

# **I. LIGAND-ACCELERATED CATALYSIS IN PALLADIUM(II)-MEDIATED C–H FUNCTIONALISATION**

## **II. HYDROGEN BONDING EFFECTS ON THE REACTIVITY OF FLUORIDE ANION**

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A thesis submitted to the Board of the Faculty of Physical Sciences in partial fulfilment of  
the requirements for the degree of Doctor of Philosophy at the University of Oxford



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# Author's Declaration

The work presented in this thesis was conducted at the Beckman Center for Chemical Sciences at The Scripps Research Institute and at the Chemistry Research Laboratory at the University of Oxford between August 2008 and April 2013 (Michaelmas Term 2008 to Trinity Term 2013) under the supervision of Professors Jin-Quan Yu (Scripps) and Véronique Gouverneur (Oxford). All the work is my own, except where otherwise stated, and has not been submitted for any other degree at this or any other university.

Keary Mark Engle

April 2013

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# Abstract

## *Part I. Ligand-Accelerated Catalysis in Palladium(II)-Mediated C–H Functionalisation*

A lingering problem in the area of Pd(II)-catalysed C–H functionalisation is the dearth of suitable ligands capable of lowering the activation energy for C–H cleavage. In our studies of aerobic Pd(II)-catalysed C–H olefination of phenylacetic acids, we discovered dramatic rate increases when mono-*N*-protected amino acids were used as ligands. In light of these findings, systematic ligand tuning was undertaken, resulting in major improvements in substrate scope, reaction rate, and catalyst turnover. A variant of this improved protocol was efficient in diolefination, offering a platform for sequential and iterative C–H functionalisation. We further demonstrated that amino acids ligands could enable efficient C–H functionalisation with other categorically distinct C–H functionalisation reactions, including C–H/R–BX<sub>*n*</sub> cross-coupling

## *Part II. Hydrogen Bonding Effects on the Reactivity of Fluoride Anion*

Fluorine-containing compounds are becoming increasingly common as medicines, agrochemicals, and materials. As such, methods for C–F bond formation using nucleophilic (F<sup>–</sup>) and electrophilic (F<sup>+</sup>) sources of fluorine have witnessed a resurgence of interest in the past decade. In the field of nucleophilic fluorination with F<sup>–</sup>, a major challenge is tuning the reactivity profile of fluoride for specific applications. To this end, we studied the effect of intermolecular hydrogen bonding on the reactivity profile of fluoride anion with the goal of developing superior fluoride reagents for synthetic applications. To obtain a comprehensive mechanistic understanding, we combined kinetic, computational, and structural techniques, which revealed the importance of weak hydrogen-bond donors, which are capable of dissociating from fluoride in solution. This mechanistic work led to the development of a new class of shelf-stable, crystalline fluoride reagents for organic synthesis.

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During graduate school, I divided my time between two outstanding institutions, Scripps and Oxford, and I owe a special thanks to the people at both locations for helping me navigate the trials and travails of a degree spanning two continents.

At Scripps, I am indebted to my many collaborators in the Yu lab. Dong-Hui Wang and Masayuki Wasa provided invaluable guidance, mentorship, and technical training during my first two years at Scripps, and it was a great thrill collaborating with both of them. My collaboration with Dong-Hui blossomed into the bulk the research programme discussed in Part I of this Thesis, and working with him in the early stages no doubt played an pivotal role in the success of that project. Later, I teamed up with Yi (Emma) Lu on alcohol-directed C–H functionalisation and with Peter Thuy-Boun on C–H/organoboron cross-coupling. In both cases, their input was essential to the development of those projects. During my second and third year, I had the opportunity to mentor two high school students, Michael Dang and David Shia. Beyond being two of the most impressive young men I have ever met, their great attitudes and kind hearts reinvigorated me and helped reaffirm my passion for chemistry.

Outside of the group, several collaborations enriched my Ph.D. experience. Studying the mechanistic nuances of our ligand-accelerated C–H olefination reaction with Dr. Dave Sale, Dr. Ryan Baxter, and Prof. Donna G. Blackmond was a highly educational experience. Together with Hengbin Wang and Prof. Huw M. L. Davies, we developed the sequential C–H functionalisation approach to the (+)-lithospermic acid core as part of the NSF Center for Stereoselective C–H Functionalization, and I appreciate their patience and persistence in seeing that project through to the end.

I thank my hoodmates Dr. Yang-Hui Zhang and later Dr. Harit Vora for the entertaining discussions and fun times. Observing their productive, engaged, and tenacious



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approach to science was pivotal in my own development as a young researcher. I would like to thank Tian-Sheng (Tyson) Mei for always smiling and for making the Yu lab a happy place to be. The rest of the Yu group, not all of whom I have space to mention, have taught me so much, and I am blessed to have had the chance to learn from all of them.

On the Yu lab website, Tanya Gresham's official position is currently listed as "the best administrative assistant ever, La Jolla," which I think suits her just right. There are countless times where I would have lost without Tanya's comforting words and organisational savvy, and she has played as vital a role as anyone over the years in keeping the Yu lab running.

As Ph.D. supervisors go, I could not have possibly done better than Prof. Jin-Quan Yu. His tireless enthusiasm and boundless creativity made the impossible seem within reach. For the countless hours Jin spent training and motivating me, I am deeply grateful.

Many of my closest friends are people I first met at Scripps, and I am confident our relationships will endure for the rest of our lives. For all the good times, thanks to Will Gutekunst, Brady Worrell, Aaron Sather, Mark Schallenberger, Hans Renata, Alex Kisluhkin, and Marisa Hovlid. I echo this sentiment in expressing my appreciation to Jamal Malik but would also like to add that it was wonderful starting the Student Sustainable Initiative (SSI) with him.

At Oxford, I also had the privilege to work closely with several outstanding colleagues. Firstly, I am indebted the CF<sub>3</sub> team—Dr. Satoshi Mizuta, Stefan Verhoog, Oscar Galicia-López, Miriam O'Duill, and Tanatorn (Plum) Khotavivattana—for their can-do attitude, creativity, and selflessness. It was a pleasure to be a part of such a wonderful group. The hydrogen-bonding project took a turn for the better when I began collaborating with Guy Giuffredi. Guy's first crystal structure of TBAF(TME)<sub>2</sub> was a game-changer, and I will never forget the butterflies in my stomach as I watched that structure spin around on his

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computer screen. Later, I had the equally good fortune to work with George Pidgeon, the best Part II student that a supervisor could ask for. George broke open the urea project by day—taking it to heights I would not have imagined in my wildest dreams—while still managing to get thrown out of Park End by night. He printed out, bound, and submitted this thesis to the Exam School on my behalf, so it quite literally wouldn't have been possible without him. Lukas Pfeifer has continued running with the hydrogen-bonding baton in the months since I've left the lab, and I am thankful that the project has been inherited by someone so generous, detail-oriented, and hard-working. All of our crystallography work was made feasible by Dr. Amber L. Thompson's tireless efforts, and she deserves special recognition, as does Dr. Hazel A. Sparkes for her help at the SXD beamline at ISIS. All computational analysis was performed by Prof. Robert S. Paton, and his insights, ideas, and feedback have been instrumental in our evolving understanding of hydrogen bonding interactions with fluoride.

The Gouverneur group, both in and out of the lab, has been wonderful. Dr. Matthew "Flash" Tredwell has been instrumental with suggestions regarding all things chemistry-related, and Charlotte "Chazzy B" Hollingworth was exceptionally gracious with her time in showing me around the department when I started. Special thanks go also to Faye Buckingham and Jamie "Wolverine" Wolstenhulme for their friendship and for never complaining about my constant presence as the third wheel during our time together. All other Gouverneur lab members have helped me immensely at one time or another, and I am grateful for their support.

I thank Prof. Véronique Gouverneur for giving me the opportunity to work in her laboratory and for providing the early inspiration for the project that turned into Part II of this Thesis. Her caring attitude in life and fearless drive in chemistry are attributes that I will always remember fondly. Working with Prof. John M. Brown was equally stimulating.

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John's passion for chemistry is infectious, and his knowledge is expansive. I left every encounter with John one new piece of chemical knowledge wealthier, and John's guidance and assistance with reaction kinetics and numerical modeling were essential.

Every now and then, I managed to sneak out of lab, and when I did it was normally for a Lincoln College event. Lincoln was my home away from home, and I was lucky to be part of the community there. To my close Lincoln friends Richard Mason, Cecilia Ng, and Lara Ehrenhofer, thanks for the fun memories.

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# Abbreviations and Acronyms

|                               |                                                |
|-------------------------------|------------------------------------------------|
| [ <sup>18</sup> F]FDG         | 2-Deoxy-2-[ <sup>18</sup> F]fluoro-D-glucose   |
| [O]                           | Generic Oxidant                                |
| ( <i>rac</i> )                | Racemic                                        |
| Å                             | Ångström (10 <sup>-10</sup> metres)            |
| β-Ala                         | β-Alanine (3-Aminopropanoic Acid)              |
| Abu                           | L-2-Aminobutyric Acid                          |
| Ac                            | Acetyl                                         |
| Ala                           | L-Alanine                                      |
| aq                            | Aqueous                                        |
| atm                           | Atmosphere (Pressure Unit)                     |
| Ar                            | Aryl                                           |
| BAr <sup>F</sup> <sub>4</sub> | Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate |
| BINAP                         | 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl    |
| BINOL                         | 1,1'-Bi-2-naphthol                             |
| bipy                          | 2,2'-Bipyridine                                |
| Bn                            | Benzyl (Also, Bzl)                             |
| Boc                           | <i>tert</i> -Butyloxycarbonyl                  |
| BPin                          | 4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl    |
| BQ                            | 1,4-Benzoquinone                               |
| Bu                            | Butyl                                          |
| Bzl                           | Benzyl (Also, Bn)                              |
| C–C                           | Carbon–Carbon (Bond)                           |
| C–H                           | Carbon–Hydrogen (Bond)                         |
| Cat                           | Catechol                                       |
| Cbz                           | Carboxybenzyl                                  |
| CI                            | Chemical Ionisation                            |
| CMD                           | Concerted Metalation/Deprotonation             |
| Cy                            | Cyclohexyl                                     |
| cod                           | 1,5-Cyclooctadiene                             |
| d.r.                          | Diastereoisomeric Ratio                        |
| dba                           | Dibenzylideneacetone                           |
| DCC                           | <i>N,N'</i> -Dicyclohexylcarbodiimide          |
| DCE                           | 1,2-Dichloroethane                             |

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|                 |                                                            |
|-----------------|------------------------------------------------------------|
| DCM             | Dichloromethane                                            |
| DFT             | Density Functional Theory                                  |
| DG              | Directing Group                                            |
| DIPT            | Diisopropyl Tartrate                                       |
| DMAP            | 4-(Dimethylamino)pyridine                                  |
| DMB             | 2,2-Dimethylbutane                                         |
| E2              | Bimolecular Elimination                                    |
| ee              | Enantiomeric Excess                                        |
| equiv.          | Equivalent(s)                                              |
| ESI             | Electrospray Ionisation                                    |
| Et              | Ethyl                                                      |
| FI              | Field Ionisation                                           |
| Fmoc            | Fluorenylmethyloxycarbonyl                                 |
| FT-IR           | Fourier Transform Infrared Spectroscopy                    |
| g               | Gram(s)                                                    |
| Gly             | L-Glycine                                                  |
| h               | Hour(s)                                                    |
| HAA             | Hydrogen Atom Abstraction                                  |
| HFIP            | Hexafluoro-2-propanol                                      |
| HPLC            | High Performance Liquid Chromatography                     |
| HRMS            | High Resolution Mass Spectrometry                          |
| HXRE            | HX Reductive Elimination                                   |
| Hz              | Hertz                                                      |
| <i>i</i>        | <i>Iso</i>                                                 |
| Ile             | L-Isoleucine                                               |
| IR              | Infrared Spectroscopy                                      |
| KIE             | Kinetic Isotope Effect                                     |
| Kryptofix-2.2.2 | 1,10-Diaza-4,7,13,16,21,24-hexaoxabicyclo[8.8.8]hexacosane |
| L               | Neutral Ligand                                             |
| Leu             | L-Leucine                                                  |
| M               | Moles per litre (mol/L)                                    |
| M.p.            | Melting Point                                              |
| Me              | Methyl                                                     |
| Men             | Menthyloxycarbonyl                                         |
| MHz             | Megahertz                                                  |

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|                          |                                                   |
|--------------------------|---------------------------------------------------|
| min                      | Minute(s)                                         |
| mL                       | Millilitre(s)                                     |
| mol                      | Mole(s)                                           |
| MOM                      | Methoxymethyl Ether                               |
| <i>n</i>                 | Normal                                            |
| NBS                      | <i>N</i> -Bromosuccinimide                        |
| NFSI                     | <i>N</i> -Fluorobenzenesulfonimide                |
| NHC                      | <i>N</i> -Heterocyclic Carbene                    |
| NHS                      | <i>N</i> -Hydroxysuccinimide                      |
| NMR                      | Nuclear Magnetic Resonance Spectroscopy           |
| NOS                      | <i>N</i> -Oxysuccinimide                          |
| NPA                      | Natural Population Analysis                       |
| NPG                      | Neopentyl Glycol                                  |
| NSAID                    | Non-Steroidal Anti-Inflammatory Drug              |
| Nu                       | Generic Nucleophile                               |
| Nva                      | L-Norvaline                                       |
| PETP                     | Pentaerythritol                                   |
| PET                      | Positron Emission Tomography                      |
| PG                       | Protecting Group                                  |
| Ph                       | Phenyl                                            |
| Phe                      | L-Phenylalanine                                   |
| PhG                      | L-Phenylglycine                                   |
| Pin                      | Pinacol                                           |
| Piv                      | Dimethylpropanoyl (Pivaloyl)                      |
| Pr                       | Propyl                                            |
| PTTL                     | <i>N</i> -Phthaloyl- <i>tert</i> -leucinate       |
| R                        | Generic Carbogenic Fragment (Aryl or Alkyl Group) |
| R–BX <sub><i>n</i></sub> | Generic Organoboron Reagent                       |
| R–M                      | Generic Organometallic Reagent                    |
| R <sub>f</sub>           | Retention Factor                                  |
| RT                       | Room Temperature                                  |
| SAR                      | Structure–Activity Relationship                   |
| Ser                      | L-Serine                                          |
| S <sub>N</sub> 2         | Bimolecular Nucleophilic Substitution             |
| <i>t</i>                 | Tertiary ( <i>tert</i> )                          |

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|--------------------|-----------------------------------------------------------------|
| <i>t</i> -AmylOH   | 2-Methyl-2-butanol                                              |
| <i>tert</i> -Leu   | L- <i>tert</i> -Leucine                                         |
| TBAF               | Tetra- <i>n</i> -butylammonium Fluoride                         |
| TBS                | <i>tert</i> -Butyldimethylsilyl                                 |
| TcBoc              | 2,2,2-Trichloro- <i>tert</i> -butyloxycarbonyl                  |
| TEAF               | Tetraethylammonium Fluoride                                     |
| TMAF               | Tetramethylammonium Fluoride                                    |
| TME                | Trimethylolethane                                               |
| Tf                 | Trifluoromethanesulfonyl (Triflyl)                              |
| TFA                | Trifluoroacetic Acid or Trifluoroacetate (Depending on Context) |
| TFAA               | Trifluoroacetic Anhydride                                       |
| THF                | Tetrahydrofuran                                                 |
| TLC                | Thin Layer Chromatography                                       |
| TOF                | Turnover Frequency                                              |
| Tol                | Tolyl                                                           |
| TON                | Turnover Number                                                 |
| Ts                 | <i>para</i> -Toluenesulfonyl (Tosyl)                            |
| TS                 | Transition State                                                |
| Val                | L-Valine                                                        |
| VSEPR              | Valence Shell Electron Pair Repulsion                           |
| X                  | Anionic Ligand                                                  |
| $\delta$           | Chemical Shift                                                  |
| $\mu\text{L}$      | Microlitre(s)                                                   |
| $^{\circ}\text{C}$ | Degrees Celsius                                                 |

## **PART I**

# **LIGAND-ACCELERATED CATALYSIS IN PALLADIUM(II)- MEDIATED C–H FUNCTIONALISATION**

## CHAPTER 1

### INTRODUCTION

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## 1.1. CONSPECTUS

Homogeneous transition metal–catalysed reactions are indispensable to all facets of modern chemical synthesis. It is thus difficult to imagine that for much of the early 20th century, the reactivity and selectivity of all known homogeneous metal catalysts paled in comparison to their heterogeneous and biological counterparts. In the intervening decades, advances in ligand design bridged this divide, such that today some of the most demanding bond-forming events are mediated by ligand-supported homogeneous metal species.

While ligand design has propelled many areas of homogeneous catalysis, in the field of Pd(II)-catalysed C–H functionalisation, suitable ligand scaffolds are lacking, which has hampered the development of broadly practical transformations based on C–H functionalisation logic. The lack of effective ligand scaffolds is at the heart of several of the long-standing problems in this field, such as controlling the stereoselectivity and site-selectivity of C–H cleavage and achieving reactivity with recalcitrant substrates (*e.g.*, aliphatic hydrocarbons and electron-poor arenes).

Part I of this Thesis describes our efforts to address these challenges through the discovery and development of mono-*N*-protected amino acids for accelerating Pd(II)-catalysed C(sp<sup>2</sup>)–H functionalisation reactions. In Chapter 1, we offer a context for this work. We begin by providing a brief overview of the role of ligand development in transition metal catalysis (Section 1.2). We then discuss the renaissance of Pd(II)-catalysed C–H functionalisation reactions (Section 1.3), before focusing specifically on the ongoing research programme of the Yu laboratory (Section 1.4). Previous work in the Yu group led to the identification of mono-*N*-protected amino acid ligands as an effective means of inducing asymmetry in enantioselective C–H activation and in achieving position-selective C–H cleavage with substituted arenes, which we describe in Section 1.5.

Chapters 2–4 focus on the application of mono-*N*-protected amino acid ligands for accelerating C–H cleavage to obtain more kinetically reactive catalysts, research that was carried out by the author in collaboration with several coworkers (see Acknowledgments) from August 2008 to June 2011 in the Yu laboratory at The Scripps Research Institute. Chapter 2 describes early work to optimise the ligand structure for C–H olefination of phenylacetic acid substrates. In Chapter 3, we describe the application of this reaction in diolefination, sequential olefination, and iterative olefination, and describe reactive catalysts for hydrocinnamic acid substrates. Chapter 4 then chronicles our efforts to apply mono-*N*-protected amino acids to improve Pd(II)-catalysed C–H functionalisation reactions with different elementary steps, specifically C–H/R–BX<sub>*n*</sub> cross-coupling of phenylacetic acid substrates. Finally, in Chapter 5, we conclude by briefly highlighting applications of mono-*N*-protected ligands in other Pd(II)-catalysed C–H functionalisation reactions, as described by the Yu group and others.

## 1.2. LIGAND DESIGN IN TRANSITION METAL CATALYSIS

### 1.2.1. Background

The importance of ligands in modern homogeneous transition metal catalysis cannot be overstated. Because ligand coordination changes the structure and reactivity of a metal catalyst, it inherently changes the activation energy of elementary steps in a given catalytic process. This change is manifested in the kinetic reactivity,<sup>1</sup> which can broaden the effective substrate scope of the reaction. Moreover, ligands can influence the selectivity (*i.e.*, enantioselectivity, diastereoselectivity, regioselectivity, and chemoselectivity) in transformations where more than one product is produced, improve the solubility of metal catalysts in organic solvents, and extend catalyst lifetimes by suppressing metal catalyst degradation pathways. For instance, in cases where precipitation of metal nanoparticles is an



irreversible catalyst deactivation pathway, strongly binding organic ligands can protect two molecules of catalyst from contacting one another and precipitating. Finally, as a consequence of these previous points, the ligand can affect the operational properties of the reaction: the compatibility with air and/or moisture, the reaction temperature, pressure, *etc.* In essence, ligands are chemists' "hands" for influencing the bond-making and -breaking processes that occur at metal centres, and arguably, in the past several decades, ligand design has been the principal force driving the improvement of known catalytic reactions and the discovery of new ones.<sup>2</sup>

During the past century, simple, commonly available metal salts (*e.g.*, CuCl, AuCl<sub>3</sub>, and Pd(OAc)<sub>2</sub>) have been applied extensively in catalysis, leading to the discovery of a myriad of different reactions, several of which have become mainstays in organic synthesis. This flurry of research in catalytic organometallic chemistry set the stage for the design of catalysts with improved reactivity and selectivity, such that desired products could be synthesised with high levels of purity and minimal amounts of waste. Because improved catalytic performance hinges on the properties of ancillary ligands, new ligand scaffolds have been vigorously pursued in all subfields of homogeneous metal catalysis.

Much of the search for new ligands has taken place in the context of research into catalytic *asymmetric* reactions, where in the absence of chiral information, the reaction will proceed *via* one of two pathways of equal energy to give a one-to-one mixture of enantiomeric products. By using a chiral nonracemic ligand, however, the reaction can be rendered enantioselective, leading to the predominant production of one enantiomer. Prominent early examples include the use of dialkyltartrate ligands in the Sharpless asymmetric epoxidation<sup>3,4</sup> and the development of chiral diphosphine ligands for asymmetric hydrogenation, such as DIOP,<sup>5</sup> DiPAMP,<sup>6</sup> chiraphos,<sup>7</sup> and BINAP<sup>8</sup> by Kagan, Knowles, Bosnich, and Noyori, respectively. Ligand design has played an equally important

role in developing *enhanced kinetic reactivity* for catalytic transformations that otherwise exhibit prohibitively slow reaction rates (or a complete lack of reactivity all together). Notable examples include the popularisation of triphenylphosphine as a ligand in the 1960s, particularly in Wilkinson's seminal applications to rhodium-catalysed hydroformylation<sup>9</sup> and hydrogenation,<sup>10</sup> and more recently, the advent of dialkylaryl- and trialkylphosphines and *N*-heterocyclic carbenes as ligands in ruthenium-catalysed olefin metathesis<sup>11,12</sup> and palladium-catalysed cross-coupling reactions.<sup>13-17</sup> Moreover, there are also important cases where the search for ligands for stereoinduction led to the identification of more reactive catalysts and *vice versa*.<sup>18,19</sup>

### 1.2.2. "Privileged" Ligands in Transition Metal Catalysis

During the past half-century of research in asymmetric transition metal catalysis, a small collection of "privileged" ligand scaffolds have emerged, a term first coined by Yoon and Jacobsen.<sup>20</sup> These ligand scaffolds have been found to be useful in many different types of asymmetric transformations, even among those with few or no mechanistic similarities (**1.1–1.9**, Figure 1.1). Privileged chiral ligands have been used extensively for reaction development in organic chemistry, and their application accounts for a high percentage of new asymmetric reactions developed each year.

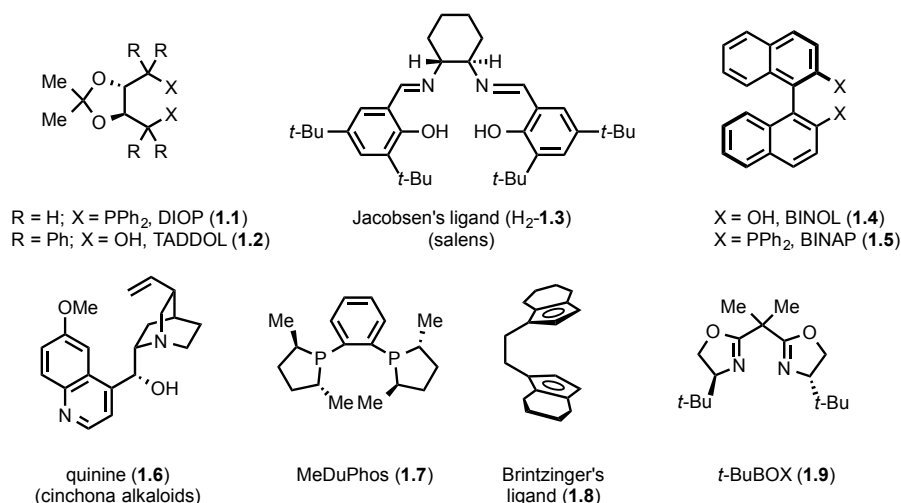


**Figure 1.1.** “Privileged” chiral ligands for asymmetric transition metal catalysis.<sup>20</sup>

As discussed above, in parallel to the progress in asymmetric catalysis, homogeneous catalytic transformations that do not induce chirality have been extensively studied. These reactions have required catalysts with high kinetic reactivity to ensure broad substrate scope, short reaction times, and favourable product distributions, and here too, ligand development has played a central role. In non-stereoselective reactions, there exist achiral “privileged” ligands, which have been utilised ubiquitously to enable a variety of different catalytic reactions, all with a myriad of distinct elementary steps (Figure 1.2). These include triaryl- and trialkylphosphines (**1.10–1.13**),<sup>21–24</sup> biaryl(dialkyl)phosphines (**1.14–1.19**),<sup>25,26</sup> diphosphines (**1.20–1.25**),<sup>27,28</sup> “pincer” ligands (**1.26–1.28**),<sup>29,30</sup> *N*-heterocyclic carbenes (**1.29–1.33**),<sup>16,31,32</sup> cyclopentadienides (**1.34–1.36**),<sup>33–38</sup> acetylacetonates (**1.37–1.38**),<sup>39</sup> diamines (**1.40–1.42**),<sup>39–41</sup> bipyridines (**1.43–1.45**),<sup>39,41–43</sup> and pyridines (**1.46–1.48**).<sup>41</sup>

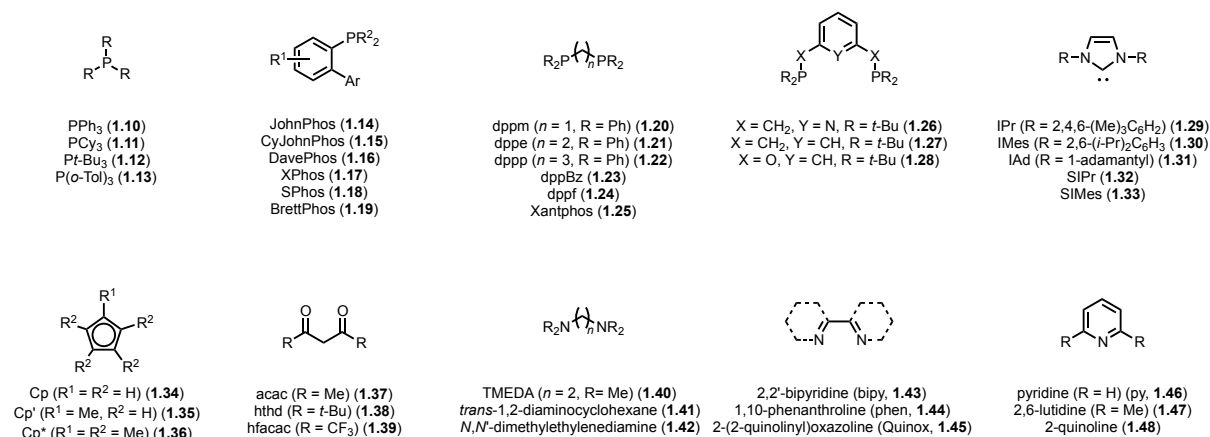
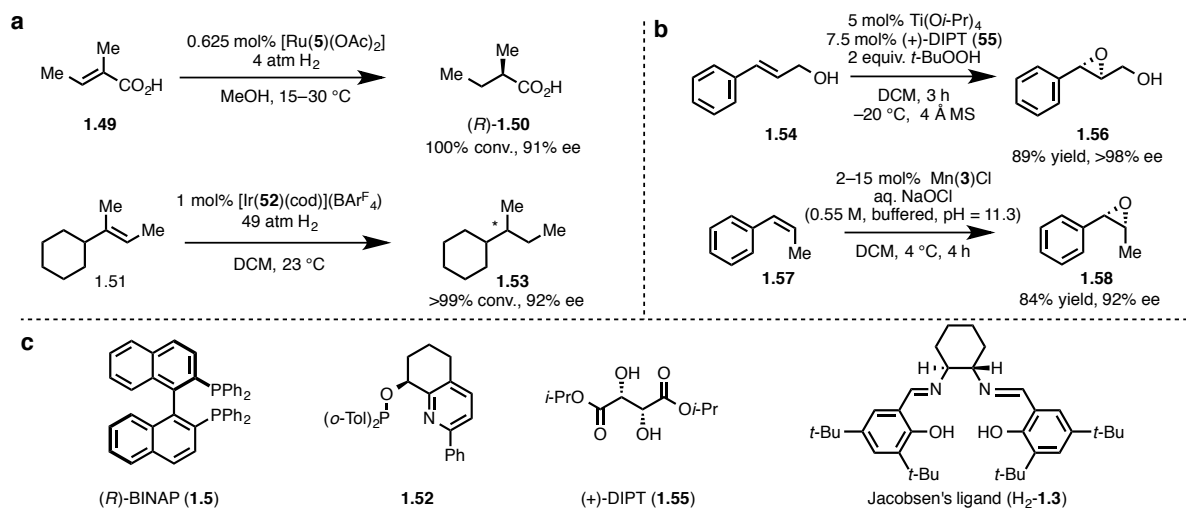


**Figure 1.2.** “Privileged” achiral ligands for high kinetic reactivity in transition metal catalysis.<sup>44</sup>

### 1.2.3. Matching Substrate to Catalyst and Identifying a Suitable Ligand Scaffold

Though privileged ligand scaffolds are remarkably general in their utility across reaction types and substrate classes, they are still not universally applicable. One common feature of ligand-controlled metal-catalysed reactions is that the catalytic system must be designed to match the properties of the substrate. Each individual class of substrates possesses a characteristic set of properties that will affect its approach to and interaction with the metal centre. The course of the reaction is dictated by the intrinsic properties of the metal centre (oxidation state, electron count, coordination geometry, *etc.*) and its established redox activity patterns. Together the properties of the substrate and metal then inform the selection and/or design of appropriate ligand scaffolds. Important substrate considerations include the steric and electronic properties (particularly those proximate to the reactive functional group), any existing stereochemistry, the presence or absence of other potentially reactive functional groups, and the presence or absence of Lewis basic chelating functional groups (directing groups).<sup>45,46</sup> For example, consider asymmetric olefin hydrogenation (Scheme 1.1a). For substrates containing a chelating functional group, such as  $\alpha,\beta$ -unsaturated carboxylic acid **1.49**, the presence of an open binding site on the metal for

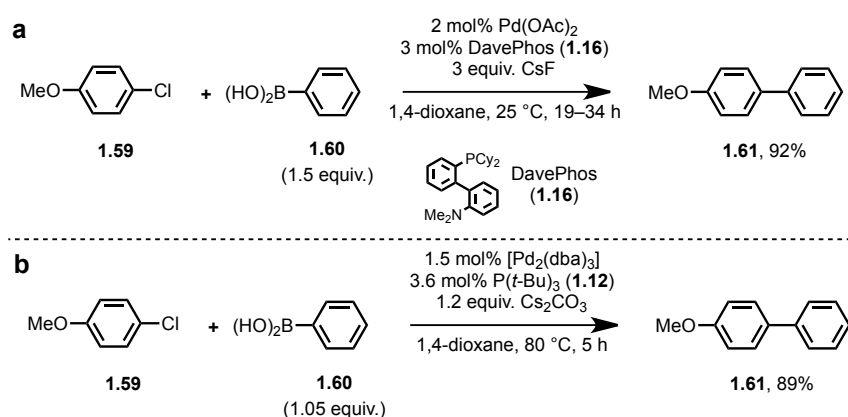
carboxylate coordination is desirable. With the  $C_2$ -symmetric Noyori [Ru(BINAP)(OAc)<sub>2</sub>] catalyst, the substrate can smoothly displace the acetate, without compromising catalyst activity, and subsequent directed asymmetric hydrogenation proceeds with excellent levels of stereoselection.<sup>47</sup> In contrast, in the Pfaltz non-directed asymmetric hydrogenation of olefins (**1.51**), a Crabtree-type catalyst<sup>48</sup> bearing a non- $C_2$ -symmetric P,N-phosphite-pyridine ligand **1.52** and a non-coordinating counterion, BAr<sub>F</sub>, is highly effective in the absence of a chelating functional group, relying on weak coordinative interactions for orienting the substrate.<sup>49,50</sup> Similarly, for asymmetric olefin epoxidation (Scheme 1.1b), the Sharpless system<sup>3,4,51</sup> is highly effective for allylic alcohols (**1.54**), and the Jacobsen system works well for internal (*Z*)-olefins not containing directing groups (**1.57**).<sup>52,53</sup> Although the net transformations appear similar in both cases, the properties of the substrate dictate the selection of a metal, the mechanistic manifold, and ultimately the ligand used for stereoselection.



**Scheme 1.1.** Application of a diverse array of catalyst/ligand structures to asymmetric transformations of olefins. (a) Asymmetric hydrogenation of olefins by Noyori<sup>47,54</sup> and Pfaltz.<sup>49</sup> (b) Asymmetric epoxidation of olefins by Sharpless<sup>3,4</sup> and Jacobsen.<sup>53</sup> (c) Ligand structures.

In non-stereoselective catalysis, tailoring ligand properties to match the substrate is similarly important. For instance in Pd-catalysed Suzuki–Miyaura<sup>55</sup> cross-coupling

reactions, unactivated aryl chlorides were traditionally an unreactive class of substrates. Ligands that are commonly used with aryl iodides, -bromides, and -triflates, such as triphenylphosphine, BINAP, and dppf are generally unreactive with electron-neutral or -rich aryl chlorides, such as **1.59**,<sup>13</sup> presumably because oxidative addition of a C(sp<sup>2</sup>)-Cl bond to a Pd(0) centre is kinetically unfavourable.<sup>56</sup> This challenge can be surmounted, however, through the application of sterically demanding, electron-rich phosphine ligands such as DavePhos (**1.16**)<sup>25</sup> and P(*t*-Bu)<sub>3</sub> (**1.12**) (Scheme 1.2).<sup>23</sup> The  $\sigma$ -donating character of these ligands increases the nucleophilicity of the Pd(0) centre which lowers the activation energy for oxidative addition. The steric bulk is thought to facilitate reductive elimination and promote formation of the catalytically active 1:1 Pd(0):ligand complex in solution.<sup>13</sup> Through the selection and design of appropriate ligands, a new class of widely available substrates was rendered reactive in this and other related cross-coupling chemistries.



**Scheme 1.2.** Application of sterically bulky, electron-rich phosphine ligands in the Suzuki–Miyaura cross-coupling of unactivated aryl chlorides with boronic acids, as reported independently by the groups of (a) Buchwald<sup>25</sup> and (b) Fu.<sup>23</sup>

#### 1.2.4. Modifiability and Modularity of Ligand Scaffolds

Because it is difficult to predict *a priori* the potentially dramatic influence that subtle changes to a ligand's structure will have on the metal centre as it cycles through many elementary steps of a catalytic process,<sup>57,58</sup> one key to the success of a ligand scaffold is that it can be readily modified. Multiple sites of variation both near and distal to the metal allow

for the steric and electronic properties to be finely tuned to meet the energetic requirements of the reaction. For instance, the BINAP/BINOL scaffold has been adapted through modification at nearly every conceivable position since its introduction in asymmetric catalysis<sup>8,59-62</sup> and has continued to play a central role in reaction discovery (Figure 1.3). In the early stages of reaction discovery and development, catalyst modifiability is particularly important, because many of the crucial reaction parameters are typically poorly understood. As evidence of the importance of modifiability, it is becoming increasingly common for commercial suppliers to offer ligand kits, containing multiple structural variants on a single ligand scaffold.

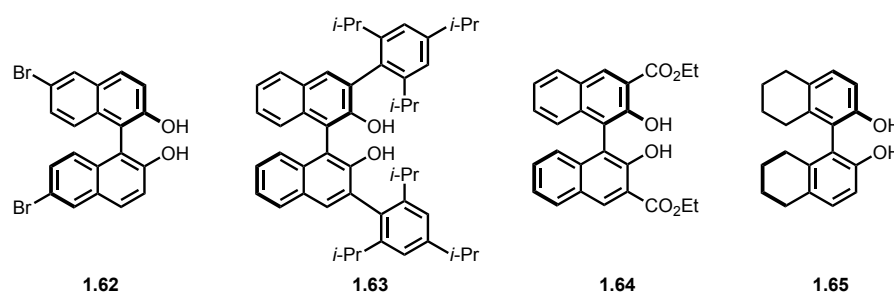


**Figure 1.3.** Selected examples of commercially available BINOL derivatives.

For similar reasons, many widely used ligand scaffolds are modular, meaning that they can be synthesised in a small number of steps from readily available components, allowing for a library of ligand candidates to be synthesised expediently.<sup>63</sup> For instance, chiral phosphine–oxazoline (PHOX, **1.66**) ligands pioneered by Pfaltz,<sup>64</sup> Helmchen,<sup>65</sup> and Williams,<sup>66</sup> possess a non-symmetrical P,N-donor system,<sup>67</sup> with one soft atom (P) and one hard atom (N) (Figure 1.4). Their unique structure has proven to be critical for challenging asymmetric metal-catalysed transformations, particularly asymmetric allylic substitution. A major practical aspect that makes this class of ligands convenient to use is the modular synthesis, where an entire family of ligand candidates can be synthesised from widely available commercial chiral building blocks.<sup>68,69</sup>

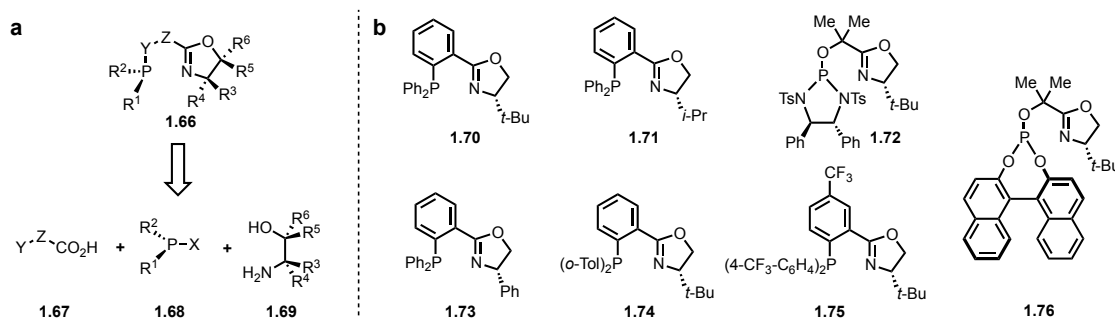


**Figure 1.4.** (a) Modular synthesis of chiral PHOX-type ligands.<sup>70</sup> (b) Representative PHOX ligands.<sup>71</sup>

Tailoring ligand properties for a desired metal-catalysed transformation requires careful consideration of the key features of the substrate class as well as the mechanism of each elementary step in the would-be catalytic process. Ligands that have a rich history of success in metal-catalysed reactions (those that are considered privileged) are often useful starting points in reaction discovery and development. In this vein modifiability and modularity are key in providing libraries of ligands for medium- and high-throughput screening campaigns. As discussed in Part I of this Thesis, many of the key advancements in the Yu laboratory have hinged upon ligand design, so the considerations outlined above are ones that have pervaded the Yu laboratory research programme in Pd(II)-catalysed C–H functionalisation.

The ensuing sections provide a concise introduction to Pd(II)-catalysed C–H functionalisation and outline the impetus and general goals of research in the Yu laboratory. The key role of ligand development in realising these objectives is discussed. Next, the challenges of identifying effective ligand scaffolds for C(sp<sup>2</sup>)–H and C(sp<sup>3</sup>)–H functionalisation using catalytic Pd(II) are considered, and previous work in the Yu laboratory, in which mono-*N*-protected acid ligands were successfully employed in enantioselective and position-selective C–H activation, is highlighted. These seminal studies directly inspired the research presented in this Thesis, which centres on the use of mono-*N*-

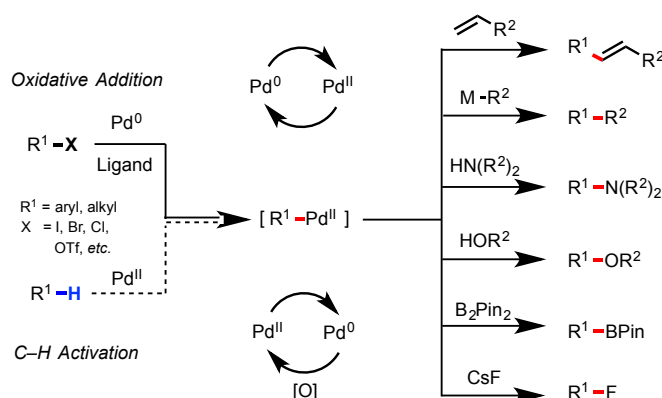


protected acid ligands to enhance kinetic reactivity in Pd(II)-catalysed C–H functionalisation.

### 1.3. THE RENAISSANCE OF PALLADIUM(II)-CATALYSED C–H FUNCTIONALISATION

#### 1.3.1. Comparison to traditional Pd(0)-catalysed cross-coupling reactions

Pd(0)-catalysed reactions of aryl and alkyl halides (R–X) have revolutionised the field of synthetic organic chemistry since the early 1970s, when the first reports describing the catalytic coupling of aryl halides and olefins were independently disclosed by Mizoroki and Heck.<sup>72</sup> Subsequent to that work, an array of carbon–carbon<sup>73–80</sup> and carbon–heteroatom<sup>79,81–84</sup> bond-forming reactions have been developed based on the Pd(0)/Pd(II) redox manifold, with increasing levels of efficiency, practicality, and reliability. The power of this class of catalytic reactions stems from the diverse reactivity of the [Pd(II)–R] intermediates, which are commonly generated from oxidative addition of the R–X group to Pd(0) (Scheme 1.3).

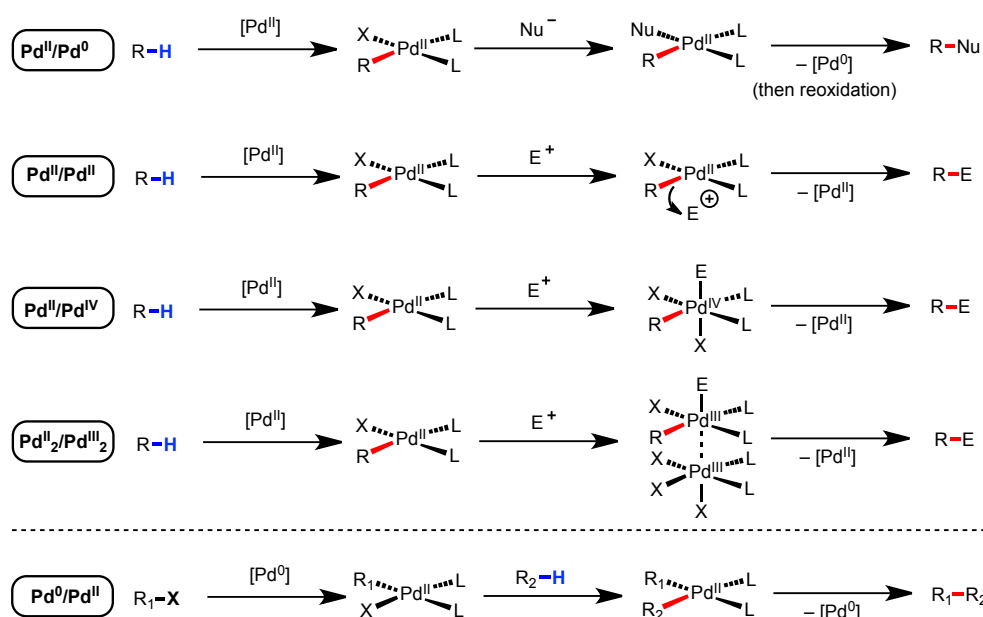


**Scheme 1.3.** Versatile reactivity of [Pd(II)–aryl] and [Pd(II)–alkyl] intermediates.<sup>85,86</sup>

A fascinating and attractive possibility would be to mimic this mode of catalysis using Pd(II)-mediated C–H cleavage, which is generally believed to be redox neutral with concomitant loss of HX (X = halide, acetate, *etc.*), as an alternative entry point to access

[Pd(II)–R] intermediates.<sup>87,88</sup> (The mechanistic details of C–H cleavage with Pd(II) will be discussed in Chapter 2.) Importantly, this would endow simple alkane and arene substrates with reactivity in these modes of bond construction and would obviate the need for pre-installing the C–X handle, which can be problematic and require multiple steps depending on the context. In considering this idea, it is important to recognise at the outset that the precise molecular structure of [Pd(II)–R] intermediates generated in this manner, which could exist as monomeric, dimeric, or trimeric species, would likely be more complex than that of those made from oxidative addition of an aryl halide to Pd(0), which are predominantly monomeric. Additionally, in this case, the proposed Pd(II)/Pd(0) catalytic cycle would require an external oxidant to close the catalytic cycle.

In addition to the putative Pd(II)/Pd(0) catalytic cycles for C–H functionalisation in Scheme 1.3, which mimic Pd(0)-catalysed cross-coupling, the [Pd(II)–R] species generated by C–H activation could also react with strong oxidants to induce reductive elimination from high-energy Pd(III)<sup>89,90</sup> or Pd(IV)<sup>91</sup> species (Scheme 1.4) to give complementary reactivity patterns.

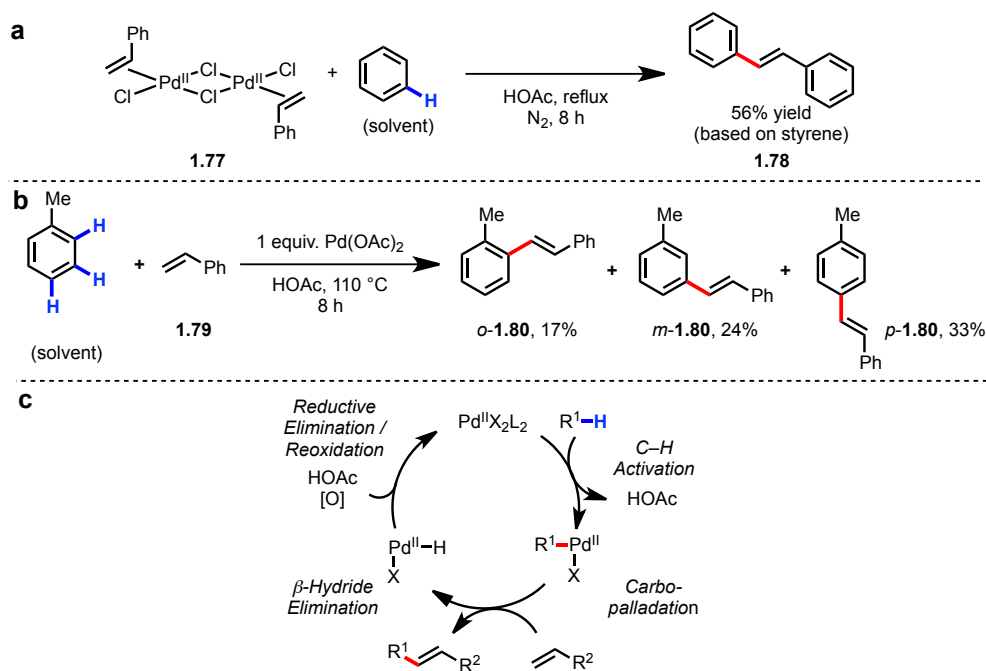


**Scheme 1.4.** Different catalytic manifolds in Pd-catalysed C–H functionalisation.

Indeed, using these approaches many notable achievements have been made in the area of Pd(II)-catalysed C–H activation, selected examples of which are highlighted in the next two sections.

### 1.3.2. Early studies

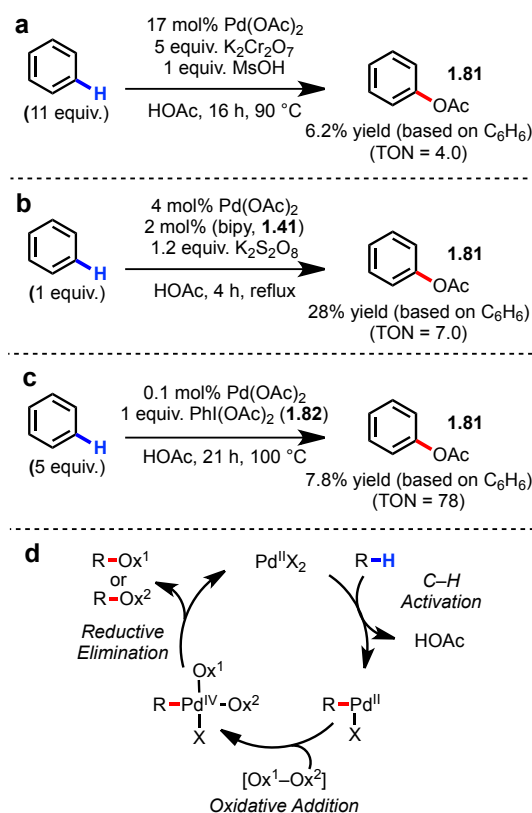
Pd(II)-catalysed C–H functionalisation reactions have been studied for the past several decades, since the pioneering work on Pd(II)-catalysed C(sp<sup>2</sup>)–H olefination of simple arenes by Fujiwara and Moritani in the late 1960s (Scheme 1.5).<sup>92-94</sup> This early work demonstrated the impressive reactivity of Pd(II) in activating C–H bonds of simple aromatic hydrocarbons, but the practical utility of this chemistry in organic synthesis has been limited due to the need for excess arene substrate (often as solvent) to achieve high effective concentration around the metal centre, the lack of positional selectivity with substituted arenes, and the poor reactivity with electron-deficient arenes. Formation of the [Ar–Pd(II)] intermediate in this reaction is thought to proceed by a Friedel–Crafts-type electrophilic palladation mechanism. It was also established that other coupling partners could react with the corresponding [Pd(II)–R] species *via* Pd(II)/Pd(0) catalysis. For instance, in 1993, Fujiwara reported a reaction in which cyclohexane could be carboxylated with CO.<sup>95</sup>



**Scheme 1.5.** (a) Initial discovery of Pd(II)-mediated C–H olefination using stoichiometric complex **1.77** by Fujiwara and Moritani in 1967.<sup>96</sup> (b) Distribution of positional isomers (*ortho*-, *meta*- and *para*-**1.80**) in the stoichiometric Pd(II)-mediated C–H olefination of toluene.<sup>97</sup> (c) General catalytic cycle for Pd(II)-catalysed C–H olefination

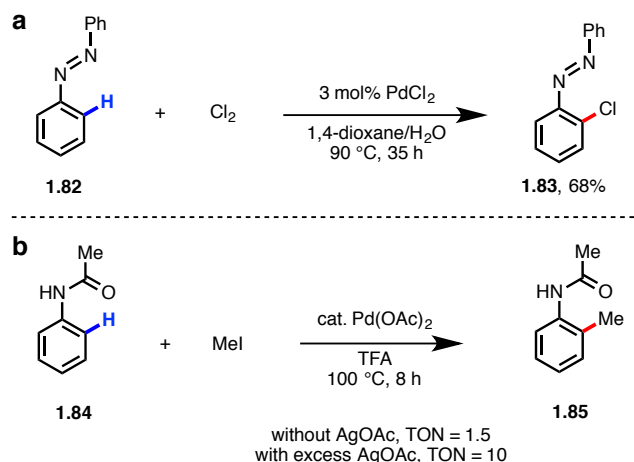
Slightly after these early reports of C–H functionalisation via Pd(II)/Pd(0) catalysis, several groups realised the potential achieving C–H functionalisation via a Pd(II)/Pd(IV) catalytic cycle (Scheme 1.6). In a pioneering study in 1971, Henry found that treatment of benzene with catalytic Pd(OAc)<sub>2</sub> in the presence of K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, a strong oxidant, and MsOH in HOAc delivered phenylacetate (**1.81**) with modest catalytic efficiency.<sup>98</sup> Subsequently, Eberson found that the presence of bipy (**1.41**) as an ancillary ligand improved catalytic turnover using K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> as the oxidant.<sup>99,100</sup> Importantly, Eberson also found that coordination of a bipy (**1.41**) ligand changes the positional selectivity (*i.e.*, product distribution) of C–H acetoxylation with substituted arenes. Later, Crabtree revisited this reaction and found that the use of PhI(OAc)<sub>2</sub> (**1.82**) as the oxidant greatly improved efficiency.<sup>101</sup> These transformations are believed to proceed *via* high-valent Pd(III) or Pd(IV) intermediates. C–O bond-forming reductive elimination from these high-energy species is more favourable than from Pd(II) centres. Similar to the Fujiwara chemistry described above, the utility of

non-directed C–H acetoxylation has been restricted by the low catalytic efficiency and the lack of positional selectivity with substituted arenes.



**Scheme 1.6.** Early high-valent approaches to Pd(II)-catalysed C–H functionalisation by (a) Henry in 1971,<sup>98</sup> (b) Eberson in 1976,<sup>100</sup> and (c) Crabtree in 1996<sup>101</sup> (d) General catalytic cycle for C–H functionalisation using strong oxidants (Ox<sup>1</sup>–Ox<sup>2</sup>) via Pd(II)/Pd(IV) catalysis.

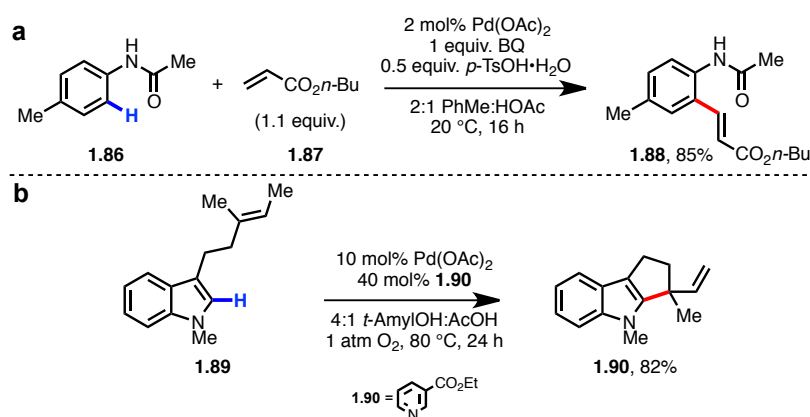
Also during this time, seminal work using cyclometallation to control regioselectivity and enhance the rate of C–H cleavage was reported by Fahey in the Pd(II)-catalysed *ortho*-C(sp<sup>2</sup>)-H chlorination of azobenzene (**1.82**) (Scheme 1.7a).<sup>102</sup> Reaction of the putative palladacycle with Cl<sub>2</sub> leads to a high-oxidation state Pd(III) or Pd(IV) intermediate, which then undergoes C–Cl reductive elimination to release the product. Another important finding came in 1984 when Tremont and Rahman found that acetanilide (**1.84**) could undergo *ortho*-methylation with MeI in good yields, and they demonstrated that TONs up to 10 could be achieved by using AgOAc as an oxidant (Scheme 1.7b).<sup>103</sup>



**Scheme 1.7.** Pd(II)-catalysed *ortho*-C–H functionalisation of substrates bearing directing groups. (a) *ortho*-C–H chlorination of azobenzene (**1.82**) by Fahey in 1971.<sup>102</sup> (b) *ortho*-C–H methylation of acetanilide (**1.84**) by Tremont in 1984.<sup>103</sup>

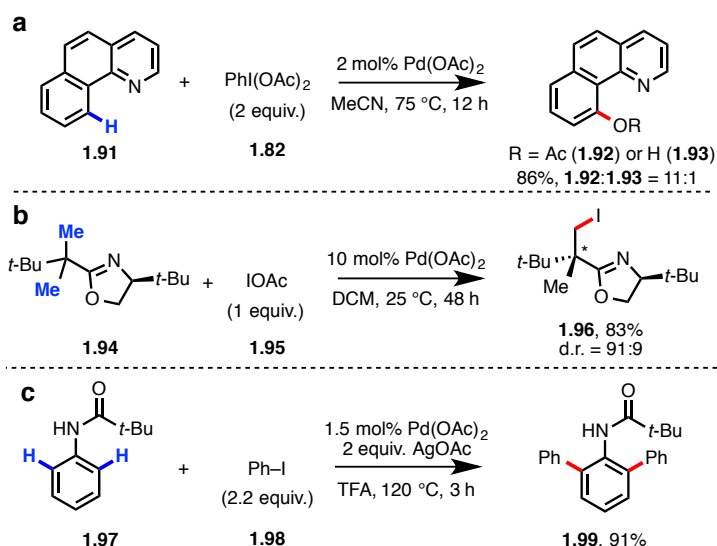
### 1.3.3. Resurgence of Interest

During the past decade, a number of groups have revisited Pd-catalysed C–H functionalisation and have developed a collection of promising new reactions (Schemes 1.8 and 1.9). First, in the context of Pd(II)-catalysed C–H olefination, the aforementioned reactivity and selectivity challenges have been partially addressed through the development of methods for position-selective C–H olefination of electron-rich heterocycles<sup>104–106</sup> and substrates containing *ortho*-directing groups (Scheme 1.8).<sup>107,108</sup>



**Scheme 1.8.** Representative examples of tactics for controlling positional selectivity in C–H olefination. (a) Intermolecular *ortho*-C–H olefination of *N*-(*p*-tolyl)acetamide (**1.86**) by de Vries and van Leeuwen in 2002.<sup>108</sup> (b) Intramolecular C–H olefination of *N*-methyl indole substrate **1.89** by Stoltz in 2003.<sup>106</sup>

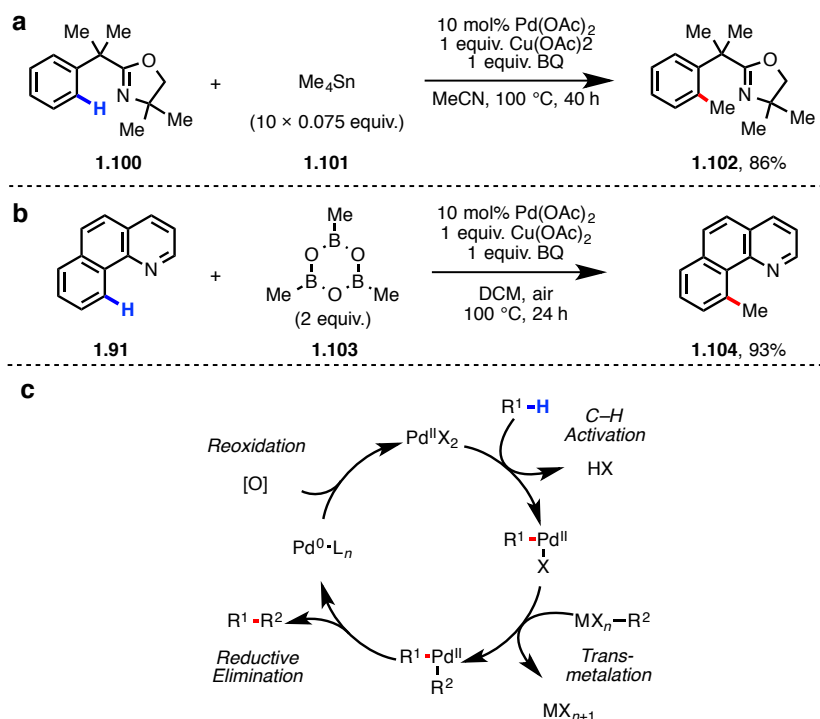
On the high-valent catalysis front, Sanford reported a C–H acetoxylation protocol using a series of different nitrogen-containing directing groups and  $\text{PhI}(\text{OAc})_2$  as the oxidant (Scheme 1.9a),<sup>109</sup> a method that could be extended to  $\text{C}(\text{sp}^3)\text{--H}$  acetoxylation as well.<sup>110</sup> Using a removable chiral oxazoline auxiliary, the Yu laboratory disclosed the first example of diastereoselective  $\text{C}(\text{sp}^3)\text{--H}$  iodination (**1.94**→**1.96**)<sup>111</sup> and acetoxylation,<sup>112</sup> methods that represent a potentially powerful approach for synthesising all-carbon quaternary stereocentres (Scheme 1.9b). Later the same year, Daugulis reported  $\text{Pd}(\text{II})$ -catalysed  $\text{C}(\text{sp}^2)\text{--H}$  arylation using anilide substrates (**50**) and aryl iodides (Scheme 1.9b).<sup>113</sup> All of these reactions are proposed to proceed through  $\text{Pd}(\text{II})/\text{Pd}(\text{IV})$  or  $\text{Pd}(\text{II})_2/\text{Pd}(\text{III})_2$  catalytic cycles.



**Scheme 1.9.** *ortho*-C–H functionalisation via  $\text{Pd}(\text{II})/\text{Pd}(\text{IV})$  or  $\text{Pd}(\text{II})_2/\text{Pd}(\text{III})_2$  catalysis. (a) *ortho*- $\text{C}(\text{sp}^2)\text{--H}$  acetoxylation by Sanford in 2004.<sup>109</sup> (b) Diastereoselective  $\text{C}(\text{sp}^3)\text{--H}$  iodination using a removable chiral oxazoline auxiliary by Yu in 2005.<sup>114</sup> (c) *ortho*- $\text{C}(\text{sp}^2)\text{--H}$  arylation by Daugulis in 2005.<sup>113</sup>

The Yu research laboratory went on to develop the first examples of C–H/R–M cross-coupling *via*  $\text{Pd}(\text{II})/\text{Pd}(0)$  catalysis (Scheme 1.10),<sup>115,116</sup> an important step toward the integration of C–H activation into classical cross-coupling-type catalytic cycles. The presence of 1,4-benzoquinone (BQ) was found to be crucial for promoting reductive

elimination from putative  $[\text{Pd(II)}\text{R}^1\text{R}^2]$  intermediates (Scheme 1.10c). In the case of organostannane coupling partners, batch-wise addition of the organotin reagent lowered the rate of homocoupling such that Pd(II)-mediated C–H cleavage could take place.



**Scheme 1.10.** Pd(II)-catalysed C–H/R– $\text{BX}_2$  cross-coupling. (a) C–H/organostannane cross-coupling using an oxazoline directing group.<sup>115</sup> (b) C–H/organoboron cross-coupling with pyridine directing group.<sup>116</sup> (c) General catalytic cycle.

Despite this impressive progress, in comparison to state-of-the-art Pd(0)-catalysed cross-coupling chemistry, Pd(II)-catalysed C–H activation reactions remain underdeveloped in terms of versatility, practicality, and catalytic efficiency. The principal driving force that has propelled Pd(0)-catalysed coupling chemistry during the past several decades has been the development of bulky phosphine and *N*-heterocyclic carbene (NHC) ligands that promote both the oxidative addition and reductive elimination steps, thereby improving the reaction rate, lowering the requisite catalyst loading, and expanding the substrate scope.<sup>13–15</sup> The advancements in ligand design have resulted in truly practical and operationally simple reactions that have found a myriad of applications, including numerous examples in natural product total synthesis.<sup>117,118</sup>



Many of these commonly used ancillary ligands, however, are incompatible with the Pd(II)-mediated C–H cleavage step (*vide infra*) in catalytic C–H functionalisation reactions.<sup>119</sup> A pervasive limitation that has hampered efforts in this field is the dearth of suitable ligand scaffolds that can accelerate C–H cleavage, which is typically the rate-limiting and selectivity-determining step in the catalytic cycles described above. Below, we provide an overview of the research efforts of the Yu laboratory to develop synthetically enabling Pd(II)-catalysed C–H functionalisation reactions. We then discuss how ligand development is a prerequisite to surmounting many of the lingering problems in the field, and introduce early work using mono-*N*-protected amino acids ligands for Pd(II)-catalysed enantioselective and position-selective C–H activation.

## **1.4. OVERVIEW OF YU LABORATORY C–H FUNCTIONALISATION RESEARCH PROGRAMME**

### **1.4.1. Philosophy and Guidelines for Reaction Development**

A primary focus of research in the Yu laboratory has been the creation of novel and strategic retrosynthetic disconnections<sup>120-123</sup> that allow C–H bonds to be viewed as dormant functional groups that can be converted to a desired C–C or C–X bond at any stage of a synthesis.<sup>85,86</sup> To make this approach broadly useful for synthetic applications, we have adhered to the following guidelines in developing C–H functionalisation reactions:

- (1) *Substrates*: We utilise substrate classes that are readily available in both bulk quantity and structural diversity, and which can lead to a variety of complex synthetic targets upon C–H functionalisation (Figure 1.5). Newly uncovered modes of reactivity can then be extended to feedstock chemicals, including those that contain weakly coordinating functional groups which can be used to facilitate C–H

cleavage.<sup>86</sup> Overall, appropriate selection of target substrate classes can further improve both the economy<sup>124</sup> and sustainability<sup>125</sup> of organic synthesis.

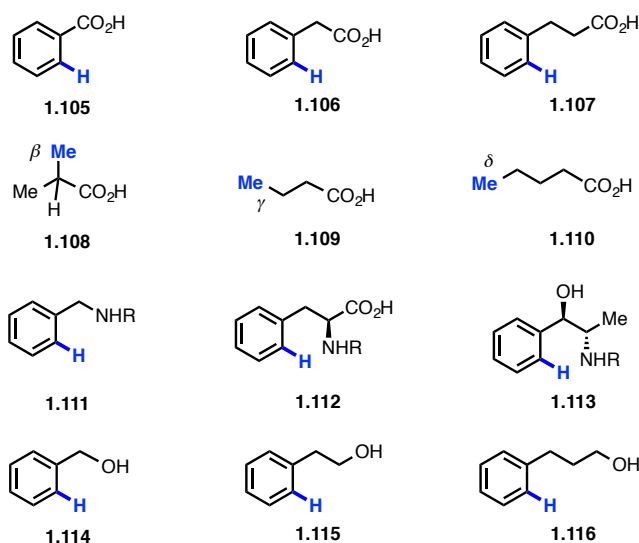
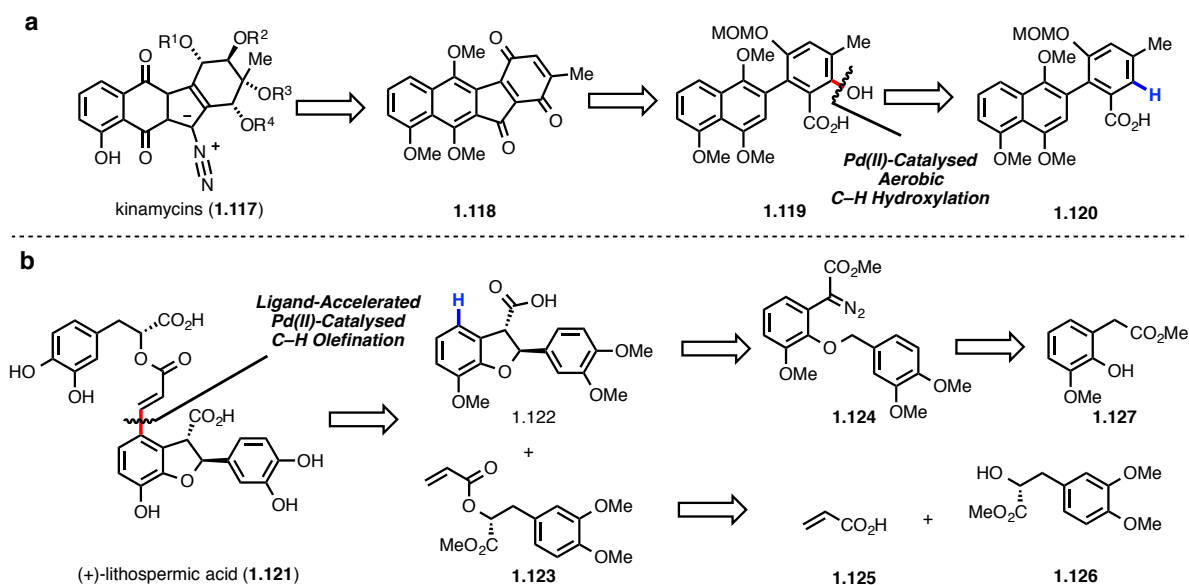


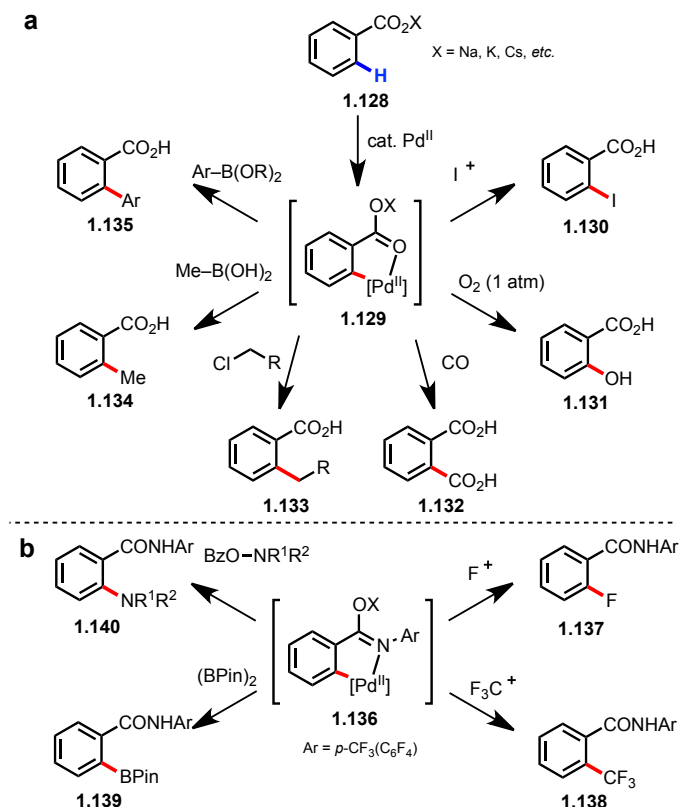
**Figure 1.5.** Aryl- and alkylcarboxylic acids, amines, and alcohols—representative starting material classes that are abundant in quantity and rich in structural diversity

(2) *Products*: Equally important is that C–H activation and subsequent functionalisation takes place at a strategic position and installs a desirable functional group so that the product represents a commonly encountered structural motif, such as a  $\beta$ -functionalised carboxylic acid, amino acid, or biaryl. Establishing reliable routes to these substructures facilitates synthesis planning that incorporates C–H activation transformations as key disconnections. When combined with the selection of simple starting materials, drastic increases in molecular complexity can be achieved using this approach (Scheme 1.11).



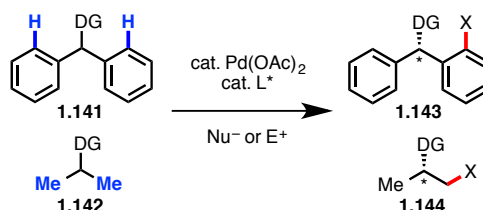
**Scheme 1.11.** Novel retrosynthetic disconnections using C–H functionalisation: routes to (a) the kinamycins (**1.117**)<sup>126</sup> and (b) (+)-lithospermic acid (**1.121**).<sup>127</sup>

(3) *Reactivity*: We preferentially target catalytic manifolds that allow flexibility in terms of the scope of nucleophiles, electrophiles, and/or radical species as reacting partners with C–H bonds. Versatility in the functionalisation step allows the [C–M] bond resulting from C–H cleavage to be efficiently mapped into any carbon–carbon or carbon–heteroatom bond (Scheme 1.12).



**Scheme 1.12.** Diverse Pd(II)-catalysed C–H functionalisation of (a) benzoic acids<sup>128-132</sup> and (b) benzoic acid-derived *N*-aryl amides<sup>133-136</sup> reported by the Yu group.

(4) *Catalysts/Ligands*: For the reasons outlined above, ligand-controlled C–H functionalisation reactions represent an especially fertile ground for discovering new modes of reactivity and for gleaning fundamental insights into chemical reactivity (Scheme 1.5). We view ligand development as the long-term solution for improving catalyst performance: reactivity (TON, TOF, and substrate scope), selectivity (site-selectivity, chemoselectivity, and stereoselectivity), and operating conditions (reaction time, temperature, and tolerance for air and moisture).



**Scheme 1.13.** Enantioselective Pd(II)-catalysed C–H activation using a chiral ligand.

(5) *Operational Convenience*: In order for novel C–H functionalisation reactions to be embraced by the synthetic community, the reactions must be operationally simple and robust. In this respect, substrates, coupling partners, catalysts, and ligands that are commercially available or easily accessible are preferable. Reactions that do not require special equipment and can be set up on the benchtop without rigorous exclusion of air or moisture are similarly desirable.

### 1.4.2 The Need for Effective Ligand Scaffolds

During the past 10 years that the Yu laboratory has been active in this area, an impediment to the group's research has been the lack of ligand scaffolds for accelerating C–H cleavage with Pd(II). The group has consistently resorted to the simplest Pd(II) salts available ( $\text{Pd}(\text{OAc})_2$ ,  $\text{Pd}(\text{TFA})_2$ ,  $\text{PdI}_2$ , *etc.*), and with these basic catalysts, many goals, including the development of methodology for functionalising bulk chemicals and for achieving site- and stereoselectivity in the C–H cleavage step, remained elusive. Thus, the lack of suitable ligand scaffolds represents a major roadblock in harnessing the full potential of Pd(II)-catalysed C–H functionalisation. Indeed, this need for ligands is at the heart of commonly cited problems in the field, like the inability to control positional selectivity of functionalised arenes<sup>137</sup> or more generally, the inability to selectively functionalise one of the many inequivalent C–H bonds present in organic small molecules.

In the Yu laboratory, these shortcomings first became apparent during work on stereoselective C–H activation methodology.<sup>138</sup> In attempting to move from a chiral auxiliary approach to a chiral catalyst approach, the group confronted a long-standing challenge in the field: uncovering a chiral metal catalyst,  $[\text{Pd}(\text{II})\text{--L}^*]$ , for enantioselective C–H activation. The group's motivation for investigating enantioselectivity was rooted in the hypothesis that a chiral ligand effective for stereoinduction is likely to be involved in the

C–H cleavage transition state. Involvement in the C–H cleavage step suggests that this ligand scaffold, or a closely related scaffold, could ultimately be used for the interrelated problems of rate enhancement and site-selectivity.

## 1.5. MONO-*N*-PROTECTED AMINO ACID LIGANDS

### 1.5.1. Considerations for Ligand Design

When considering potential ancillary ligand scaffolds for Pd(II)-catalysed C–H functionalisation, there are many interrelated challenges and complications to keep in mind:

(1) *Assembling a 1:1 ligand:substrate coordination structure.* The ligand could outcompete the substrate for coordination to the Pd(II) centre or *vice versa*. Ligands by their very nature contain coordinating functional groups (either in the form of non-bonding lone pair electrons or bonding  $\pi$ -systems). By contrast, unactivated C–H bonds are paraffin in nature, meaning that they are non-polar and have low inherent affinity for cationic metal centres. Achieving high effective molarity of the substrate in the presence of a ligand is thus difficult, particularly with simple hydrocarbon substrates, like toluene or hexane. In directed C–H activation, on the other hand, many traditional directing groups (pyridines, oxazolines, oximes, *etc.*), could inhibit ligand coordination prior to C–H cleavage (Figure 1.6).

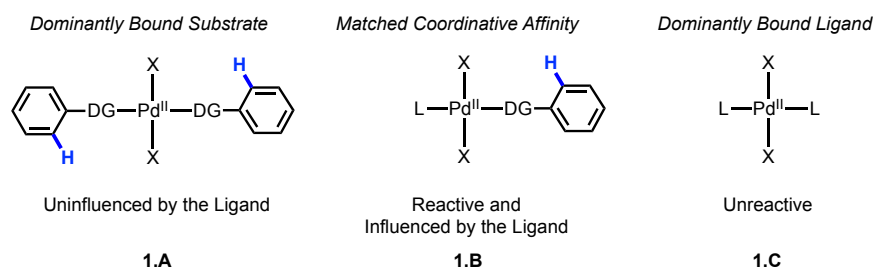


**Figure 1.6.** Depiction of three scenarios for the coordination structures in directed Pd(II)-mediated C–H cleavage: **(1.A)** The substrate contains a strong directing group (DG) and is dominantly bound to Pd(II), precluding ligand (L) coordination. The reaction may take place, but the transition state energy for C–H cleavage will be unaffected by ligand binding. **(1.B)** The substrate and ligand possess matched coordinative affinities for Pd(II), allowing one molecule of each to bind. The reaction may take place, and the transition state energy for C–H cleavage will be affected by ligand binding. **(1.C)** The ligand is a strong  $\sigma$ -donor and outcompetes substrate molecules for coordination to Pd(II). The reaction will not take place.

(2) *Productive interaction between the substrate and ligand at the metal centre.* To engineer a reaction system in which the ligand plays a dominant role in influencing the reactivity and/or selectivity, utilising a functional group capable of directing C–H cleavage via *weak coordination* is highly advantageous.<sup>86</sup> The Yu group has pursued this strategy by developing reactions that are compatible with substrates containing commonly occurring Lewis basic moieties that form low-energy interactions with Pd(II) (*e.g.*, carboxylic acids, triflimides, and alcohols). In these cases, C–H cleavage does not occur as easily as with many of the other commonly utilised directing groups (*e.g.*, pyridines, oxazolines and oximes), which offers the opportunity to probe how external ligands change the activation energy of the C–H cleavage step.

(3) *Promoting the C–H cleavage step.* Under different mechanistic paradigms for C–H cleavage, the electronic requirements of the Pd(II) centre, and thus the supporting ligand, are different. For instance in C(aryl)–H cleavage along an electrophilic palladation mechanism,<sup>139</sup> there is a need to maintain a relatively electrophilic Pd(II) centre. In a concerted metalation/deprotonation (CMD) mechanism,<sup>140–142</sup> a more nucleophilic Pd(II) centre can be effective. The operative mechanism for C–H

cleavage typically depends on a combination of factors, including the substrate, the reaction conditions, and also the ligand(s).<sup>85</sup>

(4) *Compatibility with the other steps in the catalytic cycle and the reaction conditions.* Different Pd(II)-mediated C–H functionalisation reactions proceed via different elementary steps, and each poses challenges in ligand engineering. For example, some steps may require ligand dissociation to provide a vacant coordination site, while others could require the ligand to be resistant to reductive elimination from high-valent intermediates. Additionally, under the reaction conditions, the ligand could react with the substrate, the coupling partner, or the Pd(II) catalyst along any of a number of possible degradation pathways.

(5) *Modifiability and modularity.* Because it is unlikely that a single ligand will be adequate for each combination of substrate and reaction partner, it is advantageous to pursue multiple distinct ligand scaffolds in parallel. In addition to developing multiple complementary ligand scaffolds, utilising modifiable and modular ligand scaffolds can be advantageous for fine-tuning a ligand to a specific combination of substrate and reaction type.

These general considerations and design guidelines provide a conceptual framework for ligand development in Pd(II)-catalysed C–H functionalisation. Naturally, as the Yu laboratory's research programme has progressed, our theoretical understanding of ligand design principles has evolved as a result of new insights from experimental work. Owing to the inherent unpredictability of ligand discovery, there is also an element of empiricism and serendipity to this research area, which makes it important to think carefully but still be adventurous in exploring old and new ligand architectures.



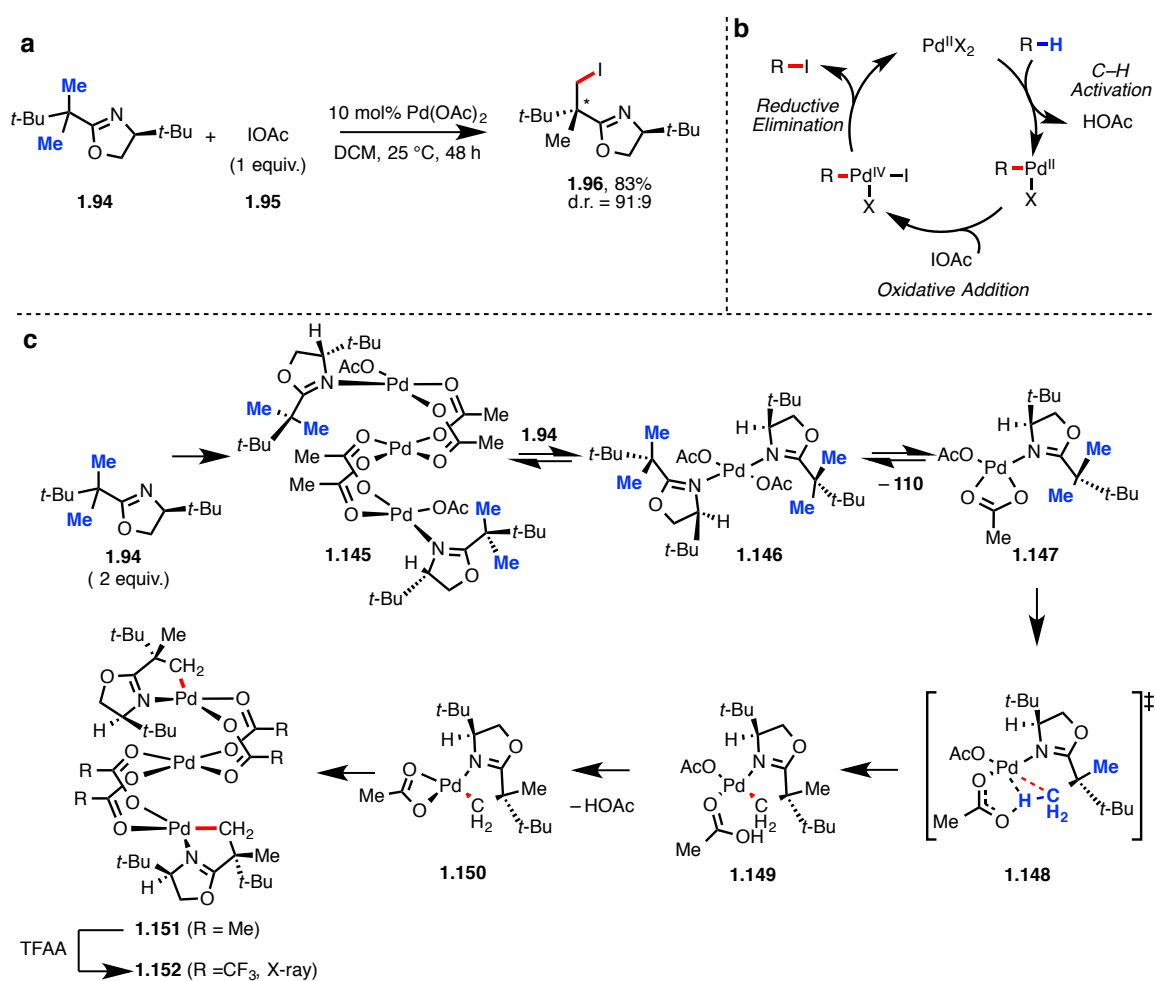
Below we summarise the discovery and development of mono-*N*-protected amino acid ligands for Pd(II)-catalysed C–H functionalisation and discuss the impetus for applying this class of ligands for rate enhancement with recalcitrant substrates.

### 1.5.2. Discovery and Applications in Enantioselective C–H Activation

Drawn to the captivating mechanistic questions and potential synthetic applications of stereoselective C–H activation chemistry, the Yu group has had a long-standing interest in investigating stereoinduction in the palladation of prochiral C–H bonds, which is fundamentally important to the understanding of C–H cleavage by Pd(II) centres.<sup>138</sup> To gain structural information concerning the transition state of directed palladation reactions, the initial focus was on reactions that would proceed through well-defined intermediates that could be easily characterised. Inspired by the important role that removable chiral auxiliaries play in modern organic synthesis, the first approach centred on the use of a chiral oxazoline group<sup>143-145</sup> that could be readily installed onto aliphatic carboxylic acids. Following this strategy, high levels of stereoinduction (>99:1 d.r.) could be achieved in the diastereoselective C–H iodination and acetoxylation of prochiral  $\alpha,\alpha$ -gem-dimethyl groups,  $\alpha,\alpha$ -gem-diphenyl groups, and cyclopropanes along a Pd(II)/Pd(IV) catalytic cycle (Scheme 1.9b and Scheme 1.14).<sup>111,112,114,146</sup>

*tert*-Butyl-substituted oxazoline **1.94** proved to be remarkably effective in directing C(sp<sup>3</sup>)–H activation, even under mild conditions (including temperatures as low as 0 °C). The origin of this pronounced reactivity has been examined through structural characterisation both in solution and in the solid state. Further studies to elucidate the transition state structure *via* computational studies have also been performed in collaboration with the Houk group (Scheme 1.14b).<sup>147</sup> Several trinuclear palladium intermediates, including **1.152**, have been characterised. DFT calculations have revealed the

involvement of monomeric precursor **1.147** as the reactive intermediate, and various possible transition states for the diastereoselective C–H cleavage step (**1.148**) have been modelled. This work has confirmed the importance of conformation and geometry in the square planar pre-transition state coordination structure **1.147**, in which the target C–H bond is approximately co-planar to the acetate anion. This arrangement minimises the dihedral angle between the C–H bond and the Pd(II)–OAc bond, which is critical during the CMD transition state.

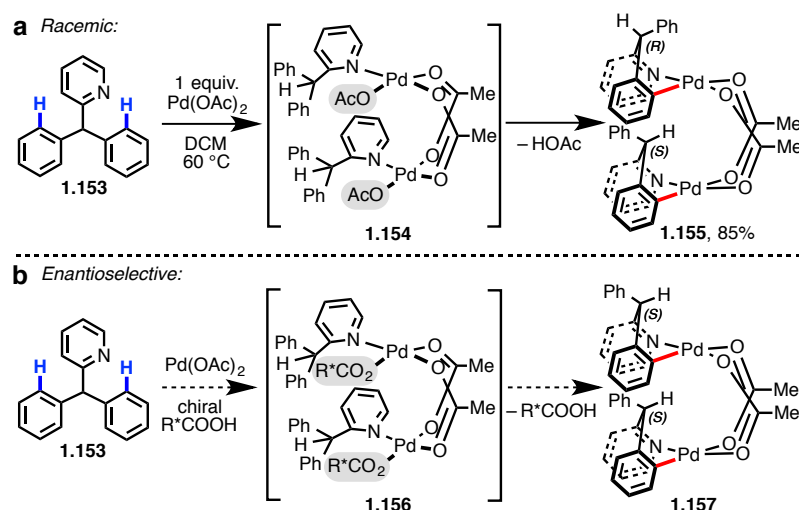


**Scheme 1.14:** (a) Disastereoselective C(sp<sup>3</sup>)–H iodination of *gem*-dimethyl groups using a removable chiral oxazoline auxiliary.<sup>111</sup> (b) General catalytic cycle for C–H iodination via Pd(II)/Pd(IV) catalysis. (c) Model for diastereocontrol, including proposed transition state structure.<sup>147</sup>

While this work was in progress, the next obvious conceptual step forward was to attempt to use a chiral ligand to achieve similar levels of stereoinduction in the absence of a

chiral auxiliary. To that end, diphenyl-2-pyridylmethane **1.153** was used as the pilot substrate, and efficient non-stereoselective conditions were first developed to achieve Pd(II)-catalysed C–H/R–BX<sub>n</sub> cross-coupling (Scheme 1.15).<sup>148</sup> In the long term, we hoped to use this reaction system as a model for developing a broad range of enantioselective carbon–carbon and carbon–heteroatom bond-forming reactions, in which C–H cleavage could be directed by a diverse collection of functional groups.

Following the isolation and characterisation of cyclopalladated dimer **1.155**, it was reasoned that prior to the C–H cleavage step, the putative pre-transition state coordination structure **1.154** offered the opportunity to replace the achiral non-bridging acetate ligands on the Pd(II) centre with chiral carboxylates. In this manner, it was hypothesised that stereoselective C–H cleavage could take place at one of the two prochiral phenyl groups. Although based on our current understanding, we now know that this line of thinking is not entirely accurate, it nonetheless served as an invaluable starting point to probe enantioselective C–H activation.



**Scheme 1.15.** (a) Racemic route to dimeric palladacycle **1.155** from prochiral starting material **1.153**. (b) *Initial hypothesis* for achieving stereoinduction in the C–H cleavage step through use of a chiral carboxylate ligand.<sup>149</sup>

To develop a catalytic enantioselective reaction, a variety of chiral acid ligands were first surveyed in an attempt to induce stereoselectivity in the Pd(II)-catalysed enantioselective C–H activation of **1.158** (Table 1.1).<sup>150</sup> Encouragingly, modest enantioselectivity (<25%) was observed using this approach. Next, it was reasoned that a more rigid backbone structure would limit the conformational degrees of freedom that the ligand possessed. For this reason, chiral cyclopropane amino acids **1.169–1.172** were examined, and it was found that the ee values could be improved to >40%, while maintaining good yield (Table 1.2). Consistent with expectations, enantiomers **1.169** and **1.171** led to product mixtures with opposite enantioselectivity values. Surprisingly, pseudo- $C_2$ -symmetric ligand **1.172** led to nearly racemic mixture. These data, in conjunction with earlier work in the literature characterising amino acid-bound palladacycles<sup>151</sup> suggested that during the C–H cleavage step, the ligand was actually bound in a *bidentate* fashion with the N–H bond possibly remaining intact, inducing chirality at the nitrogen atom. In this way, chiral information could be effectively geared from the  $\alpha$ -carbon atom of the ligand to the nitrogen atom, which would rationalise why **1.172**, which has two  $\alpha$ -substituents of similar steric bulk, was ineffective.

**Table 1.1.** Early attempts to use chiral carboxylate ligands in the catalytic enantioselective C(sp<sup>2</sup>)-H activation of **1.158**.<sup>150</sup>

| Entry            | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> | Entry            | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> |
|------------------|--------|------------------------|---------------------|------------------|--------|------------------------|---------------------|
| 1                |        | 62                     | 5                   | 6                |        | 78                     | 20                  |
| 2                |        | 75                     | 20                  | 7                |        | 63                     | 15                  |
| 3                |        | 65                     | 20                  | 8 <sup>b,e</sup> |        | 9                      | 21                  |
| 4                |        | 87                     | 6                   |                  |        |                        |                     |
| 5 <sup>c,d</sup> |        | 25                     | 0                   |                  |        |                        |                     |

<sup>a</sup> Isolated yield. <sup>b</sup> ee determined by HPLC using a chiral stationary phase. <sup>c</sup> Yield determined by <sup>1</sup>H NMR. <sup>d</sup> 10 mol% Ligand, 85 °C. <sup>e</sup> 15 mol% Ligand, 85 °C.

**Table 1.2.** Catalytic enantioselective C(sp<sup>2</sup>)-H activation of **125** with chiral cyclopropane amino acid ligands.<sup>149</sup>

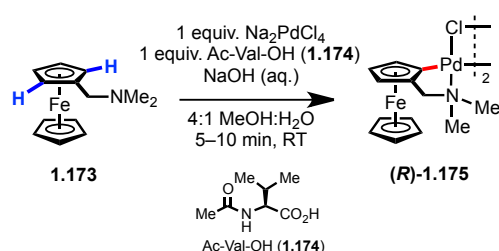
| Entry | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> | Entry | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> |
|-------|--------|------------------------|---------------------|-------|--------|------------------------|---------------------|
| 1     |        | 46                     | 46 (-)              | 3     |        | 63                     | 42 (+)              |
| 2     |        | 71                     | 41 (+)              | 4     |        | 58                     | <5 (-)              |

<sup>a</sup> Isolated yield. <sup>b</sup> ee determined by HPLC using a chiral stationary phase.

Indeed, in the literature, mono-*N*-acyl amino acids were previously employed by Sokolov and coworkers in the stoichiometric asymmetric cyclopalladation of

(dimethylamino)methylferrocene **1.173** (Table 1.3). With Ac-Val-OH (**1.174**), moderate ee values were obtained of optically enriched (*R*)-**1.175**, which possesses planar chirality. It was also established that the new Pd(II)–C bond could subsequently be coupled with electron-poor olefins or CO. However, no forays into catalytic variants of this reaction were made, so it remained unclear whether mono-*N*-protected amino acids would be compatible with other steps in a putative catalytic cycle.

**Table 1.3.** Early application of mono-*N*-acyl amino acids in asymmetric cyclopalladation.<sup>152</sup>



| Entry <sup>a</sup> | pH <sup>b</sup> | pH <sup>c</sup> | Yield (%) <sup>d</sup> | ee (%) <sup>e</sup> |
|--------------------|-----------------|-----------------|------------------------|---------------------|
| 1                  | 5.48            | 6.28            | 46                     | 8.0                 |
| 2                  | 6.00            | 7.35            | 73                     | 24.5                |
| 3                  | 6.45            | 7.90            | 83                     | 40.5                |
| 4                  | 6.70            | 8.75            | 89                     | 65.0                |
| 5                  | 7.60            | 9.30            | 85                     | 73.0                |
| 6                  | 7.95            | 9.82            | 50                     | 78.8                |
| 7                  | 8.50            | 10.30           | 37                     | 56.0                |

<sup>a</sup> Experimental procedure: an aqueous solution of equimolar NaOH and Ac-Val-OH was added to a solution of Na<sub>2</sub>PdCl<sub>4</sub> in MeOH. The pH was adjusted to appropriate value *via* addition of 50% NaOH (aq.); a solution of **1.174** in MeOH was then added, and after 5–10 min, **1.175** precipitated. <sup>b</sup> pH measured before addition of **1.174** solution. <sup>c</sup> pH measured after addition of **1.174** solution. <sup>d</sup> Isolated yield. <sup>e</sup> ee determined by optical rotation of the isolated complex.

With these results in mind, further optimisation of the ligand scaffold was carried out with an eye toward maximizing the steric difference between the two  $\alpha$ -substituents.<sup>149</sup> Gratifyingly, it was found that simple, commercially available Boc-protected amino acids gave high levels of stereinduction (Entries 1–7, Table 1.4). Among the Boc-protected amino acids examined, leucine (Entry 7) proved to be the optimal backbone structure. In an effort to improve the yield, the alkyl substituent on the carbamoyl protecting group was

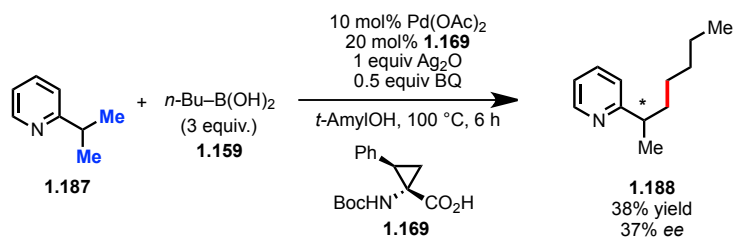
fine-tuned. Introduction of a (–)-menthyl group, improved the yield while maintaining the stereoselectivity (Entry 11).

**Table 1.4.** Catalytic enantioselective C(sp<sup>2</sup>)–H activation of **125** with mono-*N*-protected amino acid ligands.<sup>149</sup>

| Entry | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b,c</sup> | Entry | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b,c</sup> |
|-------|--------|------------------------|-----------------------|-------|--------|------------------------|-----------------------|
| 1     |        | 60                     | 52                    | 7     |        | 63                     | 90                    |
| 2     |        | 69                     | 70                    | 8     |        | 88                     | 79                    |
| 3     |        | 47                     | 85                    | 9     |        | 89                     | 85                    |
| 4     |        | 60                     | 80                    | 10    |        | 87                     | 85                    |
| 5     |        | 65                     | 88                    | 11    |        | 91                     | 87                    |
| 6     |        | 65                     | 88                    |       |        |                        |                       |

<sup>a</sup> Isolated yield. <sup>b</sup> ee determined by HPLC using a chiral stationary phase. <sup>c</sup> Absolute configuration of **1.160** determined by single-crystal X-ray diffraction.<sup>153</sup>

Importantly this concept could further be extended to enantioselective C(sp<sup>3</sup>)–H activation using pyridyl substrates containing *gem*-dimethyl groups (Scheme 1.16). In this case, one of the rigid cyclopropane amino acid ligands from above, **1.169**, was found to be optimal. Although, the alkylated product was only obtained in modest yield and ee, it served as crucial proof of concept that through future advances in ligand design, synthetically useful levels of stereoinduction could be achieved in enantioselective C(sp<sup>3</sup>)–H activation.

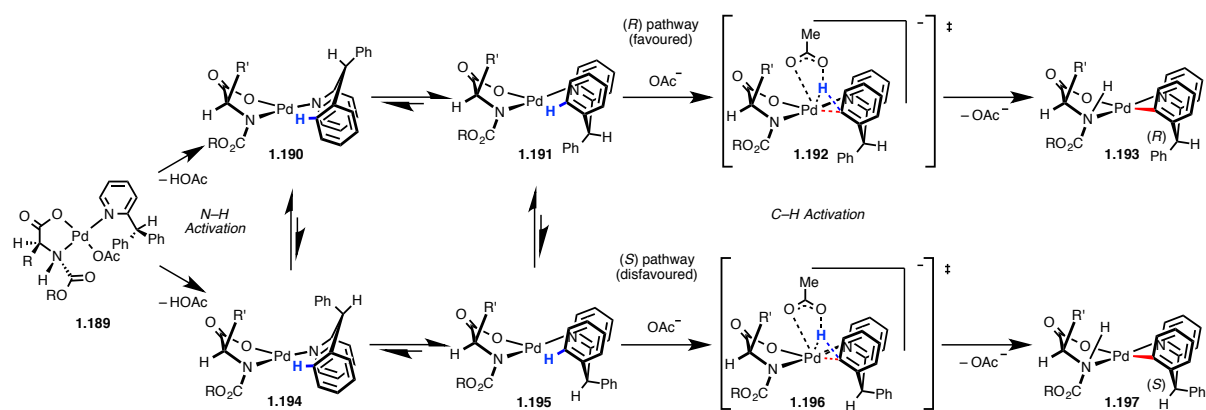


**Scheme 1.16.** Catalytic enantioselective C(sp<sup>3</sup>)–H activation of **1.187**.<sup>149</sup>

These experiments helped elucidate how chiral mono-*N*-protected amino acid ligands coordinate with the Pd(II) centre and led to the proposal of a stereomodel as a basis for further development of amino acid-based ligands to control C–H activation (Scheme 1.17).<sup>149,153</sup> Through NMR studies and inorganic synthesis of putative coordination structures, we believe that the mono-*N*-protected amino acid ligand coordinates to Pd(II) with high affinity *via* a bidentate binding mode (**1.189**). Upon complexation, the nitrogen atom becomes stereogenic, and the sterically encumbered protecting group is forced *trans* to the bulky alkyl substituent through a “gearing” effect. The pyridine moiety of the substrate coordinates *trans* to the carbamoyl group of the ligand, situating the substrate’s *ortho*-C–H bonds in close proximity to the acetate group. Computational studies performed in collaboration with the Musaev group suggest that at this stage, activation of the N–H bond by internal acetate takes place, opening a coordination site at the Pd(II) centre.<sup>153</sup> Concerted metalation/deprotonation *via* external base delivers the palladacycle with concomitant formation of a new stereocentre at the methine carbon atom. Consistent with our experimental results, pre-transition state coordination structure **1.191** and transition state **1.192** (which lead to **1.193**, containing a newly formed (*R*)-stereocentre) are computed to be lower in energy than **1.195** and **1.196** (which lead to **1.197**, containing a newly formed (*S*) stereocentre). The precise steric and electronic effects of the amino acid ligand and its influence on the relative energies of key intermediates **1.190**, **1.191**, **1.194**, and **1.195** and transition states **1.192** and **1.196** are topics of continuing investigation. After

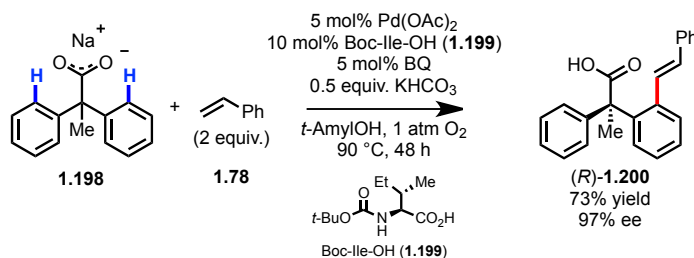


enantioselective C–H activation, palladacycle **1.193** then reacts with the boronic acid via a transmetalation/reductive elimination sequence, releasing of Pd(0), which is reoxidised by Ag(I) and re-enters the catalytic cycle.



**Scheme 1.17.** Working stereomodel, as supported by computational studies.<sup>149,153-155</sup>

The next objectives were (1) to broaden this chemistry to substrate- and product classes more relevant to organic synthesis and (2) to test the viability of other catalytic manifolds for C–C and C–heteroatom bond formation. Drawing on the extensive experience using carboxylic acid-containing substrates in the Yu group (see Scheme 1.12),<sup>86</sup> it was next questioned whether mono-*N*-protected amino acid ligands could be employed to induce enantioselectivity in a Pd(II)-catalysed aerobic C–H olefination reaction of phenylacetic acids that we had recently discovered in our laboratory.<sup>156</sup> Consistent with the group's philosophy for reaction development, it was envisioned at the outset that the carboxylate directing group<sup>107,128,132,157-159</sup> would be versatile for further functionalisation, and in this way, the reaction would offer a unique method for constructing enantioenriched chiral building blocks containing densely substituted stereocentres. Gratifyingly, exposing sodium 2,2-diphenylpropanoate (**1.198**) to our parent C–H olefination conditions in the presence of Boc-Ile-OH (**1.199**) led to the product in high yield and with high ee (Scheme 1.18).<sup>154</sup> Interestingly, the combination of the pre-formed sodium salt and  $\text{KHCO}_3$  as the base were critical; alternative combinations led to lower yield and/or ee.



**Scheme 1.18.** Enantioselective C(sp<sup>2</sup>)–H olefination of diphenylacetic acid derivative **1.198**.<sup>154</sup>

The absolute configuration of one product was confirmed through single crystal X-ray diffraction and the others were assigned by analogy, including (*R*)-**1.200**. The observation that this set of products has the same absolute configuration as (*R*)-**1.160** in Table 1.4 is consistent with the notion that the two mechanisms of stereoinduction are analogous, with the sodium carboxylate acting like the 2-pyridyl group as an L-type neutral donor during the enantioselective cyclometalation step. Importantly, this work also established the compatibility of the amino acid ligand scaffold with other elementary steps in catalysis: namely, olefin association, 1,2-migratory insertion, and  $\beta$ -hydride elimination.

### 1.5.3. Applications in Position-Selective C–H Activation

In light of mounting evidence that mono-*N*-protected amino acid ligands were intimately involved in the C–H cleavage step of the reactions described above, these ligands were next tested in a conceptually related challenge, controlling the positional selectivity in the C–H functionalisation of substituted arenes.

While exploring the substrate scope of non-stereoselective Pd(II)-catalysed *ortho*-C–H olefination of phenylacetic acids<sup>156</sup> we became interested in the functionalisation of 2-(3-methoxy-5-methylphenyl)acetic acid **1.201** because of its potential as a building unit in natural products synthesis. When we attempted the reaction under our parent reaction conditions, we observed an intractable 1.4:1 mixture of the two possible products, **1.203-A**

and **1.203-B** in 68% conversion. Upon surveying a collection of ligands, we ultimately found that the application of Formyl-Ile-OH (**1.210**) furnished **1.203-A** and **1.203-B** in a 20:1 ratio without a substantial decrease in conversion (45%) (Entry 12). Simply increasing the catalyst loading to 7% lifted the conversion to 75% with identical levels of selectivity.

**Table 1.5.** Position-selective C–H olefination of **1.215** using mono-*N*-protected amino ligands.

|       |        |                        |                  |       |        |                        |                  |
|-------|--------|------------------------|------------------|-------|--------|------------------------|------------------|
|       |        |                        |                  |       |        |                        |                  |
| Entry | Ligand | Conv. (%) <sup>a</sup> | A:B <sup>a</sup> | Entry | Ligand | Conv. (%) <sup>a</sup> | A:B <sup>a</sup> |
| 1     | ---    | 68                     | 1.4:1            | 7     |        | 50                     | 3:1              |
| 2     |        | 17                     | 3:1              | 8     |        | 16                     | 6:1              |
| 3     |        | 17                     | 5:1              | 9     |        | 24                     | 13:1             |
| 4     |        | 23                     | 6:1              | 10    |        | 16                     | 5:1              |
| 5     |        | 24                     | 7:1              | 11    |        | 23                     | 10:1             |
| 6     |        | 27                     | 8:1              | 12    |        | 45 (75) <sup>b</sup>   | 20:1             |

<sup>a</sup> The conversion and A:B ratio were determined by <sup>1</sup>H NMR of the crude reaction mixture.

<sup>b</sup> Value in parenthesis represents the conversion using 7 mol% Pd(OAc)<sub>2</sub> and 14 mol% For-Ile-OH under otherwise identical conditions.

Though a precise mechanistic rationalisation of this change in selectivity remains to be determined, one plausible explanation is that the ligand alters the mechanism of C–H cleavage. In the absence of ligand, electron-rich and electron-neutral phenylacetic acids are highly reactive, while substrates with electron-withdrawing groups are unreactive, a pattern

consistent with an electrophilic palladation mechanism for C–H cleavage.<sup>156</sup> In the presence of certain amino acid ligands, electron-deficient phenylacetic acids are preferentially reactive which is more consistent with a CMD mechanism (see Chapter 2).<sup>85</sup> It is possible that the drastic change in product distribution is a reflection of the difference in relative rates of C–H cleavage under the two mechanistic regimes. An alternative explanation is that the ligand could merely be enhancing the steric demands around the metal centre, favouring reaction away from the bulkier methyl group.<sup>160,161</sup>

#### 1.5.4. Applications in Ligand-Accelerated Catalysis

The ability of mono-*N*-protected amino acids to control enantioselectivity and positional selectivity serves as evidence that the ligand is coordinated to Pd(II) during the C–H cleavage event and is influencing the corresponding transition state energies. Accordingly, we hypothesised that this class of ligands could promote C–H activation for otherwise poorly reactive or unreactive substrates.

This central hypothesis forms the basis of Part I of this Thesis, and in Chapters 2–4, we discuss the results of experiments to test this idea. In Chapter 2, we build on the results shown in Table 1.6, using mono-*N*-protected amino acid ligands to promote C–H olefination of phenylacetic acid substrates that were previously unreactive. In Chapter 3, we apply ligand acceleration to build multiply substituted arenes through sequential and iterative C–H olefination. In Chapter 4, we draw on mono-*N*-protected amino acid ligands in the development of an improved protocol for C–H/R–BX<sub>*n*</sub> cross-coupling with phenylacetic acid substrates. Finally, Chapter 5 highlights ongoing work by the Yu group and others involving mono-*N*-protected amino acid ligands.

**1.6. REFERENCES**

- (1) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **1995**, *34*, 1059–1070.
- (2) As a point of clarification, 'ligand' can refer to any molecule that is coordinated to a metal catalyst (anionic donor, X-type; or neutral donor, L-type). Throughout the text we generally focus on ligands that possesses an element of design (*i.e.*, a molecule that was independently synthesised for the express purpose of coordinating it to the metal to influence the reactivity), rather than common counterions (OAc, OTf, Cl, *etc.*) or solvent molecules (MeCN, THF, *etc.*), but those too can have a dramatic impact on the reactivity and/or selectivity of catalytic transformations.
- (3) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.
- (4) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.
- (5) Dang, T. P.; Kagan, H. B. *J. Chem. Soc. D* **1971**, 481.
- (6) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946–5952.
- (7) Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262–6267.
- (8) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934.
- (9) Osborn, J. A.; Wilkinson, G.; Young, J. F. *Chem. Commun.* **1965**, 17.
- (10) Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711–1732.
- (11) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29.
- (12) Nolan, S. P.; Clavier, H. *Chem. Soc. Rev.* **2010**, *39*, 3305–3316.
- (13) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.

- (14) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534–1544.
- (15) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461–1473.
- (16) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290–1309.
- (17) Hillier, A. C.; Grasa, G. A.; Viciu, M. S.; Lee, H. M.; Yang, C.; Nolan, S. P. *J. Organomet. Chem.* **2002**, *653*, 69–82.
- (18) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968–1970.
- (19) Andersson, M. A.; Epple, R.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 472–475.
- (20) Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, *299*, 1691–1693.
- (21) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313–348.
- (22) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617–620.
- (23) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **1998**, *37*, 3387–3388.
- (24) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. *M. J. Org. Chem.* **1999**, *64*, 5575–5580.
- (25) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723.
- (26) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178–6179.
- (27) Hughes, O. R.; Unruh, J. D. *J. Mol. Catal.* **1981**, *12*, 71–83.
- (28) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081–3089.
- (29) Gupta, M.; Hagen, C.; Flesher, R. J.; Kaska, W. C.; Jensen, C. M. *Chem. Commun.* **1996**, 2083–2084.
- (30) Liu, F.; Pak, E. B.; Singh, B.; Jensen, C. M.; Goldman, A. S. *J. Am. Chem. Soc.* **1999**, *121*, 4086–4087.

- (31) Nolan, S. P. *Acc. Chem. Res.* **2011**, *44*, 91–100.
- (32) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.
- (33) Tajima, Y.; Kunioka, E. *J. Org. Chem.* **1968**, *33*, 1689–1690.
- (34) Stern, R.; Sajus, L. *Tetrahedron Lett.* **1968**, *9*, 6313–6314.
- (35) Miyake, A.; Kondo, H. *Angew. Chem. Int. Ed.* **1968**, *7*, 631–632.
- (36) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 5483–5484.
- (37) Uto, T.; Shimizu, M.; Ueura, K.; Tsurugi, H.; Satoh, T.; Miura, M. *J. Org. Chem.* **2007**, *73*, 298–300.
- (38) Hyster, T. K.; Rovis, T. *Chem. Sci.* **2011**, *2*, 1606–1610.
- (39) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054–3131.
- (40) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2010**, *1*, 13–31.
- (41) Togni, A.; Venanzi, L. M. *Angew. Chem. Int. Ed.* **1994**, *33*, 497–526.
- (42) Michel, B. W.; Camelio, A. M.; Cornell, C. N.; Sigman, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 6076–6077.
- (43) Campbell, A. N.; White, P. B.; Guzei, I. A.; Stahl, S. S. *J. Am. Chem. Soc.* **2010**, *132*, 15116–15119.
- (44) The examples included in this figure are not intended to constitute a comprehensive list. Additionally, it should also be noted that many of the ligands highlighted in Figure 1 are also known to give enhanced kinetic reactivity in asymmetric and non-stereoselective transformations.
- (45) Brown, J. M. *Angew. Chem. Int. Ed.* **1987**, *26*, 190–203.
- (46) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307–1370.
- (47) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174–3176.
- (48) Crabtree, R. H.; Felkin, H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *141*, 205–215.

- (49) Bell, S.; Wüstenberg, B.; Kaiser, S.; Menges, F.; Netscher, T.; Pfaltz, A. *Science* **2006**, *311*, 642–644.
- (50) Kaiser, S.; Smidt, S. P.; Pfaltz, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 5194–5197.
- (51) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922–1925.
- (52) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801–2803.
- (53) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063–7064.
- (54) Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008–2022.
- (55) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
- (56) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047–1062.
- (57) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106–112.
- (58) Reetz, M. T. *Angew. Chem. Int. Ed.* **2008**, *47*, 2556–2588.
- (59) Sakane, S.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1985**, *26*, 5535–5538.
- (60) Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418–4420.
- (61) Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467–8468.
- (62) Hoveyda, A. H.; Schrock, R. R. *Chem. Eur. J.* **2001**, *7*, 945–950.
- (63) Harper, K. C.; Sigman, M. S. *Science* **2011**, *333*, 1875–1878.
- (64) von Matt, P.; Pfaltz, A. *Angew. Chem. Int. Ed.* **1993**, *32*, 566–568.
- (65) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769–1772.
- (66) Dawson, G. J.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149–3150.
- (67) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493–4506.
- (68) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345.



- (69) Williams, J. M. J. *Synlett* **1996**, 705–710.
- (70) Pfaltz, A.; Drury, W. J., III. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5723–5726.
- (71) Tani, K.; Behenna, D. C.; McFadden, R. M.; Stoltz, B. M. *Org. Lett.* **2007**, *9*, 2529–2531.
- (72) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320–2322.
- (73) For the first reports of Pd(0)-catalysed aryl halide/alkyne coupling, see: (a) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253–257. (b) Dieck, A. H.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259–263. For an improved protocol in the presence of Cu(I) salts (the Sonogashira reaction), see: (c) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467–4470.
- (74) For the initial reports of the Ni-catalysed Kumada–Corriu coupling reaction, see: (a) Corriu, R. J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144a. (b) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374–4376. For the first Pd(0)-catalysed reaction, see: (c) Yamamura, M.; Moritani, I.; Murahashi, S.-I. *J. Organomet. Chem.* **1975**, *91*, C39–C42.
- (75) For the initial report of the Negishi coupling reaction, see: (a) Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821–1823. For a review, see: (b) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340–348.
- (76) For initial reports of the Migita–Stille reaction, see: (a) Kosugi, M.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 1423–1424. (b) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638. (c) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998.
- (77) For initial reports of the Suzuki–Miyaura coupling reaction, see: (a) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437–3440. (b) Miyaura, N.;

- Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, 866–867. For a review, see: (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, 95, 2457–2483.
- (78) For the initial report of the Hiyama coupling reaction, see: (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, 53, 918–920. For fluoride-free coupling of silanols (the Hiyama–Denmark reaction), see: (b) Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2001**, 123, 6439–6440. For a review, see: (c) Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, 41, 1486–1499.
- (79) For early reviews of the Tsuji–Trost reaction, see: (a) Trost, B. M. *Acc. Chem. Res.* **1980**, 13, 385–393. (b) Tsuji, J. *Tetrahedron* **1986**, 42, 4361–4401.
- (80) Cho, E. J.; Senecal, T. D.; Kinzel, T.; Zhang, Y.; Watson, D. A.; Buchwald, S. L. *Science* **2010**, 328, 1679–1681.
- (81) For initial reports of the Buchwald–Hartwig amination reaction, see: (a) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, 116, 5969–5970. (b) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, 116, 7901–7902. For early studies concerning C–N bond formation using Pd(0), see: (c) Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, 12, 927–928. (d) Boger, D. L.; Panek, J. S. *Tetrahedron Lett.* **1984**, 25, 3175–3178.
- (82) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, 60, 7508–7510.
- (83) For initial reports of Buchwald–Hartwig etherification, see: (a) Palucki, M.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, 118, 10333–10334. (b) Mann, G.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, 118, 13109–13110. (c) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, 121, 4369–4378. (d) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, 121, 3224–3225.

- (84) Watson, D. A.; Su, M.; Teverovskiy, G.; Zhang, Y.; Garcia-Fortanet, J.; Kinzel, T.; Buchwald, S. L. *Science* **2009**, *325*, 1661–1664.
- (85) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 14137–14151.
- (86) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788–802.
- (87) Ryabov, A. D. *Synthesis* **1985**, 233–252.
- (88) Selected reviews of Pd-catalysed C–H functionalisation: (a) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichim. Acta* **2007**, *40*, 35–41. (b) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200–205. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173–1193. (d) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115. (e) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826. (f) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (g) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169. (h) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215–1292.
- (89) For evidence and discussion of Pd(III) intermediates in C–H activation reactions, see: (a) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302–309. (b) Powers, D. C.; Geibel, M. A. L.; Klein, J. E. M. N.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050–17051. (c) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234–11241. For pioneering inorganic studies of Pd(III) species, see: (d) Cotton, F. A.; Koshevoy, I. O.; Lahuerta, P.; Murillo, C. A.; Sanaú, M.; Ubeda, M. A.; Zhao, Q. *J. Am. Chem. Soc.* **2006**, *128*, 13674–13675. For a related study concerning Pt(III) intermediates, see: (e) Whitfield, S. R.; Sanford, M. S. *Organometallic* **2008**, *27*, 1683–1689. For a recent inorganic study, see: (f) Khusnutdinova, J. R.; Rath, N. P.; Mirica, L. M. *J. Am. Chem. Soc.* **2010**, *132*, 7303–7305.
- (90) Mei, T.-S.; Wang, X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 10806–10807.

- (91) For a reviews of organopalladium(IV) chemistry, see: (a) Muñiz, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 9412–9423. (b) Xu, L.-M.; Li, B.-J.; Yang, Z.; Shi, Z.-J. *Chem. Soc. Rev.* **2010**, *39*, 712–733. (c) Sehnal, P.; Taylor, R. J. K.; Fairlamb, I. J. S. *Chem. Rev.* **2010**, *110*, 824–889. (d) Engle, K. M.; Mei, T.-S.; Wang, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 1478–1491. (e) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177–185.
- (92) Fujiwara, Y.; Moritani, I.; Matsuda, M. *Tetrahedron* **1968**, *24*, 4819–4824.
- (93) Fujiwara, Y.; Moritani, I.; Matsuda, M.; Teranishi, S. *Tetrahedron Lett.* **1968**, *9*, 3863–3865.
- (94) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91*, 7166–7169.
- (95) Nakata, K.; Miyata, T.; Jintoku, T.; Kitani, A.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3755–3759.
- (96) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119–1122.
- (97) Fujiwara, Y.; Asano, R.; Moritani, I.; Teranishi, S. *J. Org. Chem.* **1976**, *41*, 1681–1683.
- (98) Henry, P. M. *J. Org. Chem.* **1971**, *36*, 1886–1890.
- (99) Eberson, L.; Jönsson, L. *J. Chem. Soc., Chem. Commun.* **1974**, 885–886.
- (100) Eberson, L.; Jönsson, L. *Acta Chem. Scand. Ser. B* **1976**, *30*, 361–364.
- (101) Yoneyama, T.; Crabtree, R. H. *J. Mol. Catal. A: Chem.* **1996**, *108*, 35–40.
- (102) Fahey, D. R. *J. Organomet. Chem.* **1971**, *27*, 283–292.
- (103) Tremont, S. J.; Rahman, H. U. *J. Am. Chem. Soc.* **1984**, *106*, 5759–5760.
- (104) Fujiwara, Y.; Maruyama, O.; Yoshidomi, M.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 851–855.
- (105) Itahara, T.; Ikeda, M.; Sakakibara, T. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1361–1363.
- (106) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578–9579.

- (107) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211–5215.
- (108) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586–1587.
- (109) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300–2301.
- (110) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542–9543.
- (111) Giri, R.; Chen, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2005**, *44*, 2112–2115.
- (112) Giri, R.; Liang, J.; Lei, J.-G.; Li, J.-J.; Wang, D.-H.; Chen, X.; Naggar, I. C.; Guo, C.; Foxman, B. M.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2005**, *44*, 7420–7424.
- (113) Daugulis, O.; Zaitsev, V. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4046–4048.
- (114) Giri, R.; Chen, X.; Hao, X.-S.; Li, J.-J.; Liang, J.; Fan, Z.-P.; Yu, J.-Q. *Tetrahedron: Asymmetry* **2005**, *16*, 3502–3505.
- (115) Chen, X.; Li, J.-J.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 78–79.
- (116) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634–12635.
- (117) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2001**, *40*, 4544–4568.
- (118) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489.
- (119) It is important to clarify that along a Pd(0)/Pd(II) catalytic cycle, the cross-coupling of C(aryl)–H bonds with aryl halides can be promoted with phosphine and NHC ligands. Analogous to traditional Pd(0)-catalysed cross-coupling reactions, this type of reaction begins with oxidative addition of the aryl halide as the first elementary step in the catalytic cycle. Though Pd(II) salts are often used as precatalysts in these transformations, in situ reduction generates a [Pd(0)L<sub>n</sub>] species, which is the active

- catalyst. This is a distinct mechanistic manifold that is outside of the scope of this Thesis. For lead references using chiral [Pd(0)–L\*] catalysts in C–H functionalisation, see: (a) Albicker, M. R.; Cramer, N. *Angew. Chem. Int. Ed.* **2009**, *48*, 9139–9142. (b) Renaudat, A.; Jean-Gérard, L.; Jazzar, R.; Kefalidis, C. E.; Clot, E.; Baudoin, O. *Angew. Chem. Int. Ed.* **2010**, *49*, 7261–7265. (c) Nakanishi, M.; Katayev, D.; Besnard, C.; Kündig, E. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 7438–7441. (d) Anas, S.; Cordi, A.; Kagan, H. B. *Chem. Commun.* **2011**, *47*, 11483–11485. (e) Saget, T.; Lemouzy, S. J.; Cramer, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 2238–2242. (f) Martin, N.; Pierre, C.; Davi, M.; Jazzar, R.; Baudoin, O. *Chem. Eur. J.* **2012**, *18*, 4480–4484. (g) Saget, T.; Cramer, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 12842–12845.
- (120) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; John Wiley & Sons: New York, 1995.
- (121) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885–1898.
- (122) Gutekunst, W. R.; Baran, P. S. *Chem. Soc. Rev.* **2011**, *40*, 1976–1991.
- (123) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960–9009.
- (124) Newhouse, T.; Baran, P. S.; Hoffmann, R. W. *Chem. Soc. Rev.* **2009**, *38*, 3010–3021.
- (125) Li, C.-J.; Trost, B. M. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 13197–13202.
- (126) Kimura, S.; Kobayashi, S.; Kumamoto, T.; Akagi, A.; Sato, N.; Ishikawa, T. *Helv. Chim. Acta* **2011**, *94*, 578–591.
- (127) Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 5767–5769.
- (128) Mei, T.-S.; Giri, R.; Maugel, N.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 5215–5219.
- (129) Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654–14655.
- (130) Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082–14083.

- (131) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 6097–6100.
- (132) Giri, R.; Mangel, N.; Li, J.-J.; Wang, D.-H.; Breazzano, S. P.; Saunders, L. B.; Yu, J.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 3510–3511.
- (133) Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652–7655.
- (134) Chan, K. S. L.; Wasa, M.; Wang, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 9081–9084.
- (135) Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 134–137.
- (136) Zhang, X.-G.; Dai, H.-X.; Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 11948–11951.
- (137) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936–946.
- (138) Giri, R.; Shi, B.-F.; Engle, K. M.; Mangel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242–3272.
- (139) Ryabov, A. D.; Sakodinskaya, I. K.; Yatsimirsky, A. K. *J. Chem. Soc. Dalton Trans.* **1985**, 2629–2638.
- (140) Gómez, M.; Granell, J.; Martinez, M. *Organometallics* **1997**, *16*, 2539–2546.
- (141) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754–13755.
- (142) The mechanisms and associated nomenclature of metal-mediated C–H cleavage are topics of ongoing discussion in the literature. With Pd(II), oxidative addition, electrophilic palladation, and concerted metalation/deprotonation (CMD) have all been proposed, and based on our current knowledge the latter two seem to be operative in the preponderance of cases. It is important to consider, however, that in actuality these broad categories likely represent extremes on a continuum of possible mechanistic scenarios. For example, one could reasonably argue that the "CMD" category actually

encompasses nearly all base-assisted, redox-neutral C–H activation mechanisms. If proton removal at the transition state is not advanced compared to Pd–C bonding, the CMD pathway would possess electrophilic substitution character. If, on the other hand, proton removal is advanced compared to Pd–C bonding, the CMD pathway would have deprotonative character. As the community gains a deeper understanding of the true mechanism at play in each unique reaction, the adoption more precise nomenclature, such "CMD with deprotonative character" or "CMD with electrophilic substitution character" may be in order. To simplify discussion in the present review, we use "electrophilic palladation" and "CMD" in their traditional sense. The former we use to describe Pd(II)-mediated C(sp<sup>2</sup>)–H activation that likely involves a Wheland (arenium) intermediate. The latter we use to describe Pd(II)-mediated C(sp<sup>3</sup>)–H activation and C(sp<sup>2</sup>)–H activation with strongly deprotonative character (involving minimal charge build-up in the transition state).

- (143) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297–2360.
- (144) Xia, J.-B.; You, S.-L. *Organometallics* **2007**, *26*, 4869–4871.
- (145) Takebayashi, S.; Shizuno, T.; Otani, T.; Shibata, T. *Beilstein J. Org. Chem.* **2012**, *8*, 1844–1848.
- (146) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biomol. Chem.* **2006**, *4*, 4041–4047.
- (147) Giri, R.; Lan, Y.; Liu, P.; Houk, K. N.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 14118–14126.
- (148) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115.
- (149) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886.



- (150) For original data corresponding to Entries 5 and 8, see: Mangel, N. L., Palladium-Catalysed Alkylation, Arylation and Dehydrogenation of Unactivated C–H bonds. Syntheses of the Tetracyclic Aminoquinone Moiety of Marmycin A, (±)-Nosyberkol (Isotuberculosinol, Revised Structure of Edaxadiene), and (±)-Tuberculosinol. Ph.D. Thesis, Brandeis University, Waltham, MA, February 2011. For all other entries, see the Supporting Information of Ref. 149.
- (151) Navarro, R.; García, J.; Urriolabeitia, E. P.; Cativiela, C.; Diaz-de-Villegas, M. D. *J. Organomet. Chem.* **1995**, *490*, 35–43.
- (152) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.
- (153) Musaev, D. G.; Kaledin, A.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 1690–1698.
- (154) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461.
- (155) Prior to determining the absolute configuration of product (–)-**1.160** as (*R*) (see Ref. 153), we put forward a working model for stereoinduction in Ref. 149. However, the model actually predicted preferential formation of the the opposite enantiomer. That model has since been abandoned, and a revised model was put forward in Refs. 153 and 154. The discussion herein is based on the revised model.
- (156) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315–319.
- (157) Kao, L.-C.; Sen, A. *J. Chem. Soc., Chem. Commun.* **1991**, 1242–1243.
- (158) Dangel, B. D.; Johnson, J. A.; Sames, D. *J. Am. Chem. Soc.* **2001**, *123*, 8149–8150.
- (159) Lee, J. M.; Chang, S. *Tetrahedron Lett.* **2006**, *47*, 1375–1379.
- (160) Kutter, E.; Hansch, C. *J. Med. Chem.* **1969**, *12*, 647–652.
- (161) Sotomatsu, T.; Fujita, T. *J. Org. Chem.* **1989**, *54*, 4443–4448.

## CHAPTER 2

### LIGAND-ACCELERATED PALLADIUM(II)-CATALYSED C–H OLEFINATION

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## 2.1. INTRODUCTION

With the emergence of Pd(II)-catalysed C–H functionalisation for offering novel, concise routes to desirable target compounds, a lingering challenge is improving the catalytic efficiency and substrate scope of these transformations. In previous work in the Yu laboratory, it was discovered that mono-*N*-protected amino acid ligands could promote enantioselective<sup>1-3</sup> and position-selective<sup>4</sup> C–H activation. These findings are evidence that this class of ligands exhibit a dramatic influence on the metal centre during the C–H cleavage step. We thus questioned whether we could adopt these same ligands to lower the activation energy of C–H cleavage, thereby enhancing the kinetic reactivity of the Pd(II) catalyst.

Herein we report the results of our efforts to investigate this question in the context of one particular reaction, the Pd(II)-catalysed C–H olefination of phenylacetic acids. Kinetic studies have revealed a dramatic rate increase in the presence of amino acid ligands, which, taken in the context of other data, is suggestive of acceleration in the C–H cleavage step. The data from these initial rate studies prompted us to undertake further ligand optimisation, which has led to improved reaction conditions for this transformation. Finally, we present evidence from intermolecular competition experiments and kinetic isotope (KIE) experiments that suggest that coordination of amino acid ligands to Pd(II) leads to a change in the reaction mechanism of C–H cleavage from electrophilic palladation to concerted metalation/deprotonation (CMD).

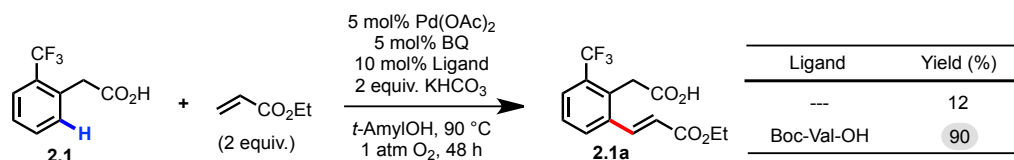
## 2.2. RESULTS AND DISCUSSION

### 2.2.1. Preliminary findings

To begin this study, we revisited an aerobic Pd(II)-catalysed C–H olefination reaction of phenylacetic acid substrates that was previously disclosed by the Yu laboratory.<sup>4</sup>

The originally reported reaction conditions gave high yields for substrates in which the aromatic ring was electron-rich or -neutral but were unreactive for electron poor substrates. Additional drawbacks of the transformation include the relatively high reaction temperature (90 °C), long reaction time (48 h), high catalyst loading (5 mol%), and the need for BQ as a co-oxidant.

In preliminary experiments,<sup>4</sup> several problematic substrates were exposed to the reaction conditions in the presence and absence of a mono-*N*-protected amino acid ligand, and dramatic improvements in yield were observed (Scheme 2.1). In the case of 2-(trifluoromethyl)phenylacetic acid (**2.1**), for example, only 12% yield was found in the absence of ligand, while a yield of 90% was obtained in the presence of Boc-Val-OH. Other substrates showed similar improvement in the presence of ligand, and hydrocinnamic acids, which were previously unreactive, could also be used to give moderate yields of the desired products.



**Scheme 2.1.** Preliminary results for ligand-promoted C–H olefination of **2.1**.<sup>4</sup>

With these results in hand, the next critical question to address was whether the improved reactivity observed using amino acid ligands is a result of ligand-induced acceleration (*i.e.*, a decrease in the activation energy) and if so, whether the amino acid core structure could be further tuned to offer improved reactivity, reduced reaction times, and lower catalyst loading.<sup>5</sup>

### 2.2.2. Reaction Kinetics

We began the next phase of our investigation by determining whether the improved yield after 48 h stemmed from improved catalyst lifetime or increased initial reaction rate. Using the C–H olefination of **2.1** to **2.1a** as a model study, we ran parallel reactions, quenching them at regular intervals and determining the conversion by  $^1\text{H}$  NMR of the crude reaction mixtures. We then plotted the conversion versus time under four different reaction conditions: (1) without Boc-Val-OH, without 1,4-benzoquinone (BQ), (2) without Boc-Val-OH, with BQ, (3) with Boc-Val-OH, without BQ, (4) with Boc-Val-OH, with BQ. The results from these studies are shown in Figure 2.1.

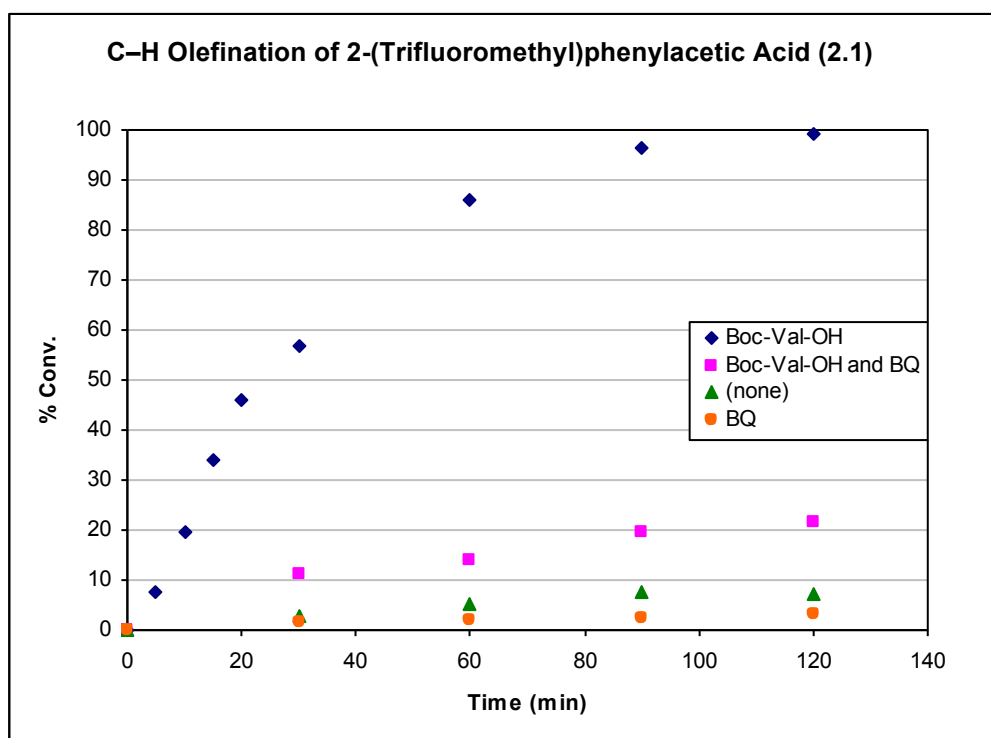
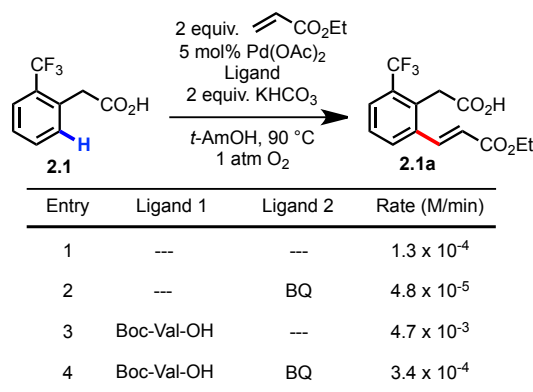


**Figure 2.1.** Initial rate studies of C–H olefination of *o*-trifluoromethylphenylacetic acid (**2.1**). BQ (5 mol%) and Boc-Val-OH (10 mol%). Each data point represents the average of three trials, with the exception of the Boc-Val-OH trials from 60 min to 120 min, which represent single trials. See the Experimental section for experimental details.

In the absence of BQ, we observed a 36-fold rate increase for reactions with Boc-Val-OH compared to those without this ligand (from  $1.3 \times 10^{-4}$  M/min to  $4.7 \times 10^{-3}$  M/min). To our surprise, we observed that BQ substantially decreased the reaction rate both with and without Boc-Val-OH. Previously, during our investigation to develop a highly mono-selective C–H olefination reaction with phenylacetic acid substrates, BQ was found to be beneficial for improving the overall yield after 48 h and controlling the mono/di selectivity

with more reactive substrates. The observation that BQ leads to a decrease in the initial reaction rate, is consistent with it being found to improve the mono/di selectivity with more reactive substrates. Additionally, though BQ lowers the initial reaction rate, it also seems to be capable of improving the overall turnover number given a sufficiently long reaction time (particularly in the case of reactions run in the absence of amino acid ligands).

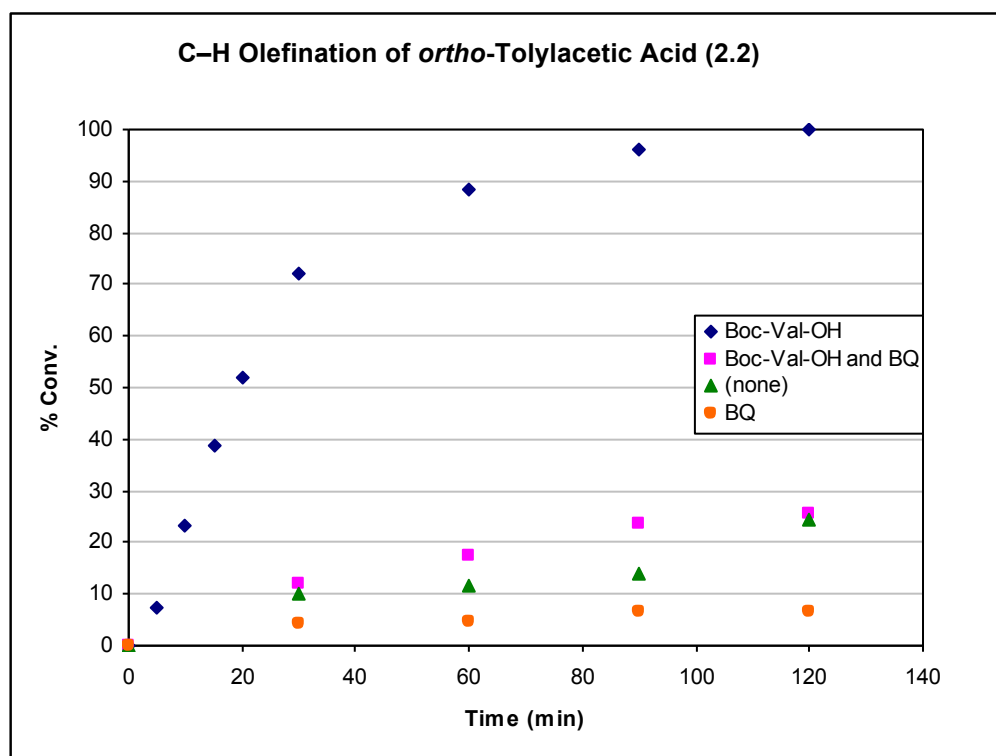
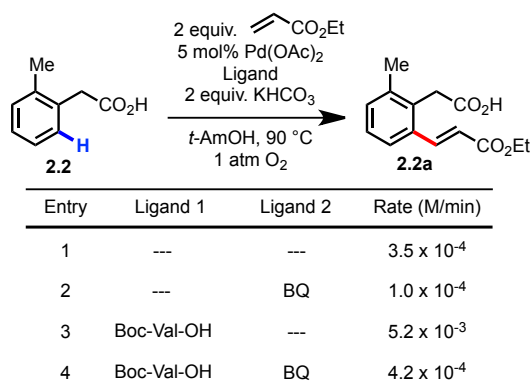


**Figure 2.2.** Kinetic studies of C–H olefination of *o*-tolylacetic acid (**2.2**). BQ (5 mol%) and Boc-Val-OH (10 mol%). Each data point represents the average of three trials, with the exception of the Boc-Val-OH trials from 60 min to 120 min, which represent single trials. See the Experimental section for experimental details.

In light of these results, we wondered whether this trend was unique to electron-deficient substrates. Thus, we performed an analogous set of experiments with a more electron-rich substrate, **2.2**, and found a 15-fold rate increase for reactions using with Boc-Val-OH compared to those without it (from  $3.5 \times 10^{-4}$  M/min to  $5.2 \times 10^{-3}$  M/min) (Figure 2.2).

With this information in hand, we next sought to determine optimal conditions for Pd(II)-catalysed C–H olefination of **2.1** in an effort to improve the reaction rate, catalytic turnover, and substrate scope, which we viewed as central to advancing the versatility and practicality of the transformation.

### 2.2.3. Ligand Optimisation

Our efforts to develop an improved reaction protocol for our aerobic Pd(II)-catalysed C–H olefination reaction centred on the identification of an optimal ligand in terms of reaction rate and overall yield. To begin, we sought to identify the most active ligand backbones by examining a set of commercially *N*-Boc-protected amino acids (Table 2.1). For our screening studies, we selected a highly abridged reaction time of 20 minutes in order to see the comparative kinetic behaviour of the different ligands. Notably, in the absence of ligand, the reaction was found to give less than 5% conversion (Entry 1). Prior to our investigation, we hypothesised that the bite angle between the two coordination sites on the amino acid ligand could have a dramatic impact on the catalytic activity of Pd(II), as it would presumably effect the geometry of the coordination assembly in the pre-transition state. We probed Boc-Gly-OH (Entry 9) (with no substitution at the alpha position, and hence a large bite angle) and a quaternary substituted amino acid with a smaller bite angle (Entry 14), and found that both of these ligand structures resulted in slower reactions than mono- $\alpha$ -substituted ligands. Among this group, Boc-Val-OH was the best, providing **1a** in



46% conversion after 20 minutes (Entry 3). As a control experiment, we also examined other commonly used organic acids, representative examples of which are shown in Table 2.1 (Entries 17 and 18; see the Experimental section for additional results). These other acids uniformly gave low conversions, suggesting that coordination of both the carboxylate group and the protected amino group with Pd(II) is crucial for rate enhancement.

**Table 2.1.** Optimisation of the ligand backbone using Boc-protected amino acids.

| Entry | Ligand                | % Conv.         | Entry | Ligand                          | % Conv. |
|-------|-----------------------|-----------------|-------|---------------------------------|---------|
| 1     | ---                   | <5              | 13    |                                 | 6       |
| 2     | BQ                    | <5              | 14    |                                 | 21      |
| 3     | Boc-Val-OH            | 46 <sup>b</sup> | 15    |                                 | 5       |
| 4     | Boc-Ile-OH            | 37              | 16    |                                 | 16      |
| 5     | Boc-Leu-OH            | 37              | 17    | PivOH                           | <5      |
| 6     | Boc- <i>t</i> -Leu-OH | 38              | 18    | <i>p</i> -TsOH·H <sub>2</sub> O | 0       |
| 7     | Boc-Nva-OH            | 30              |       |                                 |         |
| 8     | Boc-Ala-OH            | 28              |       |                                 |         |
| 9     | Boc-Gly-OH            | 17              |       |                                 |         |
| 10    | Boc-Phe-OH            | 33              |       |                                 |         |
| 11    | Boc-Ser-OH            | 8               |       |                                 |         |
| 12    | Boc- $\beta$ -Ala-OH  | 8               |       |                                 |         |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

<sup>b</sup> Average of three trials.

Following identification of valine as a highly reactive amino acid backbone, we sought to optimise the *N*-protecting group (Table 2.2). In an initial control experiment, we found that *N*-protection was required, as the reaction did not proceed with unprotected H-Val-OH (Entry 1). With this information in hand, we examined several commercially available *N*-protected valine amino acid ligands (Entries 1–3, 6, 7, and 12) and subsequently prepared several new ligands (Entries 4, 5, and 8–11). Because Boc protecting groups were found to be highly reactive, we examined other carbamate protecting groups with different

steric properties (Entries 7–11 and 13), but did not observe any improvement. We moved on to amide protecting groups (Entries 3–5 and 12). Among the amide protecting groups examined, ligands bearing less sterically demanding groups (Entries 3 and 6) were found to give better conversions than those with sterically bulky protecting groups (Entries 4, 5, and 12), with Ac-Val-OH giving the best conversion (57%) (Entry 3).

**Table 2.2.** Optimisation of the *N*-protecting group on valine.

| Entry | Ligand                  | % Conv.         | Entry | Ligand                              | % Conv. |
|-------|-------------------------|-----------------|-------|-------------------------------------|---------|
| 1     | H-Val-OH                | 0               | 8     | MeO <sub>2</sub> C-Val-OH           | 21      |
| 2     | Boc-Val-OH              | 46 <sup>b</sup> | 9     | EtO <sub>2</sub> C-Val-OH           | 26      |
| 3     | Ac-Val-OH               | 57              | 10    | <i>i</i> -BuO <sub>2</sub> C-Val-OH | 27      |
| 4     | Ada-Val-OH <sup>c</sup> | 4               | 11    | Cbz-Val-OH                          | 18      |
| 5     | Piv-Val-OH              | 2               | 12    | Bz-Val-OH                           | 3       |
| 6     | Formyl-Val-OH           | 31              | 13    | (-)-Men-Val-OH <sup>d</sup>         | 39      |
| 7     | Fmoc-Val-OH             | 19              |       |                                     |         |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

<sup>b</sup> Average of three trials. <sup>c</sup> Ada = 1-Adamantyl(OC). <sup>d</sup> (-)-Men = (-)-Menthyl(O<sub>2</sub>C).

Having found that the acetyl protecting group was highly reactive when used with valine, we wondered whether additional fine-tuning of the ligand backbone of *N*-acetyl-protected amino acids might result in further improvement in the catalyst activity (Table 2.3). To our delight, when we examined the *N*-acetyl-protected versions of a selected set of ligands from Table 2.1, we found improved yields for nearly every ligand that we probed relative to its Boc-protected counterpart. Ac-Ile-OH and Ac-Ala-OH were found to be the most reactive, giving **2.1a** in 72% and 71% conversion, respectively. Quantitative conversion of **2.1** to **2.1a** could be achieved by extending the reaction time to 2 hours (Entry 5).

**Table 2.3.** Reexamination of alternative ligand backbones using Ac as the protecting group.<sup>a</sup>

| Entry | Ligand    | % Conv.                            | Entry | Ligand    | % Conv. |
|-------|-----------|------------------------------------|-------|-----------|---------|
| 1     | Ac-Val-OH | 57                                 | 7     | Ac-Phe-OH | 60      |
| 2     | Ac-Leu-OH | 55                                 | 8     |           | 5       |
| 3     | Ac-Ala-OH | 71                                 | 9     |           | 31      |
| 4     | Ac-Gly-OH | 51                                 |       |           |         |
| 5     | Ac-Ile-OH | 72 <sup>b</sup> [>99] <sup>c</sup> |       |           |         |
| 6     | Ac-Ile-OH | 93 <sup>d</sup>                    |       |           |         |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.<sup>b</sup> Average of three trials. <sup>c</sup> The bracketed value represents the conversion after 2 h.<sup>d</sup> 110 °C.

We also probed the effect of amino acid ligand loading and found that when the reaction was run with anywhere between 5–15 mol% Ac-Ile-OH, the conversions were similar after 20 min. 2.5 mol% Ac-Ile-OH led to lower conversion (see the Experimental section). Similarly, we found that between 1 and 2 equivalents of olefin led to similar reaction rates and overall yields; with 3 equivalents of olefin, the reaction rate decreased. Because the reagents used in these experiments were readily available, we elected to use 2 equiv. Ac-Ile-OH (relative to Pd(OAc)<sub>2</sub>) and 2 equiv. olefin (relative to substrate) as the conditions for the investigations below (Sections 2.3–2.5). The reaction could be run effectively at temperatures between 50–110 °C (see the Experimental section), with lower temperatures giving decreased reaction rates. For example, at 50 °C, the reaction took 48 hours to reach >90% conversion. Running the reaction at 110 °C, >90% conversion could be achieved after 20 minutes (Entry 6, Table 3). The use of higher temperatures, such as 130 °C, reduced the reaction rate, presumably due to catalyst decomposition.

### 2.2.4. Low Catalyst Loadings/Air (1 atm) as the Reoxidant

Having identified Ac-Ile-OH as a superior ligand for reaction rate (*i.e.*, turnover frequency, TOF) in the Pd(II)-catalysed *ortho*-C–H olefination of **2.1**, we became interested in examining the efficiency of the catalytic turnover under these conditions. We began by reducing the catalyst loading to 1 mol% Pd(OAc)<sub>2</sub> and running parallel reactions under 1 atm O<sub>2</sub> (Table 2.4). Gratifyingly, we found that efficient catalysis could still be achieved under these conditions, such that **2.1a** could be prepared in 96% conversion (94% yield) after 4 h.

**Table 2.4.** C–H olefination of **2.1** using 1 mol% Pd(OAc)<sub>2</sub> and 1 atm O<sub>2</sub>.<sup>a</sup>

| Entry | Time (h) | % Conv. |
|-------|----------|---------|
| 1     | 0        | 0       |
| 2     | 1        | 34      |
| 3     | 2        | 67      |
| 4     | 3        | 93      |
| 5     | 4        | 98 (94) |

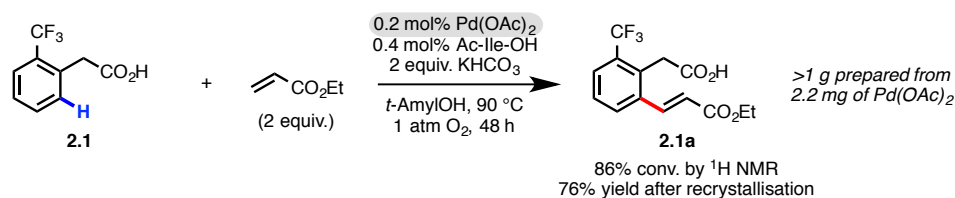
<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses.

**Table 2.5.** C–H olefination of **2.1** using 0.2 mol% Pd(OAc)<sub>2</sub> and 1 atm O<sub>2</sub>.<sup>a</sup>

| Entry | Time (h) | % Conv. |
|-------|----------|---------|
| 1     | 0        | 0       |
| 2     | 4        | 15      |
| 3     | 20       | 52      |
| 4     | 48       | 91 (83) |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

This result encouraged us to further lower the catalyst loading to 0.2 mol% Pd(OAc)<sub>2</sub> (Table 2.5). Again, we found that highly efficient catalysis could be maintained under these conditions, and we were able to synthesise **2.1a** with 91% conversion (83% yield) after an extended reaction time of 48 h. Notably, this result represents a TON of 455, which is among the highest reported for an aerobic C–H activation reaction.<sup>6,7</sup> We further demonstrated the scalability of this chemistry by using the conditions described in Table 2.5 to prepare over 1 gram of **2.1a** from **2.1** using only 2.2 mg of Pd(OAc)<sub>2</sub>. Following an aqueous quench and extraction with organic solvent, **2.1a** could be obtained from the crude reaction mixture in 76% yield after recrystallisation (Scheme 2.2).



**Scheme 2.2.** Gram-scale synthesis of **2.1a** using 0.2 mol% Pd(OAc)<sub>2</sub> and 1 atm O<sub>2</sub>.

Though 1 atm O<sub>2</sub> is a highly convenient oxidant, in terms of operational simplicity, being able to use 1 atm air (which is 21% O<sub>2</sub>) is highly desirable because it obviates the need to store compressed O<sub>2</sub> in the laboratory. To examine whether O<sub>2</sub> could be replaced with air, we used 1 mol% Pd(OAc)<sub>2</sub> and ran parallel reactions in sealed tubes under air (Table 2.6). (Having a sealed vessel is necessary due to the volatility of ethyl acrylate.) Under these conditions, **2.1a** could be synthesised in 87% conversion (78% yield) after an extended reaction time of 48 h.

**Table 2.6.** C–H olefination of **2.1** using 1 mol% Pd(OAc)<sub>2</sub> and 1 atm air.<sup>a</sup>

| Entry | Time (h) | % Conv. |
|-------|----------|---------|
| 1     | 0        | 0       |
| 2     | 1        | 2       |
| 3     | 2        | 6       |
| 4     | 12       | 29      |
| 5     | 24       | 68      |
| 6     | 48       | 87 (78) |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses.

Given the low catalyst loading, relatively mild reaction conditions, and the fact that the only byproduct in the catalytic cycle is water, this chemistry is highly atom-economical<sup>8</sup> and falls in line with goals of green chemistry.<sup>9</sup>

### 2.2.5. Substrate Scope for Accelerated C–H Olefination

Under the optimised conditions, a wide variety of phenylacetic acid substrates were highly reactive, generally giving the desired C–H olefinated products in quantitative yields (Table 2.7). The substrate scope was found to be remarkably broad, as the reaction tolerated electron-donating methoxy (**2.5a** and **2.10a**) and alkyl groups (**2.2a** and **2.4a**), as well as fluorides (**2.6a**) and chlorides (**2.7a**), the latter offering a unique opportunity for subsequent Pd(0)-mediated coupling chemistry. Bromides and iodides were found to be unreactive in C–H olefination. Arenes bearing electron-withdrawing substituents, including trifluoromethyl (**2.1a** and **2.3a**), nitro (**2.8a**), and ketone (**2.9a**) groups, gave good to excellent yields. In an effort to demonstrate the potential applicability of this chemistry in drug diversification, we targeted ketoprofen (**2.9**) and naproxen (**2.10**), two commercially

available non-steroidal anti-inflammatory drugs (NSAIDs), and observed that they could be directly *ortho*-olefinated to give **2.9a** and **2.10a** in nearly quantitative isolated yields.

For each substrate, we ran two control experiments in the absence of Ac-Ile-OH: with BQ (our original mono-selective procedure) and without. In all cases, the presence of Ac-Ile-OH led to higher conversions, but the improvement was most pronounced with electron-poor substrates. Interestingly, for electron-rich arenes (**2.2a**, **2.4a**, **2.5a**, and **2.10a**), relatively high conversions could be obtained after 2 h without Ac-Ile-OH if BQ was removed. As discussed above, in the absence of amino acid ligands, BQ allows for control of mono/di-selectivity and leads to higher TONs in many instances; however, in the case of these particular substrates (*i.e.*, electron-rich arenes containing an *ortho* or *meta*-blocking group) BQ does not offer a clear benefit and only serves to reduce the reaction rate. In general, electron-deficient substrates were found to exhibit low reactivity in the absence of ligand (**2.1a** and **2.3a**). The presence of a nitro group rendered the arene totally unreactive (**2.8a**) without ligand.

**Table 2.7.** Accelerated Pd(II)-catalysed C–H olefination of phenylacetic acid substrates **2.1–2.10**.<sup>a,b</sup>

| Product         | Additive/Ligand | % Conv.              | Product          | Additive/Ligand | % Conv.               |
|-----------------|-----------------|----------------------|------------------|-----------------|-----------------------|
| <br><b>2.1a</b> | ---             | 7 <sup>c</sup>       | <br><b>2.6a</b>  | ---             | 6                     |
|                 | BQ              | 3 <sup>c</sup>       |                  | BQ              | 2                     |
|                 | Ac-Ile-OH       | >99 (96)             |                  | Ac-Ile-OH       | >99 (99)              |
| <br><b>2.2a</b> | ---             | 25 <sup>c</sup>      | <br><b>2.7a</b>  | ---             | 8 <sup>e</sup>        |
|                 | BQ              | 7 <sup>c</sup>       |                  | BQ              | 3 <sup>e</sup>        |
|                 | Ac-Ile-OH       | 98 (97)              |                  | Ac-Ile-OH       | >99 (99) <sup>e</sup> |
| <br><b>2.3a</b> | ---             | 2                    | <br><b>2.8a</b>  | ---             | 0                     |
|                 | BQ              | 1                    |                  | BQ              | 0                     |
|                 | Ac-Ile-OH       | >99 (98)             |                  | Ac-Ile-OH       | 72 (70) <sup>f</sup>  |
| <br><b>2.4a</b> | ---             | 64                   | <br><b>2.9a</b>  | ---             | 10                    |
|                 | BQ              | 9                    |                  | BQ              | 5                     |
|                 | Ac-Ile-OH       | 88 (83) <sup>d</sup> |                  | Ac-Ile-OH       | >99 (98)              |
| <br><b>2.5a</b> | ---             | 93 (92)              | <br><b>2.10a</b> | ---             | 44 <sup>g</sup>       |
|                 | BQ              | 12                   |                  | BQ              | 23                    |
|                 | Ac-Ile-OH       | >99 (95)             |                  | Ac-Ile-OH       | >99 (94)              |

<sup>a</sup> 5 mol% BQ (when used), 10 mol% Ac-Ile-OH (when used). <sup>b</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses. <sup>c</sup> Average of three trials. <sup>d</sup> An additional 11% of the di-*ortho*-olefinated product was observed by <sup>1</sup>H NMR. <sup>e</sup> 6 h. <sup>f</sup> An additional 6% of the decarboxylated product was formed. <sup>g</sup> An additional 4% of a positional isomer was formed.

In accordance with our earlier observations,<sup>4</sup> **2.8a** was found to decarboxylate under the reaction conditions, leading to exclusive formation of the corresponding decarboxylated product **2.8a'** after 48 h. This reaction is triggered by the installation of the electron-withdrawing olefin, which further stabilises anionic charge at the benzylic position through resonance effects. It is important to note here, that prior to our identification of Ac-Ile-OH as a ligand for accelerated C–H olefination, **2.8a** could not be obtained in appreciable yields because using other ligands, it was found to decarboxylate to **2.8a'** faster than it could be generated from C–H olefination of **2.8**. In contrast, under these new conditions, **2.8a** could



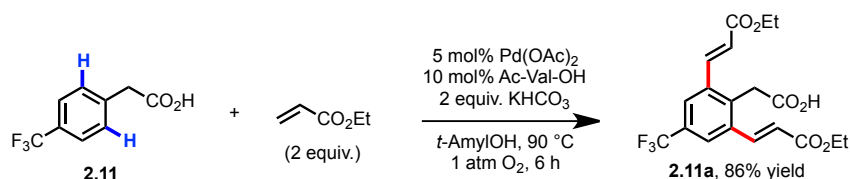
be isolated in 70% yield after 2 h. This reaction was monitored over time using  $^1\text{H}$  NMR, and the results are depicted in Table 2.8.

**Table 2.8.** Accelerated Pd(II)-catalysed C–H olefination of **2.8**.<sup>a</sup>

| Entry | Time (h) | % <b>2.8</b> | % <b>2.8a</b> | % <b>2.8a'</b> |
|-------|----------|--------------|---------------|----------------|
| 1     | 0        | 100          | 0             | 0              |
| 2     | 2        | 19           | 72 (70)       | 6 (6)          |
| 3     | 6        | 15           | 43            | 29             |
| 4     | 12       | 6            | 39            | 36             |
| 5     | 24       | 5            | 15            | 59             |
| 6     | 48       | 4            | 0             | 75 (71)        |

<sup>a</sup> The % composition was determined by  $^1\text{H}$  NMR analysis of the crude reaction mixture using  $\text{CH}_2\text{Br}_2$  as an internal standard. Isolated yield is given in parentheses. Less than 5% of 2-nitrotoluene (from direct decarboxylation of **2.8**) was observed by  $^1\text{H}$  NMR in entries 2–6.

The phenylacetic acid substrates shown in Table 2.7 all contain a sterically bulky blocking substituent at the *ortho*- or *meta*- positions. For those that are not of this type, the ligand-accelerated C–H olefination conditions that we report here will lead to significant formation of the di-*ortho*-olefinated byproduct over time. Indeed, concurrent to this work, we developed a robust method for direct 2,6-diolefination of phenylacetic and hydrocinnamic acids (Scheme 2.3; also, see Chapter 3).<sup>10</sup> For 2,6-diolefination, Ac-Ile-OH, which we use throughout this Chapter, gave irreproducible results, and Ac-Val-OH was found to be superior. Current investigations are underway in the Yu laboratory to design a ligand that will offer enhanced reactivity but will stop after a single olefination event, thereby obviating the need for a proximate blocking group.



**Scheme 2.3.** A representative example of our previously reported 2,6-diolefination reaction of phenylacetic acids using Ac-Val-OH.<sup>10</sup>

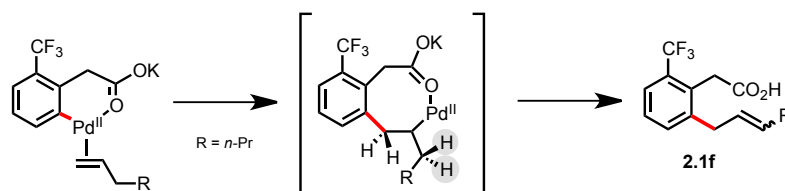
We next sought to examine the scope of olefin coupling partners that could be used under our accelerated reaction conditions (Table 2.9). A variety of acrylates (**2.1a–2.1c**), styrenes (**2.1d** and **2.1e**), and vinyl ketones (**2.1g** and **2.1h**) were found to be highly reactive, generally offering quantitative yields after 2 h (10 h in the case of **2.1e** and **2.1h**).

**Table 2.9.** Accelerated Pd(II)-catalysed C–H olefination of **2.1** with various olefin coupling partners.<sup>a,b</sup>

| Product | Additive/Ligand | % Conv.        | Product | Additive/Ligand | % Conv.               |
|---------|-----------------|----------------|---------|-----------------|-----------------------|
|         | ---             | 7 <sup>c</sup> |         | ---             | 13 <sup>d</sup>       |
|         | BQ              | 3 <sup>c</sup> |         | BQ              | 4 <sup>d</sup>        |
|         | Ac-Ile-OH       | >99 (96)       |         | Ac-Leu-OH       | 70 (65) <sup>d</sup>  |
|         | ---             | 6              |         | ---             | 0 <sup>d</sup>        |
|         | BQ              | 2              |         | BQ              | 0 <sup>d</sup>        |
|         | Ac-Ile-OH       | >99 (99)       |         | Ac-Ile-OH       | 82 (62) <sup>d</sup>  |
|         | ---             | 8              |         | ---             | 0                     |
|         | BQ              | 3              |         | BQ              | 0                     |
|         | Ac-Ile-OH       | >99 (90)       |         | Ac-Ile-OH       | >99 (94)              |
|         | ---             | 7              |         | ---             | 0 <sup>d</sup>        |
|         | BQ              | 2              |         | BQ              | 0 <sup>d</sup>        |
|         | Ac-Ile-OH       | >99 (99)       |         | Ac-Ile-OH       | >99 (97) <sup>d</sup> |

<sup>a</sup> 5 mol% BQ (when used), 10 mol% Ac-Ile-OH (when used). <sup>b</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses. <sup>c</sup> Average of three trials. <sup>d</sup> 10 h.

Consistent with our earlier observation,<sup>4,10</sup> linear alkenes were also compatible, fashioning the non-conjugated product **2.1f**. We hypothesise that this product is formed as a consequence of the mechanistic scenario depicted in Scheme 2.6, wherein coordination of the carboxylate directing group restricts bond rotation, which makes  $\beta$ -hydride elimination away from the aromatic ring more kinetically favourable. Notably, this result represents a formal C–H allylation, and as such, provides access to a novel class of non-conjugated products. Efforts to carry out C–H olefination with vinyl sulfones, sulfonates, phosphonates, and nitriles were unsuccessful. Moreover, internal alkenes, such as *trans*-methyl crotonate and *trans*-methyl cinnamate, were found to be unreactive with **2.1** under these conditions.



**Scheme 2.4.** Mechanistic hypothesis to explain the preferential formation of **2.1f**, rather than the thermodynamically favoured conjugated product.

It is worth noting here that the phenylacetic acid substrate scope and olefin scope studies were run using 5 mol% Pd(OAc)<sub>2</sub> under 1 atm O<sub>2</sub>, but using lower catalyst loadings (0.2–1 mol%) and/or air as the oxidant would likely give similar yields after extended reaction times (4–48 h), as demonstrated above.

### 2.2.6. Mechanistic Considerations.

To elucidate fully the origin of the observed ligand-promoted acceleration, insights from a number of different techniques are needed, including isolation and characterisation of the putative intermediates, kinetic determination of the rate law, and computational modelling of possible reaction pathways. In collaboration with other research groups, our laboratory is currently pursuing these investigations. In the meantime, we have performed

two key sets of experiments, measuring the intermolecular KIE and observing the relationship between initial rate and the electronic properties of the substrate through competition experiments. The resulting data provide evidence that the overall rate increase stems from acceleration in the C–H cleavage step and that the mechanism of C–H cleavage changes from electrophilic palladation to CMD when amino acid ligands are coordinated to Pd(II).

Historically speaking, the mechanism of C(*sp*<sup>2</sup>)–H cleavage by Pd(II) has attracted a great deal of attention.<sup>1,11</sup> During the past few decades, three leading transition state proposals have emerged, with the operative mechanism thought to depend on the individual system in question (Figure 2.3). One mechanism is electrophilic palladation *via* an arenium (Wheland) intermediate, originally proposed by Ryabov and coworkers in 1985 (**A**).<sup>11a</sup> In this case, Pd(II) coordinates to the  $\pi$ -system of the arene, and the resulting Wheland species transfers a proton to a bound acetate to generate the cyclopalladated intermediate. In electrophilic palladation, the efficacy of C–H activation is highly dependent on the electronic properties of the arene, with electron-rich substrates giving better reactivity. A second mechanism, oxidative addition, was proposed by Canty and van Koten in 1995, in which the C–H bond oxidatively adds to Pd(II) to generate a short-lived Pd(IV) species that can reductively eliminate HX to generate the Pd(II)-cyclopalladated intermediate (**B**).<sup>11b</sup> Lastly a third mechanism is concerted metalation/deprotonation (CMD), first put forward by Sokolov in 1979.<sup>1</sup> (**2.C**). Extensive reaction kinetics of cyclopalladation led Martinez to propose a similar mechanism in 1997 (**2.D**).<sup>11c</sup> Subsequent computational work by Davies and Macgregor in 2005 supported a similar mechanism, where electrophilic attack of the palladium on an *ortho*-C–H bond to form an agnostic complex was the rate-limiting step (**2.E**).<sup>11f</sup> In a CMD mechanism, C–H cleavage proceeds *via* the concerted transfer of the hydrogen atom to an intramolecular base, without substantial build up of positive charge on

the arene. Martinez suggested that this process proceeds *via* a four-membered transition state,<sup>11c</sup> but later evidence from Davies and Macgregor pointed to a six-membered transition state.<sup>11f</sup> CMD is thought to operate *via* an agostic interaction, rather than through a Wheland intermediate;<sup>11f</sup> as such, the rate dependence of the electronic properties of substituents is less pronounced.

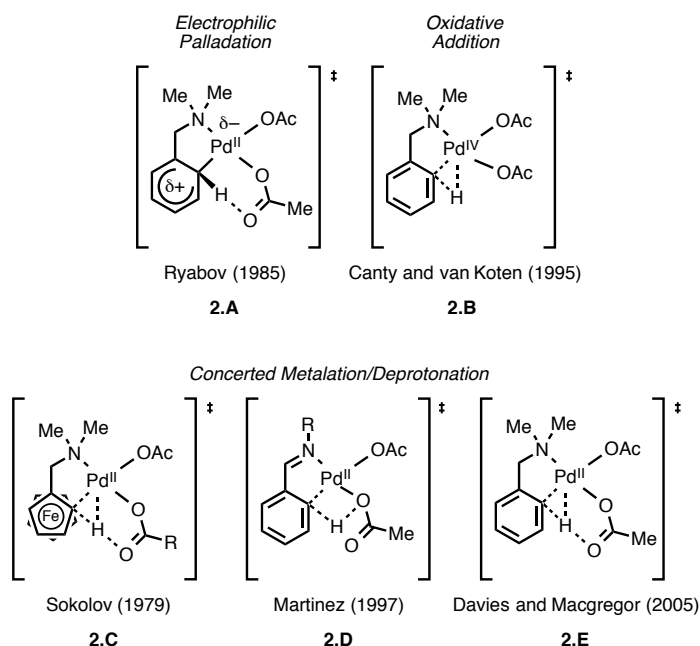


**Figure 2.3.** Mechanistic models for the C–H cleavage transition state with Pd(II).

It is worth mentioning that CMD with Pd(II) catalysts is conceptually related to the mechanism for C–H activation in Pd(0)/ArX chemistry (**2.E–2.G**, Figure 2.4).<sup>12</sup> However, the latter belongs to a different reactivity paradigm, in which the Pd(II) species is attached to a phosphine ligand and an aryl fragment and is thus rendered nucleophilic. Though the mechanism for Pd(II)-mediated C–H cleavage has been studied for a longer period of time, arguably the mechanism at play in Pd(0)/ArX chemistry is better understood due to pioneering studies by Maseras and Echavarren, as well as Fagnou.<sup>12b–f</sup>

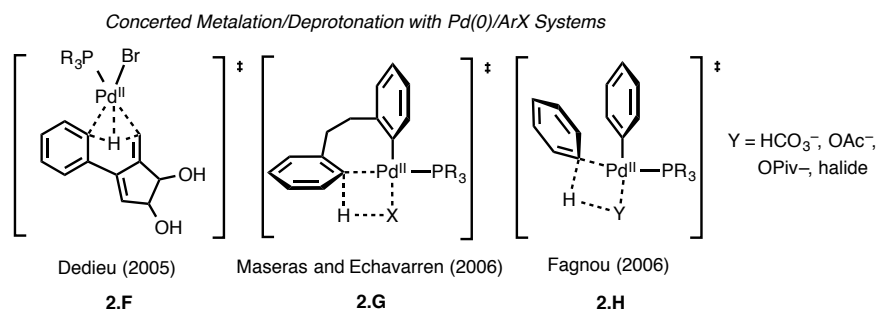
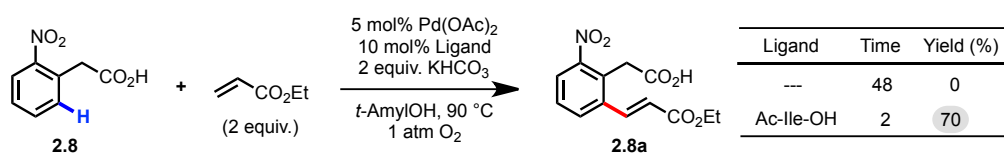


**Figure 2.4.** Conceptually relevant CMD mechanistic proposals for Pd(0)/ArX catalytic systems.

Regarding our studies of Pd(II)-mediated C–H cleavage with phenylacetic acids, qualitatively speaking, the data that we obtained using our original Pd(II)-catalysed mono-selective C–H olefination reaction<sup>4</sup> are consistent with an electrophilic palladation mechanism. The reaction was found to be high-yielding when substrates with electron-donating groups (*e.g.*, methoxy and methyl) were used, and to be low yielding or unreactive for substrates with electron-withdrawing groups (*e.g.*, CF<sub>3</sub> and NO<sub>2</sub>). In particular, without amino acid ligands, we found substrate **2.8**, which contains an *ortho*-nitro group, to be totally unreactive after 48 h, with only starting material recovered (and <5% decarboxylation) (Scheme 2.5). In sharp contrast, in the presence of Ac-Ile-OH gave 70% yield of **8a** after only 2 h. Viewed in conjunction with data in Figures 1 and 2, this data suggests two points: (1) the amino acid ligands are not merely enhancing the TON, but are generating a more reactive catalyst, (2) electrophilic palladation no longer seems to be the operative mechanism.



**Scheme 2.5.** Qualitative evidence for a change in the mechanism of C–H cleavage: C–H activation of highly electron-deficient arenes in the presence of Ac-Ile-OH.

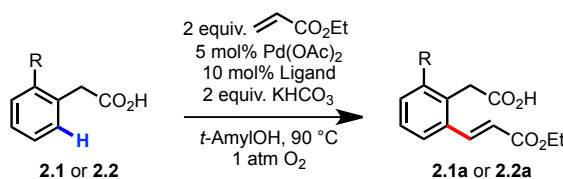
To investigate whether a departure from the electrophilic palladation pathway or a drastic increase in the electrophilic property of the Pd(II) catalyst is responsible for the reactivity of **2.8**, we carried out intermolecular competition experiments between electron-rich and electron-poor substrates (Table 2.10). We selected **2.1** and **2.2** for analysis because they are roughly isosteric to one another and do not contain strongly chelating functional groups on the aromatic ring. We began by submitting a one-to-one mixture of **2.1** and **2.2** to the reaction conditions in the absence of amino acid ligand and found that **2.2** reacted preferentially, consistent with our hypothesis for electrophilic palladation. We then repeated these experiments in the presence of two ligands: Boc-Val-OH, which we found to be an active ligand in our early studies,<sup>4</sup> and Ac-Ile-OH, which proved to be optimal throughout this investigation. When Boc-Val-OH was used, the relative reaction rate of **2.1** to **2.2** increased to the point where the two substrates were reacting almost at the same speed (*i.e.*,  $k_1/k_2$  changed from 0.22 to 0.58). Strikingly, when we examined Ac-Ile-OH, we found a reversal in relative reactivity, such that electron-poor substrate **2.1** now reacted almost twice as fast as electron-rich substrate **2.2** ( $k_1/k_2 = 1.87$ ). This same trend held for individually measured rates for the single-component reactions of **2.1** and **2.2** (Table 2.11).

**Table 2.10.** One-pot intermolecular competition experiment data.<sup>a</sup>

| Entry | Ligand     | Time (min) | % Conv. <b>2.1a</b> | % Conv. <b>2.2a</b> | $k_1 / k_2$ |
|-------|------------|------------|---------------------|---------------------|-------------|
| 1     | ---        | 120        | 3                   | 14                  | 0.22        |
| 2     | Boc-Val-OH | 10         | 18                  | 30                  | 0.58        |
| 3     | Ac-Ile-OH  | 10         | 40                  | 21                  | 1.87        |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. See the Experimental section for experimental details.

**Table 2.11.** Comparison of initial rates for single-component reactions of **2.1** and **2.2** under the different conditions shown.<sup>a</sup>

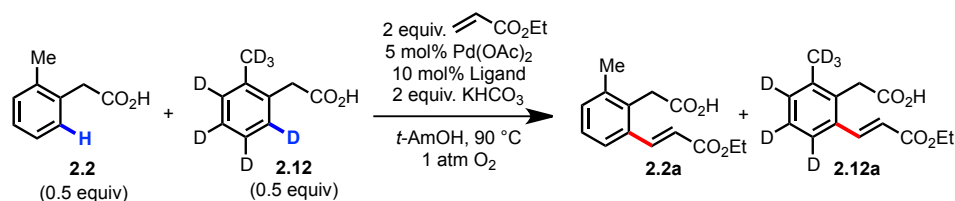


| Entry <sup>a</sup> | Ligand     | 2.1 (R = CF <sub>3</sub> ) | 2.2 (R = Me)             |                                 |
|--------------------|------------|----------------------------|--------------------------|---------------------------------|
|                    |            | k <sub>1</sub> ([M]/min)   | k <sub>2</sub> ([M]/min) | k <sub>1</sub> / k <sub>2</sub> |
| 1                  | ---        | 1.3 x 10 <sup>-4</sup>     | 3.5 x 10 <sup>-4</sup>   | 0.37                            |
| 2                  | Boc-Val-OH | 4.7 x 10 <sup>-3</sup>     | 5.2 x 10 <sup>-3</sup>   | 0.90                            |
| 3                  | Ac-Ile-OH  | 7.6 x 10 <sup>-3</sup>     | 5.5 x 10 <sup>-3</sup>   | 1.38                            |

<sup>a</sup> See the Experimental section for experimental details.

Next, we sought to determine whether the differences in these relative rate profiles could be attributed to mechanistic changes in C–H cleavage and also to test the hypothesis that the ligand-induced rate increases were a result of acceleration in the C–H cleavage step. We prepared deuterium-labelled compound **2.12**, a representative electron-rich substrate, and used it to perform intermolecular KIE experiments (Table 2.12). In the absence of ligand, we observed a large KIE of 6.1, suggesting that cleavage of the C–H bond is the rate-limiting step. In the presence of Boc-Val-OH, though the absolute reaction rates of both **2.2** and **2.12** were found to be substantially greater, the measured KIE was roughly the same (5.5), suggesting that C–H cleavage was still the rate-limiting step. Interestingly, with Ac-Ile-OH, the ligand that gives the fastest overall rate, the KIE had markedly decreased to 1.7, suggesting that the rate of C–H cleavage had increased to the point where it was no longer the slow step in the catalytic cycle. In this case, the moderate KIE (between 1 and 2) is consistent with C–H cleavage taking place before the rate-limiting step.



**Table 2.12.** Intermolecular KIE experiments.<sup>a</sup>

| Entry | Ligand     | $k_{\text{H}} / k_{\text{D}}$ |
|-------|------------|-------------------------------|
| 1     | ---        | 6.1                           |
| 2     | Boc-Val-OH | 5.5                           |
| 3     | Ac-Ile-OH  | 1.7                           |

<sup>a</sup> See the Experimental section for experimental details.

Taken together, the data from the competition experiments and the KIE experiments paint an interesting picture for the operative mechanisms in these systems. Our tentative hypothesis is that in the absence of amino acid ligands, among the three possible pathways (2.I–2.K, Figure 2.5), the reaction proceeds through an electrophilic palladation mechanism (2.H). At first glance, the large KIE of 6.1 (Entry 1, Table 2.12) would seem to contradict this proposal since electrophilic aromatic substitution reactions (including electrophilic palladation processes) often have small KIE values.<sup>13</sup> In these cases, deprotonation is assumed to be fast relative to formation of the arenium species. However, in cases where the rate of deprotonation is slow, larger KIE values have been observed.<sup>14c,15</sup> Thus if we follow this logic and invoke an electrophilic palladation mechanism, then with electron-rich substrates, such as 2.2, palladation to generate the putative Wheland intermediate is fast, and intramolecular deprotonation by internally bound acetate is the rate-limiting step, which is consistent with the large KIE of 6.1 for electron-rich substrates (2.2 and 2.12). In contrast, with electron-poor substrates, such as 2.1, palladation to form the Wheland intermediate is less favourable, and thus becomes rate-limiting, in accordance with the results of the competition experiments.

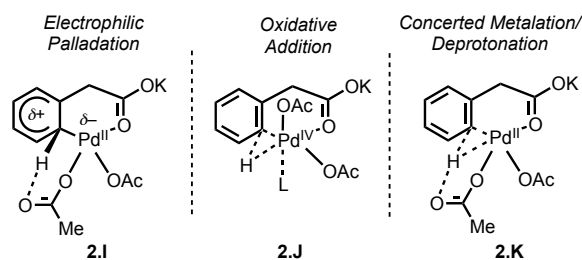


**Figure 2.5.** Possible mechanisms for C–H cleavage without ligands: electrophilic palladation (**2.I**), oxidative addition (**2.J**), and CMD (**2.K**).

With the amino acid ligands, several possibilities exist (**2.L–2.R**, Scheme 2.6), again falling within the three general classifications described above. It is important to recognise that when Ac-Ile-OH is used, the KIE data suggests that C–H cleavage is not rate-limiting; thus the results of the competition experiments (Table 2.10, Entry 3 and Table 2.11, Entry 3) need to be interpreted cautiously because the relative rate changes reflect an elementary step other than C–H cleavage. Nevertheless, the high levels of reactivity with both electron-poor and electron-rich substrates would seem to argue against an electrophilic palladation mechanism (**2.L** and **2.M**). Furthermore, in the case of Boc-Val-OH the KIE data indicates that C–H cleavage is still rate-limiting, yet in competition experiments (Table 2.10, Entry 2 and Table 2.11, Entry 2) electron-poor and electron-rich substrates were found to react with similar rates, suggesting that electrophilic palladation (which we hypothesise is operative in the ligand-free conditions) is not operative. Though we cannot rule out the possibility that Boc-Val-OH and Ac-Ile-OH promote different mechanisms, we suspect that they coordinate to Pd(II) in an identical bidentate fashion and thus affect C–H cleavage similarly. Because previous computational studies have not found oxidative addition mechanisms to be energetically favourable (**2.N**),<sup>11g</sup> our current understanding would support one of the CMD mechanisms (**2.O–2.R**). Here, the weak and reversible bidentate coordination of the amino acid ligand likely plays a crucial role in facilitating the initial agostic interaction between Pd(II) and then shuttling the proton to an internal (**2.P–2.R**) or external (**2.O**) base. Across

the various ligands that enhanced reactivity in these studies (Tables 2.1–2.3), it is possible that multiple C–H cleavage mechanisms are at play simultaneously (or that the operative mechanism is substrate-dependent).

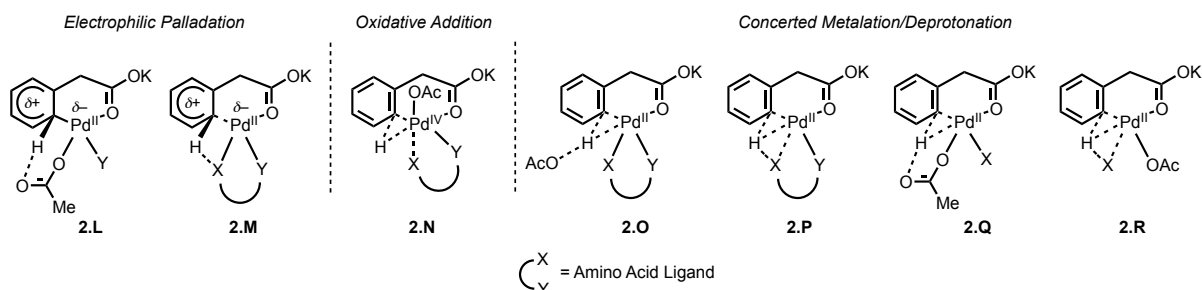


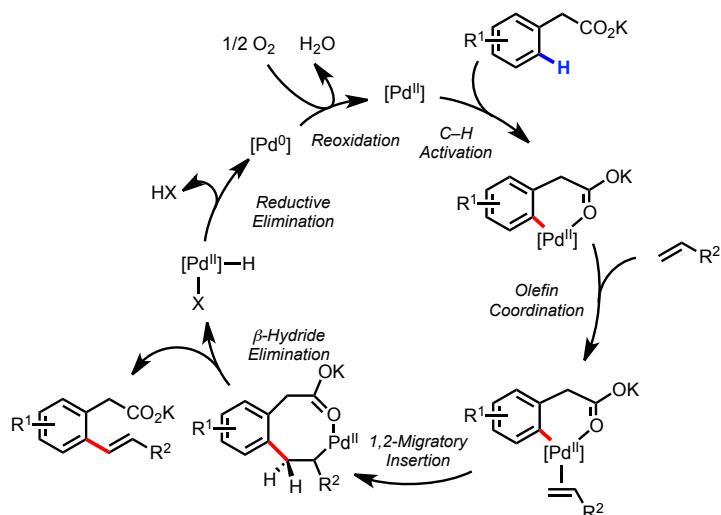
**Figure 2.6.** Possible mechanisms for C–H cleavage: electrophilic palladation (**2.L** and **2.M**), oxidative addition (**2.N**), and CMD (**2.O–2.R**).

As mentioned above, our selection of Boc-Val-OH and Ac-Ile-OH for these mechanistic studies was motivated by the finding that these ligands were highly reactive in our early work<sup>4</sup> and present work, respectively. Valine and isoleucine-derived ligands were found to show similar levels of activity when Boc-protected (Table 2.1, comparing Entries 3 and 4) and Ac-protected (Table 2.3, comparing Entries 1 and 5), consistent with the fact that their side chains differ only by a remotely located methyl group. Thus, the origin of the observed differences in catalysis between Boc-Val-OH and Ac-Ile-OH likely originate primarily from the different steric and electron properties of the *N*-protecting groups.

A detailed analysis of how the amino acid ligands affect the transition state energies of various C–H cleavage processes remains a point to be clarified by computational studies. Given the dramatic effect that small perturbations in the structure of the amino acid side chain and the *N*-protecting group have on the observed reactivity and on the competition and KIE studies, the precise role of the ligands is likely quite complex. Here, we put forward general mechanistic models to guide future analysis (Figure 2.6). An important question that remains to be addressed is what coordination mode the amino acid ligand adopts with Pd(II) in the transition state. In our previous work using mono-*N*-protected amino acid ligands for

enantioselective C–H activation,<sup>16</sup> our working stereomodel suggests that the ligand is coordinated in a bidentate fashion throughout the C–H cleavage process. However, if we invoke a bidentate coordination mode for the ligand (**2.M–2.P**), Pd(II) will be coordinatively saturated when bound to the carboxylate directing group and the C–H bond (through an agostic interaction) in the pre-transition state. This implies that traditional intramolecular deprotonation by bound acetate (**2.A** and **2.C–2.E**, Figure 2.3) is no longer viable since the bound acetate must be displaced in order for the C–H agostic interaction to occur. Thus, in this case, deprotonation is likely occurring either by an external base (**2.O**) or by one of the basic groups from the ligand (**2.M** and **2.P**). On the other hand, the amino acid ligand could adopt a monodentate coordination mode in the transition state (**2.L**, **2.Q**, and **2.R**), in which case, the models discussed in Figure 2.3 could still be applicable.

An overall proposal for the catalytic cycle is depicted in Scheme 2.6. Following coordination of the substrate to Pd(II), carboxylate-directed C–H cleavage takes place to generate the reactive cyclopalladated intermediate. Coordination of an olefin followed by 1,2-migratory cleavage effects formation of the new C–C bond.  $\beta$ -Hydride elimination and reductive elimination give the desired product with concomitant formation of a Pd(0) species, which can be reoxidised by molecular oxygen<sup>6,7,17</sup> to regenerate Pd(II) and close the catalytic cycle.



**Scheme 2.6.** Proposed catalytic cycle.

## 2.3. CONCLUSION

We have developed an improved protocol for aerobic Pd(II)-catalysed C–H olefination of phenylacetic acid substrates through the discovery of a novel ligand, Ac-Ile-OH, which is capable of accelerating the reaction. This ligand offers dramatically improved substrate scope, reaction rate, and catalyst lifetime. Catalyst loadings as low as 0.2 mol% and reaction times as fast as 20 minutes were demonstrated. Moreover, the reaction could be run using air as the terminal oxidant. We disclosed evidence based on initial rate studies, reactivity trends, competition experiments, and KIEs that suggests that the increased reaction rates stem from acceleration in the C–H cleavage step. Furthermore, this data points to a change in mechanism of C–H cleavage from electrophilic palladation to CMD or oxidative addition when amino acid ligands are added to the reaction. Efforts are currently underway in our laboratory to examine whether amino acid ligands are competent in accelerating Pd(II)-mediated C–H cleavage with other directing groups. Our preliminary results concerning ligand-enabled C–H olefination of phenethyl alcohol substrates are promising in this respect.<sup>14h</sup> Additionally, if the observed rate enhancement truly stems from acceleration in the C–H cleavage step, as we now presume, other Pd(II)-catalysed C–H

functionalisation reactions should, in principle, benefit from amino acid ligands. This hypothesis is also being actively investigated by our group at the present time.

## 2.4. EXPERIMENTAL

### 2.4.1. General Information

Unless otherwise noted, all materials were used as received from commercial sources without further purification. The phenylacetic acid substrates and olefin coupling partners were purchased from Acros, Sigma-Aldrich, TCI and Alfa-Aesar and were used as received. 2-(Trifluoromethyl)phenylacetic acid (**2.1**) was purchased from TCI; samples of **2.1** from other commercial sources were found to give irreproducible results. 1,4-Benzoquinone (BQ) was sublimed prior to used. Freshly distilled methyl vinyl ketone was used in the synthesis of **2.1g**. Commercially available organic acid ligands were purchased from Acros, Sigma Aldrich, and Alfa Aesar. In the optimisation studies **2.5a** was tested as a ligand; its synthesis is described herein. Commercially available amino acid ligands were purchased from Bachem, EMD, or Novabiochem. **2.L4** was prepared according to a method developed by Burgess.<sup>18</sup> **2.L6** was prepared according to a literature procedure.<sup>19</sup> All others were prepared following literature precedent.<sup>2,20</sup> Palladium acetate and potassium hydrogen carbonate were purchased from Sigma-Aldrich and Fisher, respectively, and were used without further purification. All reactions were run on hot plates with oil baths calibrated to an external thermometer. Prior to beginning an experiment, the hot plate was turned on, and the oil bath was allowed to equilibrate to the desired temperature for 30 minutes. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian Mercury (300 MHz and 75 MHz, respectively), Varian Inova (400 MHz and 100 MHz, respectively) and Bruker DRX (500 MHz and 125 MHz, respectively) instruments internally referenced to SiMe<sub>4</sub> or chloroform signals. The following

abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and a = apparent. High resolution mass spectra were recorded at the Centre for Mass Spectrometry, The Scripps Research Institute.

#### 2.4.2. Kinetic measurements

**General procedure for determining the initial reaction rate for C–H olefination of **2.1** (or **2.2**) under different conditions:** Four different reaction conditions were examined: (1) without Boc-Val-OH, without BQ, (2) without Boc-Val-OH, with BQ, (3) with Boc-Val-OH, without BQ, (4) with Boc-Val-OH, with BQ. To establish the initial rate under each of the conditions, four parallel reactions were set up simultaneously. Four 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) were obtained, each equipped with a magnetic stir bar. Each tube was charged with **2.1** (or **2.2**) (0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), BQ (2.7 mg, 0.025 mmol) (when used), Boc-Val-OH (10.9 mg, 0.05 mmol) (when used), ethyl acrylate (106  $\mu$ L, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tubes were capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times$  3). The reaction mixtures were stirred at room temperature for 5 min, then at 90 °C for the appropriate time. At regular intervals (every 5 minutes, or every 30 minutes), one of the reactions would be removed from the hot plate and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were then added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **2.1**, 4.01 ppm for **2.1a**, 3.67 ppm for **2.2**, and 3.84 ppm for **2.2a**). For each condition, this process was repeated three times. The resulting data was

plotted, and linear regression established the initial rate. Representative data for the determination of one initial rate are shown in Figure 2.S1.

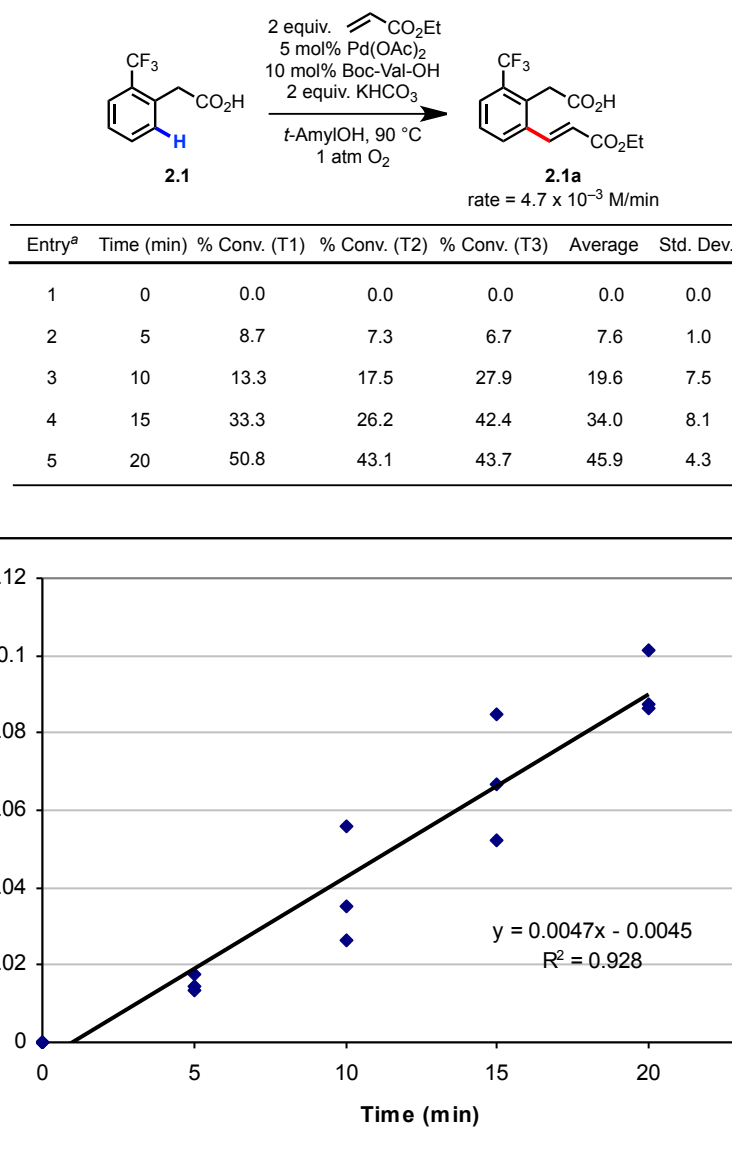
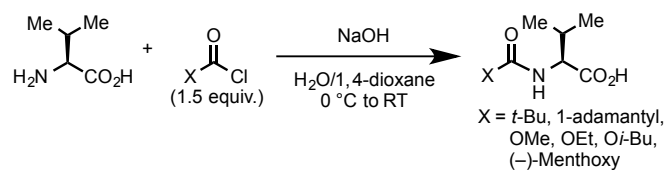


**Figure 2.S1:** Representative initial rate data for C–H olefination of **2.1** with Boc-Val-OH and without BQ.

### 2.4.3. Synthesis of New Ligands:



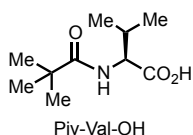
**Scheme 2.S1:** General procedure for *N*-protection for L-valine.



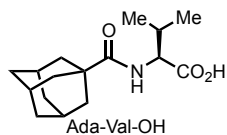
**General procedure for the synthesis of mono-*N*-protected L-valine ligands:**<sup>3,4</sup> A 500 mL round bottom flask equipped with a magnetic stir bar was charged with distilled H<sub>2</sub>O (100 mL) and NaOH (100 mmol, 4.0 g). The resulting solution was cooled to 0 °C in an ice bath. L-Valine (35 mmol, 4.1 g) was added, and the solution was stirred until it was homogeneous. The flask was equipped with an addition funnel. The corresponding carbonyl chloride (45.5 mmol) in 1,4-dioxane (40 mL) was added dropwise. The reaction mixture was then allowed to stir at room temperature overnight. The following morning, the solution was extracted with Et<sub>2</sub>O (3 × 50 mL), and the organic layers were discarded. The aqueous layer was again cooled to 0 °C in an ice bath, and concentrated HCl was added dropwise until the pH had reached 2 (as observed by pH paper). The aqueous solution was extracted with Et<sub>2</sub>O (3 × 100 mL). The organic layers were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo* to give the crude product. The pure product was obtained following recrystallisation from Et<sub>2</sub>O/hexanes or column chromatography using 15:1 DCM:MeOH as the solvent system. For a general depiction of this procedure, see Scheme 2.S1.

#### 2.4.4. Characterisation of New Ligands:

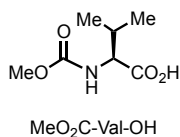
*N*-Carbamoyl-protected amino acids are known to exist as *syn*- and *anti*-rotamers,<sup>21</sup> with the latter being more thermodynamically stable than the former. In the <sup>1</sup>H and <sup>13</sup>C NMR spectra of MeO<sub>2</sub>C-Val-OH, EtO<sub>2</sub>C-Val-OH, *i*-BuO<sub>2</sub>C-Val-OH, Cbz-Val-OH, and (–)-Men-Val-OH, we detected both rotamers, generally observing <10% of the *syn*-rotamers in solution at room temperature. For simplicity, the <sup>1</sup>H and <sup>13</sup>C NMR spectral data described below correspond exclusively to the *anti*-rotamers.



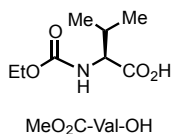
**(S)-3-methyl-2-pivalamidobutanoic acid (Piv-Val-OH):** The title compound was obtained as a white solid (4.1 g, 58% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.18 (br, 1H), 4.56 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 4.8$  Hz, 1H), 2.29–2.21 (m, 1H), 1.23 (s, 9H), 0.98 (d,  $J = 6.8$  Hz, 3H), 0.95 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.09, 175.94, 56.93, 38.91, 30.98, 27.42, 19.00, 17.67; **IR** (neat)  $\nu$  3376, 2964, 2875, 1725, 1625, 1518, 1486, 1403, 1370, 1198, 1141, 917, 840  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{10}\text{H}_{19}\text{NO}_3$   $[\text{M}+\text{H}]^+$  202.1438, found 202.1447.



**(S)-3-methyl-2-adamantanecarbonylamidobutanoic acid (Ada-Val-OH):** The title compound was obtained as a white solid (3.7 g, 75% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.11 (br, 1H), 4.51 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 5.2$  Hz, 1H), 2.30–2.22 (m, 1H), 2.06 (s, 3H), 1.90–1.86 (m, 6H), 1.77–1.69 (m, 6H), 0.98 (d,  $J = 6.8$  Hz, 3H), 0.96 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.96, 56.96, 40.83, 39.12, 36.41, 30.71, 28.02, 19.07, 17.77; **IR** (neat)  $\nu$  3375, 2962, 2906, 2852, 1728, 1624, 1520, 1301, 1207, 1147, 1110, 984  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{25}\text{NO}_3$   $[\text{M}+\text{H}]^+$  280.1907, found 280.1915.

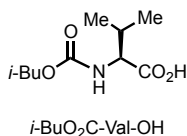


**(S)-2-(methoxycarbonylamino)-3-methylbutanoic acid (MeO<sub>2</sub>C-Val-OH):** The title compound was obtained as a white solid (4.1 g, 67% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.17 (br, 1H), 4.33 (dd,  $J_1 = 8.8$  Hz,  $J_2 = 4.4$  Hz, 1H), 3.70 (s, 3H), 2.28–2.20 (m, 1H), 1.01 (d,  $J = 6.8$  Hz, 3H), 0.94 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.97, 157.08, 58.78, 52.50, 30.96, 18.98, 17.29; **IR** (neat)  $\nu$  3324, 2966, 1695, 1526, 1466, 1373, 1304, 1214, 1098, 1041, 1021, 840, 778  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_7\text{H}_{13}\text{NO}_4$   $[\text{M}+\text{H}]^+$  176.0917, found 176.0918.

**(S)-2-(ethoxycarbonylamino)-3-methylbutanoic acid (EtO<sub>2</sub>C-Val-OH):**

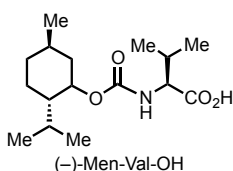
The title compound was obtained as a colourless oil (3.9 g, 59% yield). <sup>1</sup>H

**NMR** (400 MHz, CDCl<sub>3</sub>) δ 5.13 (br, 1H), 4.33 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 4.8 Hz, 1H), 4.15 (q, *J* = 6.8 Hz, 2H), 2.28–2.20 (m, 1H), 1.26 (t, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C **NMR** (100 MHz, CDCl<sub>3</sub>) δ 176.81, 156.69, 61.36, 58.68, 30.98, 18.99, 17.31, 14.45; **IR** (neat) ν 3323, 2967, 2936, 1693, 1523, 1419, 1382, 1343, 1303, 1216, 1098, 1030, 871, 778 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>8</sub>H<sub>15</sub>NO<sub>4</sub> [M+H]<sup>+</sup> 190.1074, found 190.1073.

**(S)-2-(isobutoxycarbonylamino)-3-methylbutanoic acid (*i*-BuO<sub>2</sub>C-Val-**

**OH):** The title compound was obtained as a colourless oil (7.4 g, 97%

yield). <sup>1</sup>H **NMR** (400 MHz, CDCl<sub>3</sub>) δ 5.16 (br, 1H), 4.33 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 4.4 Hz, 1H), 3.86 (d, *J* = 6.8 Hz, 2H), 2.26–2.18 (m, 1H), 1.97–1.87 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 6H); <sup>13</sup>C **NMR** (100 MHz, CDCl<sub>3</sub>) δ 176.81, 156.83, 71.47, 58.71, 31.03, 27.93, 18.96, 17.34; **IR** (neat) ν 3323, 2964, 2876, 1705, 1516, 1468, 1421, 1217, 1095, 1036, 777 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>10</sub>H<sub>19</sub>NO<sub>4</sub> [M+H]<sup>+</sup> 218.1387, found 218.1380.

**(S)-2-(((1R,2S,5R)-2-isopropyl-5-**

**methylcyclohexyloxy)carbonylamino)-3-methylbutanoic acid ((-)-**

**Men-Val-OH):** The title compound was obtained as a white solid (6.0

g, 57% yield). <sup>1</sup>H **NMR** (400 MHz, CDCl<sub>3</sub>) δ 5.10 (br, 1H), 4.58–4.54 (m, 1H), 4.33 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 4.4 Hz, 1H), 2.26–2.18 (m, 1H), 2.02 (ad, *J* = 12.0 Hz, 1H), 1.98–1.86 (m, 1H), 1.66 (ad, *J* = 12.0 Hz, 2H), 1.53–1.41 (m, 1H), 1.31 (at, *J* = 12.0 Hz, 1H), 1.09–0.99 (m, 2H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90–0.83 (m, 7H), 0.76 (d, *J* =

6.8 Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.22, 156.41, 75.16, 58.71, 47.33, 41.27, 34.25, 31.35, 31.07, 26.11, 23.45, 22.02, 20.77, 19.04, 17.37, 16.34; IR (neat)  $\nu$  3319, 2958, 2929, 2871, 1713, 1665, 1513, 1456, 1414, 1305, 1224, 1094, 1027, 983, 909  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{29}\text{NO}_4$   $[\text{M}+\text{H}]^+$  300.2169, found 300.2167.

#### 2.4.5. Optimisation Studies

**Ligand optimisation for Pd(II)-catalysed olefination with 2-(Trifluoromethyl)phenylacetic acid (2.1):** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **2.1** (102.1 mg, 0.5 mmol),  $\text{Pd}(\text{OAc})_2$  (5.6 mg, 0.025 mmol),  $\text{KHCO}_3$  (100.1 mg, 1.0 mmol), ligand (0.05 mmol), ethyl acrylate (106  $\mu\text{L}$ , 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with  $\text{O}_2$  (1 atm, balloon) ( $\times$  3). The reaction mixture was stirred at room temperature for 5 min, then at 90  $^\circ\text{C}$  for the appropriate time. The reaction vessel was removed from the oil bath and immediately cooled to 0  $^\circ\text{C}$  in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **2.1** and 4.01 ppm for **2.1a**). When indicated, the reactions were performed in triplicates, and the values shown represent the average result from the three experiments. In our initial efforts, we measured the conversion after 2 h (Table 2.S1), but we observed quantitative conversion for many ligands. We then adjusted our assay and examined the conversion after 20 min (Tables 2.S2 and 2.S3).

**Table 2.S1:** Initial results from the amino acid ligand optimisation experiments.<sup>a</sup>

| Entry | Ligand       | % Conv.        | Entry | Ligand                  | % Conv.  |
|-------|--------------|----------------|-------|-------------------------|----------|
| 1     | ---          | 7 <sup>b</sup> | 8     | Boc-Ser-OH              | 16       |
| 2     | Boc-Val-OH   | 98 (96)        | 9     | Ac-Val-OH               | >99      |
| 3     | Boc-Ile-OH   | 98             | 10    | Ac-Ile-OH               | >99 (96) |
| 4     | Boc-Leu-OH   | 92             | 11    | Ac-Leu-OH               | >99      |
| 5     | Boc-t-Leu-OH | 98             | 12    | Formyl-Ile-OH           | 36       |
| 6     | Boc-Ala-OH   | 88             | 13    | Formyl-Leu-OH           | 37       |
| 7     | Boc-Phe-OH   | 96             | 14    | Men-Leu-OH <sup>c</sup> | 71       |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses. <sup>b</sup> Average of three trials. <sup>c</sup> (-)-Men = (-)-Menthyl(O<sub>2</sub>C).

**Table 2.S2:** Results from the organic acid ligand screening experiments.<sup>a</sup>

| Entry | Ligand                          | % Conv. | Entry | Ligand | % Conv. |
|-------|---------------------------------|---------|-------|--------|---------|
| 1     | ---                             | <5      | 8     |        | <5      |
| 2     | <i>p</i> -TsOH·H <sub>2</sub> O | 0       | 9     |        | <5      |
| 3     | PivOH                           | <5      | 10    |        | 0       |
| 4     |                                 | <5      | 11    |        | <5      |
| 5     |                                 | <5      | 12    |        | <5      |
| 6     |                                 | <5      |       |        | <5      |
| 7     |                                 | <5      |       |        |         |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

**Table 2.S3:** Results from the amino acid ligand optimisation experiments.<sup>a</sup>

| Entry | Ligand                | % Conv.         | Entry | Ligand                              | % Conv.         |
|-------|-----------------------|-----------------|-------|-------------------------------------|-----------------|
| 1     | ---                   | <5              | 17    | H-Val-OH                            | 0               |
| 2     | BQ                    | <5              | 18    | Ac-Val-OH                           | 57              |
| 3     | Boc-Val-OH            | 46 <sup>b</sup> | 19    | Ada-Val-OH <sup>c</sup>             | 4               |
| 4     | Boc-Ile-OH            | 37              | 20    | Piv-Val-OH                          | 2               |
| 5     | Boc-Leu-OH            | 37              | 21    | Formyl-Val-OH                       | 31              |
| 6     | Boc- <i>t</i> -Leu-OH | 38              | 22    | Fmoc-Val-OH                         | 19              |
| 7     | Boc-Nva-OH            | 30              | 23    | MeO <sub>2</sub> C-Val-OH           | 21              |
| 8     | Boc-Ala-OH            | 28              | 24    | EtO <sub>2</sub> C-Val-OH           | 26              |
| 9     | Boc-Gly-OH            | 17              | 25    | <i>i</i> -BuO <sub>2</sub> C-Val-OH | 27              |
| 10    | Boc-Phe-OH            | 33              | 26    | Cbz-Val-OH                          | 18              |
| 11    | Boc-Ser-OH            | 8               | 27    | Bz-Val-OH                           | 3               |
| 12    | Boc- $\beta$ -Ala-OH  | 8               | 28    | Men-Val-OH <sup>d</sup>             | 39              |
| 13    |                       | 6               | 29    | Ac-Leu-OH                           | 55              |
| 14    |                       | 21              | 30    | Ac-Ala-OH                           | 71              |
| 15    |                       | 5               | 31    | Ac-Gly-OH                           | 51              |
| 16    |                       | 16              | 32    | Ac-Ile-OH                           | 72 <sup>b</sup> |
|       |                       |                 | 33    | Ac-Phe-OH                           | 60              |
|       |                       |                 | 34    |                                     | 5               |
|       |                       |                 | 35    |                                     | 31              |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.<sup>b</sup> Average of three trials. <sup>c</sup> Ada = 1-Adamantyl(OC). <sup>d</sup> (–)-Men = (–)-Menthyl(O<sub>2</sub>C).

**Additional optimisation for Pd(II)-catalysed olefination with 2-(Trifluoromethyl)phenylacetic acid (2.1):** The effects of ligand loading (Table 2.S4), olefin loading (Table 2.S5), and reaction temperature (Tables 2.S6–2.S10) were explored using Ac-Ile-OH as the ligand. A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **2.1** (102.1 mg, 0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ac-Ile-

OH, ethyl acrylate, and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times 3$ ). The reaction mixture was stirred at room temperature for 5 min, then at the appropriate temperature for the indicated time. The reaction vessel was then cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **2.1** and 4.01 ppm for **2.1a**). When indicated, the reactions were performed in triplicates, and the values shown represent the average result from the three experiments.

**Table 2.S4:** Optimisation of ligand loading.<sup>a</sup>

| Entry | Ac-Ile-OH | % Conv.         |
|-------|-----------|-----------------|
| 1     | ---       | <5 <sup>b</sup> |
| 2     | 2.5 mol%  | 56              |
| 3     | 5 mol%    | 73              |
| 4     | 10 mol%   | 72 <sup>b</sup> |
| 5     | 15 mol%   | 74              |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parenthesis. <sup>b</sup> Average of three trials.

**Table 2.S5:** Optimisation of olefin loading.<sup>a</sup>

| Entry | CO <sub>2</sub> Et | % Conv.         |
|-------|--------------------|-----------------|
| 1     | 1 equiv.           | 48 <sup>b</sup> |
| 2     | 2 equiv.           | 46 <sup>b</sup> |
| 3     | 3 equiv.           | 21 <sup>b</sup> |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parenthesis. <sup>b</sup> Average of three trials.

**Table 2.S6:** Conversion versus time at 50 °C.<sup>a</sup>

| Entry | Time (h) | % Conv. |
|-------|----------|---------|
| 1     | 0        | 0       |
| 2     | 1        | 6       |
| 3     | 8        | 37      |
| 4     | 24       | 85      |
| 5     | 48       | 96      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.



**Table 2.S7:** Conversion versus time at 70 °C.<sup>a</sup>

| Entry | Time (h) | % Conv. |
|-------|----------|---------|
| 1     | 0        | 0       |
| 2     | 1        | 54      |
| 3     | 2        | 84      |
| 4     | 3        | 94      |
| 5     | 4        | 96      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

**Table 2.S8:** Conversion versus time at 90 °C.<sup>a</sup>

| Entry | Time (min) | % Conv.         |
|-------|------------|-----------------|
| 1     | 0          | 0               |
| 2     | 5          | 10 <sup>b</sup> |
| 3     | 7.5        | 20 <sup>b</sup> |
| 4     | 10         | 29 <sup>b</sup> |
| 5     | 15         | 57 <sup>b</sup> |
| 6     | 20         | 72 <sup>b</sup> |
| 7     | 120        | >99 (96)        |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parenthesis. <sup>b</sup> Average of three trials.

**Table 2.S9:** Conversion versus time at 110 °C.<sup>a</sup>

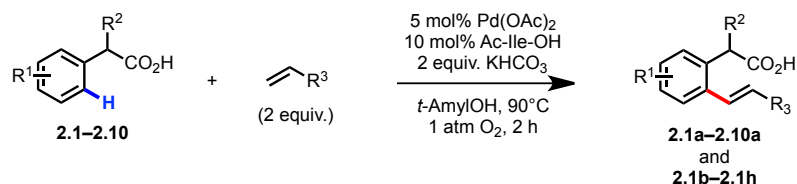
| Entry | Time (min) | % Conv. |
|-------|------------|---------|
| 1     | 0          | 0       |
| 2     | 5          | 27      |
| 3     | 10         | 66      |
| 4     | 15         | 88      |
| 5     | 20         | 93      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.**Table 2.S10:** Conversion versus time at 130 °C.<sup>a</sup>

| Entry | Time (min) | % Conv. |
|-------|------------|---------|
| 1     | 0          | 0       |
| 2     | 10         | 11      |
| 3     | 20         | 36      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

#### 2.4.6. Optimised General Procedure

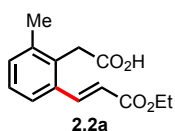
**Scheme 2.S2:** General procedure for C–H olefination of phenylacetic acids.

