# Cation-Directed Atropselective Synthesis of BINOL Derivatives

**John David Jolliffe**

*A dissertation presented in partial fulfilment of the requirements for the award of the degree of*

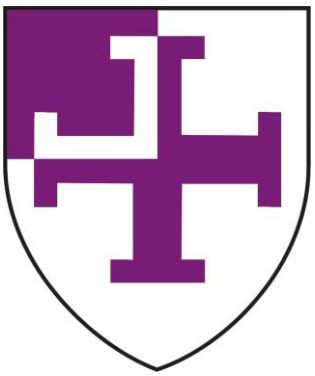
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## Dedication

I would like to dedicate this thesis to Dr Erhard Franken-Stellamans, who inspired me to pursue a career in chemistry.

## Declaration

This dissertation describes work carried out in the Chemistry Research Laboratory at the University of Oxford between October 2013 and November 2016. The dissertation is a result of my own work and includes nothing that is the outcome of work done in collaboration except where specifically indicated in the text.

John David Jolliffe

## Acknowledgements

First, I would like to thank Martin for giving me the opportunity to carry out research in his laboratories. I doubt I will ever meet another supervisor with such exuberant enthusiasm for chemistry and proper champagne etiquette (or sparkling white burgundy if necessary). I will always remain grateful for his support and patience during my time in Oxford.

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Elizabeth “shy tory” Munday, Seb “co-director of the SCC” Murphy, Niamh “this one time at rowing” Broderick, Hugo “Vicktor’s best friend” Kent-Egan, Owen “friend of the traveller community” Smith, Jack “boyband” Sutro, Elisabetta “diabetes” Ronchi and Pearse “fumehood defiler” Solon.

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Thank you to Dr Erhard Franken-Stellamans. He inspired me to pursue a career in chemistry. I will always be grateful for him sparking and nurturing my interest in chemistry and science at a young age. Hopefully I will one day have a workshop half as awesome as his.

Finally, I am eternally grateful to my friends and family for their patience and support over the years. Especially my brother Marc for putting up with “unique occurrences” and Mum and Dad for putting up with me. I know I was a bit of a £$%& from time to time (sorry!) and for providing emergency financial assistance when funds ran low ☺. Thank you, Reiner (aka stepdad) for joining our family, and for showing me how to cook properly with wine. His interactions with Baldrick will forever remain legendary. Long live the Birkenstock!

I would like to end with some wise and inspiring words that have inspired me over the years:

*“So long, and thanks for all the fish”*

## Abbreviations

| | |
|---|---|
| **Å** | Ångströms |
| **Ac** | acetyl |
| **ADP** | anisotropic displacement parameters |
| **AH/HA** | *denotes a generic Brønsted acid* |
| **aq** | aqueous |
| **Ar** | *denotes a generic aromatic system* |
| **BINAM** | 1,1′-binaphthyl-2,2′-diamine |
| **BINAP** | 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene |
| **BINOL** | [1,1'-binaphthalene]-2,2'-diol |
| **Bn** | benzyl |
| **BnMeBINOL** | 2-(benzyloxy)-2'-methoxy-1,1'-binaphthalene |
| **Boc** | *tert*-butoxycarbonyl |
| **br** | broad |
| **$^{i}$Bu** | *iso*-butyl |
| **$^{n}$Bu** | *n*-butyl |
| **$^{t}$Bu** | *tert*-butyl |
| **°C** | degrees Celsius |
| **cat** | catalytic/catalyst |
| **CCD** | charge-coupled device |
| **CCDC** | Cambridge Crystallographic Data Centre |
| **CDC** | Dr Craig D. Campbell |
| **CI** | Chemical Ionization |
| **cm** | centimetre |
| **COSY** | $^{1}$H-$^{1}$H correlation spectroscopy |
| **CPJ** | Dr Craig P. Johnston |
| **CRL** | Chemistry Research Laboratory |
| **cryo** | cryogenic |
| **CSA** | camphorsulfonic acid |
| **Cy** | cyclohexyl |
| **DDQ** | 2,3-dichloro-5,6-dicyano-1,4-benzoquinone |
| ***d.r.*** | diastereomeric ratio |
| **DABCO** | 1,4-diazabicyclo[2.2.2]octane |