**General procedure for Pd(II)-catalysed *ortho*-C–H olefination of phenylacetic acids 2.1–2.10:** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the phenylacetic acid starting

material (**2.1–2.10**) (0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), ligand (0.05 mmol), the olefin coupling partner (1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) (× 3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 2 h (longer, when noted). The reaction vessel was then cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) was then added, and the mixture was extracted with EtOAc (3 × 20 mL). The organic layers were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 3:1 hexanes:EtOAc (with 3% HOAc) as the eluent. For a general depiction of this procedure, see Scheme 2.S2.

#### 2.4.7. Characterisation of New C–H Olefinated Products

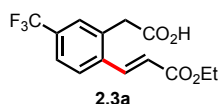
Our group has previously reported analytical data for **2.1a**, **2.5a**, **2.6a**, and **2.8a'**.<sup>4</sup> In this same publication, **2.7a**, **2.9a**, and **2.10a** were also synthesised but were isolated as their methyl esters following treatment of the crude product mixture with CH<sub>2</sub>N<sub>2</sub>. This was done to simplify the separation of the product from residual unreacted starting material. Because the reactions reported here generally gave quantitative yields, the pure products could consistently be isolated as free acids. We have included the analytical data for free acids **2.7a**, **2.9a**, and **2.10a**.



#### (*E*)-2-(2-(3-ethoxy-3-oxoprop-1-enyl)-6-methylphenyl)acetic acid (**2.2a**):

The title compound was obtained as a white solid (122 mg, 98% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.00 (d, *J* = 15.6 Hz, 1H), 7.42, (dd, *J*<sub>1</sub> = 6.8 Hz, *J*<sub>2</sub> = 2.0 Hz, 1H), 7.24–7.18 (m, 2H), 6.33 (d, *J* = 15.6 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 2H), 2.34 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 176.45,

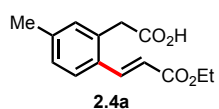
166.83, 142.47, 138.03, 134.75, 131.96, 131.50, 127.69, 124.92, 121.10, 60.61, 34.67, 20.21, 14.26; **IR** (neat)  $\nu$  2981, 2935, 1704 (br), 1631, 1446, 1368, 1313, 1269, 1237, 1179, 1162 (br), 1093, 1035, 979, 788  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{17}\text{O}_4$   $[\text{M}+\text{H}]^+$  249.1121, found 249.1124.



**(E)-2-(2-(3-ethoxy-3-oxoprop-1-enyl)-5-**

**(trifluoromethyl)phenyl)acetic acid (2.3a):** The title compound was

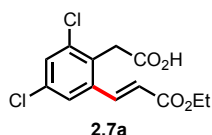
obtained as a white solid (147 mg, 97% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.91 (d,  $J = 15.6$  Hz, 1H), 7.69 (d,  $J = 8.0$  Hz, 1H), 7.58 (d,  $J = 8.0$  Hz, 1H), 7.55 (s, 1H), 6.43 (d,  $J = 15.6$  Hz, 1H), 4.28 (q,  $J = 7.2$  Hz, 2H), 3.87 (s, 2H), 1.34 (t,  $J = 7.2$  Hz, 3H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.95, 166.29, 140.01, 137.74, 133.40, 131.69 (q,  $J_{\text{C-F}} = 32.7$  Hz), 128.02 (q,  $J_{\text{C-F}} = 3.7$  Hz), 127.47, 124.90 (q,  $J_{\text{C-F}} = 3.7$  Hz), 123.60 (q,  $J_{\text{C-F}} = 270.7$  Hz), 122.24, 60.98, 38.23, 14.22; **IR** (neat)  $\nu$  2987, 2932, 1715 (br), 1638, 1422, 1335, 1283, 1222, 1167 (br), 1127, 1080, 1035, 979  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{14}\text{F}_3\text{O}_4$   $[\text{M}+\text{H}]^+$  303.0839, found 303.0844.



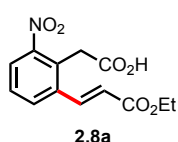
**(E)-2-(2-(3-ethoxy-3-oxoprop-1-enyl)-5-methylphenyl)acetic acid**

**(2.4a):** The title compound was obtained as a colourless oil (103 mg, 99%

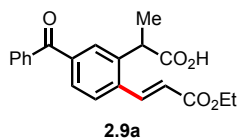
yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.90 (d,  $J = 15.6$  Hz, 1H), 7.51 (d,  $J = 8.0$  Hz, 1H), 7.12 (d,  $J = 8.0$  Hz, 1H), 7.09 (s, 1H), 6.34 (d,  $J = 15.6$  Hz, 1H), 4.25 (q,  $J = 7.2$  Hz, 2H), 3.77 (s, 2H), 2.35 (s, 3H), 1.32 (t,  $J = 7.2$  Hz, 3H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.44, 167.01, 141.31, 140.54, 132.79, 131.87, 131.14, 128.92, 126.83, 119.53, 60.56, 38.31, 21.26, 14.27; **IR** (neat)  $\nu$  2982, 2927, 1708 (br), 1632, 1610, 1368, 1315, 1283, 1179 (br), 1159, 1095, 1035, 979, 816  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{17}\text{O}_4$   $[\text{M}+\text{H}]^+$  249.1121, found 249.1118.

**(E)-2-(2,4-dichloro-6-(3-ethoxy-3-oxoprop-1-enyl)phenyl)acetic acid**

**(2.7a):** The title compound was obtained as a white solid (150 mg, 99% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d,  $J = 15.6$  Hz, 1H), 7.45 (s, 2H), 6.35 (d,  $J = 15.6$  Hz, 1H), 4.27 (q,  $J = 7.2$  Hz, 2H), 3.69 (s, 2H), 1.33 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.83, 166.03, 139.96, 137.75, 136.67, 134.17, 130.21, 129.49, 125.72, 123.73, 61.05, 34.83, 14.21; **IR** (neat)  $\nu$  2982, 2930, 1708 (br), 1637, 1584, 1553, 1446, 1398, 1368, 1310, 1274, 1237, 1178 (br), 1153, 1031, 972, 911, 859  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{13}\text{Cl}_2\text{O}_4$   $[\text{M}+\text{H}]^+$  303.0190,  $[(\text{M}+2)+\text{H}]^+$  305.0161,  $[(\text{M}+4)+\text{H}]^+$  307.0132, found 303.0188, 305.0160, 307.0140  $[\text{M}+\text{H}]^+ : [(\text{M}+2)+\text{H}]^+ : [(\text{M}+4)+\text{H}]^+ = 9:6:1$ .

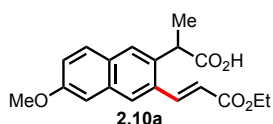
**(E)-2-(2-(3-ethoxy-3-oxoprop-1-enyl)-6-nitrophenyl)acetic acid (2.8a):**

The title compound was obtained as a white solid (98 mg, 70% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 7.6$  Hz, 1H), 7.92 (d,  $J = 15.6$  Hz, 1H), 7.78 (d,  $J = 7.6$  Hz, 1H), 7.48 (t,  $J = 7.6$  Hz, 1H), 6.38 (d,  $J = 15.6$  Hz, 1H), 4.29 (q,  $J = 7.2$  Hz, 2H), 4.08 (s, 2H), 1.35 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  174.40, 165.93, 150.32, 140.10, 137.86, 132.00, 128.61, 127.26, 125.83, 124.68, 61.15, 34.36, 14.22; **IR** (neat)  $\nu$  3089, 2985, 1710 (br), 1638, 1607, 1529, 1351, 1317, 1185 (br), 1032, 975, 894, 808, 744  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{14}\text{NO}_6$   $[\text{M}+\text{H}]^+$  280.0816, found 280.0822.

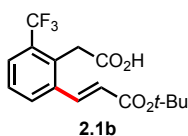
**(E)-2-(5-benzoyl-2-(3-ethoxy-3-oxoprop-1-enyl)phenyl)propanoic acid (2.9a):**

The title compound was obtained as a viscous yellow oil (188 mg, 98% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (d,  $J = 15.6$  Hz, 1H), 7.83–7.45 (m, 8H), 6.44 (d,  $J = 15.6$  Hz, 1H), 4.29 (q,  $J = 7.2$  Hz, 2H), 4.20 (q,  $J = 7.2$  Hz, 1H), 1.55 (d,  $J = 7.2$  Hz, 3H), 1.35 (t,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )

$\delta$  195.66, 178.57, 166.28, 140.56, 139.19, 138.64, 137.38, 137.06, 132.74, 130.05, 129.33, 129.18, 128.37, 127.23, 123.40, 60.91, 40.92, 18.02, 14.27; **IR** (neat)  $\nu$  2982, 2938, 1708 (br), 1657, 1635, 1598, 1447, 1410, 1368, 1314, 1272, 1217, 1178 (br), 1031, 960, 843, 754, 721  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{21}\text{O}_5$   $[\text{M}+\text{H}]^+$  353.1383, found 353.1388.

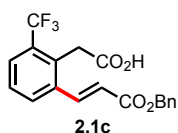


**(E)-2-(3-(3-ethoxy-3-oxoprop-1-enyl)-6-methoxynaphthalen-2-yl)propanoic acid (2.10a):** The title compound was obtained as a viscous yellow oil (153 mg, 93% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.17 (d,  $J = 15.6$  Hz, 1H), 7.92 (s, 1H), 7.72 (s, 1H), 7.67 (d,  $J = 8.8$  Hz, 1H), 7.14 (d,  $J = 9.2$  Hz, 1H), 7.09 (s, 1H), 6.46 (d,  $J = 15.6$  Hz, 1H), 4.29 (q,  $J = 7.2$  Hz, 2H), 4.21 (q,  $J = 6.8$  Hz, 1H), 3.92 (s, 3H), 1.59 (d,  $J = 6.8$  Hz, 3H), 1.35 (t,  $J = 7.2$ , 3H);  **$^{13}\text{C}$  NM** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.98, 166.70, 158.08, 142.39, 133.98, 133.42, 132.44, 129.53, 129.14, 126.11, 125.92, 121.53, 120.18, 105.56, 60.66, 55.30, 41.03, 18.31, 14.28; **IR** (neat)  $\nu$  2980, 2934, 1704 (br), 1634, 1600, 1499, 1465, 1397, 1368, 1301, 1266, 1207, 1166 (br), 1029, 975, 896, 866, 811  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{21}\text{O}_5$   $[\text{M}+\text{H}]^+$  329.1383, found 329.1378.



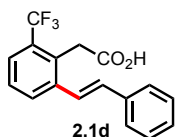
**(E)-2-(2-(3-tert-butoxy-3-oxoprop-1-enyl)-6-(trifluoromethyl)phenyl)acetic acid (2.1b):** The title compound was obtained as a white solid (163 mg, 99% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (d,  $J = 15.6$  Hz, 1H), 7.73 (d,  $J = 7.6$  Hz, 1H), 7.70 (d,  $J = 7.6$  Hz, 1H), 7.43 (t,  $J = 7.6$  Hz, 1H), 6.31 (d,  $J = 15.6$  Hz, 1H), 4.01 (s, 2H), 1.53 (s, 9H);  **$^{13}\text{C}$  NM** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.21, 165.63, 139.64, 137.37, 130.88, 130.61, 130.16 (q,  $J_{\text{C-F}} = 29.5$  Hz), 127.88, 127.06 (q,  $J_{\text{C-F}} = 5.6$  Hz), 124.66, 124.02 (q,  $J_{\text{C-F}} = 272.6$  Hz), 81.28, 34.21, 28.07; **IR** (neat)  $\nu$  2981, 2935, 1710 (br), 1637, 1454, 1324 (br), 1149, 1119, 1099, 981, 961, 842,

806, 752  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{17}\text{F}_3\text{O}_4\text{Na}$   $[\text{M}+\text{Na}]^+$  353.0971, found 353.0977.



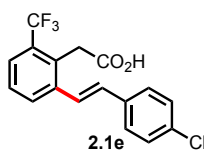
**(E)-2-(2-(3-(benzyloxy)-3-oxoprop-1-enyl)-6-(trifluoromethyl)phenyl)acetic acid (2.1c):** The title compound was

obtained as a white solid (165 mg, 90% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (d,  $J$  = 16.0 Hz, 1H), 7.74 (d,  $J$  = 7.6, 1H), 7.72 (d,  $J$  = 8.0, 1H), 7.46–7.34 (m, 6H), 6.43 (d,  $J$  = 15.6 Hz, 1H), 5.25 (s, 2H), 4.01 (s, 2H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.29, 166.06, 141.15, 137.06, 135.65, 131.00, 130.63, 130.25 (q,  $J$  = 29.6 Hz), 128.58, 128.44, 128.32, 128.27, 127.38 (q,  $J$  = 5.7 Hz), 123.96 (q,  $J$  = 272.3 Hz), 122.77, 66.71, 34.18; **IR** (neat)  $\nu$  3034, 2962, 1702 (br), 1455, 1422, 1372, 1315, 1275, 1239, 1163 (br), 1110, 1004, 975, 963, 804, 748  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{16}\text{F}_3\text{O}_4$   $[\text{M}+\text{H}]^+$  365.0995, found 365.0997.



**(E)-2-(2-styryl-6-(trifluoromethyl)phenyl)acetic acid (2.1d):** The title compound was obtained as a white solid (153 mg, 99% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 (d,  $J$  = 7.6, 1H), 7.56 (d,  $J$  = 7.6, 1H), 7.44–7.17

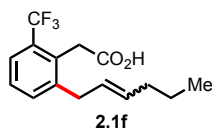
(m, 7H) 6.92 (d,  $J$  = 16.0 Hz, 1H), 3.95 (s, 2H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.53, 140.21, 136.61, 134.05, 130.29, 129.79 (q,  $J_{\text{C-F}}$  = 29.3 Hz), 129.40, 128.78, 128.35, 127.81, 126.82, 125.18 (q,  $J_{\text{C-F}}$  = 5.7 Hz), 124.71, 124.27 (q,  $J_{\text{C-F}}$  = 272.8 Hz), 34.58; **IR** (neat)  $\nu$  3026, 1708 (br), 1495, 1455, 1412, 1315 (br), 1155, 1114, 1098, 957, 798, 749  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{17}\text{H}_{14}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  307.0940, found 307.0941.



**(*E*)-2-(2-(4-chlorostyryl)-6-(trifluoromethyl)phenyl)acetic acid (2.1e):**

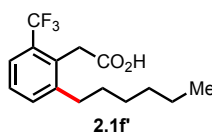
The title compound was obtained as a white solid (111 mg, 65% yield).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.45–7.32 (m, 5H), 7.22 (d, *J* = 16.0 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 4.00 (s, 2H); **<sup>13</sup>C NMR** (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO) δ 171.51, 140.93, 136.90, 134.07, 134.07, 1332.07, 132.59, 132.19, 131.02, 130.15 (q, *J*<sub>C-F</sub> = 28.9 Hz), 129.62, 129.27, 128.49, 126.70, 125.88 (q, *J*<sub>C-F</sub> = 5.9 Hz), 125.61 (q, *J*<sub>C-F</sub> = 272.0 Hz), 34.94; **IR** (neat) ν 3034, 2962, 1702 (br), 1634, 1455, 1422, 1372, 1315, 1275, 1239, 1163 (br), 1099, 1004, 975, 963, 804, 748 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>17</sub>H<sub>13</sub>ClF<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup> 341.0551, [(M+2)+H]<sup>+</sup> 343.0527, found 341.0556, 343.0527 [M+H]<sup>+</sup>: [(M+2)+H]<sup>+</sup> = 3:1.



**2-(2-(hex-2-enyl)-6-(trifluoromethyl)phenyl)acetic acid (2.1f):**

The title compound was obtained as an inseparable mixture of the *E*- and *Z*-stereoisomers (89 mg, 62% yield). By <sup>1</sup>H NMR, the *E*:*Z* ratio was determined to be approximately 4:1. The <sup>1</sup>H NMR data reported here represent only the major isomer. Following hydrogenation, **2.1f** was converted to **2.1f'**, and a complete set of analytical data were collected (included below). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.55 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 1H), 5.53–5.39 (m, 2H), 3.93 (s, 2H), 3.36 (d, *J* = 6.0 Hz, 2H), 1.98 (aq, *J* = 7.2 Hz, 2H), 1.44–1.32 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H).



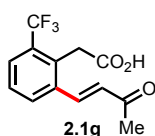
**2-(2-hexyl-6-(trifluoromethyl)phenyl)acetic acid (2.1f'):**

To a 25 mL round bottom flask equipped with a stir bar were added **2.1f** (72.5 mg, 0.25 mmol), MeOH (10 mL), and Pd/C (10 wt%) (2.7 mg, 0.0025 mmol).

The flask was evacuated under vacuum, then capped under H<sub>2</sub> (1 atm, balloon). After 6 h,

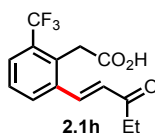


the solution was filtered through a pad of Celite. The title compound was obtained as a colourless oil (71 mg, 99% yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>) δ 7.51 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 3.89 (s, 2H), 2.60 (t, *J* = 7.8 Hz, 2H), 1.62–1.51 (m, 2H), 1.40–1.24 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 177.09, 144.06, 132.96, 129.87, 129.54 (q, *J*<sub>C-F</sub> = 28.9 Hz), 127.36, 124.48 (q, *J*<sub>C-F</sub> = 272.5 Hz), 123.76 (q, *J*<sub>C-F</sub> = 5.7 Hz), 34.10, 32.89, 31.64, 30.55, 29.25, 22.55, 14.02; **IR** (neat) ν 2929, 2856, 1713 (br), 1462, 1412, 1316, 1157, 1116 (br), 1094, 954, 803 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>15</sub>H<sub>20</sub>F<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup> 289.1410, found 289.1409.



**(*E*)-2-(2-(3-oxobut-1-enyl)-6-(trifluoromethyl)phenyl)acetic acid (2.1g):**

The title compound was obtained as an amorphous off-white solid (123 mg, 90% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.76–7.72 (m, 3H), 7.46 (t, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 4.01 (s, 2H), 2.38 (s, 3H); **<sup>13</sup>C NMR** (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO) δ 197.90, 171.27, 139.72, 138.66, 133.64, 132.04, 131.75, 130.40 (q, *J*<sub>C-F</sub> = 29.2 Hz), 128.80, 127.88 (q, *J*<sub>C-F</sub> = 5.9 Hz), 125.39 (q, *J*<sub>C-F</sub> = 272.0 Hz), 34.84, 27.72; **IR** (neat) ν 2923, 1746 (br), 1719 (br), 1604, 1467, 1321, 1245, 1155, 1115 (br), 1050, 986, 800 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>13</sub>H<sub>12</sub>F<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup> 273.0733, found 273.0740.



**(*E*)-2-(2-(3-oxopent-1-enyl)-6-(trifluoromethyl)phenyl)acetic acid (2.1h):**

The title compound was obtained as an amorphous off-white solid (138 mg, 97% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J* = 16.0 Hz, 1H), 7.76–7.71 (m, 2H), 7.45 (t, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 16.0 Hz, 1H), 4.01 (s, 2H), 2.69 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, (CDCl<sub>3</sub>)) δ 200.59, 175.18, 138.03, 137.40, 131.16, 130.59, 130.33, 130.27 (q, *J*<sub>C-F</sub> = 29.5 Hz), 128.01, 127.34 (q, *J*<sub>C-F</sub> = 5.7 Hz), 123.97 (q, *J*<sub>C-F</sub> = 273.0 Hz), 34.53, 34.25, 7.93; **IR** (neat) ν 2982, 2943, 1716,

1671, 1614, 1454, 1319, 1188, 1159, 1119, 1100, 1042, 973, 808  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{14}\text{H}_{14}\text{F}_3\text{O}_3$   $[\text{M}+\text{H}]^+$  287.0890, found 287.0902.

### 2.4.8. Competition Experiments

**Procedure for intermolecular competition experiments between compounds **2.1** and **2.2**:** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **2.1** (51.1 mg, 0.25 mmol), **2.2** (37.6 mg, 0.25 mmol),  $\text{Pd}(\text{OAc})_2$  (5.6 mg, 0.025 mmol),  $\text{KHCO}_3$  (100.1 mg, 1.0 mmol), ligand (0.05 mmol), ethyl acrylate (106  $\mu\text{L}$ , 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with  $\text{O}_2$  (1 atm, balloon) ( $\times 3$ ). The reaction mixture was stirred at room temperature for 5 min, then at 90  $^\circ\text{C}$  for the appropriate time. The reaction vessel was then cooled to 0  $^\circ\text{C}$  in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **2.1**, 4.01 ppm for **2.1a**, 3.67 ppm for **2.2**, and 3.84 ppm for **2.2a**). The results are shown in Table 2.S11.

**Table 2.S11:** Competition experiments between **2.1** and **2.2**.<sup>a</sup>

| Entry <sup>a</sup> | Ligand     | Time (min) | % Conv. <b>2.1a</b> | % Conv. <b>2.2a</b> | $k_1$ ([M]/min)      | $k_2$ ([M]/min)      | $k_1 / k_2$ |
|--------------------|------------|------------|---------------------|---------------------|----------------------|----------------------|-------------|
| 1                  | ---        | 120        | 3.0                 | 13.9                | $2.5 \times 10^{-5}$ | $1.2 \times 10^{-4}$ | 0.22        |
| 2                  | Boc-Val-OH | 10         | 17.6                | 30.5                | $1.8 \times 10^{-3}$ | $3.1 \times 10^{-3}$ | 0.58        |
| 3                  | Ac-Ile-OH  | 10         | 40.0                | 21.4                | $4.0 \times 10^{-3}$ | $2.1 \times 10^{-3}$ | 1.87        |

<sup>a</sup> The conversion was determined by  $^1\text{H}$  NMR of the crude reaction mixture.

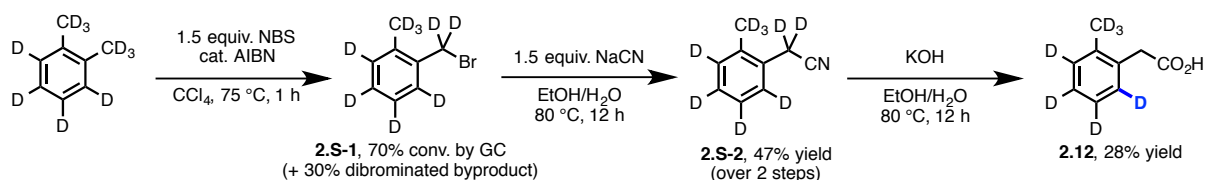
### Procedure for initial rate studies for single-component reactions of 2.1 and 2.2:

The procedure for reactions run with and without Boc-Val-OH is described in Section 2.4.2. An identical protocol was followed to determine the initial rate in the presence of Ac-Ile-OH (8.7 mg, 0.05 mmol), with reactions stopped at 5 min, 7.5 min, 10 min, and 15 min. The reactions were repeated three times, and determination of the initial rate was performed using linear regression. The overall results are shown in Table 2.S12.

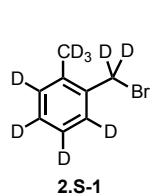
**Table S12:** Results from the single-component initial rate studies for reactions with 2.1 and 2.2. For an example data set, see Table 2.S1.

|       |            | 2.1 (R = CF <sub>3</sub> ) | 2.2 (R = Me)             |                                 |
|-------|------------|----------------------------|--------------------------|---------------------------------|
| Entry | Ligand     | k <sub>1</sub> ([M]/min)   | k <sub>2</sub> ([M]/min) | k <sub>1</sub> / k <sub>2</sub> |
| 1     | ---        | 1.3 x 10 <sup>-4</sup>     | 3.5 x 10 <sup>-4</sup>   | 0.37                            |
| 2     | Boc-Val-OH | 4.7 x 10 <sup>-3</sup>     | 5.2 x 10 <sup>-3</sup>   | 0.90                            |
| 3     | Ac-Ile-OH  | 7.6 x 10 <sup>-3</sup>     | 5.5 x 10 <sup>-3</sup>   | 1.38                            |

### 2.4.9. Kinetic Isotope Effect Experiments

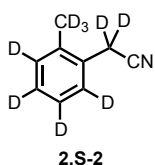


**Scheme 2.S3:** Synthetic route to 2.12.

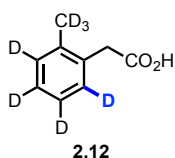


**ortho-tolyl-*d*<sub>7</sub> bromide (2.S-1):** To a 250 mL round bottom flask equipped with a magnetic stir bar, were added *ortho*-xylene-*d*<sub>10</sub> (2.4 mL, 20 mmol, 99+% atom D), NBS (5.3 g, 30 mmol), and CCl<sub>4</sub> (125 mL). The flask was fitted with a reflux condenser, and the solution was heated to refluxing conditions. Catalytic AIBN (75 mg) was added. The reaction was monitored every 20 minutes by GC-MS. After 1 h, it was observed that the reaction had progressed to completion (70% desired mono-

brominated product, 30% undesired di-brominated byproduct). The solution was allowed to cool to room temperature, at which point it was filtered to remove the succinimide precipitate. The filtrate was concentrated *in vacuo*, and the crude product mixture was obtained as a colourless oil. This mixture was taken on to the next step without further purification.



**ortho-tolyl-*d*<sub>9</sub> cyanide (2.S-2):** To a 100 mL round bottom flask equipped with a magnetic stir bar, were added crude 2.S-1 (20 mmol), NaCN (1.5 g, 30 mmol), EtOH (50 mL), and distilled H<sub>2</sub>O (10 mL). (*CAUTION: NaCN is an extremely toxic chemical and should be handled in a well-maintained fumehood. The operator should have appropriate protection at all times.*) The solution was stirred under refluxing conditions for 12 h. Following careful removal of EtOH by distillation, the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with water (3 × 100 mL) and brine (100 mL). The solution was concentrated *in vacuo*, and the crude product. Purification by column chromatography (15:1 hexanes:EtOAc) gave pure 2.S-2 as a colourless oil (1.48 g, 47% yield over two steps).



**ortho-tolyl-*d*<sub>7</sub> acetic acid (2.12):** To a 250 mL round bottom flask equipped with a magnetic stir bar, were added 2.S-2, KOH (1.7 g, 30 mmol), EtOH (100 mL), and distilled H<sub>2</sub>O (25 mL). The solution was heated to reflux for 12 h, at which point EtOH was removed *via* distillation. The resulting aqueous solution was extracted with EtOAc (3 × 50 mL), and the organic layers were discarded. Concentrated HCl was added to the aqueous layer until the pH had reached 2 (as monitored by pH paper). The solution was extracted with EtOAc (3 × 100 mL). The organic layers were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification via column

chromatography (3:1 hexanes:EtOAc, 3% HOAc) gave **2.12** as a white solid (448 mg, 28% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.69 (s, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.37, 136.95, 130.20 (t,  $J_{\text{C-D}} = 23.2$  Hz), 130.07 (t,  $J_{\text{C-D}} = 23.9$  Hz), 25.8 Hz, 127.38 (t,  $J_{\text{C-D}} = 25.8$  Hz), 125.91 (t,  $J_{\text{C-D}} = 24.5$  Hz), 39.07 (Note: the  $\text{CD}_3$  signal could not be seen in the  $^{13}\text{C}$  NMR spectrum due to its complex splitting.); IR (neat)  $\nu$  2918, 1690 (br), 1416, 1327, 1230, 908  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_9\text{H}_4\text{D}_7\text{O}_2$   $[\text{M}+\text{H}]^+$  158.1186, found 158.1190.

#### Procedure for intermolecular kinetic isotope experiments between compounds

**2.2 and 2.12:** To a 20 mL scintillation vial were added, **2.2** (15.0 mg, 0.1 mmol), **2.12** (15.7 mg, 0.1 mmol), and  $\text{CDCl}_3$  (0.5 mL). The solution was stirred until homogenous, and a small aliquot was taken for  $^1\text{H}$  NMR analysis to ensure that the weighed quantities corresponded to a mixture with  $50\% \pm 2\%$  of each component. The solvent was removed *in vacuo*, and the mixture of **2.2** and **2.12** was transferred in *t*-AmylOH (1 mL) to a 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar.  $\text{Pd}(\text{OAc})_2$  (2.2 mg, 0.01 mmol),  $\text{KHCO}_3$  (40.0 mg, 0.4 mmol), ligand (0.02 mmol), and ethyl acrylate (43  $\mu\text{L}$ , 0.4 mmol) were then added. The reaction tube was capped, then evacuated briefly under high vacuum and charged with  $\text{O}_2$  (1 atm, balloon) ( $\times$  3). The reaction mixture was stirred at room temperature for 5 min, then at 90  $^\circ\text{C}$  for the appropriate time. The reaction vessel was then cooled to 0  $^\circ\text{C}$  in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The conversion of **2.2a**,  $X_{2.2a}$ , was determined by integration of the methyl proton signals, which appear as singlets (approximately 2.32 ppm for **2.2** and 2.36 ppm for **2.2a**). The total conversion  $X_{\text{total}}$  was determined by integration of the benzylic methylene group signals, which also appear as

singlets (3.67 ppm for **2.2**/**2.12** and 3.84 ppm for **2.2a**/**2.12a**). The conversion of **2.12a**,  $X_{2.12a}$ , could then be determined from the following formula:

$$X_{2.12a} = 2 \cdot X_{total} - X_{2.2a}$$

The experiments were repeated three times without ligand, three times with Boc-Val-OH, and five times with Ac-Ile-OH. The results are shown in Table 2.S13.

**Table 2.S13:** Results from the kinetic isotope experiments with **2.2** and **2.12**.<sup>a</sup>

| Entry <sup>a</sup> | Ligand     | Time (min) | % Conv. <b>2.2a</b> | % Conv. <b>2.12a</b> | $k_H$ ([M]/min)      | $k_D$ ([M]/min)      | $k_H / k_D$ |
|--------------------|------------|------------|---------------------|----------------------|----------------------|----------------------|-------------|
| 1                  | ---        | 120        | 42.5                | 7.9                  | $3.5 \times 10^{-4}$ | $6.6 \times 10^{-5}$ | 5.38        |
| 2                  | ---        | 120        | 26.1                | 5.1                  | $2.2 \times 10^{-4}$ | $4.3 \times 10^{-5}$ | 5.12        |
| 3                  | ---        | 120        | 29.1                | 3.8                  | $2.4 \times 10^{-4}$ | $3.2 \times 10^{-5}$ | 7.67        |
| 4                  | Boc-Val-OH | 10         | 23.7                | 3.7                  | $2.4 \times 10^{-3}$ | $3.7 \times 10^{-4}$ | 6.41        |
| 5                  | Boc-Val-OH | 10         | 18.3                | 3.7                  | $1.8 \times 10^{-3}$ | $3.7 \times 10^{-4}$ | 4.90        |
| 6                  | Boc-Val-OH | 10         | 18.0                | 3.4                  | $1.8 \times 10^{-3}$ | $3.4 \times 10^{-4}$ | 5.29        |
| 7                  | Ac-Ile-OH  | 10         | 26.0                | 22.0                 | $2.6 \times 10^{-3}$ | $2.2 \times 10^{-3}$ | 1.18        |
| 8                  | Ac-Ile-OH  | 10         | 26.4                | 11.0                 | $2.6 \times 10^{-3}$ | $1.1 \times 10^{-3}$ | 2.40        |
| 9                  | Ac-Ile-OH  | 10         | 26.1                | 19.5                 | $2.6 \times 10^{-3}$ | $2.0 \times 10^{-3}$ | 1.34        |
| 10                 | Ac-Ile-OH  | 10         | 23.5                | 11.1                 | $2.4 \times 10^{-3}$ | $1.1 \times 10^{-3}$ | 2.11        |
| 11                 | Ac-Ile-OH  | 10         | 21.4                | 18.2                 | $2.1 \times 10^{-3}$ | $1.8 \times 10^{-3}$ | 1.43        |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture, as discussed in the preceding section.

## 2.5. REFERENCES

- (1) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.
- (2) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886.
- (3) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461.

- (4) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, 327, 315–319.
- (5) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **1995**, 34, 1059–1070.
- (6) Shue, R. S. *J. Chem. Soc. D* **1971**, 1510–1511.
- (7) Dams, M.; DeVos, D. E.; Celen, S.; Jacobs, P. A. *Angew. Chem. Int. Ed.* **2003**, 42, 3512–3515.
- (8) Trost, B. M. *Science* **1991**, 254, 1471–1477.
- (9) Li, C.-J.; Trost, B. M. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, 105, 13197–13202.
- (10) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2010**, 49, 6169–6173.
- (11) For studies concerning the mechanistic aspects C–H cleavage in Pd(II)-catalysed reactions, see: (a) Ryabov, A. D.; Sakodinskaya, I. K.; Yatsimirsky, A. K. *J. Chem. Soc., Dalton Trans.* **1985**, 2629–2638. (b) Canty, A. J.; van Koten, G. *Acc. Chem. Res.* **1995**, 28, 406–413. (c) Tunge, J. A.; Foresee, L. N. *Organometallics* **2005**, 24, 6440–6444. For experimental and computational evidence of concerted metalation/deprotonation, see: (d) Gómez, M.; Granell, J.; Martinez, M. *Organometallics* **1997**, 16, 2539–2546. (e) Gómez, M.; Granell, J.; Martinez, M. *J. Chem. Soc., Dalton Trans.* **1998**, 37–44. (f) Biswas, B.; Sugimoto, M.; Sakaki, S. *Organometallics* **2000**, 19, 3895–3908. (g) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, 127, 13754–13755. (h) Roiban, G.-D.; Serrano, E.; Soler, T.; Aullón, G.; Grosu, I.; Cativiela, C.; Martínez, M.; Urriolabeitia, E. P. *Inorg. Chem.* **2011**, 50, 8132–8143. For reviews of carboxylate-assisted C–H cleavage in transition metal catalysis, see: (i) Ackermann, L. *Chem. Rev.* **2011**, 111, 1315–1345. (j) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, 39, 1118–1126.
- (12) For conceptually related studies concerning C–H activation with Pd(0)–PR<sub>3</sub>/ArX catalytic systems, see: (a) Mota, A. J.; Dedieu, A.; Bour, C.; Suffert, J. *J. Am. Chem.*

- Soc.* **2005**, *127*, 7171–7182. (b) García-Cuadrado, D.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2006**, *128*, 1066–1067. (c) Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754–8756. (d) Pinto, A.; Neuville, L.; Retailleau, P.; Zhu, J. *Org. Lett.* **2006**, *8*, 4927–4930. (e) García-Cuadrado, D.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2007**, *129*, 6880–6886. (f) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Am. Chem. Soc.* **2008**, *130*, 10848–10849.
- (13) Zollinger, H. In *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic Press: London, 1964; Vol. 2, p 163–200.
- (14) Examples of Pd(II)-catalysed C–H olefination using substrates containing directing groups: (a) Miura, M.; Tsuda, T.; Satoh, T.; Nomura, M. *Chem. Lett.* **1997**, *26*, 1103–1104. (b) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211–5215. (c) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586–1587. (d) Zaitsev, V. G.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 4156–4157. (e) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666–7673. (f) Houlden, C. E.; Bailey, C. D.; Ford, J. G.; Gagné, M. R.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2008**, *130*, 10066–10067. (g) Li, J.-J.; Mei, T.-S.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 6452–6455. (h) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916–5921.
- (15) For early studies where large KIE values ( $k_1/k_2 > 5$ ) were observed in reactions thought to proceed through electrophilic Pd(II)-mediated C–H cleavage, see (a) Davidson, J. M.; Triggs, C. *J. Chem. Soc. A* **1968**, 1324–1330. (b) Shue, R. S. *J. Am. Chem. Soc.* **1971**, *93*, 7116–7117. For a related arene mercuration reaction, see: (c) Kresge, A. J.; Brennan, J. F. *J. Org. Chem.* **1967**, *32*, 752–755. For discussion of KIE values in Pd(II)-



- mediated C–H cleavage reactions, see: (d) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050–8057. (e) Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581–590.
- (16) Mono-*N*-protected amino acids were first identified as effective ligand scaffolds for Pd(II)-catalysed C–H functionalisation reactions during our studies of enantioselective C–H functionalisation: (a) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886. (b) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461. For an early report describing stoichiometric asymmetric cyclopalladation of (dimethylamino)methylferrocene in the presence of Ac-Val-OH, see: (c) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.
- (17) Reviews of aerobic Pd(II)-catalysed oxidation chemistry: (a) Stahl, S. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3400–3420. (b) Stoltz, B. M. *Chem. Lett.* **2004**, *33*, 362–367. (c) Gligorich, K. M.; Sigman, M. S. *Chem. Commun.* **2009**, 3854–3867.
- (18) Moye-Sherman, D.; Jin, S.; Ham, I.; Lim, D.; Scholtz, J. M.; Burgess, K. *J. Am. Chem. Soc.* **1998**, *120*, 9435–9443.
- (19) Pradeille, N.; Zerbe, O.; Möhle, K.; Linden, A.; Heimgartner, H. *Chem. Biodivers.* **2005**, *2*, 1127–1152.
- (20) Buckley, T. F., III; Rapoport, H. *J. Am. Chem. Soc.* **1981**, *103*, 6157–6163.
- (21) Marcovici-Mizrahi, D.; Gottlieb, H. E.; Marks, V.; Nudelman, A. *J. Org. Chem.* **1996**, *61*, 8402–8406.

## 2.6. CONTRIBUTIONS

The following individuals directly contributed to the work described in this Chapter: Keary M. Engle, Dong-Hui Wang, and Prof. Jin-Quan Yu. K.M.E. and J.-Q.Y. conceived

the project. Relevant preliminary experiments (see Ref. 4) were performed by D.-H.W. and K.M.E. All experiments described in this Chapter were carried out by K.M.E. The Chapter was adapted with permission from a published manuscript, which was written by K.M.E. and J.-Q.Y., with input from D.-H.W.

## CHAPTER 3

### LIGAND-ACCELERATED PALLADIUM(II)-CATALYSED DIOLEFINATION: APPLICATIONS TO SEQUENTIAL AND ITERATIVE C–H FUNCTIONALISATION

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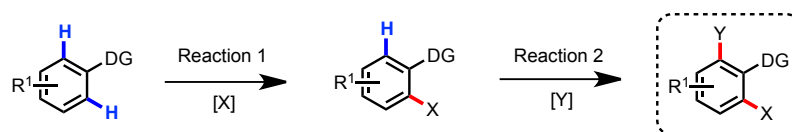
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### 3.1. INTRODUCTION

Divinylbenzene derivatives represent an important class of molecular building blocks in organic chemistry and materials science.<sup>1,2</sup> Thus, their synthesis has been an active area of research.<sup>2</sup> Indeed, shortly after the initial reports describing Pd(0)-catalysed haloarene/olefin coupling (the Mizoroki–Heck reaction),<sup>3</sup> Heck disclosed an example of divinylolation of *ortho*-dibromobenzene. Since that time, Heck<sup>4</sup> and others<sup>5</sup> have studied differential olefination of arenes containing two different halides (or pseudohalides) to synthesise unsymmetrical divinylbenzenes.<sup>6</sup>

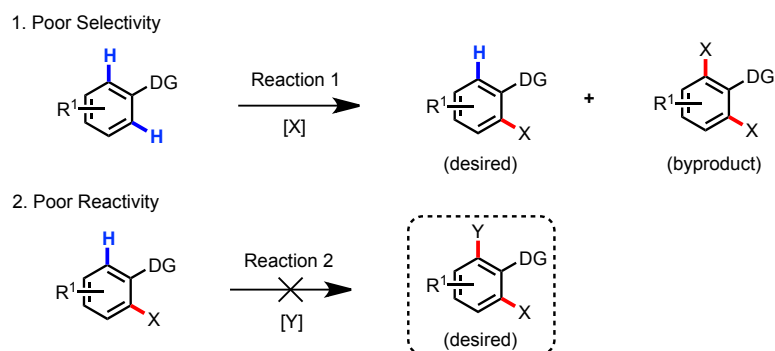
In light of the recent advances in Pd(II)-catalysed aryl C–H functionalisation reactions,<sup>7</sup> including those that directly couple aryl C–H bonds and olefins,<sup>8–17</sup> an exciting method for divinylbenzene synthesis would be to use an arene substrate containing a synthetically versatile directing group (DG) and perform sequential olefination of both *ortho*-C–H bonds (Scheme 3.1). In this way, two different alkenes could be expediently introduced in a position-selective fashion to form valuable 1,2,3-trisubstituted products,<sup>18</sup> thereby obviating the complications associated with preparing dihaloarene starting materials.



**Scheme 3.1.** Sequential directed C–H functionalisation.

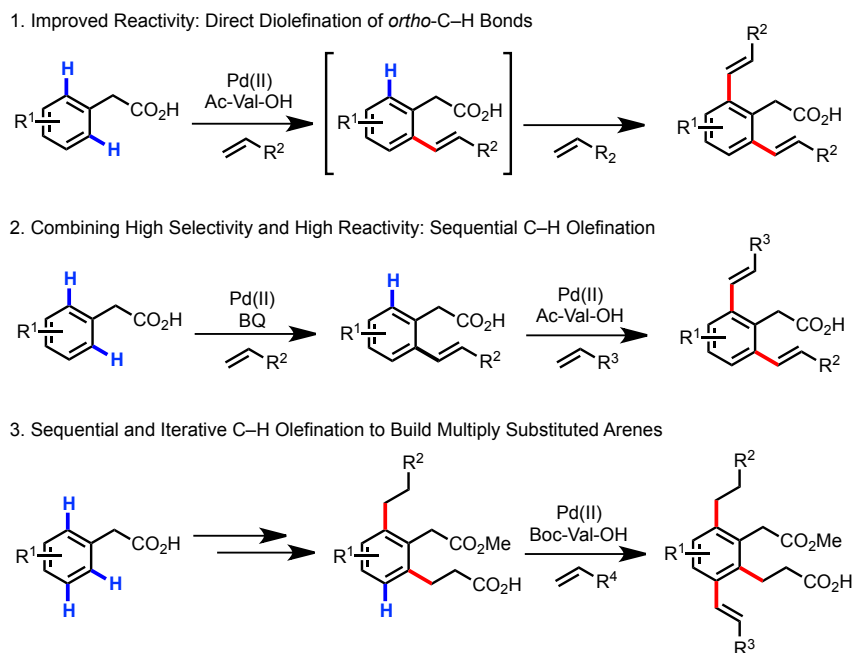
However, generally speaking, methods for sequential, directed *ortho*-C–H activation with Pd(II) remain underdeveloped<sup>19,20</sup> owing to problems rooted in both selectivity and reactivity (Scheme 3.2). In terms of selectivity, a major challenge lies in forming the mono-functionalised product in high yield while avoiding functionalising the second *ortho*-C–H bond to give the difunctionalised byproduct. Tactics to avoid this problem include

substituting the *ortho*- or *meta*-positions to block the second C–H insertion, lowering the reaction temperature or time to suboptimal levels, or using reduced equivalents of one of the reactants. However, these manoeuvres lead to limited substrate scope and/or compromised yields. Similarly, reactivity can also be a problem if the first new group is sterically bulky because it can attenuate the substrate's binding affinity for Pd(II). Alternatively, if the group is electron-withdrawing (e.g., halogen, olefin, or carboxylate), it can deactivate the aromatic ring for the second C–H activation step. Lastly, the original directing group and the newly installed functional group can coordinate to Pd(II) in a bidentate fashion, preventing the catalyst from accessing the second C–H bond.



**Scheme 3.2.** The challenges of sequential directed C–H functionalisation.

Reflecting on these two interrelated challenges, we became aware of a need for complementary catalytic systems in which the selectivity/reactivity balance of Pd(II) could be modulated through coordination of an external ligand. We report herein the realisation of this goal in the case of sequential Pd(II)-catalysed aryl C–H olefination. Furthermore, as part of our research programme to develop expedient and versatile aryl C–H functionalisation techniques, we demonstrate an example of iterative C–H functionalisation, wherein one C–H activation reaction installs a directing group for a subsequent C–H functionalisation reaction (Scheme 3.3).



**Scheme 3.3.** Outline of this chapter.

### 3.2. RESULTS AND DISCUSSION

To this end, we began by revisiting our recently disclosed *ortho*-C–H olefination reaction for phenylacetic acids.<sup>14</sup> The original conditions gave good yields and high levels of mono-selectivity with electron-rich and electron-neutral substrates. However, when we took a product from this reaction and resubmitted it to the reaction conditions in the presence of a different olefin, we observed <10% conversion of the desired unsymmetrical diolefinated product. Furthermore, we took note of the fact that during our original screening studies to develop the mono-selective reaction, we never observed more than 30% of the diolefinated byproduct, even as we extensively surveyed different reaction conditions. In light of these findings, we concluded that we faced a problem of low reactivity and needed a more reactive catalyst for the installation of a second olefin.

Encouraged by our recent success in using amino acid ligands<sup>21</sup> to enhance the reactivity of Pd(II) with electron-deficient substrates,<sup>14,22</sup> as discussed in Chapter 2, we hypothesised that we could develop a generally applicable diolefination protocol using an

optimised amino acid ligand and apply it as the second step in a two-step sequential olefination procedure. Gratifyingly, we found in our initial screening studies that an array of mono-*N*-protected amino acid ligands (10 mol%) were highly efficient in promoting diolefination with both electron-poor and electron-rich substrates, such as 4-(trifluoromethyl)phenylacetic acid (**3.1a**) and 4-methoxyphenylacetic acid (**3.1b**), fashioning the desired products in quantitative conversion after 48 h in the presence of ethyl acrylate (**3.2a**), Pd(OAc)<sub>2</sub> (5 mol%), KHCO<sub>3</sub> (2 equiv.), and *t*-AmylOH under an O<sub>2</sub> (1 atm) at 90 °C.

To determine the optimal ligand, we selected substrate **3.1a** for screening. It is worth noting that in the absence of amino acid ligands, **3.1a** was found to give only 13% yield of the mono-olefinated product **3.3a** after 48 hours. We selected an abridged reaction time of 2 h in order to see the comparative kinetic behaviour of the ligands. We found that Boc-Val-OH, Ac-Ile-OH, and Ac-Val-OH (entries 5, 11, and 12, Table 1) gave the highest conversion of **3.4a**. Ac-Ile-OH was found to be the most highly active; however, with this ligand the results varied substantially from trial to trial. Ac-Val-OH was found to be the best in terms of activity and reproducibility. Importantly, 1,4-benzoquinone (BQ), which we previously used in our mono-selective olefination procedure,<sup>14</sup> was found to decrease the reaction rate. With Ac-Val-OH, increasing the reaction time from 2 h to 6 h improved the conversion from 63% to >99% (86% isolated yield) (entry 18). Importantly, with the reaction time extended to 24 h, 2 mol% catalyst could also be used, giving 82% isolated yield of **3.4a**.

**Table 3.1.** Ligand optimisation.<sup>a</sup>

| % composition  |                       |      |      |      | % composition   |                             |      |      |          |
|----------------|-----------------------|------|------|------|-----------------|-----------------------------|------|------|----------|
| Entry          | Ligand                | 3.1a | 3.3a | 3.4a | Entry           | Ligand                      | 3.1a | 3.3a | 3.4a     |
| 1              | ---                   | 93   | 7    | 0    | 10              | Boc-Ser-OH                  | 77   | 23   | 0        |
| 2 <sup>b</sup> | BQ                    | 98   | 2    | 0    | 11 <sup>c</sup> | Ac-Val-OH                   | 4    | 33   | 63       |
| 3 <sup>b</sup> | BQ + Boc-Ile-OH       | 72   | 27   | 1    | 12 <sup>c</sup> | Ac-Ile-OH                   | 3    | 43   | 54       |
| 4              | Boc-Ile-OH            | 24   | 62   | 14   | 13              | Ac-Leu-OH                   | 54   | 43   | 3        |
| 5 <sup>c</sup> | Boc-Val-OH            | 3    | 62   | 35   | 14              | Formyl-Ile-OH               | 77   | 23   | 0        |
| 6              | Boc-Leu-OH            | 11   | 70   | 19   | 15              | Formyl-Leu-OH               | 68   | 31   | 1        |
| 7              | Boc- <i>t</i> -Leu-OH | 81   | 19   | 0    | 16              | (-)-Men-Leu-OH <sup>d</sup> | 57   | 41   | 2        |
| 8              | Boc-Ala-OH            | 25   | 65   | 10   | 17              | (-)-Men-Val-OH <sup>d</sup> | 64   | 35   | 1        |
| 9              | Boc-Phe-OH            | 47   | 49   | 4    | 18 <sup>e</sup> | Ac-Val-OH                   | 0    | 0    | >99 (86) |

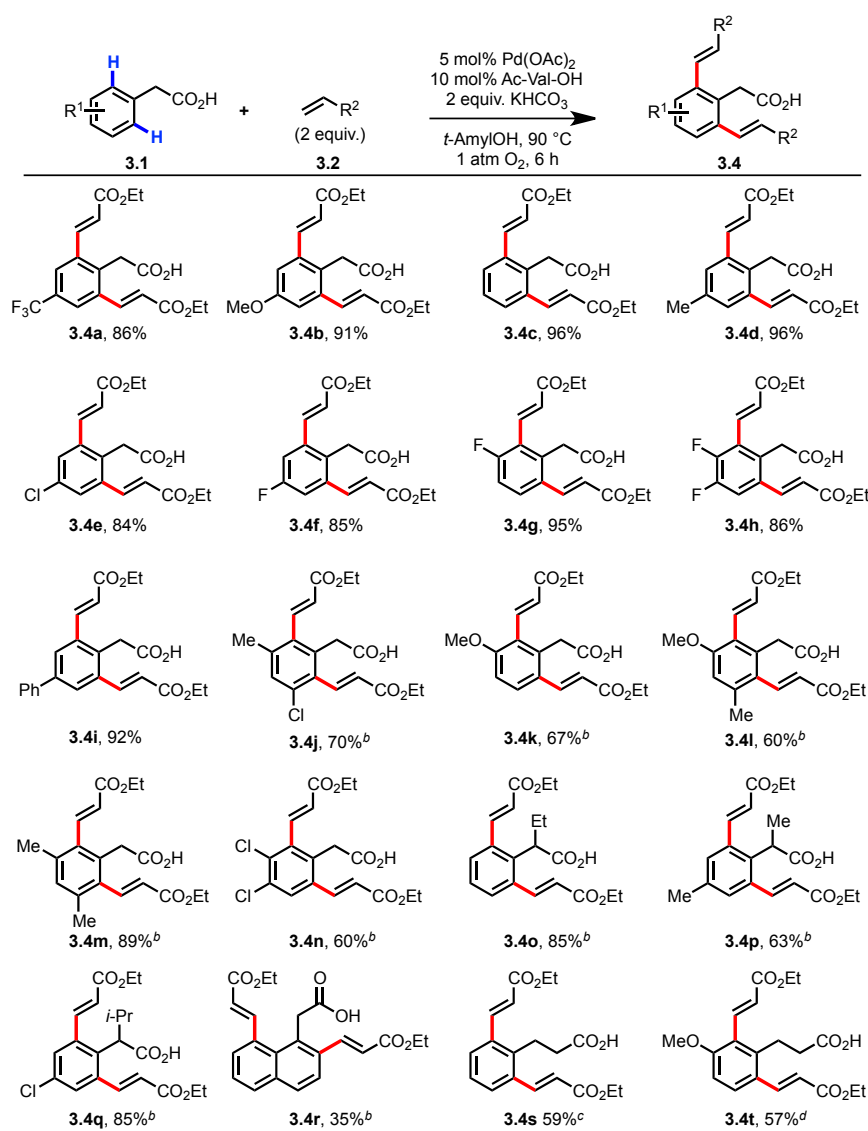
<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>b</sup> 5 mol% BQ. <sup>c</sup> Average of three trials. <sup>d</sup> (-)-Men = (-)-Menthyl(O<sub>2</sub>C). <sup>e</sup> 6 h.

Using these optimised conditions, a wide range of phenylacetic acids (**3.1**) were converted into the corresponding diolefinated products (**3.4**) (Table 3.2). The reaction worked well with electron-rich substrates containing alkoxy and alkyl groups (**3.4b**, **3.4d**, **3.4j–3.4m**, and **3.4p**) and with electron-poor substrates containing halogen atoms (**3.4a**, **3.4e–3.4h**, **3.4n**, and **3.4q**). Sterically encumbered substrates that contained bulky substituents at the  $\alpha$ -position (**3.4o–3.4q**) or at the position *meta* to the carboxylic acid directing group (**3.4j–3.4n**) required extended reaction times (48 h), but still generally gave good to excellent yields. 1-Naphthylacetic acid was also found to be a reactive substrate for diolefination (**3.4r**). Though the yield was somewhat low (35%), the second olefination proceeds via an unusual seven-membered cyclopalladated intermediate and represents a unique example of remote C–H activation at the 8-position of a naphthalene ring with a directing group at the 1-position. The reaction was also optimised for hydrocinnamic acids (see Experimental section). In these cases, Boc-Val-OH was found to be the best ligand.



Higher catalyst loadings (10–15 mol%) and extended reaction times (48–96 h) were needed to improve the yield of the diolefinated products **3.4s** and **3.4r**. In nearly all of the cases in Table 3.2 where the isolated yield is below 80%, the remaining starting material had been completely converted to the mono-olefinated product (as evidenced by  $^1\text{H}$  NMR of the crude reaction mixture).

**Table 3.2.** Substrate scope for Pd(II)-catalysed diolefination.<sup>a</sup>

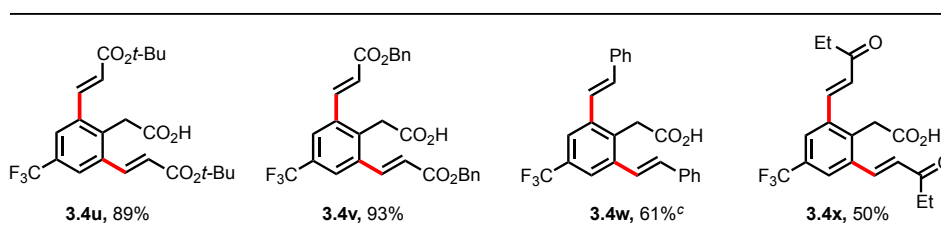


<sup>a</sup> Isolated yield. <sup>b</sup> 48 h. <sup>c</sup> 15 mol% Pd(OAc)<sub>2</sub>, 30 mol% Boc-Val-OH, 96 h. <sup>d</sup> 10 mol% Pd(OAc)<sub>2</sub>, 20 mol% Boc-Val-OH, 96 h.

Subsequently, different olefin coupling partners were examined (Table 3.3). Several acrylates (**3.2a–3.2c**) were found to be highly reactive. Styrene (**3.2d**) was also found to be a

competent coupling partner; however the reaction required extended time (48 h) and higher Pd loading (10 mol%) (**3.4w**). Ethyl vinyl ketone (**3.2e**) was found to be effective, giving 50% yield of **3.4x** after 6 h. Attempts to extend the reaction time to improve the yield of **3.4x** led to substantial product decomposition. Other olefins, such as vinyl sulfones, vinyl phosphonates, and internal alkenes were unreactive.

**Table 3.3.** Olefin scope for Pd(II)-catalysed diolefination.<sup>a,b</sup>

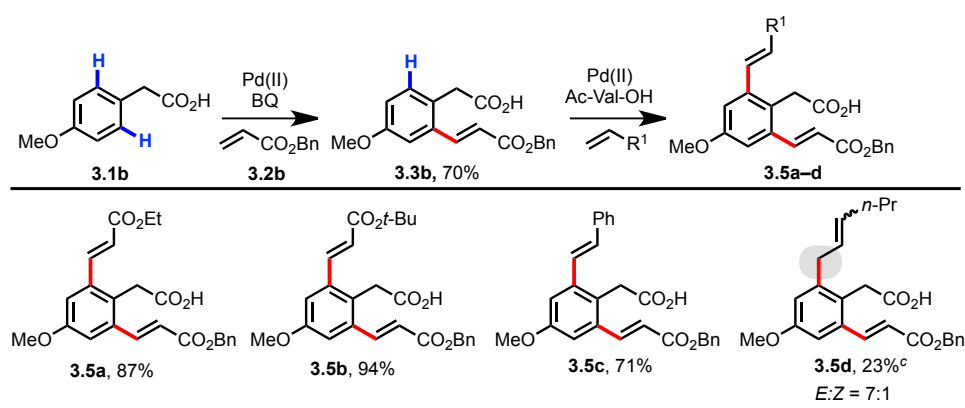


<sup>a</sup> Isolated yield. <sup>b</sup> Reaction conditions: 2 equiv. olefin, 5 mol% Pd(OAc)<sub>2</sub>, 10 mol% Ac-Val-OH, 2 equiv. KHCO<sub>3</sub>, *t*-AmylOH, 90 °C, 1 atm O<sub>2</sub>, 6 h. <sup>c</sup> 10 mol% Pd(OAc)<sub>2</sub>, 20 mol% Ac-Val-OH, 48 h.

With this robust Pd(II)-catalysed diolefination protocol in hand, we returned to our goal of effecting two sequential C–H olefination reactions to install two different alkenes (Table 3.4). We began by using our mono-selective C–H olefination reaction,<sup>14</sup> which is compatible with electron-rich and electron-neutral substrates, to couple **3.1b** and benzyl acrylate (**3.2b**), giving **3.3b** in 70% isolated yield (over 2 g prepared). Using this intermediate, we attempted to perform a second olefination reaction with representative alkene coupling partners in the presence of our more active [Pd(II)–Ac-Val-OH] catalyst. Gratifyingly, we found that orthogonally protected acrylates could be smoothly coupled to give differentially protected aromatic triacids **3.5a** and **3.5b** and that styrene (**3.2d**) could also be installed in good yield (**3.5c**). Interestingly, in accordance with our earlier observation,<sup>14</sup> when 1-hexene (**3.2f**) was used, the unique non-conjugated product **3.5d** was obtained, representing a formal C–H allylation. The isolated yield was low due to decomposition of the product during the course of the reaction. In principle, all of the

substrates used in Table 2 could be used for a similar two-step sequence. *meta*-Substituted acids offer another unique element of spatial control because the first olefin selectively reacts away from the substituent. The two-step preparation of these advanced unsymmetrical 1,2,3,5-tetrasubstituted arenes demonstrates the power of sequential aryl C–H functionalisation reactions.

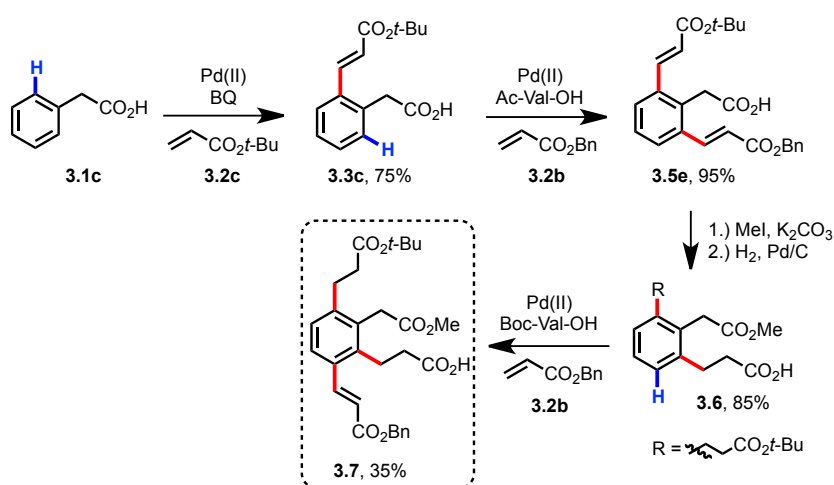
**Table 3.4.** Sequential olefination.<sup>a,b</sup>



<sup>a</sup> Isolated yield. <sup>b</sup> Reaction conditions (1<sup>st</sup> step): 2 equiv. **3.2b**, 5 mol% Pd(OAc)<sub>2</sub>, 5 mol% BQ, 2 equiv. KHCO<sub>3</sub>, *t*-AmylOH, 90 °C, 1 atm O<sub>2</sub>, 48 h. Reaction conditions (2<sup>nd</sup> step): 2 equiv. olefin, 5 mol% Pd(OAc)<sub>2</sub>, 10 mol% Ac-Val-OH, 2 equiv. KHCO<sub>3</sub>, *t*-AmylOH, 90 °C, 1 atm O<sub>2</sub>, 6 h. <sup>c</sup> 1 equiv. 1-hexene (**3.2f**).

Finally, we sought to explore the possibility of performing iterative C–H functionalisation, wherein a newly installed functional group would serve as the directing group for further C–H activation (Scheme 3.4). In particular, we envisioned using sequential olefination to install two different olefins and then, following functional group manipulations, to use one of the new moieties to direct an additional remote *ortho*-C–H functionalisation reaction. To test this idea, we prepared **3.5e** in good yield using our sequential olefination method (Scheme 3.4). Following methylation and hydrogenation, we obtained highly decorated hydrocinnamic acid **3.6**. Gratifyingly, we found that treatment of **3.6** with benzyl acrylate (**3.2b**) (2 equiv.) in the presence of Pd(OAc)<sub>2</sub> (10 mol%), Boc-Val-OH (20 mol%), and *t*-AmylOH for 12 h under O<sub>2</sub> (1 atm) effected C–H olefination to form

**3.7** in 35% isolated yield. Attempts to extend the reaction time to improve the yield led to substantial product decomposition, such that only trace quantities of **3.7** remained in solution after 24 h. Though this yield is low, given the possibility of non-productive multidentate coordination of the substrate with Pd(II), a slow reaction rate can be expected. Moreover, this case represents the most complex setting in which C–H olefination of a hydrocinnamic acid has been attempted. In the absence of Boc-Val-OH, the reaction did not proceed.



**Scheme 3.4.** Sequential and iterative C–H olefination to synthesise multiply substituted arenes. (See Experimental section for experimental details.)

### 3.3. CONCLUSION

In summary, through the discovery and development of complementary catalytic systems that exhibit tunable reactivity and selectivity, we have demonstrated a sequential C–H olefination protocol for synthesising complex divinylbenzene derivatives from simple starting materials. We first established robust reaction conditions to effect diolefination with a range of different phenylacetic and hydrocinnamic acids. We then applied these conditions as the second step in a two-step sequential C–H olefination sequence to prepare 1,2,3-trisubstituted arenes. Lastly, we used sequential C–H olefination to set the stage for a rare

example of iterative C–H functionalisation, wherein C–H activation installs a directing group for a subsequent C–H functionalisation reaction.

### 3.4. EXPERIMENTAL

#### 3.4.1. General Experimental

Unless otherwise noted, all commercial materials were used as received from commercial sources without further purification. The carboxylic acid substrates and olefin coupling partners were purchased from Acros, Sigma-Aldrich, TCI and Alfa-Aesar and were used as received. With the exception of (–)-Menthyl(O<sub>2</sub>C)-Leu-OH,<sup>23</sup> all amino acid ligands were purchased from Bachem and Novabiochem and were used as received. Palladium acetate and potassium hydrogen carbonate were purchased from Sigma-Aldrich and Fisher, respectively, and were used without further purification. All reactions were run in oil baths with the temperatures calibrated to an external thermometer. Prior to beginning an experiment, the oil bath was turned on, then allowed to equilibrate to the desired temperature for 30 minutes. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian Mercury (300 MHz and 75 MHz, respectively), Varian Inova (400 MHz and 100 MHz, respectively) and Bruker DRX (500 MHz and 125 MHz, respectively) instruments internally referenced to SiMe<sub>4</sub> or chloroform signals. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and a = apparent. High resolution mass spectra were recorded at the Centre for Mass Spectrometry, The Scripps Research Institute.

### 3.4.2. Optimisation Studies

**Ligand optimisation for Pd(II)-catalysed diolefination with 4-(trifluoromethyl)phenylacetic acid (3.1a):** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **3.1a** (102.1 mg, 0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), ligand (0.05 mmol), ethyl acrylate (**3.2a**) (106  $\mu$ L, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times$  3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 2 h. After 2 h, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The ratio of **3.1a:3.3a:3.4a** was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.72, 3.86, and 3.97 ppm, respectively). Reactions with Boc-Val-OH, Ac-Val-OH, and Ac-Ile-OH were repeated three times, and the values shown are the average results for the three experiments.

**Table 3.S1:** Results from the ligand screening experiments.<sup>a</sup>

| Entry <sup>a</sup> | Time (h) | Ligand                               | % composition |      |      |
|--------------------|----------|--------------------------------------|---------------|------|------|
|                    |          |                                      | 3.1a          | 3.3a | 3.4a |
| 1                  | 2        | ---                                  | 93            | 7    | 0    |
| 2 <sup>b</sup>     | 2        | BQ                                   | 98            | 2    | 0    |
| 3 <sup>b</sup>     | 2        | BQ + Boc-Ile-OH                      | 72            | 27   | 1    |
| 4                  | 2        | Boc-Ile-OH                           | 24            | 62   | 14   |
| 5 <sup>c</sup>     | 2        | Boc-Val-OH                           | 3             | 62   | 35   |
| 6                  | 2        | Boc-Leu-OH                           | 11            | 70   | 19   |
| 7                  | 2        | Boc- <i>t</i> -Leu-OH                | 81            | 19   | 0    |
| 8                  | 2        | Boc-Ala-OH                           | 25            | 65   | 10   |
| 9                  | 2        | Boc-Phe-OH                           | 47            | 49   | 4    |
| 10                 | 2        | Boc-Ser-OH                           | 77            | 23   | 0    |
| 11 <sup>c</sup>    | 2        | Ac-Val-OH                            | 4             | 33   | 63   |
| 12 <sup>c</sup>    | 2        | Ac-Ile-OH                            | 3             | 43   | 54   |
| 13                 | 2        | Ac-Leu-OH                            | 54            | 43   | 3    |
| 14                 | 2        | Formyl-Ile-OH                        | 77            | 23   | 0    |
| 15                 | 2        | Formyl-Leu-OH                        | 68            | 31   | 1    |
| 16                 | 2        | (-)-Menthyl(O <sub>2</sub> C)-Leu-OH | 57            | 41   | 2    |
| 17                 | 2        | (-)-Menthyl(O <sub>2</sub> C)-Val-OH | 64            | 35   | 1    |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.<sup>b</sup> 5 mol% BQ <sup>c</sup> Average of three trials.

**Reaction time optimisation for Pd(II)-catalysed diolefination with substrate 1a using Ac-Val-OH:** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **3.1a** (102.1 mg, 0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ac-Val-OH (8.0 mg, 0.05 mmol), ethyl acrylate (**3.2a**) (106 μL, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) (× 3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for the appropriate time. Subsequently, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small

aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The ratio of **3.1a**:**3.3a**:**3.4a** was determined by integration of the benzylic methylene proton signals (approximately 3.72, 3.86, and 3.97 ppm, respectively).

**Table 3.S2:** Optimisation of the diolefination protocol with respect to reaction time.<sup>a,b</sup>

| Entry          | Time (h) | % composition |             |             |
|----------------|----------|---------------|-------------|-------------|
|                |          | <b>3.1a</b>   | <b>3.3a</b> | <b>3.4a</b> |
| 1              | 1        | 5             | 63          | 32          |
| 2 <sup>c</sup> | 2        | 4             | 33          | 63          |
| 3              | 4        | 0             | 9           | 91          |
| 4              | 6        | 0             | 0           | >99 (86)    |

<sup>a</sup> Reactions condition: 5 mol% Pd(OAc)<sub>2</sub>, 10 mol% Ac-Val-OH, 2 equiv. ethyl acrylate, 2 equiv. KHCO<sub>3</sub>, *t*-AmylOH, 90 °C, 1 atm O<sub>2</sub>, 2 h. <sup>b</sup> The conversion was determined by  $^1\text{H}$  NMR analysis of the crude reaction mixture. Isolated yield is given in parentheses. <sup>c</sup> Average of three trials.

**Reaction optimisation for Pd(II)-catalysed diolefination with hydrocinnamic acid substrates (3.1s and 3.1t):** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with of the substrate (**3.1s** or **3.1t**) (0.5 mmol), Pd(OAc)<sub>2</sub>, KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), ligand (2 equiv. relative to Pd(OAc)<sub>2</sub>), ethyl acrylate (**3.2a**) (106  $\mu\text{L}$ , 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times 3$ ). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C. After the appropriate time, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The ratio of starting material to products was determined by integration of the benzylic methylene proton signals, which appear as triplets. For **3.1s**:**3.3s**:**3.4s**, the peaks appear at approximately 2.87, 3.04, and 3.18 ppm, respectively. For **3.1t**:**3.3t**:**3.4t**, the peaks appear at approximately 2.81, 2.99, and 3.15 ppm, respectively.



**Table 3.S3:** Optimisation of the diolefination protocol for substrate **3.1s**.<sup>a</sup>

| Entry            | Time (h) | Pd(OAc) <sub>2</sub> (mol%) | Ligand          | % composition |      |         |
|------------------|----------|-----------------------------|-----------------|---------------|------|---------|
|                  |          |                             |                 | 3.1s          | 3.3s | 3.4s    |
| 1                | 48       | 5                           | ---             | 95            | 5    | 0       |
| 2 <sup>b</sup>   | 48       | 5                           | BQ              | 88            | 12   | 0       |
| 3 <sup>c</sup>   | 48       | 5                           | Ac-Ile-OH       | 64            | 30   | 6       |
| 4 <sup>c</sup>   | 48       | 5                           | Ac-Val-OH       | 82            | 16   | 2       |
| 5 <sup>c</sup>   | 48       | 5                           | Boc-Leu-OH      | 50            | 30   | 20      |
| 6 <sup>c</sup>   | 48       | 5                           | Boc-Ile-OH      | 83            | 15   | 2       |
| 7 <sup>c</sup>   | 48       | 5                           | Boc-Val-OH      | 28            | 43   | 29      |
| 8 <sup>b,c</sup> | 48       | 5                           | BQ + Boc-Val-OH | 48            | 22   | 30      |
| 9 <sup>d</sup>   | 48       | 10                          | Boc-Val-OH      | 14            | 41   | 45      |
| 10 <sup>e</sup>  | 48       | 15                          | Boc-Val-OH      | 14            | 41   | 45      |
| 11 <sup>d</sup>  | 96       | 10                          | Boc-Val-OH      | 12            | 41   | 47      |
| 12 <sup>e</sup>  | 96       | 15                          | Boc-Val-OH      | 5             | 35   | 60 (59) |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.<sup>b</sup> 5 mol% BQ. <sup>c</sup> 10 mol% Ligand. <sup>d</sup> 20 mol% Ligand. <sup>e</sup> 30 mol% Ligand.

**Table 3.S4:** Optimisation of the diolefination protocol for substrate **3.1t**.

| Entry <sup>a</sup> | Time (h) | Pd(OAc) <sub>2</sub> (mol%) | Ligand     | % composition |      |         |
|--------------------|----------|-----------------------------|------------|---------------|------|---------|
|                    |          |                             |            | 3.1t          | 3.3t | 3.4t    |
| 1 <sup>b</sup>     | 48       | 5                           | BQ         | 78            | 22   | 0       |
| 2 <sup>c</sup>     | 48       | 5                           | Ac-Ile-OH  | 39            | 59   | 2       |
| 3 <sup>c</sup>     | 48       | 5                           | Ac-Val-OH  | 18            | 63   | 19      |
| 4 <sup>c</sup>     | 48       | 5                           | Boc-Leu-OH | 2             | 62   | 36      |
| 5 <sup>c</sup>     | 48       | 5                           | Boc-Ile-OH | 6             | 64   | 30      |
| 6 <sup>c</sup>     | 48       | 5                           | Boc-Val-OH | 2             | 54   | 44      |
| 7 <sup>c</sup>     | 96       | 5                           | Boc-Val-OH | 0             | 50   | 50      |
| 8 <sup>d</sup>     | 96       | 10                          | Boc-Val-OH | 0             | 42   | 58 (57) |
| 9 <sup>e</sup>     | 96       | 15                          | Boc-Val-OH | 0             | 45   | 55      |

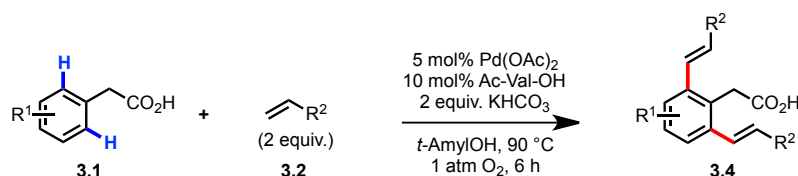
<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

<sup>b</sup> 5 mol% BQ. <sup>c</sup> 10 mol% Ligand. <sup>d</sup> 20 mol% Ligand. <sup>e</sup> 30 mol% Ligand.

### 3.4.3. Optimised General Procedure

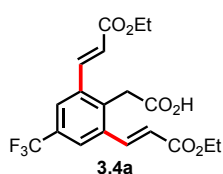
**General procedure for Pd(II)-catalysed diolefination of phenylacetic acids:** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the phenylacetic acid substrate (**3.1**) (0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ac-Val-OH (8.0 mg, 0.05 mmol), the olefin coupling partner (**3.2**) (1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) (× 3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 6 h (or 48 h in the case of less reactive substrates, see Tables 2 and 3). Subsequently, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The organic layers were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrate *in vacuo*. The resulting residue was

purified by silica gel flash column chromatography using hexanes/EtOAc (with 2–5% HOAc) as the eluent.



**Scheme 3.S1:** Dioléfination of phenylacetic acid substrates.

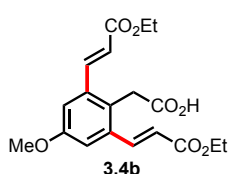
### 3.4.4. Characterisation of New Compounds:



#### 2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-4-

(trifluoromethyl)phenyl)acetic acid (**3.4a**): The title compound was prepared using the general procedure and was obtained as an off-white

solid (172 mg, 86% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (d,  $J = 16.0$  Hz, 2H), 7.79 (s, 2H), 6.42 (d,  $J = 16.0$  Hz, 2H), 4.29 (q,  $J = 7.2$  Hz, 4H), 3.98 (s, 2H), 1.35 (t,  $J = 6.8$  Hz, 6H);  $^{13}\text{C NMR}$  (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  171.21, 166.40, 141.03, 138.00, 137.67, 130.56 (q,  $J_{\text{C-F}} = 32.5$  Hz), 125.54 (q,  $J_{\text{C-F}} = 3.7$  Hz), 124.72 (q,  $J_{\text{C-F}} = 270.7$  Hz), 124.45, 61.18, 35.24, 14.53; **IR** (neat)  $\nu$  2984, 2924, 1714 (br), 1638, 1316, 1281, 1166 (br), 1127, 1037, 978, 869  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{19}\text{F}_3\text{O}_6$   $[\text{M}+\text{H}]^+$  401.1206, found 401.1206.

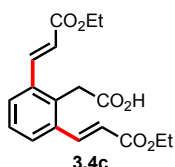


#### 2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-4-methoxyphenyl)acetic

acid (**3.4b**): The title compound was prepared using the general procedure and was obtained as an off-white solid (165 mg, 91% yield).

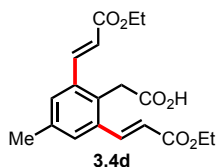
$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.93 (d,  $J = 16.0$  Hz, 2H), 7.10 (s, 2H), 6.33 (d,  $J = 16.0$  Hz, 2H), 4.26 (q,  $J = 7.5$  Hz, 4H), 3.86 (s, 2H), 3.84 (s, 3H), 1.33 (t,  $J = 7.5$  Hz, 6H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  175.07, 166.46, 158.80, 141.71, 136.79, 124.40, 122.27, 113.97, 60.80, 55.42, 33.74, 14.24; **IR** (neat)  $\nu$  2981, 2925, 1705, 1621, 1582, 1476, 1260, 1161,

1080, 1042, 979, 867, 811  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{23}\text{O}_7$   $[\text{M}+\text{H}]^+$  363.1438, found 363.1448.



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)phenyl)acetic acid (3.4c):** The

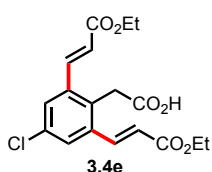
title compound was prepared using the general procedure and was obtained as an off-white solid (160 mg, 96% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (d,  $J = 15.6$  Hz, 2H), 7.58 (d,  $J = 8.0$  Hz, 2H), 7.34 (t,  $J = 7.6$  Hz, 1H), 6.35 (d,  $J = 15.6$  Hz, 2H), 4.26 (q,  $J = 7.2$  Hz, 4H), 3.94 (s, 2H), 1.33 (t,  $J = 7.2$  Hz, 6H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.20, 166.56, 141.64, 135.63, 131.82, 128.56, 128.15, 122.15, 60.80, 34.46, 14.22; **IR** (neat)  $\nu$  2982, 2939, 1707 (br), 1631, 1446, 1368, 1313, 1274, 1164 (br), 1034, 976, 800  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_6$   $[\text{M}+\text{H}]^+$  333.1333, found 333.1348.



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-4-methylphenyl)acetic acid**

**(3.4d):** The title compound was prepared using the general procedure and

was obtained as an off-white solid (166 mg, 96% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (d,  $J = 15.6$  Hz, 2H), 7.41 (s, 2H), 6.34 (d,  $J = 15.6$  Hz, 2H), 4.27 (q,  $J = 7.2$  Hz, 4H), 3.91 (s, 2H), 2.37 (s, 3H), 1.33 (t,  $J = 7.2$  Hz, 3H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.17, 166.59, 141.78, 137.67, 135.36, 129.25, 129.11, 121.72, 60.68, 34.01, 20.95, 14.16; **IR** (neat)  $\nu$  3020, 2982, 1703 (br), 1633, 1312, 1274, 1178 (br), 1039, 974, 853  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_6$   $[\text{M}+\text{H}]^+$  347.1489, found 347.1493.

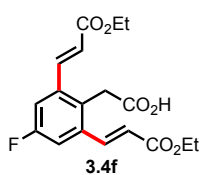


**2-(4-chloro-2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)phenyl)acetic acid**

**(3.4e):** The title compound was prepared using the general procedure and

was obtained as an off-white solid (154 mg, 84% yield).  **$^1\text{H}$  NMR** (400

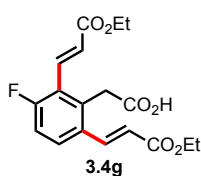
MHz, CDCl<sub>3</sub>)  $\delta$  7.91 (d,  $J$  = 15.6 Hz, 2H), 7.55 (s, 2H), 6.35 (d,  $J$  = 15.6 Hz, 2H), 4.27 (q,  $J$  = 7.2 Hz, 4H), 3.89 (s, 2H), 1.33 (t,  $J$  = 7.2 Hz, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  174.32, 166.29, 140.44, 137.31, 134.13, 130.24, 128.15, 123.27, 61.01, 34.04, 14.20; IR (neat)  $\nu$  2983, 2938, 1714 (br), 1637, 1368, 1313, 1272, 1179, 1036, 977, 911, 863 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>18</sub>H<sub>19</sub>ClO<sub>6</sub> [M+H]<sup>+</sup> 367.0948, [(M+2)+H]<sup>+</sup> 369.0919, found 367.0938, 369.0912, [M+H]<sup>+</sup>:[(M+2)+H]<sup>+</sup> = 3:1.



**2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-4-fluorophenyl)acetic acid**

**(3.4f):** The title compound was prepared using the general procedure and was obtained as an off-white solid (149 mg, 85% yield). <sup>1</sup>H NMR (400

MHz, CDCl<sub>3</sub>)  $\delta$  7.93 (d,  $J$  = 16.0 Hz, 2H), 7.28 (d,  $J$  = 9.2 Hz, 2H), 6.34 (d,  $J$  = 15.6 Hz, 2H), 4.27 (q,  $J$  = 7.2 Hz, 4H), 3.90 (s, 2H), 1.33 (t,  $J$  = 7.2 Hz, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  174.39, 166.28, 161.80 (d,  $J_{C-F}$  = 246.3 Hz), 140.61 (d,  $J_{C-F}$  = 2.1 Hz), 137.72 (d,  $J_{C-F}$  = 7.8 Hz), 127.87, 123.19, 115.13 (d,  $J_{C-F}$  = 22.3 Hz), 61.00, 33.86, 14.21; IR (neat)  $\nu$  2983, 2940, 1707 (br), 1634, 1595, 1446, 1368, 1313, 1270, 1175 (br), 1035, 975, 862 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>18</sub>H<sub>19</sub>FO<sub>6</sub> [M+H]<sup>+</sup> 351.1238, found 351.1254.

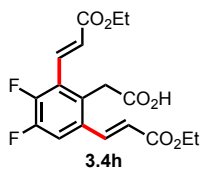


**2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-3-fluorophenyl)acetic acid**

**(3.4g):** The title compound was prepared using the general procedure and was obtained as an off-white solid (166 mg, 95% yield). <sup>1</sup>H NMR (400

MHz, CDCl<sub>3</sub>)  $\delta$  7.91 (d,  $J$  = 16.0 Hz, 1H), 7.71 (d,  $J$  = 16.0 Hz, 1H), 7.56 (at,  $J$  = 8.0 Hz, 1H), 7.10 (at,  $J$  = 9.6 Hz, 1H), 6.49 (d,  $J$  = 16.0 Hz, 1H), 6.31 (d,  $J$  = 16.0 Hz, 1H), 4.30–4.26 (m, 4H), 3.94 (s, 2H), 1.34 (t,  $J$  = 6.8 Hz, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  174.17, 166.69, 166.63, 161.78 (d,  $J_{C-F}$  = 254.8 Hz), 140.92, 135.24, 134.26 (d,  $J_{C-F}$  = 2.8 Hz), 131.58 (d,  $J_{C-F}$  = 3.6 Hz), 129.22 (d,  $J_{C-F}$  = 10.0 Hz), 123.69 (d,  $J_{C-F}$  = 12.5 Hz), 121.76,

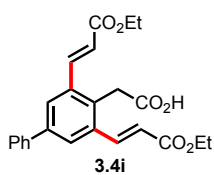
115.85 (d,  $J_{C-F} = 23.6$  Hz), 60.97, 60.90, 34.89, 14.19; **IR** (neat)  $\nu$  2983, 2940, 1708 (br), 1631, 1475, 1368, 1311, 1259, 1158 (br), 1158, 1033, 979, 826  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{18}\text{H}_{19}\text{FO}_6$   $[\text{M}+\text{H}]^+$  351.1238, found 351.1245.



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-3,4-difluorophenyl)acetic acid**

**acid (3.4h):** The title compound was prepared using the general procedure and was obtained as an off-white solid (158 mg, 86% yield).  **$^1\text{H}$  NMR**

(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.86 (d,  $J = 15.6$  Hz, 1H), 7.66 (d,  $J = 16.0$  Hz, 1H), 7.38 (dd,  $J_1 = 10.4$  Hz,  $J_2 = 8.0$  Hz, 1H), 6.50 (d,  $J = 16.0$  Hz, 1H), 6.29 (d,  $J = 15.6$  Hz, 1H), 4.31–4.24 (m, 4H), 3.88 (s, 2H), 1.36–1.31 (m, 6H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.35, 166.41, 166.16, 150.38 (dd,  $J_{I,C-F} = 245.3$  Hz,  $J_{2,C-F} = 13.9$  Hz), 150.06 (dd,  $J_{I,C-F} = 252.4$ ,  $J_{2,C-F} = 13.6$  Hz), 140.41, 135.40 (d,  $J_{C-F} = 2.9$  Hz), 132.98 (dd,  $J_{I,C-F} = 6.5$  Hz,  $J_{2,C-F} = 4.5$  Hz), 131.85 (d,  $J_{C-F} = 2.8$  Hz), 128.09 (d,  $J_{C-F} = 8.8$  Hz), 126.75 (d,  $J_{C-F} = 9.5$  Hz), 123.51, 116.79 (d,  $J_{C-F} = 18.0$  Hz), 61.34, 61.11, 35.23, 14.54, 14.50; **IR** (neat)  $\nu$  2984, 2940, 1710 (br), 1635, 1479, 1309, 1270, 1253, 1176 (br), 1094, 1037, 976, 860  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{18}\text{H}_{18}\text{F}_2\text{O}_6$   $[\text{M}+\text{H}]^+$  369.1144, found 369.1136.

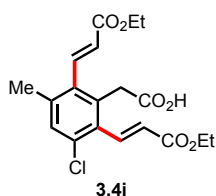


**2-(3,5-bis((E)-3-ethoxy-3-oxoprop-1-enyl)biphenyl-4-yl)acetic acid**

**(3.4i):** The title compound was prepared using the general procedure and was obtained as an off-white solid (188 mg, 92% yield).  **$^1\text{H}$  NMR** (400

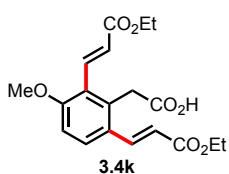
MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J = 15.6$  Hz, 2H), 7.79 (s, 2H), 7.59 (d,  $J = 7.2$  Hz, 2H), 7.47 (t,  $J = 8.0$  Hz, 2H), 7.40 (t,  $J = 7.2$  Hz, 1H), 6.44 (d,  $J = 15.6$  Hz, 2H), 4.28 (q,  $J = 7.2$  Hz, 4H), 3.99 (s, 2H), 1.34 (t,  $J = 7.2$  Hz, 6H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.68, 166.55, 141.74, 141.17, 139.51, 136.10, 130.64, 128.95, 128.01, 127.26, 127.05, 122.42, 60.86, 34.21, 14.25; **IR** (neat)  $\nu$  2983, 2938, 1701 (br), 1635, 1307, 1274, 1243, 1177 (br), 1038,

972, 906, 864  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{24}\text{H}_{24}\text{O}_6$   $[\text{M}+\text{H}]^+$  409.1646, found 409.1644.



**2-(3-chloro-2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-5-methylphenyl)acetic acid (3.4j):** The title compound was prepared using the general procedure and was obtained as an off-white solid (133 mg, 70% yield).

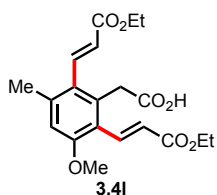
**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 (d,  $J = 16.0$  Hz, 1H), 7.69 (d,  $J = 16.0$  Hz, 1H), 7.27 (s, 1H), 6.16 (d,  $J = 16.0$  Hz, 1H), 6.01 (d,  $J = 16$  Hz, 1H), 4.27 (q,  $J = 6.8$  Hz, 4H), 3.77 (s, 2H), 2.29 (s, 3H), 1.33 (t,  $J = 6.8$  Hz, 6H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.28, 166.00, 165.92, 141.96, 140.37, 137.96, 135.12, 133.17, 132.62, 131.67, 130.56, 126.67, 126.41, 60.93, 60.90, 37.01, 20.72, 14.17; **IR** (neat)  $\nu$  2982, 1709 (br), 1642, 1447, 1368, 1303, 1279, 1174 (br), 1031, 981, 910, 868, 729  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{21}\text{ClO}_6$   $[\text{M}+\text{H}]^+$  381.1105,  $[(\text{M}+2)+\text{H}]^+$  383.1075, found 381.1093, 383.1057,  $[\text{M}+\text{H}]^+:[(\text{M}+2)+\text{H}]^+ = 3:1$ .



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-3-methoxyphenyl)acetic acid (3.4k):** The title compound was prepared using the general procedure and was obtained as an off-white solid (121 mg, 67% yield).

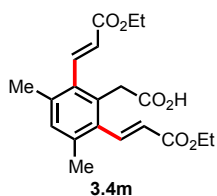
**$^1\text{H}$  NMR** (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.92 (d,  $J = 16.0$  Hz, 1H), 7.79 (d,  $J = 16.0$  Hz, 1H), 7.59 (d,  $J = 9.0$  Hz, 1H), 6.91 (d,  $J = 9.0$  Hz, 1H), 6.44 (d,  $J = 16.0$  Hz, 1H), 6.27 (d,  $J = 16.0$  Hz, 1H), 4.26 (q,  $J = 7.0$  Hz, 2H), 4.25 (q,  $J = 7.0$  Hz, 2H), 3.94 (s, 2H), 3.88 (s, 3H), 1.33 (t,  $J = 7.0$  Hz, 3H), 1.32 (t,  $J = 7.0$  Hz, 3H);  **$^{13}\text{C}$  NMR** (125 MHz,  $\text{CDCl}_3$ )  $\delta$  174.45, 167.10, 166.95, 159.53, 141.58, 138.42, 133.55, 128.86, 127.71, 125.07, 124.76, 119.52, 110.37, 60.66, 60.62, 55.72, 35.12, 14.25; **IR** (neat)  $\nu$  2981, 2940, 1705 (br), 1624, 1583, 1476,

1367, 1259, 1159 (br), 1077, 1033, 977, 812  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_7$   $[\text{M}+\text{H}]^+$  363.1438, found 363.1440.



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-3-methoxy-5-methylphenyl)acetic acid (3.4l):** The title compound was prepared using

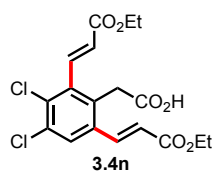
the general procedure and was obtained as an off-white solid (113 mg, 60% yield).  **$^1\text{H}$  NMR** (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.74 (d,  $J = 16.0$  Hz, 2H), 6.76 (s, 1H), 6.51 (d,  $J = 16.0$  Hz, 1H), 5.99 (d,  $J = 16.0$  Hz, 1H), 4.29–4.22 (m, 4H), 3.87 (s, 3H), 3.86 (s, 2H), 2.34 (s, 3H), 1.34–1.30 (m, 6H);  **$^{13}\text{C}$  NMR** (125 MHz,  $\text{CDCl}_3$ )  $\delta$  174.80, 167.39, 166.31, 158.12, 142.83, 139.11, 138.17, 132.60, 128.66, 125.39, 124.05, 121.97, 112.37, 60.71, 60.51, 55.54, 36.24, 21.74, 14.28, 14.25; **IR** (neat)  $\nu$  2981, 2939, 1711 (br), 1626, 1590, 1466, 1368, 1303, 1284, 1176 (br), 1123, 1034, 983, 868  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{20}\text{H}_{24}\text{O}_7$   $[\text{M}+\text{H}]^+$  377.1595, found 377.1590.



**2-(2,6-bis((E)-3-ethoxy-3-oxoprop-1-enyl)-3,5-dimethylphenyl)acetic acid (3.4m):** The title compound was prepared using the general procedure and was obtained as an off-white solid (160 mg, 89% yield).

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.75 (d,  $J = 15.6$  Hz, 2H), 7.06 (s, 1H), 6.00 (d,  $J = 15.6$  Hz, 2H), 4.25 (q,  $J = 6.8$  Hz, 4H), 3.75 (s, 2H), 2.28 (s, 6H), 1.32 (t,  $J = 7.2$  Hz, 6H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.25, 166.21, 142.92, 136.38, 133.74, 131.77, 129.66, 125.60, 60.74, 36.60, 20.84, 14.23; **IR** (neat)  $\nu$  2981, 1710 (br), 1638, 1367, 1280, 1165 (br), 1032, 988, 870  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{20}\text{H}_{24}\text{O}_6$   $[\text{M}+\text{H}]^+$  361.1646, found 361.1647.

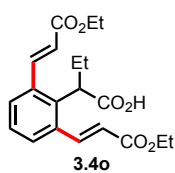




**2-(3,4-dichloro-2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)phenyl)acetic acid (3.4n):**

The title compound was prepared using the general procedure and was obtained as an off-white solid (120 mg, 60% yield).

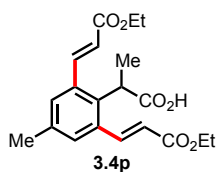
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.81 (d, *J* = 16.0 Hz, 1H), 7.70 (d, *J* = 16.0 Hz, 1H), 7.66 (s, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 6.12 (d, *J* = 16.0 Hz, 1H), 4.31–4.24 (m, 4H), 3.83 (s, 2H), 1.36–1.31 (m, 6H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 174.21, 166.23, 165.65, 140.38, 134.86, 133.06, 132.97, 130.82, 128.09, 127.42, 123.12, 61.17, 61.07, 35.79, 14.15; **IR** (neat) ν 2983, 2938, 1714 (br), 1636, 1424, 1394, 1369, 1309, 1280, 1180 (br), 1037, 976, 864 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>18</sub>H<sub>18</sub>Cl<sub>2</sub>O<sub>6</sub> [M+H]<sup>+</sup> 401.0559, [(M+2)+H]<sup>+</sup> 403.0529, [(M+4)+H]<sup>+</sup> 405.0500, found 401.0548, 403.0535, 405.0516 [M+H]<sup>+</sup>:[(M+2)+H]<sup>+</sup>:[(M+4)+H]<sup>+</sup> = 9:6:1.



**2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)phenyl)butanoic acid (3.4o):**

The title compound was prepared using the general procedure and was obtained as a yellow oil (153 mg, 85% yield).

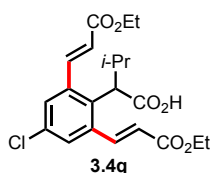
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.02 (d, *J* = 15.6 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 1H), 6.28 (d, *J* = 15.6 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 4H), 4.07 (dd, *J*<sub>1</sub> = 8.8 Hz, *J*<sub>2</sub> = 6.0 Hz, 1H), 2.38–2.29 (m, 1H), 1.85–1.74 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 6H), 0.80 (t, *J* = 7.2 Hz, 3H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 178.18, 166.37, 142.59, 136.88, 135.56, 129.16, 127.78, 122.09, 60.69, 47.42, 25.00, 14.14, 12.01; **IR** (neat) ν 2977, 2936, 1707 (br), 1631, 1367, 1308, 1268, 1163 (br), 1032, 982, 909 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>20</sub>H<sub>24</sub>O<sub>6</sub> [M+H]<sup>+</sup> 361.1646, found 361.1639.



**2-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-4-methylphenyl)propanoic**

**acid (3.4p):** The title compound was prepared using the general procedure and was obtained as a colourless oil (114 mg, 63% yield).  $^1\text{H}$

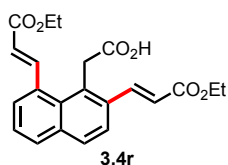
**NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.93 (d,  $J = 16.0$  Hz, 2H), 7.35 (s, 2H), 6.29 (d,  $J = 16.0$  Hz, 2H), 4.27–4.21 (m, 5H), 2.35 (s, 3H), 1.50 (d,  $J = 7.2$  Hz, 3H), 1.32 (t,  $J = 7.2$  Hz, 6H);  $^{13}\text{C}$  **NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  178.14, 166.35, 142.10, 137.47, 135.61, 134.75, 129.95, 122.19, 60.70, 39.97, 20.92, 17.35, 14.23; **IR** (neat)  $\nu$  2982, 2935, 1709 (br), 1632, 1448, 1368, 1310, 1176 (br, 1040, 980, 859  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{20}\text{H}_{24}\text{O}_6$   $[\text{M}+\text{H}]^+$  361.1646, found 361.1648.



**2-(4-chloro-2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)phenyl)-3-**

**methylbutanoic acid (3.4q):** The title compound was prepared using the general procedure and was obtained as a yellow oil (174 mg, 85% yield).

$^1\text{H}$  **NMR** (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.13 (d,  $J = 16.0$  Hz, 2H), 7.46 (s, 2H), 6.25 (d,  $J = 16.0$  Hz, 2H), 4.26 (q,  $J = 7.0$  Hz, 4H), 3.72 (d,  $J = 11.0$  Hz, 1H), 2.56–2.48 (m, 1H), 1.33 (t,  $J = 7.0$  Hz, 6H), 1.15 (d,  $J = 6.5$  Hz, 3H), 0.53 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  **NMR** (125 MHz,  $\text{CDCl}_3$ )  $\delta$  176.11, 166.04, 142.06, 138.09, 134.56, 133.77, 128.92, 123.29, 60.86, 53.51, 29.63, 22.80, 19.92, 14.21; **IR** (neat)  $\nu$  2968, 2933, 1716 (br), 1636, 1368, 1310, 1178 (br), 1036, 977, 863  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{25}\text{ClO}_6$   $[\text{M}+\text{H}]^+$  409.1418,  $[(\text{M}+2)+\text{H}]^+$  411.1388, found 409.1421, 411.1412,  $[\text{M}+\text{H}]^+:[(\text{M}+2)+\text{H}]^+ = 3:1$ .

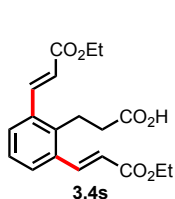


**2-(2,8-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)naphthalen-1-yl)acetic**

**acid (3.4r):** The title compound was prepared using the general procedure and was obtained as a yellow oil (67 mg, 35% yield).  $^1\text{H}$

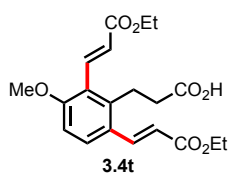
**NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.41 (d,  $J = 16.0$  Hz, 1H), 8.08 (d,  $J = 16.0$  Hz, 1H), 7.83–7.81

(m, 2H), 7.68 (d,  $J = 8.8$  Hz, 1H), 7.50–7.44 (m, 2H), 6.47 (d,  $J = 16.0$  Hz, 1H), 6.28 (d,  $J = 16.0$  Hz, 1H), 4.36 (s, 2H), 4.30–4.22 (m, 4H), 1.35–1.28 (m, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  173.88, 166.52, 147.73, 142.03, 135.32, 134.81, 134.18, 130.80, 130.00, 129.59, 129.45, 126.08, 124.45, 122.52, 120.61, 60.79, 37.33, 29.69, 14.27, 14.20; IR (neat)  $\nu$  2924, 2854, 1709 (br), 1628, 1369, 1303, 1243, 1175 (br), 1033, 828  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{22}\text{H}_{22}\text{O}_6$   $[\text{M}+\text{H}]^+$  383.1489, found 383.1487.



**3-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)phenyl)propanoic acid (3.4s):**

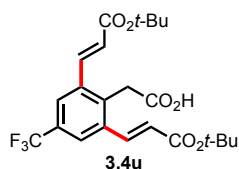
The title compound was prepared using the general procedure and was obtained as an off-white solid (102 mg, 59% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (d,  $J = 16.0$  Hz, 2H), 7.56 (d,  $J = 8.0$  Hz, 2H), 7.28 (t,  $J = 8.0$  Hz, 1H), 6.35 (d,  $J = 16.0$  Hz, 2H), 4.28 (q,  $J = 7.2$  Hz, 4H), 3.23 (t,  $J = 8.0$  Hz, 2H), 2.54 (t,  $J = 8.0$  Hz, 2H), 1.34 (t,  $J = 7.2$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.93, 166.61, 141.66, 138.55, 134.62, 128.70, 127.33, 121.80, 60.75, 34.55, 23.91, 14.28; IR (neat)  $\nu$  2981, 2924, 1710 (br), 1630, 1368, 1312, 1271, 1172 (br), 1042, 982, 869, 802  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_6$   $[\text{M}+\text{H}]^+$  347.1489, found 347.1490.



**3-(2,6-bis((*E*)-3-ethoxy-3-oxoprop-1-enyl)-3-methoxyphenyl)propanoic acid (3.4t):**

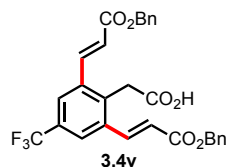
The title compound was prepared using the general procedure and was obtained as an off-white solid (107 mg, 57% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.00 (d,  $J = 16.0$  Hz, 1H), 7.82 (d,  $J = 16.0$  Hz, 1H), 7.56 (d,  $J = 8.8$  Hz, 1H), 6.86 (d,  $J = 8.8$  Hz, 1H), 6.56 (d,  $J = 16.0$  Hz, 1H), 6.27 (d,  $J = 16.0$  Hz, 1H), 4.30–4.25 (m, 4H), 3.89 (s, 3H), 3.23 (t,  $J = 8.0$  Hz, 2H), 2.54 (t,  $J = 8.0$  Hz, 2H), 1.34 (t,  $J = 7.2$  Hz, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.43, 167.38, 166.98, 159.80, 141.62, 140.67, 137.73, 129.13, 126.64, 124.72, 123.06, 119.27,

109.75, 60.60, 55.67, 34.54, 24.37, 14.28; **IR** (neat)  $\nu$  2981, 2925, 1705 (br), 1621, 1582, 1476, 1367, 1300, 1260, 1161 (br), 1080, 1042, 979, 811  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{20}\text{H}_{24}\text{O}_7$   $[\text{M}+\text{H}]^+$  377.1595, found 377.1592.



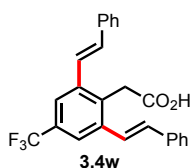
**2-(2,6-bis((E)-3-tert-butoxy-3-oxoprop-1-enyl)-4-(trifluoromethyl)phenyl)acetic acid (3.4u):** The title compound was prepared using the general procedure and was obtained as an off-white

solid (203 mg, 89% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.89 (d,  $J = 15.6$  Hz, 2H), 7.77 (s, 2H), 6.35 (d,  $J = 15.6$  Hz, 2H), 3.97 (s, 2H), 1.53 (s, 18H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  173.40, 165.57, 139.56, 136.77, 135.13, 130.50 (q,  $J_{\text{C-F}} = 32.8$  Hz), 125.49, 124.68 (q,  $J_{\text{C-F}} = 3.3$  Hz), 123.45 (q,  $J_{\text{C-F}} = 271.2$  Hz), 81.52, 34.48, 28.10; **IR** (neat)  $\nu$  2980, 2935, 1709 (br), 1637, 1321, 1283, 1230, 1147 (br), 1128 (br), 977, 922, 847  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{23}\text{H}_{27}\text{F}_3\text{O}_6$   $[\text{M}+\text{Na}]^+$  479.1652, found 479.1660.



**2-(2,6-bis((E)-3-(benzyloxy)-3-oxoprop-1-enyl)-4-(trifluoromethyl)phenyl)acetic acid (3.4v):** The title compound was prepared using the general procedure and was obtained as an off-white

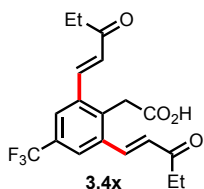
solid (244 mg, 93% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 (d,  $J = 15.6$  Hz, 2H), 7.79 (s, 2H), 7.41–7.32 (m, 10H), 6.47 (d,  $J = 15.6$  Hz, 2H), 5.23 (s, 4H), 3.97 (s, 2H);  **$^{13}\text{C}$  NMR** (100 MHz,  $((\text{CD}_3)_2\text{CO})$ )  $\delta$  171.10, 166.28, 141.60, 138.21, 137.68, 137.32, 130.63 (q,  $J_{\text{C-F}} = 32.7$  Hz), 129.33, 128.98, 128.93, 125.75 (q,  $J_{\text{C-F}} = 3.7$  Hz), 124.75 (q,  $J_{\text{C-F}} = 270.6$  Hz), 124.22, 66.86, 35.30; **IR** (neat)  $\nu$  3034, 2955, 1712 (br), 1637, 1455, 1377, 1353, 1313, 1278, 1228, 1161 (br), 1126, 1018, 975, 920  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{29}\text{H}_{23}\text{F}_3\text{O}_6$   $[\text{M}+\text{H}]^+$  525.1519, found 525.1524.



**2-(2,6-distyryl-4-(trifluoromethyl)phenyl)acetic acid (3.4w):** The title

compound was prepared using the general procedure and was obtained as an off-white solid (125 mg, 61% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$

7.76 (s, 2H), 7.52 (d,  $J = 7.2$  Hz, 4H), 7.42–7.29 (m, 8H), 7.02 (d,  $J = 16.0$  Hz, 2H), 3.99 (s, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.00, 139.20, 136.59, 134.05, 132.40, 130.31 (q,  $J_{\text{C-F}} = 32.1$ ), 128.80, 128.41, 126.87, 124.97, 124.00 (q,  $J_{\text{C-F}} = 271.2$ ), 122.29 (q,  $J_{\text{C-F}} = 3.7$ ), 35.13; IR (neat)  $\nu$  3027, 2924, 1694 (br), 1394, 1236, 1166 (br), 1120, 961, 923  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{25}\text{H}_{19}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  409.141, found 409.1404.



**2-(2,6-bis((E)-3-oxopent-1-enyl)-4-(trifluoromethyl)phenyl)acetic acid**

**(3.4x):** The title compound was prepared using the general procedure and

was obtained as an off-white solid (93 mg, 50% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.88 (d,  $J = 15.6$  Hz, 2 H), 7.80 (s, 2 H), 6.71 (d,  $J = 16.0$

Hz), 3.97 (s, 2 H), 2.71 (q,  $J = 7.2$  Hz, 4 H), 1.17 (t,  $J = 7.2$  Hz, 6 H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  200.35, 173.31, 137.69, 137.01, 135.73, 130.73 (q,  $J_{\text{C-F}} = 33.0$  Hz), 130.71, 124.81 (q,  $J = 3.5$  Hz), 123.40 (q,  $J_{\text{C-F}} = 271.1$  Hz), 34.98, 34.72, 7.90; IR (neat)  $\nu$  2980, 2941, 1730, 1697, 1671 (br), 1611, 1460, 1350, 1230, 1167, 1126 (br), 1048, 977, 899, 860, 731  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{19}\text{F}_3\text{O}_4$   $[\text{M}+\text{H}]^+$  369.1308, found 369.1308.

### 3.4.5. Sequential Olefination Studies:



**(E)-2-(2-(3-(benzyloxy)-3-oxoprop-1-enyl)-4-methoxyphenyl)acetic**

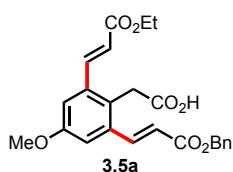
**acid (3.3b):** A 250 mL Schlenk-type sealed tube (with a Teflon high

pressure valve and side arm) equipped with a magnetic stir bar was charged with the 4-methoxyphenylacetic acid (**3.1b**) (1.66 g, 10 mmol),  $\text{Pd}(\text{OAc})_2$  (112.3 mg, 0.5 mmol),  $\text{KHCO}_3$  (2.00 g, 20 mmol), BQ (54.0 mg, 0.5 mmol), benzyl acrylate (**2b**) (3.0 mL, 20

mmol), and *t*-AmylOH (25 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times$  3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 24 h, at which point the reaction vessel was recharged with O<sub>2</sub> using the procedure described above. The reaction was allowed to stir at 90 °C for an additional 24 h (total time of 48 h). Subsequently, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (25 mL) was added, and the mixture was extracted with EtOAc (3  $\times$  75 mL). The organic layers were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 8:1 hexanes:EtOAc (with 3% HOAc) as the eluent, giving **3.3b** as an off-white solid (2.28 g, 70% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 (d, *J* = 15.6 Hz, 1H), 7.42–7.33 (m, 5H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.10 (d, *J* = 2.8 Hz, 1H), 6.91 (dd, *J*<sub>1</sub> = 8.2 Hz, *J*<sub>2</sub> = 2.4 Hz, 1H), 6.41 (d, *J* = 15.6 Hz, 1H), 5.25 (s, 2H), 3.81 (s, 3H), 3.74 (s, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  176.10, 166.46, 159.10, 142.02, 135.91, 134.90, 132.31, 128.59, 128.24, 128.22, 125.31, 120.35, 116.43, 111.55, 66.46, 55.34, 37.52; IR (neat)  $\nu$  3032, 2936, 1709 (br), 1634, 1606, 1498, 1294, 1238, 1166 (br), 1038, 976, 861, 809 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* Calcd for C<sub>19</sub>H<sub>18</sub>O<sub>5</sub> [M+H]<sup>+</sup> 327.1227 found 327.1219.

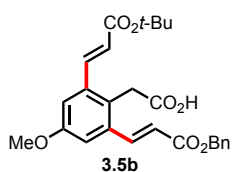
**General procedure for reaction of 3.3b with a second olefin:** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **3.3b** (163.2 mg, 0.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ac-Val-OH (8.0 mg, 0.05 mmol), the olefin coupling partner (1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times$  3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 6 h. Subsequently, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) was added, and the

mixture was extracted with EtOAc ( $3 \times 20$  mL). The organic layers were combined, dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using hexanes/EtOAc (with 2–5% HOAc) as the eluent.



**2-(2-((*E*)-3-(benzyloxy)-3-oxoprop-1-enyl)-6-((*E*)-3-ethoxy-3-oxoprop-1-enyl)-4-methoxyphenyl)acetic acid (3.5a):** The title compound was obtained as an off-white solid (185 mg, 87% yield).  $^1\text{H}$

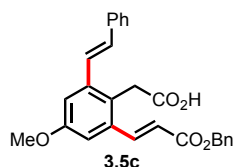
**NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 16.0$  Hz, 1H), 7.95 (d,  $J = 16.0$  Hz, 1H), 7.42–7.33 (m, 5H), 7.10 (s, 2H), 6.39 (d,  $J = 16.0$  Hz, 1H), 6.33 (d,  $J = 16.0$  Hz, 1H), 5.25 (s, 2H), 4.26 (q,  $J = 7.2$  Hz, 2H), 3.86 (s, 2H), 3.83 (s, 3H), 1.33 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  **NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.60, 166.44, 166.22, 158.79, 142.24, 141.64, 136.82, 136.61, 135.79, 128.60, 128.30, 128.27, 124.44, 122.34, 121.82, 114.17, 113.85, 66.59, 60.82, 55.43, 33.67, 14.26; IR (neat)  $\nu$  2980, 2940, 1707 (br), 1623, 1597, 1463, 1369, 1312, 1273, 1164 (br), 1035, 975, 860  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{24}\text{H}_{24}\text{O}_7$   $[\text{M}+\text{H}]^+$  425.1595, found 425.1587.



**2-(2-((*E*)-3-(benzyloxy)-3-oxoprop-1-enyl)-6-((*E*)-3-*tert*-butoxy-3-oxoprop-1-enyl)-4-methoxyphenyl)acetic acid (3.5b):** The title compound was obtained as yellow oil (213 mg, 94% yield).  $^1\text{H}$  **NMR**

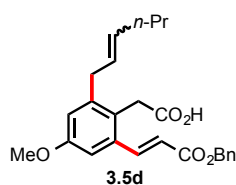
(400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 16.0$  Hz, 1H), 7.97 (d,  $J = 16.0$  Hz, 1H), 7.42–7.33 (m, 5H), 7.11–7.08 (m, 2H), 6.38 (d,  $J = 16.0$  Hz, 1H), 6.26 (d,  $J = 16.0$  Hz, 1H), 5.25 (s, 2H), 3.86 (s, 2H), 3.83 (s, 3H), 1.52 (s, 9H);  $^{13}\text{C}$  **NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  174.59, 166.24, 165.75, 158.76, 142.32, 140.66, 136.98, 136.53, 135.82, 128.59, 128.28, 128.26, 124.39, 124.10, 121.70, 114.09, 113.70, 81.01, 66.56, 55.42, 33.65, 28.14; IR (neat)  $\nu$  2976, 2936,

1706 (br), 1632, 1597, 1458, 1368, 1314, 1275, 1146 (br), 1052, 1017, 1146 (br), 1017, 974, 848  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{26}\text{H}_{28}\text{O}_7$   $[\text{M}+\text{Na}]^+$  475.1727, found 475.1742.



**2-(2-((*E*)-3-(benzyloxy)-3-oxoprop-1-enyl)-4-methoxy-6-styrylphenyl)acetic acid (3.5c):** The title compound was obtained as an

off-white solid (152 mg, 71% yield).  **$^1\text{H}$  NMR** (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07 (d,  $J = 15.6$  Hz, 1H), 7.47 (d,  $J = 7.2$  Hz, 2H), 7.35–7.22 (m, 9H), 7.15 (d,  $J = 2.7$  Hz, 1H), 7.01 (d,  $J = 2.7$  Hz, 1H), 6.92 (d,  $J = 15.9$  Hz, 1H), 6.39 (d,  $J = 15.6$  Hz, 1H), 5.23 (s, 2H), 3.84 (s, 2H), 3.82 (s, 3H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.89, 166.40, 158.74, 142.85, 139.93, 136.77, 136.01, 135.81, 132.96, 128.68, 128.53, 128.20, 128.18, 128.07, 126.74, 125.66, 123.30, 121.11, 114.01, 111.30, 66.46, 55.32, 34.14; **IR** (neat)  $\nu$  2960, 2939, 1706 (br), 1635, 1594, 1460, 1260 (br), 1052, 1016, 969, 905  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{27}\text{H}_{24}\text{O}_5$   $[\text{M}+\text{H}]^+$  429.1696, found 429.1694.

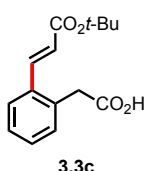


**2-(2-((*E*)-3-(benzyloxy)-3-oxoprop-1-enyl)-6-(hex-2-enyl)-4-methoxyphenyl)acetic acid (3.5d):** The title compound was obtained

as an inseparable mixture of the *E*- and *Z*-stereoisomers (49 mg, 23% yield). By  $^1\text{H}$  NMR, the *E*:*Z* ratio was determined to be approximately 7:1. Analytical data were measured using the isomeric mixture. However, the NMR data reported below represent only the major isomer.  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.01 (d,  $J = 15.6$  Hz, 1H), 7.42–7.32 (m, 5H), 6.95 (d,  $J = 2.4$  Hz, 1H), 6.82 (d,  $J = 2.4$  Hz, 1H), 6.38 (d,  $J = 15.6$  Hz, 1H), 5.52–5.38 (m, 2H), 5.24 (s, 2H), 3.80 (s, 3H), 3.78 (s, 2H), 3.34 (d,  $J = 5.2$  Hz, 2H), 1.96 (aq,  $J = 7.2$  Hz, 2H), 1.40–1.30 (m, 2H), 0.86 (t,  $J = 7.2$  Hz, 3H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.63, 166.49, 158.65, 143.12, 142.10, 135.90, 132.77, 128.56, 128.22, 128.20, 127.29, 124.09, 120.63, 117.97, 109.51, 66.41, 55.20, 36.91, 34.53, 33.53, 22.38, 13.66; **IR**



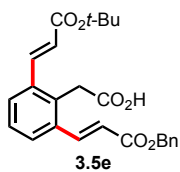
(neat)  $\nu$  2957, 2930, 1708 (br), 1633, 1599, 1464, 1315, 1268, 1268 (br), 1052, 973, 858  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{25}\text{H}_{28}\text{O}_5$   $[\text{M}+\text{H}]^+$  409.2009, found 409.201.



**(E)-2-(2-(3-tert-butoxy-3-oxoprop-1-enyl)phenyl)acetic acid (3.3c):** A 250

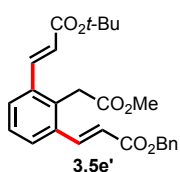
mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the phenylacetic acid

**(3.1c)** (1.36 g, 10 mmol),  $\text{Pd}(\text{OAc})_2$  (112.3 mg, 0.5 mmol),  $\text{KHCO}_3$  (2.00 g, 20 mmol), BQ (54.0 mg, 0.5 mmol), *tert*-butyl acrylate **(3.2c)** (2.9 mL, 20 mmol), and *t*-AmylOH (25 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with  $\text{O}_2$  (1 atm, balloon) ( $\times 3$ ). The reaction mixture was stirred at room temperature for 5 min, then at 90  $^\circ\text{C}$  for 24 h, at which point the reaction vessel was recharged with  $\text{O}_2$  using the procedure described above. The reaction was allowed to stir at 90  $^\circ\text{C}$  for an additional 24 h (total time of 48 h). Subsequently, the reaction vessel was cooled to 0  $^\circ\text{C}$  in an ice bath. A 2.0 N HCl solution (25 mL) was added, and the mixture was extracted with EtOAc ( $3 \times 75$  mL). The organic layers were combined, dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 8:1 hexanes:EtOAc (with 3% HOAc) as the eluent, giving **3.3c** as a colourless oil (1.97 g, 75% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85 (d,  $J = 16.0$  Hz, 1H), 7.59 (d,  $J = 7.2$  Hz, 1H), 7.35–7.28 (m, 3H), 6.31 (d,  $J = 16.0$  Hz, 1H), 3.80 (s, 2H), 1.52 (s, 9H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.59, 166.09, 140.35, 134.23, 132.73, 131.10, 129.91, 128.01, 126.88, 122.58, 80.73, 38.24, 28.16; **IR** (neat)  $\nu$  2978, 2928, 1708 (br), 1633, 1368, 1321, 1219, 1150 (br), 978, 765  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_4$   $[\text{M}+\text{Na}]^+$  285.1097, found 285.1095.



**2-(2-((*E*)-3-(benzyloxy)-3-oxoprop-1-enyl)-6-((*E*)-3-*tert*-butoxy-3-oxoprop-1-enyl)phenyl)acetic acid (**3.5e**):**

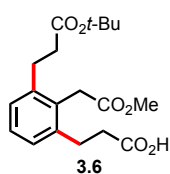
A 250 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **3.3c** (1.36 g, 7.5 mmol), Pd(OAc)<sub>2</sub> (84.2 mg, 0.375 mmol), KHCO<sub>3</sub> (1.50 g, 15 mmol), Ac-Val-OH (115.7 mg, 0.75 mmol), benzyl acrylate (**2b**) (2.3 mL, 15 mmol), and *t*-AmylOH (25 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) (× 3). The reaction mixture was stirred at room temperature for 5 min, then at 90 °C for 6 h. Subsequently, the reaction vessel was cooled to 0 °C in an ice bath. A 2.0 N HCl solution (25 mL) was added, and the mixture was extracted with EtOAc (3 × 75 mL). The organic layers were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 2:1 hexanes:EtOAc (with 3% HOAc) as the eluent, giving **3.5e** as a colourless oil (3.01 g, 95% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.07 (d, *J* = 16.0 Hz, 1H), 7.92 (d, *J* = 15.6 Hz, 1H), 7.57 (m, 7.59–7.56, 2H), 7.41–7.30 (m, 6H), 6.40 (d, *J* = 15.6 Hz, 1H), 6.28 (d, *J* = 15.6 Hz, 1H), 5.25 (s, 2H), 3.93 (s, 2H), 1.52 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 174.31, 166.33, 165.88, 142.31, 140.62, 135.85, 135.83, 135.43, 131.84, 128.67, 128.57, 128.34, 128.25, 128.23, 128.10, 124.01, 121.60, 81.00, 66.54, 34.36, 28.14; IR (neat) ν 2978, 2932, 1708 (br), 1631, 1455, 1369, 1318, 1277, 1256, 1151 (br), 981, 911, 848, 797 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* Calcd for C<sub>25</sub>H<sub>26</sub>O<sub>6</sub> [M+Na]<sup>+</sup> 445.1621, found 445.1629.



**(*E*)-benzyl 3-(3-((*E*)-3-*tert*-butoxy-3-oxoprop-1-enyl)-2-(2-methoxy-2-oxoethyl)phenyl)acrylate (**3.5e'**):**

A 250 mL Teflon-capped sealed tube equipped with a magnetic stir bar was charged with **3.5e** (3.01 g, 7.3 mmol), K<sub>2</sub>CO<sub>3</sub> (2.02 g, 14.6 mmol), and MeI (0.9 mL, 14.6 mmol), and acetone (50 mL). The

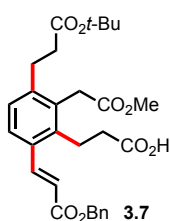
reaction was capped and stirred at 55 °C for 12 h. The reaction mixture was allowed to cool to room temperature, and the solvent and residual MeI were removed *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 10:1 hexanes:EtOAc as the eluent, giving **3.5e'** as a colourless oil (2.96 g, 93% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 8.03 (d, *J* = 15.6 Hz, 1H), 7.89 (d, *J* = 16.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.41–7.30 (m, 6H), 6.40 (d, *J* = 16.0 Hz, 1H), 6.27 (d, *J* = 15.6 Hz, 1H), 5.26 (s, 2H), 3.90 (s, 2H), 3.68 (s, 3H), 1.54 (s, 9H); **<sup>13</sup>C NMR** (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO) δ 171.41, 166.60, 166.06, 143.05, 141.55, 137.52, 136.61, 136.36, 133.95, 129.54, 129.40, 129.36, 129.06, 128.98, 128.92, 124.42, 122.22, 80.90, 66.78, 52.50, 35.10, 28.37; **IR** (neat) ν 2977, 2953, 1736 (br), 1707 (br), 1631, 1455, 1535, 1368, 1317, 1276m 1249, 1147 (br), 1012, 981, 849, 798 cm<sup>-1</sup>; **HRMS** (ESI-TOF) *m/z* Calcd for C<sub>26</sub>H<sub>28</sub>O<sub>6</sub> [M+Na]<sup>+</sup> 459.1778, found 459.1776.



**3-(3-(3-*tert*-butoxy-3-oxopropyl)-2-(2-methoxy-2-oxoethyl)phenyl)propanoic acid (3.6):** To a 100 mL round bottom flask

equipped with a stir bar were added **3.5e'** (1.14 g, 2.6 mmol), MeOH (40 mL), and Pd/C (10 wt%) (138 mg, 0.13 mmol). The flask was evacuated under vacuum, then capped under H<sub>2</sub> (1 atm, balloon). After 6 h, the solution was filtered through a pad of Celite. The title compound was obtained as a colourless oil (825 mg, 91% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.18 (t, *J* = 7.6 Hz, 1H), 7.10–7.08 (m, 2H), 3.79 (s, 2H), 3.70 (s, 3H), 2.98 (t, *J* = 7.6 Hz, 2H), 2.93 (t, *J* = 8.4 Hz, 2H), 2.64 (t, *J* = 8.0 Hz, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 1.43 (s, 9H); **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>) δ 178.03, 172.21, 171.94, 140.30, 139.54, 130.67, 127.63, 127.53, 127.22, 80.50, 52.17, 36.35, 34.86, 34.13, 28.54, 28.15, 28.07; **IR** (neat) ν 2977, 2954, 2932, 1725 (br), 1709 (br), 1457, 1434, 1367, 1249, 1210, 1144 (br),

1003, 844, 800  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{26}\text{O}_6$   $[\text{M}+\text{Na}]^+$  373.1621, found 373.1625.



**(E)-3-(6-(3-(benzyloxy)-3-oxoprop-1-enyl)-3-(3-tert-butoxy-3-oxopropyl)-2-(2-methoxy-2-oxoethyl)phenyl)propanoic acid (3.7):** A 50

mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with **3.6** (70.1 mg, 0.2 mmol),  $\text{Pd}(\text{OAc})_2$  (4.5 mg, 0.02 mmol),  $\text{KHCO}_3$  (40.0 mg, 0.4 mmol), Boc-Val-OH (8.7 mg, 0.04 mmol), benzyl acrylate (60  $\mu\text{L}$ , 0.4 mmol), and *t*-AmylOH (1.0 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with  $\text{O}_2$  (1 atm, balloon) ( $\times 3$ ). The reaction mixture was stirred at room temperature for 5 min, then at 90  $^\circ\text{C}$  for 12 h. Subsequently, the reaction vessel was cooled to 0  $^\circ\text{C}$  in an ice bath. A 2.0 N HCl solution (5 mL) was added, and the mixture was extracted with EtOAc ( $3 \times 20$  mL). The organic layers were combined, dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 2:1 hexanes:EtOAc (with 3% HOAc) as the eluent, giving **3.7** as a colourless oil (36 mg, 35% yield).  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (d,  $J = 16.0$  Hz, 1H), 7.45–7.33 (m, 6H), 7.13 (d,  $J = 8.0$  Hz, 1H), 6.39 (d,  $J = 16.0$  Hz, 1H), 5.26 (s, 2H), 3.84 (s, 2H), 3.71 (s, 3H), 3.15 (t,  $J = 8.0$  Hz, 2H), 2.94 (d,  $J = 8.0$  Hz, 2H), 2.53–2.48 (m, 4H), 1.43 (s, 9H);  **$^{13}\text{C}$  NMR** (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  173.47, 172.43, 172.27, 166.84, 143.95, 143.39, 140.76, 137.57, 133.29, 132.79, 129.33, 128.89, 128.83, 128.76, 126.96, 120.55, 80.53, 66.56, 52.31, 36.52, 35.09, 34.88, 29.50, 28.23, 25.50; **IR** (neat)  $\nu$  2977, 2954, 2926, 1714 (br), 1630, 1368, 1309, 1256, 1156 (br), 1004, 981, 846 752  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{29}\text{H}_{34}\text{O}_8$   $[\text{M}+\text{Na}]^+$  533.2146, found 533.2151.

### 3.5. REFERENCES

- (1) Burroughes, J. H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; Mackay, K.; Friend, R. H.; Burns, P. L.; Holmes, A. B. *Nature* **1990**, *347*, 539–541.
- (2) For reviews of electroluminescent conjugated polymers, see: (a) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem. Int. Ed.* **1998**, *37*, 402–428. (b) Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B. *Chem. Rev.* **2009**, *109*, 897–1091.
- (3) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320–2322.
- (4) Plevyak, J. E.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2454–2456.
- (5) For examples of differential Mizoroki–Heck reactions to construct unsymmetrical divinylbenzenes, see: (a) Plevyak, J. E.; Dickerson, J. E.; Heck, R. F. *J. Org. Chem.* **1979**, *44*, 4078–4080. (b) Spencer, A. J. *J. Organomet. Chem.* **1984**, *265*, 323–331. (c) Tao, W.; Nesbitt, S.; Heck, R. F. *J. Org. Chem.* **1990**, *55*, 63–69. (d) Carlström, A.-S.; Frejd, T. *J. Org. Chem.* **1991**, *56*, 1289–1293. (e) Sengupta, S.; Sadhukhan, S. K. *Tetrahedron Lett.* **1998**, *39*, 715–718. (f) Wang, C.; Tan, L.-S.; He, J.-P.; Hu, H.-W.; Xu, J.-H. *Synth. Commun.* **2003**, *33*, 773–782.
- (6) For examples of differential cross-coupling reactions, see: (a) Oh-e, T.; Miyaura, N.; Suzuki, A. *Synlett* **1990**, 221–223. (b) Rottländer, M.; Palmer, N.; Knochel, P. *Synlett* **1996**, 573–575. .
- (7) For reviews, see: (a) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633–639. (b) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35–41. (c) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115. (d) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (e) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169.

- (8) For the initial reports of Pd(II)-mediated C(aryl)-H olefination, see: (a) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119–1122. (b) Fujiwara, Y.; Moritani, I.; Matsuda, M.; Teranishi, S. *Tetrahedron Lett.* **1968**, *9*, 3863–3865.
- (9) For selected examples of subsequent work to establish catalytic turnover and expand the substrate scope, see: (a) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91*, 7166–7169. (b) Fujiwara, Y.; Asano, R.; Moritani, I.; Teranishi, S. *J. Org. Chem.* **1976**, *41*, 1681–1683. (c) Tsuji, J.; Nagashima, H. *Tetrahedron* **1984**, *40*, 2699–2702. (d) Jia, C.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Org. Lett.* **1999**, *1*, 2097–2100. (e) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992–1995.
- (10) Examples of non-directed Pd(II)-catalysed C–H olefination with nitrogen-containing heterocycles: (a) Fujiwara, Y.; Maruyama, O.; Yoshidomi, M.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 851–855. (b) Itahara, T.; Ikeda, M.; Sakakibara, T. *J. Chem. Soc., Perkin Trans. I* **1983**, 1361–1363. (c) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578–9579. (d) Abbiati, G.; Beccalli, E. M.; Broggini, G.; Zoni, C. *J. Org. Chem.* **2003**, *68*, 7625–7628. (e) Ma, S.; Yu, S. *Tetrahedron Lett.* **2004**, *45*, 8419–8422. (f) Liu, C.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 10250–10251. (g) Grimster, N. P.; Gauntlett, C.; Godfrey, C. R. A.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 3125–3129.
- (11) Examples of Pd(II)-catalysed C–H olefination using substrates containing directing groups: (a) Miura, M.; Tsuda, T.; Satoh, T.; Nomura, M. *Chem. Lett.* **1997**, *26*, 1103–1104. (b) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211–5215. (c) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586–1587. (d) Zaitsev, V. G.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 4156–

4157. (e) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666–7673. (f) Houlden, C. E.; Bailey, C. D.; Ford, J. G.; Gagné, M. R.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2008**, *130*, 10066–10067. (g) Li, J.-J.; Mei, T.-S.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 6452–6455. (h) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916–5921.
- (12) (a) Capito, E.; Brown, J. M.; Ricci, A. *Chem. Commun.* **2005**, 1854–1856. (b) García-Rubia, A.; Arrayás, R. G.; Carretero, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 6511–6515.
- (13) Cho, S. H.; Hwang, S. J.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 9254–9256.
- (14) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315–319.
- (15) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072–5074.
- (16) Examples of Pd(II)-mediated C–H olefination in total synthesis: (a) Trost, B. M.; Godleski, S. A.; Genet, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 3930–3931. (b) Cushing, T. D.; Sanz-Cervera, J. F.; Williams, R. M. *J. Am. Chem. Soc.* **1993**, *115*, 9323–9324. (c) Baran, P. S.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 7904–7905. (d) Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 9552–9553. (e) Beck, E. M.; Hatley, R.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2008**, *47*, 3004–3007. (f) Bowie, A. L., Jr.; Trauner, D. *J. Org. Chem.* **2009**, *74*, 1581–1586.
- (17) Arene/olefin coupling reactions have also been reported using metals other than Pd: (a) Lewis, L. N.; Smith, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 2728–2735. (b) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529–531. (c) Matsubara, T.; Koga, N.; Musaev, D. G.; Morokuma, K. *J. Am. Chem. Soc.* **1998**, *120*, 12692–12693. (d) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 6616–6623. (e) Matsumoto, T.; Taube, D. J.; Periana, R. A.; Taube, H.; Yoshida, H. *J. Am. Chem. Soc.* **2000**, *122*, 7414–7415. (f) Jun, C.-H.; Hong, J.-B.; Kim, Y.-H.; Chung, K.-Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 3440–3442. (g) Weissman, H.;

- Song, X.; Milstein, D. *J. Am. Chem. Soc.* **2000**, *123*, 337–338. (h) Thalji, R. K.; Ellman, J. A.; Bergman, R. G. *J. Am. Chem. Soc.* **2004**, *126*, 7192–7193. (i) Luedtke, A. T.; Goldberg, K. I. *Angew. Chem. Int. Ed.* **2008**, *47*, 7694–7696.
- (18) For a novel approach to construct 1,2,3-trisubstituted arenes through norbornene-mediated Pd(0)-catalysis, see: (a) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1988**, *346*, C27–C30. (b) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed.* **1997**, *36*, 119–122. For a review, see: (c) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238. For recent work, see: (d) Mariampillai, B.; Alliot, J.; Li, M.; Lautens, M. *J. Am. Chem. Soc.* **2007**, *129*, 15372–15379. (e) Gericke, K. M.; Chai, D. I.; Bieler, N.; Lautens, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 1447–1451.
- (19) For rare examples of sequential C–H activation of electron-rich heterocycles with Pd(II), see Refs. 10g, 12b, and 16e and the following: (a) Nakano, M.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett.* **2008**, *10*, 1851–1854. (b) Yanagisawa, S.; Ueda, K.; Sekizaawa, H.; Itami, K. *J. Am. Chem. Soc.* **2009**, *131*, 14622–14623.
- (20) For a recent example of sequential *ortho*-C–H olefination of 1-phenylpyrazoles using catalytic Rh(III), see: Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7094–7099.
- (21) Mono-*N*-protected amino acids were first identified as effective ligand scaffolds for Pd(II)-catalysed C–H functionalisation reactions during our studies of enantioselective C–H functionalisation: (a) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886. (b) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461. For an early report describing stoichiometric asymmetric cyclopalladation of (dimethylamino)methylferrocene in the presence of Ac-Val-OH, see: (c) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.



- (22) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 14137–14151.
- (23) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886.

### 3.6. CONTRIBUTIONS

The following individuals directly contributed to the work described in this Chapter: Keary M. Engle, Dong-Hui Wang, and Prof. Jin-Quan Yu. K.M.E., D.-H.W., and J.-Q.Y. conceived the project. Relevant preliminary experiments (see Ref. 14) were performed by D.-H.W. and K.M.E. All experiments described in this Chapter were carried out by K.M.E. Product isolation and characterisation was carried out by K.M.E. and D.-H.W. The Chapter was adapted with permission from a published manuscript, which was written by K.M.E., with input from D.-H.W. and J.-Q.Y.

## CHAPTER 4

### LIGAND-ACCELERATED PALLADIUM(II)-CATALYSED CROSS-COUPLING OF C– H BONDS WITH ARYLBORON REAGENTS

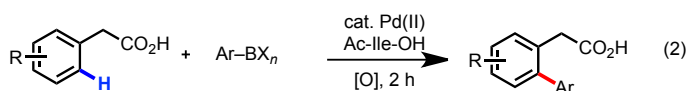
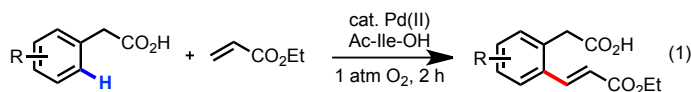
Adapted with permission from:

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## 4.1. INTRODUCTION

Since the 1970s, the discovery and development of Pd(0)-catalysed reactions of aryl and alkyl halides have revolutionised how organic chemists envision forming new carbon–carbon (C–C) and carbon–heteroatom (C–Y) bonds.<sup>1,2</sup> The versatility and practicality of these transformations stem from specially tailored phosphine and *N*-heterocyclic carbene ligands (NHC), which can accelerate both oxidative addition and reductive elimination, thereby enhancing the overall catalytic efficiency and broadening substrate scope.<sup>2</sup> In contrast, fewer ligands are compatible with analogous Pd(II)-catalysed carbon–hydrogen (C–H) bond functionalisation reactions,<sup>3–10</sup> which has hampered progress in this area. Recently, our group made strides on this front with the discovery that mono-*N*-protected amino acid ligands<sup>4</sup> could accelerate Pd(II)-catalysed C–H olefination reactions along a Pd(II)/Pd(0) catalytic cycle (Eq. 1).<sup>5</sup> Based on preliminary mechanistic data, as discussed in Chapter 2, we believe that the observed acceleration derives from an increase in the rate of C–H cleavage. This calls into question whether mono-*N*-protected amino acids would be compatible with Pd(II)-catalysed cross-coupling reactions of C–H bonds with organometallic reagents (Eq. 2),<sup>7,11,12</sup> which have completely different elementary steps following C–H cleavage (transmetalation and reductive elimination). Identification of appropriate ligand scaffolds capable of accelerating C–H/R–M cross-coupling reactions is fundamentally important for improving the scope and practicality of this new class of reactions, which are still in their infancy.



In early 2006, our group reported the first Pd(II)-catalysed cross-coupling reaction of C(sp<sup>2</sup>)-H bonds and organometallic reagents.<sup>12</sup> Since that initial report, our group<sup>13,14</sup> and others<sup>15,16</sup> have gone on to expand this mode of reactivity to an increasingly versatile collection of substrates and coupling partners.<sup>17-21</sup> Generally speaking, however, the catalytic efficiency across these examples remains unsatisfactory,<sup>16</sup> pointing to a need for ligands to enhance reactivity and turnover. Because catalytic C-H/R-M cross-coupling possesses several fundamentally distinct elementary steps (C-H cleavage, transmetalation, reductive elimination, and reoxidation), it remains a significant challenge to identify ligands that are compatible with all of these steps. Nevertheless, encouraged by our work in ligand-accelerated C-H olefination, we sought to establish a ligand-accelerated Pd(II)-catalysed cross-coupling reaction of organoboron reagents with phenylacetic acids, a major class of synthetically versatile substrates. This particular reaction intrigued us because original methodology from our lab<sup>13</sup> suffered from several limitations, including long reaction times (48 h), incompatibility with oxidants that are operationally convenient to use such as Ag(I) salts, the need for high pressure O<sub>2</sub> (20 atm), and limited substrate scope.<sup>22</sup>

Herein, we disclose the results of our studies, which represent to the best of our knowledge the first example of ligand-accelerated Pd(II)-catalysed C(sp<sup>2</sup>)-H/arylboron cross-coupling. By using amino acid ligands in conjunction with Ag<sub>2</sub>CO<sub>3</sub> as a stoichiometric reoxidant, we have developed a new protocol for the functionalisation of phenylacetic acid substrates that offers shorter reaction times, improved substrate scope, and higher yields compared to our previous method.<sup>13</sup> By using ligand acceleration under aerobic conditions, we also demonstrate that good yields can be obtained under relatively low pressures of O<sub>2</sub>. Importantly, this work establishes that mono-*N*-protected amino acids are promising ligand scaffolds for further optimisation owing to their compatibility with the transmetalation, reductive elimination, and reoxidation steps in C-H/R-M cross-coupling.

## 4.2. RESULTS AND DISCUSSION

We began by revisiting our previously reported conditions.<sup>13</sup> One of the drawbacks that hampered the practical utility of that protocol was the need for high pressure O<sub>2</sub> (20 atm), which signaled to us that reoxidation of Pd(0) to catalytically active Pd(II) was problematic (see below for a depiction of the speculative catalytic cycle). Thus for the purposes of achieving efficient turnover under mild conditions, we first turned our attention to other reoxidants, with the long term goal of developing conditions in which 1 atm air could be used as the sole reoxidant. After extensive screening, it was found that Ag<sub>2</sub>CO<sub>3</sub> functioned smoothly for these purposes, giving high conversions in this ligand accelerated C–H/arylboron cross-coupling reaction.<sup>23</sup> It should be noted that although using Ag<sub>2</sub>CO<sub>3</sub> is unsuitable for large-scale industrial production, we opted to use it here in the interest of developing a highly convenient protocol for use in academic and medicinal chemistry laboratories.

**Table 4.1.** Ligand optimisation.<sup>a</sup>

| Entry | Ligand <sup>b</sup>   | % Conv. | Entry | Ligand <sup>b</sup> | % Conv. |
|-------|-----------------------|---------|-------|---------------------|---------|
| 1     | ---                   | 13      | 9     | H-Ile-OH            | 0       |
| 2     | Boc-Gly-OH            | 61      | 10    | Me-Ile-OH           | 0       |
| 3     | Boc-Ala-OH            | 77      | 11    | Formyl-Ile-OH       | 62      |
| 4     | Boc-Phe-OH            | 83      | 12    | Ac-Ile-OH           | 89      |
| 5     | Boc-Val-OH            | 82      | 13    | Fmoc-Ile-OH         | 79      |
| 6     | Boc-Leu-OH            | 81      | 14    | Cbz-Ile-OH          | 76      |
| 7     | Boc- <i>t</i> -Leu-OH | 79      | 15    | Ac-Val-OH           | 79      |
| 8     | Boc-Ile-OH            | 81      | 16    | Ac-Leu-OH           | 87      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>b</sup> Boc = *tert*-butoxycarbonyl, Cbz = carbobenzyloxy, Fmoc = fluorenylmethyloxycarbonyl, Ac = acetyl.

For our optimisation studies, we selected 2-trifluorophenylacetic acid (**4.1a**) as our screening substrate because it was known to be relatively unreactive in the absence of ligands (Entry 1, Table 4.1).<sup>22</sup> Using  $\text{Ag}_2\text{CO}_3$  as the oxidant, we examined the effect of amino acid ligands. We first probed a range of commercially available mono-*N*-Boc-protected amino acids (Entries 2–8), and among those examined, we found those with hydrophobic residues on the backbone (*e.g.*, Ala, Val, Leu, Ile, and Phe) to be highly effective. We then optimised the *N*-protecting group (Entries 8–14), which led to identification of Ac-Ile-OH as an optimal ligand. Substitution of the nitrogen atom with an electron-withdrawing group was necessary for reactivity, as use of both Me-Ile-OH and H-Ile-OH shut down the reaction (Entries 9 and 10). This observation suggests that an electron-deficient Pd(II) centre is necessary for substrate coordination and subsequent C–H cleavage. We observed that with 5 mol%  $\text{Pd}(\text{OAc})_2$ , Ac-Ile-OH loadings of 2.5 mol%, 5 mol%, 10 mol% and 15 mol% gave nearly identical initial rates (as approximated by measuring the conversion at 20 min) and overall conversion after 2 h. Given that Ac-Ile-OH is relatively inexpensive, 10 mol% ligand was used throughout this work for convenience in weighing.

In our previous studies using  $\text{O}_2$  as the oxidant,<sup>13,14b</sup> the presence of 1,4-benzoquinone (BQ) was found to be crucial for both the C–C reductive elimination<sup>12a,24,25</sup> and reoxidation steps. In contrast, in this protocol using  $\text{Ag}_2\text{CO}_3$ , BQ was not required. 5 mol% BQ was used merely to improve reproducibility. Here, the diminished importance of BQ is likely related to the ability of  $\text{Ag}_2\text{CO}_3$  to promote both C–C reductive elimination through one-electron oxidation<sup>26</sup> and reoxidation of Pd(0) by an inner-sphere mechanism, whereby electron transfer proceeds through a putative Pd–Ag interaction.<sup>25</sup>

**Table 4.2.** Initial results with representative phenylacetic acids.<sup>a</sup>

| Product  | Ligand    | % Conv. | Product  | Ligand    | % Conv. |
|----------|-----------|---------|----------|-----------|---------|
| <br>4.3a | ---       | 13      | <br>4.3c | ---       | 12      |
| <br>4.3b | Ac-Ile-OH | 89      | <br>4.3d | Ac-Ile-OH | 77      |
|          | ---       | 16      |          | ---       | 33      |
|          | Ac-Ile-OH | 69      |          | Ac-Ile-OH | 62      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture

Acceptable conversions were obtained with representative substrates during our initial screen with 1 equiv. Ag<sub>2</sub>CO<sub>3</sub> and 1.5 equiv. PhBF<sub>3</sub>K (Table 4.2).<sup>27</sup> However, we found that phenylacetic acid starting materials were difficult to separate from the arylated products on mmol scale. Thus, in order to simplify purification and improve operational simplicity, we sought to refine the conditions to drive the reaction to completion. We further examined alternative arylboron coupling partners (Table 4.3), and found that both aryltrifluoroborates and the pinacol esters of arylboronic acids (ArBPin) provided nearly equivalent product yields. We hypothesised that under our conditions undesired homocoupling was consuming both oxidant and the arylboron reagent. We thus increased the amount of Ag<sub>2</sub>CO<sub>3</sub> to 2 equiv. and arylboron reagent to 3 equiv. and observed that quantitative conversion of **4.3a** could be achieved (Entries 1 and 2).<sup>28</sup> Under these conditions, we found that reaction worked equally well under N<sub>2</sub>, O<sub>2</sub>, or air.

**Table 4.3.** Examination of arylboron coupling partners.<sup>a</sup>

| Entry | Ph-BX <sub>2</sub>   | % Conv.               | Entry | Ph-BX <sub>2</sub>    | % Conv. |
|-------|----------------------|-----------------------|-------|-----------------------|---------|
| 1     | Ph-BF <sub>3</sub> K | 89 [>99] <sup>b</sup> | 4     | Ph-B(OH) <sub>2</sub> | 6       |
| 2     |                      | 85 [>99] <sup>b</sup> | 5     |                       | 9       |
| 3     |                      | 58                    | 6     |                       | 1       |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture <sup>b</sup> The bracketed value denotes the conversion with PhBX<sub>n</sub> (3.0 equiv.) and Ag<sub>2</sub>CO<sub>3</sub> (2.0 equiv.) under otherwise identical reaction conditions.

We also found that the reaction could also be performed at lower temperature, albeit with extended reaction time (Table 4.4). For example at 70 °C, the reaction to form **4.3a** was found to proceed to >99% conversion using Ac-Ile-OH as the ligand and 16% in the absence of ligand after 36 h.

**Table 4.4.** Conversion of **4.1a** to **4.3a** at 70 °C.<sup>a</sup>

| Entry | Ligand    | % Conv. |
|-------|-----------|---------|
| 1     | ---       | 16      |
| 2     | Ac-Ile-OH | >99     |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture.

We next examined the effect of the ligand on the rate profile with substrate **4.1a**. Two independent reactions were set up in the presence and absence of Ac-Ile-OH and allowed to run for 2 h. During this time period, small aliquots were removed at regular



intervals and analysed by  $^1\text{H}$  NMR to determine the conversion. This process was repeated three times and the data were averaged. The results, plotted in Figure 1, show a roughly 8-fold increase in the initial rate using Ac-Ile-OH.<sup>29</sup> We observed a slight deviation from strict linearity in the early part of the reaction profile, presumably due to slow release of the aryltrifluoroborate to the active boronic acid or boronate species via hydrolysis during the course of the reaction.<sup>27d</sup> This effect became more pronounced at lower temperature. Nevertheless, a clear rate increase in the presence of Ac-Ile-OH is evident from the data.

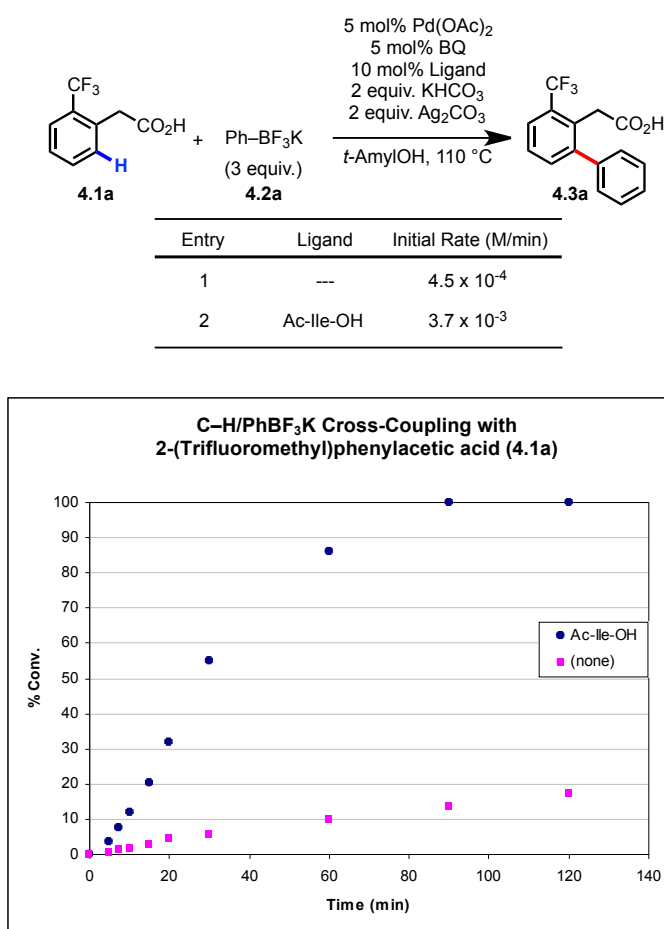


**Figure 4.1.** Rate profile for the reaction of **4.1a** with **4.2a** in the presence and absence of Ac-Ile-OH. Each data point represents the average of three independent trials. The initial rates are calculated for the data points in the 5–20 min time interval using linear regression. Beyond 2 h, no additional product conversion was observed in the trials without ligand. See the Experimental section for detailed experimental procedures.

Next, we probed phenylacetic acid substrate scope (Table 4.5). To our delight, we found that our new protocol was highly tolerant of a variety of different substituents

including alkyl groups (**4.3b** and **4.3d**), alkoxy groups (**4.3j**, **4.3k**, and (**S**)-**4.3n**), and halides (**4.3f–4.3h**). Notably strongly electron-withdrawing groups, such trifluoromethyl (**4.3a**, **4.3c**, and **4.3e**), nitro (**4.3i**), and ketone ((**rac**)-**4.3o**) groups also gave high yields, which qualitatively suggests that simple electrophilic palladation is not the operative mechanism for C–H cleavage. Our protocol was found to tolerate monosubstitution at the  $\alpha$ -position ((**rac**)-**4.3m**), (**S**)-**4.3n**, and (**rac**)-**4.3o**), providing a means for the diversification of non-steroidal anti-inflammatory drugs (NSAIDs) such as Naproxen ((**S**)-**4.1n**) and Ketoprofen ((**rac**)-**4.1o**), which gave products (**S**)-**4.3n** and (**rac**)-**4.3o**, respectively. Importantly, we found that the chiral centre in (**S**)-**4.3n** did not epimerise under the reaction condition when an enantiopure starting material was used. With chiral  $\alpha$ -substituted starting material (**rac**)-**4.3m**, racemic and enantiopure ligands were found to give comparable yields (see the Experimental section).  $\alpha,\alpha$ -Disubstituted substrates were found to give substantially lower yields under these conditions.<sup>30</sup> In the absence of a sterically bulky group at the *ortho*-, *meta*-, or  $\alpha$ -positions, the reaction gave primarily the diarylated product, but acceptable yields of the monoarylated product could be obtained by using 1 equiv. of the coupling partner (*e.g.*, **4.3e**). For each substrate, we ran a control experiment in the absence of Ac-Ile-OH. Generally, the presence of Ac-Ile-OH drastically improved the yield. In the absence of ligand, only two electron-rich substrates **4.3e** and **4.3k** gave over 60% conversion. Substrates bearing electron-withdrawing substituents (*e.g.*, **4.3a**, **4.3c**, **4.3e**, **4.3f–4.3i**) were highly unreactive in the absence of Ac-Ile-OH.

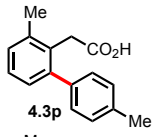
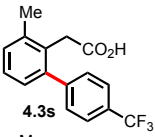
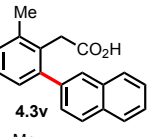
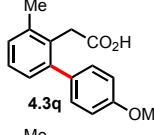
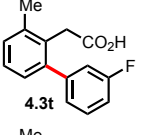
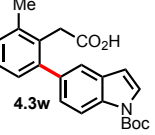
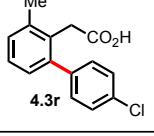
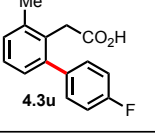
**Table 4.5.** Phenylacetic acid substrate scope.<sup>a</sup>

| Product  | Ligand    | % Conv.                | Product  | Ligand    | % Conv.  | Product  | Ligand    | % Conv.                 |
|----------|-----------|------------------------|----------|-----------|----------|----------|-----------|-------------------------|
| <br>4.3a | ---       | 17                     | <br>4.3f | ---       | 5        | <br>4.3k | ---       | 72                      |
| <br>4.3b | Ac-Ile-OH | >99 (98)               | <br>4.3g | Ac-Ile-OH | >99 (98) | <br>4.3l | Ac-Ile-OH | 96 (85)                 |
| <br>4.3c | ---       | 44                     | <br>4.3h | ---       | 20       | <br>4.3m | ---       | 22                      |
| <br>4.3d | Ac-Ile-OH | >99 (97)               | <br>4.3i | Ac-Ile-OH | 97 (96)  | <br>4.3n | Ac-Ile-OH | >99 (80)                |
| <br>4.3e | ---       | 6                      | <br>4.3j | ---       | 10       | <br>4.3o | ---       | 24 <sup>d</sup>         |
| <br>4.3a | Ac-Ile-OH | >99 (97)               | <br>4.3k | Ac-Ile-OH | >99 (98) | <br>4.3l | Ac-Ile-OH | 78 (73) <sup>d</sup>    |
| <br>4.3b | ---       | 63                     | <br>4.3g | ---       | 2        | <br>4.3m | ---       | 41 <sup>e</sup>         |
| <br>4.3c | Ac-Ile-OH | >99 (95)               | <br>4.3h | Ac-Ile-OH | 87 (69)  | <br>4.3n | Ac-Ile-OH | >99 (97) <sup>e,f</sup> |
| <br>4.3d | ---       | 6                      | <br>4.3i | ---       | 38       | <br>4.3o | ---       | 16 <sup>d</sup>         |
| <br>4.3e | Ac-Ile-OH | 57 (52) <sup>b,c</sup> | <br>4.3j | Ac-Ile-OH | >99 (94) | <br>4.3k | Ac-Ile-OH | 89 (83) <sup>d</sup>    |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture. Isolated yield is given in parentheses. <sup>b</sup> 1.0 equiv. PhBF<sub>3</sub>K was used. <sup>c</sup> 28% of the di-arylated product (**4.3e'**) was also isolated. <sup>d</sup> Racemic starting material was used. <sup>e</sup> Enantiopure starting material was used. <sup>f</sup> The product was isolated in >99:1 er, as determined by chiral HPLC (see the Experimental section).

Subsequently, we investigated the compatibility of our protocol with various substituted arylboron coupling partners (Table 4.6). We were pleased to find that several different substituted aryltrifluoroborates were well tolerated, giving excellent conversions (**4.3p–4.3v**). Importantly, we were also able to couple a heterocyclic compound under our new conditions (**4.3w**). Arylboron reagents bearing substituents at the *ortho*-position were found to be unreactive, presumably due to steric encumbrance.

**Table 4.6.** Aryltrifluoroborate scope.<sup>a,b</sup>

| Product                                                                                          | Ligand    | % Conv.  | Product                                                                                          | Ligand    | % Conv.  | Product                                                                                            | Ligand    | % Conv.                                |
|--------------------------------------------------------------------------------------------------|-----------|----------|--------------------------------------------------------------------------------------------------|-----------|----------|----------------------------------------------------------------------------------------------------|-----------|----------------------------------------|
| <br><b>4.3p</b> | ---       | 19       | <br><b>4.3s</b> | ---       | 46       | <br><b>4.3v</b> | ---       | 18                                     |
| <br><b>4.3q</b> | Ac-Ile-OH | >99 (92) | <br><b>4.3t</b> | Ac-Ile-OH | >99 (94) | <br><b>4.3w</b> | Ac-Ile-OH | 6 <sup>c</sup><br>44 (37) <sup>c</sup> |
| <br><b>4.3r</b> | Ac-Ile-OH | >99 (95) | <br><b>4.3u</b> | Ac-Ile-OH | >99 (98) |                                                                                                    |           |                                        |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture. Isolated yield is given in parentheses. <sup>b</sup> The reaction conditions were identical to those used in Table 2.

<sup>c</sup> The corresponding ArBPIn (3 equiv.) coupling partner was used.

We then shifted our focus to establishing a ligand-accelerated protocol in which O<sub>2</sub> was used as the terminal reoxidant (Table 4.7).<sup>31</sup> We again examined amino acid ligands, first turning our attention to commercially available mono-*N*-Boc-protected amino acids (Entries 2–10). Of those tested, Boc-Val-OH (Entry 10) was found to be optimal. We then sought to tune the *N*-protecting group, by modulating the steric and electronic properties of the chelating nitrogen atom (Entries 11–19). However, other amide (Entries 13–15) and carbamate (Entries 16–19) protecting groups, were found to offer no further improvements. The optimal ligand from above, Ac-Ile-OH, gave reproducibly lower conversion than Boc-Val-OH (Entry 20) For the remainder of the aerobic studies described herein, Boc-Val-OH was used as the ligand.

**Table 4.7.** Ligand optimisation under 1 atm O<sub>2</sub>.<sup>a</sup>

| Entry | Ligand <sup>b</sup>       | % Conv. | Entry | Ligand <sup>b</sup>                   | % Conv. |
|-------|---------------------------|---------|-------|---------------------------------------|---------|
| 1     | ---                       | 9       | 11    | H-Val-OH                              | 6       |
| 2     | Boc-Ala-OH                | 39      | 12    | Formyl-Val-OH                         | 52      |
| 3     | Boc-Phe-OH                | 48      | 13    | Ac-Val-OH                             | 52      |
| 4     | Boc-Ser-OH                | 26      | 14    | Piv-Val-OH                            | 9       |
| 5     | Boc-Thr( <i>t</i> -Bu)-OH | 40      | 15    | Ada-Val-OH                            | 24      |
| 6     | Boc-Aib-OH                | 44      | 16    | Me(O <sub>2</sub> C)-Val-OH           | 50      |
| 7     | Boc-Leu-OH                | 57      | 17    | Et(O <sub>2</sub> C)-Val-OH           | 46      |
| 8     | Boc- <i>t</i> -Leu-OH     | 57      | 18    | Cbz-Val-OH                            | 52      |
| 9     | Boc-Ile-OH                | 49      | 19    | <i>i</i> -Bu(O <sub>2</sub> C)-Val-OH | 49      |
| 10    | Boc-Val-OH                | 65      | 20    | Ac-Ile-OH                             | 56      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. <sup>b</sup> Aib = α-aminoisobutyric acid, Ada = 1-adamantyl(CO), Piv = pivaloyl.

To probe the efficacy of this reaction under different pressures, reactions were conducted at 1 atm, 5 atm, 20 atm O<sub>2</sub>, and 20 atm air, and three representative substrates were examined (Table 4.8).<sup>32</sup> We found that raising the O<sub>2</sub> pressure from 1 atm to 5 atm improved the conversions. However, further increasing the O<sub>2</sub> pressure from 5 atm to 20 atm had a comparatively modest effect. BQ was required for catalytic turnover. Using 5 mol% BQ gave the fastest initial rates; however, 20 mol% BQ was optimal for overall yield (see the Experimental section). Given that our old protocol required 20 atm O<sub>2</sub>/48 h to achieve moderate turnover,<sup>13,22</sup> these data serve as compelling evidence that further ligand-optimisation could lead to practical C–H/R–M cross-coupling reactions under ambient air. Moreover, the fact that both 5 atm and 20 atm O<sub>2</sub> gave similar conversions after 8 h shows that above 5 atm O<sub>2</sub>, pressure may no longer be a critical variable for enabling turnover in the presence of Boc-Val-OH. For each data point in Table 4.8, a control experiment was

performed in the absence of ligand, and substantially lower conversions were observed in each case.

**Table 4.8.** Results under different conditions using O<sub>2</sub> as the terminal oxidant.<sup>a</sup>

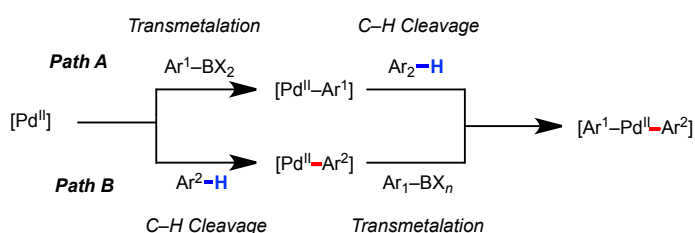
| Product         | Ligand     | 1 atm O <sub>2</sub><br>(24 h) | 5 atm O <sub>2</sub><br>(8 h) | 20 atm O <sub>2</sub><br>(8 h) | 20 atm air<br>(8 h) |
|-----------------|------------|--------------------------------|-------------------------------|--------------------------------|---------------------|
| <br><b>4.3a</b> | ---        | 12                             | 32                            | 26                             | 30                  |
|                 | Boc-Val-OH | 65                             | 96 (91)                       | 97 (93)                        | 77                  |
| <br><b>4.3d</b> | ---        | 21                             | 31                            | 49                             | 35                  |
|                 | Boc-Val-OH | 53                             | 75                            | 72 (68)                        | 73                  |
| <br><b>4.3h</b> | ---        | 4                              | 8                             | 13                             | 8                   |
|                 | Boc-Val-OH | 17                             | 62                            | 83 (74)                        | 49                  |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture. Isolated yield is given in parentheses. After the times shown, no additional product formation was observed.

A thorough understanding of the mechanism of this reaction will require detailed computational, kinetic, and structural analysis, efforts that are currently underway in our laboratory and in collaboration with other groups. In the meantime, we would like to highlight several observations that we have made thus far to help frame future mechanistic studies. The reaction begins with formation of the catalytically active Pd(II) species, which we speculate to be a monomeric Pd(II)-catalyst with a single bound amino acid, consistent with our earlier work in this area.<sup>4,33</sup> Attempts to isolate and characterise the active Ac-Ile-OH-bound Pd(II) catalyst and test its reactivity, however, have not been fruitful thus far.<sup>34,35</sup>

Two different pathways would then theoretically lead to a common [Pd(II)Ar<sup>1</sup>Ar<sup>2</sup>] intermediate (Scheme 4.1). In Path A, transmetalation to generate a [Pd(II)Ar<sup>1</sup>] species

would precede C–H cleavage. In Path B, on the other hand, C–H cleavage would take place first, followed by transmetalation. Though we cannot definitively rule out Path A, we currently favour Path b based on the fact that the reactivity trends in Table 5 (both with and without Ac-Ile-OH) closely parallel those seen in Pd(II)-catalysed C–H olefination of phenylacetic acids, where C–H cleavage is thought to be the first step of the catalytic cycle (see Chapter 2).



**Scheme 4.1.** Possible reaction pathways.

To understand the mechanism of carboxylate-directed C–H cleavage in this reaction,<sup>5c,36–38</sup> we first took note of the tolerance for both electron-donating and electron-withdrawing substituents on the aromatic ring in the presence of Ac-Ile-OH (Table 4.5). To further probe the relative reactivities of electron-rich and electron-poor phenylacetic acids, we performed competition experiments between substrates **4.1a** and **4.1b** under abridged reaction times to measure the relative initial rates (Table 4.9).<sup>39</sup> We found that in the absence of ligand, electron-rich substrate **4.1b** gave a higher initial rate. In the presence of Ac-Ile-OH, we found that electron-poor substrate **4.1a** gave a higher initial rate. The results were consistent with the single-component initial rate data (Table 4.10). Overall, the trends from these competition experiment are very similar to what we observed in ligand-accelerated C–H olefination (see Chapter 2). Based on these findings, we propose that the C–H cleavage event proceeds via a concerted metalation/deprotonation pathway in the presence of Ac-Ile-OH, and an electrophilic palladation mechanism in the absence of Ac-Ile-OH (Figure 4.2).<sup>5c,40</sup>

**Table 4.9.** One-pot intermolecular competition experiment data.<sup>a</sup>

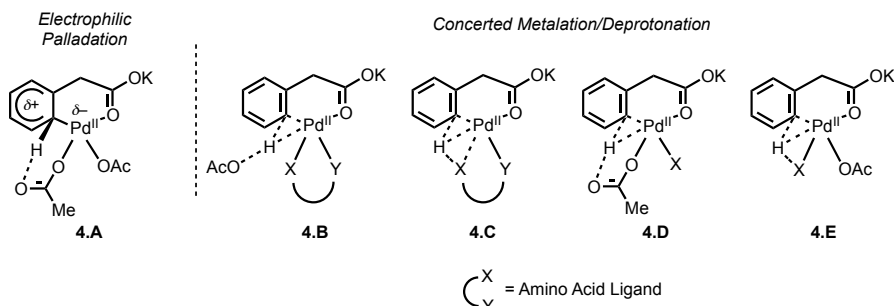
| Entry | Ligand    | Time (min) | % Conv. <b>4.3a</b> | % Conv. <b>4.3b</b> | $k_{4.3a} / k_{4.3b}$ |
|-------|-----------|------------|---------------------|---------------------|-----------------------|
| 1     | ---       | 60         | 9                   | 18                  | 0.48                  |
| 2     | Ac-Ile-OH | 20         | 36                  | 16                  | 2.17                  |

<sup>a</sup> The conversions were determined by <sup>1</sup>H NMR of the crude reaction mixture. See the Experimental section for experimental details.

**Table 4.10.** Comparison of the Initial Rates for Single-Component Reactions of **4.1a** and **4.1b** in the presence and absence of Ac-Ile-OH.<sup>a,b</sup>

| Entry | Ligand    | 4.3a (R = CF <sub>3</sub> ) |                      | 4.3b (R = Me)        |                      |
|-------|-----------|-----------------------------|----------------------|----------------------|----------------------|
|       |           | $k_{4.3a}$ ([M]/min)        | $k_{4.3b}$ ([M]/min) | $k_{4.3a}$ ([M]/min) | $k_{4.3b}$ ([M]/min) |
| 1     | ---       | $4.5 \times 10^{-4}$        | $7.1 \times 10^{-4}$ | $4.5 \times 10^{-4}$ | $7.1 \times 10^{-4}$ |
| 2     | Ac-Ile-OH | $3.7 \times 10^{-3}$        | $1.5 \times 10^{-3}$ | $3.7 \times 10^{-3}$ | $1.5 \times 10^{-3}$ |

<sup>a</sup> See the Experimental section for experimental details. <sup>b</sup> As was discussed with Figure 4.1, slight deviations from linearity were observed in the early parts of the rate profiles. Linear regression was used here with the understanding that it introduces some degree of error.

**Figure 4.2.** Proposed mechanisms for Pd(II)-mediated C–H cleavage. In the absence of ligand, we propose an electrophilic palladation mechanism (**4.A**). In the presence of ligand, we propose a concerted metalation/deprotonation mechanism with external (**4.B**) or internal (**4.C**, **4.D**, and **4.E**) base.

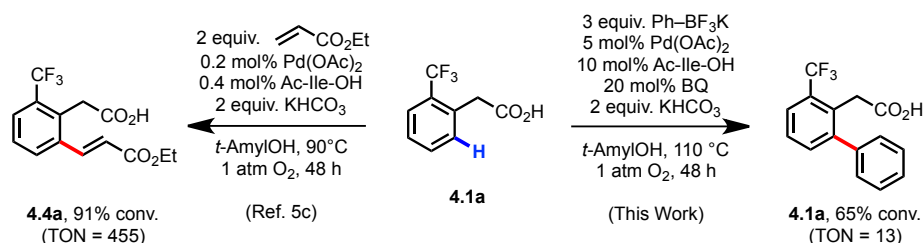


Subsequent to C–H cleavage, transmetalation takes place with the organoboron reagent to generate a diaryl Pd(II) species. Because competitive Pd(II)-mediated homocoupling of the organometallic reagents is known to be fast,<sup>12</sup> we speculate that the use of  $\text{ArBF}_3\text{K}$  reagents<sup>27</sup> as the coupling partners helps to suppress this undesired pathway.<sup>41</sup> Importantly, it has previously been found that Ag(I) salts facilitate transmetalation in cross-coupling reactions.<sup>12b,14a,18f,42</sup> Reductive elimination from the  $[\text{Pd(II)Ar}^1\text{Ar}^2]$  species, which could be induced by BQ or Ag(I),<sup>12a,24–26</sup> then forges the new key C–C bond to give the arylated phenylacetic acid product.

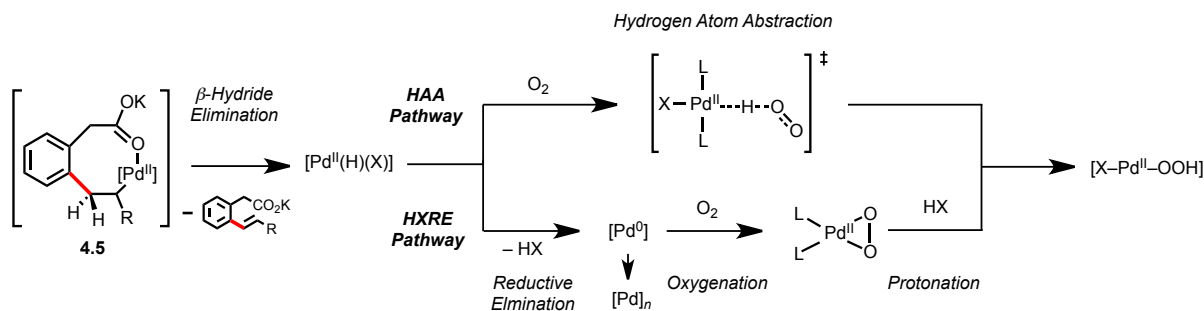
Reoxidation of Pd(0) by Ag(I) or  $\text{O}_2$  then takes place to regenerate catalytically active Pd(II) and closes the catalytic cycle. The mechanism of reoxidation with  $\text{O}_2$  warrants some additional discussion. Previously, in our ligand-accelerated C–H olefination work (see Chapter 2), efficient catalysis ( $\text{TON} > 450$ ,  $\text{TON} = \text{turnover number}$ ) was achieved under only 1 atm  $\text{O}_2$  (Scheme 2). In the present case of ligand-accelerated C–H/R– $\text{BX}_n$  cross-coupling, the maximum TONs using 1 atm  $\text{O}_2$  are roughly 30–40-fold lower. For instance, 65% conversion of product **4.3a** with 5 mol%  $\text{Pd(OAc)}_2$  was observed after 24 h at 1 atm  $\text{O}_2$ , representing a TON of 13 (Scheme 4.2 and Table 4.8). It is also noteworthy, that BQ is not required for catalysis in the case of aerobic C–H olefination but is required in aerobic C–H/R– $\text{BX}_n$  cross-coupling; in the absence of BQ, only 5% conversion of **4.3a** was observed after 24 h under 1 atm  $\text{O}_2$  (see the Experimental section).<sup>43</sup> Given the similarity of the reaction conditions in these two transformations, it is possible that this discrepancy in catalytic efficiency stems from a difference in the mechanism of reoxidation. In C–H olefination, the substrate disengages from the catalyst following a  $\beta$ -hydride elimination event, generating a  $[\text{Pd(II)(H)(X)}]$  species (Scheme 4.3). This intermediate can then react with  $\text{O}_2$  along two possible pathways, direct hydrogen atom abstraction (HAA), or a reductive elimination/oxygenation/protonation sequence (HXRE).<sup>31,44</sup> In contrast, in the case

of C–H/R–BX<sub>n</sub> cross-coupling, C–C reductive elimination, possibly promoted by BQ,<sup>12a,24,25</sup> generates the product along with concomitant formation of a [Pd(0)] species (Scheme 4.4).

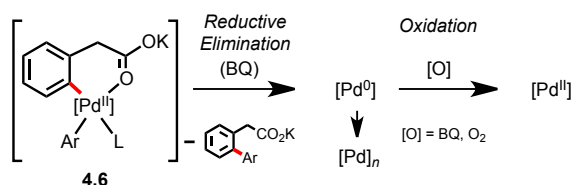
[Pd(0)] is then be reoxidised to [Pd(II)] either by BQ or by O<sub>2</sub>.<sup>45</sup>



**Scheme 4.2.** Comparison between ligand-accelerated Pd(II)-catalysed C–H olefination and C–H/R–BX<sub>n</sub> cross-coupling under 1 atm O<sub>2</sub>.<sup>5c</sup>



**Scheme 4.3.** Possible reoxidation pathways in ligand-accelerated C–H olefination.

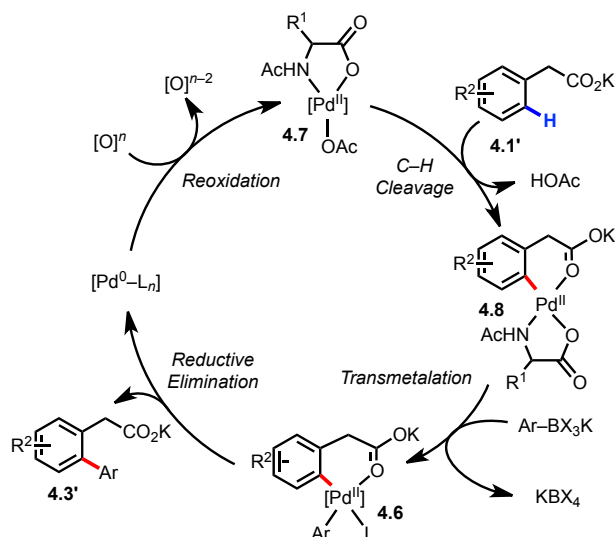


**Scheme 4.4.** Reoxidation pathway in ligand-accelerated C–H/R–BX<sub>n</sub> cross-coupling.

Detailed mechanistic and computational studies have found that either HAA or HXRE pathways can be favoured depending on the ligand environment of the [Pd(II)(H)(X)] complex and the reaction conditions.<sup>44</sup> In the presence of mono-*N*-protected amino acid ligands, however, the reactivity patterns of [Pd(H)(X)] intermediates have not yet been established. In our two catalytic systems (Schemes 4.2–4.4), catalyst deactivation is expected to take place primarily *via* aggregation of [Pd(0)] intermediates to [Pd]<sub>n</sub> (Pd black).

Thus, one possible explanation for the markedly higher catalytic efficiency in C–H olefination would be to invoke a HAA mechanism for reoxidation in that reaction (Scheme 4.3), whereby [Pd(0)] species are avoided all together. However, other explanations could also potentially account for the observed differences in catalytic efficiency between the two reactions. For example, coordination of the alkenyl  $\pi$ -system of the olefin coupling partner and/or olefinated product could serve to stabilise reduced [Pd(0)] following HXRE in the C–H olefination reaction, decreasing the likelihood of precipitation to Pd black.<sup>33</sup> Another explanation could be that the higher temperature in C–H/R–BX<sub>n</sub> cross-coupling (110 °C compared to 90 °C for C–H olefination), which we have found to be necessary for good conversion, possibly because of the higher energetic barrier for C–C reductive elimination compared with  $\beta$ -hydrogen elimination, could be detrimental for catalyst lifetime. Further mechanistic and computational studies are necessary to elucidate the viability of these different scenarios for reoxidation with O<sub>2</sub>.

The proposed Pd(II)/Pd(0) catalytic cycle is depicted in Scheme 4.5. The process begins with substrate coordination and subsequent C–H cleavage, which is presumably facilitated by the bound amino acid ligand. Transmetalation takes place, followed by reductive elimination to forge the key C–C bond with concomitant generation of Pd(0). Reoxidation with Ag(I) or O<sub>2</sub>/BQ regenerates the active catalyst.



**Scheme 4.5.** Proposed catalytic cycle.

### 4.3. CONCLUSION

In summary, we report an efficient ligand-accelerated Pd(II)-catalysed C(sp<sup>2</sup>)–H/arylboron cross-coupling reaction. Using mono-*N*-protected amino acid ligands, we were able to develop conditions to broaden phenylacetic acid substrate scope, shorten reaction times, improve product yields, and reduce catalyst loadings. We anticipate that our new operationally simple protocol using Ag<sub>2</sub>CO<sub>3</sub> will find widespread applications in academic and medicinal chemistry laboratories. Of equal importance, we have achieved progress toward the development of a complimentary practical aerobic protocol for this Pd(II)-catalysed cross-coupling reaction using 1 atm O<sub>2</sub> as the sole reoxidant. Upon further development, the aerobic reaction will provide an expedient and high yielding method for large-scale production of biaryl molecules, which are especially prevalent in pharmaceuticals.

## 4.4. EXPERIMENTAL

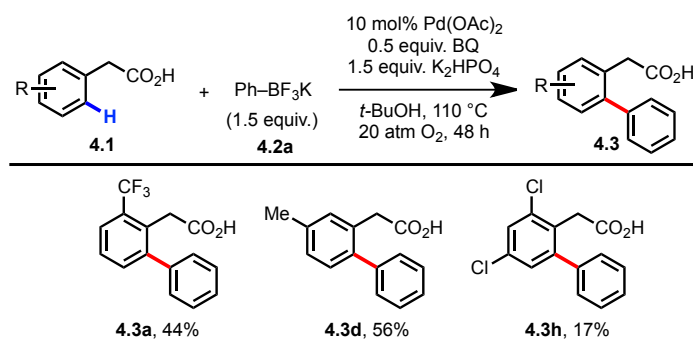
### 4.4.1. General Information

Unless otherwise noted, all materials were used as received from commercial sources without further purification. Phenylacetic acid substrates were purchased from Acros, Sigma-Aldrich, TCI, Alfa-Aesar, and MP Biomedical and were used as received. 2-(Trifluoromethyl)phenylacetic acid (**4.1a**) was purchased from TCI; samples of **4.1a** from other commercial sources were found to give inconsistent results. Organoboron coupling partners were procured from Frontier Scientific, Sigma Aldrich, and Combi-Blocks and used as received. 1,4-Benzoquinone (BQ) was sublimed prior to use. *t*-AmylOH was purchased from Sigma-Aldrich. Newly opened and/or freshly distilled samples of *t*-AmylOH gave the most consistent results. Commercially available amino acid ligands were purchased from Bachem, EMD, or Novabiochem. To examine whether racemic Ac-Ile-OH would give better yields with chiral (racemic) substrates, Ac-D-Ile-OH was prepared.<sup>46</sup> All other ligands were prepared following literature precedent.<sup>5c</sup> Palladium acetate and potassium hydrogen carbonate were purchased from Sigma-Aldrich and Fisher, respectively, and were used without further purification. All reactions were run on hot plates with oil baths calibrated to an external thermometer. Prior to beginning an experiment, the hot plate was turned on, and the oil bath was allowed to equilibrate to the desired temperature for 30 minutes. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian Inova (400 MHz and 100 MHz, respectively) and Bruker DRX equipped with a 5mm DCH cryoprobe (600 MHz and 150 MHz, respectively) instruments internally referenced to tetramethylsilane or chloroform signals. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and a = apparent. The enantiomeric ratio of **Me-(S)-4.3n** was determined by integration of the

HPLC trace, acquired using an Agilent Technologies 1200 series HPLC system with an integrate diode array detector (*vide infra*). High resolution mass spectra were recorded at the Centre for Mass Spectrometry, The Scripps Research Institute.

#### 4.4.2. Previous Conditions: Representative Problematic Substrates

**Previously reported procedure<sup>13</sup> for Pd(II)-catalysed C–H/organoboron cross-coupling with phenylacetic acids (4.1):** A 45 mL high pressure vessel equipped with a magnetic stir bar was charged with the phenylacetic acid substrate (**1**) (0.50 mmol), potassium phenyltrifluoroborate (**4.2a**) (184.0 mg, 0.75 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.05 mmol), BQ (27.0 mg, 0.25 mmol), K<sub>2</sub>HPO<sub>4</sub> (130.7 mg, 0.75 mmol), and *t*-BuOH (2.5 mL). The vessel was pressurised to 20 atm with O<sub>2</sub>, and transferred to an oil bath at 110 °C. *A note of caution: when working with high-pressure O<sub>2</sub>, proper safety measures (including the use of a blast shield) should be taken.* After being allowed to stir vigorously for 48 h, the reaction vessel was removed from the oil bath and cooled to room temperature. The pressure was released, and a 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a**, 3.79 ppm for **4.3a**, 3.61 for **4.1d** 3.60 for **4.3d** 3.79 for **4.1h**, and 3.71 for **4.3h**). The results are shown in Table 4.S1; these data were not included in the original publication.<sup>13</sup>

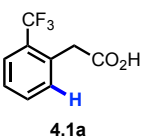
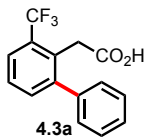
**Table 4.S1:** Representative problematic substrates using previously reported conditions.<sup>a</sup>

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

#### 4.4.3. Ligand Acceleration: Optimisation with Ag<sub>2</sub>CO<sub>3</sub> as the Oxidant

**Ligand optimisation for Pd(II)-catalysed C–H/organoboron cross-coupling with 2-(trifluoromethyl)phenylacetic acid (**4.1a**):** A 25 mL sealed tube equipped with a magnetic stir bar was charged with 2-(trifluoromethyl)phenylacetic acid (**4.1a**) (102.1 mg, 0.50 mmol), potassium phenyltrifluoroborate (**4.2a**) (184.0 mg, 0.75 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), ligand (0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ag<sub>2</sub>CO<sub>3</sub> (137.2 mg, 0.5 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for 2 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a** and 3.79 ppm for **4.3a**). The results are shown in Table 4.1 and Table 4.S2.

**Table 4.S2:** Results from the ligand screening experiments.<sup>a</sup>

| <div style="display: flex; align-items: center; justify-content: center;"> <div style="text-align: center;">  <p><b>4.1a</b></p> </div> <div style="margin: 0 10px;">+</div> <div style="text-align: center;">  <p><b>4.2a</b></p> </div> <div style="margin: 0 10px;">→</div> <div style="text-align: center;">  <p><b>4.3a</b></p> </div> </div> <div style="text-align: center; margin-top: 10px;">           5 mol% Pd(OAc)<sub>2</sub><br/>           5 mol% BQ<br/>           10 mol% Ligand<br/>           2 equiv. KHCO<sub>3</sub><br/>           1 equiv. Ag<sub>2</sub>CO<sub>3</sub><br/> <i>t</i>-AmylOH, 110 °C, 2 h         </div> |                       |         |       |                     |         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|---------|-------|---------------------|---------|
| Entry                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Ligand <sup>b</sup>   | % Conv. | Entry | Ligand <sup>b</sup> | % Conv. |
| 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ---                   | 13      | 10    | H-Ile-OH            | 0       |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Gly-OH            | 61      | 11    | Me-Ile-OH           | 0       |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Ala-OH            | 77      | 12    | Cbz-Ile-OH          | 76      |
| 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Phe-OH            | 83      | 13    | Formyl-Ile-OH       | 62      |
| 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Val-OH            | 82      | 14    | Fmoc-Ile-OH         | 79      |
| 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-allo-Ile-OH       | 83      | 15    | Ac-Ile-OH           | 89      |
| 7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc- <i>t</i> -Leu-OH | 79      | 16    | Ac-Val-OH           | 79      |
| 8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Leu-OH            | 81      | 17    | Ac-Leu-OH           | 87      |
| 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Boc-Ile-OH            | 81      | 18    | Ac-Ala-OH           | 86      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

<sup>b</sup> Boc = *tert*-butoxycarbonyl, Cbz = carbobenzyloxy, Fmoc = fluorenylmethoxycarbonyl, Ac = acetyl.

**Coupling partner optimisation for Pd(II)-catalysed C–H/organoboron cross-coupling with 2-(trifluoromethyl)phenylacetic acid (4.1a):** A 25 mL sealed tube equipped with a magnetic stir bar was charged with 2-(trifluoromethyl)phenylacetic acid **4.1a** (102.1 mg, 0.50 mmol), the phenylboron reagent (**2**) (0.75 mmol),<sup>4</sup> Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), Ac-Ile-OH (8.7 mg, 0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ag<sub>2</sub>CO<sub>3</sub> (137.2 mg, 0.5 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for 2 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a** and 3.79 ppm for **4.3a**). The results are shown in Table 4.3.



**Optimisation of PhBF<sub>3</sub>K / Ag<sub>2</sub>CO<sub>3</sub> loading with 2-(trifluoromethyl)phenylacetic acid (4.1a) and *o*-tolylacetic acid (4.1b):** A 25 mL sealed tube equipped with a magnetic stir bar was charged with the phenylacetic acid substrate (**4.1a** or **4.1b**) (0.50 mmol), phenyltrifluoroborate (**4.2a**), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), Ac-Ile-OH (8.7 mg, 0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ag<sub>2</sub>CO<sub>3</sub>, and *t*-AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for 2 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a**, 3.79 ppm for **4.3a**, 3.67 ppm for **4.1b**, and 3.63 ppm for **4.3b**). To isolate the pure product **4.3a** or **4.3b**, the biphasic mixture was basified with concentrated aqueous NaOH until the pH > 12 (as monitored by pH paper), and the resulting solution was extracted with DCM (2 × 10 mL) to remove BQ and biphenyl (the undesired homocoupling byproduct), and the organic layers were back-extracted once with 2.0 M NaOH (10 mL). The combined aqueous layers were acidified *via* dropwise addition of concentrated HCl until the pH < 2, and the solution was extracted with EtOAc (3 × 50 mL). The organic layers were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 2:1 hexanes:EtOAc (with 3% HOAc) as the eluent. The results are shown in Tables 4.2 and 4.S3.

**Table 4.S3:** Optimisation of PhBF<sub>3</sub>K / Ag<sub>2</sub>CO<sub>3</sub> loading with substrates **4.1a** and **4.1b**.<sup>a</sup>

**4.1a** (R = CF<sub>3</sub>)  
**4.1b** (R = Me)

**4.2**

**4.3a** (R = CF<sub>3</sub>)  
**4.3b** (R = Me)

---

**% Conv. (4.3a)**

|                                          |     | PhBF <sub>3</sub> (equiv.) |     |                       |
|------------------------------------------|-----|----------------------------|-----|-----------------------|
|                                          |     | 1.5                        | 2.0 | 3.0                   |
| Ag <sub>2</sub> CO <sub>3</sub> (equiv.) | 1.0 | 89                         | 87  | 86                    |
|                                          | 1.5 | 88                         | >99 | >99                   |
|                                          | 2.0 | 87                         | >99 | >99 (98) <sup>b</sup> |

|                                          |     | PhBPin (equiv.) |     |          |
|------------------------------------------|-----|-----------------|-----|----------|
|                                          |     | 1.5             | 2.0 | 3.0      |
| Ag <sub>2</sub> CO <sub>3</sub> (equiv.) | 2.0 | >99             | >99 | >99 (92) |

**% Conv. (4.3b)**

|                                          |     | PhBF <sub>3</sub> (equiv.) |     |          |
|------------------------------------------|-----|----------------------------|-----|----------|
|                                          |     | 1.5                        | 2.0 | 3.0      |
| Ag <sub>2</sub> CO <sub>3</sub> (equiv.) | 1.0 | 68                         | 68  | 70       |
|                                          | 1.5 | 75                         | 90  | 92       |
|                                          | 2.0 | 90                         | 88  | >99 (97) |

|                                          |     | PhBPin (equiv.) |     |          |
|------------------------------------------|-----|-----------------|-----|----------|
|                                          |     | 1.5             | 2.0 | 3.0      |
| Ag <sub>2</sub> CO <sub>3</sub> (equiv.) | 2.0 | 80              | 93  | >99 (96) |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Isolated yield is given in parenthesis. <sup>b</sup> Under otherwise identical conditions, 74% conversion was observed using 2 mol% Pd(OAc)<sub>2</sub>, 2 mol% BQ, and 4 mol% Ac-Ile-OH.

**Pd(II)-catalysed C–H/organoboron cross-coupling with 2-(trifluoromethyl)phenylacetic acid (4.1a) at 70 °C:** A 25 mL sealed tube equipped with a magnetic stir bar was charged with 2-(trifluoromethyl)phenylacetic acid (**4.1a**) (102.1 mg, 0.50 mmol), potassium phenyltrifluoroborate (**4.2a**) (184.0 mg, 0.75 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), ligand (0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ag<sub>2</sub>CO<sub>3</sub> (137.2 mg, 0.5 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 70 °C. After being allowed to stir vigorously for 36 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals,

which appear as singlets (approximately 3.87 ppm for **4.1a** and 3.79 ppm for **4.3a**). The results are shown in Table 4.4.

#### 4.4.4. Kinetic Measurements

**Rate profile measurements with 2-(trifluoromethyl)phenylacetic acid (4.1a) and *o*-tolylacetic acid (4.1b):** For each substrate, two different reaction conditions were examined: (1) without Ac-Ile-OH and (2) with Ac-Ile-OH. A 100 mL Schlenk tube containing a magnetic stir bar was charged with **4.1a** (or **4.1b**) (1.00 mmol), phenyltrifluoroborate (**4.2a**) (552.0 mg, 3.0 mmol), Pd(OAc)<sub>2</sub> (11.2 mg, 0.050 mmol), BQ (5.4 mg, 0.050 mmol), Ac-Ile-OH (8.7 mg, 0.05 mmol) (when used), KHCO<sub>3</sub> (200.2 mg, 2.0 mmol), Ag<sub>2</sub>CO<sub>3</sub> (551.5 mg, 2.0 mmol), and *t*-AmylOH (5.0 mL). The reaction tube was capped with a rubber septum, then stirred at 110 °C. At the indicated time points, a small aliquot (< 0.1 mL) was removed from the vial. The aliquots were added to independent 10 mL scintillation vials containing a biphasic mixture of 2.0 N HCl solution (1.0 mL) and diethyl ether (2.0 mL). An aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a**, 3.79 ppm for **4.3a**, 3.67 ppm for **4.1b**, and 3.63 ppm for **4.3b**). The procedure was repeated three times. The resulting data were plotted, and linear regression of the time points in the 5–20 min period established the initial rate. The results are shown in Tables 4.S4–4.S7 and Figures 4.S1–4.S4.

**Table 4.S4:** Rate profile measurements for **4.1a** in the absence of Ac-Ile-OH.<sup>a</sup>

5 mol% Pd(OAc)<sub>2</sub>  
5 mol% BQ  
2 equiv. KHCO<sub>3</sub>  
2 equiv. Ag<sub>2</sub>CO<sub>3</sub>  
t-AmylOH, 110 °C  
Time

| % Conv. |            |         |         |         |         |           |
|---------|------------|---------|---------|---------|---------|-----------|
| Entry   | Time (min) | Trial 1 | Trial 2 | Trial 3 | Average | Std. Dev. |
| 1       | 0          | 0.0     | 0.0     | 0.0     | 0.0     | 0.0       |
| 2       | 5          | 0.0     | 0.6     | 0.9     | 0.5     | 0.5       |
| 3       | 7.5        | 1.2     | 0.9     | 1.2     | 1.1     | 0.2       |
| 4       | 10         | 1.3     | 1.2     | 2.4     | 1.6     | 0.7       |
| 5       | 15         | 3.2     | 1.6     | 3.7     | 2.8     | 1.1       |
| 6       | 20         | 4.3     | 3.2     | 5.1     | 4.2     | 1.0       |
| 7       | 30         | 6.7     | 3.4     | 6.5     | 5.5     | 1.9       |
| 8       | 60         | 11.2    | 6.2     | 12.9    | 10.1    | 3.5       |
| 9       | 90         | 13.0    | 9.6     | 17.7    | 13.4    | 4.1       |
| 10      | 120        | 16.4    | 12.8    | 22.0    | 17.1    | 4.6       |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

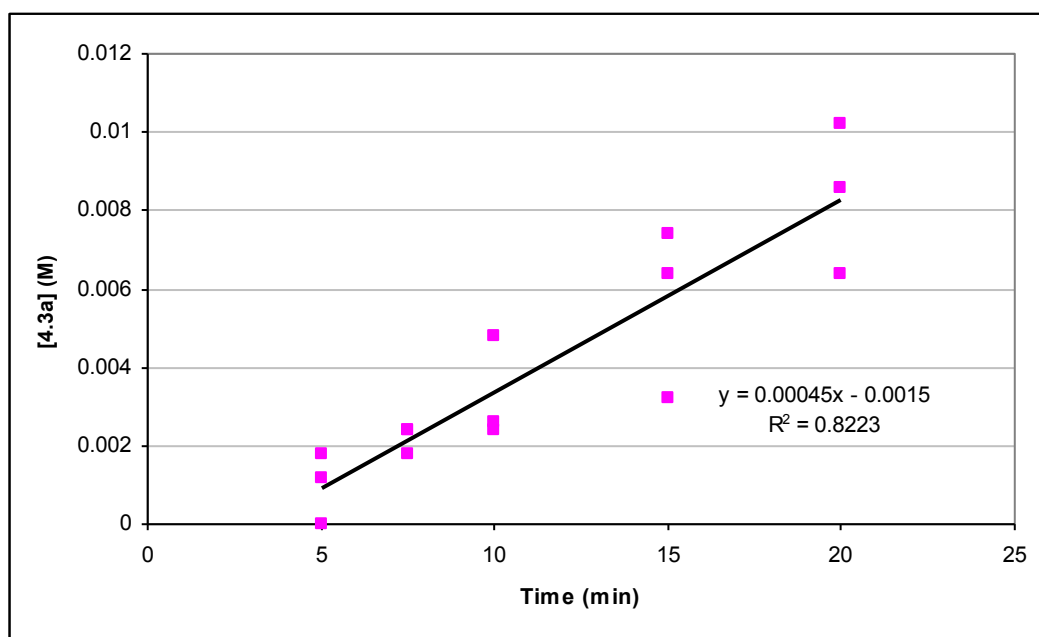
**Figure 4.S1:** Initial rate data for the formation of **4.3a** in the absence of Ac-Ile-OH.

**Table 4.S5:** Rate profile measurements for **4.1a** with Ac-Ile-OH.<sup>a</sup>

|       |            | % Conv. |         |         |         |           |
|-------|------------|---------|---------|---------|---------|-----------|
| Entry | Time (min) | Trial 1 | Trial 2 | Trial 3 | Average | Std. Dev. |
| 1     | 0          | 0.0     | 0.0     | 0.0     | 0.0     | 0.0       |
| 2     | 5          | 5.2     | 5.3     | 0.1     | 3.5     | 3.0       |
| 3     | 7.5        | 13.6    | 5.9     | 3.6     | 7.7     | 5.2       |
| 4     | 10         | 22.2    | 8.3     | 5.5     | 12.0    | 8.9       |
| 5     | 15         | 36.6    | 12.3    | 12.1    | 20.2    | 13.9      |
| 6     | 20         | 62.0    | 14.1    | 19.9    | 32.0    | 26.1      |
| 7     | 30         | 96.3    | 28.3    | 40.8    | 55.1    | 36.2      |
| 8     | 60         | 97.0    | 62.7    | 98.9    | 86.2    | 20.4      |
| 9     | 90         | 100.0   | 100.0   | 100.0   | 100.0   | 0.0       |
| 10    | 120        | 100.0   | 100.0   | 100.0   | 100.0   | 0.0       |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

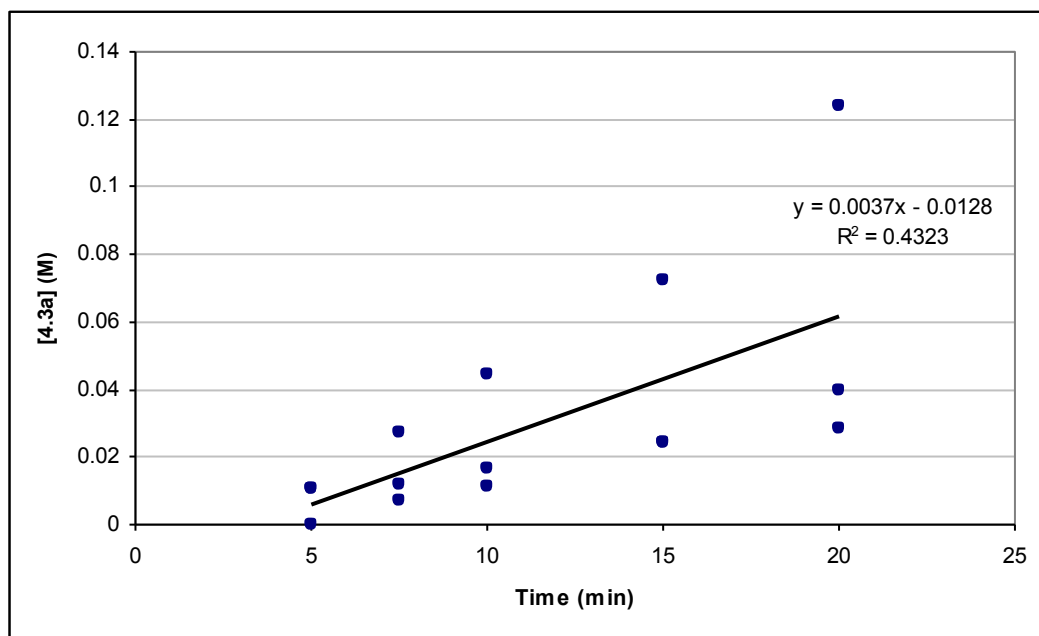
**Figure 4.S2:** Initial rate data for the formation of **4.3a** with Ac-Ile-OH.

**Table 4.S6:** Rate profile measurements for **4.1b** in the absence of Ac-Ile-OH.<sup>a</sup>

5 mol% Pd(OAc)<sub>2</sub>  
5 mol% BQ  
2 equiv. KHCO<sub>3</sub>  
2 equiv. Ag<sub>2</sub>CO<sub>3</sub>  
t-AmylOH, 110 °C  
Time

| % Conv. |            |         |         |         |         |           |
|---------|------------|---------|---------|---------|---------|-----------|
| Entry   | Time (min) | Trial 1 | Trial 2 | Trial 3 | Average | Std. Dev. |
| 1       | 0          | 0.0     | 0.0     | 0.0     | 0.0     | 0.0       |
| 2       | 5          | 0.0     | 1.4     | 0.0     | 0.5     | 0.8       |
| 3       | 7.5        | 2.8     | 2.2     | 0.0     | 1.7     | 1.5       |
| 4       | 10         | 3.1     | 4.1     | 1.1     | 2.8     | 1.5       |
| 5       | 15         | 4.5     | 6.3     | 2.2     | 4.3     | 2.1       |
| 6       | 20         | 5.1     | 8.2     | 4.4     | 5.9     | 2.0       |
| 7       | 30         | 6.5     | 12.4    | 6.7     | 8.5     | 3.4       |
| 8       | 60         | 13.0    | 20.9    | 10.8    | 14.9    | 5.3       |
| 9       | 90         | 18.2    | 21.7    | 13.7    | 17.9    | 4.0       |
| 10      | 120        | 25.6    | 33.7    | 19.5    | 26.3    | 7.1       |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

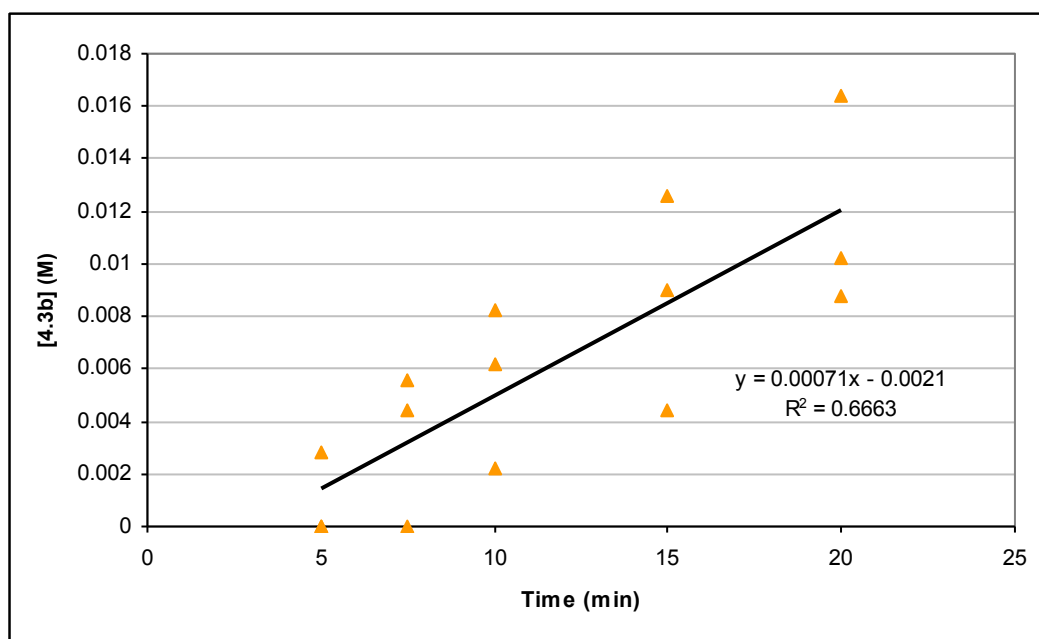
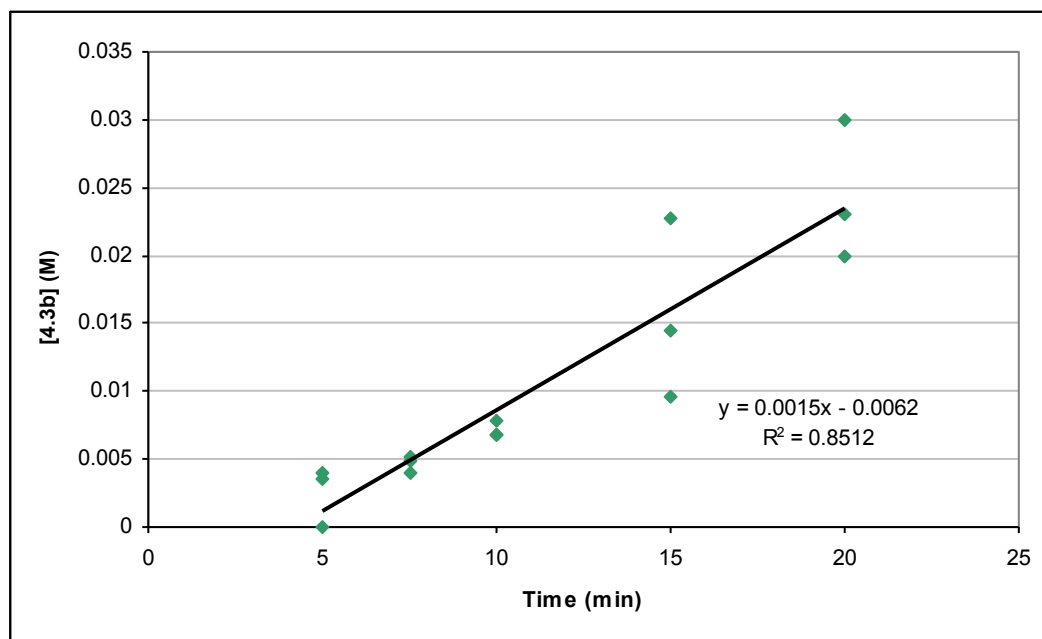
**Figure 4.S3:** Initial rate data for the formation of **4.3b** in the absence of Ac-Ile-OH.

**Table 4.S7:** Rate profile measurements for **4.1b** with Ac-Ile-OH.<sup>a</sup>

|       |            | % Conv. |         |         |         |           |
|-------|------------|---------|---------|---------|---------|-----------|
| Entry | Time (min) | Trial 1 | Trial 2 | Trial 3 | Average | Std. Dev. |
| 1     | 0          | 0.0     | 0.0     | 0.0     | 0.0     | 0.0       |
| 2     | 5          | 1.8     | 2.0     | 0.0     | 1.3     | 1.1       |
| 3     | 7.5        | 2.6     | 2.4     | 2.0     | 2.3     | 0.3       |
| 4     | 10         | 3.4     | 3.9     | 3.4     | 3.6     | 0.3       |
| 5     | 15         | 4.8     | 11.4    | 7.2     | 7.8     | 3.3       |
| 6     | 20         | 10.0    | 15.0    | 11.5    | 12.2    | 2.6       |
| 7     | 30         | 21.0    | 20.0    | 16.6    | 19.2    | 2.3       |
| 8     | 60         | 61.9    | 59.8    | 54.4    | 58.7    | 3.9       |
| 9     | 90         | 91.5    | 93.6    | 94.6    | 93.2    | 1.6       |
| 10    | 120        | 97.2    | 94.9    | 100.0   | 97.4    | 2.6       |

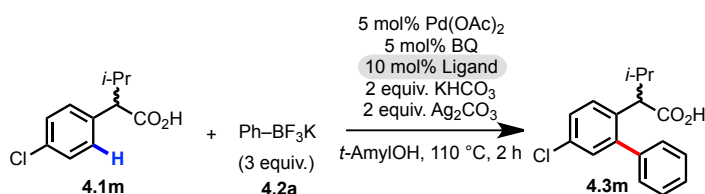
<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

**Figure 4.S4:** Initial rate data for the formation of **4.3b** with Ac-Ile-OH.

#### 4.4.5. Potential Match/Mismatch Effect with Chiral Substrates

It was observed that some  $\alpha$ -substituted phenylacetic acids gave lower conversions than their unsubstituted counterparts (*e.g.*, (*rac*)-**4.3m**). This finding prompted us to question whether we were observing a match/mismatch effect between the racemic, chiral starting material and the non-racemic, chiral catalyst. Based on this thinking, we hypothesised that one of the two enantiomers of the racemic starting material was reacting preferentially (*i.e.*, a partial kinetic resolution) and that that was leading to the low overall conversions. To test this hypothesis, we exposed 2-(4-chlorophenyl)-3-methylbutyric acid ((*rac*)-**4.1m**) to our reaction conditions using enantiopure and racemic versions of Ac-Ile-OH and Boc-Ile-OH. In both cases the racemic versions of the ligands, were prepared by mixing the L- and D-amino acids in a 1:1 ratio. Because Ac-D-Ile-OH was not commercially available, we synthesised it *via* routine *N*-acylation.<sup>46</sup> The data, which is shown in Table 4.S8, seems to refute this hypothesis, since both the (*rac*)- and the L-amino acids gave similar conversions after 2 h.

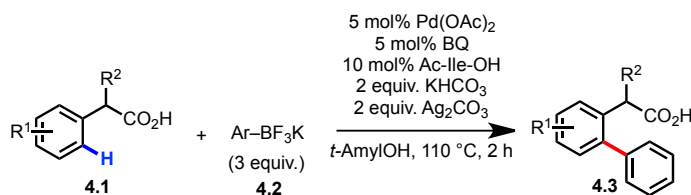
**Table 4.S8:** The effect of ligand stereochemistry on the conversion with a representative chiral starting material, (*rac*)-**4.1m**.<sup>a</sup>



| Entry | Ligand                  | % Conv. |
|-------|-------------------------|---------|
| 1     | Ac-L-Ile-OH             | 77      |
| 2     | Ac- <i>rac</i> -Ile-OH  | 77      |
| <hr/> |                         |         |
| 3     | Boc-L-Ile-OH            | 60      |
| 4     | Boc- <i>rac</i> -Ile-OH | 59      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.



4.4.6. General Procedure with  $\text{Ag}_2\text{CO}_3$  as the Oxidant

**Scheme 4.S1:** General procedure for C–H/organoboron cross-coupling using  $\text{Ag}_2\text{CO}_3$  as the oxidant.

**General procedure for Pd(II)-catalysed C–H/organoboron cross-coupling with phenylacetic acids (4.1) and potassium trifluoroborates (4.2) using  $\text{Ag}_2\text{CO}_3$  as the oxidant:** A 25 mL sealed tube equipped with a magnetic stir bar was charged with the phenylacetic acid substrate (4.1) (0.50 mmol), the aryltrifluoroborate (4.2) (1.5 mmol),  $\text{Pd}(\text{OAc})_2$  (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), Ac-Ile-OH (8.7 mg, 0.05 mmol),  $\text{KHCO}_3$  (100.1 mg, 1.0 mmol),  $\text{Ag}_2\text{CO}_3$  (275.8 mg, 1.0 mmol), and  $t$ -AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for 2 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The conversion was determined by integration of the benzylic proton signals—4.3 generally appears upfield from 4.1. To isolate the pure product 4.3, the biphasic mixture was basified with concentrated aqueous NaOH until the pH > 12 (as monitored by pH paper), and the resulting solution was extracted with DCM ( $2 \times 10$  mL) to remove BQ and the biaryl homocoupling byproduct, and the organic layers were back-extracted once with 2.0 N NaOH (10 mL). The combined aqueous layers were acidified *via* dropwise addition of concentrated HCl until the pH < 2, and the solution was extracted with EtOAc ( $3 \times 50$  mL). The organic layers were combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash

column chromatography using 2:1 hexanes:EtOAc (with 3% HOAc) as the eluent. Products **4.3i**, (*rac*)-**4.3o**, **4.3s**, and **4.3w** were prepared on a 0.2 mmol scale, using the same relative amounts of reagents. For each substrate, a control experiment in the absence of Ac-Ile-OH was run, and the conversion was determined in a similar manner; however the product (which was generally observed in scant quantities) was not isolated. The results in the presence and absence of ligand are shown in Tables 4.5 and 4.6.

#### 4.4.7. Ligand Acceleration: Optimisation of Aerobic Conditions

**Ligand optimisation for Pd(II)-catalysed C–H/organoboron cross-coupling with 2-(trifluoromethyl)phenylacetic acid (4.1a):** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with 2-(trifluoromethyl)phenylacetic acid (**4.1a**) (102.1 mg, 0.50 mmol), potassium phenyltrifluoroborate (**4.2a**) (184.0 mg, 0.75 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (10.8 mg, 0.1 mmol), ligand (0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) (× 3). It was then immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for 24 h, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a** and 3.79 ppm for **4.3a**). The results are shown in Tables 4.7 and 4.S9.

**Table 4.S9:** Results from the ligand screening experiments under aerobic conditions.<sup>a</sup>

| Entry | Ligand <sup>b</sup>       | % Conv. | Entry | Ligand <sup>b</sup>                   | % Conv. |
|-------|---------------------------|---------|-------|---------------------------------------|---------|
| 1     | ---                       | 9       | 13    | H-Val-OH                              | 6       |
| 2     | Boc-Ala-OH                | 39      | 14    | Formyl-Val-OH                         | 52      |
| 3     | Boc-Phe-OH                | 48      | 15    | Piv-Val-OH                            | 9       |
| 4     | Boc-Ser-OH                | 26      | 16    | Ada-Val-OH                            | 24      |
| 5     | Boc-Thr( <i>t</i> -Bu)-OH | 40      | 17    | Me(O <sub>2</sub> C)-Val-OH           | 50      |
| 6     | Boc-Aib-OH                | 44      | 18    | Et(O <sub>2</sub> C)-Val-OH           | 46      |
| 7     | Boc-Leu-OH                | 57      | 19    | Cbz-Val-OH                            | 52      |
| 8     | Boc- <i>t</i> -Leu-OH     | 57      | 20    | Fmoc-Val-OH                           | 20      |
| 9     | Boc-Ile-OH                | 49      | 21    | <i>i</i> -Bu(O <sub>2</sub> C)-Val-OH | 49      |
| 10    | Boc-Abu-OH                | 60      | 22    | Ac-Val-OH                             | 52      |
| 11    | Boc-Nle-OH                | 48      | 23    | Ac-Leu-OH                             | 56      |
| 12    | Boc-Val-OH                | 65      | 24    | Ac-Ile-OH                             | 56      |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.<sup>b</sup> Aib =  $\alpha$ -aminoisobutyric acid, Abu = L-2-aminobutyric acid, Nle = L-Norleucine, Ada = 1-adamantyl(CO), Piv = pivaloyl.**Optimisation of BQ loading / reaction time 2-(trifluoromethyl)phenylacetic acid**

**(4.1):** A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with 2-(trifluoromethyl)phenylacetic acid (**4.1a**) (102.1 mg, 0.50 mmol), potassium phenyltrifluoroborate (**4.2a**) (184.0 mg, 0.75 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ, Boc-Val-OH (10.9 mg, 0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped, then evacuated briefly under high vacuum and charged with O<sub>2</sub> (1 atm, balloon) ( $\times$  3). It was then immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for the appropriate amount of time, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed

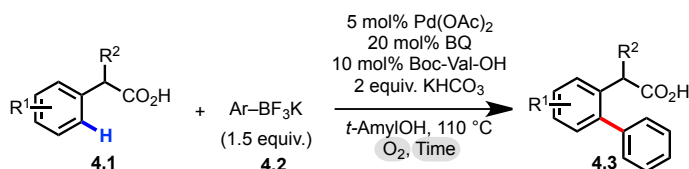
by  $^1\text{H}$  NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a** and 3.79 ppm for **4.3a**). The results are shown in Table 4.S10.

**Table 4.S10:** Optimisation of BQ loading / reaction time.<sup>a</sup>

|               |     | Time |      |      |
|---------------|-----|------|------|------|
|               |     | 2 h  | 24 h | 48 h |
| BQ<br>(mol %) | --- | 5    | 5    | 5    |
|               | 5   | 27   | 50   | 54   |
|               | 10  | 13   | 56   | 56   |
|               | 20  | 13   | 65   | 65   |
|               | 50  | 13   | 33   | 34   |

<sup>a</sup> The conversion was determined by  $^1\text{H}$  NMR analysis of the crude reaction mixture.

#### 4.4.8. General Procedure with Aerobic Conditions



**Scheme S2:** General procedure for C–H/organoboron cross-coupling under aerobic conditions.

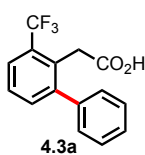
**General procedure for Pd(II)-catalysed C–H/organoboron cross-coupling of phenylacetic acids (4.1) with potassium trifluoroborates (4.2) using O<sub>2</sub> (or air) as the oxidant:** For experiments using >1 atm of pressure, a 45 mL high pressure vessel was used. For experiments using 1 atm of pressure, a 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) was used. The reaction flask was equipped with a magnetic stir bar and was charged with the phenylacetic acid substrate (**1**) (0.50 mmol), the aryltrifluoroborate (**4.2**) (0.75 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (10.8 mg, 0.1

mmol), Boc-Val-OH (10.9 mg, 0.05 mmol),  $\text{KHCO}_3$  (100.1 mg, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction vessel was capped and adjusted to the appropriate pressure of  $\text{O}_2$  (or air). *A note of caution: when working with high pressure  $\text{O}_2$ , proper safety measures (including the use of a blast shield) should be taken.* After being allowed to stir vigorously for the appropriate time, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. The pressure was released, and a 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by  $^1\text{H}$  NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets—**4.3** generally appears upfield from **4.1**. To isolate the pure product (**4.3**), the biphasic mixture was basified with concentrated aqueous NaOH until the pH > 12 (as monitored by pH paper), the resulting solution was extracted with DCM ( $2 \times 10$  mL) to remove BQ and biphenyl (the undesired homocoupling byproduct), and the organic layers were back-extracted once with 2.0 M NaOH (10 mL). The combined aqueous layers were acidified *via* dropwise addition of concentrated HCl until the pH < 2, and the solution was extracted with EtOAc ( $3 \times 50$  mL). The organic layers were combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using 2:1 hexanes:EtOAc (with 3% HOAc) as the eluent. For each substrate under each of the conditions reported, a control experiment in the absence of Ac-Ile-OH was run, and the conversion was determined in a similar manner; however the product (which was generally observed in scant quantities) was not isolated. The results are shown in Table 4.8.

#### 4.4.9. Characterisation of New Compounds

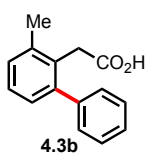
Our group has previously reported a procedure for Pd(II)-catalysed C–H/arylboron cross-coupling using benzoic and phenylacetic acid substrates under high pressure  $\text{O}_2$  (20

atm).<sup>13</sup> In that publication, **4.3i**, (*rac*)-**4.3m**, and **4.3l** were also synthesised but were isolated as their methyl esters following treatment of the crude product mixture with CH<sub>2</sub>N<sub>2</sub>. This was done to simplify the separation of the product from residual unreacted starting material, which is problematic using the free acids. Because the reactions reported here generally gave quantitative yields, the pure products could consistently be isolated as free acids. We have included the analytical data for free acids **4.3i**, (*rac*)-**4.3m**, and **4.3l**. To determine whether racemisation took place during the reaction with enantiopure (*S*)-naproxen ((*S*)-**4.1n**) as the starting material, chiral HPLC was used. Compound (*S*)-**4.3n** was prepared using the standard reaction conditions from commercially available (*S*)-naproxen ((*S*)-**4.1n**) (MP Biomedical). Compound (*rac*)-**4.3n** was prepared using the standard reaction conditions from a 1:1 mixture of commercially available (*S*)-naproxen ((*S*)-**4.1n**) (MP Biomedical) and (*R*)-naproxen ((*R*)-**4.1n**) (Aldrich). These products were converted to the corresponding methyl esters, **Me-(S)-4.3n** and **Me-(rac)-4.3n**, in order to improve separation with chiral HPLC. Because the analytical data for the enantiopure and racemic forms of **4.3n** and **Me-4.3n** are identical, only the data for (*S*)-**4.1n** and **Me-(S)-4.3n** are reported below. The chiral HPLC method was optimised using **Me-(rac)-4.3n** as the standard, and the er of **Me-(S)-4.3n** was subsequently determined

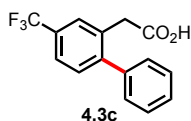


**2-(2-(trifluoromethyl)phenyl)acetic acid (4.3a):** The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (137 mg, 98% yield). *R<sub>f</sub>* = 0.82 (hexanes:EtOAc 1:1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.72 (t, *J* = 5.6 Hz, 1 H), 7.46–7.38 (m, 5 H), 7.28–7.24 (m, 2 H), 3.80 (s, 2 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 176.38, 145.41, 139.95, 133.78, 129.64, 129.55 (q, *J*<sub>C-F</sub> = 29.5 Hz), 128.88, 128.46, 127.87, 127.33, 125.45 (q, *J*<sub>C-F</sub> = 5.7 Hz), 124.38 (q, *J*<sub>C-F</sub> = 272.5 Hz), 35.18; IR

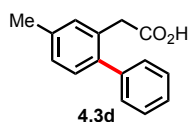
(neat)  $\nu$  3026, 2930, 1713, 1325, 1232, 1164, 1118, 1047, 942  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{12}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  281.0789, found 281.0788.



**2-(3-methylbiphenyl-2-yl)acetic acid (4.3b):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (129 mg, 97% yield).  $R_f$  = 0.74 (hexanes:EtOAc 1:1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.35 (m, 3 H), 7.31–7.21 (m, 4 H), 7.14–7.12 (m, 1 H), 3.65 (s, 2 H), 2.36 (s, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.48, 143.30, 141.65, 137.64, 129.96, 129.50, 129.09, 128.22, 127.92, 127.16, 127.13, 36.03, 20.19; **IR** (neat)  $\nu$  3.025, 2924, 1704, 1466, 1410, 1232, 762, 703  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{15}\text{O}_2$   $[\text{M}+\text{H}]^+$  227.1067, found 227.1059.

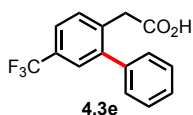


**2-(4-(trifluoromethyl)biphenyl-2-yl)acetic acid (4.3c)** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (136 mg, 97% yield).  $R_f$  = 0.66 (hexanes:EtOAc 1:1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64–7.59 (m, 2 H), 7.45–7.40 (m, 4 H), 7.30–7.26 (m, 2 H), 3.69 (s, 2 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.16, 146.14, 139.51, 131.91, 130.72, 129.82 (q,  $J_{\text{C-F}}$  = 32.6 Hz), 128.88, 128.51, 127.94, 127.35 (q,  $J_{\text{C-F}}$  = 3.7 Hz), 124.22 (q,  $J_{\text{C-F}}$  = 3.4 Hz), 123.99 (q,  $J_{\text{C-F}}$  = 270.9 Hz), 38.36; **IR** (neat)  $\nu$  3029, 2928, 1695, 1420, 1332, 1234, 1171, 1119, 1084, 912, 838  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{12}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  281.0784, found 281.0783.

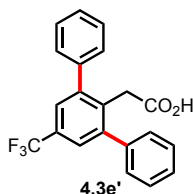


**2-(4-methylbiphenyl-2-yl)acetic acid (4.3d):** The title compound was prepared on a 0.5 mmol scale and obtained as a yellow oil (126 mg, 95% yield).  $R_f$  = 0.71 (hexanes:EtOAc 1:1);  $^1\text{H}$  NMR (400 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  7.41–7.34 (m, 3 H), 7.30–7.28 (m, 2 H), 7.19–7.16 (m, 3 H), 3.60 (s, 2 H), 2.39 (s, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  173.12, 142.22, 140.48, 137.65, 133.07, 132.13, 130.65, 130.06, 129.01,

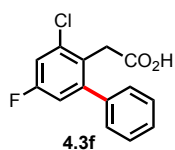
128.48, 127.78, 38.84, 21.05; **IR** (neat)  $\nu$  3024, 2922, 1705, 1484, 1412, 1291, 916, 824, 764  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{15}\text{O}_2$   $[\text{M}+\text{H}]^+$  227.1067, found 227.1062.



**2-(5-(trifluoromethyl)biphenyl-2-yl)acetic acid (4.3e):** The title compound was prepared on a 0.5 mmol scale and obtained as a white solid (73 mg, 52% yield).  $R_f$  = 0.63 (hexanes:EtOAc 1:1);  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.61 (d,  $J$  = 8.0 Hz, 1 H), 7.55 (s, 1 H), 7.50 (d,  $J$  = 8.0 Hz, 1 H), 7.45–7.41 (m, 3 H), 7.30 (d,  $J$  = 6.8 Hz, 2 H), 3.69 (s, 2 H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  175.61, 143.20, 139.42, 134.95, 130.95, 129.72 ( $J_{\text{C-F}}$  = 32.4 Hz), 129.02, 128.54, 127.93, 127.08 ( $J_{\text{C-F}}$  = 3.8 Hz), 124.28 ( $J_{\text{C-F}}$  = 3.8 Hz), 123.95 ( $J$  = 270.8 Hz), 38.10; **IR** (neat)  $\nu$  3033, 2926, 1712, 1413, 1337, 1259, 1168, 1125, 1078, 904, 771  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{12}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  281.0784, found 281.0783.



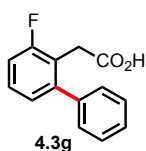
**2,6-diphenyl-4-(trifluoromethyl)phenylacetic acid (4.3e'):** The title compound was generated during the synthesis of **4.3e** and isolated as a white solid (50 mg, 28% yield).  $R_f$  = 0.71 (hexanes:EtOAc 1:1);  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.54 (s, 2 H), 7.45–7.40 (m, 6 H), 7.35–7.30 (m, 4 H), 3.59 (s, 2 H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  176.83, 144.21, 140.06, 133.24, 129.26 ( $J_{\text{C-F}}$  = 32.4 Hz), 128.89, 128.52, 127.94, 125.95 ( $J_{\text{C-F}}$  = 3.7 Hz), 123.92 ( $J_{\text{C-F}}$  = 270.9 Hz), 36.44; **IR** (neat)  $\nu$  2926, 2855, 1709, 1421, 1363, 1266, 1170, 1128, 897, 772  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{16}\text{F}_3\text{O}_2$   $[\text{M}+\text{H}]^+$  357.1097, found 357.1108.



**2-(3-chloro-5-fluorobiphenyl-2-yl)acetic acid (4.3f):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (130 mg, 98% yield).  $R_f$  = 0.56 (hexanes:EtOAc 1:1);  **$^1\text{H}$  NMR** (400 MHz,

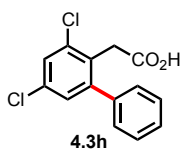


CDCl<sub>3</sub>)  $\delta$  7.46–7.39 (m, 3 H), 7.28–7.26 (m, 2 H), 7.19 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 2.8$  Hz, 1 H), 6.95 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 2.8$  Hz, 1 H), 3.71 (s, 2 H); <sup>13</sup>C NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO)  $\delta$  171.77, 161.66 (d,  $J_{C-F} = 246.3$  Hz), 147.19 (d,  $J_{C-F} = 8.5$  Hz), 140.68, 129.51, 129.42, 129.00, 128.63 (d,  $J_{C-F} = 3.6$  Hz), 116.35 (d,  $J = 22.7$  Hz), 116.34 (d,  $J = 23.2$  Hz), 36.66; IR (neat)  $\nu$  3027, 2926, 1709, 1598, 1585, 1575, 1459, 1411, 1302, 1236, 11.78, 1140, 943, 870 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>14</sub>H<sub>11</sub>ClFO<sub>2</sub> [M+H]<sup>+</sup> 265.0432, [(M+2)+H]<sup>+</sup> 267.0402, found 265.0425, 267.0413 [M+H]<sup>+</sup>: [(M+2)+H]<sup>+</sup> = 3:1.



**2-(3-fluorobiphenyl-2-yl)acetic acid (4.3g):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (110 mg, 96% yield).

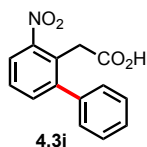
$R_f = 0.59$  (hexanes:EtOAc 1:1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.44–7.38 (m, 3 H), 7.36–7.30 (m, 3 H), 7.11–7.07 (m, 2 H), 3.66 (s, 2 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  177.04, 161.56 (d,  $J_{C-F} = 245.2$  Hz), 144.68 (d,  $J_{C-F} = 3.7$  Hz), 139.62 (d,  $J_{C-F} = 2.6$  Hz), 128.99, 128.56 (d,  $J_{C-F} = 9.2$  Hz), 128.44, 127.68, 125.62 (d,  $J_{C-F} = 3.1$  Hz), 119.31 (d,  $J_{C-F} = 15.9$  Hz), 114.08 (d,  $J_{C-F} = 22.1$  Hz), 32.20; IR (neat)  $\nu$  3025, 2927, 1707, 1573, 1462, 1410, 1289, 1238, 947, 795, 761, 703 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>14</sub>H<sub>12</sub>FO<sub>2</sub> [M+H]<sup>+</sup> 231.0816, found 231.0812.



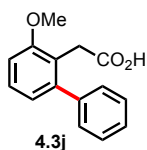
**2-(3,5-dichlorobiphenyl-2-yl)acetic acid (4.3h):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (138 mg, 98% yield).  $R_f = 0.56$  (hexanes:EtOAc 1:1); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$

7.44–7.41 (m, 4 H), 7.27–7.25 (m, 2 H), 7.21 (s, 1 H), 3.71 (s, 2 H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  176.53, 145.85, 139.27, 136.29, 133.36, 128.72, 128.67, 128.66, 128.61, 128.26, 128.17, 36.35; IR (neat)  $\nu$  3027, 2928, 1706, 1584, 1556, 1411, 1392, 1234, 1158, 937, 863, 768, 701 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  Calcd for C<sub>14</sub>H<sub>11</sub>Cl<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup> 281.0136,

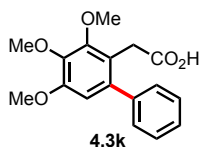
$[(M+2)+H]^+$  283.0107,  $[(M+4)+H]^+$  282.0170, found 281.0124, 283.0106, 285.0078  
 $[M+H]^+ : [(M+2)+H]^+ : [(M+4)+H]^+ = 9:6:1$ .



**2-(3-nitrophenyl-2-yl)acetic acid (4.3i):** The title compound was prepared on a 0.2 mmol scale and obtained as a white solid (35 mg, 69% yield).  $R_f = 0.40$  (hexanes:EtOAc 1:1);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.10 (dd,  $J_I = 10.1$  Hz,  $J_I = 3.0$ , 1 H), 7.58–7.43 (m, 5 H), 7.29–7.26 (m, 2 H), 3.93 (2 H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  176.44, 149.57, 145.84, 139.05, 135.23, 128.98, 128.74, 128.27, 127.90, 126.73, 124.40, 36.03; IR (neat)  $\nu$  2928, 2856, 1710, 1528, 1347, 1228, 704  $cm^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{14}H_{12}NO_4$   $[M+H]^+$  258.0761, found 258.0770.

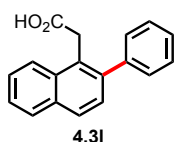


**2-(3-methoxyphenyl-2-yl)acetic acid (4.3j):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (114 mg, 94% yield).  $R_f = 0.47$  (hexanes:EtOAc 1:1);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.38–7.21 (m, 6 H), 6.87 (ad,  $J = 8.0$  Hz, 2 H), 3.83 (s, 3 H), 3.57 (s, 2 H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  178.10, 157.83, 143.92, 140.84, 129.11, 128.23, 128.01, 127.23, 122.35, 120.65, 109.26, 55.72, 33.33; IR (neat)  $\nu$  3021, 2938, 1704, 1584, 1466, 1434, 1258, 1203, 1117, 1020, 761, 703  $cm^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $C_{15}H_{15}O_3$   $[M+H]^+$  243.1016, found 243.1022

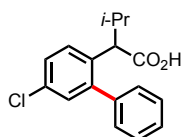


**2-(3,4,5-trimethoxyphenyl-2-yl)acetic acid (4.3k):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (128 mg, 85% yield).  $R_f = 0.50$  (hexanes:EtOAc 1:1);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.42–7.34 (m, 3 H), 7.31–7.28 (m, 2 H), 6.60 (s, 1 H), 3.95 (s, 3 H), 3.91 (s, 3 H), 3.85 (s, 3 H), 3.54 (s, 2 H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  178.02, 152.44, 152.00, 140.97,

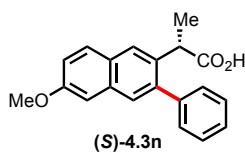
140.82, 138.19, 129.09, 128.31, 127.31, 118.19, 108.78, 60.75, 60.58, 55.94, 33.32; **IR** (neat)  $\nu$  2939, 2838, 1707, 1484, 1403, 1250, 1247, 1199, 1110, 1048, 914, 842, 772  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{17}\text{H}_{19}\text{O}_5$   $[\text{M}+\text{H}]^+$  303.1227, found 303.1224.



**2-(2-phenylnaphthalen-1-yl)acetic acid (4.3l):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (105 mg, 80% yield).  $R_f$  = 0.71 (hexanes:EtOAc 1:1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d,  $J$  = 8.4 Hz, 1 H), 7.91 (d,  $J$  = 8.0 Hz, 1 H), 7.85 (d,  $J$  = 8.4 Hz, 1 H), 7.59 (t,  $J$  = 8.0 Hz, 1 H), 7.53 (t,  $J$  = 8.0 Hz, 1 H), 7.47–7.38 (m, 6 H), 4.07 (s, 2 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.67, 141.72, 140.80, 132.90, 132.38, 129.38, 128.75, 128.32, 128.17, 127.79, 127.33, 127.03, 126.69, 125.75, 123.94, 35.65; **IR** (neat)  $\nu$  3054, 2930, 1707, 1471, 1411, 1216, 1112, 1074, 1003, 820, 766, 743  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{18}\text{H}_{15}\text{O}_2$   $[\text{M}+\text{H}]^+$  263.1067, found 263.1059.



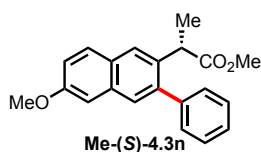
**2-(5-chlorobiphenyl-2-yl)-3-methylbutanoic acid ((rac)-4.3m):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (113 mg, 78% yield).  $R_f$  = 0.81 (hexanes:EtOAc 1:1);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.55 (d,  $J$  = 8.4 Hz, 1 H), 7.45–7.37 (m, 3 H), 7.35–7.32 (m, 3 H), 7.25 (d,  $J$  = 2.0 Hz, 1 H), 3.39 (d,  $J$  = 10.8 Hz, 1 H), 2.28–2.20 (m, 1 H), 0.92 (d,  $J$  = 6.8 Hz, 3 H), 0.52 (d,  $J$  = 6.8 Hz, 3 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  179.23, 144.81, 139.71, 134.25, 132.54, 129.99, 129.64, 128.77, 128.24, 127.89, 127.55, 53.62, 32.67, 21.35, 19.65; **IR** (neat)  $\nu$  2963, 2929, 1704, 1468, 1616, 1389, 1293, 1220, 1097, 771, 702  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{17}\text{H}_{18}\text{ClO}_2$   $[\text{M}+\text{H}]^+$  289.0995,  $[(\text{M}+2)+\text{H}]^+$  291.0966, found 289.1004, 291.0976  $[\text{M}+\text{H}]^+ : [(\text{M}+2)+\text{H}]^+ = 3:1$ .



**(S)-2-(6-methoxy-3-phenylnaphthalen-2-yl)propanoic acid ((S)-**

**4.3n)**: The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (149 mg, 97% yield).  $R_f$  = 0.80

(hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.82 (s, 1 H), 7.74 (d,  $J$  = 9.0 Hz, 1 H), 7.62 (s, 1 H), 7.47–7.40 (m, 5 H), 7.15 (dd,  $J_1$  = 9.0 Hz,  $J_2$  = 2.4 Hz, 1 H), 7.09 (d,  $J_1$  = 2.4 Hz, 1 H), 4.00 (q,  $J$  = 6.8 Hz, 1 H), 3.91 (s, 3 H), 1.44 (d,  $J$  = 6.8 Hz, 3 H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  180.45, 157.99, 141.05, 140.69, 134.26, 133.29, 129.58, 129.13, 128.37, 128.18, 127.93, 127.23, 125.72, 119.18, 105.26, 55.32, 40.81, 19.23; **IR** (neat)  $\nu$  2950, 2935, 1702, 1633, 1605, 1491, 1464, 1397, 1233, 1210, 1032, 897  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{20}\text{H}_{19}\text{O}_3$   $[\text{M}+\text{H}]^+$  307.1329, found 307.1331.



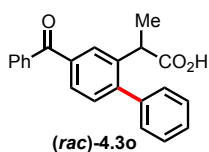
**(S)-methyl 2-(6-methoxy-3-phenylnaphthalen-2-yl)propanoate**

**(Me-(S)-4.3n)**: The title compound was synthesised from **(S)-4.3n**,

which was prepared on a 0.5 mmol scale using the standard procedure

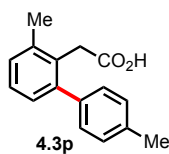
and a modified work-up that avoids strongly basic conditions (to reduce the risk of racemisation). After the reaction was stopped and cooled to 0 °C in an ice bath, a 2.0 N HCl solution (5 mL) was added. The mixture was extracted with EtOAc (3  $\times$  15 mL). The organic layers were combined, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. The resulting residue was dissolved in a 1:1 mixture of DCM:MeOH (5 mL). Excess  $\text{CH}_2\text{N}_2$ <sup>47,48</sup> was added dropwise until bubbling was no longer observed. The solution was allowed to stir for 20 min, at which point several drops of HOAc were added to quench the residual  $\text{CH}_2\text{N}_2$ . *A note of caution:  $\text{CH}_2\text{N}_2$  is explosive and toxic and should be handled in a well-maintained fumehood. The operator should have appropriate protection at all times.* Following removal of the solvent *in vacuo*, the purification was carried out using silica gel flash column chromatography with a 20:1 hexanes:EtOAc solvent system. The title

compound was obtained as a colourless oil (152 mg, 95% yield over two steps).  $R_f = 0.73$  (hexanes:EtOAc 4:1);  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (s, 1 H), 7.74 (d,  $J = 8.9$  Hz, 1 H), 7.61 (s, 1 H), 7.48–7.44 (m, 2 H), 7.41–7.39 (m, 3 H), 7.15 (d,  $J = 8.9$  Hz, 1 H), 7.09 (s, 1 H), 3.97 (q,  $J = 7.0$  Hz, 1 H), 3.91 (s, 3 H), 3.62 (s, 3 H), 1.43 (d,  $J = 7.0$  Hz, 3 H);  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  175.64, 157.93, 141.22, 140.67, 134.90, 133.18, 129.55, 129.14, 128.42, 128.14, 127.89, 127.18, 125.52, 119.11, 105.26, 55.32, 51.98, 41.01, 19.54;  $\text{IR}$  (neat)  $\nu$  2933, 2850, 1735, 1633, 1605, 1491, 1463, 1397, 1232, 1218, 1198, 1167, 1032, 897  $\text{cm}^{-1}$ ;  $\text{HRMS}$  (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{21}\text{H}_{21}\text{O}_3$   $[\text{M}+\text{H}]^+$  321.1485, found 321.1481.  $\text{HPLC}$  >99:1 er (Chiralcel OD-H, 0.5 mL/min, 10% *i*-PrOH/hexanes)  $t_R = 12.23$  min (major),  $t_R = 16.80$  min (minor).



**2-(4-benzoylbiphenyl-2-yl)propanoic acid ((rac)-4.3o):** The title compound was prepared on a 0.2 mmol scale and obtained as a yellow oil (58 mg, 88% yield).  $R_f = 0.64$  (hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,

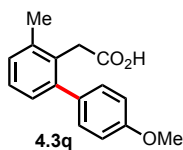
$\text{CDCl}_3$ )  $\delta$  7.92 (s, 1 H), 7.83 (d,  $J = 7.6$  Hz, 2 H), 7.73 (d,  $J = 7.6$  Hz, 1 H), 7.58 (t,  $J = 7.2$  Hz, 1 H), 7.50–7.42 (m, 5 H), 7.40–7.36 (m, 3 H), 4.00 (q,  $J = 7.2$  Hz, 1 H), 1.42 (d,  $J = 7.2$  Hz, 3 H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  196.07, 179.85, 145.97, 139.99, 138.22, 137.41, 136.90, 132.53, 130.26, 130.11, 129.12, 129.07, 128.65, 128.45, 128.29, 127.79, 40.94, 18.95;  $\text{IR}$  (neat)  $\nu$  3060, 2980, 1738, 1705, 1659, 1598, 1446, 1286, 1249, 957, 912, 700  $\text{cm}^{-1}$ ;  $\text{HRMS}$  (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{22}\text{H}_{19}\text{O}_3$   $[\text{M}+\text{H}]^+$  331.1329, found 331.1324.



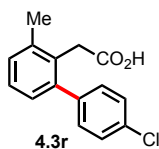
**2-(3,4'-dimethylbiphenyl-2-yl)acetic acid (4.3p):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (119 mg, 99% yield).  $R_f = 0.68$  (hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$

7.23–7.14 (m, 6 H), 7.12 (d,  $J = 7.2$  Hz, 1 H), 3.65 (s, 2 H), 2.40 (s, 3 H), 2.35 (s, 3 H);  $^{13}\text{C}$

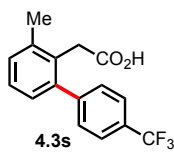
**NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  177.28, 143.28, 138.72, 137.61, 136.78, 130.06, 129.33, 128.96, 128.92, 128.00, 127.13, 36.02, 21.17, 20.20; **IR** (neat)  $\nu$  3023, 2975, 1706, 1467, 1412, 1231, 939, 822, 782 cm<sup>-1</sup>; **HRMS** (ESI-TOF)  $m/z$  Calcd for C<sub>16</sub>H<sub>17</sub>O<sub>2</sub> [M+H]<sup>+</sup> 241.1223, found 241.1218.



**2-(4'-methoxy-3-methylbiphenyl-2-yl)acetic acid (4.3q):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (118 mg, 92% yield).  $R_f$  = 0.55 (hexanes:EtOAc 1:1); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.23–7.19 (m, 4 H), 7.11 (d,  $J$  = 6.8 Hz, 1 H), 6.93 (d,  $J$  = 8.4 Hz, 2 H), 3.85 (s, 3 H), 3.66 (s, 2 H), 2.35 (s, 3 H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  177.44, 158.75, 142.96, 137.61, 134.03, 130.23, 130.18, 129.27, 128.13, 127.12, 113.63, 55.27, 36.06, 20.22; **IR** (neat)  $\nu$  3005, 2930, 1705, 1610, 1513, 1465, 1289, 1247, 1177, 1033, 837, 789 cm<sup>-1</sup>; **HRMS** (ESI-TOF)  $m/z$  Calcd for C<sub>16</sub>H<sub>17</sub>O<sub>3</sub> [M+H]<sup>+</sup> 257.1172, found 257.1172.



**2-(4'-chloro-3-methylbiphenyl-2-yl)acetic acid (4.3r):** The title compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (124 mg, 95% yield).  $R_f$  = 0.58 (hexanes:EtOAc 1:1); **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.37 (d,  $J$  = 8.4 Hz, 2 H), 7.27–7.22 (m, 4 H), 7.10–7.07 (m, 1 H), 3.61 (s, 2 H), 2.35 (s, 3 H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  177.52, 142.07, 140.06, 137.80, 133.30, 130.46, 129.89, 129.83, 128.43, 127.84, 127.29, 35.98, 20.19; **IR** (neat)  $\nu$  3027, 2923, 1704, 1493, 1464, 1412, 1233, 1090, 1016, 837, 785 cm<sup>-1</sup>; **HRMS** (ESI-TOF)  $m/z$  Calcd for C<sub>15</sub>H<sub>14</sub>ClO<sub>2</sub> [M+H]<sup>+</sup> 261.0682, [(M+2)+H]<sup>+</sup> 263.0653, found 261.0677, 263.0646 [M+H]<sup>+</sup>: [(M+2)+H]<sup>+</sup> = 3:1.



**2-(3-methyl-4'-(trifluoromethyl)biphenyl-2-yl)acetic acid (4.3s):** The title

compound was prepared on a 0.2 mmol scale and obtained as a white solid

(51 mg, 87% yield).  $R_f$  = 0.61 (hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,

$\text{CDCl}_3$ )  $\delta$  7.66 (d,  $J$  = 8.0 Hz, 2 H), 7.42 (d,  $J$  = 8.0 Hz, 2 H), 7.28–7.25 (m, 2 H), 7.10–7.08

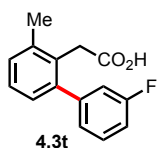
(m, 1 H), 3.60 (s, 2 H), 2.36 (s, 3 H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.42, 145.33,

141.89, 137.93, 130.14, 129.93, 129.50, 129.44 (q,  $J_{\text{C-F}}$  = 32.3 Hz), 127.71, 127.37, 125.20

(q,  $J_{\text{C-F}}$  = 3.7 Hz), 124.19 (q,  $J_{\text{C-F}}$  = 270.7 Hz); **IR** (neat)  $\nu$  3024, 2927, 1706, 1618, 1403,

1323, 1235, 1163, 1123, 1063, 849, 787  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{16}\text{H}_{14}\text{F}_3\text{O}_2$

$[\text{M}+\text{H}]^+$  295.0940, found 295.0941.



**2-(3'-fluoro-3-methylbiphenyl-2-yl)acetic acid (4.3t):** The title compound

was prepared on a 0.5 mmol scale and obtained as an off-white solid (115 mg,

94% yield).  $R_f$  = 0.67 (hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$

7.38–7.33 (m, 1 H), 7.25–7.22 (m, 2 H), 7.11–7.03 (m, 4 H), 3.63 (s, 2 H), 2.35 (s, 3 H);  $^{13}\text{C}$

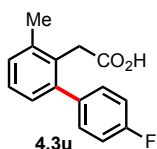
**NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.98, 162.45 (d,  $J_{\text{C-F}}$  = 245.4 Hz), 143.81 (d,  $J_{\text{C-F}}$  = 7.6 Hz),

141.99 (d,  $J_{\text{C-F}}$  = 1.8 Hz), 137.80, 129.93, 129.86, 129.72 (d,  $J_{\text{C-F}}$  = 8.4 Hz), 127.67, 127.20,

124.89 (d,  $J_{\text{C-F}}$  = 2.8 Hz), 116.17 (d,  $J_{\text{C-F}}$  = 21.3 Hz), 114.08 (d,  $J_{\text{C-F}}$  = 20.9 Hz), 36.12,

20.13; **IR** (neat)  $\nu$  3064, 2925, 1703, 1612, 1579, 1466, 1425, 1411, 1233, 1203, 889, 780

$\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{14}\text{FO}_2$   $[\text{M}+\text{H}]^+$  245.0972, found 245.0980.



**2-(4'-fluoro-3-methylbiphenyl-2-yl)acetic acid (4.3u):** The title compound

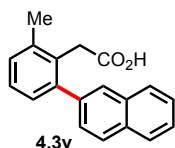
was prepared on a 0.5 mmol scale and obtained as an off-white solid (120 mg,

98% yield).  $R_f$  = 0.60 (hexanes:EtOAc 1:1);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$

7.27–7.21 (m, 4 H), 7.10–7.06 (m, 3 H), 3.61 (s, 2 H), 2.35 (s, 3 H);  $^{13}\text{C NMR}$  (100 MHz,

$\text{CDCl}_3$ )  $\delta$  178.05, 162.11 (d,  $J_{\text{C-F}}$  = 244.8 Hz), 142.26, 137.71, 137.55 (d,  $J_{\text{C-F}}$  = 3.3 Hz),

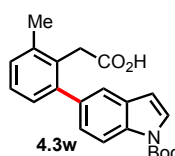
130.69 (d,  $J_{C-F} = 7.9$  Hz), 130.06, 129.67, 128.00, 127.21, 115.12 ( $J_{C-F} = 21.2$  Hz), 36.06, 20.20; **IR** (neat)  $\nu$  3023, 2920, 1702, 1604, 1509, 1465, 1413, 1221, 1158, 939, 909, 840, 785  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{15}\text{H}_{14}\text{FO}_2$   $[\text{M}+\text{H}]^+$  245.0972, found 245.0975.



**2-(2-methyl-6-(naphthalen-2-yl)phenyl)acetic acid (4.3v):** The title

compound was prepared on a 0.5 mmol scale and obtained as an off-white solid (120 mg, 87% yield).  $R_f = 0.68$  (hexanes:EtOAc 1:1);  **$^1\text{H}$  NMR** (400

MHz,  $\text{CDCl}_3$ )  $\delta$  7.90–7.81 (m, 3 H), 7.76 (s, 1 H), 7.53–7.49 (m, 2 H), 7.74 (dd,  $J_1 = 8.4$  Hz,  $J_2 = 1.6$  Hz), 7.31–7.21 (m, 4 H), 3.68 (s, 2 H), 2.39 (s, 3 H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  177.80, 143.22, 139.17, 137.74, 133.15, 132.36, 130.16, 129.61, 128.02, 127.86, 127.81, 127.68, 127.43, 127.21, 126.32, 126.02, 26.15, 20.21; **IR** (neat)  $\nu$  3055, 2956, 1704, 1410, 1233, 935, 907, 860, 823, 785, 744  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{17}\text{O}_2$   $[\text{M}+\text{H}]^+$  277.1223, found 277.1231.



**2-(2-(1-(tert-butoxycarbonyl)-1H-indol-5-yl)-6-methylphenyl)acetic acid**

**(4.3w):** The title compound was prepared on a 0.2 mmol scale and obtained as a yellow oil (27 mg, 37% yield).  $R_f = 0.69$  (hexanes:EtOAc 1:1);  **$^1\text{H}$**

**NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.14 (d,  $J = 7.2$  Hz, 1 H), 7.64 (d,  $J = 3.6$  Hz, 1 H), 7.47 (s, 1 H), 7.27–7.16 (m, 4 H), 6.57 (d,  $J = 3.6$  Hz, 1 H), 3.67 (s, 2 H), 2.34 (s, 3 H), 1.69 (s, 9 H);  **$^{13}\text{C}$  NMR** (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  173.03, 150.39, 144.36, 138.73, 137.64, 135.19, 132.59, 131.58, 130.00, 128.81, 127.52, 127.47, 126.28, 122.22, 115.48, 108.22, 84.60, 36.62, 28.30, 20.32; **IR** (neat)  $\nu$  2977, 2927, 1734, 1707, 1457, 1369, 1341, 1239, 1159, 1135, 1084, 1023  $\text{cm}^{-1}$ ; **HRMS** (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{22}\text{H}_{24}\text{NO}_4$   $[\text{M}+\text{H}]^+$  366.1700, found 366.1704.

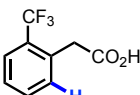


#### 4.4.10. Competition Experiments

##### Procedure for intermolecular competition experiments between compounds

**4.1a and 4.1b:** A 25 mL sealed tube equipped with a magnetic stir bar was charged with **4.1a** (51.1 mg, 0.25 mmol), **4.1b** (37.6 mg, 0.25 mmol), PhBF<sub>3</sub>K (**2a**) (276.0mg, 1.5 mmol), Pd(OAc)<sub>2</sub> (5.6 mg, 0.025 mmol), BQ (2.7 mg, 0.025 mmol), ligand (0.05 mmol), KHCO<sub>3</sub> (100.1 mg, 1.0 mmol), Ag<sub>2</sub>CO<sub>3</sub> (275.8 mg, 1.0 mmol), and *t*-AmylOH (2.5 mL). The reaction tube was capped and immediately transferred to an oil bath at 110 °C. After being allowed to stir vigorously for the appropriate time, the reaction vessel was removed from the oil bath and cooled to 0 °C in an ice bath. A 2.0 N HCl solution (5 mL) and diethyl ether (10 mL) were added. A small aliquot of the organic phase was taken, concentrated *in vacuo*, and analysed by <sup>1</sup>H NMR. The conversion was determined by integration of the benzylic methylene proton signals, which appear as singlets (approximately 3.87 ppm for **4.1a**, 3.79 ppm for **4.3a**, 3.67 ppm for **4.1b**, and 3.63 ppm for **4.3b**). The results are shown in Tables 4.8 and S11.

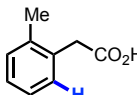
**Table 4.S11:** Competition experiments between **4.1a** and **4.1b**.<sup>a</sup>



(0.5 equiv)

**4.1a**

+

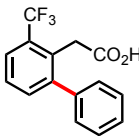


(0.5 equiv)

**4.1b**

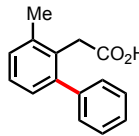
3 equiv. Ph-BF<sub>3</sub>K  
 5 mol% Pd(OAc)<sub>2</sub>  
 10 mol% Ac-Ile-OH  
 5 mol% BQ  
 2 equiv. KHCO<sub>3</sub>  
 2 equiv. Ag<sub>2</sub>CO<sub>3</sub>

*t*-AmylOH, 110 °C



**4.3a**

+



**4.3b**

| Entry <sup>a</sup> | Ligand    | Time (min) | % Conv. <b>4.3a</b> | % Conv. <b>4.3b</b> | k <sub>4.3a</sub> ([M]/min) | k <sub>4.3b</sub> ([M]/min) | k <sub>4.3a</sub> / k <sub>4.3b</sub> |
|--------------------|-----------|------------|---------------------|---------------------|-----------------------------|-----------------------------|---------------------------------------|
| 1                  | ---       | 60         | 8.6                 | 17.8                | 2.9 × 10 <sup>-4</sup>      | 5.9 × 10 <sup>-4</sup>      | 0.48                                  |
| 2                  | Ac-Ile-OH | 20         | 35.6                | 16.4                | 7.1 × 10 <sup>-3</sup>      | 3.2 × 10 <sup>-3</sup>      | 2.17                                  |

<sup>a</sup> The conversion was determined by <sup>1</sup>H NMR of the crude reaction mixture.

##### Procedure for initial rate studies for single-component reactions of **4.1a** and **4.1b**:

The procedure for reactions run with and without Ac-Ile-OH is described in Section 4.4.4.

The reactions were repeated three times, and determination of the initial rate was performed using linear regression. The overall results are shown in Table 4.9.

#### 4.5. REFERENCES

- (1) Reviews of Pd(0)-catalysed C–C bond-forming reactions in total synthesis: (a) Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2001**, *40*, 4544–4568. (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489.
- (2) For perspectives on the importance of ligand design in Pd(0) chemistry, see: (a) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211. (b) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534–1544. (c) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461–1473.
- (3) Selected reviews of Pd-catalysed C–H functionalisation: (a) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichim. Acta* **2007**, *40*, 35–41. (b) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200–205. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173–1193. (d) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115. (e) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826. (f) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (g) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147–1169. (h) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215–1292.
- (4) Mono-*N*-protected amino acids were first identified as effective ligand scaffolds for Pd(II)-catalysed C–H functionalisation reactions during our studies of enantioselective C–H functionalisation: (a) Shi, B.-F.; Maugel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886. (b) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461. For an early report describing stoichiometric asymmetric cyclopalladation of (dimethylamino)methylferrocene in the

- presence of Ac-Val-OH, see: (c) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.
- (5) (a) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315–319. (b) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2010**, *49*, 6169–6173. (c) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 14137–14151.
- (6) More recently, success has also been found using amino acid ligands to promote Pd(II)-catalysed C–H functionalisation with directing groups other than carboxylates: (a) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916–5921. (b) Dai, H.-X.; Stepan, A. F.; Plummer, M. S.; Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7222–7228. (c) Lu, Y.; Leow, D.; Wang, X.; Engle, K. M.; Yu, J.-Q. *Chem. Sci.* **2011**, *2*, 967–971. (d) Huang, C.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 12406–12409.
- (7) Reviews of Pd(II)-catalysed C–H/R–M cross-coupling from our group: (a) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115. (b) Wasa, M.; Engle, K. M.; Yu, J.-Q. *Isr. J. Chem.* **2010**, *50*, 605–616.
- (8) Pyridine ligands have been shown to enhance catalytic turnover in Pd(II)-catalysed C–H functionalisation reactions: (a) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2003**, *125*, 9578–9579. (b) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172–1175. (c) Zhang, J.; Khaskin, E.; Anderson, N. P.; Zavalij, P. Y.; Vedernikov, A. N. *Chem. Commun.* **2008**, 3625–3627. (d) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072–5074. (e) Izawa, Y.; Stahl, S. S. *Adv. Synth. Catal.* **2010**, *352*, 3223–3229. (f) Izawa, Y.; Pun, D.; Stahl, S. S. *Science* **2011**, *333*, 209–213. Arnold and Sanford have reported a bidentate NHC-alkoxide ligand that stabilises cyclopalladated Pd(IV) intermediates but leads to lower activity in Pd(II)/Pd(IV) catalysis: (g) Arnold, P. L.; Sanford, M. S.; Pearson, S. M. *J. Am. Chem. Soc.* **2009**, *131*, 13912–13913. Liu

- and coworkers have recently reported an example in which an NHC ligand was found to promote a phenol-directed C–H activation/C–O cyclisation reaction along a Pd(II)/Pd(0) catalytic cycle: (h) Xiao, B.; Gong, T.-J.; Liu, Z.-J.; Liu, J.-H.; Luo, D.-F.; Xu, J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 9250–9253.
- (9) For a review of ligand-accelerated catalysis, see: Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **1995**, *34*, 1059–1070.
- (10) For the initial reports of Pd(II)-mediated C(aryl)–H olefination, see: (a) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119–1122. (b) Fujiwara, Y.; Moritani, I.; Matsuda, M.; Teranishi, S. *Tetrahedron Lett.* **1968**, *9*, 3863–3865.
- (11) Examples of Pd-catalysed C–H arylation using other modes of catalysis: (a) Campeau, L.-C.; Rousseaux, S.; Fagnou, K. *J. Am. Chem. Soc.* **2005**, *127*, 18020–18021. (b) Daugulis, O.; Zaitsev, V. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4046–4048. (c) Kalyani, D.; Deprez, N. R.; Desai, L. V.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 7330–7331.
- (12) For the first reports of Pd(II)-catalysed C–H/R–M cross-coupling, see: (a) Chen, X.; Li, J.-J.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 78–79. (b) Chen, X.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 12634–12635.
- (13) Wang, D.-H.; Mei, T.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 17676–17677.
- (14) (a) Giri, R.; Mangel, N.; Li, J.-J.; Wang, D.-H.; Breazzano, S. P.; Saunders, L. B.; Yu, J.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 3510–3511. (b) Wang, D.-H.; Wasa, M.; Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 7190–7191. .
- (15) Examples of Pd(II)-catalysed C–H/R–M cross-coupling from other groups: (a) Yang, S.; Li, B.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 6066–6067. (b) Kawai, H.; Kobayashi, Y.; Oi, S.; Inoue, Y. *Chem. Commun.* **2008**, 1464–1466. (c) Ge, H.; Niphakis, M. J.; Georg, G. I. *J. Am. Chem. Soc.* **2008**, *130*, 3708–3709. (d) Yang, S.-D.;

- Sun, C.-L.; Fang, Z.; Li, B.-J.; Li, Y.-Z.; Shi, Z.-J. *Angew. Chem. Int. Ed.* **2008**, *47*, 1473–1476. (e) Zhao, J.; Zhang, Y.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428–7431. (f) Kirchberg, S.; Fröhlich, R.; Studer, A. *Angew. Chem. Int. Ed.* **2009**, *48*, 4235–4238. (g) Zhou, H.; Xu, Y.-H.; Chung, W.-J.; Loh, T.-P. *Angew. Chem. Int. Ed.* **2009**, *48*, 5355–5357. (h) Wei, Y.; Kan, J.; Wang, M.; Su, W.; Hong, M. *Org. Lett.* **2009**, *11*, 3346–3349. (i) Liang, Z.; Yao, B.; Zhang, Y. *Org. Lett.* **2010**, *12*, 3185–3187. (j) Tredwell, M. J.; Gulias, M.; Bremeyer, N. G.; Johansson, C. C. C.; Collins, B. S. L.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 1076–1079. (k) Kirchberg, S.; Tani, S.; Ueda, K.; Yamaguchi, J.; Studer, A.; Itami, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 2387–2391. (l) Schnapperelle, I.; Breitenlechner, S.; Bach, T. *Org. Lett.* **2011**, *13*, 3640–3643. (m) Mochida, K.; Kawasumi, K.; Segawa, Y.; Itami, K. *J. Am. Chem. Soc.* **2011**, *133*, 10716–10719.
- (16) One elegant approach to improve reactivity with electron-rich substrates has been the use of more electrophilic Pd(II) catalysts: Nishikata, T.; Abela, A. R.; Huang, S.; Lipshutz, B. H. *J. Am. Chem. Soc.* **2010**, *132*, 4978–4979.
- (17) Aryl carboxylic acid derivatives have been found to be effective organometallic reagent surrogates (*via* decarboxylation) in Pd(II)-catalysed R–H/R–CO<sub>2</sub>H cross-coupling. For leading references, see: (a) Voutchkova, A.; Coplin, A.; Leadbeater, N. E.; Crabtree, R. H. *Chem. Commun.* **2008**, 6312–6314. (b) Wang, C.; Piel, I.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 4194–4195. (c) Li, M.; Ge, H. *Org. Lett.* **2010**, *12*, 3464–3467.
- (18) Examples of stoichiometric palladacycle/R–M coupling: (a) Murahashi, S.-I.; Tanba, Y.; Yamamura, M.; Moritani, I. *Tetrahedron Lett.* **1974**, *15*, 3749–3752. (b) Yamamura, M.; Moritani, I.; Murahashi, S.-I. *Chem. Lett.* **1974**, *3*, 1423–1424. (c) Kasahara, A.; Izumi, T.; Maemura, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1878–1880. (d) Murahashi, S.-I.; Tamba, Y.; Yamamura, M.; Yoshimura, N. *J. Org. Chem.* **1978**, *43*,

- 4099–4106. (e) Louie, J.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **1996**, *35*, 2359–2361.
- (f) Dangel, B. D.; Godula, K.; Youn, S. W.; Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2002**, *124*, 11856–11857. In one case, Pd(0) was found to catalyse the intermolecular cross-coupling of 2,4,6-tri-*tert*-butylbromobenzene with arylboronic acids via an unusual intervening C(sp<sup>3</sup>)–H cleavage step following oxidative addition: (g) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685–4696. .
- (19) Examples of Rh(I)-catalysed C–H/R–M cross-coupling: (a) Oi, S.; Fukita, S.; Inoue, Y. *Chem. Commun.* **1998**, 2439–2440. (b) Vogler, T.; Studer, A. *Org. Lett.* **2007**, *10*, 129–131.
- (20) Examples of Ru(0)-catalysed C–H/R–M cross-coupling: (a) Kakiuchi, F.; Kan, S.; Igi, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **2003**, *125*, 1698–1699. (b) Pastine, S. J.; Gribkov, D. V.; Sames, D. *J. Am. Chem. Soc.* **2006**, *128*, 14220–14221. For Ru(II)-catalysed C–H/R–M cross-coupling, see: (c) Li, H.; Wei, W.; Xu, Y.; Zhang, C.; Wan, X. *Chem. Commun.* **2011**, *47*, 1497–1499.
- (21) In an intriguing recent report, it was found that nucleophilic aryl-centred radicals, generated from arylboronic acids in the presence of catalytic Ag(I), could add to electron-poor heterocycles: Seiple, I. B.; Shun, S.; Rodriguez, R. A.; Gianatassio, R.; Fujiwara, Y.; Sobel, A. L.; Baran, P. S. *J. Am. Chem. Soc.* **2010**, *132*, 13194–13196.
- (22) In Ref. 13, the substrate scope was largely limited to  $\alpha$ -substituted and  $\alpha,\alpha$ -disubstituted phenylacetic acids, in which palladation is more favourable owing to the Thorpe–Ingold effect. The reaction conditions reported in that reference were as follows: ArBF<sub>3</sub>K (1.2 equiv.), Pd(OAc)<sub>2</sub> (10 mol%), BQ (0.5 equiv.), K<sub>2</sub>HPO<sub>4</sub> (1.5 equiv.), *t*-BuOH (solvent), 110 °C, O<sub>2</sub> (20 atm), 48 h. Under those conditions, many substrates gave unsatisfactory product conversions. Representative examples include **4.3a** (44%), **4.3d** (56%), and

- 4.3h** (17%). (See Experimental section for further details.) It is important to note, that throughout this work, we used 5 mol% Pd(OAc)<sub>2</sub>.
- (23) In Ref. 13, it was stated that Ag(I) salts completely inhibited the transformation under the reported reaction conditions (given above). That claim does not seem to be true across all reaction conditions. .
- (24) For an example of olefin-promoted reductive elimination from Pd(II), see: (a) Kurosawa, H.; Emoto, M.; Ohnishi, H.; Miki, K.; Kasai, N.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1987**, *109*, 6333–6340. BQ has previously been found to promote reductive elimination in a Stille coupling reaction involving allyl halides: (b) Albéniz, A. C.; Espinet, P.; Martín-Ruiz, B. *Chem. Eur. J.* **2001**, *7*, 2481–2489. For the effects of BQ as a ligand in Pd-catalysed C–H cleavage/C–C bond-forming reactions, see: (c) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586–1587. (d) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 11904–11905.
- (25) Lanci, M. P.; Remy, M. S.; Kaminsky, W.; Mayer, J. M.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 15618–15620.
- (26) Engle, K. M.; Mei, T.-S.; Wang, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2011**, *50*, 1478–1491.
- (27) For perspectives on the use of organotrifluoroborate reagents, see: (a) Darses, S.; Genet, J.-P. *Chem. Rev.* **2007**, *108*, 288–325. (b) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286. (c) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020–3027. (d) Butters, M.; Harvey, J. N.; Jover, J.; Lennox, A. J. J.; Lloyd-Jones, G. C.; Murray, P. M. *Angew. Chem. Int. Ed.* **2010**, *49*, 5156–5160. For the use of MIDA-boronates, see: (e) E. P. Gillis, M. D. Burke, *J. Am. Chem. Soc.* **2007**, *129*, 6716–6717.

- (28) For detailed data concerning the effects of  $\text{PhBF}_3\text{K}/\text{Ag}_2\text{CO}_3$  loading, see the Experimental section.
- (29) Due to averaging effects, in Figure 1 it appears as if the reaction in the presence of Ac-Ile-OH decelerates after 20 min. However, in individual trials the rate appears to be nearly constant for time points from 20 min until the reactions proceed to completion.
- (30) High conversion with  $\alpha,\alpha$ -disubstituted phenylacetic acids can be achieved using the conditions reported in Ref. 13. With these substrates, the use of mono-*N*-protected amino acid ligands does not seem to improve the reactivity.
- (31) Reviews of aerobic Pd(II)-catalysed oxidation chemistry: (a) Stahl, S. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3400–3420. (b) Stoltz, B. M. *Chem. Lett.* **2004**, *33*, 362–367. (c) Gligorich, K. M.; Sigman, M. S. *Chem. Commun.* **2009**, 3854–3867.
- (32) Although at the present time high pressure  $\text{O}_2$  poses a safety risk when used at elevated temperatures, the advent of flow technology may soon render this approach more tenable. For leading references, see: (a) Ye, X.; Johnson, M. D.; Diao, T.; Yates, M. H.; Stahl, S. S. *Green Chem.* **2010**, *12*, 1180–1186. (b) Murphy, E. R.; Martinelli, J. R.; Zaborenko, N.; Buchwald, S. L.; Jensen, K. F. *Angew. Chem. Int. Ed.* **2007**, *46*, 1734–1737. (c) O'Brien, M.; Baxendale, I. R.; Ley, S. V. *Org. Lett.* **2010**, *12*, 1596–1598. (d) Saaby, S.; Knudsen, K. R.; Ladlow, M.; Ley, S. V. *Chem. Comm.* **2005**, 2909–2911.
- (33) Baxter, R. D.; Sale, D.; Engle, K. M.; Yu, J.-Q.; Blackmond, D. G. *J. Am. Chem. Soc.* **2012**, *134*, 4600–4606.
- (34) We have found Ac-Ile-OH-bound Pd(II) complexes to be difficult to characterise due to their poor solubility in non-polar solvents. The use of more polar coordinating solvents introduces the possibility that a solvent molecule could displace a ligand on Pd(II) and/or cause disaggregation of any oligomeric Pd(II) species. Furthermore, interpretation of the spectral data for multinuclear Ac-Ile-OH-bound Pd(II) complexes



tends to be challenging owing to the possibility of *cis/trans*-isomerism. For a report in which cyclopalladated complexes containing acetyl-protected amino acid ligands were synthesised and characterised, see: Navarro, R.; García, J.; Urriolabeitia, E. P.; Cativiela, C.; Diaz-de-Villegas, M. D. *J. Organomet. Chem.* **1995**, *490*, 35–43.

(35) We tested the activity of one amorphous "[Pd(Ac-Ile-OH)(OAc)]" complex and found that using 5 mol% catalyst with no additional ligand under otherwise identical reaction conditions to those depicted in Table 5 gave 85% conversion after 2 h. This "[Pd(Ac-Ile-OH)(OAc)]" complex was synthesised using the following procedure: To a flame-dried 20 mL round bottom flask containing a magnetic stir bar were added Pd(OAc)<sub>2</sub> (0.056g, 0.25mmol), Ac-Ile-OH (0.043g, 0.25mmol), and  $\alpha,\alpha,\alpha$ -trifluorotoluene (4 mL). The resulting mixture was capped and allowed to stir at ambient temperature for 4 h. Solvent was removed *in vacuo*, giving amorphous "[Pd(Ac-Ile-OH)(OAc)]" as a dark orange powder in quantitative yield. Broad peaks were observed in its NMR spectra (in CDCl<sub>3</sub>), and was it not further characterised.

(36) Examples of countercation-promoted, carboxylated-directed Pd(II)-catalysed C–H functionalisation from our group: (a) Mei, T.-S.; Giri, R.; Maugel, N.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 5215–5219. (b) Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082–14083. (c) Mei, T.-S.; Wang, D.-H.; Yu, J.-Q. *Org. Lett.* **2010**, *12*, 3140–3143. (d) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2009**, *48*, 6097–6100. (e) Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 14654–14655.

(37) Examples of carboxylate-directed Pd(II)-catalysed C–H functionalisation reactions from other groups: (a) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211–5215. (b) Chiong, H. A.; Pham, Q.-N.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 9879–9884. (c) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006–14008. For a review, see: (d) Satoh, T.; Miura, M. *Synthesis*

**2010**, 3395–3409. Carboxylate-directed *ortho*-thallation is a known means of generating organothallium compounds which can be used in Pd(II)-catalysed functionalisation reactions: (e) Larock, R. C.; Fellows, C. A. *J. Am. Chem. Soc.* **1982**, *104*, 1900–1907.

(38) Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306–312.

(39) It is important to clarify that if the C–H cleavage step is not rate-limiting under either of the two reaction conditions (*i.e.*, in the presence of absence of Ac-Ile-OH), then the relative reaction rates would actually be reflective of the energy barriers for other elementary steps in the catalytic cycle. Regardless of what the rate-determining step is, the qualitative observation of high reactivity with electron-poor substrates is difficult to explain were one to invoke a traditional electrophilic palladation mechanism.

(40) For studies concerning the mechanistic aspects C–H cleavage in Pd(II)-catalysed reactions, see: (a) Ryabov, A. D.; Sakodinskaya, I. K.; Yatsimirsky, A. K. *J. Chem. Soc., Dalton Trans.* **1985**, 2629–2638. (b) Canty, A. J.; van Koten, G. *Acc. Chem. Res.* **1995**, *28*, 406–413. (c) Tunge, J. A.; Foresee, L. N. *Organometallics* **2005**, *24*, 6440–6444. For experimental and computational evidence of concerted metalation/deprotonation, see: (d) Gómez, M.; Granell, J.; Martinez, M. *Organometallics* **1997**, *16*, 2539–2546. (e) Gómez, M.; Granell, J.; Martinez, M. *J. Chem. Soc., Dalton Trans.* **1998**, 37–44. (f) Biswas, B.; Sugimoto, M.; Sakaki, S. *Organometallics* **2000**, *19*, 3895–3908. (g) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754–13755. (h) Roiban, G.-D.; Serrano, E.; Soler, T.; Aullón, G.; Grosu, I.; Cativiela, C.; Martínez, M.; Urriolabeitia, E. P. *Inorg. Chem.* **2011**, *50*, 8132–8143. For reviews of carboxylate-assisted C–H cleavage in transition metal catalysis, see: (i) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315–1345. (j) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118–1126.

- (41) Even still,  $^1\text{H}$  NMR and TLC analysis of the crude reaction mixtures revealed substantial homocoupling of the  $\text{ArBF}_3\text{K}$  reagents (and the  $\text{ArBPin}$  reagents) under our optimised conditions.
- (42) Uenishi, J.; Beau, J. M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756–4758.
- (43) To clarify, we noted previously that when  $\text{Ag(I)}$  is used as the reoxidant for  $\text{C-H/R-BX}_n$  cross-coupling, BQ *is not* required and was used only to improve reproducibility. In the case of reoxidation with  $\text{O}_2$ , BQ *is* required for catalysis.
- (44) (a) Keith, J. M.; Nielsen, R. J.; Oxgaard, J.; Goddard, W. A., III *J. Am. Chem. Soc.* **2005**, *127*, 13172–13179. (b) Keith, J. M.; Nielsen, R. J.; Oxgaard, J.; Goddard, W. A., III *J. Am. Chem. Soc.* **2005**, *127*, 13172–13179. (c) Konnick, M. M.; Gandhi, B. A.; Guzei, I. A.; Stahl, S. S. *Angew. Chem. Int. Ed.* **2006**, *45*, 2904–2907. (d) Keith, J. M.; Muller, R. P.; Kemp, R. A.; Goldberg, K. I.; Goddard, W. A., III; Oxgaard, J. *Inorg. Chem.* **2006**, *45*, 9631–9633. (e) Popp, B. V.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 4410–4422. (f) Keith, J. M.; Goddard, W. A., III; Oxgaard, J. *J. Am. Chem. Soc.* **2007**, *129*, 10361–10369. (g) Konnick, M. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 5753–5762. (h) Popp, B. V.; Stahl, S. S. *Chem. Eur. J.* **2009**, *15*, 2915–2922. (i) Keith, J. M.; Goddard, W. A., III *J. Am. Chem. Soc.* **2009**, *131*, 1416–1425. (j) Konnick, M. M.; Decharin, N.; Popp, B. V.; Stahl, S. S. *Chem. Sci.* **2011**, *2*, 326–330. (k) Decharin, N.; Popp, B. V.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 13268–13271.
- (45) Decharin, N.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 5732–5735.
- (46) Sims, J. W.; Schmidt, E. W. *J. Am. Chem. Soc.* **2008**, *130*, 11149–11155.
- (47) Hudlicky, M. *J. Org. Chem.* **1980**, *45*, 5377–5378.
- (48) Please see the Aldrich Technical Bulletin AL-180, “Diazald® and Diazomethane Generators,” for a detailed experimental procedure.

## 4.6. CONTRIBUTIONS

The following individuals directly contributed to the work described in this Chapter: Keary M. Engle, Peter S. Thuy-Boun, Michael Dang, David W. Shia, and Prof. Jin-Quan Yu. K.M.E. and J.-Q.Y. conceived the project. Reaction optimisation was performed by M.D. and K.M.E. Product isolation and characterisation was carried out by K.M.E. and P.S.T.-B. Reactions under aerobic conditions were run by P.S.T.-B., M.D., and K.M.E. Reaction kinetics and other mechanistic experiments were carried out by K.M.E., M.D., D.W.S., and P.S.T.-B. The Chapter was adapted with permission from a published manuscript, which was written by K.M.E. and J.-Q.Y., with input from P.S.T.-B.

## **CHAPTER 5**

### **OUTLOOK AND CONCLUSION**

## 5.1. SUMMARY AND PERSPECTIVE

In Part I of this Thesis, we have presented our investigations concerning the use of mono-*N*-protected amino acid ligands to enhance kinetic reactivity in Pd(II)-catalysed C–H functionalisation reactions. After an introduction to the importance of ligand design in transition metal catalysis, we highlighted the dearth of ligands capable of influencing the C–H cleavage step in Pd(II)-catalysed C–H functionalisation reactions, which has been an impediment to the evolution of this field (Chapter 1). Next, we presented original research into the use of mono-*N*-protected amino acid ligands to enhance kinetic reactivity with otherwise recalcitrant phenylacetic acid substrates in Pd(II)-catalysed *ortho*-C–H olefination (Chapter 2). A variant of this protocol was used to effect efficient diolefination of phenylacetic acids and hydrocinnamic acids, and examples of sequential and iterative C–H functionalisation were presented (Chapter 3). Lastly, we tackled a catalytic cycle with different elementary steps, Pd(II)-catalysed C–H/R–BX<sub>*n*</sub> cross-coupling, and found that here too, mono-*N*-protected amino acid ligands could be used to engineer two vastly improved protocols, one using Ag<sub>2</sub>CO<sub>3</sub> as the terminal oxidant, and the other under aerobic conditions (Chapter 4).

Some of the research projects presented in the preceding chapters have continued to flourish in the Yu laboratory, and the insights from this work has spawned new lines of inquiry both in and outside of the group. During the past five years, mono-*N*-protected amino acid ligands have been adopted by the chemical community to develop an exciting collection of novel enantioselective and non-stereoselective C–H functionalisation reactions, many which represent promising new tools to expedite synthetic endeavours. We conclude Part I by highlighting these advancements.

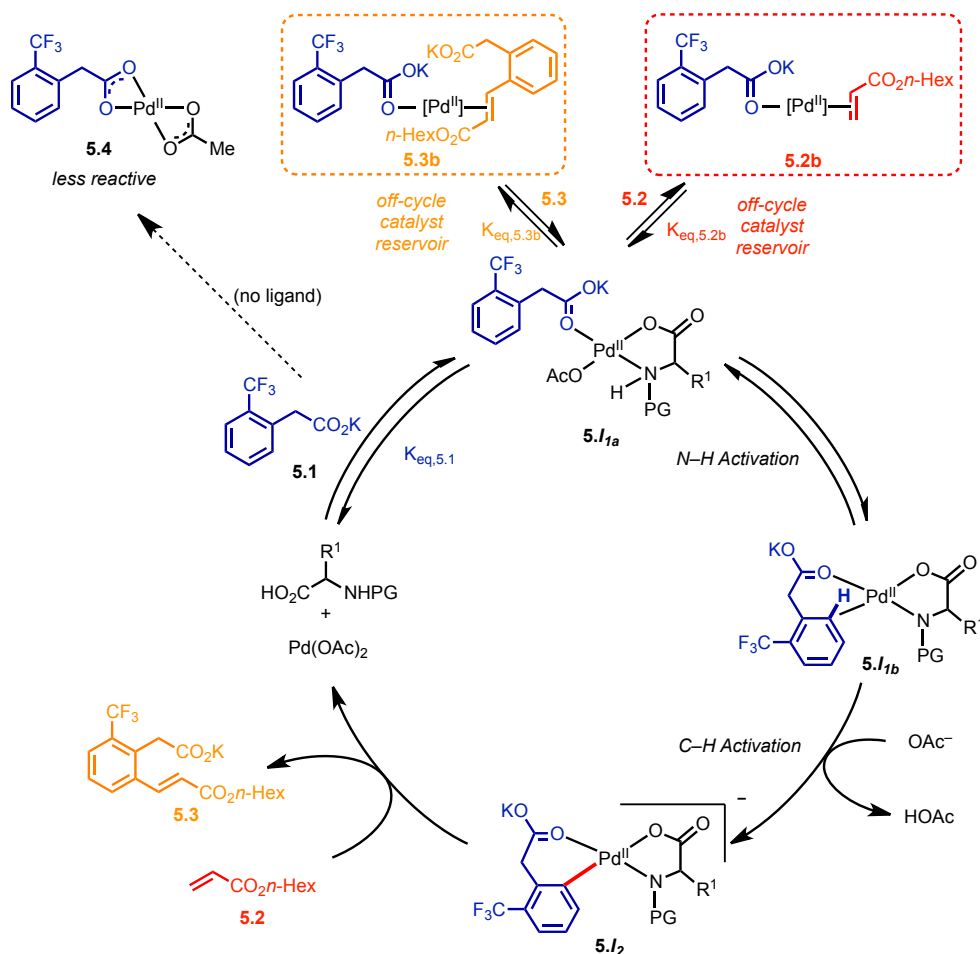
## 5.2. LIGAND-ACCELERATED PALLADIUM(II)-CATALYSED C–H OLEFINATION OF PHENYLACETIC ACIDS

Owing to its catalytic efficiency, atom economy, functional-group tolerance, and operational simplicity, the ligand-accelerated Pd(II)-catalysed C–H olefination reaction of phenylacetic acids introduced in Chapter 2 continues to be the topic of active investigation, both in terms of mechanistic elucidation and synthetic applications.

### 5.2.1. Further Mechanistic Studies

As alluded to in Chapter 2, we have continued to study the mechanism of our ligand-accelerated C–H olefination reaction using a combination of different techniques. In collaboration with the Blackmond laboratory at TSRI, reaction progress kinetic analysis and NMR experiments have been performed with potassium 2-(trifluoromethyl)phenylacetate (**5.1**), the potassium salt of a representative electron-poor substrate, and *n*-hexyl acrylate (**5.2**), a representative olefin coupling partner.<sup>1</sup> These studies revealed highly unusual reaction kinetics, in which none of the following—the phenylacetic acid substrate **5.1**, the olefin **5.2**, or the [O<sub>2</sub>] required to regenerate the catalyst—were found to exhibit positive order kinetics. In fact, both the olefin **5.2** and the reaction product **5.3** were revealed to *suppress* the reaction rate, with only the catalyst providing a positive concentration driving force in the reaction. Consideration of this data and the steady-state rate expression led to the proposal of revised catalytic cycle (Scheme 5.1), salient features of which include off-cycle catalyst reservoirs, **5.2b** and **5.3b**, which are deleterious to the rate, but may enhance catalyst lifetime. Additionally, one previously unknown role of the amino acid ligand, suppressing the formation of inactive Pd(II) species **5.4**, was deduced. The rate-determining step is proposed to involve a interplay between N–H and C–H activation, which provides an

explanation for the rate differences observed using different amino acids and helps rationalise the kinetic isotope effect (KIE) experimental data from Chapter 2.



**Scheme 5.1.** Revised catalytic cycle for ligand-accelerated Pd(II)-catalysed C-H olefination of phenylacetic acids based on a collaboration with the Blackmond laboratory.<sup>1</sup>

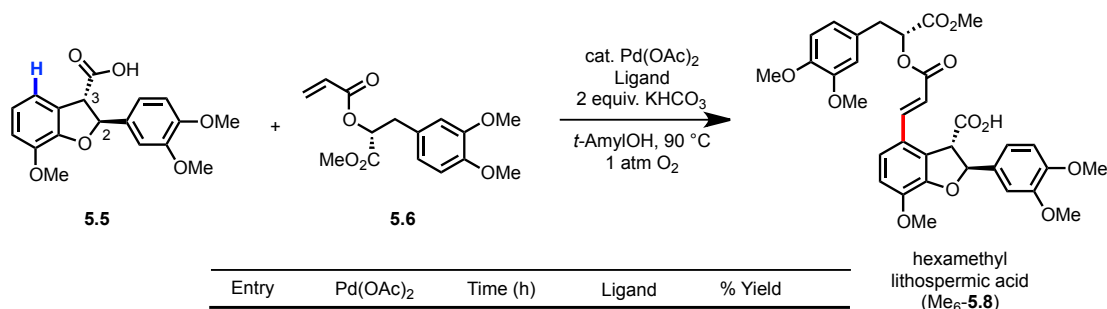
### 5.2.2. Synthetic Applications

Owing to its broad substrate scope and the synthetic versatility of the resulting molecular frameworks, this ligand-accelerated C-H olefination reaction has found several synthetic applications since its discovery. In the Yu laboratory, it played a pivotal role in the asymmetric total synthesis of (+)-lithospermic acid (**5.8**), an HIV 1 integrase inhibitor.<sup>2</sup> In the synthesis, it served as the key convergent C-C bond-forming step.<sup>3</sup> Table 5.1 shows the dramatic role played by Ac-Ile-OH (**5.7**) in facilitating the transformation. Following this late-stage union of fragments **5.5** and **5.6** to give Me<sub>6</sub>-**5.8**, a three-step global deprotection



sequence gave the natural product. This retrosynthetic approach, including the key C–H olefination step, was also later employed by the Ghosh laboratory in an independent total synthesis of (+)-lithospermic acid (**5.8**).<sup>4</sup>

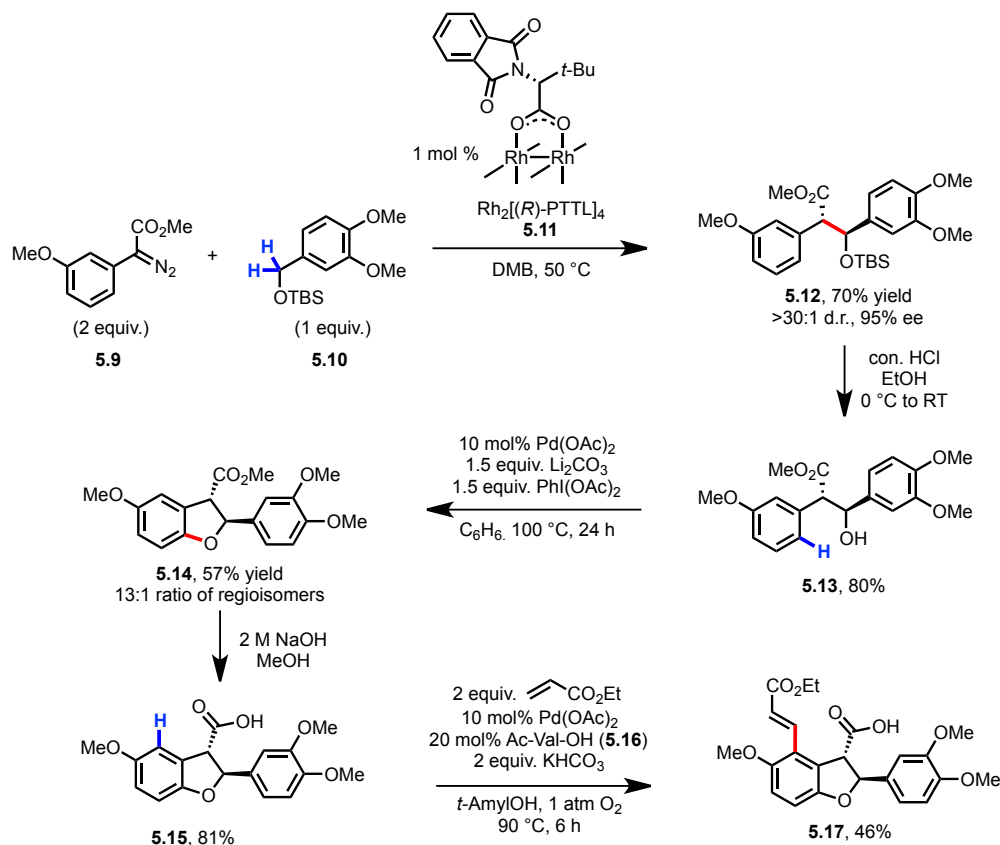
**Table 5.1.** Key C–H olefination step in the asymmetric total synthesis of (+)-lithospermic acid (**5.8**).<sup>3</sup>



| Entry | Pd(OAc) <sub>2</sub> | Time (h) | Ligand                   | % Yield |
|-------|----------------------|----------|--------------------------|---------|
| 1     | 5 mol%               | 12       | BQ                       | 31      |
| 2     | 5 mol%               | 24       | BQ                       | 50      |
| 3     | 5 mol%               | 2        | Ac-Ile-OH ( <b>5.7</b> ) | 93      |
| 4     | 2 mol%               | 10       | Ac-Ile-OH ( <b>5.7</b> ) | 91      |

In considering how to adapt this chemistry to the rapid production of analogues for biological evaluation, it was recognised that one of the limitations of this approach is the cumbersome synthesis of the starting 2-aryl-2,3-dihydrobenzofuran-3-carboxylic acid, **5.5**. In the Yu laboratory's published route, the C2–C3 bond was formed *via* Rh-catalysed C–H insertion from a progenitor compound containing a diazo group at the C3 position. In order to achieve stereocontrol during ring closure, a chiral auxiliary on the carboxylate and a chiral catalyst were required. To streamline this route for analogue synthesis, a new approach was conceived in collaboration with the Davies group at Emory University, relying on three sequential C–H functionalisation reactions (Scheme 5.2).<sup>5</sup> The sequence began with enantioselective metallocarbene C–H insertion, mediated by catalytic Rh<sub>2</sub>[(*R*)-PTTL]<sub>4</sub> (**5.11**), which efficiently forged two stereocentres in **5.12**.<sup>6</sup> Acid-mediated TBS deprotection gave **5.13**, setting the stage for application of a ring-closing *ortho*-C–H oxygenation reaction previously developed in the Yu group.<sup>7</sup> With **5.14** in hand, hydrolysis

of the methyl ester gave **5.15**. Finally, ligand-accelerated C–H olefination using Ac-Val-OH (**5.16**) forged the final C–C bond. The final product from this sequence, **5.17**, possesses the entire carbogenic skeleton of lithospermic acid with a different oxygenation pattern, making it well-suited for structure–activity relationship (SAR) testing.



**Scheme 5.2.** Synthesis of lithospermic acid analogue **5.17** using sequential C–H functionalisation logic in collaboration with the Davies laboratory.<sup>5</sup>

### 5.3. MONO-*N*-PROTECTED AMINO ACID LIGANDS

#### 5.3.1. Recent Application in Enantioselective C–H Activation

Due to their potential for expediting the synthesis of structurally complex, optically enriched chiral molecules from simple starting materials, Pd(II)-catalysed C–H activation reactions have continued to be the topic of active research efforts. In this respect, mono-*N*-protected amino acid ligands have played an important role in the development of several new transformations. Following our initial reports, which were described in Chapter 1, we

recently targeted another important and underutilised class of starting materials, cyclopropanecarboxylic acids. Encouraged by the high levels of diastereoselectivity that we previously observed in cyclopropane C–H iodination using the chiral oxazoline auxiliary approach<sup>8</sup> and by the preliminary results using amino acid ligands for enantioselective C(sp<sup>3</sup>)–H activation of *gem*-dimethyl groups,<sup>9</sup> it was reasoned that a catalytic enantioselective method for cyclopropane C–H functionalisation could be developed.

The proposed reaction was viewed as a potentially powerful and direct means of synthesising enantiopure *cis* chiral cyclopropanes, which are challenging to access using other methods. Due to the partial  $\pi$ -character of the C–C bonding system in cyclopropanes (Walsh orbital analysis), the cleavage of cyclopropyl C–H bonds is known to be more facile than that of completely unactivated C(sp<sup>3</sup>)–H bonds, and one would expect the pre-transition state coordination structure to be rigid, conceivably allowing C–H activation to take place under mild conditions. To facilitate C(sp<sup>3</sup>)–H cleavage, an acidic *N*-aryl amide directing group was installed,<sup>10,11</sup> enabling Pd(II)-catalysed C–H/R–BX<sub>2</sub> cross-coupling at temperatures as low as 40 °C.<sup>12</sup> Following optimisation of a non-stereoselective version of the reaction, systematic examination of a structurally diverse array of amino acid ligands for stereoinduction was undertaken (Table 5.2). In early screening studies, it was found that of the wide range of protecting groups examined, the TcBoc group was most successful, likely due to the large steric bulk and moderate electron-withdrawing character of the Me<sub>2</sub>(Cl<sub>3</sub>C)C moiety. Of the backbones tested, those that had aromatic rings like phenylalanine, tyrosine, and tryptophan were superior. Within the TcBoc-protected series, TcBoc-Phe-OH (**5.26**) proved to be optimal (Entry 6). Increasing the steric demands of the alkyl substituents on the TcBoc group and tuning the electronic properties on the arene led to the identification of ligand **5.32** (Entry 12). Though the yield was low, this problem could be remedied by adding the reagents consecutively in two batches, giving up to 81% yield, 91% ee for the

model reaction of **5.18** to **5.20**. This reaction was found to be compatible with aryl-, vinyl-, and alkylboron reagents and could tolerate a number of different substituents at the  $\alpha$ -position.

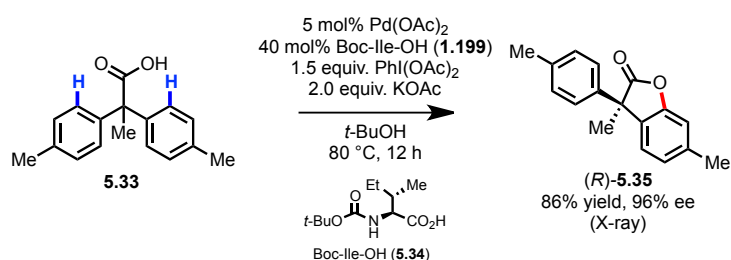
**Table 5.2.** Catalytic enantioselective C(sp<sup>3</sup>)-H activation of cyclopropanecarboxylic acid derivative **5.18** with mono-*N*-protected amino acid ligands.<sup>9</sup>

| <b>5.18</b> |        | <b>5.20</b>            |                     |       |        |                        |                     |
|-------------|--------|------------------------|---------------------|-------|--------|------------------------|---------------------|
| Entry       | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> | Entry | Ligand | Yield (%) <sup>a</sup> | ee (%) <sup>b</sup> |
| 1           |        | 55                     | 80                  | 7     |        | 51                     | 88                  |
| 2           |        | 42                     | 75                  | 8     |        | 44                     | 91                  |
| 3           |        | 47                     | 78                  | 9     |        | 50                     | 90                  |
| 4           |        | 47                     | 55                  | 10    |        | 48                     | 90                  |
| 5           |        | 31                     | 33                  | 11    |        | 40                     | 88                  |
| 6           |        | 47                     | 85                  | 12    |        | 47                     | 93                  |

<sup>a</sup> Yield determined by <sup>1</sup>H NMR analysis of the crude reaction mixture using CH<sub>2</sub>Br<sub>2</sub> as an internal standard. <sup>b</sup> ee determined by HPLC using a chiral stationary phase.

As part of a collaboration between the Wang laboratory at the University of Science and Technology in China and the Yu laboratory, an enantioselective ring-closing *ortho*-C-H oxygenation reaction of diphenylacetic acids (**5.33**) was developed to give optically enriched lactone products (**5.35**) (Scheme 5.3).<sup>13</sup> Intriguingly, the sense of stereinduction

was the same as observed previously with this class of substrates in enantioselective C–H olefination.<sup>14</sup> This suggests that enantioselective C–H activation gives a common optically enriched, chiral palladacycle, which can be channelled into a number of different C–C and C–heteroatom bond-forming reactions. Importantly, this result also established the compatibility of mono-*N*-protected amino acid ligands with enantioselective C–H activation along a Pd(II)/Pd(IV) catalytic cycle.



**Scheme 5.3.** Enantioselective C–H activation/C–O cyclisation along a Pd(II)/Pd(IV) catalytic cycle to form optimally enriched lactones.<sup>13</sup>

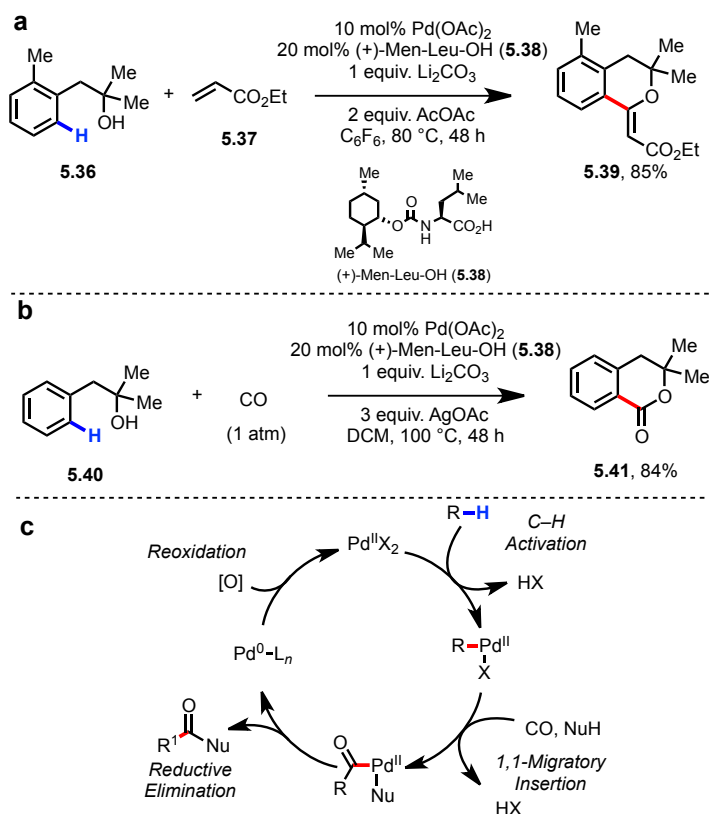
Other laboratories have revisited the asymmetric cyclopalladation of dimethylaminoferrocene using mono-*N*-protected amino acids, the stoichiometric version of which was originally reported by Sokolov in 1979,<sup>15</sup> to develop catalytic protocols. To date, stereoselective C–H/R–BX<sub>*n*</sub> cross-coupling<sup>16</sup> and C–H olefination<sup>17</sup> have been reported to give optically enriched functionalised ferrocene products with planar chirality.

### 5.3.2. Recent Applications for Enhanced Reactivity in C–H Activation

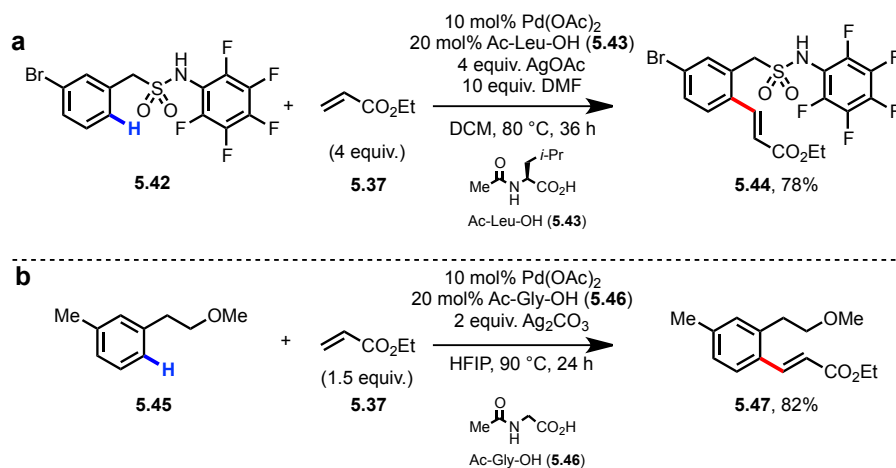
Beyond our efforts in Pd(II)-catalysed enantioselective C–H activation using mono-*N*-protected amino acid ligands, the Yu laboratory has also continued actively investigating applications of this class of ligands for enabling new reactivity in non-stereoselective reactions.

In addition to the carboxylic acid-containing substrates discussed in Chapters 2–4, we have found that other key classes of widely available, synthetically useful starting

materials can undergo Pd(II)-mediated C–H functionalisation promoted by amino acid ligands. This catalytic system has proven to be instrumental for substrates containing weakly coordinating functional groups, where in the absence of a highly reactive catalyst, cyclopalladation is sluggish. Contemporaneous to our initial studies in ligand-accelerated catalysis with phenylacetic acids, we also began exploring the effects of amino acid ligands in alcohol-directed reactions.<sup>7,18,19</sup> We viewed aryl- and alkylalcohols as ideal starting materials in C–H functionalisation because of their abundance and prevalence in desirable product motifs.<sup>20–23</sup> With the exception of examples using phenol-type directing groups,<sup>24,25</sup> hydroxy-directed C–H functionalisation using Pd catalysts had not been reported prior to our work. Through careful optimisation of the reaction conditions, we were able to achieve *ortho*-C–H olefination<sup>18</sup> and carbonylation<sup>19</sup> of phenethyl alcohols (Scheme 5.4). The use of (+)-Men-Leu-OH (**5.38**) as a supporting ligand was critical for obtaining synthetically useful yields; in both the transformations depicted in Scheme 5.4, <40% yield was observed in the absence of ligand. For both reactions, selection of a non-coordinating solvent was key due to the weak coordinative affinity of hydroxyl groups for Pd(II) centres in comparison to traditional directing groups. As part of a collaboration with Pfizer, we applied amino acid ligands to achieve high reactivity in *ortho*-C–H olefination directed by sulfonamides,<sup>26</sup> which are privileged pharmacophores in medicinal chemistry (Scheme 5.5a).<sup>27</sup> With this result as the entry point, a collection of categorically distinct, divergent C–H functionalisation reactions were developed for synthesising analogue libraries of drugs like Celebrex. With ether directing groups,<sup>28</sup> another class of prevalent, weakly coordinating functionality, the Yu group was able to develop an *ortho*-C–H olefination reactions in the presence of Ac-Gly-OH (**5.46**) and hexafluoro-2-propanol (HFIP) (Scheme 5.5b).<sup>29</sup>



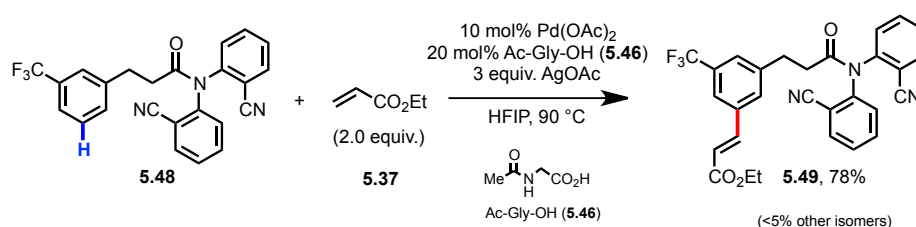
**Scheme 5.4.** Ligand-promoted *ortho*-C–H functionalisation of phenethyl alcohols: (a) olefination<sup>18</sup> and (b) carbonylation.<sup>19</sup> (c) General catalytic cycle C–H carbonylation via Pd(II)/Pd(0) catalysis; Nu = generic nucleophile.



**Scheme 5.5.** Ligand-promoted *ortho*-C–H olefination of (a) benzylsulfonamides (**5.42**)<sup>27</sup> and (b) phenethylethers (**5.45**).<sup>29</sup>

Finally, amino acid ligands were again turned to during efforts to develop a *meta*-selective Pd(II)-catalysed C–H olefination reaction of hydrocinnamic acid derivatives (Scheme 5.6).<sup>30</sup> The reaction design centred on the use of an end-on template,<sup>125,126</sup> which

was inspired by gas-phase studies of Schwarz in which metal centres were observed to adopt a linear coordination geometry with nitriles, enabling activation of remote C–H bonds.<sup>31,32</sup> To reduce this idea to practice, a simple nitrile-containing amide auxiliary was installed on a hydrocinnamic acid. End-on coordination of Pd(II) to the nitrile through the nitrogen atom situates the catalyst directly over the desired C–H bond. In this system the combination of Ac-Gly-OH (**5.46**) and HFIP were found to be critical for high activity in C–H activation. Recently, this reaction system was also applied to *meta*-C–H olefination of phenol derivatives.<sup>33</sup>

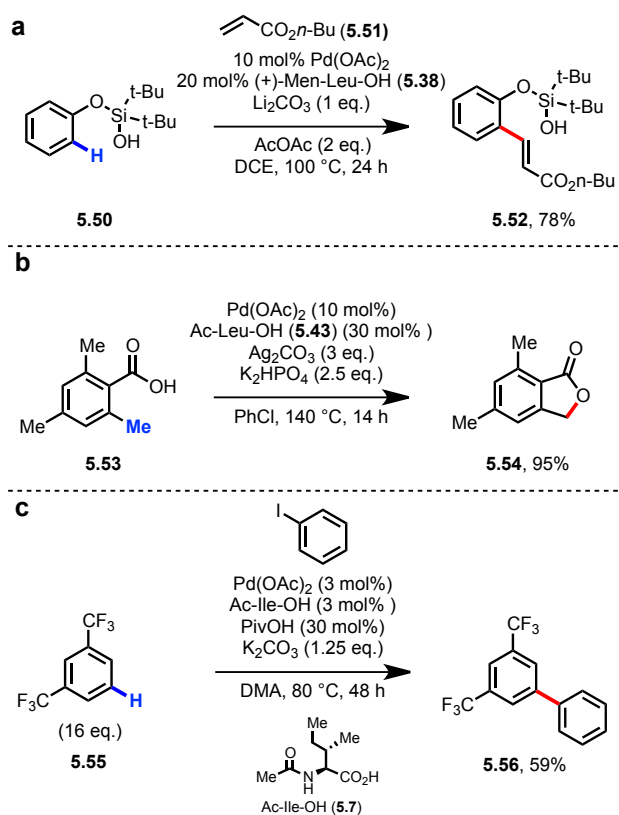


**Scheme 5.6.** Ligand-promoted *meta*-C–H olefination of hydrocinnamic acid derivative **5.48** using an end-on template approach.<sup>30</sup>

Outside of the Yu laboratory, other research groups have also had success employing mono-*N*-protected amino acid ligands to enable the development of novel Pd(II)-catalysed C–H functionalisation reactions using a diverse collection of substrates (Scheme 5.7). Based on the precedent that we established using alcohol functional groups to direct *ortho*-C–H functionalisation (Scheme 5.4), Gevorgyan reported a Pd(II)-catalysed silanol-directed C–H olefination reaction (Scheme 5.7a). (+)-Men-Leu-OH (**5.38**) was found to be crucial for obtaining high yield of the desired product.<sup>34</sup> Following C–H olefination, the silanol group could readily be removed, allowing for facile access to *ortho*-functionalised phenol products. The Martin group found success using Ac-Leu-OH (**5.43**) to facilitate C(sp<sup>3</sup>)-H oxygenation to give lactone products (Scheme 5.7b).<sup>35</sup> In the reaction, the ligand is presumably involved in C(sp<sup>3</sup>)-H cleavage to generate a Pd(II)- $\pi$ -benzyl intermediate, which is trapped with the intramolecular carboxylate nucleophile. Mono-*N*-protected ligands



also were found to improve the yield of non-directed C–H arylation of electron-poor arenes along a Pd(II)/Pd(IV) catalytic cycle by Hou and coworkers (Scheme 5.7c).<sup>36</sup>



**Scheme 5.7.** Ligand-enabled Pd(II)-Catalysed C–H functionalisation reactions employing mono-*N*-protected amino acids developed by other research groups. (a) Silanol-directed *ortho*-C(sp<sup>2</sup>)–H olefination by Gevorgyan in 2011.<sup>34</sup> Carboxylate-directed benzylic C(sp<sup>3</sup>)–H oxygenation by Martin in 2011.<sup>35</sup> (c) Non-directed C(sp<sup>2</sup>)–H arylation reported by Hou in 2012.<sup>36</sup>

While pyridine directing groups are normally highly efficient in promoting C–H activation through rigid five- and six-membered transition states, C–H cleavage with remotely disposed pyridine directing groups is known to be less facile. To overcome this challenge in the context of phenol-derived substrates containing a 2-pyridylmethyl ether linkage, in which cyclopalladation proceeds *via* a seven-membered cyclic transition state, You and coworkers applied a mono-*N*-protected amino acid ligand to obtain enhanced reactivity.<sup>37</sup> Lastly, in a recent report, Rombouts and Molander described the first example in which an amino-acid ligand was used in C–H functionalisation with a catalyst other than

Pd(II). In their report, they found that Boc-Val-OH performed favourably compared to PivOH as an additive in the Rh(III)-catalysed C–H functionalisation of benzamide derivatives.<sup>38</sup>

## 5.4. CONCLUSION

This collection of results, which has accrued over the past five years, demonstrates that mono-*N*-protected amino acid ligands effect enantioselectivity, positional selectivity, and rate enhancement in Pd(II)-catalysed C–H functionalisation. It establishes that amino acid ligands are bound to the Pd(II) centre during C–H cleavage and are capable of controlling the mechanism (and thus activation energy) of C–H cleavage. Amino acid ligands have been proven to control reactivity with many different substrate classes containing diverse directing groups, and they are compatible with a variety of elementary steps found in the catalytic cycles of Pd(II)-catalysed C–H/R–BX<sub>n</sub> cross-coupling, C–H olefination, C–H carbonylation, C–H arylation, and C–H oxygenation.

An advantage of mono-*N*-protected amino acid ligands for *directed* Pd(II)-catalysed C–H functionalisation is the non-symmetrical N,O-mixed donor system, which desymmetrises the remaining two sites on the square planar Pd(II) centre, such that the directing group can favourably bind at one, and the C–H bond react at the other. Another benefit is their practical convenience; many are commercially available and others can easily be prepared through modular synthesis. They are air- and moisture-stable and simple to employ in screening libraries. Furthermore, the mono-*N*-protected amino acid ligand scaffold offers several sites for tuning, which was pivotal in adapting the steric and electronic properties of the ligand to the unique demands of each of the transformations depicted in this chapter.

**5.5. REFERENCES**

- (1) Baxter, R. D.; Sale, D.; Engle, K. M.; Yu, J.-Q.; Blackmond, D. G. *J. Am. Chem. Soc.* **2012**, *134*, 4600–4606.
- (2) Abd-Elazem, I. S.; Chen, H. S.; Bates, R. B.; Huang, R. C. C. *Antiviral Res.* **2002**, *55*, 91–106.
- (3) Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 5767–5769.
- (4) Ghosh, A. K.; Cheng, X.; Zhou, B. *Org. Lett.* **2012**, *14*, 5046–5049.
- (5) Wang, H.; Li, G.; Engle, K. M.; Yu, J.-Q.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 6774–6777.
- (6) Davies, H. M. L.; Hedley, S. J.; Bohall, B. R. *J. Org. Chem.* **2005**, *70*, 10737–10742.
- (7) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203–12205.
- (8) Giri, R.; Chen, X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2005**, *44*, 2112–2115.
- (9) Shi, B.-F.; Mangel, N.; Zhang, Y.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886.
- (10) Wasa, M.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 9886–9887.
- (11) Wasa, M.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 3680–3681.
- (12) Wasa, M.; Engle, K. M.; Lin, D. W.; Yoo, E. J.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 19598–19601.
- (13) Cheng, X.-F.; Li, Y.; Su, Y.-M.; Yin, F.; Wang, J.; Sheng, J.; Vora, H. U.; Wang, X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 1236–1239.
- (14) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460–461.
- (15) Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537–546.

- (16) Gao, D.-W.; Shi, Y.-C.; Gu, Q.; Zhao, Z. L.; You, S.-L. *J. Am. Chem. Soc.* **2013**, *135*, 86–89.
- (17) Pi, C.; Li, Y.; Cui, X.; Zhang, H.; Han, Y.; Wu, Y. *Chem. Sci.* **2013**, *4*, 2675–2679.
- (18) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916–5921.
- (19) Lu, Y.; Leow, D.; Wang, X.; Engle, K. M.; Yu, J.-Q. *Chem. Sci.* **2011**, *2*, 967–971.
- (20) Simmons, E. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 17092–17095.
- (21) Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70–73.
- (22) Xiao, B.; Gong, T.-J.; Liu, Z.-J.; Liu, J.-H.; Luo, D.-F.; Xu, J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 9250–9253.
- (23) Wei, Y.; Yoshikai, N. *Org. Lett.* **2011**, *13*, 5504–5507.
- (24) Miura, M.; Tsuda, T.; Satoh, T.; Nomura, M. *Chem. Lett.* **1997**, *26*, 1103–1104.
- (25) Hennings, D. D.; Iwasa, S.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 2–3.
- (26) Pham, M. V.; Ye, B.; Cramer, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 10610–10614.
- (27) Dai, H.-X.; Stepan, A. F.; Plummer, M. S.; Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7222–7228.
- (28) Iglesias, Á.; Álvarez, R.; de Lera, Á. R.; Muñoz, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 2225–2228.
- (29) Li, G.; Leow, D.; Wan, L.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2013**, *52*, 1245–1247.
- (30) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518–522.
- (31) Schwarz, H. *Acc. Chem. Res.* **1989**, *22*, 282–287.
- (32) Dietl, N.; Schlangen, M.; Schwarz, H. *Chem. Eur. J.* **2011**, *17*, 1783–1788.
- (33) Dai, H.-X.; Li, G.; Zhang, X.-G.; Stepan, A. F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 7567–7571.

- (34) Huang, C.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 12406–12409.
- (35) Novák, P.; Correa, A.; Gallardo-Donaire, J.; Martin, R. *Angew. Chem. Int. Ed.* **2011**, *50*, 12236–12239.
- (36) Wang, Y.-N.; Guo, X.-Q.; Zhu, X.-H.; Zhong, R.; Cai, L.-H.; Hou, X.-F. *Chem. Commun.* **2012**, *48*, 10437–10439.
- (37) Cong, X.; You, J.; Gao, G.; Lan, J. *Chem. Commun.* **2013**, *49*, 662–664.
- (38) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *Org. Lett.* **2013**, *15*, 1528–1531.

## **PART II**

# **HYDROGEN BONDING EFFECTS ON THE REACTIVITY OF FLUORIDE ANION**

## **CHAPTER 6**

### INTRODUCTION

## 6.1. CONSPECTUS

Organic molecules containing one or more C–F bonds, organofluorine compounds, are widely used as medicines, agrochemicals, imaging agents, and high-performance materials. Generally speaking, strategies to synthesise these compounds can be classified as either electrophilic or nucleophilic fluorination, and both areas have witnessed a renaissance during the past decade, leading the development of a plethora of new, synthetically enabling transformations.

In nucleophilic fluorination reactions, a major problem in reaction development stems from fluoride's dual reactivity profile as a nucleophile and Brønsted base, and as such, developing strategies for tuning the reactivity of fluoride in organic solution for a given application is a significant challenge.

Inspired by Nature's biosynthetic approach with the fluorinase enzyme system and by previous work in organic synthesis and catalysis, we have studied the effects of intermolecular hydrogen bonding on the reactivity profile of fluoride anion with the goal of developing superior fluoride reagents for synthetic applications. In Part II of this Thesis, we present our findings from this line of inquiry. In the present chapter, we provide a brief introduction to the importance of organofluorine compounds for various applications (Section 6.2). We then outline modern approaches for C–F bond construction, with a special focus on reagent development (Section 6.3). We conclude by discussing the use of hydrogen bonding to tune the reactivity of fluoride (Section 6.4).

In Chapter 7, we disclose the results of our research, a systematic study of the influence of alcohol hydrogen-bond donors on the reactivity of fluoride, which was carried out by the author in collaboration with several coworkers (see Acknowledgments) from October 2011 to March 2013 in the Gouverneur laboratory at the University of Oxford. This investigation has combined solid-state X-ray diffraction studies of alcohol–fluoride



complexes, reactivity data, DFT calculations. Through analysis of the resulting data, we have gleaned new insights into the characteristics of effective hydrogen-bond donors and have identified highly reactive hydrogen bonding motifs. This knowledge, in turn, has led to development of a new family of shelf-stable TBAF reagents for organic synthesis. We conclude Part II by highlighting ongoing research efforts in the Gouverneur group that are advancing this theme and offer a perspective on the future evolution of the field (Chapter 8).

## 6.2. ORGANOFLUORINE COMPOUNDS

### 6.2.1. Background

Organofluorine compounds play an increasingly vital role in the modern world, and the challenges associated with their preparation continue to exert a strong influence on research in organic chemistry (Figure 6.1).<sup>1</sup> The unique set of applications in which organofluorine molecules are used stems directly from the distinctive characteristics of C–F bonds,<sup>2</sup> which are among the strongest covalent single bonds in nature (approximately 110–115 kcal/mol). Moreover, the high electronegativity and small atomic radius of fluoride make the C–F bond short (1.39 Å, compared to 1.42 for C–O) and give it especially low polarisability.

In a biological context, these basic bonding properties imbue organofluorine compounds with favourable characteristics, including improved metabolic stability (*i.e.*, resistance to cytochrome P450-mediated oxidative degradation) compared to their non-fluorinated counterparts, increased lipophilicity and bioavailability, small steric size which can be readily accommodated within enzyme binding pockets, and hydrogen bond-accepting ability that can improve enzyme binding strength.<sup>3</sup> As such, organic small molecules containing one to several C–F bonds are valued as medicinal compounds, agrochemicals, and bioactive agents. Indeed, 30% of all agrochemicals<sup>4</sup> and 20% of all

pharmaceuticals contain a fluorine atom, including blockbuster drugs, such as Prozac and Lipitor (**6.3**).<sup>5</sup>

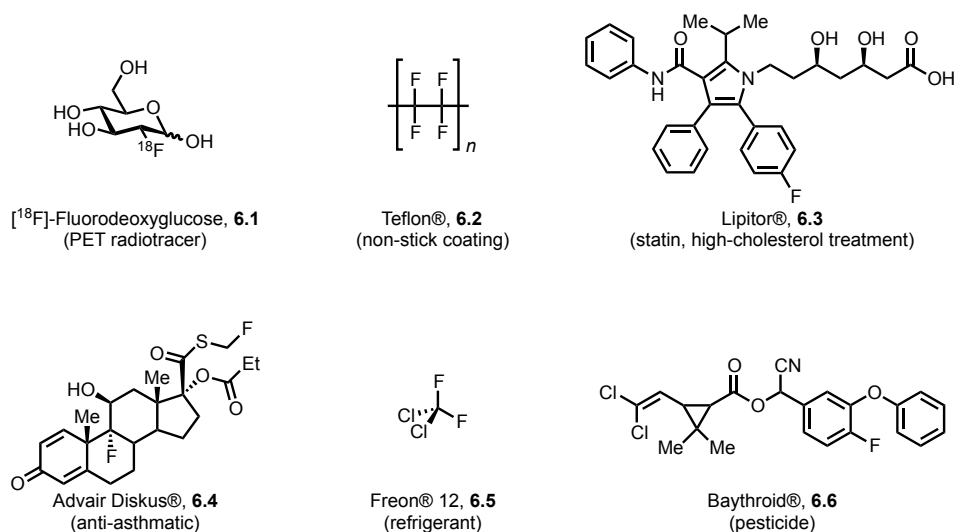


**Figure 6.1.** Representative pharmaceuticals, agrochemicals, materials, and radiotracers containing a C–F bond.

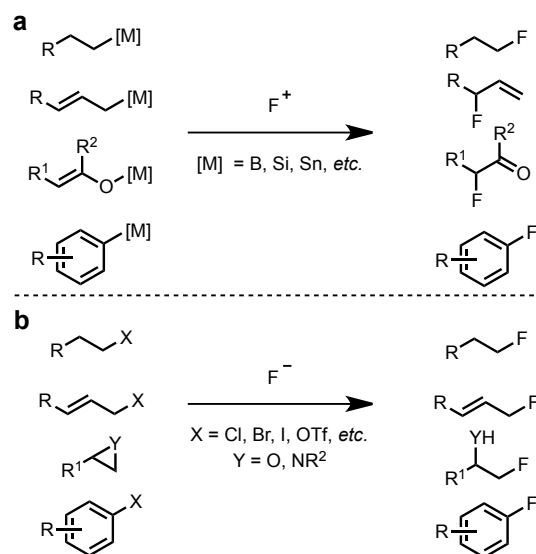
Furthermore, in the context of positron emission tomography (PET), <sup>18</sup>F is a privileged isotope, owing to a confluence of properties, including its capacity for forming a stable bond to carbon, suitable decay rate ( $t_{1/2} = 110$  min), low positron energy, small steric size, and relative ease of production.<sup>6,7</sup> Indeed, [<sup>18</sup>F]-FDG (**6.1**) was the first successfully employed radiotracer for PET imaging and remains the most widely used PET tracer, with the principal application being imaging cancer metastasis (approximately 90% of PET scans).

Beyond biological applications, the strength of the C–F bond and its general recalcitrance to many chemical transformations has been taken advantage of in the development of chemicals and materials that are robust, non-corrosive, non-flammable, and non-toxic. This includes durable polymers, such as Teflon® (**6.2**), and refrigerants, such as Freon®-12 (**6.5**).

### 6.2.2. Modern synthetic approaches

Due to the desirability of organofluorine compounds in the biological and materials sciences, methods for C–F bond formation using nucleophilic ( $F^-$ ) and electrophilic ( $F^+$ ) sources of fluorine have received widespread attention from organic chemists during the past several decades, with a particularly intense flurry of activity in the past few years.<sup>8-11</sup> The synthesis of fluorinated organic compounds is typically accomplished by employing one of two general approaches: (a) reacting an electrophilic source of fluoride ( $F^+$ ) with an alkyl, allyl, enolate, or aryl nucleophile or (b) reacting a nucleophilic source of fluoride ( $F^-$ ) with an alkyl, allyl, aryl or strained ring electrophile (Scheme 6.1). For transformations in which stereocontrol is sought or for those with a prohibitively high kinetic barrier, a variety of catalysts (*e.g.*, transition metals or organic small molecules) are capable of mediating C–F bond formation.<sup>10,11</sup> The electrophilic and nucleophilic approach are complementary, and each has advantages and disadvantages depending on the context. Both strategies have been used to realise aryl, allyl, and alkyl C–F bond formation, and both have been adapted for use with transition metal catalysis and organocatalysis.

It should be noted that C–F bond-forming reactions can also operate in the radical addition mode ( $F^\bullet$ ), but this approach has not been widely used in synthesis. Related to this idea, recently a variant of fluorination with electrophilic reagents has gained significant attention and warrants brief mention. In this approach, a carbon-centred free radical is generated from a suitable precursor (*e.g.*, radical decarboxylation). These nucleophilic high-energy species rapidly react with  $F^+$  reagents to effect C–F bond formation.<sup>12-16</sup>



**Scheme 6.1.** General strategies for C–F bond formation using (a) electrophilic fluorinating reagents ( $\text{F}^+$ ) and (b) nucleophilic fluorinating reagents ( $\text{F}^-$ ).

The unique properties of fluorine as an element pose challenges in both the electrophilic and nucleophilic mode, and in both cases, reagent development has played a critical role in ushering organofluorine chemistry into the mainstream of organic synthesis. A pervasive theme in both areas is the need to tune the reactivity profile of the fluorine source to match the inherent reactivity of the substrate and to be compatible with each step in the reaction (or catalytic cycle). Below, we give brief overviews of each of the two areas.

### 6.2.3. Electrophilic fluorination

The use of  $\text{F}_2$ , the archetypal source of  $\text{F}^+$ , and other related  $\text{F}^+$  reagents has historically been restricted by the energetic nature of these compounds and their corrosive properties, but the advent of more operationally convenient  $\text{F}^+$  reagents during the past two decades has rejuvenated this field of research (Figure 6.2). Generally, few industrial processes employ  $\text{F}_2$ , and in small-scale laboratory applications, its use was traditionally complicated by its indiscriminate reactivity, gaseous nature, and high toxicity. Though examples of synthetically useful transformations using  $\text{F}_2$  certainly exist,<sup>17</sup> the

aforementioned limitations have nonetheless persisted over time. The potent reactivity of  $F_2$  stems from the electronegativity of fluorine, which leads to a low F–F bond dissociation energy (38 kcal/mol) and makes  $F_2$  a powerful oxidising agent.

Much of the focus of  $F^+$  reagent development has thus centred on taming the reactivity of  $F_2$  to give  $F^+$  sources with lower, and consequently more discriminant, reactivity (*i.e.*, better selectivity).<sup>18</sup> A parallel and interrelated focus has been rendering this class of compounds more suitable for everyday laboratory use through improving their handling properties. Among the first of this new generation of  $F^+$  reagents designed to meet these challenges were perchloryl fluoride ( $FClO_3$ ), xenon difluoride ( $XeF_2$ , **6.7**), and various O–F reagents, including trifluoromethyl hypofluorite ( $CF_3OF$ , **6.8**). During the 80s and early 90s, the invention of N–F reagents (**6.9–6.13**) further advanced the field of electrophilic fluorination.<sup>19–21</sup> N–F reagents are typically prepared by treating the  $N(sp^2)$ - or  $N(sp^3)$ -containing precursor compound with  $F_2$ , and the reagents themselves are typically shelf-stable solids that tolerate both air and moisture. Since their introduction, N–F reagents have become widely adopted in the synthetic and organometallic communities.<sup>22,23</sup> Their use has become widespread, with applications ranging from organocatalytic asymmetric  $\alpha$ -fluorination of carbonyl-containing compounds<sup>22–24</sup> to transition metal-catalysed catalytic fluorination of C(aryl)–H bonds.<sup>25,26</sup>

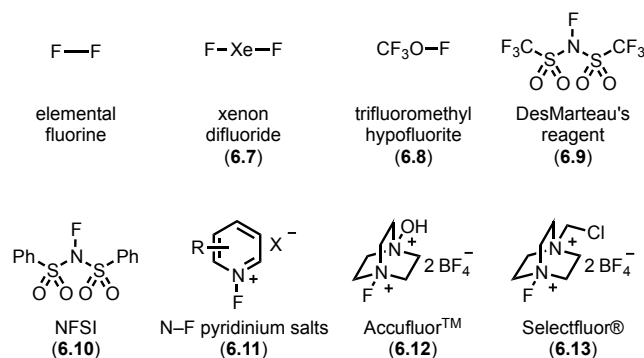


**Figure 6.2.** Commonly used electrophilic fluorinating reagents ( $F^+$ ).<sup>18</sup>

Due to the unique ability of  $F^+$  reagents to enable certain types of bond construction that are impossible with  $F^-$  sources, there has been a long-standing desire to utilise electrophilic fluorination in radiolabelling. Because electrophilic and nucleophilic fluorination offer complementary compatibility with respect to substrate reactivity (*i.e.*, nucleophile versus electrophile), it has been envisioned that development and application of  $[^{18}F]F^+$  reagents will allow access to PET imaging agents that are otherwise difficult to prepare. While  $[^{18}F]F_2$  is available, it typically suffers from low specific activity, due in part to the carrier gas that must be added to remove it following its preparation. Additionally, it suffers from the disadvantages articulated previously. Recently progress has been made to develop a new suite of  $[^{18}F]F^+$  reagents for radiolabelling. In one approach,  $[^{18}F]N-F$  reagents have been prepared, including  $[^{18}F]NFSI$ <sup>27</sup> and  $[^{18}F]Selectfluor$  bistriflate.<sup>28</sup> This approach has been facilitated by the development of high-specific activity  $[^{18}F]F_2$ ,<sup>29</sup> and these  $[^{18}F]N-F$  reagents have been successfully applied in the radiofluorination of aryl-, allyl-, and enolate nucleophiles. More recently, Ritter and coworkers have pioneered a fluoride umpolung strategy, in which  $[^{18}F]F^-$  is converted to  $[^{18}F]F^+$  *via* ligand exchange at a Pd(IV) centre.<sup>30</sup> This  $[^{18}F]F^+$  source can subsequently react with arylpalladium(II) species to effect radiofluorination.<sup>31</sup>

#### 6.2.4. Nucleophilic fluorination

While electrophilic fluorination has played an increasingly important role in the small-scale synthesis of bioactive targets and fine chemicals, nucleophilic sources of fluorine are more readily available and less expensive. Indeed, most fluorine-containing commodity chemicals and polymers are synthesised from hydrogen fluoride (HF) or another  $F^-$  source *via* nucleophilic fluorination (sometimes with the cooperative action of a Lewis acid). This general approach has been widely used in synthesis for nearly a century.<sup>32</sup> In the

broad field of nucleophilic fluorination with  $F^-$ , a major challenge has been developing strategies for tuning the reactivity profile (nucleophilicity versus basicity) of the fluoride anion in organic solution. Because only a narrow reactivity window is typically tolerated for a given synthetic transformation,<sup>11</sup> a relatively large library of  $F^-$  reagents have been developed, as described below.

The challenges in using fluoride in organic transformations stem from its high electronegativity, small size, low polarisability, and substantial charge density. These properties make fluoride an aggressive Brønsted base and strong Lewis base. It is prone to tight ion pairing with hard electrophiles, which can limit solubility in non-polar solvents, and it is a potent hydrogen-bond acceptor, rendering it susceptible to solvation with polar protic solvents, particularly with water. Indeed the strong solvation effects with water are likely the reason that despite being the 13<sup>th</sup> most abundant element in the Earth's crust, fluorine is found in fewer than 10 natural products.<sup>33</sup> Though “naked” fluoride in the gas phase is known to have high kinetic reactivity as a nucleophile,<sup>34</sup> the aforementioned characteristics make the use of fluoride in organic solution a challenge.

A variety of approaches have been developed to address these problems to facilitate nucleophilic fluorination reactions in organic solution. They all focus on one or more of the following: activating the pendent leaving group, weakening counteraction/fluoride pairing, avoiding Lewis acid complexation, improving solubility, decreasing basicity, or reducing water solvation. Based on these ideas, an array of different  $F^-$  sources have been developed (Figure 6.3). This includes deoxyfluorinating reagents (**6.14–6.18**),<sup>35–39</sup> such as  $SF_4$ , DAST (**6.14**), Fluolead<sup>TM</sup> (**6.15**), and Deoxo-Fluor® (**6.16**), which contain an electrophilic carbon or sulfur atom. Their mechanism of action involves initial attack by an oxygen atom of the substrate onto the electrophilic atom of the reagent to release  $F^-$ , which is then free to attack the resulting  $R-OSX_n$  or  $R-OCX_n$  intermediate.

These reagents can directly convert alcohols, ketones, and carboxylic acids, to the corresponding fluorides, difluoromethides, and trifluoromethides, respectively. As mentioned above, HF, typically in anhydrous form, is the most widely used  $F^-$  reagent. To improve the handling properties, reduce volatility, and increase stability, HF complexes with amine bases have been invented as a less volatile form of hydrogen fluoride (**6.19** and **6.20**).<sup>40-44</sup> Exceptionally mild  $F^-$  sources have been described for “slow release” applications that require high temperature and/or long reaction times. Prominent among them is tetrabutylammonium triphenylsilyldifluoride (TBAT, **6.22**) developed by DeShong.<sup>45</sup> Tetraalkylphosphorane<sup>46-49</sup> and tetraalkylammonium fluoride salts are highly soluble in organic solvents, and the latter have proven to be especially useful in organic synthesis.<sup>50-55</sup> Tetraalkylammonium fluorides are available as hydrates or in their anhydrous form, with the latter being more kinetically reactive and more basic.<sup>56-58</sup>

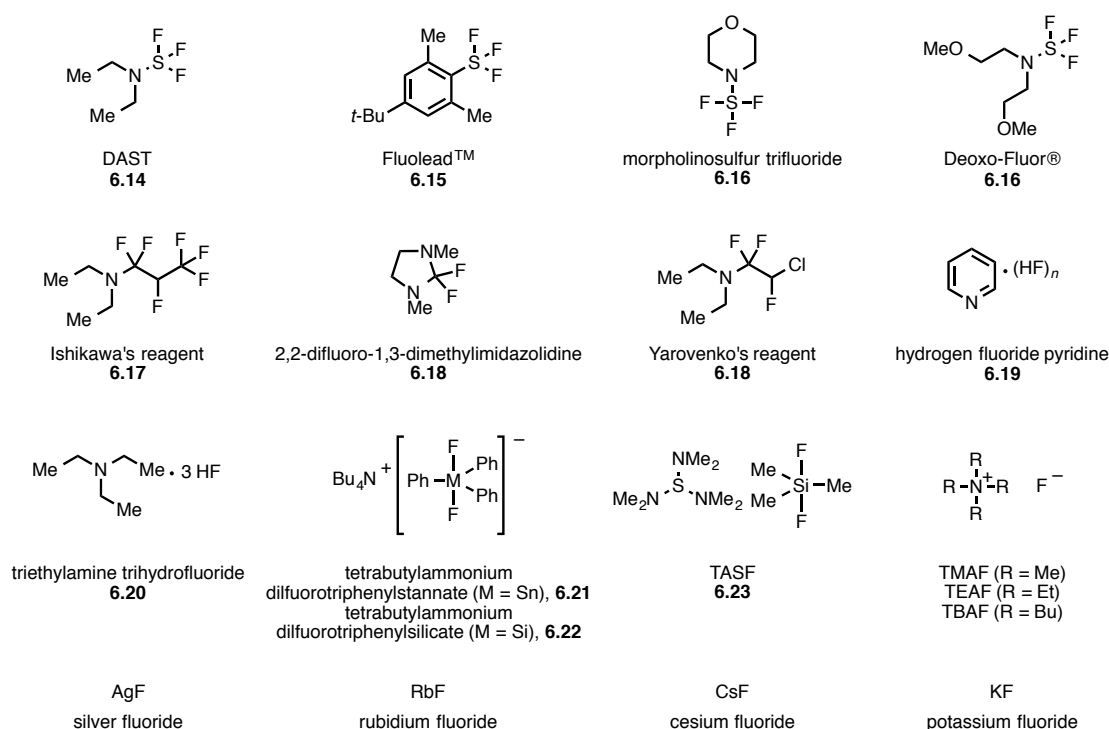


**Figure 6.3.** Commonly used nucleophilic fluorinating reagents ( $F^-$ ).<sup>11</sup>



Simple, inexpensive inorganic fluoride salts are also used extensively. However, they often suffer from low solubility in organic solvents and are difficult to obtain in anhydrous form. Therefore, strategies to activate inorganic fluoride salts have been devised (Figure 6.4). These include the use of crown ethers (**6.24**),<sup>59,60</sup> phase transfer catalysts (**6.25**),<sup>52,61-63</sup> polymer solid support resins,<sup>60,64-66</sup> spray-drying,<sup>67</sup> and ionic liquids (**6.26**).<sup>68</sup>

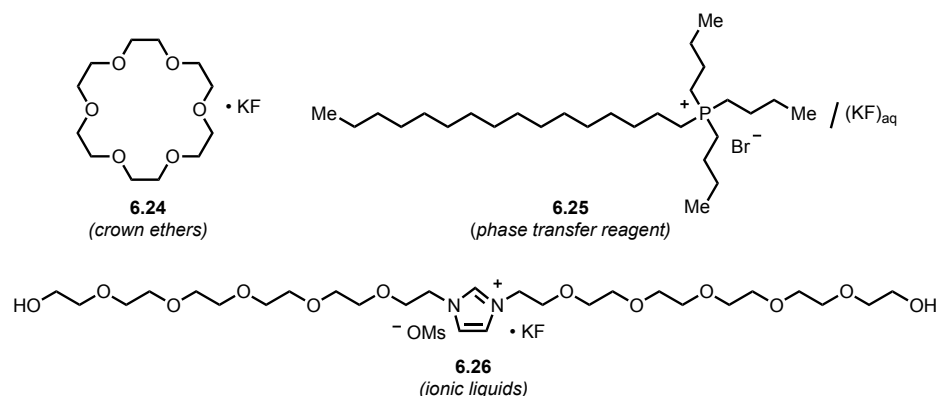


**Figure 6.4.** Representative approaches for activating inorganic fluoride salts.

In regards to radiochemistry, nucleophilic fluorination has generally been the reactivity mode of choice, largely due to the ease of producing  $[\text{}^{18}\text{F}]\text{F}^-$  with high specific activity. Off of the cyclotron,  $[\text{}^{18}\text{F}]\text{F}^-$  is obtained as an aqueous solution, but due to the low reactivity of fluoride hydrate, it must usually be dried prior to use. Following removal of water, some of the aforementioned reagents/approaches have enabled productive radiofluorination and are broadly utilised (*e.g.*,  $[\text{}^{18}\text{F}]\text{TEAF}$  and  $[\text{}^{18}\text{F}]\text{KF}\cdot\text{Kryptofix-2.2.2}$ ).

All of these  $\text{F}^-$  sources are useful in specific synthetic settings. However, many of them also suffer from disadvantages in terms of handling properties, functional group compatibility, atom economy, or operational simplicity. More broadly speaking, there remains a lack of understanding of the factors that influence the reactivity profile of individual  $\text{F}^-$  reagents. Moreover, there is an unmet need for (1) new  $\text{F}^-$  reagents with high nucleophilicity, low basicity, and little or no water content and (2) general and practical

approaches in which fluoride's reactivity profile can be fine-tuned to meet the specification of a particular substrate and reaction.

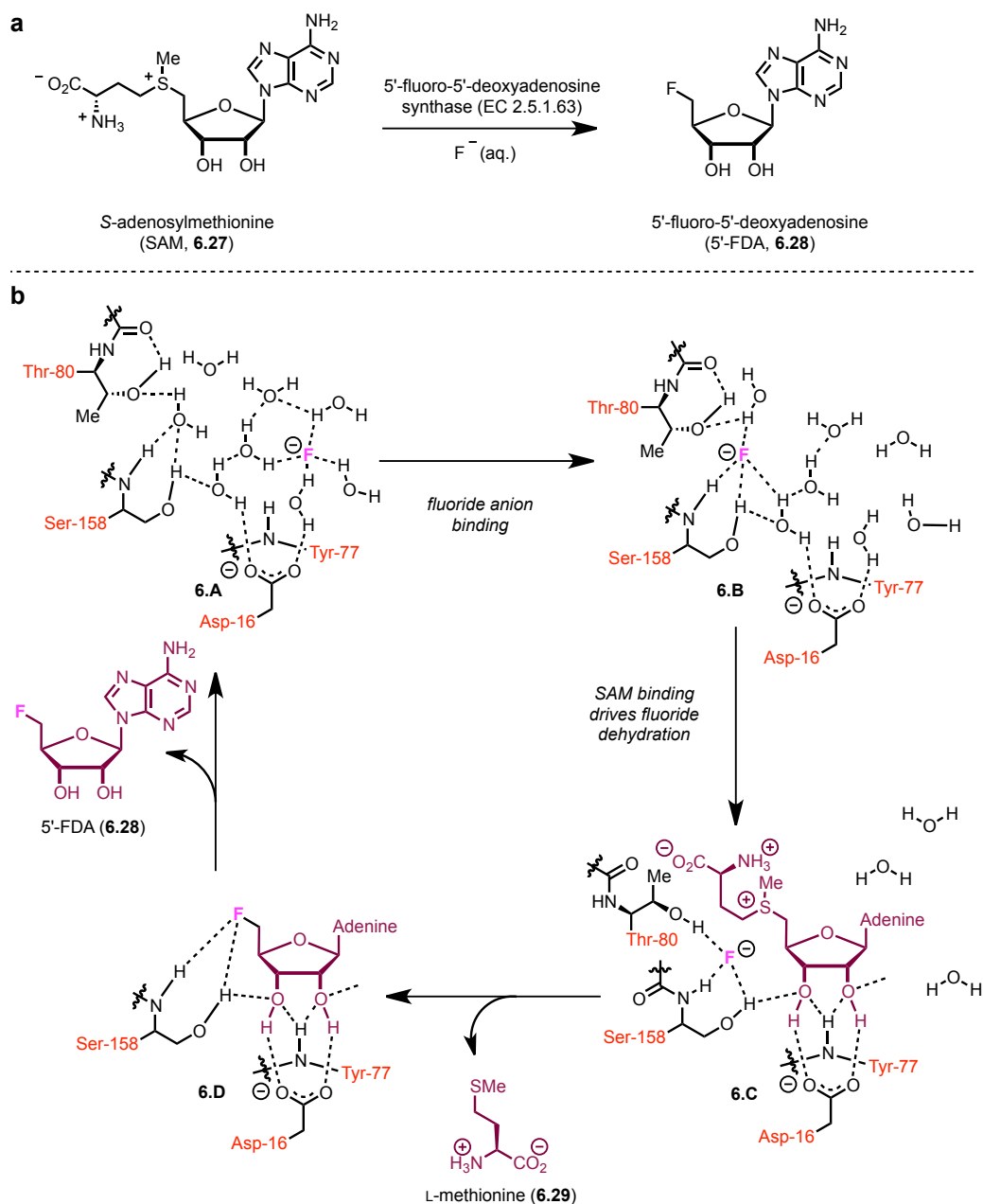
### **6.3. A HYDROGEN BONDING APPROACH TOWARDS NUCLEOPHILIC FLUORINATION**

In these respects, an attractive possibility is to use intermolecular hydrogen bonding to modulate the reactivity of fluoride. In this way, the reactivity could be precisely controlled through selection of a hydrogen-bond donor. Additionally, this approach would offer the opportunity to carry out systematic studies into the factors that govern reactivity through variation of the steric and electronic properties of the hydrogen-bond donor. Hydrogen bonding interactions to fluoride have been rather extensively applied in molecular recognition and anion sensing,<sup>69-78</sup> a subject that has recently been reviewed.<sup>79</sup> Applications of fluoride hydrogen bonding in synthesis and catalysis, on the other hand, are far less common. Below we highlight examples that are pertinent to this Thesis.

#### **6.3.1. Biocatalysis**

In a sense, a hydrogen bonding approach is Nature's solution to nucleophilic fluorination. 5'-Fluoro-5'-deoxyadenosine synthase, a fluorinase enzyme discovered by O'Hagan and coworkers in 2002,<sup>80</sup> is known to catalyse nucleophilic displacement reactions through an intricate hydrogen bonding network. Hydrogen bonding contacts play a critical role in capturing fluoride from aqueous solution, displacing coordinated water molecules, and precisely positioning fluoride anion adjacent to the substrate for nucleophilic attack (Scheme 6.2).<sup>80-82</sup> X-ray crystallography of substrate- and product-bound structures of this enzyme have revealed that fluoride forms two hydrogen bonding contacts to Ser-158 when it binds to the active site. Subsequent binding of the substrate (SAM, **6.27**) encourages

fluoride ion dehydration, which facilitates nucleophilic fluorination. An additional hydrogen bonding interaction of fluoride with Thr-80 is thought to stabilise the transition state of the  $S_N2$  fluorination process. Starting from [ $^{18}\text{F}$ ]fluoride anion, biotransformations involving the fluorinase enzyme have been used for the synthesis of [ $^{18}\text{F}$ ]5'-FDA and related compounds for PET imaging.<sup>83,84</sup>



**Scheme 6.2.** (a) Fluorinase-mediated synthesis of 5'-FDA (**6.28**), as first described by O'Hagan in 2002.<sup>80</sup> (b) Depiction of the catalytic cycle and key hydrogen bonding contacts during fluoride complexation and nucleophilic displacement.<sup>81,82</sup>

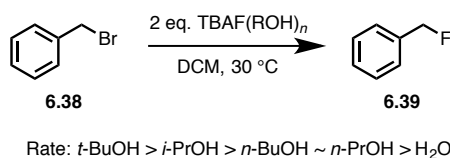
### 6.3.2. Simple alcohol solvents in S<sub>N</sub>2 reactions

In the context of organic synthesis, in a 1994 Japanese patent, Yonezawa and coworkers prepared a series of hydrogen-bonded TBAF complexes from TBAF(H<sub>2</sub>O)<sub>3</sub> using volatile alcohol solvents as the hydrogen-bond donors (Table 6.1).<sup>85</sup> Careful mixing under controlled vacuum allowed for azeotropic removal of the originally bound water molecules.

**Table 6.1.** Synthesis and properties of TBAF(ROH)<sub>*n*</sub> complexes, as reported by Yonezawa and coworkers in 1994.<sup>85</sup>

| TBAF(H <sub>2</sub> O) <sub>3</sub> |        | $\xrightarrow[\substack{40\text{ }^{\circ}\text{C, 4 h} \\ (10\text{ mmHg})}]{\text{ROH (0.13 M)}}$ |                    |                     | TBAF(ROH) <sub><i>n</i></sub> |
|-------------------------------------|--------|-----------------------------------------------------------------------------------------------------|--------------------|---------------------|-------------------------------|
| ROH                                 |        | <i>n</i>                                                                                            | % H <sub>2</sub> O | physical properties |                               |
| MeOH                                | (6.30) | 2.5                                                                                                 | 5.0                | oil                 |                               |
| EtOH                                | (6.31) | 2.5                                                                                                 | 0.0                | oil                 |                               |
| <i>n</i> -PrOH                      | (6.32) | 2.5                                                                                                 | 0.4                | crystalline         |                               |
| <i>i</i> -PrOH                      | (6.33) | 3.5                                                                                                 | 0.1                | crystalline         |                               |
| <i>n</i> -BuOH                      | (6.34) | 3.3                                                                                                 | 0.3                | oil                 |                               |
| <i>i</i> -BuOH                      | (6.35) | 5.0                                                                                                 | 0.1                | slush               |                               |
| <i>s</i> -BuOH                      | (6.36) | 2.5                                                                                                 | 2.0                | oil                 |                               |
| <i>t</i> -BuOH                      | (6.37) | 3.7                                                                                                 | 0.5                | cystalline          |                               |

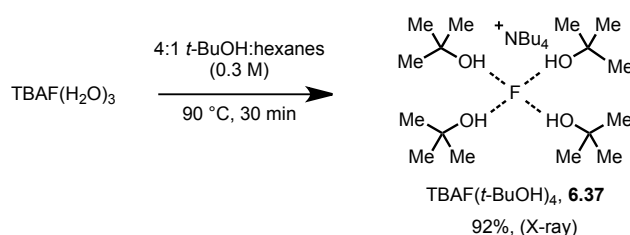
Yonezawa further found that the hydrogen-bond donor influenced the kinetic reactivity of fluoride in a representative S<sub>N</sub>2 reaction with benzyl bromide (**6.38**) in DCM (Scheme 6.3).<sup>85</sup> GC kinetic measurements revealed that reactivity roughly tracked with the steric bulk of the alcohol.



**Scheme 6.3.** Reactivity trends in the fluorination of benzyl bromide (**6.38**).<sup>85</sup>

Kim and coworkers later made several important advancements in this area. They first found that simple inorganic fluoride salts (*e.g.*, CsF) when used in bulky tertiary alcohol solvents (*e.g.*, *t*-BuOH and *t*-AmylOH) exhibited improved kinetic reactivity and

*better selectivity* for the S<sub>N</sub>2 pathway over competitive E2 elimination.<sup>86</sup> Kim and coworkers were further able to apply *t*-BuOH as a solvent with [<sup>18</sup>F]F<sup>−</sup> and demonstrate the efficiency of this protocol in radiolabelling.<sup>87</sup> Later, Kim obtained an X-ray crystal structure of TBAF(*t*-BuOH)<sub>4</sub> (**6.37**), confirming the solid-state coordination stoichiometry and geometry (Scheme 6.4).<sup>88</sup> With this isolated complex, similar reactivity and selectivity trends were found to those observed using alcohol solvents (Table 6.2).



**Scheme 6.4.** Synthesis and crystal structure of TBAF(*t*-BuOH)<sub>4</sub> (**6.37**) by Kim in 2008.<sup>88</sup>

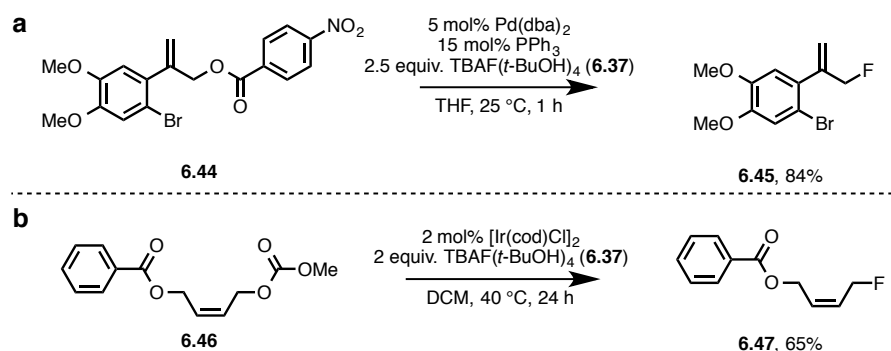
**Table 6.2.** Reactivity and selectivity of representative TBAF complexes.<sup>88</sup>

| Reagent                                            | % composition ( <sup>1</sup> H NMR) |        |         |         |
|----------------------------------------------------|-------------------------------------|--------|---------|---------|
|                                                    | Fluoride                            | Alkene | Alcohol | Bromide |
| TBAF( <i>t</i> -BuOH) <sub>4</sub> ( <b>6.37</b> ) | 80                                  | 20     | --      | --      |
| TBAF(H <sub>2</sub> O) <sub>3</sub>                | 63                                  | 30     | 6       | --      |
| TBAF (anhydrous)                                   | 22                                  | 78     | --      | --      |

### 6.3.3. Transition metal catalysis

Hydrogen bonding to fluoride sources has also played an important role in transition metal-catalysed C–F bond-forming reactions. Amelioration of the reactivity of free fluoride ion by the use of TBAF(*t*-BuOH)<sub>4</sub> (**6.37**) proved necessary for successful development of Pd(0)- and Ir(I)-catalysed allylic fluorinations reported by Gouverneur and Brown (Scheme 6.5).<sup>89,90</sup> In these reactions, the combination of high kinetic reactivity, low basicity, and minimal water content were crucial criteria in the ultimate success of TBAF(*t*-BuOH)<sub>4</sub>

(**6.37**) as the fluoride source. With slight variations to the procedures, including use of [ $^{18}\text{F}$ ]TEAF as the fluoride source, both of these reactions proved adaptable to radiolabelling.

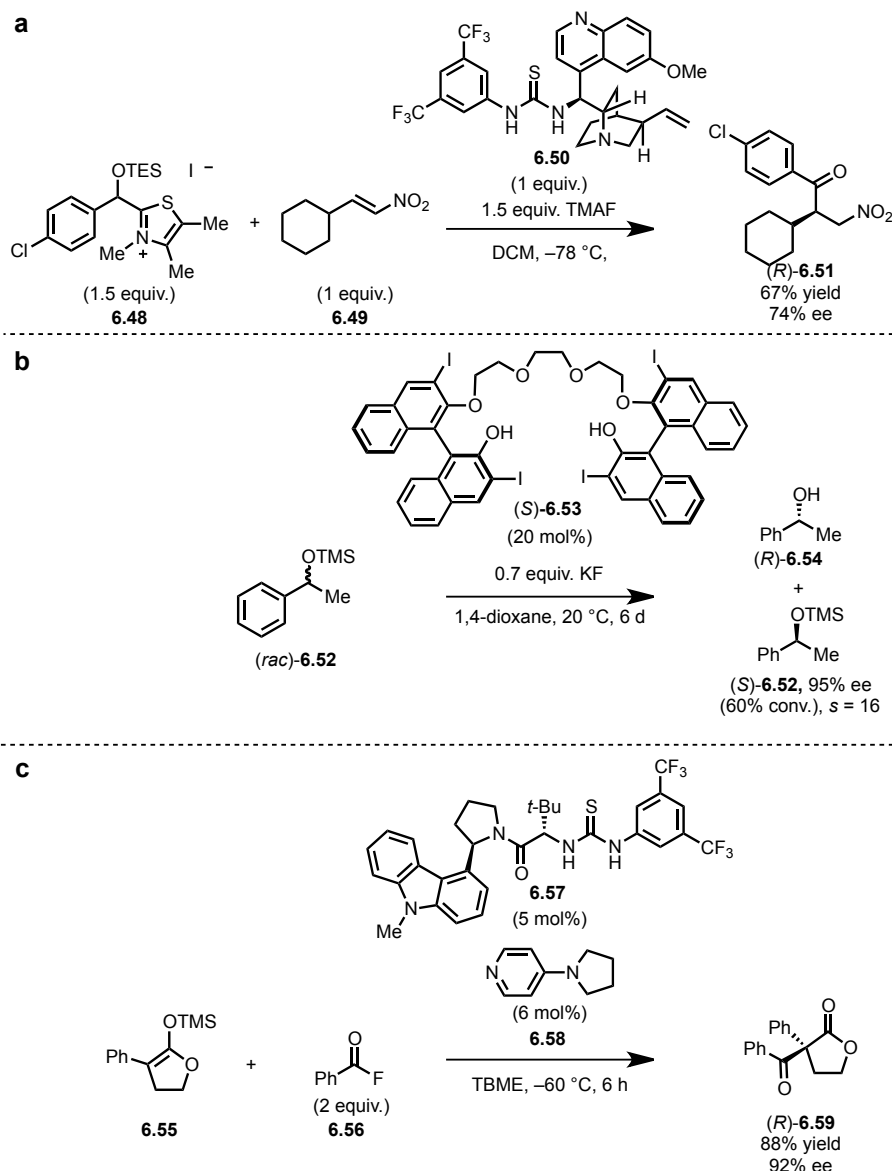


**Scheme 6.5.** Transition metal-catalysed allylic fluorination reactions using (a)  $\text{Pd}(0)^{89}$  and (b)  $\text{Ir}(\text{I})$ .<sup>90</sup>

### 6.3.4. Hydrogen bonding catalysis

Outside of the context of C–F bond forming-reactions, hydrogen bonding to fluoride has been utilised in other organic transformations, particularly those involving desilylation (Scheme 6.7). In 2006, the Scheidt group found that the combination of TMAF with stoichiometric quantities of thiourea hydrogen-bond donors was crucial for improving the conversion in the nucleophilic acylation of nitroalkenes. Use of stoichiometric amounts of chiral thiourea **6.50**<sup>91–94</sup> led to moderate ee in an asymmetric variant of the transformation (Scheme 6.7a).<sup>95</sup> Song and coworkers developed a catalytic kinetic resolution of silyl-protected secondary benzylic alcohols using chiral hydroxyl-terminated polyether **6.53**, which serves as a hybrid crown ether/hydrogen bond-donor catalyst (Scheme 6.7b).<sup>96</sup> Importantly, they were also able to obtain a crystal structure of KF complexed to the brominated version of the catalyst, confirming the presence of O–H...F hydrogen bonding in the solid state and implicating the involvement of these interactions in the solution state. In 2011, Jacobsen applied a dual-function thiourea organocatalyst in the asymmetric acylation of silyl ketene acetals (Scheme 6.7c). In the catalytic cycle for this transformation, thiourea catalyst **6.57** plays multiple roles. First, it activates benzoyl fluoride (**6.56**) for

nucleophilic attack by **6.58**, to give an *N*-acyl pyridinium fluoride species, which is thought to be stabilised by the catalyst through a cation– $\pi$  interaction and through  $F^-$ –thiourea hydrogen bonding. Subsequently, rate-limiting desilylation gives TESF and a hydrogen-bonded enolate. Stereodetermining acylation then regenerates the free catalyst and closes the catalytic cycle.



**Scheme 6.7.** Synthetic applications of fluoride hydrogen bonding for influencing the stereochemical course of desilylative reactions. (a) Asymmetric nucleophilic acylation of nitroalkenes by Scheidt in 2006.<sup>95</sup> (b) Kinetic resolution of secondary benzylic silyl ethers by Song in 2010.<sup>96</sup> (c) Asymmetric acylation of silyl ketene acetals by Jacobsen.<sup>97</sup>

### 6.3.5. Impetus for mechanistic study and further reagent development

Based on these precedents, we envisioned tuning the reactivity of fluoride by designing a hydrogen bonding system that generates a fluoride species with high nucleophilicity and low basicity in organic solution. To this end, we sought to understand comprehensively the effects of hydrogen bonding on fluoride reactivity through structural, kinetic, and computational analysis. We further aimed to harness this knowledge in pursuit of synthetically useful new  $F^-$  reagents to address unmet needs in organic and organofluorine chemistry.

These goals have motivated the research presented in Part II of this Thesis, and in Chapter 7, we describe the first comprehensive examination of alcohol–fluoride hydrogen bonding. With alcohol hydrogen-bond donors as an entry point, the Gouverneur group is well positioned extend this study to include a wide variety of O–H, N–H, S–H, and C–H hydrogen bond donors. To give the reader a sense of the direction of this line of inquiry moving forward, ongoing kinetic and structural experiments with alcohol–fluoride complex and recent progress with new hydrogen-bond donor classes are touched upon in Chapter 8.

## 6.4. REFERENCES

- (1) *Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical Aspects to Clinical Applications*; Gouverneur, V., Müller, K., Eds.; Imperial College Press: London, 2012.
- (2) *CRC Handbook of Chemistry and Physics*, 80th ed.; Lide, D.R., Ed.; CRC Press: Boca Raton, FL, 1999.
- (3) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881–1886.
- (4) Jeschke, P. *ChemBioChem* **2004**, *5*, 570–589.



- (5) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, 37, 320–330.
- (6) Phelps, M. E. *Proc. Natl. Acad. Sci. U. S. A.* **2000**, 97, 9226–9233.
- (7) Tredwell, M.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2012**, 51, 11426–11437.
- (8) Gerstenberger, M. R. C.; Haas, A. *Angew. Chem. Int. Ed.* **1981**, 20, 647–667.
- (9) Wilkinson, J. A. *Chem. Rev.* **1992**, 92, 505–519.
- (10) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, 473, 470–477.
- (11) Hollingworth, C.; Gouverneur, V. *Chem. Commun.* **2012**, 48, 2929–2942.
- (12) Rueda-Becerril, M.; Chatalova Sazepin, C.; Leung, J. C. T.; Okbinoglu, T.; Kennepohl, P.; Paquin, J.-F.; Sammis, G. M. *J. Am. Chem. Soc.* **2012**, 134, 4026–4029.
- (13) Leung, J. C. T.; Chatalova-Sazepin, C.; West, J. G.; Rueda-Becerril, M.; Paquin, J.-F.; Sammis, G. M. *Angew. Chem. Int. Ed.* **2012**, 51, 10804–10807.
- (14) Barker, T. J.; Boger, D. L. *J. Am. Chem. Soc.* **2012**, 134, 13588–13591.
- (15) Yin, F.; Wang, Z.; Li, Z.; Li, C. *J. Am. Chem. Soc.* **2012**, 134, 10401–10404.
- (16) Li, Z.; Song, L.; Li, C. *J. Am. Chem. Soc.* **2013**, 135, 4640–4643.
- (17) Purrington, S. T.; Kagen, B. S.; Patrick, T. B. *Chem. Rev.* **1986**, 86, 997–1018.
- (18) Lal, G. S.; Pez, G. P.; Syvret, R. G. *Chem. Rev.* **1996**, 96, 1737–1756.
- (19) Umemoto, T.; Kawada, K.; Tomita, K. *Tetrahedron Lett.* **1986**, 27, 4465–4468.
- (20) Resnati, G.; DesMarteau, D. D. *J. Org. Chem.* **1991**, 56, 4925–4929.
- (21) Banks, R. E.; Mohialdin-Khaffaf, S. N.; Lal, G. S.; Sharif, I.; Syvret, R. G. *J. Chem. Soc., Chem. Commun.* **1992**, 595–596.
- (22) Beeson, T. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, 127, 8826–8828.
- (23) Steiner, D. D.; Mase, N.; Barbas, C. F., III *Angew. Chem. Int. Ed.* **2005**, 44, 3706–3710.

- (24) Marigo, M.; Fielenbach, D.; Braunton, A.; Kjærsgaard, A.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2005**, *44*, 3703–3706.
- (25) Hull, K. L.; Anani, W. Q.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 7134–7135.
- (26) Wang, X.; Mei, T.-S.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 7520–7521.
- (27) Teare, H.; Robins, E. G.; Arstad, E.; Luthra, S. K.; Gouverneur, V. *Chem. Commun.* **2007**, 2330–2332.
- (28) Teare, H.; Robins, E. G.; Kirjavainen, A.; Forsback, S.; Sandford, G.; Solin, O.; Luthra, S. K.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2010**, *49*, 6821–6824.
- (29) Bergman, J.; Solin, O. *Nucl. Med. Biol.* **1997**, *24*, 677–683.
- (30) Lee, E.; Kamlet, A. S.; Powers, D. C.; Neumann, C. N.; Boursalian, G. B.; Furuya, T.; Choi, D. C.; Hooker, J. M.; Ritter, T. *Science* **2011**, *334*, 639–642.
- (31) Kamlet, A. S.; Neumann, C. N.; Lee, E.; Carlin, S. M.; Moseley, C. K.; Stephenson, N.; Hooker, J. M.; Ritter, T. *PLoS ONE* **2013**, *8*, e59187.
- (32) Dolbier, W. R., Jr. *J. Fluorine Chem.* **2005**, *126*, 157–163.
- (33) Chan, K. K. J.; O'Hagan, D. In *Methods in Enzymology*; Hopwood, D. A., Ed.; Academic Press: London, 2012; Vol. 516, p 219–235.
- (34) DePuy, C. H.; Gronert, S.; Mullin, A.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 8650–8655.
- (35) Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 574–578.
- (36) S. Lal, G.; P. Pez, G.; J. Pesaresi, R.; M. Prozonic, F. *Chem. Commun.* **1999**, 215–216.
- (37) Hayashi, H.; Sonoda, H.; Fukumura, K.; Nagata, T. *Chem. Commun.* **2002**, 1618–1619.
- (38) Beaulieu, F.; Beauregard, L.-P.; Courchesne, G.; Couturier, M.; LaFlamme, F. o.; L'Heureux, A. *Org. Lett.* **2009**, *11*, 5050–5053.
- (39) Tang, P.; Wang, W.; Ritter, T. *J. Am. Chem. Soc.* **2011**, *133*, 11482–11484.
- (40) Olah, G. A.; NojlMa, M.; Kerekes, I. *Synthesis* **1973**, 786–787.

- (41) Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872–3881.
- (42) Yoneda, N.; Abe, T.; Fukuhara, T.; Suzuki, A. *Chem. Lett.* **1983**, *12*, 1135–1136.
- (43) Yoneda, N.; Nagata, S.; Fukuhara, T.; Suzuki, A. *Chem. Lett.* **1984**, *13*, 1241–1242.
- (44) Yoneda, N. *Tetrahedron* **1991**, *47*, 5329–5365.
- (45) Pilcher, A. S.; Ammon, H. L.; DeShong, P. *J. Am. Chem. Soc.* **1995**, *117*, 5166–5167.
- (46) Leroy, J.; Hebert, E.; Wakselman, C. *J. Org. Chem.* **1979**, *44*, 3406–3408.
- (47) Bensoam, J.; Leroy, J.; Mathey, F.; Wakselman, C.; Ircha, C. *Tetrahedron Lett.* **1979**, *20*, 353–356.
- (48) Schmidbaur, H.; Mitschke, K.-H.; Buchner, W.; Stühler, H.; Weidlein, J. *Chem. Ber.* **1973**, *106*, 1226–1237.
- (49) Gasser, O.; Schmidbaur, H. *J. Am. Chem. Soc.* **1975**, *97*, 6281–6282.
- (50) Foster, A. B.; Hems, R.; Webber, J. M. *Carbohydr. Res.* **1967**, *5*, 292–301.
- (51) Rico, I.; Cantacuzene, D.; Wakselman, C. *Tetrahedron Lett.* **1981**, *22*, 3405–3408.
- (52) Tordeux, M.; Wakselman, C. *Synth. Commun.* **1982**, *12*, 513–520.
- (53) Grieco, P. A.; Williams, E.; Sugahara, T. *J. Org. Chem.* **1979**, *44*, 2194–2199.
- (54) Johnson, C. R.; Bis, K. G.; Cantillo, J. H.; Meanwell, N. A.; Reinhard, M. F. D.; Zeller, J. R.; Vonk, G. P. *J. Org. Chem.* **1983**, *48*, 1–3.
- (55) Henbest, H. B.; Jackson, W. R. *J. Chem. Soc.* **1962**, 954–959.
- (56) Cox, D. P.; Terpinski, J.; Lawrynowicz, W. *J. Org. Chem.* **1984**, *49*, 3216–3219.
- (57) Sun, H.; DiMagno, S. G. *J. Am. Chem. Soc.* **2005**, *127*, 2050–2051.
- (58) Sharma, R. K.; Fry, J. L. *J. Org. Chem.* **1983**, *48*, 2112–2114.
- (59) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250–2252.
- (60) Jadhav, V. H.; Jang, S. H.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H.; Chi, D. Y.; Kim, D. W. *Org. Lett.* **2010**, *12*, 3740–3743.

- (61) Landini, D.; Montanari, F.; Rolla, F. *Synthesis* **1974**, 428–430.
- (62) Landini, D.; Quici, S.; Rolla, F. *Synthesis* **1975**, 430–431.
- (63) Dermiek, S.; Sasson, Y. *J. Fluorine Chem.* **1983**, *22*, 431–437.
- (64) Aerts, J.; Voccia, S.; Lemaire, C.; Giacomelli, F.; Goblet, D.; Thonon, D.; Plenevaux, A.; Warnock, G.; Luxen, A. *Tetrahedron Lett.* **2010**, *51*, 64–66.
- (65) Colonna, S.; Re, A.; Gelbard, G.; Cesarotti, E. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2248–2252.
- (66) Cainelli, G.; Manescalchi, F.; Panunzio, M. *Synthesis* **1976**, 472–473.
- (67) Ishikawa, N.; Kitazume, T.; Yamazaki, T.; Mochida, Y.; Tatsuno, T. *Chem. Lett.* **1981**, *10*, 761–764.
- (68) Jadhav, V. H.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H.; Kim, D. W. *Org. Lett.* **2011**, *13*, 2502–2505.
- (69) Anzenbacher, P.; Try, A. C.; Miyaji, H.; Jursíková, K.; Lynch, V. M.; Marquez, M.; Sessler, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 10268–10272.
- (70) Mason, S.; Llinares, J. M.; Morton, M.; Clifford, T.; Bowman-James, K. *J. Am. Chem. Soc.* **2000**, *122*, 1814–1815.
- (71) Aguilar, J. A.; Clifford, T.; Danby, A.; Llinares, J. M.; Mason, S.; García-España, E.; Bowman-James, K. *Supramol. Chem.* **2001**, *13*, 405–417.
- (72) Coles, S. J.; Frey, J. G.; Gale, P. A.; Hursthouse, M. B.; Light, M. E.; Navakhun, K.; Thomas, G. L. *Chem. Commun.* **2003**, 568–569.
- (73) Cho, E. J.; Moon, J. W.; Ko, S. W.; Lee, J. Y.; Kim, S. K.; Yoon, J.; Nam, K. C. *J. Am. Chem. Soc.* **2003**, *125*, 12376–12377.
- (74) Boiocchi, M.; Del Boca, L.; Gómez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507–16514.
- (75) Esteban-Gómez, D.; Fabbrizzi, L.; Licchelli, M. *J. Org. Chem.* **2005**, *70*, 5717–5720.

- (76) Gomez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *Org. Biomol. Chem.* **2005**, *3*, 1495–1500.
- (77) Pramanik, A.; Powell, D. R.; Wong, B. M.; Hossain, M. A. *Inorg. Chem.* **2012**, *51*, 4274–4284.
- (78) Kim, S. K.; Lynch, V. M.; Young, N. J.; Hay, B. P.; Lee, C.-H.; Kim, J. S.; Moyer, B. A.; Sessler, J. L. *J. Am. Chem. Soc.* **2012**, *134*, 20837–20843.
- (79) Cametti, M.; Rissanen, K. *Chem. Soc. Rev.* **2013**, *42*, 2016–2038.
- (80) O'Hagan, D.; Schaffrath, C.; Cobb, S. L.; Hamilton, J. T. G.; Murphy, C. D. *Nature* **2002**, *416*, 279.
- (81) O'Hagan, D. *J. Fluorine Chem.* **2006**, *127*, 1479–1483.
- (82) Deng, H.; O'Hagan, D. *Curr. Opin. Chem. Biol.* **2008**, *12*, 582–592.
- (83) Deng, H.; Cobb, S. L.; Gee, A. D.; Lockhart, A.; Martarello, L.; McGlinchey, R. P.; O'Hagan, D.; Onega, M. *Chem. Commun.* **2006**, 652–654.
- (84) Onega, M.; Domarkas, J.; Deng, H.; Schweiger, L. F.; Smith, T. A. D.; Welch, A. E.; Plisson, C.; Gee, A. D.; O'Hagan, D. *Chem. Commun.* **2010**, *46*, 139–141.
- (85) Yonezawa, T.; Sakamoto, Y.; Nogawa, K. Preparation of Tetrabutylammonium Fluoride-Alcohol Adducts as Fluorination Agents. Jpn. Kokai Tokkyo Koho JP 06316551 A, Nov 15 1994.
- (86) Kim, D. W.; Jeong, Lim, S. T.; Sohn, M.-H.; Katzenellenbogen, J. A.; Chi, D. Y. *J. Org. Chem.* **2008**, *73*, 957–962.
- (87) Kim, D. W.; Ahn, D.-S.; Oh, Y.-H.; Lee, S.; Kil, H. S.; Oh, S. J.; Lee, S. J.; Kim, J. S.; Ryu, J. S.; Moon, D. H.; Chi, D. Y. *J. Am. Chem. Soc.* **2006**, *128*, 16394–16397.
- (88) Kim, D. W.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H. *Angew. Chem. Int. Ed.* **2008**, *47*, 8404–8406.

- (89) Hollingworth, C.; Hazari, A.; Hopkinson, M. N.; Tredwell, M.; Benedetto, E.; Huiban, M.; Gee, A. D.; Brown, J. M.; Gouverneur, V. *Angew. Chem. Int. Ed.* **2011**, *50*, 2613–2617.
- (90) Benedetto, E.; Tredwell, M.; Hollingworth, C.; Khotavivattana, T.; Brown, J. M.; Gouverneur, V. *Chem. Sci.* **2013**, *4*, 89–96.
- (91) Li, B.-J.; Jiang, L.; Liu, M.; Chen, Y.-C.; Ding, L.-S.; Wu, Y. *Synlett* **2005**, 603–606.
- (92) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967–1969.
- (93) Ye, J.; Dixon, D. J.; Hynes, P. S. *Chem. Commun.* **2005**, 4481–4483.
- (94) McCooey, S. H.; Connon, S. J. *Angew. Chem. Int. Ed.* **2005**, *44*, 6367–6370.
- (95) Mattson, A. E.; Zuhl, A. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 4932–4933.
- (96) Yan, H.; Jang, H. B.; Lee, J.-W.; Kim, H. K.; Lee, S. W.; Yang, J. W.; Song, C. E. *Angew. Chem. Int. Ed.* **2010**, *49*, 8915–8917.
- (97) Birrell, J. A.; Desrosiers, J.-N.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 13872–13875.

## **CHAPTER 7**

### **THE EFFECT OF ALCOHOL HYDROGEN-BOND DONORS ON THE REACTIVITY PROFILE OF FLUORIDE ANION**

## 7.1. INTRODUCTION

With the proliferation of applications for organofluorine compounds in the last half-century, efficient preparative methods have become increasingly in demand. Two complementary reactivity paradigms are used for C–F bond formation, electrophilic and nucleophilic fluorination. While both have proven synthetically valuable, nucleophilic fluorination is advantageous with respect to the widespread availability and low cost of  $F^-$  reagents compared to their  $F^+$  counterparts. Nevertheless, several challenges have persisted in applications of fluoride in organic transformations due to its high electronegativity, small size, low polarisability, and high charge density. As a consequence of these intrinsic properties, fluoride is a strong Brønsted and Lewis base. It pairs tightly with countercations and with hard electrophiles, which can restrict solubility in non-polar solvents. Furthermore, fluoride is a strong hydrogen-bond acceptor and as such tends to be highly solvated with polar protic solvents, especially water.

Organic chemists have addressed these challenges by developing a portfolio of different  $F^-$  reagents with different reactivity profiles, along with an assortment of  $F^-$  activation strategies. One appealing, if underdeveloped, approach is the use of small-molecule hydrogen-bond donors to tune the reactivity of fluoride along the reaction coordinate. In principle, this approach would allow one to use simple fluoride salts to access a broad range of different reactivity profiles, all programmed through judicious selection of the hydrogen-bond donor system. The realisation of this concept requires a detailed knowledge of hydrogen bonding interactions to fluoride and their effects on reactivity.

In this chapter, we present the results from our first inquiry into this topic. We have prepared a series of tetraalkylammonium fluoride–alcohol complexes, and studied them using single-crystal X-ray, reaction kinetics, and DFT calculations. In light of these



findings, we have proposed a mechanistic model, which provides a conceptual framework for further development of small molecule hydrogen-bond donors for fluoride activation.

## 7.2. RESULTS AND DISCUSSION

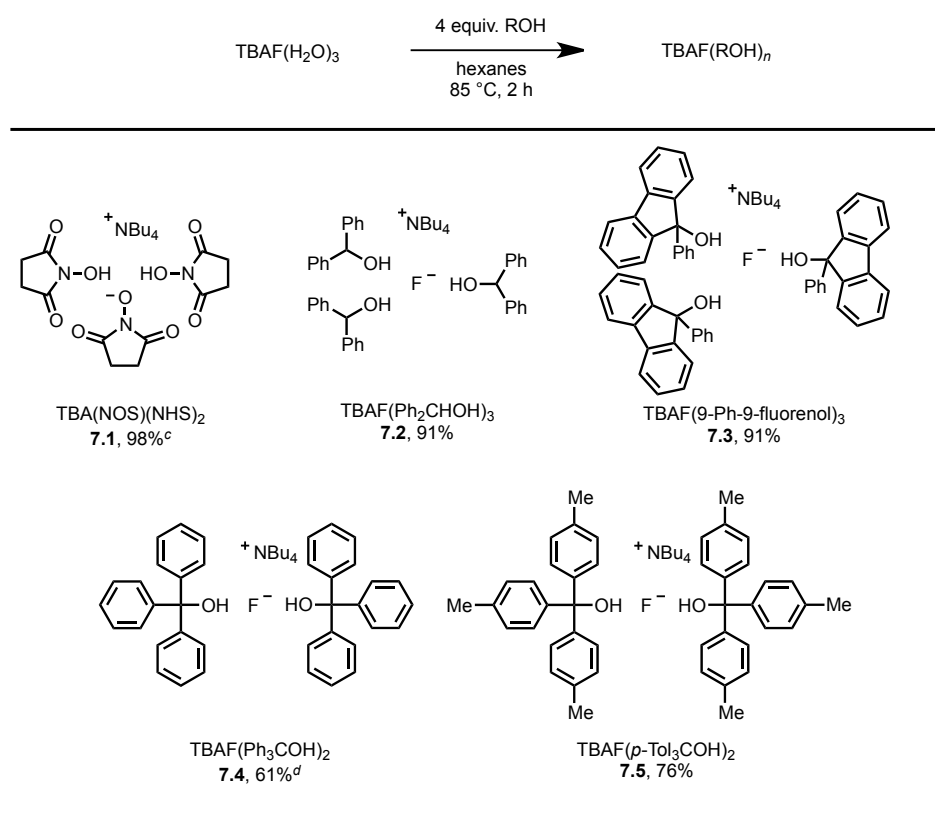
Based on the important precedents established by Yonezawa<sup>1</sup> and Kim<sup>2-4</sup> using alcohol solvents for controlling fluoride reactivity, we opted to focus this initial investigation on alcohols and related hydrogen-bond donors. This choice was also inspired by observation that two of the key hydrogen bonding interactions in the fluorinase enzyme system are with alcohol-containing amino acid side chains.<sup>5</sup> In the long term, we envision extending this research programme to other commonly encountered hydrogen-bond donors, including thiols, amines, amides, and ureas.

### 7.2.1. Fluoride complex synthesis

Our first goal was to prepare a collection of fluoride complexes with a structurally diverse collection of alcohols and polyol hydrogen-bond donors. We elected to focus on complexes with tetraalkylammonium counterions due to their comparatively high solubility in organic solvents, which we hypothesised would facilitate synthesis and characterisation. To access the target complexes, we adapted an established synthetic protocol.<sup>1,4</sup> TBAF(H<sub>2</sub>O)<sub>3</sub> was combined with the alcohol (4 equiv.) in vigorously refluxing hexanes for 2 h, which served to remove residual water from the reaction medium. The mixture was then cooled to room temperature, at which point a precipitate was observed. The precipitate was filtered, washed with excess hexanes, and then dried under high vacuum. In cases where precipitation was not observed after 12 h, the solvent was removed *in vacuo*, and the resulting residue was dried under high vacuum and then, if needed, cooled to -20 °C; in these cases, after solidification was induced, the resulting solids were similarly washed with

hexanes on a Hirsch filter and dried under high vacuum. A broad range of alcohols with different  $pK_a$  values and varying steric environments were surveyed, and those that yielded tractable solids are shown in Table 7.1. (The vast majority of the alcohols that were tested gave oils—even at  $-20\text{ }^{\circ}\text{C}$ —which were not further examined for this study). The resulting complexes were characterised by  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{19}\text{F}$  NMR spectroscopy, and a small sample of the material from each was recrystallised from EtOAc, THF, DCM, or Et<sub>2</sub>O to obtain single crystals suitable for X-ray diffraction (see Section 7.2.2). For the complexes listed in Table 7.1, samples of the bulk material had clearly defined coordination stoichiometry (based on  $^1\text{H}$  NMR), which was in good agreement with that observed in the single-crystal samples (*vide infra*).

**Table 7.1.** Preparation of TBAF(ROH)<sub>n</sub> complexes.<sup>a,b</sup>



<sup>a</sup> Isolated yields are shown. <sup>b</sup> See the Experimental section for a detailed description of the procedure in each case. <sup>c</sup> 3 equiv. of NHS. <sup>d</sup> 2 equiv. of Ph<sub>3</sub>COH.

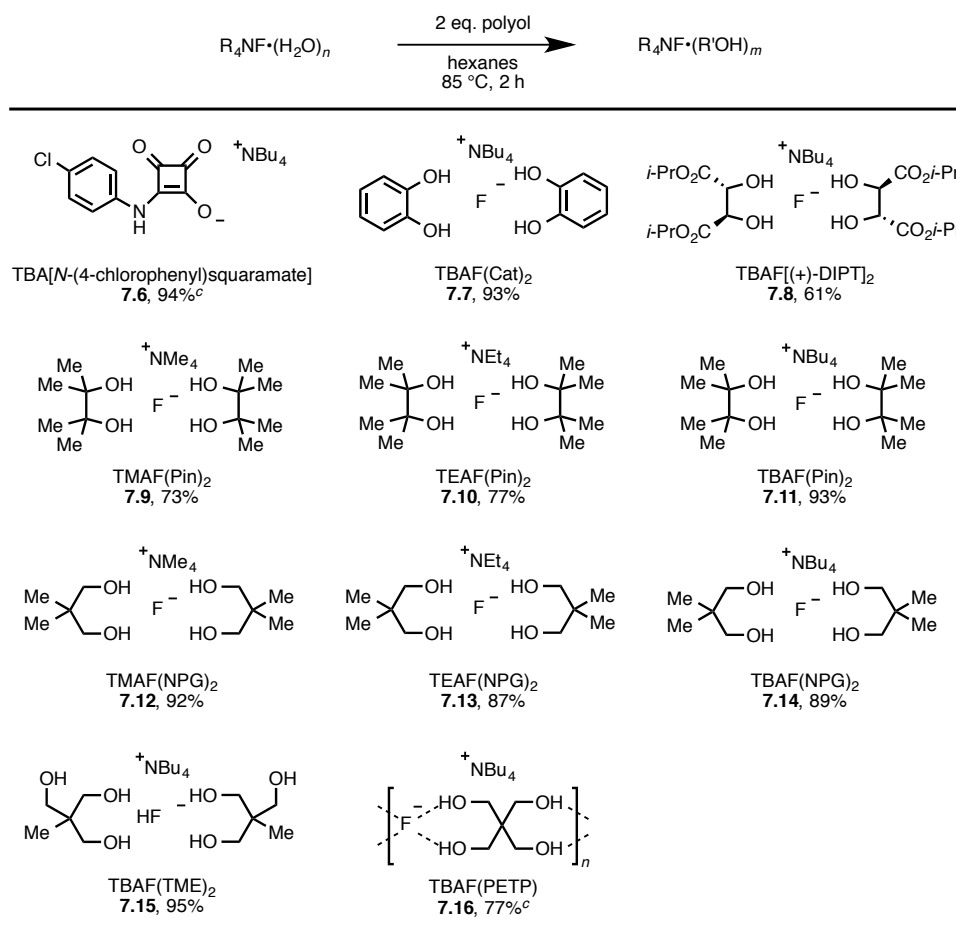
Within this series, the first obvious observation is that *N*-hydroxy succinimide (NHS), which contains an acidic O–H bond was deprotonated under the complexation conditions to give TBA(NOS)(NHS)<sub>2</sub> (**7.1**). Analysis of the <sup>19</sup>F NMR spectra of the crude material prior to recrystallisation revealed that no fluorine atoms were present in the newly synthesised complex. Single-crystal X-ray diffraction data (*vide infra*) revealed the product to be the hydrogen bond–stabilised tetrabutylammonium *N*-oxide. The p*K*<sub>a</sub> of NHS has been measured in the 5.9–6.0 range.<sup>6–8</sup> This result, in conjunction with similar findings with squaramic acid (**7.6**, Table 7.2), established that HBDs with acidic O–H bonds (p*K*<sub>a</sub> ≤ 6) are unsuitable for tuning the reactivity of fluoride because of their proclivity for participating in Brønsted acid/base chemistry. Indeed, when a 4:1 mixture of NHS and TBAF(H<sub>2</sub>O)<sub>3</sub> was combined with a primary alkyl bromide in MeCN, predominant *O*-alkylation was observed (see the Experimental section).

For the remaining alcohols, the resulting fluoride–alcohol complexes were either di- or tricoordinate. The previously published complex, TBAF(*t*-BuOH)<sub>4</sub>, is an example of a tetracoordinate complex. Notably, the variability in coordination stoichiometry in this series has not been observed previously. As a general trend, as steric bulk around the hydroxyl group increased, the coordination number was found to decrease (*e.g.*, comparing Ph<sub>2</sub>CHOH and Ph<sub>3</sub>COH, which have coordination numbers of *n* = 3 and *n* = 2, respectively).

We next hypothesised that the stability of these reagents in solution and in the solid state could be improved by having multiple hydrogen-bond donors tethered together intramolecularly. Additionally, we speculated that multiple hydrogen bonding contacts, as seen in the fluorinase enzyme, could be important for influencing the relative energies of S<sub>N</sub>2 and E2 transition states. We thus explored the possibility of preparing TBAF complexes using a variety of common diols, triols, and tetraols, as well as one *N*-aryl squaramic acid (Table 7.2). To do this, the aforementioned procedure was employed with the polyol (2

equiv.) in place of the alcohol. The results are shown in Table 7.2. Again, in these cases, the stoichiometry of the bulk material was clearly defined in the  $^1\text{H}$  NMR spectra, and the results were in good agreement with data from single-crystal samples of the same material (*vide infra*). With TMAF(Pin) $_2$  (**7.9**), TEAF(Pin) $_2$  (**7.10**), TMAF(NPG) $_2$  (**7.12**), and TEAF(NPG) $_2$  (**7.13**), single-crystals suitable for X-ray diffraction could not be obtained, despite repeated attempts. All other complexes in Table 7.2 were further characterised by single-crystal X-ray diffraction.

**Table 7.2.** Preparation of tetraalkylammonium fluoride–polyol complexes.<sup>a,b</sup>



<sup>a</sup> Isolated yields are shown. <sup>b</sup> See the Experimental section for a detailed description of the procedure in each case. <sup>c</sup> 1 equiv. of the hydrogen-bond donor.

Similar to the case with NHS, *N*-(4-chlorophenyl)squaramic acid, which bears an acidic O–H bond ( $\text{p}K_a \approx 0.8$ , based on ACD labs prediction), was deprotonated with

irreversible loss of HF during the complexation reaction to give tetrabutylammonium squaramate (**7.6**) as a dark yellow solid.

With the polyols, the coordination number was 2:1 in all cases except with pentaerythritol (PETP), which gave a 1:1 complex, TBAF(PETP) (**7.16**). With catechol (Cat), which has an intermediate  $pK_a$  between the acidic hydrogen-bond donors, NHS and *N*-(4-chlorophenyl)squaramic acid, and an aliphatic alcohol, deprotonation was not observed under the complexation conditions, and the 2:1 complex TBAF(Cat)<sub>2</sub> (**7.7**) was obtained as a pink solid in good yield.

### 7.2.2. Solid-state studies

Previous examples of crystal structures of fluoride–alcohol species are rare in the literature,<sup>4,9-11</sup> with most examples consisting of strong, phenol-type hydrogen-bond donors. Thus, relatively little is known regarding the coordination chemistry of aliphatic alcohols and polyols with fluoride. To bridge this gap, we performed an extensive series of single-crystal X-ray diffraction experiments with the complexes in Tables 7.1 and 7.2 in order to determine their solid-state coordination stoichiometry and molecular geometry.

It is important to clarify at the outset that insights gleaned from solid-state characterisation methods should be interpreted in the appropriate context, especially given the weak nature of the interactions at play in these particular complexes. Crystal structures offer a static glimpse of one local thermodynamic minimum, while solution-state behaviour, which is more relevant to chemical reactivity, is inherently dynamic. Care must thus be taken in making generalisations about these complexes solely on the basis of solid-state characterisation data. Furthermore, it should also be noted that throughout this Thesis the distances for all hydrogen bonding interactions, X–H---F (where X = C, N, or O) are quoted as the corresponding X---F distance. This is due to the inherent ambiguity concerning

hydrogen atom positions in X-ray crystal structures, a challenge that is discussed in more depth in Chapter 8.

As stated above, during the preparation of complex **7.1**, deprotonation of one of the O–H bonds took place, liberating an equivalent of HF or bifluoride,  $\text{HF}_2^-$ . In the crystal structure of **7.1**, which was previously unknown, the resulting *N*-oxide is stabilised by two intermolecular hydrogen bonds (Figure 7.1). This arrangement was preferentially observed in the solid state, even in crystal grown from samples in which 4 equiv. NHS were used in the preparation of the complex.

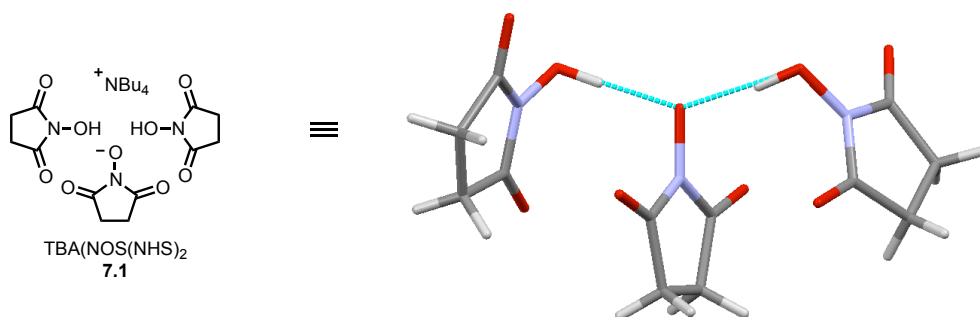


**Figure 7.1.** X-ray crystal structure of  $\text{TBA}(\text{NOS})(\text{NHS})_2$  (**7.1**). Tetrabutylammonium counteranion omitted for clarity.

For the remaining fluoride–alcohol complexes shown in Table 7.1, the resulting X-ray crystal structures revealed variability in the coordination number, which was largely independent of the number of equivalents of the alcohol used in synthesis. For example, with *p*-Tol<sub>3</sub>COH and Ph<sub>3</sub>COH, single crystals of the 2:1 alcohol:fluoride complexes grew even when 3 or 4 equiv. of the alcohol was used during complexation. The discovery that di-, tri-, and tetracoordinate fluoride can all stably exist in the solid state is important to the fundamental understanding of hydrogen bond association/dissociation to fluoride, the relative stability of different potentially equilibrating hydrogen bonding modes in solution, and ultimately to fluoride’s reactivity in different hydrogen bonding environments.

Lower coordination numbers were observed for more sterically hindered alcohols, and in the case of triarylmethanols, this low coordination stoichiometry seems to be partially explained by stabilising interactions offered by *ortho*-C–H...F interactions.

In the crystal structure of TBAF(Ph<sub>2</sub>CHOH)<sub>3</sub> (**7.2**) (Figure 7.2), fluoride is tricoordinate, and the O...F bond distances are 2.552 Å, 2.562 Å, and 2.562 Å. An  $\alpha$ -C–H...F interaction is also present between fluoride and the tetrabutylammonium counterion, with a C...F bond distance of 3.336 Å. The complex is approximately T-shaped, which allows for minimisation of the distance between fluoride and the partially positively charged  $\alpha$ -carbon atom and acidic  $\alpha$ -C–H bonds of the tetrabutylammonium counterion (not shown).

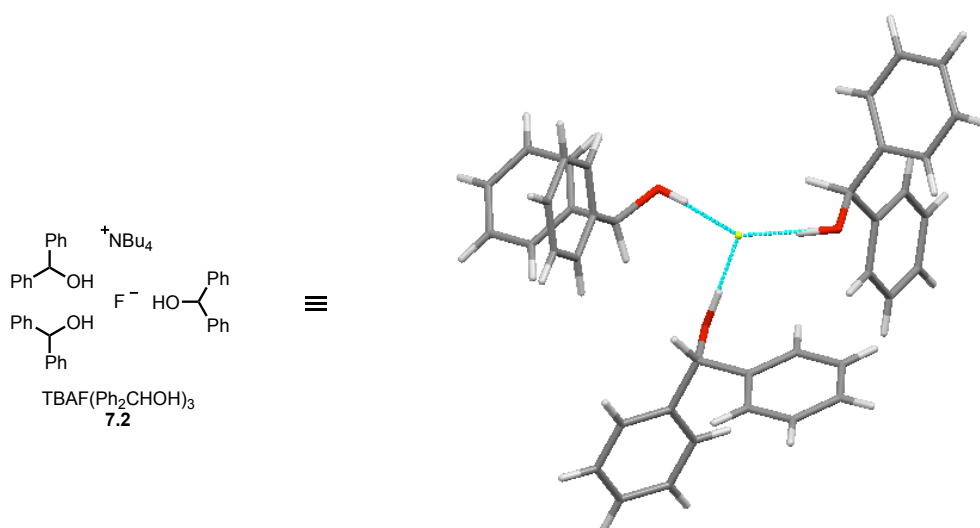


**Figure 7.2.** X-ray crystal structure of TBAF(Ph<sub>2</sub>CHOH)<sub>3</sub> (**7.2**). Tetrabutylammonium counteranion omitted for clarity.

The crystal structure of TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**7.3**) is highly unusual because the unit cell possesses two inequivalent fluoride species, one that is formally dicoordinate and one that is tricoordinate (Figure 7.3). In the dicoordinate fluoride, the third unbound 9-Ph-9-fluorenol molecule is offset, forming a hydrogen bond not with fluoride, but with an oxygen atom of one of the other 9-Ph-9-fluorenol molecules that is bound to fluoride (O...F distance = 2.433 Å). The remaining 9-Ph-9-fluorenol molecule forms a weaker hydrogen

bond to fluoride, with an O---F distance of 2.499 Å. Thus, though the alcohol:fluoride coordination stoichiometry remains 3:1, this fluoride species is actually dicoordinate. Also, in the case of the dicoordinate fluoride in this structure, one *ortho*-C–H bond appears to provide stabilisation through a C–H---F interaction (C---F bond distance = 3.175 Å). The tricoordinate fluoride, on the other hand, has longer O---F hydrogen-bond distances of 2.542 Å, 2.553 Å, and 2.639 Å. The tricoordinate fluoride has a coordination geometry that is between trigonal planar and T-shaped, while the dicoordinate fluoride is slightly bent with an O---F---O bond angle of 151.98°.

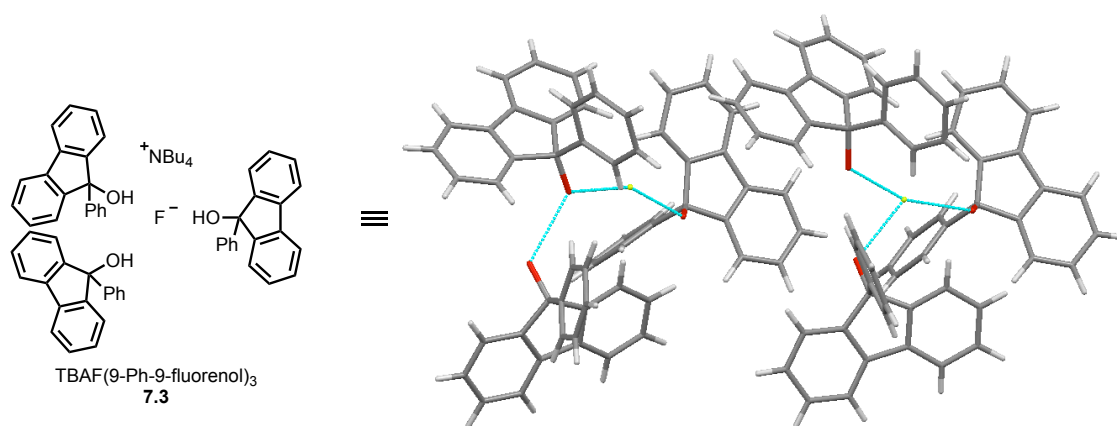


**Figure 7.3.** X-ray crystal structure of TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**7.3**), showing dicoordinate fluoride (left) and tricoordinate fluoride (right). Tetrabutylammonium counteranions omitted for clarity.

The observation of both coordination motifs within a single crystal suggests that these two coordination modes have similar energies, which lends insights into the solution-state dissociation pathway for polycordinate fluoride species and highlights the fact that multiple coordination structures can stably exist in both solution and in the solid state.

The structure of TBAF(Ph<sub>3</sub>COH)<sub>2</sub> (**7.4**) was solved as a hexane solvate, and in it, fluoride is formally dicoordinate, with O---F bond distances of 2.502 Å and 2.558 Å (Figure 7.4). Two of the *ortho*-C–H bonds from the phenyl rings also form short contacts with fluoride, with C---F distances of 3.246 Å and 3.29 Å. As mentioned above, these



interactions presumably provide stabilisation to compensate for the otherwise low coordination stoichiometry. The coordination geometry is bent with an O---F---O bond angle of 101.04.

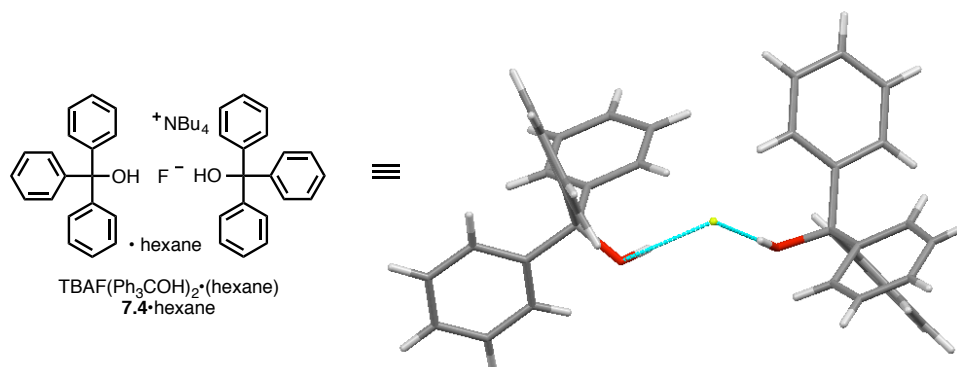


**Figure 7.4.** X-ray crystal structure of TBAF(Ph<sub>3</sub>COH)<sub>2</sub>·(hexane) (**7.4**·hexane). Tetrabutylammonium counteranion and hexane solvent omitted for clarity. Disorder was observed and modelled in four of the Ph rings and in three of the alkyl chains; the disorder is not shown here for clarity.

We were also able to solve the crystal structure of the closely related triarylmethanol complex, TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**7.5**). In the structure, there are two inequivalent, albeit highly similar, fluoride species. Both are dicoordinate, with O---F bond distances of 2.499 Å and 2.554 Å for the first, and of 2.508 Å and 2.554 Å for the second. Surrounding both fluorides, there are also two observable short contacts between the *ortho*-C–H bonds from two of the *p*-Tol groups, with C---F bond distances of 3.298 Å and 3.323 Å for the first and 3.306 Å and 3.360 Å for the second. Additionally, in each tetrabutylammonium–fluoride pair, there are observable  $\alpha$ -C–H---F and  $\beta$ -C–H---F interactions. In the structure, each of the two hydroxyl group pairs is nearly orthogonal, giving O---F---O bond angles of 85.19° and 87.64°. The compressed bond angles relative to TBAF(Ph<sub>3</sub>COH)<sub>2</sub> (**7.4**) may be a result of the added steric hindrance of the *p*-Me substituents.

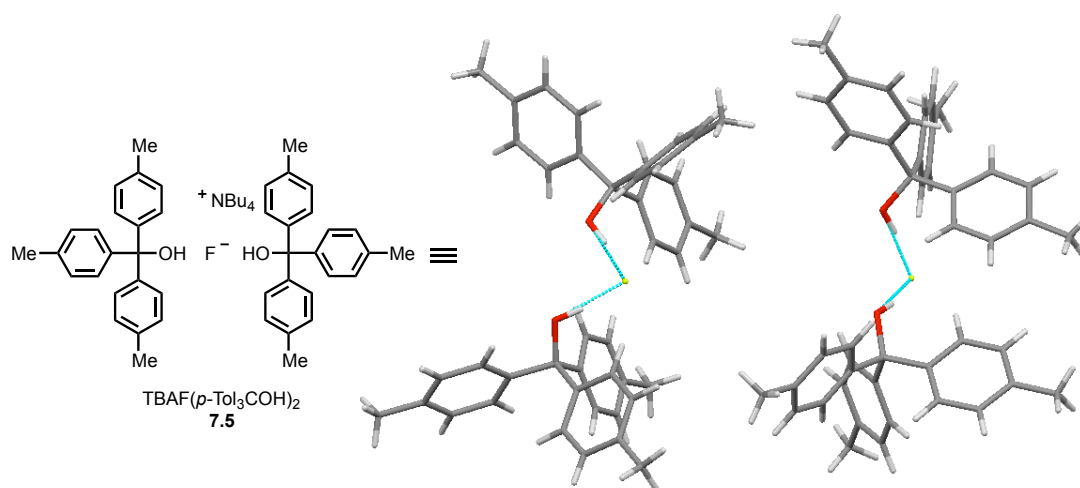


**Figure 7.5.** X-ray crystal structure of TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**7.5**). Tetrabutylammonium counteranions omitted for clarity.

We next moved on to solid-state characterisation of the complexes shown in Table 7.2. The X-ray crystal structure of TBA[*N*-(4-chlorophenyl)squaramate] (**7.6**) provided conclusive evidence that the O–H bond was deprotonated during the attempted complexation reaction (Figure 7.6). In the structure, the squaramate units are arranged as head-to-tail dimers, linked together through a 10-membered hydrogen-bonding network. To the best of our knowledge, this constitutes the first example of an X-ray crystal structure of a squaramate anion and elucidation of its solid-state packing tendencies.

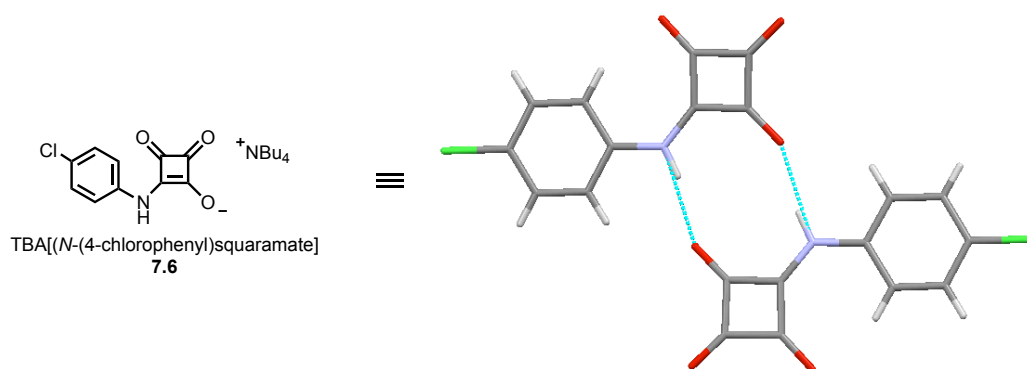


**Figure 7.6.** X-ray crystal structure of TBA[*N*-(4-chlorophenyl)squaramate] (**7.6**). Tetrabutylammonium counteranions omitted for clarity. Two unit cells are shown to illustrate the dimeric pairing that exists in the solid state.

X-ray crystal structures were obtained of TBAF bound to three 1,2-diols: catechol (Cat), (+)-diisopropyl L-tartrate ((+)-DIPT), and pinacol (Pin). Collectively, the structures of these three complexes confirm the viability of two simultaneous intramolecular hydrogen bonds to fluoride through a seven-membered cyclic hydrogen bonding network.

Two polymorphs of TBAF(Cat)<sub>2</sub> (**7.7**) were discovered (Figures 7.7.a and 7.7.b). The first, which is shown in Figure 7.7.a, was obtained from slow vapour diffusion of hexanes into a saturated solution of TBAF(Cat)<sub>2</sub> (**7.7**) in EtOAc. In the structure, there are four inequivalent fluoride species, two that are tricoordinate and two that are tetracoordinate. The average O---F bond distances of the two tricoordinate fluorides are 2.508 Å and 2.492 Å, and the average O---F bond distances of the two tetracoordinate fluorides are 2.553 Å and 2.580 Å. Overall, the average O---F distance across all four species is 2.531 Å. The two tetracoordinate fluorides have measurably longer average O---F bond distances than the tricoordinate species and have irregular coordination geometries about fluoride. The irregular coordination geometry is presumable due to strain associated with the spirocyclic hydrogen bonding system around fluoride, in which both rings contain a catechol molecule with four co-planar atoms. In each of the tricoordinate fluoride species, the remaining “unbound” hydroxyl group pairs with another tricoordinate unit, such the two catechols are linked in a head-to-head fashion through an eight-membered cyclic hydrogen bonding network.

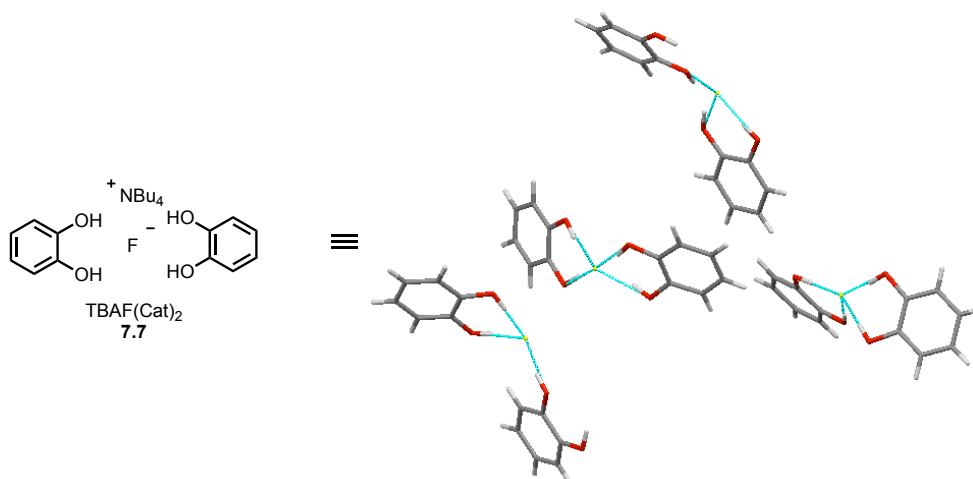


**Figure 7.7.a.** X-ray crystal structure of the first polymorph of TBAF(Cat)<sub>2</sub> (7.7). Tetrabutylammonium counteranions omitted for clarity. Disorder was observed and modeled in two of the catechol molecules and one of the fluoride ions. The disorder is not shown here for clarity.

The second polymorph, shown in Figure 7.7.b, contains two inequivalent fluoride species, one that is tricoordinate and one that is tetracoordinate. The three-coordinate fluoride species is bound to two molecules of catechol, with the *ortho*-C–H bond from one molecule of catechol occupying the “fourth” hydrogen-bonding site, similar to the tricoordinate fluoride species in the first polymorph of TBAF(Cat)<sub>2</sub> (7.7). The O---F distances are as follows: 2.495 Å, 2.495 Å, and 2.501 Å. The C---F bond distance is 3.255 Å. The tetracoordinate fluoride lies on a special position and has a highly disordered coordination environment. Due to the disorder in the tetracoordinate fluoride, its bond distances and angles are not discussed here. The overall crystal packing arrangement in the second polymorph has alternating layers of ordered and disordered fluoride–catechol hydrogen bonding networks sandwiched between layers of tetraalkylammonium cations.

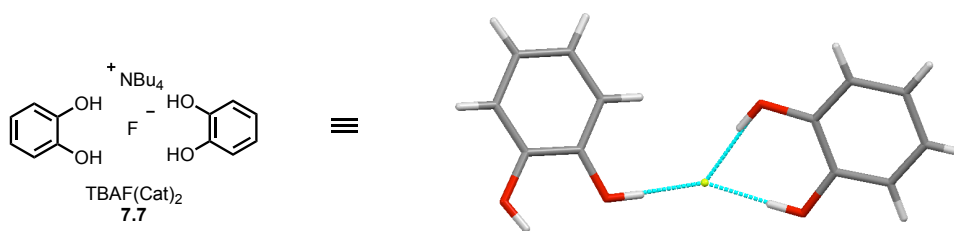


**Figure 7.7.b.** X-ray crystal structure of the second polymorph of TBAF(Cat)<sub>2</sub> (**7.7**). Tetrabutylammonium counteranion omitted for clarity. Only one of the two inequivalent fluoride ions is shown for simplicity. The coordination environment around the second fluoride has four OH donors; it is highly disordered and thus difficult to visualise.

As was mentioned earlier, previous fluoride–alcohol complexes have also employed phenol-type hydrogen-bond donors. Collectively, catechol and these previous phenol-type hydrogen bond donors have approximate  $pK_a$  values in the 9–10 range, and maintain intact O–H...F hydrogen bonds. In conjunction with the observations using NHS and *N*-(4-chlorophenyl)squaramic acid, this suggests that hydrogen-bond donors with  $pK_a$  values in the 6–9 range are the lowest that could be applied for tuning fluoride reactivity.

To demonstrate the viability of obtaining solid-state data on fluoride complexes with chiral, optically pure hydrogen-bond donors, we prepared and crystallised TBAF[(+)-DIPT]<sub>2</sub> (**7.8**) as a hexane solvate (Figure 7.8). In the structure, the four inequivalent O...F bond distances are 2.565 Å, 2.592 Å, 2.599 Å, and 2.622 Å, and the complex is roughly C<sub>2</sub>-symmetric as a consequence of the symmetry of (+)-DIPT. The coordination geometry is that of a flattened tetrahedron with O...F...O angles of 72.03°, 109.60°, 71.22°, and 129.00°.

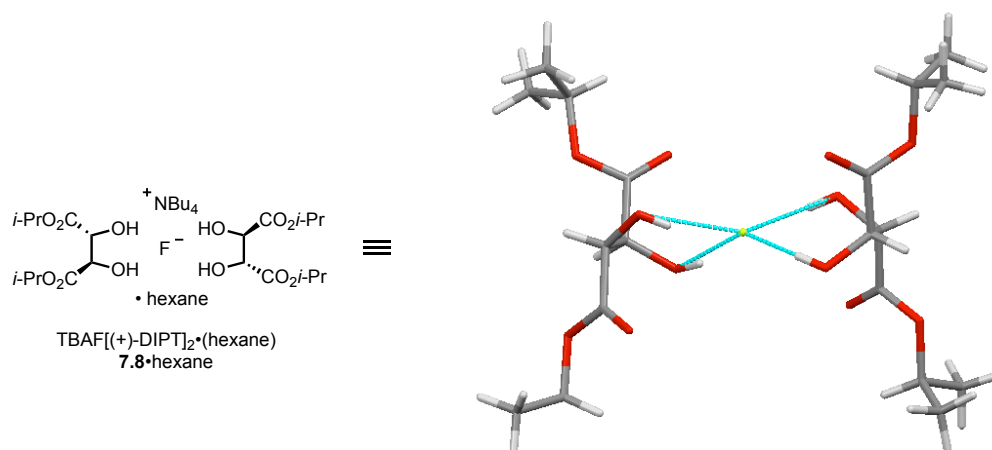


**Figure 7.8:** X-ray crystal structure of TBAF[(+)-DIPT]<sub>2</sub>·(hexane) (7.8·hexane). Tetrabutylammonium counteranion and hexane solvent omitted for clarity. Disorder was observed and modeled in one *i*-Pr group; the disorder is not shown here for clarity.

The final example of 1,2-diol complexes is TBAF(Pin)<sub>2</sub> (7.9) (Figure 7.9). In its crystal structure, the O---F bond distances are 2.614 Å, 2.614 Å, 2.623 Å, and 2.640 Å, and interestingly, all four hydrogen bonds are situated on one hemisphere of the fluoride atom. The longer bond distances in this complex compared with what is seen in TBAF[(+)-DIPT]<sub>2</sub>·(hexanes) (7.8) and the two polymorphs of TBAF(Cat)<sub>2</sub> (7.7) serve as evidence of the comparatively weak hydrogen-bond donor strength of pinacol due to steric encumbrance. Though TEAF(Pin)<sub>2</sub> and TMAF(Pin)<sub>2</sub> were also synthesised, crystals suitable for X-ray diffraction could not be grown of these complexes.

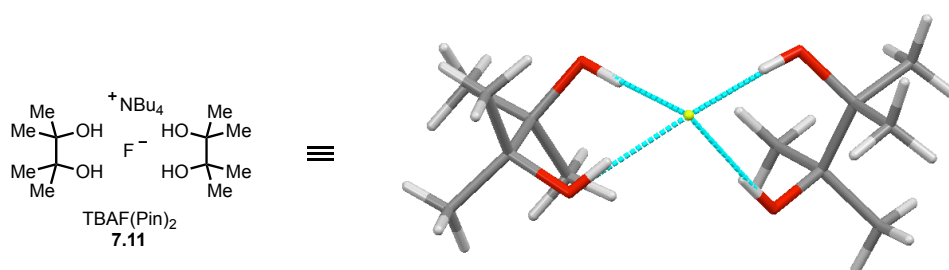


**Figure 7.9:** X-ray crystal structure of TBAF(Pin)<sub>2</sub> (7.11). Tetrabutylammonium counteranion omitted for clarity.

Several 1,3-diols and related compounds were also examined, and of them, three gave suitable crystals for X-ray diffraction, establishing that eight-membered cyclic

hydrogen bonding networks can be stably accommodated in the solid state. The first example, TBAF(NPG)<sub>2</sub> (**7.14**) is nearly square planar, possessing O---F---O angles of 78.63°, 103.43°, 79.11°, 100.83° and O---F bond distances of 2.584 Å, 2.640 Å, 2.638 Å, and 2.607 Å. TEAF(NPG)<sub>2</sub> and TMAF(NPG)<sub>2</sub>, which were also synthesised, could not be recrystallised despite repeated attempts.

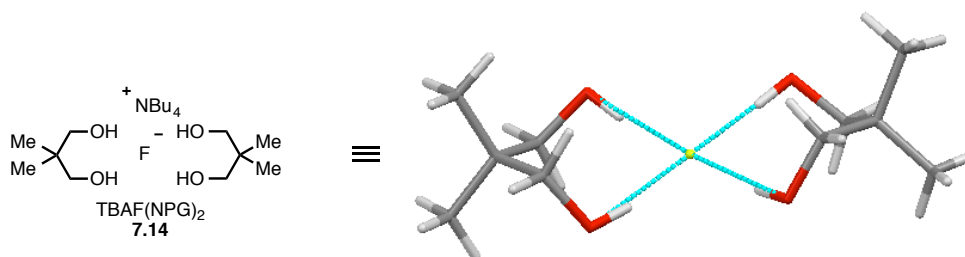


**Figure 7.10:** X-ray crystal structure of TBAF(NPG)<sub>2</sub> (**7.14**). Tetrabutylammonium counteranion omitted for clarity.

At the outset, we had speculated that trimethylolethane (TME) and pentaerythritol (PETP) would preferentially form more than two hydrogen bond contacts per molecule. In the case of TBAF(TME)<sub>2</sub> (**7.15**), however, only two hydrogen bonds to fluoride per TME molecule were observed, even in crystals grown of complexes synthesised with 1:1 alcohol:fluoride stoichiometry. Instead of binding fluoride, the third hydroxyl group forms a hydrogen bond to an adjacent oxygen atom, effectively activating one of the O-H---F bonds. In the structure, fluoride lies on a special position as an inversion center. The O---F bond distances are  $2 \times 2.612$  Å and  $2 \times 2.632$  Å, with the short bonds corresponding to those intermolecularly activated by a neighbouring TME molecule. Flattened tetrahedral coordination geometry is seen (O---F---O angles =  $2 \times 79.75^\circ$  and  $2 \times 116.07^\circ$ ).

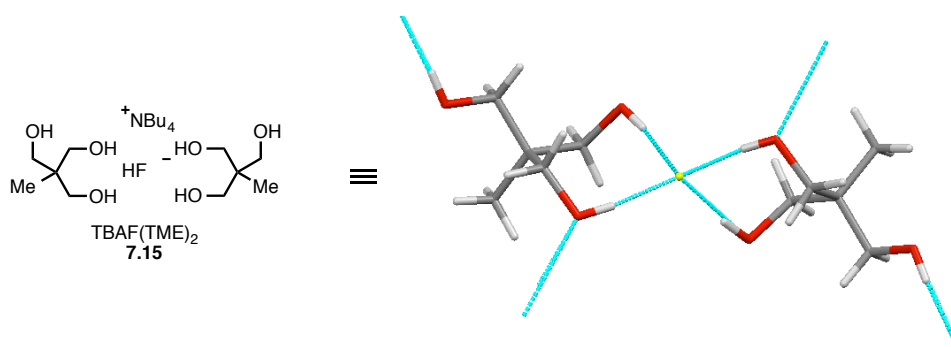


**Figure 7.11:** X-ray crystal structure of TBAF(TME)<sub>2</sub> (**7.15**). Tetrabutylammonium counteranion omitted for clarity.

Similarly, PETP was found to bind fluoride with two hydrogen bonds per PETP molecule per fluoride. Only in this case, due to the two-directional nature of the resulting arrangement, TBAF(PETP) is capable of forming an extended one-dimensional hydrogen bonding network. TBAF(PETP) (**7.16**) crystallised as its DCM solvate (Figure 7.12), revealing itself to be a one-dimensional linear hydrogen-bonding coordination polymer, with O---F bond distances of 2.587 Å, 2.656 Å, 2.668 Å, and 2.705 Å and O---F---O angles of 75.88°, 113.88°, 76.81°, and 110.24°.

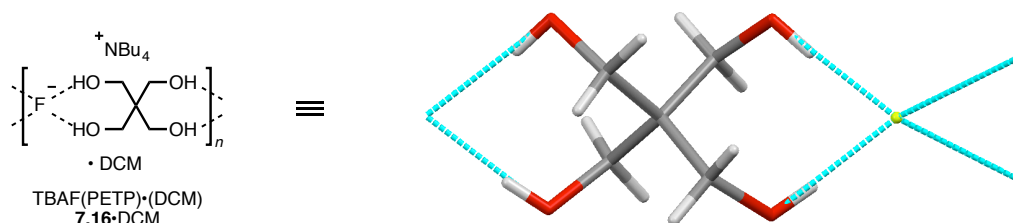


**Figure 7.12.** X-ray crystal structure of TBAF(PETP)•(DCM) (**7.16•DCM**). Tetrabutylammonium counteranion and DCM solvent omitted for clarity.

Overall, in terms of coordination geometry, the TBAF(polyol)<sub>n</sub> series displays more diversity in bonding angles than seen in the alcohol series. In TBAF(Pin)<sub>2</sub> (**7.11**), for example, all four hydrogen bonds are situated on one hemisphere of the fluoride atom, while TBAF(NPG)<sub>2</sub> (**7.14**) is roughly square planar. In contrast, TBAF[(+)-DIPT]<sub>2</sub>•(hexane) (**7.8•hexane**), TBAF(TME)<sub>2</sub> (**7.15**), and TBAF(PETP)•(DCM) (**7.16•DCM**) all possess



coordination geometry of flattened tetrahedra. Tetracoordinate TBAF(*t*-BuOH)<sub>4</sub> is approximately tetrahedral in the solid state. Together, these results demonstrate that intramolecular tethering of multiple HBDs can lead to alternative geometries, perhaps due to added energetic considerations such as ring strain and conformational biases. Additionally, we have established that both seven- and eight-membered cyclic hydrogen-bonding networks can be stably accommodated.

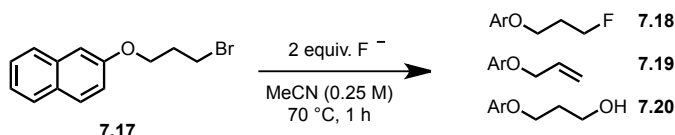
A detailed, global analysis of this set of crystal structures is currently underway in the Gouverneur, Brown, and Paton laboratories, which promises to refine our understanding of fundamental fluoride coordination chemistry. In the meantime, several trends are immediately apparent from the above data and deserve brief mention. First, the observed coordination geometries around fluoride are fairly diverse, and in many instances, for a given alcohol, several inequivalent fluoride species are present in the solid-state (either co-existing in the asymmetric unit or manifesting themselves as distinct polymorphs). Together, these observations suggest that fluoride tends to act as a point charge, rather than strictly adhering to a VSEPR model, and that the potential energy surface for geometrical rearrangement in fluoride–alcohol complexes is relatively flat. These ideas are consistent with the fact that fluoride–alcohol complexes are not held together by stereoelectronically defined covalent bonds (like inorganic and organometallic species), but rather by comparatively weak hydrogen-bonding interactions. Given that multiple coordination geometries are energetically accessible, the diversity that is observed in this series is likely due to packing effects (*e.g.*, charge distribution and space filling). Second, there is a positive correlation between the number of hydrogen-bond donors around a given fluoride atom and the resulting O---F bond distances. This is likely due to increased steric encumbrance around fluoride and decreased negative charge density as the number of hydrogen-bond donors increase. Both of these factors would be expected to weaken the strength of an

additional O–H...F hydrogen bond, which would be reflected in elongation of the measured O...F bond. More in-depth analysis of this data set through the lens of computation and NMR studies is currently underway.

### 7.2.3. Kinetic studies

Having been successful in synthesising and characterising several new tetraalkylammonium fluoride–alcohol complexes, we next tested their reactivity in a representative organic reaction. To assay the relative nucleophilicity and basicity of these complexes, we examined reactions using non-volatile primary alkyl bromide **7.17**, which is capable of participating in both S<sub>N</sub>2 and E2 reactions. To monitor reaction progress, aliquots were taken at predetermined time intervals, quenched on silica gel, and analysed by <sup>1</sup>H NMR spectroscopy. The results with selected TBAF(ROH)<sub>*n*</sub> and TBAF(polyol)<sub>*n*</sub> complexes are shown in Table 7.3 and Figures 7.13 and 7.14.

**Table 7.3.** Summary of kinetic data and reactivity studies.<sup>a,b,c</sup>



| Entry          | Fluoride Complex                                   | Reaction Composition after 2 h (% <sup>1</sup> H NMR) |         |         |       |         | <i>k</i> <sub>obs</sub> (M <sup>-1</sup> s <sup>-1</sup> ) |                        |       |
|----------------|----------------------------------------------------|-------------------------------------------------------|---------|---------|-------|---------|------------------------------------------------------------|------------------------|-------|
|                |                                                    | Fluoride                                              | Olefin  | Alcohol | Ether | Bromide | S <sub>N</sub> 2                                           | E2                     | Ratio |
| 1              | TBAF( <i>p</i> -Tol <sub>3</sub> COH) <sub>2</sub> | 67                                                    | 33      | 0       | 0     | 0       | 1.6 × 10 <sup>-2</sup>                                     | 8.4 × 10 <sup>-3</sup> | 1.9   |
| 2              | TBAF( <i>t</i> -BuOH) <sub>4</sub>                 | 66 (63)                                               | 34 (29) | 0       | 0     | 0       | 7.7 × 10 <sup>-3</sup>                                     | 3.5 × 10 <sup>-3</sup> | 2.2   |
| 3              | TBAF(H <sub>2</sub> O) <sub>3</sub>                | 59                                                    | 33      | 8       | 0     | 0       | 3.8 × 10 <sup>-3</sup>                                     | 2.4 × 10 <sup>-3</sup> | 1.6   |
| 4              | TBAF(9-phenyl-9-fluoreno) <sub>3</sub>             | 77                                                    | 22      | 0       | 0     | 1       | 3.3 × 10 <sup>-3</sup>                                     | 1.2 × 10 <sup>-3</sup> | 2.8   |
| 5              | TBAF(Pin) <sub>2</sub>                             | 67                                                    | 23      | 0       | 0     | 10      | 1.6 × 10 <sup>-3</sup>                                     | 7.7 × 10 <sup>-4</sup> | 2.1   |
| 6              | TBAF(NPG) <sub>2</sub>                             | 45                                                    | 14      | 0       | 0     | 41      | 4.0 × 10 <sup>-4</sup>                                     | 1.7 × 10 <sup>-4</sup> | 2.4   |
| 7              | TBAF(TME) <sub>2</sub>                             | 32                                                    | 8       | 0       | 0     | 60      | 1.9 × 10 <sup>-4</sup>                                     | 5.9 × 10 <sup>-5</sup> | 3.2   |
| 8 <sup>d</sup> | TBAF (anhydrous)                                   | 22                                                    | 78      | 0       | 0     | 0       | ---                                                        | ---                    | ---   |
| 9              | TBAF(Cat) <sub>2</sub>                             | 11                                                    | 2       | 7       | 29    | 51      | ---                                                        | ---                    | ---   |

<sup>a</sup> The % composition was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Values represent the average of three independent trials, except in the case of TBAF(Cat)<sub>2</sub>, in which they represent a single trial. Isolated yields from a fourth independent run (0.5 mmol scale) shown in parentheses. <sup>b</sup> Entries are ordered by *k*<sub>obs,SN2</sub>. <sup>c</sup> *k*<sub>obs</sub> values were derived from the kinetic data by modelling the reactions as second-order using the Berkeley Madonna application (see the Experimental section for details). <sup>d</sup> Value taken from Ref. 4. Reaction conditions: CD<sub>3</sub>CN (0.25 M), 25 °C, 1 h. Anhydrous TBAF generated from tetrabutylammonium cyanide and hexafluorobenzene using the procedure of Ref. 12.