| | |
|---|---|
| **dba** | dibenzylideneacetone |
| **dec.** | decomposed |
| **DEPT** | distortionless enhancement by polarization transfer |
| **DIPEA** | *N*,*N*-diisopropylethylamine |
| **DMAP** | *N*,*N*-dimethylpyridin-4-amine |
| **DME** | 1,2-dimethoxyethane |
| **DMF** | *N*,*N*-dimethylformamide |
| **DMSO** | dimethylsulfoxide |
| **DPhil** | Doctor of Philosophy |
| **E** | *denotes a generic electrophile* |
| ***e.e.*** | enantiomeric excess |
| ***e.r.*** | enantiomeric ratio |
| **eq** | equivalents |
| **ESI** | electrospray ionization |
| **ESPT** | excited state proton transfer |
| **Et** | Ethyl |
| **FI** | field ionization |
| **FTIR** | Fourier-transform infra-red spectroscopy |
| **h** | hours |
| **HA/AH** | *denotes a generic Brønsted acid* |
| **HMBC** | heteronuclear multiple-bond correlation spectroscopy |
| **HMPA** | hexamethylphosphoramide |
| **HPLC** | high-performance liquid chromatography |
| **HRMS** | high-resolution mass spectrometry |
| **HSAB** | hard and soft acids and bases |
| **HSQC** | heteronuclear single-quantum correlation spectroscopy |
| **hν** | *denotes irradiation with either visible light or UV photons* |
| ***i*** | *iso* |
| **IPA** | *iso*-propanol |
| **ISC** | intersystem crossing |
| **IUPAC** | International Union of Pure and Applied Chemistry |
| ***J*** | coupling constant |
| **JMG** | Prof. Jonathan M. Goodman |
| **K** | Kelvin |

| | |
|---|---|
| **kcal** | kilocalorie |
| **λ** | wavelength |
| **LA** | *denotes a generic Lewis acid* |
| **LiHMDS** | lithium bis(trimethylsilyl)amide |
| **LRMS** | low-resolution mass spectrometry |
| **M** | moles per litre |
| ***m*** | *meta*- |
| **maj** | major enantiomer |
| **mAU** | milli-absorbance unit |
| **mbar** | millibar |
| ***m*-CPBA** | *meta*-chloroperoxybenzoic acid |
| **Me** | Methyl |
| **MeBINOL** | 2'-Methoxy-[1,1'-binaphthalen]-2-ol |
| **MeCN** | acetonitrile |
| **MHz** | megahertz |
| **min** | minutes/minor enantiomer |
| **mL** | millilitres |
| **mm** | millimetres |
| **mol** | moles |
| **MS** | molecular sieves/mass spectrometry |
| **Ms** | mesyl |
| **μL** | microlitres |
| **NBP** | *N*-bromophthalimide |
| **NBS** | *N*-bromosuccinimide |
| **NHC** | *N*-heterocyclic carbene |
| **NIS** | *N*-iodosuccinimide |
| **nm** | nanometres |
| **NMR** | nuclear magnetic resonance |
| **NOBIN** | 2-amino-2'-hydroxy-1,1'-binaphthyl |
| ***o*** | *ortho*- |
| **$^{i}$Pr** | isopropyl |
| **petrol 40-60** | petroleum ether, boiling point range 40-60 °C |
| **Ph** | phenyl |
| **PhEt** | ethyl benzene |

| | |
|---|---|
| **PhH** | benzene |
| **PhMe** | toluene |
| **PhSH** | benzene thiol |
| **PhEt** | ethyl benzene |
| **PMB** | 4-methoxybenzyl ether |
| **PPA** | polyphosphoric acid |
| **ppm** | parts per million |
| **PTC** | phase-transfer catalysis |
| ***p*-TSA** | p-toluenesulfonic acid |
| **QUINAP** | 1-(2-diphenylphosphino-1-naphthyl)isoquinoline |
| **quant.** | quantitative |
| **Quat** | quaternary |
| **R** | *denotes a generic substituent* |
| **r.t.** | room temperature |
| **rac** | racemization/racemic |
| **RJA** | Dr Roland J. Armstrong |
| **rpm** | revolutions per minute |
| **S** | Selectivity factor |
| **s** | seconds |
| **semi-prep** | semi-preparative |
| **SENS** | *denotes a generic sensitizer* |
| ***t*** | tertiary |
| **T1** | longitudinal relaxation time |
| **TBAB** | tetra-*n*-butylammonium bromide |
| **TBDPS** | *tert*-Butyldiphenylsilyl |
| **TBME** | methyl tert-butyl ether |
| **TET** | triplet energy transfer |
| **Tf** | triflyl |
| **THF** | tetrahydrofuran |
| **TLC** | thin-layer chromatography |
| **TMS** | trimethylsilyl |
| **TRIP** | 3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl hydrogenphosphate |
| **Ts** | *p*-toluenesulfonyl |

| | |
|---|---|
| **Uni-Club** | University-Club, a local tavern |
| **UV** | ultraviolet |
| **VANOL** | 3,3'-diphenyl-2,2'-bi-1-naphthalol |
| **vs.** | versus |
| **w/w** | ratio of weights |
| **wt** | weight |