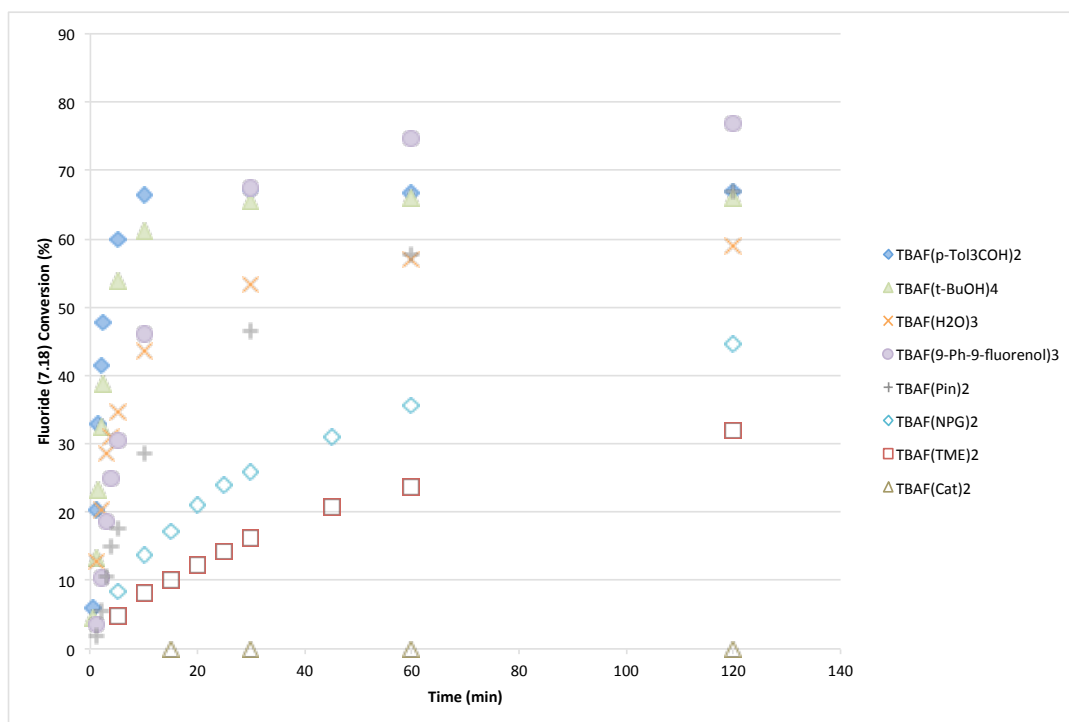


**Figure 7.13.** Rate profiles for fluoride (7.18) product formation using selected TBAF(ROH)<sub>n</sub> and TBAF(polyol)<sub>n</sub> complexes. Each data point represents the average value of three independent trials, with the exception of TBAF(Cat)<sub>2</sub>, for which it represents a single trial.

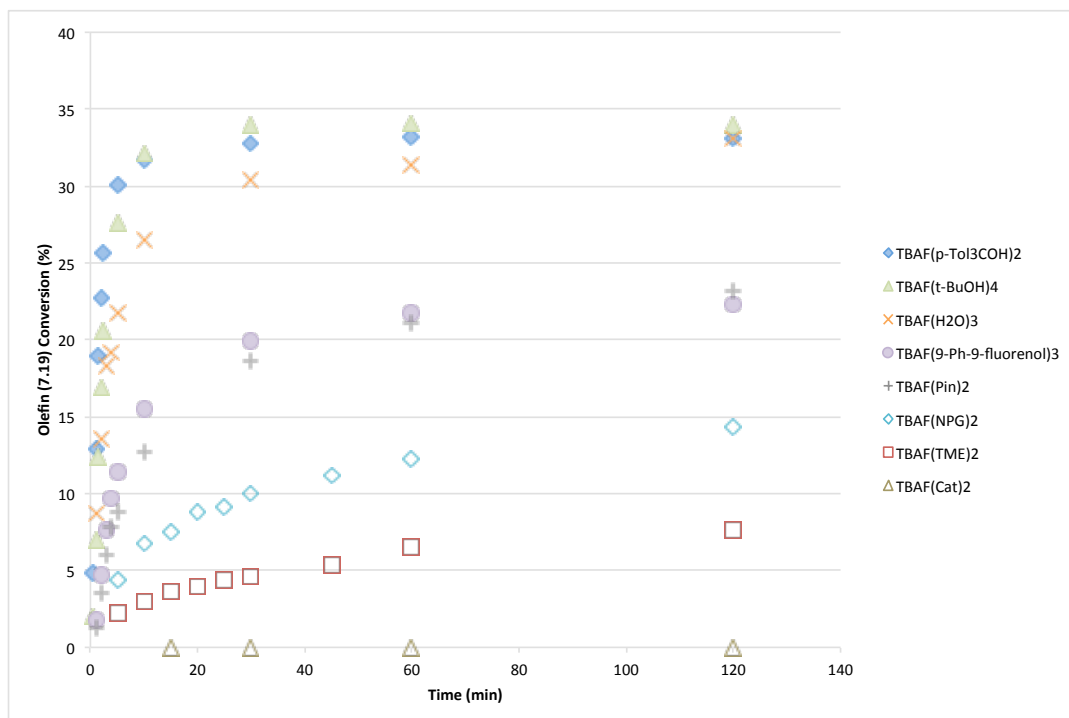


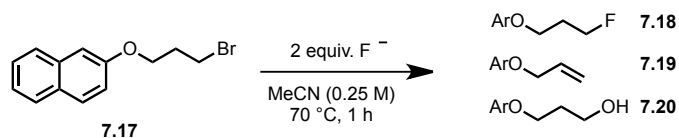
**Figure 7.14.** Rate profiles for olefin (7.19) product formation using selected TBAF(ROH)<sub>n</sub> and TBAF(polyol)<sub>n</sub> complexes. Each data point represents the average value of three independent trials, with the exception of TBAF(Cat)<sub>2</sub>, for which it represents a single trial.

From these results several conclusions can be drawn. Firstly, nearly all of the newly synthesised  $\text{TBAF}(\text{ROH})_n$  complexes were indeed reactive  $\text{F}^-$  sources for  $\text{S}_{\text{N}}2$  and E2 with **7.17**.  $\text{TBAF}(\text{polyol})_n$  complexes were found to be less reactive than  $\text{TBAF}(\text{alcohol})_n$  complexes, with  $\text{TBAF}(\text{Pin})_2$  (**7.11**) showing the best reactivity among them. Secondly, the reactivity profile, both in terms of the reaction kinetics,<sup>13</sup> overall yield, and product distribution, changed dramatically as a result of the coordinated hydrogen-bond donor.<sup>1</sup> Thirdly, the TBAF complexes derived from triarylmethanols, which are exceptionally bulky and relatively weak hydrogen-bond donors, were among the best in terms of rate and selectivity for the  $\text{S}_{\text{N}}2$  pathway. While the reaction rates for  $\text{S}_{\text{N}}2$  and E2 tended to track with one another,  $\text{TBAF}(9\text{-Ph-9-fluoreno})_3$  (**7.3**) was found to be somewhat of an exception, giving high  $\text{S}_{\text{N}}2$  reactivity with relatively low basicity, which led to the best overall product distribution (Entry 4). Interestingly,  $\text{TBAF}(\text{Cat})_2$  (**7.7**) was found to be unreactive, despite still containing fluoride (as evidenced by the two X-ray crystal structures). Given the strong hydrogen-bond donating ability of catechol, we believe that the absence of reactivity in this case is due to the formation of tightly bound polycordinate fluoride species in solution. Dissociation of catechol from fluoride kinetically unfavourable; thus fluoride cannot subsequently participate in  $\text{S}_{\text{N}}2$  or E2. We have observed similar effects with other strong hydrogen-bond donors ( $8 < \text{p}K_{\text{a}} < 11$ ).

To verify that the hydrogen-bond donor plays a dominant role in dictating the observed reactivity profile, we next performed a set of control experiment by varying the alkyl chain length of the tetraalkylammonium counterion and keeping the hydrogen-bond donor the same (Table 7.4 and Figures 7.15 and 7.16). It was found that the identify of the alcohol hydrogen-bond donor and not the counterion primarily influenced the kinetic reactivity and overall product distribution. In recent experiments, we have found that the reactivity trends seen in Figures 7.13 and 7.14 are the same but are more pronounced in

magnitude when the reactions are performed in a less polar solvent, PhMe, rather than in MeCN (data not shown).

**Table 7.4.** Counterion control experiments.<sup>a</sup>



| Reaction Composition after 2 h (% <sup>1</sup> H NMR) |                        |          |        |         |       |         |
|-------------------------------------------------------|------------------------|----------|--------|---------|-------|---------|
| Entry                                                 | Fluoride Complex       | Fluoride | Olefin | Alcohol | Ether | Bromide |
| 1                                                     | TMAF(Pin) <sub>2</sub> | 68       | 38     | 1       | 0     | 3       |
| 2                                                     | TEAF(Pin) <sub>2</sub> | 68       | 25     | 0       | 0     | 7       |
| 3                                                     | TBAF(Pin) <sub>2</sub> | 67       | 23     | 0       | 0     | 10      |
| 4                                                     | TMAF(NPG) <sub>2</sub> | 47       | 16     | 0       | 0     | 37      |
| 5                                                     | TEAF(NPG) <sub>2</sub> | 54       | 18     | 0       | 0     | 27      |
| 6                                                     | TBAF(NPG) <sub>2</sub> | 45       | 14     | 0       | 0     | 41      |

<sup>a</sup> The % composition was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Values for TBAF(Pin)<sub>2</sub> and TBAF(NPG)<sub>2</sub> represent the average of three independent trials, while the other values represent single trials.

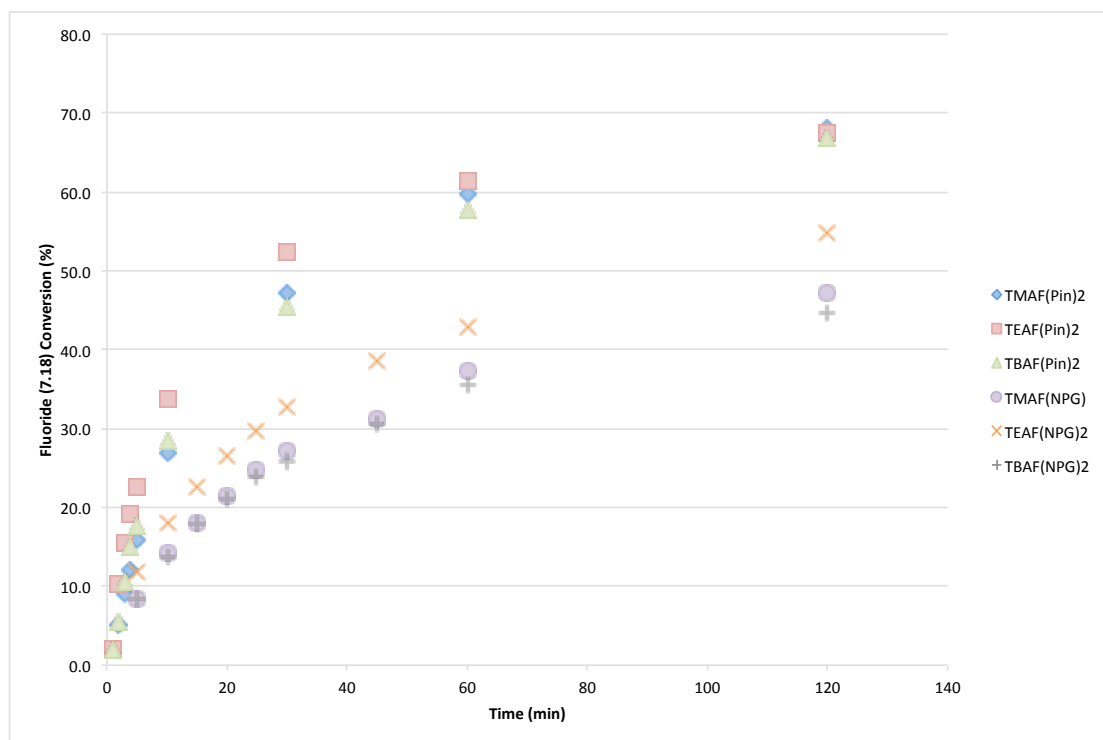


**Figure 7.15.** Counterion control experiments. Summary of rate profiles for fluoride (**7.18**) product formation. The data for TBAF(NPG)<sub>2</sub> and TBAF(Pin)<sub>2</sub>. Values for TBAF(Pin)<sub>2</sub> and TBAF(NPG)<sub>2</sub> represent the average of three independent trials, while the other values represent single trials.

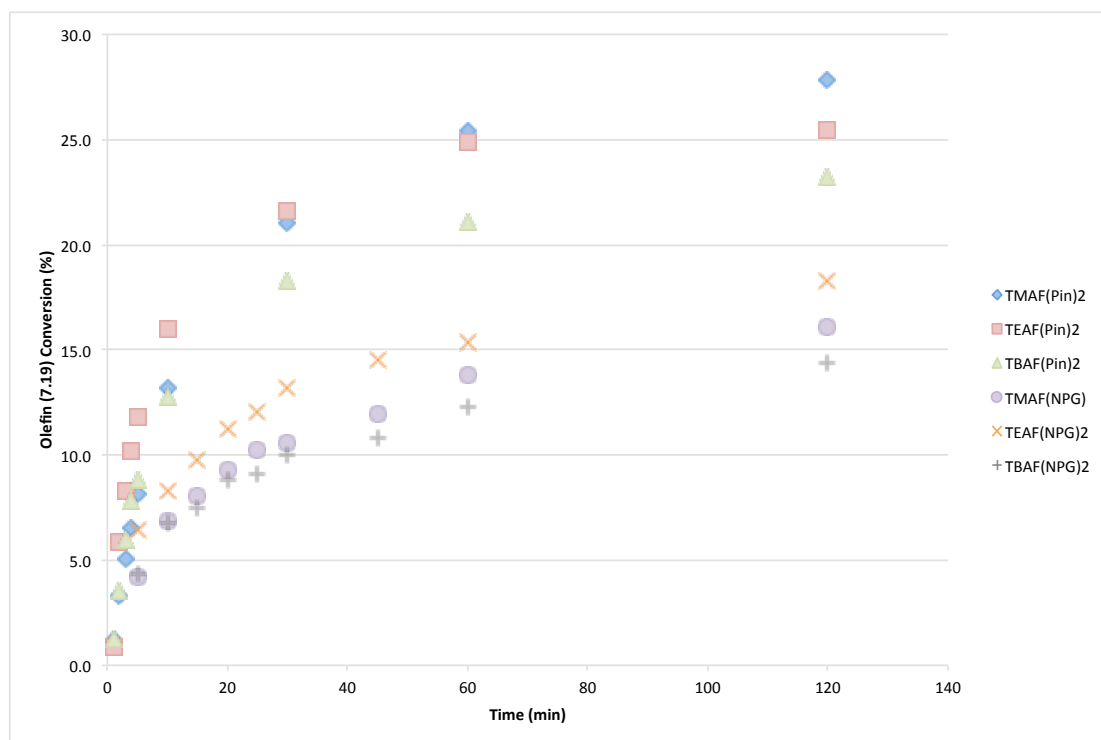


**Figure 7.16.** Counterion control experiments. Summary of rate profiles for olefin (7.19) product formation. Values for TBAF(Pin)<sub>2</sub> and TBAF(NPG)<sub>2</sub> represent the average of three independent trials, while the other values represent single trials.

From the above data, it is clear that there is an intimate relationship between the hydrogen bonding environment around fluoride and the observed reactivity profile. The precise nature of this relationship, however, is complicated. This is due to the fact that fluoride–alcohol and –polyol complexes are held together by weak interactions. As a result, association/dissociation of the hydrogen-bond donors can readily take place in solution, and the energy barrier to geometrical rearrangement is relatively low. Nevertheless, some insights connecting reactivity and solid-state characterisation (Section 7.2.2) merit brief discussion. First, there is a negative correlation between coordination number and observed kinetic reactivity (both in S<sub>N</sub>2 and E2), and there is a positive correlation between coordination number and selectivity for S<sub>N</sub>2. Qualitatively, this first observation is consistent with the notion that highly coordinated fluoride (*e.g.*, tetracoordinate) is unreactive, meaning that dissociation must take place prior to a reaction with an

electrophile. Because, complexes with low coordination numbers also generally have shorter O---F bonds, there is an overall negative correlation between O---F bond distance and kinetic reactivity. At first glance, this result seems at odds both with intuition and with the working mechanistic model proposed below, since one would expect short O---F bond distances to imply strong hydrogen bonding, low charge density on fluoride, and low reactivity. Within a given series (e.g., tetracoordinate), however, there is a positive correlation between O---F bond length and reactivity. Thus, both coordination number and O---F bond strength play a crucial role in governing the reactivity of fluoride. Second, hydrogen-bond donors that form multiple hydrogen bonding contacts to fluoride per molecule in the solid-state are less reactive in solution. For example, TBAF(Pin)<sub>2</sub> (**7.11**) is less kinetically reactive than structurally similar TBAF(*t*-BuOH)<sub>4</sub>. This observation is again consistent with the notion that dissociation from highly coordinated fluoride is required prior to a reaction. The observation that TBAF(TME)<sub>2</sub> (**7.15**) is less reactive and more selective for S<sub>N</sub>2 than TBAF(NPG)<sub>2</sub> (**7.14**), both of which have two hydrogen bonding contacts to fluoride per hydrogen-bond donor in the solid state, suggests that in solution the third unbound hydroxyl group on TME may nevertheless dynamically coordinate to fluoride to attenuate reactivity. The relationship between solid-state structure and reactivity is the subject of ongoing investigation in Gouverneur, Brown, and Paton groups.

In terms of practical features, these new complexes are straightforward to prepare and nearly all of them are free-flowing crystalline solids that are easy to handle. The complexes show improved stability to air and moisture compared with TBAF(H<sub>2</sub>O)<sub>3</sub> and TBAF(*t*-BuOH)<sub>4</sub>, both of which are hygroscopic and difficult to handle. TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**7.3**), TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**7.5**), and TBAF(Pin)<sub>2</sub> (**7.11**), three of the most reactive new complexes, are particularly robust and can be exposed to air for several days without any detectable changes to their physical properties.

#### 7.2.4. Computational studies

Next, computational modelling studies were undertaken at the density functional level of theory to gain insight into the role of hydrogen-bonding additives on modulating both the reactivity and selectivity of fluoride.<sup>14,15</sup> Taking tetracoordinated  $(t\text{-BuOH})_4\text{F}^-$  as a representative example, the reactivity of each fluoride species  $(t\text{-BuOH})_n\text{F}^-$ , where  $n = 3, 2, 1, 0$ , formed by the successive loss of one  $t\text{-BuOH}$  was examined. Transition structures for nucleophilic substitution ( $\text{S}_{\text{N}}2$ ) and elimination (E2) pathways were located for the reaction with EtBr and  $n\text{-PrBr}$ . Although *syn* elimination is a possibility, in the absence of a coordinating counteraction, it is typically much less favourable than antiperiplanar elimination, which in the end was the only pathway considered. Optimisations were performed in a surrounding continuum dielectric medium to describe bulk solvation due to acetonitrile. For dynamic reasons, the transfer of alcohol molecules from  $\text{F}^-$  to the leaving group ( $\text{Br}^-$ ) during either reaction is considered to be relatively inefficient,<sup>16</sup> so in our model, the leaving group is initially formed in unsolvated (apart from bulk dielectric) form. While the underestimation of  $\text{S}_{\text{N}}2$  barriers by DFT is well known, the relative energetics of substitution and elimination pathways for  $\text{F}^- + \text{EtBr}$  obtained with wB97XD ( $\text{DDG}^\ddagger = 5.0$  kcal/mol) compares favourably with WFT (MP2/CBS ( $\text{DDG}^\ddagger = 6.0$  kcal/mol)).

As expected, the computed activation barriers illustrate the greater kinetic reactivity of a fluoride anion without any alcohol coordination whatsoever ( $n = 0$ ) towards both substitution and elimination pathways. The thermodynamic consequence of coordination to fluoride by  $t\text{-BuOH}$  results in a selective stabilisation of the reactants with respect to products, making both  $\text{S}_{\text{N}}2$  and E2 reactions less exergonic. This effect causes both substitution and elimination transition structures to be shifted later (more product-like) along the reaction coordinate whilst the activation barriers also increase, a manifestation of



the Lefler–Hammond postulate or alternatively viewed in terms of the Marcus equation for which  $\Delta G_0$  becomes less negative.

What is perhaps most interesting is the contrast between substitution and elimination as a function of coordinated alcohol molecules: the activation barrier for E2 elimination progressively increases with increasing coordination number in  $(t\text{-BuOH})_n\text{F}^-$ , rising incrementally from 18 to 27 kcal/mol, whereas the  $\text{S}_{\text{N}}2$  barrier is essentially converged at 18–20 kcal/mol by  $n = 1$  and does not grow any larger with increasing coordination. This divergence between elimination and substitution has implications for selectivity, since the more highly coordinated fluoride is computed to show greater preference for substitution.

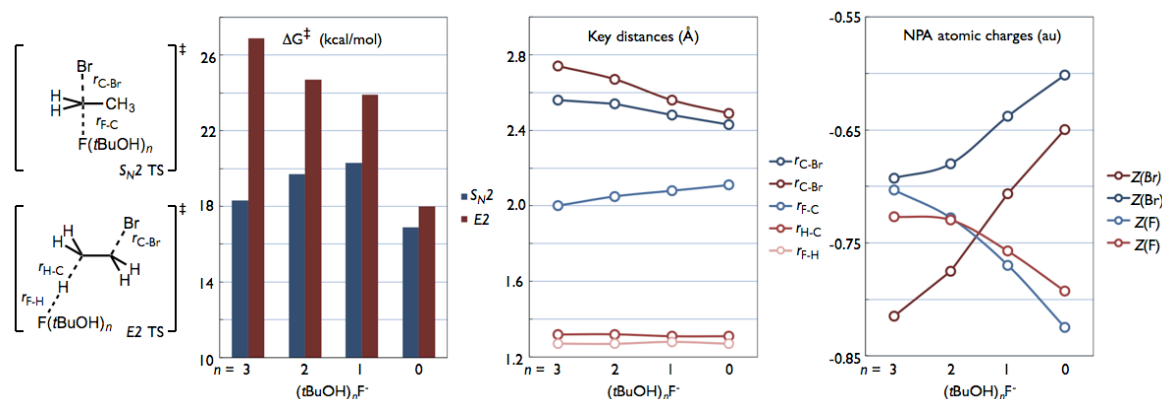


**Figure 7.17.** Computed activation free energies, geometries, and electronic features of  $\text{S}_{\text{N}}2$  and E2 transition structures for  $(t\text{-BuOH})_n\text{F}^-$  reacting with EtBr.

What causes this marked contrast in behaviour between the two transition structures and hence mechanisms? As both TSs are shifted later with higher fluoride coordination numbers, the extent of C–Br breaking is magnified and in the case of E2 elimination, this is more pronounced, where the breaking C–Br bond is elongated from 2.5 to 2.8 Å (Fig. 7.17, middle). At the same time, the extent of charge transfer from F towards Br increases in both mechanisms, with the E2 TS showing a much more negative bromide according to the computed NPA charges. Due to the much greater transfer of charge to the leaving group in the E2 mechanism as the coordination number increases, microsolvation by  $t\text{-BuOH}$  of

fluoride in the TS is weakened relative to fluoride, and it is this that causes the activation barrier to increase. For the  $S_N2$  barriers, a similar trend would be expected, albeit this would be a smaller increase in barriers since the loss of negative charge from fluoride is less pronounced in the substitution TS. That the  $S_N2$  barriers are effectively the same for  $n = 1-3$  suggests that there may be a mitigating effect that acts to stabilise the TS which could arise from a reduction in electrostatic repulsion between nucleophile and leaving group.

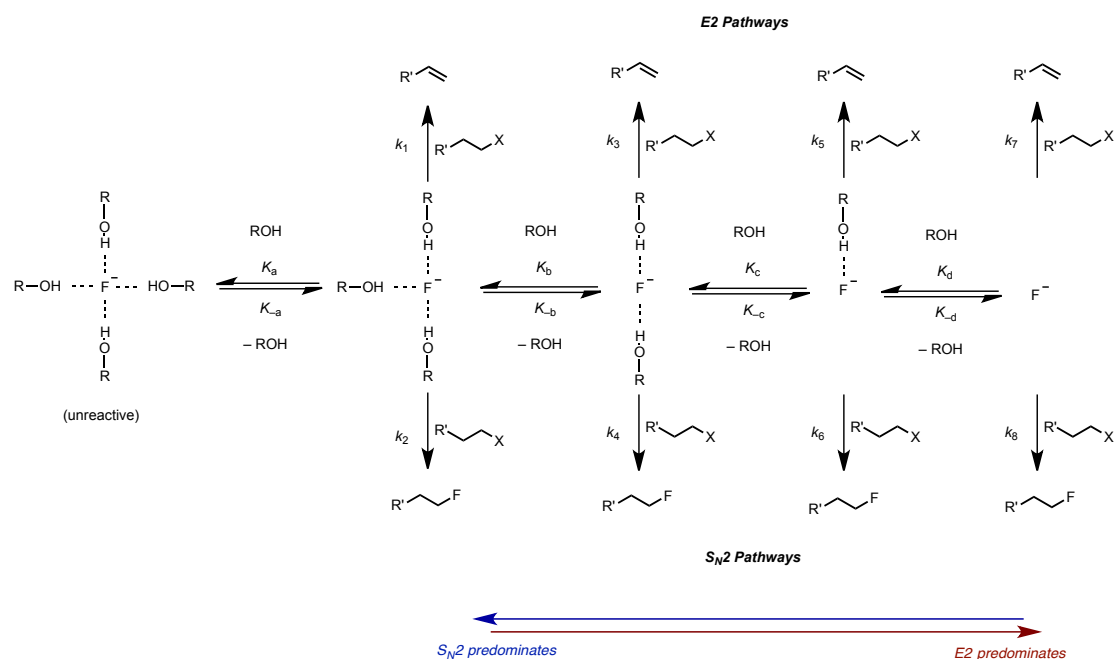
### 7.3. MECHANISTIC MODEL

The insights obtained from our combined structural, kinetic, and computational investigations have shed new light on the mechanisms at play in these reactions. Though additional data is need to piece together a comprehensive explanation for the effects of hydrogen bonding on fluoride reactivity, at the present time, we wish to outline a conceptual framework based on our observations to help guide future work (Scheme 7.1).

We hypothesise that in solution, several hydrogen-bonded fluoride species equilibrate *via* association/dissociation. “Naked” fluoride, as well as mono-, di-, and tricoordinate fluoride are all reactive and have different reactivity profiles. Based on our DFT calculations, the coordination of hydrogen-bond donors serves to decrease Brønsted basicity without substantially lowering nucleophilicity. Experimentally, the measured reactivity patterns are consistent with this idea, as “anhydrous” TBAF led predominantly to elimination, while all alcohol-bound fluoride sources preferentially yielded fluorinated product.

In our model, when fluoride is in a tetracoordinate state, one or more hydrogen-bond donors must dissociate to reach a reactive tri-, di-, or monocoordinate intermediate. Thus, strong hydrogen-bond donors, as exemplified by Cat, can sequester fluoride in “off-cycle” coordination reservoirs, where fluoride is neither a competent nucleophile nor a strong base.

One would expect dissociation of a hydrogen-bond donor to be accelerated by two factors: (1) weak hydrogen bonding strength, and (2) intermolecular steric clashing. Thus high (though not necessarily discriminate) reactivity would be expected with fluoride sources that have a low coordination number or can readily dissociate to a low coordination state. Indeed these predictions track with our reactivity data, as well as with the earlier studies by Yonezawa and coworkers.<sup>1</sup> Obtaining high  $S_N2$  versus E2 *selectivity* on the other hand seems to require stronger hydrogen-bond donors or reaction systems that favour population of di- and tricoordinate fluoride states. Taken together, these considerations suggest that “balanced” hydrogen-bond donor strength is needed: strong enough to tamp down basicity, and weak enough to allow for the smooth release of reactive fluoride.



**Scheme 7.1.** Working mechanistic model.

Additionally, there are other explanations that should be considered in this analysis. For instance, hydrogen-bond donors bearing large hydrophobic groups would be expected to facilitate lipophilic pairing with organic substrate and improve solubility of fluoride in organic solution (a form of phase transfer catalysis). It is likely that many of these

phenomena act in concert, which makes designing reagents with a balanced set of properties a significant challenge.

## 7.4. CONCLUSION

In summary, we have studied the effects of alcohol hydrogen-bond donors on the structure and reactivity of fluoride anion. We synthesised a diverse collection of novel fluoride–alcohol complexes and characterised them using X-ray crystallography. We then tested their reactivity and found that the hydrogen-bond donor played a substantial role in modulating the kinetic reactivity profile of fluoride. Weakly coordinating triarylmethanols were identified as superior hydrogen-bond donors that encouraged high nucleophilicity and low basicity. Within the series of new complexes, several represent promising reagents for use in organic synthesis due to their high reactivity and favourable handling properties. Initial computational results suggest that increasing the coordination stoichiometry around fluoride raises the activation energy for E2 elimination but does not substantially raise the activation energy for the S<sub>N</sub>2 pathway, consistent with experimental findings. In the long term, we hope that this line of inquiry will lead to the development of a small-molecule hydrogen-bond donor catalyst to activate inexpensive and widely available sources of fluoride (*e.g.*, NaF, KF, and CsF).

## 7.5. EXPERIMENTAL

### 7.5.1. General information

Unless otherwise noted, all materials were used as received from commercial sources without further purification. TMAF(H<sub>2</sub>O)<sub>4</sub>, TEAF(H<sub>2</sub>O)<sub>2</sub>, and TBAF(H<sub>2</sub>O)<sub>3</sub> were purchased from Acros, Sigma-Aldrich, and Apollo, respectively. All alcohol hydrogen-bond donors were purchased from Sigma-Aldrich or Alfa Aesar. 2-Naphthol and 3-bromo-1-

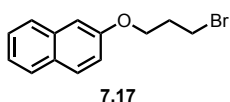
propanol were purchased from Sigma-Aldrich; 1,3-dibromopropane was purchased from Fluorochem. TBAF(*t*-BuOH)<sub>4</sub> was prepared according to the procedure of Kim.<sup>4</sup>

All NMR spectra were recorded on Bruker DPX250 and AV400 spectrometers. <sup>1</sup>H and <sup>13</sup>C NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using the Bruker internal referencing procedure (edlock). <sup>19</sup>F NMR spectra are referenced relative to CFCl<sub>3</sub> in CDCl<sub>3</sub>. Coupling constants (*J*) are reported in units of hertz (Hz). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, qr = quartet, qn = quintet, sx = sextet, m = multiplet, and a = apparent. High-resolution mass spectra (HRMS, *m/z*) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionisation (ESI+). Infrared spectra were recorded using a Bruker Tensor 27 FT-IR spectrometer. Absorptions are reported in wavenumbers (cm<sup>-1</sup>), and only peaks of interest are reported.

X-ray diffraction data were collected variously on a Nonius Kappa CCD and an Agilent SuperNova diffractometer at 150 K. Data were reduced using the instrument manufacturer software, DENZO-SMN<sup>17</sup> and CrysAlisPro.<sup>18</sup> All structures could be solved *ab initio* using SIR92<sup>19</sup> or SuperFlip;<sup>20</sup> however, in the final refinements a common model was used to provide the initial phases, and the structure was refined using CRYSTALS.<sup>21,22</sup>

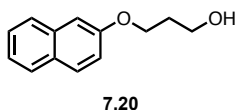
All reactions were performed in flame-dried apparatus with magnetic stirring under an inert atmosphere. All solvents were dried on a column of alumina prior to use. Flash column chromatography was performed over Merck Geduran® silica gel 60 (40–63 μm) using eluent systems as described for each experiment.

### 7.5.2. Synthesis of starting material and reference compound



**2-(3-Bromopropoxy)naphthalene (7.17):** The title compound was prepared according to a modified version of a procedure developed by

Kim and coworkers.<sup>23</sup> To a 250 mL round-bottom flask containing a magnetic stir bar were added, 2-naphthol (2.02 g, 14.0 mmol), 1,3-dibromopropane (280 mmol, 28.6 mL), K<sub>2</sub>CO<sub>3</sub> (140 mmol, 19.3 g), and DMF (2.0 mL). The resulting slurry solution was stirred at 50 °C for 48 h. The reaction mixture was cooled to room temperature, and water (100 mL) was added. The resulting biphasic mixture was extracted with DCM (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried over MgSO<sub>4</sub>, filtered, and then concentrated *in vacuo*. Excess 1,3-dibromopropane (b.p. = 166–167 °C) was removed using a rotary evaporator connected to a well-maintained vacuum pump and a water bath at elevated temperature (70–80 °C). The resulting residue was further dried under high vacuum for several hours. Purification via silica gel column chromatography (10:1 hexanes:DCM → 4:1 hexanes:DCM) delivered analytically pure **7.17** as a colourless oil, which over time transformed into a white crystalline solid (2.56 g, 69% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.78–7.72 (m, 3H), 7.45 (ddd, *J*<sub>1</sub> = 8.4 Hz, *J*<sub>2</sub> = 7.2 Hz, *J*<sub>3</sub> = 1.2 Hz, 1H), 7.35 (ddd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 6.8 Hz, *J*<sub>3</sub> = 1.2 Hz, 1H), 7.17–7.13 (m, 2H), 4.23 (t, *J* = 6.0 Hz, 2H), 3.66 (t, *J* = 6.8 Hz, 2H), 2.39 (qn, *J* = 6.0 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.60, 134.49, 129.44, 129.02, 127.63, 126.74, 126.40, 123.59, 118.77, 106.71, 65.30, 32.33, 30.07. IR (solid) ν 3060, 2949, 2899, 1629, 1599, 1510, 1461, 1390, 1254, 1215, 1182, 1027, 841, 816, 748 cm<sup>-1</sup>; HRMS (EI/FI) *m/z* Calcd for C<sub>13</sub>H<sub>13</sub>BrO [M]<sup>+</sup> 264.0150, [(M+2)]<sup>+</sup> 266.0130, found 264.0146, 266.0153 [M]<sup>+</sup> : [(M+2)]<sup>+</sup> = 1:1.



**3-(Naphthalen-2-yloxy)propan-1-ol (7.20):** The title compound was prepared according to a procedure described by Shi and He.<sup>24</sup> To a 250

mL round-bottom flask equipped with a magnetic stir bar, were added distilled water (100 mL) and naphthol (7.21 g, 50 mmol), giving a suspension. NaOH pellets were added one-by-one until the mixture became a transparent, homogenous, purple solution. 3-

Bromopropanol (2.70 mL, 30 mmol) was added dropwise. The flask was capped with a rubber septum, and the reaction mixture was allowed to stir at room temperature for 24 h. The aqueous reaction mixture was extracted with DCM ( $3 \times 100$  mL). The combined organic layers were washed with H<sub>2</sub>O ( $3 \times 100$  mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo* to give the crude product as an off-white solid in approximately 60% yield by mass. To remove trace quantities of 3-bromopropanol, which proved to be difficult to separate via silica gel column chromatography, the crude product was recrystallised (10:1 Et<sub>2</sub>O:hexanes), giving analytically pure **7.20** as an off-white solid (852 mg, 14% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.78–7.72 (m, 3H), 7.44 (at,  $J = 8.0$  Hz, 1H), 7.34 (at,  $J = 8.0$  Hz, 1H), 7.16–7.13 (m, 2H), 4.25 (t,  $J = 6.0$  Hz, 2H), 3.92 (t,  $J = 6.0$  Hz, 2H), 2.12 (qn,  $J = 6.0$  Hz, 2 H), 1.70 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  156.68, 134.50, 129.41, 128.99, 127.63, 126.74, 126.38, 123.66, 118.77, 106.68, 65.74, 60.58, 31.96; IR (film, CDCl<sub>3</sub>)  $\nu$  3267, 2955, 2878, 1629, 1600, 1509, 1467, 1389, 1261, 1219, 1184, 1055, 1040, 837, 815, 749 cm<sup>-1</sup>; HRMS (ESI)  $m/z$  Calcd for C<sub>13</sub>H<sub>14</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup> 255.0886, found 225.0880.

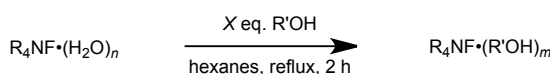
### 7.5.3. Complex synthesis and characterisation

#### General Procedure for Synthesising [Tetraalkylammonium Fluoride–Alcohol]

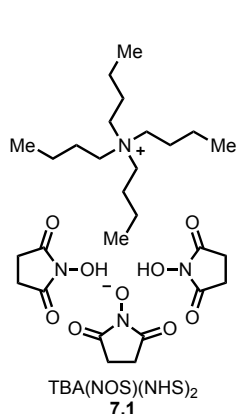
**Complexes:** To a flame-dried 250 mL round-bottom flask under a nitrogen atmosphere and equipped with a stir bar and reflux condenser, were added hexanes (125 mL), tetraalkylammonium fluoride hydrate (4.0 mmol) and the alcohol hydrogen-bond donor (8.0 mmol). The resulting suspension was allowed to stir in an oil bath at vigorous reflux (80–85 °C) for 2 h. After approximately 30 min, droplets of water were observed on the inside walls of the reflux condenser. During the course of the reaction the persistent presence of a white solid precipitate was observed. The solution was allowed to cool to room temperature, filtered quickly, washed with hexanes ( $3 \times 50$  ml), and dried under high vacuum, giving the

desired [tetraalkylammonium fluoride–alcohol] complex, which was used without further purification.

*Note:* In all  $^{13}\text{C}$  NMR spectra of [tetraalkylammonium fluoride–alcohol] complexes taken in  $\text{CDCl}_3$ , we observed a singlet at approximately 77.20 ppm, which we attribute to  $\text{CHCl}_3$ . We surmise that  $\text{CHCl}_3$  is formed *in situ* from  $\text{CDCl}_3$  via proton exchange, which is presumably mediated by fluoride acting as a Brønsted base. This signal has been omitted from the peak listings below.



**Scheme 7.S1:** General procedure for synthesising [tetraalkylammonium fluoride–alcohol] complexes.



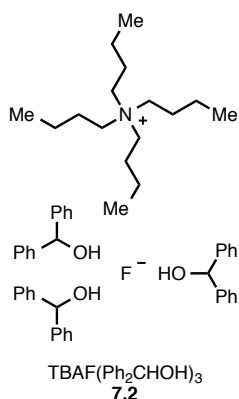
**tetra-*n*-butylammonium**                      ***N*-oxysuccinimide**                      **bis(*N*-**

**hydroxysuccinimide) (TBA(NOS)(NHS)<sub>2</sub>, 7.1):** The title compound was prepared using the standard procedure with 4.0 mmol of TBAF( $\text{H}_2\text{O}$ )<sub>3</sub> and 12.0 mmol of *N*-hydroxysuccinimide. The complex was thus obtained as a crystalline white solid (2.30 g, 98% yield).

Single-crystal X-ray diffraction of a recrystallised sample (see below)

established that the complex is an *N*-oxyanion.  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 (bs, 2H), 3.26–3.22 (m, 8H), 1.63 (qn,  $J = 7.6$  Hz, 8H), 1.39 (sx,  $J = 7.2$  Hz, 8H), 0.94 (t,  $J = 7.2$  Hz, 12H);  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  173.58, 58.44, 25.53, 23.77, 19.50, 13.57; **IR** (solid)  $\nu$  2959, 2876, 2345, 1712, 1211, 1095, 1074, 883, 817, 714, 651  $\text{cm}^{-1}$ ; **X-ray** (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.1** in THF, which had previously been prepared by dissolving **7.1** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

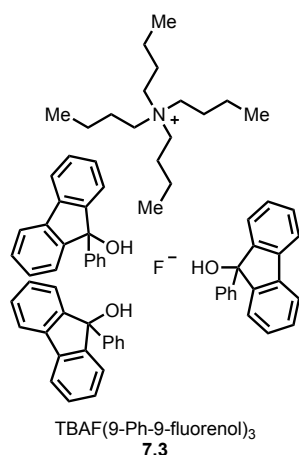




**tetra-*n*-butylammonium      fluoride      tris(diphenylmethanol)**

**(TBAF(Ph<sub>2</sub>CHOH)<sub>3</sub>, 7.2):** The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 16.0 mmol of diphenylmethanol. The complex was thus obtained as a chalky off-white solid (2.96 g, 91% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39–

7.36 (m, 12H), 7.30–7.27 (m, 12H), 7.23–7.19 (m, 6H), 5.81 (s, 3H), 3.26–3.16 (m, 8H), 1.58–1.46 (m, 8H), 1.38–1.31 (m, 8H), 0.95 (t, *J* = 7.6 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 128.12, 128.07, 126.4, 126.71, 75.21, 58.11, 23.94, 19.64, 13.65; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ –156.49; IR (solid) ν 3024, 2961, 2873, 2693, 1490, 1453, 1181, 1052, 1027, 914, 884, 755, 737, 700 cm<sup>–1</sup>. **X-ray** (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.2** in THF, which had previously been prepared by dissolving **7.2** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

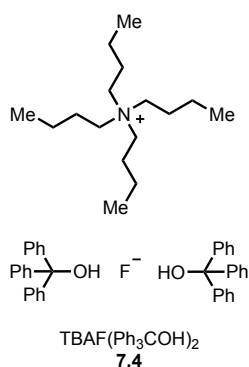


**tetra-*n*-butylammonium      fluoride      tris(9-phenyl-9-fluorenol)**

**(TBAF(9-Ph-9-fluorenol)<sub>3</sub>, 7.3):** The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 16.0 mmol of 9-phenyl-9-fluorenol. The complex was thus obtained as a chalky off-white solid (3.76 g, 91% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.67 (d, *J* = 7.6 Hz,

6H), 7.41 (d, *J* = 8.0 Hz, 6H), 7.36 (t, *J* = 7.6 Hz, 12H), 7.27–7.19 (m, 15H), 3.27–2.23 (m, 8H), 1.59–1.51 (m, 8H), 1.35 (sx, *J* = 7.2 Hz, 8H), 0.95 (t, *J* = 7.2 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 150.79, 143.67, 139.55, 128.81, 128.32, 128.09,

126.99, 125.45, 124.92, 119.90, 83.43, 58.65, 24.00, 19.65, 13.65;  $^{19}\text{F}$  NMR (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$  -155.79; **IR** (solid)  $\nu$  3276, 3058, 2960, 2937, 2872, 2555, 1738, 1478, 1442, 1180, 1054, 1030, 924, 889, 730, 694  $\text{cm}^{-1}$ . **X-ray** (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.3** in EtOAc, which had previously been prepared by dissolving **7.3** in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

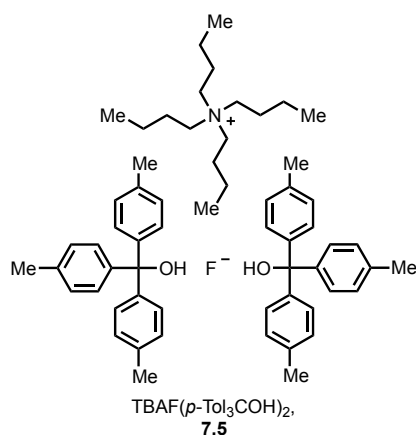


**tetra-*n*-butylammonium      fluoride      bis(triphenylmethanol)**

**(TBAF( $\text{Ph}_3\text{COH}$ )<sub>2</sub>, **7.4**):** The title compound was prepared according to the general procedure with 2.0 mmol of TBAF( $\text{H}_2\text{O}$ )<sub>3</sub> and 4.0 mmol of triphenylmethanol. After heating at reflux for 2 h, a viscous yellow oil was observed at the bottom of the reaction vessel, which solidified when allowed to stand at room temperature for 2 h. The reaction

mixture was filtered, washed quickly with acetone ( $\times$  1) and hexanes ( $\times$  3), and dried under high vacuum. The complex was thus obtained as a crystalline yellow solid (954 mg, 61% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27–7.24 (m, 30H), 3.31–3.27 (m, 8H), 1.62 (qn,  $J$  = 7.2 Hz, 8H), 1.40 (sx,  $J$  = 7.2 Hz, 8H), 0.97 (t,  $J$  = 7.2 Hz, 12H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  147.00, 127.86, 127.66, 126.91, 81.61, 58.54, 23.88, 19.58, 13.56;  $^{19}\text{F}$  NMR (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$  -155.21; **IR** (solid)  $\nu$  3059, 2960, 2932, 2874, 2451, 1488, 1444, 1380, 1162, 1050, 1031, 884, 757, 698, 638  $\text{cm}^{-1}$ . **X-ray** (single-crystal) A distinct sample of TBAF( $\text{Ph}_3\text{COH}$ )<sub>*n*</sub> was synthesised using the general procedure with a 4:1 ratio of TBAF( $\text{H}_2\text{O}$ )<sub>3</sub> and triphenylmethanol. After being filtered, washed with hexanes ( $\times$  3), and dried under high vacuum,  $^1\text{H}$  NMR analysis of this material revealed an alcohol:fluoride ratio of 3.8:1. This material was used to grow single crystals of the 2:1 complex. Colourless

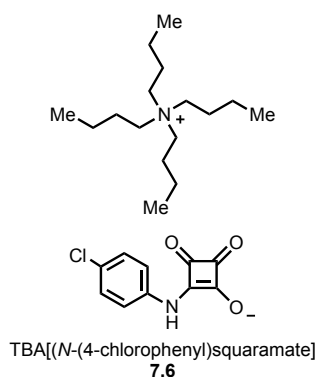
needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of  $\text{TBAF}(\text{Ph}_3\text{COH})_n$  in EtOAc, which had previously been prepared by dissolving  $\text{TBAF}(\text{Ph}_3\text{COH})_n$  in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. The crystal was found to be an *n*-hexane solvate.



**tetra-*n*-butylammonium fluoride bis(tri-*p*-tolylmethanol) (TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub>, **7.5**):**

The title compound was prepared according to the general procedure with 4.0 mmol of  $\text{TBAF}(\text{H}_2\text{O})_3$  and 16.0 mmol of tri-*p*-tolylmethanol. During the course of the reaction, the solution became homogenous. After 2 h of heating at reflux, the flask was removed from the oil bath and

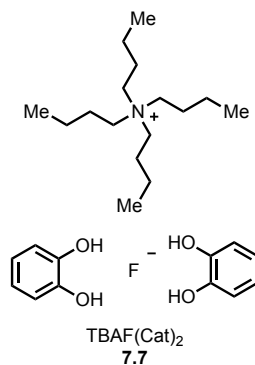
allowed to stand at room temperature for 4 h, during which time a pale yellow precipitate was observed. Following the standard work-up, **7.5** was obtained as a crystalline pale-yellow solid (2.62 g, 76% yield). **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.15 (d,  $J$  = 8.0 Hz, 12H), 7.09 (d,  $J$  = 8.0 Hz, 12H), 3.39–3.34 (m, 8H), 2.33 (s, 18H), 1.67 (qn,  $J$  = 7.2 Hz, 8H), 1.45 (sx,  $J$  = 7.2 Hz, 8H), 1.01 (t,  $J$  = 7.2 Hz, 12H); **<sup>13</sup>C NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  144.28, 136.66, 128.49, 127.74, 81.14, 58.87, 24.09, 20.98, 19.75, 13.66; **<sup>19</sup>F NMR** (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$  –156.48; **IR** (solid)  $\nu$  2962, 2935, 2874, 2482, 1508, 1488, 1456, 1380, 1182, 1155, 1063, 916, 886, 812, 781  $\text{cm}^{-1}$ ; **X-ray** (single-crystal) Colourless needles of X-ray quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.5** in  $\text{Et}_2\text{O}$ , which had previously been prepared by dissolving **7.5** in refluxing  $\text{Et}_2\text{O}$  (approximately 35 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.



**tetra-*n*-butylammonium      *N*-(4-chlorophenyl)squaramate**

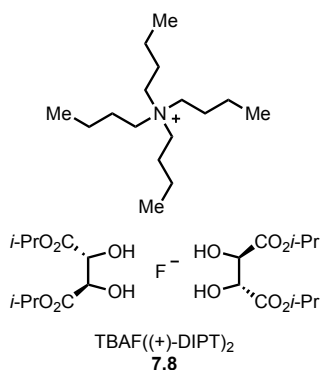
**(TBA[*N*-(4-chlorophenyl)squaramate, 7.6):** To an oven-dried 100 mL round bottom flask under a nitrogen atmosphere and equipped with a stir bar and reflux condenser, were added hexanes (50 mL), TBAF(H<sub>2</sub>O)<sub>3</sub> (315 mg, 1.0 mmol) and **7.6** (224 mg, 1.0 mmol). The resulting suspension was allowed to stir in an

oil bath at vigorous reflux (80–85 °C) for 2 h. After approximately 30 min, droplets of water were observed on the inside walls of the reflux condenser. During the course of the reaction, a dark-yellow solid precipitate was observed. The solution was allowed to cool to room temperature, filtered quickly, washed with hexanes (× 3), and dried under high vacuum, giving **7.6** (438 mg, 94% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.58 (ad, *J* = 8.8 Hz, 2H), 7.11 (ad, *J* = 8.8 Hz, 2H), 3.20–3.16 (m, 8H), 1.55 (qn, *J* = 8.0 Hz, 8H), 1.34 (sx, *J* = 7.6 Hz, 8H), 0.91 (t, *J* = 7.2 Hz, 12H); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 188.57, 177.02, 139.29, 128.99, 125.83, 118.78, 99.97, 58.78, 23.91, 19.69, 13.61; **IR** (solid) ν 2998, 2874, 1782, 1664, 1598, 1554, 1537, 1494, 1411, 1381, 1189, 1108, 826 cm<sup>-1</sup>; **X-ray** (single-crystal) Yellow needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.6** in THF, which had previously been prepared by dissolving **7.6** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min at room temperature to cool to near room temperature.



**tetra-*n*-butylammonium flouride bis(catechol) (TBAF(Cat)<sub>2</sub>, 7.7):**

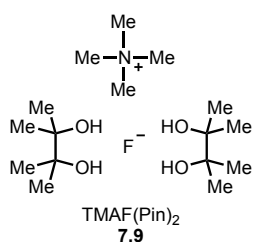
The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 8.0 mmol of catechol. After heating at reflux for 2 h, a viscous pink oil was observed at the bottom of the reaction vessel, which solidified when allowed to stand at room temperature for 4 h. Following the standard work-up, the complex was obtained as a pink solid that became brown/purple over time (1.79 g, 93% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.84 (bs, 4H), 6.79–6.76 (m, 4H), 6.67–6.63 (m, 4H), 2.90–2.86 (m, 8H), 1.35–1.31 (m, 8H), 1.25 (sx, *J* = 7.2 Hz, 8H), 0.88 (t, *J* = 7.2 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 145.46, 119.67, 116.61, 58.00, 23.47, 19.38, 13.47; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ –113.40; IR (solid) ν 3147, 3065, 2960, 2901, 2876, 1600, 1495, 1471, 1363, 1279, 1249, 921, 881, 747 cm<sup>–1</sup>. X-ray (single-crystal, 1<sup>st</sup> polymorph) Colourless plates of X-ray diffraction quality were obtained by vapour diffusion of hexanes into a saturated solution of 7.7 in EtOAc, which had previously been prepared by dissolving 7.7 in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. (2<sup>nd</sup> polymorph) Pink plate-like crystals of X-ray diffraction quality were obtained directly from the reaction mixture.



**tetra-*n*-butylammonium flouride bis((+)-diisopropyl L-tartrate)) (TBAF((+)-DIPT)<sub>2</sub>, 7.8):**

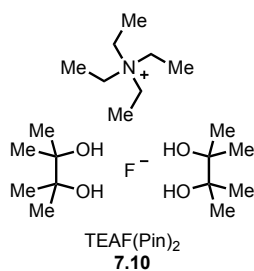
The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 8.0 mmol of (+)-diisopropyl tartrate. After heating at reflux for 2 h, a viscous colourless oil was observed at the bottom of the reaction vessel. The reaction was allowed to

cool to room temperature, and the solvent was removed *in vacuo*. After further drying under high vacuum for 8 h, the complex was transferred to a  $-20\text{ }^{\circ}\text{C}$  fridge for 8 h, at which point it was observed to have solidified. The resulting material was warmed to room temperature and washed with hexanes ( $\times 3$ ) on a sinter funnel, then dried under high vacuum. The complex was thus obtained as sticky colourless solid (1.79 g, 61% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.09–5.01 (m, 4H), 4.45 (s, 4H), 3.29–3.25 (m, 8H), 1.61 (qn,  $J = 7.6$  Hz, 8H), 1.39 (sx,  $J = 7.6$  Hz, 8H), 1.25–1.21 (m, 32H), 0.95 (t,  $J = 0.72$  Hz, 12H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.43, 72.79, 69.25, 58.48, 23.87, 21.69, 21.63, 19.59, 13.58;  $^{19}\text{F}$  NMR (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$   $-156.27$ ; IR (solid)  $\nu$  3143, 2962, 2875, 1744, 1468, 1375, 1265, 1217, 1197, 1150, 1096  $\text{cm}^{-1}$ ; X-ray (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.8** in THF, which had previously been prepared by dissolving **7.8** in refluxing THF (approximately  $66\text{ }^{\circ}\text{C}$ ) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. The crystal was found to be an *n*-hexane solvate.

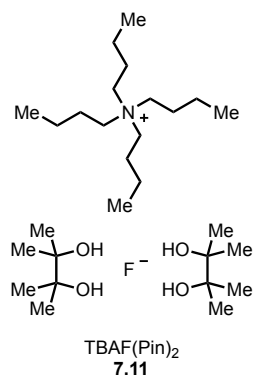


**tetramethylammonium fluoride bis(pinacol) (TMAF(Pin)<sub>2</sub>, 7.9):**

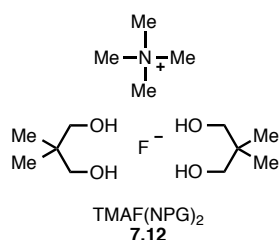
The title compound was prepared according to the general procedure with 4.0 mmol of TMAF( $\text{H}_2\text{O}$ )<sub>4</sub> and 8.0 mmol of pinacol. The complex was thus obtained as a chalky white solid (964 mg, 73% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.37 (s, 12H), 1.16 (s, 24H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  74.82, 55.76, 25.12;  $^{19}\text{F}$  NMR (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$   $-108.01$ ; IR (solid)  $\nu$  3182, 2983, 2937, 1489, 1381, 1358, 1191, 1150, 949, 762  $\text{cm}^{-1}$ .

**tetraethylammonium flouride bis(pinacol) (TEAF(Pin)<sub>2</sub>, 7.10):**

The title compound was prepared according to the general procedure with 4.0 mmol of TEAF(H<sub>2</sub>O)<sub>2</sub> and 8.0 mmol of pinacol. The complex was thus obtained as a chalky white solid (1.19 mg, 77% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.40 (qr, *J* = 7.2 Hz, 8H), 1.34 (t, *J* = 7.2 Hz, 12H), 1.18 (s, 24H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 74.66, 52.39, 25.09, 7.64; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -115.51; IR (solid) ν 3170, 2974, 2939, 1490, 1379, 1149, 1002, 952, 787 cm<sup>-1</sup>.

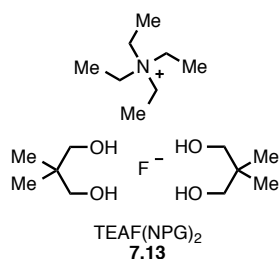
**tetra-*n*-butylammonium flouride bis(pinacol) (TBAF(Pin)<sub>2</sub>, 7.11):**

The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 8.0 mmol of pinacol. The complex was thus obtained as flocculent white solid (1.86 g, 93% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.28–3.24 (m, 8H), 1.64–1.56 (m, 8H), 1.40 (sx, *J* = 7.6 Hz, 8H), 1.15 (s, 24H), 0.96 (t, *J* = 7.2 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 74.46, 58.42, 25.17, 23.95, 19.64, 13.62; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -114.53; IR (solid) ν 3159, 2965, 2944, 2878, 1463, 1380, 1150, 953, 887 cm<sup>-1</sup>. X-ray (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.11** in THF, which had previously been prepared by dissolving **7.11** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.



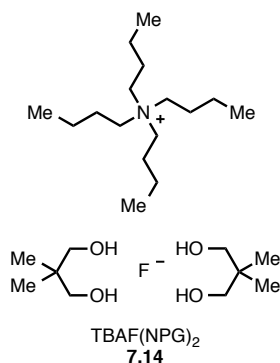
**tetramethylammonium fluoride bis(neopentyl glycol)**

**(TMAF(NPG)<sub>2</sub>, 7.12):** The title compound was prepared according to the general procedure with 4.0 mmol of TMAF(H<sub>2</sub>O)<sub>4</sub> and 8.0 mmol of neopentylglycol. The complex was thus obtained as a crystalline white solid (1.11 g, 92% yield). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 3.29 (as, 20H), 0.77 (s, 12H), <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 68.68, 55.66, 37.00, 21.80; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -134.44; IR (solid) ν 3113, 2955, 2867, 1489, 1392, 1357, 1042, 990 cm<sup>-1</sup>.



**tetraethylammonium fluoride bis(neopentyl glycol)**

**(TEAF(NPG)<sub>2</sub>, 7.13):** The title compound was prepared according to the general procedure with 4.0 mmol of TEAF(H<sub>2</sub>O)<sub>2</sub> and 8.0 mmol of neopentylglycol. The complex was thus obtained as a flocculent white solid (1.25 g, 87% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.38–3.32 (m, 16H), 1.35 (t, *J* = 7.2 Hz, 12H), 0.83 (s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 77.20, 69.69, 52.43, 36.86, 21.74, 7.53; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -139.49; IR (solid) ν 3192, 2985, 1904, 2863, 1470, 1393, 1043, 1003, 747 cm<sup>-1</sup>.

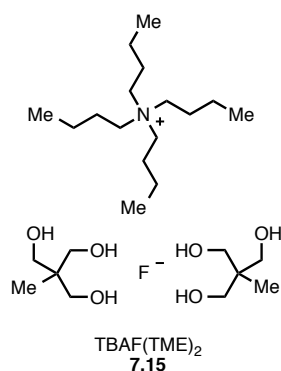


**tetra-*n*-butylammonium fluoride bis(neopentyl glycol)**

**(TBAF(NPG)<sub>2</sub>, 7.14):** The title compound was prepared according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 8.0 mmol of neopentylglycol. The complex was thus obtained as a crystalline white solid (1.76 g, 89% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 3.27 (s, 8H), 3.20–3.16 (m, 8H), 1.61–1.53 (m, 8H), 1.35 (sx, *J* = 7.6 Hz, 8H), 0.95 (t, *J* = 7.2 Hz, 12H), 0.74 (s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 68.74, 58.42, 36.90, 23.75, 21.79, 19.55, 13.52; <sup>19</sup>F NMR (376.5 MHz, CDCl<sub>3</sub>) δ -142.34;

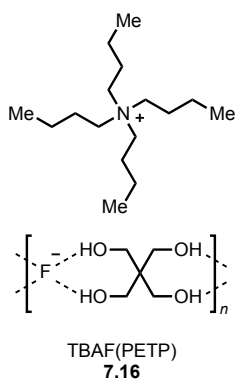


**IR** (solid)  $\nu$  3177, 2960, 2865, 1485, 1354, 1049, 884, 739  $\text{cm}^{-1}$ . **X-ray** (single-crystal) Colourless plate-like crystals of X-ray quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.14** in THF, which had previously been prepared by dissolving **7.14** in THF at room temperature and filtering to remove residual solid.



**tetra-*n*-butylammonium fluoride bis(1,1,1-tris(hydroxymethyl)ethane) (TBAF(TME)<sub>2</sub>, 7.15):** The title compound was prepared using according to the general procedure with 4.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 8.0 mmol of 1,1,1-tris(hydroxymethyl)ethane. After heating at reflux for 2 h, a viscous oil was observed at the bottom of the reaction vessel, which

solidified when allowed to stand at room temperature for 8 h. Following the standard work-up, **7.15** was obtained as a chalky white solid (1.90 g, 95% yield). **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.07 (bs, 2H), 3.61 (s, 12H), 3.25–3.21 (m, 8H), 1.67–1.59 (m, 8H), 1.43 (sx,  $J$  = 7.2 Hz, 8H), 1.01 (t,  $J$  = 7.2 Hz, 12H), 0.66 (s, 6H), **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>)  $\delta$  67.71, 58.71, 41.00, 23.89, 19.70, 17.38, 13.63; **<sup>19</sup>F NMR** (376.5 MHz, CDCl<sub>3</sub>)  $\delta$  –140.48; **IR** (solid)  $\nu$  3337, 3181, 2962, 2929, 2876, 1473, 1039, 885  $\text{cm}^{-1}$ . **X-ray** (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.15** in THF, which had previously been prepared by dissolving **7.15** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.



**tetra-*n*-butylammonium flouride pentaerythritol (TBAF(PETP),**

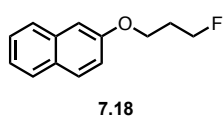
**7.16)** The title compound was prepared according to the general procedure with 2.0 mmol of TBAF(H<sub>2</sub>O)<sub>3</sub> and 2.0 mmol of pentaerythritol. The complex was thus obtained as a crystalline white solid (616 mg, 77% yield). <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 6.18 (bs, 2H), 3.47 (s, 8H), 3.21–3.17 (m, 8H), 3.04 (bs, 2H), 1.63 (qn, *J* = 7.2

Hz, 8H), 1.42 (sx, *J* = 7.2 Hz, 8H), 1.01 (t, *J* = 7.2 Hz, 12H); <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 63.94, 59.27, 46.24, 24.39, 20.25, 13.95; <sup>19</sup>F NMR (376.5 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ –136.81; IR (solid) ν 3197, 2961, 2930, 2873, 1489, 1463, 1374, 1124, 1017, 886, 742 cm<sup>–1</sup>; X-ray (single-crystal) Colourless plate-like crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.16** in DCM, which had previously been prepared by dissolving **7.16** in refluxing DCM (approximately 40 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. The crystal was found to be a DCM solvate.

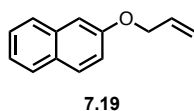
**7.5.4. General procedure for nucleophilic fluorination (preparative scale) and product characterisation**

To a 14 mL screw-top vial, were added **7.17** (48.8 mg, 0.2 mmol), MeCN (0.8 mL), and TBAF(*t*-BuOH)<sub>4</sub> (0.8 mmol, 223.2 mg). The vial was capped and transferred to an oil bath, which had been pre-heated to 70 °C. After 1 h, the vial was removed from the oil bath and allowed to cool to room temperature. Et<sub>2</sub>O (4 mL) and H<sub>2</sub>O (4 mL) were added to quench the reaction. A sample of the organic phases was removed, and the solvent was removed *in vacuo*. The resulting residue was dissolved in CDCl<sub>3</sub> for analysis by <sup>1</sup>H NMR spectroscopy. The NMR sample was combined with the reaction mixture and the layers were separated. The aqueous layer was further extracted with Et<sub>2</sub>O (2 × 5 mL). The

combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated *in vacuo*. Subsequent purification was carried out using silica gel column chromatography, using a gradient solvent system of pure hexanes  $\rightarrow$  10:1 hexanes:EtOAc. (Hexanes was used as an eluent until the olefin, **7.19**, eluted, and 10:1 hexanes:EtOAc was used to elute the fluoride, **7.20**.) The olefin byproduct and fluorinated product were obtained as pure compounds; the spectral data were in accordance with literature precedents.<sup>4,25</sup>

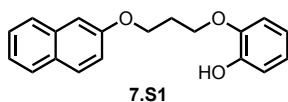


**2-(3-fluoropropoxy)naphthalene (7.18):** The title compound was prepared according to the general procedure and isolated via silica gel column chromatography (10:1 hexanes:EtOAc) (63 mg, 63% yield). **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78–7.71 (m, 3H), 7.44 (ddd,  $J_1 = 8.0$  Hz,  $J_2 = 6.8$  Hz,  $J_3 = 1.2$  Hz, 1 H), 7.34 (ddd,  $J_1 = 8.0$  Hz,  $J_2 = 6.8$  Hz,  $J_3 = 1.2$  Hz, 1H), 7.15–7.13 (m, 2H), 4.70 (dt,  $J_{\text{H-F}} = 47.2$ ,  $J_{\text{H-H}} = 6.0$  Hz, 2H), 4.23 (t,  $J = 6.0$  Hz, 2H), 2.25 (dqn,  $J_{\text{H-F}} = 26.0$  Hz,  $J_{\text{H-H}} = 6.0$  Hz, 2H); **<sup>13</sup>C NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.65, 134.49, 129.39, 128.97, 127.60, 126.72, 126.35, 123.63, 118.77, 106.62, 80.77 (d,  $J_{\text{C-F}} = 163.5$  Hz), 63.46 (d,  $J_{\text{C-F}} = 5.2$  Hz), 30.35 (d,  $J_{\text{C-F}} = 19.9$  Hz); **<sup>19</sup>F NMR** (376.5 MHz,  $\text{CDCl}_3$ )  $\delta$  -222.11; **IR** (film,  $\text{CDCl}_3$ )  $\nu$  3058, 2969, 1629, 1601, 1510, 1465, 1390, 1258, 1216, 1181, 1097, 1052, 838, 747  $\text{cm}^{-1}$ ; **HRMS** (EI/FI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{13}\text{FO}$   $[\text{M}]^+$  204.0950, found 205.0957.



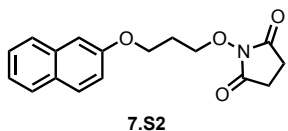
**2-(allyloxy)naphthalene (7.19):** The title compound was prepared according to the general procedure and isolated via silica gel column chromatography (hexanes) (27 mg, 29% yield). **<sup>1</sup>H NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78–7.71 (m, 3 H), 7.43 (td,  $J_1 = 8.0$  Hz,  $J_2 = 1.2$  Hz, 1 H), 7.33 (td,  $J_1 = 8.0$  Hz,  $J_2 = 1.2$  Hz, 1 H), 7.18 (dd,  $J_1 = 8.8$  Hz,  $J_2 = 2.8$  Hz, 1H), 7.15–7.14 (m, 1H), 6.14 (ddt,  $J_1 = 10.6$  Hz,  $J_2 = 17.4$  Hz,  $J_3 = 5.6$  Hz, 1H), 5.51–5.45 (m, 1H), 5.35–5.31 (m, 1H), 4.66 (adt,  $J = 5.6$  Hz,  $J_2 = 1.2$

Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.51, 134.48, 133.17, 129.40, 129.00, 127.63, 126.74, 126.33, 123.64, 118.96, 117.79, 106.98, 68.81; IR (film,  $\text{CDCl}_3$ )  $\nu$  3058, 1630, 1600, 1258, 1217, 1182, 1017, 837, 747  $\text{cm}^{-1}$ ; HRMS (EI/CI)  $m/z$  Calcd for  $\text{C}_{13}\text{H}_{12}\text{O}$   $[\text{M}]^+$  184.0888, found 184.0891.



**2-(3-(naphthalen-2-yloxy)propoxy)phenol (7.S1):** The title compound was prepared following the general procedure using

0.5 mmol of **7.17** and 1.0 mmol of TBAF(Cat)<sub>2</sub> and a reaction time of 48 h. The reaction was allowed to cool to room temperature, and the solvent was removed *in vacuo*. The resulting residue was purified via silica gel column chromatography (1:1 hexanes:DCM  $\rightarrow$  1:2 hexanes:DCM) to give **7.S1** as a colourless oil (27 mg, 18% yield).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69–7.63 (m, 3H), 7.36 (ddd,  $J_1 = 8.0$  Hz,  $J_2 = 6.8$  Hz,  $J_3 = 1.2$  Hz, 1 H), 7.26 (ddd,  $J_1 = 8.0$  Hz,  $J_2 = 6.8$  Hz,  $J_3 = 1.2$  Hz, 1H), 7.16–7.07 (m, 2H), 6.88–6.73 (m, 4H), 4.21 (qr,  $J = 6.0$  Hz, 4H), 2.27 (qn,  $J = 6.0$  Hz, 2H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.57, 145.95, 145.71, 134.47, 129.49, 129.02, 127.63, 126.73, 126.40, 123.70, 121.78, 120.14, 118.78, 114.70, 112.15, 106.67, 66.09, 64.60, 29.18; IR (film,  $\text{CDCl}_3$ )  $\nu$  3528, 3055, 2935, 2881, 1629, 1599, 1501, 1465, 1390, 1357, 1258, 1216, 1181, 1110, 1056, 838, 744  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  Calcd for  $\text{C}_{19}\text{H}_{18}\text{NaO}_3$   $[\text{M}+\text{Na}]^+$  317.1148, found 317.1145.



**1-(3-(naphthalen-2-yloxy)propoxy)pyrrolidine-2,5-dione (7.S2):**

To a 10 mL screw-top vial containing a magnetic stir bar, the following were successively added: **7.17** (132.6 mg, 0.5 mmol), *N*-hydroxysuccinimide (160.4 mg, 4.0 mmol), anhydrous MeCN (2.0 mL), and TBAF( $\text{H}_2\text{O}$ )<sub>3</sub> (315.5 mg, 1.0 mmol). The vial was capped, and the reaction mixture was placed in a pre-heated oil bath at 70  $^\circ\text{C}$ , and allowed to stir for 1 h. Subsequently, the vial was removed from the oil bath and

allowed to cool to room temperature. The reaction mixture was quenched with distilled H<sub>2</sub>O (10 mL), and extracted with Et<sub>2</sub>O (3 × 10 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (2:1 hexanes:ethyl acetate), giving pure **7.S2** as a white solid (34.8 mg, 23% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.77–7.72 (m, 3H), 7.43 (at, *J* = 7.2 Hz, 1H), 7.33 (at, *J* = 7.2 Hz, 1H), 7.18–7.12 (m, 2H), 4.35 (t, *J* = 6.4 Hz, 2H), 4.30 (t, *J* = 6.4 Hz, 2H), 2.68 (s, 4H), 2.26 (qn, *J* = 6.4 Hz, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.17, 156.63, 134.51, 129.36, 128.98, 127.58, 126.77, 126.32, 123.61, 118.81, 106.81, 74.36, 64.03, 28.27, 25.44; IR (film, CDCl<sub>3</sub>) ν 2944, 1721, 1629, 1600, 1260, 1204, 1073, 841, 814 cm<sup>-1</sup>; HRMS (ESI) *m/z* Calcd for C<sub>17</sub>H<sub>17</sub>NFNaO<sub>4</sub> [M+Na]<sup>+</sup> 322.1050, found 322.1044.

#### 7.5.5. Reaction kinetics

**Rate profile measurements with tetraalkylammonium fluoride–alcohol complexes:** To a 14 mL screw-top vial, were added **7.17** (53.0 mg, 0.2 mmol), MeCN (0.8 mL), and the [tetraalkylammonium fluoride–alcohol] complex (0.8 mmol). The vial was capped with a rubber septum, then stirred at 70 °C for 2 h (48 h in the case of TBAF(Cat)<sub>2</sub>). At the indicated time points, a small aliquot (< 80 μL) was taken with a syringe and needle. Each aliquot was filtered through a short plug of silica gel to quench the reaction, and the silica gel was washed with EtOAc (3 × 2 mL). The combined rinsings were concentrated *in vacuo*, and the resulting residue was analysed by <sup>1</sup>H NMR. The conversion at each time point was determined by integration of the methylene/allylic proton signals depicted in Figure 7.S1. The procedure was repeated three times for each complex. The resulting data were plotted, and numerical modelling established the second-order rate constant. The results are summarised in Table 7.3. For a representative complete data set, see below (Table 7.S1 and Figures 7.S2 and 7.S3).

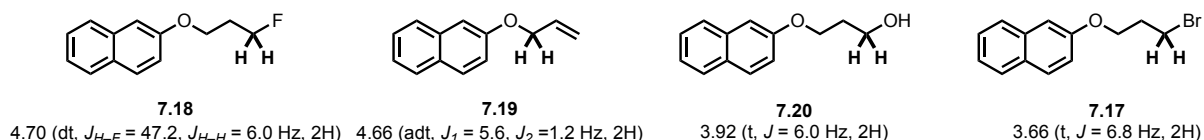


**Figure 7.S1.** Summary of key peaks for integration. The chemical shifts shown here are based on pure, isolated samples of each of these compounds. The corresponding alkoxyated products were generally not observed in measurable amounts, except in the case of TBAF(Cat)<sub>2</sub>, where the product was isolated and characterised. In the reaction mixture, the signal for the alcohol product (**7.20**) can appear as a broad triplet or broad quartet, depending on the concentration and pH of the solution.

### 7.5.6. Representative kinetic data

**Table 7.S1:** Kinetic measurements using TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub>.<sup>a</sup>

|       |         | Composition (%), Trial 1 |        |         |       |         | Composition (%), Trial 2 |        |         |       |         | Composition (%), Trial 3 |        |         |       |         | Fluoride (%) |           | Olefin (%) |           | Alcohol (%) |           | Ether (%) |           | Bromide (%) |           |
|-------|---------|--------------------------|--------|---------|-------|---------|--------------------------|--------|---------|-------|---------|--------------------------|--------|---------|-------|---------|--------------|-----------|------------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|
| Entry | t (min) | Fluoride                 | Olefin | Alcohol | Ether | Bromide | Fluoride                 | Olefin | Alcohol | Ether | Bromide | Fluoride                 | Olefin | Alcohol | Ether | Bromide | Ave.         | Std. Dev. | Ave.       | Std. Dev. | Ave.        | Std. Dev. | Ave.      | Std. Dev. | Ave.        | Std. Dev. |
| 1     | 0.5     | 6.5                      | 5.1    | 0.0     | 0.0   | 88.4    | 5.3                      | 4.6    | 0.0     | 0.0   | 90.1    | 6.1                      | 4.6    | 0.0     | 0.0   | 89.3    | 6.0          | 0.6       | 4.8        | 0.2       | 0.0         | 0.0       | 0.0       | 0.0       | 89.3        | 0.8       |
| 2     | 1       | 19.9                     | 12.4   | 0.0     | 0.0   | 67.7    | 20.3                     | 12.8   | 0.0     | 0.0   | 66.9    | 21.1                     | 13.4   | 0.0     | 0.0   | 65.5    | 20.4         | 0.6       | 12.9       | 0.5       | 0.0         | 0.0       | 0.0       | 0.0       | 66.7        | 1.1       |
| 3     | 1.5     | 31.3                     | 18.2   | 0.0     | 0.0   | 50.5    | 33.3                     | 19.0   | 0.0     | 0.0   | 47.7    | 33.9                     | 19.7   | 0.0     | 0.0   | 46.4    | 32.9         | 1.4       | 18.9       | 0.8       | 0.0         | 0.0       | 0.0       | 0.0       | 48.2        | 2.1       |
| 4     | 2       | 40.1                     | 21.5   | 0.0     | 0.0   | 38.3    | 41.4                     | 23.0   | 0.0     | 0.0   | 35.6    | 42.9                     | 23.8   | 0.0     | 0.0   | 33.3    | 41.5         | 1.4       | 22.8       | 1.2       | 0.0         | 0.0       | 0.0       | 0.0       | 35.7        | 2.5       |
| 5     | 2.5     | 46.2                     | 24.6   | 0.0     | 0.0   | 29.2    | 47.6                     | 26.1   | 0.0     | 0.0   | 26.3    | 49.1                     | 26.4   | 0.0     | 0.0   | 24.4    | 47.7         | 1.5       | 25.7       | 1.0       | 0.0         | 0.0       | 0.0       | 0.0       | 26.6        | 2.4       |
| 6     | 5       | 59.3                     | 29.8   | 0.0     | 0.0   | 10.9    | 59.6                     | 30.0   | 0.0     | 0.0   | 10.4    | 61.1                     | 30.4   | 0.0     | 0.0   | 8.5     | 60.0         | 1.0       | 30.1       | 0.3       | 0.0         | 0.0       | 0.0       | 0.0       | 9.9         | 1.3       |
| 7     | 10      | 66.2                     | 31.1   | 0.0     | 0.0   | 2.7     | 66.7                     | 31.7   | 0.0     | 0.0   | 1.7     | 66.2                     | 32.5   | 0.0     | 0.0   | 1.3     | 66.4         | 0.3       | 31.7       | 0.7       | 0.0         | 0.0       | 0.0       | 0.0       | 1.9         | 0.7       |
| 8     | 30      | 67.8                     | 32.2   | 0.0     | 0.0   | 0.0     | 67.6                     | 32.4   | 0.0     | 0.0   | 0.0     | 66.3                     | 33.7   | 0.0     | 0.0   | 0.0     | 67.2         | 0.8       | 32.8       | 0.8       | 0.0         | 0.0       | 0.0       | 0.0       | 0.0         | 0.0       |
| 9     | 60      | 67.2                     | 32.8   | 0.0     | 0.0   | 0.0     | 66.7                     | 33.3   | 0.0     | 0.0   | 0.0     | 66.4                     | 33.6   | 0.0     | 0.0   | 0.0     | 66.8         | 0.4       | 33.2       | 0.4       | 0.0         | 0.0       | 0.0       | 0.0       | 0.0         | 0.0       |
| 10    | 120     | 67.2                     | 32.8   | 0.0     | 0.0   | 0.0     | 66.7                     | 33.3   | 0.0     | 0.0   | 0.0     | 66.7                     | 33.3   | 0.0     | 0.0   | 0.0     | 66.9         | 0.3       | 33.1       | 0.3       | 0.0         | 0.0       | 0.0       | 0.0       | 0.0         | 0.0       |

|       |         | Concentration (M), Trial 1 |        |         |       |         | Concentration (M), Trial 2 |        |         |       |         | Concentration (M), Trial 3 |        |         |       |         | Fluoride (M) |           | Olefin (M) |           | Alcohol (M) |           | Ether (M) |           | Bromide (M) |           |
|-------|---------|----------------------------|--------|---------|-------|---------|----------------------------|--------|---------|-------|---------|----------------------------|--------|---------|-------|---------|--------------|-----------|------------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|
| Entry | t (min) | Fluoride                   | Olefin | Alcohol | Ether | Bromide | Fluoride                   | Olefin | Alcohol | Ether | Bromide | Fluoride                   | Olefin | Alcohol | Ether | Bromide | Ave.         | Std. Dev. | Ave.       | Std. Dev. | Ave.        | Std. Dev. | Ave.      | Std. Dev. | Ave.        | Std. Dev. |
| 1     | 0.5     | 0.016                      | 0.013  | 0.000   | 0.000 | 0.221   | 0.013                      | 0.012  | 0.000   | 0.000 | 0.225   | 0.015                      | 0.012  | 0.000   | 0.000 | 0.223   | 0.015        | 0.002     | 0.012      | 0.001     | 0.000       | 0.000     | 0.000     | 0.000     | 0.223       | 0.002     |
| 2     | 1       | 0.050                      | 0.031  | 0.000   | 0.000 | 0.169   | 0.051                      | 0.032  | 0.000   | 0.000 | 0.167   | 0.053                      | 0.033  | 0.000   | 0.000 | 0.164   | 0.051        | 0.001     | 0.032      | 0.001     | 0.000       | 0.000     | 0.000     | 0.000     | 0.167       | 0.003     |
| 3     | 1.5     | 0.078                      | 0.045  | 0.000   | 0.000 | 0.126   | 0.083                      | 0.047  | 0.000   | 0.000 | 0.119   | 0.085                      | 0.049  | 0.000   | 0.000 | 0.116   | 0.082        | 0.003     | 0.047      | 0.002     | 0.000       | 0.000     | 0.000     | 0.000     | 0.120       | 0.005     |
| 4     | 2       | 0.100                      | 0.054  | 0.000   | 0.000 | 0.096   | 0.104                      | 0.057  | 0.000   | 0.000 | 0.089   | 0.107                      | 0.060  | 0.000   | 0.000 | 0.083   | 0.104        | 0.004     | 0.057      | 0.003     | 0.000       | 0.000     | 0.000     | 0.000     | 0.089       | 0.006     |
| 5     | 2.5     | 0.116                      | 0.061  | 0.000   | 0.000 | 0.073   | 0.119                      | 0.065  | 0.000   | 0.000 | 0.066   | 0.123                      | 0.066  | 0.000   | 0.000 | 0.061   | 0.119        | 0.004     | 0.064      | 0.002     | 0.000       | 0.000     | 0.000     | 0.000     | 0.067       | 0.006     |
| 6     | 5       | 0.148                      | 0.074  | 0.000   | 0.000 | 0.027   | 0.149                      | 0.075  | 0.000   | 0.000 | 0.026   | 0.153                      | 0.076  | 0.000   | 0.000 | 0.021   | 0.150        | 0.002     | 0.075      | 0.001     | 0.000       | 0.000     | 0.000     | 0.000     | 0.025       | 0.003     |
| 7     | 10      | 0.166                      | 0.078  | 0.000   | 0.000 | 0.007   | 0.167                      | 0.079  | 0.000   | 0.000 | 0.004   | 0.166                      | 0.081  | 0.000   | 0.000 | 0.003   | 0.166        | 0.001     | 0.079      | 0.002     | 0.000       | 0.000     | 0.000     | 0.000     | 0.005       | 0.002     |
| 8     | 30      | 0.170                      | 0.080  | 0.000   | 0.000 | 0.000   | 0.169                      | 0.081  | 0.000   | 0.000 | 0.000   | 0.166                      | 0.084  | 0.000   | 0.000 | 0.000   | 0.168        | 0.002     | 0.082      | 0.002     | 0.000       | 0.000     | 0.000     | 0.000     | 0.000       | 0.000     |
| 9     | 60      | 0.168                      | 0.082  | 0.000   | 0.000 | 0.000   | 0.167                      | 0.083  | 0.000   | 0.000 | 0.000   | 0.166                      | 0.084  | 0.000   | 0.000 | 0.000   | 0.167        | 0.001     | 0.083      | 0.001     | 0.000       | 0.000     | 0.000     | 0.000     | 0.000       | 0.000     |
| 10    | 120     | 0.168                      | 0.082  | 0.000   | 0.000 | 0.000   | 0.167                      | 0.083  | 0.000   | 0.000 | 0.000   | 0.167                      | 0.083  | 0.000   | 0.000 | 0.000   | 0.167        | 0.001     | 0.083      | 0.001     | 0.000       | 0.000     | 0.000     | 0.000     | 0.000       | 0.000     |

<sup>a</sup> The % composition was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture.

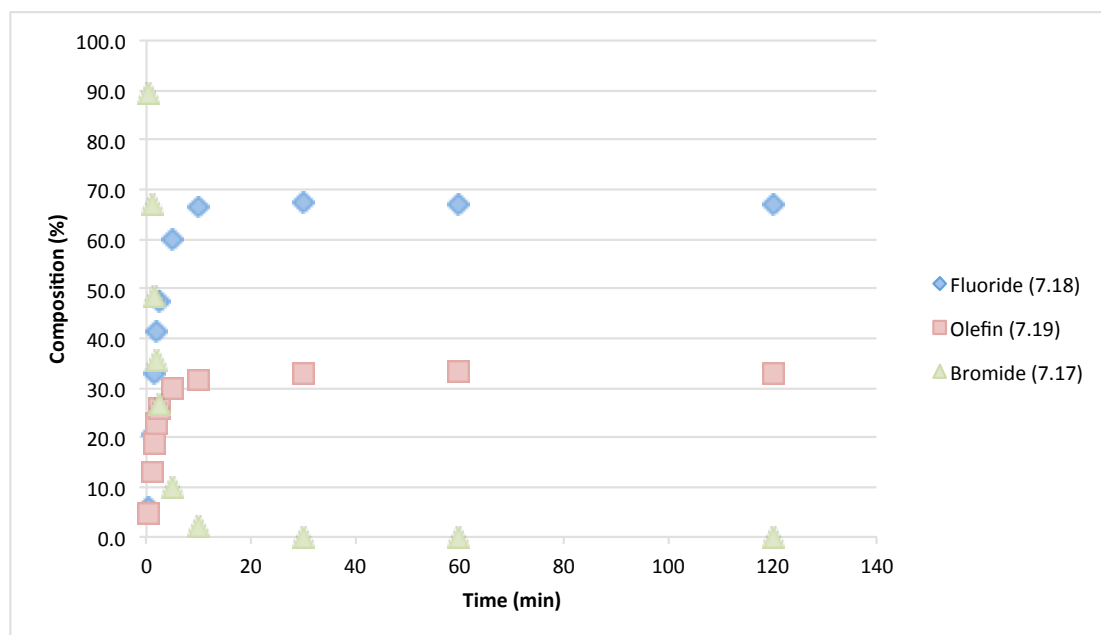


**Figure 7.S2:** Rate profile with TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub>. Each data point represents the average value of three independent trials.

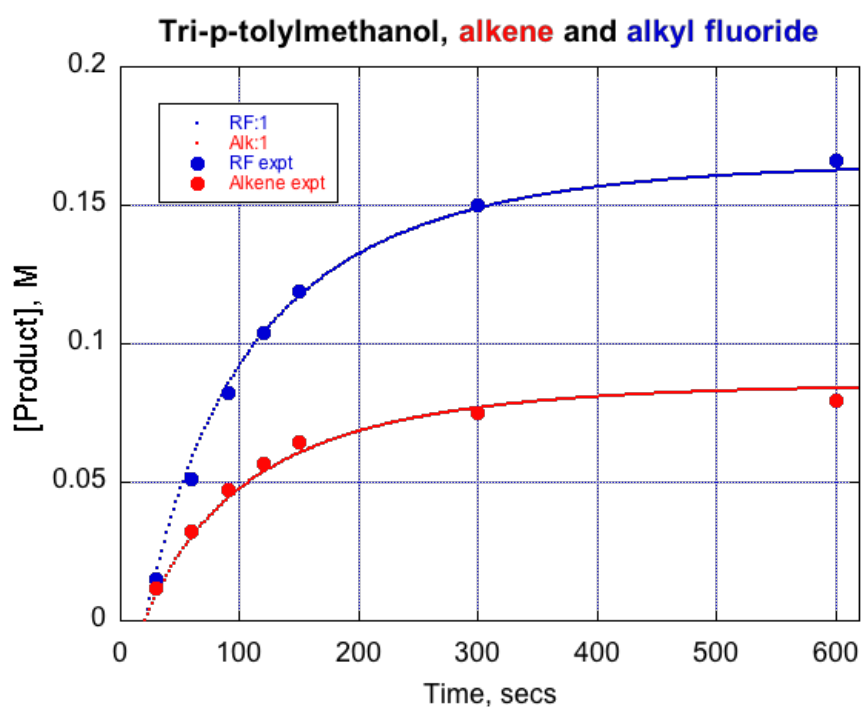


**Figure 7.S3:** Resulting curve fits. The reaction was modelled as second-order, following a rate equation of the form,  $\text{rate} = k_{\text{obs}}[\text{F}^-][\text{SM}]$ . Data points from 30 sec to 10 min were included, and analysis was performed using the Berkeley Madonna application. Output values are shown in Table 7.3.

### 7.5.7. Computational methods

Optimisations were performed with *Gaussian09*, rev C.1 at the density functional level of theory.<sup>26</sup> Stationary points were optimised with the dispersion-corrected range-separated wB97XD functional<sup>27</sup> in combination with the 6-31G(d) basis set for C, H and O, 6-31+G(d) for F, and the LANL08 scalar relativistic effective core potential<sup>28</sup> and associated triple zeta valence + diffuse basis set for Br. All optimisations were performed with a conductor-like polarisable continuum model of the reaction solvent, acetonitrile.<sup>26,29</sup> Free energies calculated in the solution phase incorporate a correction factor of  $RT\ln(24.5) = 2.1$  kcal/mol to account for the change from a standard state of 1 atm to 1 mol/L. Stationary points were confirmed as minima and transition structures by the presence of zero and exactly one imaginary harmonic vibrational frequency, respectively. Free energies include unscaled zero point vibrational energies and are corrected for the presence of low frequencies ( $< 50\text{ cm}^{-1}$ ), which are unlikely to be well described by a harmonic oscillator, by scaling these values to  $50\text{ cm}^{-1}$  in the evaluation of vibrational components to the entropy.<sup>30</sup> Calculation of natural atomic charges was performed using *NBO v3.1*.<sup>31</sup> Unless otherwise stated, Gibbs free energies are quoted in kcal/mol at 298 K at a standard state of 1 mol/L.

## 7.6. REFERENCES

- (1) Yonezawa, T.; Sakamoto, Y.; Nogawa, K. Preparation of Tetrabutylammonium Fluoride-Alcohol Adducts as Fluorination Agents. *Jpn. Kokai Tokkyo Koho JP 06316551 A*, Nov 15 1994.
- (2) Kim, D. W.; Ahn, D.-S.; Oh, Y.-H.; Lee, S.; Kil, H. S.; Oh, S. J.; Lee, S. J.; Kim, J. S.; Ryu, J. S.; Moon, D. H.; Chi, D. Y. *J. Am. Chem. Soc.* **2006**, *128*, 16394–16397.



- (3) Kim, D. W.; Jeong, Lim, S. T.; Sohn, M.-H.; Katzenellenbogen, J. A.; Chi, D. Y. *J. Org. Chem.* **2008**, *73*, 957–962.
- (4) Kim, D. W.; Jeong, H.-J.; Lim, S. T.; Sohn, M.-H. *Angew. Chem. Int. Ed.* **2008**, *47*, 8404–8406.
- (5) Deng, H.; O'Hagan, D. *Curr. Opin. Chem. Biol.* **2008**, *12*, 582–592.
- (6) Adalsteinsson, O.; Lamotte, A.; Baddour, R. F.; Colton, C. K.; Pollak, A.; Whitesides, G. M. *J. Mol. Catal.* **1979**, *6*, 199–225.
- (7) Notari, R. E. *J. Pharm. Sci.* **1969**, *58*, 1064–1068.
- (8) Ames, D. E.; Grey, T. F. *J. Chem. Soc.* **1955**, 631–636.
- (9) Anzenbacher, P.; Jursíková, K.; Lynch, V. M.; Gale, P. A.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 11020–11021.
- (10) Libra, E. R.; Scott, M. J. *Chem. Commun.* **2006**, 1485–1487.
- (11) Chen, C.-H.; Leung, M.-k. *Tetrahedron* **2011**, *67*, 3924–3935.
- (12) Sun, H.; DiMagno, S. G. *J. Am. Chem. Soc.* **2005**, *127*, 2050–2051.
- (13) Nolte, C.; Ammer, J.; Mayr, H. *J. Org. Chem.* **2012**, *77*, 3325–3335.
- (14) Oh, Y.-H.; Ahn, D.-S.; Chung, S.-Y.; Jeon, J.-H.; Park, S.-W.; Oh, S. J.; Kim, D. W.; Kil, H. S.; Chi, D. Y.; Lee, S. *J. Phys. Chem. A* **2007**, *111*, 10152–10161.
- (15) Pliego, J. R.; Piló-Veloso, D. *J. Phys. Chem. B* **2007**, *111*, 1752–1758.
- (16) Matthias Bickelhaupt, F.; Baerends, E. J.; Anibbering, N. M. M. *Chem. Eur. J.* **1996**, *2*, 196–207.
- (17) Otwinowski, Z.; Minor, W. In *Methods in Enzymology*; Carter, C. W., Jr., Sweet, R. M., Eds.; Academic Press: New York, 1997; Vol. Volume 276, p 307–326.
- (18) CrysAlisPro (Agilent Technologies, Oxford, 2011).
- (19) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.

- (20) Palatinus, L.; Chapuis, G. *J. Appl. Crystallogr.* **2007**, *40*, 786–790.
- (21) Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Crystallogr.* **2003**, *36*, 1487.
- (22) Cooper, R. I.; Thompson, A. L.; Watkin, D. J. *J. Appl. Crystallogr.* **2010**, *43*, 1100–1107.
- (23) Jeon, W. S.; Kim, E.; Ko, Y. H.; Hwang, I.; Lee, J. W.; Kim, S.-Y.; Kim, H.-J.; Kim, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 87–91.
- (24) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596–13597.
- (25) Gozzo, F. C.; Fernandes, S. A.; Rodrigues, D. C.; Eberlin, M. N.; Marsaioli, A. J. *J. Org. Chem.* **2003**, *68*, 5493–5499.
- (26) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995–2001.
- (27) Chai, J.-D.; Head-Gordon, M. *PCCP* **2008**, *10*, 6615–6620.
- (28) Roy, L. E.; Hay, P. J.; Martin, R. L. *J. Chem. Theory Comput.* **2008**, *4*, 1029–1031.
- (29) Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669–681.
- (30) Ribeiro, R. F.; Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2011**, *115*, 14556–14562.
- (31) NBO Version 3.1, E. D. Glendening, A. E. Reed, J. E. Carpenter, and F. Weinhold.

## 7.7. CONTRIBUTIONS

The following individuals directly contributed to the work described in this Chapter: Keary M. Engle, George, W. Pidgeon, Guy T. Giuffredi, Dr. Amber L. Thompson, Prof. Robert S. Paton, Prof. John M. Brown, and Prof. Véronique Gouverneur. K.M.E., J.M.B., and V.G. conceived the project. Complexes were synthesised and spectroscopically characterised by K.M.E. and G.W.P. X-ray crystallography was performed by G.W.P., G.T.G., K.M.E., and A.L.T. Reaction kinetics were carried out by K.M.E., and the resulting

data was numerically modelled by J.M.B. Computational work was undertaken by R.S.P. Section 7.2.4 was adapted with permission from original work by R.S.P. The rest of the Chapter was written by K.M.E. with input from J.M.B. and V.G.

## **CHAPTER 8**

### **OUTLOOK AND CONCLUSION**

## 8.1. SUMMARY AND PERSPECTIVE

Part II of this Thesis has presented a hydrogen bonding approach for tuning the reactivity of fluoride anion. Chapter 6 began with an introduction of organofluorine compounds, their growing importance to human life, and representative synthetic approaches to access them. Focus then shifted specifically to the idea of using hydrogen bonding contacts to control the reactivity profile of fluoride. Chapter 7 discussed our original research in this area, in which alcohol and polyol hydrogen-bond donors were studied using a three-pronged approach combining structural characterisation, kinetic analysis, and DFT calculations (Chapter 7). These studies have provided a valuable foundation for the development of improved hydrogen bonding systems for diverse applications. Current efforts in the Gouverneur, Brown, and Paton laboratories are focused on addressing some of the lingering questions pertaining to fluoride–alcohol complexes and extending this concept to other hydrogen-bond donors. Part II of this Thesis concludes by highlighting these ongoing efforts.

## 8.2. ALCOHOL HYDROGEN-BOND DONORS

### 8.2.1. Neutron diffraction studies

Though much insight has been gained through the single-crystal X-ray diffraction studies of alcohol–fluoride complexes presented in Chapter 7, one of the fundamental limitations of X-ray crystallography is its poor ability to resolve hydrogen atom positions. Generally, in structures of organic molecules based on X-ray diffraction data, hydrogen atoms are positioned using computational modelling based on established geometrical constraints and partial electron-density maps. In our study, there are several points of concern in this respect. Firstly, fluoride is known to be a strong Brønsted base, meaning that (1) the O–H---F bond could be elongated compared to related O–H---X model systems and

(2) the extent of elongation would not be accurately determinable with X-ray data. Moreover, one of our major goals is to understand the correlation (if any) between solid-state O–H...F bond distances and reactivity trends. Although we are able to see the hydrogen atoms in the difference Fourier maps of our X-ray structures, we have been unable to measure the O–H...F bond distances with a high level of accuracy, which is an impediment to the realisation of this goal.

To rectify this problem, we have calibrated our X-ray measurements by performing neutron diffraction on two representative alcohol–fluoride complexes, TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**8.1**) and TBAF(NPG)<sub>2</sub> (**8.2**) (Figure 8.1). Key to the success of this effort was the ability to grow large crystals of both samples. The single-crystal for TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**8.1**) that was used for analysis, for example, was approximately 8 cm<sup>3</sup> in volume and was grown *via* repeated seeding through eight generations over a one-month period. To the best of our knowledge, these are the first examples of alcohol–fluoride complexes that have been characterised with single-crystal neutron diffraction. The experiments were completed at the SXD beamline at ISIS,<sup>1</sup> and the structures are currently being refined.

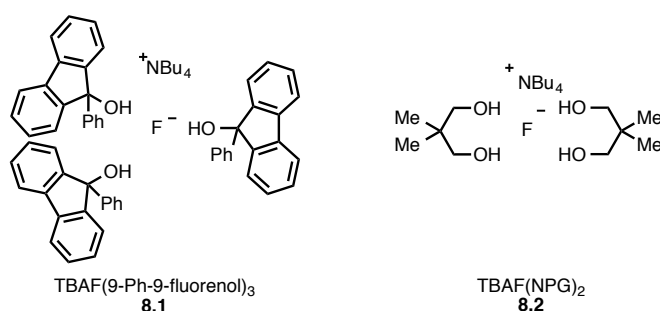


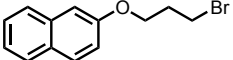
**Figure 8.1:** TBAF–alcohol complexes that have recently been characterised by single-crystal neutron diffraction at ISIS.

### 8.2.2. Further mechanistic studies

Beyond deepening our structural investigations of fluoride–alcohol complexes, we have continued to perform additional kinetic experiments to understand the root cause of their observed reactivity profiles. While the first-pass kinetic data described in Chapter 7 established that the hydrogen-bond donor can play a dominant role in influencing kinetic reactivity and selectivity in nucleophilic fluorination reactions, further experiments are still needed to elucidate the mechanistic nuances of these reaction systems. To this end, a series of follow-up studies are currently underway in the Gouverneur laboratory in collaboration with the Brown group at Oxford.

As an illustrative example of the type of insights that have arisen from this work, one interesting set of experiments revealed that the reaction concentration dramatically influences the observed  $S_N2$  versus E2 selectivity (Entries 2–4, Table 8.1, and Figures 8.2 and 8.3). When the concentration was decreased, reactions with TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**8.4**) began to give preferentially E2 elimination. An explanation for this observation is that as the effective concentration of alcohol around fluoride decreases, fluoride displays a reactivity profile that is more akin to that of its “naked” state (*e.g.*, as seen in “anhydrous” TBAF), which supports the mechanistic model outlined in Chapter 7. Indeed, when the amount of *p*-Tol<sub>3</sub>COH in solution was increased while keeping other variables constant, the selectivity improved (Entry 1). These findings suggest that caution must be taken in extrapolating insights from solid-state structural data to conclusions about solution-state behaviour. By virtue of the weak coordination strength of fluoride–alcohol molecular assemblies, the complexes become fragile at low concentration, which was borne out in the reactivity data. Our preliminary analysis suggests that the reaction follows a second-order rate law, and further experiments are ongoing.

**Table 8.1.** Summary of reactivity data for concentration study.<sup>a</sup>



**8.3**

2 equiv. TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**8.4**)

Additive

MeCN

70 °C, 2 h



ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>F **8.5**

ArOCH<sub>2</sub>CH=CH<sub>2</sub> **8.6**

ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH **8.7**

ArOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OR **8.8**

| Reaction Composition after 2 h (% , <sup>1</sup> H NMR) |                    |                                      |          |        |         |       |         |
|---------------------------------------------------------|--------------------|--------------------------------------|----------|--------|---------|-------|---------|
| Entry                                                   | [ <b>8.3</b> ] (M) | Additive                             | Fluoride | Olefin | Alcohol | Ether | Bromide |
| 1                                                       | 0.25               | 4 eq. <i>p</i> -Tol <sub>3</sub> COH | 79       | 21     | 0       | 0     | 0       |
| 2                                                       | 0.25               | ---                                  | 67       | 33     | 0       | 0     | 0       |
| 3                                                       | 0.0625             | ---                                  | 51       | 49     | 0       | 0     | 0       |
| 4                                                       | 0.025              | ---                                  | 43       | 57     | 0       | 0     | 0       |

<sup>a</sup> The % composition was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. Values for 0.25 M (additive free) represent average of three independent trials. Other values are the result of single trials.

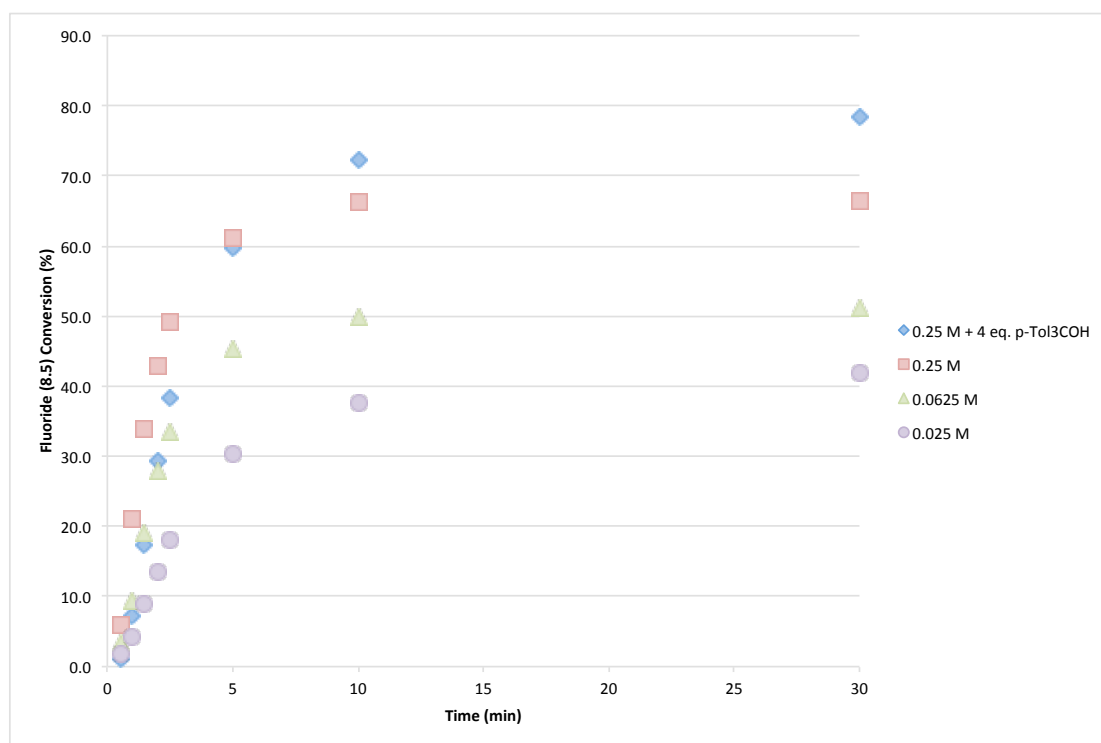


**Figure 8.2.** Summary of rate profiles for fluoride (**8.5**) product formation with TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**8.4**) in MeCN at different concentrations. Values for 0.25 M (additive-free) represent the average of three independent trials. Other values represent single trials.



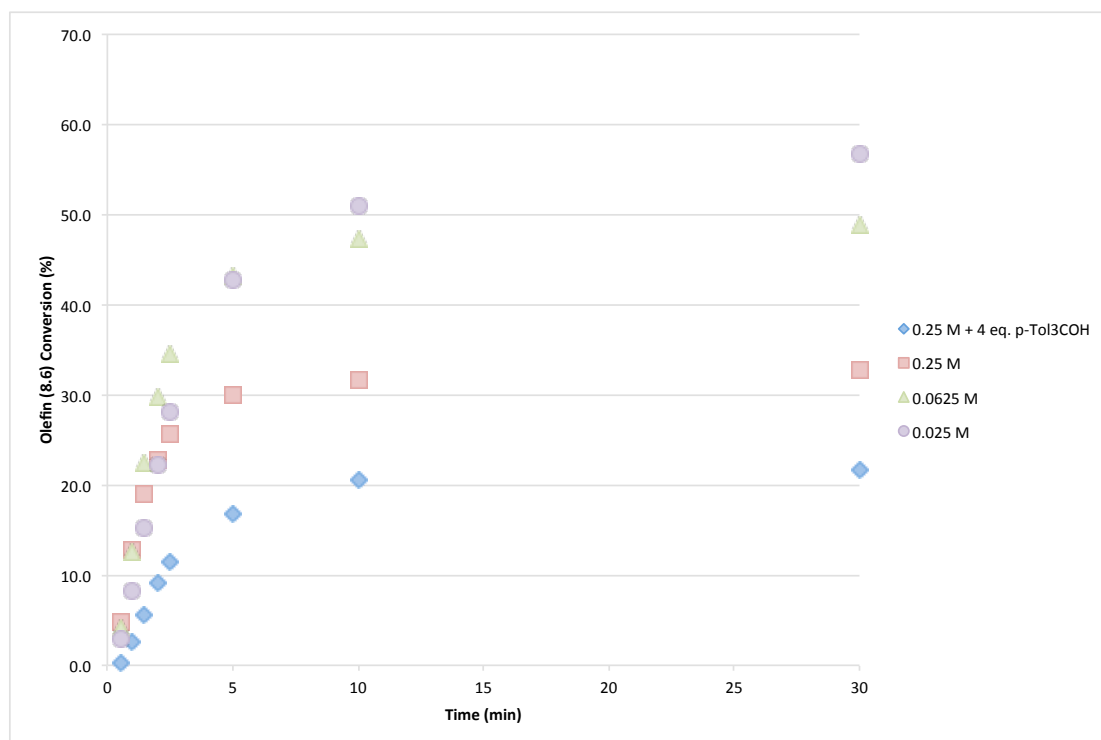


**Figure 8.3.** Summary of rate profiles for olefin (**8.6**) product formation with TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**8.4**) in MeCN at different concentrations. Values for 0.25 M (additive-free) represent the average of three independent trials. Other values represent single trials.

### 8.3. UREA HYDROGEN-BOND DONORS

#### 8.3.1. Synthesis, Structure, and Reactivity

A major component of the long-term vision for this project is to gain an understanding of the coordination chemistry and reactivity trends of fluoride anion with a variety of different hydrogen bonding motifs. Thus far, we have primarily focused on alcohols, but we have recently initiated experiments with other functional groups.

Our results in the alcohol series have suggested that relatively weak, non-acidic hydrogen-bond donors ( $pK_a > 11$ ) are suitable for controlling the reactivity of fluoride anion, but thus far, only a very limited subset of hydrogen-bond donors have been assayed, both in terms of hydrogen-bonding strength and anion-binding geometry. Intriguing classes of hydrogen-bond donors for future study include thiols, amines, amides, thioamides,

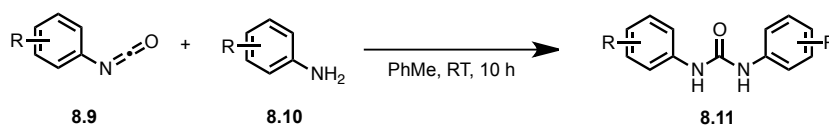
carbamates, thiocarbamates, guanidines, amidines, ureas, and thioureas. The latter four, in particular, are enticing vehicles for delivering chiral F<sup>-</sup> for asymmetric C–F bond formation.

Due to their unique hydrogen-bond donor capabilities, ureas and thioureas are widely used in a range of different molecular recognition applications.<sup>2,3</sup> With fluoride, ureas and thiourea hydrogen-bonding motifs have been used for anion sensing<sup>4-9</sup> and organocatalysis.<sup>10,11</sup> However, despite extensive solid-state characterisation of (thio)urea hydrogen bond complexes with other anions and hydrogen-bond acceptors,<sup>2</sup> comparatively little X-ray crystallographic data is available with fluoride. Rare exceptions include Mak's early studies with tetraalkylammonium fluoride salts in complexation with unfunctionalised urea<sup>12</sup> and thiourea.<sup>13,14</sup> Additionally, there are important examples of structurally similar polyamides that have been complexed with fluoride and examined by X-ray crystallography.<sup>15</sup> Thus, while the interaction between (thio)ureas and fluoride has often been invoked and has been studied analytically, spectroscopically, and computationally,<sup>9</sup> it has not yet been systematically examined in the solid state. Moreover, despite the attention placed on using (thio)ureas for fluoride recognition, very little is known regarding their impact on the reactivity profile of fluoride through hydrogen bonding.

At the outset, we were attracted to the idea of using 1,3-diarylureas as hydrogen-bond donors for several reasons. We hypothesised that aromatic substitution on the nitrogen atoms would provide added planarity and rigidity, which could potentially encourage the corresponding tetraalkylammonium fluoride complexes to be crystalline solids at room temperature. Furthermore, 1,3-diaryl substitution would provide the opportunity to vary systematically the acidity of the N–H bond through the introduction of substituents on the aromatic ring, which would allow linear free-energy relationships to be examined.

To initiate this study, we prepared a series of different 1,3-diarylureas. Based on preliminary experiments, the most convenient and high-yielding procedure for our purposes

was found to be direct coupling of a 1:1 ratio of the corresponding commercially available isocyanate and aniline (Scheme 8.1). This methodology proved to be reliable, high-yielding, and functional group-tolerant. Purification could be performed *via* filtration, as the 1,3-diarylureas readily precipitated from PhMe, while both starting materials remained in solution. Lower yields were observed with electron-deficient anilines, presumably because of attenuated nucleophilicity.



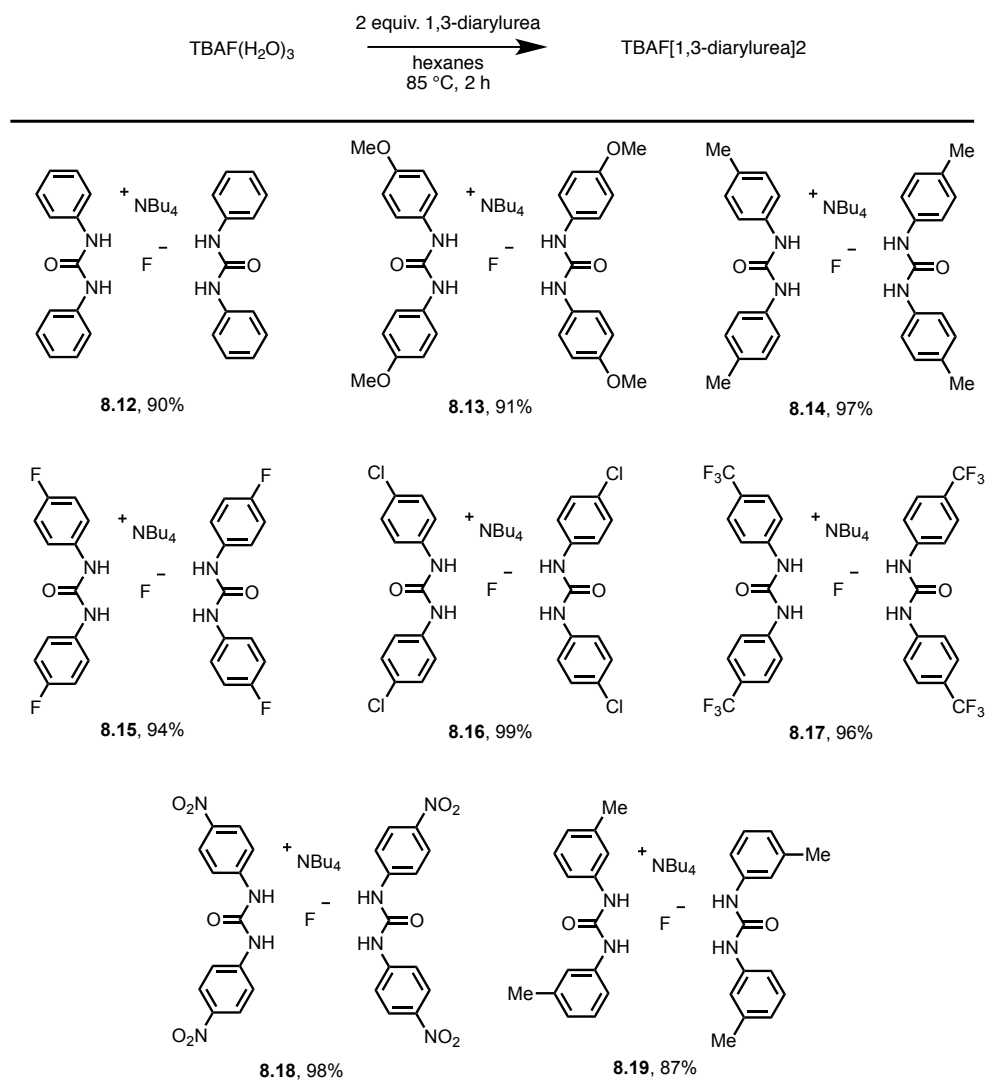
**Scheme 8.1:** Synthesis of 1,3-diarylureas.

To attempt complexation with fluoride, we employed the same method that we used previously for synthesising the fluoride–alcohol complexes: refluxing a 2:1 mixture of the 1,3-diarylurea and TBAF(H<sub>2</sub>O)<sub>3</sub> for 2 h in hexanes (pseudo-Dean–Stark conditions). We proceed to test the ureas that we had synthesised, as well as other commercially available 1,3-diarylureas.

We were delighted to find that nearly all of the 1,3-diarylureas that were examined formed solid complexes with tetraalkylammonium fluoride salts (Table 8.2), a far higher success rate than we saw with the alcohol series. In general, 1,3-diarylureas tended to give complexes with well-defined 2:1 coordination stoichiometry. The complexes were found to be more soluble in organic solvents than the 1,3-diarylureas themselves, which was important for characterisation, as well as for ultimately growing crystals for X-ray diffraction experiments. Literature precedent suggested that with stronger electron-withdrawing groups, such as CF<sub>3</sub> and NO<sub>2</sub>, deprotonation to form bifluoride and the corresponding *N*-anion could take place in MeCN if excess fluoride was used.<sup>5</sup> We found, however, that under our conditions, this was not the case. In the preparation of **8.18**, for

instance, we observed only trace amounts of a red solid, which we presumed to be the deprotonated urea anion.

**Table 8.2.** Preparation of TBAF[1,3-diarylurea]<sub>2</sub> complexes.<sup>a</sup>



<sup>a</sup> Isolated yields are shown.

In addition to having a tendency to exist as solids, complexes in this series were found to possess inherently high crystallinity. Indeed, X-ray crystal structures for all of the complexes shown in Table 8.2 have been solved. As a representative example, the crystal structure of TBAF[1,3-diphenylurea]<sub>2</sub> (**8.12**) is shown in Figure 8.4. We found that large block crystals of this complex could be grown overnight by layering hexanes onto a

saturated solution of the complex in EtOAc. The crystal structure shows clear 2:1 coordination stoichiometry. In the unit cell, fluoride lies on a special position, such that there are in effect two distinct fluoride hydrogen bonding environments, with each fluoride anion serving as an inversion centre bound to two symmetrically disposed 1,3-diphenylurea molecules. The first fluoride has N---F bond distances of  $2 \times 2.625$  Å and  $2 \times 2.862$  Å and a torsion angle between urea planes of  $64.11^\circ$ . The second fluoride has N---F bond distances of  $2 \times 2.689$  Å and  $2 \times 2.705$  Å and a torsion angle between urea planes of  $43.11^\circ$ . The average N---F bond distance, 2.719 Å, is substantially longer than typical O---F bond distances observed in the fluoride–alcohol series.

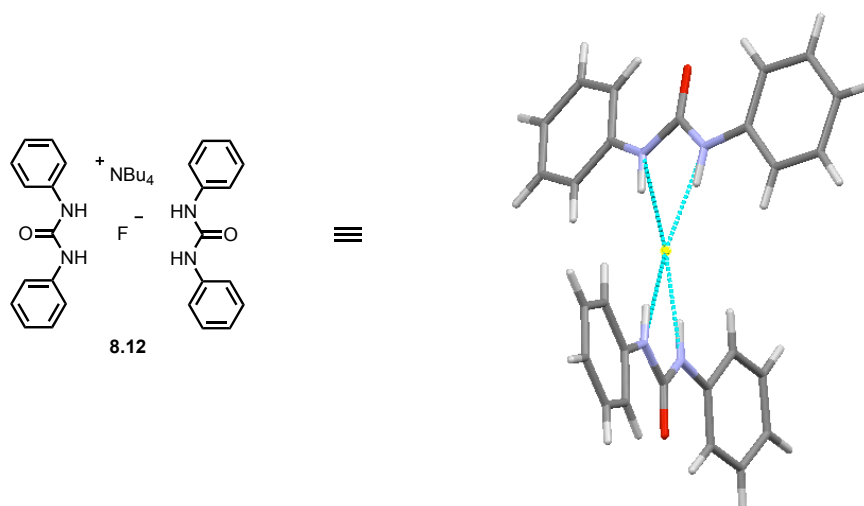


**Figure 8.4:** X-ray crystal structure of TBAF[1,3-diphenylurea]<sub>2</sub> (**8.12**). Tetrabutylammonium counteranion omitted for clarity.

In addition to the complexes shown in Table 8.2, we have solved X-ray crystal structures for more than 10 other fluoride–1,3-diarylurea complexes, and we have identified four recurring solid-state binding motifs (Figure 8.5).

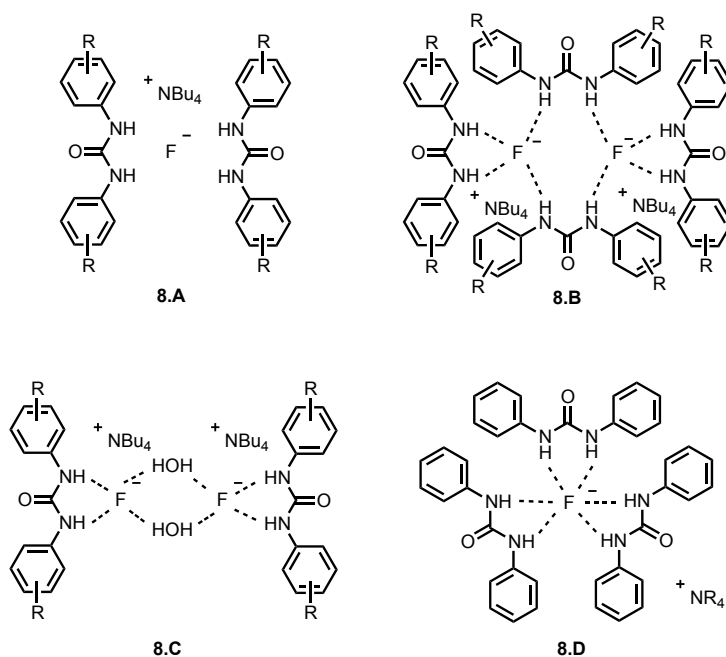
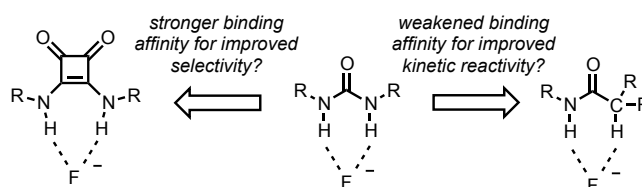


**Figure 8.5:** Four urea–fluoride binding modes observed in X-ray crystal structures of the 1,3-diarylurea series.

Having established the viability of forming stable fluoride–1,3-diarylurea complexes and determining their crystal structures, the next phase of the investigation will be to observe how the reactivity profile of fluoride varies as the electronic properties of the aryl ring are changed. Our preliminary findings are quite revealing. The kinetic reactivities of all of the complexes shown in Table 8.2 are 2–3 orders of magnitude lower than with fluoride–alcohol complexes. Reactions typically take 48 h to run to completion but exhibit a higher ratio of  $S_N2$  to E2. Interestingly, the  $S_N2$  pathway seems to be less sensitive than the E2 pathway to the electronic influence of the substituents on the aryl ring. These results are consistent with the computational results presented in Chapter 7 and with our working mechanistic model. DFT calculations and mechanistic studies are currently underway in collaboration with the Paton and Brown groups, respectively, at Oxford.

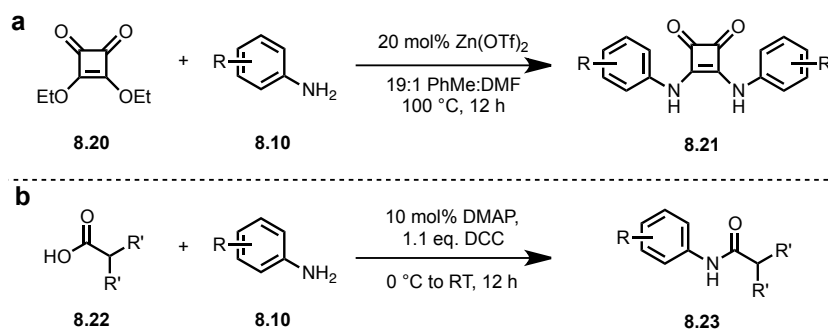
### 8.3.2. Related Complexes

With the knowledge gleaned from the fluoride–urea project, we have begun exploring whether it is possible to tune fluoride reactivity in a more dramatic fashion through the use of alternative N–H hydrogen-bond donors (Scheme 8.2). In the case of *N,N'*-disubstituted squaramides, we hypothesised that increased N–H bond acidity might improve the  $S_N2$  to E2 ratio, by decreasing the effective basicity of fluoride while maintaining its nucleophilicity. In the case of amides bearing an acidic  $\alpha$ -C–H bond, we hypothesised that we could obtain enhanced kinetic reactivity by reducing the strength of second hydrogen-bond donor relative to the urea case.



**Scheme 8.2.** Design ideas for alternative N–H hydrogen-bond donor systems.

Both classes of hydrogen-bond donors could readily be synthesised using the reactions shown in Scheme 8.3. To prepare *N,N'*-diarylsquaramides, we employed the procedure developed by Taylor and coworkers, condensing diethyl squarate with 2 equiv. of the desired aniline in the presence of catalytic  $Zn(OTf)_2$  (Scheme 8.3a).<sup>16</sup> For *N*-aryl amides, we used DCC coupling of the corresponding carboxylic acid and aniline (Scheme 8.3b). Both procedures were found to be highly robust, scalable, and operationally simple to conduct.

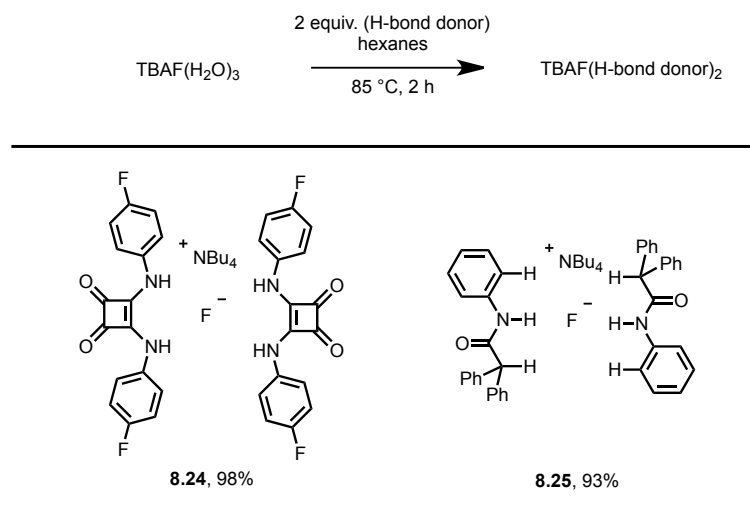


**Scheme 8.3.** Synthesis of (a) *N*-arylamide and (b) *N,N'*-diarylsquaramide<sup>16</sup> hydrogen-bond donors.

With straightforward routes to access these two classes of hydrogen-bond donors in place, we then moved on to examine their potential for binding fluoride in the solid state. Based on our results with the 1,3-diarylsquaramide series, we were fairly confident that *N*-arylamides would be stable against deprotonation by  $\text{F}^-$ . *N,N'*-Diarylsquaramides, on the other hand, are known to have more acidic N–H bonds than 1,3-diarylsquaramides. This is due to the capability of the squaramide conjugate base to delocalise negative charge over the cyclobutene-1,2-dione ring. While evidence for the formation of a 1:1 fluoride:squaramide complex in solution has been put forward,<sup>17</sup> the introduction of additional equivalents of fluoride in this same system was found to trigger deprotonation. With other squaramide-based anion receptors, deprotonation by fluoride was found to be predominant even with one equivalent of  $\text{F}^-$ .<sup>18</sup>

With these considerations in mind, we exposed both new classes of N–H hydrogen-bond donors to our standard complexation conditions. To our delight, in both cases, complexation was successful with no evidence of deprotonation. In this way, we have been able to synthesise a new series of  $\text{TBAF}[N,N'\text{-diarylsquaramide}]_2$  and  $\text{TBAF}[N,2,2\text{-triarylsquaramide}]_2$  complexes, representative examples of which are shown in Table 8.3.



**Table 8.3.** Preparation of TBAF[H-bond donor]<sub>2</sub> complexes.<sup>a</sup>

<sup>a</sup> Isolated yields are shown.

Both of these new classes of complexes have proven to be amenable to characterisation by single-crystal X-ray diffraction. In the resulting structure of TBAF[*N,N'*-bis(4-fluorophenyl)squaramide]<sub>2</sub> (**8.24**), which crystallised as a THF solvate, fluoride is four-coordinate, bound to two molecules of *N,N'*-bis(4-fluorophenyl)squaramide (Figure 8.6). The average N---F bond distance is 2.67 Å, compared to approximately 2.70–2.72 Å observed in TBAF[1,3-diarylurea]<sub>2</sub> complexes. This shortening in N---F bond distance is consistent with the expected increase in the hydrogen-bond donor strength of squaramides relative to ureas. The torsion angle of the two squaramides around fluoride is approximately 60°, which is in the range of many TBAF[1,3-diarylurea]<sub>2</sub> complexes. Notably, **8.24**•THF and other members of this series (not shown) are the first fluoride–squaramide complexes to be characterised by X-ray crystallography.

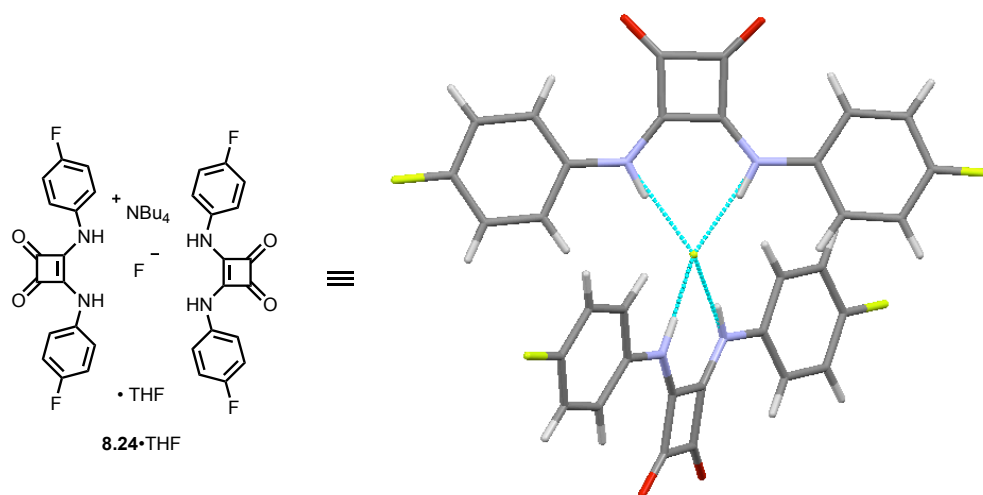


**Figure 8.6:** X-ray crystal structure of TBAF[*N,N'*-bis(4-fluorophenyl)squaramide]<sub>2</sub>•(THF) (**8.24**•THF). Tetrabutylammonium counteranion and THF solvent omitted for clarity.

The crystal structure of TBAF(*N*,2,2-triphenylacetamide)<sub>2</sub> (**8.25**) shows two canonical N–H...F hydrogen bonds with N...F distances of 2.606 Å and 2.547 Å (Figure 8.7). Additionally, fluoride is stabilised by short contacts with the *ortho*-C–H bond of the phenyl group attached to nitrogen and the acidic  $\alpha$ -C–H bond. The two  $\alpha$ -C...F distances are 3.244 Å and 3.220 Å, and the two *ortho*-C...F distances are 3.332 Å and 3.406 Å.

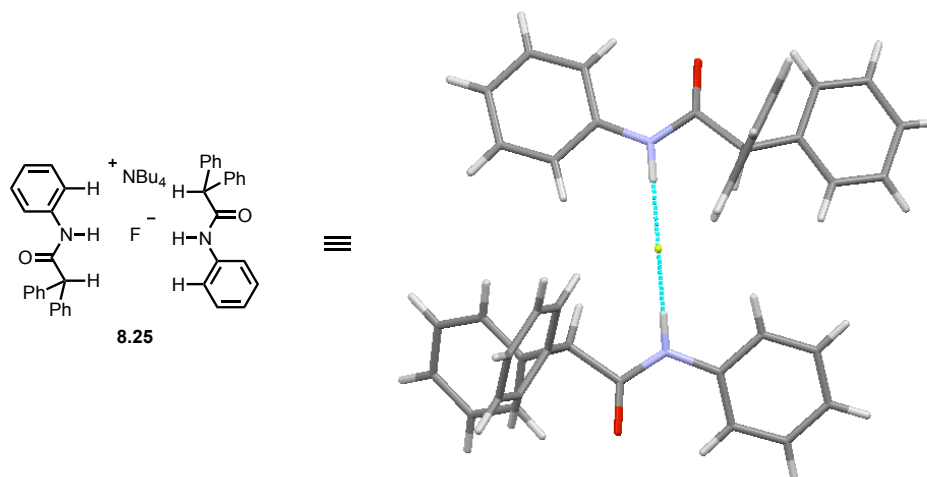


**Figure 8.6:** X-ray crystal structure of TBAF[*N*,2,2-triphenylacetamide]<sub>2</sub> (**8.25**). Tetrabutylammonium counteranion omitted for clarity.

With the synthetic routes to these complexes established and their solid-state structures confirmed, analysis of their reactivity is presently underway in the Gouverneur group. Among the intriguing questions that we aim to address in these systems, we are

particularly curious whether the reactivity trends follow expectations based on the anion binding designs put forward in Scheme 8.2.

## 8.4. CONCLUSIONS

Part II of this Thesis has highlighted recent progress towards understanding the influence of hydrogen bonding on the reactivity of fluoride anion and exploiting this knowledge to design superior reagents. Our initial work with alcohol and polyol hydrogen-bond donors has served as the foundation for the continued evolution of this research programme. The combination of solid-state characterisation, reaction kinetics, and computational analysis offers a powerful platform for the analysis of fluoride reactivity under different hydrogen bonding environments. The working mechanistic model that has arisen from this work takes into account the ability of di-, tri-, and tetracoordinate fluoride species to equilibrate in solution, with each of these species having different activation barriers for  $S_N2$  and E2. Higher coordination states give preferential reactivity for the  $S_N2$  pathway, a pattern that has been borne out experimentally and computationally.

More broadly, the notion of tuning fluoride nucleophilicity versus basicity in this manner extends to other reaction types, and it is anticipated that it will have far-reaching implications across a range of different contexts. Practical fallout from this line of inquiry includes the discovery of new shelf-stable TBAF reagents such as TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub> (**8.4**) and TBAF(9-Ph-9-fluorenol)<sub>3</sub> (**8.1**), which are convenient to prepare and offer high kinetic reactivity, low basicity, and improved handling properties, compared to other TBAF sources.

More recently, new projects have been initiated that use other hydrogen-bond donors, including 1,3-diarylsureas, *N,N'*-diarylsquaramides, and *N*-arylamides. Complexes with all of these hydrogen-bond donors have been characterised by X-ray crystallography,

which has led to new insights into recurring solid-state fluoride coordination motifs. The diverse reactivity exhibited by these complexes compared to the fluoride–alcohol series further speaks to the dramatic influence of hydrogen bonding on fluoride reactivity.

Moving forward, it is anticipated that this research programme will continue to sharpen the scientific community's understanding of fundamental fluorine chemistry and that this reactivity paradigm will have a positive practical impact on the synthesis of organofluorine compounds.

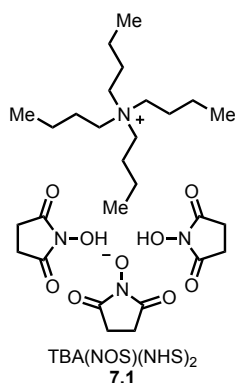
## 8.5. REFERENCES

- (1) Keen, D. A.; Gutmann, M. J.; Wilson, C. C. *J. Appl. Crystallogr.* **2006**, *39*, 714–722.
- (2) Etter, M. C.; Urbanczyk-Lipkowska, Z.; Zia-Ebrahimi, M.; Panunto, T. W. *J. Am. Chem. Soc.* **1990**, *112*, 8415–8426.
- (3) Dydio, P.; Lichosyt, D.; Jurczak, J. *Chem. Soc. Rev.* **2011**, *40*, 2971–2985.
- (4) Cho, E. J.; Moon, J. W.; Ko, S. W.; Lee, J. Y.; Kim, S. K.; Yoon, J.; Nam, K. C. *J. Am. Chem. Soc.* **2003**, *125*, 12376–12377.
- (5) Boiocchi, M.; Del Boca, L.; Gómez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507–16514.
- (6) Esteban-Gómez, D.; Fabbrizzi, L.; Licchelli, M. *J. Org. Chem.* **2005**, *70*, 5717–5720.
- (7) Ghosh, K.; Adhikari, S.; Fröhlich, R.; Petsalakis, I. D.; Theodorakopoulos, G. *J. Mol. Struct.* **2011**, *1004*, 193–203.
- (8) Pérez-Ruiz, R.; Griesbeck, A. G.; Sampedro, D. *Tetrahedron* **2012**, *68*, 5724–5729.
- (9) Pramanik, A.; Powell, D. R.; Wong, B. M.; Hossain, M. A. *Inorg. Chem.* **2012**, *51*, 4274–4284.
- (10) Mattson, A. E.; Zuhl, A. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 4932–4933.

- (11) Birrell, J. A.; Desrosiers, J.-N.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 13872–13875.
- (12) Li, Q.; Mak, T. C. W. *Acta Crystallogr., Sect. B: Struct. Sci* **1998**, *54*, 180–192.
- (13) Mak, T. C. W. *J. Mol. Struct.* **1988**, *189*, 393–396.
- (14) Mak, T. C. W. *J. Inclusion Phenom. Macrocyclic Chem.* **1990**, *8*, 199–214.
- (15) Coles, S. J.; Frey, J. G.; Gale, P. A.; Hursthouse, M. B.; Light, M. E.; Navakhun, K.; Thomas, G. L. *Chem. Commun.* **2003**, 568–569.
- (16) Rostami, A.; Colin, A.; Li, X. Y.; Chudzinski, M. G.; Lough, A. J.; Taylor, M. S. *J. Org. Chem.* **2010**, *75*, 3983–3992.
- (17) Amendola, V.; Bergamaschi, G.; Boiocchi, M.; Fabbrizzi, L.; Milani, M. *Chem. Eur. J.* **2010**, *16*, 4368–4380.
- (18) Ramalingam, V.; Domaradzki, M. E.; Jang, S.; Muthyala, R. S. *Org. Lett.* **2008**, *10*, 3315–3318.

## **APPENDIX**

### **X-RAY CRYSTALLOGRAPHY DATA**



**tetra-*n*-butylammonium *N*-oxysuccinimide bis(*N*-hydroxysuccinimide) (TBA(NOS)(NHS)<sub>2</sub>, 7.1):**

**X-ray** (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.1** in THF, which had previously been prepared by dissolving **7.1** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 006KME12

## Crystal Data

$a = 9.8919(2) \text{ \AA}$   $\alpha = 90^\circ$

$b = 20.5429(4) \text{ \AA}$   $\beta = 98.5668(10)^\circ$

$c = 16.0649(3) \text{ \AA}$   $\gamma = 90^\circ$

Volume 3228.10(11)  $\text{\AA}^3$

Space group  $P 1 2_1/n 1$

Formula  $\text{C}_{28} \text{H}_{50} \text{N}_4 \text{O}_9$

Cell determined from 5999 reflections

Temperature 150K

Shape prism

Colour clear\_pale\_colourless

$D_x$  1.21  $\text{Mg m}^{-3}$

$\mu$  0.090  $\text{mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$  0.80

Crystal Class monoclinic

$Z = 4$

$M_r$  586.73

Cell  $\theta$  range = 5 - 25°

Size 0.16 × 0.20 × 0.40 mm

$F_{000}$  1272.000

$T_{\max}$  0.99

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 39670

Independent reflections 5837

$R_{\text{int}}$  0.0359

$\theta_{\max}$  25.3138

$h = -11 \rightarrow 11$

$k = -24 \rightarrow 24$

$l = -19 \rightarrow 19$

## Refinement

$\Delta\rho_{\min} = -0.43 \text{ e \AA}^{-3}$

$\Delta\rho_{\max} = 0.36 \text{ e \AA}^{-3}$

Reflections used 5835  
 Cutoff: I > -3.00σ(I)  
 Parameters refined 370  
 S = 1.05  
 R-factor 0.084  
 weighted R-factor 0.134  
 Δ/σ<sub>max</sub> 0.0003  
 Refinement on F<sup>2</sup>  
 w =  $1/[\sigma^2(F_{\text{obs}}^2) + (0.043 \times P)^2 + 2.260 \times P + 0.000 + 0.000 \times \sin\theta]$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| N31   | 0.32836(17) | 0.67168(8)  | 0.83847(11) | 0.0263                 | 1.0000    |
| C32   | 0.4449(2)   | 0.71989(11) | 0.83795(14) | 0.0314                 | 1.0000    |
| C33   | 0.4505(2)   | 0.77600(11) | 0.89928(16) | 0.0385                 | 1.0000    |
| C34   | 0.5814(3)   | 0.81430(13) | 0.89746(19) | 0.0495                 | 1.0000    |
| C35   | 0.6094(3)   | 0.86499(14) | 0.9663(2)   | 0.0644                 | 1.0000    |
| C36   | 0.3285(2)   | 0.64303(11) | 0.92538(13) | 0.0277                 | 1.0000    |
| C37   | 0.4621(2)   | 0.61438(11) | 0.96741(14) | 0.0322                 | 1.0000    |
| C38   | 0.4442(2)   | 0.58545(12) | 1.05224(14) | 0.0353                 | 1.0000    |
| C39   | 0.5793(3)   | 0.56340(13) | 1.10226(16) | 0.0461                 | 1.0000    |
| C40   | 0.3504(2)   | 0.61931(11) | 0.77493(14) | 0.0307                 | 1.0000    |
| C41   | 0.2434(2)   | 0.56613(11) | 0.76113(14) | 0.0329                 | 1.0000    |
| C42   | 0.2714(3)   | 0.52188(12) | 0.68911(15) | 0.0386                 | 1.0000    |
| C43   | 0.1704(3)   | 0.46605(13) | 0.67459(17) | 0.0494                 | 1.0000    |
| C44   | 0.1905(2)   | 0.70487(11) | 0.81533(14) | 0.0294                 | 1.0000    |
| C45   | 0.1631(2)   | 0.73497(13) | 0.72846(15) | 0.0388                 | 1.0000    |
| C46   | 0.0242(3)   | 0.76867(13) | 0.71594(18) | 0.0470                 | 1.0000    |
| C47   | 0.0166(3)   | 0.82720(15) | 0.7712(2)   | 0.0593                 | 1.0000    |
| O1    | 0.68937(16) | 0.79464(8)  | 0.65625(11) | 0.0429                 | 1.0000    |
| N2    | 0.57355(18) | 0.79125(9)  | 0.59780(12) | 0.0321                 | 1.0000    |
| C3    | 0.4478(2)   | 0.81312(11) | 0.61439(15) | 0.0333                 | 1.0000    |
| O4    | 0.42842(17) | 0.83880(8)  | 0.67915(11) | 0.0427                 | 1.0000    |
| C5    | 0.3467(2)   | 0.79852(13) | 0.53707(15) | 0.0392                 | 1.0000    |
| C6    | 0.4272(2)   | 0.76388(12) | 0.47665(14) | 0.0369                 | 1.0000    |
| C7    | 0.5697(2)   | 0.75876(11) | 0.52263(15) | 0.0334                 | 1.0000    |
| O8    | 0.66759(16) | 0.73085(8)  | 0.50101(11) | 0.0416                 | 1.0000    |
| O11   | 0.73363(16) | 0.61939(8)  | 0.85691(10) | 0.0381                 | 1.0000    |
| N12   | 0.79748(18) | 0.56077(9)  | 0.84853(12) | 0.0308                 | 1.0000    |



|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| C13  | 0.7386(2)   | 0.51116(11) | 0.79773(15) | 0.0350 | 1.0000 |
| O14  | 0.62608(17) | 0.51451(8)  | 0.75566(12) | 0.0479 | 1.0000 |
| C15  | 0.8396(2)   | 0.45635(11) | 0.80427(16) | 0.0402 | 1.0000 |
| C16  | 0.9596(2)   | 0.47919(11) | 0.86879(16) | 0.0394 | 1.0000 |
| C17  | 0.9285(2)   | 0.54838(11) | 0.88776(14) | 0.0330 | 1.0000 |
| O18  | 1.00029(17) | 0.58741(8)  | 0.93096(11) | 0.0437 | 1.0000 |
| O21  | 0.70276(17) | 0.68060(7)  | 0.72141(10) | 0.0373 | 1.0000 |
| N22  | 0.69438(19) | 0.63690(9)  | 0.65716(12) | 0.0328 | 1.0000 |
| C23  | 0.5754(3)   | 0.62476(12) | 0.60417(15) | 0.0386 | 1.0000 |
| O24  | 0.46736(18) | 0.65253(10) | 0.60666(11) | 0.0510 | 1.0000 |
| C25  | 0.6062(4)   | 0.57251(15) | 0.54477(19) | 0.0670 | 1.0000 |
| C26  | 0.7574(4)   | 0.55865(17) | 0.56744(19) | 0.0746 | 1.0000 |
| C27  | 0.8040(3)   | 0.59983(13) | 0.64286(17) | 0.0460 | 1.0000 |
| O28  | 0.9151(2)   | 0.60109(11) | 0.68609(14) | 0.0680 | 1.0000 |
| H72  | 0.3071(2)   | 0.83902(13) | 0.51319(15) | 0.0464 | 1.0000 |
| H71  | 0.2771(2)   | 0.77144(13) | 0.55375(15) | 0.0472 | 1.0000 |
| H81  | 0.4267(2)   | 0.78863(12) | 0.42534(14) | 0.0439 | 1.0000 |
| H82  | 0.3926(2)   | 0.71978(12) | 0.46320(14) | 0.0445 | 1.0000 |
| H131 | 0.9682(2)   | 0.45310(11) | 0.91976(16) | 0.0480 | 1.0000 |
| H132 | 1.0469(2)   | 0.47736(11) | 0.84711(16) | 0.0473 | 1.0000 |
| H142 | 0.7983(2)   | 0.41694(11) | 0.82189(16) | 0.0485 | 1.0000 |
| H141 | 0.8683(2)   | 0.45040(11) | 0.74970(16) | 0.0485 | 1.0000 |
| H211 | 0.5842(4)   | 0.58691(15) | 0.48746(19) | 0.0799 | 1.0000 |
| H212 | 0.5531(4)   | 0.53522(15) | 0.55249(19) | 0.0807 | 1.0000 |
| H221 | 0.8065(4)   | 0.57050(17) | 0.52174(19) | 0.0907 | 1.0000 |
| H222 | 0.7753(4)   | 0.51304(17) | 0.58150(19) | 0.0903 | 1.0000 |
| H262 | 0.1841(2)   | 0.73855(11) | 0.85682(14) | 0.0343 | 1.0000 |
| H261 | 0.1232(2)   | 0.67159(11) | 0.82033(14) | 0.0349 | 1.0000 |
| H271 | 0.2340(2)   | 0.76681(13) | 0.72192(15) | 0.0464 | 1.0000 |
| H272 | 0.1633(2)   | 0.70085(13) | 0.68676(15) | 0.0475 | 1.0000 |
| H281 | 0.0032(3)   | 0.78370(13) | 0.65676(18) | 0.0562 | 1.0000 |
| H282 | -0.0458(3)  | 0.73612(13) | 0.72577(18) | 0.0561 | 1.0000 |
| H292 | -0.0710(3)  | 0.84865(15) | 0.7568(2)   | 0.0893 | 1.0000 |
| H291 | 0.0862(3)   | 0.85843(15) | 0.7632(2)   | 0.0886 | 1.0000 |
| H293 | 0.0312(3)   | 0.81516(15) | 0.8311(2)   | 0.0879 | 1.0000 |
| H302 | 0.3032(2)   | 0.67803(11) | 0.96064(13) | 0.0329 | 1.0000 |
| H301 | 0.2586(2)   | 0.60933(11) | 0.92012(13) | 0.0329 | 1.0000 |
| H312 | 0.5302(2)   | 0.64881(11) | 0.97659(14) | 0.0385 | 1.0000 |
| H311 | 0.4950(2)   | 0.58009(11) | 0.93328(14) | 0.0395 | 1.0000 |
| H322 | 0.4044(2)   | 0.61804(12) | 1.08478(14) | 0.0416 | 1.0000 |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| H321 | 0.3829(2)   | 0.54862(12) | 1.04289(14) | 0.0420 | 1.0000 |
| H331 | 0.5663(3)   | 0.54322(13) | 1.15576(16) | 0.0684 | 1.0000 |
| H333 | 0.6391(3)   | 0.60141(13) | 1.11593(16) | 0.0687 | 1.0000 |
| H332 | 0.6243(3)   | 0.53264(13) | 1.06878(16) | 0.0684 | 1.0000 |
| H341 | 0.4412(2)   | 0.60042(11) | 0.79415(14) | 0.0360 | 1.0000 |
| H342 | 0.3538(2)   | 0.64143(11) | 0.72255(14) | 0.0366 | 1.0000 |
| H351 | 0.2484(2)   | 0.53992(11) | 0.81320(14) | 0.0395 | 1.0000 |
| H352 | 0.1537(2)   | 0.58504(11) | 0.74790(14) | 0.0402 | 1.0000 |
| H362 | 0.3647(3)   | 0.50446(12) | 0.70299(15) | 0.0459 | 1.0000 |
| H361 | 0.2657(3)   | 0.54748(12) | 0.63818(15) | 0.0458 | 1.0000 |
| H371 | 0.1898(3)   | 0.44029(13) | 0.62750(17) | 0.0731 | 1.0000 |
| H373 | 0.1781(3)   | 0.43861(13) | 0.72482(17) | 0.0731 | 1.0000 |
| H372 | 0.0781(3)   | 0.48295(13) | 0.66001(17) | 0.0737 | 1.0000 |
| H381 | 0.5293(2)   | 0.69489(11) | 0.85068(14) | 0.0371 | 1.0000 |
| H382 | 0.4366(2)   | 0.73626(11) | 0.77940(14) | 0.0380 | 1.0000 |
| H391 | 0.4487(2)   | 0.76013(11) | 0.95596(16) | 0.0460 | 1.0000 |
| H392 | 0.3727(2)   | 0.80509(11) | 0.88349(16) | 0.0463 | 1.0000 |
| H402 | 0.5764(3)   | 0.83528(13) | 0.84191(19) | 0.0593 | 1.0000 |
| H401 | 0.6540(3)   | 0.78134(13) | 0.90322(19) | 0.0600 | 1.0000 |
| H411 | 0.6972(3)   | 0.88592(14) | 0.9639(2)   | 0.0971 | 1.0000 |
| H413 | 0.5388(3)   | 0.89788(14) | 0.9598(2)   | 0.0968 | 1.0000 |
| H412 | 0.6124(3)   | 0.84472(14) | 1.0219(2)   | 0.0972 | 1.0000 |
| H91  | 0.72682(16) | 0.63817(8)  | 0.80624(10) | 0.0568 | 1.0000 |
| H41  | 0.69379(16) | 0.75548(8)  | 0.67760(11) | 0.0641 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| N31   | 0.0193(9)       | 0.0300(10)      | 0.0302(10)      | 0.0042(8)       | 0.0056(7)       | 0.0018(7)       |
| C32   | 0.0201(11)      | 0.0372(13)      | 0.0373(13)      | 0.0070(10)      | 0.0050(9)       | -0.0013(9)      |
| C33   | 0.0304(13)      | 0.0327(13)      | 0.0521(15)      | 0.0030(11)      | 0.0055(11)      | -0.0014(10)     |
| C34   | 0.0338(14)      | 0.0479(16)      | 0.0634(18)      | 0.0042(13)      | -0.0040(12)     | -0.0098(12)     |
| C35   | 0.0530(18)      | 0.0451(17)      | 0.087(2)        | -0.0008(16)     | -0.0177(16)     | -0.0070(13)     |
| C36   | 0.0241(11)      | 0.0326(12)      | 0.0271(11)      | 0.0029(9)       | 0.0061(9)       | 0.0002(9)       |
| C37   | 0.0293(12)      | 0.0348(12)      | 0.0323(12)      | 0.0050(10)      | 0.0038(9)       | 0.0009(10)      |
| C38   | 0.0384(13)      | 0.0355(13)      | 0.0313(12)      | 0.0017(10)      | 0.0026(10)      | -0.0010(10)     |
| C39   | 0.0529(16)      | 0.0474(15)      | 0.0355(14)      | 0.0060(12)      | -0.0017(12)     | 0.0065(12)      |
| C40   | 0.0279(12)      | 0.0363(13)      | 0.0287(11)      | 0.0008(10)      | 0.0067(9)       | 0.0038(10)      |
| C41   | 0.0278(12)      | 0.0370(13)      | 0.0339(12)      | 0.0000(10)      | 0.0046(10)      | 0.0014(10)      |

|     |            |            |            |             |             |             |
|-----|------------|------------|------------|-------------|-------------|-------------|
| C42 | 0.0394(14) | 0.0452(14) | 0.0306(12) | -0.0014(11) | 0.0029(10)  | -0.0010(11) |
| C43 | 0.0481(16) | 0.0516(16) | 0.0477(16) | -0.0107(13) | 0.0039(12)  | -0.0037(13) |
| C44 | 0.0178(11) | 0.0341(12) | 0.0364(12) | 0.0051(10)  | 0.0043(9)   | 0.0031(9)   |
| C45 | 0.0316(13) | 0.0450(14) | 0.0388(13) | 0.0082(11)  | 0.0015(10)  | 0.0035(11)  |
| C46 | 0.0317(14) | 0.0456(15) | 0.0595(17) | 0.0160(13)  | -0.0067(12) | 0.0047(11)  |
| C47 | 0.0571(18) | 0.0552(18) | 0.0656(19) | 0.0155(15)  | 0.0093(15)  | 0.0195(14)  |
| O1  | 0.0323(9)  | 0.0343(9)  | 0.0566(11) | 0.0041(8)   | -0.0111(8)  | -0.0034(7)  |
| N2  | 0.0233(10) | 0.0343(10) | 0.0366(11) | 0.0057(8)   | -0.0026(8)  | -0.0022(8)  |
| C3  | 0.0321(13) | 0.0311(12) | 0.0378(13) | 0.0092(10)  | 0.0083(10)  | -0.0022(10) |
| O4  | 0.0449(10) | 0.0413(10) | 0.0431(10) | -0.0008(8)  | 0.0106(8)   | -0.0020(8)  |
| C5  | 0.0267(12) | 0.0505(15) | 0.0412(14) | 0.0073(12)  | 0.0075(10)  | -0.0007(11) |
| C6  | 0.0322(13) | 0.0465(14) | 0.0315(12) | 0.0065(11)  | 0.0032(10)  | 0.0003(11)  |
| C7  | 0.0269(12) | 0.0342(12) | 0.0406(13) | 0.0110(10)  | 0.0095(10)  | -0.0026(10) |
| O8  | 0.0331(9)  | 0.0459(10) | 0.0493(10) | 0.0106(8)   | 0.0169(8)   | 0.0033(8)   |
| O11 | 0.0405(9)  | 0.0404(9)  | 0.0339(9)  | 0.0004(7)   | 0.0076(7)   | 0.0146(7)   |
| N12 | 0.0267(10) | 0.0289(10) | 0.0368(10) | 0.0028(8)   | 0.0052(8)   | 0.0056(8)   |
| C13 | 0.0305(13) | 0.0322(13) | 0.0433(14) | 0.0051(11)  | 0.0089(11)  | -0.0027(10) |
| O14 | 0.0292(9)  | 0.0471(11) | 0.0634(12) | 0.0044(9)   | -0.0059(8)  | -0.0023(8)  |
| C15 | 0.0380(14) | 0.0297(12) | 0.0526(15) | 0.0030(11)  | 0.0050(12)  | -0.0004(10) |
| C16 | 0.0314(13) | 0.0366(13) | 0.0504(15) | 0.0050(11)  | 0.0069(11)  | 0.0050(10)  |
| C17 | 0.0276(12) | 0.0386(13) | 0.0341(12) | 0.0072(11)  | 0.0087(10)  | 0.0005(10)  |
| O18 | 0.0363(10) | 0.0445(10) | 0.0476(10) | -0.0021(8)  | -0.0024(8)  | -0.0020(8)  |
| O21 | 0.0440(10) | 0.0310(8)  | 0.0357(9)  | -0.0028(7)  | 0.0024(7)   | 0.0049(7)   |
| N22 | 0.0351(11) | 0.0309(10) | 0.0326(10) | -0.0014(8)  | 0.0064(8)   | -0.0002(8)  |
| C23 | 0.0425(15) | 0.0383(14) | 0.0349(13) | 0.0095(11)  | 0.0053(11)  | -0.0121(12) |
| O24 | 0.0317(10) | 0.0699(13) | 0.0514(11) | 0.0215(10)  | 0.0064(8)   | -0.0095(9)  |
| C25 | 0.102(3)   | 0.0511(18) | 0.0443(17) | -0.0077(14) | -0.0020(17) | -0.0176(17) |
| C26 | 0.104(3)   | 0.071(2)   | 0.0502(18) | -0.0102(16) | 0.0166(18)  | 0.030(2)    |
| C27 | 0.0527(18) | 0.0464(15) | 0.0415(15) | 0.0033(12)  | 0.0160(13)  | 0.0099(13)  |
| O28 | 0.0450(12) | 0.0847(16) | 0.0742(14) | 0.0059(12)  | 0.0082(11)  | 0.0237(11)  |

## Distances

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| N31 | C32  | 1.521(3)Å |  | N31 | C36  | 1.515(3)Å |
| N31 | C40  | 1.521(3)Å |  | N31 | C44  | 1.521(3)Å |
| C32 | C33  | 1.512(3)Å |  | C32 | H381 | 0.976Å    |
| C32 | H382 | 0.991Å    |  | C33 | C34  | 1.519(3)Å |
| C33 | H391 | 0.970Å    |  | C33 | H392 | 0.978Å    |
| C34 | C35  | 1.514(4)Å |  | C34 | H402 | 0.986Å    |
| C34 | H401 | 0.982Å    |  | C35 | H411 | 0.975Å    |

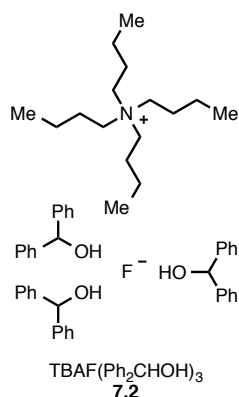
|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| C35 | H413 | 0.966Å    |  | C35 | H412 | 0.983Å    |
| C36 | C37  | 1.511(3)Å |  | C36 | H302 | 0.971Å    |
| C36 | H301 | 0.974Å    |  | C37 | C38  | 1.521(3)Å |
| C37 | H312 | 0.973Å    |  | C37 | H311 | 0.978Å    |
| C38 | C39  | 1.521(3)Å |  | C38 | H322 | 0.969Å    |
| C38 | H321 | 0.967Å    |  | C39 | H331 | 0.980Å    |
| C39 | H333 | 0.985Å    |  | C39 | H332 | 0.979Å    |
| C40 | C41  | 1.515(3)Å |  | C40 | H341 | 0.984Å    |
| C40 | H342 | 0.961Å    |  | C41 | C42  | 1.529(3)Å |
| C41 | H351 | 0.990Å    |  | C41 | H352 | 0.963Å    |
| C42 | C43  | 1.516(3)Å |  | C42 | H362 | 0.984Å    |
| C42 | H361 | 0.967Å    |  | C43 | H371 | 0.966Å    |
| C43 | H373 | 0.978Å    |  | C43 | H372 | 0.973Å    |
| C44 | C45  | 1.514(3)Å |  | C44 | H262 | 0.969Å    |
| C44 | H261 | 0.966Å    |  | C45 | C46  | 1.525(3)Å |
| C45 | H271 | 0.976Å    |  | C45 | H272 | 0.970Å    |
| C46 | C47  | 1.504(4)Å |  | C46 | H281 | 0.992Å    |
| C46 | H282 | 0.992Å    |  | C47 | H292 | 0.969Å    |
| C47 | H291 | 0.964Å    |  | C47 | H293 | 0.983Å    |
| O1  | N2   | 1.371(2)Å |  | O1  | H41  | 0.873Å    |
| N2  | C3   | 1.385(3)Å |  | N2  | C7   | 1.375(3)Å |
| C3  | O4   | 1.207(3)Å |  | C3  | C5   | 1.504(3)Å |
| C5  | C6   | 1.520(3)Å |  | C5  | H72  | 0.974Å    |
| C5  | H71  | 0.954Å    |  | C6  | C7   | 1.495(3)Å |
| C6  | H81  | 0.968Å    |  | C6  | H82  | 0.981Å    |
| C7  | O8   | 1.219(3)Å |  | O11 | N12  | 1.376(2)Å |
| O11 | H91  | 0.894Å    |  | N12 | C13  | 1.379(3)Å |
| N12 | C17  | 1.378(3)Å |  | C13 | O14  | 1.215(3)Å |
| C13 | C15  | 1.499(3)Å |  | C15 | C16  | 1.528(3)Å |
| C15 | H142 | 0.968Å    |  | C15 | H141 | 0.969Å    |
| C16 | C17  | 1.495(3)Å |  | C16 | H131 | 0.972Å    |
| C16 | H132 | 0.980Å    |  | C17 | O18  | 1.217(3)Å |
| O21 | N22  | 1.361(2)Å |  | N22 | C23  | 1.369(3)Å |
| N22 | C27  | 1.372(3)Å |  | C23 | O24  | 1.218(3)Å |
| C23 | C25  | 1.497(4)Å |  | C25 | C26  | 1.512(5)Å |
| C25 | H211 | 0.961Å    |  | C25 | H212 | 0.947Å    |
| C26 | C27  | 1.493(4)Å |  | C26 | H221 | 0.970Å    |
| C26 | H222 | 0.974Å    |  | C27 | O28  | 1.210(3)Å |

## Angles

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C32  | N31 | C36  | 111.18(16)° |  | C32  | N31 | C40  | 105.80(15)° |
| C36  | N31 | C40  | 111.29(16)° |  | C32  | N31 | C44  | 111.07(16)° |
| C36  | N31 | C44  | 106.10(15)° |  | C40  | N31 | C44  | 111.49(16)° |
| N31  | C32 | C33  | 116.58(17)° |  | N31  | C32 | H381 | 106.368°    |
| C33  | C32 | H381 | 108.503°    |  | N31  | C32 | H382 | 105.693°    |
| C33  | C32 | H382 | 110.468°    |  | H381 | C32 | H382 | 108.966°    |
| C32  | C33 | C34  | 109.3(2)°   |  | C32  | C33 | H391 | 110.571°    |
| C34  | C33 | H391 | 109.117°    |  | C32  | C33 | H392 | 110.214°    |
| C34  | C33 | H392 | 108.600°    |  | H391 | C33 | H392 | 108.959°    |
| C33  | C34 | C35  | 114.0(2)°   |  | C33  | C34 | H402 | 108.466°    |
| C35  | C34 | H402 | 109.847°    |  | C33  | C34 | H401 | 104.781°    |
| C35  | C34 | H401 | 110.703°    |  | H402 | C34 | H401 | 108.870°    |
| C34  | C35 | H411 | 110.015°    |  | C34  | C35 | H413 | 110.605°    |
| H411 | C35 | H413 | 108.731°    |  | C34  | C35 | H412 | 110.522°    |
| H411 | C35 | H412 | 108.392°    |  | H413 | C35 | H412 | 108.517°    |
| N31  | C36 | C37  | 116.36(16)° |  | N31  | C36 | H302 | 106.551°    |
| C37  | C36 | H302 | 108.189°    |  | N31  | C36 | H301 | 107.042°    |
| C37  | C36 | H301 | 108.962°    |  | H302 | C36 | H301 | 109.600°    |
| C36  | C37 | C38  | 110.00(18)° |  | C36  | C37 | H312 | 108.927°    |
| C38  | C37 | H312 | 108.572°    |  | C36  | C37 | H311 | 111.849°    |
| C38  | C37 | H311 | 108.281°    |  | H312 | C37 | H311 | 109.151°    |
| C37  | C38 | C39  | 112.3(2)°   |  | C37  | C38 | H322 | 108.935°    |
| C39  | C38 | H322 | 108.464°    |  | C37  | C38 | H321 | 108.685°    |
| C39  | C38 | H321 | 109.257°    |  | H322 | C38 | H321 | 109.147°    |
| C38  | C39 | H331 | 111.696°    |  | C38  | C39 | H333 | 109.431°    |
| H331 | C39 | H333 | 107.039°    |  | C38  | C39 | H332 | 109.736°    |
| H331 | C39 | H332 | 109.794°    |  | H333 | C39 | H332 | 109.077°    |
| N31  | C40 | C41  | 116.18(17)° |  | N31  | C40 | H341 | 106.477°    |
| C41  | C40 | H341 | 110.278°    |  | N31  | C40 | H342 | 106.274°    |
| C41  | C40 | H342 | 109.130°    |  | H341 | C40 | H342 | 108.174°    |
| C40  | C41 | C42  | 109.77(18)° |  | C40  | C41 | H351 | 108.819°    |
| C42  | C41 | H351 | 108.924°    |  | C40  | C41 | H352 | 110.027°    |
| C42  | C41 | H352 | 109.727°    |  | H351 | C41 | H352 | 109.553°    |
| C41  | C42 | C43  | 112.2(2)°   |  | C41  | C42 | H362 | 108.310°    |
| C43  | C42 | H362 | 109.500°    |  | C41  | C42 | H361 | 108.840°    |
| C43  | C42 | H361 | 109.126°    |  | H362 | C42 | H361 | 108.848°    |
| C42  | C43 | H371 | 109.404°    |  | C42  | C43 | H373 | 109.929°    |
| H371 | C43 | H373 | 109.291°    |  | C42  | C43 | H372 | 109.900°    |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| H371 | C43 | H372 | 107.216°    |  | H373 | C43 | H372 | 111.047°    |
| N31  | C44 | C45  | 116.07(17)° |  | N31  | C44 | H262 | 107.475°    |
| C45  | C44 | H262 | 108.750°    |  | N31  | C44 | H261 | 105.436°    |
| C45  | C44 | H261 | 109.573°    |  | H262 | C44 | H261 | 109.360°    |
| C44  | C45 | C46  | 109.9(2)°   |  | C44  | C45 | H271 | 109.886°    |
| C46  | C45 | H271 | 109.232°    |  | C44  | C45 | H272 | 108.853°    |
| C46  | C45 | H272 | 109.375°    |  | H271 | C45 | H272 | 109.540°    |
| C45  | C46 | C47  | 114.1(2)°   |  | C45  | C46 | H281 | 108.911°    |
| C47  | C46 | H281 | 107.185°    |  | C45  | C46 | H282 | 108.025°    |
| C47  | C46 | H282 | 110.338°    |  | H281 | C46 | H282 | 108.108°    |
| C46  | C47 | H292 | 110.138°    |  | C46  | C47 | H291 | 110.703°    |
| H292 | C47 | H291 | 107.231°    |  | C46  | C47 | H293 | 111.342°    |
| H292 | C47 | H293 | 110.186°    |  | H291 | C47 | H293 | 107.116°    |
| N2   | O1  | H41  | 102.136°    |  | O1   | N2  | C3   | 122.32(19)° |
| O1   | N2  | C7   | 122.48(18)° |  | C3   | N2  | C7   | 114.72(18)° |
| N2   | C3  | O4   | 124.7(2)°   |  | N2   | C3  | C5   | 106.38(19)° |
| O4   | C3  | C5   | 128.9(2)°   |  | C3   | C5  | C6   | 105.89(19)° |
| C3   | C5  | H72  | 109.499°    |  | C6   | C5  | H72  | 111.484°    |
| C3   | C5  | H71  | 107.647°    |  | C6   | C5  | H71  | 112.006°    |
| H72  | C5  | H71  | 110.133°    |  | C5   | C6  | C7   | 105.21(19)° |
| C5   | C6  | H81  | 111.191°    |  | C7   | C6  | H81  | 109.983°    |
| C5   | C6  | H82  | 111.983°    |  | C7   | C6  | H82  | 108.434°    |
| H81  | C6  | H82  | 109.896°    |  | N2   | C7  | C6   | 107.47(19)° |
| N2   | C7  | O8   | 124.0(2)°   |  | C6   | C7  | O8   | 128.5(2)°   |
| N12  | O11 | H91  | 105.180°    |  | O11  | N12 | C13  | 123.04(18)° |
| O11  | N12 | C17  | 122.09(18)° |  | C13  | N12 | C17  | 114.81(19)° |
| N12  | C13 | O14  | 123.9(2)°   |  | N12  | C13 | C15  | 107.18(19)° |
| O14  | C13 | C15  | 128.9(2)°   |  | C13  | C15 | C16  | 105.01(19)° |
| C13  | C15 | H142 | 110.045°    |  | C16  | C15 | H142 | 112.166°    |
| C13  | C15 | H141 | 108.287°    |  | C16  | C15 | H141 | 110.470°    |
| H142 | C15 | H141 | 110.649°    |  | C15  | C16 | C17  | 105.54(19)° |
| C15  | C16 | H131 | 111.346°    |  | C17  | C16 | H131 | 110.337°    |
| C15  | C16 | H132 | 112.581°    |  | C17  | C16 | H132 | 109.142°    |
| H131 | C16 | H132 | 107.882°    |  | N12  | C17 | C16  | 106.9(2)°   |
| N12  | C17 | O18  | 124.6(2)°   |  | C16  | C17 | O18  | 128.5(2)°   |
| O21  | N22 | C23  | 122.78(19)° |  | O21  | N22 | C27  | 122.2(2)°   |
| C23  | N22 | C27  | 115.0(2)°   |  | N22  | C23 | O24  | 124.9(2)°   |
| N22  | C23 | C25  | 106.8(2)°   |  | O24  | C23 | C25  | 128.3(3)°   |
| C23  | C25 | C26  | 105.6(2)°   |  | C23  | C25 | H211 | 110.586°    |
| C26  | C25 | H211 | 111.297°    |  | C23  | C25 | H212 | 109.102°    |

|     |     |      |           |  |      |     |      |           |
|-----|-----|------|-----------|--|------|-----|------|-----------|
| C26 | C25 | H212 | 111.309°  |  | H211 | C25 | H212 | 108.889°  |
| C25 | C26 | C27  | 105.3(2)° |  | C25  | C26 | H221 | 111.063°  |
| C27 | C26 | H221 | 110.057°  |  | C25  | C26 | H222 | 112.138°  |
| C27 | C26 | H222 | 109.461°  |  | H221 | C26 | H222 | 108.800°  |
| N22 | C27 | C26  | 107.1(2)° |  | N22  | C27 | O28  | 124.4(3)° |
| C26 | C27 | O28  | 128.5(3)° |  |      |     |      |           |



**tetra-*n*-butylammonium fluoride tris(diphenylmethanol) (TBAF(Ph<sub>2</sub>CHOH)<sub>3</sub>, 7.2):**

**X-ray** (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.2** in THF, which had previously been prepared by dissolving **7.2** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 065GGKE02

## Crystal Data

$a = 9.49530(10) \text{ \AA}$   $\alpha = 81.8444(6)^\circ$

$b = 12.1501(2) \text{ \AA}$   $\beta = 89.1604(6)^\circ$

$c = 21.4618(4) \text{ \AA}$   $\gamma = 78.5486(7)^\circ$

Volume  $2401.96(7) \text{ \AA}^3$

Space group  $P -1$

Formula  $C_{55} H_{72} F_1 N_1 O_3$

Cell determined from 10032 reflections

Temperature 150K

Shape block

Colour clear\_pale\_colourless

$D_x$   $1.13 \text{ Mg m}^{-3}$

$\mu$   $0.070 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$  0.65

Crystal Class triclinic

$Z = 2$

$M_r$  814.18

Cell  $\theta$  range =  $5 - 27^\circ$

Size  $0.14 \times 0.18 \times 0.65 \text{ mm}$

$F_{000}$  884.000

$T_{\max}$  0.99

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 40263

Independent reflections 10827

$R_{\text{int}}$  0.0224

$\theta_{\max}$   $27.5680$

$h = -12 \rightarrow 12$

$k = -15 \rightarrow 15$

$l = -27 \rightarrow 27$

## Refinement

$\Delta\rho_{\min} = -0.35 \text{ e \AA}^{-3}$

$\Delta\rho_{\max} = 0.53 \text{ e \AA}^{-3}$



Reflections used 8998  
 Cutoff: I > -3.00σ(I)  
 Parameters refined 597  
 S = 1.00  
 R-factor 0.061  
 weighted R-factor 0.128  
 Δ/σ<sub>max</sub> 0.0006  
 Refinement on F<sup>2</sup>  
 w =  $\frac{1}{[\sigma^2(F_{\text{obs}}^2) + (0.053 \times P)^2 + 0.963 \times P + 0.000 + 0.000 \times \sin\theta]}$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| O1    | 0.55996(14) | 0.19758(12) | 0.69367(6)  | 0.0598                 | 1.0000    |
| O2    | 0.26656(12) | 0.55784(9)  | 0.70626(5)  | 0.0440                 | 1.0000    |
| O3    | 0.25801(12) | 0.30950(11) | 0.82809(5)  | 0.0500                 | 1.0000    |
| C11   | 0.51437(18) | 0.21305(13) | 0.63082(7)  | 0.0450                 | 1.0000    |
| C59   | 0.49700(19) | 0.13028(15) | 0.85187(9)  | 0.0488                 | 1.0000    |
| C13   | 0.6203(10)  | 0.3094(9)   | 0.5355(4)   | 0.0565                 | 0.50(3)   |
| C61   | 0.6831(2)   | 0.01465(18) | 0.92049(12) | 0.0678                 | 1.0000    |
| C15   | 0.8553(10)  | 0.2382(12)  | 0.5010(3)   | 0.0551                 | 0.50(3)   |
| C16   | 0.8727(8)   | 0.1522(11)  | 0.5506(4)   | 0.0530                 | 0.50(3)   |
| C17   | 0.7619(9)   | 0.1440(10)  | 0.5927(5)   | 0.0469                 | 0.50(3)   |
| C18   | 0.42759(17) | 0.12389(13) | 0.61968(7)  | 0.0391                 | 1.0000    |
| C19   | 0.3601(2)   | 0.07012(18) | 0.66890(9)  | 0.0571                 | 1.0000    |
| C20   | 0.2756(2)   | -0.0059(2)  | 0.65850(10) | 0.0660                 | 1.0000    |
| C21   | 0.25578(19) | 0.02951(16) | 0.59881(9)  | 0.0531                 | 1.0000    |
| C22   | 0.32217(19) | 0.02300(15) | 0.54951(8)  | 0.0485                 | 1.0000    |
| C23   | 0.40794(18) | 0.09849(14) | 0.55984(7)  | 0.0423                 | 1.0000    |
| C31   | 0.20272(16) | 0.59655(13) | 0.76102(7)  | 0.0371                 | 1.0000    |
| C32   | 0.06383(16) | 0.68016(12) | 0.74281(7)  | 0.0359                 | 1.0000    |
| C33   | 0.03781(18) | 0.73647(14) | 0.68196(8)  | 0.0448                 | 1.0000    |
| C34   | -0.0877(2)  | 0.81644(15) | 0.66739(10) | 0.0537                 | 1.0000    |
| C35   | 0.18808(19) | 0.84033(15) | 0.71303(10) | 0.0551                 | 1.0000    |
| C36   | 0.16380(18) | 0.78465(15) | 0.77340(10) | 0.0518                 | 1.0000    |
| C37   | 0.03885(17) | 0.70527(14) | 0.78811(8)  | 0.0420                 | 1.0000    |
| C38   | 0.29970(15) | 0.65427(13) | 0.79561(7)  | 0.0354                 | 1.0000    |
| C39   | 0.37417(18) | 0.73045(16) | 0.76215(8)  | 0.0463                 | 1.0000    |
| C40   | 0.45436(19) | 0.78969(18) | 0.79291(9)  | 0.0549                 | 1.0000    |
| C41   | 0.46330(19) | 0.77379(17) | 0.85775(9)  | 0.0537                 | 1.0000    |

|      |             |             |             |        |         |
|------|-------------|-------------|-------------|--------|---------|
| C42  | 0.3913(2)   | 0.69763(17) | 0.89143(8)  | 0.0534 | 1.0000  |
| C43  | 0.30978(18) | 0.63857(14) | 0.86068(8)  | 0.0441 | 1.0000  |
| C51  | 0.31863(16) | 0.29157(13) | 0.88924(7)  | 0.0395 | 1.0000  |
| C52  | 0.19986(16) | 0.27592(13) | 0.93566(7)  | 0.0366 | 1.0000  |
| C53  | 0.12801(17) | 0.18789(14) | 0.93460(8)  | 0.0406 | 1.0000  |
| C54  | 0.01791(18) | 0.17422(16) | 0.97642(9)  | 0.0529 | 1.0000  |
| C55  | -0.0186(2)  | 0.24727(18) | 1.02038(9)  | 0.0609 | 1.0000  |
| C56  | 0.0525(2)   | 0.33431(19) | 1.02167(9)  | 0.0641 | 1.0000  |
| C57  | 0.1605(2)   | 0.34891(16) | 0.97951(9)  | 0.0528 | 1.0000  |
| C58  | 0.44577(15) | 0.19159(13) | 0.89947(7)  | 0.0360 | 1.0000  |
| C81  | 0.75296(17) | 0.39829(14) | 0.83219(7)  | 0.0399 | 1.0000  |
| C60  | 0.6157(2)   | 0.04210(17) | 0.86237(11) | 0.0652 | 1.0000  |
| C83  | 0.6519(2)   | 0.43151(17) | 0.93853(8)  | 0.0527 | 1.0000  |
| C62  | 0.6322(2)   | 0.07420(18) | 0.96799(11) | 0.0619 | 1.0000  |
| C63  | 0.51450(18) | 0.16207(15) | 0.95808(8)  | 0.0468 | 1.0000  |
| F1   | 0.43490(11) | 0.36839(8)  | 0.74413(5)  | 0.0513 | 1.0000  |
| N71  | 0.87553(13) | 0.37386(10) | 0.72580(5)  | 0.0317 | 1.0000  |
| C72  | 1.01109(15) | 0.39787(13) | 0.69277(7)  | 0.0335 | 1.0000  |
| C73  | 1.03410(18) | 0.36276(14) | 0.62773(7)  | 0.0410 | 1.0000  |
| C74  | 1.14053(18) | 0.42431(16) | 0.59186(8)  | 0.0475 | 1.0000  |
| C75  | 1.1729(2)   | 0.38915(18) | 0.52742(8)  | 0.0563 | 1.0000  |
| C76  | 0.74142(16) | 0.43273(13) | 0.68705(7)  | 0.0343 | 1.0000  |
| C77  | 0.72701(17) | 0.55884(13) | 0.66730(8)  | 0.0407 | 1.0000  |
| C78  | 0.59162(16) | 0.60566(14) | 0.62740(7)  | 0.0401 | 1.0000  |
| C79  | 0.57277(19) | 0.73214(15) | 0.60606(8)  | 0.0484 | 1.0000  |
| C80  | 0.87532(16) | 0.41747(12) | 0.78863(6)  | 0.0324 | 1.0000  |
| C117 | 0.7658(7)   | 0.1228(9)   | 0.6018(5)   | 0.0397 | 0.50(3) |
| C82  | 0.76057(18) | 0.45768(15) | 0.88926(7)  | 0.0435 | 1.0000  |
| C115 | 0.8855(10)  | 0.1985(12)  | 0.5113(5)   | 0.0532 | 0.50(3) |
| C84  | 0.87347(17) | 0.24787(12) | 0.73452(7)  | 0.0380 | 1.0000  |
| C85  | 0.98957(19) | 0.17241(13) | 0.77734(8)  | 0.0437 | 1.0000  |
| C86  | 0.9823(2)   | 0.04878(14) | 0.77733(9)  | 0.0503 | 1.0000  |
| C87  | 1.0880(2)   | 0.03090(15) | 0.82321(10) | 0.0626 | 1.0000  |
| C112 | 0.6470(9)   | 0.2081(9)   | 0.5890(5)   | 0.0405 | 0.50(3) |
| C116 | 0.8858(6)   | 0.1179(10)  | 0.5636(5)   | 0.0474 | 0.50(3) |
| C12  | 0.6335(9)   | 0.2214(9)   | 0.5853(5)   | 0.0414 | 0.50(3) |
| C14  | 0.7296(12)  | 0.3160(11)  | 0.4928(3)   | 0.0617 | 0.50(3) |
| C114 | 0.7694(13)  | 0.2840(9)   | 0.4975(4)   | 0.0548 | 0.50(3) |
| C113 | 0.6494(11)  | 0.2889(9)   | 0.5354(4)   | 0.0511 | 0.50(3) |
| H591 | 0.45326(19) | 0.14950(15) | 0.81105(9)  | 0.0587 | 1.0000  |

|      |             |             |             |        |         |
|------|-------------|-------------|-------------|--------|---------|
| H131 | 0.5355(10)  | 0.3652(9)   | 0.5312(4)   | 0.0681 | 0.50(3) |
| H611 | 0.7628(2)   | 0.04407(18) | 0.92750(12) | 0.0813 | 1.0000  |
| H151 | 0.9299(10)  | 0.2449(12)  | 0.4714(3)   | 0.0664 | 0.50(3) |
| H161 | 0.9591(8)   | 0.0988(11)  | 0.5565(4)   | 0.0639 | 0.50(3) |
| H171 | 0.7728(9)   | 0.0861(10)  | 0.6263(5)   | 0.0556 | 0.50(3) |
| H191 | 0.3752(2)   | 0.08391(18) | 0.70958(9)  | 0.0696 | 1.0000  |
| H201 | 0.2311(2)   | -0.0417(2)  | 0.69225(10) | 0.0799 | 1.0000  |
| H211 | 0.19638(19) | 0.08029(16) | 0.59144(9)  | 0.0633 | 1.0000  |
| H221 | 0.31125(19) | 0.00696(15) | 0.50839(8)  | 0.0578 | 1.0000  |
| H231 | 0.45111(18) | 0.13457(14) | 0.52492(7)  | 0.0508 | 1.0000  |
| H311 | 0.18189(16) | 0.53233(13) | 0.78939(7)  | 0.0433 | 1.0000  |
| H331 | 0.10621(18) | 0.72089(14) | 0.65031(8)  | 0.0540 | 1.0000  |
| H341 | -0.1054(2)  | 0.85208(15) | 0.62523(10) | 0.0641 | 1.0000  |
| H351 | 0.27254(19) | 0.89311(15) | 0.70282(10) | 0.0663 | 1.0000  |
| H361 | 0.23358(18) | 0.80050(15) | 0.80490(10) | 0.0621 | 1.0000  |
| H371 | 0.02399(17) | 0.66801(14) | 0.83029(8)  | 0.0495 | 1.0000  |
| H391 | 0.36894(18) | 0.74284(16) | 0.71786(8)  | 0.0552 | 1.0000  |
| H401 | 0.50208(19) | 0.84388(18) | 0.76924(9)  | 0.0668 | 1.0000  |
| H411 | 0.51713(19) | 0.81591(17) | 0.87904(9)  | 0.0639 | 1.0000  |
| H421 | 0.3985(2)   | 0.68482(17) | 0.93599(8)  | 0.0641 | 1.0000  |
| H431 | 0.25958(18) | 0.58564(14) | 0.88361(8)  | 0.0529 | 1.0000  |
| H511 | 0.35354(16) | 0.36299(13) | 0.89418(7)  | 0.0472 | 1.0000  |
| H531 | 0.15454(17) | 0.13756(14) | 0.90503(8)  | 0.0471 | 1.0000  |
| H541 | 0.02967(18) | 0.11577(16) | 0.97380(9)  | 0.0628 | 1.0000  |
| H551 | -0.0896(2)  | 0.23677(18) | 1.04918(9)  | 0.0724 | 1.0000  |
| H561 | 0.0294(2)   | 0.38525(19) | 1.05275(9)  | 0.0775 | 1.0000  |
| H571 | 0.2080(2)   | 0.40949(16) | 0.98113(9)  | 0.0642 | 1.0000  |
| H811 | 0.76039(17) | 0.31771(14) | 0.84671(7)  | 0.0494 | 1.0000  |
| H812 | 0.66290(17) | 0.42692(14) | 0.81096(7)  | 0.0491 | 1.0000  |
| H601 | 0.6509(2)   | 0.00258(17) | 0.82870(11) | 0.0784 | 1.0000  |
| H831 | 0.6572(2)   | 0.47119(17) | 0.97460(8)  | 0.0783 | 1.0000  |
| H832 | 0.6682(2)   | 0.34947(17) | 0.95226(8)  | 0.0787 | 1.0000  |
| H833 | 0.5555(2)   | 0.45481(17) | 0.92040(8)  | 0.0787 | 1.0000  |
| H621 | 0.6751(2)   | 0.05482(18) | 1.00775(11) | 0.0751 | 1.0000  |
| H631 | 0.47935(18) | 0.20190(15) | 0.99120(8)  | 0.0560 | 1.0000  |
| H721 | 1.08938(15) | 0.35919(13) | 0.72019(7)  | 0.0382 | 1.0000  |
| H722 | 1.00547(15) | 0.47992(13) | 0.68997(7)  | 0.0380 | 1.0000  |
| H731 | 1.07124(18) | 0.28162(14) | 0.63101(7)  | 0.0514 | 1.0000  |
| H732 | 0.94562(18) | 0.38082(14) | 0.60446(7)  | 0.0492 | 1.0000  |
| H741 | 1.22677(18) | 0.41337(16) | 0.61673(8)  | 0.0583 | 1.0000  |

|       |             |             |             |        |         |
|-------|-------------|-------------|-------------|--------|---------|
| H742  | 1.09908(18) | 0.50558(16) | 0.58772(8)  | 0.0581 | 1.0000  |
| H753  | 1.2412(2)   | 0.43055(18) | 0.50571(8)  | 0.0847 | 1.0000  |
| H752  | 1.2140(2)   | 0.30949(18) | 0.53062(8)  | 0.0832 | 1.0000  |
| H751  | 1.0855(2)   | 0.40317(18) | 0.50086(8)  | 0.0825 | 1.0000  |
| H762  | 0.66148(16) | 0.41655(13) | 0.71245(7)  | 0.0393 | 1.0000  |
| H761  | 0.74367(16) | 0.39474(13) | 0.65073(7)  | 0.0395 | 1.0000  |
| H771  | 0.72003(17) | 0.59820(13) | 0.70423(8)  | 0.0495 | 1.0000  |
| H772  | 0.81060(17) | 0.57318(13) | 0.64323(8)  | 0.0502 | 1.0000  |
| H781  | 0.50820(16) | 0.58867(14) | 0.65177(7)  | 0.0474 | 1.0000  |
| H782  | 0.59780(16) | 0.56589(14) | 0.59042(7)  | 0.0473 | 1.0000  |
| H793  | 0.48484(19) | 0.76079(15) | 0.58131(8)  | 0.0723 | 1.0000  |
| H792  | 0.56805(19) | 0.77370(15) | 0.64247(8)  | 0.0709 | 1.0000  |
| H791  | 0.65363(19) | 0.74906(15) | 0.57943(8)  | 0.0719 | 1.0000  |
| H801  | 0.96733(16) | 0.38182(12) | 0.80923(6)  | 0.0374 | 1.0000  |
| H802  | 0.87201(16) | 0.49726(12) | 0.77867(6)  | 0.0372 | 1.0000  |
| H1171 | 0.7647(7)   | 0.0690(9)   | 0.6361(5)   | 0.0475 | 0.50(3) |
| H821  | 0.85785(18) | 0.43425(15) | 0.90828(7)  | 0.0523 | 1.0000  |
| H822  | 0.74215(18) | 0.53911(15) | 0.87567(7)  | 0.0520 | 1.0000  |
| H1151 | 0.9670(10)  | 0.1942(12)  | 0.4846(5)   | 0.0649 | 0.50(3) |
| H841  | 0.77721(17) | 0.24106(12) | 0.75040(7)  | 0.0454 | 1.0000  |
| H842  | 0.88293(17) | 0.22545(12) | 0.69229(7)  | 0.0453 | 1.0000  |
| H851  | 0.97884(19) | 0.18960(13) | 0.81969(8)  | 0.0517 | 1.0000  |
| H852  | 1.08219(19) | 0.18436(13) | 0.76332(8)  | 0.0530 | 1.0000  |
| H862  | 0.8836(2)   | 0.03942(14) | 0.78716(9)  | 0.0607 | 1.0000  |
| H861  | 1.0029(2)   | 0.03168(14) | 0.73501(9)  | 0.0608 | 1.0000  |
| H873  | 1.0892(2)   | 0.10649(15) | 0.81732(10) | 0.0928 | 1.0000  |
| H872  | 1.0587(2)   | 0.02108(15) | 0.86632(10) | 0.0928 | 1.0000  |
| H871  | 1.1861(2)   | 0.01667(15) | 0.81701(10) | 0.0929 | 1.0000  |
| H1161 | 0.9649(6)   | 0.0590(10)  | 0.5737(5)   | 0.0570 | 0.50(3) |
| H141  | 0.7165(12)  | 0.3736(11)  | 0.4585(3)   | 0.0740 | 0.50(3) |
| H1141 | 0.7712(13)  | 0.3398(9)   | 0.4615(4)   | 0.0663 | 0.50(3) |
| H1131 | 0.5698(11)  | 0.3469(9)   | 0.5250(4)   | 0.0615 | 0.50(3) |
| H111  | 0.44970(18) | 0.29578(13) | 0.63002(7)  | 0.0481 | 1.0000  |
| H31   | 0.32456(12) | 0.32599(11) | 0.79979(5)  | 0.0760 | 1.0000  |
| H21   | 0.32667(12) | 0.49866(9)  | 0.72024(5)  | 0.0671 | 1.0000  |
| H11   | 0.51282(14) | 0.26062(12) | 0.71544(6)  | 0.0919 | 1.0000  |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| O1    | 0.0633(8)       | 0.0668(8)       | 0.0483(7)       | -0.0215(6)      | -0.0110(6)      | -0.0004(7)      |
| O2    | 0.0489(7)       | 0.0428(6)       | 0.0401(6)       | -0.0146(5)      | 0.0078(5)       | -0.0025(5)      |
| O3    | 0.0381(6)       | 0.0653(8)       | 0.0411(6)       | 0.0100(5)       | -0.0029(5)      | -0.0090(5)      |
| C11   | 0.0511(9)       | 0.0413(9)       | 0.0423(9)       | -0.0154(7)      | -0.0104(7)      | -0.0011(7)      |
| C59   | 0.0489(10)      | 0.0477(10)      | 0.0496(10)      | -0.0088(8)      | 0.0004(8)       | -0.0077(8)      |
| C13   | 0.063(3)        | 0.042(3)        | 0.065(3)        | 0.005(3)        | -0.030(2)       | -0.018(2)       |
| C61   | 0.0388(10)      | 0.0513(11)      | 0.1027(18)      | 0.0094(12)      | 0.0023(11)      | 0.0019(8)       |
| C15   | 0.064(3)        | 0.058(5)        | 0.047(2)        | 0.007(3)        | -0.017(3)       | -0.029(3)       |
| C16   | 0.062(3)        | 0.052(4)        | 0.044(3)        | 0.003(3)        | -0.017(2)       | -0.014(2)       |
| C17   | 0.065(3)        | 0.040(3)        | 0.034(3)        | -0.0005(19)     | -0.010(2)       | -0.010(2)       |
| C18   | 0.0380(8)       | 0.0405(8)       | 0.0362(8)       | -0.0096(7)      | -0.0013(6)      | 0.0018(7)       |
| C19   | 0.0580(11)      | 0.0765(13)      | 0.0384(9)       | -0.0140(9)      | 0.0055(8)       | -0.0134(10)     |
| C20   | 0.0601(12)      | 0.0823(15)      | 0.0561(12)      | -0.0010(11)     | 0.0157(10)      | -0.0228(11)     |
| C21   | 0.0407(9)       | 0.0514(10)      | 0.0683(12)      | -0.0099(9)      | 0.0040(8)       | -0.0110(8)      |
| C22   | 0.0499(10)      | 0.0524(10)      | 0.0462(10)      | -0.0144(8)      | -0.0020(8)      | -0.0121(8)      |
| C23   | 0.0485(9)       | 0.0454(9)       | 0.0348(8)       | -0.0073(7)      | -0.0003(7)      | -0.0126(7)      |
| C31   | 0.0414(8)       | 0.0345(8)       | 0.0363(8)       | -0.0085(6)      | 0.0092(6)       | -0.0082(6)      |
| C32   | 0.0362(8)       | 0.0312(7)       | 0.0447(9)       | -0.0116(6)      | 0.0038(6)       | -0.0133(6)      |
| C33   | 0.0437(9)       | 0.0432(9)       | 0.0486(10)      | -0.0049(7)      | 0.0053(7)       | -0.0125(7)      |
| C34   | 0.0517(10)      | 0.0454(10)      | 0.0622(12)      | 0.0024(8)       | -0.0068(9)      | -0.0117(8)      |
| C35   | 0.0362(9)       | 0.0432(10)      | 0.0867(15)      | -0.0134(9)      | -0.0021(9)      | -0.0063(7)      |
| C36   | 0.0378(9)       | 0.0518(10)      | 0.0709(13)      | -0.0228(9)      | 0.0098(8)       | -0.0121(8)      |
| C37   | 0.0391(8)       | 0.0428(9)       | 0.0492(9)       | -0.0152(7)      | 0.0073(7)       | -0.0148(7)      |
| C38   | 0.0313(7)       | 0.0372(8)       | 0.0365(8)       | -0.0072(6)      | 0.0070(6)       | -0.0029(6)      |
| C39   | 0.0411(9)       | 0.0674(11)      | 0.0337(8)       | -0.0072(8)      | 0.0071(7)       | -0.0192(8)      |
| C40   | 0.0461(10)      | 0.0764(13)      | 0.0485(10)      | -0.0050(9)      | 0.0057(8)       | -0.0306(9)      |
| C41   | 0.0464(10)      | 0.0724(12)      | 0.0479(10)      | -0.0102(9)      | -0.0050(8)      | -0.0237(9)      |
| C42   | 0.0605(11)      | 0.0670(12)      | 0.0340(9)       | -0.0057(8)      | -0.0029(8)      | -0.0166(9)      |
| C43   | 0.0501(10)      | 0.0457(9)       | 0.0360(8)       | -0.0021(7)      | 0.0041(7)       | -0.0112(8)      |
| C51   | 0.0359(8)       | 0.0400(8)       | 0.0418(9)       | -0.0021(7)      | -0.0035(6)      | -0.0081(7)      |
| C52   | 0.0335(8)       | 0.0382(8)       | 0.0350(8)       | -0.0012(6)      | -0.0045(6)      | -0.0021(6)      |
| C53   | 0.0368(8)       | 0.0416(9)       | 0.0417(9)       | -0.0048(7)      | -0.0031(7)      | -0.0041(7)      |
| C54   | 0.0397(9)       | 0.0522(10)      | 0.0618(11)      | 0.0106(9)       | -0.0025(8)      | -0.0101(8)      |
| C55   | 0.0496(11)      | 0.0712(13)      | 0.0467(10)      | 0.0124(9)       | 0.0141(8)       | 0.0088(10)      |
| C56   | 0.0737(13)      | 0.0683(13)      | 0.0455(11)      | -0.0146(9)      | 0.0103(9)       | 0.0018(11)      |
| C57   | 0.0588(11)      | 0.0515(10)      | 0.0498(10)      | -0.0143(8)      | 0.0004(8)       | -0.0097(9)      |
| C58   | 0.0305(7)       | 0.0384(8)       | 0.0398(8)       | -0.0015(6)      | -0.0019(6)      | -0.0108(6)      |

|      |            |            |            |             |             |             |
|------|------------|------------|------------|-------------|-------------|-------------|
| C81  | 0.0419(8)  | 0.0460(9)  | 0.0349(8)  | -0.0050(7)  | -0.0012(6)  | -0.0166(7)  |
| C60  | 0.0612(12) | 0.0489(11) | 0.0826(15) | -0.0147(10) | 0.0173(11)  | -0.0013(9)  |
| C83  | 0.0555(11) | 0.0676(12) | 0.0409(9)  | -0.0134(8)  | 0.0099(8)   | -0.0231(9)  |
| C62  | 0.0424(10) | 0.0662(13) | 0.0705(13) | 0.0159(11)  | -0.0191(9)  | -0.0114(9)  |
| C63  | 0.0422(9)  | 0.0522(10) | 0.0454(9)  | -0.0002(8)  | -0.0070(7)  | -0.0118(8)  |
| F1   | 0.0584(6)  | 0.0447(5)  | 0.0476(6)  | -0.0089(4)  | 0.0183(5)   | -0.0023(5)  |
| N71  | 0.0351(6)  | 0.0328(6)  | 0.0297(6)  | -0.0040(5)  | -0.0041(5)  | -0.0126(5)  |
| C72  | 0.0324(7)  | 0.0351(8)  | 0.0340(8)  | -0.0045(6)  | -0.0019(6)  | -0.0096(6)  |
| C73  | 0.0453(9)  | 0.0422(9)  | 0.0367(8)  | -0.0094(7)  | 0.0007(7)   | -0.0092(7)  |
| C74  | 0.0361(8)  | 0.0644(11) | 0.0442(9)  | -0.0147(8)  | 0.0063(7)   | -0.0103(8)  |
| C75  | 0.0493(10) | 0.0717(13) | 0.0461(10) | -0.0145(9)  | 0.0108(8)   | -0.0045(9)  |
| C76  | 0.0336(7)  | 0.0414(8)  | 0.0296(7)  | -0.0040(6)  | -0.0049(6)  | -0.0116(6)  |
| C77  | 0.0385(8)  | 0.0429(9)  | 0.0396(8)  | 0.0005(7)   | -0.0077(7)  | -0.0097(7)  |
| C78  | 0.0337(8)  | 0.0521(9)  | 0.0322(8)  | -0.0037(7)  | -0.0004(6)  | -0.0048(7)  |
| C79  | 0.0444(9)  | 0.0544(10) | 0.0395(9)  | 0.0018(8)   | -0.0027(7)  | 0.0010(8)   |
| C80  | 0.0376(8)  | 0.0326(7)  | 0.0295(7)  | -0.0050(6)  | -0.0046(6)  | -0.0124(6)  |
| C117 | 0.040(2)   | 0.041(3)   | 0.038(3)   | -0.0060(18) | -0.0065(18) | -0.0069(18) |
| C82  | 0.0490(9)  | 0.0506(10) | 0.0357(8)  | -0.0077(7)  | 0.0025(7)   | -0.0203(8)  |
| C115 | 0.053(3)   | 0.058(4)   | 0.053(3)   | -0.011(3)   | 0.002(3)    | -0.021(3)   |
| C84  | 0.0483(9)  | 0.0337(8)  | 0.0360(8)  | -0.0058(6)  | -0.0058(7)  | -0.0165(7)  |
| C85  | 0.0546(10) | 0.0341(8)  | 0.0445(9)  | -0.0057(7)  | -0.0090(7)  | -0.0130(7)  |
| C86  | 0.0593(11) | 0.0343(9)  | 0.0604(11) | -0.0106(8)  | -0.0007(9)  | -0.0136(8)  |
| C87  | 0.0854(15) | 0.0298(9)  | 0.0710(13) | -0.0059(8)  | -0.0098(11) | -0.0078(9)  |
| C112 | 0.050(3)   | 0.036(3)   | 0.038(3)   | -0.008(2)   | -0.011(2)   | -0.011(2)   |
| C116 | 0.040(2)   | 0.051(4)   | 0.052(3)   | -0.011(2)   | -0.006(2)   | -0.006(2)   |
| C12  | 0.050(3)   | 0.035(3)   | 0.042(3)   | -0.010(2)   | -0.020(2)   | -0.010(2)   |
| C14  | 0.069(3)   | 0.057(4)   | 0.060(3)   | 0.020(3)    | -0.026(3)   | -0.033(3)   |
| C114 | 0.065(4)   | 0.047(4)   | 0.051(3)   | 0.002(2)    | 0.000(3)    | -0.014(3)   |
| C113 | 0.061(3)   | 0.043(3)   | 0.048(3)   | -0.003(2)   | -0.008(2)   | -0.009(2)   |

## Distances

|     |      |             |  |     |      |           |
|-----|------|-------------|--|-----|------|-----------|
| O1  | C11  | 1.3982(19)Å |  | O1  | H11  | 0.982Å    |
| O2  | C31  | 1.4116(18)Å |  | O2  | H21  | 0.845Å    |
| O3  | C51  | 1.4117(19)Å |  | O3  | H31  | 0.901Å    |
| C11 | C18  | 1.531(2)Å   |  | C11 | C112 | 1.532(4)Å |
| C11 | C12  | 1.493(5)Å   |  | C11 | H111 | 1.067Å    |
| C59 | C58  | 1.376(2)Å   |  | C59 | C60  | 1.389(3)Å |
| C59 | H591 | 0.953Å      |  | C13 | C112 | 1.542(5)Å |
| C13 | C12  | 1.388(4)Å   |  | C13 | C14  | 1.382(4)Å |

|     |       |           |  |     |       |           |
|-----|-------|-----------|--|-----|-------|-----------|
| C13 | C114  | 1.622(9)Å |  | C13 | C113  | 0.334(7)Å |
| C13 | H131  | 0.941Å    |  | C13 | H1131 | 0.613Å    |
| C61 | C60   | 1.378(3)Å |  | C61 | C62   | 1.361(3)Å |
| C61 | H611  | 0.929Å    |  | C15 | C16   | 1.369(4)Å |
| C15 | C115  | 0.530(7)Å |  | C15 | C14   | 1.364(4)Å |
| C15 | C114  | 0.889(8)Å |  | C15 | H151  | 0.952Å    |
| C15 | H1151 | 1.163Å    |  | C16 | C17   | 1.385(5)Å |
| C16 | C117  | 1.537(9)Å |  | C16 | C115  | 0.966(9)Å |
| C16 | C116  | 0.464(8)Å |  | C16 | H161  | 0.937Å    |
| C17 | C117  | 0.297(8)Å |  | C17 | C112  | 1.204(6)Å |
| C17 | C116  | 1.327(9)Å |  | C17 | C12   | 1.379(4)Å |
| C17 | H171  | 0.926Å    |  | C17 | H1171 | 1.205Å    |
| C18 | C19   | 1.380(2)Å |  | C18 | C23   | 1.386(2)Å |
| C19 | C20   | 1.380(3)Å |  | C19 | H191  | 0.930Å    |
| C20 | C21   | 1.375(3)Å |  | C20 | H201  | 0.931Å    |
| C21 | C22   | 1.368(3)Å |  | C21 | H211  | 0.945Å    |
| C22 | C23   | 1.383(2)Å |  | C22 | H221  | 0.942Å    |
| C23 | H231  | 0.944Å    |  | C31 | C32   | 1.515(2)Å |
| C31 | C38   | 1.522(2)Å |  | C31 | H311  | 0.970Å    |
| C32 | C33   | 1.387(2)Å |  | C32 | C37   | 1.388(2)Å |
| C33 | C34   | 1.388(2)Å |  | C33 | H331  | 0.945Å    |
| C34 | C35   | 1.377(3)Å |  | C34 | H341  | 0.948Å    |
| C35 | C36   | 1.374(3)Å |  | C35 | H351  | 0.929Å    |
| C36 | C37   | 1.381(2)Å |  | C36 | H361  | 0.952Å    |
| C37 | H371  | 0.952Å    |  | C38 | C39   | 1.389(2)Å |
| C38 | C43   | 1.384(2)Å |  | C39 | C40   | 1.379(2)Å |
| C39 | H391  | 0.941Å    |  | C40 | C41   | 1.379(3)Å |
| C40 | H401  | 0.956Å    |  | C41 | C42   | 1.376(3)Å |
| C41 | H411  | 0.953Å    |  | C42 | C43   | 1.386(2)Å |
| C42 | H421  | 0.948Å    |  | C43 | H431  | 0.953Å    |
| C51 | C52   | 1.516(2)Å |  | C51 | C58   | 1.527(2)Å |
| C51 | H511  | 1.008Å    |  | C52 | C53   | 1.381(2)Å |
| C52 | C57   | 1.381(2)Å |  | C53 | C54   | 1.387(2)Å |
| C53 | H531  | 0.940Å    |  | C54 | C55   | 1.380(3)Å |
| C54 | H541  | 0.923Å    |  | C55 | C56   | 1.366(3)Å |
| C55 | H551  | 0.924Å    |  | C56 | C57   | 1.379(3)Å |
| C56 | H561  | 0.967Å    |  | C57 | H571  | 0.941Å    |
| C58 | C63   | 1.393(2)Å |  | C81 | C80   | 1.514(2)Å |
| C81 | C82   | 1.517(2)Å |  | C81 | H811  | 0.973Å    |
| C81 | H812  | 0.953Å    |  | C60 | H601  | 0.945Å    |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C83  | C82   | 1.512(2)Å   |  | C83  | H831  | 0.975Å      |
| C83  | H832  | 0.980Å      |  | C83  | H833  | 0.972Å      |
| C62  | C63   | 1.380(3)Å   |  | C62  | H621  | 0.930Å      |
| C63  | H631  | 0.937Å      |  | N71  | C72   | 1.5193(18)Å |
| N71  | C76   | 1.5249(18)Å |  | N71  | C80   | 1.5170(17)Å |
| N71  | C84   | 1.5197(18)Å |  | C72  | C73   | 1.517(2)Å   |
| C72  | H721  | 0.957Å      |  | C72  | H722  | 0.981Å      |
| C73  | C74   | 1.512(2)Å   |  | C73  | H731  | 0.972Å      |
| C73  | H732  | 0.955Å      |  | C74  | C75   | 1.514(2)Å   |
| C74  | H741  | 0.960Å      |  | C74  | H742  | 0.980Å      |
| C75  | H753  | 0.972Å      |  | C75  | H752  | 0.962Å      |
| C75  | H751  | 0.986Å      |  | C76  | C77   | 1.510(2)Å   |
| C76  | H762  | 0.964Å      |  | C76  | H761  | 0.959Å      |
| C77  | C78   | 1.521(2)Å   |  | C77  | H771  | 0.977Å      |
| C77  | H772  | 0.972Å      |  | C78  | C79   | 1.516(2)Å   |
| C78  | H781  | 0.983Å      |  | C78  | H782  | 0.981Å      |
| C79  | H793  | 0.973Å      |  | C79  | H792  | 0.985Å      |
| C79  | H791  | 0.987Å      |  | C80  | H801  | 0.976Å      |
| C80  | H802  | 0.957Å      |  | C117 | C112  | 1.374(4)Å   |
| C117 | C116  | 1.390(4)Å   |  | C117 | C12   | 1.560(5)Å   |
| C117 | H171  | 0.635Å      |  | C117 | H1171 | 0.915Å      |
| C82  | H821  | 0.987Å      |  | C82  | H822  | 0.972Å      |
| C115 | C116  | 1.381(4)Å   |  | C115 | C114  | 1.360(4)Å   |
| C115 | H151  | 1.084Å      |  | C115 | H1151 | 0.954Å      |
| C84  | C85   | 1.513(2)Å   |  | C84  | H841  | 0.986Å      |
| C84  | H842  | 0.981Å      |  | C85  | C86   | 1.517(2)Å   |
| C85  | H851  | 0.961Å      |  | C85  | H852  | 0.957Å      |
| C86  | C87   | 1.512(3)Å   |  | C86  | H862  | 0.983Å      |
| C86  | H861  | 0.969Å      |  | C87  | H873  | 0.942Å      |
| C87  | H872  | 0.979Å      |  | C87  | H871  | 0.985Å      |
| C112 | C12   | 0.192(4)Å   |  | C112 | C113  | 1.405(4)Å   |
| C116 | H161  | 0.710Å      |  | C116 | H1161 | 0.932Å      |
| C12  | C113  | 1.280(6)Å   |  | C14  | C114  | 0.485(8)Å   |
| C14  | C113  | 1.233(9)Å   |  | C14  | H141  | 0.932Å      |
| C14  | H1141 | 0.820Å      |  | C114 | C113  | 1.387(4)Å   |
| C114 | H1141 | 0.954Å      |  | C113 | H131  | 1.272Å      |
| C113 | H1131 | 0.931Å      |  | H131 | H1131 | 0.389Å      |
| H151 | H1151 | 0.672Å      |  | H161 | H1161 | 0.559Å      |
| H171 | H1171 | 0.295Å      |  | H141 | H1141 | 0.593Å      |



## Angles

|      |     |       |            |  |      |     |       |             |
|------|-----|-------|------------|--|------|-----|-------|-------------|
| C11  | O1  | H11   | 111.501°   |  | C31  | O2  | H21   | 103.793°    |
| C51  | O3  | H31   | 109.185°   |  | O1   | C11 | C18   | 110.71(14)° |
| O1   | C11 | C112  | 108.4(5)°  |  | C18  | C11 | C112  | 111.8(6)°   |
| O1   | C11 | C12   | 113.1(5)°  |  | C18  | C11 | C12   | 113.6(7)°   |
| C112 | C11 | C12   | 7.14(13)°  |  | O1   | C11 | H111  | 97.236°     |
| C18  | C11 | H111  | 113.084°   |  | C112 | C11 | H111  | 114.567°    |
| C12  | C11 | H111  | 108.053°   |  | C58  | C59 | C60   | 120.24(18)° |
| C58  | C59 | H591  | 120.302°   |  | C60  | C59 | H591  | 119.428°    |
| C112 | C13 | C12   | 4.5(3)°    |  | C112 | C13 | C14   | 116.5(3)°   |
| C12  | C13 | C14   | 121.01(6)° |  | C112 | C13 | C114  | 100.3(3)°   |
| C12  | C13 | C114  | 104.8(3)°  |  | C14  | C13 | C114  | 16.2(3)°    |
| C112 | C13 | C113  | 59.9(13)°  |  | C12  | C13 | C113  | 64.3(15)°   |
| C14  | C13 | C113  | 57.0(15)°  |  | C114 | C13 | C113  | 40.9(14)°   |
| C112 | C13 | H131  | 123.591°   |  | C12  | C13 | H131  | 119.072°    |
| C14  | C13 | H131  | 119.918°   |  | C114 | C13 | H131  | 136.108°    |
| C113 | C13 | H131  | 173.206°   |  | C112 | C13 | H1131 | 137.466°    |
| C12  | C13 | H1131 | 132.995°   |  | C14  | C13 | H1131 | 105.487°    |
| C114 | C13 | H1131 | 121.464°   |  | C113 | C13 | H1131 | 158.169°    |
| H131 | C13 | H1131 | 15.924°    |  | C60  | C61 | C62   | 119.58(18)° |
| C60  | C61 | H611  | 120.585°   |  | C62  | C61 | H611  | 119.836°    |
| C16  | C15 | C115  | 32.6(11)°  |  | C16  | C15 | C14   | 120.36(6)°  |
| C115 | C15 | C14   | 151.0(11)° |  | C16  | C15 | C114  | 115.6(5)°   |
| C115 | C15 | C114  | 145.8(15)° |  | C14  | C15 | C114  | 5.3(6)°     |
| C16  | C15 | H151  | 121.083°   |  | C115 | C15 | H151  | 89.332°     |
| C14  | C15 | H151  | 118.558°   |  | C114 | C15 | H151  | 123.202°    |
| C16  | C15 | H1151 | 86.089°    |  | C115 | C15 | H1151 | 54.031°     |
| C14  | C15 | H1151 | 153.097°   |  | C114 | C15 | H1151 | 156.988°    |
| H151 | C15 | H1151 | 35.304°    |  | C15  | C16 | C17   | 119.82(6)°  |
| C15  | C16 | C117  | 129.7(2)°  |  | C17  | C16 | C117  | 10.0(3)°    |
| C15  | C16 | C115  | 17.2(5)°   |  | C17  | C16 | C115  | 136.3(5)°   |
| C117 | C16 | C115  | 145.8(7)°  |  | C15  | C16 | C116  | 164.9(17)°  |
| C17  | C16 | C116  | 73.1(12)°  |  | C117 | C16 | C116  | 63.0(11)°   |
| C115 | C16 | C116  | 148.1(18)° |  | C15  | C16 | H161  | 120.548°    |
| C17  | C16 | H161  | 119.636°   |  | C117 | C16 | H161  | 109.733°    |
| C115 | C16 | H161  | 103.877°   |  | C116 | C16 | H161  | 47.337°     |
| C16  | C17 | C117  | 115.6(19)° |  | C16  | C17 | C112  | 124.5(3)°   |
| C117 | C17 | C112  | 119(2)°    |  | C16  | C17 | C116  | 19.5(3)°    |
| C117 | C17 | C116  | 96.1(19)°  |  | C112 | C17 | C116  | 143.7(6)°   |

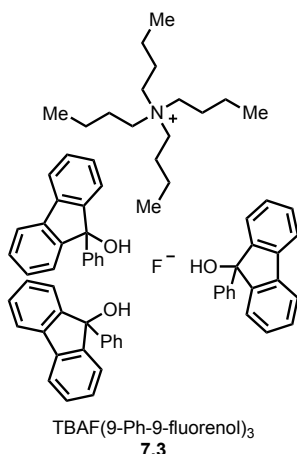
|      |     |       |             |  |      |     |       |             |
|------|-----|-------|-------------|--|------|-----|-------|-------------|
| C16  | C17 | C12   | 120.98(6)°  |  | C117 | C17 | C12   | 122.6(20)°  |
| C112 | C17 | C12   | 3.6(3)°     |  | C116 | C17 | C12   | 140.2(3)°   |
| C16  | C17 | H171  | 120.338°    |  | C117 | C17 | H171  | 9.906°      |
| C112 | C17 | H171  | 115.119°    |  | C116 | C17 | H171  | 101.003°    |
| C12  | C17 | H171  | 118.677°    |  | C16  | C17 | H1171 | 124.672°    |
| C117 | C17 | H1171 | 10.749°     |  | C112 | C17 | H1171 | 110.703°    |
| C116 | C17 | H1171 | 105.220°    |  | C12  | C17 | H1171 | 114.271°    |
| H171 | C17 | H1171 | 5.102°      |  | C11  | C18 | C19   | 120.66(15)° |
| C11  | C18 | C23   | 121.53(14)° |  | C19  | C18 | C23   | 117.73(16)° |
| C18  | C19 | C20   | 120.81(17)° |  | C18  | C19 | H191  | 118.833°    |
| C20  | C19 | H191  | 120.321°    |  | C19  | C20 | C21   | 120.91(18)° |
| C19  | C20 | H201  | 119.713°    |  | C21  | C20 | H201  | 119.381°    |
| C20  | C21 | C22   | 118.99(17)° |  | C20  | C21 | H211  | 121.078°    |
| C22  | C21 | H211  | 119.924°    |  | C21  | C22 | C23   | 120.26(17)° |
| C21  | C22 | H221  | 120.251°    |  | C23  | C22 | H221  | 119.482°    |
| C18  | C23 | C22   | 121.30(16)° |  | C18  | C23 | H231  | 120.123°    |
| C22  | C23 | H231  | 118.546°    |  | O2   | C31 | C32   | 109.01(12)° |
| O2   | C31 | C38   | 112.49(12)° |  | C32  | C31 | C38   | 108.77(12)° |
| O2   | C31 | H311  | 108.988°    |  | C32  | C31 | H311  | 109.265°    |
| C38  | C31 | H311  | 108.279°    |  | C31  | C32 | C33   | 121.67(14)° |
| C31  | C32 | C37   | 119.93(14)° |  | C33  | C32 | C37   | 118.36(15)° |
| C32  | C33 | C34   | 120.31(16)° |  | C32  | C33 | H331  | 119.909°    |
| C34  | C33 | H331  | 119.780°    |  | C33  | C34 | C35   | 120.45(18)° |
| C33  | C34 | H341  | 119.180°    |  | C35  | C34 | H341  | 120.318°    |
| C34  | C35 | C36   | 119.76(17)° |  | C34  | C35 | H351  | 120.018°    |
| C36  | C35 | H351  | 120.219°    |  | C35  | C36 | C37   | 119.96(17)° |
| C35  | C36 | H361  | 119.851°    |  | C37  | C36 | H361  | 120.187°    |
| C32  | C37 | C36   | 121.17(17)° |  | C32  | C37 | H371  | 120.279°    |
| C36  | C37 | H371  | 118.554°    |  | C31  | C38 | C39   | 120.06(14)° |
| C31  | C38 | C43   | 121.74(14)° |  | C39  | C38 | C43   | 118.07(15)° |
| C38  | C39 | C40   | 120.91(15)° |  | C38  | C39 | H391  | 119.786°    |
| C40  | C39 | H391  | 119.301°    |  | C39  | C40 | C41   | 120.59(16)° |
| C39  | C40 | H401  | 119.879°    |  | C41  | C40 | H401  | 119.506°    |
| C40  | C41 | C42   | 119.06(16)° |  | C40  | C41 | H411  | 120.575°    |
| C42  | C41 | H411  | 120.357°    |  | C41  | C42 | C43   | 120.50(16)° |
| C41  | C42 | H421  | 119.711°    |  | C43  | C42 | H421  | 119.787°    |
| C38  | C43 | C42   | 120.87(16)° |  | C38  | C43 | H431  | 118.051°    |
| C42  | C43 | H431  | 121.082°    |  | O3   | C51 | C52   | 107.60(12)° |
| O3   | C51 | C58   | 113.19(13)° |  | C52  | C51 | C58   | 111.51(12)° |
| O3   | C51 | H511  | 105.958°    |  | C52  | C51 | H511  | 109.792°    |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C58  | C51 | H511 | 108.613°    |  | C51  | C52 | C53  | 120.27(14)° |
| C51  | C52 | C57  | 121.21(15)° |  | C53  | C52 | C57  | 118.53(15)° |
| C52  | C53 | C54  | 120.44(16)° |  | C52  | C53 | H531 | 119.043°    |
| C54  | C53 | H531 | 120.517°    |  | C53  | C54 | C55  | 120.11(18)° |
| C53  | C54 | H541 | 118.354°    |  | C55  | C54 | H541 | 121.537°    |
| C54  | C55 | C56  | 119.62(17)° |  | C54  | C55 | H551 | 120.240°    |
| C56  | C55 | H551 | 120.135°    |  | C55  | C56 | C57  | 120.28(18)° |
| C55  | C56 | H561 | 120.540°    |  | C57  | C56 | H561 | 119.164°    |
| C52  | C57 | C56  | 121.01(18)° |  | C52  | C57 | H571 | 120.042°    |
| C56  | C57 | H571 | 118.942°    |  | C59  | C58 | C51  | 121.85(14)° |
| C59  | C58 | C63  | 118.47(15)° |  | C51  | C58 | C63  | 119.67(15)° |
| C80  | C81 | C82  | 109.29(12)° |  | C80  | C81 | H811 | 110.483°    |
| C82  | C81 | H811 | 108.172°    |  | C80  | C81 | H812 | 110.404°    |
| C82  | C81 | H812 | 109.748°    |  | H811 | C81 | H812 | 108.712°    |
| C59  | C60 | C61  | 120.5(2)°   |  | C59  | C60 | H601 | 118.887°    |
| C61  | C60 | H601 | 120.565°    |  | C82  | C83 | H831 | 111.375°    |
| C82  | C83 | H832 | 109.650°    |  | H831 | C83 | H832 | 109.999°    |
| C82  | C83 | H833 | 109.641°    |  | H831 | C83 | H833 | 108.577°    |
| H832 | C83 | H833 | 107.512°    |  | C61  | C62 | C63  | 120.40(19)° |
| C61  | C62 | H621 | 120.270°    |  | C63  | C62 | H621 | 119.307°    |
| C58  | C63 | C62  | 120.77(18)° |  | C58  | C63 | H631 | 119.381°    |
| C62  | C63 | H631 | 119.840°    |  | C72  | N71 | C76  | 111.28(11)° |
| C72  | N71 | C80  | 106.13(10)° |  | C76  | N71 | C80  | 110.89(11)° |
| C72  | N71 | C84  | 111.10(11)° |  | C76  | N71 | C84  | 106.17(10)° |
| C80  | N71 | C84  | 111.35(11)° |  | N71  | C72 | C73  | 115.89(12)° |
| N71  | C72 | H721 | 106.002°    |  | C73  | C72 | H721 | 110.051°    |
| N71  | C72 | H722 | 106.094°    |  | C73  | C72 | H722 | 109.549°    |
| H721 | C72 | H722 | 108.994°    |  | C72  | C73 | C74  | 110.37(13)° |
| C72  | C73 | H731 | 110.274°    |  | C74  | C73 | H731 | 108.588°    |
| C72  | C73 | H732 | 110.324°    |  | C74  | C73 | H732 | 108.412°    |
| H731 | C73 | H732 | 108.820°    |  | C73  | C74 | C75  | 112.91(15)° |
| C73  | C74 | H741 | 109.381°    |  | C75  | C74 | H741 | 111.278°    |
| C73  | C74 | H742 | 107.061°    |  | C75  | C74 | H742 | 109.986°    |
| H741 | C74 | H742 | 105.909°    |  | C74  | C75 | H753 | 110.634°    |
| C74  | C75 | H752 | 111.099°    |  | H753 | C75 | H752 | 107.675°    |
| C74  | C75 | H751 | 111.912°    |  | H753 | C75 | H751 | 108.192°    |
| H752 | C75 | H751 | 107.149°    |  | N71  | C76 | C77  | 115.78(11)° |
| N71  | C76 | H762 | 105.476°    |  | C77  | C76 | H762 | 110.946°    |
| N71  | C76 | H761 | 105.889°    |  | C77  | C76 | H761 | 110.245°    |
| H762 | C76 | H761 | 108.088°    |  | C76  | C77 | C78  | 110.20(13)° |

|      |      |       |             |  |      |      |       |             |
|------|------|-------|-------------|--|------|------|-------|-------------|
| C76  | C77  | H771  | 110.423°    |  | C78  | C77  | H771  | 108.003°    |
| C76  | C77  | H772  | 109.398°    |  | C78  | C77  | H772  | 109.641°    |
| H771 | C77  | H772  | 109.148°    |  | C77  | C78  | C79   | 112.20(14)° |
| C77  | C78  | H781  | 108.880°    |  | C79  | C78  | H781  | 110.347°    |
| C77  | C78  | H782  | 108.277°    |  | C79  | C78  | H782  | 109.423°    |
| H781 | C78  | H782  | 107.581°    |  | C78  | C79  | H793  | 111.036°    |
| C78  | C79  | H792  | 110.824°    |  | H793 | C79  | H792  | 108.097°    |
| C78  | C79  | H791  | 110.561°    |  | H793 | C79  | H791  | 107.546°    |
| H792 | C79  | H791  | 108.664°    |  | C81  | C80  | N71   | 116.36(11)° |
| C81  | C80  | H801  | 110.137°    |  | N71  | C80  | H801  | 106.663°    |
| C81  | C80  | H802  | 109.038°    |  | N71  | C80  | H802  | 105.611°    |
| H801 | C80  | H802  | 108.734°    |  | C16  | C117 | C17   | 54.4(18)°   |
| C16  | C117 | C112  | 103.9(3)°   |  | C17  | C117 | C112  | 50.0(19)°   |
| C16  | C117 | C116  | 17.3(3)°    |  | C17  | C117 | C116  | 71.7(18)°   |
| C112 | C117 | C116  | 121.04(6)°  |  | C16  | C117 | C12   | 102.0(4)°   |
| C17  | C117 | C12   | 48.1(17)°   |  | C112 | C117 | C12   | 1.9(3)°     |
| C116 | C117 | C12   | 119.1(3)°   |  | C16  | C117 | H171  | 131.956°    |
| C17  | C117 | H171  | 165.477°    |  | C112 | C117 | H171  | 123.542°    |
| C116 | C117 | H171  | 115.176°    |  | C12  | C117 | H171  | 125.440°    |
| C16  | C117 | H1171 | 137.419°    |  | C17  | C117 | H1171 | 165.777°    |
| C112 | C117 | H1171 | 118.657°    |  | C116 | C117 | H1171 | 120.308°    |
| C12  | C117 | H1171 | 120.569°    |  | H171 | C117 | H1171 | 6.981°      |
| C81  | C82  | C83   | 112.41(13)° |  | C81  | C82  | H821  | 109.468°    |
| C83  | C82  | H821  | 108.912°    |  | C81  | C82  | H822  | 108.667°    |
| C83  | C82  | H822  | 108.674°    |  | H821 | C82  | H822  | 108.638°    |
| C15  | C115 | C16   | 130.2(15)°  |  | C15  | C115 | C116  | 140.3(11)°  |
| C16  | C115 | C116  | 10.2(5)°    |  | C15  | C115 | C114  | 21.5(10)°   |
| C16  | C115 | C114  | 110.8(5)°   |  | C116 | C115 | C114  | 120.37(6)°  |
| C15  | C115 | H151  | 61.413°     |  | C16  | C115 | H151  | 164.504°    |
| C116 | C115 | H151  | 157.042°    |  | C114 | C115 | H151  | 82.161°     |
| C15  | C115 | H1151 | 99.251°     |  | C16  | C115 | H1151 | 129.312°    |
| C116 | C115 | H1151 | 119.912°    |  | C114 | C115 | H1151 | 119.717°    |
| H151 | C115 | H1151 | 37.840°     |  | N71  | C84  | C85   | 115.82(12)° |
| N71  | C84  | H841  | 105.791°    |  | C85  | C84  | H841  | 110.908°    |
| N71  | C84  | H842  | 105.946°    |  | C85  | C84  | H842  | 109.332°    |
| H841 | C84  | H842  | 108.733°    |  | C84  | C85  | C86   | 110.08(13)° |
| C84  | C85  | H851  | 110.880°    |  | C86  | C85  | H851  | 108.984°    |
| C84  | C85  | H852  | 110.055°    |  | C86  | C85  | H852  | 109.231°    |
| H851 | C85  | H852  | 107.557°    |  | C85  | C86  | C87   | 112.78(15)° |
| C85  | C86  | H862  | 108.411°    |  | C87  | C86  | H862  | 110.498°    |

|      |      |       |            |  |      |      |       |            |
|------|------|-------|------------|--|------|------|-------|------------|
| C85  | C86  | H861  | 107.335°   |  | C87  | C86  | H861  | 109.579°   |
| H862 | C86  | H861  | 108.086°   |  | C86  | C87  | H873  | 109.631°   |
| C86  | C87  | H872  | 109.459°   |  | H873 | C87  | H872  | 109.031°   |
| C86  | C87  | H871  | 111.496°   |  | H873 | C87  | H871  | 108.069°   |
| H872 | C87  | H871  | 109.111°   |  | C11  | C112 | C13   | 109.4(3)°  |
| C11  | C112 | C17   | 131.7(4)°  |  | C13  | C112 | C17   | 118.9(6)°  |
| C11  | C112 | C117  | 121.00(6)° |  | C13  | C112 | C117  | 129.6(3)°  |
| C17  | C112 | C117  | 10.9(4)°   |  | C11  | C112 | C12   | 75(2)°     |
| C13  | C112 | C12   | 35(2)°     |  | C17  | C112 | C12   | 153(3)°    |
| C117 | C112 | C12   | 164(2)°    |  | C11  | C112 | C113  | 121.07(6)° |
| C13  | C112 | C113  | 11.9(3)°   |  | C17  | C112 | C113  | 107.2(4)°  |
| C117 | C112 | C113  | 117.91(6)° |  | C12  | C112 | C113  | 46(2)°     |
| C16  | C116 | C17   | 87.4(11)°  |  | C16  | C116 | C117  | 99.7(12)°  |
| C17  | C116 | C117  | 12.3(3)°   |  | C16  | C116 | C115  | 21.7(13)°  |
| C17  | C116 | C115  | 107.8(3)°  |  | C117 | C116 | C115  | 119.89(6)° |
| C16  | C116 | H161  | 103.988°   |  | C17  | C116 | H161  | 164.703°   |
| C117 | C116 | H161  | 154.291°   |  | C115 | C116 | H161  | 85.124°    |
| C16  | C116 | H1161 | 140.757°   |  | C17  | C116 | H1161 | 131.007°   |
| C117 | C116 | H1161 | 118.886°   |  | C115 | C116 | H1161 | 121.217°   |
| H161 | C116 | H1161 | 36.770°    |  | C11  | C12  | C13   | 121.02(6)° |
| C11  | C12  | C17   | 121.02(6)° |  | C13  | C12  | C17   | 117.93(6)° |
| C11  | C12  | C117  | 111.9(3)°  |  | C13  | C12  | C117  | 127.0(3)°  |
| C17  | C12  | C117  | 9.2(4)°    |  | C11  | C12  | C112  | 98(2)°     |
| C13  | C12  | C112  | 141(2)°    |  | C17  | C12  | C112  | 23(2)°     |
| C117 | C12  | C112  | 14(2)°     |  | C11  | C12  | C113  | 134.4(3)°  |
| C13  | C12  | C113  | 13.6(4)°   |  | C17  | C12  | C113  | 104.5(3)°  |
| C117 | C12  | C113  | 113.6(5)°  |  | C112 | C12  | C113  | 127(3)°    |
| C13  | C14  | C15   | 119.82(6)° |  | C13  | C14  | C114  | 111.2(10)° |
| C15  | C14  | C114  | 9.7(12)°   |  | C13  | C14  | C113  | 13.1(3)°   |
| C15  | C14  | C113  | 106.9(3)°  |  | C114 | C14  | C113  | 98.2(11)°  |
| C13  | C14  | H141  | 119.592°   |  | C15  | C14  | H141  | 120.586°   |
| C114 | C14  | H141  | 128.952°   |  | C113 | C14  | H141  | 132.456°   |
| C13  | C14  | H1141 | 158.476°   |  | C15  | C14  | H1141 | 81.694°    |
| C114 | C14  | H1141 | 90.172°    |  | C113 | C14  | H1141 | 170.903°   |
| H141 | C14  | H1141 | 38.894°    |  | C13  | C114 | C15   | 140.4(8)°  |
| C13  | C114 | C115  | 128.7(2)°  |  | C15  | C114 | C115  | 12.6(6)°   |
| C13  | C114 | C14   | 52.6(9)°   |  | C15  | C114 | C14   | 165.0(18)° |
| C115 | C114 | C14   | 177(2)°    |  | C13  | C114 | C113  | 9.1(3)°    |
| C15  | C114 | C113  | 131.7(6)°  |  | C115 | C114 | C113  | 119.79(6)° |
| C14  | C114 | C113  | 61.6(11)°  |  | C13  | C114 | H1141 | 111.797°   |

|      |       |       |            |  |      |       |       |            |
|------|-------|-------|------------|--|------|-------|-------|------------|
| C15  | C114  | H1141 | 107.431°   |  | C115 | C114  | H1141 | 119.478°   |
| C14  | C114  | H1141 | 59.255°    |  | C113 | C114  | H1141 | 120.733°   |
| C13  | C113  | C112  | 108.3(16)° |  | C13  | C113  | C12   | 102.1(18)° |
| C112 | C113  | C12   | 6.3(3)°    |  | C13  | C113  | C14   | 109.8(16)° |
| C112 | C113  | C14   | 141.1(4)°  |  | C12  | C113  | C14   | 147.4(6)°  |
| C13  | C113  | C114  | 130.0(17)° |  | C112 | C113  | C114  | 120.98(6)° |
| C12  | C113  | C114  | 127.2(3)°  |  | C14  | C113  | C114  | 20.3(3)°   |
| C13  | C113  | H131  | 5.017°     |  | C112 | C113  | H131  | 110.915°   |
| C12  | C113  | H131  | 104.667°   |  | C14  | C113  | H131  | 107.677°   |
| C114 | C113  | H131  | 127.940°   |  | C13  | C113  | H1131 | 14.177°    |
| C112 | C113  | H1131 | 120.004°   |  | C12  | C113  | H1131 | 113.756°   |
| C14  | C113  | H1131 | 98.813°    |  | C114 | C113  | H1131 | 119.020°   |
| H131 | C113  | H1131 | 9.859°     |  | C13  | H131  | C113  | 1.777°     |
| C13  | H131  | H1131 | 25.638°    |  | C113 | H131  | H1131 | 24.203°    |
| C15  | H151  | C115  | 29.255°    |  | C15  | H151  | H1151 | 89.760°    |
| C115 | H151  | H1151 | 60.508°    |  | C16  | H161  | C116  | 28.675°    |
| C16  | H161  | H1161 | 122.415°   |  | C116 | H161  | H1161 | 93.740°    |
| C17  | H171  | C117  | 4.618°     |  | C17  | H171  | H1171 | 158.668°   |
| C117 | H171  | H1171 | 157.826°   |  | C17  | H1171 | C117  | 3.474°     |
| C17  | H1171 | H171  | 16.231°    |  | C117 | H1171 | H171  | 15.193°    |
| C15  | H1151 | C115  | 26.719°    |  | C15  | H1151 | H151  | 54.936°    |
| C115 | H1151 | H151  | 81.653°    |  | C116 | H1161 | H161  | 49.490°    |
| C14  | H141  | H1141 | 60.283°    |  | C14  | H1141 | C114  | 30.573°    |
| C14  | H1141 | H141  | 80.823°    |  | C114 | H1141 | H141  | 111.320°   |
| C13  | H1131 | C113  | 7.653°     |  | C13  | H1131 | H131  | 138.437°   |
| C113 | H1131 | H131  | 145.938°   |  |      |       |       |            |



**tetra-*n*-butylammonium fluoride tris(9-phenyl-9-fluorenol) (TBAF(9-Ph-9-fluorenol)<sub>3</sub>, 7.3):**

**X-ray** (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.3** in EtOAc, which had previously been prepared by dissolving **7.3** in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 004GWP12

## Crystal Data

$$a = 14.56830(10) \text{ \AA} \quad \alpha = 91.2454(7)^\circ$$

$$b = 19.9837(2) \text{ \AA} \quad \beta = 94.4191(7)^\circ$$

$$c = 20.7534(2) \text{ \AA} \quad \gamma = 103.9009(8)^\circ$$

$$\text{Volume} \quad 5842.46(9) \text{ \AA}^3$$

$$\text{Space group} \quad P -1$$

$$\text{Formula} \quad \text{C}_{73} \text{H}_{78} \text{F}_1 \text{N}_1 \text{O}_3$$

$$\text{Cell determined from} \quad 141894 \text{ reflections}$$

$$\text{Temperature} \quad 150\text{K}$$

$$\text{Shape} \quad \text{block}$$

$$\text{Colour} \quad \text{clear\_pale\_colourless}$$

$$D_x \quad 1.18 \text{ Mg m}^{-3}$$

$$\mu \quad 0.561 \text{ mm}^{-1}$$

$$\text{Absorption correction} \quad \text{multi-scan}$$

$$T_{\min} \quad 0.47$$

$$\text{Crystal Class} \quad \text{triclinic}$$

$$Z = \quad 4$$

$$M_r \quad 1036.43$$

$$\text{Cell } \theta \text{ range} = 3 - 76^\circ$$

$$\text{Size} \quad 0.21 \times 0.24 \times 0.26 \text{ mm}$$

$$F000 \quad 2224.000$$

$$T_{\max} \quad 0.89$$

## Data Collection

$$\text{Diffractometer} \quad \text{multi-scan}$$

$$\text{Scan type} \quad \omega \text{ scans}$$

$$\text{Reflections measured} \quad 227665$$

$$\text{Independent reflections} \quad 24424$$

$$R_{\text{int}} \quad 0.0260$$

$$\theta_{\max} \quad 76.6556$$

$$h = \quad -18 \rightarrow 18$$

$$k = \quad -24 \rightarrow 25$$

$$l = \quad -26 \rightarrow 26$$

## Refinement

$$\Delta\rho_{\min} = \quad -0.30 \text{ e \AA}^{-3}$$

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\max}$ =  | 0.52 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 20878                                                                                                                                                                                       |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 1406                                                                                                                                                                                        |
| S =                    | 0.99                                                                                                                                                                                        |
| R-factor               | 0.043                                                                                                                                                                                       |
| weighted R-factor      | 0.098                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0122                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.039 \times P)^2 + 2.940 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | <i>x</i>    | <i>y</i>   | <i>z</i>   | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|------------|------------|------------------------|-----------|
| F1    | 0.61935(5)  | 0.85750(4) | 0.25220(4) | 0.0359                 | 1.0000    |
| F2    | 0.19771(5)  | 0.41171(5) | 0.29033(4) | 0.0417                 | 1.0000    |
| O11   | 0.45609(6)  | 0.83384(4) | 0.29473(4) | 0.0282                 | 1.0000    |
| O12   | 0.51011(6)  | 0.79247(4) | 0.15152(4) | 0.0273                 | 1.0000    |
| O13   | 0.79470(6)  | 0.91173(4) | 0.24144(5) | 0.0309                 | 1.0000    |
| O14   | 0.36029(6)  | 0.42842(4) | 0.25275(4) | 0.0285                 | 1.0000    |
| O15   | 0.02598(6)  | 0.37027(4) | 0.27411(4) | 0.0248                 | 1.0000    |
| O16   | 0.05572(6)  | 0.30606(4) | 0.15706(4) | 0.0305                 | 1.0000    |
| C101  | 0.43484(9)  | 0.86095(6) | 0.35367(6) | 0.0257                 | 1.0000    |
| C102  | 0.47445(9)  | 0.82895(6) | 0.41257(6) | 0.0272                 | 1.0000    |
| C103  | 0.56831(10) | 0.83423(7) | 0.43346(7) | 0.0361                 | 1.0000    |
| C104  | 0.58839(12) | 0.80008(8) | 0.48850(8) | 0.0449                 | 1.0000    |
| C105  | 0.51622(12) | 0.76217(8) | 0.52206(7) | 0.0440                 | 1.0000    |
| C106  | 0.42188(11) | 0.75666(7) | 0.50122(7) | 0.0374                 | 1.0000    |
| C107  | 0.40110(10) | 0.79022(6) | 0.44576(6) | 0.0291                 | 1.0000    |
| C108  | 0.30992(9)  | 0.79335(6) | 0.41168(6) | 0.0284                 | 1.0000    |
| C109  | 0.32832(9)  | 0.83423(6) | 0.35819(6) | 0.0260                 | 1.0000    |
| C110  | 0.25541(10) | 0.84589(7) | 0.31706(7) | 0.0332                 | 1.0000    |
| C111  | 0.16243(10) | 0.81616(8) | 0.32954(7) | 0.0379                 | 1.0000    |
| C112  | 0.14374(10) | 0.77540(7) | 0.38256(8) | 0.0387                 | 1.0000    |
| C113  | 0.21703(10) | 0.76344(7) | 0.42393(7) | 0.0358                 | 1.0000    |
| C114  | 0.46352(9)  | 0.93981(6) | 0.35987(6) | 0.0278                 | 1.0000    |
| C115  | 0.51315(11) | 0.97950(7) | 0.31417(7) | 0.0368                 | 1.0000    |
| C116  | 0.53611(13) | 1.05105(8) | 0.32155(8) | 0.0480                 | 1.0000    |
| C117  | 0.50972(13) | 1.08338(8) | 0.37381(8) | 0.0483                 | 1.0000    |
| C118  | 0.46148(13) | 1.04431(8) | 0.41987(8) | 0.0475                 | 1.0000    |



|      |             |            |             |        |        |
|------|-------------|------------|-------------|--------|--------|
| C119 | 0.43912(12) | 0.97333(7) | 0.41305(7)  | 0.0411 | 1.0000 |
| C120 | 0.50458(9)  | 0.82856(6) | 0.09374(6)  | 0.0246 | 1.0000 |
| C121 | 0.60208(8)  | 0.86367(6) | 0.07264(6)  | 0.0243 | 1.0000 |
| C122 | 0.66987(9)  | 0.91684(7) | 0.10439(6)  | 0.0279 | 1.0000 |
| C123 | 0.75475(9)  | 0.94084(7) | 0.07660(7)  | 0.0351 | 1.0000 |
| C124 | 0.77100(10) | 0.91249(8) | 0.01826(7)  | 0.0399 | 1.0000 |
| C125 | 0.70246(10) | 0.85947(8) | 0.01406(7)  | 0.0365 | 1.0000 |
| C126 | 0.61746(9)  | 0.83533(7) | 0.01333(6)  | 0.0284 | 1.0000 |
| C127 | 0.53224(9)  | 0.78139(7) | 0.00917(6)  | 0.0299 | 1.0000 |
| C128 | 0.46676(9)  | 0.77575(6) | 0.03755(6)  | 0.0278 | 1.0000 |
| C129 | 0.38039(10) | 0.72804(7) | 0.02904(7)  | 0.0349 | 1.0000 |
| C130 | 0.35929(11) | 0.68611(8) | 0.02738(8)  | 0.0427 | 1.0000 |
| C131 | 0.42336(11) | 0.69305(8) | 0.07444(8)  | 0.0439 | 1.0000 |
| C132 | 0.51055(11) | 0.74022(8) | 0.06583(7)  | 0.0387 | 1.0000 |
| C133 | 0.44274(8)  | 0.88043(6) | 0.09774(6)  | 0.0241 | 1.0000 |
| C134 | 0.39453(10) | 0.88666(7) | 0.15146(6)  | 0.0336 | 1.0000 |
| C135 | 0.33905(12) | 0.93441(9) | 0.15307(7)  | 0.0435 | 1.0000 |
| C136 | 0.33056(10) | 0.97554(7) | 0.10161(7)  | 0.0361 | 1.0000 |
| C137 | 0.37837(9)  | 0.96941(7) | 0.04772(7)  | 0.0323 | 1.0000 |
| C138 | 0.43416(9)  | 0.92250(7) | 0.04603(6)  | 0.0295 | 1.0000 |
| C139 | 0.86191(9)  | 0.87399(6) | 0.26143(7)  | 0.0302 | 1.0000 |
| C140 | 0.88268(10) | 0.87826(7) | 0.33487(7)  | 0.0334 | 1.0000 |
| C141 | 0.82261(11) | 0.85151(7) | 0.38114(7)  | 0.0396 | 1.0000 |
| C142 | 0.85635(14) | 0.86421(8) | 0.44595(8)  | 0.0525 | 1.0000 |
| C143 | 0.94928(16) | 0.90324(9) | 0.46275(9)  | 0.0623 | 1.0000 |
| C144 | 1.00863(13) | 0.92968(9) | 0.41656(10) | 0.0540 | 1.0000 |
| C145 | 0.97530(11) | 0.91734(7) | 0.35232(8)  | 0.0427 | 1.0000 |
| C146 | 1.02189(10) | 0.93885(7) | 0.29313(9)  | 0.0421 | 1.0000 |
| C147 | 0.95814(9)  | 0.91293(7) | 0.23983(8)  | 0.0359 | 1.0000 |
| C148 | 0.98457(11) | 0.92315(7) | 0.17719(9)  | 0.0443 | 1.0000 |
| C149 | 1.07563(12) | 0.96134(8) | 0.16830(11) | 0.0542 | 1.0000 |
| C150 | 1.13846(12) | 0.98820(9) | 0.22054(11) | 0.0584 | 1.0000 |
| C151 | 1.11398(11) | 0.97765(8) | 0.28318(11) | 0.0561 | 1.0000 |
| C152 | 0.83492(9)  | 0.80008(6) | 0.23232(7)  | 0.0292 | 1.0000 |
| C153 | 0.76752(10) | 0.78241(7) | 0.17999(7)  | 0.0336 | 1.0000 |
| C154 | 0.74454(11) | 0.71603(7) | 0.15192(7)  | 0.0387 | 1.0000 |
| C155 | 0.78912(11) | 0.66694(7) | 0.17587(8)  | 0.0412 | 1.0000 |
| C156 | 0.85678(11) | 0.68406(7) | 0.22784(8)  | 0.0416 | 1.0000 |
| C157 | 0.87973(10) | 0.75025(7) | 0.25598(8)  | 0.0360 | 1.0000 |
| C158 | 0.42158(8)  | 0.38946(6) | 0.27920(6)  | 0.0254 | 1.0000 |

|      |             |            |            |        |        |
|------|-------------|------------|------------|--------|--------|
| C159 | 0.43657(9)  | 0.39591(6) | 0.35311(6) | 0.0275 | 1.0000 |
| C160 | 0.36967(10) | 0.37883(7) | 0.39753(7) | 0.0326 | 1.0000 |
| C161 | 0.39969(11) | 0.38949(8) | 0.46307(7) | 0.0419 | 1.0000 |
| C162 | 0.49458(12) | 0.41662(8) | 0.48347(8) | 0.0462 | 1.0000 |
| C163 | 0.56151(11) | 0.43444(8) | 0.43925(8) | 0.0422 | 1.0000 |
| C164 | 0.53222(9)  | 0.42415(7) | 0.37361(7) | 0.0320 | 1.0000 |
| C165 | 0.58529(9)  | 0.44051(6) | 0.31631(7) | 0.0324 | 1.0000 |
| C166 | 0.52186(9)  | 0.42232(6) | 0.26108(7) | 0.0286 | 1.0000 |
| C167 | 0.55218(10) | 0.43465(7) | 0.20004(7) | 0.0353 | 1.0000 |
| C168 | 0.64784(11) | 0.46592(7) | 0.19480(9) | 0.0442 | 1.0000 |
| C169 | 0.71074(10) | 0.48317(7) | 0.24955(9) | 0.0467 | 1.0000 |
| C170 | 0.68060(10) | 0.47049(7) | 0.31051(9) | 0.0415 | 1.0000 |
| C171 | 0.39170(8)  | 0.31355(6) | 0.25491(6) | 0.0246 | 1.0000 |
| C172 | 0.30860(9)  | 0.28814(7) | 0.21580(6) | 0.0309 | 1.0000 |
| C173 | 0.28542(11) | 0.22001(7) | 0.19177(7) | 0.0379 | 1.0000 |
| C174 | 0.34440(11) | 0.17692(7) | 0.20659(7) | 0.0401 | 1.0000 |
| C175 | 0.42696(11) | 0.20178(7) | 0.24638(8) | 0.0392 | 1.0000 |
| C176 | 0.45012(9)  | 0.26928(7) | 0.27052(7) | 0.0320 | 1.0000 |
| C177 | 0.02015(8)  | 0.38010(6) | 0.32984(6) | 0.0221 | 1.0000 |
| C178 | 0.01826(8)  | 0.34971(6) | 0.39036(6) | 0.0227 | 1.0000 |
| C179 | 0.10865(9)  | 0.36809(7) | 0.42166(6) | 0.0277 | 1.0000 |
| C180 | 0.12750(10) | 0.33364(7) | 0.47692(6) | 0.0321 | 1.0000 |
| C181 | 0.05785(10) | 0.28165(7) | 0.49989(6) | 0.0325 | 1.0000 |
| C182 | 0.03297(10) | 0.26318(7) | 0.46866(6) | 0.0295 | 1.0000 |
| C183 | 0.05278(9)  | 0.29849(6) | 0.41428(6) | 0.0244 | 1.0000 |
| C184 | 0.14136(9)  | 0.29197(6) | 0.37277(6) | 0.0239 | 1.0000 |
| C185 | 0.12305(8)  | 0.33730(6) | 0.32236(6) | 0.0227 | 1.0000 |
| C186 | 0.19432(9)  | 0.34149(6) | 0.27576(6) | 0.0264 | 1.0000 |
| C187 | 0.28537(9)  | 0.30059(7) | 0.28061(7) | 0.0306 | 1.0000 |
| C188 | 0.30396(9)  | 0.25635(7) | 0.33122(7) | 0.0316 | 1.0000 |
| C189 | 0.23232(9)  | 0.25126(6) | 0.37770(6) | 0.0286 | 1.0000 |
| C190 | 0.01887(8)  | 0.45622(6) | 0.34364(6) | 0.0237 | 1.0000 |
| C191 | 0.02483(10) | 0.50809(7) | 0.30523(6) | 0.0310 | 1.0000 |
| C192 | 0.02268(11) | 0.57628(7) | 0.31885(8) | 0.0402 | 1.0000 |
| C193 | 0.02300(11) | 0.59288(7) | 0.37031(8) | 0.0404 | 1.0000 |
| C194 | 0.06545(11) | 0.54163(7) | 0.40941(8) | 0.0417 | 1.0000 |
| C195 | 0.06327(10) | 0.47401(7) | 0.39625(7) | 0.0351 | 1.0000 |
| C196 | 0.03124(9)  | 0.33444(7) | 0.09638(6) | 0.0273 | 1.0000 |
| C197 | 0.07545(9)  | 0.35082(7) | 0.08884(6) | 0.0271 | 1.0000 |
| C198 | 0.14815(9)  | 0.39727(7) | 0.12481(6) | 0.0318 | 1.0000 |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| C199 | 0.24079(10) | 0.40356(8)  | 0.10892(7)  | 0.0393 | 1.0000 |
| C200 | 0.26010(10) | 0.36424(9)  | 0.05832(8)  | 0.0439 | 1.0000 |
| C201 | 0.18765(11) | 0.31765(8)  | 0.02204(7)  | 0.0412 | 1.0000 |
| C202 | 0.09489(10) | 0.31140(7)  | 0.03756(6)  | 0.0321 | 1.0000 |
| C203 | 0.00487(10) | 0.26648(7)  | 0.00920(7)  | 0.0355 | 1.0000 |
| C204 | 0.06850(10) | 0.27770(7)  | 0.04412(6)  | 0.0315 | 1.0000 |
| C205 | 0.16093(11) | 0.24029(8)  | 0.02918(7)  | 0.0402 | 1.0000 |
| C206 | 0.17963(12) | 0.19226(9)  | 0.02263(9)  | 0.0524 | 1.0000 |
| C207 | 0.10738(14) | 0.18251(9)  | 0.05823(9)  | 0.0568 | 1.0000 |
| C208 | 0.01417(13) | 0.21890(9)  | 0.04274(8)  | 0.0490 | 1.0000 |
| C209 | 0.06968(9)  | 0.39843(7)  | 0.08376(6)  | 0.0304 | 1.0000 |
| C210 | 0.07503(11) | 0.44350(8)  | 0.13419(7)  | 0.0401 | 1.0000 |
| C211 | 0.10616(13) | 0.50301(9)  | 0.12268(9)  | 0.0532 | 1.0000 |
| C212 | 0.13256(12) | 0.51845(9)  | 0.06111(10) | 0.0574 | 1.0000 |
| C213 | 0.12733(14) | 0.47456(10) | 0.01088(10) | 0.0629 | 1.0000 |
| C214 | 0.09597(13) | 0.41500(9)  | 0.02161(8)  | 0.0489 | 1.0000 |
| N501 | 0.39356(8)  | 0.62633(5)  | 0.25215(5)  | 0.0298 | 1.0000 |
| C502 | 0.40806(10) | 0.58018(6)  | 0.19655(7)  | 0.0320 | 1.0000 |
| C503 | 0.47422(10) | 0.61455(7)  | 0.14753(7)  | 0.0341 | 1.0000 |
| C504 | 0.46065(11) | 0.56716(7)  | 0.08719(7)  | 0.0400 | 1.0000 |
| C505 | 0.53697(13) | 0.59150(8)  | 0.04125(8)  | 0.0476 | 1.0000 |
| C506 | 0.48760(10) | 0.66945(6)  | 0.28295(7)  | 0.0326 | 1.0000 |
| C507 | 0.55709(10) | 0.62999(7)  | 0.31036(7)  | 0.0357 | 1.0000 |
| C508 | 0.64785(11) | 0.68117(8)  | 0.33734(8)  | 0.0419 | 1.0000 |
| C509 | 0.72310(12) | 0.64693(9)  | 0.36535(8)  | 0.0472 | 1.0000 |
| C510 | 0.34140(10) | 0.57764(6)  | 0.30012(6)  | 0.0313 | 1.0000 |
| C511 | 0.30912(10) | 0.61050(7)  | 0.35816(7)  | 0.0332 | 1.0000 |
| C512 | 0.26507(10) | 0.55260(7)  | 0.40149(6)  | 0.0337 | 1.0000 |
| C513 | 0.21872(11) | 0.57707(8)  | 0.45754(7)  | 0.0421 | 1.0000 |
| C514 | 0.33713(10) | 0.67721(7)  | 0.22857(7)  | 0.0337 | 1.0000 |
| C515 | 0.23974(11) | 0.64581(8)  | 0.19568(7)  | 0.0417 | 1.0000 |
| C516 | 0.18237(12) | 0.69886(10) | 0.18863(10) | 0.0561 | 1.0000 |
| C517 | 0.08371(14) | 0.67016(13) | 0.15643(9)  | 0.0686 | 1.0000 |
| N521 | 0.91099(8)  | 0.12775(5)  | 0.25054(5)  | 0.0295 | 1.0000 |
| C522 | 0.95255(10) | 0.09809(7)  | 0.19449(7)  | 0.0356 | 1.0000 |
| C523 | 0.99814(12) | 0.15182(8)  | 0.14763(8)  | 0.0446 | 1.0000 |
| C524 | 1.04692(11) | 0.12134(8)  | 0.09573(8)  | 0.0443 | 1.0000 |
| C525 | 0.97611(13) | 0.06964(11) | 0.05057(9)  | 0.0591 | 1.0000 |
| C526 | 0.98754(10) | 0.18358(7)  | 0.28712(7)  | 0.0327 | 1.0000 |
| C527 | 1.07731(11) | 0.16122(8)  | 0.30862(8)  | 0.0419 | 1.0000 |

|       |             |             |             |        |        |
|-------|-------------|-------------|-------------|--------|--------|
| C528  | 1.14766(11) | 0.21694(8)  | 0.34841(8)  | 0.0448 | 1.0000 |
| C529  | 1.23624(12) | 0.19414(9)  | 0.37079(8)  | 0.0501 | 1.0000 |
| C530  | 0.87384(10) | 0.06891(6)  | 0.29456(7)  | 0.0321 | 1.0000 |
| C531  | 0.82498(11) | 0.08747(7)  | 0.35193(7)  | 0.0366 | 1.0000 |
| C532  | 0.79489(12) | 0.02516(8)  | 0.39314(8)  | 0.0460 | 1.0000 |
| C533  | 0.74752(14) | 0.04120(11) | 0.45189(9)  | 0.0605 | 1.0000 |
| C534  | 0.83161(10) | 0.16069(7)  | 0.22590(7)  | 0.0315 | 1.0000 |
| C535  | 0.74787(11) | 0.11178(8)  | 0.18870(8)  | 0.0421 | 1.0000 |
| C536  | 0.66803(11) | 0.14674(8)  | 0.17063(8)  | 0.0419 | 1.0000 |
| C537  | 0.58118(14) | 0.09706(11) | 0.13624(9)  | 0.0623 | 1.0000 |
| H1031 | 0.61897(10) | 0.86103(7)  | 0.41029(7)  | 0.0441 | 1.0000 |
| H1041 | 0.65288(12) | 0.80234(8)  | 0.50358(8)  | 0.0543 | 1.0000 |
| H1051 | 0.53139(12) | 0.73934(8)  | 0.55950(7)  | 0.0531 | 1.0000 |
| H1061 | 0.37168(11) | 0.72983(7)  | 0.52369(7)  | 0.0439 | 1.0000 |
| H1101 | 0.26873(10) | 0.87362(7)  | 0.28042(7)  | 0.0400 | 1.0000 |
| H1111 | 0.11168(10) | 0.82267(8)  | 0.30148(7)  | 0.0455 | 1.0000 |
| H1121 | 0.07935(10) | 0.75587(7)  | 0.39053(8)  | 0.0451 | 1.0000 |
| H1131 | 0.20351(10) | 0.73419(7)  | 0.46043(7)  | 0.0433 | 1.0000 |
| H1151 | 0.53103(11) | 0.95722(7)  | 0.27670(7)  | 0.0446 | 1.0000 |
| H1161 | 0.57017(13) | 1.07771(8)  | 0.28899(8)  | 0.0587 | 1.0000 |
| H1171 | 0.52441(13) | 1.13302(8)  | 0.37850(8)  | 0.0578 | 1.0000 |
| H1181 | 0.44284(13) | 1.06594(8)  | 0.45571(8)  | 0.0570 | 1.0000 |
| H1191 | 0.40548(12) | 0.94679(7)  | 0.44501(7)  | 0.0497 | 1.0000 |
| H1221 | 0.65938(9)  | 0.93624(7)  | 0.14444(6)  | 0.0327 | 1.0000 |
| H1231 | 0.80273(9)  | 0.97632(7)  | 0.09848(7)  | 0.0420 | 1.0000 |
| H1241 | 0.83030(10) | 0.93056(8)  | 0.00018(7)  | 0.0481 | 1.0000 |
| H1251 | 0.71376(10) | 0.84024(8)  | 0.05434(7)  | 0.0442 | 1.0000 |
| H1291 | 0.33516(10) | 0.72456(7)  | 0.06081(7)  | 0.0415 | 1.0000 |
| H1301 | 0.30059(11) | 0.65336(8)  | 0.03391(8)  | 0.0507 | 1.0000 |
| H1311 | 0.40690(11) | 0.66414(8)  | 0.11316(8)  | 0.0531 | 1.0000 |
| H1321 | 0.55477(11) | 0.74453(8)  | 0.09815(7)  | 0.0470 | 1.0000 |
| H1341 | 0.40112(10) | 0.85912(7)  | 0.18713(6)  | 0.0410 | 1.0000 |
| H1351 | 0.30627(12) | 0.93895(9)  | 0.19066(7)  | 0.0528 | 1.0000 |
| H1361 | 0.29230(10) | 1.00834(7)  | 0.10244(7)  | 0.0428 | 1.0000 |
| H1371 | 0.37294(9)  | 0.99723(7)  | 0.01256(7)  | 0.0387 | 1.0000 |
| H1381 | 0.46752(9)  | 0.91833(7)  | 0.00963(6)  | 0.0361 | 1.0000 |
| H1411 | 0.75982(11) | 0.82601(7)  | 0.36982(7)  | 0.0452 | 1.0000 |
| H1421 | 0.81489(14) | 0.84728(8)  | 0.47700(8)  | 0.0595 | 1.0000 |
| H1431 | 0.96764(16) | 0.91077(9)  | 0.50611(9)  | 0.0750 | 1.0000 |
| H1441 | 1.07353(13) | 0.95646(9)  | 0.42983(10) | 0.0653 | 1.0000 |

|       |             |            |             |        |        |
|-------|-------------|------------|-------------|--------|--------|
| H1481 | 0.93824(11) | 0.90147(7) | 0.13929(9)  | 0.0550 | 1.0000 |
| H1491 | 1.09742(12) | 0.96857(8) | 0.12314(11) | 0.0668 | 1.0000 |
| H1501 | 1.20208(12) | 1.01492(9) | 0.21294(11) | 0.0697 | 1.0000 |
| H1511 | 1.15169(11) | 0.99172(8) | 0.32131(11) | 0.0647 | 1.0000 |
| H1531 | 0.73621(10) | 0.81592(7) | 0.16389(7)  | 0.0395 | 1.0000 |
| H1541 | 0.69714(11) | 0.70550(7) | 0.11572(7)  | 0.0462 | 1.0000 |
| H1551 | 0.77399(11) | 0.62132(7) | 0.15653(8)  | 0.0493 | 1.0000 |
| H1561 | 0.88752(11) | 0.65027(7) | 0.24510(8)  | 0.0504 | 1.0000 |
| H1571 | 0.92612(10) | 0.76179(7) | 0.29221(8)  | 0.0435 | 1.0000 |
| H1601 | 0.30392(10) | 0.36058(7) | 0.38413(7)  | 0.0377 | 1.0000 |
| H1611 | 0.35360(11) | 0.37750(8) | 0.49509(7)  | 0.0506 | 1.0000 |
| H1621 | 0.51385(12) | 0.42396(8) | 0.52951(8)  | 0.0557 | 1.0000 |
| H1631 | 0.62669(11) | 0.45406(8) | 0.45264(8)  | 0.0506 | 1.0000 |
| H1671 | 0.50826(10) | 0.42286(7) | 0.16230(7)  | 0.0404 | 1.0000 |
| H1681 | 0.66783(11) | 0.47471(7) | 0.15334(9)  | 0.0529 | 1.0000 |
| H1691 | 0.77667(10) | 0.50370(7) | 0.24508(9)  | 0.0557 | 1.0000 |
| H1701 | 0.72423(10) | 0.48155(7) | 0.34831(9)  | 0.0505 | 1.0000 |
| H1721 | 0.26781(9)  | 0.31835(7) | 0.20499(6)  | 0.0377 | 1.0000 |
| H1731 | 0.22763(11) | 0.20400(7) | 0.16382(7)  | 0.0469 | 1.0000 |
| H1741 | 0.32906(11) | 0.13060(7) | 0.18902(7)  | 0.0485 | 1.0000 |
| H1751 | 0.46836(11) | 0.17292(7) | 0.25780(8)  | 0.0476 | 1.0000 |
| H1761 | 0.50716(9)  | 0.28569(7) | 0.29817(7)  | 0.0387 | 1.0000 |
| H1791 | 0.15754(9)  | 0.40284(7) | 0.40493(6)  | 0.0330 | 1.0000 |
| H1801 | 0.18981(10) | 0.34576(7) | 0.49825(6)  | 0.0388 | 1.0000 |
| H1811 | 0.07250(10) | 0.25845(7) | 0.53706(6)  | 0.0387 | 1.0000 |
| H1821 | 0.08084(10) | 0.22684(7) | 0.48401(6)  | 0.0344 | 1.0000 |
| H1861 | 0.18242(9)  | 0.37210(6) | 0.24082(6)  | 0.0317 | 1.0000 |
| H1871 | 0.33541(9)  | 0.30328(7) | 0.24930(7)  | 0.0370 | 1.0000 |
| H1881 | 0.36731(9)  | 0.22894(7) | 0.33393(7)  | 0.0373 | 1.0000 |
| H1891 | 0.24461(9)  | 0.22056(6) | 0.41227(6)  | 0.0337 | 1.0000 |
| H1911 | 0.05677(10) | 0.49709(7) | 0.26940(6)  | 0.0370 | 1.0000 |
| H1921 | 0.05442(11) | 0.61179(7) | 0.29215(8)  | 0.0493 | 1.0000 |
| H1931 | 0.02537(11) | 0.63956(7) | 0.37891(8)  | 0.0478 | 1.0000 |
| H1941 | 0.09546(11) | 0.55343(7) | 0.44578(8)  | 0.0508 | 1.0000 |
| H1951 | 0.09245(10) | 0.43872(7) | 0.42382(7)  | 0.0428 | 1.0000 |
| H1981 | 0.13532(9)  | 0.42482(7) | 0.16056(6)  | 0.0380 | 1.0000 |
| H1991 | 0.29233(10) | 0.43506(8) | 0.13391(7)  | 0.0476 | 1.0000 |
| H2001 | 0.32456(10) | 0.36907(9) | 0.04901(8)  | 0.0531 | 1.0000 |
| H2011 | 0.20028(11) | 0.28948(8) | 0.01222(7)  | 0.0489 | 1.0000 |
| H2051 | 0.21134(11) | 0.24699(8) | 0.05437(7)  | 0.0474 | 1.0000 |

|       |             |             |             |        |        |
|-------|-------------|-------------|-------------|--------|--------|
| H2061 | 0.24353(12) | 0.16601(9)  | 0.03312(9)  | 0.0632 | 1.0000 |
| H2071 | 0.12130(14) | 0.14931(9)  | 0.09437(9)  | 0.0681 | 1.0000 |
| H2081 | 0.03597(13) | 0.21073(9)  | 0.06685(8)  | 0.0587 | 1.0000 |
| H2101 | 0.05751(11) | 0.43340(8)  | 0.17758(7)  | 0.0492 | 1.0000 |
| H2111 | 0.11044(13) | 0.53369(9)  | 0.15823(9)  | 0.0656 | 1.0000 |
| H2121 | 0.15422(12) | 0.55950(9)  | 0.05301(10) | 0.0696 | 1.0000 |
| H2131 | 0.14409(14) | 0.48460(10) | 0.03155(10) | 0.0777 | 1.0000 |
| H2141 | 0.09147(13) | 0.38490(9)  | 0.01243(8)  | 0.0587 | 1.0000 |
| H5021 | 0.43104(10) | 0.54285(6)  | 0.21642(7)  | 0.0371 | 1.0000 |
| H5022 | 0.34395(10) | 0.56133(6)  | 0.17553(7)  | 0.0364 | 1.0000 |
| H5031 | 0.46231(10) | 0.65878(7)  | 0.13556(7)  | 0.0405 | 1.0000 |
| H5032 | 0.54137(10) | 0.62384(7)  | 0.16612(7)  | 0.0415 | 1.0000 |
| H5041 | 0.39752(11) | 0.56519(7)  | 0.06443(7)  | 0.0472 | 1.0000 |
| H5042 | 0.46191(11) | 0.52064(7)  | 0.10039(7)  | 0.0478 | 1.0000 |
| H5052 | 0.52288(13) | 0.56361(8)  | 0.00092(8)  | 0.0700 | 1.0000 |
| H5053 | 0.54100(13) | 0.63941(8)  | 0.03194(8)  | 0.0693 | 1.0000 |
| H5051 | 0.59876(13) | 0.58747(8)  | 0.06106(8)  | 0.0700 | 1.0000 |
| H5061 | 0.47145(10) | 0.69771(6)  | 0.31658(7)  | 0.0376 | 1.0000 |
| H5062 | 0.51475(10) | 0.69890(6)  | 0.24917(7)  | 0.0380 | 1.0000 |
| H5071 | 0.53033(10) | 0.60079(7)  | 0.34492(7)  | 0.0439 | 1.0000 |
| H5072 | 0.57245(10) | 0.59997(7)  | 0.27648(7)  | 0.0428 | 1.0000 |
| H5081 | 0.63145(11) | 0.71054(8)  | 0.37025(8)  | 0.0505 | 1.0000 |
| H5082 | 0.67175(11) | 0.70971(8)  | 0.30247(8)  | 0.0502 | 1.0000 |
| H5093 | 0.77874(12) | 0.68222(9)  | 0.38416(8)  | 0.0698 | 1.0000 |
| H5092 | 0.69805(12) | 0.61524(9)  | 0.39885(8)  | 0.0703 | 1.0000 |
| H5091 | 0.74385(12) | 0.62052(9)  | 0.33063(8)  | 0.0696 | 1.0000 |
| H5101 | 0.38492(10) | 0.54899(6)  | 0.31413(6)  | 0.0374 | 1.0000 |
| H5102 | 0.28653(10) | 0.54856(6)  | 0.27561(6)  | 0.0368 | 1.0000 |
| H5111 | 0.36262(10) | 0.64338(7)  | 0.38241(7)  | 0.0400 | 1.0000 |
| H5112 | 0.26153(10) | 0.63581(7)  | 0.34427(7)  | 0.0398 | 1.0000 |
| H5121 | 0.31402(10) | 0.52969(7)  | 0.41777(6)  | 0.0396 | 1.0000 |
| H5122 | 0.21712(10) | 0.51824(7)  | 0.37538(6)  | 0.0401 | 1.0000 |
| H5133 | 0.19253(11) | 0.53849(8)  | 0.48408(7)  | 0.0623 | 1.0000 |
| H5131 | 0.26459(11) | 0.61199(8)  | 0.48522(7)  | 0.0614 | 1.0000 |
| H5132 | 0.16680(11) | 0.59744(8)  | 0.44182(7)  | 0.0621 | 1.0000 |
| H5141 | 0.33170(10) | 0.70480(7)  | 0.26663(7)  | 0.0395 | 1.0000 |
| H5142 | 0.37669(10) | 0.70698(7)  | 0.19932(7)  | 0.0395 | 1.0000 |
| H5151 | 0.20634(11) | 0.60774(8)  | 0.21960(7)  | 0.0502 | 1.0000 |
| H5152 | 0.24442(11) | 0.62623(8)  | 0.15269(7)  | 0.0518 | 1.0000 |
| H5161 | 0.17632(12) | 0.71753(10) | 0.23327(10) | 0.0701 | 1.0000 |

|       |             |             |             |        |        |
|-------|-------------|-------------|-------------|--------|--------|
| H5162 | 0.21260(12) | 0.73703(10) | 0.16484(10) | 0.0671 | 1.0000 |
| H5172 | 0.04540(14) | 0.70430(13) | 0.15885(9)  | 0.1023 | 1.0000 |
| H5171 | 0.04975(14) | 0.62642(13) | 0.17459(9)  | 0.1028 | 1.0000 |
| H5173 | 0.08757(14) | 0.66010(13) | 0.11080(9)  | 0.1039 | 1.0000 |
| H5221 | 0.99835(10) | 0.07436(7)  | 0.21486(7)  | 0.0408 | 1.0000 |
| H5222 | 0.89892(10) | 0.06433(7)  | 0.17587(7)  | 0.0394 | 1.0000 |
| H5231 | 1.04808(12) | 0.19144(8)  | 0.17316(8)  | 0.0557 | 1.0000 |
| H5232 | 0.94451(12) | 0.16875(8)  | 0.12592(8)  | 0.0554 | 1.0000 |
| H5241 | 1.09364(11) | 0.09994(8)  | 0.11688(8)  | 0.0450 | 1.0000 |
| H5242 | 1.08313(11) | 0.15978(8)  | 0.07055(8)  | 0.0537 | 1.0000 |
| H5261 | 1.00107(10) | 0.22236(7)  | 0.26008(7)  | 0.0381 | 1.0000 |
| H5262 | 0.95947(10) | 0.19741(7)  | 0.32368(7)  | 0.0371 | 1.0000 |
| H5271 | 1.10842(11) | 0.14966(8)  | 0.27027(8)  | 0.0512 | 1.0000 |
| H5272 | 1.06422(11) | 0.12138(8)  | 0.33737(8)  | 0.0524 | 1.0000 |
| H5281 | 1.16228(11) | 0.25830(8)  | 0.32074(8)  | 0.0548 | 1.0000 |
| H5282 | 1.11437(11) | 0.22921(8)  | 0.38728(8)  | 0.0559 | 1.0000 |
| H5291 | 1.28141(12) | 0.23112(9)  | 0.39885(8)  | 0.0755 | 1.0000 |
| H5292 | 1.26829(12) | 0.18341(9)  | 0.33361(8)  | 0.0753 | 1.0000 |
| H5293 | 1.21973(12) | 0.15183(9)  | 0.39303(8)  | 0.0709 | 1.0000 |
| H5301 | 0.92845(10) | 0.05237(6)  | 0.30977(7)  | 0.0386 | 1.0000 |
| H5302 | 0.83063(10) | 0.03229(6)  | 0.26646(7)  | 0.0384 | 1.0000 |
| H5311 | 0.86686(11) | 0.12418(7)  | 0.37850(7)  | 0.0447 | 1.0000 |
| H5312 | 0.76871(11) | 0.10326(7)  | 0.33710(7)  | 0.0443 | 1.0000 |
| H5321 | 0.85052(12) | 0.00925(8)  | 0.40650(8)  | 0.0557 | 1.0000 |
| H5322 | 0.74954(12) | 0.01053(8)  | 0.36651(8)  | 0.0565 | 1.0000 |
| H5331 | 0.73046(14) | 0.00100(11) | 0.47790(9)  | 0.0899 | 1.0000 |
| H5332 | 0.78835(14) | 0.07867(11) | 0.47908(9)  | 0.0892 | 1.0000 |
| H5333 | 0.68986(14) | 0.05566(11) | 0.43916(9)  | 0.0898 | 1.0000 |
| H5342 | 0.85870(10) | 0.19839(7)  | 0.19841(7)  | 0.0378 | 1.0000 |
| H5341 | 0.81072(10) | 0.18028(7)  | 0.26410(7)  | 0.0355 | 1.0000 |
| H5352 | 0.76724(11) | 0.09469(8)  | 0.14942(8)  | 0.0531 | 1.0000 |
| H5351 | 0.72056(11) | 0.07292(8)  | 0.21409(8)  | 0.0510 | 1.0000 |
| H5361 | 0.69180(11) | 0.18484(8)  | 0.14474(8)  | 0.0525 | 1.0000 |
| H5362 | 0.64922(11) | 0.16577(8)  | 0.21036(8)  | 0.0505 | 1.0000 |
| H5371 | 0.53264(14) | 0.12177(11) | 0.12264(9)  | 0.0929 | 1.0000 |
| H5372 | 0.59865(14) | 0.07543(11) | 0.09837(9)  | 0.0946 | 1.0000 |
| H5373 | 0.55257(14) | 0.06006(11) | 0.16585(9)  | 0.0953 | 1.0000 |
| H151  | 0.08955(6)  | 0.38545(4)  | 0.28095(4)  | 0.0407 | 1.0000 |
| H131  | 0.73658(6)  | 0.88967(4)  | 0.24874(5)  | 0.0482 | 1.0000 |
| H121  | 0.54700(6)  | 0.81842(4)  | 0.18079(4)  | 0.0428 | 1.0000 |

|       |             |             |            |        |        |
|-------|-------------|-------------|------------|--------|--------|
| H161  | 0.02474(6)  | 0.33122(4)  | 0.18858(4) | 0.0468 | 1.0000 |
| H141  | 0.30514(6)  | 0.41778(4)  | 0.26845(4) | 0.0445 | 1.0000 |
| H111  | 0.51575(6)  | 0.84602(4)  | 0.28899(4) | 0.0444 | 1.0000 |
| H5251 | 1.00749(13) | 0.05989(11) | 0.00923(9) | 0.0894 | 1.0000 |
| H5252 | 0.96770(13) | 0.02620(11) | 0.07628(9) | 0.0857 | 1.0000 |
| H5253 | 0.91359(13) | 0.08523(11) | 0.03947(9) | 0.0898 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0261(4)       | 0.0466(5)       | 0.0343(4)       | -0.0029(3)      | 0.0069(3)       | 0.0067(3)       |
| F2    | 0.0224(4)       | 0.0647(6)       | 0.0368(4)       | -0.0047(4)      | 0.0059(3)       | 0.0080(4)       |
| O11   | 0.0282(4)       | 0.0300(5)       | 0.0254(4)       | -0.0044(4)      | 0.0075(3)       | 0.0038(4)       |
| O12   | 0.0313(5)       | 0.0235(4)       | 0.0257(4)       | 0.0029(3)       | 0.0043(4)       | 0.0030(4)       |
| O13   | 0.0241(4)       | 0.0230(4)       | 0.0465(5)       | 0.0006(4)       | 0.0034(4)       | 0.0073(4)       |
| O14   | 0.0239(4)       | 0.0270(4)       | 0.0375(5)       | 0.0070(4)       | 0.0080(4)       | 0.0099(4)       |
| O15   | 0.0205(4)       | 0.0322(5)       | 0.0220(4)       | -0.0022(3)      | 0.0050(3)       | 0.0060(3)       |
| O16   | 0.0354(5)       | 0.0285(5)       | 0.0230(4)       | 0.0025(4)       | 0.0050(4)       | -0.0017(4)      |
| C101  | 0.0292(6)       | 0.0253(6)       | 0.0231(6)       | -0.0005(5)      | 0.0062(5)       | 0.0068(5)       |
| C102  | 0.0346(7)       | 0.0227(6)       | 0.0255(6)       | -0.0039(5)      | 0.0035(5)       | 0.0093(5)       |
| C103  | 0.0354(7)       | 0.0354(7)       | 0.0379(8)       | -0.0042(6)      | -0.0004(6)      | 0.0109(6)       |
| C104  | 0.0454(9)       | 0.0476(9)       | 0.0434(8)       | -0.0034(7)      | -0.0092(7)      | 0.0193(7)       |
| C105  | 0.0619(10)      | 0.0418(8)       | 0.0330(7)       | 0.0012(6)       | -0.0069(7)      | 0.0251(8)       |
| C106  | 0.0544(9)       | 0.0318(7)       | 0.0293(7)       | 0.0042(6)       | 0.0075(6)       | 0.0154(6)       |
| C107  | 0.0389(7)       | 0.0244(6)       | 0.0266(6)       | -0.0005(5)      | 0.0055(5)       | 0.0119(5)       |
| C108  | 0.0355(7)       | 0.0242(6)       | 0.0277(6)       | 0.0014(5)       | 0.0096(5)       | 0.0095(5)       |
| C109  | 0.0300(7)       | 0.0231(6)       | 0.0263(6)       | 0.0006(5)       | 0.0071(5)       | 0.0076(5)       |
| C110  | 0.0337(7)       | 0.0347(7)       | 0.0331(7)       | 0.0079(6)       | 0.0069(6)       | 0.0100(6)       |
| C111  | 0.0301(7)       | 0.0412(8)       | 0.0442(8)       | 0.0045(6)       | 0.0039(6)       | 0.0115(6)       |
| C112  | 0.0299(7)       | 0.0364(8)       | 0.0502(9)       | 0.0049(6)       | 0.0136(6)       | 0.0053(6)       |
| C113  | 0.0393(8)       | 0.0312(7)       | 0.0391(8)       | 0.0088(6)       | 0.0156(6)       | 0.0082(6)       |
| C114  | 0.0303(7)       | 0.0263(6)       | 0.0271(6)       | 0.0011(5)       | 0.0033(5)       | 0.0070(5)       |
| C115  | 0.0457(8)       | 0.0313(7)       | 0.0337(7)       | 0.0023(6)       | 0.0125(6)       | 0.0072(6)       |
| C116  | 0.0646(11)      | 0.0310(8)       | 0.0479(9)       | 0.0087(7)       | 0.0196(8)       | 0.0055(7)       |
| C117  | 0.0690(11)      | 0.0244(7)       | 0.0507(9)       | 0.0014(6)       | 0.0108(8)       | 0.0082(7)       |
| C118  | 0.0714(11)      | 0.0315(8)       | 0.0420(8)       | -0.0053(6)      | 0.0171(8)       | 0.0136(7)       |
| C119  | 0.0591(10)      | 0.0304(7)       | 0.0350(8)       | 0.0013(6)       | 0.0189(7)       | 0.0086(7)       |
| C120  | 0.0254(6)       | 0.0239(6)       | 0.0232(6)       | 0.0009(5)       | 0.0046(5)       | 0.0025(5)       |
| C121  | 0.0237(6)       | 0.0243(6)       | 0.0254(6)       | 0.0030(5)       | 0.0037(5)       | 0.0063(5)       |
| C122  | 0.0273(6)       | 0.0284(6)       | 0.0275(6)       | 0.0012(5)       | 0.0021(5)       | 0.0058(5)       |



|      |            |            |            |            |             |            |
|------|------------|------------|------------|------------|-------------|------------|
| C123 | 0.0248(7)  | 0.0348(7)  | 0.0418(8)  | 0.0002(6)  | 0.0019(6)   | 0.0004(5)  |
| C124 | 0.0260(7)  | 0.0459(8)  | 0.0466(8)  | 0.0027(7)  | 0.0135(6)   | 0.0031(6)  |
| C125 | 0.0342(7)  | 0.0420(8)  | 0.0346(7)  | -0.0015(6) | 0.0132(6)   | 0.0087(6)  |
| C126 | 0.0289(7)  | 0.0282(6)  | 0.0286(6)  | 0.0011(5)  | 0.0058(5)   | 0.0073(5)  |
| C127 | 0.0320(7)  | 0.0284(6)  | 0.0294(7)  | -0.0017(5) | 0.0044(5)   | 0.0072(5)  |
| C128 | 0.0284(6)  | 0.0254(6)  | 0.0288(6)  | -0.0014(5) | 0.0026(5)   | 0.0053(5)  |
| C129 | 0.0302(7)  | 0.0315(7)  | 0.0407(8)  | -0.0042(6) | 0.0050(6)   | 0.0029(6)  |
| C130 | 0.0349(8)  | 0.0348(8)  | 0.0528(9)  | -0.0130(7) | -0.0035(7)  | 0.0012(6)  |
| C131 | 0.0478(9)  | 0.0406(8)  | 0.0406(8)  | -0.0175(7) | -0.0025(7)  | 0.0091(7)  |
| C132 | 0.0446(8)  | 0.0390(8)  | 0.0329(7)  | -0.0080(6) | 0.0071(6)   | 0.0102(6)  |
| C133 | 0.0210(6)  | 0.0240(6)  | 0.0243(6)  | -0.0011(5) | 0.0021(5)   | -0.0001(5) |
| C134 | 0.0389(7)  | 0.0402(8)  | 0.0262(6)  | 0.0067(6)  | 0.0085(6)   | 0.0163(6)  |
| C135 | 0.0530(9)  | 0.0566(10) | 0.0317(7)  | 0.0077(7)  | 0.0164(7)   | 0.0299(8)  |
| C136 | 0.0360(7)  | 0.0377(8)  | 0.0391(8)  | 0.0039(6)  | 0.0058(6)   | 0.0167(6)  |
| C137 | 0.0303(7)  | 0.0332(7)  | 0.0330(7)  | 0.0097(6)  | 0.0033(5)   | 0.0058(6)  |
| C138 | 0.0287(6)  | 0.0331(7)  | 0.0264(6)  | 0.0044(5)  | 0.0078(5)   | 0.0049(5)  |
| C139 | 0.0240(6)  | 0.0224(6)  | 0.0446(8)  | -0.0002(5) | 0.0040(5)   | 0.0065(5)  |
| C140 | 0.0309(7)  | 0.0216(6)  | 0.0484(8)  | -0.0027(6) | -0.0021(6)  | 0.0093(5)  |
| C141 | 0.0467(8)  | 0.0269(7)  | 0.0448(8)  | -0.0019(6) | -0.0011(7)  | 0.0103(6)  |
| C142 | 0.0773(12) | 0.0381(8)  | 0.0446(9)  | 0.0025(7)  | 0.0011(8)   | 0.0202(8)  |
| C143 | 0.0873(14) | 0.0466(10) | 0.0528(11) | -0.0116(8) | -0.0316(10) | 0.0288(10) |
| C144 | 0.0509(10) | 0.0405(9)  | 0.0675(12) | -0.0037(8) | -0.0193(9)  | 0.0130(8)  |
| C145 | 0.0358(8)  | 0.0259(7)  | 0.0654(10) | -0.0076(7) | -0.0150(7)  | 0.0125(6)  |
| C146 | 0.0262(7)  | 0.0241(7)  | 0.0774(11) | -0.0001(7) | 0.0039(7)   | 0.0093(5)  |
| C147 | 0.0261(7)  | 0.0194(6)  | 0.0634(10) | -0.0017(6) | 0.0065(6)   | 0.0072(5)  |
| C148 | 0.0414(8)  | 0.0264(7)  | 0.0693(11) | 0.0016(7)  | 0.0237(8)   | 0.0101(6)  |
| C149 | 0.0435(9)  | 0.0297(8)  | 0.0942(14) | 0.0032(8)  | 0.0306(9)   | 0.0107(7)  |
| C150 | 0.0359(9)  | 0.0362(9)  | 0.1093(16) | 0.0098(9)  | 0.0330(10)  | 0.0117(7)  |
| C151 | 0.0307(8)  | 0.0267(7)  | 0.1085(16) | -0.0070(8) | -0.0098(9)  | 0.0080(6)  |
| C152 | 0.0243(6)  | 0.0227(6)  | 0.0410(7)  | 0.0003(5)  | 0.0089(5)   | 0.0044(5)  |
| C153 | 0.0344(7)  | 0.0268(7)  | 0.0404(8)  | 0.0010(6)  | 0.0054(6)   | 0.0082(6)  |
| C154 | 0.0414(8)  | 0.0326(7)  | 0.0398(8)  | -0.0051(6) | 0.0055(6)   | 0.0046(6)  |
| C155 | 0.0496(9)  | 0.0240(7)  | 0.0499(9)  | -0.0052(6) | 0.0141(7)   | 0.0065(6)  |
| C156 | 0.0439(8)  | 0.0272(7)  | 0.0581(10) | 0.0029(6)  | 0.0103(7)   | 0.0153(6)  |
| C157 | 0.0304(7)  | 0.0289(7)  | 0.0496(8)  | 0.0001(6)  | 0.0033(6)   | 0.0092(6)  |
| C158 | 0.0213(6)  | 0.0231(6)  | 0.0326(7)  | 0.0012(5)  | 0.0049(5)   | 0.0064(5)  |
| C159 | 0.0272(6)  | 0.0216(6)  | 0.0344(7)  | -0.0024(5) | 0.0020(5)   | 0.0081(5)  |
| C160 | 0.0316(7)  | 0.0322(7)  | 0.0352(7)  | -0.0009(6) | 0.0050(6)   | 0.0099(6)  |
| C161 | 0.0478(9)  | 0.0456(9)  | 0.0346(8)  | -0.0009(6) | 0.0066(6)   | 0.0148(7)  |
| C162 | 0.0556(10) | 0.0471(9)  | 0.0347(8)  | -0.0057(7) | -0.0059(7)  | 0.0141(8)  |

|      |           |            |            |            |            |            |
|------|-----------|------------|------------|------------|------------|------------|
| C163 | 0.0387(8) | 0.0378(8)  | 0.0470(9)  | -0.0064(7) | -0.0110(7) | 0.0082(6)  |
| C164 | 0.0291(7) | 0.0236(6)  | 0.0427(8)  | -0.0031(5) | -0.0011(6) | 0.0071(5)  |
| C165 | 0.0255(6) | 0.0207(6)  | 0.0507(8)  | -0.0022(6) | 0.0025(6)  | 0.0055(5)  |
| C166 | 0.0242(6) | 0.0194(6)  | 0.0433(7)  | 0.0000(5)  | 0.0083(5)  | 0.0059(5)  |
| C167 | 0.0330(7) | 0.0273(7)  | 0.0474(8)  | 0.0025(6)  | 0.0136(6)  | 0.0074(6)  |
| C168 | 0.0412(8) | 0.0301(7)  | 0.0641(10) | 0.0059(7)  | 0.0267(8)  | 0.0067(6)  |
| C169 | 0.0269(7) | 0.0279(7)  | 0.0841(12) | 0.0015(7)  | 0.0168(8)  | 0.0008(6)  |
| C170 | 0.0255(7) | 0.0275(7)  | 0.0690(10) | -0.0025(7) | 0.0019(7)  | 0.0028(6)  |
| C171 | 0.0235(6) | 0.0244(6)  | 0.0259(6)  | 0.0024(5)  | 0.0076(5)  | 0.0041(5)  |
| C172 | 0.0292(7) | 0.0310(7)  | 0.0310(7)  | 0.0032(5)  | 0.0025(5)  | 0.0043(5)  |
| C173 | 0.0383(8) | 0.0364(8)  | 0.0321(7)  | -0.0032(6) | 0.0017(6)  | -0.0038(6) |
| C174 | 0.0518(9) | 0.0253(7)  | 0.0404(8)  | -0.0049(6) | 0.0136(7)  | 0.0013(6)  |
| C175 | 0.0429(8) | 0.0278(7)  | 0.0504(9)  | 0.0016(6)  | 0.0104(7)  | 0.0132(6)  |
| C176 | 0.0279(7) | 0.0282(7)  | 0.0404(7)  | -0.0001(6) | 0.0036(6)  | 0.0077(5)  |
| C177 | 0.0210(6) | 0.0238(6)  | 0.0221(6)  | -0.0003(5) | 0.0049(4)  | 0.0057(5)  |
| C178 | 0.0253(6) | 0.0225(6)  | 0.0223(6)  | -0.0017(5) | 0.0056(5)  | 0.0086(5)  |
| C179 | 0.0264(6) | 0.0300(6)  | 0.0268(6)  | -0.0012(5) | 0.0036(5)  | 0.0069(5)  |
| C180 | 0.0298(7) | 0.0404(7)  | 0.0276(6)  | -0.0010(6) | -0.0007(5) | 0.0122(6)  |
| C181 | 0.0402(8) | 0.0378(7)  | 0.0241(6)  | 0.0046(5)  | 0.0044(5)  | 0.0175(6)  |
| C182 | 0.0349(7) | 0.0287(6)  | 0.0276(6)  | 0.0044(5)  | 0.0100(5)  | 0.0105(5)  |
| C183 | 0.0270(6) | 0.0237(6)  | 0.0245(6)  | -0.0016(5) | 0.0069(5)  | 0.0087(5)  |
| C184 | 0.0253(6) | 0.0213(6)  | 0.0270(6)  | -0.0018(5) | 0.0068(5)  | 0.0079(5)  |
| C185 | 0.0225(6) | 0.0202(6)  | 0.0264(6)  | -0.0023(5) | 0.0064(5)  | 0.0062(5)  |
| C186 | 0.0247(6) | 0.0258(6)  | 0.0297(6)  | 0.0011(5)  | 0.0043(5)  | 0.0077(5)  |
| C187 | 0.0231(6) | 0.0315(7)  | 0.0373(7)  | -0.0017(5) | 0.0012(5)  | 0.0078(5)  |
| C188 | 0.0219(6) | 0.0282(7)  | 0.0434(8)  | -0.0010(6) | 0.0076(5)  | 0.0026(5)  |
| C189 | 0.0286(6) | 0.0239(6)  | 0.0343(7)  | 0.0024(5)  | 0.0104(5)  | 0.0056(5)  |
| C190 | 0.0203(6) | 0.0242(6)  | 0.0260(6)  | 0.0003(5)  | 0.0008(5)  | 0.0044(5)  |
| C191 | 0.0346(7) | 0.0292(7)  | 0.0294(7)  | 0.0046(5)  | 0.0066(5)  | 0.0065(5)  |
| C192 | 0.0474(9) | 0.0266(7)  | 0.0459(8)  | 0.0098(6)  | 0.0078(7)  | 0.0058(6)  |
| C193 | 0.0426(8) | 0.0236(7)  | 0.0556(9)  | -0.0027(6) | 0.0038(7)  | 0.0096(6)  |
| C194 | 0.0454(8) | 0.0310(7)  | 0.0505(9)  | -0.0065(6) | 0.0173(7)  | 0.0096(6)  |
| C195 | 0.0402(8) | 0.0265(7)  | 0.0396(8)  | 0.0006(6)  | 0.0172(6)  | 0.0060(6)  |
| C196 | 0.0269(6) | 0.0301(6)  | 0.0221(6)  | 0.0017(5)  | 0.0034(5)  | 0.0011(5)  |
| C197 | 0.0276(6) | 0.0293(6)  | 0.0227(6)  | 0.0063(5)  | 0.0021(5)  | 0.0029(5)  |
| C198 | 0.0324(7) | 0.0313(7)  | 0.0278(6)  | 0.0062(5)  | -0.0013(5) | 0.0009(5)  |
| C199 | 0.0298(7) | 0.0432(8)  | 0.0387(8)  | 0.0134(6)  | -0.0026(6) | -0.0023(6) |
| C200 | 0.0271(7) | 0.0603(10) | 0.0438(8)  | 0.0179(7)  | 0.0083(6)  | 0.0066(7)  |
| C201 | 0.0390(8) | 0.0534(9)  | 0.0337(7)  | 0.0063(7)  | 0.0118(6)  | 0.0132(7)  |
| C202 | 0.0325(7) | 0.0374(7)  | 0.0253(6)  | 0.0045(5)  | 0.0042(5)  | 0.0058(6)  |

|      |            |            |            |            |            |            |
|------|------------|------------|------------|------------|------------|------------|
| C203 | 0.0378(8)  | 0.0390(8)  | 0.0276(7)  | -0.0021(6) | 0.0018(6)  | 0.0059(6)  |
| C204 | 0.0321(7)  | 0.0327(7)  | 0.0267(6)  | 0.0003(5)  | -0.0004(5) | 0.0030(6)  |
| C205 | 0.0337(8)  | 0.0407(8)  | 0.0409(8)  | -0.0014(6) | -0.0035(6) | 0.0009(6)  |
| C206 | 0.0452(9)  | 0.0471(9)  | 0.0552(10) | -0.0108(8) | -0.0134(8) | -0.0013(7) |
| C207 | 0.0658(12) | 0.0506(10) | 0.0475(10) | -0.0209(8) | -0.0107(8) | 0.0084(9)  |
| C208 | 0.0555(10) | 0.0527(10) | 0.0378(8)  | -0.0128(7) | 0.0023(7)  | 0.0133(8)  |
| C209 | 0.0235(6)  | 0.0325(7)  | 0.0330(7)  | 0.0078(5)  | 0.0059(5)  | 0.0010(5)  |
| C210 | 0.0455(8)  | 0.0374(8)  | 0.0407(8)  | 0.0086(6)  | 0.0163(7)  | 0.0120(6)  |
| C211 | 0.0577(10) | 0.0416(9)  | 0.0689(11) | 0.0150(8)  | 0.0304(9)  | 0.0199(8)  |
| C212 | 0.0470(10) | 0.0449(9)  | 0.0868(14) | 0.0272(10) | 0.0177(9)  | 0.0177(8)  |
| C213 | 0.0643(12) | 0.0588(11) | 0.0638(12) | 0.0307(10) | -0.0082(9) | 0.0131(9)  |
| C214 | 0.0599(10) | 0.0465(9)  | 0.0381(8)  | 0.0097(7)  | -0.0016(7) | 0.0098(8)  |
| N501 | 0.0349(6)  | 0.0197(5)  | 0.0335(6)  | -0.0005(4) | 0.0126(5)  | 0.0014(4)  |
| C502 | 0.0390(7)  | 0.0212(6)  | 0.0348(7)  | -0.0021(5) | 0.0134(6)  | 0.0025(5)  |
| C503 | 0.0413(8)  | 0.0242(6)  | 0.0360(7)  | 0.0019(5)  | 0.0147(6)  | 0.0027(6)  |
| C504 | 0.0509(9)  | 0.0280(7)  | 0.0391(8)  | -0.0012(6) | 0.0179(7)  | 0.0017(6)  |
| C505 | 0.0630(10) | 0.0352(8)  | 0.0436(9)  | -0.0023(6) | 0.0265(8)  | 0.0032(7)  |
| C506 | 0.0366(7)  | 0.0213(6)  | 0.0376(7)  | -0.0020(5) | 0.0114(6)  | 0.0000(5)  |
| C507 | 0.0421(8)  | 0.0267(7)  | 0.0363(7)  | 0.0011(6)  | 0.0082(6)  | 0.0033(6)  |
| C508 | 0.0442(8)  | 0.0343(8)  | 0.0438(8)  | -0.0055(6) | 0.0047(7)  | 0.0029(6)  |
| C509 | 0.0495(9)  | 0.0519(9)  | 0.0356(8)  | 0.0028(7)  | -0.0006(7) | 0.0044(7)  |
| C510 | 0.0363(7)  | 0.0220(6)  | 0.0336(7)  | 0.0010(5)  | 0.0123(6)  | 0.0005(5)  |
| C511 | 0.0376(7)  | 0.0275(7)  | 0.0333(7)  | -0.0013(5) | 0.0107(6)  | 0.0038(6)  |
| C512 | 0.0362(7)  | 0.0320(7)  | 0.0306(7)  | 0.0016(5)  | 0.0070(6)  | 0.0027(6)  |
| C513 | 0.0432(8)  | 0.0502(9)  | 0.0340(8)  | 0.0053(6)  | 0.0120(6)  | 0.0105(7)  |
| C514 | 0.0391(8)  | 0.0251(6)  | 0.0376(7)  | 0.0021(5)  | 0.0136(6)  | 0.0059(6)  |
| C515 | 0.0452(9)  | 0.0396(8)  | 0.0387(8)  | -0.0003(6) | 0.0072(7)  | 0.0058(7)  |
| C516 | 0.0457(10) | 0.0583(11) | 0.0678(12) | 0.0073(9)  | 0.0114(8)  | 0.0171(8)  |
| C517 | 0.0539(11) | 0.1064(17) | 0.0472(10) | 0.0159(10) | 0.0063(8)  | 0.0213(11) |
| N521 | 0.0342(6)  | 0.0236(5)  | 0.0330(6)  | -0.0011(4) | 0.0054(5)  | 0.0109(5)  |
| C522 | 0.0382(8)  | 0.0346(7)  | 0.0378(7)  | -0.0061(6) | 0.0051(6)  | 0.0165(6)  |
| C523 | 0.0482(9)  | 0.0461(9)  | 0.0452(9)  | 0.0055(7)  | 0.0148(7)  | 0.0187(7)  |
| C524 | 0.0408(8)  | 0.0440(9)  | 0.0478(9)  | -0.0024(7) | 0.0147(7)  | 0.0064(7)  |
| C525 | 0.0460(10) | 0.0710(12) | 0.0547(10) | -0.0066(9) | 0.0148(8)  | 0.0006(9)  |
| C526 | 0.0348(7)  | 0.0246(6)  | 0.0393(7)  | -0.0014(5) | 0.0096(6)  | 0.0066(5)  |
| C527 | 0.0425(8)  | 0.0405(8)  | 0.0446(8)  | -0.0063(7) | 0.0008(7)  | 0.0151(7)  |
| C528 | 0.0431(9)  | 0.0397(8)  | 0.0491(9)  | -0.0014(7) | 0.0065(7)  | 0.0049(7)  |
| C529 | 0.0457(9)  | 0.0576(10) | 0.0439(9)  | 0.0061(8)  | -0.0022(7) | 0.0077(8)  |
| C530 | 0.0363(7)  | 0.0207(6)  | 0.0402(7)  | 0.0022(5)  | 0.0023(6)  | 0.0091(5)  |
| C531 | 0.0411(8)  | 0.0288(7)  | 0.0420(8)  | 0.0061(6)  | 0.0080(6)  | 0.0107(6)  |

|      |            |            |            |            |            |            |
|------|------------|------------|------------|------------|------------|------------|
| C532 | 0.0481(9)  | 0.0392(8)  | 0.0541(10) | 0.0164(7)  | 0.0127(7)  | 0.0132(7)  |
| C533 | 0.0650(12) | 0.0677(12) | 0.0564(11) | 0.0260(9)  | 0.0221(9)  | 0.0232(10) |
| C534 | 0.0369(7)  | 0.0271(6)  | 0.0346(7)  | 0.0029(5)  | 0.0068(6)  | 0.0145(6)  |
| C535 | 0.0465(9)  | 0.0426(8)  | 0.0394(8)  | -0.0091(6) | -0.0040(7) | 0.0185(7)  |
| C536 | 0.0413(8)  | 0.0478(9)  | 0.0404(8)  | 0.0070(7)  | 0.0054(6)  | 0.0170(7)  |
| C537 | 0.0588(11) | 0.0837(14) | 0.0466(10) | -0.0174(9) | -0.0172(8) | 0.0300(10) |

## Distances

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| O11  | C101  | 1.4126(14)Å |  | O11  | H111  | 0.863Å      |
| O12  | C120  | 1.4197(14)Å |  | O12  | H121  | 0.854Å      |
| O13  | C139  | 1.4163(15)Å |  | O13  | H131  | 0.882Å      |
| O14  | C158  | 1.4079(15)Å |  | O14  | H141  | 0.871Å      |
| O15  | C177  | 1.4146(14)Å |  | O15  | H151  | 0.901Å      |
| O16  | C196  | 1.4274(14)Å |  | O16  | H161  | 0.846Å      |
| C101 | C102  | 1.5292(17)Å |  | C101 | C109  | 1.5260(17)Å |
| C101 | C114  | 1.5301(17)Å |  | C102 | C103  | 1.3807(19)Å |
| C102 | C107  | 1.3981(18)Å |  | C103 | C104  | 1.391(2)Å   |
| C103 | H1031 | 0.969Å      |  | C104 | C105  | 1.385(2)Å   |
| C104 | H1041 | 0.957Å      |  | C105 | C106  | 1.386(2)Å   |
| C105 | H1051 | 0.948Å      |  | C106 | C107  | 1.3940(19)Å |
| C106 | H1061 | 0.956Å      |  | C107 | C108  | 1.4717(19)Å |
| C108 | C109  | 1.3970(17)Å |  | C108 | C113  | 1.3871(19)Å |
| C109 | C110  | 1.3780(19)Å |  | C110 | C111  | 1.3888(19)Å |
| C110 | H1101 | 0.955Å      |  | C111 | C112  | 1.388(2)Å   |
| C111 | H1111 | 0.941Å      |  | C112 | C113  | 1.387(2)Å   |
| C112 | H1121 | 0.954Å      |  | C113 | H1131 | 0.970Å      |
| C114 | C115  | 1.3834(18)Å |  | C114 | C119  | 1.3914(19)Å |
| C115 | C116  | 1.390(2)Å   |  | C115 | H1151 | 0.971Å      |
| C116 | C117  | 1.376(2)Å   |  | C116 | H1161 | 0.963Å      |
| C117 | C118  | 1.375(2)Å   |  | C117 | H1171 | 0.964Å      |
| C118 | C119  | 1.379(2)Å   |  | C118 | H1181 | 0.942Å      |
| C119 | H1191 | 0.950Å      |  | C120 | C121  | 1.5271(16)Å |
| C120 | C128  | 1.5314(17)Å |  | C120 | C133  | 1.5328(17)Å |
| C121 | C122  | 1.3797(18)Å |  | C121 | C126  | 1.3996(17)Å |
| C122 | C123  | 1.3888(18)Å |  | C122 | H1221 | 0.948Å      |
| C123 | C124  | 1.386(2)Å   |  | C123 | H1231 | 0.947Å      |
| C124 | C125  | 1.388(2)Å   |  | C124 | H1241 | 0.961Å      |
| C125 | C126  | 1.3867(18)Å |  | C125 | H1251 | 0.954Å      |
| C126 | C127  | 1.4722(18)Å |  | C127 | C128  | 1.3994(18)Å |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C127 | C132  | 1.3911(19)Å |  | C128 | C129  | 1.3804(18)Å |
| C129 | C130  | 1.395(2)Å   |  | C129 | H1291 | 0.960Å      |
| C130 | C131  | 1.389(2)Å   |  | C130 | H1301 | 0.942Å      |
| C131 | C132  | 1.384(2)Å   |  | C131 | H1311 | 0.959Å      |
| C132 | H1321 | 0.956Å      |  | C133 | C134  | 1.3815(18)Å |
| C133 | C138  | 1.3938(18)Å |  | C134 | C135  | 1.392(2)Å   |
| C134 | H1341 | 0.945Å      |  | C135 | C136  | 1.378(2)Å   |
| C135 | H1351 | 0.959Å      |  | C136 | C137  | 1.3806(19)Å |
| C136 | H1361 | 0.958Å      |  | C137 | C138  | 1.3819(19)Å |
| C137 | H1371 | 0.937Å      |  | C138 | H1381 | 0.942Å      |
| C139 | C140  | 1.527(2)Å   |  | C139 | C147  | 1.5361(18)Å |
| C139 | C152  | 1.5319(17)Å |  | C140 | C141  | 1.379(2)Å   |
| C140 | C145  | 1.403(2)Å   |  | C141 | C142  | 1.392(2)Å   |
| C141 | H1411 | 0.943Å      |  | C142 | C143  | 1.404(3)Å   |
| C142 | H1421 | 0.930Å      |  | C143 | C144  | 1.370(3)Å   |
| C143 | H1431 | 0.917Å      |  | C144 | C145  | 1.379(2)Å   |
| C144 | H1441 | 0.983Å      |  | C145 | C146  | 1.472(2)Å   |
| C146 | C147  | 1.393(2)Å   |  | C146 | C151  | 1.412(2)Å   |
| C147 | C148  | 1.390(2)Å   |  | C148 | C149  | 1.391(2)Å   |
| C148 | H1481 | 1.012Å      |  | C149 | C150  | 1.374(3)Å   |
| C149 | H1491 | 1.015Å      |  | C150 | C151  | 1.382(3)Å   |
| C150 | H1501 | 0.978Å      |  | C151 | H1511 | 0.925Å      |
| C152 | C153  | 1.386(2)Å   |  | C152 | C157  | 1.3940(19)Å |
| C153 | C154  | 1.3907(19)Å |  | C153 | H1531 | 0.949Å      |
| C154 | C155  | 1.382(2)Å   |  | C154 | H1541 | 0.964Å      |
| C155 | C156  | 1.382(2)Å   |  | C155 | H1551 | 0.956Å      |
| C156 | C157  | 1.388(2)Å   |  | C156 | H1561 | 0.957Å      |
| C157 | H1571 | 0.956Å      |  | C158 | C159  | 1.5308(18)Å |
| C158 | C166  | 1.5301(16)Å |  | C158 | C171  | 1.5363(17)Å |
| C159 | C160  | 1.3814(19)Å |  | C159 | C164  | 1.4005(18)Å |
| C160 | C161  | 1.392(2)Å   |  | C160 | H1601 | 0.956Å      |
| C161 | C162  | 1.387(2)Å   |  | C161 | H1611 | 0.974Å      |
| C162 | C163  | 1.380(2)Å   |  | C162 | H1621 | 0.973Å      |
| C163 | C164  | 1.392(2)Å   |  | C163 | H1631 | 0.953Å      |
| C164 | C165  | 1.468(2)Å   |  | C165 | C166  | 1.3990(19)Å |
| C165 | C170  | 1.3895(19)Å |  | C166 | C167  | 1.381(2)Å   |
| C167 | C168  | 1.397(2)Å   |  | C167 | H1671 | 0.960Å      |
| C168 | C169  | 1.386(2)Å   |  | C168 | H1681 | 0.936Å      |
| C169 | C170  | 1.380(2)Å   |  | C169 | H1691 | 0.962Å      |
| C170 | H1701 | 0.957Å      |  | C171 | C172  | 1.3847(18)Å |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C171 | C176  | 1.3942(18)Å |  | C172 | C173  | 1.3928(19)Å |
| C172 | H1721 | 0.962Å      |  | C173 | C174  | 1.379(2)Å   |
| C173 | H1731 | 0.967Å      |  | C174 | C175  | 1.385(2)Å   |
| C174 | H1741 | 0.955Å      |  | C175 | C176  | 1.3821(19)Å |
| C175 | H1751 | 0.951Å      |  | C176 | H1761 | 0.956Å      |
| C177 | C178  | 1.5321(16)Å |  | C177 | C185  | 1.5314(16)Å |
| C177 | C190  | 1.5371(16)Å |  | C178 | C179  | 1.3843(17)Å |
| C178 | C183  | 1.3992(17)Å |  | C179 | C180  | 1.3933(18)Å |
| C179 | H1791 | 0.960Å      |  | C180 | C181  | 1.388(2)Å   |
| C180 | H1801 | 0.952Å      |  | C181 | C182  | 1.3891(19)Å |
| C181 | H1811 | 0.945Å      |  | C182 | C183  | 1.3918(18)Å |
| C182 | H1821 | 0.957Å      |  | C183 | C184  | 1.4723(17)Å |
| C184 | C185  | 1.3980(17)Å |  | C184 | C189  | 1.3910(17)Å |
| C185 | C186  | 1.3823(18)Å |  | C186 | C187  | 1.3931(18)Å |
| C186 | H1861 | 0.958Å      |  | C187 | C188  | 1.3883(19)Å |
| C187 | H1871 | 0.951Å      |  | C188 | C189  | 1.3894(19)Å |
| C188 | H1881 | 0.960Å      |  | C189 | H1891 | 0.953Å      |
| C190 | C191  | 1.3829(17)Å |  | C190 | C195  | 1.3926(18)Å |
| C191 | C192  | 1.3939(19)Å |  | C191 | H1911 | 0.956Å      |
| C192 | C193  | 1.376(2)Å   |  | C192 | H1921 | 0.961Å      |
| C193 | C194  | 1.378(2)Å   |  | C193 | H1931 | 0.955Å      |
| C194 | C195  | 1.3812(19)Å |  | C194 | H1941 | 0.954Å      |
| C195 | H1951 | 0.957Å      |  | C196 | C197  | 1.5307(17)Å |
| C196 | C204  | 1.5222(18)Å |  | C196 | C209  | 1.5340(19)Å |
| C197 | C198  | 1.3843(18)Å |  | C197 | C202  | 1.3965(19)Å |
| C198 | C199  | 1.391(2)Å   |  | C198 | H1981 | 0.970Å      |
| C199 | C200  | 1.384(2)Å   |  | C199 | H1991 | 0.963Å      |
| C200 | C201  | 1.387(2)Å   |  | C200 | H2001 | 0.956Å      |
| C201 | C202  | 1.390(2)Å   |  | C201 | H2011 | 0.953Å      |
| C202 | C203  | 1.4712(19)Å |  | C203 | C204  | 1.395(2)Å   |
| C203 | C208  | 1.388(2)Å   |  | C204 | C205  | 1.3822(19)Å |
| C205 | C206  | 1.391(2)Å   |  | C205 | H2051 | 0.966Å      |
| C206 | C207  | 1.380(3)Å   |  | C206 | H2061 | 0.958Å      |
| C207 | C208  | 1.387(2)Å   |  | C207 | H2071 | 0.967Å      |
| C208 | H2081 | 0.960Å      |  | C209 | C210  | 1.385(2)Å   |
| C209 | C214  | 1.387(2)Å   |  | C210 | C211  | 1.390(2)Å   |
| C210 | H2101 | 0.956Å      |  | C211 | C212  | 1.369(3)Å   |
| C211 | H2111 | 0.964Å      |  | C212 | C213  | 1.366(3)Å   |
| C212 | H2121 | 0.961Å      |  | C213 | C214  | 1.390(3)Å   |
| C213 | H2131 | 0.935Å      |  | C214 | H2141 | 0.934Å      |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| N501 | C502  | 1.5203(16)Å |  | N501 | C506  | 1.5172(17)Å |
| N501 | C510  | 1.5229(16)Å |  | N501 | C514  | 1.5199(18)Å |
| C502 | C503  | 1.5163(17)Å |  | C502 | H5021 | 0.975Å      |
| C502 | H5022 | 0.983Å      |  | C503 | C504  | 1.5246(19)Å |
| C503 | H5031 | 0.974Å      |  | C503 | H5032 | 0.996Å      |
| C504 | C505  | 1.518(2)Å   |  | C504 | H5041 | 0.993Å      |
| C504 | H5042 | 0.979Å      |  | C505 | H5052 | 0.975Å      |
| C505 | H5053 | 0.970Å      |  | C505 | H5051 | 0.982Å      |
| C506 | C507  | 1.512(2)Å   |  | C506 | H5061 | 0.966Å      |
| C506 | H5062 | 0.971Å      |  | C507 | C508  | 1.523(2)Å   |
| C507 | H5071 | 0.979Å      |  | C507 | H5072 | 0.987Å      |
| C508 | C509  | 1.512(2)Å   |  | C508 | H5081 | 0.971Å      |
| C508 | H5082 | 0.965Å      |  | C509 | H5093 | 0.986Å      |
| C509 | H5092 | 0.982Å      |  | C509 | H5091 | 0.991Å      |
| C510 | C511  | 1.5179(18)Å |  | C510 | H5101 | 0.983Å      |
| C510 | H5102 | 0.968Å      |  | C511 | C512  | 1.5286(18)Å |
| C511 | H5111 | 0.986Å      |  | C511 | H5112 | 0.982Å      |
| C512 | C513  | 1.5175(19)Å |  | C512 | H5121 | 0.979Å      |
| C512 | H5122 | 0.974Å      |  | C513 | H5133 | 0.976Å      |
| C513 | H5131 | 0.981Å      |  | C513 | H5132 | 0.980Å      |
| C514 | C515  | 1.509(2)Å   |  | C514 | H5141 | 0.972Å      |
| C514 | H5142 | 0.980Å      |  | C515 | C516  | 1.502(2)Å   |
| C515 | H5151 | 0.968Å      |  | C515 | H5152 | 0.980Å      |
| C516 | C517  | 1.510(3)Å   |  | C516 | H5161 | 1.009Å      |
| C516 | H5162 | 0.953Å      |  | C517 | H5172 | 0.983Å      |
| C517 | H5171 | 0.993Å      |  | C517 | H5173 | 0.972Å      |
| N521 | C522  | 1.5238(16)Å |  | N521 | C526  | 1.5163(17)Å |
| N521 | C530  | 1.5256(17)Å |  | N521 | C534  | 1.5236(16)Å |
| C522 | C523  | 1.530(2)Å   |  | C522 | H5221 | 0.983Å      |
| C522 | H5222 | 0.951Å      |  | C523 | C524  | 1.528(2)Å   |
| C523 | H5231 | 1.041Å      |  | C523 | H5232 | 1.004Å      |
| C524 | C525  | 1.519(2)Å   |  | C524 | H5241 | 0.970Å      |
| C524 | H5242 | 1.003Å      |  | C525 | H5251 | 1.039Å      |
| C525 | H5252 | 1.016Å      |  | C525 | H5253 | 1.043Å      |
| C526 | C527  | 1.519(2)Å   |  | C526 | H5261 | 0.958Å      |
| C526 | H5262 | 0.955Å      |  | C527 | C528  | 1.501(2)Å   |
| C527 | H5271 | 0.995Å      |  | C527 | H5272 | 0.996Å      |
| C528 | C529  | 1.513(2)Å   |  | C528 | H5281 | 1.007Å      |
| C528 | H5282 | 1.027Å      |  | C529 | H5291 | 1.003Å      |
| C529 | H5292 | 0.978Å      |  | C529 | H5293 | 0.960Å      |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C530 | C531  | 1.5166(19)Å |  | C530 | H5301 | 0.966Å      |
| C530 | H5302 | 0.988Å      |  | C531 | C532  | 1.5219(19)Å |
| C531 | H5311 | 0.964Å      |  | C531 | H5312 | 0.978Å      |
| C532 | C533  | 1.512(2)Å   |  | C532 | H5321 | 0.963Å      |
| C532 | H5322 | 0.975Å      |  | C533 | H5331 | 0.971Å      |
| C533 | H5332 | 0.974Å      |  | C533 | H5333 | 0.972Å      |
| C534 | C535  | 1.513(2)Å   |  | C534 | H5342 | 0.980Å      |
| C534 | H5341 | 0.977Å      |  | C535 | C536  | 1.522(2)Å   |
| C535 | H5352 | 0.965Å      |  | C535 | H5351 | 0.970Å      |
| C536 | C537  | 1.524(2)Å   |  | C536 | H5361 | 0.953Å      |
| C536 | H5362 | 0.985Å      |  | C537 | H5371 | 0.983Å      |
| C537 | H5372 | 0.969Å      |  | C537 | H5373 | 1.005Å      |

## Angles

|      |      |       |             |  |      |      |       |             |
|------|------|-------|-------------|--|------|------|-------|-------------|
| C101 | O11  | H111  | 112.564°    |  | C120 | O12  | H121  | 110.444°    |
| C139 | O13  | H131  | 111.679°    |  | C158 | O14  | H141  | 111.926°    |
| C177 | O15  | H151  | 111.959°    |  | C196 | O16  | H161  | 111.923°    |
| O11  | C101 | C102  | 112.45(10)° |  | O11  | C101 | C109  | 106.99(10)° |
| C102 | C101 | C109  | 101.02(10)° |  | O11  | C101 | C114  | 113.59(10)° |
| C102 | C101 | C114  | 111.27(10)° |  | C109 | C101 | C114  | 110.72(10)° |
| C101 | C102 | C103  | 128.08(12)° |  | C101 | C102 | C107  | 110.93(11)° |
| C103 | C102 | C107  | 120.99(12)° |  | C102 | C103 | C104  | 118.42(14)° |
| C102 | C103 | H1031 | 120.793°    |  | C104 | C103 | H1031 | 120.791°    |
| C103 | C104 | C105  | 120.99(14)° |  | C103 | C104 | H1041 | 120.023°    |
| C105 | C104 | H1041 | 118.983°    |  | C104 | C105 | C106  | 120.79(14)° |
| C104 | C105 | H1051 | 119.699°    |  | C106 | C105 | H1051 | 119.510°    |
| C105 | C106 | C107  | 118.59(14)° |  | C105 | C106 | H1061 | 121.211°    |
| C107 | C106 | H1061 | 120.185°    |  | C102 | C107 | C106  | 120.22(13)° |
| C102 | C107 | C108  | 108.48(11)° |  | C106 | C107 | C108  | 131.31(13)° |
| C107 | C108 | C109  | 108.49(11)° |  | C107 | C108 | C113  | 131.50(12)° |
| C109 | C108 | C113  | 120.01(13)° |  | C101 | C109 | C108  | 111.08(11)° |
| C101 | C109 | C110  | 127.83(11)° |  | C108 | C109 | C110  | 121.09(12)° |
| C109 | C110 | C111  | 118.85(12)° |  | C109 | C110 | H1101 | 120.456°    |
| C111 | C110 | H1101 | 120.695°    |  | C110 | C111 | C112  | 120.31(13)° |
| C110 | C111 | H1111 | 120.121°    |  | C112 | C111 | H1111 | 119.555°    |
| C111 | C112 | C113  | 120.95(13)° |  | C111 | C112 | H1121 | 118.977°    |
| C113 | C112 | H1121 | 120.070°    |  | C108 | C113 | C112  | 118.79(13)° |
| C108 | C113 | H1131 | 120.658°    |  | C112 | C113 | H1131 | 120.543°    |
| C101 | C114 | C115  | 122.27(11)° |  | C101 | C114 | C119  | 119.39(11)° |



|      |      |       |             |  |      |      |       |             |
|------|------|-------|-------------|--|------|------|-------|-------------|
| C115 | C114 | C119  | 118.34(12)° |  | C114 | C115 | C116  | 119.98(13)° |
| C114 | C115 | H1151 | 119.768°    |  | C116 | C115 | H1151 | 120.242°    |
| C115 | C116 | C117  | 120.89(14)° |  | C115 | C116 | H1161 | 118.642°    |
| C117 | C116 | H1161 | 120.464°    |  | C116 | C117 | C118  | 119.49(14)° |
| C116 | C117 | H1171 | 120.966°    |  | C118 | C117 | H1171 | 119.546°    |
| C117 | C118 | C119  | 119.88(14)° |  | C117 | C118 | H1181 | 120.143°    |
| C119 | C118 | H1181 | 119.973°    |  | C114 | C119 | C118  | 121.40(13)° |
| C114 | C119 | H1191 | 119.347°    |  | C118 | C119 | H1191 | 119.245°    |
| O12  | C120 | C121  | 112.73(10)° |  | O12  | C120 | C128  | 108.49(10)° |
| C121 | C120 | C128  | 100.92(10)° |  | O12  | C120 | C133  | 112.70(10)° |
| C121 | C120 | C133  | 110.55(10)° |  | C128 | C120 | C133  | 110.83(10)° |
| C120 | C121 | C122  | 127.82(11)° |  | C120 | C121 | C126  | 111.14(10)° |
| C122 | C121 | C126  | 121.03(11)° |  | C121 | C122 | C123  | 118.32(12)° |
| C121 | C122 | H1221 | 121.096°    |  | C123 | C122 | H1221 | 120.582°    |
| C122 | C123 | C124  | 121.00(13)° |  | C122 | C123 | H1231 | 119.286°    |
| C124 | C123 | H1231 | 119.692°    |  | C123 | C124 | C125  | 120.73(13)° |
| C123 | C124 | H1241 | 118.883°    |  | C125 | C124 | H1241 | 120.381°    |
| C124 | C125 | C126  | 118.59(13)° |  | C124 | C125 | H1251 | 120.502°    |
| C126 | C125 | H1251 | 120.908°    |  | C121 | C126 | C125  | 120.31(12)° |
| C121 | C126 | C127  | 108.45(11)° |  | C125 | C126 | C127  | 131.24(12)° |
| C126 | C127 | C128  | 108.46(11)° |  | C126 | C127 | C132  | 130.91(12)° |
| C128 | C127 | C132  | 120.62(13)° |  | C120 | C128 | C127  | 111.00(11)° |
| C120 | C128 | C129  | 128.34(12)° |  | C127 | C128 | C129  | 120.64(12)° |
| C128 | C129 | C130  | 118.66(13)° |  | C128 | C129 | H1291 | 120.660°    |
| C130 | C129 | H1291 | 120.660°    |  | C129 | C130 | C131  | 120.58(13)° |
| C129 | C130 | H1301 | 119.658°    |  | C131 | C130 | H1301 | 119.755°    |
| C130 | C131 | C132  | 121.00(13)° |  | C130 | C131 | H1311 | 119.110°    |
| C132 | C131 | H1311 | 119.880°    |  | C127 | C132 | C131  | 118.45(13)° |
| C127 | C132 | H1321 | 120.767°    |  | C131 | C132 | H1321 | 120.779°    |
| C120 | C133 | C134  | 121.70(11)° |  | C120 | C133 | C138  | 119.65(11)° |
| C134 | C133 | C138  | 118.65(12)° |  | C133 | C134 | C135  | 119.83(12)° |
| C133 | C134 | H1341 | 119.209°    |  | C135 | C134 | H1341 | 120.936°    |
| C134 | C135 | C136  | 121.15(13)° |  | C134 | C135 | H1351 | 119.577°    |
| C136 | C135 | H1351 | 119.274°    |  | C135 | C136 | C137  | 119.27(13)° |
| C135 | C136 | H1361 | 121.436°    |  | C137 | C136 | H1361 | 119.294°    |
| C136 | C137 | C138  | 119.87(12)° |  | C136 | C137 | H1371 | 119.724°    |
| C138 | C137 | H1371 | 120.408°    |  | C133 | C138 | C137  | 121.23(12)° |
| C133 | C138 | H1381 | 118.380°    |  | C137 | C138 | H1381 | 120.390°    |
| O13  | C139 | C140  | 111.66(10)° |  | O13  | C139 | C147  | 107.26(10)° |
| C140 | C139 | C147  | 101.23(11)° |  | O13  | C139 | C152  | 112.10(11)° |

|      |      |       |             |  |      |      |       |             |
|------|------|-------|-------------|--|------|------|-------|-------------|
| C140 | C139 | C152  | 113.69(11)° |  | C147 | C139 | C152  | 110.18(10)° |
| C139 | C140 | C141  | 128.35(12)° |  | C139 | C140 | C145  | 110.46(13)° |
| C141 | C140 | C145  | 121.15(14)° |  | C140 | C141 | C142  | 118.19(15)° |
| C140 | C141 | H1411 | 121.655°    |  | C142 | C141 | H1411 | 120.140°    |
| C141 | C142 | C143  | 120.07(18)° |  | C141 | C142 | H1421 | 117.840°    |
| C143 | C142 | H1421 | 122.059°    |  | C142 | C143 | C144  | 121.47(16)° |
| C142 | C143 | H1431 | 116.591°    |  | C144 | C143 | H1431 | 121.924°    |
| C143 | C144 | C145  | 118.58(16)° |  | C143 | C144 | H1441 | 119.584°    |
| C145 | C144 | H1441 | 121.833°    |  | C140 | C145 | C144  | 120.53(17)° |
| C140 | C145 | C146  | 108.83(13)° |  | C144 | C145 | C146  | 130.65(15)° |
| C145 | C146 | C147  | 108.56(12)° |  | C145 | C146 | C151  | 132.10(16)° |
| C147 | C146 | C151  | 119.33(17)° |  | C139 | C147 | C146  | 110.81(13)° |
| C139 | C147 | C148  | 128.14(14)° |  | C146 | C147 | C148  | 121.05(14)° |
| C147 | C148 | C149  | 118.82(17)° |  | C147 | C148 | H1481 | 119.579°    |
| C149 | C148 | H1481 | 121.574°    |  | C148 | C149 | C150  | 120.57(18)° |
| C148 | C149 | H1491 | 120.518°    |  | C150 | C149 | H1491 | 118.886°    |
| C149 | C150 | C151  | 121.44(15)° |  | C149 | C150 | H1501 | 118.932°    |
| C151 | C150 | H1501 | 119.625°    |  | C146 | C151 | C150  | 118.77(17)° |
| C146 | C151 | H1511 | 113.144°    |  | C150 | C151 | H1511 | 128.043°    |
| C139 | C152 | C153  | 120.07(12)° |  | C139 | C152 | C157  | 121.10(12)° |
| C153 | C152 | C157  | 118.78(12)° |  | C152 | C153 | C154  | 120.58(13)° |
| C152 | C153 | H1531 | 119.283°    |  | C154 | C153 | H1531 | 120.127°    |
| C153 | C154 | C155  | 120.20(14)° |  | C153 | C154 | H1541 | 118.346°    |
| C155 | C154 | H1541 | 121.456°    |  | C154 | C155 | C156  | 119.74(13)° |
| C154 | C155 | H1551 | 120.569°    |  | C156 | C155 | H1551 | 119.693°    |
| C155 | C156 | C157  | 120.16(14)° |  | C155 | C156 | H1561 | 120.367°    |
| C157 | C156 | H1561 | 119.467°    |  | C152 | C157 | C156  | 120.54(14)° |
| C152 | C157 | H1571 | 119.515°    |  | C156 | C157 | H1571 | 119.940°    |
| O14  | C158 | C159  | 113.50(10)° |  | O14  | C158 | C166  | 108.08(10)° |
| C159 | C158 | C166  | 100.83(10)° |  | O14  | C158 | C171  | 112.34(10)° |
| C159 | C158 | C171  | 111.43(10)° |  | C166 | C158 | C171  | 109.96(10)° |
| C158 | C159 | C160  | 128.40(12)° |  | C158 | C159 | C164  | 110.91(11)° |
| C160 | C159 | C164  | 120.69(13)° |  | C159 | C160 | C161  | 118.50(13)° |
| C159 | C160 | H1601 | 121.504°    |  | C161 | C160 | H1601 | 119.992°    |
| C160 | C161 | C162  | 120.88(14)° |  | C160 | C161 | H1611 | 119.663°    |
| C162 | C161 | H1611 | 119.457°    |  | C161 | C162 | C163  | 120.82(14)° |
| C161 | C162 | H1621 | 119.450°    |  | C163 | C162 | H1621 | 119.720°    |
| C162 | C163 | C164  | 118.76(14)° |  | C162 | C163 | H1631 | 121.609°    |
| C164 | C163 | H1631 | 119.628°    |  | C159 | C164 | C163  | 120.35(13)° |
| C159 | C164 | C165  | 108.59(12)° |  | C163 | C164 | C165  | 131.02(13)° |

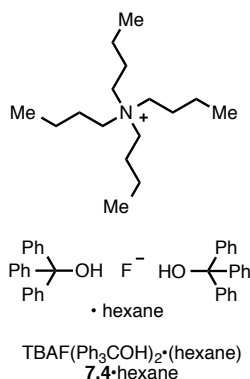
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| C166 | C165 | C170  | 120.29(14)° |  | C158 | C166 | C165  | 111.04(11)° |
| C158 | C166 | C167  | 128.06(12)° |  | C165 | C166 | C167  | 120.90(12)° |
| C166 | C167 | C168  | 118.34(14)° |  | C166 | C167 | H1671 | 120.677°    |
| C168 | C167 | H1671 | 120.975°    |  | C167 | C168 | C169  | 120.64(15)° |
| C167 | C168 | H1681 | 117.972°    |  | C169 | C168 | H1681 | 121.385°    |
| C168 | C169 | C170  | 121.04(13)° |  | C168 | C169 | H1691 | 119.639°    |
| C170 | C169 | H1691 | 119.314°    |  | C165 | C170 | C169  | 118.77(15)° |
| C165 | C170 | H1701 | 120.124°    |  | C169 | C170 | H1701 | 121.099°    |
| C158 | C171 | C172  | 121.32(11)° |  | C158 | C171 | C176  | 119.99(11)° |
| C172 | C171 | C176  | 118.66(12)° |  | C171 | C172 | C173  | 120.22(13)° |
| C171 | C172 | H1721 | 119.099°    |  | C173 | C172 | H1721 | 120.674°    |
| C172 | C173 | C174  | 120.72(13)° |  | C172 | C173 | H1731 | 118.370°    |
| C174 | C173 | H1731 | 120.905°    |  | C173 | C174 | C175  | 119.32(13)° |
| C173 | C174 | H1741 | 120.391°    |  | C175 | C174 | H1741 | 120.283°    |
| C174 | C175 | C176  | 120.18(14)° |  | C174 | C175 | H1751 | 120.937°    |
| C176 | C175 | H1751 | 118.878°    |  | C171 | C176 | C175  | 120.89(13)° |
| C171 | C176 | H1761 | 119.807°    |  | C175 | C176 | H1761 | 119.307°    |
| O15  | C177 | C178  | 113.31(9)°  |  | O15  | C177 | C185  | 109.98(9)°  |
| C178 | C177 | C185  | 100.94(9)°  |  | O15  | C177 | C190  | 112.61(9)°  |
| C178 | C177 | C190  | 110.04(9)°  |  | C185 | C177 | C190  | 109.30(9)°  |
| C177 | C178 | C179  | 128.34(11)° |  | C177 | C178 | C183  | 110.93(10)° |
| C179 | C178 | C183  | 120.71(11)° |  | C178 | C179 | C180  | 118.41(12)° |
| C178 | C179 | H1791 | 120.663°    |  | C180 | C179 | H1791 | 120.901°    |
| C179 | C180 | C181  | 121.03(12)° |  | C179 | C180 | H1801 | 118.625°    |
| C181 | C180 | H1801 | 120.331°    |  | C180 | C181 | C182  | 120.69(12)° |
| C180 | C181 | H1811 | 119.593°    |  | C182 | C181 | H1811 | 119.718°    |
| C181 | C182 | C183  | 118.51(12)° |  | C181 | C182 | H1821 | 120.833°    |
| C183 | C182 | H1821 | 120.654°    |  | C178 | C183 | C182  | 120.60(12)° |
| C178 | C183 | C184  | 108.52(11)° |  | C182 | C183 | C184  | 130.88(11)° |
| C183 | C184 | C185  | 108.59(10)° |  | C183 | C184 | C189  | 130.92(12)° |
| C185 | C184 | C189  | 120.49(12)° |  | C177 | C185 | C184  | 110.94(10)° |
| C177 | C185 | C186  | 128.24(11)° |  | C184 | C185 | C186  | 120.76(11)° |
| C185 | C186 | C187  | 118.75(12)° |  | C185 | C186 | H1861 | 121.426°    |
| C187 | C186 | H1861 | 119.821°    |  | C186 | C187 | C188  | 120.54(12)° |
| C186 | C187 | H1871 | 119.849°    |  | C188 | C187 | H1871 | 119.612°    |
| C187 | C188 | C189  | 120.95(12)° |  | C187 | C188 | H1881 | 119.249°    |
| C189 | C188 | H1881 | 119.796°    |  | C184 | C189 | C188  | 118.50(12)° |
| C184 | C189 | H1891 | 120.258°    |  | C188 | C189 | H1891 | 121.242°    |
| C177 | C190 | C191  | 122.12(11)° |  | C177 | C190 | C195  | 119.40(11)° |

|      |      |       |             |  |      |      |       |             |
|------|------|-------|-------------|--|------|------|-------|-------------|
| C191 | C190 | C195  | 118.49(12)° |  | C190 | C191 | C192  | 120.16(13)° |
| C190 | C191 | H1911 | 119.799°    |  | C192 | C191 | H1911 | 120.044°    |
| C191 | C192 | C193  | 120.67(13)° |  | C191 | C192 | H1921 | 119.056°    |
| C193 | C192 | H1921 | 120.269°    |  | C192 | C193 | C194  | 119.52(13)° |
| C192 | C193 | H1931 | 120.335°    |  | C194 | C193 | H1931 | 120.144°    |
| C193 | C194 | C195  | 120.04(13)° |  | C193 | C194 | H1941 | 119.398°    |
| C195 | C194 | H1941 | 120.560°    |  | C190 | C195 | C194  | 121.11(13)° |
| C190 | C195 | H1951 | 119.294°    |  | C194 | C195 | H1951 | 119.592°    |
| O16  | C196 | C197  | 113.27(10)° |  | O16  | C196 | C204  | 107.68(10)° |
| C197 | C196 | C204  | 101.17(10)° |  | O16  | C196 | C209  | 111.81(10)° |
| C197 | C196 | C209  | 110.27(10)° |  | C204 | C196 | C209  | 112.19(11)° |
| C196 | C197 | C198  | 128.68(12)° |  | C196 | C197 | C202  | 110.73(11)° |
| C198 | C197 | C202  | 120.59(12)° |  | C197 | C198 | C199  | 118.57(13)° |
| C197 | C198 | H1981 | 121.153°    |  | C199 | C198 | H1981 | 120.279°    |
| C198 | C199 | C200  | 120.85(13)° |  | C198 | C199 | H1991 | 119.664°    |
| C200 | C199 | H1991 | 119.479°    |  | C199 | C200 | C201  | 120.91(14)° |
| C199 | C200 | H2001 | 118.988°    |  | C201 | C200 | H2001 | 120.094°    |
| C200 | C201 | C202  | 118.45(14)° |  | C200 | C201 | H2011 | 121.610°    |
| C202 | C201 | H2011 | 119.923°    |  | C197 | C202 | C201  | 120.63(13)° |
| C197 | C202 | C203  | 108.43(12)° |  | C201 | C202 | C203  | 130.92(13)° |
| C202 | C203 | C204  | 108.64(12)° |  | C202 | C203 | C208  | 130.94(14)° |
| C204 | C203 | C208  | 120.42(14)° |  | C196 | C204 | C203  | 110.92(11)° |
| C196 | C204 | C205  | 128.16(13)° |  | C203 | C204 | C205  | 120.92(13)° |
| C204 | C205 | C206  | 118.46(15)° |  | C204 | C205 | H2051 | 120.806°    |
| C206 | C205 | H2051 | 120.735°    |  | C205 | C206 | C207  | 120.56(15)° |
| C205 | C206 | H2061 | 118.854°    |  | C207 | C206 | H2061 | 120.583°    |
| C206 | C207 | C208  | 121.30(15)° |  | C206 | C207 | H2071 | 119.833°    |
| C208 | C207 | H2071 | 118.866°    |  | C203 | C208 | C207  | 118.31(16)° |
| C203 | C208 | H2081 | 120.895°    |  | C207 | C208 | H2081 | 120.790°    |
| C196 | C209 | C210  | 120.75(12)° |  | C196 | C209 | C214  | 121.53(13)° |
| C210 | C209 | C214  | 117.66(14)° |  | C209 | C210 | C211  | 120.94(15)° |
| C209 | C210 | H2101 | 119.573°    |  | C211 | C210 | H2101 | 119.481°    |
| C210 | C211 | C212  | 120.75(17)° |  | C210 | C211 | H2111 | 120.203°    |
| C212 | C211 | H2111 | 119.040°    |  | C211 | C212 | C213  | 118.93(16)° |
| C211 | C212 | H2121 | 120.939°    |  | C213 | C212 | H2121 | 120.126°    |
| C212 | C213 | C214  | 120.97(17)° |  | C212 | C213 | H2131 | 120.180°    |
| C214 | C213 | H2131 | 118.846°    |  | C209 | C214 | C213  | 120.75(17)° |
| C209 | C214 | H2141 | 117.584°    |  | C213 | C214 | H2141 | 121.668°    |
| C502 | N501 | C506  | 111.28(10)° |  | C502 | N501 | C510  | 105.51(9)°  |
| C506 | N501 | C510  | 111.27(10)° |  | C502 | N501 | C514  | 111.05(10)° |

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|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C506  | N501 | C514  | 106.1(1)°   |  | C510  | N501 | C514  | 111.71(10)° |
| N501  | C502 | C503  | 116.32(10)° |  | N501  | C502 | H5021 | 105.956°    |
| C503  | C502 | H5021 | 110.544°    |  | N501  | C502 | H5022 | 104.407°    |
| C503  | C502 | H5022 | 110.272°    |  | H5021 | C502 | H5022 | 108.962°    |
| C502  | C503 | C504  | 109.20(11)° |  | C502  | C503 | H5031 | 111.627°    |
| C504  | C503 | H5031 | 109.296°    |  | C502  | C503 | H5032 | 110.126°    |
| C504  | C503 | H5032 | 109.537°    |  | H5031 | C503 | H5032 | 107.020°    |
| C503  | C504 | C505  | 112.23(12)° |  | C503  | C504 | H5041 | 109.001°    |
| C505  | C504 | H5041 | 109.225°    |  | C503  | C504 | H5042 | 108.772°    |
| C505  | C504 | H5042 | 109.287°    |  | H5041 | C504 | H5042 | 108.238°    |
| C504  | C505 | H5052 | 110.782°    |  | C504  | C505 | H5053 | 109.653°    |
| H5052 | C505 | H5053 | 109.327°    |  | C504  | C505 | H5051 | 110.032°    |
| H5052 | C505 | H5051 | 108.218°    |  | H5053 | C505 | H5051 | 108.788°    |
| N501  | C506 | C507  | 116.16(10)° |  | N501  | C506 | H5061 | 105.439°    |
| C507  | C506 | H5061 | 110.337°    |  | N501  | C506 | H5062 | 105.138°    |
| C507  | C506 | H5062 | 110.438°    |  | H5061 | C506 | H5062 | 108.962°    |
| C506  | C507 | C508  | 108.95(11)° |  | C506  | C507 | H5071 | 110.658°    |
| C508  | C507 | H5071 | 109.375°    |  | C506  | C507 | H5072 | 110.728°    |
| C508  | C507 | H5072 | 109.061°    |  | H5071 | C507 | H5072 | 108.044°    |
| C507  | C508 | C509  | 113.32(13)° |  | C507  | C508 | H5081 | 108.017°    |
| C509  | C508 | H5081 | 110.095°    |  | C507  | C508 | H5082 | 107.404°    |
| C509  | C508 | H5082 | 109.809°    |  | H5081 | C508 | H5082 | 108.019°    |
| C508  | C509 | H5093 | 109.927°    |  | C508  | C509 | H5092 | 110.497°    |
| H5093 | C509 | H5092 | 109.528°    |  | C508  | C509 | H5091 | 109.702°    |
| H5093 | C509 | H5091 | 108.220°    |  | H5092 | C509 | H5091 | 108.924°    |
| N501  | C510 | C511  | 116.89(10)° |  | N501  | C510 | H5101 | 105.305°    |
| C511  | C510 | H5101 | 110.634°    |  | N501  | C510 | H5102 | 106.017°    |
| C511  | C510 | H5102 | 109.057°    |  | H5101 | C510 | H5102 | 108.583°    |
| C510  | C511 | C512  | 107.70(11)° |  | C510  | C511 | H5111 | 111.326°    |
| C512  | C511 | H5111 | 110.145°    |  | C510  | C511 | H5112 | 110.530°    |
| C512  | C511 | H5112 | 109.355°    |  | H5111 | C511 | H5112 | 107.782°    |
| C511  | C512 | C513  | 113.51(12)° |  | C511  | C512 | H5121 | 109.038°    |
| C513  | C512 | H5121 | 110.019°    |  | C511  | C512 | H5122 | 108.689°    |
| C513  | C512 | H5122 | 108.393°    |  | H5121 | C512 | H5122 | 106.973°    |
| C512  | C513 | H5133 | 110.457°    |  | C512  | C513 | H5131 | 111.230°    |
| H5133 | C513 | H5131 | 108.182°    |  | C512  | C513 | H5132 | 110.850°    |
| H5133 | C513 | H5132 | 107.996°    |  | H5131 | C513 | H5132 | 108.007°    |
| N501  | C514 | C515  | 115.76(11)° |  | N501  | C514 | H5141 | 105.822°    |
| C515  | C514 | H5141 | 109.739°    |  | N501  | C514 | H5142 | 105.899°    |
| C515  | C514 | H5142 | 110.695°    |  | H5141 | C514 | H5142 | 108.602°    |

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|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C514  | C515 | C516  | 110.93(13)° |  | C514  | C515 | H5151 | 110.854°    |
| C516  | C515 | H5151 | 109.631°    |  | C514  | C515 | H5152 | 110.696°    |
| C516  | C515 | H5152 | 108.796°    |  | H5151 | C515 | H5152 | 105.791°    |
| C515  | C516 | C517  | 113.27(17)° |  | C515  | C516 | H5161 | 108.034°    |
| C517  | C516 | H5161 | 108.142°    |  | C515  | C516 | H5162 | 112.190°    |
| C517  | C516 | H5162 | 107.958°    |  | H5161 | C516 | H5162 | 106.996°    |
| C516  | C517 | H5172 | 110.654°    |  | C516  | C517 | H5171 | 113.535°    |
| H5172 | C517 | H5171 | 109.394°    |  | C516  | C517 | H5173 | 109.446°    |
| H5172 | C517 | H5173 | 106.971°    |  | H5171 | C517 | H5173 | 106.559°    |
| C522  | N521 | C526  | 109.46(10)° |  | C522  | N521 | C530  | 107.74(10)° |
| C526  | N521 | C530  | 110.54(10)° |  | C522  | N521 | C534  | 110.83(10)° |
| C526  | N521 | C534  | 107.55(10)° |  | C530  | N521 | C534  | 110.72(10)° |
| N521  | C522 | C523  | 114.17(11)° |  | N521  | C522 | H5221 | 105.124°    |
| C523  | C522 | H5221 | 112.071°    |  | N521  | C522 | H5222 | 101.522°    |
| C523  | C522 | H5222 | 114.447°    |  | H5221 | C522 | H5222 | 108.606°    |
| C522  | C523 | C524  | 112.64(13)° |  | C522  | C523 | H5231 | 109.657°    |
| C524  | C523 | H5231 | 108.624°    |  | C522  | C523 | H5232 | 105.575°    |
| C524  | C523 | H5232 | 108.487°    |  | H5231 | C523 | H5232 | 111.873°    |
| C523  | C524 | C525  | 111.76(14)° |  | C523  | C524 | H5241 | 108.590°    |
| C525  | C524 | H5241 | 110.804°    |  | C523  | C524 | H5242 | 109.017°    |
| C525  | C524 | H5242 | 110.204°    |  | H5241 | C524 | H5242 | 106.290°    |
| C524  | C525 | H5251 | 110.039°    |  | C524  | C525 | H5252 | 101.415°    |
| H5251 | C525 | H5252 | 106.293°    |  | C524  | C525 | H5253 | 112.332°    |
| H5251 | C525 | H5253 | 111.877°    |  | H5252 | C525 | H5253 | 114.260°    |
| N521  | C526 | C527  | 114.34(11)° |  | N521  | C526 | H5261 | 107.458°    |
| C527  | C526 | H5261 | 111.133°    |  | N521  | C526 | H5262 | 106.017°    |
| C527  | C526 | H5262 | 110.496°    |  | H5261 | C526 | H5262 | 107.008°    |
| C526  | C527 | C528  | 111.89(12)° |  | C526  | C527 | H5271 | 110.160°    |
| C528  | C527 | H5271 | 107.805°    |  | C526  | C527 | H5272 | 111.818°    |
| C528  | C527 | H5272 | 104.624°    |  | H5271 | C527 | H5272 | 110.357°    |
| C527  | C528 | C529  | 111.82(14)° |  | C527  | C528 | H5281 | 106.734°    |
| C529  | C528 | H5281 | 111.819°    |  | C527  | C528 | H5282 | 107.160°    |
| C529  | C528 | H5282 | 110.699°    |  | H5281 | C528 | H5282 | 108.383°    |
| C528  | C529 | H5291 | 110.967°    |  | C528  | C529 | H5292 | 110.331°    |
| H5291 | C529 | H5292 | 108.811°    |  | C528  | C529 | H5293 | 110.163°    |
| H5291 | C529 | H5293 | 111.126°    |  | H5292 | C529 | H5293 | 105.288°    |
| N521  | C530 | C531  | 115.78(10)° |  | N521  | C530 | H5301 | 105.740°    |
| C531  | C530 | H5301 | 109.537°    |  | N521  | C530 | H5302 | 105.989°    |
| C531  | C530 | H5302 | 111.025°    |  | H5301 | C530 | H5302 | 108.410°    |
| C530  | C531 | C532  | 110.46(12)° |  | C530  | C531 | H5311 | 110.681°    |

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| C532  | C531 | H5311 | 108.662°    |  | C530  | C531 | H5312 | 110.280° |
| C532  | C531 | H5312 | 108.787°    |  | H5311 | C531 | H5312 | 107.902° |
| C531  | C532 | C533  | 112.68(14)° |  | C531  | C532 | H5321 | 108.133° |
| C533  | C532 | H5321 | 109.793°    |  | C531  | C532 | H5322 | 107.878° |
| C533  | C532 | H5322 | 108.119°    |  | H5321 | C532 | H5322 | 110.213° |
| C532  | C533 | H5331 | 111.078°    |  | C532  | C533 | H5332 | 111.768° |
| H5331 | C533 | H5332 | 108.388°    |  | C532  | C533 | H5333 | 110.797° |
| H5331 | C533 | H5333 | 107.846°    |  | H5332 | C533 | H5333 | 106.777° |
| N521  | C534 | C535  | 114.80(11)° |  | N521  | C534 | H5342 | 107.934° |
| C535  | C534 | H5342 | 109.455°    |  | N521  | C534 | H5341 | 106.099° |
| C535  | C534 | H5341 | 109.775°    |  | H5342 | C534 | H5341 | 108.578° |
| C534  | C535 | C536  | 111.84(12)° |  | C534  | C535 | H5352 | 110.126° |
| C536  | C535 | H5352 | 108.227°    |  | C534  | C535 | H5351 | 111.623° |
| C536  | C535 | H5351 | 105.978°    |  | H5352 | C535 | H5351 | 108.893° |
| C535  | C536 | C537  | 112.37(14)° |  | C535  | C536 | H5361 | 108.553° |
| C537  | C536 | H5361 | 111.383°    |  | C535  | C536 | H5362 | 108.831° |
| C537  | C536 | H5362 | 108.651°    |  | H5361 | C536 | H5362 | 106.877° |
| C536  | C537 | H5371 | 110.408°    |  | C536  | C537 | H5372 | 110.263° |
| H5371 | C537 | H5372 | 108.798°    |  | C536  | C537 | H5373 | 110.546° |
| H5371 | C537 | H5373 | 108.089°    |  | H5372 | C537 | H5373 | 108.676° |



**tetra-*n*-butylammonium fluoride bis(triphenylmethanol), *n*-hexane solvate (TBAF(Ph<sub>3</sub>COH)<sub>2</sub>•(hexane), 7.4•(hexane)):**

**X-ray** (single-crystal) A distinct sample of TBAF(Ph<sub>3</sub>COH)<sub>n</sub> was synthesised using the general procedure with a 4:1 ratio of TBAF(H<sub>2</sub>O)<sub>3</sub> and triphenylmethanol. After being filtered, washed with hexanes (×3), and dried under high vacuum, <sup>1</sup>H NMR analysis of this material revealed a ratio of 3.8:1. This material was used to grow single crystals of the 2:1 complex. Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of TBAF(Ph<sub>3</sub>COH)<sub>n</sub> in EtOAc, which had previously been prepared by dissolving TBAF(Ph<sub>3</sub>COH)<sub>n</sub> in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering while hot, and then allowing to stand for 1 min to cool to near room temperature. The crystal was found to be an *n*-hexane solvate.

Oxford Crystallography Number: 010GWP12

## Crystal Data

$a = 11.28870(10) \text{ \AA}$   $\alpha = 90^\circ$

$b = 17.60250(10) \text{ \AA}$   $\beta = 98.4318(7)^\circ$

$c = 24.9660(2) \text{ \AA}$   $\gamma = 90^\circ$

Volume  $4907.35(7) \text{ \AA}^3$

Space group  $P 2_1/n$

Formula  $C_{54.00} H_{68} F_1 N_1 O_2$

Cell determined from 49297 reflections

Temperature 150K

Shape block

Colour clear\_pale\_colourless

$D_x$   $1.06 \text{ Mg m}^{-3}$

$\mu$   $0.504 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$  0.20

Crystal Class monoclinic

$Z = 4$

$M_r$  782.14

Cell  $\theta$  range =  $3 - 77^\circ$

Size  $0.22 \times 0.24 \times 0.30 \text{ mm}$

$F_{000}$  1696.000

$T_{\max}$  0.90

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 117478

Independent reflections 10345

Rint 0.0354

$\theta_{\max}$  76.9172

$h = -14 \rightarrow 14$

$k = 0 \rightarrow 22$



l = 0  $\rightarrow$  31

## Refinement

$\Delta\rho_{\min}$  = -0.60 e Å<sup>-3</sup>  
 $\Delta\rho_{\max}$  = 0.69 e Å<sup>-3</sup>  
 Reflections used 10304  
 Cutoff: I > -3.00σ(I)  
 Parameters refined 836  
 S = 0.98  
 R-factor 0.061  
 weighted R-factor 0.145  
 $\Delta/\sigma_{\max}$  0.0008  
 Refinement on F<sup>2</sup>  
 $w = \frac{1}{[\sigma^2(F_{\text{obs}}^2) + (0.067 \times P)^2 + 1.955 \times P + 0.000 + 0.000 \times \sin\theta]}$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | x           | y           | z           | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| F1    | 0.70392(8)  | 0.66013(5)  | 0.69178(3)  | 0.0436                 | 1.0000    |
| O1    | 0.57356(9)  | 0.72725(6)  | 0.74912(4)  | 0.0376                 | 1.0000    |
| C101  | 0.55234(12) | 0.69143(8)  | 0.79752(5)  | 0.0368                 | 1.0000    |
| C102  | 0.47219(13) | 0.62057(8)  | 0.78477(6)  | 0.0373                 | 1.0000    |
| C103  | 0.47379(14) | 0.58051(9)  | 0.73709(6)  | 0.0393                 | 1.0000    |
| C104  | 0.40159(16) | 0.51694(10) | 0.72553(8)  | 0.0510                 | 1.0000    |
| C105  | 0.32842(16) | 0.49216(11) | 0.76173(10) | 0.0609                 | 1.0000    |
| C106  | 0.32726(19) | 0.53095(11) | 0.80915(10) | 0.0652                 | 1.0000    |
| C107  | 0.39740(18) | 0.59467(10) | 0.82057(8)  | 0.0538                 | 1.0000    |
| C108  | 0.4744(5)   | 0.7485(4)   | 0.8236(2)   | 0.0468                 | 0.63(2)   |
| C109  | 0.3612(5)   | 0.7663(5)   | 0.79861(18) | 0.0451                 | 0.63(2)   |
| C110  | 0.2942(6)   | 0.8225(4)   | 0.8197(3)   | 0.0527                 | 0.63(2)   |
| C111  | 0.3398(8)   | 0.8602(3)   | 0.8669(4)   | 0.0527                 | 0.63(2)   |
| C112  | 0.4520(8)   | 0.8433(3)   | 0.8922(3)   | 0.0533                 | 0.63(2)   |
| C113  | 0.5210(6)   | 0.7886(4)   | 0.8706(3)   | 0.0496                 | 0.63(2)   |
| C114  | 0.6649(3)   | 0.6654(5)   | 0.8344(3)   | 0.0428                 | 0.60(2)   |
| C115  | 0.6569(7)   | 0.6206(4)   | 0.8798(3)   | 0.0582                 | 0.60(2)   |
| C116  | 0.7589(9)   | 0.6008(4)   | 0.9149(2)   | 0.0687                 | 0.60(2)   |
| C117  | 0.8696(7)   | 0.6256(5)   | 0.9056(3)   | 0.0654                 | 0.60(2)   |
| C118  | 0.8787(4)   | 0.6700(5)   | 0.8614(3)   | 0.0609                 | 0.60(2)   |
| C119  | 0.7765(4)   | 0.6893(5)   | 0.8254(3)   | 0.0507                 | 0.60(2)   |

|      |             |             |             |        |           |
|------|-------------|-------------|-------------|--------|-----------|
| O2   | 0.70003(10) | 0.74871(6)  | 0.61047(4)  | 0.0449 | 1.0000    |
| C201 | 0.65432(15) | 0.71905(8)  | 0.55807(5)  | 0.0451 | 1.0000    |
| C202 | 0.51994(16) | 0.70406(8)  | 0.55372(6)  | 0.0417 | 1.0000    |
| C203 | 0.4382(2)   | 0.72169(10) | 0.50784(7)  | 0.0551 | 1.0000    |
| C204 | 0.3181(2)   | 0.70540(12) | 0.50516(8)  | 0.0669 | 1.0000    |
| C205 | 0.2754(2)   | 0.67142(12) | 0.54800(9)  | 0.0663 | 1.0000    |
| C206 | 0.35483(19) | 0.65287(11) | 0.59360(8)  | 0.0595 | 1.0000    |
| C207 | 0.47535(17) | 0.66902(10) | 0.59648(7)  | 0.0492 | 1.0000    |
| C208 | 0.6734(3)   | 0.78135(11) | 0.51717(10) | 0.0425 | 0.746(10) |
| C209 | 0.7009(4)   | 0.76293(16) | 0.46545(11) | 0.0529 | 0.746(10) |
| C210 | 0.7154(3)   | 0.8197(2)   | 0.42869(12) | 0.0602 | 0.746(10) |
| C211 | 0.7003(3)   | 0.8945(2)   | 0.44176(14) | 0.0614 | 0.746(10) |
| C212 | 0.6700(6)   | 0.91285(16) | 0.4917(2)   | 0.0549 | 0.746(10) |
| C213 | 0.6548(5)   | 0.85634(17) | 0.52874(16) | 0.0425 | 0.746(10) |
| C214 | 0.7298(4)   | 0.6513(3)   | 0.5466(3)   | 0.0553 | 0.538(14) |
| C215 | 0.8455(5)   | 0.6420(4)   | 0.5740(3)   | 0.0570 | 0.538(14) |
| C216 | 0.9165(5)   | 0.5819(4)   | 0.5613(3)   | 0.0576 | 0.538(14) |
| C217 | 0.8711(7)   | 0.5290(3)   | 0.5239(2)   | 0.0524 | 0.538(14) |
| C218 | 0.7582(9)   | 0.5378(3)   | 0.49665(16) | 0.0638 | 0.538(14) |
| C219 | 0.6880(7)   | 0.6000(4)   | 0.50756(18) | 0.0611 | 0.538(14) |
| C308 | 0.4915(8)   | 0.7551(5)   | 0.8270(3)   | 0.0288 | 0.37(2)   |
| C309 | 0.3841(11)  | 0.7852(7)   | 0.8044(3)   | 0.0470 | 0.37(2)   |
| C310 | 0.3248(13)  | 0.8377(6)   | 0.8329(6)   | 0.0574 | 0.37(2)   |
| C311 | 0.3783(15)  | 0.8648(5)   | 0.8821(6)   | 0.0536 | 0.37(2)   |
| C312 | 0.4872(14)  | 0.8373(6)   | 0.9044(5)   | 0.0558 | 0.37(2)   |
| C313 | 0.5441(11)  | 0.7821(7)   | 0.8777(4)   | 0.0450 | 0.37(2)   |
| C314 | 0.6779(5)   | 0.6747(8)   | 0.8301(5)   | 0.0465 | 0.40(2)   |
| C315 | 0.6914(10)  | 0.6230(6)   | 0.8730(4)   | 0.0603 | 0.40(2)   |
| C316 | 0.8032(13)  | 0.6108(5)   | 0.9036(5)   | 0.0682 | 0.40(2)   |
| C317 | 0.9029(9)   | 0.6462(7)   | 0.8901(5)   | 0.0657 | 0.40(2)   |
| C318 | 0.8916(5)   | 0.6955(8)   | 0.8467(5)   | 0.0588 | 0.40(2)   |
| C319 | 0.7792(5)   | 0.7098(7)   | 0.8168(4)   | 0.0471 | 0.40(2)   |
| C408 | 0.6890(12)  | 0.7898(3)   | 0.5254(4)   | 0.0652 | 0.254(10) |
| C409 | 0.7540(13)  | 0.7811(4)   | 0.4818(5)   | 0.0696 | 0.254(10) |
| C410 | 0.7681(15)  | 0.8421(5)   | 0.4476(5)   | 0.0808 | 0.254(10) |
| C411 | 0.7227(14)  | 0.9120(5)   | 0.4574(5)   | 0.0736 | 0.254(10) |
| C412 | 0.665(2)    | 0.9223(5)   | 0.5023(6)   | 0.0596 | 0.254(10) |
| C413 | 0.6516(18)  | 0.8612(4)   | 0.5369(6)   | 0.0556 | 0.254(10) |
| C414 | 0.7130(3)   | 0.6418(3)   | 0.5462(3)   | 0.0494 | 0.462(14) |
| C415 | 0.8326(5)   | 0.6293(4)   | 0.5628(4)   | 0.0561 | 0.462(14) |

|       |             |             |             |        |           |
|-------|-------------|-------------|-------------|--------|-----------|
| C416  | 0.8870(5)   | 0.5615(4)   | 0.5494(3)   | 0.0528 | 0.462(14) |
| C417  | 0.8227(7)   | 0.5086(3)   | 0.5157(2)   | 0.0504 | 0.462(14) |
| C418  | 0.7025(7)   | 0.5198(3)   | 0.49874(17) | 0.0488 | 0.462(14) |
| C419  | 0.6459(5)   | 0.5847(3)   | 0.51440(18) | 0.0453 | 0.462(14) |
| N501  | 0.85385(12) | 0.46070(6)  | 0.75228(6)  | 0.0468 | 1.0000    |
| C502  | 0.75633(13) | 0.46358(7)  | 0.78823(6)  | 0.0398 | 1.0000    |
| C503  | 0.69081(16) | 0.38999(8)  | 0.79425(7)  | 0.0484 | 1.0000    |
| C504  | 0.60346(15) | 0.40073(8)  | 0.83410(7)  | 0.0480 | 1.0000    |
| C505  | 0.51875(18) | 0.33445(11) | 0.83462(8)  | 0.0631 | 1.0000    |
| C506  | 0.8954(12)  | 0.5434(3)   | 0.7506(7)   | 0.0456 | 0.56(3)   |
| C507  | 1.0013(7)   | 0.5581(4)   | 0.7204(5)   | 0.0522 | 0.56(3)   |
| C508  | 1.0400(7)   | 0.6410(4)   | 0.7282(6)   | 0.0569 | 0.56(3)   |
| C509  | 1.1365(7)   | 0.6631(6)   | 0.6952(6)   | 0.0640 | 0.56(3)   |
| C510  | 0.9597(10)  | 0.4092(5)   | 0.7812(3)   | 0.0590 | 0.491(15) |
| C511  | 1.0172(7)   | 0.4343(4)   | 0.8390(3)   | 0.0583 | 0.491(15) |
| C512  | 1.1097(6)   | 0.3722(3)   | 0.8636(5)   | 0.0732 | 0.491(15) |
| C513  | 1.1669(6)   | 0.3896(5)   | 0.9186(5)   | 0.0781 | 0.491(15) |
| C514  | 0.80564(18) | 0.42998(8)  | 0.69679(7)  | 0.0595 | 1.0000    |
| C515  | 0.70087(18) | 0.47211(9)  | 0.66620(7)  | 0.0623 | 1.0000    |
| C516  | 0.6733(4)   | 0.4383(2)   | 0.61267(17) | 0.0744 | 0.468(5)  |
| C517  | 0.5662(5)   | 0.4600(3)   | 0.58572(18) | 0.0758 | 0.468(5)  |
| C606  | 0.9004(15)  | 0.5402(4)   | 0.7470(8)   | 0.0468 | 0.44(3)   |
| C607  | 0.9913(10)  | 0.5500(5)   | 0.7089(5)   | 0.0527 | 0.44(3)   |
| C608  | 1.0307(9)   | 0.6323(5)   | 0.7096(7)   | 0.0595 | 0.44(3)   |
| C609  | 1.1278(9)   | 0.6466(7)   | 0.6763(6)   | 0.0610 | 0.44(3)   |
| C610  | 0.9485(9)   | 0.4064(5)   | 0.7703(3)   | 0.0566 | 0.509(15) |
| C611  | 1.0125(7)   | 0.4176(4)   | 0.8259(3)   | 0.0569 | 0.509(15) |
| C612  | 1.1082(5)   | 0.3590(3)   | 0.8377(4)   | 0.0622 | 0.509(15) |
| C613  | 1.1733(5)   | 0.3638(4)   | 0.8936(4)   | 0.0684 | 0.509(15) |
| C617  | 0.6383(4)   | 0.4219(2)   | 0.61637(12) | 0.0791 | 0.532(5)  |
| C618  | 0.5413(4)   | 0.3712(2)   | 0.63072(14) | 0.0629 | 0.532(5)  |
| H1031 | 0.52406(14) | 0.59685(9)  | 0.71266(6)  | 0.0463 | 1.0000    |
| H1041 | 0.40288(16) | 0.49120(10) | 0.69264(8)  | 0.0614 | 1.0000    |
| H1051 | 0.27944(16) | 0.44872(11) | 0.75383(10) | 0.0732 | 1.0000    |
| H1061 | 0.27790(19) | 0.51314(11) | 0.83457(10) | 0.0780 | 1.0000    |
| H1071 | 0.39360(18) | 0.62181(10) | 0.85331(8)  | 0.0658 | 1.0000    |
| H1091 | 0.3287(5)   | 0.7396(5)   | 0.76690(18) | 0.0536 | 0.63(2)   |
| H1101 | 0.2171(6)   | 0.8341(4)   | 0.8016(3)   | 0.0631 | 0.63(2)   |
| H1111 | 0.2917(8)   | 0.8968(3)   | 0.8818(4)   | 0.0628 | 0.63(2)   |
| H1121 | 0.4825(8)   | 0.8689(3)   | 0.9243(3)   | 0.0644 | 0.63(2)   |

|       |             |             |             |        |           |
|-------|-------------|-------------|-------------|--------|-----------|
| H1131 | 0.5985(6)   | 0.7787(4)   | 0.8888(3)   | 0.0600 | 0.63(2)   |
| H1151 | 0.5817(7)   | 0.6034(4)   | 0.8870(3)   | 0.0695 | 0.60(2)   |
| H1161 | 0.7509(9)   | 0.5708(4)   | 0.9456(2)   | 0.0820 | 0.60(2)   |
| H1171 | 0.9388(7)   | 0.6118(5)   | 0.9295(3)   | 0.0778 | 0.60(2)   |
| H1181 | 0.9535(4)   | 0.6869(5)   | 0.8548(3)   | 0.0736 | 0.60(2)   |
| H1191 | 0.7818(4)   | 0.7190(5)   | 0.7945(3)   | 0.0606 | 0.60(2)   |
| H2031 | 0.4677(2)   | 0.74469(10) | 0.47896(7)  | 0.0658 | 1.0000    |
| H2041 | 0.2650(2)   | 0.71883(12) | 0.47452(8)  | 0.0799 | 1.0000    |
| H2051 | 0.1921(2)   | 0.66105(12) | 0.54555(9)  | 0.0794 | 1.0000    |
| H2061 | 0.32554(19) | 0.62819(11) | 0.62373(8)  | 0.0713 | 1.0000    |
| H2071 | 0.52924(17) | 0.65494(10) | 0.62746(7)  | 0.0589 | 1.0000    |
| H2091 | 0.7138(4)   | 0.71156(16) | 0.45559(11) | 0.0634 | 0.746(10) |
| H2101 | 0.7363(3)   | 0.8073(2)   | 0.39362(12) | 0.0713 | 0.746(10) |
| H2111 | 0.7099(3)   | 0.9342(2)   | 0.41673(14) | 0.0743 | 0.746(10) |
| H2121 | 0.6570(6)   | 0.96367(16) | 0.5016(2)   | 0.0664 | 0.746(10) |
| H2131 | 0.6317(5)   | 0.86686(17) | 0.56314(16) | 0.0507 | 0.746(10) |
| H2151 | 0.8745(5)   | 0.6766(4)   | 0.6014(3)   | 0.0681 | 0.538(14) |
| H2161 | 0.9968(5)   | 0.5766(4)   | 0.5791(3)   | 0.0700 | 0.538(14) |
| H2171 | 0.9172(7)   | 0.4866(3)   | 0.5162(2)   | 0.0628 | 0.538(14) |
| H2181 | 0.7257(9)   | 0.5022(3)   | 0.47046(16) | 0.0762 | 0.538(14) |
| H2191 | 0.6098(7)   | 0.6067(4)   | 0.48866(18) | 0.0732 | 0.538(14) |
| H3091 | 0.3521(11)  | 0.7701(7)   | 0.7691(3)   | 0.0562 | 0.37(2)   |
| H3101 | 0.2480(13)  | 0.8541(6)   | 0.8181(6)   | 0.0695 | 0.37(2)   |
| H3111 | 0.3388(15)  | 0.9022(5)   | 0.9001(6)   | 0.0642 | 0.37(2)   |
| H3121 | 0.5235(14)  | 0.8561(6)   | 0.9382(5)   | 0.0671 | 0.37(2)   |
| H3131 | 0.6173(11)  | 0.7629(7)   | 0.8945(4)   | 0.0539 | 0.37(2)   |
| H3151 | 0.6241(10)  | 0.5974(6)   | 0.8812(4)   | 0.0718 | 0.40(2)   |
| H3161 | 0.8115(13)  | 0.5779(5)   | 0.9332(5)   | 0.0823 | 0.40(2)   |
| H3171 | 0.9789(9)   | 0.6364(7)   | 0.9101(5)   | 0.0790 | 0.40(2)   |
| H3181 | 0.9600(5)   | 0.7193(8)   | 0.8369(5)   | 0.0712 | 0.40(2)   |
| H3191 | 0.7718(5)   | 0.7435(7)   | 0.7872(4)   | 0.0565 | 0.40(2)   |
| H4091 | 0.7887(13)  | 0.7341(4)   | 0.4753(5)   | 0.0840 | 0.254(10) |
| H4101 | 0.8080(15)  | 0.8349(5)   | 0.4177(5)   | 0.0971 | 0.254(10) |
| H4111 | 0.7310(14)  | 0.9527(5)   | 0.4341(5)   | 0.0880 | 0.254(10) |
| H4121 | 0.635(2)    | 0.9700(5)   | 0.5096(6)   | 0.0708 | 0.254(10) |
| H4131 | 0.6163(18)  | 0.8687(4)   | 0.5682(6)   | 0.0669 | 0.254(10) |
| H4151 | 0.8744(5)   | 0.6666(4)   | 0.5830(4)   | 0.0669 | 0.462(14) |
| H4161 | 0.9667(5)   | 0.5528(4)   | 0.5637(3)   | 0.0631 | 0.462(14) |
| H4171 | 0.8630(7)   | 0.4652(3)   | 0.5050(2)   | 0.0598 | 0.462(14) |
| H4181 | 0.6590(7)   | 0.4823(3)   | 0.47745(17) | 0.0595 | 0.462(14) |

|       |             |             |             |        |           |
|-------|-------------|-------------|-------------|--------|-----------|
| H4191 | 0.5619(5)   | 0.5904(3)   | 0.50335(18) | 0.0540 | 0.462(14) |
| H5022 | 0.79494(13) | 0.48143(7)  | 0.82405(6)  | 0.0483 | 1.0000    |
| H5021 | 0.69925(13) | 0.50173(7)  | 0.77280(6)  | 0.0458 | 1.0000    |
| H5031 | 0.74770(16) | 0.34910(8)  | 0.80606(7)  | 0.0589 | 1.0000    |
| H5032 | 0.64414(16) | 0.37551(8)  | 0.75913(7)  | 0.0593 | 1.0000    |
| H5042 | 0.64715(15) | 0.40892(8)  | 0.87004(7)  | 0.0582 | 1.0000    |
| H5041 | 0.55875(15) | 0.44735(8)  | 0.82645(7)  | 0.0581 | 1.0000    |
| H5053 | 0.46426(18) | 0.34345(11) | 0.86197(8)  | 0.0944 | 1.0000    |
| H5052 | 0.56334(18) | 0.28825(11) | 0.84478(8)  | 0.0940 | 1.0000    |
| H5051 | 0.47120(18) | 0.32690(11) | 0.79822(8)  | 0.0949 | 1.0000    |
| H5061 | 0.9151(12)  | 0.5590(3)   | 0.7890(7)   | 0.0547 | 0.56(3)   |
| H5062 | 0.8265(12)  | 0.5720(3)   | 0.7336(7)   | 0.0539 | 0.56(3)   |
| H5071 | 1.0684(7)   | 0.5256(4)   | 0.7343(5)   | 0.0627 | 0.56(3)   |
| H5072 | 0.9780(7)   | 0.5473(4)   | 0.6821(5)   | 0.0634 | 0.56(3)   |
| H5082 | 1.0766(7)   | 0.6499(4)   | 0.7661(6)   | 0.0677 | 0.56(3)   |
| H5081 | 0.9705(7)   | 0.6737(4)   | 0.7202(6)   | 0.0671 | 0.56(3)   |
| H5093 | 1.1608(7)   | 0.7159(6)   | 0.7025(6)   | 0.0956 | 0.56(3)   |
| H5092 | 1.2066(7)   | 0.6315(6)   | 0.7052(6)   | 0.0953 | 0.56(3)   |
| H5091 | 1.1074(7)   | 0.6585(6)   | 0.6557(6)   | 0.0963 | 0.56(3)   |
| H5101 | 1.0219(10)  | 0.4091(5)   | 0.7571(3)   | 0.0707 | 0.491(15) |
| H5102 | 0.9257(10)  | 0.3596(5)   | 0.7843(3)   | 0.0708 | 0.491(15) |
| H5112 | 1.0573(7)   | 0.4822(4)   | 0.8373(3)   | 0.0697 | 0.491(15) |
| H5111 | 0.9542(7)   | 0.4413(4)   | 0.8617(3)   | 0.0696 | 0.491(15) |
| H5122 | 1.1758(6)   | 0.3564(3)   | 0.8426(5)   | 0.0849 | 0.491(15) |
| H5121 | 1.0614(6)   | 0.3270(3)   | 0.8658(5)   | 0.0872 | 0.491(15) |
| H5131 | 1.2274(6)   | 0.3506(5)   | 0.9313(5)   | 0.1166 | 0.491(15) |
| H5132 | 1.2053(6)   | 0.4393(5)   | 0.9196(5)   | 0.1168 | 0.491(15) |
| H5133 | 1.1041(6)   | 0.3906(5)   | 0.9419(5)   | 0.1172 | 0.491(15) |
| H5142 | 0.87217(18) | 0.42960(8)  | 0.67639(7)  | 0.0701 | 1.0000    |
| H5141 | 0.78190(18) | 0.37780(8)  | 0.70219(7)  | 0.0697 | 1.0000    |
| H5161 | 0.7393(4)   | 0.4514(2)   | 0.59252(17) | 0.0889 | 0.468(5)  |
| H5162 | 0.6734(4)   | 0.3797(2)   | 0.61917(17) | 0.0901 | 0.468(5)  |
| H5172 | 0.5608(5)   | 0.4414(3)   | 0.54914(18) | 0.1135 | 0.468(5)  |
| H5171 | 0.5620(5)   | 0.5141(3)   | 0.58760(18) | 0.1135 | 0.468(5)  |
| H5173 | 0.5085(5)   | 0.4356(3)   | 0.60423(18) | 0.1128 | 0.468(5)  |
| H6062 | 0.9354(15)  | 0.5551(4)   | 0.7838(8)   | 0.0563 | 0.44(3)   |
| H6061 | 0.8307(15)  | 0.5717(4)   | 0.7348(8)   | 0.0551 | 0.44(3)   |
| H6071 | 1.0597(10)  | 0.5177(5)   | 0.7192(5)   | 0.0627 | 0.44(3)   |
| H6072 | 0.9560(10)  | 0.5365(5)   | 0.6718(5)   | 0.0630 | 0.44(3)   |
| H6082 | 1.0631(9)   | 0.6478(5)   | 0.7475(7)   | 0.0713 | 0.44(3)   |

|       |             |            |             |        |           |
|-------|-------------|------------|-------------|--------|-----------|
| H6081 | 0.9600(9)   | 0.6629(5)  | 0.6958(7)   | 0.0704 | 0.44(3)   |
| H6091 | 1.1486(9)   | 0.7012(7)  | 0.6764(6)   | 0.0917 | 0.44(3)   |
| H6092 | 1.1973(9)   | 0.6167(7)  | 0.6900(6)   | 0.0915 | 0.44(3)   |
| H6093 | 1.0997(9)   | 0.6309(7)  | 0.6392(6)   | 0.0920 | 0.44(3)   |
| H6102 | 1.0052(9)   | 0.4094(5)  | 0.7436(3)   | 0.0670 | 0.509(15) |
| H6101 | 0.9109(9)   | 0.3570(5)  | 0.7676(3)   | 0.0673 | 0.509(15) |
| H6112 | 1.0449(7)   | 0.4681(4)  | 0.8301(3)   | 0.0678 | 0.509(15) |
| H6111 | 0.9551(7)   | 0.4114(4)  | 0.8507(3)   | 0.0681 | 0.509(15) |
| H6121 | 1.1709(5)   | 0.3661(3)  | 0.8153(4)   | 0.0750 | 0.509(15) |
| H6122 | 1.0760(5)   | 0.3085(3)  | 0.8328(4)   | 0.0747 | 0.509(15) |
| H6133 | 1.2345(5)   | 0.3234(4)  | 0.8982(4)   | 0.1027 | 0.509(15) |
| H6132 | 1.2132(5)   | 0.4133(4)  | 0.8985(4)   | 0.1030 | 0.509(15) |
| H6131 | 1.1156(5)   | 0.3560(4)  | 0.9186(4)   | 0.1031 | 0.509(15) |
| H6172 | 0.7001(4)   | 0.3937(2)  | 0.59886(12) | 0.0959 | 0.532(5)  |
| H6171 | 0.5905(4)   | 0.4548(2)  | 0.59137(12) | 0.0933 | 0.532(5)  |
| H6181 | 0.4990(4)   | 0.3486(2)  | 0.59877(14) | 0.0938 | 0.532(5)  |
| H6182 | 0.5793(4)   | 0.3314(2)  | 0.65376(14) | 0.0941 | 0.532(5)  |
| H6183 | 0.4872(4)   | 0.3986(2)  | 0.65004(14) | 0.0945 | 0.532(5)  |
| H11   | 0.62085(9)  | 0.69952(6) | 0.73207(4)  | 0.0574 | 1.0000    |
| H21   | 0.69853(10) | 0.71584(6) | 0.63518(4)  | 0.0670 | 1.0000    |
| H5151 | 0.71981(18) | 0.52521(9) | 0.66279(7)  | 0.0745 | 0.468(5)  |
| H5152 | 0.63453(18) | 0.46766(9) | 0.68697(7)  | 0.0748 | 0.468(5)  |
| H5153 | 0.64310(18) | 0.48515(9) | 0.69010(7)  | 0.0745 | 0.532(5)  |
| H5154 | 0.72958(18) | 0.51914(9) | 0.65205(7)  | 0.0745 | 0.532(5)  |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0517(5)       | 0.0464(5)       | 0.0345(4)       | 0.0029(3)       | 0.0130(4)       | 0.0096(4)       |
| O1    | 0.0454(6)       | 0.0352(5)       | 0.0345(5)       | 0.0032(4)       | 0.0136(4)       | 0.0036(4)       |
| C101  | 0.0465(8)       | 0.0360(7)       | 0.0287(6)       | 0.0015(5)       | 0.0082(5)       | 0.0057(6)       |
| C102  | 0.0422(8)       | 0.0358(7)       | 0.0350(7)       | 0.0076(5)       | 0.0091(6)       | 0.0072(6)       |
| C103  | 0.0400(7)       | 0.0409(7)       | 0.0368(7)       | 0.0045(6)       | 0.0052(6)       | 0.0006(6)       |
| C104  | 0.0487(9)       | 0.0450(9)       | 0.0568(10)      | -0.0007(7)      | -0.0005(7)      | -0.0025(7)      |
| C105  | 0.0435(9)       | 0.0422(9)       | 0.0976(15)      | 0.0112(9)       | 0.0120(9)       | -0.0026(7)      |
| C106  | 0.0631(12)      | 0.0490(10)      | 0.0923(15)      | 0.0190(10)      | 0.0411(11)      | 0.0047(8)       |
| C107  | 0.0657(11)      | 0.0458(9)       | 0.0562(10)      | 0.0116(7)       | 0.0303(9)       | 0.0076(8)       |
| C108  | 0.061(2)        | 0.040(2)        | 0.042(2)        | 0.0035(16)      | 0.0157(16)      | 0.0025(19)      |
| C109  | 0.0527(19)      | 0.039(2)        | 0.0450(17)      | -0.0032(13)     | 0.0112(13)      | 0.0089(17)      |
| C110  | 0.058(2)        | 0.055(2)        | 0.047(2)        | -0.0012(17)     | 0.0126(17)      | 0.0172(19)      |

|      |            |            |            |             |             |             |
|------|------------|------------|------------|-------------|-------------|-------------|
| C111 | 0.067(3)   | 0.0505(19) | 0.044(3)   | -0.0053(17) | 0.019(2)    | 0.0156(19)  |
| C112 | 0.065(3)   | 0.0528(19) | 0.043(2)   | -0.0058(17) | 0.010(2)    | 0.0127(19)  |
| C113 | 0.057(2)   | 0.046(2)   | 0.047(2)   | 0.0036(18)  | 0.0108(15)  | 0.0069(17)  |
| C114 | 0.0519(19) | 0.036(2)   | 0.037(2)   | -0.0109(14) | -0.0042(15) | 0.0065(15)  |
| C115 | 0.070(3)   | 0.058(2)   | 0.042(2)   | 0.0064(17)  | -0.008(2)   | 0.013(2)    |
| C116 | 0.080(3)   | 0.069(2)   | 0.050(2)   | 0.0065(17)  | -0.015(2)   | 0.013(2)    |
| C117 | 0.068(3)   | 0.061(3)   | 0.058(3)   | -0.008(2)   | -0.021(3)   | 0.016(2)    |
| C118 | 0.055(2)   | 0.056(3)   | 0.066(3)   | -0.010(2)   | -0.0115(18) | 0.0125(18)  |
| C119 | 0.053(2)   | 0.043(3)   | 0.053(2)   | -0.0105(16) | -0.0058(15) | 0.0110(15)  |
| O2   | 0.0571(7)  | 0.0447(6)  | 0.0349(5)  | 0.0027(4)   | 0.0137(5)   | 0.0037(5)   |
| C201 | 0.0649(10) | 0.0435(8)  | 0.0301(7)  | 0.0036(6)   | 0.0177(6)   | 0.0145(7)   |
| C202 | 0.0660(10) | 0.0297(7)  | 0.0302(7)  | -0.0040(5)  | 0.0099(6)   | 0.0075(6)   |
| C203 | 0.0870(14) | 0.0439(9)  | 0.0328(8)  | 0.0000(6)   | 0.0034(8)   | -0.0026(9)  |
| C204 | 0.0826(14) | 0.0584(11) | 0.0510(10) | 0.0003(9)   | -0.0193(10) | -0.0136(10) |
| C205 | 0.0732(13) | 0.0532(11) | 0.0672(12) | -0.0004(9)  | -0.0073(10) | -0.0186(9)  |
| C206 | 0.0679(12) | 0.0563(11) | 0.0537(10) | 0.0062(8)   | 0.0067(9)   | -0.0097(9)  |
| C207 | 0.0616(10) | 0.0488(9)  | 0.0375(8)  | 0.0049(7)   | 0.0080(7)   | 0.0037(8)   |
| C208 | 0.0484(14) | 0.0486(13) | 0.0332(12) | 0.0059(10)  | 0.0148(10)  | 0.0109(11)  |
| C209 | 0.0617(18) | 0.0639(16) | 0.0359(12) | 0.0030(11)  | 0.0170(12)  | 0.0092(13)  |
| C210 | 0.0655(19) | 0.0794(19) | 0.0388(13) | 0.0095(13)  | 0.0186(13)  | 0.0000(15)  |
| C211 | 0.0649(17) | 0.074(2)   | 0.0450(16) | 0.0178(14)  | 0.0070(13)  | -0.0153(15) |
| C212 | 0.0644(18) | 0.0495(17) | 0.049(2)   | 0.0039(14)  | 0.0006(17)  | -0.0094(15) |
| C213 | 0.0460(15) | 0.0470(17) | 0.0345(16) | -0.0025(11) | 0.0058(12)  | -0.0031(13) |
| C214 | 0.088(3)   | 0.047(2)   | 0.037(2)   | 0.0118(18)  | 0.028(2)    | 0.025(2)    |
| C215 | 0.070(3)   | 0.053(2)   | 0.056(3)   | -0.0040(18) | 0.0348(19)  | 0.018(2)    |
| C216 | 0.070(3)   | 0.049(3)   | 0.059(3)   | -0.011(2)   | 0.026(2)    | 0.012(2)    |
| C217 | 0.069(3)   | 0.043(2)   | 0.048(2)   | -0.0043(18) | 0.017(2)    | 0.018(2)    |
| C218 | 0.082(4)   | 0.057(3)   | 0.054(2)   | -0.0115(18) | 0.016(2)    | 0.026(3)    |
| C219 | 0.086(3)   | 0.064(3)   | 0.0364(18) | 0.0003(17)  | 0.018(2)    | 0.035(2)    |
| C308 | 0.043(3)   | 0.025(2)   | 0.022(3)   | -0.0001(18) | 0.0154(18)  | 0.001(2)    |
| C309 | 0.065(4)   | 0.035(3)   | 0.042(3)   | -0.004(2)   | 0.010(2)    | 0.006(3)    |
| C310 | 0.073(4)   | 0.049(3)   | 0.051(4)   | -0.006(3)   | 0.012(3)    | 0.016(3)    |
| C311 | 0.079(5)   | 0.045(3)   | 0.040(4)   | -0.009(3)   | 0.021(4)    | 0.001(3)    |
| C312 | 0.075(5)   | 0.048(3)   | 0.046(4)   | -0.015(3)   | 0.012(3)    | 0.004(3)    |
| C313 | 0.067(4)   | 0.035(3)   | 0.035(3)   | -0.016(3)   | 0.013(2)    | -0.001(3)   |
| C314 | 0.063(3)   | 0.039(3)   | 0.035(3)   | -0.006(2)   | -0.001(2)   | 0.013(3)    |
| C315 | 0.078(4)   | 0.052(3)   | 0.046(3)   | -0.002(2)   | -0.007(3)   | 0.006(3)    |
| C316 | 0.079(5)   | 0.063(3)   | 0.055(4)   | 0.003(3)    | -0.017(4)   | 0.004(4)    |
| C317 | 0.074(4)   | 0.058(4)   | 0.056(4)   | -0.008(3)   | -0.021(3)   | 0.013(3)    |
| C318 | 0.060(3)   | 0.054(4)   | 0.057(4)   | -0.012(3)   | -0.008(2)   | 0.016(2)    |

|      |            |            |            |             |             |             |
|------|------------|------------|------------|-------------|-------------|-------------|
| C319 | 0.048(3)   | 0.042(4)   | 0.049(3)   | -0.010(2)   | -0.002(2)   | 0.017(2)    |
| C408 | 0.087(5)   | 0.064(4)   | 0.047(4)   | 0.019(3)    | 0.019(4)    | 0.004(4)    |
| C409 | 0.101(6)   | 0.062(4)   | 0.052(4)   | 0.011(3)    | 0.030(4)    | -0.001(4)   |
| C410 | 0.120(6)   | 0.075(4)   | 0.053(5)   | 0.019(4)    | 0.033(5)    | -0.013(5)   |
| C411 | 0.117(6)   | 0.063(4)   | 0.041(4)   | 0.019(4)    | 0.011(4)    | -0.020(4)   |
| C412 | 0.094(6)   | 0.046(4)   | 0.035(4)   | 0.007(3)    | -0.002(4)   | -0.021(4)   |
| C413 | 0.083(6)   | 0.045(4)   | 0.036(4)   | 0.012(3)    | 0.002(4)    | -0.012(4)   |
| C414 | 0.070(3)   | 0.047(3)   | 0.035(3)   | 0.007(2)    | 0.023(2)    | 0.023(2)    |
| C415 | 0.072(3)   | 0.056(3)   | 0.043(3)   | -0.009(2)   | 0.018(2)    | 0.013(2)    |
| C416 | 0.059(3)   | 0.051(3)   | 0.048(3)   | -0.017(2)   | 0.009(2)    | 0.012(2)    |
| C417 | 0.053(3)   | 0.045(2)   | 0.053(2)   | -0.0112(19) | 0.009(2)    | 0.007(2)    |
| C418 | 0.045(3)   | 0.046(2)   | 0.060(2)   | -0.0064(16) | 0.0203(18)  | 0.0028(18)  |
| C419 | 0.057(2)   | 0.041(2)   | 0.044(2)   | 0.0000(15)  | 0.0290(17)  | 0.0060(17)  |
| N501 | 0.0492(7)  | 0.0276(6)  | 0.0684(8)  | 0.0024(5)   | 0.0248(6)   | 0.0072(5)   |
| C502 | 0.0413(7)  | 0.0320(7)  | 0.0477(8)  | -0.0022(6)  | 0.0117(6)   | 0.0038(6)   |
| C503 | 0.0560(9)  | 0.0363(7)  | 0.0554(9)  | 0.0002(7)   | 0.0167(7)   | -0.0027(7)  |
| C504 | 0.0464(8)  | 0.0490(9)  | 0.0494(9)  | 0.0034(7)   | 0.0090(7)   | -0.0035(7)  |
| C505 | 0.0597(11) | 0.0608(11) | 0.0705(12) | 0.0091(9)   | 0.0149(9)   | -0.0131(9)  |
| C506 | 0.042(2)   | 0.028(2)   | 0.070(3)   | 0.008(2)    | 0.021(2)    | 0.005(2)    |
| C507 | 0.042(2)   | 0.044(2)   | 0.074(3)   | 0.0093(19)  | 0.022(2)    | 0.0073(17)  |
| C508 | 0.046(2)   | 0.046(2)   | 0.082(4)   | 0.016(2)    | 0.020(2)    | 0.0005(16)  |
| C509 | 0.044(2)   | 0.055(3)   | 0.095(5)   | 0.018(3)    | 0.020(3)    | 0.0038(19)  |
| C510 | 0.050(2)   | 0.033(2)   | 0.097(3)   | 0.018(2)    | 0.021(3)    | 0.019(2)    |
| C511 | 0.044(2)   | 0.038(2)   | 0.093(3)   | 0.025(2)    | 0.009(2)    | 0.0112(18)  |
| C512 | 0.063(2)   | 0.044(2)   | 0.106(4)   | 0.031(3)    | -0.011(3)   | 0.0076(19)  |
| C513 | 0.068(3)   | 0.057(3)   | 0.103(5)   | 0.029(3)    | -0.006(3)   | 0.002(2)    |
| C514 | 0.0822(12) | 0.0366(8)  | 0.0685(10) | -0.0099(7)  | 0.0409(9)   | 0.0002(8)   |
| C515 | 0.0799(12) | 0.0512(9)  | 0.0603(10) | -0.0183(8)  | 0.0252(9)   | -0.0171(8)  |
| C516 | 0.131(3)   | 0.041(2)   | 0.051(2)   | 0.0012(16)  | 0.014(2)    | -0.036(2)   |
| C517 | 0.100(3)   | 0.067(3)   | 0.058(2)   | -0.018(2)   | 0.005(2)    | -0.015(2)   |
| C606 | 0.044(3)   | 0.028(2)   | 0.070(4)   | 0.006(3)    | 0.013(2)    | 0.009(2)    |
| C607 | 0.046(3)   | 0.043(3)   | 0.071(4)   | 0.008(2)    | 0.015(2)    | 0.000(2)    |
| C608 | 0.053(3)   | 0.050(3)   | 0.077(4)   | 0.010(3)    | 0.018(3)    | -0.001(2)   |
| C609 | 0.052(3)   | 0.058(4)   | 0.077(5)   | 0.011(3)    | 0.023(3)    | -0.004(3)   |
| C610 | 0.052(3)   | 0.035(2)   | 0.089(3)   | 0.017(2)    | 0.031(2)    | 0.0092(19)  |
| C611 | 0.047(2)   | 0.041(2)   | 0.087(3)   | 0.021(2)    | 0.026(2)    | 0.007(2)    |
| C612 | 0.051(2)   | 0.051(2)   | 0.084(4)   | 0.021(2)    | 0.006(2)    | 0.0001(17)  |
| C613 | 0.056(2)   | 0.050(3)   | 0.096(4)   | 0.024(3)    | 0.000(3)    | -0.002(2)   |
| C617 | 0.138(3)   | 0.058(2)   | 0.0427(18) | -0.0067(16) | 0.018(2)    | -0.039(2)   |
| C618 | 0.077(2)   | 0.055(2)   | 0.0536(19) | -0.0149(15) | -0.0034(16) | -0.0117(16) |



## Distances

|      |       |             |  |      |       |            |
|------|-------|-------------|--|------|-------|------------|
| O1   | C101  | 1.4142(16)Å |  | O1   | H11   | 0.878Å     |
| C101 | C102  | 1.546(2)Å   |  | C101 | C108  | 1.541(4)Å  |
| C101 | C114  | 1.526(3)Å   |  | C101 | C308  | 1.555(4)Å  |
| C101 | C314  | 1.556(5)Å   |  | C102 | C103  | 1.386(2)Å  |
| C102 | C107  | 1.393(2)Å   |  | C103 | C104  | 1.390(2)Å  |
| C103 | H1031 | 0.937Å      |  | C104 | C105  | 1.381(3)Å  |
| C104 | H1041 | 0.940Å      |  | C105 | C106  | 1.368(3)Å  |
| C105 | H1051 | 0.947Å      |  | C106 | C107  | 1.378(3)Å  |
| C106 | H1061 | 0.957Å      |  | C107 | H1071 | 0.953Å     |
| C108 | C109  | 1.373(4)Å   |  | C108 | C113  | 1.405(4)Å  |
| C108 | C308  | 0.230(12)Å  |  | C108 | C309  | 1.242(7)Å  |
| C108 | C313  | 1.575(6)Å   |  | C109 | C110  | 1.394(4)Å  |
| C109 | C308  | 1.549(6)Å   |  | C109 | C309  | 0.433(11)Å |
| C109 | C310  | 1.607(9)Å   |  | C109 | H1091 | 0.947Å     |
| C109 | H3091 | 0.732Å      |  | C110 | C111  | 1.384(4)Å  |
| C110 | C309  | 1.311(9)Å   |  | C110 | C310  | 0.516(10)Å |
| C110 | H1101 | 0.942Å      |  | C110 | H3101 | 0.760Å     |
| C111 | C112  | 1.363(4)Å   |  | C111 | C310  | 0.928(10)Å |
| C111 | C311  | 0.540(10)Å  |  | C111 | H1111 | 0.954Å     |
| C111 | H3111 | 1.113Å      |  | C112 | C113  | 1.395(4)Å  |
| C112 | C311  | 0.915(11)Å  |  | C112 | C312  | 0.476(10)Å |
| C112 | C313  | 1.576(9)Å   |  | C112 | H1121 | 0.941Å     |
| C113 | C308  | 1.240(6)Å   |  | C113 | C312  | 1.299(9)Å  |
| C113 | C313  | 0.314(9)Å   |  | C113 | H1131 | 0.942Å     |
| C113 | H3131 | 1.246Å      |  | C114 | C115  | 1.396(4)Å  |
| C114 | C119  | 1.377(4)Å   |  | C114 | C314  | 0.253(5)Å  |
| C114 | C315  | 1.221(6)Å   |  | C114 | C319  | 1.623(6)Å  |
| C115 | C116  | 1.385(4)Å   |  | C115 | C314  | 1.610(5)Å  |
| C115 | C315  | 0.450(10)Å  |  | C115 | C316  | 1.680(9)Å  |
| C115 | H1151 | 0.943Å      |  | C115 | H3151 | 0.556Å     |
| C116 | C117  | 1.376(4)Å   |  | C116 | C315  | 1.262(9)Å  |
| C116 | C316  | 0.634(9)Å   |  | C116 | H1161 | 0.947Å     |
| C116 | H3161 | 0.803Å      |  | C117 | C118  | 1.368(4)Å  |
| C117 | C316  | 0.788(9)Å   |  | C117 | C317  | 0.682(8)Å  |
| C117 | H1171 | 0.943Å      |  | C117 | H3171 | 1.237Å     |
| C118 | C119  | 1.396(4)Å   |  | C118 | C317  | 0.840(7)Å  |
| C118 | C318  | 0.610(7)Å   |  | C118 | C319  | 1.620(7)Å  |
| C118 | H1181 | 0.933Å      |  | C119 | C314  | 1.164(6)Å  |

|      |       |            |  |      |       |             |
|------|-------|------------|--|------|-------|-------------|
| C119 | C318  | 1.334(8)Å  |  | C119 | C319  | 0.423(7)Å   |
| C119 | H1191 | 0.940Å     |  | O2   | C201  | 1.4325(18)Å |
| O2   | H21   | 0.848Å     |  | C201 | C202  | 1.528(2)Å   |
| C201 | C208  | 1.535(3)Å  |  | C201 | C214  | 1.517(3)Å   |
| C201 | C408  | 1.570(5)Å  |  | C201 | C414  | 1.560(4)Å   |
| C202 | C203  | 1.396(2)Å  |  | C202 | C207  | 1.390(2)Å   |
| C203 | C204  | 1.378(3)Å  |  | C203 | H2031 | 0.930Å      |
| C204 | C205  | 1.373(3)Å  |  | C204 | H2041 | 0.931Å      |
| C205 | C206  | 1.381(3)Å  |  | C205 | H2051 | 0.951Å      |
| C206 | C207  | 1.381(3)Å  |  | C206 | H2061 | 0.968Å      |
| C207 | H2071 | 0.944Å     |  | C208 | C209  | 1.409(3)Å   |
| C208 | C213  | 1.374(3)Å  |  | C208 | C408  | 0.291(15)Å  |
| C208 | C409  | 1.359(7)Å  |  | C208 | C413  | 1.522(7)Å   |
| C209 | C210  | 1.383(3)Å  |  | C209 | C408  | 1.593(8)Å   |
| C209 | C409  | 0.745(15)Å |  | C209 | C410  | 1.678(10)Å  |
| C209 | H2091 | 0.954Å     |  | C209 | H4091 | 1.109Å      |
| C210 | C211  | 1.374(3)Å  |  | C210 | C409  | 1.496(11)Å  |
| C210 | C410  | 0.806(16)Å |  | C210 | H2101 | 0.964Å      |
| C210 | H4101 | 1.151Å     |  | C211 | C212  | 1.379(3)Å   |
| C211 | C410  | 1.194(12)Å |  | C211 | C411  | 0.531(13)Å  |
| C211 | C412  | 1.689(13)Å |  | C211 | H2111 | 0.954Å      |
| C211 | H4111 | 1.107Å     |  | C212 | C213  | 1.386(3)Å   |
| C212 | C411  | 1.112(11)Å |  | C212 | C412  | 0.323(14)Å  |
| C212 | C413  | 1.486(10)Å |  | C212 | H2121 | 0.945Å      |
| C212 | H4121 | 1.193Å     |  | C213 | C408  | 1.240(6)Å   |
| C213 | C412  | 1.349(9)Å  |  | C213 | C413  | 0.229(11)Å  |
| C213 | H2131 | 0.951Å     |  | C213 | H4131 | 1.155Å      |
| C214 | C215  | 1.393(4)Å  |  | C214 | C219  | 1.362(4)Å   |
| C214 | C414  | 0.251(11)Å |  | C214 | C415  | 1.234(6)Å   |
| C214 | C419  | 1.640(5)Å  |  | C215 | C216  | 1.391(4)Å   |
| C215 | C414  | 1.554(4)Å  |  | C215 | C415  | 0.371(6)Å   |
| C215 | C416  | 1.639(7)Å  |  | C215 | H2151 | 0.938Å      |
| C215 | H4151 | 0.569Å     |  | C216 | C217  | 1.364(4)Å   |
| C216 | C415  | 1.266(7)Å  |  | C216 | C416  | 0.546(5)Å   |
| C216 | H2161 | 0.954Å     |  | C216 | H4161 | 0.760Å      |
| C217 | C218  | 1.363(4)Å  |  | C217 | C416  | 0.856(6)Å   |
| C217 | C417  | 0.660(5)Å  |  | C217 | H2171 | 0.945Å      |
| C217 | H4171 | 1.217Å     |  | C218 | C219  | 1.402(4)Å   |
| C218 | C417  | 0.959(6)Å  |  | C218 | C418  | 0.713(6)Å   |
| C218 | C419  | 1.628(5)Å  |  | C218 | H2181 | 0.940Å      |

|      |       |             |  |      |       |            |
|------|-------|-------------|--|------|-------|------------|
| C219 | C414  | 1.214(5)Å   |  | C219 | C418  | 1.441(6)Å  |
| C219 | C419  | 0.592(6)Å   |  | C219 | H2191 | 0.945Å     |
| C308 | C309  | 1.367(5)Å   |  | C308 | C313  | 1.399(5)Å  |
| C309 | C310  | 1.395(5)Å   |  | C309 | H3091 | 0.941Å     |
| C310 | C311  | 1.372(5)Å   |  | C310 | H3101 | 0.937Å     |
| C311 | C312  | 1.362(5)Å   |  | C311 | H1111 | 1.128Å     |
| C311 | H3111 | 0.945Å      |  | C312 | C313  | 1.389(5)Å  |
| C312 | H1121 | 0.753Å      |  | C312 | H3121 | 0.942Å     |
| C313 | H1131 | 0.639Å      |  | C313 | H3131 | 0.934Å     |
| C314 | C315  | 1.396(5)Å   |  | C314 | C319  | 1.382(5)Å  |
| C315 | C316  | 1.393(5)Å   |  | C315 | H3151 | 0.932Å     |
| C316 | C317  | 1.371(5)Å   |  | C316 | H3161 | 0.934Å     |
| C317 | C318  | 1.378(5)Å   |  | C317 | H1171 | 1.176Å     |
| C317 | H3171 | 0.944Å      |  | C318 | C319  | 1.397(5)Å  |
| C318 | H1181 | 0.715Å      |  | C318 | H3181 | 0.943Å     |
| C319 | H1191 | 0.585Å      |  | C319 | H3191 | 0.942Å     |
| C408 | C409  | 1.408(5)Å   |  | C408 | C413  | 1.370(6)Å  |
| C409 | C410  | 1.395(5)Å   |  | C409 | H4091 | 0.939Å     |
| C410 | C411  | 1.367(6)Å   |  | C410 | H4101 | 0.936Å     |
| C411 | C412  | 1.386(6)Å   |  | C411 | H2111 | 1.078Å     |
| C411 | H4111 | 0.937Å      |  | C412 | C413  | 1.401(6)Å  |
| C412 | H2121 | 0.735Å      |  | C412 | H4121 | 0.938Å     |
| C413 | H2131 | 0.730Å      |  | C413 | H4131 | 0.938Å     |
| C414 | C415  | 1.371(5)Å   |  | C414 | C419  | 1.427(4)Å  |
| C415 | C416  | 1.404(5)Å   |  | C415 | H4151 | 0.916Å     |
| C416 | C417  | 1.387(4)Å   |  | C416 | H4161 | 0.931Å     |
| C417 | C418  | 1.376(4)Å   |  | C417 | H2171 | 1.133Å     |
| C417 | H4171 | 0.948Å      |  | C418 | C419  | 1.393(4)Å  |
| C418 | H2181 | 0.847Å      |  | C418 | H4181 | 0.939Å     |
| C419 | H2191 | 0.807Å      |  | C419 | H4191 | 0.953Å     |
| N501 | C502  | 1.5199(18)Å |  | N501 | C506  | 1.531(6)Å  |
| N501 | C510  | 1.587(6)Å   |  | N501 | C514  | 1.512(2)Å  |
| N501 | C606  | 1.507(7)Å   |  | N501 | C610  | 1.456(6)Å  |
| C502 | C503  | 1.510(2)Å   |  | C502 | H5022 | 0.987Å     |
| C502 | H5021 | 0.971Å      |  | C503 | C504  | 1.512(2)Å  |
| C503 | H5031 | 0.981Å      |  | C503 | H5032 | 0.988Å     |
| C504 | C505  | 1.510(2)Å   |  | C504 | H5042 | 0.969Å     |
| C504 | H5041 | 0.968Å      |  | C505 | H5053 | 0.996Å     |
| C505 | H5052 | 0.970Å      |  | C505 | H5051 | 0.994Å     |
| C506 | C507  | 1.527(6)Å   |  | C506 | C606  | 0.126(10)Å |

|      |       |            |  |      |       |            |
|------|-------|------------|--|------|-------|------------|
| C506 | C607  | 1.613(9)Å  |  | C506 | H5061 | 0.991Å     |
| C506 | H5062 | 0.971Å     |  | C506 | H6062 | 0.907Å     |
| C506 | H6061 | 0.924Å     |  | C507 | C508  | 1.527(6)Å  |
| C507 | C606  | 1.436(9)Å  |  | C507 | C607  | 0.324(15)Å |
| C507 | C608  | 1.384(11)Å |  | C507 | H5071 | 0.972Å     |
| C507 | H5072 | 0.972Å     |  | C507 | H6071 | 0.974Å     |
| C508 | C509  | 1.510(6)Å  |  | C508 | C607  | 1.737(10)Å |
| C508 | C608  | 0.484(9)Å  |  | C508 | H5082 | 0.989Å     |
| C508 | H5081 | 0.970Å     |  | C508 | H6082 | 0.528Å     |
| C508 | H6081 | 1.184Å     |  | C509 | C608  | 1.406(13)Å |
| C509 | C609  | 0.551(9)Å  |  | C509 | H5093 | 0.977Å     |
| C509 | H5092 | 0.969Å     |  | C509 | H5091 | 0.996Å     |
| C509 | H6091 | 0.840Å     |  | C509 | H6092 | 1.087Å     |
| C510 | C511  | 1.557(6)Å  |  | C510 | C610  | 0.287(7)Å  |
| C510 | C611  | 1.195(7)Å  |  | C510 | H5101 | 0.990Å     |
| C510 | H5102 | 0.962Å     |  | C510 | H6102 | 1.134Å     |
| C510 | H6101 | 1.100Å     |  | C511 | C512  | 1.574(6)Å  |
| C511 | C611  | 0.437(6)Å  |  | C511 | C612  | 1.680(8)Å  |
| C511 | H5112 | 0.961Å     |  | C511 | H5111 | 0.979Å     |
| C511 | H6112 | 0.721Å     |  | C511 | H6111 | 0.894Å     |
| C512 | C513  | 1.461(6)Å  |  | C512 | C611  | 1.557(8)Å  |
| C512 | C612  | 0.685(7)Å  |  | C512 | C613  | 0.970(8)Å  |
| C512 | H5122 | 1.012Å     |  | C512 | H5121 | 0.971Å     |
| C513 | C613  | 0.782(7)Å  |  | C513 | H5131 | 0.988Å     |
| C513 | H5132 | 0.975Å     |  | C513 | H5133 | 0.981Å     |
| C513 | H6132 | 0.881Å     |  | C513 | H6131 | 0.828Å     |
| C514 | C515  | 1.506(3)Å  |  | C514 | H5142 | 0.967Å     |
| C514 | H5141 | 0.972Å     |  | C515 | C516  | 1.454(4)Å  |
| C515 | C617  | 1.603(4)Å  |  | C515 | H5151 | 0.965Å     |
| C515 | H5152 | 0.974Å     |  | C515 | H5153 | 0.974Å     |
| C515 | H5154 | 0.974Å     |  | C516 | C517  | 1.350(6)Å  |
| C516 | C617  | 0.509(6)Å  |  | C516 | H5161 | 0.985Å     |
| C516 | H5162 | 1.045Å     |  | C516 | H6172 | 0.926Å     |
| C516 | H6171 | 1.046Å     |  | C517 | C617  | 1.232(6)Å  |
| C517 | H5172 | 0.964Å     |  | C517 | H5171 | 0.955Å     |
| C517 | H5173 | 0.955Å     |  | C517 | H6171 | 0.304Å     |
| C606 | C607  | 1.508(8)Å  |  | C606 | H5061 | 1.089Å     |
| C606 | H5062 | 1.020Å     |  | C606 | H6062 | 0.980Å     |
| C606 | H6061 | 0.975Å     |  | C607 | C608  | 1.514(7)Å  |
| C607 | H5071 | 1.088Å     |  | C607 | H5072 | 0.667Å     |

|       |       |           |  |       |       |           |
|-------|-------|-----------|--|-------|-------|-----------|
| C607  | H6071 | 0.964Å    |  | C607  | H6072 | 0.983Å    |
| C608  | C609  | 1.491(7)Å |  | C608  | H5081 | 1.056Å    |
| C608  | H6082 | 1.001Å    |  | C608  | H6081 | 0.982Å    |
| C609  | H5092 | 1.092Å    |  | C609  | H5091 | 0.571Å    |
| C609  | H6091 | 0.990Å    |  | C609  | H6092 | 0.965Å    |
| C609  | H6093 | 0.973Å    |  | C610  | C611  | 1.482(6)Å |
| C610  | H5101 | 0.937Å    |  | C610  | H5102 | 0.945Å    |
| C610  | H6102 | 0.991Å    |  | C610  | H6101 | 0.965Å    |
| C611  | C612  | 1.491(6)Å |  | C611  | H5112 | 1.260Å    |
| C611  | H5111 | 1.255Å    |  | C611  | H6112 | 0.960Å    |
| C611  | H6111 | 0.965Å    |  | C612  | C613  | 1.482(5)Å |
| C612  | H5122 | 0.757Å    |  | C612  | H5121 | 1.094Å    |
| C612  | H6121 | 0.974Å    |  | C612  | H6122 | 0.962Å    |
| C613  | H5122 | 1.284Å    |  | C613  | H5131 | 1.070Å    |
| C613  | H6133 | 0.987Å    |  | C613  | H6132 | 0.980Å    |
| C613  | H6131 | 0.975Å    |  | C617  | C618  | 1.495(5)Å |
| C617  | H5162 | 0.839Å    |  | C617  | H6172 | 1.006Å    |
| C617  | H6171 | 0.958Å    |  | C618  | H6181 | 0.954Å    |
| C618  | H6182 | 0.967Å    |  | C618  | H6183 | 0.962Å    |
| H1091 | H3091 | 0.598Å    |  | H1101 | H3101 | 0.612Å    |
| H1111 | H3111 | 0.655Å    |  | H1121 | H3121 | 0.582Å    |
| H1131 | H3131 | 0.365Å    |  | H1151 | H3151 | 0.531Å    |
| H1161 | H3161 | 0.801Å    |  | H1171 | H3171 | 0.832Å    |
| H1181 | H3181 | 0.735Å    |  | H1191 | H3191 | 0.476Å    |
| H2111 | H4111 | 0.566Å    |  | H2121 | H4121 | 0.362Å    |
| H2131 | H4131 | 0.233Å    |  | H2151 | H4151 | 0.491Å    |
| H2161 | H4161 | 0.633Å    |  | H2171 | H4171 | 0.739Å    |
| H2191 | H4191 | 0.753Å    |  | H5061 | H6062 | 0.287Å    |
| H5062 | H6061 | 0.053Å    |  | H5071 | H6071 | 0.402Å    |
| H5072 | H6072 | 0.381Å    |  | H5082 | H6082 | 0.468Å    |
| H5081 | H6081 | 0.631Å    |  | H5093 | H6091 | 0.694Å    |
| H5092 | H6092 | 0.459Å    |  | H5091 | H6093 | 0.634Å    |
| H5101 | H6102 | 0.361Å    |  | H5102 | H6101 | 0.428Å    |
| H5112 | H6112 | 0.326Å    |  | H5111 | H6111 | 0.595Å    |
| H5122 | H6121 | 0.699Å    |  | H5132 | H6132 | 0.713Å    |
| H5162 | H6172 | 0.674Å    |  | H5151 | H5154 | 0.323Å    |
| H5152 | H5153 | 0.328Å    |  |       |       |           |

## Angles

|      |      |       |             |  |       |      |       |             |
|------|------|-------|-------------|--|-------|------|-------|-------------|
| C101 | O1   | H11   | 110.937°    |  | O1    | C101 | C102  | 110.56(11)° |
| O1   | C101 | C108  | 104.4(3)°   |  | C102  | C101 | C108  | 105.1(3)°   |
| O1   | C101 | C114  | 114.7(2)°   |  | C102  | C101 | C114  | 107.0(3)°   |
| C108 | C101 | C114  | 114.7(4)°   |  | O1    | C101 | C308  | 103.0(4)°   |
| C102 | C101 | C308  | 113.1(5)°   |  | C108  | C101 | C308  | 8.5(4)°     |
| C114 | C101 | C308  | 108.5(5)°   |  | O1    | C101 | C314  | 106.0(3)°   |
| C102 | C101 | C314  | 114.6(5)°   |  | C108  | C101 | C314  | 115.8(6)°   |
| C114 | C101 | C314  | 9.36(18)°   |  | C308  | C101 | C314  | 108.7(7)°   |
| C101 | C102 | C103  | 120.40(13)° |  | C101  | C102 | C107  | 121.56(14)° |
| C103 | C102 | C107  | 118.03(15)° |  | C102  | C103 | C104  | 120.46(15)° |
| C102 | C103 | H1031 | 119.225°    |  | C104  | C103 | H1031 | 120.319°    |
| C103 | C104 | C105  | 120.48(18)° |  | C103  | C104 | H1041 | 119.069°    |
| C105 | C104 | H1041 | 120.451°    |  | C104  | C105 | C106  | 119.41(17)° |
| C104 | C105 | H1051 | 120.347°    |  | C106  | C105 | H1051 | 120.245°    |
| C105 | C106 | C107  | 120.45(17)° |  | C105  | C106 | H1061 | 119.395°    |
| C107 | C106 | H1061 | 120.147°    |  | C102  | C107 | C106  | 121.16(18)° |
| C102 | C107 | H1071 | 119.588°    |  | C106  | C107 | H1071 | 119.248°    |
| C101 | C108 | C109  | 120.54(7)°  |  | C101  | C108 | C113  | 120.92(7)°  |
| C109 | C108 | C113  | 118.29(6)°  |  | C101  | C108 | C308  | 89.3(19)°   |
| C109 | C108 | C308  | 137(3)°     |  | C113  | C108 | C308  | 41(3)°      |
| C101 | C108 | C309  | 131.6(5)°   |  | C109  | C108 | C309  | 18.2(5)°    |
| C113 | C108 | C309  | 104.2(4)°   |  | C308  | C108 | C309  | 119(3)°     |
| C101 | C108 | C313  | 111.2(4)°   |  | C109  | C108 | C313  | 128.2(4)°   |
| C113 | C108 | C313  | 10.2(4)°    |  | C308  | C108 | C313  | 37(3)°      |
| C309 | C108 | C313  | 114.4(5)°   |  | C108  | C109 | C110  | 120.73(7)°  |
| C108 | C109 | C308  | 5.9(6)°     |  | C110  | C109 | C308  | 116.7(3)°   |
| C108 | C109 | C309  | 63.5(11)°   |  | C110  | C109 | C309  | 70.1(13)°   |
| C308 | C109 | C309  | 57.6(10)°   |  | C108  | C109 | C310  | 103.3(4)°   |
| C110 | C109 | C310  | 18.1(4)°    |  | C308  | C109 | C310  | 98.9(4)°    |
| C309 | C109 | C310  | 53.7(12)°   |  | C108  | C109 | H1091 | 119.062°    |
| C110 | C109 | H1091 | 120.202°    |  | C308  | C109 | H1091 | 122.963°    |
| C309 | C109 | H1091 | 143.215°    |  | C310  | C109 | H1091 | 137.395°    |
| C108 | C109 | H3091 | 117.495°    |  | C110  | C109 | H3091 | 108.112°    |
| C308 | C109 | H3091 | 117.170°    |  | C309  | C109 | H3091 | 104.849°    |
| C310 | C109 | H3091 | 117.110°    |  | H1091 | C109 | H3091 | 39.149°     |
| C109 | C110 | C111  | 120.43(7)°  |  | C109  | C110 | C309  | 18.1(5)°    |
| C111 | C110 | C309  | 106.3(4)°   |  | C109  | C110 | C310  | 105.0(10)°  |
| C111 | C110 | C310  | 22.6(14)°   |  | C309  | C110 | C310  | 88.3(12)°   |

|       |      |       |            |  |       |      |       |            |
|-------|------|-------|------------|--|-------|------|-------|------------|
| C109  | C110 | H1101 | 119.106°   |  | C111  | C110 | H1101 | 120.460°   |
| C309  | C110 | H1101 | 131.972°   |  | C310  | C110 | H1101 | 132.854°   |
| C109  | C110 | H3101 | 155.026°   |  | C111  | C110 | H3101 | 81.928°    |
| C309  | C110 | H3101 | 155.005°   |  | C310  | C110 | H3101 | 92.540°    |
| H1101 | C110 | H3101 | 40.389°    |  | C110  | C111 | C112  | 119.66(7)° |
| C110  | C111 | C310  | 12.3(8)°   |  | C112  | C111 | C310  | 111.3(6)°  |
| C110  | C111 | C311  | 146.3(10)° |  | C112  | C111 | C311  | 27.0(10)°  |
| C310  | C111 | C311  | 136.6(15)° |  | C110  | C111 | H1111 | 119.688°   |
| C112  | C111 | H1111 | 120.636°   |  | C310  | C111 | H1111 | 127.459°   |
| C311  | C111 | H1111 | 93.908°    |  | C110  | C111 | H3111 | 155.500°   |
| C112  | C111 | H3111 | 84.821°    |  | C310  | C111 | H3111 | 160.665°   |
| C311  | C111 | H3111 | 58.012°    |  | H1111 | C111 | H3111 | 35.896°    |
| C111  | C112 | C113  | 120.31(7)° |  | C111  | C112 | C311  | 15.6(5)°   |
| C113  | C112 | C311  | 135.7(5)°  |  | C111  | C112 | C312  | 167.7(20)° |
| C113  | C112 | C312  | 68.6(11)°  |  | C311  | C112 | C312  | 155.1(16)° |
| C111  | C112 | C313  | 129.9(3)°  |  | C113  | C112 | C313  | 9.9(3)°    |
| C311  | C112 | C313  | 145.4(7)°  |  | C312  | C112 | C313  | 58.7(10)°  |
| C111  | C112 | H1121 | 119.356°   |  | C113  | C112 | H1121 | 120.331°   |
| C311  | C112 | H1121 | 103.929°   |  | C312  | C112 | H1121 | 52.542°    |
| C313  | C112 | H1121 | 110.660°   |  | C108  | C113 | C112  | 120.53(7)° |
| C108  | C113 | C308  | 7.0(7)°    |  | C112  | C113 | C308  | 125.0(3)°  |
| C108  | C113 | C312  | 139.9(5)°  |  | C112  | C113 | C312  | 20.0(5)°   |
| C308  | C113 | C312  | 144.9(7)°  |  | C108  | C113 | C313  | 117.5(18)° |
| C112  | C113 | C313  | 120.1(18)° |  | C308  | C113 | C313  | 114.3(19)° |
| C312  | C113 | C313  | 100.2(18)° |  | C108  | C113 | H1131 | 121.163°   |
| C112  | C113 | H1131 | 118.298°   |  | C308  | C113 | H1131 | 116.478°   |
| C312  | C113 | H1131 | 98.629°    |  | C313  | C113 | H1131 | 12.945°    |
| C108  | C113 | H3131 | 114.229°   |  | C112  | C113 | H3131 | 124.327°   |
| C308  | C113 | H3131 | 110.461°   |  | C312  | C113 | H3131 | 104.376°   |
| C313  | C113 | H3131 | 5.609°     |  | H1131 | C113 | H3131 | 10.714°    |
| C101  | C114 | C115  | 120.80(7)° |  | C101  | C114 | C119  | 120.72(6)° |
| C115  | C114 | C119  | 118.36(6)° |  | C101  | C114 | C314  | 92.1(16)°  |
| C115  | C114 | C314  | 145(3)°    |  | C119  | C114 | C314  | 30(2)°     |
| C101  | C114 | C315  | 138.2(4)°  |  | C115  | C114 | C315  | 18.2(5)°   |
| C119  | C114 | C315  | 101.1(4)°  |  | C314  | C114 | C315  | 129.5(20)° |
| C101  | C114 | C319  | 108.5(3)°  |  | C115  | C114 | C319  | 129.9(3)°  |
| C119  | C114 | C319  | 13.2(3)°   |  | C314  | C114 | C319  | 16.8(18)°  |
| C315  | C114 | C319  | 113.3(5)°  |  | C114  | C115 | C116  | 120.58(7)° |
| C114  | C115 | C314  | 5.2(4)°    |  | C116  | C115 | C314  | 115.7(3)°  |
| C114  | C115 | C315  | 58.3(11)°  |  | C116  | C115 | C315  | 65.0(12)°  |

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|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C314  | C115 | C315  | 54.3(10)°   |  | C114  | C115 | C316  | 99.6(3)°    |
| C116  | C115 | C316  | 21.2(3)°    |  | C314  | C115 | C316  | 94.8(3)°    |
| C315  | C115 | C316  | 44.2(12)°   |  | C114  | C115 | H1151 | 120.197°    |
| C116  | C115 | H1151 | 119.225°    |  | C314  | C115 | H1151 | 125.086°    |
| C315  | C115 | H1151 | 163.002°    |  | C316  | C115 | H1151 | 140.033°    |
| C114  | C115 | H3151 | 126.127°    |  | C116  | C115 | H3151 | 105.945°    |
| C314  | C115 | H3151 | 131.143°    |  | C315  | C115 | H3151 | 135.616°    |
| C316  | C115 | H3151 | 122.096°    |  | H1151 | C115 | H3151 | 29.037°     |
| C115  | C116 | C117  | 120.36(7)°  |  | C115  | C116 | C315  | 18.8(5)°    |
| C117  | C116 | C315  | 102.4(3)°   |  | C115  | C116 | C316  | 106.7(7)°   |
| C117  | C116 | C316  | 16.4(9)°    |  | C315  | C116 | C316  | 88.0(8)°    |
| C115  | C116 | H1161 | 118.917°    |  | C117  | C116 | H1161 | 120.713°    |
| C315  | C116 | H1161 | 136.636°    |  | C316  | C116 | H1161 | 133.656°    |
| C115  | C116 | H3161 | 164.449°    |  | C117  | C116 | H3161 | 68.986°     |
| C315  | C116 | H3161 | 159.045°    |  | C316  | C116 | H3161 | 80.039°     |
| H1161 | C116 | H3161 | 53.736°     |  | C116  | C117 | C118  | 119.66(7)°  |
| C116  | C117 | C316  | 13.2(8)°    |  | C118  | C117 | C316  | 108.7(5)°   |
| C116  | C117 | C317  | 148.7(7)°   |  | C118  | C117 | C317  | 29.1(7)°    |
| C316  | C117 | C317  | 137.6(12)°  |  | C116  | C117 | H1171 | 119.987°    |
| C118  | C117 | H1171 | 120.352°    |  | C316  | C117 | H1171 | 130.258°    |
| C317  | C117 | H1171 | 91.301°     |  | C116  | C117 | H3171 | 162.192°    |
| C118  | C117 | H3171 | 78.147°     |  | C316  | C117 | H3171 | 169.482°    |
| C317  | C117 | H3171 | 49.104°     |  | H1171 | C117 | H3171 | 42.205°     |
| C117  | C118 | C119  | 120.38(7)°  |  | C117  | C118 | C317  | 23.2(6)°    |
| C119  | C118 | C317  | 143.6(6)°   |  | C117  | C118 | C318  | 163.1(12)°  |
| C119  | C118 | C318  | 71.5(8)°    |  | C317  | C118 | C318  | 143.3(13)°  |
| C117  | C118 | C319  | 132.4(3)°   |  | C119  | C118 | C319  | 13.7(3)°    |
| C317  | C118 | C319  | 155.1(8)°   |  | C318  | C118 | C319  | 58.1(7)°    |
| C117  | C118 | H1181 | 120.070°    |  | C119  | C118 | H1181 | 119.543°    |
| C317  | C118 | H1181 | 96.852°     |  | C318  | C118 | H1181 | 49.999°     |
| C319  | C118 | H1181 | 107.182°    |  | C114  | C119 | C118  | 120.65(7)°  |
| C114  | C119 | C314  | 6.2(4)°     |  | C118  | C119 | C314  | 126.3(3)°   |
| C114  | C119 | C318  | 145.1(4)°   |  | C118  | C119 | C318  | 25.7(3)°    |
| C314  | C119 | C318  | 150.1(7)°   |  | C114  | C119 | C319  | 118.6(13)°  |
| C118  | C119 | C319  | 114.8(14)°  |  | C314  | C119 | C319  | 112.4(15)°  |
| C318  | C119 | C319  | 89.7(13)°   |  | C114  | C119 | H1191 | 118.213°    |
| C118  | C119 | H1191 | 121.139°    |  | C314  | C119 | H1191 | 112.463°    |
| C318  | C119 | H1191 | 96.122°     |  | C319  | C119 | H1191 | 25.020°     |
| C201  | O2   | H21   | 111.886°    |  | O2    | C201 | C202  | 110.42(11)° |
| O2    | C201 | C208  | 106.28(14)° |  | C202  | C201 | C208  | 108.08(16)° |



|      |      |       |             |  |       |      |       |             |
|------|------|-------|-------------|--|-------|------|-------|-------------|
| O2   | C201 | C214  | 108.75(17)° |  | C202  | C201 | C214  | 115.4(3)°   |
| C208 | C201 | C214  | 107.4(4)°   |  | O2    | C201 | C408  | 95.9(5)°    |
| C202 | C201 | C408  | 114.9(5)°   |  | C208  | C201 | C408  | 10.7(6)°    |
| C214 | C201 | C408  | 109.7(4)°   |  | O2    | C201 | C414  | 112.6(2)°   |
| C202 | C201 | C414  | 106.3(2)°   |  | C208  | C201 | C414  | 113.1(4)°   |
| C214 | C201 | C414  | 9.2(4)°     |  | C408  | C201 | C414  | 116.6(4)°   |
| C201 | C202 | C203  | 123.34(15)° |  | C201  | C202 | C207  | 119.32(14)° |
| C203 | C202 | C207  | 117.31(17)° |  | C202  | C203 | C204  | 121.37(17)° |
| C202 | C203 | H2031 | 117.697°    |  | C204  | C203 | H2031 | 120.931°    |
| C203 | C204 | C205  | 120.56(18)° |  | C203  | C204 | H2041 | 119.846°    |
| C205 | C204 | H2041 | 119.566°    |  | C204  | C205 | C206  | 119.0(2)°   |
| C204 | C205 | H2051 | 119.369°    |  | C206  | C205 | H2051 | 121.622°    |
| C205 | C206 | C207  | 120.67(18)° |  | C205  | C206 | H2061 | 119.474°    |
| C207 | C206 | H2061 | 119.859°    |  | C202  | C207 | C206  | 121.08(17)° |
| C202 | C207 | H2071 | 118.896°    |  | C206  | C207 | H2071 | 120.003°    |
| C201 | C208 | C209  | 121.08(6)°  |  | C201  | C208 | C213  | 120.40(6)°  |
| C209 | C208 | C213  | 118.33(6)°  |  | C201  | C208 | C408  | 91.5(14)°   |
| C209 | C208 | C408  | 124.8(16)°  |  | C213  | C208 | C408  | 57.1(19)°   |
| C201 | C208 | C409  | 127.1(4)°   |  | C209  | C208 | C409  | 31.2(6)°    |
| C213 | C208 | C409  | 106.1(4)°   |  | C408  | C208 | C409  | 93.7(18)°   |
| C201 | C208 | C413  | 113.6(4)°   |  | C209  | C208 | C413  | 125.2(4)°   |
| C213 | C208 | C413  | 6.9(5)°     |  | C408  | C208 | C413  | 53.8(14)°   |
| C409 | C208 | C413  | 111.7(5)°   |  | C208  | C209 | C210  | 120.36(6)°  |
| C208 | C209 | C408  | 8.6(5)°     |  | C210  | C209 | C408  | 116.3(2)°   |
| C208 | C209 | C409  | 70.7(5)°    |  | C210  | C209 | C409  | 83.6(6)°    |
| C408 | C209 | C409  | 62.1(6)°    |  | C208  | C209 | C410  | 102.8(3)°   |
| C210 | C209 | C410  | 28.5(5)°    |  | C408  | C209 | C410  | 96.1(5)°    |
| C409 | C209 | C410  | 55.3(7)°    |  | C208  | C209 | H2091 | 121.133°    |
| C210 | C209 | H2091 | 118.435°    |  | C408  | C209 | H2091 | 124.106°    |
| C409 | C209 | H2091 | 113.936°    |  | C410  | C209 | H2091 | 128.814°    |
| C208 | C209 | H4091 | 102.203°    |  | C210  | C209 | H4091 | 106.799°    |
| C408 | C209 | H4091 | 97.041°     |  | C409  | C209 | H4091 | 56.843°     |
| C410 | C209 | H4091 | 90.862°     |  | H2091 | C209 | H4091 | 57.188°     |
| C209 | C210 | C211  | 120.28(6)°  |  | C209  | C210 | C409  | 29.7(5)°    |
| C211 | C210 | C409  | 104.8(3)°   |  | C209  | C210 | C410  | 96.6(6)°    |
| C211 | C210 | C410  | 59.9(8)°    |  | C409  | C210 | C410  | 67.0(8)°    |
| C209 | C210 | H2101 | 120.543°    |  | C211  | C210 | H2101 | 119.181°    |
| C409 | C210 | H2101 | 128.574°    |  | C410  | C210 | H2101 | 112.679°    |
| C209 | C210 | H4101 | 121.828°    |  | C211  | C210 | H4101 | 88.992°     |
| C409 | C210 | H4101 | 99.250°     |  | C410  | C210 | H4101 | 53.715°     |

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|-------|------|-------|------------|--|-------|------|-------|------------|
| H2101 | C210 | H4101 | 58.994°    |  | C210  | C211 | C212  | 119.68(6)° |
| C210  | C211 | C410  | 35.7(8)°   |  | C212  | C211 | C410  | 108.0(5)°  |
| C210  | C211 | C411  | 131.8(14)° |  | C212  | C211 | C411  | 49.8(13)°  |
| C410  | C211 | C411  | 97.4(17)°  |  | C210  | C211 | C412  | 122.9(3)°  |
| C212  | C211 | C412  | 3.3(5)°    |  | C410  | C211 | C412  | 110.1(8)°  |
| C411  | C211 | C412  | 47.4(15)°  |  | C210  | C211 | H2111 | 121.095°   |
| C212  | C211 | H2111 | 119.223°   |  | C410  | C211 | H2111 | 120.863°   |
| C411  | C211 | H2111 | 88.309°    |  | C412  | C211 | H2111 | 115.990°   |
| C210  | C211 | H4111 | 142.470°   |  | C212  | C211 | H4111 | 93.741°    |
| C410  | C211 | H4111 | 121.621°   |  | C411  | C211 | H4111 | 57.619°    |
| C412  | C211 | H4111 | 90.401°    |  | H2111 | C211 | H4111 | 30.749°    |
| C211  | C212 | C213  | 120.45(7)° |  | C211  | C212 | C411  | 21.3(7)°   |
| C213  | C212 | C411  | 129.5(5)°  |  | C211  | C212 | C412  | 162(2)°    |
| C213  | C212 | C412  | 76.8(17)°  |  | C411  | C212 | C412  | 144(4)°    |
| C211  | C212 | C413  | 128.6(3)°  |  | C213  | C212 | C413  | 8.2(4)°    |
| C411  | C212 | C413  | 136.5(8)°  |  | C412  | C212 | C413  | 68.6(18)°  |
| C211  | C212 | H2121 | 121.799°   |  | C213  | C212 | H2121 | 117.739°   |
| C411  | C212 | H2121 | 109.642°   |  | C412  | C212 | H2121 | 41.326°    |
| C413  | C212 | H2121 | 109.594°   |  | C211  | C212 | H4121 | 132.546°   |
| C213  | C212 | H4121 | 105.995°   |  | C411  | C212 | H4121 | 123.088°   |
| C412  | C212 | H4121 | 32.600°    |  | C413  | C212 | H4121 | 98.085°    |
| H2121 | C212 | H4121 | 14.235°    |  | C208  | C213 | C212  | 120.80(6)° |
| C208  | C213 | C408  | 11.3(8)°   |  | C212  | C213 | C408  | 124.3(3)°  |
| C208  | C213 | C412  | 134.1(5)°  |  | C212  | C213 | C412  | 13.5(6)°   |
| C408  | C213 | C412  | 136.8(7)°  |  | C208  | C213 | C413  | 127(2)°    |
| C212  | C213 | C413  | 112(2)°    |  | C408  | C213 | C413  | 121(3)°    |
| C412  | C213 | C413  | 99(2)°     |  | C208  | C213 | H2131 | 116.567°   |
| C212  | C213 | H2131 | 122.637°   |  | C408  | C213 | H2131 | 111.978°   |
| C412  | C213 | H2131 | 109.252°   |  | C413  | C213 | H2131 | 12.437°    |
| C208  | C213 | H4131 | 116.626°   |  | C212  | C213 | H4131 | 122.233°   |
| C408  | C213 | H4131 | 113.287°   |  | C412  | C213 | H4131 | 109.113°   |
| C413  | C213 | H4131 | 16.467°    |  | H2131 | C213 | H4131 | 6.170°     |
| C201  | C214 | C215  | 120.83(6)° |  | C201  | C214 | C219  | 120.73(6)° |
| C215  | C214 | C219  | 118.36(6)° |  | C201  | C214 | C414  | 95.1(14)°  |
| C215  | C214 | C414  | 126(3)°    |  | C219  | C214 | C414  | 50(3)°     |
| C201  | C214 | C415  | 135.4(3)°  |  | C215  | C214 | C415  | 14.7(3)°   |
| C219  | C214 | C415  | 103.7(3)°  |  | C414  | C214 | C415  | 118(2)°    |
| C201  | C214 | C419  | 110.7(3)°  |  | C215  | C214 | C419  | 126.1(3)°  |
| C219  | C214 | C419  | 20.1(3)°   |  | C414  | C214 | C419  | 30(3)°     |
| C415  | C214 | C419  | 112.6(4)°  |  | C214  | C215 | C216  | 120.52(7)° |

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| C214  | C215 | C414  | 7.5(6)°    |  | C216  | C215 | C414  | 116.5(2)°  |
| C214  | C215 | C415  | 57.6(13)°  |  | C216  | C215 | C415  | 63.0(13)°  |
| C414  | C215 | C415  | 54.3(12)°  |  | C214  | C215 | C416  | 102.5(2)°  |
| C216  | C215 | C416  | 18.56(19)° |  | C414  | C215 | C416  | 98.1(3)°   |
| C415  | C215 | C416  | 45.5(13)°  |  | C214  | C215 | H2151 | 118.874°   |
| C216  | C215 | H2151 | 120.602°   |  | C414  | C215 | H2151 | 122.428°   |
| C415  | C215 | H2151 | 176.121°   |  | C416  | C215 | H2151 | 138.231°   |
| C214  | C215 | H4151 | 123.149°   |  | C216  | C215 | H4151 | 110.751°   |
| C414  | C215 | H4151 | 129.535°   |  | C415  | C215 | H4151 | 153.817°   |
| C416  | C215 | H4151 | 128.963°   |  | H2151 | C215 | H4151 | 25.532°    |
| C215  | C216 | C217  | 120.27(7)° |  | C215  | C216 | C415  | 15.1(2)°   |
| C217  | C216 | C415  | 105.2(2)°  |  | C215  | C216 | C416  | 107.3(7)°  |
| C217  | C216 | C416  | 16.8(10)°  |  | C415  | C216 | C416  | 92.9(7)°   |
| C215  | C216 | H2161 | 120.488°   |  | C217  | C216 | H2161 | 119.223°   |
| C415  | C216 | H2161 | 135.542°   |  | C416  | C216 | H2161 | 130.542°   |
| C215  | C216 | H4161 | 160.429°   |  | C217  | C216 | H4161 | 78.134°    |
| C415  | C216 | H4161 | 173.626°   |  | C416  | C216 | H4161 | 89.280°    |
| H2161 | C216 | H4161 | 41.462°    |  | C216  | C217 | C218  | 119.59(7)° |
| C216  | C217 | C416  | 10.6(6)°   |  | C218  | C217 | C416  | 112.0(4)°  |
| C216  | C217 | C417  | 142.5(7)°  |  | C218  | C217 | C417  | 40.3(6)°   |
| C416  | C217 | C417  | 131.9(10)° |  | C216  | C217 | H2171 | 121.035°   |
| C218  | C217 | H2171 | 119.366°   |  | C416  | C217 | H2171 | 128.171°   |
| C417  | C217 | H2171 | 87.860°    |  | C216  | C217 | H4171 | 153.579°   |
| C218  | C217 | H4171 | 84.207°    |  | C416  | C217 | H4171 | 154.459°   |
| C417  | C217 | H4171 | 50.652°    |  | H2171 | C217 | H4171 | 37.342°    |
| C217  | C218 | C219  | 120.40(7)° |  | C217  | C218 | C417  | 26.4(3)°   |
| C219  | C218 | C417  | 137.1(4)°  |  | C217  | C218 | C418  | 133.2(8)°  |
| C219  | C218 | C418  | 78.6(5)°   |  | C417  | C218 | C418  | 109.9(9)°  |
| C217  | C218 | C419  | 129.1(2)°  |  | C219  | C218 | C419  | 20.9(3)°   |
| C417  | C218 | C419  | 134.6(6)°  |  | C418  | C218 | C419  | 58.3(4)°   |
| C217  | C218 | H2181 | 120.828°   |  | C219  | C218 | H2181 | 118.772°   |
| C417  | C218 | H2181 | 100.309°   |  | C418  | C218 | H2181 | 59.813°    |
| C419  | C218 | H2181 | 106.722°   |  | C214  | C219 | C218  | 120.70(7)° |
| C214  | C219 | C414  | 9.1(7)°    |  | C218  | C219 | C414  | 123.8(3)°  |
| C214  | C219 | C418  | 136.3(4)°  |  | C218  | C219 | C418  | 29.0(2)°   |
| C414  | C219 | C418  | 134.2(6)°  |  | C214  | C219 | C419  | 107.6(7)°  |
| C218  | C219 | C419  | 101.7(7)°  |  | C414  | C219 | C419  | 98.5(8)°   |
| C418  | C219 | C419  | 73.4(7)°   |  | C214  | C219 | H2191 | 118.391°   |
| C218  | C219 | H2191 | 120.885°   |  | C414  | C219 | H2191 | 114.410°   |
| C418  | C219 | H2191 | 99.432°    |  | C419  | C219 | H2191 | 58.038°    |

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|-------|------|-------|------------|--|-------|------|-------|------------|
| C101  | C308 | C108  | 82.2(18)°  |  | C101  | C308 | C109  | 109.3(3)°  |
| C108  | C308 | C109  | 37(3)°     |  | C101  | C308 | C113  | 132.7(4)°  |
| C108  | C308 | C113  | 132(4)°    |  | C109  | C308 | C113  | 117.1(6)°  |
| C101  | C308 | C309  | 120.70(6)° |  | C108  | C308 | C309  | 53(3)°     |
| C109  | C308 | C309  | 15.5(4)°   |  | C113  | C308 | C309  | 106.6(4)°  |
| C101  | C308 | C313  | 120.97(6)° |  | C108  | C308 | C313  | 137(4)°    |
| C109  | C308 | C313  | 128.3(4)°  |  | C113  | C308 | C313  | 11.8(4)°   |
| C309  | C308 | C313  | 118.32(6)° |  | C108  | C309 | C109  | 98.4(13)°  |
| C108  | C309 | C110  | 140.9(8)°  |  | C109  | C309 | C110  | 91.9(15)°  |
| C108  | C309 | C308  | 8.5(7)°    |  | C109  | C309 | C308  | 106.9(12)° |
| C110  | C309 | C308  | 138.7(5)°  |  | C108  | C309 | C310  | 125.2(3)°  |
| C109  | C309 | C310  | 111.8(15)° |  | C110  | C309 | C310  | 21.7(5)°   |
| C308  | C309 | C310  | 120.61(7)° |  | C108  | C309 | H3091 | 113.236°   |
| C109  | C309 | H3091 | 48.735°    |  | C110  | C309 | H3091 | 101.894°   |
| C308  | C309 | H3091 | 118.212°   |  | C310  | C309 | H3091 | 121.176°   |
| C109  | C310 | C110  | 56.9(9)°   |  | C109  | C310 | C111  | 142.5(9)°  |
| C110  | C310 | C111  | 145(2)°    |  | C109  | C310 | C309  | 14.5(5)°   |
| C110  | C310 | C309  | 70.0(11)°  |  | C111  | C310 | C309  | 135.3(6)°  |
| C109  | C310 | C311  | 129.5(3)°  |  | C110  | C310 | C311  | 157(2)°    |
| C111  | C310 | C311  | 15.7(6)°   |  | C309  | C310 | C311  | 120.37(7)° |
| C109  | C310 | H3101 | 108.974°   |  | C110  | C310 | H3101 | 54.065°    |
| C111  | C310 | H3101 | 105.192°   |  | C309  | C310 | H3101 | 119.257°   |
| C311  | C310 | H3101 | 120.369°   |  | C111  | C311 | C112  | 137.4(14)° |
| C111  | C311 | C310  | 27.7(10)°  |  | C112  | C311 | C310  | 111.4(5)°  |
| C111  | C311 | C312  | 145.0(10)° |  | C112  | C311 | C312  | 8.4(5)°    |
| C310  | C311 | C312  | 119.66(7)° |  | C111  | C311 | H1111 | 57.527°    |
| C112  | C311 | H1111 | 163.898°   |  | C310  | C311 | H1111 | 84.316°    |
| C312  | C311 | H1111 | 155.449°   |  | C111  | C311 | H3111 | 92.977°    |
| C112  | C311 | H3111 | 129.136°   |  | C310  | C311 | H3111 | 119.414°   |
| C312  | C311 | H3111 | 120.922°   |  | H1111 | C311 | H3111 | 35.450°    |
| C112  | C312 | C113  | 91.5(11)°  |  | C112  | C312 | C311  | 16.4(11)°  |
| C113  | C312 | C311  | 107.6(4)°  |  | C112  | C312 | C313  | 104.3(11)° |
| C113  | C312 | C313  | 12.9(4)°   |  | C311  | C312 | C313  | 120.32(7)° |
| C112  | C312 | H1121 | 97.336°    |  | C113  | C312 | H1121 | 166.427°   |
| C311  | C312 | H1121 | 82.025°    |  | C313  | C312 | H1121 | 156.416°   |
| C112  | C312 | H3121 | 135.249°   |  | C113  | C312 | H3121 | 133.036°   |
| C311  | C312 | H3121 | 119.370°   |  | C313  | C312 | H3121 | 120.310°   |
| H1121 | C312 | H3121 | 38.142°    |  | C108  | C313 | C112  | 101.0(5)°  |
| C108  | C313 | C113  | 52.3(15)°  |  | C112  | C313 | C113  | 50.0(16)°  |
| C108  | C313 | C308  | 5.7(7)°    |  | C112  | C313 | C308  | 103.5(3)°  |

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|------|------|-------|------------|--|-------|------|-------|------------|
| C113 | C313 | C308  | 53.9(16)°  |  | C108  | C313 | C312  | 117.8(3)°  |
| C112 | C313 | C312  | 17.0(3)°   |  | C113  | C313 | C312  | 67.0(17)°  |
| C308 | C313 | C312  | 120.50(7)° |  | C108  | C313 | H1131 | 131.724°   |
| C112 | C313 | H1131 | 126.035°   |  | C113  | C313 | H1131 | 160.731°   |
| C308 | C313 | H1131 | 127.963°   |  | C312  | C313 | H1131 | 109.816°   |
| C108 | C313 | H3131 | 123.195°   |  | C112  | C313 | H3131 | 135.601°   |
| C113 | C313 | H3131 | 172.506°   |  | C308  | C313 | H3131 | 120.905°   |
| C312 | C313 | H3131 | 118.587°   |  | H1131 | C313 | H3131 | 16.099°    |
| C101 | C314 | C114  | 78.6(16)°  |  | C101  | C314 | C115  | 106.8(3)°  |
| C114 | C314 | C115  | 30(2)°     |  | C101  | C314 | C119  | 135.7(4)°  |
| C114 | C314 | C119  | 144(3)°    |  | C115  | C314 | C119  | 117.4(5)°  |
| C101 | C314 | C315  | 120.83(6)° |  | C114  | C314 | C315  | 42.4(17)°  |
| C115 | C314 | C315  | 15.2(4)°   |  | C119  | C314 | C315  | 102.9(4)°  |
| C101 | C314 | C319  | 120.80(6)° |  | C114  | C314 | C319  | 160(2)°    |
| C115 | C314 | C319  | 132.1(3)°  |  | C119  | C314 | C319  | 16.5(4)°   |
| C315 | C314 | C319  | 118.36(6)° |  | C114  | C315 | C115  | 103.5(14)° |
| C114 | C315 | C116  | 153.0(8)°  |  | C115  | C315 | C116  | 96.1(14)°  |
| C114 | C315 | C314  | 8.0(3)°    |  | C115  | C315 | C314  | 110.5(13)° |
| C116 | C315 | C314  | 145.3(5)°  |  | C114  | C315 | C316  | 128.6(3)°  |
| C115 | C315 | C316  | 122.9(15)° |  | C116  | C315 | C316  | 27.1(4)°   |
| C314 | C315 | C316  | 120.59(7)° |  | C114  | C315 | H3151 | 110.953°   |
| C115 | C315 | H3151 | 24.655°    |  | C116  | C315 | H3151 | 94.560°    |
| C314 | C315 | H3151 | 118.979°   |  | C316  | C315 | H3151 | 120.427°   |
| C115 | C316 | C116  | 52.1(6)°   |  | C115  | C316 | C117  | 149.9(7)°  |
| C116 | C316 | C117  | 150.4(17)° |  | C115  | C316 | C315  | 13.0(4)°   |
| C116 | C316 | C315  | 64.9(8)°   |  | C117  | C316 | C315  | 139.5(5)°  |
| C115 | C316 | C317  | 131.8(3)°  |  | C116  | C316 | C317  | 164.8(17)° |
| C117 | C316 | C317  | 19.6(6)°   |  | C315  | C316 | C317  | 120.34(7)° |
| C115 | C316 | H3161 | 108.807°   |  | C116  | C316 | H3161 | 57.954°    |
| C117 | C316 | H3161 | 99.890°    |  | C315  | C316 | H3161 | 120.508°   |
| C317 | C316 | H3161 | 119.142°   |  | C117  | C317 | C118  | 127.7(12)° |
| C117 | C317 | C316  | 22.8(7)°   |  | C118  | C317 | C316  | 105.1(5)°  |
| C117 | C317 | C318  | 141.7(7)°  |  | C118  | C317 | C318  | 15.3(6)°   |
| C316 | C317 | C318  | 119.65(7)° |  | C117  | C317 | H1171 | 53.275°    |
| C118 | C317 | H1171 | 178.103°   |  | C316  | C317 | H1171 | 75.773°    |
| C318 | C317 | H1171 | 164.242°   |  | C117  | C317 | H3171 | 97.794°    |
| C118 | C317 | H3171 | 134.426°   |  | C316  | C317 | H3171 | 120.098°   |
| C318 | C317 | H3171 | 120.248°   |  | H1171 | C317 | H3171 | 44.527°    |
| C118 | C318 | C119  | 82.8(8)°   |  | C118  | C318 | C317  | 21.4(8)°   |
| C119 | C318 | C317  | 103.6(3)°  |  | C118  | C318 | C319  | 100.1(8)°  |

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| C119  | C318 | C319  | 17.6(3)°   |  | C317  | C318 | C319  | 120.36(7)° |
| C118  | C318 | H1181 | 89.156°    |  | C119  | C318 | H1181 | 161.981°   |
| C317  | C318 | H1181 | 70.806°    |  | C319  | C318 | H1181 | 164.429°   |
| C118  | C318 | H3181 | 139.479°   |  | C119  | C318 | H3181 | 136.037°   |
| C317  | C318 | H3181 | 119.942°   |  | C319  | C318 | H3181 | 119.696°   |
| H1181 | C318 | H3181 | 50.353°    |  | C114  | C319 | C118  | 96.0(3)°   |
| C114  | C319 | C119  | 48.2(11)°  |  | C118  | C319 | C119  | 51.5(11)°  |
| C114  | C319 | C314  | 3.0(3)°    |  | C118  | C319 | C314  | 99.0(3)°   |
| C119  | C319 | C314  | 51.2(12)°  |  | C114  | C319 | C318  | 117.7(2)°  |
| C118  | C319 | C318  | 21.8(3)°   |  | C119  | C319 | C318  | 72.7(12)°  |
| C314  | C319 | C318  | 120.60(7)° |  | C114  | C319 | H1191 | 122.848°   |
| C118  | C319 | H1191 | 130.300°   |  | C119  | C319 | H1191 | 137.151°   |
| C314  | C319 | H1191 | 120.665°   |  | C318  | C319 | H1191 | 112.954°   |
| C114  | C319 | H3191 | 122.231°   |  | C118  | C319 | H3191 | 141.628°   |
| C119  | C319 | H3191 | 158.333°   |  | C314  | C319 | H3191 | 119.301°   |
| C318  | C319 | H3191 | 120.101°   |  | H1191 | C319 | H3191 | 24.485°    |
| C201  | C408 | C208  | 77.8(13)°  |  | C201  | C408 | C209  | 108.3(4)°  |
| C208  | C408 | C209  | 46.6(12)°  |  | C201  | C408 | C213  | 127.6(5)°  |
| C208  | C408 | C213  | 112(3)°    |  | C209  | C408 | C213  | 114.5(7)°  |
| C201  | C408 | C409  | 120.90(7)° |  | C208  | C408 | C409  | 74.4(14)°  |
| C209  | C408 | C409  | 27.9(5)°   |  | C213  | C408 | C409  | 111.0(4)°  |
| C201  | C408 | C413  | 120.72(7)° |  | C208  | C408 | C413  | 116.3(20)° |
| C209  | C408 | C413  | 122.7(5)°  |  | C213  | C408 | C413  | 8.3(6)°    |
| C409  | C408 | C413  | 118.30(6)° |  | C208  | C409 | C209  | 78.2(8)°   |
| C208  | C409 | C210  | 116.0(9)°  |  | C209  | C409 | C210  | 66.7(8)°   |
| C208  | C409 | C408  | 11.9(7)°   |  | C209  | C409 | C408  | 90.0(8)°   |
| C210  | C409 | C408  | 121.2(7)°  |  | C208  | C409 | C410  | 122.8(4)°  |
| C209  | C409 | C410  | 98.7(10)°  |  | C210  | C409 | C410  | 32.1(6)°   |
| C408  | C409 | C410  | 120.49(7)° |  | C208  | C409 | H4091 | 116.794°   |
| C209  | C409 | H4091 | 81.518°    |  | C210  | C409 | H4091 | 108.892°   |
| C408  | C409 | H4091 | 120.415°   |  | C410  | C409 | H4091 | 119.094°   |
| C209  | C410 | C210  | 54.9(5)°   |  | C209  | C410 | C211  | 111.6(10)° |
| C210  | C410 | C211  | 84.4(13)°  |  | C209  | C410 | C409  | 26.0(6)°   |
| C210  | C410 | C409  | 80.8(8)°   |  | C211  | C410 | C409  | 122.8(6)°  |
| C209  | C410 | C411  | 120.2(6)°  |  | C210  | C410 | C411  | 106.3(12)° |
| C211  | C410 | C411  | 22.6(6)°   |  | C409  | C410 | C411  | 120.26(7)° |
| C209  | C410 | H4101 | 112.886°   |  | C210  | C410 | H4101 | 82.317°    |
| C211  | C410 | H4101 | 112.471°   |  | C409  | C410 | H4101 | 119.650°   |
| C411  | C410 | H4101 | 120.086°   |  | C211  | C411 | C212  | 108.9(19)° |
| C211  | C411 | C410  | 60.0(14)°  |  | C212  | C411 | C410  | 114.0(4)°  |

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| C211  | C411 | C412  | 116(2)°    |  | C212  | C411 | C412  | 7.9(10)°   |
| C410  | C411 | C412  | 119.60(7)° |  | C211  | C411 | H2111 | 62.223°    |
| C212  | C411 | H2111 | 135.035°   |  | C410  | C411 | H2111 | 99.226°    |
| C412  | C411 | H2111 | 134.468°   |  | C211  | C411 | H4111 | 93.803°    |
| C212  | C411 | H4111 | 125.510°   |  | C410  | C411 | H4111 | 120.195°   |
| C412  | C411 | H4111 | 120.198°   |  | H2111 | C411 | H4111 | 31.641°    |
| C211  | C412 | C212  | 14.4(18)°  |  | C211  | C412 | C213  | 103.8(7)°  |
| C212  | C412 | C213  | 89.7(17)°  |  | C211  | C412 | C411  | 16.4(6)°   |
| C212  | C412 | C411  | 28(3)°     |  | C213  | C412 | C411  | 111.6(4)°  |
| C211  | C412 | C413  | 113.0(5)°  |  | C212  | C412 | C413  | 99.0(18)°  |
| C213  | C412 | C413  | 9.3(5)°    |  | C411  | C412 | C413  | 120.34(7)° |
| C211  | C412 | H2121 | 108.239°   |  | C212  | C412 | H2121 | 121.821°   |
| C213  | C412 | H2121 | 147.549°   |  | C411  | C412 | H2121 | 100.703°   |
| C413  | C412 | H2121 | 138.477°   |  | C211  | C412 | H4121 | 125.040°   |
| C212  | C412 | H4121 | 136.723°   |  | C213  | C412 | H4121 | 127.921°   |
| C411  | C412 | H4121 | 120.296°   |  | C413  | C412 | H4121 | 119.357°   |
| H2121 | C412 | H4121 | 20.764°    |  | C208  | C413 | C212  | 105.8(6)°  |
| C208  | C413 | C213  | 46(2)°     |  | C212  | C413 | C213  | 60(2)°     |
| C208  | C413 | C408  | 9.9(7)°    |  | C212  | C413 | C408  | 108.7(4)°  |
| C213  | C413 | C408  | 51(3)°     |  | C208  | C413 | C412  | 118.1(4)°  |
| C212  | C413 | C412  | 12.4(5)°   |  | C213  | C413 | C412  | 72(2)°     |
| C408  | C413 | C412  | 120.59(7)° |  | C208  | C413 | H2131 | 120.092°   |
| C212  | C413 | H2131 | 133.930°   |  | C213  | C413 | H2131 | 163.696°   |
| C408  | C413 | H2131 | 117.230°   |  | C412  | C413 | H2131 | 121.719°   |
| C208  | C413 | H4131 | 120.488°   |  | C212  | C413 | H4131 | 132.173°   |
| C213  | C413 | H4131 | 159.571°   |  | C408  | C413 | H4131 | 118.995°   |
| C412  | C413 | H4131 | 120.418°   |  | H2131 | C413 | H4131 | 7.215°     |
| C201  | C414 | C214  | 75.7(13)°  |  | C201  | C414 | C215  | 108.8(3)°  |
| C214  | C414 | C215  | 46(2)°     |  | C201  | C414 | C219  | 128.6(4)°  |
| C214  | C414 | C219  | 121(3)°    |  | C215  | C414 | C219  | 116.9(5)°  |
| C201  | C414 | C415  | 120.65(7)° |  | C214  | C414 | C415  | 52.5(18)°  |
| C215  | C414 | C415  | 12.7(3)°   |  | C219  | C414 | C415  | 104.3(3)°  |
| C201  | C414 | C419  | 120.90(7)° |  | C214  | C414 | C419  | 145(3)°    |
| C215  | C414 | C419  | 130.3(3)°  |  | C219  | C414 | C419  | 24.2(3)°   |
| C415  | C414 | C419  | 118.27(6)° |  | C214  | C415 | C215  | 107.8(15)° |
| C214  | C415 | C216  | 150.3(4)°  |  | C215  | C415 | C216  | 101.9(14)° |
| C214  | C415 | C414  | 9.3(6)°    |  | C215  | C415 | C414  | 113.1(14)° |
| C216  | C415 | C414  | 143.6(2)°  |  | C214  | C415 | C416  | 127.7(2)°  |
| C215  | C415 | C416  | 123.6(15)° |  | C216  | C415 | C416  | 22.9(2)°   |
| C414  | C415 | C416  | 120.69(7)° |  | C214  | C415 | H4151 | 109.829°   |

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| C215  | C415 | H4151 | 15.900°     |  | C216  | C415 | H4151 | 99.318°     |
| C414  | C415 | H4151 | 117.126°    |  | C416  | C415 | H4151 | 122.177°    |
| C215  | C416 | C216  | 54.1(6)°    |  | C215  | C416 | C217  | 144.7(6)°   |
| C216  | C416 | C217  | 152.5(15)°  |  | C215  | C416 | C415  | 10.9(3)°    |
| C216  | C416 | C415  | 64.3(7)°    |  | C217  | C416 | C415  | 133.9(5)°   |
| C215  | C416 | C417  | 130.9(2)°   |  | C216  | C416 | C417  | 173.3(13)°  |
| C217  | C416 | C417  | 20.8(4)°    |  | C415  | C416 | C417  | 120.46(7)°  |
| C215  | C416 | H4161 | 108.238°    |  | C216  | C416 | H4161 | 54.781°     |
| C217  | C416 | H4161 | 105.044°    |  | C415  | C416 | H4161 | 118.781°    |
| C417  | C416 | H4161 | 120.758°    |  | C217  | C417 | C218  | 113.3(8)°   |
| C217  | C417 | C416  | 27.4(6)°    |  | C218  | C417 | C416  | 103.5(3)°   |
| C217  | C417 | C418  | 138.7(6)°   |  | C218  | C417 | C418  | 29.1(4)°    |
| C416  | C417 | C418  | 119.68(7)°  |  | C217  | C417 | H2171 | 56.494°     |
| C218  | C417 | H2171 | 146.447°    |  | C416  | C417 | H2171 | 79.348°     |
| C418  | C417 | H2171 | 159.561°    |  | C217  | C417 | H4171 | 96.747°     |
| C218  | C417 | H4171 | 130.688°    |  | C416  | C417 | H4171 | 118.953°    |
| C418  | C417 | H4171 | 121.368°    |  | H2171 | C417 | H4171 | 40.387°     |
| C218  | C418 | C219  | 72.4(5)°    |  | C218  | C418 | C417  | 41.0(6)°    |
| C219  | C418 | C417  | 102.9(2)°   |  | C218  | C418 | C419  | 95.9(5)°    |
| C219  | C418 | C419  | 24.0(2)°    |  | C417  | C418 | C419  | 120.23(7)°  |
| C218  | C418 | H2181 | 73.524°     |  | C219  | C418 | H2181 | 122.760°    |
| C417  | C418 | H2181 | 77.986°     |  | C419  | C418 | H2181 | 138.134°    |
| C218  | C418 | H4181 | 131.582°    |  | C219  | C418 | H4181 | 135.473°    |
| C417  | C418 | H4181 | 118.895°    |  | C419  | C418 | H4181 | 120.842°    |
| H2181 | C418 | H4181 | 58.110°     |  | C214  | C419 | C218  | 94.6(3)°    |
| C214  | C419 | C219  | 52.3(6)°    |  | C218  | C419 | C219  | 57.5(6)°    |
| C214  | C419 | C414  | 5.0(6)°     |  | C218  | C419 | C414  | 97.9(2)°    |
| C219  | C419 | C414  | 57.3(6)°    |  | C214  | C419 | C418  | 117.9(2)°   |
| C218  | C419 | C418  | 25.8(2)°    |  | C219  | C419 | C418  | 82.6(6)°    |
| C414  | C419 | C418  | 120.41(7)°  |  | C214  | C419 | H2191 | 103.749°    |
| C218  | C419 | H2191 | 110.410°    |  | C219  | C419 | H2191 | 83.505°     |
| C414  | C419 | H2191 | 105.806°    |  | C418  | C419 | H2191 | 111.561°    |
| C214  | C419 | H4191 | 123.091°    |  | C218  | C419 | H4191 | 139.028°    |
| C219  | C419 | H4191 | 132.493°    |  | C414  | C419 | H4191 | 120.820°    |
| C418  | C419 | H4191 | 118.768°    |  | H2191 | C419 | H4191 | 49.794°     |
| C502  | N501 | C506  | 103.62(19)° |  | C502  | N501 | C510  | 108.2(5)°   |
| C506  | N501 | C510  | 110.0(8)°   |  | C502  | N501 | C514  | 111.00(12)° |
| C506  | N501 | C514  | 112.7(7)°   |  | C510  | N501 | C514  | 111.0(2)°   |
| C502  | N501 | C606  | 108.2(2)°   |  | C506  | N501 | C606  | 4.7(4)°     |
| C510  | N501 | C606  | 108.7(10)°  |  | C514  | N501 | C606  | 109.6(8)°   |



|       |      |       |           |  |       |      |       |             |
|-------|------|-------|-----------|--|-------|------|-------|-------------|
| C502  | N501 | C610  | 113.7(4)° |  | C506  | N501 | C610  | 114.8(7)°   |
| C510  | N501 | C610  | 9.6(2)°   |  | C514  | N501 | C610  | 101.39(19)° |
| C606  | N501 | C610  | 112.8(9)° |  | N501  | C502 | C503  | 115.97(8)°  |
| N501  | C502 | H5022 | 106.490°  |  | C503  | C502 | H5022 | 109.919°    |
| N501  | C502 | H5021 | 106.546°  |  | C503  | C502 | H5021 | 109.071°    |
| H5022 | C502 | H5021 | 108.582°  |  | C502  | C503 | C504  | 109.54(7)°  |
| C502  | C503 | H5031 | 110.529°  |  | C504  | C503 | H5031 | 110.833°    |
| C502  | C503 | H5032 | 109.770°  |  | C504  | C503 | H5032 | 107.578°    |
| H5031 | C503 | H5032 | 108.535°  |  | C503  | C504 | C505  | 112.59(9)°  |
| C503  | C504 | H5042 | 109.591°  |  | C505  | C504 | H5042 | 110.118°    |
| C503  | C504 | H5041 | 110.355°  |  | C505  | C504 | H5041 | 110.146°    |
| H5042 | C504 | H5041 | 103.679°  |  | C504  | C505 | H5053 | 109.781°    |
| C504  | C505 | H5052 | 110.180°  |  | H5053 | C505 | H5052 | 107.637°    |
| C504  | C505 | H5051 | 110.674°  |  | H5053 | C505 | H5051 | 110.044°    |
| H5052 | C505 | H5051 | 108.464°  |  | N501  | C506 | C507  | 116.10(10)° |
| N501  | C506 | C606  | 77(6)°    |  | C507  | C506 | C606  | 42(8)°      |
| N501  | C506 | C607  | 108.9(5)° |  | C507  | C506 | C607  | 11.4(6)°    |
| C606  | C506 | C607  | 33(6)°    |  | N501  | C506 | H5061 | 105.324°    |
| C507  | C506 | H5061 | 110.463°  |  | C606  | C506 | H5061 | 138.501°    |
| C607  | C506 | H5061 | 121.796°  |  | N501  | C506 | H5062 | 106.100°    |
| C507  | C506 | H5062 | 109.201°  |  | C606  | C506 | H5062 | 109.580°    |
| C607  | C506 | H5062 | 104.409°  |  | H5061 | C506 | H5062 | 109.409°    |
| N501  | C506 | H6062 | 107.745°  |  | C507  | C506 | H6062 | 95.296°     |
| C606  | C506 | H6062 | 122.210°  |  | C607  | C506 | H6062 | 106.363°    |
| H5061 | C506 | H6062 | 16.650°   |  | N501  | C506 | H6061 | 107.371°    |
| C507  | C506 | H6061 | 108.885°  |  | C606  | C506 | H6061 | 110.296°    |
| C607  | C506 | H6061 | 104.353°  |  | H5061 | C506 | H6061 | 108.414°    |
| H5062 | C506 | H6062 | 122.771°  |  | H5062 | C506 | H6061 | 1.380°      |
| H6062 | C506 | H6061 | 121.610°  |  | C506  | C507 | C508  | 109.22(10)° |
| C506  | C507 | C606  | 3.4(7)°   |  | C508  | C507 | C606  | 112.5(4)°   |
| C506  | C507 | C607  | 100(2)°   |  | C508  | C507 | C607  | 126(3)°     |
| C606  | C507 | C607  | 97(3)°    |  | C506  | C507 | C608  | 118.9(6)°   |
| C508  | C507 | C608  | 18.3(4)°  |  | C606  | C507 | C608  | 121.8(8)°   |
| C607  | C507 | C608  | 108(3)°   |  | C506  | C507 | H5071 | 110.329°    |
| C508  | C507 | H5071 | 108.892°  |  | C606  | C507 | H5071 | 109.453°    |
| C607  | C507 | H5071 | 102.112°  |  | C608  | C507 | H5071 | 115.402°    |
| C506  | C507 | H5072 | 109.541°  |  | C508  | C507 | H5072 | 110.075°    |
| C606  | C507 | H5072 | 107.122°  |  | C607  | C507 | H5072 | 16.006°     |
| C608  | C507 | H5072 | 91.833°   |  | C506  | C507 | H6071 | 118.279°    |
| C508  | C507 | H6071 | 121.319°  |  | C606  | C507 | H6071 | 116.126°    |

|       |      |       |            |  |       |      |       |             |
|-------|------|-------|------------|--|-------|------|-------|-------------|
| C607  | C507 | H6071 | 78.598°    |  | C608  | C507 | H6071 | 120.068°    |
| H5071 | C507 | H5072 | 108.771°   |  | H5071 | C507 | H6071 | 23.815°     |
| H5072 | C507 | H6071 | 85.070°    |  | C507  | C508 | C509  | 113.12(10)° |
| C507  | C508 | C607  | 8.7(6)°    |  | C509  | C508 | C607  | 108.1(4)°   |
| C507  | C508 | C608  | 63.8(15)°  |  | C509  | C508 | C608  | 68.4(16)°   |
| C607  | C508 | C608  | 55.2(13)°  |  | C507  | C508 | H5082 | 110.216°    |
| C509  | C508 | H5082 | 104.355°   |  | C607  | C508 | H5082 | 118.830°    |
| C608  | C508 | H5082 | 165.333°   |  | C507  | C508 | H5081 | 109.451°    |
| C509  | C508 | H5081 | 111.171°   |  | C607  | C508 | H5081 | 106.042°    |
| C608  | C508 | H5081 | 86.314°    |  | H5082 | C508 | H5081 | 108.333°    |
| C507  | C508 | H6082 | 115.266°   |  | C509  | C508 | H6082 | 98.120°     |
| C607  | C508 | H6082 | 123.753°   |  | C608  | C508 | H6082 | 162.699°    |
| H5082 | C508 | H6082 | 6.590°     |  | C507  | C508 | H6081 | 92.780°     |
| C509  | C508 | H6081 | 94.776°    |  | C607  | C508 | H6081 | 86.128°     |
| C608  | C508 | H6081 | 54.159°    |  | H5082 | C508 | H6081 | 140.462°    |
| H5081 | C508 | H6082 | 109.284°   |  | H5081 | C508 | H6081 | 32.173°     |
| H6082 | C508 | H6081 | 140.840°   |  | C508  | C509 | C608  | 18.7(4)°    |
| C508  | C509 | C609  | 106.1(15)° |  | C608  | C509 | C609  | 87.9(16)°   |
| C508  | C509 | H5093 | 110.414°   |  | C608  | C509 | H5093 | 122.983°    |
| C609  | C509 | H5093 | 132.216°   |  | C508  | C509 | H5092 | 109.787°    |
| C608  | C509 | H5092 | 113.850°   |  | C609  | C509 | H5092 | 87.282°     |
| H5093 | C509 | H5092 | 107.543°   |  | C508  | C509 | H5091 | 111.039°    |
| C608  | C509 | H5091 | 93.030°    |  | C609  | C509 | H5091 | 28.036°     |
| H5093 | C509 | H5091 | 107.769°   |  | H5092 | C509 | H5091 | 110.207°    |
| C508  | C509 | H6091 | 134.365°   |  | C608  | C509 | H6091 | 131.640°    |
| C609  | C509 | H6091 | 88.173°    |  | H5093 | C509 | H6091 | 44.119°     |
| H5092 | C509 | H6091 | 114.070°   |  | C508  | C509 | H6092 | 112.911°    |
| C608  | C509 | H6092 | 108.369°   |  | C609  | C509 | H6092 | 62.417°     |
| H5093 | C509 | H6092 | 124.849°   |  | H5092 | C509 | H6092 | 24.939°     |
| H5091 | C509 | H6091 | 64.578°    |  | H5091 | C509 | H6092 | 86.727°     |
| H6091 | C509 | H6092 | 112.107°   |  | N501  | C510 | C511  | 116.30(10)° |
| N501  | C510 | C610  | 58.1(17)°  |  | C511  | C510 | C610  | 174(3)°     |
| N501  | C510 | C611  | 126.4(4)°  |  | C511  | C510 | C611  | 10.3(4)°    |
| C610  | C510 | C611  | 175(3)°    |  | N501  | C510 | H5101 | 106.107°    |
| C511  | C510 | H5101 | 109.172°   |  | C610  | C510 | H5101 | 71.036°     |
| C611  | C510 | H5101 | 105.572°   |  | N501  | C510 | H5102 | 105.772°    |
| C511  | C510 | H5102 | 107.546°   |  | C610  | C510 | H5102 | 77.962°     |
| C611  | C510 | H5102 | 100.853°   |  | H5101 | C510 | H5102 | 111.994°    |
| N501  | C510 | H6102 | 91.364°    |  | C511  | C510 | H6102 | 126.079°    |
| C610  | C510 | H6102 | 53.498°    |  | C611  | C510 | H6102 | 123.314°    |

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|-------|------|-------|------------|--|-------|------|-------|-------------|
| H5101 | C510 | H6102 | 17.942°    |  | N501  | C510 | H6101 | 91.564°     |
| C511  | C510 | H6101 | 130.222°   |  | C610  | C510 | H6101 | 55.276°     |
| C611  | C510 | H6101 | 123.405°   |  | H5101 | C510 | H6101 | 100.277°    |
| H5102 | C510 | H6102 | 107.616°   |  | H5102 | C510 | H6101 | 22.695°     |
| H6102 | C510 | H6101 | 90.751°    |  | C510  | C511 | C512  | 109.06(10)° |
| C510  | C511 | C611  | 29.3(13)°  |  | C512  | C511 | C611  | 79.8(13)°   |
| C510  | C511 | C612  | 86.0(2)°   |  | C512  | C511 | C612  | 24.0(2)°    |
| C611  | C511 | C612  | 57.4(13)°  |  | C510  | C511 | H5112 | 110.094°    |
| C512  | C511 | H5112 | 109.710°   |  | C611  | C511 | H5112 | 124.431°    |
| C612  | C511 | H5112 | 113.459°   |  | C510  | C511 | H5111 | 109.424°    |
| C512  | C511 | H5111 | 110.993°   |  | C611  | C511 | H5111 | 119.826°    |
| C612  | C511 | H5111 | 127.452°   |  | H5112 | C511 | H5111 | 107.546°    |
| C510  | C511 | H6112 | 95.107°    |  | C512  | C511 | H6112 | 113.531°    |
| C611  | C511 | H6112 | 109.620°   |  | C612  | C511 | H6112 | 110.433°    |
| H5112 | C511 | H6112 | 15.339°    |  | C510  | C511 | H6111 | 86.303°     |
| C512  | C511 | H6111 | 93.704°    |  | C611  | C511 | H6111 | 85.675°     |
| C612  | C511 | H6111 | 99.216°    |  | H5112 | C511 | H6111 | 143.856°    |
| H5111 | C511 | H6112 | 117.333°   |  | H5111 | C511 | H6111 | 36.662°     |
| H6112 | C511 | H6111 | 150.348°   |  | C511  | C512 | C513  | 113.42(10)° |
| C511  | C512 | C611  | 16.0(2)°   |  | C513  | C512 | C611  | 129.4(3)°   |
| C511  | C512 | C612  | 86.8(7)°   |  | C513  | C512 | C612  | 154.7(9)°   |
| C611  | C512 | C612  | 71.7(6)°   |  | C511  | C512 | C613  | 141.3(4)°   |
| C513  | C512 | C613  | 29.6(4)°   |  | C611  | C512 | C613  | 157.0(5)°   |
| C612  | C512 | C613  | 126.2(11)° |  | C511  | C512 | H5122 | 119.122°    |
| C513  | C512 | H5122 | 106.552°   |  | C611  | C512 | H5122 | 109.686°    |
| C612  | C512 | H5122 | 48.435°    |  | C613  | C512 | H5122 | 80.738°     |
| C511  | C512 | H5121 | 104.224°   |  | C513  | C512 | H5121 | 107.094°    |
| C611  | C512 | H5121 | 95.903°    |  | C612  | C512 | H5121 | 80.753°     |
| C613  | C512 | H5121 | 101.008°   |  | H5122 | C512 | H5121 | 105.550°    |
| C512  | C513 | C613  | 37.8(6)°   |  | C512  | C513 | H5131 | 110.288°    |
| C613  | C513 | H5131 | 73.382°    |  | C512  | C513 | H5132 | 110.236°    |
| C613  | C513 | H5132 | 116.623°   |  | H5131 | C513 | H5132 | 109.385°    |
| C512  | C513 | H5133 | 107.637°   |  | C613  | C513 | H5133 | 129.915°    |
| H5131 | C513 | H5133 | 110.250°   |  | H5132 | C513 | H5133 | 109.019°    |
| C512  | C513 | H6132 | 77.400°    |  | C613  | C513 | H6132 | 71.918°     |
| H5131 | C513 | H6132 | 94.208°    |  | H5132 | C513 | H6132 | 44.834°     |
| H5133 | C513 | H6132 | 150.474°   |  | C512  | C513 | H6131 | 68.682°     |
| C613  | C513 | H6131 | 74.440°    |  | H5131 | C513 | H6131 | 87.414°     |
| H5132 | C513 | H6131 | 161.659°   |  | H5133 | C513 | H6131 | 56.384°     |
| H6132 | C513 | H6131 | 144.270°   |  | N501  | C514 | C515  | 116.03(6)°  |

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|-------|------|-------|-------------|--|-------|------|-------|-------------|
| N501  | C514 | H5142 | 106.369°    |  | C515  | C514 | H5142 | 110.448°    |
| N501  | C514 | H5141 | 106.282°    |  | C515  | C514 | H5141 | 108.897°    |
| H5142 | C514 | H5141 | 108.531°    |  | C514  | C515 | C516  | 108.11(9)°  |
| C514  | C515 | C617  | 110.21(10)° |  | C516  | C515 | C617  | 18.3(2)°    |
| C514  | C515 | H5151 | 110.734°    |  | C516  | C515 | H5151 | 109.575°    |
| C617  | C515 | H5151 | 122.935°    |  | C514  | C515 | H5152 | 107.362°    |
| C516  | C515 | H5152 | 112.255°    |  | C617  | C515 | H5152 | 94.778°     |
| H5151 | C515 | H5152 | 108.791°    |  | C514  | C515 | H5153 | 110.632°    |
| C516  | C515 | H5153 | 125.964°    |  | C617  | C515 | H5153 | 110.312°    |
| H5151 | C515 | H5153 | 90.160°     |  | H5152 | C515 | H5153 | 19.415°     |
| C514  | C515 | H5154 | 108.918°    |  | C516  | C515 | H5154 | 92.966°     |
| C617  | C515 | H5154 | 108.630°    |  | H5151 | C515 | H5154 | 19.152°     |
| H5152 | C515 | H5154 | 125.717°    |  | H5153 | C515 | H5154 | 108.081°    |
| C515  | C516 | C517  | 113.44(10)° |  | C515  | C516 | C617  | 97.6(7)°    |
| C517  | C516 | C617  | 65.8(5)°    |  | C515  | C516 | H5161 | 107.375°    |
| C517  | C516 | H5161 | 111.641°    |  | C617  | C516 | H5161 | 152.842°    |
| C515  | C516 | H5162 | 105.421°    |  | C517  | C516 | H5162 | 109.680°    |
| C617  | C516 | H5162 | 52.558°     |  | H5161 | C516 | H5162 | 109.019°    |
| C515  | C516 | H6172 | 130.649°    |  | C517  | C516 | H6172 | 111.817°    |
| C617  | C516 | H6172 | 83.620°     |  | H5161 | C516 | H6172 | 72.208°     |
| H5162 | C516 | H6172 | 39.407°     |  | C515  | C516 | H6171 | 114.137°    |
| C517  | C516 | H6171 | 0.699°      |  | C617  | C516 | H6171 | 65.855°     |
| H5161 | C516 | H6171 | 111.220°    |  | H5162 | C516 | H6171 | 109.415°    |
| H6172 | C516 | H6171 | 111.187°    |  | C516  | C517 | C617  | 22.1(3)°    |
| C516  | C517 | H5172 | 107.649°    |  | C617  | C517 | H5172 | 110.304°    |
| C516  | C517 | H5171 | 107.720°    |  | C617  | C517 | H5171 | 123.097°    |
| H5172 | C517 | H5171 | 112.901°    |  | C516  | C517 | H5173 | 104.861°    |
| C617  | C517 | H5173 | 83.661°     |  | H5172 | C517 | H5173 | 110.672°    |
| H5171 | C517 | H5173 | 112.549°    |  | C516  | C517 | H6171 | 2.407°      |
| C617  | C517 | H6171 | 22.584°     |  | H5172 | C517 | H6171 | 105.246°    |
| H5171 | C517 | H6171 | 109.094°    |  | H5173 | C517 | H6171 | 105.859°    |
| N501  | C606 | C506  | 99(6)°      |  | N501  | C606 | C507  | 123.7(5)°   |
| C506  | C606 | C507  | 135(8)°     |  | N501  | C606 | C607  | 116.09(10)° |
| C506  | C606 | C607  | 145(6)°     |  | C507  | C606 | C607  | 12.3(6)°    |
| N501  | C606 | H5061 | 101.812°    |  | C506  | C606 | H5061 | 37.101°     |
| C507  | C606 | H5061 | 111.115°    |  | C607  | C606 | H5061 | 123.414°    |
| N501  | C606 | H5062 | 105.066°    |  | C506  | C606 | H5062 | 63.740°     |
| C507  | C606 | H5062 | 113.077°    |  | C607  | C606 | H5062 | 109.127°    |
| H5061 | C606 | H5062 | 98.776°     |  | N501  | C606 | H6062 | 105.339°    |
| C506  | C606 | H6062 | 51.549°     |  | C507  | C606 | H6062 | 97.939°     |

|       |      |       |            |  |       |      |       |             |
|-------|------|-------|------------|--|-------|------|-------|-------------|
| C607  | C606 | H6062 | 110.045°   |  | H5061 | C606 | H6062 | 14.788°     |
| N501  | C606 | H6061 | 106.218°   |  | C506  | C606 | H6061 | 62.740°     |
| C507  | C606 | H6061 | 112.863°   |  | C607  | C606 | H6061 | 109.242°    |
| H5061 | C606 | H6061 | 97.551°    |  | H5062 | C606 | H6062 | 111.046°    |
| H5062 | C606 | H6061 | 1.502°     |  | H6062 | C606 | H6061 | 109.705°    |
| C506  | C607 | C507  | 69(2)°     |  | C506  | C607 | C508  | 95.9(5)°    |
| C507  | C607 | C508  | 45(2)°     |  | C506  | C607 | C606  | 2.6(5)°     |
| C507  | C607 | C606  | 71(2)°     |  | C508  | C607 | C606  | 98.5(4)°    |
| C506  | C607 | C608  | 106.6(4)°  |  | C507  | C607 | C608  | 60(2)°      |
| C508  | C607 | C608  | 15.2(4)°   |  | C606  | C607 | C608  | 109.18(10)° |
| C506  | C607 | H5071 | 98.617°    |  | C507  | C607 | H5071 | 60.943°     |
| C508  | C607 | H5071 | 90.573°    |  | C606  | C607 | H5071 | 98.408°     |
| C608  | C607 | H5071 | 99.399°    |  | C506  | C607 | H5072 | 124.735°    |
| C507  | C607 | H5072 | 156.291°   |  | C508  | C607 | H5072 | 111.097°    |
| C606  | C607 | H5072 | 123.501°   |  | C608  | C607 | H5072 | 95.916°     |
| C506  | C607 | H6071 | 111.916°   |  | C507  | C607 | H6071 | 82.149°     |
| C508  | C607 | H6071 | 105.227°   |  | C606  | C607 | H6071 | 110.931°    |
| C608  | C607 | H6071 | 109.851°   |  | C506  | C607 | H6072 | 111.887°    |
| C507  | C607 | H6072 | 167.910°   |  | C508  | C607 | H6072 | 123.540°    |
| C606  | C607 | H6072 | 110.328°   |  | C608  | C607 | H6072 | 108.718°    |
| H5071 | C607 | H5072 | 126.960°   |  | H5071 | C607 | H6071 | 21.505°     |
| H5072 | C607 | H6071 | 106.169°   |  | H5071 | C607 | H6072 | 129.289°    |
| H5072 | C607 | H6072 | 15.074°    |  | H6071 | C607 | H6072 | 107.800°    |
| C507  | C608 | C508  | 97.9(17)°  |  | C507  | C608 | C509  | 130.6(10)°  |
| C508  | C608 | C509  | 92.9(18)°  |  | C507  | C608 | C607  | 11.8(7)°    |
| C508  | C608 | C607  | 109.5(16)° |  | C509  | C608 | C607  | 128.7(6)°   |
| C507  | C608 | C609  | 118.9(5)°  |  | C508  | C608 | C609  | 114.0(18)°  |
| C509  | C608 | C609  | 21.7(4)°   |  | C607  | C608 | C609  | 113.15(10)° |
| C507  | C608 | H5081 | 114.897°   |  | C508  | C608 | H5081 | 66.445°     |
| C509  | C608 | H5081 | 113.591°   |  | C607  | C608 | H5081 | 117.619°    |
| C609  | C608 | H5081 | 125.177°   |  | C507  | C608 | H6082 | 97.956°     |
| C508  | C608 | H6082 | 9.028°     |  | C509  | C608 | H6082 | 86.063°     |
| C607  | C608 | H6082 | 109.704°   |  | C609  | C608 | H6082 | 106.591°    |
| C507  | C608 | H6081 | 112.268°   |  | C508  | C608 | H6081 | 102.284°    |
| C509  | C608 | H6081 | 112.094°   |  | C607  | C608 | H6081 | 107.293°    |
| C609  | C608 | H6081 | 109.775°   |  | H5081 | C608 | H6082 | 74.671°     |
| H5081 | C608 | H6081 | 35.856°    |  | H6082 | C608 | H6081 | 110.348°    |
| C509  | C609 | C608  | 70.4(15)°  |  | C509  | C609 | H5092 | 62.455°     |
| C608  | C609 | H5092 | 100.650°   |  | C509  | C609 | H5091 | 125.012°    |
| C608  | C609 | H5091 | 109.385°   |  | H5092 | C609 | H5091 | 149.806°    |

|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C509  | C609 | H6091 | 58.027°     |  | C608  | C609 | H6091 | 110.801°    |
| H5092 | C609 | H6091 | 93.643°     |  | H5091 | C609 | H6091 | 73.175°     |
| C509  | C609 | H6092 | 87.162°     |  | C608  | C609 | H6092 | 109.639°    |
| H5092 | C609 | H6092 | 24.780°     |  | H5091 | C609 | H6092 | 135.956°    |
| H6091 | C609 | H6092 | 110.355°    |  | C509  | C609 | H6093 | 163.039°    |
| C608  | C609 | H6093 | 108.618°    |  | H5092 | C609 | H6093 | 132.776°    |
| H5091 | C609 | H6093 | 38.411°     |  | H6091 | C609 | H6093 | 108.831°    |
| H6092 | C609 | H6093 | 108.543°    |  | N501  | C610 | C510  | 112.3(17)°  |
| N501  | C610 | C611  | 115.88(10)° |  | C510  | C610 | C611  | 4(2)°       |
| N501  | C610 | H5101 | 120.243°    |  | C510  | C610 | H5101 | 92.096°     |
| C611  | C610 | H5101 | 89.383°     |  | N501  | C610 | H5102 | 117.319°    |
| C510  | C610 | H5102 | 84.729°     |  | C611  | C610 | H5102 | 83.813°     |
| H5101 | C610 | H5102 | 118.633°    |  | N501  | C610 | H6102 | 105.908°    |
| C510  | C610 | H6102 | 113.019°    |  | C611  | C610 | H6102 | 110.479°    |
| H5101 | C610 | H6102 | 21.336°     |  | H5102 | C610 | H6102 | 122.233°    |
| N501  | C610 | H6101 | 105.950°    |  | C510  | C610 | H6101 | 110.564°    |
| C611  | C610 | H6101 | 109.553°    |  | H5101 | C610 | H6101 | 115.134°    |
| H5102 | C610 | H6101 | 25.844°     |  | H6102 | C610 | H6101 | 108.766°    |
| C510  | C611 | C511  | 140.4(17)°  |  | C510  | C611 | C512  | 135.3(5)°   |
| C511  | C611 | C512  | 84.1(13)°   |  | C510  | C611 | C610  | 0.9(5)°     |
| C511  | C611 | C610  | 141.2(14)°  |  | C512  | C611 | C610  | 134.5(3)°   |
| C510  | C611 | C612  | 110.2(4)°   |  | C511  | C611 | C612  | 108.3(14)°  |
| C512  | C611 | C612  | 25.8(2)°    |  | C610  | C611 | C612  | 109.36(10)° |
| C510  | C611 | H5112 | 116.780°    |  | C511  | C611 | H5112 | 38.959°     |
| C512  | C611 | H5112 | 95.943°     |  | C610  | C611 | H5112 | 117.126°    |
| C612  | C611 | H5112 | 108.939°    |  | C510  | C611 | H5111 | 117.657°    |
| C511  | C611 | H5111 | 42.604°     |  | C512  | C611 | H5111 | 97.939°     |
| C610  | C611 | H5111 | 118.484°    |  | C612  | C611 | H5111 | 122.024°    |
| C510  | C611 | H6112 | 110.189°    |  | C511  | C611 | H6112 | 45.022°     |
| C512  | C611 | H6112 | 100.710°    |  | C610  | C611 | H6112 | 110.513°    |
| C612  | C611 | H6112 | 111.368°    |  | C510  | C611 | H6111 | 107.232°    |
| C511  | C611 | H6111 | 67.502°     |  | C512  | C611 | H6111 | 91.941°     |
| C610  | C611 | H6111 | 107.813°    |  | C612  | C611 | H6111 | 109.253°    |
| H5112 | C611 | H5111 | 76.953°     |  | H5112 | C611 | H6112 | 6.767°      |
| H5111 | C611 | H6112 | 81.179°     |  | H5112 | C611 | H6111 | 104.046°    |
| H5111 | C611 | H6111 | 27.289°     |  | H6112 | C611 | H6111 | 108.458°    |
| C511  | C612 | C512  | 69.2(6)°    |  | C511  | C612 | C611  | 14.3(3)°    |
| C512  | C612 | C611  | 82.4(7)°    |  | C511  | C612 | C613  | 99.0(3)°    |
| C512  | C612 | C613  | 31.9(7)°    |  | C611  | C612 | C613  | 113.01(10)° |
| C511  | C612 | H5122 | 130.490°    |  | C512  | C612 | H5122 | 88.993°     |

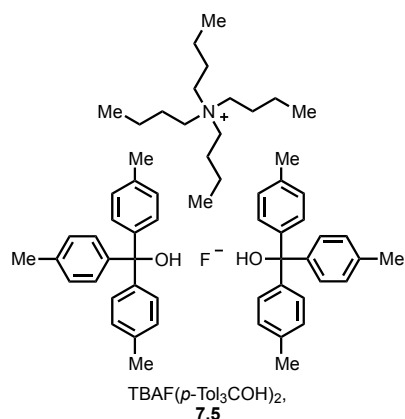
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| C611  | C612  | H5122 | 139.295°  |  | C613  | C612  | H5122 | 60.068°     |
| C511  | C612  | H5121 | 92.302°   |  | C512  | C612  | H5121 | 61.110°     |
| C611  | C612  | H5121 | 94.497°   |  | C613  | C612  | H5121 | 69.238°     |
| H5122 | C612  | H5121 | 115.828°  |  | C511  | C612  | H6121 | 114.118°    |
| C512  | C612  | H6121 | 125.542°  |  | C611  | C612  | H6121 | 111.433°    |
| C613  | C612  | H6121 | 103.472°  |  | H5122 | C612  | H6121 | 45.522°     |
| C511  | C612  | H6122 | 120.745°  |  | C512  | C612  | H6122 | 112.884°    |
| C611  | C612  | H6122 | 111.415°  |  | C613  | C612  | H6122 | 107.347°    |
| H5122 | C612  | H6122 | 108.586°  |  | H5121 | C612  | H6121 | 153.545°    |
| H5121 | C612  | H6122 | 52.790°   |  | H6121 | C612  | H6122 | 109.805°    |
| C512  | C613  | C513  | 112.6(9)° |  | C512  | C613  | C612  | 21.9(4)°    |
| C513  | C613  | C612  | 133.9(7)° |  | C512  | C613  | H5122 | 51.042°     |
| C513  | C613  | H5122 | 150.041°  |  | C612  | C613  | H5122 | 30.727°     |
| C512  | C613  | H5131 | 167.190°  |  | C513  | C613  | H5131 | 62.171°     |
| C612  | C613  | H5131 | 163.063°  |  | H5122 | C613  | H5131 | 139.178°    |
| C512  | C613  | H6133 | 128.688°  |  | C513  | C613  | H6133 | 118.051°    |
| C612  | C613  | H6133 | 108.055°  |  | H5122 | C613  | H6133 | 85.651°     |
| H5131 | C613  | H6133 | 56.018°   |  | C512  | C613  | H6132 | 103.634°    |
| C513  | C613  | H6132 | 58.731°   |  | C612  | C613  | H6132 | 108.834°    |
| H5122 | C613  | H6132 | 97.805°   |  | H5131 | C613  | H6132 | 83.814°     |
| C512  | C613  | H6131 | 91.515°   |  | C513  | C613  | H6131 | 54.919°     |
| C612  | C613  | H6131 | 107.935°  |  | H5122 | C613  | H6131 | 137.145°    |
| H5131 | C613  | H6131 | 75.905°   |  | H6133 | C613  | H6132 | 108.949°    |
| H6133 | C613  | H6131 | 110.288°  |  | H6132 | C613  | H6131 | 112.663°    |
| C515  | C617  | C516  | 64.0(7)°  |  | C515  | C617  | C517  | 110.9(3)°   |
| C516  | C617  | C517  | 92.1(6)°  |  | C515  | C617  | C618  | 113.42(10)° |
| C516  | C617  | C618  | 175.9(7)° |  | C517  | C617  | C618  | 91.9(4)°    |
| C515  | C617  | H5162 | 105.944°  |  | C516  | C617  | H5162 | 98.634°     |
| C517  | C617  | H5162 | 142.629°  |  | C618  | C617  | H5162 | 78.810°     |
| C515  | C617  | H6172 | 110.752°  |  | C516  | C617  | H6172 | 66.168°     |
| C517  | C617  | H6172 | 115.826°  |  | C618  | C617  | H6172 | 112.922°    |
| H5162 | C617  | H6172 | 41.626°   |  | C515  | C617  | H6171 | 108.292°    |
| C516  | C617  | H6171 | 85.134°   |  | C517  | C617  | H6171 | 6.997°      |
| C618  | C617  | H6171 | 98.856°   |  | H5162 | C617  | H6171 | 143.402°    |
| H6172 | C617  | H6171 | 112.002°  |  | C617  | C618  | H6181 | 110.048°    |
| C617  | C618  | H6182 | 107.386°  |  | H6181 | C618  | H6182 | 108.567°    |
| C617  | C618  | H6183 | 111.292°  |  | H6181 | C618  | H6183 | 110.543°    |
| H6182 | C618  | H6183 | 108.905°  |  | C109  | H1091 | H3091 | 50.560°     |
| C110  | H1101 | H3101 | 53.566°   |  | C111  | H1111 | C311  | 28.565°     |
| C111  | H1111 | H3111 | 85.440°   |  | C311  | H1111 | H3111 | 56.875°     |

|      |       |       |          |  |      |       |       |          |
|------|-------|-------|----------|--|------|-------|-------|----------|
| C112 | H1121 | C312  | 30.122°  |  | C112 | H1121 | H3121 | 118.808° |
| C312 | H1121 | H3121 | 88.836°  |  | C113 | H1131 | C313  | 6.324°   |
| C113 | H1131 | H3131 | 140.662° |  | C313 | H1131 | H3131 | 134.882° |
| C115 | H1151 | H3151 | 30.540°  |  | C116 | H1161 | H3161 | 53.959°  |
| C117 | H1171 | C317  | 35.424°  |  | C117 | H1171 | H3171 | 88.168°  |
| C317 | H1171 | H3171 | 52.750°  |  | C118 | H1181 | C318  | 40.845°  |
| C118 | H1181 | H3181 | 121.950° |  | C318 | H1181 | H3181 | 81.124°  |
| C119 | H1191 | C319  | 17.829°  |  | C119 | H1191 | H3191 | 141.098° |
| C319 | H1191 | H3191 | 124.901° |  | C211 | H2111 | C411  | 29.469°  |
| C211 | H2111 | H4111 | 89.685°  |  | C411 | H2111 | H4111 | 60.271°  |
| C212 | H2121 | C412  | 16.853°  |  | C212 | H2121 | H4121 | 125.779° |
| C412 | H2121 | H4121 | 113.181° |  | C213 | H2131 | C413  | 3.867°   |
| C213 | H2131 | H4131 | 147.747° |  | C413 | H2131 | H4131 | 149.573° |
| C215 | H2151 | H4151 | 29.973°  |  | C216 | H2161 | H4161 | 52.657°  |
| C217 | H2171 | C417  | 35.646°  |  | C217 | H2171 | H4171 | 91.771°  |
| C417 | H2171 | H4171 | 56.245°  |  | C218 | H2181 | C418  | 46.663°  |
| C219 | H2191 | C419  | 38.457°  |  | C219 | H2191 | H4191 | 113.180° |
| C419 | H2191 | H4191 | 75.233°  |  | C109 | H3091 | C309  | 26.416°  |
| C109 | H3091 | H1091 | 90.291°  |  | C309 | H3091 | H1091 | 116.329° |
| C110 | H3101 | C310  | 33.396°  |  | C110 | H3101 | H1101 | 86.045°  |
| C310 | H3101 | H1101 | 119.387° |  | C111 | H3111 | C311  | 29.011°  |
| C111 | H3111 | H1111 | 58.664°  |  | C311 | H3111 | H1111 | 87.675°  |
| C312 | H3121 | H1121 | 53.021°  |  | C113 | H3131 | C313  | 1.885°   |
| C113 | H3131 | H1131 | 28.624°  |  | C313 | H3131 | H1131 | 29.019°  |
| C115 | H3151 | C315  | 19.729°  |  | C115 | H3151 | H1151 | 120.423° |
| C315 | H3151 | H1151 | 139.540° |  | C116 | H3161 | C316  | 42.007°  |
| C116 | H3161 | H1161 | 72.305°  |  | C316 | H3161 | H1161 | 114.237° |
| C117 | H3171 | C317  | 33.102°  |  | C117 | H3171 | H1171 | 49.627°  |
| C317 | H3171 | H1171 | 82.723°  |  | C318 | H3181 | H1181 | 48.522°  |
| C319 | H3191 | H1191 | 30.615°  |  | C209 | H4091 | C409  | 41.639°  |
| C210 | H4101 | C410  | 43.968°  |  | C211 | H4111 | C411  | 28.579°  |
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| C412 | H4121 | H2121 | 46.055°  |  | C213 | H4131 | C413  | 3.961°   |
| C213 | H4131 | H2131 | 26.084°  |  | C413 | H4131 | H2131 | 23.213°  |
| C215 | H4151 | C415  | 10.283°  |  | C215 | H4151 | H2151 | 124.496° |
| C415 | H4151 | H2151 | 134.640° |  | C216 | H4161 | C416  | 35.939°  |
| C216 | H4161 | H2161 | 85.881°  |  | C416 | H4161 | H2161 | 121.663° |
| C217 | H4171 | C417  | 32.601°  |  | C217 | H4171 | H2171 | 50.887°  |
| C417 | H4171 | H2171 | 83.368°  |  | C419 | H4191 | H2191 | 54.972°  |



|      |       |       |          |  |      |       |       |          |
|------|-------|-------|----------|--|------|-------|-------|----------|
| C506 | H5061 | C606  | 4.398°   |  | C506 | H5061 | H6062 | 64.948°  |
| C606 | H5061 | H6062 | 60.678°  |  | C506 | H5062 | C606  | 6.680°   |
| C506 | H5062 | H6061 | 24.958°  |  | C606 | H5062 | H6061 | 28.977°  |
| C507 | H5071 | C607  | 16.945°  |  | C507 | H5071 | H6071 | 78.315°  |
| C607 | H5071 | H6071 | 61.613°  |  | C507 | H5072 | C607  | 7.704°   |
| C507 | H5072 | H6072 | 144.620° |  | C607 | H5072 | H6072 | 137.850° |
| C508 | H5082 | H6082 | 7.433°   |  | C508 | H5081 | C608  | 27.240°  |
| C508 | H5081 | H6081 | 92.934°  |  | C608 | H5081 | H6081 | 65.707°  |
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| C510 | H5101 | H6102 | 104.364° |  | C610 | H5101 | H6102 | 87.809°  |
| C510 | H5102 | C610  | 17.309°  |  | C510 | H5102 | H6101 | 97.103°  |
| C610 | H5102 | H6101 | 79.799°  |  | C511 | H5112 | C611  | 16.610°  |
| C511 | H5112 | H6112 | 35.763°  |  | C611 | H5112 | H6112 | 20.283°  |
| C511 | H5111 | C611  | 17.570°  |  | C511 | H5111 | H6111 | 63.859°  |
| C611 | H5111 | H6111 | 48.071°  |  | C512 | H5122 | C612  | 42.572°  |
| C512 | H5122 | C613  | 48.220°  |  | C612 | H5122 | C613  | 89.206°  |
| C512 | H5122 | H6121 | 118.724° |  | C612 | H5122 | H6121 | 83.838°  |
| C613 | H5122 | H6121 | 159.247° |  | C512 | H5121 | C612  | 38.136°  |
| C513 | H5131 | C613  | 44.447°  |  | C513 | H5132 | H6132 | 60.608°  |
| C516 | H5162 | C617  | 28.808°  |  | C516 | H5162 | H6172 | 60.719°  |
| C617 | H5162 | H6172 | 82.558°  |  | C506 | H6062 | C606  | 6.241°   |
| C506 | H6062 | H5061 | 98.402°  |  | C606 | H6062 | H5061 | 104.534° |
| C506 | H6061 | C606  | 6.964°   |  | C506 | H6061 | H5062 | 153.662° |
| C606 | H6061 | H5062 | 149.523° |  | C507 | H6071 | C607  | 19.253°  |
| C507 | H6071 | H5071 | 77.870°  |  | C607 | H6071 | H5071 | 96.882°  |
| C607 | H6072 | H5072 | 27.076°  |  | C508 | H6082 | C608  | 8.273°   |
| C508 | H6082 | H5082 | 165.977° |  | C608 | H6082 | H5082 | 168.372° |
| C508 | H6081 | C608  | 23.557°  |  | C508 | H6081 | H5081 | 54.893°  |
| C608 | H6081 | H5081 | 78.437°  |  | C509 | H6091 | C609  | 33.800°  |
| C509 | H6091 | H5093 | 78.479°  |  | C609 | H6091 | H5093 | 112.232° |
| C509 | H6092 | C609  | 30.421°  |  | C509 | H6092 | H5092 | 63.049°  |
| C609 | H6092 | H5092 | 93.383°  |  | C609 | H6093 | H5091 | 34.072°  |
| C510 | H6102 | C610  | 13.483°  |  | C510 | H6102 | H5101 | 57.694°  |
| C610 | H6102 | H5101 | 70.856°  |  | C510 | H6101 | C610  | 14.161°  |
| C510 | H6101 | H5102 | 60.203°  |  | C610 | H6101 | H5102 | 74.357°  |
| C511 | H6112 | C611  | 25.358°  |  | C511 | H6112 | H5112 | 128.898° |
| C611 | H6112 | H5112 | 152.950° |  | C511 | H6111 | C611  | 26.823°  |

|      |       |       |          |  |      |       |       |          |
|------|-------|-------|----------|--|------|-------|-------|----------|
| C511 | H6111 | H5111 | 79.479°  |  | C611 | H6111 | H5111 | 104.640° |
| C612 | H6121 | H5122 | 50.640°  |  | C513 | H6132 | C613  | 49.352°  |
| C513 | H6132 | H5132 | 74.558°  |  | C613 | H6132 | H5132 | 123.757° |
| C513 | H6131 | C613  | 50.641°  |  | C516 | H6172 | C617  | 30.211°  |
| C516 | H6172 | H5162 | 79.875°  |  | C617 | H6172 | H5162 | 55.816°  |
| C516 | H6171 | C517  | 176.894° |  | C516 | H6171 | C617  | 29.011°  |
| C517 | H6171 | C617  | 150.420° |  | C515 | H5151 | H5154 | 81.947°  |
| C515 | H5152 | H5153 | 80.144°  |  | C515 | H5153 | H5152 | 80.441°  |
| C515 | H5154 | H5151 | 78.901°  |  |      |       |       |          |



**tetra-*n*-butylammonium fluoride bis(tri-*p*-tolylmethanol) (TBAF(*p*-Tol<sub>3</sub>COH)<sub>2</sub>, 7.5):**

**X-ray** (single-crystal) Colourless needles of X-ray quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.5** in Et<sub>2</sub>O, which had previously been prepared by dissolving **7.5** in refluxing Et<sub>2</sub>O (approximately 35 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 048GWP12

## Crystal Data

$a = 13.4717(3) \text{ \AA}$   $\alpha = 78.8655(19)^\circ$

$b = 17.5643(4) \text{ \AA}$   $\beta = 80.5422(17)^\circ$

$c = 24.8506(5) \text{ \AA}$   $\gamma = 69.645(2)^\circ$

Volume 5379.0(2)  $\text{\AA}^3$

Space group P -1

Formula C<sub>60</sub> H<sub>80</sub> F<sub>1</sub> N<sub>1</sub> O<sub>2</sub>

Cell determined from 46180 reflections

Temperature 150K

Shape block

Colour clear\_pale\_colourless

$D_x = 1.07 \text{ Mg m}^{-3}$

$\mu = 0.500 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min} = 0.82$

Crystal Class triclinic

$Z = 4$

$M_r = 866.30$

Cell  $\theta$  range = 3 - 77°

Size 0.18 × 0.20 × 0.21 mm

$F_{000} = 1888.000$

$T_{\max} = 0.91$

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 110583

Independent reflections 22463

$R_{\text{int}} = 0.0331$

$\theta_{\max} = 77.1663$

$h = -17 \rightarrow 16$

$k = -21 \rightarrow 22$

$l = -31 \rightarrow 31$

## Refinement

$\Delta\rho_{\min} = -0.21 \text{ e \AA}^{-3}$

$\Delta\rho_{\max} = 0.33 \text{ e \AA}^{-3}$

Reflections used 22370  
 Cutoff: I > -3.00σ(I)  
 Parameters refined 1154  
 S = 0.99  
 R-factor 0.050  
 weighted R-factor 0.120  
 Δ/σ<sub>max</sub> 0.0009  
 Refinement on F<sup>2</sup>  
 w =  $\frac{1}{[\sigma^2(F_{\text{obs}}^2) + (0.060 \times P)^2 + 1.555 \times P + 0.000 + 0.000 \times \sin\theta]}$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| C91   | 0.03783(13) | 0.59782(8)  | 0.51970(6)  | 0.0465                 | 1.0000    |
| C11   | 0.34783(9)  | 0.67176(7)  | 0.84329(4)  | 0.0289                 | 1.0000    |
| C12   | 0.22826(10) | 0.68207(7)  | 0.84943(5)  | 0.0299                 | 1.0000    |
| C13   | 0.16170(10) | 0.73928(8)  | 0.81269(5)  | 0.0353                 | 1.0000    |
| C14   | 0.05323(11) | 0.74962(9)  | 0.81826(6)  | 0.0416                 | 1.0000    |
| C15   | 0.00784(11) | 0.70327(9)  | 0.86007(6)  | 0.0432                 | 1.0000    |
| C16   | 0.07434(11) | 0.64644(9)  | 0.89678(6)  | 0.0428                 | 1.0000    |
| C17   | 0.18239(10) | 0.63581(8)  | 0.89172(5)  | 0.0360                 | 1.0000    |
| C18   | 0.10973(13) | 0.71478(12) | 0.86618(8)  | 0.0608                 | 1.0000    |
| C19   | 0.41380(9)  | 0.57990(7)  | 0.85390(5)  | 0.0314                 | 1.0000    |
| C20   | 0.45336(10) | 0.53465(8)  | 0.81028(6)  | 0.0368                 | 1.0000    |
| C21   | 0.51105(11) | 0.45139(8)  | 0.82029(7)  | 0.0452                 | 1.0000    |
| C22   | 0.53031(10) | 0.41072(8)  | 0.87306(7)  | 0.0458                 | 1.0000    |
| C23   | 0.49131(11) | 0.45607(8)  | 0.91630(6)  | 0.0435                 | 1.0000    |
| C24   | 0.43436(10) | 0.53958(8)  | 0.90690(6)  | 0.0375                 | 1.0000    |
| C25   | 0.59102(13) | 0.32011(9)  | 0.88310(10) | 0.0651                 | 1.0000    |
| C26   | 0.37441(10) | 0.71668(7)  | 0.88340(5)  | 0.0304                 | 1.0000    |
| C27   | 0.47830(11) | 0.71902(8)  | 0.87763(5)  | 0.0362                 | 1.0000    |
| C28   | 0.50768(12) | 0.76052(8)  | 0.91090(6)  | 0.0420                 | 1.0000    |
| C29   | 0.43556(13) | 0.80012(9)  | 0.95165(6)  | 0.0451                 | 1.0000    |
| C30   | 0.33356(13) | 0.79619(9)  | 0.95807(6)  | 0.0473                 | 1.0000    |
| C31   | 0.30246(11) | 0.75551(8)  | 0.92416(5)  | 0.0395                 | 1.0000    |
| C32   | 0.46746(18) | 0.84628(12) | 0.98764(8)  | 0.0661                 | 1.0000    |
| C41   | 0.52119(9)  | 0.71831(7)  | 0.60481(5)  | 0.0304                 | 1.0000    |
| C42   | 0.45812(9)  | 0.71932(7)  | 0.55810(5)  | 0.0302                 | 1.0000    |
| C43   | 0.36209(10) | 0.70350(8)  | 0.57052(6)  | 0.0382                 | 1.0000    |
| C44   | 0.30725(11) | 0.70073(9)  | 0.52868(6)  | 0.0427                 | 1.0000    |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| C45  | 0.34603(11) | 0.71282(7)  | 0.47343(6)  | 0.0378 | 1.0000 |
| C46  | 0.44210(11) | 0.72812(8)  | 0.46129(5)  | 0.0382 | 1.0000 |
| C47  | 0.49710(10) | 0.73196(8)  | 0.50266(5)  | 0.0350 | 1.0000 |
| C48  | 0.28886(13) | 0.70763(10) | 0.42788(7)  | 0.0521 | 1.0000 |
| C49  | 0.58817(9)  | 0.62931(7)  | 0.62422(5)  | 0.0306 | 1.0000 |
| C50  | 0.60049(10) | 0.60176(8)  | 0.67981(5)  | 0.0347 | 1.0000 |
| C51  | 0.66022(10) | 0.52115(8)  | 0.69737(5)  | 0.0376 | 1.0000 |
| C52  | 0.71043(10) | 0.46557(8)  | 0.66064(5)  | 0.0360 | 1.0000 |
| C53  | 0.70002(12) | 0.49392(8)  | 0.60506(6)  | 0.0421 | 1.0000 |
| C54  | 0.63885(12) | 0.57400(8)  | 0.58726(5)  | 0.0395 | 1.0000 |
| C55  | 0.77009(12) | 0.37741(9)  | 0.68107(7)  | 0.0472 | 1.0000 |
| C56  | 0.59118(10) | 0.77284(7)  | 0.58356(5)  | 0.0310 | 1.0000 |
| C57  | 0.54124(11) | 0.85719(8)  | 0.57504(6)  | 0.0399 | 1.0000 |
| C58  | 0.59864(12) | 0.91018(8)  | 0.55344(6)  | 0.0429 | 1.0000 |
| C59  | 0.70799(11) | 0.88087(8)  | 0.53971(5)  | 0.0379 | 1.0000 |
| C60  | 0.75734(10) | 0.79663(8)  | 0.54753(5)  | 0.0382 | 1.0000 |
| C61  | 0.70030(10) | 0.74318(8)  | 0.56935(5)  | 0.0357 | 1.0000 |
| C62  | 0.77081(13) | 0.93848(10) | 0.51741(7)  | 0.0522 | 1.0000 |
| C71  | 0.14929(9)  | 0.27551(7)  | 0.65868(4)  | 0.0278 | 1.0000 |
| C72  | 0.08264(9)  | 0.22584(7)  | 0.64714(5)  | 0.0303 | 1.0000 |
| C73  | 0.04644(10) | 0.17482(8)  | 0.69016(6)  | 0.0380 | 1.0000 |
| C74  | 0.01132(11) | 0.12836(9)  | 0.67951(7)  | 0.0482 | 1.0000 |
| C75  | 0.03417(11) | 0.13024(9)  | 0.62689(8)  | 0.0498 | 1.0000 |
| C76  | 0.00172(11) | 0.18141(9)  | 0.58423(7)  | 0.0458 | 1.0000 |
| C77  | 0.05891(10) | 0.22855(8)  | 0.59424(6)  | 0.0368 | 1.0000 |
| C78  | 0.09467(15) | 0.07777(12) | 0.61574(11) | 0.0767 | 1.0000 |
| C79  | 0.26836(9)  | 0.22437(7)  | 0.65235(5)  | 0.0286 | 1.0000 |
| C80  | 0.33592(10) | 0.22677(8)  | 0.68817(5)  | 0.0352 | 1.0000 |
| C81  | 0.44400(11) | 0.18101(9)  | 0.68287(6)  | 0.0420 | 1.0000 |
| C82  | 0.48776(10) | 0.13126(8)  | 0.64226(6)  | 0.0422 | 1.0000 |
| C83  | 0.42040(10) | 0.12931(8)  | 0.60620(6)  | 0.0402 | 1.0000 |
| C84  | 0.31261(10) | 0.17475(7)  | 0.61114(5)  | 0.0334 | 1.0000 |
| C85  | 0.60529(12) | 0.08204(11) | 0.63613(8)  | 0.0608 | 1.0000 |
| C86  | 0.12463(9)  | 0.35769(7)  | 0.61947(4)  | 0.0277 | 1.0000 |
| C87  | 0.02339(10) | 0.41506(7)  | 0.62743(5)  | 0.0318 | 1.0000 |
| C88  | 0.00460(10) | 0.49183(7)  | 0.59535(5)  | 0.0347 | 1.0000 |
| C89  | 0.06792(11) | 0.51396(7)  | 0.55413(5)  | 0.0349 | 1.0000 |
| C90  | 0.16768(11) | 0.45658(8)  | 0.54571(5)  | 0.0394 | 1.0000 |
| C238 | 0.19643(10) | 0.37917(7)  | 0.57799(5)  | 0.0350 | 1.0000 |
| C101 | 0.01223(9)  | 0.27858(7)  | 0.89457(5)  | 0.0291 | 1.0000 |

|      |             |             |            |        |        |
|------|-------------|-------------|------------|--------|--------|
| C102 | 0.04948(9)  | 0.22036(7)  | 0.94166(5) | 0.0301 | 1.0000 |
| C103 | 0.14655(10) | 0.16118(8)  | 0.92963(6) | 0.0388 | 1.0000 |
| C104 | 0.20360(11) | 0.10934(9)  | 0.97177(6) | 0.0451 | 1.0000 |
| C105 | 0.16604(12) | 0.11470(8)  | 1.02673(6) | 0.0421 | 1.0000 |
| C106 | 0.06742(12) | 0.17175(8)  | 1.03866(5) | 0.0418 | 1.0000 |
| C107 | 0.01002(11) | 0.22422(8)  | 0.99679(5) | 0.0362 | 1.0000 |
| C108 | 0.23118(17) | 0.06159(10) | 1.07220(8) | 0.0630 | 1.0000 |
| C109 | 0.07834(9)  | 0.23716(7)  | 0.87328(5) | 0.0292 | 1.0000 |
| C110 | 0.09583(10) | 0.25448(7)  | 0.81790(5) | 0.0326 | 1.0000 |
| C111 | 0.15419(10) | 0.21696(8)  | 0.79765(5) | 0.0346 | 1.0000 |
| C112 | 0.19756(10) | 0.16130(8)  | 0.83180(6) | 0.0358 | 1.0000 |
| C113 | 0.18085(11) | 0.14456(8)  | 0.88711(6) | 0.0384 | 1.0000 |
| C114 | 0.12172(10) | 0.18127(8)  | 0.90751(5) | 0.0345 | 1.0000 |
| C115 | 0.26102(14) | 0.12167(10) | 0.80874(7) | 0.0532 | 1.0000 |
| C116 | 0.08167(9)  | 0.35902(7)  | 0.91566(5) | 0.0297 | 1.0000 |
| C117 | 0.03104(10) | 0.41025(8)  | 0.92645(6) | 0.0368 | 1.0000 |
| C118 | 0.08824(11) | 0.48211(8)  | 0.94800(6) | 0.0384 | 1.0000 |
| C119 | 0.19818(11) | 0.50549(8)  | 0.95951(5) | 0.0363 | 1.0000 |
| C120 | 0.24848(11) | 0.45442(9)  | 0.94886(6) | 0.0422 | 1.0000 |
| C121 | 0.19142(10) | 0.38218(8)  | 0.92726(6) | 0.0382 | 1.0000 |
| C122 | 0.26056(13) | 0.58408(9)  | 0.98219(7) | 0.0505 | 1.0000 |
| O1   | 0.37936(7)  | 0.70867(5)  | 0.79038(3) | 0.0333 | 1.0000 |
| O2   | 0.45136(7)  | 0.75422(5)  | 0.64912(4) | 0.0357 | 1.0000 |
| O3   | 0.11807(7)  | 0.29878(5)  | 0.71198(3) | 0.0334 | 1.0000 |
| O4   | 0.05955(7)  | 0.30119(5)  | 0.85101(3) | 0.0328 | 1.0000 |
| F1   | 0.33533(6)  | 0.67338(5)  | 0.70647(3) | 0.0388 | 1.0000 |
| F2   | 0.16882(6)  | 0.18923(4)  | 0.79331(3) | 0.0383 | 1.0000 |
| H41  | 0.09649(7)  | 0.25946(5)  | 0.83487(3) | 0.0512 | 1.0000 |
| H31  | 0.13616(7)  | 0.25611(5)  | 0.73721(3) | 0.0521 | 1.0000 |
| H11  | 0.36401(7)  | 0.69050(5)  | 0.76345(3) | 0.0521 | 1.0000 |
| H21  | 0.41140(7)  | 0.72424(5)  | 0.66536(4) | 0.0559 | 1.0000 |
| N201 | 0.33695(8)  | 0.04113(6)  | 0.76782(4) | 0.0298 | 1.0000 |
| C202 | 0.43463(10) | 0.11765(7)  | 0.76764(5) | 0.0331 | 1.0000 |
| C203 | 0.53261(11) | 0.10901(8)  | 0.73085(6) | 0.0397 | 1.0000 |
| C204 | 0.62333(12) | 0.19013(10) | 0.73690(7) | 0.0507 | 1.0000 |
| C205 | 0.72639(13) | 0.18611(13) | 0.70340(8) | 0.0654 | 1.0000 |
| C206 | 0.36077(10) | 0.03019(7)  | 0.78247(5) | 0.0324 | 1.0000 |
| C207 | 0.40576(11) | 0.01575(8)  | 0.83697(6) | 0.0402 | 1.0000 |
| C208 | 0.43767(13) | 0.08928(9)  | 0.84106(7) | 0.0479 | 1.0000 |
| C209 | 0.48530(14) | 0.08102(12) | 0.89373(7) | 0.0587 | 1.0000 |

|       |             |             |            |        |        |
|-------|-------------|-------------|------------|--------|--------|
| C210  | 0.29834(10) | 0.01204(7)  | 0.71102(5) | 0.0329 | 1.0000 |
| C211  | 0.26187(11) | 0.07072(8)  | 0.68831(5) | 0.0375 | 1.0000 |
| C212  | 0.23208(10) | 0.03449(8)  | 0.63002(5) | 0.0373 | 1.0000 |
| C213  | 0.18700(14) | 0.08776(10) | 0.60672(7) | 0.0531 | 1.0000 |
| C214  | 0.25274(10) | 0.06445(7)  | 0.81007(5) | 0.0346 | 1.0000 |
| C215  | 0.14295(11) | 0.00001(9)  | 0.81273(6) | 0.0435 | 1.0000 |
| C216  | 0.06756(12) | 0.02967(10) | 0.85836(7) | 0.0526 | 1.0000 |
| C217  | 0.08626(14) | 0.02625(11) | 0.91598(7) | 0.0588 | 1.0000 |
| N221  | 0.16323(8)  | 0.51952(6)  | 0.73344(4) | 0.0330 | 1.0000 |
| C222  | 0.06297(10) | 0.49709(8)  | 0.73613(5) | 0.0363 | 1.0000 |
| C223  | 0.03160(11) | 0.54199(8)  | 0.77347(6) | 0.0390 | 1.0000 |
| C224  | 0.12620(12) | 0.51360(11) | 0.77384(7) | 0.0510 | 1.0000 |
| C225  | 0.22525(13) | 0.56337(12) | 0.80653(7) | 0.0562 | 1.0000 |
| C226  | 0.14120(10) | 0.61127(7)  | 0.71751(5) | 0.0351 | 1.0000 |
| C227  | 0.09193(12) | 0.65011(8)  | 0.66395(6) | 0.0423 | 1.0000 |
| C228  | 0.06400(13) | 0.74255(9)  | 0.65776(7) | 0.0503 | 1.0000 |
| C229  | 0.01023(15) | 0.78796(11) | 0.60666(8) | 0.0580 | 1.0000 |
| C230  | 0.20417(10) | 0.49725(8)  | 0.78967(5) | 0.0345 | 1.0000 |
| C231  | 0.23796(11) | 0.40700(8)  | 0.81312(6) | 0.0399 | 1.0000 |
| H1031 | 0.17410(10) | 0.15755(8)  | 0.89158(6) | 0.0465 | 1.0000 |
| C232  | 0.26681(11) | 0.39568(9)  | 0.87157(6) | 0.0394 | 1.0000 |
| C233  | 0.30821(14) | 0.30587(10) | 0.89584(7) | 0.0539 | 1.0000 |
| C234  | 0.24553(11) | 0.47243(8)  | 0.69120(5) | 0.0386 | 1.0000 |
| C235  | 0.35653(12) | 0.47822(10) | 0.68786(7) | 0.0488 | 1.0000 |
| C236  | 0.43247(14) | 0.43223(10) | 0.64245(7) | 0.0558 | 1.0000 |
| C237  | 0.41682(15) | 0.47783(11) | 0.58505(7) | 0.0603 | 1.0000 |
| H1041 | 0.27041(11) | 0.06915(9)  | 0.96229(6) | 0.0551 | 1.0000 |
| H1061 | 0.03850(12) | 0.17658(8)  | 1.07637(5) | 0.0496 | 1.0000 |
| H1071 | 0.05741(11) | 0.26349(8)  | 1.00641(5) | 0.0432 | 1.0000 |
| H1081 | 0.18654(17) | 0.04784(10) | 1.10478(8) | 0.0958 | 1.0000 |
| H1083 | 0.27047(17) | 0.09166(10) | 1.08359(8) | 0.0953 | 1.0000 |
| H1082 | 0.28115(17) | 0.01088(10) | 1.06000(8) | 0.0945 | 1.0000 |
| H1171 | 0.04617(10) | 0.39435(8)  | 0.91880(6) | 0.0458 | 1.0000 |
| H1181 | 0.05117(11) | 0.51671(8)  | 0.95557(6) | 0.0473 | 1.0000 |
| H1201 | 0.32495(11) | 0.46996(9)  | 0.95602(6) | 0.0521 | 1.0000 |
| H1211 | 0.22762(10) | 0.34710(8)  | 0.92123(6) | 0.0474 | 1.0000 |
| H1223 | 0.30030(13) | 0.57473(9)  | 1.01812(7) | 0.0764 | 1.0000 |
| H1221 | 0.31176(13) | 0.62131(9)  | 0.95791(7) | 0.0783 | 1.0000 |
| H1222 | 0.21368(13) | 0.61436(9)  | 0.98694(7) | 0.0766 | 1.0000 |
| H1101 | 0.06687(10) | 0.29243(7)  | 0.79325(5) | 0.0391 | 1.0000 |

|       |             |             |             |        |        |
|-------|-------------|-------------|-------------|--------|--------|
| H1111 | 0.16509(10) | 0.22981(8)  | 0.75957(5)  | 0.0418 | 1.0000 |
| H1131 | 0.20964(11) | 0.10649(8)  | 0.91114(6)  | 0.0469 | 1.0000 |
| H1141 | 0.11030(10) | 0.16914(8)  | 0.94640(5)  | 0.0414 | 1.0000 |
| H1151 | 0.31374(14) | 0.10856(10) | 0.83412(7)  | 0.0822 | 1.0000 |
| H1152 | 0.28642(14) | 0.15085(10) | 0.77590(7)  | 0.0831 | 1.0000 |
| H1153 | 0.21659(14) | 0.06952(10) | 0.79945(7)  | 0.0828 | 1.0000 |
| H731  | 0.06018(10) | 0.17263(8)  | 0.72741(6)  | 0.0456 | 1.0000 |
| H741  | 0.03462(11) | 0.09380(9)  | 0.70945(7)  | 0.0584 | 1.0000 |
| H761  | 0.01250(11) | 0.18445(9)  | 0.54770(7)  | 0.0554 | 1.0000 |
| H771  | 0.08227(10) | 0.26344(8)  | 0.56363(6)  | 0.0445 | 1.0000 |
| H781  | 0.12800(15) | 0.09945(12) | 0.58239(11) | 0.1157 | 1.0000 |
| H782  | 0.15042(15) | 0.07600(12) | 0.64413(11) | 0.1153 | 1.0000 |
| H783  | 0.05198(15) | 0.02185(12) | 0.61356(11) | 0.1165 | 1.0000 |
| H801  | 0.30888(10) | 0.26009(8)  | 0.71631(5)  | 0.0417 | 1.0000 |
| H811  | 0.48760(11) | 0.18601(9)  | 0.70727(6)  | 0.0504 | 1.0000 |
| H831  | 0.44803(10) | 0.09542(8)  | 0.57701(6)  | 0.0488 | 1.0000 |
| H841  | 0.26766(10) | 0.17091(7)  | 0.58559(5)  | 0.0402 | 1.0000 |
| H853  | 0.64057(12) | 0.10389(11) | 0.60290(8)  | 0.0911 | 1.0000 |
| H852  | 0.61552(12) | 0.02471(11) | 0.63440(8)  | 0.0915 | 1.0000 |
| H851  | 0.63569(12) | 0.08600(11) | 0.66698(8)  | 0.0910 | 1.0000 |
| H871  | 0.02767(10) | 0.40132(7)  | 0.65547(5)  | 0.0386 | 1.0000 |
| H881  | 0.07399(10) | 0.53066(7)  | 0.60202(5)  | 0.0414 | 1.0000 |
| H901  | 0.21912(11) | 0.46973(8)  | 0.51745(5)  | 0.0472 | 1.0000 |
| H2381 | 0.26621(10) | 0.34135(7)  | 0.57149(5)  | 0.0424 | 1.0000 |
| H912  | 0.03383(13) | 0.64094(8)  | 0.53868(6)  | 0.0726 | 1.0000 |
| H911  | 0.03236(13) | 0.61293(8)  | 0.50863(6)  | 0.0740 | 1.0000 |
| H913  | 0.08040(13) | 0.60010(8)  | 0.48618(6)  | 0.0738 | 1.0000 |
| H201  | 0.44167(10) | 0.56058(8)  | 0.77429(6)  | 0.0434 | 1.0000 |
| H211  | 0.53691(11) | 0.42202(8)  | 0.78968(7)  | 0.0546 | 1.0000 |
| H231  | 0.50191(11) | 0.42874(8)  | 0.95453(6)  | 0.0526 | 1.0000 |
| H241  | 0.40883(10) | 0.56940(8)  | 0.93723(6)  | 0.0449 | 1.0000 |
| H253  | 0.55646(13) | 0.28941(9)  | 0.86912(10) | 0.0986 | 1.0000 |
| H252  | 0.59654(13) | 0.30069(9)  | 0.92177(10) | 0.0994 | 1.0000 |
| H251  | 0.66178(13) | 0.30879(9)  | 0.86425(10) | 0.0975 | 1.0000 |
| H131  | 0.19186(10) | 0.76956(8)  | 0.78319(5)  | 0.0411 | 1.0000 |
| H141  | 0.00950(11) | 0.79017(9)  | 0.79309(6)  | 0.0505 | 1.0000 |
| H161  | 0.04333(11) | 0.61442(9)  | 0.92724(6)  | 0.0514 | 1.0000 |
| H171  | 0.22707(10) | 0.59552(8)  | 0.91820(5)  | 0.0438 | 1.0000 |
| H181  | 0.14716(13) | 0.74039(12) | 0.89842(8)  | 0.0913 | 1.0000 |
| H183  | 0.14045(13) | 0.75015(12) | 0.83478(8)  | 0.0914 | 1.0000 |



|       |             |             |            |        |        |
|-------|-------------|-------------|------------|--------|--------|
| H182  | 0.12345(13) | 0.66364(12) | 0.86826(8) | 0.0929 | 1.0000 |
| H271  | 0.52809(11) | 0.69224(8)  | 0.85109(5) | 0.0429 | 1.0000 |
| H281  | 0.57791(12) | 0.76278(8)  | 0.90453(6) | 0.0511 | 1.0000 |
| H301  | 0.28214(13) | 0.82324(9)  | 0.98614(6) | 0.0581 | 1.0000 |
| H311  | 0.22955(11) | 0.75519(8)  | 0.92960(5) | 0.0486 | 1.0000 |
| H321  | 0.42044(18) | 0.85459(12) | 1.02093(8) | 0.1002 | 1.0000 |
| H322  | 0.53574(18) | 0.81558(12) | 0.99865(8) | 0.1003 | 1.0000 |
| H323  | 0.46980(18) | 0.89859(12) | 0.96942(8) | 0.1004 | 1.0000 |
| H431  | 0.33334(10) | 0.69494(8)  | 0.60857(6) | 0.0448 | 1.0000 |
| H441  | 0.24133(11) | 0.68950(9)  | 0.53857(6) | 0.0516 | 1.0000 |
| H461  | 0.47040(11) | 0.73738(8)  | 0.42326(5) | 0.0467 | 1.0000 |
| H471  | 0.56245(10) | 0.74339(8)  | 0.49244(5) | 0.0418 | 1.0000 |
| H481  | 0.21990(13) | 0.70269(10) | 0.44164(7) | 0.0788 | 1.0000 |
| H482  | 0.32807(13) | 0.65825(10) | 0.41145(7) | 0.0787 | 1.0000 |
| H483  | 0.28029(13) | 0.75474(10) | 0.39988(7) | 0.0807 | 1.0000 |
| H501  | 0.56541(10) | 0.63848(8)  | 0.70590(5) | 0.0430 | 1.0000 |
| H511  | 0.66407(10) | 0.50342(8)  | 0.73605(5) | 0.0455 | 1.0000 |
| H531  | 0.73594(12) | 0.45766(8)  | 0.57875(6) | 0.0505 | 1.0000 |
| H541  | 0.63156(12) | 0.59108(8)  | 0.54854(5) | 0.0470 | 1.0000 |
| H552  | 0.82011(12) | 0.35061(9)  | 0.65191(7) | 0.0715 | 1.0000 |
| H551  | 0.72159(12) | 0.34662(9)  | 0.69403(7) | 0.0709 | 1.0000 |
| H553  | 0.80820(12) | 0.37315(9)  | 0.71166(7) | 0.0697 | 1.0000 |
| H571  | 0.46590(11) | 0.87921(8)  | 0.58438(6) | 0.0490 | 1.0000 |
| H581  | 0.56169(12) | 0.96809(8)  | 0.54758(6) | 0.0515 | 1.0000 |
| H601  | 0.83386(10) | 0.77399(8)  | 0.53764(5) | 0.0473 | 1.0000 |
| H611  | 0.73722(10) | 0.68533(8)  | 0.57466(5) | 0.0434 | 1.0000 |
| H623  | 0.72414(13) | 0.99415(10) | 0.50879(7) | 0.0776 | 1.0000 |
| H622  | 0.81240(13) | 0.94114(10) | 0.54433(7) | 0.0799 | 1.0000 |
| H621  | 0.81682(13) | 0.92401(10) | 0.48390(7) | 0.0791 | 1.0000 |
| H2021 | 0.45124(10) | 0.13406(7)  | 0.80535(5) | 0.0402 | 1.0000 |
| H2022 | 0.41301(10) | 0.15976(7)  | 0.75696(5) | 0.0398 | 1.0000 |
| H2031 | 0.51829(11) | 0.09289(8)  | 0.69322(6) | 0.0490 | 1.0000 |
| H2032 | 0.55466(11) | 0.06700(8)  | 0.74071(6) | 0.0489 | 1.0000 |
| H2041 | 0.60220(12) | 0.23309(10) | 0.72645(7) | 0.0640 | 1.0000 |
| H2042 | 0.63690(12) | 0.20511(10) | 0.77573(7) | 0.0626 | 1.0000 |
| H2051 | 0.74968(13) | 0.14639(13) | 0.71605(8) | 0.0980 | 1.0000 |
| H2052 | 0.71563(13) | 0.16821(13) | 0.66366(8) | 0.0972 | 1.0000 |
| H2053 | 0.78316(13) | 0.23999(13) | 0.70755(8) | 0.0970 | 1.0000 |
| H2061 | 0.29538(10) | 0.07569(7)  | 0.78220(5) | 0.0379 | 1.0000 |
| H2062 | 0.41342(10) | 0.04171(7)  | 0.75304(5) | 0.0377 | 1.0000 |

|       |             |             |            |        |        |
|-------|-------------|-------------|------------|--------|--------|
| H2071 | 0.35269(11) | 0.00802(8)  | 0.86803(6) | 0.0499 | 1.0000 |
| H2072 | 0.46740(11) | 0.03387(8)  | 0.83975(6) | 0.0496 | 1.0000 |
| H2081 | 0.37575(13) | 0.13840(9)  | 0.83768(7) | 0.0586 | 1.0000 |
| H2082 | 0.49085(13) | 0.09466(9)  | 0.80986(7) | 0.0591 | 1.0000 |
| H2091 | 0.54565(14) | 0.03053(12) | 0.89736(7) | 0.0871 | 1.0000 |
| H2092 | 0.51008(14) | 0.12722(12) | 0.89495(7) | 0.0867 | 1.0000 |
| H2093 | 0.43430(14) | 0.07720(12) | 0.92518(7) | 0.0887 | 1.0000 |
| H2101 | 0.24045(10) | 0.04051(7)  | 0.71282(5) | 0.0369 | 1.0000 |
| H2102 | 0.35729(10) | 0.00050(7)  | 0.68700(5) | 0.0363 | 1.0000 |
| H2111 | 0.31647(11) | 0.12409(8)  | 0.68734(5) | 0.0462 | 1.0000 |
| H2112 | 0.19861(11) | 0.07997(8)  | 0.71204(5) | 0.0449 | 1.0000 |
| H2121 | 0.17923(10) | 0.02038(8)  | 0.63006(5) | 0.0439 | 1.0000 |
| H2122 | 0.29637(10) | 0.02782(8)  | 0.60593(5) | 0.0452 | 1.0000 |
| H2133 | 0.23844(14) | 0.14236(10) | 0.60546(7) | 0.0803 | 1.0000 |
| H2132 | 0.12473(14) | 0.09411(10) | 0.63022(7) | 0.0786 | 1.0000 |
| H2131 | 0.16751(14) | 0.06340(10) | 0.56893(7) | 0.0784 | 1.0000 |
| H2141 | 0.24860(10) | 0.11557(7)  | 0.80137(5) | 0.0391 | 1.0000 |
| H2142 | 0.28187(10) | 0.07752(7)  | 0.84609(5) | 0.0404 | 1.0000 |
| H2151 | 0.11487(11) | 0.00948(9)  | 0.77684(6) | 0.0520 | 1.0000 |
| H2152 | 0.14712(11) | 0.05191(9)  | 0.81919(6) | 0.0516 | 1.0000 |
| H2161 | 0.07228(12) | 0.08628(10) | 0.85488(7) | 0.0627 | 1.0000 |
| H2162 | 0.00541(12) | 0.00400(10) | 0.85166(7) | 0.0628 | 1.0000 |
| H2173 | 0.03826(14) | 0.04604(11) | 0.94436(7) | 0.0870 | 1.0000 |
| H2172 | 0.07532(14) | 0.03040(11) | 0.92023(7) | 0.0862 | 1.0000 |
| H2171 | 0.15996(14) | 0.05826(11) | 0.92378(7) | 0.0876 | 1.0000 |
| H2221 | 0.04508(10) | 0.50774(8)  | 0.69886(5) | 0.0440 | 1.0000 |
| H2222 | 0.08219(10) | 0.43874(8)  | 0.74826(5) | 0.0441 | 1.0000 |
| H2231 | 0.05233(11) | 0.60064(8)  | 0.76182(6) | 0.0478 | 1.0000 |
| H2232 | 0.01199(11) | 0.53041(8)  | 0.81125(6) | 0.0476 | 1.0000 |
| H2241 | 0.14041(12) | 0.51953(11) | 0.73637(7) | 0.0623 | 1.0000 |
| H2242 | 0.10399(12) | 0.45371(11) | 0.78960(7) | 0.0643 | 1.0000 |
| H2253 | 0.24651(13) | 0.61946(12) | 0.78909(7) | 0.0848 | 1.0000 |
| H2252 | 0.21019(13) | 0.56187(12) | 0.84395(7) | 0.0828 | 1.0000 |
| H2251 | 0.28412(13) | 0.54109(12) | 0.81017(7) | 0.0841 | 1.0000 |
| H2261 | 0.09251(10) | 0.63597(7)  | 0.74773(5) | 0.0411 | 1.0000 |
| H2262 | 0.20945(10) | 0.62027(7)  | 0.71639(5) | 0.0426 | 1.0000 |
| H2271 | 0.02754(12) | 0.63754(8)  | 0.66304(6) | 0.0520 | 1.0000 |
| H2272 | 0.14090(12) | 0.63106(8)  | 0.63286(6) | 0.0515 | 1.0000 |
| H2281 | 0.12907(13) | 0.75514(9)  | 0.65793(7) | 0.0605 | 1.0000 |
| H2282 | 0.01280(13) | 0.76190(9)  | 0.68973(7) | 0.0616 | 1.0000 |

|       |             |             |            |        |        |
|-------|-------------|-------------|------------|--------|--------|
| H2291 | 0.05678(15) | 0.76952(11) | 0.57340(8) | 0.0875 | 1.0000 |
| H2292 | 0.00764(15) | 0.84908(11) | 0.60336(8) | 0.0862 | 1.0000 |
| H2293 | 0.05597(15) | 0.77529(11) | 0.60694(8) | 0.0866 | 1.0000 |
| H2301 | 0.26298(10) | 0.51830(8)  | 0.78585(5) | 0.0401 | 1.0000 |
| H2302 | 0.14744(10) | 0.52854(8)  | 0.81463(5) | 0.0405 | 1.0000 |
| H2311 | 0.18002(11) | 0.38564(8)  | 0.81339(6) | 0.0484 | 1.0000 |
| H2312 | 0.30072(11) | 0.37584(8)  | 0.78956(6) | 0.0474 | 1.0000 |
| H2321 | 0.20227(11) | 0.42456(9)  | 0.89499(6) | 0.0466 | 1.0000 |
| H2322 | 0.31922(11) | 0.42154(9)  | 0.87193(6) | 0.0464 | 1.0000 |
| H2331 | 0.25248(14) | 0.28127(10) | 0.89828(7) | 0.0811 | 1.0000 |
| H2332 | 0.32760(14) | 0.29851(10) | 0.93335(7) | 0.0801 | 1.0000 |
| H2333 | 0.37014(14) | 0.27597(10) | 0.87273(7) | 0.0779 | 1.0000 |
| H2341 | 0.24712(11) | 0.41505(8)  | 0.70064(5) | 0.0444 | 1.0000 |
| H2342 | 0.21651(11) | 0.49387(8)  | 0.65599(5) | 0.0461 | 1.0000 |
| H2351 | 0.38468(12) | 0.45256(10) | 0.72422(7) | 0.0599 | 1.0000 |
| H2352 | 0.35211(12) | 0.53573(10) | 0.68135(7) | 0.0574 | 1.0000 |
| H2361 | 0.50772(14) | 0.42498(10) | 0.64675(7) | 0.0687 | 1.0000 |
| H2362 | 0.42521(14) | 0.37641(10) | 0.64480(7) | 0.0665 | 1.0000 |
| H2373 | 0.34068(15) | 0.49161(11) | 0.57877(7) | 0.0903 | 1.0000 |
| H2372 | 0.46532(15) | 0.44571(11) | 0.55660(7) | 0.0889 | 1.0000 |
| H2371 | 0.43285(15) | 0.52983(11) | 0.58234(7) | 0.0896 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| C91   | 0.0679(9)       | 0.0304(6)       | 0.0402(7)       | 0.0016(5)       | -0.0159(6)      | -0.0136(6)      |
| C11   | 0.0357(6)       | 0.0287(5)       | 0.0244(5)       | -0.0044(4)      | 0.0015(4)       | -0.0151(5)      |
| C12   | 0.0362(6)       | 0.0279(5)       | 0.0286(5)       | -0.0102(4)      | 0.0007(4)       | -0.0130(5)      |
| C13   | 0.0411(7)       | 0.0342(6)       | 0.0322(6)       | -0.0095(5)      | -0.0029(5)      | -0.0122(5)      |
| C14   | 0.0409(7)       | 0.0436(7)       | 0.0414(7)       | -0.0176(6)      | -0.0079(5)      | -0.0075(6)      |
| C15   | 0.0372(7)       | 0.0467(7)       | 0.0524(8)       | -0.0263(6)      | 0.0023(6)       | -0.0150(6)      |
| C16   | 0.0406(7)       | 0.0420(7)       | 0.0494(8)       | -0.0143(6)      | 0.0091(6)       | -0.0202(6)      |
| C17   | 0.0386(6)       | 0.0326(6)       | 0.0375(6)       | -0.0071(5)      | 0.0027(5)       | -0.0147(5)      |
| C18   | 0.0395(8)       | 0.0705(11)      | 0.0816(12)      | -0.0348(9)      | 0.0014(8)       | -0.0202(8)      |
| C19   | 0.0300(6)       | 0.0303(6)       | 0.0357(6)       | -0.0061(5)      | 0.0026(4)       | -0.0143(5)      |
| C20   | 0.0353(6)       | 0.0353(6)       | 0.0418(7)       | -0.0111(5)      | 0.0075(5)       | -0.0163(5)      |
| C21   | 0.0345(7)       | 0.0376(7)       | 0.0646(9)       | -0.0202(6)      | 0.0127(6)       | -0.0145(5)      |
| C22   | 0.0271(6)       | 0.0325(6)       | 0.0767(10)      | -0.0052(6)      | -0.0024(6)      | -0.0111(5)      |
| C23   | 0.0350(6)       | 0.0380(7)       | 0.0574(8)       | 0.0042(6)       | -0.0099(6)      | -0.0155(5)      |
| C24   | 0.0392(7)       | 0.0345(6)       | 0.0394(7)       | -0.0022(5)      | -0.0038(5)      | -0.0147(5)      |

|     |            |            |            |             |             |             |
|-----|------------|------------|------------|-------------|-------------|-------------|
| C25 | 0.0397(8)  | 0.0351(7)  | 0.1167(16) | -0.0076(8)  | -0.0137(9)  | -0.0068(6)  |
| C26 | 0.0405(6)  | 0.0269(5)  | 0.0259(5)  | -0.0017(4)  | -0.0047(4)  | -0.0142(5)  |
| C27 | 0.0412(7)  | 0.0360(6)  | 0.0344(6)  | -0.0049(5)  | -0.0035(5)  | -0.0165(5)  |
| C28 | 0.0494(8)  | 0.0420(7)  | 0.0419(7)  | 0.0012(5)   | -0.0152(6)  | -0.0233(6)  |
| C29 | 0.0671(9)  | 0.0405(7)  | 0.0356(7)  | -0.0037(5)  | -0.0182(6)  | -0.0225(7)  |
| C30 | 0.0604(9)  | 0.0510(8)  | 0.0352(7)  | -0.0176(6)  | -0.0027(6)  | -0.0191(7)  |
| C31 | 0.0458(7)  | 0.0427(7)  | 0.0336(6)  | -0.0117(5)  | -0.0006(5)  | -0.0172(6)  |
| C32 | 0.0964(14) | 0.0677(11) | 0.0529(9)  | -0.0152(8)  | -0.0260(9)  | -0.0385(10) |
| C41 | 0.0327(6)  | 0.0310(5)  | 0.0280(5)  | -0.0090(4)  | 0.0059(4)   | -0.0124(5)  |
| C42 | 0.0314(6)  | 0.0260(5)  | 0.0319(6)  | -0.0072(4)  | 0.0028(4)   | -0.0089(4)  |
| C43 | 0.0368(6)  | 0.0428(7)  | 0.0373(6)  | -0.0116(5)  | 0.0058(5)   | -0.0170(5)  |
| C44 | 0.0346(6)  | 0.0466(7)  | 0.0505(8)  | -0.0139(6)  | 0.0009(6)   | -0.0165(6)  |
| C45 | 0.0405(7)  | 0.0283(6)  | 0.0433(7)  | -0.0073(5)  | -0.0094(5)  | -0.0062(5)  |
| C46 | 0.0467(7)  | 0.0353(6)  | 0.0314(6)  | -0.0028(5)  | -0.0032(5)  | -0.0135(5)  |
| C47 | 0.0367(6)  | 0.0367(6)  | 0.0317(6)  | -0.0045(5)  | 0.0014(5)   | -0.0148(5)  |
| C48 | 0.0559(9)  | 0.0485(8)  | 0.0550(9)  | -0.0085(7)  | -0.0204(7)  | -0.0139(7)  |
| C49 | 0.0333(6)  | 0.0315(6)  | 0.0288(5)  | -0.0055(4)  | 0.0025(4)   | -0.0151(5)  |
| C50 | 0.0352(6)  | 0.0446(7)  | 0.0289(6)  | -0.0092(5)  | -0.0003(5)  | -0.0180(5)  |
| C51 | 0.0378(6)  | 0.0486(7)  | 0.0301(6)  | 0.0010(5)   | -0.0074(5)  | -0.0206(6)  |
| C52 | 0.0354(6)  | 0.0364(6)  | 0.0388(6)  | 0.0023(5)   | -0.0069(5)  | -0.0177(5)  |
| C53 | 0.0544(8)  | 0.0313(6)  | 0.0352(6)  | -0.0055(5)  | -0.0007(6)  | -0.0088(6)  |
| C54 | 0.0540(8)  | 0.0319(6)  | 0.0265(6)  | -0.0032(5)  | 0.0011(5)   | -0.0094(6)  |
| C55 | 0.0505(8)  | 0.0397(7)  | 0.0527(8)  | 0.0083(6)   | -0.0181(6)  | -0.0186(6)  |
| C56 | 0.0343(6)  | 0.0320(6)  | 0.0283(5)  | -0.0079(4)  | 0.0021(4)   | -0.0135(5)  |
| C57 | 0.0349(6)  | 0.0332(6)  | 0.0497(7)  | -0.0104(5)  | 0.0045(5)   | -0.0104(5)  |
| C58 | 0.0475(7)  | 0.0300(6)  | 0.0500(8)  | -0.0065(5)  | 0.0007(6)   | -0.0137(6)  |
| C59 | 0.0450(7)  | 0.0391(6)  | 0.0344(6)  | -0.0057(5)  | 0.0009(5)   | -0.0219(6)  |
| C60 | 0.0336(6)  | 0.0416(7)  | 0.0401(7)  | -0.0065(5)  | 0.0020(5)   | -0.0155(5)  |
| C61 | 0.0354(6)  | 0.0325(6)  | 0.0378(6)  | -0.0057(5)  | 0.0016(5)   | -0.0114(5)  |
| C62 | 0.0576(9)  | 0.0493(8)  | 0.0561(9)  | -0.0038(7)  | 0.0034(7)   | -0.0317(7)  |
| C71 | 0.0318(6)  | 0.0254(5)  | 0.0239(5)  | -0.0046(4)  | 0.0018(4)   | -0.0079(4)  |
| C72 | 0.0257(5)  | 0.0255(5)  | 0.0361(6)  | -0.0075(4)  | 0.0027(4)   | -0.0050(4)  |
| C73 | 0.0338(6)  | 0.0307(6)  | 0.0453(7)  | -0.0069(5)  | 0.0074(5)   | -0.0095(5)  |
| C74 | 0.0349(7)  | 0.0353(7)  | 0.0714(10) | -0.0082(6)  | 0.0096(6)   | -0.0145(5)  |
| C75 | 0.0281(6)  | 0.0363(7)  | 0.0872(12) | -0.0200(7)  | -0.0038(7)  | -0.0086(5)  |
| C76 | 0.0356(7)  | 0.0410(7)  | 0.0627(9)  | -0.0188(6)  | -0.0121(6)  | -0.0058(6)  |
| C77 | 0.0347(6)  | 0.0334(6)  | 0.0414(7)  | -0.0088(5)  | -0.0044(5)  | -0.0080(5)  |
| C78 | 0.0455(9)  | 0.0563(10) | 0.141(2)   | -0.0295(11) | -0.0146(11) | -0.0218(8)  |
| C79 | 0.0312(6)  | 0.0236(5)  | 0.0290(5)  | -0.0002(4)  | 0.0002(4)   | -0.0098(4)  |
| C80 | 0.0385(6)  | 0.0354(6)  | 0.0324(6)  | -0.0019(5)  | -0.0034(5)  | -0.0144(5)  |

|      |            |           |            |            |            |            |
|------|------------|-----------|------------|------------|------------|------------|
| C81  | 0.0371(7)  | 0.0465(7) | 0.0428(7)  | 0.0085(6)  | -0.0097(5) | -0.0196(6) |
| C82  | 0.0313(6)  | 0.0354(6) | 0.0522(8)  | 0.0063(6)  | 0.0013(5)  | -0.0107(5) |
| C83  | 0.0343(6)  | 0.0319(6) | 0.0492(7)  | -0.0080(5) | 0.0067(5)  | -0.0081(5) |
| C84  | 0.0330(6)  | 0.0292(5) | 0.0364(6)  | -0.0069(5) | 0.0011(5)  | -0.0091(5) |
| C85  | 0.0321(7)  | 0.0534(9) | 0.0843(12) | 0.0038(8)  | -0.0007(7) | -0.0081(6) |
| C86  | 0.0341(6)  | 0.0254(5) | 0.0240(5)  | -0.0049(4) | -0.0030(4) | -0.0096(4) |
| C87  | 0.0337(6)  | 0.0305(6) | 0.0303(6)  | -0.0060(4) | -0.0018(4) | -0.0092(5) |
| C88  | 0.0372(6)  | 0.0292(6) | 0.0356(6)  | -0.0081(5) | -0.0084(5) | -0.0044(5) |
| C89  | 0.0491(7)  | 0.0273(5) | 0.0297(6)  | -0.0028(4) | -0.0109(5) | -0.0119(5) |
| C90  | 0.0475(7)  | 0.0352(6) | 0.0318(6)  | 0.0008(5)  | 0.0011(5)  | -0.0144(6) |
| C238 | 0.0363(6)  | 0.0304(6) | 0.0323(6)  | -0.0025(5) | 0.0024(5)  | -0.0074(5) |
| C101 | 0.0301(5)  | 0.0302(5) | 0.0271(5)  | -0.0046(4) | 0.0038(4)  | -0.0130(4) |
| C102 | 0.0305(6)  | 0.0302(5) | 0.0314(6)  | -0.0050(4) | 0.0004(4)  | -0.0137(5) |
| C103 | 0.0368(6)  | 0.0368(6) | 0.0377(6)  | -0.0052(5) | 0.0036(5)  | -0.0091(5) |
| C104 | 0.0384(7)  | 0.0369(7) | 0.0529(8)  | -0.0024(6) | -0.0034(6) | -0.0063(5) |
| C105 | 0.0526(8)  | 0.0315(6) | 0.0459(7)  | 0.0011(5)  | -0.0158(6) | -0.0171(6) |
| C106 | 0.0578(8)  | 0.0376(6) | 0.0319(6)  | -0.0043(5) | -0.0053(6) | -0.0181(6) |
| C107 | 0.0393(6)  | 0.0358(6) | 0.0316(6)  | -0.0064(5) | 0.0006(5)  | -0.0109(5) |
| C108 | 0.0828(12) | 0.0422(8) | 0.0632(10) | 0.0044(7)  | -0.0348(9) | -0.0137(8) |
| C109 | 0.0289(5)  | 0.0266(5) | 0.0311(6)  | -0.0064(4) | 0.0026(4)  | -0.0091(4) |
| C110 | 0.0338(6)  | 0.0300(5) | 0.0325(6)  | -0.0016(4) | -0.0006(5) | -0.0112(5) |
| C111 | 0.0348(6)  | 0.0350(6) | 0.0322(6)  | -0.0046(5) | -0.0041(5) | -0.0091(5) |
| C112 | 0.0335(6)  | 0.0316(6) | 0.0431(7)  | -0.0074(5) | -0.0043(5) | -0.0105(5) |
| C113 | 0.0418(7)  | 0.0360(6) | 0.0401(7)  | -0.0019(5) | 0.0004(5)  | -0.0201(5) |
| C114 | 0.0389(6)  | 0.0348(6) | 0.0306(6)  | -0.0033(5) | 0.0013(5)  | -0.0162(5) |
| C115 | 0.0606(9)  | 0.0561(9) | 0.0551(9)  | -0.0057(7) | -0.0137(7) | -0.0322(8) |
| C116 | 0.0319(6)  | 0.0299(5) | 0.0274(5)  | -0.0037(4) | 0.0002(4)  | -0.0121(5) |
| C117 | 0.0335(6)  | 0.0346(6) | 0.0443(7)  | -0.0080(5) | -0.0010(5) | -0.0140(5) |
| C118 | 0.0440(7)  | 0.0326(6) | 0.0426(7)  | -0.0072(5) | -0.0049(5) | -0.0165(5) |
| C119 | 0.0442(7)  | 0.0322(6) | 0.0300(6)  | -0.0053(5) | -0.0024(5) | -0.0097(5) |
| C120 | 0.0326(6)  | 0.0449(7) | 0.0487(8)  | -0.0171(6) | 0.0015(5)  | -0.0094(5) |
| C121 | 0.0332(6)  | 0.0415(7) | 0.0450(7)  | -0.0158(5) | 0.0010(5)  | -0.0157(5) |
| C122 | 0.0579(9)  | 0.0389(7) | 0.0499(8)  | -0.0152(6) | -0.0011(7) | -0.0075(6) |
| O1   | 0.0462(5)  | 0.0362(4) | 0.0242(4)  | -0.0047(3) | 0.0015(3)  | -0.0241(4) |
| O2   | 0.0390(5)  | 0.0365(4) | 0.0331(4)  | -0.0146(3) | 0.0111(3)  | -0.0159(4) |
| O3   | 0.0430(5)  | 0.0274(4) | 0.0232(4)  | -0.0044(3) | 0.0019(3)  | -0.0055(3) |
| O4   | 0.0348(4)  | 0.0340(4) | 0.0307(4)  | -0.0061(3) | 0.0075(3)  | -0.0166(3) |
| F1   | 0.0427(4)  | 0.0540(4) | 0.0285(3)  | -0.0115(3) | 0.0043(3)  | -0.0275(3) |
| F2   | 0.0425(4)  | 0.0333(4) | 0.0286(3)  | -0.0020(3) | 0.0031(3)  | -0.0038(3) |
| N201 | 0.0317(5)  | 0.0231(4) | 0.0327(5)  | -0.0017(4) | -0.0013(4) | -0.0089(4) |

|      |            |            |            |            |            |            |
|------|------------|------------|------------|------------|------------|------------|
| C202 | 0.0346(6)  | 0.0235(5)  | 0.0380(6)  | -0.0023(4) | -0.0041(5) | -0.0063(5) |
| C203 | 0.0381(7)  | 0.0370(6)  | 0.0406(7)  | -0.0064(5) | 0.0009(5)  | -0.0098(5) |
| C204 | 0.0386(7)  | 0.0459(8)  | 0.0597(9)  | -0.0118(7) | -0.0003(6) | -0.0041(6) |
| C205 | 0.0413(8)  | 0.0808(12) | 0.0618(10) | -0.0174(9) | 0.0041(7)  | -0.0053(8) |
| C206 | 0.0350(6)  | 0.0247(5)  | 0.0373(6)  | -0.0053(4) | -0.0013(5) | -0.0104(5) |
| C207 | 0.0432(7)  | 0.0395(7)  | 0.0384(7)  | -0.0060(5) | -0.0047(5) | -0.0139(6) |
| C208 | 0.0504(8)  | 0.0472(8)  | 0.0515(8)  | -0.0128(6) | -0.0105(6) | -0.0177(6) |
| C209 | 0.0547(9)  | 0.0779(11) | 0.0546(9)  | -0.0211(8) | -0.0089(7) | -0.0282(8) |
| C210 | 0.0366(6)  | 0.0264(5)  | 0.0337(6)  | -0.0002(4) | -0.0040(5) | -0.0100(5) |
| C211 | 0.0440(7)  | 0.0288(6)  | 0.0401(7)  | -0.0046(5) | -0.0062(5) | -0.0116(5) |
| C212 | 0.0365(6)  | 0.0360(6)  | 0.0386(7)  | -0.0077(5) | -0.0034(5) | -0.0098(5) |
| C213 | 0.0644(10) | 0.0474(8)  | 0.0546(9)  | -0.0082(7) | -0.0170(7) | -0.0219(7) |
| C214 | 0.0357(6)  | 0.0302(6)  | 0.0361(6)  | -0.0008(5) | 0.0011(5)  | -0.0130(5) |
| C215 | 0.0366(7)  | 0.0386(7)  | 0.0504(8)  | -0.0050(6) | 0.0023(6)  | -0.0102(5) |
| C216 | 0.0420(8)  | 0.0512(8)  | 0.0667(10) | -0.0196(7) | 0.0147(7)  | -0.0213(7) |
| C217 | 0.0579(10) | 0.0531(9)  | 0.0605(10) | -0.0113(7) | 0.0167(8)  | -0.0208(8) |
| N221 | 0.0388(5)  | 0.0328(5)  | 0.0340(5)  | -0.0122(4) | -0.0020(4) | -0.0168(4) |
| C222 | 0.0421(7)  | 0.0361(6)  | 0.0396(6)  | -0.0082(5) | -0.0082(5) | -0.0206(5) |
| C223 | 0.0414(7)  | 0.0428(7)  | 0.0397(7)  | -0.0077(5) | -0.0053(5) | -0.0209(6) |
| C224 | 0.0457(8)  | 0.0663(10) | 0.0532(8)  | -0.0134(7) | -0.0065(6) | -0.0305(7) |
| C225 | 0.0479(8)  | 0.0874(12) | 0.0440(8)  | -0.0135(8) | -0.0029(6) | -0.0342(8) |
| C226 | 0.0400(6)  | 0.0322(6)  | 0.0393(6)  | -0.0117(5) | -0.0002(5) | -0.0180(5) |
| C227 | 0.0526(8)  | 0.0402(7)  | 0.0399(7)  | -0.0082(5) | -0.0045(6) | -0.0214(6) |
| C228 | 0.0545(9)  | 0.0389(7)  | 0.0624(9)  | -0.0057(6) | -0.0180(7) | -0.0167(6) |
| C229 | 0.0614(10) | 0.0498(9)  | 0.0633(10) | -0.0007(7) | -0.0174(8) | -0.0180(8) |
| C230 | 0.0363(6)  | 0.0392(6)  | 0.0350(6)  | -0.0129(5) | -0.0028(5) | -0.0174(5) |
| C231 | 0.0451(7)  | 0.0389(7)  | 0.0415(7)  | -0.0080(5) | -0.0068(5) | -0.0188(6) |
| C232 | 0.0357(6)  | 0.0456(7)  | 0.0410(7)  | -0.0065(5) | -0.0029(5) | -0.0191(6) |
| C233 | 0.0566(9)  | 0.0485(8)  | 0.0586(9)  | -0.0011(7) | -0.0172(7) | -0.0184(7) |
| C234 | 0.0466(7)  | 0.0353(6)  | 0.0371(6)  | -0.0151(5) | 0.0001(5)  | -0.0140(5) |
| C235 | 0.0454(8)  | 0.0516(8)  | 0.0522(8)  | -0.0222(7) | 0.0065(6)  | -0.0167(6) |
| C236 | 0.0523(9)  | 0.0491(8)  | 0.0610(10) | -0.0192(7) | 0.0136(7)  | -0.0134(7) |
| C237 | 0.0607(10) | 0.0587(10) | 0.0611(10) | -0.0191(8) | 0.0133(8)  | -0.0225(8) |

## Distances

|     |      |             |  |     |      |             |
|-----|------|-------------|--|-----|------|-------------|
| C91 | C89  | 1.5093(16)Å |  | C91 | H912 | 0.949Å      |
| C91 | H911 | 0.961Å      |  | C91 | H913 | 0.933Å      |
| C11 | C12  | 1.5421(16)Å |  | C11 | C19  | 1.5419(16)Å |
| C11 | C26  | 1.5369(15)Å |  | C11 | O1   | 1.4172(13)Å |

|     |      |             |  |     |      |             |
|-----|------|-------------|--|-----|------|-------------|
| C12 | C13  | 1.3911(17)Å |  | C12 | C17  | 1.3973(16)Å |
| C13 | C14  | 1.3951(19)Å |  | C13 | H131 | 0.942Å      |
| C14 | C15  | 1.388(2)Å   |  | C14 | H141 | 0.950Å      |
| C15 | C16  | 1.388(2)Å   |  | C15 | C18  | 1.511(2)Å   |
| C16 | C17  | 1.3891(19)Å |  | C16 | H161 | 0.979Å      |
| C17 | H171 | 0.975Å      |  | C18 | H181 | 0.973Å      |
| C18 | H183 | 0.952Å      |  | C18 | H182 | 0.969Å      |
| C19 | C20  | 1.3926(17)Å |  | C19 | C24  | 1.3914(18)Å |
| C20 | C21  | 1.3918(19)Å |  | C20 | H201 | 0.933Å      |
| C21 | C22  | 1.385(2)Å   |  | C21 | H211 | 0.952Å      |
| C22 | C23  | 1.385(2)Å   |  | C22 | C25  | 1.5074(19)Å |
| C23 | C24  | 1.3923(19)Å |  | C23 | H231 | 0.987Å      |
| C24 | H241 | 0.950Å      |  | C25 | H253 | 0.963Å      |
| C25 | H252 | 0.962Å      |  | C25 | H251 | 0.962Å      |
| C26 | C27  | 1.3974(18)Å |  | C26 | C31  | 1.3837(18)Å |
| C27 | C28  | 1.3829(18)Å |  | C27 | H271 | 0.928Å      |
| C28 | C29  | 1.390(2)Å   |  | C28 | H281 | 0.947Å      |
| C29 | C30  | 1.381(2)Å   |  | C29 | C32  | 1.5133(19)Å |
| C30 | C31  | 1.3976(19)Å |  | C30 | H301 | 0.966Å      |
| C31 | H311 | 0.971Å      |  | C32 | H321 | 0.958Å      |
| C32 | H322 | 0.945Å      |  | C32 | H323 | 0.951Å      |
| C41 | C42  | 1.5413(17)Å |  | C41 | C49  | 1.5365(16)Å |
| C41 | C56  | 1.5345(15)Å |  | C41 | O2   | 1.4179(13)Å |
| C42 | C43  | 1.3899(17)Å |  | C42 | C47  | 1.3957(16)Å |
| C43 | C44  | 1.388(2)Å   |  | C43 | H431 | 0.965Å      |
| C44 | C45  | 1.390(2)Å   |  | C44 | H441 | 0.959Å      |
| C45 | C46  | 1.3860(19)Å |  | C45 | C48  | 1.5024(19)Å |
| C46 | C47  | 1.3866(18)Å |  | C46 | H461 | 0.965Å      |
| C47 | H471 | 0.954Å      |  | C48 | H481 | 0.963Å      |
| C48 | H482 | 0.972Å      |  | C48 | H483 | 0.959Å      |
| C49 | C50  | 1.3898(17)Å |  | C49 | C54  | 1.3894(17)Å |
| C50 | C51  | 1.3881(19)Å |  | C50 | H501 | 0.953Å      |
| C51 | C52  | 1.388(2)Å   |  | C51 | H511 | 0.956Å      |
| C52 | C53  | 1.3874(18)Å |  | C52 | C55  | 1.5054(18)Å |
| C53 | C54  | 1.3880(18)Å |  | C53 | H531 | 0.954Å      |
| C54 | H541 | 0.962Å      |  | C55 | H552 | 0.975Å      |
| C55 | H551 | 0.966Å      |  | C55 | H553 | 0.963Å      |
| C56 | C57  | 1.3873(17)Å |  | C56 | C61  | 1.3874(17)Å |
| C57 | C58  | 1.3869(18)Å |  | C57 | H571 | 0.958Å      |
| C58 | C59  | 1.388(2)Å   |  | C58 | H581 | 0.958Å      |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C59  | C60   | 1.3842(19)Å |  | C59  | C62   | 1.5075(18)Å |
| C60  | C61   | 1.3908(17)Å |  | C60  | H601  | 0.975Å      |
| C61  | H611  | 0.957Å      |  | C62  | H623  | 0.966Å      |
| C62  | H622  | 0.958Å      |  | C62  | H621  | 0.972Å      |
| C71  | C72   | 1.5414(16)Å |  | C71  | C79   | 1.5407(16)Å |
| C71  | C86   | 1.5405(15)Å |  | C71  | O3    | 1.4160(13)Å |
| C72  | C73   | 1.3952(17)Å |  | C72  | C77   | 1.3913(18)Å |
| C73  | C74   | 1.391(2)Å   |  | C73  | H731  | 0.964Å      |
| C74  | C75   | 1.384(2)Å   |  | C74  | H741  | 0.950Å      |
| C75  | C76   | 1.390(2)Å   |  | C75  | C78   | 1.512(2)Å   |
| C76  | C77   | 1.3883(19)Å |  | C76  | H761  | 0.946Å      |
| C77  | H771  | 0.964Å      |  | C78  | H781  | 0.956Å      |
| C78  | H782  | 0.947Å      |  | C78  | H783  | 0.957Å      |
| C79  | C80   | 1.3892(17)Å |  | C79  | C84   | 1.3951(17)Å |
| C80  | C81   | 1.3954(19)Å |  | C80  | H801  | 0.944Å      |
| C81  | C82   | 1.384(2)Å   |  | C81  | H811  | 0.945Å      |
| C82  | C83   | 1.389(2)Å   |  | C82  | C85   | 1.5156(19)Å |
| C83  | C84   | 1.3906(18)Å |  | C83  | H831  | 0.971Å      |
| C84  | H841  | 0.972Å      |  | C85  | H853  | 0.964Å      |
| C85  | H852  | 0.976Å      |  | C85  | H851  | 0.951Å      |
| C86  | C87   | 1.3954(16)Å |  | C86  | C238  | 1.3844(16)Å |
| C87  | C88   | 1.3878(17)Å |  | C87  | H871  | 0.954Å      |
| C88  | C89   | 1.3914(18)Å |  | C88  | H881  | 0.957Å      |
| C89  | C90   | 1.3830(19)Å |  | C90  | C238  | 1.3988(17)Å |
| C90  | H901  | 0.957Å      |  | C238 | H2381 | 0.953Å      |
| C101 | C102  | 1.5402(16)Å |  | C101 | C109  | 1.5351(16)Å |
| C101 | C116  | 1.5334(16)Å |  | C101 | O4    | 1.4219(13)Å |
| C102 | C103  | 1.3877(17)Å |  | C102 | C107  | 1.3913(17)Å |
| C103 | C104  | 1.3878(19)Å |  | C103 | H1031 | 0.963Å      |
| C104 | C105  | 1.385(2)Å   |  | C104 | H1041 | 0.957Å      |
| C105 | C106  | 1.384(2)Å   |  | C105 | C108  | 1.506(2)Å   |
| C106 | C107  | 1.3885(18)Å |  | C106 | H1061 | 0.962Å      |
| C107 | H1071 | 0.956Å      |  | C108 | H1081 | 0.970Å      |
| C108 | H1083 | 0.970Å      |  | C108 | H1082 | 0.979Å      |
| C109 | C110  | 1.3919(17)Å |  | C109 | C114  | 1.3936(16)Å |
| C110 | C111  | 1.3871(17)Å |  | C110 | H1101 | 0.957Å      |
| C111 | C112  | 1.3898(18)Å |  | C111 | H1111 | 0.953Å      |
| C112 | C113  | 1.3877(19)Å |  | C112 | C115  | 1.5076(18)Å |
| C113 | C114  | 1.3871(18)Å |  | C113 | H1131 | 0.951Å      |
| C114 | H1141 | 0.974Å      |  | C115 | H1151 | 0.930Å      |



|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C115 | H1152 | 0.924Å      |  | C115 | H1153 | 0.952Å      |
| C116 | C117  | 1.3881(17)Å |  | C116 | C121  | 1.3862(17)Å |
| C117 | C118  | 1.3866(18)Å |  | C117 | H1171 | 0.974Å      |
| C118 | C119  | 1.3882(19)Å |  | C118 | H1181 | 0.970Å      |
| C119 | C120  | 1.3811(19)Å |  | C119 | C122  | 1.5059(18)Å |
| C120 | C121  | 1.3920(18)Å |  | C120 | H1201 | 0.964Å      |
| C121 | H1211 | 0.953Å      |  | C122 | H1223 | 0.979Å      |
| C122 | H1221 | 0.969Å      |  | C122 | H1222 | 0.989Å      |
| O1   | H11   | 0.875Å      |  | O2   | H21   | 0.880Å      |
| O3   | H31   | 0.869Å      |  | O4   | H41   | 0.860Å      |
| N201 | C202  | 1.5192(14)Å |  | N201 | C206  | 1.5162(14)Å |
| N201 | C210  | 1.5173(15)Å |  | N201 | C214  | 1.5239(15)Å |
| C202 | C203  | 1.5134(17)Å |  | C202 | H2021 | 0.965Å      |
| C202 | H2022 | 0.976Å      |  | C203 | C204  | 1.5207(19)Å |
| C203 | H2031 | 0.955Å      |  | C203 | H2032 | 0.969Å      |
| C204 | C205  | 1.514(2)Å   |  | C204 | H2041 | 0.983Å      |
| C204 | H2042 | 0.980Å      |  | C205 | H2051 | 0.976Å      |
| C205 | H2052 | 0.995Å      |  | C205 | H2053 | 0.988Å      |
| C206 | C207  | 1.5151(18)Å |  | C206 | H2061 | 0.962Å      |
| C206 | H2062 | 0.975Å      |  | C207 | C208  | 1.5213(19)Å |
| C207 | H2071 | 0.985Å      |  | C207 | H2072 | 0.973Å      |
| C208 | C209  | 1.511(2)Å   |  | C208 | H2081 | 0.970Å      |
| C208 | H2082 | 0.979Å      |  | C209 | H2091 | 0.973Å      |
| C209 | H2092 | 0.986Å      |  | C209 | H2093 | 0.960Å      |
| C210 | C211  | 1.5134(17)Å |  | C210 | H2101 | 0.983Å      |
| C210 | H2102 | 0.975Å      |  | C211 | C212  | 1.5236(18)Å |
| C211 | H2111 | 0.971Å      |  | C211 | H2112 | 0.997Å      |
| C212 | C213  | 1.5164(19)Å |  | C212 | H2121 | 0.979Å      |
| C212 | H2122 | 0.998Å      |  | C213 | H2133 | 0.971Å      |
| C213 | H2132 | 0.968Å      |  | C213 | H2131 | 0.991Å      |
| C214 | C215  | 1.5184(18)Å |  | C214 | H2141 | 0.985Å      |
| C214 | H2142 | 0.991Å      |  | C215 | C216  | 1.5331(19)Å |
| C215 | H2151 | 0.988Å      |  | C215 | H2152 | 0.977Å      |
| C216 | C217  | 1.510(3)Å   |  | C216 | H2161 | 0.994Å      |
| C216 | H2162 | 0.977Å      |  | C217 | H2173 | 0.974Å      |
| C217 | H2172 | 0.978Å      |  | C217 | H2171 | 0.986Å      |
| N221 | C222  | 1.5213(15)Å |  | N221 | C226  | 1.5170(15)Å |
| N221 | C230  | 1.5172(15)Å |  | N221 | C234  | 1.5265(16)Å |
| C222 | C223  | 1.5170(19)Å |  | C222 | H2221 | 0.962Å      |
| C222 | H2222 | 0.964Å      |  | C223 | C224  | 1.5195(18)Å |

|      |       |             |  |      |       |             |  |
|------|-------|-------------|--|------|-------|-------------|--|
| C223 | H2231 | 0.967Å      |  | C223 | H2232 | 0.981Å      |  |
| C224 | C225  | 1.520(2)Å   |  | C224 | H2241 | 0.960Å      |  |
| C224 | H2242 | 1.005Å      |  | C225 | H2253 | 0.959Å      |  |
| C225 | H2252 | 0.977Å      |  | C225 | H2251 | 0.984Å      |  |
| C226 | C227  | 1.5172(19)Å |  | C226 | H2261 | 0.974Å      |  |
| C226 | H2262 | 0.981Å      |  | C227 | C228  | 1.5163(19)Å |  |
| C227 | H2271 | 0.971Å      |  | C227 | H2272 | 0.961Å      |  |
| C228 | C229  | 1.511(2)Å   |  | C228 | H2281 | 0.977Å      |  |
| C228 | H2282 | 0.992Å      |  | C229 | H2291 | 0.986Å      |  |
| C229 | H2292 | 1.005Å      |  | C229 | H2293 | 0.990Å      |  |
| C230 | C231  | 1.5127(18)Å |  | C230 | H2301 | 0.969Å      |  |
| C230 | H2302 | 0.977Å      |  | C231 | C232  | 1.5236(18)Å |  |
| C231 | H2311 | 0.975Å      |  | C231 | H2312 | 0.998Å      |  |
| C232 | C233  | 1.515(2)Å   |  | C232 | H2321 | 0.996Å      |  |
| C232 | H2322 | 0.965Å      |  | C233 | H2331 | 0.977Å      |  |
| C233 | H2332 | 0.982Å      |  | C233 | H2333 | 0.978Å      |  |
| C234 | C235  | 1.522(2)Å   |  | C234 | H2341 | 0.983Å      |  |
| C234 | H2342 | 0.971Å      |  | C235 | C236  | 1.540(2)Å   |  |
| C235 | H2351 | 1.000Å      |  | C235 | H2352 | 0.974Å      |  |
| C236 | C237  | 1.504(3)Å   |  | C236 | H2361 | 0.998Å      |  |
| C236 | H2362 | 1.009Å      |  | C237 | H2373 | 1.000Å      |  |
| C237 | H2372 | 0.995Å      |  | C237 | H2371 | 0.997Å      |  |

## Angles

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C89  | C91 | H912 | 114.093°    |  | C89  | C91 | H911 | 110.884°    |
| H912 | C91 | H911 | 103.890°    |  | C89  | C91 | H913 | 113.381°    |
| H912 | C91 | H913 | 110.463°    |  | H911 | C91 | H913 | 103.158°    |
| C12  | C11 | C19  | 109.90(9)°  |  | C12  | C11 | C26  | 112.26(9)°  |
| C19  | C11 | C26  | 108.66(9)°  |  | C12  | C11 | O1   | 110.69(9)°  |
| C19  | C11 | O1   | 111.03(9)°  |  | C26  | C11 | O1   | 104.17(8)°  |
| C11  | C12 | C13  | 120.36(10)° |  | C11  | C12 | C17  | 122.07(11)° |
| C13  | C12 | C17  | 117.56(11)° |  | C12  | C13 | C14  | 120.76(12)° |
| C12  | C13 | H131 | 118.574°    |  | C14  | C13 | H131 | 120.628°    |
| C13  | C14 | C15  | 121.65(13)° |  | C13  | C14 | H141 | 118.781°    |
| C15  | C14 | H141 | 119.561°    |  | C14  | C15 | C16  | 117.47(12)° |
| C14  | C15 | C18  | 121.58(15)° |  | C16  | C15 | C18  | 120.94(14)° |
| C15  | C16 | C17  | 121.37(13)° |  | C15  | C16 | H161 | 118.633°    |
| C17  | C16 | H161 | 119.984°    |  | C12  | C17 | C16  | 121.19(13)° |
| C12  | C17 | H171 | 119.325°    |  | C16  | C17 | H171 | 119.489°    |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C15  | C18 | H181 | 112.038°    |  | C15  | C18 | H183 | 109.143°    |
| H181 | C18 | H183 | 107.098°    |  | C15  | C18 | H182 | 112.430°    |
| H181 | C18 | H182 | 108.816°    |  | H183 | C18 | H182 | 107.060°    |
| C11  | C19 | C20  | 120.42(11)° |  | C11  | C19 | C24  | 121.46(11)° |
| C20  | C19 | C24  | 118.11(12)° |  | C19  | C20 | C21  | 120.10(13)° |
| C19  | C20 | H201 | 119.668°    |  | C21  | C20 | H201 | 120.226°    |
| C20  | C21 | C22  | 121.99(13)° |  | C20  | C21 | H211 | 118.222°    |
| C22  | C21 | H211 | 119.787°    |  | C21  | C22 | C23  | 117.71(12)° |
| C21  | C22 | C25  | 121.12(16)° |  | C23  | C22 | C25  | 121.17(16)° |
| C22  | C23 | C24  | 120.98(14)° |  | C22  | C23 | H231 | 119.861°    |
| C24  | C23 | H231 | 119.128°    |  | C19  | C24 | C23  | 121.09(13)° |
| C19  | C24 | H241 | 119.532°    |  | C23  | C24 | H241 | 119.379°    |
| C22  | C25 | H253 | 110.560°    |  | C22  | C25 | H252 | 111.262°    |
| H253 | C25 | H252 | 108.775°    |  | C22  | C25 | H251 | 110.403°    |
| H253 | C25 | H251 | 107.396°    |  | H252 | C25 | H251 | 108.329°    |
| C11  | C26 | C27  | 117.35(11)° |  | C11  | C26 | C31  | 124.55(11)° |
| C27  | C26 | C31  | 118.09(11)° |  | C26  | C27 | C28  | 120.92(13)° |
| C26  | C27 | H271 | 119.317°    |  | C28  | C27 | H271 | 119.759°    |
| C27  | C28 | C29  | 121.23(13)° |  | C27  | C28 | H281 | 118.272°    |
| C29  | C28 | H281 | 120.472°    |  | C28  | C29 | C30  | 117.72(12)° |
| C28  | C29 | C32  | 121.19(15)° |  | C30  | C29 | C32  | 121.08(15)° |
| C29  | C30 | C31  | 121.57(13)° |  | C29  | C30 | H301 | 119.148°    |
| C31  | C30 | H301 | 119.268°    |  | C26  | C31 | C30  | 120.43(13)° |
| C26  | C31 | H311 | 120.693°    |  | C30  | C31 | H311 | 118.872°    |
| C29  | C32 | H321 | 112.281°    |  | C29  | C32 | H322 | 109.880°    |
| H321 | C32 | H322 | 106.112°    |  | C29  | C32 | H323 | 112.900°    |
| H321 | C32 | H323 | 107.626°    |  | H322 | C32 | H323 | 107.716°    |
| C42  | C41 | C49  | 109.08(9)°  |  | C42  | C41 | C56  | 109.02(9)°  |
| C49  | C41 | C56  | 111.61(10)° |  | C42  | C41 | O2   | 110.69(10)° |
| C49  | C41 | O2   | 110.96(9)°  |  | C56  | C41 | O2   | 105.44(9)°  |
| C41  | C42 | C43  | 120.18(10)° |  | C41  | C42 | C47  | 121.76(10)° |
| C43  | C42 | C47  | 117.99(12)° |  | C42  | C43 | C44  | 120.46(12)° |
| C42  | C43 | H431 | 119.441°    |  | C44  | C43 | H431 | 120.099°    |
| C43  | C44 | C45  | 121.77(12)° |  | C43  | C44 | H441 | 118.495°    |
| C45  | C44 | H441 | 119.731°    |  | C44  | C45 | C46  | 117.52(12)° |
| C44  | C45 | C48  | 122.21(13)° |  | C46  | C45 | C48  | 120.25(13)° |
| C45  | C46 | C47  | 121.29(12)° |  | C45  | C46 | H461 | 119.212°    |
| C47  | C46 | H461 | 119.484°    |  | C42  | C47 | C46  | 120.96(12)° |
| C42  | C47 | H471 | 120.526°    |  | C46  | C47 | H471 | 118.514°    |
| C45  | C48 | H481 | 111.562°    |  | C45  | C48 | H482 | 110.024°    |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| H481 | C48 | H482 | 105.421°    |  | C45  | C48 | H483 | 111.332°    |
| H481 | C48 | H483 | 108.973°    |  | H482 | C48 | H483 | 109.341°    |
| C41  | C49 | C50  | 120.57(11)° |  | C41  | C49 | C54  | 121.66(10)° |
| C50  | C49 | C54  | 117.77(11)° |  | C49  | C50 | C51  | 120.55(12)° |
| C49  | C50 | H501 | 119.080°    |  | C51  | C50 | H501 | 120.334°    |
| C50  | C51 | C52  | 121.86(11)° |  | C50  | C51 | H511 | 118.421°    |
| C52  | C51 | H511 | 119.672°    |  | C51  | C52 | C53  | 117.36(12)° |
| C51  | C52 | C55  | 120.74(12)° |  | C53  | C52 | C55  | 121.86(13)° |
| C52  | C53 | C54  | 121.12(12)° |  | C52  | C53 | H531 | 119.190°    |
| C54  | C53 | H531 | 119.692°    |  | C49  | C54 | C53  | 121.30(12)° |
| C49  | C54 | H541 | 119.799°    |  | C53  | C54 | H541 | 118.896°    |
| C52  | C55 | H552 | 111.537°    |  | C52  | C55 | H551 | 110.758°    |
| H552 | C55 | H551 | 107.239°    |  | C52  | C55 | H553 | 111.259°    |
| H552 | C55 | H553 | 109.077°    |  | H551 | C55 | H553 | 106.774°    |
| C41  | C56 | C57  | 117.82(11)° |  | C41  | C56 | C61  | 124.24(11)° |
| C57  | C56 | C61  | 117.83(11)° |  | C56  | C57 | C58  | 121.10(12)° |
| C56  | C57 | H571 | 119.445°    |  | C58  | C57 | H571 | 119.455°    |
| C57  | C58 | C59  | 121.30(12)° |  | C57  | C58 | H581 | 119.095°    |
| C59  | C58 | H581 | 119.599°    |  | C58  | C59 | C60  | 117.45(12)° |
| C58  | C59 | C62  | 121.35(13)° |  | C60  | C59 | C62  | 121.20(13)° |
| C59  | C60 | C61  | 121.52(12)° |  | C59  | C60 | H601 | 119.512°    |
| C61  | C60 | H601 | 118.970°    |  | C56  | C61 | C60  | 120.79(12)° |
| C56  | C61 | H611 | 119.984°    |  | C60  | C61 | H611 | 119.224°    |
| C59  | C62 | H623 | 111.074°    |  | C59  | C62 | H622 | 111.507°    |
| H623 | C62 | H622 | 104.659°    |  | C59  | C62 | H621 | 112.657°    |
| H623 | C62 | H621 | 107.088°    |  | H622 | C62 | H621 | 109.462°    |
| C72  | C71 | C79  | 109.53(9)°  |  | C72  | C71 | C86  | 109.38(9)°  |
| C79  | C71 | C86  | 112.02(9)°  |  | C72  | C71 | O3   | 110.95(9)°  |
| C79  | C71 | O3   | 110.76(9)°  |  | C86  | C71 | O3   | 104.12(8)°  |
| C71  | C72 | C73  | 120.01(11)° |  | C71  | C72 | C77  | 121.88(10)° |
| C73  | C72 | C77  | 118.09(12)° |  | C72  | C73 | C74  | 120.01(14)° |
| C72  | C73 | H731 | 120.002°    |  | C74  | C73 | H731 | 119.977°    |
| C73  | C74 | C75  | 122.09(14)° |  | C73  | C74 | H741 | 118.414°    |
| C75  | C74 | H741 | 119.487°    |  | C74  | C75 | C76  | 117.64(13)° |
| C74  | C75 | C78  | 121.48(17)° |  | C76  | C75 | C78  | 120.87(17)° |
| C75  | C76 | C77  | 120.96(14)° |  | C75  | C76 | H761 | 120.106°    |
| C77  | C76 | H761 | 118.934°    |  | C72  | C77 | C76  | 121.20(13)° |
| C72  | C77 | H771 | 120.229°    |  | C76  | C77 | H771 | 118.574°    |
| C75  | C78 | H781 | 111.901°    |  | C75  | C78 | H782 | 110.899°    |
| H781 | C78 | H782 | 105.822°    |  | C75  | C78 | H783 | 114.020°    |

|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| H781  | C78  | H783  | 107.735°    |  | H782  | C78  | H783  | 105.964°    |
| C71   | C79  | C80   | 120.20(10)° |  | C71   | C79  | C84   | 122.24(10)° |
| C80   | C79  | C84   | 117.57(11)° |  | C79   | C80  | C81   | 120.89(12)° |
| C79   | C80  | H801  | 119.888°    |  | C81   | C80  | H801  | 119.223°    |
| C80   | C81  | C82   | 121.56(13)° |  | C80   | C81  | H811  | 118.086°    |
| C82   | C81  | H811  | 120.333°    |  | C81   | C82  | C83   | 117.56(12)° |
| C81   | C82  | C85   | 121.65(14)° |  | C83   | C82  | C85   | 120.77(15)° |
| C82   | C83  | C84   | 121.28(13)° |  | C82   | C83  | H831  | 120.150°    |
| C84   | C83  | H831  | 118.569°    |  | C79   | C84  | C83   | 121.14(12)° |
| C79   | C84  | H841  | 119.960°    |  | C83   | C84  | H841  | 118.893°    |
| C82   | C85  | H853  | 110.619°    |  | C82   | C85  | H852  | 110.630°    |
| H853  | C85  | H852  | 108.461°    |  | C82   | C85  | H851  | 108.023°    |
| H853  | C85  | H851  | 108.802°    |  | H852  | C85  | H851  | 110.292°    |
| C71   | C86  | C87   | 117.33(10)° |  | C71   | C86  | C238  | 124.66(10)° |
| C87   | C86  | C238  | 117.99(10)° |  | C86   | C87  | C88   | 121.31(11)° |
| C86   | C87  | H871  | 119.435°    |  | C88   | C87  | H871  | 119.256°    |
| C87   | C88  | C89   | 120.79(11)° |  | C87   | C88  | H881  | 119.921°    |
| C89   | C88  | H881  | 119.279°    |  | C91   | C89  | C88   | 120.75(12)° |
| C91   | C89  | C90   | 121.40(12)° |  | C88   | C89  | C90   | 117.85(11)° |
| C89   | C90  | C238  | 121.62(12)° |  | C89   | C90  | H901  | 119.867°    |
| C238  | C90  | H901  | 118.510°    |  | C86   | C238 | C90   | 120.43(12)° |
| C86   | C238 | H2381 | 120.042°    |  | C90   | C238 | H2381 | 119.523°    |
| C102  | C101 | C109  | 110.10(9)°  |  | C102  | C101 | C116  | 108.78(9)°  |
| C109  | C101 | C116  | 112.11(9)°  |  | C102  | C101 | O4    | 110.21(9)°  |
| C109  | C101 | O4    | 110.36(9)°  |  | C116  | C101 | O4    | 105.16(9)°  |
| C101  | C102 | C103  | 120.01(11)° |  | C101  | C102 | C107  | 121.84(11)° |
| C103  | C102 | C107  | 118.14(11)° |  | C102  | C103 | C104  | 120.45(12)° |
| C102  | C103 | H1031 | 118.771°    |  | C104  | C103 | H1031 | 120.770°    |
| C103  | C104 | C105  | 121.53(13)° |  | C103  | C104 | H1041 | 118.692°    |
| C105  | C104 | H1041 | 119.780°    |  | C104  | C105 | C106  | 117.93(12)° |
| C104  | C105 | C108  | 121.24(15)° |  | C106  | C105 | C108  | 120.81(14)° |
| C105  | C106 | C107  | 120.93(13)° |  | C105  | C106 | H1061 | 120.112°    |
| C107  | C106 | H1061 | 118.933°    |  | C102  | C107 | C106  | 120.95(12)° |
| C102  | C107 | H1071 | 120.158°    |  | C106  | C107 | H1071 | 118.893°    |
| C105  | C108 | H1081 | 111.704°    |  | C105  | C108 | H1083 | 109.373°    |
| H1081 | C108 | H1083 | 106.045°    |  | C105  | C108 | H1082 | 111.085°    |
| H1081 | C108 | H1082 | 109.120°    |  | H1083 | C108 | H1082 | 109.370°    |
| C101  | C109 | C110  | 119.94(10)° |  | C101  | C109 | C114  | 122.31(11)° |
| C110  | C109 | C114  | 117.74(11)° |  | C109  | C110 | C111  | 120.89(11)° |
| C109  | C110 | H1101 | 119.828°    |  | C111  | C110 | H1101 | 119.284°    |

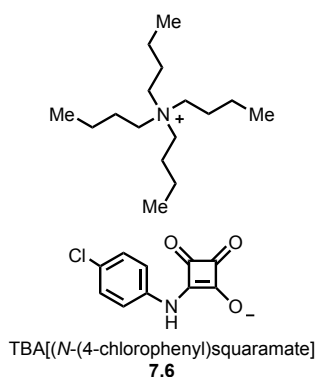
|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C110  | C111 | C112  | 121.37(12)° |  | C110  | C111 | H1111 | 119.344°    |
| C112  | C111 | H1111 | 119.284°    |  | C111  | C112 | C113  | 117.73(11)° |
| C111  | C112 | C115  | 120.25(12)° |  | C113  | C112 | C115  | 122.01(12)° |
| C112  | C113 | C114  | 121.18(11)° |  | C112  | C113 | H1131 | 119.049°    |
| C114  | C113 | H1131 | 119.762°    |  | C109  | C114 | C113  | 121.08(12)° |
| C109  | C114 | H1141 | 118.253°    |  | C113  | C114 | H1141 | 120.660°    |
| C112  | C115 | H1151 | 113.765°    |  | C112  | C115 | H1152 | 112.525°    |
| H1151 | C115 | H1152 | 112.599°    |  | C112  | C115 | H1153 | 110.146°    |
| H1151 | C115 | H1153 | 102.649°    |  | H1152 | C115 | H1153 | 104.220°    |
| C101  | C116 | C117  | 117.95(10)° |  | C101  | C116 | C121  | 124.31(10)° |
| C117  | C116 | C121  | 117.65(11)° |  | C116  | C117 | C118  | 121.18(12)° |
| C116  | C117 | H1171 | 118.420°    |  | C118  | C117 | H1171 | 120.401°    |
| C117  | C118 | C119  | 121.23(12)° |  | C117  | C118 | H1181 | 119.800°    |
| C119  | C118 | H1181 | 118.967°    |  | C118  | C119 | C120  | 117.56(12)° |
| C118  | C119 | C122  | 121.29(12)° |  | C120  | C119 | C122  | 121.14(13)° |
| C119  | C120 | C121  | 121.43(12)° |  | C119  | C120 | H1201 | 118.885°    |
| C121  | C120 | H1201 | 119.672°    |  | C116  | C121 | C120  | 120.94(12)° |
| C116  | C121 | H1211 | 119.081°    |  | C120  | C121 | H1211 | 119.953°    |
| C119  | C122 | H1223 | 112.525°    |  | C119  | C122 | H1221 | 112.132°    |
| H1223 | C122 | H1221 | 106.898°    |  | C119  | C122 | H1222 | 111.648°    |
| H1223 | C122 | H1222 | 107.116°    |  | H1221 | C122 | H1222 | 106.131°    |
| C11   | O1   | H11   | 113.086°    |  | C41   | O2   | H21   | 111.150°    |
| C71   | O3   | H31   | 110.611°    |  | C101  | O4   | H41   | 109.920°    |
| C202  | N201 | C206  | 111.83(9)°  |  | C202  | N201 | C210  | 111.01(9)°  |
| C206  | N201 | C210  | 105.67(8)°  |  | C202  | N201 | C214  | 106.27(8)°  |
| C206  | N201 | C214  | 110.85(9)°  |  | C210  | N201 | C214  | 111.30(9)°  |
| N201  | C202 | C203  | 116.56(10)° |  | N201  | C202 | H2021 | 105.846°    |
| C203  | C202 | H2021 | 109.086°    |  | N201  | C202 | H2022 | 106.530°    |
| C203  | C202 | H2022 | 109.792°    |  | H2021 | C202 | H2022 | 108.740°    |
| C202  | C203 | C204  | 109.68(11)° |  | C202  | C203 | H2031 | 110.748°    |
| C204  | C203 | H2031 | 109.761°    |  | C202  | C203 | H2032 | 110.778°    |
| C204  | C203 | H2032 | 108.787°    |  | H2031 | C203 | H2032 | 107.033°    |
| C203  | C204 | C205  | 113.32(14)° |  | C203  | C204 | H2041 | 109.492°    |
| C205  | C204 | H2041 | 109.884°    |  | C203  | C204 | H2042 | 108.221°    |
| C205  | C204 | H2042 | 107.258°    |  | H2041 | C204 | H2042 | 108.526°    |
| C204  | C205 | H2051 | 109.309°    |  | C204  | C205 | H2052 | 110.273°    |
| H2051 | C205 | H2052 | 108.598°    |  | C204  | C205 | H2053 | 111.302°    |
| H2051 | C205 | H2053 | 108.385°    |  | H2052 | C205 | H2053 | 108.912°    |
| N201  | C206 | C207  | 116.45(10)° |  | N201  | C206 | H2061 | 106.860°    |
| C207  | C206 | H2061 | 109.518°    |  | N201  | C206 | H2062 | 105.197°    |

|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C207  | C206 | H2062 | 108.061°    |  | H2061 | C206 | H2062 | 110.664°    |
| C206  | C207 | C208  | 108.82(11)° |  | C206  | C207 | H2071 | 110.608°    |
| C208  | C207 | H2071 | 110.015°    |  | C206  | C207 | H2072 | 110.717°    |
| C208  | C207 | H2072 | 109.745°    |  | H2071 | C207 | H2072 | 106.922°    |
| C207  | C208 | C209  | 113.45(13)° |  | C207  | C208 | H2081 | 108.866°    |
| C209  | C208 | H2081 | 110.080°    |  | C207  | C208 | H2082 | 107.695°    |
| C209  | C208 | H2082 | 108.345°    |  | H2081 | C208 | H2082 | 108.257°    |
| C208  | C209 | H2091 | 109.337°    |  | C208  | C209 | H2092 | 112.886°    |
| H2091 | C209 | H2092 | 108.283°    |  | C208  | C209 | H2093 | 110.455°    |
| H2091 | C209 | H2093 | 107.194°    |  | H2092 | C209 | H2093 | 108.503°    |
| N201  | C210 | C211  | 116.16(9)°  |  | N201  | C210 | H2101 | 107.089°    |
| C211  | C210 | H2101 | 110.158°    |  | N201  | C210 | H2102 | 105.338°    |
| C211  | C210 | H2102 | 111.188°    |  | H2101 | C210 | H2102 | 106.342°    |
| C210  | C211 | C212  | 109.43(10)° |  | C210  | C211 | H2111 | 112.195°    |
| C212  | C211 | H2111 | 108.826°    |  | C210  | C211 | H2112 | 110.073°    |
| C212  | C211 | H2112 | 109.210°    |  | H2111 | C211 | H2112 | 107.039°    |
| C211  | C212 | C213  | 111.76(11)° |  | C211  | C212 | H2121 | 109.798°    |
| C213  | C212 | H2121 | 108.946°    |  | C211  | C212 | H2122 | 109.067°    |
| C213  | C212 | H2122 | 110.232°    |  | H2121 | C212 | H2122 | 106.923°    |
| C212  | C213 | H2133 | 110.751°    |  | C212  | C213 | H2132 | 109.949°    |
| H2133 | C213 | H2132 | 107.106°    |  | C212  | C213 | H2131 | 111.002°    |
| H2133 | C213 | H2131 | 108.577°    |  | H2132 | C213 | H2131 | 109.360°    |
| N201  | C214 | C215  | 115.73(10)° |  | N201  | C214 | H2141 | 106.733°    |
| C215  | C214 | H2141 | 110.157°    |  | N201  | C214 | H2142 | 105.632°    |
| C215  | C214 | H2142 | 110.581°    |  | H2141 | C214 | H2142 | 107.607°    |
| C214  | C215 | C216  | 110.36(12)° |  | C214  | C215 | H2151 | 108.417°    |
| C216  | C215 | H2151 | 109.249°    |  | C214  | C215 | H2152 | 110.560°    |
| C216  | C215 | H2152 | 110.121°    |  | H2151 | C215 | H2152 | 108.072°    |
| C215  | C216 | C217  | 114.14(13)° |  | C215  | C216 | H2161 | 109.667°    |
| C217  | C216 | H2161 | 110.178°    |  | C215  | C216 | H2162 | 107.949°    |
| C217  | C216 | H2162 | 109.637°    |  | H2161 | C216 | H2162 | 104.834°    |
| C216  | C217 | H2173 | 112.864°    |  | C216  | C217 | H2172 | 109.947°    |
| H2173 | C217 | H2172 | 107.223°    |  | C216  | C217 | H2171 | 111.840°    |
| H2173 | C217 | H2171 | 108.128°    |  | H2172 | C217 | H2171 | 106.539°    |
| C222  | N221 | C226  | 111.38(10)° |  | C222  | N221 | C230  | 110.40(9)°  |
| C226  | N221 | C230  | 106.06(9)°  |  | C222  | N221 | C234  | 107.31(9)°  |
| C226  | N221 | C234  | 110.84(10)° |  | C230  | N221 | C234  | 110.90(10)° |
| N221  | C222 | C223  | 115.57(10)° |  | N221  | C222 | H2221 | 106.296°    |
| C223  | C222 | H2221 | 110.208°    |  | N221  | C222 | H2222 | 106.635°    |
| C223  | C222 | H2222 | 109.760°    |  | H2221 | C222 | H2222 | 108.055°    |

|       |      |       |             |  |       |      |       |          |
|-------|------|-------|-------------|--|-------|------|-------|----------|
| C222  | C223 | C224  | 111.01(11)° |  | C222  | C223 | H2231 | 110.976° |
| C224  | C223 | H2231 | 109.023°    |  | C222  | C223 | H2232 | 109.093° |
| C224  | C223 | H2232 | 108.351°    |  | H2231 | C223 | H2232 | 108.315° |
| C223  | C224 | C225  | 112.05(13)° |  | C223  | C224 | H2241 | 108.179° |
| C225  | C224 | H2241 | 109.148°    |  | C223  | C224 | H2242 | 106.753° |
| C225  | C224 | H2242 | 111.752°    |  | H2241 | C224 | H2242 | 108.838° |
| C224  | C225 | H2253 | 109.428°    |  | C224  | C225 | H2252 | 110.143° |
| H2253 | C225 | H2252 | 108.278°    |  | C224  | C225 | H2251 | 111.902° |
| H2253 | C225 | H2251 | 110.332°    |  | H2252 | C225 | H2251 | 106.665° |
| N221  | C226 | C227  | 116.37(10)° |  | N221  | C226 | H2261 | 105.345° |
| C227  | C226 | H2261 | 108.749°    |  | N221  | C226 | H2262 | 106.106° |
| C227  | C226 | H2262 | 110.686°    |  | H2261 | C226 | H2262 | 109.305° |
| C226  | C227 | C228  | 109.28(11)° |  | C226  | C227 | H2271 | 111.770° |
| C228  | C227 | H2271 | 108.475°    |  | C226  | C227 | H2272 | 110.922° |
| C228  | C227 | H2272 | 108.300°    |  | H2271 | C227 | H2272 | 107.998° |
| C227  | C228 | C229  | 113.80(13)° |  | C227  | C228 | H2281 | 108.382° |
| C229  | C228 | H2281 | 110.376°    |  | C227  | C228 | H2282 | 107.908° |
| C229  | C228 | H2282 | 106.541°    |  | H2281 | C228 | H2282 | 109.751° |
| C228  | C229 | H2291 | 110.092°    |  | C228  | C229 | H2292 | 112.522° |
| H2291 | C229 | H2292 | 108.314°    |  | C228  | C229 | H2293 | 109.904° |
| H2291 | C229 | H2293 | 106.914°    |  | H2292 | C229 | H2293 | 108.922° |
| N221  | C230 | C231  | 115.96(10)° |  | N221  | C230 | H2301 | 105.913° |
| C231  | C230 | H2301 | 110.764°    |  | N221  | C230 | H2302 | 106.536° |
| C231  | C230 | H2302 | 109.956°    |  | H2301 | C230 | H2302 | 107.269° |
| C230  | C231 | C232  | 109.55(11)° |  | C230  | C231 | H2311 | 109.639° |
| C232  | C231 | H2311 | 109.959°    |  | C230  | C231 | H2312 | 109.880° |
| C232  | C231 | H2312 | 109.673°    |  | H2311 | C231 | H2312 | 108.116° |
| C231  | C232 | C233  | 111.90(12)° |  | C231  | C232 | H2321 | 108.624° |
| C233  | C232 | H2321 | 109.739°    |  | C231  | C232 | H2322 | 110.119° |
| C233  | C232 | H2322 | 109.819°    |  | H2321 | C232 | H2322 | 106.488° |
| C232  | C233 | H2331 | 109.330°    |  | C232  | C233 | H2332 | 111.945° |
| H2331 | C233 | H2332 | 107.028°    |  | C232  | C233 | H2333 | 111.042° |
| H2331 | C233 | H2333 | 108.400°    |  | H2332 | C233 | H2333 | 108.954° |
| N221  | C234 | C235  | 115.21(10)° |  | N221  | C234 | H2341 | 106.333° |
| C235  | C234 | H2341 | 110.967°    |  | N221  | C234 | H2342 | 105.767° |
| C235  | C234 | H2342 | 110.804°    |  | H2341 | C234 | H2342 | 107.308° |
| C234  | C235 | C236  | 111.45(13)° |  | C234  | C235 | H2351 | 107.880° |
| C236  | C235 | H2351 | 108.785°    |  | C234  | C235 | H2352 | 109.396° |
| C236  | C235 | H2352 | 110.665°    |  | H2351 | C235 | H2352 | 108.576° |
| C235  | C236 | C237  | 113.92(14)° |  | C235  | C236 | H2361 | 110.186° |



|       |      |       |          |  |       |      |       |          |
|-------|------|-------|----------|--|-------|------|-------|----------|
| C237  | C236 | H2361 | 104.130° |  | C235  | C236 | H2362 | 110.236° |
| C237  | C236 | H2362 | 109.385° |  | H2361 | C236 | H2362 | 108.725° |
| C236  | C237 | H2373 | 108.783° |  | C236  | C237 | H2372 | 111.960° |
| H2373 | C237 | H2372 | 110.808° |  | C236  | C237 | H2371 | 108.067° |
| H2373 | C237 | H2371 | 108.867° |  | H2372 | C237 | H2371 | 108.271° |



**tetra-*n*-butylammonium** ***N*-(4-chlorophenyl)squaramate**  
**(TBA[*N*-(4-chlorophenyl)squaramate, 7.6):**

**X-ray** (single-crystal) Yellow needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.6** in THF, which had previously been prepared by dissolving **7.6** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 062GWP13

## Crystal Data

$a = 17.4111(6) \text{ \AA}$   $\alpha = 90^\circ$

$b = 20.7877(6) \text{ \AA}$   $\beta = 90^\circ$

$c = 14.7572(7) \text{ \AA}$   $\gamma = 90^\circ$

Volume  $5341.2(3) \text{ \AA}^3$

Space group  $P c c n$

Formula  $C_{26} H_{41} Cl_1 N_2 O_3$

Cell determined from 6524 reflections

Temperature 150K

Shape needle

Colour clear\_pale\_colourless

$D_x$   $1.16 \text{ Mg m}^{-3}$

$\mu$   $1.477 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$  0.60

Crystal Class orthorhombic

$Z = 8$

$M_r$  465.08

Cell  $\theta$  range =  $3 - 77^\circ$

Size  $0.02 \times 0.04 \times 0.20 \text{ mm}$

$F_{000}$  2016.000

$T_{\max}$  0.97

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 10427

Independent reflections 5615

$R_{\text{int}}$  0.0382

$\theta_{\max}$   $77.0734$

$h = -21 \rightarrow 21$

$k = -26 \rightarrow 23$

$l = -17 \rightarrow 18$

## Refinement

$\Delta\rho_{\min} = -0.53 \text{ e \AA}^{-3}$

$\Delta\rho_{\max} = 0.51 \text{ e \AA}^{-3}$

Reflections used 5592  
 Cutoff: I > -3.00σ(I)  
 Parameters refined 289  
 S = 1.07  
 R-factor 0.101  
 weighted R-factor 0.170  
 Δ/σ<sub>max</sub> 0.0003  
 Refinement on F<sup>2</sup>  
 w =  $\frac{1}{[\sigma^2(F_{\text{obs}}^2) + (0.030 \times P)^2 + 6.735 \times P + 0.000 + 0.000 \times \sin\theta]}$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| N1    | 0.11544(14) | 0.26699(12) | 0.61922(19) | 0.0352                 | 1.0000    |
| C2    | 0.13470(17) | 0.32911(14) | 0.6311(2)   | 0.0332                 | 1.0000    |
| C3    | 0.21071(18) | 0.35570(15) | 0.6360(2)   | 0.0368                 | 1.0000    |
| C4    | 0.17820(18) | 0.42091(15) | 0.6488(2)   | 0.0362                 | 1.0000    |
| C5    | 0.09946(19) | 0.39201(16) | 0.6413(2)   | 0.0395                 | 1.0000    |
| O6    | 0.27700(13) | 0.33340(11) | 0.6286(2)   | 0.0485                 | 1.0000    |
| O7    | 0.20395(14) | 0.47512(11) | 0.65882(18) | 0.0457                 | 1.0000    |
| O8    | 0.03429(14) | 0.41555(12) | 0.6412(2)   | 0.0573                 | 1.0000    |
| C9    | 0.04152(17) | 0.23958(15) | 0.6091(2)   | 0.0352                 | 1.0000    |
| C10   | 0.03553(19) | 0.17418(16) | 0.5978(2)   | 0.0408                 | 1.0000    |
| C11   | -0.0361(2)  | 0.14501(16) | 0.5903(3)   | 0.0480                 | 1.0000    |
| C12   | -0.1013(2)  | 0.18283(18) | 0.5949(3)   | 0.0501                 | 1.0000    |
| C13   | -0.0964(2)  | 0.24792(19) | 0.6039(3)   | 0.0511                 | 1.0000    |
| C14   | 0.02465(19) | 0.27749(15) | 0.6113(3)   | 0.0420                 | 1.0000    |
| Cl15  | 0.19169(6)  | 0.14660(6)  | 0.58870(10) | 0.0762                 | 1.0000    |
| N21   | 0.12290(15) | 0.42736(13) | 0.34825(18) | 0.0359                 | 1.0000    |
| C22   | 0.04619(19) | 0.43749(16) | 0.3972(2)   | 0.0416                 | 1.0000    |
| C23   | -0.0233(2)  | 0.4068(2)   | 0.3539(3)   | 0.0557                 | 1.0000    |
| C24   | -0.0912(2)  | 0.4089(2)   | 0.4182(3)   | 0.0633                 | 1.0000    |
| C25   | -0.1602(3)  | 0.3729(2)   | 0.3805(5)   | 0.0859                 | 1.0000    |
| C26   | 0.12433(18) | 0.46547(17) | 0.2597(2)   | 0.0389                 | 1.0000    |
| C27   | 0.1302(2)   | 0.53757(17) | 0.2687(3)   | 0.0428                 | 1.0000    |
| C28   | 0.1231(2)   | 0.56918(19) | 0.1755(3)   | 0.0516                 | 1.0000    |
| C29   | 0.1324(2)   | 0.6419(2)   | 0.1805(3)   | 0.0607                 | 1.0000    |
| C30   | 0.18470(19) | 0.44997(15) | 0.4134(2)   | 0.0381                 | 1.0000    |
| C31   | 0.26669(19) | 0.44413(15) | 0.3790(2)   | 0.0393                 | 1.0000    |
| C32   | 0.3218(2)   | 0.46559(18) | 0.4534(3)   | 0.0494                 | 1.0000    |

|      |             |             |           |        |        |
|------|-------------|-------------|-----------|--------|--------|
| C33  | 0.4056(2)   | 0.46203(19) | 0.4220(4) | 0.0623 | 1.0000 |
| C34  | 0.13501(18) | 0.35699(16) | 0.3240(2) | 0.0386 | 1.0000 |
| C35  | 0.13898(19) | 0.31136(16) | 0.4040(2) | 0.0416 | 1.0000 |
| C36  | 0.1366(2)   | 0.24089(17) | 0.3719(3) | 0.0467 | 1.0000 |
| C37  | 0.0561(2)   | 0.21966(18) | 0.3456(3) | 0.0531 | 1.0000 |
| H31  | -0.1407     | 0.2735      | 0.6055    | 0.0614 | 1.0000 |
| H41  | -0.0205     | 0.3223      | 0.6174    | 0.0488 | 1.0000 |
| H141 | 0.0802      | 0.1485      | 0.5952    | 0.0491 | 1.0000 |
| H151 | -0.0400     | 0.1010      | 0.5824    | 0.0573 | 1.0000 |
| H171 | 0.1745      | 0.4947      | 0.4266    | 0.0451 | 1.0000 |
| H172 | 0.1787      | 0.4244      | 0.4680    | 0.0456 | 1.0000 |
| H181 | 0.2736      | 0.4714      | 0.3258    | 0.0469 | 1.0000 |
| H182 | 0.2772      | 0.3997      | 0.3638    | 0.0463 | 1.0000 |
| H191 | 0.3102      | 0.5101      | 0.4693    | 0.0584 | 1.0000 |
| H192 | 0.3149      | 0.4383      | 0.5058    | 0.0594 | 1.0000 |
| H203 | 0.4388      | 0.4785      | 0.4690    | 0.0929 | 1.0000 |
| H202 | 0.4119      | 0.4881      | 0.3682    | 0.0929 | 1.0000 |
| H201 | 0.4186      | 0.4176      | 0.4087    | 0.0926 | 1.0000 |
| H211 | 0.1682      | 0.4501      | 0.2255    | 0.0467 | 1.0000 |
| H212 | 0.0773      | 0.4550      | 0.2274    | 0.0471 | 1.0000 |
| H221 | 0.1797      | 0.5493      | 0.2947    | 0.0513 | 1.0000 |
| H222 | 0.0905      | 0.5542      | 0.3077    | 0.0514 | 1.0000 |
| H231 | 0.1636      | 0.5518      | 0.1358    | 0.0619 | 1.0000 |
| H232 | 0.0729      | 0.5590      | 0.1502    | 0.0621 | 1.0000 |
| H241 | 0.1283      | 0.6606      | 0.1207    | 0.0908 | 1.0000 |
| H242 | 0.1822      | 0.6525      | 0.2052    | 0.0908 | 1.0000 |
| H243 | 0.0933      | 0.6604      | 0.2188    | 0.0906 | 1.0000 |
| H251 | 0.0378      | 0.4834      | 0.4013    | 0.0493 | 1.0000 |
| H252 | 0.0524      | 0.4197      | 0.4583    | 0.0501 | 1.0000 |
| H261 | -0.0361     | 0.4300      | 0.2990    | 0.0671 | 1.0000 |
| H262 | -0.0127     | 0.3620      | 0.3406    | 0.0668 | 1.0000 |
| H271 | -0.1053     | 0.4549      | 0.4275    | 0.0763 | 1.0000 |
| H272 | -0.0762     | 0.3893      | 0.4758    | 0.0764 | 1.0000 |
| H281 | -0.2030     | 0.3756      | 0.4225    | 0.1291 | 1.0000 |
| H282 | -0.1757     | 0.3915      | 0.3231    | 0.1289 | 1.0000 |
| H283 | -0.1468     | 0.3283      | 0.3717    | 0.1287 | 1.0000 |
| H291 | 0.1822      | 0.3542      | 0.2898    | 0.0457 | 1.0000 |
| H292 | 0.0930      | 0.3446      | 0.2845    | 0.0456 | 1.0000 |
| H301 | 0.1862      | 0.3192      | 0.4376    | 0.0500 | 1.0000 |
| H302 | 0.0954      | 0.3197      | 0.4442    | 0.0502 | 1.0000 |

|      |        |        |        |        |        |
|------|--------|--------|--------|--------|--------|
| H311 | 0.1545 | 0.2131 | 0.4207 | 0.0560 | 1.0000 |
| H312 | 0.1704 | 0.2360 | 0.3196 | 0.0557 | 1.0000 |
| H323 | 0.0572 | 0.1758 | 0.3222 | 0.0797 | 1.0000 |
| H322 | 0.0230 | 0.2200 | 0.3986 | 0.0798 | 1.0000 |
| H321 | 0.0341 | 0.2481 | 0.2998 | 0.0797 | 1.0000 |
| H61  | 0.1531 | 0.2400 | 0.6168 | 0.0424 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| N1    | 0.0305(13)      | 0.0343(14)      | 0.0408(15)      | 0.0019(11)      | -0.0009(11)     | 0.0059(10)      |
| C2    | 0.0344(16)      | 0.0332(15)      | 0.0320(15)      | 0.0011(13)      | -0.0014(13)     | 0.0044(12)      |
| C3    | 0.0361(17)      | 0.0374(16)      | 0.0370(17)      | 0.0022(14)      | -0.0049(13)     | 0.0009(13)      |
| C4    | 0.0387(16)      | 0.0349(16)      | 0.0352(17)      | 0.0020(14)      | -0.0038(13)     | 0.0044(13)      |
| C5    | 0.0383(17)      | 0.0374(17)      | 0.0427(19)      | -0.0004(15)     | -0.0005(15)     | 0.0024(13)      |
| O6    | 0.0331(12)      | 0.0381(13)      | 0.0743(19)      | -0.0043(12)     | -0.0054(12)     | 0.0050(9)       |
| O7    | 0.0470(14)      | 0.0347(12)      | 0.0554(16)      | -0.0025(11)     | -0.0078(12)     | 0.0012(10)      |
| O8    | 0.0349(13)      | 0.0423(14)      | 0.095(2)        | -0.0033(14)     | 0.0011(14)      | 0.0083(10)      |
| C9    | 0.0339(15)      | 0.0402(17)      | 0.0315(16)      | 0.0011(13)      | -0.0016(12)     | -0.0002(13)     |
| C10   | 0.0381(17)      | 0.0376(17)      | 0.047(2)        | 0.0026(15)      | -0.0016(15)     | 0.0021(13)      |
| C11   | 0.051(2)        | 0.0345(17)      | 0.059(2)        | -0.0034(17)     | -0.0004(18)     | -0.0060(15)     |
| C12   | 0.0344(17)      | 0.053(2)        | 0.062(2)        | -0.0060(19)     | -0.0040(17)     | -0.0091(15)     |
| C13   | 0.0369(17)      | 0.053(2)        | 0.064(3)        | -0.0072(19)     | -0.0071(17)     | 0.0046(16)      |
| C14   | 0.0361(17)      | 0.0329(16)      | 0.057(2)        | -0.0060(15)     | -0.0048(15)     | 0.0027(13)      |
| C115  | 0.0430(5)       | 0.0718(7)       | 0.1137(10)      | -0.0141(7)      | -0.0050(6)      | -0.0158(5)      |
| N21   | 0.0335(13)      | 0.0405(14)      | 0.0337(14)      | -0.0039(12)     | 0.0015(11)      | 0.0017(11)      |
| C22   | 0.0361(17)      | 0.0467(19)      | 0.0421(19)      | -0.0035(15)     | 0.0077(14)      | 0.0016(14)      |
| C23   | 0.0366(18)      | 0.061(2)        | 0.069(3)        | -0.016(2)       | 0.0082(18)      | -0.0031(16)     |
| C24   | 0.0383(19)      | 0.080(3)        | 0.072(3)        | 0.022(2)        | 0.0076(19)      | 0.0039(19)      |
| C25   | 0.042(2)        | 0.077(3)        | 0.139(5)        | 0.021(3)        | 0.007(3)        | -0.007(2)       |
| C26   | 0.0326(16)      | 0.0488(19)      | 0.0352(17)      | 0.0003(15)      | 0.0009(13)      | 0.0032(13)      |
| C27   | 0.0395(18)      | 0.0440(19)      | 0.045(2)        | -0.0004(15)     | 0.0033(15)      | 0.0047(14)      |
| C28   | 0.049(2)        | 0.055(2)        | 0.050(2)        | 0.0108(18)      | 0.0009(17)      | 0.0070(17)      |
| C29   | 0.059(2)        | 0.061(2)        | 0.063(3)        | 0.013(2)        | 0.009(2)        | 0.016(2)        |
| C30   | 0.0415(17)      | 0.0374(16)      | 0.0355(17)      | -0.0054(14)     | -0.0025(14)     | 0.0000(13)      |
| C31   | 0.0396(18)      | 0.0335(16)      | 0.0448(19)      | -0.0044(14)     | -0.0043(14)     | 0.0013(13)      |
| C32   | 0.049(2)        | 0.045(2)        | 0.054(2)        | -0.0021(17)     | -0.0110(17)     | -0.0028(16)     |
| C33   | 0.044(2)        | 0.051(2)        | 0.092(4)        | -0.003(2)       | -0.015(2)       | -0.0062(17)     |
| C34   | 0.0363(16)      | 0.0408(18)      | 0.0386(17)      | -0.0066(15)     | -0.0008(14)     | 0.0014(14)      |
| C35   | 0.0431(18)      | 0.0428(18)      | 0.0390(18)      | -0.0017(15)     | -0.0037(15)     | 0.0017(14)      |

|     |          |            |          |             |             |             |
|-----|----------|------------|----------|-------------|-------------|-------------|
| C36 | 0.054(2) | 0.0397(19) | 0.046(2) | -0.0040(16) | -0.0016(17) | 0.0025(15)  |
| C37 | 0.062(2) | 0.048(2)   | 0.049(2) | -0.0029(18) | -0.0006(18) | -0.0120(18) |

## Distances

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| N1  | C2   | 1.345(4)Å |  | N1  | C9   | 1.415(4)Å |
| N1  | H61  | 0.863Å    |  | C2  | C3   | 1.436(4)Å |
| C2  | C5   | 1.452(4)Å |  | C3  | C4   | 1.481(4)Å |
| C3  | O6   | 1.249(4)Å |  | C4  | C5   | 1.501(4)Å |
| C4  | O7   | 1.222(4)Å |  | C5  | O8   | 1.236(4)Å |
| C9  | C10  | 1.374(5)Å |  | C9  | C14  | 1.396(4)Å |
| C10 | C11  | 1.391(5)Å |  | C10 | H141 | 0.945Å    |
| C11 | C12  | 1.383(5)Å |  | C11 | H151 | 0.925Å    |
| C12 | C13  | 1.362(5)Å |  | C12 | Cl15 | 1.747(3)Å |
| C13 | C14  | 1.397(5)Å |  | C13 | H31  | 0.938Å    |
| C14 | H41  | 0.939Å    |  | N21 | C22  | 1.533(4)Å |
| N21 | C26  | 1.528(4)Å |  | N21 | C30  | 1.518(4)Å |
| N21 | C34  | 1.521(4)Å |  | C22 | C23  | 1.509(5)Å |
| C22 | H251 | 0.968Å    |  | C22 | H252 | 0.981Å    |
| C23 | C24  | 1.516(5)Å |  | C23 | H261 | 0.969Å    |
| C23 | H262 | 0.969Å    |  | C24 | C25  | 1.523(6)Å |
| C24 | H271 | 0.996Å    |  | C24 | H272 | 0.978Å    |
| C25 | H281 | 0.971Å    |  | C25 | H282 | 0.969Å    |
| C25 | H283 | 0.964Å    |  | C26 | C27  | 1.508(5)Å |
| C26 | H211 | 0.969Å    |  | C26 | H212 | 0.973Å    |
| C27 | C28  | 1.530(5)Å |  | C27 | H221 | 0.974Å    |
| C27 | H222 | 0.964Å    |  | C28 | C29  | 1.522(6)Å |
| C28 | H231 | 0.985Å    |  | C28 | H232 | 0.974Å    |
| C29 | H241 | 0.967Å    |  | C29 | H242 | 0.967Å    |
| C29 | H243 | 0.963Å    |  | C30 | C31  | 1.520(5)Å |
| C30 | H171 | 0.966Å    |  | C30 | H172 | 0.970Å    |
| C31 | C32  | 1.524(5)Å |  | C31 | H181 | 0.977Å    |
| C31 | H182 | 0.968Å    |  | C32 | C33  | 1.532(6)Å |
| C32 | H191 | 0.976Å    |  | C32 | H192 | 0.967Å    |
| C33 | H203 | 0.965Å    |  | C33 | H202 | 0.967Å    |
| C33 | H201 | 0.970Å    |  | C34 | C35  | 1.516(5)Å |
| C34 | H291 | 0.966Å    |  | C34 | H292 | 0.968Å    |
| C35 | C36  | 1.540(5)Å |  | C35 | H301 | 0.974Å    |
| C35 | H302 | 0.978Å    |  | C36 | C37  | 1.520(5)Å |
| C36 | H311 | 0.975Å    |  | C36 | H312 | 0.975Å    |

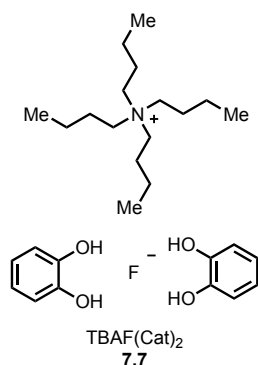
|     |      |        |  |     |      |        |
|-----|------|--------|--|-----|------|--------|
| C37 | H323 | 0.974Å |  | C37 | H322 | 0.971Å |
| C37 | H321 | 0.977Å |  |     |      |        |

## Angles

|      |     |      |           |  |      |     |      |           |
|------|-----|------|-----------|--|------|-----|------|-----------|
| C2   | N1  | C9   | 128.8(3)° |  | C2   | N1  | H61  | 116.081°  |
| C9   | N1  | H61  | 115.104°  |  | N1   | C2  | C3   | 127.3(3)° |
| N1   | C2  | C5   | 140.6(3)° |  | C3   | C2  | C5   | 92.1(3)°  |
| C2   | C3  | C4   | 90.4(2)°  |  | C2   | C3  | O6   | 134.8(3)° |
| C4   | C3  | O6   | 134.8(3)° |  | C3   | C4  | C5   | 88.5(2)°  |
| C3   | C4  | O7   | 136.0(3)° |  | C5   | C4  | O7   | 135.5(3)° |
| C2   | C5  | C4   | 89.0(2)°  |  | C2   | C5  | O8   | 138.1(3)° |
| C4   | C5  | O8   | 132.9(3)° |  | N1   | C9  | C10  | 118.7(3)° |
| N1   | C9  | C14  | 121.4(3)° |  | C10  | C9  | C14  | 119.9(3)° |
| C9   | C10 | C11  | 120.6(3)° |  | C9   | C10 | H141 | 120.187°  |
| C11  | C10 | H141 | 119.203°  |  | C10  | C11 | C12  | 119.0(3)° |
| C10  | C11 | H151 | 120.464°  |  | C12  | C11 | H151 | 120.554°  |
| C11  | C12 | C13  | 121.2(3)° |  | C11  | C12 | Cl15 | 119.5(3)° |
| C13  | C12 | Cl15 | 119.3(3)° |  | C12  | C13 | C14  | 120.0(3)° |
| C12  | C13 | H31  | 121.014°  |  | C14  | C13 | H31  | 118.953°  |
| C9   | C14 | C13  | 119.2(3)° |  | C9   | C14 | H41  | 119.926°  |
| C13  | C14 | H41  | 120.859°  |  | C22  | N21 | C26  | 110.2(2)° |
| C22  | N21 | C30  | 106.1(2)° |  | C26  | N21 | C30  | 111.7(2)° |
| C22  | N21 | C34  | 111.4(2)° |  | C26  | N21 | C34  | 107.1(2)° |
| C30  | N21 | C34  | 110.4(2)° |  | N21  | C22 | C23  | 116.2(3)° |
| N21  | C22 | H251 | 107.309°  |  | C23  | C22 | H251 | 108.761°  |
| N21  | C22 | H252 | 106.603°  |  | C23  | C22 | H252 | 108.595°  |
| H251 | C22 | H252 | 109.264°  |  | C22  | C23 | C24  | 110.3(4)° |
| C22  | C23 | H261 | 109.220°  |  | C24  | C23 | H261 | 109.244°  |
| C22  | C23 | H262 | 109.848°  |  | C24  | C23 | H262 | 107.646°  |
| H261 | C23 | H262 | 110.545°  |  | C23  | C24 | C25  | 111.9(4)° |
| C23  | C24 | H271 | 107.856°  |  | C25  | C24 | H271 | 109.169°  |
| C23  | C24 | H272 | 108.936°  |  | C25  | C24 | H272 | 108.803°  |
| H271 | C24 | H272 | 110.209°  |  | C24  | C25 | H281 | 110.107°  |
| C24  | C25 | H282 | 110.020°  |  | H281 | C25 | H282 | 108.729°  |
| C24  | C25 | H283 | 109.296°  |  | H281 | C25 | H283 | 109.148°  |
| H282 | C25 | H283 | 109.523°  |  | N21  | C26 | C27  | 116.2(3)° |
| N21  | C26 | H211 | 106.716°  |  | C27  | C26 | H211 | 108.671°  |
| N21  | C26 | H212 | 106.802°  |  | C27  | C26 | H212 | 108.814°  |
| H211 | C26 | H212 | 109.546°  |  | C26  | C27 | C28  | 110.0(3)° |

|      |     |      |          |  |      |     |      |           |
|------|-----|------|----------|--|------|-----|------|-----------|
| C26  | C27 | H221 | 110.095° |  | C28  | C27 | H221 | 108.447°  |
| C26  | C27 | H222 | 111.198° |  | C28  | C27 | H222 | 108.968°  |
| H221 | C27 | H222 | 108.055° |  | C27  | C28 | C29  | 112.0(3)° |
| C27  | C28 | H231 | 108.612° |  | C29  | C28 | H231 | 108.545°  |
| C27  | C28 | H232 | 108.886° |  | C29  | C28 | H232 | 109.254°  |
| H231 | C28 | H232 | 109.534° |  | C28  | C29 | H241 | 110.322°  |
| C28  | C29 | H242 | 109.799° |  | H241 | C29 | H242 | 108.518°  |
| C28  | C29 | H243 | 110.541° |  | H241 | C29 | H243 | 108.784°  |
| H242 | C29 | H243 | 108.830° |  | N21  | C30 | C31  | 115.4(3)° |
| N21  | C30 | H171 | 107.168° |  | C31  | C30 | H171 | 108.481°  |
| N21  | C30 | H172 | 106.240° |  | C31  | C30 | H172 | 109.510°  |
| H171 | C30 | H172 | 109.903° |  | C30  | C31 | C32  | 109.1(3)° |
| C30  | C31 | H181 | 109.764° |  | C32  | C31 | H181 | 109.312°  |
| C30  | C31 | H182 | 109.367° |  | C32  | C31 | H182 | 109.122°  |
| H181 | C31 | H182 | 110.133° |  | C31  | C32 | C33  | 111.6(3)° |
| C31  | C32 | H191 | 108.716° |  | C33  | C32 | H191 | 108.439°  |
| C31  | C32 | H192 | 109.011° |  | C33  | C32 | H192 | 109.359°  |
| H191 | C32 | H192 | 109.720° |  | C32  | C33 | H203 | 109.626°  |
| C32  | C33 | H202 | 109.244° |  | H203 | C33 | H202 | 108.814°  |
| C32  | C33 | H201 | 109.235° |  | H203 | C33 | H201 | 110.051°  |
| H202 | C33 | H201 | 109.856° |  | N21  | C34 | C35  | 115.1(3)° |
| N21  | C34 | H291 | 107.390° |  | C35  | C34 | H291 | 109.237°  |
| N21  | C34 | H292 | 106.967° |  | C35  | C34 | H292 | 109.655°  |
| H291 | C34 | H292 | 108.264° |  | C34  | C35 | C36  | 110.8(3)° |
| C34  | C35 | H301 | 109.252° |  | C36  | C35 | H301 | 109.837°  |
| C34  | C35 | H302 | 109.004° |  | C36  | C35 | H302 | 109.536°  |
| H301 | C35 | H302 | 108.418° |  | C35  | C36 | C37  | 112.3(3)° |
| C35  | C36 | H311 | 109.110° |  | C37  | C36 | H311 | 108.184°  |
| C35  | C36 | H312 | 109.070° |  | C37  | C36 | H312 | 108.878°  |
| H311 | C36 | H312 | 109.241° |  | C36  | C37 | H323 | 110.078°  |
| C36  | C37 | H322 | 109.917° |  | H323 | C37 | H322 | 107.672°  |
| C36  | C37 | H321 | 111.261° |  | H323 | C37 | H321 | 109.212°  |
| H322 | C37 | H321 | 108.618° |  |      |     |      |           |





**tetra-*n*-butylammonium fluoride bis(catechol), 1<sup>st</sup> polymorph (TBAF(Cat)<sub>2</sub>, 7.7):**

**X-ray** (single-crystal, 1<sup>st</sup> polymorph) Colourless plates of X-ray diffraction quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.7** in EtOAc, which had previously been prepared by dissolving **7.7** in refluxing EtOAc (approximately 77 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 066GWP13

## Crystal Data

$a = 27.2660(3) \text{ \AA}$   $\alpha = 90^\circ$

$b = 27.8831(2) \text{ \AA}$   $\beta = 110.3660(11)^\circ$

$c = 15.9412(2) \text{ \AA}$   $\gamma = 90^\circ$

Volume 11361.9(2)  $\text{\AA}^3$

Space group

C c

Formula

C<sub>28</sub> H<sub>48</sub> F<sub>1</sub> N<sub>1</sub> O<sub>4</sub>

Cell determined from 52222 reflections

Temperature

150K

Shape

plate

Colour

clear\_pale\_colourless

D<sub>x</sub>

1.13 Mg m<sup>-3</sup>

$\mu$

0.625 mm<sup>-1</sup>

Absorption correction multi-scan

T<sub>min</sub>

0.88

Crystal Class monoclinic

Z =

16

M<sub>r</sub>

481.69

Cell  $\theta$  range = 3 - 77°

Size

0.03 × 0.09 × 0.15 mm

F000

4224.000

T<sub>max</sub>

0.98

## Data Collection

Diffractometer

multi-scan

Scan type

$\omega$  scans

Reflections measured

131227

Independent reflections

22907

R<sub>int</sub>

0.0316

$\theta_{\text{max}}$

76.8386

h =

-34 → 32

k =

-34 → 35

l =

-20 → 20

## Refinement

$\Delta\rho_{\text{min}} =$

-0.22 e  $\text{\AA}^{-3}$

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\max}$ =  | 0.28 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 22810                                                                                                                                                                                       |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 1381                                                                                                                                                                                        |
| S =                    | 0.99                                                                                                                                                                                        |
| R-factor               | 0.038                                                                                                                                                                                       |
| weighted R-factor      | 0.093                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0052                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.055 \times P)^2 + 2.085 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| F1    | 0.89162(6)  | 0.85639(6)  | 0.63664(10) | 0.0848                 | 1.0000    |
| F2    | 0.58304(5)  | 0.49173(4)  | 0.13628(8)  | 0.0647                 | 1.0000    |
| F3    | 0.7191(4)   | 0.78411(19) | 0.0373(12)  | 0.1082                 | 0.72(4)   |
| F4    | 0.7354(12)  | 0.7774(6)   | 0.0175(5)   | 0.0781                 | 0.28(4)   |
| F5    | 0.50815(7)  | 0.90717(4)  | 0.50176(10) | 0.0794                 | 1.0000    |
| O1    | 0.95558(6)  | 0.87200(4)  | 0.56621(9)  | 0.0559                 | 1.0000    |
| O2    | 1.04266(7)  | 0.88955(6)  | 0.52545(11) | 0.0755                 | 1.0000    |
| C3    | 0.98748(7)  | 0.83420(6)  | 0.56593(10) | 0.0483                 | 1.0000    |
| C4    | 1.03114(8)  | 0.84461(7)  | 0.54359(12) | 0.0565                 | 1.0000    |
| C5    | 1.06563(9)  | 0.80838(9)  | 0.54195(13) | 0.0748                 | 1.0000    |
| C6    | 1.05608(11) | 0.76193(9)  | 0.56274(15) | 0.0843                 | 1.0000    |
| C7    | 1.01324(12) | 0.75166(8)  | 0.58584(14) | 0.0800                 | 1.0000    |
| C8    | 0.97848(9)  | 0.78756(6)  | 0.58781(11) | 0.0613                 | 1.0000    |
| O11   | 0.82889(7)  | 0.78937(5)  | 0.62653(9)  | 0.0626                 | 1.0000    |
| O12   | 0.79992(6)  | 0.89038(4)  | 0.60588(8)  | 0.0546                 | 1.0000    |
| C13   | 0.77825(8)  | 0.80578(6)  | 0.60127(10) | 0.0500                 | 1.0000    |
| C14   | 0.76461(7)  | 0.85450(5)  | 0.59156(9)  | 0.0440                 | 1.0000    |
| C15   | 0.71227(8)  | 0.86720(8)  | 0.56486(11) | 0.0578                 | 1.0000    |
| C16   | 0.67380(8)  | 0.83130(11) | 0.54908(13) | 0.0763                 | 1.0000    |
| C17   | 0.68940(11) | 0.78328(9)  | 0.55982(13) | 0.0745                 | 1.0000    |
| C18   | 0.74042(10) | 0.77153(7)  | 0.58536(12) | 0.0646                 | 1.0000    |
| O21   | 0.49674(6)  | 0.52182(4)  | 0.03789(8)  | 0.0501                 | 1.0000    |
| O22   | 0.39474(6)  | 0.55102(4)  | 0.01878(9)  | 0.0555                 | 1.0000    |
| C23   | 0.45908(7)  | 0.48888(5)  | 0.03455(9)  | 0.0411                 | 1.0000    |
| C24   | 0.40731(7)  | 0.50426(5)  | 0.00527(9)  | 0.0423                 | 1.0000    |
| C25   | 0.36756(7)  | 0.47250(6)  | 0.00008(10) | 0.0477                 | 1.0000    |

|     |             |             |             |        |           |
|-----|-------------|-------------|-------------|--------|-----------|
| C26 | 0.37834(8)  | 0.42481(6)  | 0.02390(11) | 0.0510 | 1.0000    |
| C27 | 0.42963(8)  | 0.40938(6)  | 0.05273(11) | 0.0539 | 1.0000    |
| C28 | 0.46982(8)  | 0.44102(5)  | 0.05800(10) | 0.0486 | 1.0000    |
| O31 | 0.67578(6)  | 0.48790(5)  | 0.13940(12) | 0.0760 | 1.0000    |
| O32 | 0.60841(7)  | 0.40503(5)  | 0.12608(11) | 0.0695 | 1.0000    |
| C33 | 0.68351(7)  | 0.44460(6)  | 0.10739(12) | 0.0524 | 1.0000    |
| C34 | 0.65108(7)  | 0.40469(6)  | 0.10092(10) | 0.0477 | 1.0000    |
| C35 | 0.66324(8)  | 0.36198(6)  | 0.06734(11) | 0.0557 | 1.0000    |
| C36 | 0.70651(9)  | 0.35847(7)  | 0.04180(11) | 0.0617 | 1.0000    |
| C37 | 0.73858(9)  | 0.39741(8)  | 0.04917(14) | 0.0668 | 1.0000    |
| C38 | 0.72645(8)  | 0.44029(8)  | 0.08102(15) | 0.0668 | 1.0000    |
| O41 | 0.80233(7)  | 0.73337(6)  | 0.12205(12) | 0.0818 | 1.0000    |
| O42 | 0.69663(7)  | 0.69492(6)  | 0.04317(10) | 0.0759 | 1.0000    |
| C43 | 0.78913(8)  | 0.68658(7)  | 0.13081(12) | 0.0578 | 1.0000    |
| C44 | 0.73853(8)  | 0.66825(7)  | 0.09210(10) | 0.0528 | 1.0000    |
| C45 | 0.72931(9)  | 0.62006(7)  | 0.10355(12) | 0.0599 | 1.0000    |
| C46 | 0.76855(10) | 0.59041(8)  | 0.15470(16) | 0.0717 | 1.0000    |
| C47 | 0.81796(10) | 0.60861(8)  | 0.19466(19) | 0.0837 | 1.0000    |
| C48 | 0.82825(9)  | 0.65622(9)  | 0.18214(18) | 0.0792 | 1.0000    |
| O51 | 0.7547(2)   | 0.86862(19) | 0.0381(5)   | 0.0697 | 0.684(17) |
| O52 | 0.6497(2)   | 0.8472(3)   | 0.0373(3)   | 0.0842 | 0.684(17) |
| C53 | 0.72348(14) | 0.90134(15) | 0.0583(4)   | 0.0569 | 0.684(17) |
| C54 | 0.67275(13) | 0.8913(2)   | 0.0568(4)   | 0.0602 | 0.684(17) |
| C55 | 0.64259(12) | 0.9283(3)   | 0.0715(3)   | 0.0626 | 0.684(17) |
| C56 | 0.6619(2)   | 0.9746(3)   | 0.0874(3)   | 0.0693 | 0.684(17) |
| C57 | 0.7123(3)   | 0.98401(17) | 0.0911(4)   | 0.0695 | 0.684(17) |
| C58 | 0.7429(2)   | 0.94733(16) | 0.0779(5)   | 0.0607 | 0.684(17) |
| O61 | 0.7648(4)   | 0.8662(3)   | 0.0545(8)   | 0.0583 | 0.316(17) |
| O62 | 0.6630(5)   | 0.8287(5)   | 0.0426(6)   | 0.0745 | 0.316(17) |
| C63 | 0.7237(3)   | 0.8941(3)   | 0.0559(7)   | 0.0530 | 0.316(17) |
| C64 | 0.6761(3)   | 0.8758(4)   | 0.0551(7)   | 0.0588 | 0.316(17) |
| C65 | 0.6405(3)   | 0.9062(6)   | 0.0720(6)   | 0.0684 | 0.316(17) |
| C66 | 0.6510(4)   | 0.9545(5)   | 0.0873(6)   | 0.0722 | 0.316(17) |
| C67 | 0.6969(5)   | 0.9730(4)   | 0.0835(8)   | 0.0735 | 0.316(17) |
| C68 | 0.7323(4)   | 0.9431(3)   | 0.0655(9)   | 0.0617 | 0.316(17) |
| O71 | 0.54653(15) | 0.82446(12) | 0.5292(4)   | 0.0705 | 0.820(12) |
| O72 | 0.44573(17) | 0.84793(15) | 0.5441(4)   | 0.0615 | 0.820(12) |
| C73 | 0.51896(11) | 0.79367(9)  | 0.5625(3)   | 0.0522 | 0.820(12) |
| C74 | 0.47025(13) | 0.80428(11) | 0.5676(3)   | 0.0501 | 0.820(12) |
| C75 | 0.44442(13) | 0.76961(14) | 0.5989(3)   | 0.0614 | 0.820(12) |

|      |             |             |             |        |           |
|------|-------------|-------------|-------------|--------|-----------|
| C76  | 0.4659(2)   | 0.72478(11) | 0.6237(2)   | 0.0679 | 0.820(12) |
| C77  | 0.5142(2)   | 0.71439(7)  | 0.61925(19) | 0.0712 | 0.820(12) |
| C78  | 0.54045(13) | 0.74865(11) | 0.5886(2)   | 0.0638 | 0.820(12) |
| O81  | 0.5481(5)   | 0.8199(4)   | 0.5590(9)   | 0.0556 | 0.180(12) |
| O82  | 0.4456(6)   | 0.8580(5)   | 0.5408(13)  | 0.0548 | 0.180(12) |
| C83  | 0.5100(6)   | 0.7938(4)   | 0.5751(11)  | 0.0549 | 0.180(12) |
| C84  | 0.4616(6)   | 0.8123(4)   | 0.5687(13)  | 0.0498 | 0.180(12) |
| C85  | 0.4269(6)   | 0.7837(6)   | 0.5923(8)   | 0.0609 | 0.180(12) |
| C86  | 0.4394(8)   | 0.7367(6)   | 0.6200(8)   | 0.0697 | 0.180(12) |
| C87  | 0.4875(9)   | 0.7185(4)   | 0.6271(11)  | 0.0638 | 0.180(12) |
| C88  | 0.5220(7)   | 0.7463(3)   | 0.6028(10)  | 0.0619 | 0.180(12) |
| O91  | 0.43559(8)  | 0.96047(5)  | 0.40278(10) | 0.0757 | 1.0000    |
| O92  | 0.53046(7)  | 0.99510(5)  | 0.53818(10) | 0.0647 | 1.0000    |
| C93  | 0.43913(9)  | 1.00386(6)  | 0.44343(11) | 0.0570 | 1.0000    |
| C94  | 0.48511(9)  | 1.02080(6)  | 0.50874(11) | 0.0537 | 1.0000    |
| C95  | 0.48491(9)  | 1.06662(6)  | 0.54355(13) | 0.0605 | 1.0000    |
| C96  | 0.44067(10) | 1.09483(6)  | 0.51566(13) | 0.0667 | 1.0000    |
| C97  | 0.39534(10) | 1.07797(7)  | 0.45210(14) | 0.0685 | 1.0000    |
| C98  | 0.39504(10) | 1.03253(7)  | 0.41627(13) | 0.0642 | 1.0000    |
| N101 | 0.53649(5)  | 0.93078(4)  | 0.78394(7)  | 0.0311 | 1.0000    |
| C102 | 0.56040(6)  | 0.97432(4)  | 0.84095(9)  | 0.0343 | 1.0000    |
| C103 | 0.57145(6)  | 1.01712(5)  | 0.79159(10) | 0.0398 | 1.0000    |
| C104 | 0.59461(7)  | 1.05793(5)  | 0.85652(11) | 0.0466 | 1.0000    |
| C105 | 0.60675(8)  | 1.10156(6)  | 0.81009(13) | 0.0563 | 1.0000    |
| C106 | 0.57374(6)  | 0.90979(5)  | 0.74180(9)  | 0.0349 | 1.0000    |
| C107 | 0.62574(6)  | 0.89115(5)  | 0.80513(9)  | 0.0377 | 1.0000    |
| C108 | 0.65762(7)  | 0.87299(7)  | 0.74989(12) | 0.0529 | 1.0000    |
| C109 | 0.71090(8)  | 0.85418(7)  | 0.80619(14) | 0.0605 | 1.0000    |
| C110 | 0.52463(6)  | 0.89475(4)  | 0.84600(8)  | 0.0337 | 1.0000    |
| C111 | 0.50174(6)  | 0.84706(5)  | 0.80450(9)  | 0.0369 | 1.0000    |
| C112 | 0.49472(8)  | 0.81500(5)  | 0.87659(10) | 0.0494 | 1.0000    |
| C113 | 0.47232(7)  | 0.76602(5)  | 0.84243(10) | 0.0460 | 1.0000    |
| C114 | 0.48738(6)  | 0.94431(5)  | 0.70654(9)  | 0.0350 | 1.0000    |
| C115 | 0.44553(6)  | 0.97020(5)  | 0.73041(10) | 0.0414 | 1.0000    |
| C116 | 0.40183(7)  | 0.98466(7)  | 0.64493(13) | 0.0597 | 1.0000    |
| C117 | 0.36071(8)  | 1.01559(7)  | 0.66100(17) | 0.0684 | 1.0000    |
| N121 | 0.79830(5)  | 0.67898(4)  | 0.83496(7)  | 0.0339 | 1.0000    |
| C122 | 0.82667(6)  | 0.72133(5)  | 0.89156(9)  | 0.0364 | 1.0000    |
| C123 | 0.82861(7)  | 0.76588(5)  | 0.83779(10) | 0.0404 | 1.0000    |
| C124 | 0.85653(8)  | 0.80730(5)  | 0.89700(10) | 0.0491 | 1.0000    |

|      |             |            |             |        |        |
|------|-------------|------------|-------------|--------|--------|
| C125 | 0.86095(8)  | 0.85008(6) | 0.84063(11) | 0.0516 | 1.0000 |
| C126 | 0.82318(6)  | 0.66614(5) | 0.76594(9)  | 0.0367 | 1.0000 |
| C127 | 0.88003(7)  | 0.65031(5) | 0.80358(10) | 0.0405 | 1.0000 |
| C128 | 0.90367(7)  | 0.65021(5) | 0.72976(10) | 0.0447 | 1.0000 |
| C129 | 0.95968(8)  | 0.63185(7) | 0.76270(13) | 0.0559 | 1.0000 |
| C130 | 0.80194(7)  | 0.63704(5) | 0.89809(9)  | 0.0390 | 1.0000 |
| C131 | 0.77456(8)  | 0.59154(5) | 0.85335(11) | 0.0477 | 1.0000 |
| C132 | 0.78159(10) | 0.55151(6) | 0.92089(12) | 0.0609 | 1.0000 |
| C133 | 0.75219(11) | 0.50622(7) | 0.87772(17) | 0.0752 | 1.0000 |
| C134 | 0.74160(6)  | 0.69178(5) | 0.78296(9)  | 0.0372 | 1.0000 |
| C135 | 0.70950(6)  | 0.70731(5) | 0.83943(10) | 0.0413 | 1.0000 |
| C136 | 0.65428(7)  | 0.72077(6) | 0.77859(11) | 0.0480 | 1.0000 |
| C137 | 0.62108(7)  | 0.73963(7) | 0.83052(12) | 0.0541 | 1.0000 |
| N141 | 0.54156(5)  | 0.56579(3) | 0.32066(7)  | 0.0297 | 1.0000 |
| C142 | 0.53409(6)  | 0.60774(4) | 0.37558(8)  | 0.0333 | 1.0000 |
| C143 | 0.50806(6)  | 0.65151(5) | 0.32246(9)  | 0.0377 | 1.0000 |
| C144 | 0.50368(7)  | 0.69077(6) | 0.38580(12) | 0.0512 | 1.0000 |
| C145 | 0.47672(8)  | 0.73550(6) | 0.33663(14) | 0.0598 | 1.0000 |
| C146 | 0.57401(6)  | 0.58044(4) | 0.26410(8)  | 0.0335 | 1.0000 |
| C147 | 0.62804(6)  | 0.59951(5) | 0.31612(10) | 0.0403 | 1.0000 |
| C148 | 0.65550(7)  | 0.61692(6) | 0.25353(11) | 0.0507 | 1.0000 |
| C149 | 0.70893(7)  | 0.63817(7) | 0.30454(12) | 0.0529 | 1.0000 |
| C150 | 0.56880(6)  | 0.52638(4) | 0.38669(9)  | 0.0353 | 1.0000 |
| C151 | 0.57823(7)  | 0.48029(5) | 0.34481(10) | 0.0440 | 1.0000 |
| C152 | 0.61365(8)  | 0.44646(6) | 0.41477(12) | 0.0534 | 1.0000 |
| C153 | 0.62049(9)  | 0.39914(6) | 0.37360(15) | 0.0685 | 1.0000 |
| C154 | 0.48900(6)  | 0.54842(4) | 0.25591(8)  | 0.0318 | 1.0000 |
| C155 | 0.44847(6)  | 0.53570(5) | 0.29696(9)  | 0.0353 | 1.0000 |
| C156 | 0.39914(6)  | 0.51762(5) | 0.22430(9)  | 0.0399 | 1.0000 |
| C157 | 0.35547(7)  | 0.50763(6) | 0.26069(11) | 0.0513 | 1.0000 |
| N161 | 0.79176(5)  | 0.82760(3) | 0.33317(7)  | 0.0301 | 1.0000 |
| C162 | 0.78586(6)  | 0.87093(4) | 0.38705(8)  | 0.0313 | 1.0000 |
| C163 | 0.76232(6)  | 0.91546(5) | 0.33309(9)  | 0.0372 | 1.0000 |
| C164 | 0.74565(7)  | 0.95031(5) | 0.39178(10) | 0.0414 | 1.0000 |
| C165 | 0.72674(8)  | 0.99793(6) | 0.34534(12) | 0.0529 | 1.0000 |
| C166 | 0.82047(6)  | 0.84096(4) | 0.27012(8)  | 0.0334 | 1.0000 |
| C167 | 0.87635(6)  | 0.85770(5) | 0.31656(9)  | 0.0369 | 1.0000 |
| C168 | 0.90015(7)  | 0.87353(6) | 0.24759(11) | 0.0475 | 1.0000 |
| C169 | 0.95740(8)  | 0.88717(8) | 0.29133(14) | 0.0608 | 1.0000 |
| C170 | 0.82184(6)  | 0.79003(4) | 0.40027(8)  | 0.0335 | 1.0000 |

|      |             |             |             |        |           |
|------|-------------|-------------|-------------|--------|-----------|
| C171 | 0.83053(7)  | 0.74347(5)  | 0.35810(10) | 0.0419 | 1.0000    |
| C172 | 0.86240(7)  | 0.70810(5)  | 0.42945(12) | 0.0479 | 1.0000    |
| C173 | 0.83280(8)  | 0.69033(6)  | 0.48820(12) | 0.0560 | 1.0000    |
| C174 | 0.73820(6)  | 0.80847(5)  | 0.27568(9)  | 0.0353 | 1.0000    |
| C175 | 0.70494(6)  | 0.78889(5)  | 0.32702(9)  | 0.0393 | 1.0000    |
| C176 | 0.65260(7)  | 0.77124(6)  | 0.26229(11) | 0.0477 | 1.0000    |
| C177 | 0.61799(7)  | 0.75098(7)  | 0.31067(13) | 0.0573 | 1.0000    |
| H51  | 1.09386(9)  | 0.81675(9)  | 0.52598(13) | 0.0901 | 1.0000    |
| H61  | 1.08024(11) | 0.73735(9)  | 0.56489(15) | 0.1012 | 1.0000    |
| H71  | 1.00641(12) | 0.71926(8)  | 0.59978(14) | 0.0965 | 1.0000    |
| H81  | 0.94916(9)  | 0.77403(6)  | 0.60907(11) | 0.0666 | 1.0000    |
| H151 | 0.70298(8)  | 0.89911(8)  | 0.55908(11) | 0.0697 | 1.0000    |
| H161 | 0.63953(8)  | 0.84191(11) | 0.53109(13) | 0.0899 | 1.0000    |
| H171 | 0.66290(11) | 0.75868(9)  | 0.54916(13) | 0.0900 | 1.0000    |
| H181 | 0.75121(10) | 0.73772(7)  | 0.59029(12) | 0.0775 | 1.0000    |
| H251 | 0.33164(7)  | 0.48369(6)  | 0.01972(10) | 0.0577 | 1.0000    |
| H261 | 0.34976(8)  | 0.40314(6)  | 0.02110(11) | 0.0615 | 1.0000    |
| H271 | 0.43784(8)  | 0.37642(6)  | 0.06881(11) | 0.0666 | 1.0000    |
| H281 | 0.50346(8)  | 0.43057(5)  | 0.07710(10) | 0.0585 | 1.0000    |
| H351 | 0.64076(8)  | 0.33562(6)  | 0.06292(11) | 0.0673 | 1.0000    |
| H361 | 0.71429(9)  | 0.32992(7)  | 0.01692(11) | 0.0739 | 1.0000    |
| H371 | 0.76823(9)  | 0.39481(8)  | 0.03052(14) | 0.0805 | 1.0000    |
| H381 | 0.74792(8)  | 0.46738(8)  | 0.08765(15) | 0.0805 | 1.0000    |
| H451 | 0.69516(9)  | 0.60837(7)  | 0.07880(12) | 0.0717 | 1.0000    |
| H461 | 0.76017(10) | 0.55689(8)  | 0.16317(16) | 0.0859 | 1.0000    |
| H471 | 0.84660(10) | 0.58840(8)  | 0.23087(19) | 0.1001 | 1.0000    |
| H481 | 0.86260(9)  | 0.66887(9)  | 0.20796(18) | 0.0945 | 1.0000    |
| H551 | 0.60835(12) | 0.9224(3)   | 0.0695(3)   | 0.0767 | 0.684(17) |
| H561 | 0.6401(2)   | 0.9994(3)   | 0.0949(3)   | 0.0816 | 0.684(17) |
| H571 | 0.7263(3)   | 1.01545(17) | 0.1028(4)   | 0.0818 | 0.684(17) |
| H581 | 0.7776(2)   | 0.95324(16) | 0.0814(5)   | 0.0706 | 0.684(17) |
| H651 | 0.6084(3)   | 0.8936(6)   | 0.0719(6)   | 0.0831 | 0.316(17) |
| H661 | 0.6263(4)   | 0.9745(5)   | 0.0997(6)   | 0.0881 | 0.316(17) |
| H671 | 0.7039(5)   | 1.0055(4)   | 0.0937(8)   | 0.0884 | 0.316(17) |
| H681 | 0.7635(4)   | 0.9562(3)   | 0.0634(9)   | 0.0780 | 0.316(17) |
| H751 | 0.41139(13) | 0.77665(14) | 0.6028(3)   | 0.0739 | 0.820(12) |
| H761 | 0.4478(2)   | 0.70036(11) | 0.6448(2)   | 0.0800 | 0.820(12) |
| H771 | 0.5292(2)   | 0.68343(7)  | 0.63585(19) | 0.0844 | 0.820(12) |
| H781 | 0.57409(13) | 0.74325(11) | 0.5856(2)   | 0.0762 | 0.820(12) |
| H851 | 0.3942(6)   | 0.7959(6)   | 0.5894(8)   | 0.0714 | 0.180(12) |

|       |             |            |             |        |           |
|-------|-------------|------------|-------------|--------|-----------|
| H861  | 0.4154(8)   | 0.7171(6)  | 0.6343(8)   | 0.0830 | 0.180(12) |
| H871  | 0.4969(9)   | 0.6871(4)  | 0.6476(11)  | 0.0769 | 0.180(12) |
| H881  | 0.5541(7)   | 0.7343(3)  | 0.6049(10)  | 0.0761 | 0.180(12) |
| H951  | 0.51534(9)  | 1.07728(6) | 0.58397(13) | 0.0723 | 1.0000    |
| H961  | 0.44105(10) | 1.12579(6) | 0.53897(13) | 0.0794 | 1.0000    |
| H971  | 0.36511(10) | 1.09820(7) | 0.43136(14) | 0.0820 | 1.0000    |
| H981  | 0.36366(10) | 1.02035(7) | 0.37184(13) | 0.0758 | 1.0000    |
| H1022 | 0.59241(6)  | 0.96328(4) | 0.88657(9)  | 0.0404 | 1.0000    |
| H1021 | 0.53585(6)  | 0.98274(4) | 0.87094(9)  | 0.0395 | 1.0000    |
| H1032 | 0.59563(6)  | 1.00776(5) | 0.76041(10) | 0.0479 | 1.0000    |
| H1031 | 0.53882(6)  | 1.02758(5) | 0.74578(10) | 0.0498 | 1.0000    |
| H1041 | 0.62686(7)  | 1.04844(5) | 0.90238(11) | 0.0564 | 1.0000    |
| H1042 | 0.56967(7)  | 1.06693(5) | 0.88601(11) | 0.0569 | 1.0000    |
| H1052 | 0.62416(8)  | 1.12587(6) | 0.85454(13) | 0.0847 | 1.0000    |
| H1051 | 0.63011(8)  | 1.09288(6) | 0.77744(13) | 0.0828 | 1.0000    |
| H1053 | 0.57550(8)  | 1.11559(6) | 0.76690(13) | 0.0830 | 1.0000    |
| H1062 | 0.58032(6)  | 0.93496(5) | 0.70541(9)  | 0.0409 | 1.0000    |
| H1061 | 0.55461(6)  | 0.88403(5) | 0.70249(9)  | 0.0405 | 1.0000    |
| H1072 | 0.64592(6)  | 0.91628(5) | 0.84586(9)  | 0.0457 | 1.0000    |
| H1071 | 0.61984(6)  | 0.86493(5) | 0.84079(9)  | 0.0456 | 1.0000    |
| H1081 | 0.66335(7)  | 0.89880(7) | 0.71358(12) | 0.0639 | 1.0000    |
| H1082 | 0.63838(7)  | 0.84698(7) | 0.71236(12) | 0.0658 | 1.0000    |
| H1092 | 0.72961(8)  | 0.84266(7) | 0.76829(14) | 0.0905 | 1.0000    |
| H1091 | 0.73218(8)  | 0.87909(7) | 0.84636(14) | 0.0901 | 1.0000    |
| H1093 | 0.70818(8)  | 0.82693(7) | 0.84309(14) | 0.0904 | 1.0000    |
| H1102 | 0.55898(6)  | 0.88973(4) | 0.89516(8)  | 0.0378 | 1.0000    |
| H1101 | 0.50011(6)  | 0.91078(4) | 0.87004(8)  | 0.0389 | 1.0000    |
| H1112 | 0.52356(6)  | 0.83049(5) | 0.77705(9)  | 0.0452 | 1.0000    |
| H1111 | 0.46768(6)  | 0.85077(5) | 0.75790(9)  | 0.0462 | 1.0000    |
| H1121 | 0.53058(8)  | 0.81090(5) | 0.92205(10) | 0.0620 | 1.0000    |
| H1122 | 0.47282(8)  | 0.83034(5) | 0.90482(10) | 0.0615 | 1.0000    |
| H1132 | 0.46768(7)  | 0.74677(5) | 0.88944(10) | 0.0683 | 1.0000    |
| H1131 | 0.49524(7)  | 0.75059(5) | 0.81630(10) | 0.0683 | 1.0000    |
| H1133 | 0.43828(7)  | 0.77033(5) | 0.79723(10) | 0.0675 | 1.0000    |
| H1142 | 0.49864(6)  | 0.96461(5) | 0.66804(9)  | 0.0427 | 1.0000    |
| H1141 | 0.47381(6)  | 0.91526(5) | 0.67616(9)  | 0.0411 | 1.0000    |
| H1152 | 0.45987(6)  | 0.99914(5) | 0.76278(10) | 0.0507 | 1.0000    |
| H1151 | 0.43201(6)  | 0.95079(5) | 0.76770(10) | 0.0515 | 1.0000    |
| H1161 | 0.41786(7)  | 1.00225(7) | 0.60736(13) | 0.0731 | 1.0000    |
| H1162 | 0.38492(7)  | 0.95511(7) | 0.61267(13) | 0.0727 | 1.0000    |

|       |             |            |             |        |        |
|-------|-------------|------------|-------------|--------|--------|
| H1172 | 0.33531(8)  | 1.02688(7) | 0.60463(17) | 0.1031 | 1.0000 |
| H1171 | 0.37743(8)  | 1.04291(7) | 0.69798(17) | 0.1035 | 1.0000 |
| H1173 | 0.34187(8)  | 0.99803(7) | 0.69382(17) | 0.1012 | 1.0000 |
| H1222 | 0.86213(6)  | 0.71003(5) | 0.92565(9)  | 0.0419 | 1.0000 |
| H1221 | 0.80921(6)  | 0.72737(5) | 0.93388(9)  | 0.0430 | 1.0000 |
| H1232 | 0.84665(7)  | 0.75844(5) | 0.79741(10) | 0.0505 | 1.0000 |
| H1231 | 0.79346(7)  | 0.77593(5) | 0.80237(10) | 0.0495 | 1.0000 |
| H1241 | 0.89121(8)  | 0.79615(5) | 0.93479(10) | 0.0585 | 1.0000 |
| H1242 | 0.83917(8)  | 0.81596(5) | 0.93836(10) | 0.0602 | 1.0000 |
| H1252 | 0.87896(8)  | 0.87757(6) | 0.87882(11) | 0.0759 | 1.0000 |
| H1251 | 0.87925(8)  | 0.84079(6) | 0.79988(11) | 0.0757 | 1.0000 |
| H1253 | 0.82573(8)  | 0.86091(6) | 0.80565(11) | 0.0755 | 1.0000 |
| H1262 | 0.82041(6)  | 0.69464(5) | 0.72876(9)  | 0.0442 | 1.0000 |
| H1261 | 0.80109(6)  | 0.64183(5) | 0.72799(9)  | 0.0434 | 1.0000 |
| H1271 | 0.90082(7)  | 0.67178(5) | 0.85202(10) | 0.0488 | 1.0000 |
| H1272 | 0.88149(7)  | 0.61731(5) | 0.82810(10) | 0.0488 | 1.0000 |
| H1281 | 0.90120(7)  | 0.68243(5) | 0.70523(10) | 0.0555 | 1.0000 |
| H1282 | 0.88240(7)  | 0.63049(5) | 0.68076(10) | 0.0540 | 1.0000 |
| H1292 | 0.97286(8)  | 0.63406(7) | 0.71464(13) | 0.0826 | 1.0000 |
| H1291 | 0.98163(8)  | 0.65132(7) | 0.81272(13) | 0.0828 | 1.0000 |
| H1293 | 0.96056(8)  | 0.59835(7) | 0.78123(13) | 0.0839 | 1.0000 |
| H1302 | 0.83823(7)  | 0.63100(5) | 0.92866(9)  | 0.0457 | 1.0000 |
| H1301 | 0.78699(7)  | 0.64714(5) | 0.94275(9)  | 0.0467 | 1.0000 |
| H1311 | 0.78871(8)  | 0.58230(5) | 0.80841(11) | 0.0586 | 1.0000 |
| H1312 | 0.73705(8)  | 0.59788(5) | 0.82502(11) | 0.0571 | 1.0000 |
| H1322 | 0.81865(10) | 0.54524(6) | 0.94605(12) | 0.0738 | 1.0000 |
| H1321 | 0.76921(10) | 0.56235(6) | 0.96715(12) | 0.0726 | 1.0000 |
| H1333 | 0.75941(11) | 0.48053(7) | 0.92008(17) | 0.1131 | 1.0000 |
| H1332 | 0.76340(11) | 0.49658(7) | 0.82851(17) | 0.1116 | 1.0000 |
| H1331 | 0.71581(11) | 0.51253(7) | 0.85484(17) | 0.1125 | 1.0000 |
| H1342 | 0.74348(6)  | 0.71816(5) | 0.74212(9)  | 0.0443 | 1.0000 |
| H1341 | 0.72669(6)  | 0.66273(5) | 0.74894(9)  | 0.0433 | 1.0000 |
| H1351 | 0.72666(6)  | 0.73464(5) | 0.87820(10) | 0.0504 | 1.0000 |
| H1352 | 0.70758(6)  | 0.68052(5) | 0.87796(10) | 0.0492 | 1.0000 |
| H1362 | 0.65710(7)  | 0.74582(6) | 0.73851(11) | 0.0585 | 1.0000 |
| H1361 | 0.63741(7)  | 0.69221(6) | 0.74442(11) | 0.0585 | 1.0000 |
| H1373 | 0.58556(7)  | 0.74806(7) | 0.78943(12) | 0.0815 | 1.0000 |
| H1372 | 0.63776(7)  | 0.76740(7) | 0.86659(12) | 0.0800 | 1.0000 |
| H1371 | 0.61677(7)  | 0.71480(7) | 0.86906(12) | 0.0803 | 1.0000 |
| H1422 | 0.56866(6)  | 0.61616(4) | 0.41742(8)  | 0.0368 | 1.0000 |



|       |            |            |             |        |        |
|-------|------------|------------|-------------|--------|--------|
| H1421 | 0.51340(6) | 0.59572(4) | 0.40966(8)  | 0.0396 | 1.0000 |
| H1431 | 0.52764(6) | 0.66292(5) | 0.28600(9)  | 0.0428 | 1.0000 |
| H1432 | 0.47327(6) | 0.64152(5) | 0.28300(9)  | 0.0450 | 1.0000 |
| H1442 | 0.53946(7) | 0.69938(6) | 0.42439(12) | 0.0620 | 1.0000 |
| H1441 | 0.48417(7) | 0.67921(6) | 0.42279(12) | 0.0598 | 1.0000 |
| H1453 | 0.47370(8) | 0.75954(6) | 0.37840(14) | 0.0900 | 1.0000 |
| H1452 | 0.49689(8) | 0.74867(6) | 0.30251(14) | 0.0901 | 1.0000 |
| H1451 | 0.44095(8) | 0.72855(6) | 0.29639(14) | 0.0878 | 1.0000 |
| H1462 | 0.55334(6) | 0.60592(4) | 0.22369(8)  | 0.0397 | 1.0000 |
| H1461 | 0.57613(6) | 0.55273(4) | 0.22863(8)  | 0.0392 | 1.0000 |
| H1471 | 0.62550(6) | 0.62734(5) | 0.35210(10) | 0.0510 | 1.0000 |
| H1472 | 0.64970(6) | 0.57564(5) | 0.35582(10) | 0.0492 | 1.0000 |
| H1482 | 0.63299(7) | 0.64299(6) | 0.21693(11) | 0.0609 | 1.0000 |
| H1481 | 0.65791(7) | 0.59012(6) | 0.21535(11) | 0.0627 | 1.0000 |
| H1493 | 0.72604(7) | 0.64991(7) | 0.26251(12) | 0.0783 | 1.0000 |
| H1492 | 0.70547(7) | 0.66594(7) | 0.34248(12) | 0.0776 | 1.0000 |
| H1491 | 0.73192(7) | 0.61405(7) | 0.34482(12) | 0.0802 | 1.0000 |
| H1502 | 0.60213(6) | 0.54016(4) | 0.42392(9)  | 0.0402 | 1.0000 |
| H1501 | 0.54876(6) | 0.51995(4) | 0.42399(9)  | 0.0425 | 1.0000 |
| H1511 | 0.59393(7) | 0.48748(5) | 0.29977(10) | 0.0537 | 1.0000 |
| H1512 | 0.54544(7) | 0.46418(5) | 0.31703(10) | 0.0550 | 1.0000 |
| H1522 | 0.64805(8) | 0.46243(6) | 0.44280(12) | 0.0646 | 1.0000 |
| H1521 | 0.59929(8) | 0.44148(6) | 0.46245(12) | 0.0646 | 1.0000 |
| H1533 | 0.64348(9) | 0.37752(6) | 0.41809(15) | 0.1023 | 1.0000 |
| H1532 | 0.63427(9) | 0.40523(6) | 0.32597(15) | 0.1026 | 1.0000 |
| H1531 | 0.58600(9) | 0.38346(6) | 0.34579(15) | 0.1025 | 1.0000 |
| H1542 | 0.47610(6) | 0.57472(4) | 0.21295(8)  | 0.0378 | 1.0000 |
| H1541 | 0.49646(6) | 0.51960(4) | 0.22684(8)  | 0.0381 | 1.0000 |
| H1551 | 0.43919(6) | 0.56409(5) | 0.32462(9)  | 0.0426 | 1.0000 |
| H1552 | 0.46130(6) | 0.51165(5) | 0.34471(9)  | 0.0430 | 1.0000 |
| H1562 | 0.38718(6) | 0.54251(5) | 0.17782(9)  | 0.0500 | 1.0000 |
| H1561 | 0.40656(6) | 0.48800(5) | 0.19736(9)  | 0.0495 | 1.0000 |
| H1573 | 0.32343(7) | 0.49524(6) | 0.21243(11) | 0.0770 | 1.0000 |
| H1572 | 0.34660(7) | 0.53660(6) | 0.28682(11) | 0.0779 | 1.0000 |
| H1571 | 0.36569(7) | 0.48307(6) | 0.30774(11) | 0.0761 | 1.0000 |
| H1622 | 0.81951(6) | 0.87769(4) | 0.42923(8)  | 0.0381 | 1.0000 |
| H1621 | 0.76312(6) | 0.86077(4) | 0.41981(8)  | 0.0366 | 1.0000 |
| H1631 | 0.78852(6) | 0.93149(5) | 0.31220(9)  | 0.0455 | 1.0000 |
| H1632 | 0.73070(6) | 0.90698(5) | 0.28145(9)  | 0.0455 | 1.0000 |
| H1642 | 0.77551(7) | 0.95639(5) | 0.44563(10) | 0.0496 | 1.0000 |

|       |            |            |             |        |        |
|-------|------------|------------|-------------|--------|--------|
| H1641 | 0.71680(7) | 0.93533(5) | 0.40785(10) | 0.0500 | 1.0000 |
| H1653 | 0.71613(8) | 1.02023(6) | 0.38448(12) | 0.0767 | 1.0000 |
| H1652 | 0.75487(8) | 1.01395(6) | 0.33269(12) | 0.0785 | 1.0000 |
| H1651 | 0.69819(8) | 0.99396(6) | 0.29001(12) | 0.0782 | 1.0000 |
| H1662 | 0.79925(6) | 0.86605(4) | 0.23192(8)  | 0.0395 | 1.0000 |
| H1661 | 0.81953(6) | 0.81297(4) | 0.23303(8)  | 0.0394 | 1.0000 |
| H1671 | 0.87672(6) | 0.88421(5) | 0.35510(9)  | 0.0448 | 1.0000 |
| H1672 | 0.89776(6) | 0.83212(5) | 0.35377(9)  | 0.0458 | 1.0000 |
| H1682 | 0.88002(7) | 0.90095(6) | 0.21248(11) | 0.0575 | 1.0000 |
| H1681 | 0.89633(7) | 0.84745(6) | 0.20476(11) | 0.0581 | 1.0000 |
| H1693 | 0.97131(8) | 0.89902(8) | 0.24705(14) | 0.0901 | 1.0000 |
| H1692 | 0.95869(8) | 0.91207(8) | 0.33413(14) | 0.0901 | 1.0000 |
| H1691 | 0.97720(8) | 0.85970(8) | 0.32210(14) | 0.0898 | 1.0000 |
| H1702 | 0.85510(6) | 0.80431(4) | 0.43585(8)  | 0.0388 | 1.0000 |
| H1701 | 0.80296(6) | 0.78447(4) | 0.43995(8)  | 0.0379 | 1.0000 |
| H1711 | 0.84800(7) | 0.75024(5) | 0.31570(10) | 0.0508 | 1.0000 |
| H1712 | 0.79670(7) | 0.72904(5) | 0.32392(10) | 0.0495 | 1.0000 |
| H1722 | 0.89595(7) | 0.72186(5) | 0.46597(12) | 0.0590 | 1.0000 |
| H1721 | 0.86986(7) | 0.67944(5) | 0.39804(12) | 0.0579 | 1.0000 |
| H1733 | 0.85468(8) | 0.66566(6) | 0.52897(12) | 0.0837 | 1.0000 |
| H1732 | 0.82562(8) | 0.71743(6) | 0.52278(12) | 0.0832 | 1.0000 |
| H1731 | 0.79888(8) | 0.67576(6) | 0.44945(12) | 0.0850 | 1.0000 |
| H1742 | 0.71949(6) | 0.83455(5) | 0.23697(9)  | 0.0411 | 1.0000 |
| H1741 | 0.74467(6) | 0.78230(5) | 0.23755(9)  | 0.0402 | 1.0000 |
| H1751 | 0.69845(6) | 0.81455(5) | 0.36586(9)  | 0.0464 | 1.0000 |
| H1752 | 0.72343(6) | 0.76172(5) | 0.36480(9)  | 0.0480 | 1.0000 |
| H1762 | 0.63579(7) | 0.79744(6) | 0.22404(11) | 0.0569 | 1.0000 |
| H1761 | 0.65984(7) | 0.74646(6) | 0.22397(11) | 0.0568 | 1.0000 |
| H1773 | 0.58625(7) | 0.73896(7) | 0.26685(13) | 0.0854 | 1.0000 |
| H1772 | 0.60929(7) | 0.77650(7) | 0.34557(13) | 0.0855 | 1.0000 |
| H1771 | 0.63551(7) | 0.72464(7) | 0.35111(13) | 0.0860 | 1.0000 |
| H11   | 0.93178(6) | 0.86213(4) | 0.58081(9)  | 0.0840 | 1.0000 |
| H21   | 1.01777(7) | 0.90955(6) | 0.53085(11) | 0.1138 | 1.0000 |
| H111  | 0.85930(7) | 0.81188(5) | 0.62918(9)  | 0.0962 | 1.0000 |
| H121  | 0.82913(6) | 0.87676(4) | 0.61672(8)  | 0.0802 | 1.0000 |
| H211  | 0.52601(6) | 0.50944(4) | 0.06651(8)  | 0.0747 | 1.0000 |
| H221  | 0.42064(6) | 0.56744(4) | 0.00493(9)  | 0.0826 | 1.0000 |
| H311  | 0.64507(6) | 0.49303(5) | 0.13807(12) | 0.1137 | 1.0000 |
| H321  | 0.60090(7) | 0.43401(5) | 0.13325(11) | 0.1040 | 1.0000 |
| H411  | 0.77550(7) | 0.74977(6) | 0.08821(12) | 0.1220 | 1.0000 |

|      |             |             |             |        |           |
|------|-------------|-------------|-------------|--------|-----------|
| H421 | 0.70712(7)  | 0.72254(6)  | 0.05781(10) | 0.1123 | 1.0000    |
| H511 | 0.7438(2)   | 0.84007(19) | 0.0341(5)   | 0.1065 | 0.684(17) |
| H521 | 0.6742(2)   | 0.8293(3)   | 0.0383(3)   | 0.1243 | 0.684(17) |
| H611 | 0.7493(4)   | 0.8356(3)   | 0.0535(8)   | 0.0983 | 0.316(17) |
| H621 | 0.6844(5)   | 0.8011(5)   | 0.0297(6)   | 0.1140 | 0.316(17) |
| H711 | 0.53267(15) | 0.85304(12) | 0.5122(4)   | 0.1046 | 0.820(12) |
| H721 | 0.46738(17) | 0.86697(15) | 0.5328(4)   | 0.0916 | 0.820(12) |
| H811 | 0.5338(5)   | 0.8507(4)   | 0.5390(9)   | 0.0808 | 0.180(12) |
| H821 | 0.4702(6)   | 0.8774(5)   | 0.5263(13)  | 0.0829 | 0.180(12) |
| H911 | 0.46029(8)  | 0.94169(5)  | 0.43475(10) | 0.1149 | 1.0000    |
| H921 | 0.52118(7)  | 0.96657(5)  | 0.51959(10) | 0.0966 | 1.0000    |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0551(6)       | 0.1142(10)      | 0.0937(9)       | 0.0220(8)       | 0.0367(6)       | 0.0030(6)       |
| F2    | 0.0538(6)       | 0.0748(7)       | 0.0661(6)       | -0.0144(5)      | 0.0214(5)       | 0.0131(5)       |
| F3    | 0.113(4)        | 0.0644(14)      | 0.114(5)        | -0.013(2)       | -0.001(3)       | -0.0003(17)     |
| F4    | 0.123(9)        | 0.051(5)        | 0.052(4)        | -0.005(2)       | 0.020(3)        | -0.011(4)       |
| F5    | 0.1021(9)       | 0.0526(6)       | 0.0873(8)       | 0.0091(5)       | 0.0378(7)       | 0.0042(6)       |
| O1    | 0.0614(7)       | 0.0527(6)       | 0.0616(7)       | -0.0022(5)      | 0.0317(6)       | 0.0065(5)       |
| O2    | 0.0671(8)       | 0.0849(10)      | 0.0856(10)      | -0.0121(8)      | 0.0404(8)       | -0.0031(7)      |
| C3    | 0.0534(9)       | 0.0510(8)       | 0.0361(6)       | -0.0093(6)      | 0.0100(6)       | 0.0040(6)       |
| C4    | 0.0533(9)       | 0.0679(10)      | 0.0455(8)       | -0.0174(7)      | 0.0136(7)       | -0.0009(8)      |
| C5    | 0.0511(10)      | 0.1081(17)      | 0.0539(10)      | -0.0361(10)     | 0.0039(8)       | 0.0127(10)      |
| C6    | 0.0784(15)      | 0.0852(15)      | 0.0599(11)      | -0.0303(10)     | -0.0131(10)     | 0.0366(12)      |
| C7    | 0.1079(19)      | 0.0573(10)      | 0.0512(10)      | -0.0092(8)      | -0.0022(11)     | 0.0198(11)      |
| C8    | 0.0815(12)      | 0.0521(9)       | 0.0402(7)       | -0.0091(6)      | 0.0085(8)       | -0.0004(8)      |
| O11   | 0.0737(8)       | 0.0610(7)       | 0.0538(6)       | 0.0014(5)       | 0.0229(6)       | 0.0163(6)       |
| O12   | 0.0589(7)       | 0.0508(6)       | 0.0544(6)       | -0.0037(5)      | 0.0201(5)       | -0.0085(5)      |
| C13   | 0.0722(11)      | 0.0509(8)       | 0.0303(6)       | -0.0016(5)      | 0.0221(7)       | -0.0044(7)      |
| C14   | 0.0548(8)       | 0.0492(7)       | 0.0326(6)       | -0.0011(5)      | 0.0211(6)       | -0.0027(6)      |
| C15   | 0.0582(10)      | 0.0770(11)      | 0.0433(8)       | 0.0028(7)       | 0.0242(7)       | 0.0042(8)       |
| C16   | 0.0456(9)       | 0.144(2)        | 0.0446(9)       | -0.0027(11)     | 0.0219(7)       | -0.0129(11)     |
| C17   | 0.0949(16)      | 0.0848(14)      | 0.0477(9)       | -0.0040(9)      | 0.0296(10)      | -0.0398(12)     |
| C18   | 0.0859(14)      | 0.0658(10)      | 0.0426(8)       | -0.0030(7)      | 0.0229(8)       | -0.0244(10)     |
| O21   | 0.0506(6)       | 0.0525(6)       | 0.0501(6)       | 0.0029(4)       | 0.0211(5)       | 0.0012(5)       |
| O22   | 0.0511(6)       | 0.0447(5)       | 0.0623(7)       | 0.0092(5)       | 0.0091(5)       | 0.0054(4)       |
| C23   | 0.0498(8)       | 0.0471(7)       | 0.0293(6)       | -0.0011(5)      | 0.0176(5)       | 0.0016(6)       |
| C24   | 0.0521(8)       | 0.0432(7)       | 0.0302(6)       | 0.0016(5)       | 0.0126(5)       | 0.0053(6)       |

|     |            |            |            |             |            |             |
|-----|------------|------------|------------|-------------|------------|-------------|
| C25 | 0.0503(8)  | 0.0523(8)  | 0.0376(7)  | -0.0041(6)  | 0.0115(6)  | 0.0000(6)   |
| C26 | 0.0612(10) | 0.0499(8)  | 0.0416(7)  | -0.0065(6)  | 0.0174(7)  | -0.0072(7)  |
| C27 | 0.0692(10) | 0.0424(7)  | 0.0473(8)  | 0.0006(6)   | 0.0168(7)  | 0.0026(7)   |
| C28 | 0.0573(9)  | 0.0463(7)  | 0.0417(7)  | -0.0007(6)  | 0.0166(6)  | 0.0087(6)   |
| O31 | 0.0561(7)  | 0.0653(8)  | 0.1070(11) | -0.0372(8)  | 0.0288(7)  | -0.0059(6)  |
| O32 | 0.0661(8)  | 0.0632(7)  | 0.0892(10) | 0.0039(7)   | 0.0397(7)  | 0.0003(6)   |
| C33 | 0.0393(8)  | 0.0584(9)  | 0.0523(8)  | -0.0126(7)  | 0.0070(6)  | 0.0035(6)   |
| C34 | 0.0451(8)  | 0.0521(8)  | 0.0401(7)  | 0.0051(6)   | 0.0075(6)  | 0.0075(6)   |
| C35 | 0.0710(11) | 0.0475(8)  | 0.0403(7)  | 0.0068(6)   | 0.0089(7)  | 0.0102(7)   |
| C36 | 0.0778(12) | 0.0594(10) | 0.0421(8)  | 0.0037(7)   | 0.0134(8)  | 0.0296(9)   |
| C37 | 0.0555(10) | 0.0801(13) | 0.0651(11) | -0.0025(9)  | 0.0213(8)  | 0.0174(9)   |
| C38 | 0.0416(9)  | 0.0760(12) | 0.0805(12) | -0.0163(10) | 0.0184(8)  | -0.0007(8)  |
| O41 | 0.0808(10) | 0.0789(9)  | 0.0859(10) | -0.0136(8)  | 0.0294(8)  | -0.0298(8)  |
| O42 | 0.0657(8)  | 0.0825(9)  | 0.0660(8)  | 0.0173(7)   | 0.0060(7)  | -0.0117(7)  |
| C43 | 0.0579(10) | 0.0647(10) | 0.0551(9)  | -0.0193(8)  | 0.0253(8)  | -0.0120(8)  |
| C44 | 0.0546(9)  | 0.0706(10) | 0.0360(7)  | -0.0070(6)  | 0.0193(6)  | -0.0081(8)  |
| C45 | 0.0630(10) | 0.0696(10) | 0.0521(9)  | -0.0132(8)  | 0.0264(8)  | -0.0156(8)  |
| C46 | 0.0806(14) | 0.0617(11) | 0.0766(13) | -0.0200(9)  | 0.0320(11) | 0.0037(9)   |
| C47 | 0.0740(14) | 0.0727(13) | 0.0994(17) | -0.0255(12) | 0.0239(12) | 0.0197(11)  |
| C48 | 0.0514(10) | 0.0870(14) | 0.0944(15) | -0.0343(12) | 0.0192(10) | -0.0007(10) |
| O51 | 0.0622(19) | 0.084(2)   | 0.057(3)   | -0.0083(16) | 0.013(2)   | -0.0021(15) |
| O52 | 0.0687(19) | 0.080(3)   | 0.0905(18) | 0.0103(18)  | 0.0102(14) | -0.0196(18) |
| C53 | 0.0571(18) | 0.074(2)   | 0.0359(18) | 0.0048(16)  | 0.0111(15) | -0.0048(15) |
| C54 | 0.0544(17) | 0.074(2)   | 0.0437(15) | 0.0037(18)  | 0.0059(12) | -0.0101(15) |
| C55 | 0.0490(15) | 0.084(4)   | 0.0454(15) | 0.002(2)    | 0.0044(12) | -0.0040(17) |
| C56 | 0.064(2)   | 0.079(3)   | 0.0512(15) | -0.0005(18) | 0.0030(15) | 0.009(2)    |
| C57 | 0.074(2)   | 0.068(2)   | 0.0512(17) | -0.0009(16) | 0.0018(18) | -0.0038(17) |
| C58 | 0.0605(19) | 0.0723(19) | 0.042(2)   | -0.0033(14) | 0.0080(18) | -0.0114(14) |
| O61 | 0.060(3)   | 0.053(3)   | 0.041(3)   | 0.0061(19)  | -0.009(3)  | -0.011(2)   |
| O62 | 0.079(4)   | 0.070(4)   | 0.064(3)   | -0.002(3)   | 0.013(3)   | -0.034(3)   |
| C63 | 0.066(3)   | 0.052(3)   | 0.025(3)   | 0.003(2)    | -0.005(3)  | -0.019(2)   |
| C64 | 0.067(3)   | 0.071(4)   | 0.027(2)   | -0.001(3)   | 0.003(2)   | -0.026(3)   |
| C65 | 0.075(4)   | 0.077(5)   | 0.037(3)   | 0.000(3)    | -0.002(2)  | -0.020(3)   |
| C66 | 0.078(4)   | 0.070(5)   | 0.051(3)   | 0.003(4)    | 0.001(3)   | 0.000(4)    |
| C67 | 0.085(5)   | 0.066(4)   | 0.048(3)   | 0.003(3)    | -0.003(4)  | -0.015(3)   |
| C68 | 0.071(4)   | 0.065(4)   | 0.035(3)   | 0.006(3)    | -0.001(3)  | -0.021(3)   |
| O71 | 0.0532(12) | 0.0694(13) | 0.091(2)   | 0.0137(14)  | 0.0283(14) | 0.0029(9)   |
| O72 | 0.0541(13) | 0.0661(14) | 0.0644(14) | 0.0029(13)  | 0.0209(10) | 0.0054(10)  |
| C73 | 0.0502(12) | 0.0520(12) | 0.0477(15) | -0.0059(9)  | 0.0085(9)  | -0.0052(10) |
| C74 | 0.0546(14) | 0.0548(12) | 0.0339(11) | -0.0064(11) | 0.0065(10) | -0.0050(10) |

|      |            |            |            |             |            |             |
|------|------------|------------|------------|-------------|------------|-------------|
| C75  | 0.0695(18) | 0.0725(18) | 0.0408(13) | -0.0105(12) | 0.0176(13) | -0.0186(14) |
| C76  | 0.091(3)   | 0.0630(15) | 0.0441(15) | -0.0065(12) | 0.016(2)   | -0.0230(16) |
| C77  | 0.096(3)   | 0.0496(13) | 0.0525(12) | -0.0045(9)  | 0.0070(14) | -0.0041(14) |
| C78  | 0.0664(17) | 0.0568(13) | 0.0570(15) | -0.0039(10) | 0.0073(12) | 0.0046(11)  |
| O81  | 0.056(4)   | 0.052(4)   | 0.053(5)   | 0.011(3)    | 0.012(3)   | 0.020(3)    |
| O82  | 0.061(6)   | 0.067(5)   | 0.039(5)   | -0.016(4)   | 0.020(4)   | -0.010(4)   |
| C83  | 0.066(5)   | 0.050(4)   | 0.037(4)   | -0.008(3)   | 0.005(4)   | -0.010(4)   |
| C84  | 0.063(5)   | 0.061(5)   | 0.021(4)   | -0.015(4)   | 0.009(4)   | -0.020(4)   |
| C85  | 0.078(6)   | 0.071(5)   | 0.019(3)   | -0.003(4)   | -0.002(4)  | -0.030(4)   |
| C86  | 0.086(7)   | 0.072(5)   | 0.033(4)   | 0.004(4)    | -0.002(4)  | -0.024(5)   |
| C87  | 0.083(7)   | 0.052(5)   | 0.038(5)   | 0.008(4)    | -0.003(5)  | -0.017(5)   |
| C88  | 0.078(7)   | 0.051(4)   | 0.043(4)   | 0.000(3)    | 0.004(5)   | -0.006(4)   |
| O91  | 0.1125(12) | 0.0454(6)  | 0.0610(7)  | -0.0077(5)  | 0.0198(8)  | -0.0023(7)  |
| O92  | 0.0744(9)  | 0.0642(7)  | 0.0660(7)  | 0.0006(6)   | 0.0375(7)  | -0.0090(6)  |
| C93  | 0.0888(13) | 0.0414(7)  | 0.0471(8)  | 0.0031(6)   | 0.0314(8)  | -0.0068(8)  |
| C94  | 0.0781(12) | 0.0455(8)  | 0.0497(8)  | 0.0044(6)   | 0.0375(8)  | -0.0090(7)  |
| C95  | 0.0866(13) | 0.0512(9)  | 0.0537(9)  | -0.0023(7)  | 0.0371(9)  | -0.0165(8)  |
| C96  | 0.1056(16) | 0.0435(8)  | 0.0600(10) | -0.0002(7)  | 0.0401(11) | -0.0006(9)  |
| C97  | 0.0955(15) | 0.0526(9)  | 0.0636(11) | 0.0079(8)   | 0.0356(10) | 0.0069(9)   |
| C98  | 0.0883(14) | 0.0517(9)  | 0.0539(9)  | 0.0054(7)   | 0.0263(9)  | -0.0062(9)  |
| N101 | 0.0317(5)  | 0.0353(5)  | 0.0279(4)  | -0.0007(4)  | 0.0123(4)  | -0.0002(4)  |
| C102 | 0.0337(6)  | 0.0366(6)  | 0.0346(6)  | -0.0035(5)  | 0.0145(5)  | -0.0018(5)  |
| C103 | 0.0384(7)  | 0.0404(6)  | 0.0411(7)  | 0.0007(5)   | 0.0145(5)  | -0.0045(5)  |
| C104 | 0.0458(8)  | 0.0426(7)  | 0.0540(8)  | -0.0063(6)  | 0.0206(6)  | -0.0079(6)  |
| C105 | 0.0507(9)  | 0.0437(8)  | 0.0719(10) | -0.0005(7)  | 0.0182(8)  | -0.0101(6)  |
| C106 | 0.0366(6)  | 0.0397(6)  | 0.0321(5)  | 0.0007(5)   | 0.0166(5)  | 0.0031(5)   |
| C107 | 0.0340(6)  | 0.0419(6)  | 0.0388(6)  | 0.0011(5)   | 0.0148(5)  | 0.0036(5)   |
| C108 | 0.0451(8)  | 0.0663(10) | 0.0536(8)  | 0.0059(7)   | 0.0250(7)  | 0.0178(7)   |
| C109 | 0.0459(9)  | 0.0649(10) | 0.0758(11) | 0.0085(8)   | 0.0275(8)  | 0.0167(7)   |
| C110 | 0.0366(6)  | 0.0372(6)  | 0.0303(5)  | 0.0009(4)   | 0.0155(5)  | -0.0018(5)  |
| C111 | 0.0400(7)  | 0.0380(6)  | 0.0343(6)  | -0.0008(5)  | 0.0149(5)  | -0.0033(5)  |
| C112 | 0.0698(10) | 0.0411(7)  | 0.0416(7)  | -0.0017(6)  | 0.0247(7)  | -0.0108(7)  |
| C113 | 0.0509(8)  | 0.0424(7)  | 0.0451(7)  | 0.0001(6)   | 0.0174(6)  | -0.0074(6)  |
| C114 | 0.0324(6)  | 0.0410(6)  | 0.0312(6)  | 0.0030(5)   | 0.0105(5)  | -0.0007(5)  |
| C115 | 0.0327(6)  | 0.0449(7)  | 0.0470(7)  | 0.0022(5)   | 0.0144(5)  | 0.0014(5)   |
| C116 | 0.0395(8)  | 0.0809(12) | 0.0591(9)  | 0.0261(9)   | 0.0177(7)  | 0.0116(8)   |
| C117 | 0.0391(8)  | 0.0571(9)  | 0.1029(15) | 0.0201(10)  | 0.0170(9)  | 0.0092(7)   |
| N121 | 0.0357(5)  | 0.0352(5)  | 0.0297(5)  | -0.0015(4)  | 0.0098(4)  | 0.0011(4)   |
| C122 | 0.0342(6)  | 0.0400(6)  | 0.0338(6)  | -0.0061(5)  | 0.0105(5)  | -0.0005(5)  |
| C123 | 0.0399(7)  | 0.0389(6)  | 0.0403(6)  | -0.0013(5)  | 0.0113(5)  | -0.0018(5)  |

|      |            |            |            |            |            |            |
|------|------------|------------|------------|------------|------------|------------|
| C124 | 0.0634(10) | 0.0460(7)  | 0.0405(7)  | -0.0094(6) | 0.0214(7)  | -0.0105(7) |
| C125 | 0.0659(10) | 0.0439(7)  | 0.0477(8)  | -0.0053(6) | 0.0230(7)  | -0.0110(7) |
| C126 | 0.0434(7)  | 0.0370(6)  | 0.0307(5)  | -0.0011(5) | 0.0142(5)  | 0.0031(5)  |
| C127 | 0.0433(7)  | 0.0429(7)  | 0.0376(6)  | 0.0028(5)  | 0.0170(5)  | 0.0070(5)  |
| C128 | 0.0528(8)  | 0.0439(7)  | 0.0426(7)  | 0.0021(5)  | 0.0230(6)  | 0.0055(6)  |
| C129 | 0.0545(9)  | 0.0611(9)  | 0.0600(9)  | 0.0014(7)  | 0.0300(8)  | 0.0092(7)  |
| C130 | 0.0436(7)  | 0.0389(6)  | 0.0347(6)  | 0.0035(5)  | 0.0139(5)  | 0.0037(5)  |
| C131 | 0.0545(9)  | 0.0405(7)  | 0.0460(7)  | 0.0027(6)  | 0.0148(6)  | -0.0024(6) |
| C132 | 0.0932(14) | 0.0407(8)  | 0.0548(9)  | 0.0032(7)  | 0.0333(9)  | 0.0012(8)  |
| C133 | 0.0962(16) | 0.0465(9)  | 0.0856(14) | 0.0063(9)  | 0.0350(12) | -0.0112(9) |
| C134 | 0.0333(6)  | 0.0400(6)  | 0.0350(6)  | -0.0008(5) | 0.0079(5)  | 0.0015(5)  |
| C135 | 0.0368(7)  | 0.0448(7)  | 0.0418(7)  | -0.0023(5) | 0.0132(5)  | 0.0017(5)  |
| C136 | 0.0376(7)  | 0.0544(8)  | 0.0492(8)  | 0.0003(6)  | 0.0116(6)  | 0.0047(6)  |
| C137 | 0.0406(8)  | 0.0611(9)  | 0.0594(9)  | -0.0037(7) | 0.0158(7)  | 0.0078(7)  |
| N141 | 0.0313(5)  | 0.0306(4)  | 0.0271(4)  | -0.0009(4) | 0.0098(4)  | -0.0006(4) |
| C142 | 0.0352(6)  | 0.0354(6)  | 0.0296(5)  | -0.0056(4) | 0.0117(5)  | -0.0022(5) |
| C143 | 0.0394(7)  | 0.0348(6)  | 0.0396(6)  | -0.0034(5) | 0.0146(5)  | 0.0010(5)  |
| C144 | 0.0522(9)  | 0.0436(7)  | 0.0550(8)  | -0.0122(6) | 0.0151(7)  | 0.0071(6)  |
| C145 | 0.0610(10) | 0.0398(7)  | 0.0804(12) | -0.0067(7) | 0.0267(9)  | 0.0091(7)  |
| C146 | 0.0367(6)  | 0.0354(6)  | 0.0310(5)  | 0.0002(4)  | 0.0150(5)  | -0.0020(5) |
| C147 | 0.0371(7)  | 0.0469(7)  | 0.0385(6)  | 0.0010(5)  | 0.0153(5)  | -0.0046(5) |
| C148 | 0.0491(8)  | 0.0638(9)  | 0.0439(7)  | -0.0086(7) | 0.0221(6)  | -0.0197(7) |
| C149 | 0.0478(8)  | 0.0624(9)  | 0.0555(9)  | -0.0113(7) | 0.0268(7)  | -0.0164(7) |
| C150 | 0.0351(6)  | 0.0364(6)  | 0.0325(6)  | 0.0047(5)  | 0.0096(5)  | 0.0009(5)  |
| C151 | 0.0467(8)  | 0.0362(6)  | 0.0450(7)  | 0.0031(5)  | 0.0108(6)  | 0.0058(5)  |
| C152 | 0.0586(9)  | 0.0436(8)  | 0.0560(9)  | 0.0119(6)  | 0.0175(7)  | 0.0117(7)  |
| C153 | 0.0762(12) | 0.0449(8)  | 0.0769(12) | 0.0080(8)  | 0.0170(10) | 0.0231(8)  |
| C154 | 0.0336(6)  | 0.0340(5)  | 0.0258(5)  | -0.0019(4) | 0.0079(4)  | -0.0024(4) |
| C155 | 0.0362(6)  | 0.0395(6)  | 0.0301(5)  | -0.0032(5) | 0.0116(5)  | -0.0052(5) |
| C156 | 0.0379(7)  | 0.0467(7)  | 0.0324(6)  | -0.0013(5) | 0.0090(5)  | -0.0075(5) |
| C157 | 0.0411(8)  | 0.0656(9)  | 0.0473(8)  | -0.0046(7) | 0.0154(6)  | -0.0154(7) |
| N161 | 0.0325(5)  | 0.0317(5)  | 0.0266(4)  | -0.0017(4) | 0.0110(4)  | -0.0023(4) |
| C162 | 0.0338(6)  | 0.0330(5)  | 0.0291(5)  | -0.0026(4) | 0.0133(4)  | -0.0021(4) |
| C163 | 0.0407(7)  | 0.0370(6)  | 0.0372(6)  | 0.0020(5)  | 0.0179(5)  | 0.0025(5)  |
| C164 | 0.0399(7)  | 0.0404(7)  | 0.0441(7)  | -0.0027(5) | 0.0149(6)  | 0.0038(5)  |
| C165 | 0.0537(9)  | 0.0452(8)  | 0.0552(9)  | 0.0002(6)  | 0.0129(7)  | 0.0145(6)  |
| C166 | 0.0383(6)  | 0.0365(6)  | 0.0291(5)  | -0.0010(4) | 0.0162(5)  | -0.0032(5) |
| C167 | 0.0372(6)  | 0.0396(6)  | 0.0368(6)  | -0.0012(5) | 0.0163(5)  | -0.0044(5) |
| C168 | 0.0480(8)  | 0.0567(8)  | 0.0445(7)  | -0.0046(6) | 0.0247(6)  | -0.0112(7) |
| C169 | 0.0466(9)  | 0.0781(12) | 0.0644(10) | -0.0015(9) | 0.0278(8)  | -0.0168(8) |

|      |            |            |            |            |           |            |
|------|------------|------------|------------|------------|-----------|------------|
| C170 | 0.0344(6)  | 0.0348(6)  | 0.0316(5)  | 0.0023(4)  | 0.0117(5) | -0.0002(5) |
| C171 | 0.0521(8)  | 0.0362(6)  | 0.0426(7)  | 0.0012(5)  | 0.0231(6) | 0.0048(6)  |
| C172 | 0.0458(8)  | 0.0382(7)  | 0.0594(9)  | 0.0055(6)  | 0.0180(7) | 0.0062(6)  |
| C173 | 0.0713(11) | 0.0487(8)  | 0.0505(8)  | 0.0120(7)  | 0.0244(8) | 0.0074(7)  |
| C174 | 0.0331(6)  | 0.0393(6)  | 0.0311(5)  | -0.0035(4) | 0.0083(5) | -0.0051(5) |
| C175 | 0.0351(6)  | 0.0440(7)  | 0.0391(6)  | -0.0021(5) | 0.0130(5) | -0.0060(5) |
| C176 | 0.0378(7)  | 0.0528(8)  | 0.0486(8)  | -0.0008(6) | 0.0103(6) | -0.0109(6) |
| C177 | 0.0411(8)  | 0.0660(10) | 0.0630(10) | -0.0008(8) | 0.0157(7) | -0.0156(7) |

## Distances

|     |      |             |  |     |      |           |
|-----|------|-------------|--|-----|------|-----------|
| F3  | F4   | 0.655(12)Å  |  | F3  | H621 | 1.027Å    |
| O1  | C3   | 1.3675(19)Å |  | O1  | H11  | 0.810Å    |
| O2  | C4   | 1.348(3)Å   |  | O2  | H21  | 0.905Å    |
| C3  | C4   | 1.387(3)Å   |  | C3  | C8   | 1.390(3)Å |
| C4  | C5   | 1.387(3)Å   |  | C5  | C6   | 1.384(4)Å |
| C5  | H51  | 0.921Å      |  | C6  | C7   | 1.371(4)Å |
| C6  | H61  | 0.943Å      |  | C7  | C8   | 1.386(3)Å |
| C7  | H71  | 0.964Å      |  | C8  | H81  | 1.042Å    |
| O11 | C13  | 1.375(2)Å   |  | O11 | H111 | 1.029Å    |
| O12 | C14  | 1.3518(19)Å |  | O12 | H121 | 0.844Å    |
| C13 | C14  | 1.403(2)Å   |  | C13 | C18  | 1.363(3)Å |
| C14 | C15  | 1.386(2)Å   |  | C15 | C16  | 1.408(3)Å |
| C15 | H151 | 0.921Å      |  | C16 | C17  | 1.397(4)Å |
| C16 | H161 | 0.926Å      |  | C17 | C18  | 1.347(3)Å |
| C17 | H171 | 0.967Å      |  | C18 | H181 | 0.983Å    |
| O21 | C23  | 1.3648(19)Å |  | O21 | H211 | 0.843Å    |
| O22 | C24  | 1.3685(18)Å |  | O22 | H221 | 0.816Å    |
| C23 | C24  | 1.391(2)Å   |  | C23 | C28  | 1.389(2)Å |
| C24 | C25  | 1.380(2)Å   |  | C25 | C26  | 1.386(2)Å |
| C25 | H251 | 0.970Å      |  | C26 | C27  | 1.380(3)Å |
| C26 | H261 | 0.975Å      |  | C27 | C28  | 1.386(3)Å |
| C27 | H271 | 0.959Å      |  | C28 | H281 | 0.908Å    |
| O31 | C33  | 1.355(2)Å   |  | O31 | H311 | 0.842Å    |
| O32 | C34  | 1.356(2)Å   |  | O32 | H321 | 0.851Å    |
| C33 | C34  | 1.403(2)Å   |  | C33 | C38  | 1.380(3)Å |
| C34 | C35  | 1.392(2)Å   |  | C35 | C36  | 1.379(3)Å |
| C35 | H351 | 0.944Å      |  | C36 | C37  | 1.373(3)Å |
| C36 | H361 | 0.946Å      |  | C37 | C38  | 1.383(3)Å |
| C37 | H371 | 0.956Å      |  | C38 | H381 | 0.939Å    |

|     |      |            |  |     |      |            |
|-----|------|------------|--|-----|------|------------|
| O41 | C43  | 1.373(2)Å  |  | O41 | H411 | 0.872Å     |
| O42 | C44  | 1.359(2)Å  |  | O42 | H421 | 0.826Å     |
| C43 | C44  | 1.397(2)Å  |  | C43 | C48  | 1.384(3)Å  |
| C44 | C45  | 1.391(3)Å  |  | C45 | C46  | 1.373(3)Å  |
| C45 | H451 | 0.934Å     |  | C46 | C47  | 1.371(3)Å  |
| C46 | H461 | 0.983Å     |  | C47 | C48  | 1.386(4)Å  |
| C47 | H471 | 0.973Å     |  | C48 | H481 | 0.950Å     |
| O51 | C53  | 1.361(4)Å  |  | O51 | O61  | 0.313(14)Å |
| O51 | C63  | 1.212(10)Å |  | O51 | H511 | 0.845Å     |
| O51 | H611 | 0.977Å     |  | O52 | C54  | 1.366(3)Å  |
| O52 | O62  | 0.619(10)Å |  | O52 | C64  | 1.043(8)Å  |
| O52 | H521 | 0.829Å     |  | C53 | C54  | 1.403(3)Å  |
| C53 | C58  | 1.381(3)Å  |  | C53 | O61  | 1.509(10)Å |
| C53 | C63  | 0.205(9)Å  |  | C53 | C64  | 1.461(8)Å  |
| C53 | C68  | 1.188(10)Å |  | C54 | C55  | 1.390(3)Å  |
| C54 | C63  | 1.397(8)Å  |  | C54 | C64  | 0.446(9)Å  |
| C54 | C65  | 1.075(9)Å  |  | C55 | C56  | 1.382(4)Å  |
| C55 | C65  | 0.619(9)Å  |  | C55 | C66  | 0.780(9)Å  |
| C55 | H551 | 0.938Å     |  | C56 | C57  | 1.379(4)Å  |
| C56 | C66  | 0.632(10)Å |  | C56 | C67  | 0.979(11)Å |
| C56 | H561 | 0.946Å     |  | C56 | H661 | 1.056Å     |
| C57 | C58  | 1.382(4)Å  |  | C57 | C67  | 0.498(9)Å  |
| C57 | C68  | 1.385(12)Å |  | C57 | H571 | 0.949Å     |
| C57 | H671 | 0.646Å     |  | C58 | C63  | 1.571(9)Å  |
| C58 | C67  | 1.474(12)Å |  | C58 | C68  | 0.310(12)Å |
| C58 | H581 | 0.943Å     |  | C58 | H681 | 0.721Å     |
| O61 | C63  | 1.370(6)Å  |  | O61 | H511 | 0.915Å     |
| O61 | H611 | 0.950Å     |  | O62 | C64  | 1.356(5)Å  |
| O62 | H521 | 0.337Å     |  | O62 | H621 | 1.030Å     |
| C63 | C64  | 1.392(5)Å  |  | C63 | C68  | 1.386(5)Å  |
| C64 | C65  | 1.386(5)Å  |  | C65 | C66  | 1.380(5)Å  |
| C65 | H551 | 0.974Å     |  | C65 | H651 | 0.943Å     |
| C66 | C67  | 1.374(5)Å  |  | C66 | H661 | 0.948Å     |
| C67 | C68  | 1.379(5)Å  |  | C67 | H671 | 0.926Å     |
| C68 | H581 | 1.204Å     |  | C68 | H681 | 0.935Å     |
| O71 | C73  | 1.364(3)Å  |  | O71 | O81  | 0.479(12)Å |
| O71 | C83  | 1.663(13)Å |  | O71 | H711 | 0.883Å     |
| O71 | H811 | 0.847Å     |  | O72 | C74  | 1.376(3)Å  |
| O72 | O82  | 0.287(14)Å |  | O72 | C84  | 1.099(12)Å |
| O72 | H721 | 0.858Å     |  | O72 | H821 | 1.154Å     |



|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C73  | C74   | 1.390(3)Å   |  | C73  | C78   | 1.387(3)Å   |
| C73  | O81   | 1.096(14)Å  |  | C73  | C83   | 0.368(17)Å  |
| C73  | C84   | 1.685(16)Å  |  | C73  | C88   | 1.458(10)Å  |
| C74  | C75   | 1.387(3)Å   |  | C74  | O82   | 1.638(13)Å  |
| C74  | C83   | 1.087(15)Å  |  | C74  | C84   | 0.332(16)Å  |
| C74  | C85   | 1.486(14)Å  |  | C75  | C76   | 1.379(3)Å   |
| C75  | C84   | 1.423(10)Å  |  | C75  | C85   | 0.599(17)Å  |
| C75  | C86   | 1.004(10)Å  |  | C75  | H751  | 0.945Å      |
| C76  | C77   | 1.373(3)Å   |  | C76  | C86   | 0.78(2)Å    |
| C76  | C87   | 0.60(2)Å    |  | C76  | H761  | 0.968Å      |
| C77  | C78   | 1.381(3)Å   |  | C77  | C87   | 0.79(2)Å    |
| C77  | C88   | 0.972(11)Å  |  | C77  | H771  | 0.952Å      |
| C77  | H871  | 1.075Å      |  | C78  | C83   | 1.483(12)Å  |
| C78  | C88   | 0.623(19)Å  |  | C78  | H781  | 0.947Å      |
| C78  | H881  | 0.547Å      |  | O81  | C83   | 1.365(7)Å   |
| O81  | H711  | 1.169Å      |  | O81  | H811  | 0.950Å      |
| O82  | C84   | 1.371(7)Å   |  | O82  | H721  | 0.696Å      |
| O82  | H821  | 0.950Å      |  | C83  | C84   | 1.388(5)Å   |
| C83  | C88   | 1.399(5)Å   |  | C84  | C85   | 1.386(5)Å   |
| C85  | C86   | 1.387(5)Å   |  | C85  | H751  | 0.542Å      |
| C85  | H851  | 0.940Å      |  | C86  | C87   | 1.374(6)Å   |
| C86  | H761  | 1.082Å      |  | C86  | H861  | 0.939Å      |
| C87  | C88   | 1.374(5)Å   |  | C87  | H871  | 0.939Å      |
| C88  | H881  | 0.927Å      |  | O91  | C93   | 1.360(2)Å   |
| O91  | H911  | 0.865Å      |  | O92  | C94   | 1.363(2)Å   |
| O92  | H921  | 0.856Å      |  | C93  | C94   | 1.404(3)Å   |
| C93  | C98   | 1.382(3)Å   |  | C94  | C95   | 1.394(2)Å   |
| C95  | C96   | 1.378(3)Å   |  | C95  | H951  | 0.905Å      |
| C96  | C97   | 1.380(3)Å   |  | C96  | H961  | 0.938Å      |
| C97  | C98   | 1.389(3)Å   |  | C97  | H971  | 0.958Å      |
| C98  | H981  | 0.963Å      |  | N101 | C102  | 1.5208(15)Å |
| N101 | C106  | 1.5165(16)Å |  | N101 | C110  | 1.5216(15)Å |
| N101 | C114  | 1.5191(15)Å |  | C102 | C103  | 1.5163(18)Å |
| C102 | H1022 | 0.971Å      |  | C102 | H1021 | 0.977Å      |
| C103 | C104  | 1.5198(19)Å |  | C103 | H1032 | 0.989Å      |
| C103 | H1031 | 0.979Å      |  | C104 | C105  | 1.519(2)Å   |
| C104 | H1041 | 0.965Å      |  | C104 | H1042 | 0.984Å      |
| C105 | H1052 | 0.976Å      |  | C105 | H1051 | 0.983Å      |
| C105 | H1053 | 0.972Å      |  | C106 | C107  | 1.5175(18)Å |
| C106 | H1062 | 0.966Å      |  | C106 | H1061 | 0.976Å      |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C107 | C108  | 1.523(2)Å   |  | C107 | H1072 | 0.983Å      |
| C107 | H1071 | 0.973Å      |  | C108 | C109  | 1.511(2)Å   |
| C108 | H1081 | 0.969Å      |  | C108 | H1082 | 0.970Å      |
| C109 | H1092 | 0.971Å      |  | C109 | H1091 | 0.985Å      |
| C109 | H1093 | 0.979Å      |  | C110 | C111  | 1.5195(17)Å |
| C110 | H1102 | 1.000Å      |  | C110 | H1101 | 0.986Å      |
| C111 | C112  | 1.5196(19)Å |  | C111 | H1112 | 0.970Å      |
| C111 | H1111 | 0.972Å      |  | C112 | C113  | 1.518(2)Å   |
| C112 | H1121 | 1.000Å      |  | C112 | H1122 | 0.964Å      |
| C113 | H1132 | 0.965Å      |  | C113 | H1131 | 0.964Å      |
| C113 | H1133 | 0.964Å      |  | C114 | C115  | 1.5067(19)Å |
| C114 | H1142 | 0.960Å      |  | C114 | H1141 | 0.950Å      |
| C115 | C116  | 1.520(2)Å   |  | C115 | H1152 | 0.964Å      |
| C115 | H1151 | 0.967Å      |  | C116 | C117  | 1.505(3)Å   |
| C116 | H1161 | 0.986Å      |  | C116 | H1162 | 0.995Å      |
| C117 | H1172 | 0.976Å      |  | C117 | H1171 | 0.974Å      |
| C117 | H1173 | 0.982Å      |  | N121 | C122  | 1.5234(15)Å |
| N121 | C126  | 1.5227(17)Å |  | N121 | C130  | 1.5234(16)Å |
| N121 | C134  | 1.5206(16)Å |  | C122 | C123  | 1.5205(19)Å |
| C122 | H1222 | 0.982Å      |  | C122 | H1221 | 0.966Å      |
| C123 | C124  | 1.5180(19)Å |  | C123 | H1232 | 0.959Å      |
| C123 | H1231 | 0.969Å      |  | C124 | C125  | 1.523(2)Å   |
| C124 | H1241 | 0.978Å      |  | C124 | H1242 | 0.967Å      |
| C125 | H1252 | 0.996Å      |  | C125 | H1251 | 0.982Å      |
| C125 | H1253 | 0.975Å      |  | C126 | C127  | 1.5199(19)Å |
| C126 | H1262 | 0.978Å      |  | C126 | H1261 | 0.967Å      |
| C127 | C128  | 1.526(2)Å   |  | C127 | H1271 | 0.986Å      |
| C127 | H1272 | 0.995Å      |  | C128 | C129  | 1.521(2)Å   |
| C128 | H1281 | 0.973Å      |  | C128 | H1282 | 0.966Å      |
| C129 | H1292 | 0.955Å      |  | C129 | H1291 | 0.978Å      |
| C129 | H1293 | 0.977Å      |  | C130 | C131  | 1.518(2)Å   |
| C130 | H1302 | 0.954Å      |  | C130 | H1301 | 0.977Å      |
| C131 | C132  | 1.516(2)Å   |  | C131 | H1311 | 0.960Å      |
| C131 | H1312 | 0.980Å      |  | C132 | C133  | 1.525(3)Å   |
| C132 | H1322 | 0.965Å      |  | C132 | H1321 | 0.961Å      |
| C133 | H1333 | 0.957Å      |  | C133 | H1332 | 0.974Å      |
| C133 | H1331 | 0.947Å      |  | C134 | C135  | 1.5207(19)Å |
| C134 | H1342 | 0.995Å      |  | C134 | H1341 | 0.981Å      |
| C135 | C136  | 1.5271(19)Å |  | C135 | H1351 | 0.990Å      |
| C135 | H1352 | 0.980Å      |  | C136 | C137  | 1.518(2)Å   |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C136 | H1362 | 0.968Å      |  | C136 | H1361 | 0.984Å      |
| C137 | H1373 | 0.990Å      |  | C137 | H1372 | 0.977Å      |
| C137 | H1371 | 0.960Å      |  | N141 | C142  | 1.5166(15)Å |
| N141 | C146  | 1.5225(16)Å |  | N141 | C150  | 1.5241(15)Å |
| N141 | C154  | 1.5246(15)Å |  | C142 | C143  | 1.5139(17)Å |
| C142 | H1422 | 0.975Å      |  | C142 | H1421 | 0.969Å      |
| C143 | C144  | 1.5219(19)Å |  | C143 | H1431 | 0.969Å      |
| C143 | H1432 | 0.979Å      |  | C144 | C145  | 1.520(2)Å   |
| C144 | H1442 | 0.985Å      |  | C144 | H1441 | 0.976Å      |
| C145 | H1453 | 0.968Å      |  | C145 | H1452 | 0.970Å      |
| C145 | H1451 | 0.982Å      |  | C146 | C147  | 1.5135(18)Å |
| C146 | H1462 | 0.992Å      |  | C146 | H1461 | 0.971Å      |
| C147 | C148  | 1.520(2)Å   |  | C147 | H1471 | 0.982Å      |
| C147 | H1472 | 0.965Å      |  | C148 | C149  | 1.520(2)Å   |
| C148 | H1482 | 0.998Å      |  | C148 | H1481 | 0.980Å      |
| C149 | H1493 | 0.996Å      |  | C149 | H1492 | 1.007Å      |
| C149 | H1491 | 0.989Å      |  | C150 | C151  | 1.5108(19)Å |
| C150 | H1502 | 0.975Å      |  | C150 | H1501 | 0.954Å      |
| C151 | C152  | 1.5221(19)Å |  | C151 | H1511 | 0.976Å      |
| C151 | H1512 | 0.960Å      |  | C152 | C153  | 1.514(2)Å   |
| C152 | H1522 | 0.993Å      |  | C152 | H1521 | 0.979Å      |
| C153 | H1533 | 0.975Å      |  | C153 | H1532 | 0.972Å      |
| C153 | H1531 | 0.991Å      |  | C154 | C155  | 1.5096(18)Å |
| C154 | H1542 | 0.981Å      |  | C154 | H1541 | 0.984Å      |
| C155 | C156  | 1.5233(17)Å |  | C155 | H1551 | 0.981Å      |
| C155 | H1552 | 0.983Å      |  | C156 | C157  | 1.521(2)Å   |
| C156 | H1562 | 0.984Å      |  | C156 | H1561 | 0.984Å      |
| C157 | H1573 | 1.003Å      |  | C157 | H1572 | 0.977Å      |
| C157 | H1571 | 0.982Å      |  | N161 | C162  | 1.5230(15)Å |
| N161 | C166  | 1.5197(15)Å |  | N161 | C170  | 1.5176(15)Å |
| N161 | C174  | 1.5249(15)Å |  | C162 | C163  | 1.5196(17)Å |
| C162 | H1622 | 0.949Å      |  | C162 | H1621 | 0.981Å      |
| C163 | C164  | 1.5241(19)Å |  | C163 | H1631 | 0.993Å      |
| C163 | H1632 | 0.992Å      |  | C164 | C165  | 1.520(2)Å   |
| C164 | H1642 | 0.971Å      |  | C164 | H1641 | 1.000Å      |
| C165 | H1653 | 0.993Å      |  | C165 | H1652 | 0.967Å      |
| C165 | H1651 | 0.958Å      |  | C166 | C167  | 1.5172(18)Å |
| C166 | H1662 | 0.975Å      |  | C166 | H1661 | 0.974Å      |
| C167 | C168  | 1.5236(19)Å |  | C167 | H1671 | 0.959Å      |
| C167 | H1672 | 0.980Å      |  | C168 | C169  | 1.520(2)Å   |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C168 | H1682 | 0.993Å      |  | C168 | H1681 | 0.978Å      |
| C169 | H1693 | 0.968Å      |  | C169 | H1692 | 0.965Å      |
| C169 | H1691 | 0.967Å      |  | C170 | C171  | 1.5183(18)Å |
| C170 | H1702 | 0.972Å      |  | C170 | H1701 | 0.957Å      |
| C171 | C172  | 1.5276(19)Å |  | C171 | H1711 | 0.971Å      |
| C171 | H1712 | 0.980Å      |  | C172 | C173  | 1.517(2)Å   |
| C172 | H1722 | 0.976Å      |  | C172 | H1721 | 1.001Å      |
| C173 | H1733 | 0.991Å      |  | C173 | H1732 | 0.994Å      |
| C173 | H1731 | 1.002Å      |  | C174 | C175  | 1.5189(19)Å |
| C174 | H1742 | 0.975Å      |  | C174 | H1741 | 1.004Å      |
| C175 | C176  | 1.5227(18)Å |  | C175 | H1751 | 1.001Å      |
| C175 | H1752 | 0.990Å      |  | C176 | C177  | 1.520(2)Å   |
| C176 | H1762 | 0.960Å      |  | C176 | H1761 | 0.987Å      |
| C177 | H1773 | 0.964Å      |  | C177 | H1772 | 0.982Å      |
| C177 | H1771 | 0.984Å      |  | H551 | H651  | 0.804Å      |
| H561 | H661  | 0.808Å      |  | H571 | H671  | 0.641Å      |
| H581 | H681  | 0.401Å      |  | H751 | H851  | 0.696Å      |
| H781 | H881  | 0.757Å      |  | H511 | H611  | 0.319Å      |
| H711 | H811  | 0.422Å      |  | H721 | H821  | 0.327Å      |

## Angles

|     |     |      |             |  |     |     |      |             |
|-----|-----|------|-------------|--|-----|-----|------|-------------|
| F4  | F3  | H621 | 145.750°    |  | C3  | O1  | H11  | 108.270°    |
| C4  | O2  | H21  | 108.299°    |  | O1  | C3  | C4   | 116.32(15)° |
| O1  | C3  | C8   | 123.51(17)° |  | C4  | C3  | C8   | 120.16(17)° |
| O2  | C4  | C3   | 122.33(16)° |  | O2  | C4  | C5   | 117.6(2)°   |
| C3  | C4  | C5   | 120.1(2)°   |  | C4  | C5  | C6   | 119.5(2)°   |
| C4  | C5  | H51  | 117.266°    |  | C6  | C5  | H51  | 123.271°    |
| C5  | C6  | C7   | 120.57(19)° |  | C5  | C6  | H61  | 120.098°    |
| C7  | C6  | H61  | 119.209°    |  | C6  | C7  | C8   | 120.5(2)°   |
| C6  | C7  | H71  | 120.571°    |  | C8  | C7  | H71  | 118.879°    |
| C3  | C8  | C7   | 119.2(2)°   |  | C3  | C8  | H81  | 130.011°    |
| C7  | C8  | H81  | 110.733°    |  | C13 | O11 | H111 | 121.447°    |
| C14 | O12 | H121 | 105.498°    |  | O11 | C13 | C14  | 123.73(15)° |
| O11 | C13 | C18  | 116.05(17)° |  | C14 | C13 | C18  | 120.22(18)° |
| O12 | C14 | C13  | 123.51(15)° |  | O12 | C14 | C15  | 117.36(15)° |
| C13 | C14 | C15  | 119.12(16)° |  | C14 | C15 | C16  | 119.79(19)° |
| C14 | C15 | H151 | 119.725°    |  | C16 | C15 | H151 | 120.463°    |
| C15 | C16 | C17  | 118.9(2)°   |  | C15 | C16 | H161 | 115.929°    |
| C17 | C16 | H161 | 125.151°    |  | C16 | C17 | C18  | 120.55(18)° |

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|------|-----|------|-------------|--|-----|-----|------|-------------|
| C16  | C17 | H171 | 118.768°    |  | C18 | C17 | H171 | 120.683°    |
| C13  | C18 | C17  | 121.4(2)°   |  | C13 | C18 | H181 | 118.098°    |
| C17  | C18 | H181 | 120.437°    |  | C23 | O21 | H211 | 107.661°    |
| C24  | O22 | H221 | 108.233°    |  | O21 | C23 | C24  | 117.87(13)° |
| O21  | C23 | C28  | 123.40(14)° |  | C24 | C23 | C28  | 118.73(14)° |
| O22  | C24 | C23  | 120.90(14)° |  | O22 | C24 | C25  | 118.67(14)° |
| C23  | C24 | C25  | 120.43(13)° |  | C24 | C25 | C26  | 120.80(15)° |
| C24  | C25 | H251 | 119.762°    |  | C26 | C25 | H251 | 119.431°    |
| C25  | C26 | C27  | 118.94(16)° |  | C25 | C26 | H261 | 119.489°    |
| C27  | C26 | H261 | 121.557°    |  | C26 | C27 | C28  | 120.65(15)° |
| C26  | C27 | H271 | 120.166°    |  | C28 | C27 | H271 | 119.179°    |
| C23  | C28 | C27  | 120.45(15)° |  | C23 | C28 | H281 | 119.496°    |
| C27  | C28 | H281 | 120.058°    |  | C33 | O31 | H311 | 115.170°    |
| C34  | O32 | H321 | 108.522°    |  | O31 | C33 | C34  | 123.90(16)° |
| O31  | C33 | C38  | 116.85(17)° |  | C34 | C33 | C38  | 119.25(16)° |
| O32  | C34 | C33  | 123.81(15)° |  | O32 | C34 | C35  | 117.61(16)° |
| C33  | C34 | C35  | 118.58(16)° |  | C34 | C35 | C36  | 121.14(18)° |
| C34  | C35 | H351 | 117.336°    |  | C36 | C35 | H351 | 121.525°    |
| C35  | C36 | C37  | 120.22(17)° |  | C35 | C36 | H361 | 121.560°    |
| C37  | C36 | H361 | 118.182°    |  | C36 | C37 | C38  | 119.23(19)° |
| C36  | C37 | H371 | 119.692°    |  | C38 | C37 | H371 | 121.047°    |
| C33  | C38 | C37  | 121.6(2)°   |  | C33 | C38 | H381 | 117.239°    |
| C37  | C38 | H381 | 121.154°    |  | C43 | O41 | H411 | 111.591°    |
| C44  | O42 | H421 | 102.053°    |  | O41 | C43 | C44  | 123.78(19)° |
| O41  | C43 | C48  | 117.76(18)° |  | C44 | C43 | C48  | 118.45(18)° |
| O42  | C44 | C43  | 123.84(17)° |  | O42 | C44 | C45  | 116.74(16)° |
| C43  | C44 | C45  | 119.42(18)° |  | C44 | C45 | C46  | 121.37(18)° |
| C44  | C45 | H451 | 118.720°    |  | C46 | C45 | H451 | 119.793°    |
| C45  | C46 | C47  | 119.3(2)°   |  | C45 | C46 | H461 | 118.926°    |
| C47  | C46 | H461 | 121.731°    |  | C46 | C47 | C48  | 120.2(2)°   |
| C46  | C47 | H471 | 121.155°    |  | C48 | C47 | H471 | 118.638°    |
| C43  | C48 | C47  | 121.2(2)°   |  | C43 | C48 | H481 | 118.010°    |
| C47  | C48 | H481 | 120.776°    |  | C53 | O51 | O61  | 113(3)°     |
| C53  | O51 | C63  | 6.3(4)°     |  | O61 | O51 | C63  | 114(3)°     |
| C53  | O51 | H511 | 114.545°    |  | O61 | O51 | H511 | 92.693°     |
| C63  | O51 | H511 | 108.293°    |  | C53 | O51 | H611 | 114.231°    |
| O61  | O51 | H611 | 75.821°     |  | C63 | O51 | H611 | 108.413°    |
| H511 | O51 | H611 | 18.371°     |  | C54 | O52 | O62  | 121.3(9)°   |
| C54  | O52 | C64  | 14.8(5)°    |  | O62 | O52 | C64  | 106.6(12)°  |
| C54  | O52 | H521 | 103.499°    |  | O62 | O52 | H521 | 21.210°     |

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|------|-----|------|------------|--|------|-----|------|------------|
| C64  | O52 | H521 | 88.796°    |  | O51  | C53 | C54  | 123.82(6)° |
| O51  | C53 | C58  | 116.95(6)° |  | C54  | C53 | C58  | 119.17(5)° |
| O51  | C53 | O61  | 11.0(6)°   |  | C54  | C53 | O61  | 127.9(5)°  |
| C58  | C53 | O61  | 112.2(5)°  |  | O51  | C53 | C63  | 40(3)°     |
| C54  | C53 | C63  | 84(2)°     |  | C58  | C53 | C63  | 156(2)°    |
| O61  | C53 | C63  | 44(2)°     |  | O51  | C53 | C64  | 106.4(3)°  |
| C54  | C53 | C64  | 17.8(3)°   |  | C58  | C53 | C64  | 136.6(3)°  |
| O61  | C53 | C64  | 110.2(6)°  |  | C63  | C53 | C64  | 66(2)°     |
| O51  | C53 | C68  | 123.9(5)°  |  | C54  | C53 | C68  | 111.3(5)°  |
| C58  | C53 | C68  | 10.8(7)°   |  | O61  | C53 | C68  | 120.7(6)°  |
| C63  | C53 | C68  | 164(3)°    |  | C64  | C53 | C68  | 129.1(7)°  |
| O52  | C54 | C53  | 123.77(6)° |  | O52  | C54 | C55  | 117.06(6)° |
| C53  | C54 | C55  | 119.09(5)° |  | O52  | C54 | C63  | 115.4(4)°  |
| C53  | C54 | C63  | 8.4(4)°    |  | C55  | C54 | C63  | 127.5(4)°  |
| O52  | C54 | C64  | 36.7(10)°  |  | C53  | C54 | C64  | 88.5(10)°  |
| C55  | C54 | C64  | 151.5(11)° |  | C63  | C54 | C64  | 80.1(10)°  |
| O52  | C54 | C65  | 93.0(5)°   |  | C53  | C54 | C65  | 143.0(5)°  |
| C55  | C54 | C65  | 25.2(5)°   |  | C63  | C54 | C65  | 151.1(7)°  |
| C64  | C54 | C65  | 126.4(14)° |  | C54  | C55 | C56  | 120.94(6)° |
| C54  | C55 | C65  | 47.6(8)°   |  | C56  | C55 | C65  | 163.2(9)°  |
| C54  | C55 | C66  | 128.6(7)°  |  | C56  | C55 | C66  | 10.7(8)°   |
| C65  | C55 | C66  | 161.0(14)° |  | C54  | C55 | H551 | 120.269°   |
| C56  | C55 | H551 | 118.778°   |  | C65  | C55 | H551 | 74.275°    |
| C66  | C55 | H551 | 110.723°   |  | C55  | C56 | C57  | 119.74(6)° |
| C55  | C56 | C66  | 13.3(9)°   |  | C57  | C56 | C66  | 128.9(8)°  |
| C55  | C56 | C67  | 105.4(5)°  |  | C57  | C56 | C67  | 14.7(5)°   |
| C66  | C56 | C67  | 115.3(12)° |  | C55  | C56 | H561 | 119.382°   |
| C57  | C56 | H561 | 120.870°   |  | C66  | C56 | H561 | 109.505°   |
| C67  | C56 | H561 | 135.036°   |  | C55  | C56 | H661 | 73.494°    |
| C57  | C56 | H661 | 163.527°   |  | C66  | C56 | H661 | 62.498°    |
| C67  | C56 | H661 | 172.837°   |  | H561 | C56 | H661 | 47.186°    |
| C56  | C57 | C58  | 119.83(6)° |  | C56  | C57 | C67  | 29.8(13)°  |
| C58  | C57 | C67  | 90.6(13)°  |  | C56  | C57 | C68  | 108.6(3)°  |
| C58  | C57 | C68  | 12.8(5)°   |  | C67  | C57 | C68  | 78.9(13)°  |
| C56  | C57 | H571 | 120.931°   |  | C58  | C57 | H571 | 119.241°   |
| C67  | C57 | H571 | 149.688°   |  | C68  | C57 | H571 | 130.020°   |
| C56  | C57 | H671 | 79.175°    |  | C58  | C57 | H671 | 159.930°   |
| C67  | C57 | H671 | 107.395°   |  | C68  | C57 | H671 | 164.531°   |
| H571 | C57 | H671 | 42.299°    |  | C53  | C58 | C57  | 121.13(6)° |
| C53  | C58 | C63  | 3.0(3)°    |  | C57  | C58 | C63  | 124.1(3)°  |

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|-----|-----|------|------------|--|------|-----|------|------------|
| C53 | C58 | C67  | 101.4(3)°  |  | C57  | C58 | C67  | 19.8(3)°   |
| C63 | C58 | C67  | 104.4(5)°  |  | C53  | C58 | C68  | 46(2)°     |
| C57 | C58 | C68  | 84(2)°     |  | C63  | C58 | C68  | 49(2)°     |
| C67 | C58 | C68  | 66(2)°     |  | C53  | C58 | H581 | 118.279°   |
| C57 | C58 | H581 | 120.589°   |  | C63  | C58 | H581 | 115.313°   |
| C67 | C58 | H581 | 140.257°   |  | C68  | C58 | H581 | 142.805°   |
| C53 | C58 | H681 | 121.828°   |  | C57  | C58 | H681 | 111.909°   |
| C63 | C58 | H681 | 119.303°   |  | C67  | C58 | H681 | 128.720°   |
| C68 | C58 | H681 | 125.625°   |  | H581 | C58 | H681 | 23.376°    |
| O51 | O61 | C53  | 56(2)°     |  | O51  | O61 | C63  | 54(2)°     |
| C53 | O61 | C63  | 6.0(3)°    |  | O51  | O61 | H511 | 67.336°    |
| C53 | O61 | H511 | 98.506°    |  | C63  | O61 | H511 | 92.563°    |
| O51 | O61 | H611 | 85.564°    |  | C53  | O61 | H611 | 104.517°   |
| C63 | O61 | H611 | 98.653°    |  | H511 | O61 | H611 | 19.560°    |
| O52 | O62 | C64  | 47.5(8)°   |  | O52  | O62 | H521 | 117.171°   |
| C64 | O62 | H521 | 76.471°    |  | O52  | O62 | H621 | 160.222°   |
| C64 | O62 | H621 | 127.766°   |  | H521 | O62 | H621 | 51.580°    |
| O51 | C63 | C53  | 134(3)°    |  | O51  | C63 | C54  | 138.3(8)°  |
| C53 | C63 | C54  | 88(2)°     |  | O51  | C63 | C58  | 113.7(6)°  |
| C53 | C63 | C58  | 21(2)°     |  | C54  | C63 | C58  | 107.9(6)°  |
| O51 | C63 | O61  | 12.0(7)°   |  | C53  | C63 | O61  | 130(2)°    |
| C54 | C63 | O61  | 142.1(4)°  |  | C58  | C63 | O61  | 109.2(4)°  |
| O51 | C63 | C64  | 120.4(6)°  |  | C53  | C63 | C64  | 106(2)°    |
| C54 | C63 | C64  | 18.4(3)°   |  | C58  | C63 | C64  | 126.0(4)°  |
| O61 | C63 | C64  | 123.75(7)° |  | O51  | C63 | C68  | 120.0(6)°  |
| C53 | C63 | C68  | 14(3)°     |  | C54  | C63 | C68  | 100.7(4)°  |
| C58 | C63 | C68  | 9.6(6)°    |  | O61  | C63 | C68  | 116.99(7)° |
| C64 | C63 | C68  | 119.08(6)° |  | O52  | C64 | C53  | 154.1(9)°  |
| O52 | C64 | C54  | 128.4(14)° |  | C53  | C64 | C54  | 73.8(9)°   |
| O52 | C64 | O62  | 25.9(6)°   |  | C53  | C64 | O62  | 131.5(4)°  |
| C54 | C64 | O62  | 154.2(10)° |  | O52  | C64 | C63  | 146.8(6)°  |
| C53 | C64 | C63  | 7.8(4)°    |  | C54  | C64 | C63  | 81.5(10)°  |
| O62 | C64 | C63  | 123.77(6)° |  | O52  | C64 | C65  | 93.3(6)°   |
| C53 | C64 | C65  | 111.4(4)°  |  | C54  | C64 | C65  | 38.6(10)°  |
| O62 | C64 | C65  | 117.04(6)° |  | C63  | C64 | C65  | 119.11(6)° |
| C54 | C65 | C55  | 107.2(10)° |  | C54  | C65 | C64  | 15.0(4)°   |
| C55 | C65 | C64  | 122.2(8)°  |  | C54  | C65 | C66  | 106.3(4)°  |
| C55 | C65 | C66  | 10.6(8)°   |  | C64  | C65 | C66  | 121.02(7)° |
| C54 | C65 | H551 | 165.063°   |  | C55  | C65 | H551 | 68.012°    |
| C64 | C65 | H551 | 163.238°   |  | C66  | C65 | H551 | 71.649°    |

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| C54  | C65 | H651 | 133.358°   |  | C55 | C65 | H651 | 117.582°   |
| C64  | C65 | H651 | 118.870°   |  | C66 | C65 | H651 | 120.101°   |
| H551 | C65 | H651 | 49.595°    |  | C55 | C66 | C56  | 156.0(17)° |
| C55  | C66 | C65  | 8.4(7)°    |  | C56 | C66 | C65  | 158.6(10)° |
| C55  | C66 | C67  | 120.6(6)°  |  | C56 | C66 | C67  | 40.1(9)°   |
| C65  | C66 | C67  | 119.74(7)° |  | C55 | C66 | H661 | 117.732°   |
| C56  | C66 | H661 | 81.228°    |  | C65 | C66 | H661 | 119.315°   |
| C67  | C66 | H661 | 120.944°   |  | C56 | C67 | C57  | 135.5(18)° |
| C56  | C67 | C58  | 153.4(8)°  |  | C57 | C67 | C58  | 69.7(13)°  |
| C56  | C67 | C66  | 24.6(5)°   |  | C57 | C67 | C66  | 157.1(18)° |
| C58  | C67 | C66  | 128.8(4)°  |  | C56 | C67 | C68  | 143.9(5)°  |
| C57  | C67 | C68  | 80.3(15)°  |  | C58 | C67 | C68  | 11.9(5)°   |
| C66  | C67 | C68  | 119.72(7)° |  | C56 | C67 | H671 | 95.344°    |
| C57  | C67 | H671 | 41.726°    |  | C58 | C67 | H671 | 110.932°   |
| C66  | C67 | H671 | 119.640°   |  | C68 | C67 | H671 | 120.633°   |
| C53  | C68 | C57  | 138.4(8)°  |  | C53 | C68 | C58  | 123(3)°    |
| C57  | C68 | C58  | 83(2)°     |  | C53 | C68 | C63  | 2.3(5)°    |
| C57  | C68 | C63  | 140.8(5)°  |  | C58 | C68 | C63  | 122(3)°    |
| C53  | C68 | C67  | 118.7(4)°  |  | C57 | C68 | C67  | 20.8(4)°   |
| C58  | C68 | C67  | 102(3)°    |  | C63 | C68 | C67  | 121.00(7)° |
| C53  | C68 | H581 | 114.130°   |  | C57 | C68 | H581 | 103.106°   |
| C58  | C68 | H581 | 28.254°    |  | C63 | C68 | H581 | 112.064°   |
| C67  | C68 | H581 | 123.761°   |  | C53 | C68 | H681 | 122.394°   |
| C57  | C68 | H681 | 98.399°    |  | C58 | C68 | H681 | 38.767°    |
| C63  | C68 | H681 | 120.103°   |  | C67 | C68 | H681 | 118.789°   |
| H581 | C68 | H681 | 16.133°    |  | C73 | O71 | O81  | 47.1(17)°  |
| C73  | O71 | C83  | 8.1(6)°    |  | O81 | O71 | C83  | 44.6(17)°  |
| C73  | O71 | H711 | 116.853°   |  | O81 | O71 | H711 | 115.020°   |
| C83  | O71 | H711 | 109.864°   |  | C73 | O71 | H811 | 98.912°    |
| O81  | O71 | H811 | 86.911°    |  | C83 | O71 | H811 | 90.876°    |
| H711 | O71 | H811 | 28.122°    |  | C74 | O72 | O82  | 153(4)°    |
| C74  | O72 | C84  | 8.5(9)°    |  | O82 | O72 | C84  | 159(5)°    |
| C74  | O72 | H721 | 107.439°   |  | O82 | O72 | H721 | 47.224°    |
| C84  | O72 | H721 | 114.885°   |  | C74 | O72 | H821 | 115.433°   |
| O82  | O72 | H821 | 39.420°    |  | C84 | O72 | H821 | 122.884°   |
| H721 | O72 | H821 | 8.003°     |  | O71 | C73 | C74  | 123.76(5)° |
| O71  | C73 | C78  | 117.01(6)° |  | C74 | C73 | C78  | 119.17(5)° |
| O71  | C73 | O81  | 18.7(7)°   |  | C74 | C73 | O81  | 125.8(8)°  |
| C78  | C73 | O81  | 112.4(8)°  |  | O71 | C73 | C83  | 140.2(19)° |
| C74  | C73 | C83  | 30(2)°     |  | C78 | C73 | C83  | 98.0(16)°  |



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|------|-----|------|------------|--|-----|-----|------|------------|
| O81  | C73 | C83  | 131(3)°    |  | O71 | C73 | C84  | 118.5(4)°  |
| C74  | C73 | C84  | 5.7(5)°    |  | C78 | C73 | C84  | 124.4(3)°  |
| O81  | C73 | C84  | 120.1(9)°  |  | C83 | C73 | C84  | 32(2)°     |
| O71  | C73 | C88  | 141.9(7)°  |  | C74 | C73 | C88  | 94.3(7)°   |
| C78  | C73 | C88  | 25.1(7)°   |  | O81 | C73 | C88  | 134.1(11)° |
| C83  | C73 | C88  | 73.5(15)°  |  | C84 | C73 | C88  | 99.5(8)°   |
| O72  | C74 | C73  | 123.75(5)° |  | O72 | C74 | C75  | 117.06(6)° |
| C73  | C74 | C75  | 119.19(5)° |  | O72 | C74 | O82  | 4.5(7)°    |
| C73  | C74 | O82  | 119.6(6)°  |  | C75 | C74 | O82  | 121.2(6)°  |
| O72  | C74 | C83  | 129.6(5)°  |  | C73 | C74 | C83  | 9.7(9)°    |
| C75  | C74 | C83  | 112.6(5)°  |  | O82 | C74 | C83  | 125.3(9)°  |
| O72  | C74 | C84  | 29(2)°     |  | C73 | C74 | C84  | 150(2)°    |
| C75  | C74 | C84  | 89(2)°     |  | O82 | C74 | C84  | 32.7(18)°  |
| C83  | C74 | C84  | 152(4)°    |  | O72 | C74 | C85  | 93.3(6)°   |
| C73  | C74 | C85  | 142.9(6)°  |  | C75 | C74 | C85  | 23.7(6)°   |
| O82  | C74 | C85  | 97.5(9)°   |  | C83 | C74 | C85  | 136.1(8)°  |
| C84  | C74 | C85  | 66(2)°     |  | C74 | C75 | C76  | 121.07(6)° |
| C74  | C75 | C84  | 13.5(7)°   |  | C76 | C75 | C84  | 134.3(6)°  |
| C74  | C75 | C85  | 87.5(12)°  |  | C76 | C75 | C85  | 151.4(12)° |
| C84  | C75 | C85  | 74.3(10)°  |  | C74 | C75 | C86  | 154.7(13)° |
| C76  | C75 | C86  | 33.8(12)°  |  | C84 | C75 | C86  | 168.1(18)° |
| C85  | C75 | C86  | 117.6(19)° |  | C74 | C75 | H751 | 119.602°   |
| C76  | C75 | H751 | 119.324°   |  | C84 | C75 | H751 | 106.322°   |
| C85  | C75 | H751 | 32.192°    |  | C86 | C75 | H751 | 85.601°    |
| C75  | C76 | C77  | 119.75(6)° |  | C75 | C76 | C86  | 45.7(7)°   |
| C77  | C76 | C86  | 165.3(7)°  |  | C75 | C76 | C87  | 126.8(9)°  |
| C77  | C76 | C87  | 9.1(14)°   |  | C86 | C76 | C87  | 171.9(16)° |
| C75  | C76 | H761 | 121.292°   |  | C77 | C76 | H761 | 118.951°   |
| C86  | C76 | H761 | 75.640°    |  | C87 | C76 | H761 | 111.579°   |
| C76  | C77 | C78  | 119.76(6)° |  | C76 | C77 | C87  | 6.9(9)°    |
| C78  | C77 | C87  | 125.2(6)°  |  | C76 | C77 | C88  | 97.1(11)°  |
| C78  | C77 | C88  | 23.4(11)°  |  | C87 | C77 | C88  | 102.1(14)° |
| C76  | C77 | H771 | 120.232°   |  | C78 | C77 | H771 | 119.993°   |
| C87  | C77 | H771 | 114.746°   |  | C88 | C77 | H771 | 142.378°   |
| C76  | C77 | H871 | 63.834°    |  | C78 | C77 | H871 | 175.071°   |
| C87  | C77 | H871 | 58.128°    |  | C88 | C77 | H871 | 158.641°   |
| H771 | C77 | H871 | 56.625°    |  | C73 | C78 | C77  | 121.05(6)° |
| C73  | C78 | C83  | 14.2(6)°   |  | C77 | C78 | C83  | 107.8(5)°  |
| C73  | C78 | C88  | 83.9(9)°   |  | C77 | C78 | C88  | 38.3(10)°  |
| C83  | C78 | C88  | 70.0(12)°  |  | C73 | C78 | H781 | 116.362°   |

|     |     |      |            |  |      |     |      |            |
|-----|-----|------|------------|--|------|-----|------|------------|
| C77 | C78 | H781 | 122.570°   |  | C83  | C78 | H781 | 129.139°   |
| C88 | C78 | H781 | 157.145°   |  | C73  | C78 | H881 | 162.319°   |
| C77 | C78 | H881 | 70.976°    |  | C83  | C78 | H881 | 160.953°   |
| C88 | C78 | H881 | 104.594°   |  | H781 | C78 | H881 | 53.025°    |
| O71 | O81 | C73  | 114(2)°    |  | O71  | O81 | C83  | 121(2)°    |
| C73 | O81 | C83  | 11.8(9)°   |  | O71  | O81 | H711 | 43.182°    |
| C73 | O81 | H711 | 116.927°   |  | C83  | O81 | H711 | 114.338°   |
| O71 | O81 | H811 | 62.852°    |  | C73  | O81 | H811 | 113.541°   |
| C83 | O81 | H811 | 107.081°   |  | H711 | O81 | H811 | 19.682°    |
| O72 | O82 | C74  | 22(3)°     |  | O72  | O82 | C84  | 17(4)°     |
| C74 | O82 | C84  | 7.5(6)°    |  | O72  | O82 | H721 | 115.184°   |
| C74 | O82 | H721 | 94.322°    |  | C84  | O82 | H721 | 101.360°   |
| O72 | O82 | H821 | 129.533°   |  | C74  | O82 | H821 | 108.835°   |
| C84 | O82 | H821 | 115.864°   |  | H721 | O82 | H821 | 14.514°    |
| O71 | C83 | C73  | 31.7(15)°  |  | O71  | C83 | C74  | 122.7(8)°  |
| C73 | C83 | C74  | 140(3)°    |  | O71  | C83 | C78  | 96.3(9)°   |
| C73 | C83 | C78  | 67.8(17)°  |  | C74  | C83 | C78  | 136.9(10)° |
| O71 | C83 | O81  | 14.3(5)°   |  | C73  | C83 | O81  | 37(2)°     |
| C74 | C83 | O81  | 129.1(5)°  |  | C78  | C83 | O81  | 93.2(7)°   |
| O71 | C83 | C84  | 118.5(6)°  |  | C73  | C83 | C84  | 140(3)°    |
| C74 | C83 | C84  | 6.5(9)°    |  | C78  | C83 | C84  | 142.8(7)°  |
| O81 | C83 | C84  | 123.77(6)° |  | O71  | C83 | C88  | 121.0(6)°  |
| C73 | C83 | C88  | 92.0(17)°  |  | C74  | C83 | C88  | 113.8(5)°  |
| C78 | C83 | C88  | 24.7(7)°   |  | O81  | C83 | C88  | 117.04(6)° |
| C84 | C83 | C88  | 119.15(6)° |  | O72  | C84 | C73  | 121.0(10)° |
| O72 | C84 | C74  | 142(3)°    |  | C73  | C84 | C74  | 24.6(20)°  |
| O72 | C84 | C75  | 138.0(14)° |  | C73  | C84 | C75  | 100.5(7)°  |
| C74 | C84 | C75  | 77.2(18)°  |  | O72  | C84 | O82  | 4.3(10)°   |
| C73 | C84 | O82  | 117.7(4)°  |  | C74  | C84 | O82  | 140(2)°    |
| C75 | C84 | O82  | 141.6(7)°  |  | O72  | C84 | C83  | 127.3(9)°  |
| C73 | C84 | C83  | 8.1(6)°    |  | C74  | C84 | C83  | 22(3)°     |
| C75 | C84 | C83  | 94.6(7)°   |  | O82  | C84 | C83  | 123.79(6)° |
| O72 | C84 | C85  | 113.4(9)°  |  | C73  | C84 | C85  | 125.0(4)°  |
| C74 | C84 | C85  | 101(2)°    |  | C75  | C84 | C85  | 24.6(7)°   |
| O82 | C84 | C85  | 117.05(6)° |  | C83  | C84 | C85  | 119.16(6)° |
| C74 | C85 | C75  | 68.8(13)°  |  | C74  | C85 | C84  | 12.6(5)°   |
| C75 | C85 | C84  | 81.1(11)°  |  | C74  | C85 | C86  | 108.6(5)°  |
| C75 | C85 | C86  | 39.9(11)°  |  | C84  | C85 | C86  | 121.04(7)° |
| C74 | C85 | H751 | 177.196°   |  | C75  | C85 | H751 | 111.744°   |
| C84 | C85 | H751 | 165.932°   |  | C86  | C85 | H751 | 72.087°    |

|       |      |       |             |  |      |      |       |             |
|-------|------|-------|-------------|--|------|------|-------|-------------|
| C74   | C85  | H851  | 132.407°    |  | C75  | C85  | H851  | 158.758°    |
| C84   | C85  | H851  | 120.099°    |  | C86  | C85  | H851  | 118.857°    |
| H751  | C85  | H851  | 47.116°     |  | C75  | C86  | C76   | 100.5(15)°  |
| C75   | C86  | C85   | 22.5(10)°   |  | C76  | C86  | C85   | 123.0(7)°   |
| C75   | C86  | C87   | 97.3(10)°   |  | C76  | C86  | C87   | 3.5(7)°     |
| C85   | C86  | C87   | 119.76(7)°  |  | C75  | C86  | H761  | 160.384°    |
| C76   | C86  | H761  | 60.082°     |  | C85  | C86  | H761  | 176.103°    |
| C87   | C86  | H761  | 63.238°     |  | C75  | C86  | H861  | 143.204°    |
| C76   | C86  | H861  | 116.278°    |  | C85  | C86  | H861  | 120.719°    |
| C87   | C86  | H861  | 119.517°    |  | H761 | C86  | H861  | 56.327°     |
| C76   | C87  | C77   | 164(2)°     |  | C76  | C87  | C86   | 4.6(9)°     |
| C77   | C87  | C86   | 161.5(11)°  |  | C76  | C87  | C88   | 123.9(8)°   |
| C77   | C87  | C88   | 43.8(7)°    |  | C86  | C87  | C88   | 119.75(7)°  |
| C76   | C87  | H871  | 116.462°    |  | C77  | C87  | H871  | 76.364°     |
| C86   | C87  | H871  | 120.646°    |  | C88  | C87  | H871  | 119.601°    |
| C73   | C88  | C77   | 164.6(15)°  |  | C73  | C88  | C78   | 71.0(9)°    |
| C77   | C88  | C78   | 118.3(18)°  |  | C73  | C88  | C83   | 14.6(7)°    |
| C77   | C88  | C83   | 154.6(12)°  |  | C78  | C88  | C83   | 85.2(10)°   |
| C73   | C88  | C87   | 134.1(6)°   |  | C77  | C88  | C87   | 34.1(13)°   |
| C78   | C88  | C87   | 151.6(13)°  |  | C83  | C88  | C87   | 121.04(7)°  |
| C73   | C88  | H881  | 104.614°    |  | C77  | C88  | H881  | 87.126°     |
| C78   | C88  | H881  | 34.818°     |  | C83  | C88  | H881  | 117.979°    |
| C87   | C88  | H881  | 120.978°    |  | C93  | O91  | H911  | 110.244°    |
| C94   | O92  | H921  | 104.239°    |  | O91  | C93  | C94   | 123.35(18)° |
| O91   | C93  | C98   | 117.11(18)° |  | C94  | C93  | C98   | 119.53(16)° |
| O92   | C94  | C93   | 123.19(16)° |  | O92  | C94  | C95   | 118.26(18)° |
| C93   | C94  | C95   | 118.53(18)° |  | C94  | C95  | C96   | 121.28(19)° |
| C94   | C95  | H951  | 117.050°    |  | C96  | C95  | H951  | 121.650°    |
| C95   | C96  | C97   | 120.15(17)° |  | C95  | C96  | H961  | 120.633°    |
| C97   | C96  | H961  | 119.211°    |  | C96  | C97  | C98   | 119.3(2)°   |
| C96   | C97  | H971  | 119.744°    |  | C98  | C97  | H971  | 120.942°    |
| C93   | C98  | C97   | 121.3(2)°   |  | C93  | C98  | H981  | 118.677°    |
| C97   | C98  | H981  | 120.065°    |  | C102 | N101 | C106  | 111.04(10)° |
| C102  | N101 | C110  | 106.40(9)°  |  | C106 | N101 | C110  | 111.10(9)°  |
| C102  | N101 | C114  | 111.13(9)°  |  | C106 | N101 | C114  | 105.84(9)°  |
| C110  | N101 | C114  | 111.43(9)°  |  | N101 | C102 | C103  | 116.07(10)° |
| N101  | C102 | H1022 | 106.325°    |  | C103 | C102 | H1022 | 110.410°    |
| N101  | C102 | H1021 | 105.083°    |  | C103 | C102 | H1021 | 111.000°    |
| H1022 | C102 | H1021 | 107.460°    |  | C102 | C103 | C104  | 110.27(12)° |
| C102  | C103 | H1032 | 109.913°    |  | C104 | C103 | H1032 | 110.378°    |

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|-------|------|-------|----------|--|-------|------|-------|-------------|
| C102  | C103 | H1031 | 109.183° |  | C104  | C103 | H1031 | 109.843°    |
| H1032 | C103 | H1031 | 107.196° |  | C103  | C104 | C105  | 112.15(14)° |
| C103  | C104 | H1041 | 111.339° |  | C105  | C104 | H1041 | 107.049°    |
| C103  | C104 | H1042 | 108.887° |  | C105  | C104 | H1042 | 109.430°    |
| H1041 | C104 | H1042 | 107.876° |  | C104  | C105 | H1052 | 109.619°    |
| C104  | C105 | H1051 | 110.622° |  | H1052 | C105 | H1051 | 108.311°    |
| C104  | C105 | H1053 | 112.423° |  | H1052 | C105 | H1053 | 108.646°    |
| H1051 | C105 | H1053 | 107.097° |  | N101  | C106 | C107  | 116.88(10)° |
| N101  | C106 | H1062 | 106.169° |  | C107  | C106 | H1062 | 108.807°    |
| N101  | C106 | H1061 | 106.119° |  | C107  | C106 | H1061 | 109.993°    |
| H1062 | C106 | H1061 | 108.565° |  | C106  | C107 | C108  | 108.55(11)° |
| C106  | C107 | H1072 | 111.956° |  | C108  | C107 | H1072 | 108.538°    |
| C106  | C107 | H1071 | 109.862° |  | C108  | C107 | H1071 | 109.357°    |
| H1072 | C107 | H1071 | 108.537° |  | C107  | C108 | C109  | 113.33(14)° |
| C107  | C108 | H1081 | 109.961° |  | C109  | C108 | H1081 | 106.907°    |
| C107  | C108 | H1082 | 108.068° |  | C109  | C108 | H1082 | 107.973°    |
| H1081 | C108 | H1082 | 110.595° |  | C108  | C109 | H1092 | 110.476°    |
| C108  | C109 | H1091 | 111.615° |  | H1092 | C109 | H1091 | 108.623°    |
| C108  | C109 | H1093 | 111.589° |  | H1092 | C109 | H1093 | 106.450°    |
| H1091 | C109 | H1093 | 107.892° |  | N101  | C110 | C111  | 116.28(10)° |
| N101  | C110 | H1102 | 104.418° |  | C111  | C110 | H1102 | 110.444°    |
| N101  | C110 | H1101 | 106.250° |  | C111  | C110 | H1101 | 109.555°    |
| H1102 | C110 | H1101 | 109.627° |  | C110  | C111 | C112  | 109.05(11)° |
| C110  | C111 | H1112 | 112.949° |  | C112  | C111 | H1112 | 108.641°    |
| C110  | C111 | H1111 | 112.201° |  | C112  | C111 | H1111 | 107.608°    |
| H1112 | C111 | H1111 | 106.194° |  | C111  | C112 | C113  | 113.51(12)° |
| C111  | C112 | H1121 | 105.450° |  | C113  | C112 | H1121 | 109.089°    |
| C111  | C112 | H1122 | 110.698° |  | C113  | C112 | H1122 | 109.234°    |
| H1121 | C112 | H1122 | 108.704° |  | C112  | C113 | H1132 | 111.535°    |
| C112  | C113 | H1131 | 108.424° |  | H1132 | C113 | H1131 | 111.517°    |
| C112  | C113 | H1133 | 108.589° |  | H1132 | C113 | H1133 | 107.293°    |
| H1131 | C113 | H1133 | 109.426° |  | N101  | C114 | C115  | 116.41(11)° |
| N101  | C114 | H1142 | 106.136° |  | C115  | C114 | H1142 | 108.516°    |
| N101  | C114 | H1141 | 106.210° |  | C115  | C114 | H1141 | 110.016°    |
| H1142 | C114 | H1141 | 109.338° |  | C114  | C115 | C116  | 109.09(13)° |
| C114  | C115 | H1152 | 109.544° |  | C116  | C115 | H1152 | 107.640°    |
| C114  | C115 | H1151 | 111.806° |  | C116  | C115 | H1151 | 110.616°    |
| H1152 | C115 | H1151 | 108.048° |  | C115  | C116 | C117  | 113.42(17)° |
| C115  | C116 | H1161 | 107.557° |  | C117  | C116 | H1161 | 109.412°    |
| C115  | C116 | H1162 | 108.734° |  | C117  | C116 | H1162 | 108.881°    |

|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| H1161 | C116 | H1162 | 108.744°    |  | C116  | C117 | H1172 | 111.096°    |
| C116  | C117 | H1171 | 109.369°    |  | H1172 | C117 | H1171 | 109.716°    |
| C116  | C117 | H1173 | 111.337°    |  | H1172 | C117 | H1173 | 108.425°    |
| H1171 | C117 | H1173 | 106.795°    |  | C122  | N121 | C126  | 110.37(10)° |
| C122  | N121 | C130  | 107.50(9)°  |  | C126  | N121 | C130  | 110.72(10)° |
| C122  | N121 | C134  | 110.57(10)° |  | C126  | N121 | C134  | 106.58(9)°  |
| C130  | N121 | C134  | 111.13(10)° |  | N121  | C122 | C123  | 114.17(10)° |
| N121  | C122 | H1222 | 106.168°    |  | C123  | C122 | H1222 | 110.705°    |
| N121  | C122 | H1221 | 106.058°    |  | C123  | C122 | H1221 | 111.928°    |
| H1222 | C122 | H1221 | 107.392°    |  | C122  | C123 | C124  | 112.29(11)° |
| C122  | C123 | H1232 | 109.165°    |  | C124  | C123 | H1232 | 108.580°    |
| C122  | C123 | H1231 | 110.082°    |  | C124  | C123 | H1231 | 108.801°    |
| H1232 | C123 | H1231 | 107.807°    |  | C123  | C124 | C125  | 110.76(12)° |
| C123  | C124 | H1241 | 108.008°    |  | C125  | C124 | H1241 | 110.752°    |
| C123  | C124 | H1242 | 110.830°    |  | C125  | C124 | H1242 | 111.389°    |
| H1241 | C124 | H1242 | 104.901°    |  | C124  | C125 | H1252 | 111.447°    |
| C124  | C125 | H1251 | 110.269°    |  | H1252 | C125 | H1251 | 110.584°    |
| C124  | C125 | H1253 | 108.398°    |  | H1252 | C125 | H1253 | 106.808°    |
| H1251 | C125 | H1253 | 109.228°    |  | N121  | C126 | C127  | 115.63(10)° |
| N121  | C126 | H1262 | 106.675°    |  | C127  | C126 | H1262 | 109.154°    |
| N121  | C126 | H1261 | 106.247°    |  | C127  | C126 | H1261 | 111.783°    |
| H1262 | C126 | H1261 | 106.885°    |  | C126  | C127 | C128  | 110.03(11)° |
| C126  | C127 | H1271 | 111.253°    |  | C128  | C127 | H1271 | 108.841°    |
| C126  | C127 | H1272 | 108.639°    |  | C128  | C127 | H1272 | 109.354°    |
| H1271 | C127 | H1272 | 108.691°    |  | C127  | C128 | C129  | 112.17(13)° |
| C127  | C128 | H1281 | 108.641°    |  | C129  | C128 | H1281 | 111.760°    |
| C127  | C128 | H1282 | 109.178°    |  | C129  | C128 | H1282 | 109.618°    |
| H1281 | C128 | H1282 | 105.217°    |  | C128  | C129 | H1292 | 108.324°    |
| C128  | C129 | H1291 | 110.528°    |  | H1292 | C129 | H1291 | 108.903°    |
| C128  | C129 | H1293 | 110.009°    |  | H1292 | C129 | H1293 | 109.139°    |
| H1291 | C129 | H1293 | 109.899°    |  | N121  | C130 | C131  | 115.02(11)° |
| N121  | C130 | H1302 | 106.898°    |  | C131  | C130 | H1302 | 110.216°    |
| N121  | C130 | H1301 | 108.205°    |  | C131  | C130 | H1301 | 108.756°    |
| H1302 | C130 | H1301 | 107.482°    |  | C130  | C131 | C132  | 111.21(13)° |
| C130  | C131 | H1311 | 108.374°    |  | C132  | C131 | H1311 | 110.377°    |
| C130  | C131 | H1312 | 109.239°    |  | C132  | C131 | H1312 | 108.299°    |
| H1311 | C131 | H1312 | 109.321°    |  | C131  | C132 | C133  | 111.86(16)° |
| C131  | C132 | H1322 | 106.502°    |  | C133  | C132 | H1322 | 110.347°    |
| C131  | C132 | H1321 | 108.799°    |  | C133  | C132 | H1321 | 109.688°    |
| H1322 | C132 | H1321 | 109.570°    |  | C132  | C133 | H1333 | 110.766°    |

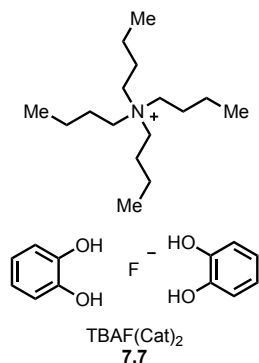
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|-------|------|-------|------------|--|-------|------|-------|-------------|
| C132  | C133 | H1332 | 109.213°   |  | H1333 | C133 | H1332 | 108.470°    |
| C132  | C133 | H1331 | 109.610°   |  | H1333 | C133 | H1331 | 109.972°    |
| H1332 | C133 | H1331 | 108.771°   |  | N121  | C134 | C135  | 115.43(10)° |
| N121  | C134 | H1342 | 104.829°   |  | C135  | C134 | H1342 | 110.359°    |
| N121  | C134 | H1341 | 104.760°   |  | C135  | C134 | H1341 | 110.451°    |
| H1342 | C134 | H1341 | 110.765°   |  | C134  | C135 | C136  | 109.71(12)° |
| C134  | C135 | H1351 | 110.148°   |  | C136  | C135 | H1351 | 110.773°    |
| C134  | C135 | H1352 | 108.740°   |  | C136  | C135 | H1352 | 109.230°    |
| H1351 | C135 | H1352 | 108.191°   |  | C135  | C136 | C137  | 112.47(13)° |
| C135  | C136 | H1362 | 108.023°   |  | C137  | C136 | H1362 | 108.034°    |
| C135  | C136 | H1361 | 108.687°   |  | C137  | C136 | H1361 | 109.251°    |
| H1362 | C136 | H1361 | 110.365°   |  | C136  | C137 | H1373 | 110.690°    |
| C136  | C137 | H1372 | 110.580°   |  | H1373 | C137 | H1372 | 110.437°    |
| C136  | C137 | H1371 | 109.161°   |  | H1373 | C137 | H1371 | 106.571°    |
| H1372 | C137 | H1371 | 109.302°   |  | C142  | N141 | C146  | 110.94(9)°  |
| C142  | N141 | C150  | 106.77(9)° |  | C146  | N141 | C150  | 111.00(9)°  |
| C142  | N141 | C154  | 110.64(9)° |  | C146  | N141 | C154  | 106.70(9)°  |
| C150  | N141 | C154  | 110.85(9)° |  | N141  | C142 | C143  | 115.46(10)° |
| N141  | C142 | H1422 | 106.777°   |  | C143  | C142 | H1422 | 109.996°    |
| N141  | C142 | H1421 | 106.142°   |  | C143  | C142 | H1421 | 109.956°    |
| H1422 | C142 | H1421 | 108.214°   |  | C142  | C143 | C144  | 109.79(12)° |
| C142  | C143 | H1431 | 110.553°   |  | C144  | C143 | H1431 | 110.388°    |
| C142  | C143 | H1432 | 106.909°   |  | C144  | C143 | H1432 | 110.424°    |
| H1431 | C143 | H1432 | 108.716°   |  | C143  | C144 | C145  | 112.57(14)° |
| C143  | C144 | H1442 | 107.483°   |  | C145  | C144 | H1442 | 108.557°    |
| C143  | C144 | H1441 | 110.386°   |  | C145  | C144 | H1441 | 108.369°    |
| H1442 | C144 | H1441 | 109.427°   |  | C144  | C145 | H1453 | 110.798°    |
| C144  | C145 | H1452 | 109.443°   |  | H1453 | C145 | H1452 | 108.915°    |
| C144  | C145 | H1451 | 111.531°   |  | H1453 | C145 | H1451 | 106.439°    |
| H1452 | C145 | H1451 | 109.645°   |  | N141  | C146 | C147  | 115.17(10)° |
| N141  | C146 | H1462 | 105.124°   |  | C147  | C146 | H1462 | 109.197°    |
| N141  | C146 | H1461 | 107.220°   |  | C147  | C146 | H1461 | 110.768°    |
| H1462 | C146 | H1461 | 109.100°   |  | C146  | C147 | C148  | 111.12(11)° |
| C146  | C147 | H1471 | 110.160°   |  | C148  | C147 | H1471 | 106.383°    |
| C146  | C147 | H1472 | 111.941°   |  | C148  | C147 | H1472 | 108.774°    |
| H1471 | C147 | H1472 | 108.262°   |  | C147  | C148 | C149  | 111.87(13)° |
| C147  | C148 | H1482 | 105.840°   |  | C149  | C148 | H1482 | 107.989°    |
| C147  | C148 | H1481 | 108.577°   |  | C149  | C148 | H1481 | 111.758°    |
| H1482 | C148 | H1481 | 110.651°   |  | C148  | C149 | H1493 | 110.765°    |
| C148  | C149 | H1492 | 110.390°   |  | H1493 | C149 | H1492 | 108.371°    |

|       |      |       |            |  |       |      |       |             |
|-------|------|-------|------------|--|-------|------|-------|-------------|
| C148  | C149 | H1491 | 110.817°   |  | H1493 | C149 | H1491 | 108.712°    |
| H1492 | C149 | H1491 | 107.692°   |  | N141  | C150 | C151  | 115.16(10)° |
| N141  | C150 | H1502 | 105.276°   |  | C151  | C150 | H1502 | 109.774°    |
| N141  | C150 | H1501 | 108.585°   |  | C151  | C150 | H1501 | 109.739°    |
| H1502 | C150 | H1501 | 108.021°   |  | C150  | C151 | C152  | 111.44(12)° |
| C150  | C151 | H1511 | 109.637°   |  | C152  | C151 | H1511 | 109.703°    |
| C150  | C151 | H1512 | 109.125°   |  | C152  | C151 | H1512 | 107.428°    |
| H1511 | C151 | H1512 | 109.462°   |  | C151  | C152 | C153  | 111.41(15)° |
| C151  | C152 | H1522 | 108.120°   |  | C153  | C152 | H1522 | 110.259°    |
| C151  | C152 | H1521 | 109.499°   |  | C153  | C152 | H1521 | 110.854°    |
| H1522 | C152 | H1521 | 106.541°   |  | C152  | C153 | H1533 | 111.636°    |
| C152  | C153 | H1532 | 109.008°   |  | H1533 | C153 | H1532 | 110.544°    |
| C152  | C153 | H1531 | 109.723°   |  | H1533 | C153 | H1531 | 108.818°    |
| H1532 | C153 | H1531 | 107.001°   |  | N141  | C154 | C155  | 116.01(9)°  |
| N141  | C154 | H1542 | 105.024°   |  | C155  | C154 | H1542 | 109.850°    |
| N141  | C154 | H1541 | 106.189°   |  | C155  | C154 | H1541 | 108.353°    |
| H1542 | C154 | H1541 | 111.373°   |  | C154  | C155 | C156  | 109.50(10)° |
| C154  | C155 | H1551 | 110.333°   |  | C156  | C155 | H1551 | 108.136°    |
| C154  | C155 | H1552 | 112.279°   |  | C156  | C155 | H1552 | 110.191°    |
| H1551 | C155 | H1552 | 106.279°   |  | C155  | C156 | C157  | 111.83(11)° |
| C155  | C156 | H1562 | 108.213°   |  | C157  | C156 | H1562 | 108.546°    |
| C155  | C156 | H1561 | 110.397°   |  | C157  | C156 | H1561 | 108.654°    |
| H1562 | C156 | H1561 | 109.150°   |  | C156  | C157 | H1573 | 111.035°    |
| C156  | C157 | H1572 | 110.722°   |  | H1573 | C157 | H1572 | 109.452°    |
| C156  | C157 | H1571 | 111.568°   |  | H1573 | C157 | H1571 | 106.598°    |
| H1572 | C157 | H1571 | 107.307°   |  | C162  | N161 | C166  | 110.99(9)°  |
| C162  | N161 | C170  | 106.69(9)° |  | C166  | N161 | C170  | 111.04(9)°  |
| C162  | N161 | C174  | 110.45(9)° |  | C166  | N161 | C174  | 107.11(9)°  |
| C170  | N161 | C174  | 110.60(9)° |  | N161  | C162 | C163  | 115.83(10)° |
| N161  | C162 | H1622 | 106.950°   |  | C163  | C162 | H1622 | 110.643°    |
| N161  | C162 | H1621 | 106.332°   |  | C163  | C162 | H1621 | 108.460°    |
| H1622 | C162 | H1621 | 108.337°   |  | C162  | C163 | C164  | 109.32(11)° |
| C162  | C163 | H1631 | 110.252°   |  | C164  | C163 | H1631 | 108.772°    |
| C162  | C163 | H1632 | 110.429°   |  | C164  | C163 | H1632 | 107.618°    |
| H1631 | C163 | H1632 | 110.384°   |  | C163  | C164 | C165  | 112.39(13)° |
| C163  | C164 | H1642 | 108.463°   |  | C165  | C164 | H1642 | 108.422°    |
| C163  | C164 | H1641 | 108.688°   |  | C165  | C164 | H1641 | 109.035°    |
| H1642 | C164 | H1641 | 109.818°   |  | C164  | C165 | H1653 | 111.381°    |
| C164  | C165 | H1652 | 110.236°   |  | H1653 | C165 | H1652 | 105.500°    |
| C164  | C165 | H1651 | 112.119°   |  | H1653 | C165 | H1651 | 109.239°    |

|       |      |       |          |  |       |      |       |             |
|-------|------|-------|----------|--|-------|------|-------|-------------|
| H1652 | C165 | H1651 | 108.103° |  | N161  | C166 | C167  | 114.44(10)° |
| N161  | C166 | H1662 | 105.009° |  | C167  | C166 | H1662 | 111.153°    |
| N161  | C166 | H1661 | 107.115° |  | C167  | C166 | H1661 | 110.635°    |
| H1662 | C166 | H1661 | 108.141° |  | C166  | C167 | C168  | 110.16(11)° |
| C166  | C167 | H1671 | 109.562° |  | C168  | C167 | H1671 | 109.082°    |
| C166  | C167 | H1672 | 110.913° |  | C168  | C167 | H1672 | 109.499°    |
| H1671 | C167 | H1672 | 107.564° |  | C167  | C168 | C169  | 111.65(13)° |
| C167  | C168 | H1682 | 109.812° |  | C169  | C168 | H1682 | 110.131°    |
| C167  | C168 | H1681 | 108.652° |  | C169  | C168 | H1681 | 110.436°    |
| H1682 | C168 | H1681 | 105.991° |  | C168  | C169 | H1693 | 110.564°    |
| C168  | C169 | H1692 | 106.446° |  | H1693 | C169 | H1692 | 110.025°    |
| C168  | C169 | H1691 | 109.733° |  | H1693 | C169 | H1691 | 110.435°    |
| H1692 | C169 | H1691 | 109.554° |  | N161  | C170 | C171  | 114.04(10)° |
| N161  | C170 | H1702 | 107.108° |  | C171  | C170 | H1702 | 110.539°    |
| N161  | C170 | H1701 | 107.144° |  | C171  | C170 | H1701 | 110.908°    |
| H1702 | C170 | H1701 | 106.750° |  | C170  | C171 | C172  | 111.00(12)° |
| C170  | C171 | H1711 | 109.389° |  | C172  | C171 | H1711 | 110.731°    |
| C170  | C171 | H1712 | 109.602° |  | C172  | C171 | H1712 | 109.297°    |
| H1711 | C171 | H1712 | 106.719° |  | C171  | C172 | C173  | 112.56(13)° |
| C171  | C172 | H1722 | 111.260° |  | C173  | C172 | H1722 | 110.473°    |
| C171  | C172 | H1721 | 107.756° |  | C173  | C172 | H1721 | 107.017°    |
| H1722 | C172 | H1721 | 107.511° |  | C172  | C173 | H1733 | 107.681°    |
| C172  | C173 | H1732 | 110.127° |  | H1733 | C173 | H1732 | 110.714°    |
| C172  | C173 | H1731 | 109.093° |  | H1733 | C173 | H1731 | 109.785°    |
| H1732 | C173 | H1731 | 109.408° |  | N161  | C174 | C175  | 115.37(10)° |
| N161  | C174 | H1742 | 107.473° |  | C175  | C174 | H1742 | 109.282°    |
| N161  | C174 | H1741 | 106.546° |  | C175  | C174 | H1741 | 109.187°    |
| H1742 | C174 | H1741 | 108.798° |  | C174  | C175 | C176  | 110.22(11)° |
| C174  | C175 | H1751 | 110.074° |  | C176  | C175 | H1751 | 108.934°    |
| C174  | C175 | H1752 | 109.254° |  | C176  | C175 | H1752 | 108.891°    |
| H1751 | C175 | H1752 | 109.449° |  | C175  | C176 | C177  | 112.16(13)° |
| C175  | C176 | H1762 | 108.194° |  | C177  | C176 | H1762 | 111.197°    |
| C175  | C176 | H1761 | 107.668° |  | C177  | C176 | H1761 | 110.322°    |
| H1762 | C176 | H1761 | 107.100° |  | C176  | C177 | H1773 | 108.722°    |
| C176  | C177 | H1772 | 109.458° |  | H1773 | C177 | H1772 | 109.261°    |
| C176  | C177 | H1771 | 111.351° |  | H1773 | C177 | H1771 | 108.898°    |
| H1772 | C177 | H1771 | 109.122° |  | C55   | H551 | C65   | 37.713°     |
| C55   | H551 | H651  | 100.917° |  | C65   | H551 | H651  | 63.222°     |
| C56   | H561 | H661  | 73.557°  |  | C57   | H571 | H671  | 42.696°     |
| C58   | H581 | C68   | 8.941°   |  | C58   | H581 | H681  | 45.423°     |



|     |      |      |          |  |     |      |      |          |
|-----|------|------|----------|--|-----|------|------|----------|
| C68 | H581 | H681 | 40.361°  |  | C65 | H651 | H551 | 67.184°  |
| C56 | H661 | C66  | 36.274°  |  | C56 | H661 | H561 | 59.256°  |
| C66 | H661 | H561 | 95.398°  |  | C57 | H671 | C67  | 30.879°  |
| C57 | H671 | H571 | 95.005°  |  | C67 | H671 | H571 | 125.881° |
| C58 | H681 | C68  | 15.609°  |  | C58 | H681 | H581 | 111.201° |
| C68 | H681 | H581 | 123.506° |  | C75 | H751 | C85  | 36.064°  |
| C75 | H751 | H851 | 134.110° |  | C85 | H751 | H851 | 98.090°  |
| C76 | H761 | C86  | 44.279°  |  | C78 | H781 | H881 | 35.234°  |
| C85 | H851 | H751 | 34.794°  |  | C77 | H871 | C87  | 45.507°  |
| C78 | H881 | C88  | 40.588°  |  | C78 | H881 | H781 | 91.742°  |
| C88 | H881 | H781 | 132.123° |  | O51 | H511 | O61  | 19.971°  |
| O51 | H511 | H611 | 104.931° |  | O61 | H511 | H611 | 86.482°  |
| O52 | H521 | O62  | 41.619°  |  | O51 | H611 | O61  | 18.615°  |
| O51 | H611 | H511 | 56.698°  |  | O61 | H611 | H511 | 73.959°  |
| F3  | H621 | O62  | 152.273° |  | O71 | H711 | O81  | 21.798°  |
| O71 | H711 | H811 | 71.143°  |  | O81 | H711 | H811 | 49.359°  |
| O72 | H721 | O82  | 17.592°  |  | O72 | H721 | H821 | 150.530° |
| O82 | H721 | H821 | 133.189° |  | O71 | H811 | O81  | 30.237°  |
| O71 | H811 | H711 | 80.735°  |  | O81 | H811 | H711 | 110.959° |
| O72 | H821 | O82  | 11.047°  |  | O72 | H821 | H721 | 21.467°  |
| O82 | H821 | H721 | 32.297°  |  |     |      |      |          |



**tetra-*n*-butylammonium fluoride bis(catechol), 2<sup>nd</sup> polymorph (TBAF(Cat)<sub>2</sub>, 7.7):**

**X-ray** (single-crystal, 2<sup>nd</sup> *polymorph*). Pink plate-like crystals of X-ray diffraction quality were obtained directly from the reaction mixture.

Oxford Crystallography Number: 026KME12

## Crystal Data

$a = 13.2624(3) \text{ \AA}$   $\alpha = 67.629(2)^\circ$

$b = 13.9265(4) \text{ \AA}$   $\beta = 74.866(2)^\circ$

$c = 17.0611(4) \text{ \AA}$   $\gamma = 87.898(2)^\circ$

Volume 2806.00(13)  $\text{\AA}^3$

Space group P -1

Formula  $\text{C}_{28} \text{H}_{48} \text{F}_1 \text{N}_1 \text{O}_4$

Cell determined from 33684 reflections

Temperature 150K

Shape needle

Colour clear\_pale\_pink

$D_x = 1.14 \text{ Mg m}^{-3}$

$\mu = 0.632 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min} = 0.77$

Crystal Class triclinic

$Z = 4$

$M_r = 481.69$

Cell  $\theta$  range = 3 - 77°

Size  $0.01 \times 0.02 \times 0.09 \text{ mm}$

$F(000) = 1056.000$

$T_{\max} = 0.99$

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 116266

Independent reflections 11735

$R_{\text{int}} = 0.0935$

$\theta_{\max} = 77.2842$

$h = -16 \rightarrow 16$

$k = -17 \rightarrow 17$

$l = -21 \rightarrow 21$

## Refinement

$\Delta\rho_{\min} = -1.09 \text{ e \AA}^{-3}$

$\Delta\rho_{\max} = 0.84 \text{ e \AA}^{-3}$

Reflections used 7698

Cutoff:  $I > -3.00\sigma(I)$   
 Parameters refined 766  
 $S = 1.02$   
 R-factor 0.101  
 weighted R-factor 0.208  
 $\Delta/\sigma_{\max} 0.0034$   
 Refinement on  $F^2$   
 $w = 1/[\sigma^2(F_{\text{obs}}^2) + (0.049 \times P)^2 + 9.325 \times P + 0.000 + 0.000 \times \sin\theta]$ ,  
 $P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$

## Parameters

| Label | <i>x</i>  | <i>y</i>  | <i>z</i>    | $U_{\text{iso/equiv}}$ | Occupancy |
|-------|-----------|-----------|-------------|------------------------|-----------|
| F1    | 0.6132(2) | 0.5095(2) | 0.5779(2)   | 0.0599                 | 1.0000    |
| O1    | 0.7744(3) | 0.6321(3) | 0.5171(2)   | 0.0509                 | 1.0000    |
| O2    | 0.5587(2) | 0.6899(2) | 0.5568(2)   | 0.0437                 | 1.0000    |
| F2    | 0.5290(6) | 0.0209(5) | 1.0200(4)   | 0.0811                 | 0.5000    |
| C3    | 0.7473(4) | 0.7311(4) | 0.5032(3)   | 0.0388                 | 1.0000    |
| F3    | 1.0377(6) | 0.4811(5) | 0.9809(5)   | 0.0816                 | 0.5000    |
| C4    | 0.6441(3) | 0.7592(3) | 0.5226(3)   | 0.0353                 | 1.0000    |
| C5    | 0.6261(4) | 0.8623(4) | 0.5067(3)   | 0.0385                 | 1.0000    |
| C6    | 0.7069(4) | 0.9387(4) | 0.4706(3)   | 0.0456                 | 1.0000    |
| C7    | 0.8086(4) | 0.9113(4) | 0.4514(3)   | 0.0481                 | 1.0000    |
| C8    | 0.8283(4) | 0.8090(4) | 0.4660(3)   | 0.0429                 | 1.0000    |
| O11   | 0.6038(2) | 0.3585(2) | 0.53274(19) | 0.0401                 | 1.0000    |
| H11   | 0.7241(3) | 0.5866(3) | 0.5391(2)   | 0.0770                 | 1.0000    |
| O12   | 0.6234(2) | 0.2062(3) | 0.4699(2)   | 0.0507                 | 1.0000    |
| C13   | 0.6962(3) | 0.3134(3) | 0.5268(3)   | 0.0326                 | 1.0000    |
| C14   | 0.7044(3) | 0.2338(3) | 0.4945(3)   | 0.0359                 | 1.0000    |
| C15   | 0.7953(3) | 0.1828(3) | 0.4871(3)   | 0.0397                 | 1.0000    |
| C16   | 0.8788(3) | 0.2096(3) | 0.5109(3)   | 0.0385                 | 1.0000    |
| C17   | 0.8718(3) | 0.2886(3) | 0.5413(3)   | 0.0390                 | 1.0000    |
| C18   | 0.7805(3) | 0.3412(4) | 0.5484(3)   | 0.0388                 | 1.0000    |
| O21   | 0.8482(6) | 0.4403(5) | 0.9855(5)   | 0.0669                 | 0.5000    |
| H21   | 0.5759(2) | 0.6304(2) | 0.5616(2)   | 0.0665                 | 1.0000    |
| O22   | 1.0235(5) | 0.3447(6) | 0.9140(5)   | 0.0720                 | 0.5000    |
| C23   | 0.8398(4) | 0.3454(6) | 0.9820(7)   | 0.0647                 | 0.5000    |
| C24   | 0.9238(4) | 0.2995(6) | 0.9472(7)   | 0.0673                 | 0.5000    |
| C25   | 0.9084(6) | 0.2053(7) | 0.9413(8)   | 0.0692                 | 0.5000    |
| C26   | 0.8086(7) | 0.1562(7) | 0.9705(9)   | 0.0713                 | 0.5000    |
| C27   | 0.7244(6) | 0.2022(9) | 1.0055(12)  | 0.0696                 | 0.5000    |

|     |           |           |            |        |        |
|-----|-----------|-----------|------------|--------|--------|
| C28 | 0.7399(5) | 0.2976(9) | 1.0099(11) | 0.0681 | 0.5000 |
| O31 | 0.7855(5) | 0.4385(5) | 1.0165(5)  | 0.0681 | 0.5000 |
| O32 | 0.9912(5) | 0.4092(5) | 0.9256(5)  | 0.0649 | 0.5000 |
| C33 | 0.8093(4) | 0.3533(6) | 0.9957(8)  | 0.0606 | 0.5000 |
| C34 | 0.9090(4) | 0.3376(5) | 0.9551(6)  | 0.0617 | 0.5000 |
| C35 | 0.9271(5) | 0.2498(6) | 0.9354(7)  | 0.0621 | 0.5000 |
| C36 | 0.8458(7) | 0.1759(6) | 0.9586(8)  | 0.0611 | 0.5000 |
| C37 | 0.7463(6) | 0.1899(8) | 1.0021(11) | 0.0591 | 0.5000 |
| C38 | 0.7278(5) | 0.2795(8) | 1.0192(11) | 0.0593 | 0.5000 |
| O41 | 0.4630(5) | 0.1710(6) | 1.0503(5)  | 0.0844 | 0.5000 |
| O42 | 0.2945(4) | 0.0384(6) | 1.0521(5)  | 0.0930 | 0.5000 |
| C43 | 0.3754(5) | 0.2090(5) | 1.0257(5)  | 0.0701 | 0.5000 |
| C44 | 0.2916(4) | 0.1435(4) | 1.0271(4)  | 0.0716 | 0.5000 |
| C45 | 0.2012(5) | 0.1843(6) | 1.0144(7)  | 0.0756 | 0.5000 |
| C46 | 0.1918(6) | 0.2904(6) | 0.9896(6)  | 0.0775 | 0.5000 |
| C47 | 0.2717(8) | 0.3538(5) | 0.9898(8)  | 0.0747 | 0.5000 |
| C48 | 0.3627(7) | 0.3109(5) | 1.0088(8)  | 0.0713 | 0.5000 |
| O51 | 0.4744(5) | 0.1052(6) | 1.0663(5)  | 0.0801 | 0.5000 |
| H51 | 0.5578(4) | 0.8810(4) | 0.5191(3)  | 0.0465 | 1.0000 |
| O52 | 0.3053(4) | 0.0429(5) | 1.0267(5)  | 0.0740 | 0.5000 |
| C53 | 0.3964(5) | 0.1671(5) | 1.0445(5)  | 0.0620 | 0.5000 |
| C54 | 0.3146(4) | 0.1348(4) | 1.0292(5)  | 0.0567 | 0.5000 |
| C55 | 0.2372(5) | 0.2042(6) | 1.0052(7)  | 0.0553 | 0.5000 |
| C56 | 0.2479(6) | 0.3052(6) | 0.9969(7)  | 0.0559 | 0.5000 |
| C57 | 0.3355(7) | 0.3398(5) | 1.0077(7)  | 0.0579 | 0.5000 |
| C58 | 0.4111(5) | 0.2716(5) | 1.0305(6)  | 0.0622 | 0.5000 |
| N61 | 0.8649(3) | 0.6654(3) | 0.7408(2)  | 0.0301 | 1.0000 |
| H61 | 0.6921(4) | 1.0089(4) | 0.4602(3)  | 0.0542 | 1.0000 |
| C62 | 0.9155(3) | 0.6150(3) | 0.6759(3)  | 0.0317 | 1.0000 |
| C63 | 0.9359(3) | 0.5016(3) | 0.7167(3)  | 0.0364 | 1.0000 |
| C64 | 0.9964(4) | 0.4634(4) | 0.6460(3)  | 0.0423 | 1.0000 |
| C65 | 1.0215(4) | 0.3507(4) | 0.6853(3)  | 0.0472 | 1.0000 |
| C66 | 0.7633(3) | 0.6044(3) | 0.8031(3)  | 0.0334 | 1.0000 |
| C67 | 0.6810(3) | 0.5928(3) | 0.7597(3)  | 0.0365 | 1.0000 |
| C68 | 0.5830(4) | 0.5322(4) | 0.8294(3)  | 0.0502 | 1.0000 |
| C69 | 0.4977(4) | 0.5207(4) | 0.7883(3)  | 0.0552 | 1.0000 |
| C70 | 0.8449(3) | 0.7754(3) | 0.6872(3)  | 0.0303 | 1.0000 |
| C71 | 0.8003(3) | 0.8416(3) | 0.7399(3)  | 0.0355 | 1.0000 |
| H71 | 0.8645(4) | 0.9620(4) | 0.4277(3)  | 0.0574 | 1.0000 |
| C72 | 0.7907(4) | 0.9520(3) | 0.6780(3)  | 0.0396 | 1.0000 |

|      |           |            |             |        |        |
|------|-----------|------------|-------------|--------|--------|
| C73  | 0.7429(4) | 1.0209(4)  | 0.7268(3)   | 0.0455 | 1.0000 |
| C74  | 0.9369(3) | 0.6659(3)  | 0.7974(3)   | 0.0320 | 1.0000 |
| C75  | 1.0389(3) | 0.7332(3)  | 0.7477(3)   | 0.0358 | 1.0000 |
| C76  | 1.1039(4) | 0.7278(4)  | 0.8108(3)   | 0.0450 | 1.0000 |
| C77  | 1.2052(4) | 0.7960(4)  | 0.7635(3)   | 0.0526 | 1.0000 |
| N81  | 0.3682(3) | 0.1705(3)  | 0.7541(2)   | 0.0295 | 1.0000 |
| H81  | 0.8956(4) | 0.7896(4)  | 0.4514(3)   | 0.0525 | 1.0000 |
| C82  | 0.4198(3) | 0.1110(3)  | 0.6970(3)   | 0.0333 | 1.0000 |
| C83  | 0.4350(3) | -0.0021(3) | 0.7466(3)   | 0.0376 | 1.0000 |
| C84  | 0.4885(4) | -0.0535(4) | 0.6835(3)   | 0.0448 | 1.0000 |
| C85  | 0.5072(4) | -0.1658(4) | 0.7317(3)   | 0.0496 | 1.0000 |
| C86  | 0.2648(3) | 0.1140(3)  | 0.8169(3)   | 0.0318 | 1.0000 |
| C87  | 0.1829(3) | 0.0989(3)  | 0.7735(3)   | 0.0378 | 1.0000 |
| C88  | 0.0902(4) | 0.0298(4)  | 0.8410(3)   | 0.0549 | 1.0000 |
| C89  | 0.0029(4) | 0.0207(5)  | 0.8010(4)   | 0.0646 | 1.0000 |
| C90  | 0.3510(3) | 0.2781(3)  | 0.6924(3)   | 0.0330 | 1.0000 |
| C91  | 0.3038(3) | 0.3507(3)  | 0.7371(3)   | 0.0353 | 1.0000 |
| C92  | 0.2946(4) | 0.4581(3)  | 0.6697(3)   | 0.0428 | 1.0000 |
| C93  | 0.2412(4) | 0.5305(4)  | 0.7129(3)   | 0.0516 | 1.0000 |
| C94  | 0.4376(3) | 0.1768(3)  | 0.8108(3)   | 0.0313 | 1.0000 |
| C95  | 0.5438(3) | 0.2344(3)  | 0.7616(3)   | 0.0340 | 1.0000 |
| C96  | 0.6024(4) | 0.2389(4)  | 0.8261(3)   | 0.0418 | 1.0000 |
| C97  | 0.7097(4) | 0.2961(4)  | 0.7795(3)   | 0.0479 | 1.0000 |
| H111 | 0.6053(2) | 0.4118(2)  | 0.54532(19) | 0.0597 | 1.0000 |
| H121 | 0.5735(2) | 0.2461(3)  | 0.4686(2)   | 0.0756 | 1.0000 |
| H151 | 0.8003(3) | 0.1290(3)  | 0.4673(3)   | 0.0486 | 1.0000 |
| H161 | 0.9414(3) | 0.1705(3)  | 0.5070(3)   | 0.0461 | 1.0000 |
| H171 | 0.9283(3) | 0.3084(3)  | 0.5574(3)   | 0.0482 | 1.0000 |
| H181 | 0.7768(3) | 0.3999(4)  | 0.5653(3)   | 0.0475 | 1.0000 |
| H211 | 0.9183(6) | 0.4555(5)  | 0.9837(5)   | 0.0817 | 0.5000 |
| H221 | 1.0286(5) | 0.3948(6)  | 0.9384(5)   | 0.0878 | 0.5000 |
| H251 | 0.9666(6) | 0.1749(7)  | 0.9172(8)   | 0.0843 | 0.5000 |
| H261 | 0.7992(7) | 0.0910(7)  | 0.9670(9)   | 0.0888 | 0.5000 |
| H271 | 0.6572(6) | 0.1696(9)  | 1.0250(12)  | 0.0866 | 0.5000 |
| H281 | 0.6831(5) | 0.3297(9)  | 1.0321(11)  | 0.0837 | 0.5000 |
| H311 | 0.8488(5) | 0.4671(5)  | 1.0176(5)   | 0.0831 | 0.5000 |
| H321 | 0.9805(5) | 0.4501(5)  | 0.9604(5)   | 0.0783 | 0.5000 |
| H351 | 0.9956(5) | 0.2402(6)  | 0.9059(7)   | 0.0749 | 0.5000 |
| H361 | 0.8587(7) | 0.1153(6)  | 0.9458(8)   | 0.0717 | 0.5000 |
| H371 | 0.6907(6) | 0.1402(8)  | 1.0187(11)  | 0.0687 | 0.5000 |

|      |           |           |            |        |        |
|------|-----------|-----------|------------|--------|--------|
| H381 | 0.6604(5) | 0.2902(8) | 1.0461(11) | 0.0685 | 0.5000 |
| H411 | 0.4877(5) | 0.1118(6) | 1.0382(5)  | 0.0945 | 0.5000 |
| H421 | 0.3680(4) | 0.0331(6) | 1.0421(5)  | 0.1199 | 0.5000 |
| H451 | 0.1467(5) | 0.1397(6) | 1.0198(7)  | 0.0891 | 0.5000 |
| H461 | 0.1302(6) | 0.3180(6) | 0.9730(6)  | 0.0945 | 0.5000 |
| H471 | 0.2615(8) | 0.4245(5) | 0.9765(8)  | 0.0904 | 0.5000 |
| H481 | 0.4146(7) | 0.3539(5) | 1.0098(8)  | 0.0823 | 0.5000 |
| H511 | 0.4738(5) | 0.0608(6) | 1.0357(5)  | 0.0918 | 0.5000 |
| H521 | 0.3709(4) | 0.0175(5) | 1.0080(5)  | 0.0912 | 0.5000 |
| H551 | 0.1790(5) | 0.1835(6) | 0.9932(7)  | 0.0633 | 0.5000 |
| H561 | 0.1989(6) | 0.3525(6) | 0.9843(7)  | 0.0639 | 0.5000 |
| H571 | 0.3482(7) | 0.4095(5) | 0.9997(7)  | 0.0669 | 0.5000 |
| H581 | 0.4719(5) | 0.2926(5) | 1.0381(6)  | 0.0717 | 0.5000 |
| H621 | 0.9829(3) | 0.6534(3) | 0.6429(3)  | 0.0373 | 1.0000 |
| H622 | 0.8706(3) | 0.6233(3) | 0.6383(3)  | 0.0372 | 1.0000 |
| H631 | 0.8687(3) | 0.4613(3) | 0.7474(3)  | 0.0427 | 1.0000 |
| H632 | 0.9775(3) | 0.4933(3) | 0.7571(3)  | 0.0431 | 1.0000 |
| H641 | 1.0619(4) | 0.5073(4) | 0.6139(3)  | 0.0508 | 1.0000 |
| H642 | 0.9523(4) | 0.4693(4) | 0.6061(3)  | 0.0517 | 1.0000 |
| H651 | 1.0611(4) | 0.3412(4) | 0.7288(3)  | 0.0706 | 1.0000 |
| H652 | 1.0652(4) | 0.3298(4) | 0.6399(3)  | 0.0711 | 1.0000 |
| H653 | 0.9575(4) | 0.3049(4) | 0.7137(3)  | 0.0706 | 1.0000 |
| H661 | 0.7825(3) | 0.5360(3) | 0.8368(3)  | 0.0396 | 1.0000 |
| H662 | 0.7348(3) | 0.6403(3) | 0.8408(3)  | 0.0397 | 1.0000 |
| H671 | 0.7076(3) | 0.5535(3) | 0.7227(3)  | 0.0432 | 1.0000 |
| H672 | 0.6631(3) | 0.6614(3) | 0.7250(3)  | 0.0425 | 1.0000 |
| H681 | 0.5579(4) | 0.5690(4) | 0.8674(3)  | 0.0593 | 1.0000 |
| H682 | 0.6016(4) | 0.4627(4) | 0.8626(3)  | 0.0588 | 1.0000 |
| H691 | 0.4767(4) | 0.5878(4) | 0.7559(3)  | 0.0818 | 1.0000 |
| H692 | 0.4376(4) | 0.4795(4) | 0.8329(3)  | 0.0820 | 1.0000 |
| H693 | 0.5240(4) | 0.4843(4) | 0.7495(3)  | 0.0819 | 1.0000 |
| H701 | 0.7968(3) | 0.7699(3) | 0.6553(3)  | 0.0355 | 1.0000 |
| H702 | 0.9118(3) | 0.8074(3) | 0.6472(3)  | 0.0353 | 1.0000 |
| H711 | 0.7309(3) | 0.8103(3) | 0.7804(3)  | 0.0401 | 1.0000 |
| H712 | 0.8486(3) | 0.8450(3) | 0.7734(3)  | 0.0399 | 1.0000 |
| H721 | 0.8592(4) | 0.9819(3) | 0.6426(3)  | 0.0480 | 1.0000 |
| H722 | 0.7470(4) | 0.9466(3) | 0.6420(3)  | 0.0481 | 1.0000 |
| H731 | 0.7875(4) | 1.0252(4) | 0.7620(3)  | 0.0660 | 1.0000 |
| H732 | 0.7385(4) | 1.0923(4) | 0.6863(3)  | 0.0661 | 1.0000 |
| H733 | 0.6728(4) | 0.9928(4) | 0.7629(3)  | 0.0654 | 1.0000 |

|      |            |            |           |        |        |
|------|------------|------------|-----------|--------|--------|
| H741 | 0.9540(3)  | 0.5951(3)  | 0.8239(3) | 0.0387 | 1.0000 |
| H742 | 0.8971(3)  | 0.6908(3)  | 0.8414(3) | 0.0391 | 1.0000 |
| H751 | 1.0224(3)  | 0.8052(3)  | 0.7206(3) | 0.0428 | 1.0000 |
| H752 | 1.0797(3)  | 0.7092(3)  | 0.7025(3) | 0.0435 | 1.0000 |
| H761 | 1.1196(4)  | 0.6565(4)  | 0.8380(3) | 0.0539 | 1.0000 |
| H762 | 1.0618(4)  | 0.7524(4)  | 0.8557(3) | 0.0543 | 1.0000 |
| H771 | 1.2462(4)  | 0.7747(4)  | 0.7179(3) | 0.0789 | 1.0000 |
| H772 | 1.1917(4)  | 0.8682(4)  | 0.7385(3) | 0.0787 | 1.0000 |
| H773 | 1.2453(4)  | 0.7886(4)  | 0.8050(3) | 0.0792 | 1.0000 |
| H821 | 0.3753(3)  | 0.1145(3)  | 0.6595(3) | 0.0401 | 1.0000 |
| H822 | 0.4865(3)  | 0.1492(3)  | 0.6614(3) | 0.0393 | 1.0000 |
| H831 | 0.4785(3)  | -0.0070(3) | 0.7845(3) | 0.0466 | 1.0000 |
| H832 | 0.3660(3)  | -0.0388(3) | 0.7794(3) | 0.0455 | 1.0000 |
| H841 | 0.4452(4)  | -0.0505(4) | 0.6454(3) | 0.0536 | 1.0000 |
| H842 | 0.5547(4)  | -0.0148(4) | 0.6478(3) | 0.0530 | 1.0000 |
| H851 | 0.4417(4)  | -0.2039(4) | 0.7680(3) | 0.0741 | 1.0000 |
| H852 | 0.5531(4)  | -0.1712(4) | 0.7685(3) | 0.0740 | 1.0000 |
| H853 | 0.5402(4)  | -0.1972(4) | 0.6906(3) | 0.0743 | 1.0000 |
| H861 | 0.2820(3)  | 0.0469(3)  | 0.8536(3) | 0.0390 | 1.0000 |
| H862 | 0.2369(3)  | 0.1559(3)  | 0.8511(3) | 0.0388 | 1.0000 |
| H871 | 0.1574(3)  | 0.1644(3)  | 0.7435(3) | 0.0459 | 1.0000 |
| H872 | 0.2133(3)  | 0.0680(3)  | 0.7323(3) | 0.0468 | 1.0000 |
| H881 | 0.1147(4)  | -0.0386(4) | 0.8662(3) | 0.0673 | 1.0000 |
| H882 | 0.0643(4)  | 0.0573(4)  | 0.8859(3) | 0.0671 | 1.0000 |
| H891 | -0.0536(4) | -0.0270(5) | 0.8429(4) | 0.0969 | 1.0000 |
| H892 | 0.0293(4)  | -0.0044(5) | 0.7541(4) | 0.0973 | 1.0000 |
| H893 | -0.0238(4) | 0.0876(5)  | 0.7769(4) | 0.0971 | 1.0000 |
| H901 | 0.4194(3)  | 0.3093(3)  | 0.6533(3) | 0.0386 | 1.0000 |
| H902 | 0.3064(3)  | 0.2664(3)  | 0.6599(3) | 0.0384 | 1.0000 |
| H911 | 0.2349(3)  | 0.3212(3)  | 0.7765(3) | 0.0410 | 1.0000 |
| H912 | 0.3507(3)  | 0.3599(3)  | 0.7707(3) | 0.0414 | 1.0000 |
| H921 | 0.2549(4)  | 0.4490(3)  | 0.6311(3) | 0.0517 | 1.0000 |
| H922 | 0.3657(4)  | 0.4893(3)  | 0.6344(3) | 0.0512 | 1.0000 |
| H931 | 0.2349(4)  | 0.5973(4)  | 0.6693(3) | 0.0749 | 1.0000 |
| H932 | 0.1711(4)  | 0.5018(4)  | 0.7492(3) | 0.0745 | 1.0000 |
| H933 | 0.2815(4)  | 0.5431(4)  | 0.7478(3) | 0.0751 | 1.0000 |
| H941 | 0.3978(3)  | 0.2143(3)  | 0.8471(3) | 0.0373 | 1.0000 |
| H942 | 0.4459(3)  | 0.1057(3)  | 0.8466(3) | 0.0358 | 1.0000 |
| H951 | 0.5855(3)  | 0.1972(3)  | 0.7267(3) | 0.0410 | 1.0000 |
| H952 | 0.5367(3)  | 0.3051(3)  | 0.7226(3) | 0.0409 | 1.0000 |

|      |           |           |           |        |        |
|------|-----------|-----------|-----------|--------|--------|
| H961 | 0.6112(4) | 0.1687(4) | 0.8632(3) | 0.0500 | 1.0000 |
| H962 | 0.5597(4) | 0.2762(4) | 0.8602(3) | 0.0504 | 1.0000 |
| H971 | 0.7424(4) | 0.3030(4) | 0.8214(3) | 0.0701 | 1.0000 |
| H972 | 0.7538(4) | 0.2569(4) | 0.7500(3) | 0.0697 | 1.0000 |
| H973 | 0.7061(4) | 0.3660(4) | 0.7381(3) | 0.0699 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.070(2)        | 0.0463(17)      | 0.0667(19)      | -0.0274(15)     | -0.0153(16)     | 0.0092(14)      |
| O1    | 0.048(2)        | 0.051(2)        | 0.061(2)        | -0.0257(18)     | -0.0202(17)     | 0.0154(16)      |
| O2    | 0.0395(18)      | 0.0363(18)      | 0.054(2)        | -0.0161(15)     | -0.0130(15)     | 0.0027(14)      |
| F2    | 0.106(6)        | 0.050(4)        | 0.061(5)        | -0.003(3)       | -0.009(4)       | 0.027(4)        |
| C3    | 0.048(3)        | 0.048(3)        | 0.028(2)        | -0.019(2)       | -0.017(2)       | 0.009(2)        |
| F3    | 0.098(7)        | 0.055(5)        | 0.087(6)        | -0.008(4)       | -0.042(5)       | -0.021(4)       |
| C4    | 0.041(3)        | 0.045(3)        | 0.028(2)        | -0.018(2)       | -0.0159(19)     | 0.005(2)        |
| C5    | 0.041(3)        | 0.046(3)        | 0.037(3)        | -0.022(2)       | -0.017(2)       | 0.005(2)        |
| C6    | 0.058(3)        | 0.047(3)        | 0.041(3)        | -0.021(2)       | -0.025(2)       | 0.005(2)        |
| C7    | 0.048(3)        | 0.063(4)        | 0.038(3)        | -0.022(2)       | -0.012(2)       | -0.008(3)       |
| C8    | 0.038(3)        | 0.063(3)        | 0.037(3)        | -0.027(2)       | -0.013(2)       | 0.004(2)        |
| O11   | 0.0416(18)      | 0.0378(17)      | 0.0372(17)      | -0.0131(14)     | -0.0064(14)     | 0.0030(14)      |
| O12   | 0.0427(19)      | 0.051(2)        | 0.069(2)        | -0.0317(18)     | -0.0193(17)     | 0.0043(16)      |
| C13   | 0.036(2)        | 0.030(2)        | 0.023(2)        | -0.0038(18)     | -0.0030(18)     | 0.0037(19)      |
| C14   | 0.033(2)        | 0.036(3)        | 0.033(2)        | -0.007(2)       | -0.0058(19)     | -0.005(2)       |
| C15   | 0.042(3)        | 0.036(3)        | 0.036(3)        | -0.012(2)       | -0.004(2)       | -0.001(2)       |
| C16   | 0.035(2)        | 0.034(2)        | 0.037(2)        | -0.006(2)       | -0.004(2)       | -0.0012(19)     |
| C17   | 0.038(3)        | 0.042(3)        | 0.035(2)        | -0.012(2)       | -0.011(2)       | -0.003(2)       |
| C18   | 0.044(3)        | 0.039(3)        | 0.032(2)        | -0.014(2)       | -0.006(2)       | -0.002(2)       |
| O21   | 0.077(4)        | 0.065(4)        | 0.054(4)        | -0.008(3)       | -0.030(3)       | -0.006(3)       |
| O22   | 0.076(4)        | 0.075(4)        | 0.062(4)        | -0.016(3)       | -0.027(3)       | -0.005(3)       |
| C23   | 0.077(3)        | 0.067(3)        | 0.050(3)        | -0.008(3)       | -0.036(3)       | -0.008(3)       |
| C24   | 0.077(3)        | 0.070(3)        | 0.054(3)        | -0.011(3)       | -0.034(3)       | -0.007(3)       |
| C25   | 0.080(4)        | 0.070(4)        | 0.056(4)        | -0.009(3)       | -0.035(3)       | -0.011(3)       |
| C26   | 0.082(4)        | 0.071(4)        | 0.055(4)        | -0.005(3)       | -0.038(3)       | -0.013(3)       |
| C27   | 0.080(4)        | 0.071(4)        | 0.053(4)        | -0.003(3)       | -0.039(4)       | -0.013(3)       |
| C28   | 0.079(4)        | 0.070(4)        | 0.051(4)        | -0.004(3)       | -0.037(3)       | -0.009(3)       |
| O31   | 0.073(4)        | 0.061(3)        | 0.055(4)        | -0.001(3)       | -0.022(3)       | -0.009(3)       |
| O32   | 0.069(4)        | 0.058(3)        | 0.055(3)        | 0.001(3)        | -0.028(3)       | -0.009(3)       |
| C33   | 0.067(3)        | 0.058(3)        | 0.046(3)        | 0.002(3)        | -0.029(3)       | -0.009(3)       |
| C34   | 0.067(3)        | 0.059(3)        | 0.047(3)        | 0.003(3)        | -0.029(3)       | -0.009(3)       |



|     |            |            |            |             |             |             |
|-----|------------|------------|------------|-------------|-------------|-------------|
| C35 | 0.065(3)   | 0.061(3)   | 0.047(4)   | 0.002(3)    | -0.025(3)   | -0.010(3)   |
| C36 | 0.064(3)   | 0.061(3)   | 0.045(4)   | 0.001(3)    | -0.023(3)   | -0.010(3)   |
| C37 | 0.064(3)   | 0.059(3)   | 0.043(4)   | 0.000(3)    | -0.023(3)   | -0.010(3)   |
| C38 | 0.066(3)   | 0.059(3)   | 0.043(4)   | 0.000(3)    | -0.025(3)   | -0.008(3)   |
| O41 | 0.084(4)   | 0.109(4)   | 0.034(3)   | -0.005(3)   | -0.013(3)   | 0.043(4)    |
| O42 | 0.135(5)   | 0.091(4)   | 0.020(4)   | -0.014(3)   | 0.022(4)    | 0.015(4)    |
| C43 | 0.081(3)   | 0.096(3)   | 0.022(3)   | -0.015(3)   | -0.010(3)   | 0.033(3)    |
| C44 | 0.090(3)   | 0.091(3)   | 0.020(3)   | -0.019(3)   | 0.001(3)    | 0.024(3)    |
| C45 | 0.084(4)   | 0.103(4)   | 0.025(3)   | -0.019(3)   | 0.001(3)    | 0.021(3)    |
| C46 | 0.083(4)   | 0.104(4)   | 0.027(3)   | -0.016(3)   | -0.002(3)   | 0.027(3)    |
| C47 | 0.082(4)   | 0.099(4)   | 0.028(3)   | -0.017(3)   | -0.003(3)   | 0.030(3)    |
| C48 | 0.081(4)   | 0.095(4)   | 0.025(3)   | -0.017(3)   | -0.005(3)   | 0.030(3)    |
| O51 | 0.065(3)   | 0.114(4)   | 0.033(3)   | 0.002(3)    | -0.016(3)   | 0.037(3)    |
| O52 | 0.094(3)   | 0.089(3)   | 0.022(3)   | -0.022(3)   | 0.011(3)    | 0.018(3)    |
| C53 | 0.054(3)   | 0.102(3)   | 0.021(3)   | -0.012(3)   | -0.015(2)   | 0.028(3)    |
| C54 | 0.063(3)   | 0.088(3)   | 0.017(2)   | -0.022(2)   | -0.006(2)   | 0.021(3)    |
| C55 | 0.055(3)   | 0.091(3)   | 0.018(3)   | -0.023(3)   | -0.005(3)   | 0.019(3)    |
| C56 | 0.054(3)   | 0.091(4)   | 0.020(3)   | -0.022(3)   | -0.006(3)   | 0.021(3)    |
| C57 | 0.056(3)   | 0.093(4)   | 0.020(3)   | -0.020(3)   | -0.006(3)   | 0.020(3)    |
| C58 | 0.056(3)   | 0.102(4)   | 0.018(3)   | -0.016(3)   | -0.008(3)   | 0.022(3)    |
| N61 | 0.0311(19) | 0.0327(19) | 0.0254(18) | -0.0098(15) | -0.0075(15) | -0.0007(15) |
| C62 | 0.035(2)   | 0.034(2)   | 0.028(2)   | -0.0128(19) | -0.0075(18) | -0.0011(19) |
| C63 | 0.034(2)   | 0.037(3)   | 0.037(2)   | -0.013(2)   | -0.0086(19) | -0.0001(19) |
| C64 | 0.046(3)   | 0.043(3)   | 0.044(3)   | -0.021(2)   | -0.017(2)   | 0.009(2)    |
| C65 | 0.047(3)   | 0.043(3)   | 0.056(3)   | -0.023(2)   | -0.016(2)   | 0.009(2)    |
| C66 | 0.033(2)   | 0.032(2)   | 0.029(2)   | -0.0074(19) | -0.0042(18) | -0.0030(18) |
| C67 | 0.036(2)   | 0.035(2)   | 0.036(2)   | -0.012(2)   | -0.008(2)   | -0.0014(19) |
| C68 | 0.042(3)   | 0.062(3)   | 0.042(3)   | -0.017(3)   | -0.005(2)   | -0.012(2)   |
| C69 | 0.040(3)   | 0.064(3)   | 0.052(3)   | -0.012(3)   | -0.011(2)   | -0.014(2)   |
| C70 | 0.034(2)   | 0.031(2)   | 0.025(2)   | -0.0087(18) | -0.0092(18) | -0.0015(18) |
| C71 | 0.035(2)   | 0.039(3)   | 0.030(2)   | -0.012(2)   | -0.0077(19) | 0.003(2)    |
| C72 | 0.047(3)   | 0.034(3)   | 0.031(2)   | -0.009(2)   | -0.006(2)   | 0.004(2)    |
| C73 | 0.049(3)   | 0.046(3)   | 0.041(3)   | -0.017(2)   | -0.011(2)   | 0.008(2)    |
| C74 | 0.037(2)   | 0.034(2)   | 0.027(2)   | -0.0101(19) | -0.0129(18) | 0.0026(19)  |
| C75 | 0.036(2)   | 0.040(3)   | 0.031(2)   | -0.012(2)   | -0.0113(19) | 0.001(2)    |
| C76 | 0.045(3)   | 0.053(3)   | 0.042(3)   | -0.016(2)   | -0.021(2)   | -0.003(2)   |
| C77 | 0.045(3)   | 0.063(3)   | 0.056(3)   | -0.023(3)   | -0.023(2)   | -0.003(3)   |
| N81 | 0.0317(19) | 0.0341(19) | 0.0212(17) | -0.0086(15) | -0.0077(14) | 0.0019(15)  |
| C82 | 0.034(2)   | 0.044(3)   | 0.028(2)   | -0.019(2)   | -0.0100(18) | 0.0051(19)  |
| C83 | 0.035(2)   | 0.045(3)   | 0.036(2)   | -0.020(2)   | -0.009(2)   | 0.005(2)    |

|     |          |          |          |             |             |             |
|-----|----------|----------|----------|-------------|-------------|-------------|
| C84 | 0.051(3) | 0.049(3) | 0.041(3) | -0.022(2)   | -0.018(2)   | 0.015(2)    |
| C85 | 0.050(3) | 0.050(3) | 0.054(3) | -0.026(3)   | -0.015(2)   | 0.016(2)    |
| C86 | 0.033(2) | 0.035(2) | 0.025(2) | -0.0098(19) | -0.0059(18) | -0.0002(19) |
| C87 | 0.039(3) | 0.038(3) | 0.038(3) | -0.016(2)   | -0.012(2)   | 0.004(2)    |
| C88 | 0.046(3) | 0.066(4) | 0.047(3) | -0.018(3)   | -0.007(2)   | -0.012(3)   |
| C89 | 0.046(3) | 0.073(4) | 0.070(4) | -0.020(3)   | -0.015(3)   | -0.012(3)   |
| C90 | 0.034(2) | 0.037(2) | 0.025(2) | -0.0080(19) | -0.0093(18) | -0.0005(19) |
| C91 | 0.037(2) | 0.037(2) | 0.032(2) | -0.012(2)   | -0.0106(19) | 0.002(2)    |
| C92 | 0.047(3) | 0.037(3) | 0.039(3) | -0.008(2)   | -0.011(2)   | 0.002(2)    |
| C93 | 0.059(3) | 0.040(3) | 0.054(3) | -0.015(2)   | -0.017(3)   | 0.008(2)    |
| C94 | 0.036(2) | 0.037(2) | 0.024(2) | -0.0122(19) | -0.0116(18) | 0.0008(19)  |
| C95 | 0.035(2) | 0.039(3) | 0.027(2) | -0.0104(19) | -0.0089(18) | 0.0023(19)  |
| C96 | 0.043(3) | 0.046(3) | 0.032(2) | -0.009(2)   | -0.012(2)   | -0.011(2)   |
| C97 | 0.046(3) | 0.055(3) | 0.040(3) | -0.011(2)   | -0.018(2)   | -0.008(2)   |

## Distances

|     |          |            |  |     |          |            |
|-----|----------|------------|--|-----|----------|------------|
| O1  | C3       | 1.358(5)Å  |  | O1  | H11      | 0.842Å     |
| O2  | C4       | 1.364(5)Å  |  | O2  | H21      | 0.831Å     |
| F2  | F2 2_657 | 1.417(15)Å |  | F2  | O51      | 1.693(10)Å |
| F2  | H511     | 0.946Å     |  | C3  | C4       | 1.400(6)Å  |
| C3  | C8       | 1.393(6)Å  |  | F3  | F3 2_767 | 1.258(14)Å |
| F3  | H321     | 1.078Å     |  | C4  | C5       | 1.380(6)Å  |
| C5  | C6       | 1.378(6)Å  |  | C5  | H51      | 0.927Å     |
| C6  | C7       | 1.378(7)Å  |  | C6  | H61      | 0.948Å     |
| C7  | C8       | 1.376(7)Å  |  | C7  | H71      | 0.936Å     |
| C8  | H81      | 0.922Å     |  | O11 | C13      | 1.354(5)Å  |
| O11 | H111     | 0.851Å     |  | O12 | C14      | 1.365(5)Å  |
| O12 | H121     | 0.848Å     |  | C13 | C14      | 1.405(6)Å  |
| C13 | C18      | 1.375(6)Å  |  | C14 | C15      | 1.378(6)Å  |
| C15 | C16      | 1.383(6)Å  |  | C15 | H151     | 0.925Å     |
| C16 | C17      | 1.375(6)Å  |  | C16 | H161     | 0.978Å     |
| C17 | C18      | 1.394(6)Å  |  | C17 | H171     | 0.945Å     |
| C18 | H181     | 0.960Å     |  | O21 | C23      | 1.355(6)Å  |
| O21 | O31      | 0.858(8)Å  |  | O21 | C33      | 1.266(9)Å  |
| O21 | H211     | 0.950Å     |  | O21 | H311     | 0.773Å     |
| O22 | C24      | 1.367(6)Å  |  | O22 | O32      | 1.046(8)Å  |
| O22 | C34      | 1.487(8)Å  |  | O22 | H221     | 0.950Å     |
| C23 | C24      | 1.377(5)Å  |  | C23 | C28      | 1.385(5)Å  |
| C23 | O31      | 1.684(10)Å |  | C23 | C33      | 0.443(8)Å  |

|     |      |            |  |     |      |            |
|-----|------|------------|--|-----|------|------------|
| C23 | C34  | 0.936(8)Å  |  | C23 | C38  | 1.617(8)Å  |
| C24 | C25  | 1.379(5)Å  |  | C24 | O32  | 1.666(8)Å  |
| C24 | C34  | 0.610(8)Å  |  | C24 | C35  | 0.787(8)Å  |
| C25 | C26  | 1.390(5)Å  |  | C25 | C35  | 0.638(9)Å  |
| C25 | C36  | 0.866(10)Å |  | C25 | H251 | 0.941Å     |
| C25 | H351 | 1.179Å     |  | C26 | C27  | 1.380(5)Å  |
| C26 | C36  | 0.524(10)Å |  | C26 | C37  | 1.060(14)Å |
| C26 | H261 | 0.947Å     |  | C26 | H361 | 0.976Å     |
| C27 | C28  | 1.385(5)Å  |  | C27 | C36  | 1.695(13)Å |
| C27 | C37  | 0.335(16)Å |  | C27 | C38  | 1.190(14)Å |
| C27 | H271 | 0.934Å     |  | C27 | H371 | 0.907Å     |
| C28 | C33  | 1.140(9)Å  |  | C28 | C37  | 1.553(13)Å |
| C28 | C38  | 0.271(15)Å |  | C28 | H281 | 0.930Å     |
| C28 | H381 | 1.060Å     |  | O31 | C33  | 1.367(6)Å  |
| O31 | H311 | 0.950Å     |  | O32 | C34  | 1.360(6)Å  |
| O32 | H221 | 0.591Å     |  | O32 | H321 | 0.950Å     |
| C33 | C34  | 1.375(5)Å  |  | C33 | C38  | 1.388(5)Å  |
| C34 | C35  | 1.384(5)Å  |  | C35 | C36  | 1.389(5)Å  |
| C35 | H251 | 1.257Å     |  | C35 | H351 | 0.948Å     |
| C36 | C37  | 1.381(5)Å  |  | C36 | H361 | 0.948Å     |
| C37 | C38  | 1.385(5)Å  |  | C37 | H271 | 1.153Å     |
| C37 | H371 | 0.939Å     |  | C38 | H281 | 0.953Å     |
| C38 | H381 | 0.928Å     |  | O41 | C43  | 1.359(6)Å  |
| O41 | O51  | 0.871(8)Å  |  | O41 | C53  | 0.920(8)Å  |
| O41 | C58  | 1.498(8)Å  |  | O41 | H411 | 0.950Å     |
| O42 | C44  | 1.363(8)Å  |  | O42 | O52  | 0.400(13)Å |
| O42 | C54  | 1.265(10)Å |  | O42 | H421 | 0.950Å     |
| O42 | H521 | 1.194Å     |  | C43 | C44  | 1.453(5)Å  |
| C43 | C48  | 1.350(5)Å  |  | C43 | C53  | 0.643(7)Å  |
| C43 | C54  | 1.308(8)Å  |  | C43 | C58  | 1.046(8)Å  |
| C44 | C45  | 1.342(5)Å  |  | C44 | O52  | 1.410(8)Å  |
| C44 | C53  | 1.565(6)Å  |  | C44 | C54  | 0.330(4)Å  |
| C44 | C55  | 1.109(7)Å  |  | C45 | C46  | 1.383(5)Å  |
| C45 | C54  | 1.672(6)Å  |  | C45 | C55  | 0.516(9)Å  |
| C45 | C56  | 1.703(11)Å |  | C45 | H451 | 0.934Å     |
| C45 | H551 | 0.526Å     |  | C46 | C47  | 1.406(5)Å  |
| C46 | C55  | 1.288(10)Å |  | C46 | C56  | 0.831(10)Å |
| C46 | H461 | 0.954Å     |  | C46 | H561 | 0.841Å     |
| C47 | C48  | 1.385(5)Å  |  | C47 | C56  | 0.712(11)Å |
| C47 | C57  | 0.962(10)Å |  | C47 | H471 | 0.936Å     |

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| C47 | H561 | 0.996Å    |  | C48 | C56  | 1.596(9)Å |
| C48 | C57  | 0.527(9)Å |  | C48 | C58  | 0.890(9)Å |
| C48 | H481 | 0.936Å    |  | O51 | C53  | 1.357(6)Å |
| O51 | H411 | 0.438Å    |  | O51 | H511 | 0.950Å    |
| O52 | C54  | 1.309(6)Å |  | O52 | H421 | 0.926Å    |
| O52 | H521 | 0.950Å    |  | C53 | C54  | 1.310(5)Å |
| C53 | C58  | 1.395(5)Å |  | C54 | C55  | 1.415(5)Å |
| C55 | C56  | 1.367(5)Å |  | C55 | H551 | 0.929Å    |
| C56 | C57  | 1.356(5)Å |  | C56 | H561 | 0.914Å    |
| C57 | C58  | 1.381(5)Å |  | C57 | H481 | 1.086Å    |
| C57 | H571 | 0.943Å    |  | C58 | H481 | 1.061Å    |
| C58 | H581 | 0.924Å    |  | N61 | C62  | 1.529(5)Å |
| N61 | C66  | 1.522(5)Å |  | N61 | C70  | 1.511(5)Å |
| N61 | C74  | 1.526(5)Å |  | C62 | C63  | 1.510(6)Å |
| C62 | H621 | 0.972Å    |  | C62 | H622 | 0.958Å    |
| C63 | C64  | 1.529(6)Å |  | C63 | H631 | 0.976Å    |
| C63 | H632 | 0.962Å    |  | C64 | C65  | 1.517(6)Å |
| C64 | H641 | 0.981Å    |  | C64 | H642 | 0.986Å    |
| C65 | H651 | 0.984Å    |  | C65 | H652 | 0.973Å    |
| C65 | H653 | 0.976Å    |  | C66 | C67  | 1.514(6)Å |
| C66 | H661 | 0.972Å    |  | C66 | H662 | 0.954Å    |
| C67 | C68  | 1.525(6)Å |  | C67 | H671 | 0.976Å    |
| C67 | H672 | 0.973Å    |  | C68 | C69  | 1.519(7)Å |
| C68 | H681 | 0.960Å    |  | C68 | H682 | 0.978Å    |
| C69 | H691 | 0.962Å    |  | C69 | H692 | 0.963Å    |
| C69 | H693 | 0.969Å    |  | C70 | C71  | 1.523(6)Å |
| C70 | H701 | 0.962Å    |  | C70 | H702 | 0.966Å    |
| C71 | C72  | 1.522(6)Å |  | C71 | H711 | 0.991Å    |
| C71 | H712 | 0.977Å    |  | C72 | C73  | 1.517(6)Å |
| C72 | H721 | 0.955Å    |  | C72 | H722 | 0.972Å    |
| C73 | H731 | 0.964Å    |  | C73 | H732 | 0.981Å    |
| C73 | H733 | 0.969Å    |  | C74 | C75  | 1.522(6)Å |
| C74 | H741 | 0.962Å    |  | C74 | H742 | 0.970Å    |
| C75 | C76  | 1.525(6)Å |  | C75 | H751 | 0.974Å    |
| C75 | H752 | 0.983Å    |  | C76 | C77  | 1.517(6)Å |
| C76 | H761 | 0.964Å    |  | C76 | H762 | 0.989Å    |
| C77 | H771 | 0.964Å    |  | C77 | H772 | 0.963Å    |
| C77 | H773 | 0.966Å    |  | N81 | C82  | 1.526(5)Å |
| N81 | C86  | 1.523(5)Å |  | N81 | C90  | 1.518(5)Å |
| N81 | C94  | 1.526(5)Å |  | C82 | C83  | 1.513(6)Å |

|      |      |           |  |      |      |           |
|------|------|-----------|--|------|------|-----------|
| C82  | H821 | 0.966Å    |  | C82  | H822 | 0.971Å    |
| C83  | C84  | 1.525(6)Å |  | C83  | H831 | 0.955Å    |
| C83  | H832 | 0.981Å    |  | C84  | C85  | 1.511(7)Å |
| C84  | H841 | 0.962Å    |  | C84  | H842 | 0.968Å    |
| C85  | H851 | 0.960Å    |  | C85  | H852 | 0.965Å    |
| C85  | H853 | 0.966Å    |  | C86  | C87  | 1.525(6)Å |
| C86  | H861 | 0.966Å    |  | C86  | H862 | 0.973Å    |
| C87  | C88  | 1.506(6)Å |  | C87  | H871 | 0.959Å    |
| C87  | H872 | 0.956Å    |  | C88  | C89  | 1.520(7)Å |
| C88  | H881 | 0.969Å    |  | C88  | H882 | 0.964Å    |
| C89  | H891 | 0.954Å    |  | C89  | H892 | 0.971Å    |
| C89  | H893 | 0.960Å    |  | C90  | C91  | 1.512(6)Å |
| C90  | H901 | 0.973Å    |  | C90  | H902 | 0.966Å    |
| C91  | C92  | 1.525(6)Å |  | C91  | H911 | 0.976Å    |
| C91  | H912 | 0.990Å    |  | C92  | C93  | 1.517(7)Å |
| C92  | H921 | 0.988Å    |  | C92  | H922 | 0.987Å    |
| C93  | H931 | 0.963Å    |  | C93  | H932 | 0.973Å    |
| C93  | H933 | 0.961Å    |  | C94  | C95  | 1.512(6)Å |
| C94  | H941 | 0.994Å    |  | C94  | H942 | 0.965Å    |
| C95  | C96  | 1.523(6)Å |  | C95  | H951 | 0.984Å    |
| C95  | H952 | 0.974Å    |  | C96  | C97  | 1.517(6)Å |
| C96  | H961 | 0.964Å    |  | C96  | H962 | 0.982Å    |
| C97  | H971 | 0.963Å    |  | C97  | H972 | 0.962Å    |
| C97  | H973 | 0.970Å    |  | H211 | H321 | 0.832Å    |
| H261 | H361 | 0.804Å    |  | H271 | H371 | 0.610Å    |
| H281 | H381 | 0.571Å    |  | H411 | H511 | 0.761Å    |
| H421 | H521 | 0.687Å    |  | H451 | H551 | 0.685Å    |

## Angles

|          |    |      |           |  |          |    |      |           |
|----------|----|------|-----------|--|----------|----|------|-----------|
| C3       | O1 | H11  | 115.337°  |  | C4       | O2 | H21  | 111.284°  |
| F2 2_657 | F2 | O51  | 119.8(8)° |  | F2 2_657 | F2 | H511 | 92.990°   |
| O51      | F2 | H511 | 26.849°   |  | O1       | C3 | C4   | 124.3(4)° |
| O1       | C3 | C8   | 117.2(4)° |  | C4       | C3 | C8   | 118.6(4)° |
| F3 2_767 | F3 | H321 | 86.167°   |  | O2       | C4 | C3   | 123.6(4)° |
| O2       | C4 | C5   | 117.3(4)° |  | C3       | C4 | C5   | 119.1(4)° |
| C4       | C5 | C6   | 121.8(4)° |  | C4       | C5 | H51  | 119.088°  |
| C6       | C5 | H51  | 119.094°  |  | C5       | C6 | C7   | 119.2(5)° |
| C5       | C6 | H61  | 119.850°  |  | C7       | C6 | H61  | 120.907°  |
| C6       | C7 | C8   | 119.9(5)° |  | C6       | C7 | H71  | 120.406°  |

|     |     |      |            |  |      |     |      |            |
|-----|-----|------|------------|--|------|-----|------|------------|
| C8  | C7  | H71  | 119.646°   |  | C3   | C8  | C7   | 121.3(4)°  |
| C3  | C8  | H81  | 117.492°   |  | C7   | C8  | H81  | 121.217°   |
| C13 | O11 | H111 | 112.531°   |  | C14  | O12 | H121 | 114.919°   |
| O11 | C13 | C14  | 115.8(4)°  |  | O11  | C13 | C18  | 125.0(4)°  |
| C14 | C13 | C18  | 119.2(4)°  |  | O12  | C14 | C13  | 120.8(4)°  |
| O12 | C14 | C15  | 119.4(4)°  |  | C13  | C14 | C15  | 119.8(4)°  |
| C14 | C15 | C16  | 120.6(4)°  |  | C14  | C15 | H151 | 120.032°   |
| C16 | C15 | H151 | 119.365°   |  | C15  | C16 | C17  | 119.9(4)°  |
| C15 | C16 | H161 | 118.879°   |  | C17  | C16 | H161 | 121.246°   |
| C16 | C17 | C18  | 120.0(4)°  |  | C16  | C17 | H171 | 120.978°   |
| C18 | C17 | H171 | 119.013°   |  | C13  | C18 | C17  | 120.5(4)°  |
| C13 | C18 | H181 | 118.851°   |  | C17  | C18 | H181 | 120.537°   |
| C23 | O21 | O31  | 96.5(8)°   |  | C23  | O21 | C33  | 19.1(4)°   |
| O31 | O21 | C33  | 77.5(7)°   |  | C23  | O21 | H211 | 109.557°   |
| O31 | O21 | H211 | 139.992°   |  | C33  | O21 | H211 | 126.262°   |
| C23 | O21 | H311 | 142.215°   |  | O31  | O21 | H311 | 71.042°    |
| C33 | O21 | H311 | 133.103°   |  | H211 | O21 | H311 | 69.757°    |
| C24 | O22 | O32  | 86.3(5)°   |  | C24  | O22 | C34  | 24.2(3)°   |
| O32 | O22 | C34  | 62.1(5)°   |  | C24  | O22 | H221 | 108.511°   |
| O32 | O22 | H221 | 34.025°    |  | C34  | O22 | H221 | 85.994°    |
| O21 | C23 | C24  | 123.05(7)° |  | O21  | C23 | C28  | 116.91(7)° |
| C24 | C23 | C28  | 119.89(6)° |  | O21  | C23 | O31  | 30.4(3)°   |
| C24 | C23 | O31  | 153.0(4)°  |  | C28  | C23 | O31  | 87.1(4)°   |
| O21 | C23 | C33  | 69.0(12)°  |  | C24  | C23 | C33  | 167.5(14)° |
| C28 | C23 | C33  | 48.5(12)°  |  | O31  | C23 | C33  | 38.8(9)°   |
| O21 | C23 | C34  | 101.6(5)°  |  | C24  | C23 | C34  | 21.4(5)°   |
| C28 | C23 | C34  | 141.2(5)°  |  | O31  | C23 | C34  | 131.7(7)°  |
| C33 | C23 | C34  | 170.2(19)° |  | O21  | C23 | C38  | 120.9(5)°  |
| C24 | C23 | C38  | 116.1(5)°  |  | C28  | C23 | C38  | 5.4(10)°   |
| O31 | C23 | C38  | 90.7(4)°   |  | C33  | C23 | C38  | 52.0(9)°   |
| C34 | C23 | C38  | 137.5(8)°  |  | O22  | C24 | C23  | 123.09(6)° |
| O22 | C24 | C25  | 116.94(6)° |  | C23  | C24 | C25  | 119.92(6)° |
| O22 | C24 | O32  | 38.8(3)°   |  | C23  | C24 | O32  | 84.4(3)°   |
| C25 | C24 | O32  | 155.1(4)°  |  | O22  | C24 | C34  | 89.0(7)°   |
| C23 | C24 | C34  | 34.1(7)°   |  | C25  | C24 | C34  | 153.8(7)°  |
| O32 | C24 | C34  | 50.3(6)°   |  | O22  | C24 | C35  | 104.6(7)°  |
| C23 | C24 | C35  | 131.8(7)°  |  | C25  | C24 | C35  | 13.1(8)°   |
| O32 | C24 | C35  | 142.2(9)°  |  | C34  | C24 | C35  | 164.2(19)° |
| C24 | C25 | C26  | 120.37(7)° |  | C24  | C25 | C35  | 16.2(10)°  |
| C26 | C25 | C35  | 135.0(9)°  |  | C24  | C25 | C36  | 119.8(8)°  |

|      |     |      |            |  |      |     |      |            |
|------|-----|------|------------|--|------|-----|------|------------|
| C26  | C25 | C36  | 1.3(13)°   |  | C35  | C25 | C36  | 134.3(16)° |
| C24  | C25 | H251 | 118.890°   |  | C26  | C25 | H251 | 120.737°   |
| C35  | C25 | H251 | 103.806°   |  | C36  | C25 | H251 | 121.343°   |
| C24  | C25 | H351 | 68.798°    |  | C26  | C25 | H351 | 168.988°   |
| C35  | C25 | H351 | 53.315°    |  | C36  | C25 | H351 | 168.770°   |
| H251 | C25 | H351 | 50.521°    |  | C25  | C26 | C27  | 119.72(7)° |
| C25  | C26 | C36  | 2(2)°      |  | C27  | C26 | C36  | 118.7(13)° |
| C25  | C26 | C37  | 118.1(5)°  |  | C27  | C26 | C37  | 4.8(17)°   |
| C36  | C26 | C37  | 117.3(16)° |  | C25  | C26 | H261 | 119.605°   |
| C27  | C26 | H261 | 120.664°   |  | C36  | C26 | H261 | 120.633°   |
| C37  | C26 | H261 | 121.971°   |  | C25  | C26 | H361 | 70.296°    |
| C27  | C26 | H361 | 169.804°   |  | C36  | C26 | H361 | 71.253°    |
| C37  | C26 | H361 | 171.116°   |  | H261 | C26 | H361 | 49.395°    |
| C26  | C27 | C28  | 119.71(7)° |  | C26  | C27 | C36  | 15.7(3)°   |
| C28  | C27 | C36  | 104.0(3)°  |  | C26  | C27 | C37  | 15(5)°     |
| C28  | C27 | C37  | 114(2)°    |  | C36  | C27 | C37  | 19(4)°     |
| C26  | C27 | C38  | 126.5(5)°  |  | C28  | C27 | C38  | 8.4(10)°   |
| C36  | C27 | C38  | 110.8(6)°  |  | C37  | C27 | C38  | 119(3)°    |
| C26  | C27 | H271 | 119.930°   |  | C28  | C27 | H271 | 120.351°   |
| C36  | C27 | H271 | 135.654°   |  | C37  | C27 | H271 | 123.612°   |
| C38  | C27 | H271 | 113.463°   |  | C26  | C27 | H371 | 82.125°    |
| C28  | C27 | H371 | 157.138°   |  | C36  | C27 | H371 | 97.778°    |
| C37  | C27 | H371 | 85.019°    |  | C38  | C27 | H371 | 148.977°   |
| H271 | C27 | H371 | 38.669°    |  | C23  | C28 | C27  | 120.35(7)° |
| C23  | C28 | C33  | 16.9(5)°   |  | C27  | C28 | C33  | 137.1(5)°  |
| C23  | C28 | C37  | 109.3(4)°  |  | C27  | C28 | C37  | 11.3(5)°   |
| C33  | C28 | C37  | 125.9(8)°  |  | C23  | C28 | C38  | 146(5)°    |
| C27  | C28 | C38  | 40(4)°     |  | C33  | C28 | C38  | 153(8)°    |
| C37  | C28 | C38  | 48(3)°     |  | C23  | C28 | H281 | 119.615°   |
| C27  | C28 | H281 | 120.032°   |  | C33  | C28 | H281 | 102.821°   |
| C37  | C28 | H281 | 130.967°   |  | C38  | C28 | H281 | 86.421°    |
| C23  | C28 | H381 | 149.958°   |  | C27  | C28 | H381 | 88.517°    |
| C33  | C28 | H381 | 133.228°   |  | C37  | C28 | H381 | 98.969°    |
| C38  | C28 | H381 | 54.201°    |  | H281 | C28 | H381 | 32.505°    |
| O21  | O31 | C23  | 53.1(6)°   |  | O21  | O31 | C33  | 64.7(7)°   |
| C23  | O31 | C33  | 11.7(2)°   |  | O21  | O31 | H311 | 50.337°    |
| C23  | O31 | H311 | 96.313°    |  | C33  | O31 | H311 | 107.181°   |
| O22  | O32 | C24  | 54.9(4)°   |  | O22  | O32 | C34  | 75.1(5)°   |
| C24  | O32 | C34  | 20.2(3)°   |  | O22  | O32 | H221 | 64.055°    |
| C24  | O32 | H221 | 103.802°   |  | C34  | O32 | H221 | 116.488°   |

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|------|-----|------|------------|--|------|-----|------|------------|
| O22  | O32 | H321 | 148.691°   |  | C24  | O32 | H321 | 127.063°   |
| C34  | O32 | H321 | 109.736°   |  | H221 | O32 | H321 | 87.447°    |
| O21  | C33 | C23  | 91.9(12)°  |  | O21  | C33 | C28  | 152.0(9)°  |
| C23  | C33 | C28  | 114.6(16)° |  | O21  | C33 | O31  | 37.8(4)°   |
| C23  | C33 | O31  | 129.5(11)° |  | C28  | C33 | O31  | 115.6(6)°  |
| O21  | C33 | C34  | 85.6(4)°   |  | C23  | C33 | C34  | 6.7(13)°   |
| C28  | C33 | C34  | 121.2(6)°  |  | O31  | C33 | C34  | 123.09(6)° |
| O21  | C33 | C38  | 154.3(4)°  |  | C23  | C33 | C38  | 113.5(11)° |
| C28  | C33 | C38  | 5.0(16)°   |  | O31  | C33 | C38  | 116.97(6)° |
| C34  | C33 | C38  | 119.93(6)° |  | O22  | C34 | C23  | 168.7(7)°  |
| O22  | C34 | C24  | 66.8(7)°   |  | C23  | C34 | C24  | 124.5(10)° |
| O22  | C34 | O32  | 42.8(3)°   |  | C23  | C34 | O32  | 126.0(5)°  |
| C24  | C34 | O32  | 109.5(7)°  |  | O22  | C34 | C33  | 165.6(3)°  |
| C23  | C34 | C33  | 3.1(6)°    |  | C24  | C34 | C33  | 127.5(7)°  |
| O32  | C34 | C33  | 123.02(7)° |  | O22  | C34 | C35  | 74.5(3)°   |
| C23  | C34 | C35  | 116.8(5)°  |  | C24  | C34 | C35  | 8.9(11)°   |
| O32  | C34 | C35  | 116.86(7)° |  | C33  | C34 | C35  | 119.86(6)° |
| C24  | C35 | C25  | 150.8(18)° |  | C24  | C35 | C34  | 6.9(8)°    |
| C25  | C35 | C34  | 145.9(11)° |  | C24  | C35 | C36  | 126.2(6)°  |
| C25  | C35 | C36  | 26.5(10)°  |  | C34  | C35 | C36  | 120.39(7)° |
| C24  | C35 | H251 | 158.810°   |  | C25  | C35 | H251 | 46.648°    |
| C34  | C35 | H251 | 165.665°   |  | C36  | C35 | H251 | 72.925°    |
| C24  | C35 | H351 | 113.690°   |  | C25  | C35 | H351 | 93.996°    |
| C34  | C35 | H351 | 119.631°   |  | C36  | C35 | H351 | 119.982°   |
| H251 | C35 | H351 | 47.378°    |  | C25  | C36 | C26  | 177(4)°    |
| C25  | C36 | C27  | 136.0(10)° |  | C26  | C36 | C27  | 45.6(11)°  |
| C25  | C36 | C35  | 19.2(7)°   |  | C26  | C36 | C35  | 162.7(14)° |
| C27  | C36 | C35  | 117.1(4)°  |  | C25  | C36 | C37  | 138.3(7)°  |
| C26  | C36 | C37  | 43.0(14)°  |  | C27  | C36 | C37  | 4.4(11)°   |
| C35  | C36 | C37  | 119.72(7)° |  | C25  | C36 | H361 | 101.260°   |
| C26  | C36 | H361 | 77.169°    |  | C27  | C36 | H361 | 122.692°   |
| C35  | C36 | H361 | 120.125°   |  | C37  | C36 | H361 | 120.139°   |
| C26  | C37 | C27  | 160(7)°    |  | C26  | C37 | C28  | 131.5(7)°  |
| C27  | C37 | C28  | 54.4(19)°  |  | C26  | C37 | C36  | 19.7(5)°   |
| C27  | C37 | C36  | 157(5)°    |  | C28  | C37 | C36  | 112.0(4)°  |
| C26  | C37 | C38  | 139.3(5)°  |  | C27  | C37 | C38  | 49(2)°     |
| C28  | C37 | C38  | 8.3(7)°    |  | C36  | C37 | C38  | 119.69(7)° |
| C26  | C37 | H271 | 131.047°   |  | C27  | C37 | H271 | 42.389°    |
| C28  | C37 | H271 | 95.699°    |  | C36  | C37 | H271 | 150.345°   |
| C38  | C37 | H271 | 88.639°    |  | C26  | C37 | H371 | 100.911°   |



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|------|-----|------|------------|--|------|-----|------|------------|
| C27  | C37 | H371 | 74.163°    |  | C28  | C37 | H371 | 127.183°   |
| C36  | C37 | H371 | 120.607°   |  | C38  | C37 | H371 | 119.677°   |
| H271 | C37 | H371 | 31.843°    |  | C23  | C38 | C27  | 117.0(8)°  |
| C23  | C38 | C28  | 29(4)°     |  | C27  | C38 | C28  | 132(5)°    |
| C23  | C38 | C33  | 14.6(3)°   |  | C27  | C38 | C33  | 131.5(6)°  |
| C28  | C38 | C33  | 22(6)°     |  | C23  | C38 | C37  | 105.8(3)°  |
| C27  | C38 | C37  | 12.2(7)°   |  | C28  | C38 | C37  | 124(3)°    |
| C33  | C38 | C37  | 120.34(7)° |  | C23  | C38 | H281 | 100.007°   |
| C27  | C38 | H281 | 140.492°   |  | C28  | C38 | H281 | 77.076°    |
| C33  | C38 | H281 | 85.713°    |  | C37  | C38 | H281 | 152.657°   |
| C23  | C38 | H381 | 134.639°   |  | C27  | C38 | H381 | 108.167°   |
| C28  | C38 | H381 | 112.085°   |  | C33  | C38 | H381 | 120.100°   |
| C37  | C38 | H381 | 119.563°   |  | H281 | C38 | H381 | 35.304°    |
| C43  | O41 | O51  | 122.2(6)°  |  | C43  | O41 | C53  | 24.3(5)°   |
| O51  | O41 | C53  | 98.5(9)°   |  | C43  | O41 | C58  | 42.6(3)°   |
| O51  | O41 | C58  | 163.2(9)°  |  | C53  | O41 | C58  | 65.5(5)°   |
| C43  | O41 | H411 | 116.346°   |  | O51  | O41 | H411 | 27.396°    |
| C53  | O41 | H411 | 98.147°    |  | C58  | O41 | H411 | 153.102°   |
| C44  | O42 | O52  | 88.4(17)°  |  | C44  | O42 | C54  | 13.8(2)°   |
| O52  | O42 | C54  | 87.3(16)°  |  | C44  | O42 | H421 | 99.290°    |
| O52  | O42 | H421 | 74.392°    |  | C54  | O42 | H421 | 85.761°    |
| C44  | O42 | H521 | 110.388°   |  | O52  | O42 | H521 | 44.340°    |
| C54  | O42 | H521 | 100.540°   |  | H421 | O42 | H521 | 35.122°    |
| O41  | C43 | C44  | 123.16(7)° |  | O41  | C43 | C48  | 116.79(7)° |
| C44  | C43 | C48  | 119.64(7)° |  | O41  | C43 | C53  | 36.0(7)°   |
| C44  | C43 | C53  | 87.7(7)°   |  | C48  | C43 | C53  | 149.6(8)°  |
| O41  | C43 | C54  | 111.1(2)°  |  | C44  | C43 | C54  | 12.4(2)°   |
| C48  | C43 | C54  | 131.9(2)°  |  | C53  | C43 | C54  | 76.0(8)°   |
| O41  | C43 | C58  | 75.8(4)°   |  | C44  | C43 | C58  | 158.2(6)°  |
| C48  | C43 | C58  | 41.2(5)°   |  | C53  | C43 | C58  | 109.0(9)°  |
| C54  | C43 | C58  | 169.0(10)° |  | O42  | C44 | C43  | 122.98(9)° |
| O42  | C44 | C45  | 116.89(9)° |  | C43  | C44 | C45  | 119.58(6)° |
| O42  | C44 | O52  | 16.5(5)°   |  | C43  | C44 | O52  | 123.20(9)° |
| C45  | C44 | O52  | 116.37(9)° |  | O42  | C44 | C53  | 98.9(3)°   |
| C43  | C44 | C53  | 24.2(3)°   |  | C45  | C44 | C53  | 142.5(3)°  |
| O52  | C44 | C53  | 101.2(3)°  |  | O42  | C44 | C54  | 66.0(13)°  |
| C43  | C44 | C54  | 58.0(13)°  |  | C45  | C44 | C54  | 176.4(18)° |
| O52  | C44 | C54  | 65.7(13)°  |  | C53  | C44 | C54  | 35.7(12)°  |
| O42  | C44 | C55  | 137.9(5)°  |  | C43  | C44 | C55  | 99.1(5)°   |
| C45  | C44 | C55  | 21.8(5)°   |  | O52  | C44 | C55  | 134.1(6)°  |

|      |     |      |            |  |      |     |      |            |
|------|-----|------|------------|--|------|-----|------|------------|
| C53  | C44 | C55  | 123.0(6)°  |  | C54  | C44 | C55  | 154.9(19)° |
| C44  | C45 | C46  | 120.37(7)° |  | C44  | C45 | C54  | 0.7(3)°    |
| C46  | C45 | C54  | 119.8(3)°  |  | C44  | C45 | C55  | 52.9(11)°  |
| C46  | C45 | C55  | 68.7(11)°  |  | C54  | C45 | C55  | 52.2(9)°   |
| C44  | C45 | C56  | 91.8(3)°   |  | C46  | C45 | C56  | 28.9(3)°   |
| C54  | C45 | C56  | 91.3(4)°   |  | C55  | C45 | C56  | 42.4(11)°  |
| C44  | C45 | H451 | 118.104°   |  | C46  | C45 | H451 | 121.444°   |
| C54  | C45 | H451 | 118.634°   |  | C55  | C45 | H451 | 163.338°   |
| C56  | C45 | H451 | 150.062°   |  | C44  | C45 | H551 | 132.063°   |
| C46  | C45 | H551 | 89.972°    |  | C54  | C45 | H551 | 131.990°   |
| C55  | C45 | H551 | 126.241°   |  | C56  | C45 | H551 | 114.917°   |
| H451 | C45 | H551 | 46.226°    |  | C45  | C46 | C47  | 119.80(7)° |
| C45  | C46 | C55  | 21.9(4)°   |  | C47  | C46 | C55  | 99.1(4)°   |
| C45  | C46 | C56  | 97.5(6)°   |  | C47  | C46 | C56  | 22.4(6)°   |
| C55  | C46 | C56  | 77.0(6)°   |  | C45  | C46 | H461 | 118.107°   |
| C47  | C46 | H461 | 122.087°   |  | C55  | C46 | H461 | 138.255°   |
| C56  | C46 | H461 | 144.423°   |  | C45  | C46 | H561 | 162.125°   |
| C47  | C46 | H561 | 44.291°    |  | C55  | C46 | H561 | 143.299°   |
| C56  | C46 | H561 | 66.276°    |  | H461 | C46 | H561 | 78.321°    |
| C46  | C47 | C48  | 119.76(7)° |  | C46  | C47 | C56  | 26.3(7)°   |
| C48  | C47 | C56  | 93.6(6)°   |  | C46  | C47 | C57  | 133.6(6)°  |
| C48  | C47 | C57  | 15.6(6)°   |  | C56  | C47 | C57  | 107.3(10)° |
| C46  | C47 | H471 | 118.186°   |  | C48  | C47 | H471 | 122.055°   |
| C56  | C47 | H471 | 144.322°   |  | C57  | C47 | H471 | 107.757°   |
| C46  | C47 | H561 | 36.153°    |  | C48  | C47 | H561 | 155.547°   |
| C56  | C47 | H561 | 62.112°    |  | C57  | C47 | H561 | 165.911°   |
| H471 | C47 | H561 | 82.213°    |  | C43  | C48 | C47  | 120.27(7)° |
| C43  | C48 | C56  | 93.9(4)°   |  | C47  | C48 | C56  | 26.4(4)°   |
| C43  | C48 | C57  | 145.8(13)° |  | C47  | C48 | C57  | 29.4(12)°  |
| C56  | C48 | C57  | 54.1(9)°   |  | C43  | C48 | C58  | 50.7(6)°   |
| C47  | C48 | C58  | 167.0(12)° |  | C56  | C48 | C58  | 142.6(9)°  |
| C57  | C48 | C58  | 153(2)°    |  | C43  | C48 | H481 | 120.957°   |
| C47  | C48 | H481 | 118.777°   |  | C56  | C48 | H481 | 145.124°   |
| C57  | C48 | H481 | 91.449°    |  | C58  | C48 | H481 | 71.003°    |
| F2   | O51 | O41  | 139.0(10)° |  | F2   | O51 | C53  | 126.0(5)°  |
| O41  | O51 | C53  | 42.1(6)°   |  | F2   | O51 | H411 | 52.640°    |
| O41  | O51 | H411 | 86.376°    |  | C53  | O51 | H411 | 88.212°    |
| F2   | O51 | H511 | 26.740°    |  | O41  | O51 | H511 | 128.681°   |
| C53  | O51 | H511 | 101.201°   |  | H411 | O51 | H511 | 51.769°    |
| O42  | O52 | C44  | 75.1(16)°  |  | O42  | O52 | C54  | 74.9(16)°  |

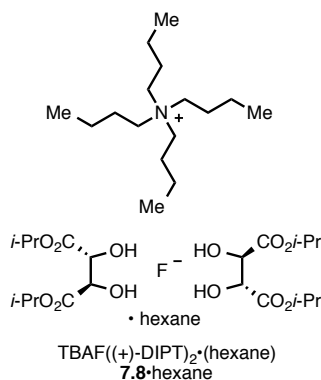
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|-----|-----|------|------------|--|------|-----|------|------------|
| C44 | O52 | C54  | 13.29(18)° |  | O42  | O52 | H421 | 81.052°    |
| C44 | O52 | H421 | 97.321°    |  | C54  | O52 | H421 | 84.177°    |
| O42 | O52 | H521 | 118.560°   |  | C44  | O52 | H521 | 124.747°   |
| C54 | O52 | H521 | 112.767°   |  | H421 | O52 | H521 | 42.957°    |
| O41 | C53 | C43  | 119.7(11)° |  | O41  | C53 | C44  | 168.5(9)°  |
| C43 | C53 | C44  | 68.1(6)°   |  | O41  | C53 | O51  | 39.4(5)°   |
| C43 | C53 | O51  | 157.4(10)° |  | C44  | C53 | O51  | 131.1(3)°  |
| O41 | C53 | C54  | 160.3(7)°  |  | C43  | C53 | C54  | 75.6(7)°   |
| C44 | C53 | C54  | 8.4(3)°    |  | O51  | C53 | C54  | 122.88(6)° |
| O41 | C53 | C58  | 77.7(5)°   |  | C43  | C53 | C58  | 45.1(7)°   |
| C44 | C53 | C58  | 111.9(3)°  |  | O51  | C53 | C58  | 116.88(6)° |
| C54 | C53 | C58  | 119.97(6)° |  | O42  | C54 | C43  | 148.2(4)°  |
| O42 | C54 | C44  | 100.2(14)° |  | C43  | C54 | C44  | 109.7(15)° |
| O42 | C54 | C45  | 102.5(4)°  |  | C43  | C54 | C45  | 107.7(4)°  |
| C44 | C54 | C45  | 2.9(14)°   |  | O42  | C54 | O52  | 17.8(6)°   |
| C43 | C54 | O52  | 148.4(4)°  |  | C44  | C54 | O52  | 101.0(14)° |
| C45 | C54 | O52  | 102.7(4)°  |  | O42  | C54 | C53  | 119.8(3)°  |
| C43 | C54 | C53  | 28.4(3)°   |  | C44  | C54 | C53  | 135.9(14)° |
| C45 | C54 | C53  | 134.4(4)°  |  | O52  | C54 | C53  | 122.82(7)° |
| O42 | C54 | C55  | 118.9(3)°  |  | C43  | C54 | C55  | 92.1(3)°   |
| C44 | C54 | C55  | 19.4(15)°  |  | C45  | C54 | C55  | 16.8(4)°   |
| O52 | C54 | C55  | 116.94(7)° |  | C53  | C54 | C55  | 119.90(6)° |
| C44 | C55 | C45  | 105.4(15)° |  | C44  | C55 | C46  | 160.8(9)°  |
| C45 | C55 | C46  | 89.4(10)°  |  | C44  | C55 | C54  | 5.7(4)°    |
| C45 | C55 | C54  | 111.0(12)° |  | C46  | C55 | C54  | 156.4(5)°  |
| C44 | C55 | C56  | 125.1(4)°  |  | C45  | C55 | C56  | 122.8(13)° |
| C46 | C55 | C56  | 36.3(5)°   |  | C54  | C55 | C56  | 120.24(7)° |
| C44 | C55 | H551 | 116.739°   |  | C45  | C55 | H551 | 27.140°    |
| C46 | C55 | H551 | 81.943°    |  | C54  | C55 | H551 | 121.616°   |
| C56 | C55 | H551 | 118.127°   |  | C45  | C56 | C46  | 53.6(6)°   |
| C45 | C56 | C47  | 174.9(9)°  |  | C46  | C56 | C47  | 131.3(11)° |
| C45 | C56 | C48  | 115.0(5)°  |  | C46  | C56 | C48  | 167.8(10)° |
| C47 | C56 | C48  | 60.0(7)°   |  | C45  | C56 | C55  | 14.8(4)°   |
| C46 | C56 | C55  | 66.7(7)°   |  | C47  | C56 | C55  | 160.3(10)° |
| C48 | C56 | C55  | 101.5(3)°  |  | C45  | C56 | C57  | 132.5(3)°  |
| C46 | C56 | C57  | 173.7(7)°  |  | C47  | C56 | C57  | 42.6(7)°   |
| C48 | C56 | C57  | 18.4(3)°   |  | C55  | C56 | C57  | 119.58(7)° |
| C45 | C56 | H561 | 110.673°   |  | C46  | C56 | H561 | 57.426°    |
| C47 | C56 | H561 | 74.366°    |  | C48  | C56 | H561 | 134.304°   |
| C55 | C56 | H561 | 124.100°   |  | C57  | C56 | H561 | 116.317°   |

|      |     |      |            |  |      |     |      |            |
|------|-----|------|------------|--|------|-----|------|------------|
| C47  | C57 | C48  | 134.9(18)° |  | C47  | C57 | C56  | 30.1(6)°   |
| C48  | C57 | C56  | 107.5(11)° |  | C47  | C57 | C58  | 149.2(6)°  |
| C48  | C57 | C58  | 17.0(16)°  |  | C56  | C57 | C58  | 119.65(7)° |
| C47  | C57 | H481 | 158.239°   |  | C48  | C57 | H481 | 59.517°    |
| C56  | C57 | H481 | 165.984°   |  | C58  | C57 | H481 | 49.196°    |
| C47  | C57 | H571 | 92.905°    |  | C48  | C57 | H571 | 127.971°   |
| C56  | C57 | H571 | 122.789°   |  | C58  | C57 | H571 | 117.554°   |
| H481 | C57 | H571 | 68.951°    |  | O41  | C58 | C43  | 61.6(5)°   |
| O41  | C58 | C48  | 149.0(9)°  |  | C43  | C58 | C48  | 88.0(7)°   |
| O41  | C58 | C53  | 36.9(3)°   |  | C43  | C58 | C53  | 25.8(4)°   |
| C48  | C58 | C53  | 113.6(6)°  |  | O41  | C58 | C57  | 157.1(3)°  |
| C43  | C58 | C57  | 95.5(4)°   |  | C48  | C58 | C57  | 10.0(9)°   |
| C53  | C58 | C57  | 120.39(7)° |  | O41  | C58 | H481 | 150.896°   |
| C43  | C58 | H481 | 143.254°   |  | C48  | C58 | H481 | 56.534°    |
| C53  | C58 | H481 | 168.594°   |  | C57  | C58 | H481 | 50.777°    |
| O41  | C58 | H581 | 80.846°    |  | C43  | C58 | H581 | 142.070°   |
| C48  | C58 | H581 | 128.372°   |  | C53  | C58 | H581 | 117.593°   |
| C57  | C58 | H581 | 122.007°   |  | H481 | C58 | H581 | 71.849°    |
| C62  | N61 | C66  | 110.7(3)°  |  | C62  | N61 | C70  | 107.2(3)°  |
| C66  | N61 | C70  | 110.9(3)°  |  | C62  | N61 | C74  | 110.7(3)°  |
| C66  | N61 | C74  | 107.0(3)°  |  | C70  | N61 | C74  | 110.5(3)°  |
| N61  | C62 | C63  | 115.5(3)°  |  | N61  | C62 | H621 | 105.834°   |
| C63  | C62 | H621 | 107.345°   |  | N61  | C62 | H622 | 107.106°   |
| C63  | C62 | H622 | 109.959°   |  | H621 | C62 | H622 | 111.003°   |
| C62  | C63 | C64  | 110.5(4)°  |  | C62  | C63 | H631 | 108.436°   |
| C64  | C63 | H631 | 109.767°   |  | C62  | C63 | H632 | 109.471°   |
| C64  | C63 | H632 | 108.109°   |  | H631 | C63 | H632 | 110.537°   |
| C63  | C64 | C65  | 111.8(4)°  |  | C63  | C64 | H641 | 108.454°   |
| C65  | C64 | H641 | 109.311°   |  | C63  | C64 | H642 | 107.911°   |
| C65  | C64 | H642 | 108.672°   |  | H641 | C64 | H642 | 110.712°   |
| C64  | C65 | H651 | 110.714°   |  | C64  | C65 | H652 | 110.464°   |
| H651 | C65 | H652 | 106.907°   |  | C64  | C65 | H653 | 110.796°   |
| H651 | C65 | H653 | 108.977°   |  | H652 | C65 | H653 | 108.879°   |
| N61  | C66 | C67  | 115.5(3)°  |  | N61  | C66 | H661 | 106.239°   |
| C67  | C66 | H661 | 109.519°   |  | N61  | C66 | H662 | 106.808°   |
| C67  | C66 | H662 | 108.262°   |  | H661 | C66 | H662 | 110.407°   |
| C66  | C67 | C68  | 110.1(4)°  |  | C66  | C67 | H671 | 109.637°   |
| C68  | C67 | H671 | 107.694°   |  | C66  | C67 | H672 | 109.414°   |
| C68  | C67 | H672 | 109.274°   |  | H671 | C67 | H672 | 110.690°   |
| C67  | C68 | C69  | 111.6(4)°  |  | C67  | C68 | H681 | 108.144°   |

|      |     |      |           |  |      |     |      |           |
|------|-----|------|-----------|--|------|-----|------|-----------|
| C69  | C68 | H681 | 109.458°  |  | C67  | C68 | H682 | 108.460°  |
| C69  | C68 | H682 | 108.560°  |  | H681 | C68 | H682 | 110.600°  |
| C68  | C69 | H691 | 110.636°  |  | C68  | C69 | H692 | 110.664°  |
| H691 | C69 | H692 | 109.273°  |  | C68  | C69 | H693 | 108.904°  |
| H691 | C69 | H693 | 110.016°  |  | H692 | C69 | H693 | 107.286°  |
| N61  | C70 | C71  | 115.4(3)° |  | N61  | C70 | H701 | 106.488°  |
| C71  | C70 | H701 | 109.383°  |  | N61  | C70 | H702 | 105.829°  |
| C71  | C70 | H702 | 109.144°  |  | H701 | C70 | H702 | 110.506°  |
| C70  | C71 | C72  | 110.0(3)° |  | C70  | C71 | H711 | 109.853°  |
| C72  | C71 | H711 | 110.276°  |  | C70  | C71 | H712 | 108.783°  |
| C72  | C71 | H712 | 107.841°  |  | H711 | C71 | H712 | 110.001°  |
| C71  | C72 | C73  | 112.6(4)° |  | C71  | C72 | H721 | 108.451°  |
| C73  | C72 | H721 | 108.085°  |  | C71  | C72 | H722 | 106.709°  |
| C73  | C72 | H722 | 110.104°  |  | H721 | C72 | H722 | 110.941°  |
| C72  | C73 | H731 | 108.676°  |  | C72  | C73 | H732 | 111.877°  |
| H731 | C73 | H732 | 106.766°  |  | C72  | C73 | H733 | 109.829°  |
| H731 | C73 | H733 | 111.349°  |  | H732 | C73 | H733 | 108.328°  |
| N61  | C74 | C75  | 115.1(3)° |  | N61  | C74 | H741 | 106.740°  |
| C75  | C74 | H741 | 108.032°  |  | N61  | C74 | H742 | 106.391°  |
| C75  | C74 | H742 | 109.277°  |  | H741 | C74 | H742 | 111.345°  |
| C74  | C75 | C76  | 110.4(3)° |  | C74  | C75 | H751 | 108.712°  |
| C76  | C75 | H751 | 108.473°  |  | C74  | C75 | H752 | 110.101°  |
| C76  | C75 | H752 | 108.926°  |  | H751 | C75 | H752 | 110.259°  |
| C75  | C76 | C77  | 111.6(4)° |  | C75  | C76 | H761 | 108.477°  |
| C77  | C76 | H761 | 109.414°  |  | C75  | C76 | H762 | 107.846°  |
| C77  | C76 | H762 | 108.979°  |  | H761 | C76 | H762 | 110.501°  |
| C76  | C77 | H771 | 110.126°  |  | C76  | C77 | H772 | 111.168°  |
| H771 | C77 | H772 | 109.874°  |  | C76  | C77 | H773 | 109.216°  |
| H771 | C77 | H773 | 108.547°  |  | H772 | C77 | H773 | 107.839°  |
| C82  | N81 | C86  | 110.5(3)° |  | C82  | N81 | C90  | 107.2(3)° |
| C86  | N81 | C90  | 110.9(3)° |  | C82  | N81 | C94  | 110.4(3)° |
| C86  | N81 | C94  | 106.7(3)° |  | C90  | N81 | C94  | 111.3(3)° |
| N81  | C82 | C83  | 115.4(3)° |  | N81  | C82 | H821 | 106.406°  |
| C83  | C82 | H821 | 108.745°  |  | N81  | C82 | H822 | 105.717°  |
| C83  | C82 | H822 | 110.836°  |  | H821 | C82 | H822 | 109.551°  |
| C82  | C83 | C84  | 111.0(4)° |  | C82  | C83 | H831 | 109.782°  |
| C84  | C83 | H831 | 107.832°  |  | C82  | C83 | H832 | 108.415°  |
| C84  | C83 | H832 | 107.827°  |  | H831 | C83 | H832 | 112.022°  |
| C83  | C84 | C85  | 111.9(4)° |  | C83  | C84 | H841 | 109.061°  |
| C85  | C84 | H841 | 109.078°  |  | C83  | C84 | H842 | 108.502°  |

|      |     |      |           |  |      |     |      |          |
|------|-----|------|-----------|--|------|-----|------|----------|
| C85  | C84 | H842 | 109.585°  |  | H841 | C84 | H842 | 108.611° |
| C84  | C85 | H851 | 109.601°  |  | C84  | C85 | H852 | 111.048° |
| H851 | C85 | H852 | 108.708°  |  | C84  | C85 | H853 | 110.700° |
| H851 | C85 | H853 | 109.435°  |  | H852 | C85 | H853 | 107.293° |
| N81  | C86 | C87  | 115.5(3)° |  | N81  | C86 | H861 | 106.049° |
| C87  | C86 | H861 | 109.335°  |  | N81  | C86 | H862 | 105.891° |
| C87  | C86 | H862 | 108.752°  |  | H861 | C86 | H862 | 111.234° |
| C86  | C87 | C88  | 111.1(4)° |  | C86  | C87 | H871 | 110.609° |
| C88  | C87 | H871 | 107.341°  |  | C86  | C87 | H872 | 109.519° |
| C88  | C87 | H872 | 109.017°  |  | H871 | C87 | H872 | 109.237° |
| C87  | C88 | C89  | 112.4(4)° |  | C87  | C88 | H881 | 107.097° |
| C89  | C88 | H881 | 108.647°  |  | C87  | C88 | H882 | 108.828° |
| C89  | C88 | H882 | 109.804°  |  | H881 | C88 | H882 | 109.996° |
| C88  | C89 | H891 | 112.311°  |  | C88  | C89 | H892 | 110.074° |
| H891 | C89 | H892 | 107.089°  |  | C88  | C89 | H893 | 109.979° |
| H891 | C89 | H893 | 108.648°  |  | H892 | C89 | H893 | 108.632° |
| N81  | C90 | C91  | 115.0(3)° |  | N81  | C90 | H901 | 106.855° |
| C91  | C90 | H901 | 108.028°  |  | N81  | C90 | H902 | 105.300° |
| C91  | C90 | H902 | 111.008°  |  | H901 | C90 | H902 | 110.584° |
| C90  | C91 | C92  | 111.0(4)° |  | C90  | C91 | H911 | 109.502° |
| C92  | C91 | H911 | 109.968°  |  | C90  | C91 | H912 | 108.888° |
| C92  | C91 | H912 | 107.107°  |  | H911 | C91 | H912 | 110.320° |
| C91  | C92 | C93  | 112.1(4)° |  | C91  | C92 | H921 | 107.848° |
| C93  | C92 | H921 | 110.521°  |  | C91  | C92 | H922 | 108.638° |
| C93  | C92 | H922 | 108.145°  |  | H921 | C92 | H922 | 109.585° |
| C92  | C93 | H931 | 110.753°  |  | C92  | C93 | H932 | 110.653° |
| H931 | C93 | H932 | 107.677°  |  | C92  | C93 | H933 | 111.103° |
| H931 | C93 | H933 | 106.499°  |  | H932 | C93 | H933 | 110.018° |
| N81  | C94 | C95  | 115.9(3)° |  | N81  | C94 | H941 | 105.406° |
| C95  | C94 | H941 | 108.139°  |  | N81  | C94 | H942 | 105.870° |
| C95  | C94 | H942 | 109.896°  |  | H941 | C94 | H942 | 111.647° |
| C94  | C95 | C96  | 110.2(3)° |  | C94  | C95 | H951 | 109.453° |
| C96  | C95 | H951 | 108.093°  |  | C94  | C95 | H952 | 110.737° |
| C96  | C95 | H952 | 108.920°  |  | H951 | C95 | H952 | 109.368° |
| C95  | C96 | C97  | 112.0(4)° |  | C95  | C96 | H961 | 108.436° |
| C97  | C96 | H961 | 108.511°  |  | C95  | C96 | H962 | 106.885° |
| C97  | C96 | H962 | 109.248°  |  | H961 | C96 | H962 | 111.762° |
| C96  | C97 | H971 | 110.259°  |  | C96  | C97 | H972 | 109.725° |
| H971 | C97 | H972 | 107.591°  |  | C96  | C97 | H973 | 112.310° |
| H971 | C97 | H973 | 106.503°  |  | H972 | C97 | H973 | 110.305° |

|     |      |      |          |  |     |      |      |          |
|-----|------|------|----------|--|-----|------|------|----------|
| O21 | H211 | H321 | 143.175° |  | O22 | H221 | O32  | 81.920°  |
| C25 | H251 | C35  | 29.546°  |  | C26 | H261 | H361 | 67.169°  |
| C27 | H271 | C37  | 13.999°  |  | C27 | H271 | H371 | 68.286°  |
| C37 | H271 | H371 | 54.327°  |  | C28 | H281 | C38  | 16.503°  |
| C28 | H281 | H381 | 86.322°  |  | C38 | H281 | H381 | 69.949°  |
| O21 | H311 | O31  | 58.621°  |  | F3  | H321 | O32  | 128.398° |
| F3  | H321 | H211 | 115.578° |  | O32 | H321 | H211 | 115.391° |
| C25 | H351 | C35  | 32.689°  |  | C26 | H361 | C36  | 31.578°  |
| C26 | H361 | H261 | 63.435°  |  | C36 | H361 | H261 | 95.005°  |
| C27 | H371 | C37  | 20.818°  |  | C27 | H371 | H271 | 73.045°  |
| C37 | H371 | H271 | 93.829°  |  | C28 | H381 | C38  | 13.714°  |
| C28 | H381 | H281 | 61.173°  |  | C38 | H381 | H281 | 74.747°  |
| O41 | H411 | O51  | 66.228°  |  | O41 | H411 | H511 | 147.083° |
| O51 | H411 | H511 | 101.356° |  | O42 | H421 | O52  | 24.556°  |
| O42 | H421 | H521 | 92.209°  |  | O52 | H421 | H521 | 70.365°  |
| C45 | H451 | H551 | 33.663°  |  | C48 | H481 | C57  | 29.034°  |
| C48 | H481 | C58  | 52.464°  |  | C57 | H481 | C58  | 80.027°  |
| F2  | H511 | O51  | 126.412° |  | F2  | H511 | H411 | 118.276° |
| O51 | H511 | H411 | 26.875°  |  | O42 | H521 | O52  | 17.100°  |
| O42 | H521 | H421 | 52.669°  |  | O52 | H521 | H421 | 66.678°  |
| C45 | H551 | C55  | 26.619°  |  | C45 | H551 | H451 | 100.111° |
| C55 | H551 | H451 | 124.944° |  | C46 | H561 | C47  | 99.556°  |
| C46 | H561 | C56  | 56.298°  |  | C47 | H561 | C56  | 43.522°  |



**tetra-*n*-butylammonium fluoride bis((+)-diisopropyl L-tartrate)) hexane solvate (TBAF((+)-DIPT)<sub>2</sub>•(hexane), 7.8•hexane):**

**X-ray** (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.8** in THF, which had previously been prepared by dissolving **7.8** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. The crystal was found to be an *n*-hexane solvate.

Oxford Crystallography Number: 066GGKE01

## Crystal Data

$a = 18.9780(2) \text{ \AA}$      $\alpha = 90^\circ$

$b = 24.2645(2) \text{ \AA}$      $\beta = 90^\circ$

$c = 10.32180(10) \text{ \AA}$      $\gamma = 90^\circ$

Volume                     $4753.10(8) \text{ \AA}^3$

Space group             $P 2_1 2_1 2$

Formula                  $C_{38.39} H_{77.58} F_1 N_1 O_{12}$

Cell determined from 5976 reflections

Temperature            150K

Shape                    prism

Colour                   clear\_pale\_colourless

$D_x$                          $1.07 \text{ Mg m}^{-3}$

$\mu$                            $0.080 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$                     0.75

Crystal Class    orthorhombic

$Z =$                         4

$M_r$                         764.30

Cell  $\theta$  range = 5 - 27°

Size                       $0.10 \times 0.10 \times 0.43 \text{ mm}$

$F_{000}$                     1679.681

$T_{\max}$                     0.99

## Data Collection

Diffractometer        multi-scan

Scan type                 $\omega$  scans

Reflections measured 65091

Independent reflections 10799

$R_{\text{int}}$                     0.0440

$\theta_{\max}$                     27.4798

$h =$                          $0 \rightarrow 24$

$k =$                          $0 \rightarrow 31$

$l =$                          $-13 \rightarrow 13$

## Refinement

$\Delta\rho_{\min} =$                  $-0.25 \text{ e \AA}^{-3}$



|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\max}$ =  | 0.30 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 10798                                                                                                                                                                                       |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 525                                                                                                                                                                                         |
| S =                    | 0.98                                                                                                                                                                                        |
| R-factor               | 0.067                                                                                                                                                                                       |
| weighted R-factor      | 0.098                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0006                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.035 \times P)^2 + 1.090 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| F1    | 0.38987(6)  | 0.66501(4)  | 0.55042(11) | 0.0562                 | 1.0000    |
| O1    | 0.41033(6)  | 0.76097(5)  | 0.64710(11) | 0.0467                 | 1.0000    |
| O2    | 0.47328(6)  | 0.71936(5)  | 0.39319(11) | 0.0418                 | 1.0000    |
| C11   | 0.47021(9)  | 0.78025(7)  | 0.58129(16) | 0.0378                 | 1.0000    |
| C12   | 0.53757(10) | 0.75258(7)  | 0.62622(15) | 0.0403                 | 1.0000    |
| O13   | 0.54185(7)  | 0.71738(5)  | 0.70782(12) | 0.0519                 | 1.0000    |
| O14   | 0.59264(6)  | 0.77369(5)  | 0.56172(12) | 0.0448                 | 1.0000    |
| C15   | 0.66275(9)  | 0.75182(8)  | 0.59001(18) | 0.0457                 | 1.0000    |
| C16   | 0.69355(12) | 0.78477(12) | 0.6989(2)   | 0.0734                 | 1.0000    |
| C17   | 0.70371(11) | 0.75631(9)  | 0.46650(19) | 0.0575                 | 1.0000    |
| C21   | 0.46447(9)  | 0.77395(7)  | 0.43383(15) | 0.0367                 | 1.0000    |
| C22   | 0.39556(9)  | 0.79820(7)  | 0.38627(18) | 0.0426                 | 1.0000    |
| O23   | 0.35312(7)  | 0.77425(6)  | 0.32158(14) | 0.0577                 | 1.0000    |
| O24   | 0.38858(7)  | 0.85058(5)  | 0.42566(16) | 0.0596                 | 1.0000    |
| C25   | 0.32136(12) | 0.87790(9)  | 0.4010(3)   | 0.0744                 | 1.0000    |
| C26   | 0.30962(17) | 0.91663(12) | 0.5145(4)   | 0.1059                 | 1.0000    |
| C27   | 0.32673(18) | 0.90662(15) | 0.2725(3)   | 0.1128                 | 1.0000    |
| O3    | 0.29555(6)  | 0.61281(5)  | 0.41622(12) | 0.0448                 | 1.0000    |
| O4    | 0.35730(6)  | 0.57468(5)  | 0.67130(11) | 0.0434                 | 1.0000    |
| C31   | 0.29994(9)  | 0.55846(7)  | 0.46107(16) | 0.0363                 | 1.0000    |
| C32   | 0.36461(9)  | 0.52865(7)  | 0.41062(17) | 0.0389                 | 1.0000    |
| O33   | 0.41043(7)  | 0.54899(6)  | 0.34677(14) | 0.0559                 | 1.0000    |
| O34   | 0.36194(6)  | 0.47567(5)  | 0.44535(13) | 0.0502                 | 1.0000    |
| C35   | 0.42043(7)  | 0.43892(7)  | 0.41075(15) | 0.0508                 | 1.0000    |
| C36   | 0.45195(17) | 0.41837(14) | 0.5328(3)   | 0.0817                 | 0.829(5)  |
| C37   | 0.39098(15) | 0.39389(13) | 0.3282(3)   | 0.0836                 | 0.829(5)  |

|      |             |             |             |        |          |
|------|-------------|-------------|-------------|--------|----------|
| C41  | 0.29656(8)  | 0.55510(7)  | 0.61007(16) | 0.0352 | 1.0000   |
| C42  | 0.23008(9)  | 0.58516(7)  | 0.65513(17) | 0.0384 | 1.0000   |
| O43  | 0.22842(7)  | 0.62320(5)  | 0.72902(13) | 0.0490 | 1.0000   |
| O44  | 0.17333(6)  | 0.56223(5)  | 0.59978(13) | 0.0454 | 1.0000   |
| C45  | 0.10487(9)  | 0.58799(8)  | 0.6218(2)   | 0.0524 | 1.0000   |
| C46  | 0.07139(13) | 0.56248(11) | 0.7393(3)   | 0.0754 | 1.0000   |
| C47  | 0.06346(12) | 0.57784(10) | 0.4992(3)   | 0.0729 | 1.0000   |
| C136 | 0.4162(5)   | 0.3902(4)   | 0.4961(11)  | 0.0640 | 0.171(5) |
| C137 | 0.4131(5)   | 0.4253(5)   | 0.2735(7)   | 0.0691 | 0.171(5) |
| N51  | 0.40169(8)  | 0.67074(6)  | 1.00236(12) | 0.0390 | 1.0000   |
| C52  | 0.44769(10) | 0.63533(8)  | 0.91481(17) | 0.0476 | 1.0000   |
| C53  | 0.50461(12) | 0.60213(8)  | 0.9808(2)   | 0.0571 | 1.0000   |
| C54  | 0.54774(14) | 0.57168(10) | 0.8789(3)   | 0.0813 | 1.0000   |
| C55  | 0.60603(18) | 0.53728(12) | 0.9350(4)   | 0.1118 | 1.0000   |
| C56  | 0.44696(9)  | 0.70737(7)  | 1.08770(16) | 0.0397 | 1.0000   |
| C57  | 0.49863(10) | 0.74387(8)  | 1.01570(17) | 0.0458 | 1.0000   |
| C58  | 0.53989(10) | 0.77993(8)  | 1.10932(18) | 0.0517 | 1.0000   |
| C59  | 0.59497(12) | 0.81480(9)  | 1.0419(2)   | 0.0622 | 1.0000   |
| C60  | 0.35509(10) | 0.70491(8)  | 0.91370(16) | 0.0461 | 1.0000   |
| C61  | 0.30676(11) | 0.74521(9)  | 0.98112(19) | 0.0548 | 1.0000   |
| C62  | 0.25904(12) | 0.77342(11) | 0.8840(2)   | 0.0730 | 1.0000   |
| C63  | 0.21368(16) | 0.81727(12) | 0.9466(3)   | 0.0986 | 1.0000   |
| C64  | 0.35733(9)  | 0.63501(7)  | 1.09236(16) | 0.0417 | 1.0000   |
| C65  | 0.30009(11) | 0.60185(8)  | 1.02640(18) | 0.0527 | 1.0000   |
| C66  | 0.26653(12) | 0.56089(10) | 1.1176(2)   | 0.0629 | 1.0000   |
| C67  | 0.20779(15) | 0.52851(12) | 1.0541(3)   | 0.0935 | 1.0000   |
| C101 | 0.4168(6)   | 0.8875(4)   | 0.8986(8)   | 0.0999 | 0.398(4) |
| C102 | 0.4533(4)   | 0.9371(2)   | 0.9509(6)   | 0.0865 | 0.398(4) |
| C103 | 0.4804(5)   | 0.9787(3)   | 0.8486(5)   | 0.0892 | 0.398(4) |
| C104 | 0.5174(4)   | 1.0298(3)   | 0.9155(5)   | 0.0858 | 0.398(4) |
| C105 | 0.5433(4)   | 1.0721(2)   | 0.8128(6)   | 0.0933 | 0.398(4) |
| C106 | 0.5957(7)   | 1.1135(4)   | 0.8596(8)   | 0.0951 | 0.398(4) |
| H111 | 0.47361(9)  | 0.81917(7)  | 0.59948(16) | 0.0429 | 1.0000   |
| H151 | 0.65699(9)  | 0.71325(8)  | 0.61744(18) | 0.0534 | 1.0000   |
| H163 | 0.74135(12) | 0.77273(12) | 0.7154(2)   | 0.1098 | 1.0000   |
| H162 | 0.66396(12) | 0.78035(12) | 0.7750(2)   | 0.1085 | 1.0000   |
| H161 | 0.69257(12) | 0.82344(12) | 0.6744(2)   | 0.1109 | 1.0000   |
| H172 | 0.75148(11) | 0.74214(9)  | 0.47890(19) | 0.0855 | 1.0000   |
| H171 | 0.68004(11) | 0.73437(9)  | 0.39791(19) | 0.0860 | 1.0000   |
| H173 | 0.70673(11) | 0.79570(9)  | 0.44039(19) | 0.0852 | 1.0000   |

|       |             |             |             |        |          |
|-------|-------------|-------------|-------------|--------|----------|
| H211  | 0.50262(9)  | 0.79583(7)  | 0.39452(15) | 0.0407 | 1.0000   |
| H251  | 0.28040(12) | 0.85109(9)  | 0.4039(3)   | 0.0883 | 1.0000   |
| H261  | 0.26353(17) | 0.93549(12) | 0.5038(4)   | 0.1586 | 1.0000   |
| H263  | 0.31012(17) | 0.89418(12) | 0.5952(4)   | 0.1593 | 1.0000   |
| H262  | 0.34932(17) | 0.94318(12) | 0.5111(4)   | 0.1589 | 1.0000   |
| H273  | 0.28096(18) | 0.92453(15) | 0.2580(3)   | 0.1689 | 1.0000   |
| H272  | 0.33685(18) | 0.87835(15) | 0.2090(3)   | 0.1686 | 1.0000   |
| H271  | 0.36385(18) | 0.93423(15) | 0.2784(3)   | 0.1681 | 1.0000   |
| H311  | 0.26027(9)  | 0.53868(7)  | 0.42759(16) | 0.0428 | 1.0000   |
| H361  | 0.49081(17) | 0.39464(14) | 0.5124(3)   | 0.1217 | 0.829(5) |
| H362  | 0.46566(17) | 0.44986(14) | 0.5822(3)   | 0.1229 | 0.829(5) |
| H363  | 0.41508(17) | 0.39721(14) | 0.5781(3)   | 0.1220 | 0.829(5) |
| H371  | 0.43109(15) | 0.37015(13) | 0.3057(3)   | 0.1244 | 0.829(5) |
| H373  | 0.36873(15) | 0.40972(13) | 0.2510(3)   | 0.1248 | 0.829(5) |
| H372  | 0.35589(15) | 0.37474(13) | 0.3788(3)   | 0.1241 | 0.829(5) |
| H411  | 0.29043(8)  | 0.51639(7)  | 0.63236(16) | 0.0392 | 1.0000   |
| H451  | 0.11380(9)  | 0.62728(8)  | 0.6319(2)   | 0.0618 | 1.0000   |
| H461  | 0.02563(13) | 0.58033(11) | 0.7555(3)   | 0.1117 | 1.0000   |
| H463  | 0.10106(13) | 0.56739(11) | 0.8172(3)   | 0.1127 | 1.0000   |
| H462  | 0.06318(13) | 0.52332(11) | 0.7241(3)   | 0.1106 | 1.0000   |
| H472  | 0.01557(12) | 0.59352(10) | 0.5136(3)   | 0.1079 | 1.0000   |
| H471  | 0.08873(12) | 0.59576(10) | 0.4269(3)   | 0.1082 | 1.0000   |
| H473  | 0.06233(12) | 0.53808(10) | 0.4845(3)   | 0.1060 | 1.0000   |
| H1361 | 0.4597(5)   | 0.3694(4)   | 0.4895(11)  | 0.0958 | 0.171(5) |
| H1363 | 0.4093(5)   | 0.4014(4)   | 0.5841(11)  | 0.0958 | 0.171(5) |
| H1362 | 0.3770(5)   | 0.3680(4)   | 0.4701(11)  | 0.0957 | 0.171(5) |
| H1372 | 0.4547(5)   | 0.4056(5)   | 0.2474(7)   | 0.1040 | 0.171(5) |
| H1371 | 0.4093(5)   | 0.4587(5)   | 0.2250(7)   | 0.1039 | 0.171(5) |
| H1373 | 0.3715(5)   | 0.4030(5)   | 0.2606(7)   | 0.1039 | 0.171(5) |
| H522  | 0.47009(10) | 0.66003(8)  | 0.85189(17) | 0.0559 | 1.0000   |
| H521  | 0.41548(10) | 0.60969(8)  | 0.86869(17) | 0.0576 | 1.0000   |
| H532  | 0.53564(12) | 0.62801(8)  | 1.0300(2)   | 0.0681 | 1.0000   |
| H531  | 0.48406(12) | 0.57458(8)  | 1.0405(2)   | 0.0659 | 1.0000   |
| H541  | 0.57092(14) | 0.59903(10) | 0.8227(3)   | 0.0979 | 1.0000   |
| H542  | 0.51583(14) | 0.54979(10) | 0.8270(3)   | 0.0971 | 1.0000   |
| H551  | 0.62957(18) | 0.51657(12) | 0.8657(4)   | 0.1676 | 1.0000   |
| H553  | 0.63927(18) | 0.56200(12) | 0.9808(4)   | 0.1679 | 1.0000   |
| H552  | 0.58422(18) | 0.51038(12) | 0.9957(4)   | 0.1677 | 1.0000   |
| H562  | 0.41403(9)  | 0.72904(7)  | 1.14019(16) | 0.0453 | 1.0000   |
| H561  | 0.47362(9)  | 0.68257(7)  | 1.14400(16) | 0.0463 | 1.0000   |

|       |             |             |             |        |          |
|-------|-------------|-------------|-------------|--------|----------|
| H571  | 0.47263(10) | 0.76717(8)  | 0.95666(17) | 0.0554 | 1.0000   |
| H572  | 0.53138(10) | 0.72104(8)  | 0.96687(17) | 0.0549 | 1.0000   |
| H581  | 0.50485(10) | 0.80391(8)  | 1.15435(18) | 0.0624 | 1.0000   |
| H582  | 0.56285(10) | 0.75588(8)  | 1.17367(18) | 0.0622 | 1.0000   |
| H591  | 0.62226(12) | 0.83618(9)  | 1.1060(2)   | 0.0926 | 1.0000   |
| H593  | 0.57266(12) | 0.83965(9)  | 0.9791(2)   | 0.0917 | 1.0000   |
| H592  | 0.62848(12) | 0.79186(9)  | 0.9935(2)   | 0.0920 | 1.0000   |
| H602  | 0.38605(10) | 0.72538(8)  | 0.85580(16) | 0.0535 | 1.0000   |
| H601  | 0.32761(10) | 0.67883(8)  | 0.86354(16) | 0.0553 | 1.0000   |
| H612  | 0.33377(11) | 0.77382(9)  | 1.02688(19) | 0.0654 | 1.0000   |
| H611  | 0.27809(11) | 0.72653(9)  | 1.04274(19) | 0.0669 | 1.0000   |
| H621  | 0.28988(12) | 0.79058(11) | 0.8201(2)   | 0.0882 | 1.0000   |
| H622  | 0.22890(12) | 0.74682(11) | 0.8452(2)   | 0.0884 | 1.0000   |
| H632  | 0.18254(16) | 0.83271(12) | 0.8858(3)   | 0.1477 | 1.0000   |
| H633  | 0.24558(16) | 0.84778(12) | 0.9736(3)   | 0.1466 | 1.0000   |
| H631  | 0.18892(16) | 0.80383(12) | 1.0220(3)   | 0.1466 | 1.0000   |
| H641  | 0.33716(9)  | 0.66031(7)  | 1.15489(16) | 0.0491 | 1.0000   |
| H642  | 0.39037(9)  | 0.61129(7)  | 1.13809(16) | 0.0485 | 1.0000   |
| H651  | 0.26312(11) | 0.62779(8)  | 0.99380(18) | 0.0628 | 1.0000   |
| H652  | 0.31996(11) | 0.58145(8)  | 0.95611(18) | 0.0633 | 1.0000   |
| H661  | 0.25174(12) | 0.58020(10) | 1.1978(2)   | 0.0754 | 1.0000   |
| H662  | 0.30357(12) | 0.53483(10) | 1.1434(2)   | 0.0751 | 1.0000   |
| H671  | 0.18725(15) | 0.50349(12) | 1.1168(3)   | 0.1394 | 1.0000   |
| H672  | 0.17110(15) | 0.55053(12) | 1.0197(3)   | 0.1402 | 1.0000   |
| H673  | 0.22782(15) | 0.50639(12) | 0.9822(3)   | 0.1395 | 1.0000   |
| H11   | 0.40410(6)  | 0.72887(5)  | 0.62085(11) | 0.0686 | 1.0000   |
| H21   | 0.44537(6)  | 0.69967(5)  | 0.43414(11) | 0.0627 | 1.0000   |
| H41   | 0.36679(6)  | 0.60438(5)  | 0.63872(11) | 0.0652 | 1.0000   |
| H31   | 0.32712(6)  | 0.63170(5)  | 0.45314(12) | 0.0670 | 1.0000   |
| H1021 | 0.4212(4)   | 0.9539(2)   | 1.0112(6)   | 0.1049 | 0.398(4) |
| H1022 | 0.4940(4)   | 0.9233(2)   | 0.9952(6)   | 0.1050 | 0.398(4) |
| H1031 | 0.4402(5)   | 0.9904(3)   | 0.7937(5)   | 0.1083 | 0.398(4) |
| H1032 | 0.5148(5)   | 0.9573(3)   | 0.7938(5)   | 0.1076 | 0.398(4) |
| H1041 | 0.4831(4)   | 1.0487(3)   | 0.9719(5)   | 0.1039 | 0.398(4) |
| H1042 | 0.5569(4)   | 1.0160(3)   | 0.9695(5)   | 0.1039 | 0.398(4) |
| H1051 | 0.5033(4)   | 1.0916(2)   | 0.7874(6)   | 0.1125 | 0.398(4) |
| H1052 | 0.5657(4)   | 1.0549(2)   | 0.7396(6)   | 0.1116 | 0.398(4) |
| H351  | 0.45568(7)  | 0.45962(7)  | 0.35708(15) | 0.0606 | 0.829(5) |
| H352  | 0.46523(7)  | 0.45803(7)  | 0.42549(15) | 0.0607 | 0.171(5) |
| H1061 | 0.5797(7)   | 1.1498(4)   | 0.8412(8)   | 0.1444 | 0.398(4) |

|       |           |           |           |        |          |
|-------|-----------|-----------|-----------|--------|----------|
| H1062 | 0.6004(7) | 1.1076(4) | 0.9536(8) | 0.1435 | 0.398(4) |
| H1063 | 0.6390(7) | 1.1065(4) | 0.8128(8) | 0.1435 | 0.398(4) |
| H1011 | 0.3673(6) | 0.8926(4) | 0.9104(8) | 0.1517 | 0.398(4) |
| H1012 | 0.4314(6) | 0.8876(4) | 0.8095(8) | 0.1518 | 0.398(4) |
| H1013 | 0.4336(6) | 0.8574(4) | 0.9487(8) | 0.1522 | 0.398(4) |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0614(7)       | 0.0446(6)       | 0.0625(7)       | -0.0015(5)      | -0.0015(6)      | -0.0170(5)      |
| O1    | 0.0469(7)       | 0.0507(7)       | 0.0427(7)       | -0.0091(6)      | 0.0186(6)       | -0.0132(6)      |
| O2    | 0.0469(7)       | 0.0440(6)       | 0.0345(6)       | -0.0054(5)      | 0.0049(5)       | 0.0032(5)       |
| C11   | 0.0416(9)       | 0.0354(8)       | 0.0365(8)       | -0.0046(7)      | 0.0097(8)       | -0.0073(7)      |
| C12   | 0.0486(10)      | 0.0435(9)       | 0.0287(8)       | -0.0049(8)      | 0.0055(8)       | -0.0140(8)      |
| O13   | 0.0610(8)       | 0.0571(8)       | 0.0375(6)       | 0.0119(6)       | 0.0030(6)       | -0.0124(7)      |
| O14   | 0.0376(6)       | 0.0516(7)       | 0.0453(7)       | 0.0129(6)       | 0.0019(5)       | -0.0068(5)      |
| C15   | 0.0420(10)      | 0.0525(10)      | 0.0428(10)      | 0.0107(9)       | -0.0013(8)      | -0.0021(8)      |
| C16   | 0.0516(13)      | 0.111(2)        | 0.0575(13)      | -0.0137(13)     | -0.0061(11)     | -0.0033(13)     |
| C17   | 0.0483(11)      | 0.0734(13)      | 0.0509(11)      | 0.0110(11)      | 0.0043(9)       | 0.0025(10)      |
| C21   | 0.0358(8)       | 0.0394(8)       | 0.0348(8)       | 0.0002(7)       | 0.0074(7)       | -0.0011(7)      |
| C22   | 0.0363(9)       | 0.0450(10)      | 0.0465(10)      | 0.0035(8)       | 0.0084(8)       | -0.0014(8)      |
| O23   | 0.0427(7)       | 0.0679(9)       | 0.0626(8)       | -0.0078(7)      | -0.0060(7)      | 0.0051(7)       |
| O24   | 0.0417(7)       | 0.0409(7)       | 0.0963(11)      | 0.0037(7)       | 0.0001(7)       | 0.0036(6)       |
| C25   | 0.0535(13)      | 0.0513(12)      | 0.119(2)        | 0.0137(14)      | -0.0054(14)     | 0.0116(10)      |
| C26   | 0.098(2)        | 0.0809(18)      | 0.139(3)        | -0.0035(19)     | 0.018(2)        | 0.0429(16)      |
| C27   | 0.117(3)        | 0.111(2)        | 0.111(2)        | 0.022(2)        | -0.023(2)       | 0.037(2)        |
| O3    | 0.0511(7)       | 0.0382(6)       | 0.0450(7)       | 0.0055(6)       | -0.0107(6)      | 0.0005(5)       |
| O4    | 0.0395(6)       | 0.0479(7)       | 0.0427(7)       | 0.0041(6)       | -0.0107(6)      | -0.0061(5)      |
| C31   | 0.0335(8)       | 0.0348(8)       | 0.0407(9)       | 0.0025(7)       | -0.0065(7)      | -0.0031(7)      |
| C32   | 0.0359(9)       | 0.0438(9)       | 0.0368(9)       | 0.0021(8)       | -0.0062(8)      | -0.0041(8)      |
| O33   | 0.0437(7)       | 0.0601(8)       | 0.0640(9)       | 0.0191(7)       | 0.0078(7)       | -0.0005(6)      |
| O34   | 0.0458(7)       | 0.0359(6)       | 0.0688(9)       | -0.0007(6)      | 0.0172(6)       | 0.0005(5)       |
| C35   | 0.0475(10)      | 0.0456(9)       | 0.0593(11)      | -0.0023(9)      | 0.0101(9)       | 0.0062(8)       |
| C36   | 0.075(2)        | 0.102(2)        | 0.0686(18)      | -0.0072(17)     | -0.0032(15)     | 0.0212(19)      |
| C37   | 0.083(2)        | 0.076(2)        | 0.092(2)        | -0.0349(19)     | 0.0036(18)      | 0.0119(17)      |
| C41   | 0.0338(8)       | 0.0337(8)       | 0.0381(9)       | 0.0033(7)       | -0.0050(7)      | -0.0026(7)      |
| C42   | 0.0416(9)       | 0.0351(9)       | 0.0386(9)       | 0.0040(8)       | -0.0025(8)      | -0.0026(7)      |
| O43   | 0.0511(8)       | 0.0461(7)       | 0.0497(7)       | -0.0105(6)      | -0.0027(6)      | 0.0003(6)       |
| O44   | 0.0316(6)       | 0.0406(6)       | 0.0638(8)       | -0.0095(6)      | -0.0024(6)      | -0.0012(5)      |
| C45   | 0.0349(10)      | 0.0411(10)      | 0.0813(14)      | -0.0078(10)     | -0.0006(10)     | 0.0018(8)       |

|      |            |            |            |             |             |             |
|------|------------|------------|------------|-------------|-------------|-------------|
| C46  | 0.0544(13) | 0.0775(16) | 0.0944(18) | -0.0073(14) | 0.0192(12)  | -0.0032(12) |
| C47  | 0.0482(12) | 0.0690(14) | 0.1014(19) | -0.0040(14) | -0.0205(13) | 0.0107(11)  |
| C136 | 0.074(6)   | 0.045(5)   | 0.073(6)   | 0.001(4)    | 0.002(5)    | 0.020(5)    |
| C137 | 0.077(6)   | 0.063(6)   | 0.068(5)   | -0.011(5)   | 0.014(5)    | 0.016(5)    |
| N51  | 0.0458(8)  | 0.0464(8)  | 0.0248(6)  | 0.0019(6)   | -0.0005(6)  | -0.0090(7)  |
| C52  | 0.0582(12) | 0.0497(10) | 0.0348(9)  | -0.0073(8)  | 0.0067(9)   | -0.0147(9)  |
| C53  | 0.0615(13) | 0.0525(11) | 0.0572(12) | -0.0100(10) | 0.0085(10)  | -0.0013(10) |
| C54  | 0.0900(18) | 0.0627(14) | 0.0913(18) | -0.0206(13) | 0.0302(15)  | -0.0046(13) |
| C55  | 0.101(2)   | 0.0770(18) | 0.158(3)   | -0.024(2)   | 0.029(2)    | 0.0215(17)  |
| C56  | 0.0437(10) | 0.0466(10) | 0.0289(8)  | -0.0037(8)  | -0.0030(8)  | -0.0042(7)  |
| C57  | 0.0517(11) | 0.0495(10) | 0.0361(9)  | -0.0050(8)  | 0.0018(8)   | -0.0097(9)  |
| C58  | 0.0543(11) | 0.0568(11) | 0.0441(10) | -0.0116(9)  | 0.0047(9)   | -0.0139(9)  |
| C59  | 0.0591(13) | 0.0675(13) | 0.0598(12) | -0.0133(11) | 0.0112(11)  | -0.0208(11) |
| C60  | 0.0547(11) | 0.0554(11) | 0.0283(8)  | 0.0096(8)   | -0.0075(8)  | -0.0135(9)  |
| C61  | 0.0603(12) | 0.0597(12) | 0.0443(10) | 0.0111(10)  | -0.0115(10) | -0.0025(10) |
| C62  | 0.0638(14) | 0.0868(16) | 0.0684(14) | 0.0293(13)  | -0.0164(12) | 0.0000(13)  |
| C63  | 0.0820(19) | 0.0939(19) | 0.120(2)   | 0.0297(19)  | -0.0222(18) | 0.0235(16)  |
| C64  | 0.0453(10) | 0.0495(10) | 0.0302(8)  | 0.0067(8)   | -0.0004(8)  | -0.0076(8)  |
| C65  | 0.0559(12) | 0.0610(12) | 0.0413(10) | 0.0073(9)   | -0.0043(9)  | -0.0180(10) |
| C66  | 0.0631(13) | 0.0720(14) | 0.0536(12) | 0.0098(11)  | -0.0028(10) | -0.0265(11) |
| C67  | 0.0890(19) | 0.1003(19) | 0.0912(19) | 0.0181(16)  | -0.0151(16) | -0.0523(16) |
| C101 | 0.082(5)   | 0.085(5)   | 0.132(6)   | 0.002(5)    | -0.035(5)   | 0.014(4)    |
| C102 | 0.073(4)   | 0.087(4)   | 0.099(4)   | -0.006(3)   | -0.020(3)   | 0.018(3)    |
| C103 | 0.073(4)   | 0.098(4)   | 0.096(5)   | -0.006(3)   | 0.000(3)    | 0.006(3)    |
| C104 | 0.074(4)   | 0.093(4)   | 0.091(5)   | 0.004(3)    | -0.004(3)   | 0.007(3)    |
| C105 | 0.096(4)   | 0.094(4)   | 0.090(4)   | 0.010(3)    | -0.022(3)   | -0.015(3)   |
| C106 | 0.113(7)   | 0.073(5)   | 0.099(5)   | 0.004(4)    | -0.012(5)   | -0.015(4)   |

## Distances

|     |      |             |  |     |      |           |
|-----|------|-------------|--|-----|------|-----------|
| O1  | C11  | 1.4042(19)Å |  | O1  | H11  | 0.833Å    |
| O2  | C21  | 1.3993(19)Å |  | O2  | H21  | 0.829Å    |
| C11 | C12  | 1.517(2)Å   |  | C11 | C21  | 1.534(2)Å |
| C11 | H111 | 0.965Å      |  | C12 | O13  | 1.202(2)Å |
| C12 | O14  | 1.341(2)Å   |  | O14 | C15  | 1.462(2)Å |
| C15 | C16  | 1.498(3)Å   |  | C15 | C17  | 1.497(3)Å |
| C15 | H151 | 0.984Å      |  | C16 | H163 | 0.968Å    |
| C16 | H162 | 0.972Å      |  | C16 | H161 | 0.972Å    |
| C17 | H172 | 0.978Å      |  | C17 | H171 | 0.993Å    |
| C17 | H173 | 0.995Å      |  | C21 | C22  | 1.516(2)Å |

|      |       |             |  |      |       |             |
|------|-------|-------------|--|------|-------|-------------|
| C21  | H211  | 0.985Å      |  | C22  | O23   | 1.197(2)Å   |
| C22  | O24   | 1.341(2)Å   |  | O24  | C25   | 1.460(2)Å   |
| C25  | C26   | 1.518(4)Å   |  | C25  | C27   | 1.502(4)Å   |
| C25  | H251  | 1.014Å      |  | C26  | H261  | 0.993Å      |
| C26  | H263  | 0.996Å      |  | C26  | H262  | 0.992Å      |
| C27  | H273  | 0.983Å      |  | C27  | H272  | 0.968Å      |
| C27  | H271  | 0.974Å      |  | O3   | C31   | 1.4003(19)Å |
| O3   | H31   | 0.845Å      |  | O4   | C41   | 1.3979(19)Å |
| O4   | H41   | 0.815Å      |  | C31  | C32   | 1.517(2)Å   |
| C31  | C41   | 1.541(2)Å   |  | C31  | H311  | 0.957Å      |
| C32  | O33   | 1.198(2)Å   |  | C32  | O34   | 1.335(2)Å   |
| O34  | C35   | 1.4679(18)Å |  | C35  | C36   | 1.481(3)Å   |
| C35  | C37   | 1.494(3)Å   |  | C35  | C136  | 1.477(6)Å   |
| C35  | C137  | 1.461(6)Å   |  | C35  | H351  | 1.003Å      |
| C35  | H352  | 0.980Å      |  | C36  | C136  | 1.036(13)Å  |
| C36  | H361  | 0.959Å      |  | C36  | H362  | 0.955Å      |
| C36  | H363  | 0.986Å      |  | C36  | H1361 | 1.279Å      |
| C36  | H1363 | 1.050Å      |  | C37  | C137  | 1.037(12)Å  |
| C37  | H371  | 0.982Å      |  | C37  | H373  | 0.980Å      |
| C37  | H372  | 0.965Å      |  | C37  | H1373 | 0.819Å      |
| C41  | C42   | 1.530(2)Å   |  | C41  | H411  | 0.974Å      |
| C42  | O43   | 1.198(2)Å   |  | C42  | O44   | 1.340(2)Å   |
| O44  | C45   | 1.460(2)Å   |  | C45  | C46   | 1.502(3)Å   |
| C45  | C47   | 1.510(3)Å   |  | C45  | H451  | 0.974Å      |
| C46  | H461  | 0.985Å      |  | C46  | H463  | 0.989Å      |
| C46  | H462  | 0.976Å      |  | C47  | H472  | 0.997Å      |
| C47  | H471  | 0.988Å      |  | C47  | H473  | 0.977Å      |
| C136 | H363  | 0.864Å      |  | C136 | H1361 | 0.970Å      |
| C136 | H1363 | 0.958Å      |  | C136 | H1362 | 0.957Å      |
| C137 | H373  | 0.952Å      |  | C137 | H1372 | 0.962Å      |
| C137 | H1371 | 0.956Å      |  | C137 | H1373 | 0.966Å      |
| N51  | C52   | 1.522(2)Å   |  | N51  | C56   | 1.518(2)Å   |
| N51  | C60   | 1.519(2)Å   |  | N51  | C64   | 1.524(2)Å   |
| C52  | C53   | 1.510(3)Å   |  | C52  | H522  | 0.981Å      |
| C52  | H521  | 0.994Å      |  | C53  | C54   | 1.524(3)Å   |
| C53  | H532  | 1.000Å      |  | C53  | H531  | 0.989Å      |
| C54  | C55   | 1.502(4)Å   |  | C54  | H541  | 0.985Å      |
| C54  | H542  | 0.967Å      |  | C55  | H551  | 0.982Å      |
| C55  | H553  | 0.990Å      |  | C55  | H552  | 0.995Å      |
| C56  | C57   | 1.516(2)Å   |  | C56  | H562  | 0.980Å      |

|       |             |            |  |      |             |            |
|-------|-------------|------------|--|------|-------------|------------|
| C56   | H561        | 0.978Å     |  | C57  | C58         | 1.521(2)Å  |
| C57   | H571        | 0.967Å     |  | C57  | H572        | 0.973Å     |
| C58   | C59         | 1.514(3)Å  |  | C58  | H581        | 0.998Å     |
| C58   | H582        | 0.986Å     |  | C59  | H591        | 0.988Å     |
| C59   | H593        | 0.981Å     |  | C59  | H592        | 0.982Å     |
| C60   | C61         | 1.511(3)Å  |  | C60  | H602        | 0.974Å     |
| C60   | H601        | 0.970Å     |  | C61  | C62         | 1.515(3)Å  |
| C61   | H612        | 0.984Å     |  | C61  | H611        | 0.952Å     |
| C62   | C63         | 1.513(4)Å  |  | C62  | H621        | 0.975Å     |
| C62   | H622        | 0.951Å     |  | C63  | H632        | 0.940Å     |
| C63   | H633        | 0.996Å     |  | C63  | H631        | 0.966Å     |
| C64   | C65         | 1.514(3)Å  |  | C64  | H641        | 0.969Å     |
| C64   | H642        | 0.973Å     |  | C65  | C66         | 1.510(3)Å  |
| C65   | H651        | 1.001Å     |  | C65  | H652        | 0.956Å     |
| C66   | C67         | 1.513(3)Å  |  | C66  | H661        | 0.992Å     |
| C66   | H662        | 0.982Å     |  | C67  | H671        | 0.969Å     |
| C67   | H672        | 0.947Å     |  | C67  | H673        | 0.992Å     |
| C101  | C102        | 1.489(5)Å  |  | C101 | C105 4_675  | 1.523(10)Å |
| C101  | C106 4_675  | 0.468(15)Å |  | C101 | H1061 4_675 | 1.083Å     |
| C101  | H1062 4_675 | 0.666Å     |  | C101 | H1011       | 0.955Å     |
| C101  | H1012       | 0.961Å     |  | C101 | H1013       | 0.949Å     |
| C102  | C103        | 1.549(5)Å  |  | C102 | C104 4_675  | 1.044(8)Å  |
| C102  | C105 4_675  | 1.443(8)Å  |  | C102 | H1021       | 0.963Å     |
| C102  | H1022       | 0.958Å     |  | C102 | H1041 4_675 | 1.274Å     |
| C102  | H1042 4_675 | 1.171Å     |  | C103 | C103 4_675  | 1.275(10)Å |
| C103  | C104        | 1.584(5)Å  |  | C103 | C104 4_675  | 0.723(5)Å  |
| C103  | C105 4_675  | 1.362(8)Å  |  | C103 | H1031       | 0.991Å     |
| C103  | H1032       | 1.008Å     |  | C104 | C104 4_675  | 1.589(10)Å |
| C104  | C105        | 1.555(5)Å  |  | C104 | H1041       | 0.987Å     |
| C104  | H1042       | 0.992Å     |  | C105 | C106        | 1.494(5)Å  |
| C105  | H1051       | 0.932Å     |  | C105 | H1052       | 0.962Å     |
| C105  | H1012 4_675 | 1.091Å     |  | C106 | H1061       | 0.951Å     |
| C106  | H1062       | 0.985Å     |  | C106 | H1063       | 0.969Å     |
| C106  | H1011 4_675 | 0.889Å     |  | C106 | H1012 4_675 | 0.730Å     |
| C106  | H1013 4_675 | 1.285Å     |  | H363 | H1363       | 0.162Å     |
| H373  | H1373       | 0.199Å     |  | H351 | H352        | 0.730Å     |
| H1062 | H1011 4_675 | 0.758Å     |  |      |             |            |



## Angles

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C11  | O1  | H11  | 105.604°    |  | C21  | O2  | H21  | 108.441°    |
| O1   | C11 | C12  | 112.75(13)° |  | O1   | C11 | C21  | 112.92(13)° |
| C12  | C11 | C21  | 108.61(13)° |  | O1   | C11 | H111 | 106.626°    |
| C12  | C11 | H111 | 108.498°    |  | C21  | C11 | H111 | 107.191°    |
| C11  | C12 | O13  | 125.86(15)° |  | C11  | C12 | O14  | 109.64(14)° |
| O13  | C12 | O14  | 124.50(17)° |  | C12  | O14 | C15  | 118.14(13)° |
| O14  | C15 | C16  | 108.14(16)° |  | O14  | C15 | C17  | 106.02(15)° |
| C16  | C15 | C17  | 113.41(17)° |  | O14  | C15 | H151 | 107.553°    |
| C16  | C15 | H151 | 109.598°    |  | C17  | C15 | H151 | 111.836°    |
| C15  | C16 | H163 | 109.689°    |  | C15  | C16 | H162 | 108.790°    |
| H163 | C16 | H162 | 111.427°    |  | C15  | C16 | H161 | 108.232°    |
| H163 | C16 | H161 | 110.818°    |  | H162 | C16 | H161 | 107.796°    |
| C15  | C17 | H172 | 110.131°    |  | C15  | C17 | H171 | 109.469°    |
| H172 | C17 | H171 | 108.900°    |  | C15  | C17 | H173 | 109.304°    |
| H172 | C17 | H173 | 108.656°    |  | H171 | C17 | H173 | 110.368°    |
| O2   | C21 | C11  | 112.55(13)° |  | O2   | C21 | C22  | 111.93(14)° |
| C11  | C21 | C22  | 110.12(14)° |  | O2   | C21 | H211 | 107.390°    |
| C11  | C21 | H211 | 107.618°    |  | C22  | C21 | H211 | 106.942°    |
| C21  | C22 | O23  | 124.95(16)° |  | C21  | C22 | O24  | 110.79(16)° |
| O23  | C22 | O24  | 124.25(17)° |  | C22  | O24 | C25  | 117.63(16)° |
| O24  | C25 | C26  | 106.0(2)°   |  | O24  | C25 | C27  | 107.8(2)°   |
| C26  | C25 | C27  | 113.8(2)°   |  | O24  | C25 | H251 | 111.930°    |
| C26  | C25 | H251 | 105.193°    |  | C27  | C25 | H251 | 112.055°    |
| C25  | C26 | H261 | 109.215°    |  | C25  | C26 | H263 | 107.783°    |
| H261 | C26 | H263 | 110.682°    |  | C25  | C26 | H262 | 105.267°    |
| H261 | C26 | H262 | 111.474°    |  | H263 | C26 | H262 | 112.176°    |
| C25  | C27 | H273 | 106.276°    |  | C25  | C27 | H272 | 106.431°    |
| H273 | C27 | H272 | 112.641°    |  | C25  | C27 | H271 | 108.287°    |
| H273 | C27 | H271 | 110.156°    |  | H272 | C27 | H271 | 112.682°    |
| C31  | O3  | H31  | 108.639°    |  | C41  | O4  | H41  | 107.225°    |
| O3   | C31 | C32  | 112.56(14)° |  | O3   | C31 | C41  | 112.16(14)° |
| C32  | C31 | C41  | 110.55(13)° |  | O3   | C31 | H311 | 107.828°    |
| C32  | C31 | H311 | 105.859°    |  | C41  | C31 | H311 | 107.514°    |
| C31  | C32 | O33  | 125.44(16)° |  | C31  | C32 | O34  | 109.64(14)° |
| O33  | C32 | O34  | 124.89(16)° |  | C32  | O34 | C35  | 119.39(12)° |
| O34  | C35 | C36  | 107.64(7)°  |  | O34  | C35 | C37  | 107.46(7)°  |
| C36  | C35 | C37  | 112.95(7)°  |  | O34  | C35 | C136 | 107.47(7)°  |
| C36  | C35 | C136 | 41.0(5)°    |  | C37  | C35 | C136 | 74.6(5)°    |

|      |     |       |             |  |       |      |       |             |
|------|-----|-------|-------------|--|-------|------|-------|-------------|
| O34  | C35 | C137  | 107.56(7)°  |  | C36   | C35  | C137  | 141.9(2)°   |
| C37  | C35 | C137  | 41.0(5)°    |  | C136  | C35  | C137  | 113.03(7)°  |
| O34  | C35 | H351  | 109.543°    |  | C36   | C35  | H351  | 111.645°    |
| C37  | C35 | H351  | 107.494°    |  | C136  | C35  | H351  | 140.034°    |
| C137 | C35 | H351  | 69.001°     |  | O34   | C35  | H352  | 109.315°    |
| C36  | C35 | H352  | 71.152°     |  | C37   | C35  | H352  | 139.363°    |
| C136 | C35 | H352  | 109.483°    |  | C137  | C35  | H352  | 109.882°    |
| H351 | C35 | H352  | 43.167°     |  | C35   | C36  | C136  | 69.3(4)°    |
| C35  | C36 | H361  | 109.041°    |  | C136  | C36  | H361  | 91.534°     |
| C35  | C36 | H362  | 107.154°    |  | C136  | C36  | H362  | 154.539°    |
| H361 | C36 | H362  | 112.839°    |  | C35   | C36  | H363  | 106.964°    |
| C136 | C36 | H363  | 50.502°     |  | H361  | C36  | H363  | 109.703°    |
| H362 | C36 | H363  | 110.922°    |  | C35   | C36  | H1361 | 93.553°     |
| C136 | C36 | H1361 | 48.135°     |  | H361  | C36  | H1361 | 43.683°     |
| H362 | C36 | H1361 | 154.113°    |  | H363  | C36  | H1361 | 76.278°     |
| C35  | C36 | H1363 | 104.468°    |  | C136  | C36  | H1363 | 54.659°     |
| H361 | C36 | H1363 | 117.880°    |  | H362  | C36  | H1363 | 104.681°    |
| H363 | C36 | H1363 | 8.369°      |  | H1361 | C36  | H1363 | 84.307°     |
| C35  | C37 | C137  | 67.8(4)°    |  | C35   | C37  | H371  | 105.881°    |
| C137 | C37 | H371  | 89.321°     |  | C35   | C37  | H373  | 109.767°    |
| C137 | C37 | H373  | 56.240°     |  | H371  | C37  | H373  | 111.809°    |
| C35  | C37 | H372  | 107.557°    |  | C137  | C37  | H372  | 158.040°    |
| H371 | C37 | H372  | 112.334°    |  | H373  | C37  | H372  | 109.337°    |
| C35  | C37 | H1373 | 117.217°    |  | C137  | C37  | H1373 | 61.412°     |
| H371 | C37 | H1373 | 107.779°    |  | H373  | C37  | H1373 | 7.472°      |
| H372 | C37 | H1373 | 106.225°    |  | O4    | C41  | C31   | 113.50(13)° |
| O4   | C41 | C42   | 112.37(13)° |  | C31   | C41  | C42   | 108.21(13)° |
| O4   | C41 | H411  | 108.634°    |  | C31   | C41  | H411  | 106.953°    |
| C42  | C41 | H411  | 106.828°    |  | C41   | C42  | O43   | 125.65(16)° |
| C41  | C42 | O44   | 109.59(13)° |  | O43   | C42  | O44   | 124.76(16)° |
| C42  | O44 | C45   | 118.12(14)° |  | O44   | C45  | C46   | 109.01(17)° |
| O44  | C45 | C47   | 105.24(16)° |  | C46   | C45  | C47   | 112.89(18)° |
| O44  | C45 | H451  | 106.320°    |  | C46   | C45  | H451  | 112.974°    |
| C47  | C45 | H451  | 109.892°    |  | C45   | C46  | H461  | 109.217°    |
| C45  | C46 | H463  | 111.464°    |  | H461  | C46  | H463  | 108.094°    |
| C45  | C46 | H462  | 109.850°    |  | H461  | C46  | H462  | 108.351°    |
| H463 | C46 | H462  | 109.793°    |  | C45   | C47  | H472  | 106.674°    |
| C45  | C47 | H471  | 107.983°    |  | H472  | C47  | H471  | 112.815°    |
| C45  | C47 | H473  | 107.599°    |  | H472  | C47  | H473  | 112.343°    |
| H471 | C47 | H473  | 109.176°    |  | C35   | C136 | C36   | 69.7(5)°    |

|       |      |       |             |  |       |      |       |             |
|-------|------|-------|-------------|--|-------|------|-------|-------------|
| C35   | C136 | H363  | 115.261°    |  | C36   | C136 | H363  | 61.738°     |
| C35   | C136 | H1361 | 109.174°    |  | C36   | C136 | H1361 | 79.162°     |
| H363  | C136 | H1361 | 101.121°    |  | C35   | C136 | H1363 | 110.130°    |
| C36   | C136 | H1363 | 63.439°     |  | H363  | C136 | H1363 | 8.301°      |
| H1361 | C136 | H1363 | 109.312°    |  | C35   | C136 | H1362 | 109.028°    |
| C36   | C136 | H1362 | 169.722°    |  | H363  | C136 | H1362 | 111.524°    |
| H1361 | C136 | H1362 | 110.466°    |  | H1363 | C136 | H1362 | 108.722°    |
| C35   | C137 | C37   | 71.2(5)°    |  | C35   | C137 | H373  | 114.268°    |
| C37   | C137 | H373  | 58.888°     |  | C35   | C137 | H1372 | 107.869°    |
| C37   | C137 | H1372 | 96.914°     |  | H373  | C137 | H1372 | 117.440°    |
| C35   | C137 | H1371 | 108.812°    |  | C37   | C137 | H1371 | 151.327°    |
| H373  | C137 | H1371 | 98.095°     |  | H1372 | C137 | H1371 | 109.715°    |
| C35   | C137 | H1373 | 109.786°    |  | C37   | C137 | H1373 | 48.134°     |
| H373  | C137 | H1373 | 11.881°     |  | H1372 | C137 | H1373 | 110.684°    |
| H1371 | C137 | H1373 | 109.927°    |  | C52   | N51  | C56   | 110.51(13)° |
| C52   | N51  | C60   | 106.52(13)° |  | C56   | N51  | C60   | 111.08(13)° |
| C52   | N51  | C64   | 110.94(13)° |  | C56   | N51  | C64   | 106.98(12)° |
| C60   | N51  | C64   | 110.86(13)° |  | N51   | C52  | C53   | 116.34(15)° |
| N51   | C52  | H522  | 107.248°    |  | C53   | C52  | H522  | 108.356°    |
| N51   | C52  | H521  | 106.551°    |  | C53   | C52  | H521  | 108.811°    |
| H522  | C52  | H521  | 109.389°    |  | C52   | C53  | C54   | 109.35(19)° |
| C52   | C53  | H532  | 108.395°    |  | C54   | C53  | H532  | 109.802°    |
| C52   | C53  | H531  | 111.082°    |  | C54   | C53  | H531  | 108.325°    |
| H532  | C53  | H531  | 109.877°    |  | C53   | C54  | C55   | 113.5(2)°   |
| C53   | C54  | H541  | 108.642°    |  | C55   | C54  | H541  | 105.803°    |
| C53   | C54  | H542  | 108.192°    |  | C55   | C54  | H542  | 111.674°    |
| H541  | C54  | H542  | 108.922°    |  | C54   | C55  | H551  | 109.778°    |
| C54   | C55  | H553  | 108.456°    |  | H551  | C55  | H553  | 111.584°    |
| C54   | C55  | H552  | 107.520°    |  | H551  | C55  | H552  | 108.188°    |
| H553  | C55  | H552  | 111.230°    |  | N51   | C56  | C57   | 115.07(13)° |
| N51   | C56  | H562  | 105.911°    |  | C57   | C56  | H562  | 111.714°    |
| N51   | C56  | H561  | 106.105°    |  | C57   | C56  | H561  | 108.437°    |
| H562  | C56  | H561  | 109.365°    |  | C56   | C57  | C58   | 110.96(14)° |
| C56   | C57  | H571  | 108.700°    |  | C58   | C57  | H571  | 109.079°    |
| C56   | C57  | H572  | 109.540°    |  | C58   | C57  | H572  | 109.131°    |
| H571  | C57  | H572  | 109.409°    |  | C57   | C58  | C59   | 112.64(16)° |
| C57   | C58  | H581  | 106.755°    |  | C59   | C58  | H581  | 110.376°    |
| C57   | C58  | H582  | 108.371°    |  | C59   | C58  | H582  | 109.589°    |
| H581  | C58  | H582  | 109.007°    |  | C58   | C59  | H591  | 110.332°    |
| C58   | C59  | H593  | 110.421°    |  | H591  | C59  | H593  | 110.242°    |

|                |      |                |            |  |                |      |                |             |
|----------------|------|----------------|------------|--|----------------|------|----------------|-------------|
| C58            | C59  | H592           | 111.363°   |  | H591           | C59  | H592           | 107.413°    |
| H593           | C59  | H592           | 106.977°   |  | N51            | C60  | C61            | 115.42(14)° |
| N51            | C60  | H602           | 107.263°   |  | C61            | C60  | H602           | 108.585°    |
| N51            | C60  | H601           | 106.182°   |  | C61            | C60  | H601           | 109.983°    |
| H602           | C60  | H601           | 109.247°   |  | C60            | C61  | C62            | 110.53(17)° |
| C60            | C61  | H612           | 111.204°   |  | C62            | C61  | H612           | 108.079°    |
| C60            | C61  | H611           | 110.292°   |  | C62            | C61  | H611           | 108.402°    |
| H612           | C61  | H611           | 108.237°   |  | C61            | C62  | C63            | 112.1(2)°   |
| C61            | C62  | H621           | 106.369°   |  | C63            | C62  | H621           | 109.264°    |
| C61            | C62  | H622           | 109.355°   |  | C63            | C62  | H622           | 108.349°    |
| H621           | C62  | H622           | 111.473°   |  | C62            | C63  | H632           | 110.674°    |
| C62            | C63  | H633           | 107.250°   |  | H632           | C63  | H633           | 105.868°    |
| C62            | C63  | H631           | 112.522°   |  | H632           | C63  | H631           | 111.508°    |
| H633           | C63  | H631           | 108.685°   |  | N51            | C64  | C65            | 115.13(13)° |
| N51            | C64  | H641           | 105.284°   |  | C65            | C64  | H641           | 110.658°    |
| N51            | C64  | H642           | 106.022°   |  | C65            | C64  | H642           | 111.476°    |
| H641           | C64  | H642           | 107.821°   |  | C64            | C65  | C66            | 111.85(15)° |
| C64            | C65  | H651           | 108.649°   |  | C66            | C65  | H651           | 109.141°    |
| C64            | C65  | H652           | 109.487°   |  | C66            | C65  | H652           | 107.400°    |
| H651           | C65  | H652           | 110.307°   |  | C65            | C66  | C67            | 112.50(19)° |
| C65            | C66  | H661           | 109.204°   |  | C67            | C66  | H661           | 113.466°    |
| C65            | C66  | H662           | 106.897°   |  | C67            | C66  | H662           | 108.057°    |
| H661           | C66  | H662           | 106.312°   |  | C66            | C67  | H671           | 109.439°    |
| C66            | C67  | H672           | 114.274°   |  | H671           | C67  | H672           | 107.946°    |
| C66            | C67  | H673           | 108.824°   |  | H671           | C67  | H673           | 108.358°    |
| H672           | C67  | H673           | 107.843°   |  | C102           | C101 | C105<br>4_675  | 57.2(3)°    |
| C102           | C101 | C106<br>4_675  | 126.0(20)° |  | C105<br>4_675  | C101 | C106<br>4_675  | 77.6(14)°   |
| C102           | C101 | H1061<br>4_675 | 147.583°   |  | C105<br>4_675  | C101 | H1061<br>4_675 | 100.918°    |
| C106<br>4_675  | C101 | H1061<br>4_675 | 61.208°    |  | C102           | C101 | H1062<br>4_675 | 76.975°     |
| C105<br>4_675  | C101 | H1062<br>4_675 | 128.653°   |  | C106<br>4_675  | C101 | H1062<br>4_675 | 119.630°    |
| H1061<br>4_675 | C101 | H1062<br>4_675 | 130.221°   |  | C102           | C101 | H1011          | 107.779°    |
| C105<br>4_675  | C101 | H1011          | 118.644°   |  | C106<br>4_675  | C101 | H1011          | 67.560°     |
| H1061<br>4_675 | C101 | H1011          | 103.834°   |  | H1062<br>4_675 | C101 | H1011          | 52.077°     |
| C102           | C101 | H1012          | 102.175°   |  | C105           | C101 | H1012          | 45.454°     |

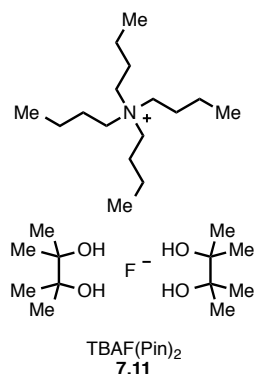
|                |      |                |            |  |                |      |                |            |
|----------------|------|----------------|------------|--|----------------|------|----------------|------------|
|                |      |                |            |  | 4_675          |      |                |            |
| C106<br>4_675  | C101 | H1012          | 47.338°    |  | H1061<br>4_675 | C101 | H1012          | 57.361°    |
| H1062<br>4_675 | C101 | H1012          | 163.281°   |  | C102           | C101 | H1013          | 105.538°   |
| C105<br>4_675  | C101 | H1013          | 130.132°   |  | C106<br>4_675  | C101 | H1013          | 126.856°   |
| H1061<br>4_675 | C101 | H1013          | 68.604°    |  | H1062<br>4_675 | C101 | H1013          | 80.661°    |
| H1011          | C101 | H1012          | 113.935°   |  | H1011          | C101 | H1013          | 111.141°   |
| H1012          | C101 | H1013          | 115.227°   |  | C101           | C102 | C103           | 115.71(7)° |
| C101           | C102 | C104<br>4_675  | 138.1(3)°  |  | C103           | C102 | C104<br>4_675  | 23.5(4)°   |
| C101           | C102 | C105<br>4_675  | 62.5(4)°   |  | C103           | C102 | C105<br>4_675  | 54.0(4)°   |
| C104<br>4_675  | C102 | C105<br>4_675  | 75.5(4)°   |  | C101           | C102 | H1021          | 106.423°   |
| C103           | C102 | H1021          | 111.966°   |  | C104<br>4_675  | C102 | H1021          | 103.665°   |
| C105<br>4_675  | C102 | H1021          | 137.081°   |  | C101           | C102 | H1022          | 105.407°   |
| C103           | C102 | H1022          | 106.648°   |  | C104<br>4_675  | C102 | H1022          | 90.384°    |
| C105<br>4_675  | C102 | H1022          | 112.423°   |  | H1021          | C102 | H1022          | 110.488°   |
| C101           | C102 | H1041<br>4_675 | 136.101°   |  | C103           | C102 | H1041<br>4_675 | 68.039°    |
| C104<br>4_675  | C102 | H1041<br>4_675 | 49.188°    |  | C105<br>4_675  | C102 | H1041<br>4_675 | 99.619°    |
| H1021          | C102 | H1041<br>4_675 | 112.053°   |  | C101           | C102 | H1042<br>4_675 | 140.205°   |
| C103           | C102 | H1042<br>4_675 | 62.126°    |  | C104<br>4_675  | C102 | H1042<br>4_675 | 52.824°    |
| C105<br>4_675  | C102 | H1042<br>4_675 | 108.619°   |  | H1021          | C102 | H1042<br>4_675 | 51.412°    |
| H1022          | C102 | H1041<br>4_675 | 41.334°    |  | H1022          | C102 | H1042<br>4_675 | 113.225°   |
| H1041<br>4_675 | C102 | H1042<br>4_675 | 82.284°    |  | C102           | C103 | C103<br>4_675  | 136.3(2)°  |
| C102           | C103 | C104           | 111.08(7)° |  | C103<br>4_675  | C103 | C104           | 26.6(2)°   |
| C102           | C103 | C104<br>4_675  | 35.1(7)°   |  | C103<br>4_675  | C103 | C104<br>4_675  | 101.3(7)°  |
| C104           | C103 | C104<br>4_675  | 77.2(7)°   |  | C102           | C103 | C105<br>4_675  | 59.0(4)°   |

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|---------------|------|---------------|------------|--|---------------|------|---------------|-------------|
| C103<br>4_675 | C103 | C105<br>4_675 | 157.9(9)°  |  | C104          | C103 | C105<br>4_675 | 166.5(6)°   |
| C104<br>4_675 | C103 | C105<br>4_675 | 91.2(8)°   |  | C102          | C103 | H1031         | 108.749°    |
| C103<br>4_675 | C103 | H1031         | 102.528°   |  | C104          | C103 | H1031         | 111.462°    |
| C104<br>4_675 | C103 | H1031         | 132.343°   |  | C105<br>4_675 | C103 | H1031         | 81.477°     |
| C102          | C103 | H1032         | 105.182°   |  | C103<br>4_675 | C103 | H1032         | 92.197°     |
| C104          | C103 | H1032         | 111.097°   |  | C104<br>4_675 | C103 | H1032         | 110.600°    |
| C105<br>4_675 | C103 | H1032         | 66.182°    |  | H1031         | C103 | H1032         | 109.045°    |
| C102<br>4_675 | C104 | C103          | 172.8(7)°  |  | C102<br>4_675 | C104 | C103<br>4_675 | 121.5(10)°  |
| C103          | C104 | C103<br>4_675 | 52.1(7)°   |  | C102<br>4_675 | C104 | C104<br>4_675 | 157.3(6)°   |
| C103          | C104 | C104<br>4_675 | 26.33(16)° |  | C103<br>4_675 | C104 | C104<br>4_675 | 76.5(7)°    |
| C102<br>4_675 | C104 | C105          | 64.0(5)°   |  | C103          | C104 | C105          | 111.05(7)°  |
| C103<br>4_675 | C104 | C105          | 61.1(7)°   |  | C104<br>4_675 | C104 | C105          | 137.03(15)° |
| C102<br>4_675 | C104 | H1041         | 77.670°    |  | C103          | C104 | H1041         | 109.243°    |
| C103<br>4_675 | C104 | H1041         | 137.359°   |  | C104<br>4_675 | C104 | H1041         | 98.635°     |
| C105          | C104 | H1041         | 107.594°   |  | C102<br>4_675 | C104 | H1042         | 70.206°     |
| C103          | C104 | H1042         | 108.415°   |  | C103<br>4_675 | C104 | H1042         | 113.356°    |
| C104<br>4_675 | C104 | H1042         | 90.377°    |  | C105          | C104 | H1042         | 111.526°    |
| H1041         | C104 | H1042         | 108.966°   |  | C101<br>4_675 | C105 | C102<br>4_675 | 60.2(4)°    |
| C101<br>4_675 | C105 | C103<br>4_675 | 126.1(6)°  |  | C102<br>4_675 | C105 | C103<br>4_675 | 66.9(3)°    |
| C101<br>4_675 | C105 | C104          | 100.7(5)°  |  | C102<br>4_675 | C105 | C104          | 40.5(3)°    |
| C103<br>4_675 | C105 | C104          | 27.7(2)°   |  | C101<br>4_675 | C105 | C106          | 17.8(6)°    |
| C102<br>4_675 | C105 | C106          | 75.8(3)°   |  | C103<br>4_675 | C105 | C106          | 137.7(4)°   |
| C104          | C105 | C106          | 115.72(7)° |  | C101<br>4_675 | C105 | H1051         | 104.002°    |

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|----------------|------|----------------|----------|--|----------------|------|----------------|-----------|
| C102<br>4_675  | C105 | H1051          | 113.159° |  | C103<br>4_675  | C105 | H1051          | 105.531°  |
| C104           | C105 | H1051          | 105.685° |  | C106           | C105 | H1051          | 106.974°  |
| C101<br>4_675  | C105 | H1052          | 121.008° |  | C102<br>4_675  | C105 | H1052          | 133.522°  |
| C103<br>4_675  | C105 | H1052          | 88.086°  |  | C104           | C105 | H1052          | 112.910°  |
| C106           | C105 | H1052          | 104.484° |  | C101<br>4_675  | C105 | H1012<br>4_675 | 38.878°   |
| C102<br>4_675  | C105 | H1012<br>4_675 | 98.608°  |  | C103<br>4_675  | C105 | H1012<br>4_675 | 164.841°  |
| C104           | C105 | H1012<br>4_675 | 138.850° |  | C106           | C105 | H1012<br>4_675 | 27.575°   |
| H1051          | C105 | H1052          | 111.002° |  | H1051          | C105 | H1012<br>4_675 | 83.933°   |
| H1052          | C105 | H1012<br>4_675 | 99.695°  |  | C101<br>4_675  | C106 | C105           | 84.6(14)° |
| C101<br>4_675  | C106 | H1061          | 93.246°  |  | C105           | C106 | H1061          | 110.237°  |
| C101<br>4_675  | C106 | H1062          | 35.979°  |  | C105           | C106 | H1062          | 106.341°  |
| H1061          | C106 | H1062          | 111.080° |  | C101<br>4_675  | C106 | H1063          | 148.236°  |
| C105           | C106 | H1063          | 106.646° |  | H1061          | C106 | H1063          | 109.532°  |
| H1062          | C106 | H1063          | 112.855° |  | C101<br>4_675  | C106 | H1011<br>4_675 | 83.334°   |
| C105           | C106 | H1011<br>4_675 | 127.196° |  | H1061          | C106 | H1011<br>4_675 | 121.625°  |
| H1062          | C106 | H1011<br>4_675 | 47.361°  |  | H1063          | C106 | H1011<br>4_675 | 66.056°   |
| C101<br>4_675  | C106 | H1012<br>4_675 | 104.532° |  | C105           | C106 | H1012<br>4_675 | 43.782°   |
| H1061          | C106 | H1012<br>4_675 | 70.514°  |  | H1062          | C106 | H1012<br>4_675 | 139.204°  |
| H1063          | C106 | H1012<br>4_675 | 103.833° |  | C101<br>4_675  | C106 | H1013<br>4_675 | 36.212°   |
| C105           | C106 | H1013<br>4_675 | 108.210° |  | H1061          | C106 | H1013<br>4_675 | 59.725°   |
| H1062          | C106 | H1013<br>4_675 | 54.133°  |  | H1063          | C106 | H1013<br>4_675 | 145.061°  |
| H1011<br>4_675 | C106 | H1012<br>4_675 | 165.684° |  | H1011<br>4_675 | C106 | H1013<br>4_675 | 90.621°   |
| H1012<br>4_675 | C106 | H1013<br>4_675 | 102.805° |  | C36            | H363 | C136           | 67.760°   |
| C36            | H363 | H1363          | 109.264° |  | C136           | H363 | H1363          | 121.358°  |

|               |       |                |          |  |               |       |                |          |
|---------------|-------|----------------|----------|--|---------------|-------|----------------|----------|
| C37           | H373  | C137           | 64.872°  |  | C37           | H373  | H1373          | 32.370°  |
| C137          | H373  | H1373          | 88.071°  |  | C36           | H1361 | C136           | 52.703°  |
| C36           | H1363 | C136           | 61.902°  |  | C36           | H1363 | H363           | 62.366°  |
| C136          | H1363 | H363           | 50.341°  |  | C37           | H1373 | C137           | 70.454°  |
| C37           | H1373 | H373           | 140.158° |  | C137          | H1373 | H373           | 80.048°  |
| C102<br>4_675 | H1041 | C104           | 53.142°  |  | C102<br>4_675 | H1042 | C104           | 56.970°  |
| C35           | H351  | H352           | 66.735°  |  | C35           | H352  | H351           | 70.098°  |
| C101<br>4_675 | H1061 | C106           | 25.545°  |  | C101<br>4_675 | H1062 | C106           | 24.391°  |
| C101<br>4_675 | H1062 | H1011<br>4_675 | 84.058°  |  | C106          | H1062 | H1011<br>4_675 | 59.672°  |
| C101          | H1011 | C106<br>4_675  | 29.106°  |  | C101          | H1011 | H1062<br>4_675 | 43.865°  |
| C106<br>4_675 | H1011 | H1062<br>4_675 | 72.967°  |  | C101          | H1012 | C105<br>4_675  | 95.668°  |
| C101          | H1012 | C106<br>4_675  | 28.131°  |  | C105<br>4_675 | H1012 | C106<br>4_675  | 108.643° |
| C101          | H1013 | C106<br>4_675  | 16.931°  |  |               |       |                |          |





**tetra-*n*-butylammonium fluoride bis(pinacol) (TBAF(Pin)<sub>2</sub>, 7.11):**

**X-ray** (single-crystal) Colourless needles of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.11** in THF, which had previously been prepared by dissolving **7.11** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography Number: 064GGKE01

## Crystal Data

$$a = 18.6017(3) \text{ \AA} \quad \alpha = 90^\circ$$

$$b = 18.6158(3) \text{ \AA} \quad \beta = 90^\circ$$

$$c = 19.1084(3) \text{ \AA} \quad \gamma = 90^\circ$$

$$\text{Volume} \quad 6616.96(18) \text{ \AA}^3$$

$$\text{Space group} \quad P b c a$$

$$\text{Formula} \quad C_{28} H_{64} F_1 N_1 O_4$$

$$\text{Cell determined from} \quad 7082 \text{ reflections}$$

$$\text{Temperature} \quad 150 \text{ K}$$

$$\text{Shape} \quad \text{prism}$$

$$\text{Colour} \quad \text{clear\_pale\_colourless}$$

$$D_x \quad 1.00 \text{ Mg m}^{-3}$$

$$\mu \quad 0.068 \text{ mm}^{-1}$$

$$\text{Absorption correction} \quad \text{multi-scan}$$

$$T_{\min} \quad 0.79$$

$$\text{Crystal Class} \quad \text{orthorhombic}$$

$$Z = \quad 8$$

$$M_r \quad 497.82$$

$$\text{Cell } \theta \text{ range} = 5 - 26^\circ$$

$$\text{Size} \quad 0.08 \times 0.10 \times 0.49 \text{ mm}$$

$$F000 \quad 2240.000$$

$$T_{\max} \quad 0.99$$

## Data Collection

$$\text{Diffractometer} \quad \text{multi-scan}$$

$$\text{Scan type} \quad \omega \text{ scans}$$

$$\text{Reflections measured} \quad 96568$$

$$\text{Independent reflections} \quad 6466$$

$$R_{\text{int}} \quad 0.0219$$

$$\theta_{\max} \quad 26.0203$$

$$h = \quad -22 \rightarrow 22$$

$$k = \quad -22 \rightarrow 22$$

$$l = \quad -23 \rightarrow 23$$

## Refinement

$$\Delta\rho_{\min} = \quad -0.14 \text{ e \AA}^{-3}$$

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\max}$ =  | 0.20 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 6466                                                                                                                                                                                        |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 308                                                                                                                                                                                         |
| S =                    | 0.99                                                                                                                                                                                        |
| R-factor               | 0.056                                                                                                                                                                                       |
| weighted R-factor      | 0.104                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0004                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.050 \times P)^2 + 1.370 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| O11   | 0.56788(7)  | 0.72138(8)  | 0.30033(6)  | 0.0513                 | 1.0000    |
| O12   | 0.54606(7)  | 0.65605(7)  | 0.44062(6)  | 0.0501                 | 1.0000    |
| C13   | 0.62234(10) | 0.71496(12) | 0.35288(9)  | 0.0477                 | 1.0000    |
| C14   | 0.62025(14) | 0.78300(13) | 0.39782(11) | 0.0615                 | 1.0000    |
| C15   | 0.69275(13) | 0.71186(18) | 0.31307(11) | 0.0764                 | 1.0000    |
| C16   | 0.60849(10) | 0.64646(12) | 0.39733(9)  | 0.0471                 | 1.0000    |
| C17   | 0.59632(15) | 0.58091(14) | 0.35078(12) | 0.0698                 | 1.0000    |
| C18   | 0.66914(13) | 0.63180(14) | 0.44888(11) | 0.0663                 | 1.0000    |
| O21   | 0.37360(8)  | 0.81345(7)  | 0.29469(6)  | 0.0539                 | 1.0000    |
| O22   | 0.41449(8)  | 0.83041(7)  | 0.44283(6)  | 0.0519                 | 1.0000    |
| C23   | 0.33862(10) | 0.86068(10) | 0.34234(9)  | 0.0412                 | 1.0000    |
| C24   | 0.27629(13) | 0.82080(13) | 0.37657(12) | 0.0628                 | 1.0000    |
| C25   | 0.30923(14) | 0.92073(12) | 0.29649(10) | 0.0597                 | 1.0000    |
| C26   | 0.39302(11) | 0.88796(10) | 0.39833(9)  | 0.0440                 | 1.0000    |
| C27   | 0.46051(14) | 0.91905(16) | 0.36375(13) | 0.0755                 | 1.0000    |
| C28   | 0.35884(15) | 0.94266(12) | 0.44785(11) | 0.0673                 | 1.0000    |
| F1    | 0.44450(6)  | 0.71655(6)  | 0.36576(6)  | 0.0533                 | 1.0000    |
| N31   | 0.48187(7)  | 0.73666(7)  | 0.62204(6)  | 0.0265                 | 1.0000    |
| C32   | 0.54096(8)  | 0.77609(9)  | 0.58261(7)  | 0.0293                 | 1.0000    |
| C33   | 0.59799(9)  | 0.81016(10) | 0.62899(8)  | 0.0366                 | 1.0000    |
| C34   | 0.65669(10) | 0.84451(10) | 0.58584(9)  | 0.0389                 | 1.0000    |
| C35   | 0.71542(11) | 0.87771(11) | 0.63084(10) | 0.0455                 | 1.0000    |
| C36   | 0.44411(9)  | 0.78604(9)  | 0.67381(7)  | 0.0295                 | 1.0000    |
| C37   | 0.41070(10) | 0.85332(9)  | 0.64273(8)  | 0.0375                 | 1.0000    |
| C38   | 0.37834(11) | 0.89881(10) | 0.70092(9)  | 0.0449                 | 1.0000    |
| C39   | 0.34221(12) | 0.96574(12) | 0.67396(12) | 0.0595                 | 1.0000    |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| C40  | 0.51289(9)  | 0.67500(8)  | 0.66476(7)  | 0.0295 | 1.0000 |
| C41  | 0.55143(10) | 0.61832(9)  | 0.62258(8)  | 0.0372 | 1.0000 |
| C42  | 0.57587(13) | 0.55634(11) | 0.66721(10) | 0.0540 | 1.0000 |
| C43  | 0.61050(15) | 0.49724(12) | 0.62429(12) | 0.0672 | 1.0000 |
| C44  | 0.42948(8)  | 0.70879(9)  | 0.56737(7)  | 0.0287 | 1.0000 |
| C45  | 0.37106(9)  | 0.66015(10) | 0.59495(8)  | 0.0359 | 1.0000 |
| C46  | 0.32062(11) | 0.63635(11) | 0.53737(10) | 0.0461 | 1.0000 |
| C47  | 0.26771(11) | 0.58014(11) | 0.56125(11) | 0.0509 | 1.0000 |
| H253 | 0.28235(14) | 0.95456(12) | 0.32385(10) | 0.0882 | 1.0000 |
| H252 | 0.34914(14) | 0.94699(12) | 0.27573(10) | 0.0894 | 1.0000 |
| H251 | 0.27917(14) | 0.90107(12) | 0.26049(10) | 0.0890 | 1.0000 |
| H241 | 0.24818(13) | 0.85434(13) | 0.40561(12) | 0.0934 | 1.0000 |
| H242 | 0.24631(13) | 0.79846(13) | 0.34115(12) | 0.0942 | 1.0000 |
| H243 | 0.29520(13) | 0.78456(13) | 0.40886(12) | 0.0925 | 1.0000 |
| H281 | 0.39389(15) | 0.95631(12) | 0.48441(11) | 0.0996 | 1.0000 |
| H282 | 0.34643(15) | 0.98577(12) | 0.42098(11) | 0.1003 | 1.0000 |
| H283 | 0.31407(15) | 0.92261(12) | 0.46889(11) | 0.1005 | 1.0000 |
| H273 | 0.49416(14) | 0.93434(16) | 0.39788(13) | 0.1127 | 1.0000 |
| H272 | 0.44589(14) | 0.95857(16) | 0.33390(13) | 0.1119 | 1.0000 |
| H271 | 0.48174(14) | 0.88289(16) | 0.33356(13) | 0.1129 | 1.0000 |
| H152 | 0.69625(13) | 0.75570(18) | 0.28185(11) | 0.1138 | 1.0000 |
| H153 | 0.73223(13) | 0.71112(18) | 0.34831(11) | 0.1132 | 1.0000 |
| H151 | 0.69319(13) | 0.66704(18) | 0.28383(11) | 0.1141 | 1.0000 |
| H142 | 0.62888(14) | 0.82717(13) | 0.36794(11) | 0.0912 | 1.0000 |
| H141 | 0.65852(14) | 0.78109(13) | 0.43274(11) | 0.0906 | 1.0000 |
| H143 | 0.57247(14) | 0.78507(13) | 0.42142(11) | 0.0911 | 1.0000 |
| H181 | 0.71139(13) | 0.62428(14) | 0.42343(11) | 0.0984 | 1.0000 |
| H183 | 0.67505(13) | 0.67209(14) | 0.47875(11) | 0.0985 | 1.0000 |
| H182 | 0.65695(13) | 0.58983(14) | 0.47572(11) | 0.0991 | 1.0000 |
| H173 | 0.63914(15) | 0.57171(14) | 0.32189(12) | 0.1019 | 1.0000 |
| H171 | 0.58482(15) | 0.53992(14) | 0.38015(12) | 0.1049 | 1.0000 |
| H172 | 0.55603(15) | 0.59100(14) | 0.32018(12) | 0.1046 | 1.0000 |
| H401 | 0.54427(9)  | 0.69762(8)  | 0.69796(7)  | 0.0346 | 1.0000 |
| H402 | 0.47344(9)  | 0.65408(8)  | 0.68842(7)  | 0.0345 | 1.0000 |
| H411 | 0.59331(10) | 0.64016(9)  | 0.60220(8)  | 0.0465 | 1.0000 |
| H412 | 0.52140(10) | 0.60097(9)  | 0.58562(8)  | 0.0460 | 1.0000 |
| H421 | 0.61106(13) | 0.57524(11) | 0.70291(10) | 0.0653 | 1.0000 |
| H422 | 0.53474(13) | 0.53739(11) | 0.69202(10) | 0.0665 | 1.0000 |
| H431 | 0.62597(15) | 0.45662(12) | 0.65453(12) | 0.1004 | 1.0000 |
| H433 | 0.65309(15) | 0.51604(12) | 0.60050(12) | 0.1016 | 1.0000 |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| H432 | 0.57638(15) | 0.47822(12) | 0.59075(12) | 0.1009 | 1.0000 |
| H321 | 0.56304(8)  | 0.74295(9)  | 0.55016(7)  | 0.0333 | 1.0000 |
| H322 | 0.51673(8)  | 0.81123(9)  | 0.55570(7)  | 0.0340 | 1.0000 |
| H331 | 0.61906(9)  | 0.77300(10) | 0.65914(8)  | 0.0462 | 1.0000 |
| H332 | 0.57681(9)  | 0.84644(10) | 0.65818(8)  | 0.0453 | 1.0000 |
| H341 | 0.67923(10) | 0.80815(10) | 0.55467(9)  | 0.0476 | 1.0000 |
| H342 | 0.63445(10) | 0.88029(10) | 0.55648(9)  | 0.0490 | 1.0000 |
| H351 | 0.74791(11) | 0.90538(11) | 0.60129(10) | 0.0665 | 1.0000 |
| H352 | 0.74051(11) | 0.84069(11) | 0.65474(10) | 0.0674 | 1.0000 |
| H353 | 0.69491(11) | 0.91069(11) | 0.66623(10) | 0.0669 | 1.0000 |
| H441 | 0.45536(8)  | 0.68293(9)  | 0.53340(7)  | 0.0320 | 1.0000 |
| H442 | 0.40807(8)  | 0.75122(9)  | 0.54610(7)  | 0.0327 | 1.0000 |
| H451 | 0.39223(9)  | 0.61785(10) | 0.61477(8)  | 0.0452 | 1.0000 |
| H452 | 0.34494(9)  | 0.68354(10) | 0.63098(8)  | 0.0447 | 1.0000 |
| H461 | 0.34966(11) | 0.61578(11) | 0.50139(10) | 0.0573 | 1.0000 |
| H462 | 0.29636(11) | 0.67614(11) | 0.51813(10) | 0.0583 | 1.0000 |
| H473 | 0.23461(11) | 0.56692(11) | 0.52450(11) | 0.0761 | 1.0000 |
| H472 | 0.29289(11) | 0.53718(11) | 0.57718(11) | 0.0764 | 1.0000 |
| H471 | 0.24103(11) | 0.59835(11) | 0.60296(11) | 0.0752 | 1.0000 |
| H362 | 0.47839(9)  | 0.79998(9)  | 0.70907(7)  | 0.0347 | 1.0000 |
| H361 | 0.40861(9)  | 0.75719(9)  | 0.69723(7)  | 0.0364 | 1.0000 |
| H372 | 0.44774(10) | 0.88200(9)  | 0.61893(8)  | 0.0453 | 1.0000 |
| H371 | 0.37266(10) | 0.84056(9)  | 0.60951(8)  | 0.0463 | 1.0000 |
| H382 | 0.41614(11) | 0.91199(10) | 0.73348(9)  | 0.0554 | 1.0000 |
| H381 | 0.34398(11) | 0.86896(10) | 0.72466(9)  | 0.0546 | 1.0000 |
| H393 | 0.31885(12) | 0.99445(12) | 0.71105(12) | 0.0884 | 1.0000 |
| H391 | 0.37852(12) | 0.99646(12) | 0.65063(12) | 0.0891 | 1.0000 |
| H392 | 0.30590(12) | 0.95286(12) | 0.63999(12) | 0.0890 | 1.0000 |
| H221 | 0.42546(8)  | 0.79461(7)  | 0.41868(6)  | 0.0776 | 1.0000 |
| H121 | 0.51107(7)  | 0.66929(7)  | 0.41337(6)  | 0.0755 | 1.0000 |
| H211 | 0.39551(8)  | 0.78065(7)  | 0.31484(6)  | 0.0810 | 1.0000 |
| H111 | 0.52716(7)  | 0.72174(8)  | 0.32370(6)  | 0.0768 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| O11   | 0.0511(8)       | 0.0796(10)      | 0.0231(5)       | 0.0024(6)       | -0.0066(5)      | 0.0045(7)       |
| O12   | 0.0539(8)       | 0.0644(9)       | 0.0320(6)       | 0.0059(6)       | 0.0056(6)       | 0.0184(7)       |
| C13   | 0.0422(10)      | 0.0768(14)      | 0.0240(7)       | -0.0014(8)      | -0.0033(7)      | 0.0044(10)      |
| C14   | 0.0692(14)      | 0.0720(15)      | 0.0435(10)      | -0.0023(10)     | -0.0099(10)     | -0.0085(12)     |

|     |            |            |            |             |             |             |
|-----|------------|------------|------------|-------------|-------------|-------------|
| C15 | 0.0491(13) | 0.137(2)   | 0.0426(11) | 0.0001(14)  | 0.0049(10)  | -0.0054(14) |
| C16 | 0.0472(11) | 0.0659(13) | 0.0282(8)  | -0.0041(8)  | 0.0017(8)   | 0.0180(10)  |
| C17 | 0.0774(16) | 0.0736(16) | 0.0583(12) | -0.0163(12) | -0.0040(12) | 0.0215(13)  |
| C18 | 0.0621(14) | 0.0955(18) | 0.0412(10) | -0.0019(11) | -0.0070(10) | 0.0345(13)  |
| O21 | 0.0733(9)  | 0.0592(9)  | 0.0293(6)  | -0.0062(6)  | 0.0018(6)   | 0.0297(7)   |
| O22 | 0.0766(10) | 0.0490(8)  | 0.0302(6)  | 0.0042(5)   | -0.0029(6)  | 0.0186(7)   |
| C23 | 0.0499(11) | 0.0418(10) | 0.0319(8)  | -0.0032(7)  | 0.0036(8)   | 0.0150(8)   |
| C24 | 0.0572(13) | 0.0650(14) | 0.0662(13) | -0.0079(11) | 0.0099(11)  | -0.0051(11) |
| C25 | 0.0774(15) | 0.0557(13) | 0.0461(10) | 0.0012(9)   | -0.0108(11) | 0.0221(11)  |
| C26 | 0.0569(12) | 0.0413(10) | 0.0339(9)  | 0.0050(8)   | -0.0003(8)  | 0.0061(9)   |
| C27 | 0.0691(16) | 0.0837(18) | 0.0737(15) | 0.0207(14)  | -0.0043(13) | -0.0189(13) |
| C28 | 0.106(2)   | 0.0471(12) | 0.0488(11) | -0.0107(10) | -0.0121(12) | 0.0186(12)  |
| F1  | 0.0467(6)  | 0.0531(7)  | 0.0601(6)  | -0.0014(5)  | -0.0021(5)  | 0.0159(5)   |
| N31 | 0.0293(7)  | 0.0307(7)  | 0.0197(5)  | 0.0010(5)   | -0.0001(5)  | 0.0013(6)   |
| C32 | 0.0321(8)  | 0.0323(8)  | 0.0236(7)  | 0.0018(6)   | 0.0033(6)   | -0.0001(7)  |
| C33 | 0.0382(9)  | 0.0437(10) | 0.0279(8)  | -0.0023(7)  | 0.0006(7)   | -0.0068(8)  |
| C34 | 0.0424(10) | 0.0431(10) | 0.0311(8)  | 0.0010(7)   | 0.0016(7)   | -0.0095(8)  |
| C35 | 0.0475(11) | 0.0495(11) | 0.0395(9)  | -0.0028(8)  | 0.0011(8)   | -0.0150(9)  |
| C36 | 0.0325(8)  | 0.0351(8)  | 0.0208(6)  | -0.0016(6)  | 0.0026(6)   | 0.0020(7)   |
| C37 | 0.0437(10) | 0.0378(9)  | 0.0310(8)  | -0.0017(7)  | 0.0000(7)   | 0.0073(8)   |
| C38 | 0.0456(10) | 0.0474(11) | 0.0418(9)  | -0.0136(8)  | -0.0018(8)  | 0.0103(9)   |
| C39 | 0.0614(13) | 0.0510(12) | 0.0660(13) | -0.0198(10) | -0.0141(11) | 0.0202(10)  |
| C40 | 0.0323(8)  | 0.0332(9)  | 0.0229(7)  | 0.0048(6)   | -0.0013(6)  | -0.0005(7)  |
| C41 | 0.0426(9)  | 0.0379(9)  | 0.0310(8)  | 0.0028(7)   | 0.0023(7)   | 0.0086(8)   |
| C42 | 0.0703(14) | 0.0475(11) | 0.0444(10) | 0.0133(9)   | 0.0126(10)  | 0.0218(10)  |
| C43 | 0.0909(17) | 0.0490(12) | 0.0617(13) | 0.0185(11)  | 0.0264(13)  | 0.0331(12)  |
| C44 | 0.0306(8)  | 0.0350(9)  | 0.0205(6)  | -0.0008(6)  | -0.0033(6)  | 0.0024(7)   |
| C45 | 0.0358(9)  | 0.0410(10) | 0.0307(8)  | 0.0014(7)   | -0.0006(7)  | -0.0024(7)  |
| C46 | 0.0469(11) | 0.0508(11) | 0.0405(9)  | 0.0031(8)   | -0.0077(8)  | -0.0104(9)  |
| C47 | 0.0459(12) | 0.0451(11) | 0.0619(12) | 0.0072(9)   | -0.0122(9)  | -0.0102(9)  |

## Distances

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| O11 | C13  | 1.431(2)Å |  | O11 | H111 | 0.879Å    |
| O12 | C16  | 1.437(2)Å |  | O12 | H121 | 0.869Å    |
| C13 | C14  | 1.531(3)Å |  | C13 | C15  | 1.516(3)Å |
| C13 | C16  | 1.554(3)Å |  | C14 | H142 | 1.014Å    |
| C14 | H141 | 0.976Å    |  | C14 | H143 | 0.997Å    |
| C15 | H152 | 1.013Å    |  | C15 | H153 | 0.997Å    |
| C15 | H151 | 1.004Å    |  | C16 | C17  | 1.527(3)Å |

|     |      |             |  |     |      |             |
|-----|------|-------------|--|-----|------|-------------|
| C16 | C18  | 1.522(3)Å   |  | C17 | H173 | 0.984Å      |
| C17 | H171 | 0.971Å      |  | C17 | H172 | 0.969Å      |
| C18 | H181 | 0.935Å      |  | C18 | H183 | 0.949Å      |
| C18 | H182 | 0.962Å      |  | O21 | C23  | 1.423(2)Å   |
| O21 | H211 | 0.829Å      |  | O22 | C26  | 1.425(2)Å   |
| O22 | H221 | 0.836Å      |  | C23 | C24  | 1.524(3)Å   |
| C23 | C25  | 1.522(3)Å   |  | C23 | C26  | 1.558(3)Å   |
| C24 | H241 | 0.985Å      |  | C24 | H242 | 0.971Å      |
| C24 | H243 | 0.980Å      |  | C25 | H253 | 0.959Å      |
| C25 | H252 | 0.974Å      |  | C25 | H251 | 0.959Å      |
| C26 | C27  | 1.532(3)Å   |  | C26 | C28  | 1.528(3)Å   |
| C27 | H273 | 0.948Å      |  | C27 | H272 | 0.970Å      |
| C27 | H271 | 0.971Å      |  | C28 | H281 | 0.989Å      |
| C28 | H282 | 0.980Å      |  | C28 | H283 | 0.997Å      |
| N31 | C32  | 1.5216(19)Å |  | N31 | C36  | 1.5221(18)Å |
| N31 | C40  | 1.5222(19)Å |  | N31 | C44  | 1.5201(18)Å |
| C32 | C33  | 1.521(2)Å   |  | C32 | H321 | 0.966Å      |
| C32 | H322 | 0.946Å      |  | C33 | C34  | 1.510(2)Å   |
| C33 | H331 | 0.982Å      |  | C33 | H332 | 0.960Å      |
| C34 | C35  | 1.521(2)Å   |  | C34 | H341 | 0.994Å      |
| C34 | H342 | 0.964Å      |  | C35 | H351 | 0.974Å      |
| C35 | H352 | 0.949Å      |  | C35 | H353 | 0.990Å      |
| C36 | C37  | 1.519(2)Å   |  | C36 | H362 | 0.963Å      |
| C36 | H361 | 0.962Å      |  | C37 | C38  | 1.522(2)Å   |
| C37 | H372 | 0.983Å      |  | C37 | H371 | 0.980Å      |
| C38 | C39  | 1.507(3)Å   |  | C38 | H382 | 0.971Å      |
| C38 | H381 | 0.961Å      |  | C39 | H393 | 0.988Å      |
| C39 | H391 | 0.991Å      |  | C39 | H392 | 0.967Å      |
| C40 | C41  | 1.509(2)Å   |  | C40 | H401 | 0.959Å      |
| C40 | H402 | 0.946Å      |  | C41 | C42  | 1.505(2)Å   |
| C41 | H411 | 0.961Å      |  | C41 | H412 | 0.957Å      |
| C42 | C43  | 1.516(3)Å   |  | C42 | H421 | 1.009Å      |
| C42 | H422 | 0.967Å      |  | C43 | H431 | 0.994Å      |
| C43 | H433 | 0.978Å      |  | C43 | H432 | 0.969Å      |
| C44 | C45  | 1.509(2)Å   |  | C44 | H441 | 0.941Å      |
| C44 | H442 | 0.973Å      |  | C45 | C46  | 1.512(2)Å   |
| C45 | H451 | 0.959Å      |  | C45 | H452 | 0.949Å      |
| C46 | C47  | 1.507(3)Å   |  | C46 | H461 | 0.954Å      |
| C46 | H462 | 0.942Å      |  | C47 | H473 | 0.966Å      |
| C47 | H472 | 0.975Å      |  | C47 | H471 | 0.998Å      |

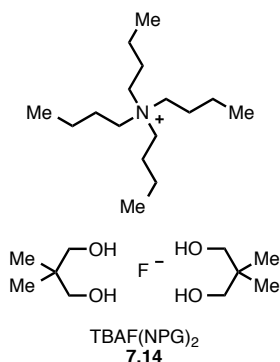
## Angles

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C13  | O11 | H111 | 104.719°    |  | C16  | O12 | H121 | 107.193°    |
| O11  | C13 | C14  | 107.84(17)° |  | O11  | C13 | C15  | 105.23(14)° |
| C14  | C13 | C15  | 109.6(2)°   |  | O11  | C13 | C16  | 109.55(16)° |
| C14  | C13 | C16  | 111.61(15)° |  | C15  | C13 | C16  | 112.74(19)° |
| C13  | C14 | H142 | 110.561°    |  | C13  | C14 | H141 | 109.554°    |
| H142 | C14 | H141 | 107.402°    |  | C13  | C14 | H143 | 107.943°    |
| H142 | C14 | H143 | 111.379°    |  | H141 | C14 | H143 | 110.000°    |
| C13  | C15 | H152 | 108.697°    |  | C13  | C15 | H153 | 107.357°    |
| H152 | C15 | H153 | 111.203°    |  | C13  | C15 | H151 | 108.537°    |
| H152 | C15 | H151 | 109.946°    |  | H153 | C15 | H151 | 111.001°    |
| O12  | C16 | C13  | 110.29(15)° |  | O12  | C16 | C17  | 108.35(18)° |
| C13  | C16 | C17  | 111.23(15)° |  | O12  | C16 | C18  | 104.40(14)° |
| C13  | C16 | C18  | 112.21(18)° |  | C17  | C16 | C18  | 110.09(18)° |
| C16  | C17 | H173 | 110.235°    |  | C16  | C17 | H171 | 108.912°    |
| H173 | C17 | H171 | 111.450°    |  | C16  | C17 | H172 | 108.138°    |
| H173 | C17 | H172 | 108.732°    |  | H171 | C17 | H172 | 109.310°    |
| C16  | C18 | H181 | 108.251°    |  | C16  | C18 | H183 | 109.482°    |
| H181 | C18 | H183 | 109.493°    |  | C16  | C18 | H182 | 108.419°    |
| H181 | C18 | H182 | 110.741°    |  | H183 | C18 | H182 | 110.410°    |
| C23  | O21 | H211 | 112.494°    |  | C26  | O22 | H221 | 109.791°    |
| O21  | C23 | C24  | 108.76(17)° |  | O21  | C23 | C25  | 104.46(14)° |
| C24  | C23 | C25  | 109.36(18)° |  | O21  | C23 | C26  | 110.11(15)° |
| C24  | C23 | C26  | 110.99(15)° |  | C25  | C23 | C26  | 112.91(16)° |
| C23  | C24 | H241 | 109.681°    |  | C23  | C24 | H242 | 110.273°    |
| H241 | C24 | H242 | 111.063°    |  | C23  | C24 | H243 | 109.418°    |
| H241 | C24 | H243 | 105.796°    |  | H242 | C24 | H243 | 110.509°    |
| C23  | C25 | H253 | 110.840°    |  | C23  | C25 | H252 | 109.236°    |
| H253 | C25 | H252 | 106.855°    |  | C23  | C25 | H251 | 110.001°    |
| H253 | C25 | H251 | 109.739°    |  | H252 | C25 | H251 | 110.120°    |
| O22  | C26 | C23  | 110.29(15)° |  | O22  | C26 | C27  | 108.16(18)° |
| C23  | C26 | C27  | 111.05(15)° |  | O22  | C26 | C28  | 104.36(14)° |
| C23  | C26 | C28  | 111.85(17)° |  | C27  | C26 | C28  | 110.9(2)°   |
| C26  | C27 | H273 | 110.970°    |  | C26  | C27 | H272 | 108.084°    |
| H273 | C27 | H272 | 111.237°    |  | C26  | C27 | H271 | 109.134°    |
| H273 | C27 | H271 | 110.398°    |  | H272 | C27 | H271 | 106.892°    |
| C26  | C28 | H281 | 109.528°    |  | C26  | C28 | H282 | 108.606°    |
| H281 | C28 | H282 | 108.350°    |  | C26  | C28 | H283 | 110.349°    |
| H281 | C28 | H283 | 111.235°    |  | H282 | C28 | H283 | 108.708°    |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C32  | N31 | C36  | 111.34(12)° |  | C32  | N31 | C40  | 110.82(11)° |
| C36  | N31 | C40  | 106.37(10)° |  | C32  | N31 | C44  | 106.71(10)° |
| C36  | N31 | C44  | 110.92(11)° |  | C40  | N31 | C44  | 110.74(12)° |
| N31  | C32 | C33  | 114.61(11)° |  | N31  | C32 | H321 | 108.473°    |
| C33  | C32 | H321 | 110.108°    |  | N31  | C32 | H322 | 104.968°    |
| C33  | C32 | H322 | 111.144°    |  | H321 | C32 | H322 | 107.166°    |
| C32  | C33 | C34  | 111.27(12)° |  | C32  | C33 | H331 | 109.065°    |
| C34  | C33 | H331 | 109.272°    |  | C32  | C33 | H332 | 110.205°    |
| C34  | C33 | H332 | 108.423°    |  | H331 | C33 | H332 | 108.564°    |
| C33  | C34 | C35  | 112.49(13)° |  | C33  | C34 | H341 | 110.106°    |
| C35  | C34 | H341 | 108.199°    |  | C33  | C34 | H342 | 107.451°    |
| C35  | C34 | H342 | 110.870°    |  | H341 | C34 | H342 | 107.617°    |
| C34  | C35 | H351 | 109.427°    |  | C34  | C35 | H352 | 109.265°    |
| H351 | C35 | H352 | 110.947°    |  | C34  | C35 | H353 | 111.184°    |
| H351 | C35 | H353 | 107.888°    |  | H352 | C35 | H353 | 108.123°    |
| N31  | C36 | C37  | 115.63(11)° |  | N31  | C36 | H362 | 108.170°    |
| C37  | C36 | H362 | 108.796°    |  | N31  | C36 | H361 | 106.374°    |
| C37  | C36 | H361 | 111.187°    |  | H362 | C36 | H361 | 106.240°    |
| C36  | C37 | C38  | 109.57(13)° |  | C36  | C37 | H372 | 109.988°    |
| C38  | C37 | H372 | 108.239°    |  | C36  | C37 | H371 | 110.418°    |
| C38  | C37 | H371 | 108.827°    |  | H372 | C37 | H371 | 109.754°    |
| C37  | C38 | C39  | 112.77(16)° |  | C37  | C38 | H382 | 108.816°    |
| C39  | C38 | H382 | 109.471°    |  | C37  | C38 | H381 | 106.642°    |
| C39  | C38 | H381 | 110.057°    |  | H382 | C38 | H381 | 108.992°    |
| C38  | C39 | H393 | 113.465°    |  | C38  | C39 | H391 | 109.083°    |
| H393 | C39 | H391 | 108.073°    |  | C38  | C39 | H392 | 109.636°    |
| H393 | C39 | H392 | 107.973°    |  | H391 | C39 | H392 | 108.490°    |
| N31  | C40 | C41  | 114.90(11)° |  | N31  | C40 | H401 | 104.723°    |
| C41  | C40 | H401 | 111.777°    |  | N31  | C40 | H402 | 105.829°    |
| C41  | C40 | H402 | 109.639°    |  | H401 | C40 | H402 | 109.678°    |
| C40  | C41 | C42  | 112.14(13)° |  | C40  | C41 | H411 | 107.809°    |
| C42  | C41 | H411 | 107.990°    |  | C40  | C41 | H412 | 110.677°    |
| C42  | C41 | H412 | 109.622°    |  | H411 | C41 | H412 | 108.481°    |
| C41  | C42 | C43  | 112.23(15)° |  | C41  | C42 | H421 | 108.166°    |
| C43  | C42 | H421 | 110.079°    |  | C41  | C42 | H422 | 108.563°    |
| C43  | C42 | H422 | 109.685°    |  | H421 | C42 | H422 | 108.008°    |
| C42  | C43 | H431 | 111.131°    |  | C42  | C43 | H433 | 109.628°    |
| H431 | C43 | H433 | 107.938°    |  | C42  | C43 | H432 | 110.151°    |
| H431 | C43 | H432 | 107.227°    |  | H433 | C43 | H432 | 110.723°    |
| N31  | C44 | C45  | 115.24(12)° |  | N31  | C44 | H441 | 108.714°    |



|      |     |      |             |  |      |     |      |          |
|------|-----|------|-------------|--|------|-----|------|----------|
| C45  | C44 | H441 | 107.605°    |  | N31  | C44 | H442 | 105.790° |
| C45  | C44 | H442 | 109.755°    |  | H441 | C44 | H442 | 109.668° |
| C44  | C45 | C46  | 111.61(13)° |  | C44  | C45 | H451 | 109.577° |
| C46  | C45 | H451 | 107.563°    |  | C44  | C45 | H452 | 110.293° |
| C46  | C45 | H452 | 110.163°    |  | H451 | C45 | H452 | 107.505° |
| C45  | C46 | C47  | 112.84(15)° |  | C45  | C46 | H461 | 106.889° |
| C47  | C46 | H461 | 107.998°    |  | C45  | C46 | H462 | 110.540° |
| C47  | C46 | H462 | 110.560°    |  | H461 | C46 | H462 | 107.781° |
| C46  | C47 | H473 | 111.904°    |  | C46  | C47 | H472 | 110.493° |
| H473 | C47 | H472 | 108.913°    |  | C46  | C47 | H471 | 109.309° |
| H473 | C47 | H471 | 110.487°    |  | H472 | C47 | H471 | 105.545° |



**tetra-*n*-butylammonium fluoride bis(neopentyl glycol) (TBAF(NPG)<sub>2</sub>, 7.14):**

**X-ray** (single-crystal) Colourless plate-like crystals of X-ray quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.14** in THF, which had previously been prepared by dissolving **7.14** in THF at room temperature and filtering to remove residual solid.

Oxford Crystallography Number: 034KME12

## Crystal Data

$a = 22.51660(10) \text{ \AA}$   $\alpha = 90^\circ$

$b = 14.28630(10) \text{ \AA}$   $\beta = 103.6255(5)^\circ$

$c = 19.87830(10) \text{ \AA}$   $\gamma = 90^\circ$

Volume  $6214.47(6) \text{ \AA}^3$   
 Space group  $C 1 2/c 1$   
 Formula  $C_{26} H_{60} F_1 N_1 O_4$   
 Cell determined from 39155 reflections  
 Temperature 150K  
 Shape block  
 Colour clear\_pale\_colourless  
 $D_x$   $1.00 \text{ Mg m}^{-3}$   
 $\mu$   $0.549 \text{ mm}^{-1}$   
 Absorption correction multi-scan  
 $T_{\min}$  0.67

Crystal Class monoclinic  
 $Z = 8$   
 $M_r$  469.76  
 Cell  $\theta$  range =  $4 - 77^\circ$   
 Size  $0.18 \times 0.20 \times 0.28 \text{ mm}$   
 $F_{000}$  2112.000  
 $T_{\max}$  0.91

## Data Collection

Diffractometer multi-scan  
 Scan type  $\omega$  scans  
 Reflections measured 66092  
 Independent reflections 6505  
 $R_{\text{int}}$  0.0232  
 $\theta_{\max}$   $76.7106$   
 $h = -28 \rightarrow 28$   
 $k = -17 \rightarrow 18$   
 $l = -21 \rightarrow 24$

## Refinement

$\Delta\rho_{\min} = -0.24 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\max} = 0.49 \text{ e \AA}^{-3}$   
 Reflections used 5509

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cutoff: I >            | -3.00 $\sigma$ (I)                                                                                                                                                                          |
| Parameters refined     | 289                                                                                                                                                                                         |
| S =                    | 0.99                                                                                                                                                                                        |
| R-factor               | 0.058                                                                                                                                                                                       |
| weighted R-factor      | 0.152                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0005                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.079 \times P)^2 + 5.765 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | <i>x</i>    | <i>y</i>    | <i>z</i>    | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| F1    | 0.27929(5)  | 0.55808(9)  | 0.84295(6)  | 0.0629                 | 1.0000    |
| O11   | 0.19226(6)  | 0.56868(9)  | 0.90730(6)  | 0.0512                 | 1.0000    |
| C12   | 0.17577(9)  | 0.47292(14) | 0.90524(9)  | 0.0525                 | 1.0000    |
| C13   | 0.12471(7)  | 0.44455(13) | 0.84337(9)  | 0.0468                 | 1.0000    |
| C14   | 0.06545(10) | 0.4930(3)   | 0.84832(14) | 0.0936                 | 1.0000    |
| C15   | 0.14046(8)  | 0.47872(15) | 0.77642(9)  | 0.0543                 | 1.0000    |
| C16   | 0.11831(15) | 0.33954(19) | 0.84267(17) | 0.0964                 | 1.0000    |
| O21   | 0.19725(6)  | 0.44414(10) | 0.76830(7)  | 0.0583                 | 1.0000    |
| O31   | 0.36838(6)  | 0.64090(10) | 0.93026(7)  | 0.0624                 | 1.0000    |
| C32   | 0.41744(9)  | 0.58453(19) | 0.92155(9)  | 0.0637                 | 1.0000    |
| C33   | 0.44791(7)  | 0.61732(13) | 0.86506(9)  | 0.0459                 | 1.0000    |
| C34   | 0.47911(13) | 0.7110(2)   | 0.88439(19) | 0.1093                 | 1.0000    |
| C35   | 0.40052(9)  | 0.62826(15) | 0.79771(9)  | 0.0552                 | 1.0000    |
| C36   | 0.49523(10) | 0.5444(2)   | 0.85677(14) | 0.0776                 | 1.0000    |
| O41   | 0.36741(7)  | 0.54633(13) | 0.77632(7)  | 0.0789                 | 1.0000    |
| N51   | 0.30616(5)  | 0.37557(8)  | 0.62249(5)  | 0.0277                 | 1.0000    |
| C52   | 0.30821(7)  | 0.35878(10) | 0.69880(7)  | 0.0307                 | 1.0000    |
| C53   | 0.29169(8)  | 0.26154(11) | 0.71804(8)  | 0.0422                 | 1.0000    |
| C54   | 0.30035(8)  | 0.25731(12) | 0.79648(8)  | 0.0401                 | 1.0000    |
| C55   | 0.28373(13) | 0.16493(14) | 0.82282(10) | 0.0678                 | 1.0000    |
| C56   | 0.24257(6)  | 0.35633(10) | 0.57777(7)  | 0.0307                 | 1.0000    |
| C57   | 0.19228(7)  | 0.41868(12) | 0.59140(8)  | 0.0395                 | 1.0000    |
| C58   | 0.13093(7)  | 0.38828(13) | 0.54628(8)  | 0.0425                 | 1.0000    |
| C59   | 0.07871(8)  | 0.44949(17) | 0.55641(11) | 0.0619                 | 1.0000    |
| C60   | 0.32372(7)  | 0.47761(10) | 0.61749(7)  | 0.0310                 | 1.0000    |
| C61   | 0.32710(8)  | 0.51198(11) | 0.54635(8)  | 0.0401                 | 1.0000    |
| C62   | 0.33514(9)  | 0.61783(12) | 0.54818(9)  | 0.0473                 | 1.0000    |
| C63   | 0.34632(12) | 0.65723(16) | 0.48130(11) | 0.0705                 | 1.0000    |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| C64  | 0.34973(6)  | 0.31102(10) | 0.59677(7)  | 0.0302 | 1.0000 |
| C65  | 0.41536(7)  | 0.31184(12) | 0.63904(8)  | 0.0404 | 1.0000 |
| C66  | 0.45651(8)  | 0.25982(15) | 0.60124(9)  | 0.0503 | 1.0000 |
| C67  | 0.52172(9)  | 0.25000(19) | 0.64297(14) | 0.0748 | 1.0000 |
| H121 | 0.16097(9)  | 0.45755(14) | 0.94701(9)  | 0.0631 | 1.0000 |
| H122 | 0.21146(9)  | 0.43170(14) | 0.90473(9)  | 0.0631 | 1.0000 |
| H142 | 0.03519(10) | 0.4729(3)   | 0.80698(14) | 0.1396 | 1.0000 |
| H141 | 0.05276(10) | 0.4716(3)   | 0.88967(14) | 0.1399 | 1.0000 |
| H143 | 0.07140(10) | 0.5626(3)   | 0.84935(14) | 0.1401 | 1.0000 |
| H151 | 0.14010(8)  | 0.54959(15) | 0.77709(9)  | 0.0658 | 1.0000 |
| H152 | 0.10779(8)  | 0.45452(15) | 0.73587(9)  | 0.0657 | 1.0000 |
| H162 | 0.08383(15) | 0.32645(19) | 0.80253(17) | 0.1448 | 1.0000 |
| H163 | 0.11014(15) | 0.32393(19) | 0.88902(17) | 0.1448 | 1.0000 |
| H161 | 0.15715(15) | 0.31299(19) | 0.83529(17) | 0.1454 | 1.0000 |
| H322 | 0.44815(9)  | 0.58397(19) | 0.96501(9)  | 0.0778 | 1.0000 |
| H321 | 0.40296(9)  | 0.51956(19) | 0.90941(9)  | 0.0750 | 1.0000 |
| H341 | 0.49974(13) | 0.7300(2)   | 0.84809(19) | 0.1634 | 1.0000 |
| H342 | 0.50924(13) | 0.7070(2)   | 0.92908(19) | 0.1648 | 1.0000 |
| H343 | 0.44859(13) | 0.7592(2)   | 0.88778(19) | 0.1632 | 1.0000 |
| H351 | 0.37175(9)  | 0.67917(15) | 0.80513(9)  | 0.0650 | 1.0000 |
| H352 | 0.42222(9)  | 0.64611(15) | 0.76203(9)  | 0.0664 | 1.0000 |
| H361 | 0.52060(10) | 0.5709(2)   | 0.82703(14) | 0.1152 | 1.0000 |
| H362 | 0.52121(10) | 0.5277(2)   | 0.90178(14) | 0.1162 | 1.0000 |
| H363 | 0.47274(10) | 0.4876(2)   | 0.83468(14) | 0.1163 | 1.0000 |
| H522 | 0.34912(7)  | 0.37484(10) | 0.72307(7)  | 0.0361 | 1.0000 |
| H521 | 0.28007(7)  | 0.40383(10) | 0.71137(7)  | 0.0347 | 1.0000 |
| H531 | 0.31824(8)  | 0.21813(11) | 0.70527(8)  | 0.0529 | 1.0000 |
| H532 | 0.25008(8)  | 0.24675(11) | 0.69595(8)  | 0.0529 | 1.0000 |
| H541 | 0.34158(8)  | 0.27207(12) | 0.81770(8)  | 0.0498 | 1.0000 |
| H542 | 0.27530(8)  | 0.30517(12) | 0.80959(8)  | 0.0497 | 1.0000 |
| H551 | 0.28928(13) | 0.16519(14) | 0.87295(10) | 0.0996 | 1.0000 |
| H553 | 0.30935(13) | 0.11790(14) | 0.81143(10) | 0.1024 | 1.0000 |
| H552 | 0.24270(13) | 0.14781(14) | 0.80195(10) | 0.1035 | 1.0000 |
| H561 | 0.23417(6)  | 0.29184(10) | 0.58566(7)  | 0.0367 | 1.0000 |
| H562 | 0.24524(6)  | 0.36311(10) | 0.52955(7)  | 0.0359 | 1.0000 |
| H572 | 0.19145(7)  | 0.41504(12) | 0.63861(8)  | 0.0480 | 1.0000 |
| H571 | 0.20037(7)  | 0.48273(12) | 0.58125(8)  | 0.0476 | 1.0000 |
| H581 | 0.12427(7)  | 0.32424(13) | 0.55645(8)  | 0.0508 | 1.0000 |
| H582 | 0.13283(7)  | 0.39232(13) | 0.49873(8)  | 0.0500 | 1.0000 |
| H592 | 0.04099(8)  | 0.42925(17) | 0.52622(11) | 0.0913 | 1.0000 |

|      |             |             |             |        |        |
|------|-------------|-------------|-------------|--------|--------|
| H591 | 0.07464(8)  | 0.44342(17) | 0.60221(11) | 0.0920 | 1.0000 |
| H593 | 0.08544(8)  | 0.51449(17) | 0.54685(11) | 0.0922 | 1.0000 |
| H602 | 0.36241(7)  | 0.48568(10) | 0.64965(7)  | 0.0353 | 1.0000 |
| H601 | 0.29427(7)  | 0.51391(10) | 0.63368(7)  | 0.0364 | 1.0000 |
| H611 | 0.36161(8)  | 0.48281(11) | 0.53270(8)  | 0.0488 | 1.0000 |
| H612 | 0.29126(8)  | 0.49529(11) | 0.51322(8)  | 0.0493 | 1.0000 |
| H622 | 0.36949(9)  | 0.63496(12) | 0.58673(9)  | 0.0567 | 1.0000 |
| H621 | 0.29845(9)  | 0.64589(12) | 0.55723(9)  | 0.0583 | 1.0000 |
| H631 | 0.34815(12) | 0.72397(16) | 0.48544(11) | 0.1045 | 1.0000 |
| H632 | 0.38479(12) | 0.63558(16) | 0.47392(11) | 0.1069 | 1.0000 |
| H633 | 0.31418(12) | 0.64052(16) | 0.44208(11) | 0.1057 | 1.0000 |
| H641 | 0.33355(6)  | 0.24930(10) | 0.59666(7)  | 0.0355 | 1.0000 |
| H642 | 0.34769(6)  | 0.33002(10) | 0.55057(7)  | 0.0345 | 1.0000 |
| H652 | 0.42950(7)  | 0.37486(12) | 0.64716(8)  | 0.0507 | 1.0000 |
| H651 | 0.41833(7)  | 0.28210(12) | 0.68352(8)  | 0.0497 | 1.0000 |
| H661 | 0.45636(8)  | 0.29127(15) | 0.55744(9)  | 0.0621 | 1.0000 |
| H662 | 0.43842(8)  | 0.19825(15) | 0.59005(9)  | 0.0613 | 1.0000 |
| H672 | 0.54640(9)  | 0.21882(19) | 0.61591(14) | 0.1111 | 1.0000 |
| H671 | 0.53927(9)  | 0.30843(19) | 0.65874(14) | 0.1118 | 1.0000 |
| H673 | 0.52189(9)  | 0.21174(19) | 0.68344(14) | 0.1115 | 1.0000 |
| H111 | 0.22248(6)  | 0.57185(9)  | 0.88729(6)  | 0.0771 | 1.0000 |
| H411 | 0.33740(7)  | 0.54808(13) | 0.79565(7)  | 0.1168 | 1.0000 |
| H311 | 0.33625(6)  | 0.62686(10) | 0.90077(7)  | 0.0932 | 1.0000 |
| H211 | 0.22265(6)  | 0.47827(10) | 0.79240(7)  | 0.0863 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0383(5)       | 0.0881(8)       | 0.0639(7)       | -0.0014(6)      | 0.0156(5)       | -0.0146(5)      |
| O11   | 0.0519(7)       | 0.0594(8)       | 0.0461(7)       | -0.0151(5)      | 0.0190(5)       | -0.0122(6)      |
| C12   | 0.0523(10)      | 0.0678(12)      | 0.0406(9)       | 0.0050(8)       | 0.0170(8)       | -0.0030(9)      |
| C13   | 0.0378(8)       | 0.0622(11)      | 0.0443(9)       | -0.0095(8)      | 0.0173(7)       | -0.0106(7)      |
| C14   | 0.0405(11)      | 0.170(3)        | 0.0732(15)      | -0.0311(17)     | 0.0183(10)      | -0.0004(14)     |
| C15   | 0.0469(10)      | 0.0759(13)      | 0.0399(9)       | -0.0083(9)      | 0.0099(7)       | -0.0063(9)      |
| C16   | 0.112(2)        | 0.0799(17)      | 0.110(2)        | -0.0166(15)     | 0.0509(18)      | -0.0468(16)     |
| O21   | 0.0531(7)       | 0.0777(9)       | 0.0522(7)       | -0.0216(6)      | 0.0287(6)       | -0.0085(6)      |
| O31   | 0.0592(8)       | 0.0860(10)      | 0.0531(7)       | -0.0269(7)      | 0.0355(6)       | -0.0210(7)      |
| C32   | 0.0478(10)      | 0.1098(17)      | 0.0337(9)       | 0.0013(10)      | 0.0101(8)       | -0.0051(11)     |
| C33   | 0.0372(8)       | 0.0609(11)      | 0.0443(9)       | -0.0137(8)      | 0.0187(7)       | -0.0109(7)      |
| C34   | 0.0838(18)      | 0.108(2)        | 0.160(3)        | -0.074(2)       | 0.078(2)        | -0.0546(16)     |

|     |            |            |            |             |            |             |
|-----|------------|------------|------------|-------------|------------|-------------|
| C35 | 0.0562(11) | 0.0725(13) | 0.0448(10) | 0.0122(9)   | 0.0274(8)  | 0.0055(9)   |
| C36 | 0.0523(12) | 0.1033(19) | 0.0816(16) | 0.0093(14)  | 0.0246(11) | 0.0191(12)  |
| O41 | 0.0630(9)  | 0.1239(14) | 0.0537(8)  | -0.0448(9)  | 0.0217(7)  | -0.0293(9)  |
| N51 | 0.0315(6)  | 0.0319(6)  | 0.0213(5)  | -0.0021(4)  | 0.0095(4)  | -0.0027(5)  |
| C52 | 0.0369(7)  | 0.0365(7)  | 0.0207(6)  | -0.0016(5)  | 0.0107(5)  | -0.0022(6)  |
| C53 | 0.0615(10) | 0.0385(8)  | 0.0318(8)  | -0.0001(6)  | 0.0215(7)  | -0.0067(7)  |
| C54 | 0.0451(9)  | 0.0473(9)  | 0.0304(8)  | 0.0058(6)   | 0.0138(6)  | -0.0016(7)  |
| C55 | 0.1182(19) | 0.0529(11) | 0.0401(10) | 0.0064(8)   | 0.0343(11) | -0.0149(11) |
| C56 | 0.0315(7)  | 0.0357(7)  | 0.0255(7)  | -0.0044(5)  | 0.0079(5)  | -0.0044(6)  |
| C57 | 0.0359(8)  | 0.0491(9)  | 0.0339(8)  | -0.0072(6)  | 0.0092(6)  | 0.0031(7)   |
| C58 | 0.0331(8)  | 0.0554(10) | 0.0401(8)  | 0.0002(7)   | 0.0108(6)  | -0.0017(7)  |
| C59 | 0.0383(9)  | 0.0863(15) | 0.0616(12) | 0.0001(10)  | 0.0127(8)  | 0.0126(9)   |
| C60 | 0.0350(7)  | 0.0317(7)  | 0.0274(7)  | -0.0023(5)  | 0.0092(6)  | -0.0045(6)  |
| C61 | 0.0493(9)  | 0.0420(9)  | 0.0282(7)  | 0.0030(6)   | 0.0075(6)  | -0.0094(7)  |
| C62 | 0.0537(10) | 0.0410(9)  | 0.0494(10) | 0.0102(7)   | 0.0169(8)  | -0.0023(7)  |
| C63 | 0.0909(16) | 0.0643(13) | 0.0522(11) | 0.0225(10)  | 0.0088(11) | -0.0222(11) |
| C64 | 0.0331(7)  | 0.0355(7)  | 0.0241(6)  | -0.0024(5)  | 0.0111(5)  | -0.0006(6)  |
| C65 | 0.0349(8)  | 0.0500(9)  | 0.0360(8)  | -0.0058(7)  | 0.0076(6)  | 0.0012(7)   |
| C66 | 0.0386(9)  | 0.0701(12) | 0.0434(9)  | -0.0039(8)  | 0.0121(7)  | 0.0089(8)   |
| C67 | 0.0380(10) | 0.0959(17) | 0.0870(16) | -0.0242(13) | 0.0081(10) | 0.0128(10)  |

## Distances

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| O11 | C12  | 1.416(2)Å |  | O11 | H111 | 0.866Å    |
| C12 | C13  | 1.527(2)Å |  | C12 | H121 | 0.989Å    |
| C12 | H122 | 0.998Å    |  | C13 | C14  | 1.527(3)Å |
| C13 | C15  | 1.536(2)Å |  | C13 | C16  | 1.507(3)Å |
| C14 | H142 | 0.979Å    |  | C14 | H141 | 0.980Å    |
| C14 | H143 | 1.003Å    |  | C15 | O21  | 1.415(2)Å |
| C15 | H151 | 1.013Å    |  | C15 | H152 | 1.015Å    |
| C16 | H162 | 0.991Å    |  | C16 | H163 | 1.006Å    |
| C16 | H161 | 0.995Å    |  | O21 | H211 | 0.816Å    |
| O31 | C32  | 1.410(3)Å |  | O31 | H311 | 0.841Å    |
| C32 | C33  | 1.521(2)Å |  | C32 | H322 | 0.971Å    |
| C32 | H321 | 0.994Å    |  | C33 | C34  | 1.518(3)Å |
| C33 | C35  | 1.511(3)Å |  | C33 | C36  | 1.526(3)Å |
| C34 | H341 | 0.984Å    |  | C34 | H342 | 0.984Å    |
| C34 | H343 | 0.986Å    |  | C35 | O41  | 1.399(3)Å |
| C35 | H351 | 1.008Å    |  | C35 | H352 | 0.985Å    |
| C36 | H361 | 0.989Å    |  | C36 | H362 | 0.976Å    |

|     |      |             |  |     |      |             |
|-----|------|-------------|--|-----|------|-------------|
| C36 | H363 | 1.002Å      |  | O41 | H411 | 0.853Å      |
| N51 | C52  | 1.5255(16)Å |  | N51 | C56  | 1.5219(17)Å |
| N51 | C60  | 1.5198(17)Å |  | N51 | C64  | 1.5200(17)Å |
| C52 | C53  | 1.511(2)Å   |  | C52 | H522 | 0.961Å      |
| C52 | H521 | 0.976Å      |  | C53 | C54  | 1.526(2)Å   |
| C53 | H531 | 0.937Å      |  | C53 | H532 | 0.960Å      |
| C54 | C55  | 1.500(2)Å   |  | C54 | H541 | 0.949Å      |
| C54 | H542 | 0.961Å      |  | C55 | H551 | 0.975Å      |
| C55 | H553 | 0.947Å      |  | C55 | H552 | 0.951Å      |
| C56 | C57  | 1.515(2)Å   |  | C56 | H561 | 0.961Å      |
| C56 | H562 | 0.979Å      |  | C57 | C58  | 1.522(2)Å   |
| C57 | H572 | 0.944Å      |  | C57 | H571 | 0.964Å      |
| C58 | C59  | 1.516(2)Å   |  | C58 | H581 | 0.956Å      |
| C58 | H582 | 0.958Å      |  | C59 | H592 | 0.962Å      |
| C59 | H591 | 0.940Å      |  | C59 | H593 | 0.967Å      |
| C60 | C61  | 1.5158(19)Å |  | C60 | H602 | 0.958Å      |
| C60 | H601 | 0.955Å      |  | C61 | C62  | 1.522(2)Å   |
| C61 | H611 | 0.975Å      |  | C61 | H612 | 0.944Å      |
| C62 | C63  | 1.518(2)Å   |  | C62 | H622 | 0.983Å      |
| C62 | H621 | 0.972Å      |  | C63 | H631 | 0.957Å      |
| C63 | H632 | 0.963Å      |  | C63 | H633 | 0.961Å      |
| C64 | C65  | 1.518(2)Å   |  | C64 | H641 | 0.954Å      |
| C64 | H642 | 0.948Å      |  | C65 | C66  | 1.518(2)Å   |
| C65 | H652 | 0.956Å      |  | C65 | H651 | 0.969Å      |
| C66 | C67  | 1.513(3)Å   |  | C66 | H661 | 0.979Å      |
| C66 | H662 | 0.973Å      |  | C67 | H672 | 0.968Å      |
| C67 | H671 | 0.945Å      |  | C67 | H673 | 0.972Å      |

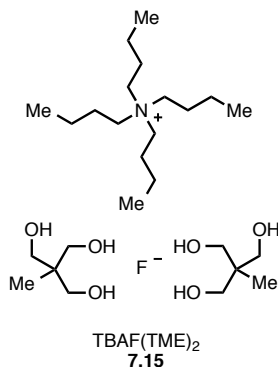
## Angles

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C12  | O11 | H111 | 105.431°    |  | O11  | C12 | C13  | 114.98(15)° |
| O11  | C12 | H121 | 109.150°    |  | C13  | C12 | H121 | 106.166°    |
| O11  | C12 | H122 | 111.351°    |  | C13  | C12 | H122 | 106.885°    |
| H121 | C12 | H122 | 107.974°    |  | C12  | C13 | C14  | 109.36(16)° |
| C12  | C13 | C15  | 109.26(14)° |  | C14  | C13 | C15  | 107.19(18)° |
| C12  | C13 | C16  | 108.9(2)°   |  | C14  | C13 | C16  | 111.6(2)°   |
| C15  | C13 | C16  | 110.46(18)° |  | C13  | C14 | H142 | 105.026°    |
| C13  | C14 | H141 | 110.174°    |  | H142 | C14 | H141 | 109.259°    |
| C13  | C14 | H143 | 109.644°    |  | H142 | C14 | H143 | 111.784°    |
| H141 | C14 | H143 | 110.803°    |  | C13  | C15 | O21  | 112.79(16)° |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C13  | C15 | H151 | 107.597°    |  | O21  | C15 | H151 | 111.149°    |
| C13  | C15 | H152 | 107.925°    |  | O21  | C15 | H152 | 107.196°    |
| H151 | C15 | H152 | 110.142°    |  | C13  | C16 | H162 | 104.496°    |
| C13  | C16 | H163 | 104.461°    |  | H162 | C16 | H163 | 114.709°    |
| C13  | C16 | H161 | 107.170°    |  | H162 | C16 | H161 | 110.992°    |
| H163 | C16 | H161 | 114.025°    |  | C15  | O21 | H211 | 104.584°    |
| C32  | O31 | H311 | 110.377°    |  | O31  | C32 | C33  | 114.67(18)° |
| O31  | C32 | H322 | 108.032°    |  | C33  | C32 | H322 | 107.984°    |
| O31  | C32 | H321 | 109.956°    |  | C33  | C32 | H321 | 106.708°    |
| H322 | C32 | H321 | 109.400°    |  | C32  | C33 | C34  | 110.30(18)° |
| C32  | C33 | C35  | 109.81(14)° |  | C34  | C33 | C35  | 108.7(2)°   |
| C32  | C33 | C36  | 108.50(18)° |  | C34  | C33 | C36  | 109.61(18)° |
| C35  | C33 | C36  | 109.89(16)° |  | C33  | C34 | H341 | 109.143°    |
| C33  | C34 | H342 | 110.903°    |  | H341 | C34 | H342 | 109.498°    |
| C33  | C34 | H343 | 110.134°    |  | H341 | C34 | H343 | 108.317°    |
| H342 | C34 | H343 | 108.802°    |  | C33  | C35 | O41  | 113.41(16)° |
| C33  | C35 | H351 | 106.804°    |  | O41  | C35 | H351 | 109.481°    |
| C33  | C35 | H352 | 107.355°    |  | O41  | C35 | H352 | 108.481°    |
| H351 | C35 | H352 | 111.329°    |  | C33  | C36 | H361 | 108.638°    |
| C33  | C36 | H362 | 110.513°    |  | H361 | C36 | H362 | 109.598°    |
| C33  | C36 | H363 | 107.868°    |  | H361 | C36 | H363 | 110.588°    |
| H362 | C36 | H363 | 109.615°    |  | C35  | O41 | H411 | 105.103°    |
| C52  | N51 | C56  | 110.88(10)° |  | C52  | N51 | C60  | 105.57(10)° |
| C56  | N51 | C60  | 111.01(10)° |  | C52  | N51 | C64  | 111.61(10)° |
| C56  | N51 | C64  | 106.67(10)° |  | C60  | N51 | C64  | 111.19(10)° |
| N51  | C52 | C53  | 116.41(11)° |  | N51  | C52 | H522 | 105.232°    |
| C53  | C52 | H522 | 110.873°    |  | N51  | C52 | H521 | 106.351°    |
| C53  | C52 | H521 | 109.147°    |  | H522 | C52 | H521 | 108.480°    |
| C52  | C53 | C54  | 108.38(12)° |  | C52  | C53 | H531 | 109.222°    |
| C54  | C53 | H531 | 108.328°    |  | C52  | C53 | H532 | 111.021°    |
| C54  | C53 | H532 | 109.547°    |  | H531 | C53 | H532 | 110.278°    |
| C53  | C54 | C55  | 114.16(14)° |  | C53  | C54 | H541 | 108.752°    |
| C55  | C54 | H541 | 109.816°    |  | C53  | C54 | H542 | 107.888°    |
| C55  | C54 | H542 | 108.722°    |  | H541 | C54 | H542 | 107.262°    |
| C54  | C55 | H551 | 111.797°    |  | C54  | C55 | H553 | 108.936°    |
| H551 | C55 | H553 | 107.971°    |  | C54  | C55 | H552 | 111.756°    |
| H551 | C55 | H552 | 108.927°    |  | H553 | C55 | H552 | 107.282°    |
| N51  | C56 | C57  | 115.43(11)° |  | N51  | C56 | H561 | 105.789°    |
| C57  | C56 | H561 | 110.518°    |  | N51  | C56 | H562 | 106.721°    |
| C57  | C56 | H562 | 109.737°    |  | H561 | C56 | H562 | 108.340°    |



|      |     |      |             |  |      |     |      |          |
|------|-----|------|-------------|--|------|-----|------|----------|
| C56  | C57 | C58  | 109.86(12)° |  | C56  | C57 | H572 | 109.629° |
| C58  | C57 | H572 | 110.018°    |  | C56  | C57 | H571 | 109.563° |
| C58  | C57 | H571 | 109.728°    |  | H572 | C57 | H571 | 108.015° |
| C57  | C58 | C59  | 112.43(15)° |  | C57  | C58 | H581 | 108.304° |
| C59  | C58 | H581 | 111.001°    |  | C57  | C58 | H582 | 108.609° |
| C59  | C58 | H582 | 108.210°    |  | H581 | C58 | H582 | 108.171° |
| C58  | C59 | H592 | 110.006°    |  | C58  | C59 | H591 | 109.316° |
| H592 | C59 | H591 | 107.666°    |  | C58  | C59 | H593 | 111.426° |
| H592 | C59 | H593 | 108.805°    |  | H591 | C59 | H593 | 109.541° |
| N51  | C60 | C61  | 116.28(11)° |  | N51  | C60 | H602 | 106.349° |
| C61  | C60 | H602 | 110.236°    |  | N51  | C60 | H601 | 106.659° |
| C61  | C60 | H601 | 109.251°    |  | H602 | C60 | H601 | 107.699° |
| C60  | C61 | C62  | 109.35(13)° |  | C60  | C61 | H611 | 109.853° |
| C62  | C61 | H611 | 109.452°    |  | C60  | C61 | H612 | 110.274° |
| C62  | C61 | H612 | 110.177°    |  | H611 | C61 | H612 | 107.717° |
| C61  | C62 | C63  | 112.99(16)° |  | C61  | C62 | H622 | 109.470° |
| C63  | C62 | H622 | 109.154°    |  | C61  | C62 | H621 | 108.211° |
| C63  | C62 | H621 | 109.412°    |  | H622 | C62 | H621 | 107.446° |
| C62  | C63 | H631 | 107.860°    |  | C62  | C63 | H632 | 110.779° |
| H631 | C63 | H632 | 108.121°    |  | C62  | C63 | H633 | 111.710° |
| H631 | C63 | H633 | 109.048°    |  | H632 | C63 | H633 | 109.233° |
| N51  | C64 | C65  | 115.49(11)° |  | N51  | C64 | H641 | 106.576° |
| C65  | C64 | H641 | 109.253°    |  | N51  | C64 | H642 | 105.321° |
| C65  | C64 | H642 | 110.638°    |  | H641 | C64 | H642 | 109.332° |
| C64  | C65 | C66  | 110.52(13)° |  | C64  | C65 | H652 | 110.043° |
| C66  | C65 | H652 | 109.088°    |  | C64  | C65 | H651 | 110.518° |
| C66  | C65 | H651 | 108.553°    |  | H652 | C65 | H651 | 108.065° |
| C65  | C66 | C67  | 113.62(15)° |  | C65  | C66 | H661 | 109.936° |
| C67  | C66 | H661 | 109.250°    |  | C65  | C66 | H662 | 106.525° |
| C67  | C66 | H662 | 109.963°    |  | H661 | C66 | H662 | 107.335° |
| C66  | C67 | H672 | 110.357°    |  | C66  | C67 | H671 | 112.082° |
| H672 | C67 | H671 | 109.928°    |  | C66  | C67 | H673 | 108.675° |
| H672 | C67 | H673 | 108.073°    |  | H671 | C67 | H673 | 107.595° |



**tetra-*n*-butylammonium fluoride bis(1,1,1-tris(hydroxymethyl)ethane) (TBAF(TME)<sub>2</sub>, 7.15):**

**X-ray** (single-crystal) Colourless block crystals of X-ray diffraction quality were obtained by vapour diffusion of hexanes into a saturated solution of **7.15** in THF, which had previously been prepared by dissolving **7.15** in refluxing THF (approximately 66 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature.

Oxford Crystallography File Name: 063GGKE01

## Crystal Data

$a = 9.91330(10) \text{ \AA}$   $\alpha = 90^\circ$

$b = 17.3454(3) \text{ \AA}$   $\beta = 90^\circ$

$c = 18.3631(3) \text{ \AA}$   $\gamma = 90^\circ$

Volume  $3157.54(8) \text{ \AA}^3$

Space group  $P b c n$

Formula  $C_{26} H_{60} F_1 N_1 O_6$

Cell determined from 4020 reflections

Temperature 150K

Shape plate

Colour clear\_pale\_colourless

$D_x$   $1.06 \text{ Mg m}^{-3}$

$\mu$   $0.076 \text{ mm}^{-1}$

Absorption correction multi-scan

$T_{\min}$  0.91

Crystal Class orthorhombic

$Z = 4$

$M_r$  501.76

Cell  $\theta$  range =  $5 - 27^\circ$

Size  $0.10 \times 0.20 \times 0.35 \text{ mm}$

$F_{000}$  1120.000

$T_{\max}$  0.99

## Data Collection

Diffractometer multi-scan

Scan type  $\omega$  scans

Reflections measured 46870

Independent reflections 3597

$R_{\text{int}}$  0.0199

$\theta_{\max}$  27.4919

$h = -12 \rightarrow 12$

$k = -22 \rightarrow 22$

$l = -23 \rightarrow 23$

## Refinement

$\Delta\rho_{\min} = -0.25 \text{ e \AA}^{-3}$

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\max}$ =  | 0.34 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 3597                                                                                                                                                                                        |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 155                                                                                                                                                                                         |
| S =                    | 0.96                                                                                                                                                                                        |
| R-factor               | 0.062                                                                                                                                                                                       |
| weighted R-factor      | 0.106                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0005                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.042 \times P)^2 + 1.175 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | x           | y           | z          | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|------------|------------------------|-----------|
| F1    | 0.5000      | 0.27953(8)  | 0.7500     | 0.0484                 | 1.0000    |
| O11   | 0.40012(9)  | 0.24409(6)  | 0.62274(5) | 0.0429                 | 1.0000    |
| O12   | 0.65488(9)  | 0.36391(6)  | 0.66504(5) | 0.0439                 | 1.0000    |
| O13   | 0.65601(9)  | 0.28057(7)  | 0.44334(5) | 0.0482                 | 1.0000    |
| C14   | 0.51408(13) | 0.25017(8)  | 0.57553(7) | 0.0332                 | 1.0000    |
| C15   | 0.54159(12) | 0.33180(8)  | 0.54877(6) | 0.0308                 | 1.0000    |
| C16   | 0.55852(14) | 0.38750(8)  | 0.61275(7) | 0.0388                 | 1.0000    |
| C17   | 0.67155(13) | 0.33030(9)  | 0.50427(7) | 0.0397                 | 1.0000    |
| C18   | 0.42407(15) | 0.36007(10) | 0.50219(8) | 0.0467                 | 1.0000    |
| N21   | 0.0000      | 0.27575(8)  | 0.7500     | 0.0241                 | 1.0000    |
| C22   | 0.01982(11) | 0.32476(7)  | 0.81779(6) | 0.0266                 | 1.0000    |
| C23   | 0.08660(12) | 0.38576(7)  | 0.83215(6) | 0.0301                 | 1.0000    |
| C24   | 0.05989(13) | 0.42255(7)  | 0.90624(7) | 0.0341                 | 1.0000    |
| C25   | 0.14602(16) | 0.49324(8)  | 0.92037(8) | 0.0440                 | 1.0000    |
| C26   | 0.12487(11) | 0.22620(7)  | 0.76156(6) | 0.0269                 | 1.0000    |
| C27   | 0.15489(12) | 0.16644(7)  | 0.70371(7) | 0.0323                 | 1.0000    |
| C28   | 0.27869(15) | 0.12033(8)  | 0.72610(8) | 0.0414                 | 1.0000    |
| C29   | 0.31618(18) | 0.05819(9)  | 0.67198(9) | 0.0546                 | 1.0000    |
| H111  | 0.42535(9)  | 0.25530(6)  | 0.66597(5) | 0.0641                 | 1.0000    |
| H121  | 0.61175(9)  | 0.33751(6)  | 0.69673(5) | 0.0666                 | 1.0000    |
| H131  | 0.73126(9)  | 0.27420(7)  | 0.42400(5) | 0.0718                 | 1.0000    |
| H141  | 0.49455(13) | 0.21704(8)  | 0.53240(7) | 0.0380                 | 1.0000    |
| H142  | 0.59422(13) | 0.23005(8)  | 0.60027(7) | 0.0408                 | 1.0000    |
| H161  | 0.59073(14) | 0.43700(8)  | 0.59304(7) | 0.0480                 | 1.0000    |
| H162  | 0.46982(14) | 0.39448(8)  | 0.63676(7) | 0.0465                 | 1.0000    |
| H171  | 0.74529(13) | 0.31332(9)  | 0.53535(7) | 0.0465                 | 1.0000    |

|      |             |             |            |        |        |
|------|-------------|-------------|------------|--------|--------|
| H172 | 0.68952(13) | 0.38252(9)  | 0.48766(7) | 0.0488 | 1.0000 |
| H181 | 0.43689(15) | 0.41262(10) | 0.48603(8) | 0.0709 | 1.0000 |
| H182 | 0.33764(15) | 0.35704(10) | 0.53066(8) | 0.0683 | 1.0000 |
| H183 | 0.41796(15) | 0.32984(10) | 0.45801(8) | 0.0689 | 1.0000 |
| H221 | 0.02070(11) | 0.28765(7)  | 0.85787(6) | 0.0313 | 1.0000 |
| H222 | 0.10804(11) | 0.34903(7)  | 0.81342(6) | 0.0313 | 1.0000 |
| H231 | 0.17453(12) | 0.36237(7)  | 0.83251(6) | 0.0358 | 1.0000 |
| H232 | 0.08390(12) | 0.42587(7)  | 0.79381(6) | 0.0353 | 1.0000 |
| H241 | 0.07649(13) | 0.38432(7)  | 0.94329(7) | 0.0423 | 1.0000 |
| H242 | 0.03564(13) | 0.43637(7)  | 0.90837(7) | 0.0403 | 1.0000 |
| H251 | 0.12235(16) | 0.53355(8)  | 0.88629(8) | 0.0639 | 1.0000 |
| H252 | 0.13150(16) | 0.51173(8)  | 0.97042(8) | 0.0659 | 1.0000 |
| H253 | 0.24236(16) | 0.48098(8)  | 0.91345(8) | 0.0649 | 1.0000 |
| H261 | 0.11466(11) | 0.20079(7)  | 0.80899(6) | 0.0327 | 1.0000 |
| H262 | 0.20169(11) | 0.26157(7)  | 0.76484(6) | 0.0306 | 1.0000 |
| H271 | 0.07940(12) | 0.13339(7)  | 0.69750(7) | 0.0398 | 1.0000 |
| H272 | 0.17225(12) | 0.19140(7)  | 0.65677(7) | 0.0398 | 1.0000 |
| H281 | 0.35563(15) | 0.15643(8)  | 0.73071(8) | 0.0512 | 1.0000 |
| H282 | 0.26220(15) | 0.09547(8)  | 0.77250(8) | 0.0530 | 1.0000 |
| H291 | 0.33130(18) | 0.08034(9)  | 0.62211(9) | 0.0824 | 1.0000 |
| H292 | 0.24229(18) | 0.01959(9)  | 0.66797(9) | 0.0828 | 1.0000 |
| H293 | 0.40223(18) | 0.03106(9)  | 0.68626(9) | 0.0810 | 1.0000 |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| F1    | 0.0514(7)       | 0.0726(8)       | 0.0211(5)       | 0.0000          | -0.0021(5)      | 0.0000          |
| O11   | 0.0312(5)       | 0.0744(7)       | 0.0232(4)       | -0.0007(4)      | 0.0016(4)       | -0.0145(5)      |
| O12   | 0.0315(5)       | 0.0676(7)       | 0.0326(5)       | -0.0081(5)      | -0.0050(4)      | -0.0063(4)      |
| O13   | 0.0305(5)       | 0.0859(8)       | 0.0282(5)       | -0.0151(5)      | 0.0055(4)       | -0.0024(5)      |
| C14   | 0.0289(6)       | 0.0449(7)       | 0.0260(6)       | -0.0027(5)      | 0.0023(5)       | -0.0020(5)      |
| C15   | 0.0264(6)       | 0.0423(7)       | 0.0237(6)       | -0.0011(5)      | -0.0005(5)      | 0.0018(5)       |
| C16   | 0.0398(7)       | 0.0439(8)       | 0.0329(7)       | -0.0054(6)      | -0.0025(6)      | 0.0009(6)       |
| C17   | 0.0336(7)       | 0.0583(9)       | 0.0272(6)       | -0.0025(6)      | 0.0048(5)       | -0.0080(6)      |
| C18   | 0.0436(8)       | 0.0645(10)      | 0.0320(7)       | 0.0029(7)       | -0.0063(6)      | 0.0142(7)       |
| N21   | 0.0211(6)       | 0.0300(7)       | 0.0213(6)       | 0.0000          | 0.0016(5)       | 0.0000          |
| C22   | 0.0254(6)       | 0.0319(6)       | 0.0224(5)       | -0.0032(4)      | -0.0008(4)      | -0.0005(5)      |
| C23   | 0.0272(6)       | 0.0344(6)       | 0.0286(6)       | -0.0037(5)      | 0.0002(5)       | 0.0013(5)       |
| C24   | 0.0395(7)       | 0.0335(7)       | 0.0294(6)       | -0.0035(5)      | 0.0008(5)       | 0.0006(5)       |
| C25   | 0.0503(8)       | 0.0393(7)       | 0.0426(8)       | -0.0097(6)      | 0.0023(6)       | 0.0051(6)       |

|     |           |           |            |            |           |            |
|-----|-----------|-----------|------------|------------|-----------|------------|
| C26 | 0.0232(6) | 0.0334(6) | 0.0240(6)  | -0.0003(5) | 0.0033(4) | -0.0039(5) |
| C27 | 0.0293(6) | 0.0364(7) | 0.0313(6)  | -0.0056(5) | 0.0027(5) | -0.0041(5) |
| C28 | 0.0431(8) | 0.0398(7) | 0.0412(7)  | -0.0033(6) | 0.0035(6) | -0.0132(6) |
| C29 | 0.0562(9) | 0.0437(8) | 0.0638(10) | -0.0125(7) | 0.0007(8) | -0.0148(7) |

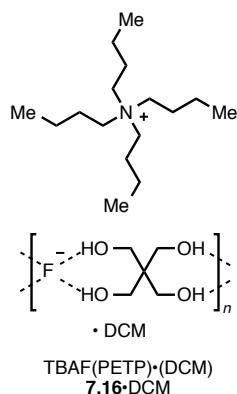
## Distances

|     |           |             |  |     |      |             |
|-----|-----------|-------------|--|-----|------|-------------|
| O11 | C14       | 1.4279(15)Å |  | O11 | H111 | 0.855Å      |
| O12 | C16       | 1.4148(16)Å |  | O12 | H121 | 0.855Å      |
| O13 | C17       | 1.4211(16)Å |  | O13 | H131 | 0.834Å      |
| C14 | C15       | 1.5233(18)Å |  | C14 | H141 | 0.998Å      |
| C14 | H142      | 0.980Å      |  | C15 | C16  | 1.5304(17)Å |
| C15 | C17       | 1.5258(17)Å |  | C15 | C18  | 1.5263(17)Å |
| C16 | H161      | 0.985Å      |  | C16 | H162 | 0.991Å      |
| C17 | H171      | 0.973Å      |  | C17 | H172 | 0.972Å      |
| C18 | H181      | 0.967Å      |  | C18 | H182 | 1.005Å      |
| C18 | H183      | 0.968Å      |  | N21 | C22  | 1.5202(13)Å |
| N21 | C22 7_556 | 1.5202(13)Å |  | N21 | C26  | 1.5219(13)Å |
| N21 | C26 7_556 | 1.5219(13)Å |  | C22 | C23  | 1.5172(16)Å |
| C22 | H221      | 0.978Å      |  | C22 | H222 | 0.974Å      |
| C23 | C24       | 1.5260(16)Å |  | C23 | H231 | 0.961Å      |
| C23 | H232      | 0.990Å      |  | C24 | C25  | 1.5165(18)Å |
| C24 | H241      | 0.964Å      |  | C24 | H242 | 0.978Å      |
| C25 | H251      | 0.967Å      |  | C25 | H252 | 0.984Å      |
| C25 | H253      | 0.987Å      |  | C26 | C27  | 1.5137(16)Å |
| C26 | H261      | 0.981Å      |  | C26 | H262 | 0.980Å      |
| C27 | C28       | 1.5215(17)Å |  | C27 | H271 | 0.950Å      |
| C27 | H272      | 0.980Å      |  | C28 | C29  | 1.5124(19)Å |
| C28 | H281      | 0.990Å      |  | C28 | H282 | 0.969Å      |
| C29 | H291      | 1.004Å      |  | C29 | H292 | 0.995Å      |
| C29 | H293      | 1.009Å      |  |     |      |             |

## Angles

|      |     |      |             |  |     |     |      |             |
|------|-----|------|-------------|--|-----|-----|------|-------------|
| C14  | O11 | H111 | 108.396°    |  | C16 | O12 | H121 | 106.213°    |
| C17  | O13 | H131 | 108.591°    |  | O11 | C14 | C15  | 113.96(10)° |
| O11  | C14 | H141 | 106.618°    |  | C15 | C14 | H141 | 108.309°    |
| O11  | C14 | H142 | 109.499°    |  | C15 | C14 | H142 | 109.604°    |
| H141 | C14 | H142 | 108.687°    |  | C14 | C15 | C16  | 111.03(10)° |
| C14  | C15 | C17  | 107.94(11)° |  | C16 | C15 | C17  | 109.23(10)° |

|      |     |           |             |  |           |     |           |             |
|------|-----|-----------|-------------|--|-----------|-----|-----------|-------------|
| C14  | C15 | C18       | 110.04(11)° |  | C16       | C15 | C18       | 108.13(11)° |
| C17  | C15 | C18       | 110.48(11)° |  | O12       | C16 | C15       | 114.36(11)° |
| O12  | C16 | H161      | 106.417°    |  | C15       | C16 | H161      | 107.685°    |
| O12  | C16 | H162      | 109.418°    |  | C15       | C16 | H162      | 108.744°    |
| H161 | C16 | H162      | 110.154°    |  | O13       | C17 | C15       | 109.91(10)° |
| O13  | C17 | H171      | 111.073°    |  | C15       | C17 | H171      | 108.985°    |
| O13  | C17 | H172      | 109.786°    |  | C15       | C17 | H172      | 107.867°    |
| H171 | C17 | H172      | 109.157°    |  | C15       | C18 | H181      | 111.999°    |
| C15  | C18 | H182      | 110.024°    |  | H181      | C18 | H182      | 108.724°    |
| C15  | C18 | H183      | 110.087°    |  | H181      | C18 | H183      | 105.159°    |
| H182 | C18 | H183      | 110.754°    |  | C22       | N21 | C22 7_556 | 112.00(12)° |
| C22  | N21 | C26       | 107.86(6)°  |  | C22 7_556 | N21 | C26       | 108.96(6)°  |
| C22  | N21 | C26 7_556 | 108.96(6)°  |  | C22 7_556 | N21 | C26 7_556 | 107.86(6)°  |
| C26  | N21 | C26 7_556 | 111.23(12)° |  | N21       | C22 | C23       | 116.25(9)°  |
| N21  | C22 | H221      | 104.447°    |  | C23       | C22 | H221      | 109.544°    |
| N21  | C22 | H222      | 106.872°    |  | C23       | C22 | H222      | 109.711°    |
| H221 | C22 | H222      | 109.788°    |  | C22       | C23 | C24       | 109.02(10)° |
| C22  | C23 | H231      | 109.721°    |  | C24       | C23 | H231      | 109.125°    |
| C22  | C23 | H232      | 110.348°    |  | C24       | C23 | H232      | 109.587°    |
| H231 | C23 | H232      | 109.022°    |  | C23       | C24 | C25       | 113.14(11)° |
| C23  | C24 | H241      | 108.166°    |  | C25       | C24 | H241      | 109.839°    |
| C23  | C24 | H242      | 107.836°    |  | C25       | C24 | H242      | 109.897°    |
| H241 | C24 | H242      | 107.800°    |  | C24       | C25 | H251      | 109.705°    |
| C24  | C25 | H252      | 109.932°    |  | H251      | C25 | H252      | 109.464°    |
| C24  | C25 | H253      | 110.407°    |  | H251      | C25 | H253      | 107.897°    |
| H252 | C25 | H253      | 109.402°    |  | N21       | C26 | C27       | 116.66(9)°  |
| N21  | C26 | H261      | 107.068°    |  | C27       | C26 | H261      | 109.609°    |
| N21  | C26 | H262      | 106.689°    |  | C27       | C26 | H262      | 108.612°    |
| H261 | C26 | H262      | 107.865°    |  | C26       | C27 | C28       | 109.20(10)° |
| C26  | C27 | H271      | 110.055°    |  | C28       | C27 | H271      | 110.535°    |
| C26  | C27 | H272      | 110.448°    |  | C28       | C27 | H272      | 109.161°    |
| H271 | C27 | H272      | 107.420°    |  | C27       | C28 | C29       | 113.29(12)° |
| C27  | C28 | H281      | 108.176°    |  | C29       | C28 | H281      | 108.519°    |
| C27  | C28 | H282      | 109.598°    |  | C29       | C28 | H282      | 107.582°    |
| H281 | C28 | H282      | 109.638°    |  | C28       | C29 | H291      | 111.293°    |
| C28  | C29 | H292      | 110.323°    |  | H291      | C29 | H292      | 107.445°    |
| C28  | C29 | H293      | 111.676°    |  | H291      | C29 | H293      | 106.810°    |
| H292 | C29 | H293      | 109.134°    |  |           |     |           |             |



**tetra-*n*-butylammonium fluoride pentaerythritol, DCM solvate (TBAF(PETP)•(DCM), 7.16•DCM)**

**X-ray** (single-crystal) Colourless plate-like crystals of X-ray diffraction quality were obtained by carefully layering hexanes onto a saturated solution of **7.16** in DCM, which had previously been prepared by dissolving **7.16** in refluxing DCM (approximately 40 °C) until visibly saturated, filtering the solution while hot, and then allowing the filtrate to stand for roughly 1 min to cool to near room temperature. The crystal was found to be a DCM solvate.

Oxford Crystallography Number: 043GWP12

## Crystal Data

$$a = 9.9446(3) \text{ \AA} \quad \alpha = 90^\circ$$

$$b = 18.0891(7) \text{ \AA} \quad \beta = 103.523(4)^\circ$$

$$c = 15.7361(6) \text{ \AA} \quad \gamma = 90^\circ$$

$$\text{Volume} \quad 2752.27(18) \text{ \AA}^3$$

$$\text{Space group} \quad P 2_1/c$$

$$\text{Formula} \quad \text{C}_{22} \text{H}_{50} \text{Cl}_2 \text{F}_1 \text{N}_1 \text{O}_4$$

$$\text{Cell determined from} \quad 6459 \text{ reflections}$$

$$\text{Temperature} \quad 150 \text{ K}$$

$$\text{Shape} \quad \text{plate}$$

$$\text{Colour} \quad \text{clear\_pale\_colourless}$$

$$D_x \quad 1.16 \text{ Mg m}^{-3}$$

$$\mu \quad 2.380 \text{ mm}^{-1}$$

$$\text{Absorption correction} \quad \text{multi-scan}$$

$$T_{\min} \quad 0.61$$

$$\text{Crystal Class} \quad \text{monoclinic}$$

$$Z = \quad 4$$

$$M_r \quad 482.55$$

$$\text{Cell } \theta \text{ range} = 3 - 75^\circ$$

$$\text{Size} \quad 0.04 \times 0.15 \times 0.18 \text{ mm}$$

$$F000 \quad 1056.000$$

$$T_{\max} \quad 0.91$$

## Data Collection

$$\text{Diffractometer} \quad \text{multi-scan}$$

$$\text{Scan type} \quad \omega \text{ scans}$$

$$\text{Reflections measured} \quad 19286$$

$$\text{Independent reflections} \quad 5597$$

$$R_{\text{int}} \quad 0.0471$$

$$\theta_{\max} \quad 75.2470$$

$$h = \quad -12 \rightarrow 10$$

$$k = \quad -21 \rightarrow 22$$

$$l = \quad -19 \rightarrow 18$$

## Refinement

|                        |                                                                                                                                                                                             |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\Delta\rho_{\min}$ =  | -0.47 e Å <sup>-3</sup>                                                                                                                                                                     |
| $\Delta\rho_{\max}$ =  | 0.60 e Å <sup>-3</sup>                                                                                                                                                                      |
| Reflections used       | 4548                                                                                                                                                                                        |
| Cutoff: I >            | -3.00σ(I)                                                                                                                                                                                   |
| Parameters refined     | 293                                                                                                                                                                                         |
| S =                    | 0.99                                                                                                                                                                                        |
| R-factor               | 0.069                                                                                                                                                                                       |
| weighted R-factor      | 0.151                                                                                                                                                                                       |
| $\Delta/\sigma_{\max}$ | 0.0003                                                                                                                                                                                      |
| Refinement on          | F <sup>2</sup>                                                                                                                                                                              |
| w =                    | $1/[\sigma^2(F_{\text{obs}}^2) + (0.067 \times P)^2 + 2.175 \times P + 0.000 + 0.000 \times \sin\theta]$ ,<br>$P = 0.333 \times \max(F_{\text{obs}}^2, 0) + 0.667 \times F_{\text{calc}}^2$ |

## Parameters

| Label | x           | y           | z           | U <sub>iso/equiv</sub> | Occupancy |
|-------|-------------|-------------|-------------|------------------------|-----------|
| C15   | 0.3401(2)   | 0.22442(14) | 0.51870(16) | 0.0372                 | 1.0000    |
| C16   | 0.4999(2)   | 0.17925(14) | 0.65279(16) | 0.0367                 | 1.0000    |
| C17   | 0.4146(3)   | 0.31148(15) | 0.64459(17) | 0.0402                 | 1.0000    |
| C18   | 0.5833(2)   | 0.27377(14) | 0.56003(16) | 0.0359                 | 1.0000    |
| C19   | 0.4598(2)   | 0.24753(13) | 0.59429(14) | 0.0303                 | 1.0000    |
| N21   | 0.94353(17) | 0.29272(10) | 0.83012(11) | 0.0255                 | 1.0000    |
| C22   | 1.0718(2)   | 0.34140(12) | 0.84625(15) | 0.0295                 | 1.0000    |
| C23   | 1.0807(2)   | 0.39672(13) | 0.77594(16) | 0.0356                 | 1.0000    |
| C24   | 1.2065(3)   | 0.44576(16) | 0.8077(2)   | 0.0506                 | 1.0000    |
| C25   | 1.2220(4)   | 0.5026(2)   | 0.7403(2)   | 0.0745                 | 1.0000    |
| C26   | 0.9264(2)   | 0.24858(12) | 0.74660(14) | 0.0290                 | 1.0000    |
| C27   | 1.0374(3)   | 0.19318(14) | 0.74197(16) | 0.0378                 | 1.0000    |
| C28   | 0.9987(4)   | 0.15681(19) | 0.6518(2)   | 0.0659                 | 1.0000    |
| C29   | 1.0885(4)   | 0.09432(18) | 0.6382(2)   | 0.0616                 | 1.0000    |
| C30   | 0.8117(2)   | 0.33796(13) | 0.81902(15) | 0.0298                 | 1.0000    |
| C31   | 0.8003(3)   | 0.38832(14) | 0.89383(16) | 0.0362                 | 1.0000    |
| C32   | 0.6616(3)   | 0.42858(16) | 0.87052(19) | 0.0489                 | 1.0000    |
| C33   | 0.6378(4)   | 0.47591(19) | 0.9446(2)   | 0.0678                 | 1.0000    |
| C34   | 0.9635(2)   | 0.24205(12) | 0.90935(14) | 0.0281                 | 1.0000    |
| C35   | 0.8533(2)   | 0.18352(14) | 0.90641(16) | 0.0365                 | 1.0000    |
| C36   | 0.8837(3)   | 0.14019(16) | 0.99208(17) | 0.0461                 | 1.0000    |
| C37   | 1.0218(3)   | 0.10234(18) | 1.0142(2)   | 0.0593                 | 1.0000    |
| C41   | 0.6347(7)   | 0.5624(5)   | 0.6058(7)   | 0.0863                 | 0.644(12) |



|      |             |             |             |        |           |
|------|-------------|-------------|-------------|--------|-----------|
| C142 | 0.4816(5)   | 0.5390(4)   | 0.6317(4)   | 0.1180 | 0.644(12) |
| C143 | 0.7433(8)   | 0.4874(4)   | 0.6317(6)   | 0.0653 | 0.356(12) |
| C51  | 0.6327(9)   | 0.5637(7)   | 0.6291(12)  | 0.0719 | 0.356(12) |
| C152 | 0.4749(7)   | 0.5180(5)   | 0.6017(6)   | 0.1078 | 0.356(12) |
| C153 | 0.7761(5)   | 0.5046(3)   | 0.6402(3)   | 0.0653 | 0.644(12) |
| F1   | 0.4633(2)   | 0.24550(12) | 0.84601(10) | 0.0689 | 1.0000    |
| O11  | 0.30475(17) | 0.27917(10) | 0.45204(11) | 0.0415 | 1.0000    |
| O12  | 0.59920(17) | 0.19404(10) | 0.73180(11) | 0.0424 | 1.0000    |
| O13  | 0.3132(2)   | 0.29090(13) | 0.69156(13) | 0.0568 | 1.0000    |
| O14  | 0.6277(2)   | 0.22220(12) | 0.50429(13) | 0.0523 | 1.0000    |
| H121 | 0.54785(17) | 0.20758(10) | 0.76351(11) | 0.0643 | 1.0000    |
| H162 | 0.5372(2)   | 0.14280(14) | 0.61901(16) | 0.0448 | 1.0000    |
| H161 | 0.4170(2)   | 0.15755(14) | 0.66518(16) | 0.0437 | 1.0000    |
| H151 | 0.2573(2)   | 0.21582(14) | 0.53949(16) | 0.0447 | 1.0000    |
| H152 | 0.3628(2)   | 0.17801(14) | 0.49360(16) | 0.0452 | 1.0000    |
| H111 | 0.35391(17) | 0.27406(10) | 0.41721(11) | 0.0624 | 1.0000    |
| H181 | 0.6606(2)   | 0.28242(14) | 0.61070(16) | 0.0426 | 1.0000    |
| H182 | 0.5587(2)   | 0.32037(14) | 0.53014(16) | 0.0418 | 1.0000    |
| H141 | 0.5705(2)   | 0.23054(12) | 0.45942(13) | 0.0774 | 1.0000    |
| H171 | 0.4953(3)   | 0.33185(15) | 0.68498(17) | 0.0476 | 1.0000    |
| H172 | 0.3723(3)   | 0.34968(15) | 0.60284(17) | 0.0477 | 1.0000    |
| H131 | 0.3499(2)   | 0.27184(13) | 0.73887(13) | 0.0852 | 1.0000    |
| H261 | 0.8396(2)   | 0.22367(12) | 0.73787(14) | 0.0343 | 1.0000    |
| H262 | 0.9200(2)   | 0.28454(12) | 0.69961(14) | 0.0350 | 1.0000    |
| H272 | 1.0407(3)   | 0.15426(14) | 0.78561(16) | 0.0449 | 1.0000    |
| H271 | 1.1281(3)   | 0.21660(14) | 0.75179(16) | 0.0456 | 1.0000    |
| H281 | 0.9973(4)   | 0.19365(19) | 0.6073(2)   | 0.0790 | 1.0000    |
| H282 | 0.9093(4)   | 0.13075(19) | 0.6422(2)   | 0.0794 | 1.0000    |
| H291 | 1.1859(4)   | 0.11071(18) | 0.6484(2)   | 0.0922 | 1.0000    |
| H292 | 1.0619(4)   | 0.07359(18) | 0.5785(2)   | 0.0922 | 1.0000    |
| H293 | 1.0848(4)   | 0.05277(18) | 0.6794(2)   | 0.0922 | 1.0000    |
| H301 | 0.7374(2)   | 0.30278(13) | 0.81059(15) | 0.0349 | 1.0000    |
| H302 | 0.8023(2)   | 0.36565(13) | 0.76543(15) | 0.0360 | 1.0000    |
| H312 | 0.8743(3)   | 0.42491(14) | 0.90526(16) | 0.0431 | 1.0000    |
| H311 | 0.8025(3)   | 0.35864(14) | 0.94595(16) | 0.0435 | 1.0000    |
| H321 | 0.6571(3)   | 0.45818(16) | 0.81908(19) | 0.0591 | 1.0000    |
| H322 | 0.5888(3)   | 0.39147(16) | 0.85697(19) | 0.0587 | 1.0000    |
| H333 | 0.6396(4)   | 0.44511(19) | 0.9951(2)   | 0.1017 | 1.0000    |
| H331 | 0.7116(4)   | 0.51274(19) | 0.9585(2)   | 0.1011 | 1.0000    |
| H332 | 0.5493(4)   | 0.50070(19) | 0.9287(2)   | 0.1016 | 1.0000    |

|      |           |             |             |        |           |
|------|-----------|-------------|-------------|--------|-----------|
| H222 | 1.1480(2) | 0.30756(12) | 0.85368(15) | 0.0349 | 1.0000    |
| H221 | 1.0756(2) | 0.36743(12) | 0.90168(15) | 0.0359 | 1.0000    |
| H231 | 0.9983(2) | 0.42627(13) | 0.76268(16) | 0.0435 | 1.0000    |
| H232 | 1.0881(2) | 0.37115(13) | 0.72259(16) | 0.0429 | 1.0000    |
| H241 | 1.2862(3) | 0.41513(16) | 0.8215(2)   | 0.0615 | 1.0000    |
| H242 | 1.1975(3) | 0.47024(16) | 0.8610(2)   | 0.0610 | 1.0000    |
| H253 | 1.2443(4) | 0.4768(2)   | 0.6914(2)   | 0.1121 | 1.0000    |
| H252 | 1.1356(4) | 0.5286(2)   | 0.7200(2)   | 0.1123 | 1.0000    |
| H251 | 1.2946(4) | 0.5367(2)   | 0.7658(2)   | 0.1118 | 1.0000    |
| H341 | 1.0521(2) | 0.21718(12) | 0.91470(14) | 0.0336 | 1.0000    |
| H342 | 0.9645(2) | 0.27347(12) | 0.96020(14) | 0.0348 | 1.0000    |
| H352 | 0.7640(2) | 0.20569(14) | 0.89932(16) | 0.0451 | 1.0000    |
| H351 | 0.8509(2) | 0.14980(14) | 0.85888(16) | 0.0437 | 1.0000    |
| H362 | 0.8132(3) | 0.10157(16) | 0.98988(17) | 0.0547 | 1.0000    |
| H361 | 0.8778(3) | 0.17433(16) | 1.04074(17) | 0.0562 | 1.0000    |
| H371 | 1.0353(3) | 0.07515(18) | 0.9637(2)   | 0.0891 | 1.0000    |
| H373 | 1.0965(3) | 0.13895(18) | 1.0310(2)   | 0.0894 | 1.0000    |
| H372 | 1.0253(3) | 0.06845(18) | 1.0628(2)   | 0.0880 | 1.0000    |
| H411 | 0.6609(7) | 0.6085(5)   | 0.6355(7)   | 0.1037 | 0.644(12) |
| H412 | 0.6204(7) | 0.5680(5)   | 0.5442(7)   | 0.1031 | 0.644(12) |
| H511 | 0.6467(9) | 0.5889(7)   | 0.6851(12)  | 0.0869 | 0.356(12) |
| H512 | 0.6419(9) | 0.5980(7)   | 0.5831(12)  | 0.0869 | 0.356(12) |

## Thermal Parameters

| Label | U <sub>11</sub> | U <sub>22</sub> | U <sub>33</sub> | U <sub>23</sub> | U <sub>13</sub> | U <sub>12</sub> |
|-------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| C15   | 0.0303(12)      | 0.0416(14)      | 0.0333(13)      | 0.0048(11)      | -0.0052(10)     | -0.0088(10)     |
| C16   | 0.0310(12)      | 0.0397(13)      | 0.0342(13)      | 0.0040(10)      | -0.0031(10)     | -0.0046(10)     |
| C17   | 0.0375(13)      | 0.0439(14)      | 0.0378(13)      | -0.0012(11)     | 0.0061(11)      | 0.0022(11)      |
| C18   | 0.0256(11)      | 0.0448(14)      | 0.0340(12)      | 0.0041(11)      | 0.0005(10)      | -0.0037(10)     |
| C19   | 0.0224(10)      | 0.0357(12)      | 0.0290(12)      | 0.0001(10)      | -0.0020(9)      | -0.0039(9)      |
| N21   | 0.0230(9)       | 0.0299(10)      | 0.0213(9)       | 0.0019(7)       | 0.0008(7)       | 0.0031(7)       |
| C22   | 0.0223(10)      | 0.0301(12)      | 0.0325(12)      | -0.0001(9)      | -0.0011(9)      | -0.0015(9)      |
| C23   | 0.0342(12)      | 0.0340(13)      | 0.0366(13)      | 0.0040(10)      | 0.0042(10)      | -0.0023(10)     |
| C24   | 0.0478(16)      | 0.0470(16)      | 0.0533(17)      | -0.0004(13)     | 0.0045(13)      | -0.0172(13)     |
| C25   | 0.085(2)        | 0.065(2)        | 0.072(2)        | 0.0121(18)      | 0.0141(19)      | -0.0389(19)     |
| C26   | 0.0338(12)      | 0.0297(11)      | 0.0218(10)      | -0.0009(9)      | 0.0026(9)       | 0.0009(9)       |
| C27   | 0.0449(14)      | 0.0363(13)      | 0.0342(13)      | 0.0000(10)      | 0.0137(11)      | 0.0055(11)      |
| C28   | 0.104(3)        | 0.0555(19)      | 0.0380(16)      | -0.0030(13)     | 0.0168(16)      | 0.0296(18)      |
| C29   | 0.073(2)        | 0.0550(19)      | 0.061(2)        | -0.0091(15)     | 0.0246(17)      | 0.0065(16)      |

|      |            |            |            |             |            |             |
|------|------------|------------|------------|-------------|------------|-------------|
| C30  | 0.0222(10) | 0.0354(12) | 0.0298(12) | 0.0034(10)  | 0.0021(9)  | 0.0071(9)   |
| C31  | 0.0379(13) | 0.0376(13) | 0.0343(13) | -0.0023(10) | 0.0107(10) | 0.0048(10)  |
| C32  | 0.0495(16) | 0.0502(16) | 0.0516(16) | 0.0074(13)  | 0.0211(13) | 0.0183(13)  |
| C33  | 0.086(2)   | 0.0577(19) | 0.074(2)   | 0.0038(17)  | 0.046(2)   | 0.0259(17)  |
| C34  | 0.0270(11) | 0.0311(11) | 0.0232(10) | 0.0040(9)   | -0.0001(9) | 0.0019(9)   |
| C35  | 0.0298(12) | 0.0463(14) | 0.0316(12) | 0.0061(11)  | 0.0037(10) | -0.0025(10) |
| C36  | 0.0479(15) | 0.0515(16) | 0.0379(14) | 0.0101(12)  | 0.0079(12) | -0.0064(12) |
| C37  | 0.0582(18) | 0.0522(18) | 0.063(2)   | 0.0242(15)  | 0.0053(15) | 0.0019(14)  |
| C41  | 0.069(4)   | 0.069(4)   | 0.115(6)   | 0.053(4)    | 0.010(3)   | 0.001(3)    |
| Cl42 | 0.0860(18) | 0.155(3)   | 0.126(3)   | 0.015(2)    | 0.0507(19) | 0.0403(19)  |
| Cl43 | 0.0599(18) | 0.0655(18) | 0.0702(11) | 0.0084(13)  | 0.0143(13) | 0.0088(13)  |
| C51  | 0.061(5)   | 0.073(6)   | 0.087(6)   | -0.008(5)   | 0.029(5)   | 0.004(4)    |
| Cl52 | 0.073(2)   | 0.139(4)   | 0.124(4)   | -0.033(3)   | 0.047(2)   | -0.029(3)   |
| Cl53 | 0.0599(18) | 0.0655(18) | 0.0702(11) | 0.0084(13)  | 0.0143(13) | 0.0088(13)  |
| F1   | 0.0848(13) | 0.0954(14) | 0.0286(8)  | 0.0011(8)   | 0.0174(8)  | 0.0032(11)  |
| O11  | 0.0330(9)  | 0.0502(11) | 0.0342(9)  | 0.0079(8)   | -0.0063(7) | -0.0046(8)  |
| O12  | 0.0298(9)  | 0.0572(11) | 0.0334(9)  | 0.0074(8)   | -0.0063(7) | -0.0041(8)  |
| O13  | 0.0451(11) | 0.0810(15) | 0.0482(11) | 0.0023(10)  | 0.0188(9)  | 0.0121(10)  |
| O14  | 0.0473(11) | 0.0668(13) | 0.0456(11) | -0.0005(10) | 0.0164(9)  | 0.0097(9)   |

## Distances

|     |      |           |  |     |      |           |
|-----|------|-----------|--|-----|------|-----------|
| C15 | C19  | 1.532(3)Å |  | C15 | O11  | 1.426(3)Å |
| C15 | H151 | 0.967Å    |  | C15 | H152 | 0.977Å    |
| C16 | C19  | 1.536(3)Å |  | C16 | O12  | 1.421(3)Å |
| C16 | H162 | 0.973Å    |  | C16 | H161 | 0.973Å    |
| C17 | C19  | 1.528(3)Å |  | C17 | O13  | 1.432(3)Å |
| C17 | H171 | 0.973Å    |  | C17 | H172 | 0.978Å    |
| C18 | C19  | 1.527(3)Å |  | C18 | O14  | 1.420(3)Å |
| C18 | H181 | 0.982Å    |  | C18 | H182 | 0.968Å    |
| N21 | C22  | 1.522(3)Å |  | N21 | C26  | 1.513(3)Å |
| N21 | C30  | 1.521(3)Å |  | N21 | C34  | 1.523(3)Å |
| C22 | C23  | 1.510(3)Å |  | C22 | H222 | 0.960Å    |
| C22 | H221 | 0.984Å    |  | C23 | C24  | 1.520(3)Å |
| C23 | H231 | 0.960Å    |  | C23 | H232 | 0.976Å    |
| C24 | C25  | 1.511(4)Å |  | C24 | H241 | 0.950Å    |
| C24 | H242 | 0.970Å    |  | C25 | H253 | 0.968Å    |
| C25 | H252 | 0.966Å    |  | C25 | H251 | 0.963Å    |
| C26 | C27  | 1.505(3)Å |  | C26 | H261 | 0.955Å    |
| C26 | H262 | 0.975Å    |  | C27 | C28  | 1.530(4)Å |

|      |      |            |  |      |      |            |  |
|------|------|------------|--|------|------|------------|--|
| C27  | H272 | 0.979Å     |  | C27  | H271 | 0.976Å     |  |
| C28  | C29  | 1.487(4)Å  |  | C28  | H281 | 0.964Å     |  |
| C28  | H282 | 0.986Å     |  | C29  | H291 | 0.989Å     |  |
| C29  | H292 | 0.987Å     |  | C29  | H293 | 1.000Å     |  |
| C30  | C31  | 1.514(3)Å  |  | C30  | H301 | 0.960Å     |  |
| C30  | H302 | 0.966Å     |  | C31  | C32  | 1.526(3)Å  |  |
| C31  | H312 | 0.975Å     |  | C31  | H311 | 0.976Å     |  |
| C32  | C33  | 1.508(4)Å  |  | C32  | H321 | 0.963Å     |  |
| C32  | H322 | 0.973Å     |  | C33  | H333 | 0.968Å     |  |
| C33  | H331 | 0.977Å     |  | C33  | H332 | 0.967Å     |  |
| C34  | C35  | 1.517(3)Å  |  | C34  | H341 | 0.975Å     |  |
| C34  | H342 | 0.980Å     |  | C35  | C36  | 1.527(3)Å  |  |
| C35  | H352 | 0.956Å     |  | C35  | H351 | 0.961Å     |  |
| C36  | C37  | 1.501(4)Å  |  | C36  | H362 | 0.985Å     |  |
| C36  | H361 | 0.996Å     |  | C37  | H371 | 0.971Å     |  |
| C37  | H373 | 0.984Å     |  | C37  | H372 | 0.974Å     |  |
| C41  | Cl42 | 1.718(7)Å  |  | C41  | Cl43 | 1.723(7)Å  |  |
| C41  | C51  | 0.37(2)Å   |  | C41  | Cl52 | 1.767(11)Å |  |
| C41  | Cl53 | 1.734(9)Å  |  | C41  | H411 | 0.962Å     |  |
| C41  | H412 | 0.952Å     |  | C41  | H512 | 0.749Å     |  |
| Cl42 | C51  | 1.577(12)Å |  | Cl42 | Cl52 | 0.598(6)Å  |  |
| Cl43 | C51  | 1.760(16)Å |  | Cl43 | Cl53 | 0.449(7)Å  |  |
| C51  | Cl52 | 1.736(9)Å  |  | C51  | Cl53 | 1.758(9)Å  |  |
| C51  | H411 | 0.856Å     |  | C51  | H511 | 0.972Å     |  |
| C51  | H512 | 0.975Å     |  | O11  | H111 | 0.820Å     |  |
| O12  | H121 | 0.830Å     |  | O13  | H131 | 0.824Å     |  |
| O14  | H141 | 0.810Å     |  | H411 | H512 | 0.824Å     |  |
| H412 | H512 | 0.808Å     |  |      |      |            |  |

## Angles

|     |     |      |             |  |      |     |      |          |
|-----|-----|------|-------------|--|------|-----|------|----------|
| C19 | C15 | O11  | 113.26(19)° |  | C19  | C15 | H151 | 110.508° |
| O11 | C15 | H151 | 106.134°    |  | C19  | C15 | H152 | 109.712° |
| O11 | C15 | H152 | 109.879°    |  | H151 | C15 | H152 | 107.122° |
| C19 | C16 | O12  | 113.75(19)° |  | C19  | C16 | H162 | 107.212° |
| O12 | C16 | H162 | 109.275°    |  | C19  | C16 | H161 | 109.331° |
| O12 | C16 | H161 | 110.416°    |  | H162 | C16 | H161 | 106.561° |
| C19 | C17 | O13  | 113.5(2)°   |  | C19  | C17 | H171 | 109.087° |
| O13 | C17 | H171 | 109.563°    |  | C19  | C17 | H172 | 108.616° |
| O13 | C17 | H172 | 106.660°    |  | H171 | C17 | H172 | 109.320° |

|      |     |      |             |  |      |     |      |             |
|------|-----|------|-------------|--|------|-----|------|-------------|
| C19  | C18 | O14  | 113.9(2)°   |  | C19  | C18 | H181 | 107.706°    |
| O14  | C18 | H181 | 107.980°    |  | C19  | C18 | H182 | 108.055°    |
| O14  | C18 | H182 | 110.573°    |  | H181 | C18 | H182 | 108.435°    |
| C15  | C19 | C16  | 106.95(18)° |  | C15  | C19 | C17  | 109.8(2)°   |
| C16  | C19 | C17  | 111.4(2)°   |  | C15  | C19 | C18  | 110.73(19)° |
| C16  | C19 | C18  | 110.14(19)° |  | C17  | C19 | C18  | 107.82(19)° |
| C22  | N21 | C26  | 111.70(17)° |  | C22  | N21 | C30  | 111.98(17)° |
| C26  | N21 | C30  | 105.40(15)° |  | C22  | N21 | C34  | 105.55(15)° |
| C26  | N21 | C34  | 111.12(16)° |  | C30  | N21 | C34  | 111.22(16)° |
| N21  | C22 | C23  | 116.85(17)° |  | N21  | C22 | H222 | 104.974°    |
| C23  | C22 | H222 | 109.405°    |  | N21  | C22 | H221 | 106.361°    |
| C23  | C22 | H221 | 109.613°    |  | H222 | C22 | H221 | 109.374°    |
| C22  | C23 | C24  | 109.3(2)°   |  | C22  | C23 | H231 | 109.594°    |
| C24  | C23 | H231 | 109.997°    |  | C22  | C23 | H232 | 110.206°    |
| C24  | C23 | H232 | 109.718°    |  | H231 | C23 | H232 | 108.000°    |
| C23  | C24 | C25  | 112.2(2)°   |  | C23  | C24 | H241 | 108.285°    |
| C25  | C24 | H241 | 109.916°    |  | C23  | C24 | H242 | 108.382°    |
| C25  | C24 | H242 | 109.972°    |  | H241 | C24 | H242 | 107.995°    |
| C24  | C25 | H253 | 108.074°    |  | C24  | C25 | H252 | 109.543°    |
| H253 | C25 | H252 | 108.864°    |  | C24  | C25 | H251 | 109.405°    |
| H253 | C25 | H251 | 110.610°    |  | H252 | C25 | H251 | 110.304°    |
| N21  | C26 | C27  | 117.31(18)° |  | N21  | C26 | H261 | 106.723°    |
| C27  | C26 | H261 | 109.128°    |  | N21  | C26 | H262 | 106.300°    |
| C27  | C26 | H262 | 109.026°    |  | H261 | C26 | H262 | 107.991°    |
| C26  | C27 | C28  | 107.6(2)°   |  | C26  | C27 | H272 | 110.451°    |
| C28  | C27 | H272 | 107.556°    |  | C26  | C27 | H271 | 111.367°    |
| C28  | C27 | H271 | 110.899°    |  | H272 | C27 | H271 | 108.868°    |
| C27  | C28 | C29  | 115.5(3)°   |  | C27  | C28 | H281 | 109.521°    |
| C29  | C28 | H281 | 109.128°    |  | C27  | C28 | H282 | 111.654°    |
| C29  | C28 | H282 | 99.512°     |  | H281 | C28 | H282 | 111.163°    |
| C28  | C29 | H291 | 110.286°    |  | C28  | C29 | H292 | 112.892°    |
| H291 | C29 | H292 | 107.689°    |  | C28  | C29 | H293 | 111.301°    |
| H291 | C29 | H293 | 107.621°    |  | H292 | C29 | H293 | 106.816°    |
| N21  | C30 | C31  | 117.01(18)° |  | N21  | C30 | H301 | 105.892°    |
| C31  | C30 | H301 | 108.121°    |  | N21  | C30 | H302 | 106.519°    |
| C31  | C30 | H302 | 110.924°    |  | H301 | C30 | H302 | 107.963°    |
| C30  | C31 | C32  | 109.2(2)°   |  | C30  | C31 | H312 | 111.163°    |
| C32  | C31 | H312 | 108.756°    |  | C30  | C31 | H311 | 109.353°    |
| C32  | C31 | H311 | 107.816°    |  | H312 | C31 | H311 | 110.524°    |
| C31  | C32 | C33  | 112.4(3)°   |  | C31  | C32 | H321 | 109.227°    |

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|------|------|------|-------------|--|------|------|------|-----------|
| C33  | C32  | H321 | 110.410°    |  | C31  | C32  | H322 | 107.885°  |
| C33  | C32  | H322 | 108.551°    |  | H321 | C32  | H322 | 108.258°  |
| C32  | C33  | H333 | 109.394°    |  | C32  | C33  | H331 | 108.351°  |
| H333 | C33  | H331 | 109.891°    |  | C32  | C33  | H332 | 111.151°  |
| H333 | C33  | H332 | 108.643°    |  | H331 | C33  | H332 | 109.403°  |
| N21  | C34  | C35  | 116.12(17)° |  | N21  | C34  | H341 | 106.890°  |
| C35  | C34  | H341 | 108.216°    |  | N21  | C34  | H342 | 107.091°  |
| C35  | C34  | H342 | 107.419°    |  | H341 | C34  | H342 | 111.133°  |
| C34  | C35  | C36  | 109.80(19)° |  | C34  | C35  | H352 | 110.805°  |
| C36  | C35  | H352 | 107.766°    |  | C34  | C35  | H351 | 110.659°  |
| C36  | C35  | H351 | 108.967°    |  | H352 | C35  | H351 | 108.777°  |
| C35  | C36  | C37  | 114.9(2)°   |  | C35  | C36  | H362 | 109.910°  |
| C37  | C36  | H362 | 106.858°    |  | C35  | C36  | H361 | 108.987°  |
| C37  | C36  | H361 | 108.639°    |  | H362 | C36  | H361 | 107.301°  |
| C36  | C37  | H371 | 109.623°    |  | C36  | C37  | H373 | 110.351°  |
| H371 | C37  | H373 | 108.700°    |  | C36  | C37  | H372 | 109.404°  |
| H371 | C37  | H372 | 109.728°    |  | H373 | C37  | H372 | 109.019°  |
| Cl42 | C41  | Cl43 | 107.0(5)°   |  | Cl42 | C41  | C51  | 62(2)°    |
| Cl43 | C41  | C51  | 90(3)°      |  | Cl42 | C41  | Cl52 | 19.7(2)°  |
| Cl43 | C41  | Cl52 | 99.2(6)°    |  | C51  | C41  | Cl52 | 79(2)°    |
| Cl42 | C41  | Cl53 | 118.5(5)°   |  | Cl43 | C41  | Cl53 | 14.9(2)°  |
| C51  | C41  | Cl53 | 88(2)°      |  | Cl52 | C41  | Cl53 | 113.3(6)° |
| Cl42 | C41  | H411 | 104.638°    |  | Cl43 | C41  | H411 | 119.030°  |
| C51  | C41  | H411 | 62.446°     |  | Cl52 | C41  | H411 | 123.424°  |
| Cl53 | C41  | H411 | 105.307°    |  | Cl42 | C41  | H412 | 109.822°  |
| Cl43 | C41  | H412 | 105.147°    |  | C51  | C41  | H412 | 164.995°  |
| Cl52 | C41  | H412 | 95.339°     |  | Cl53 | C41  | H412 | 107.383°  |
| Cl42 | C41  | H512 | 120.937°    |  | Cl43 | C41  | H512 | 131.775°  |
| C51  | C41  | H512 | 116.568°    |  | Cl52 | C41  | H512 | 123.981°  |
| Cl53 | C41  | H512 | 120.407°    |  | H411 | C41  | H412 | 111.039°  |
| H411 | C41  | H512 | 55.860°     |  | H412 | C41  | H512 | 55.183°   |
| C41  | Cl42 | C51  | 12.0(9)°    |  | C41  | Cl42 | Cl52 | 84.8(10)° |
| C51  | Cl42 | Cl52 | 95.2(10)°   |  | C41  | Cl43 | C51  | 12.2(8)°  |
| C41  | Cl43 | Cl53 | 83.9(14)°   |  | C51  | Cl43 | Cl53 | 82.4(15)° |
| C41  | C51  | Cl42 | 106(3)°     |  | C41  | C51  | Cl43 | 78(2)°    |
| Cl42 | C51  | Cl43 | 111.8(8)°   |  | C41  | C51  | Cl52 | 89(3)°    |
| Cl42 | C51  | Cl52 | 20.1(2)°    |  | Cl43 | C51  | Cl52 | 99.0(8)°  |
| C41  | C51  | Cl53 | 80(2)°      |  | Cl42 | C51  | Cl53 | 125.5(9)° |
| Cl43 | C51  | Cl53 | 14.7(2)°    |  | Cl52 | C51  | Cl53 | 113.6(8)° |
| C41  | C51  | H411 | 94.846°     |  | Cl42 | C51  | H411 | 123.563°  |

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|------|------|------|-----------|--|------|------|------|-----------|
| Cl43 | C51  | H411 | 123.704°  |  | Cl52 | C51  | H411 | 137.028°  |
| Cl53 | C51  | H411 | 109.184°  |  | C41  | C51  | H511 | 153.170°  |
| Cl42 | C51  | H511 | 92.596°   |  | Cl43 | C51  | H511 | 112.994°  |
| Cl52 | C51  | H511 | 112.244°  |  | Cl53 | C51  | H511 | 104.746°  |
| C41  | C51  | H512 | 43.422°   |  | Cl42 | C51  | H512 | 117.066°  |
| Cl43 | C51  | H512 | 110.490°  |  | Cl52 | C51  | H512 | 110.764°  |
| Cl53 | C51  | H512 | 104.208°  |  | H411 | C51  | H511 | 58.456°   |
| H411 | C51  | H512 | 52.981°   |  | H511 | C51  | H512 | 110.862°  |
| C41  | Cl52 | Cl42 | 75.5(10)° |  | C41  | Cl52 | C51  | 12.2(8)°  |
| Cl42 | Cl52 | C51  | 64.7(10)° |  | C41  | Cl53 | Cl43 | 81.1(14)° |
| C41  | Cl53 | C51  | 12.2(8)°  |  | Cl43 | Cl53 | C51  | 82.9(15)° |
| C15  | O11  | H111 | 109.292°  |  | C16  | O12  | H121 | 100.500°  |
| C17  | O13  | H131 | 111.010°  |  | C18  | O14  | H141 | 99.207°   |
| C41  | H411 | C51  | 22.707°   |  | C41  | H411 | H512 | 48.831°   |
| C51  | H411 | H512 | 70.893°   |  | C41  | H412 | H512 | 49.546°   |
| C41  | H512 | C51  | 20.010°   |  | C41  | H512 | H411 | 75.308°   |
| C51  | H512 | H411 | 56.126°   |  | C41  | H512 | H412 | 75.271°   |
| C51  | H512 | H412 | 94.665°   |  | H411 | H512 | H412 | 150.568°  |