## Abstract

The use of chiral counterions to facilitate enantioselective mono-*C*-alkylation of enolates has been explored extensively over the past century. We have demonstrated that an alternative mode of reactivity – *O*-alkylation – predominates if the *C*-alkylation is impeded. We have applied this concept to the atropselective dynamic kinetic resolution of 1-aryl-2-tetralones, leading to an organocatalytic synthesis of enantio-enriched BINOL derivatives (**Figure i**).

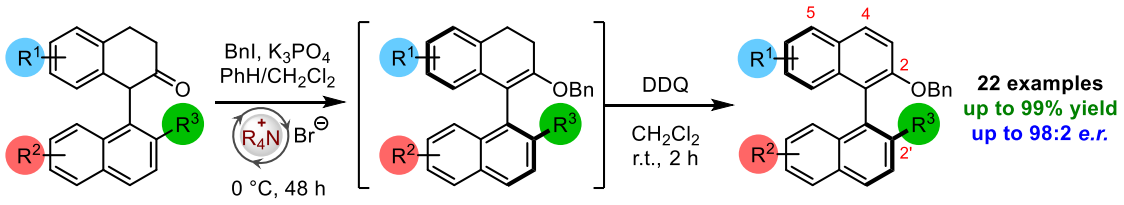



**Figure i** Organocatalytic enantioselective synthesis of BINOL derivatives by atropselective *O*-alkylation of ketones.

In this reaction, the chiral counterion plays a key role as both a phase-transfer catalyst and also as the agent to facilitate atropselective alkylation of rapidly interconverting axially chiral enolates. Treatment of 2-tetralones with base in the presence of an ammonium salt leads to intermediate atropisomeric dihydro-BINOL; oxidation with DDQ leads to BINOLs without loss of *e.r*. This transformation leads to high enantioselectivity and the scope of this reaction is significant: we can insert substituents into any position around the BINOL core, and we can also generate heavily functionalized derivatives without compromising stereochemical integrity.

By employing a substoichiometric amount of alkylating agent, we have applied our reaction protocol to the kinetic resolution of MeBINOL with good selectivity (**Figure ii)**.

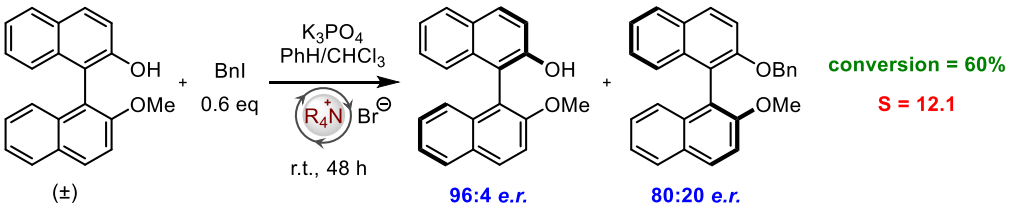



**Figure ii** Cation-directed kinetic resolution of MeBINOL.

# Table of Contents


**1. Introduction ..... 1**

1.1. Atropisomerism ..... 1

1.2. Asymmetric Phase-Transfer Catalysis ..... 3

1.3. Atropselective Synthesis of Biaryls ..... 5

*1.3.1. Method A: Point to Axial Chirality Transfer* ..... 6

*1.3.2. Method B: Atropselective Biaryl Bond Formation* ..... 9

*1.3.3. Method C: Desymmetrization of Prochiral Biaryls* ..... 11

*1.3.4. Method D: De-Novo Construction of an Aromatic Ring* ..... 14

*1.3.5. Method E: Kinetic Resolution of Axially Chiral Biaryls* ..... 17

*1.3.6. Method F: Dynamic Kinetic Resolution of Biaryls* ..... 19

**2. Binaphthyl Synthesis by Iodocyclization of Yne-ones and Yne-ols ..... 24**

2.1. Background and Project Aims ..... 24

2.2. Substrate Synthesis and Racemic Reaction ..... 25

2.3. Attempted Enantioselective Iodocyclizations ..... 30

2.4. Attempted Point to Axial Chirality Transfer ..... 32

**3. Binaphthyl Synthesis by Atropselective Ketone O-Alkylation ..... 33**

3.1. Background and Project Aims ..... 33

3.2. Substrate Synthesis and a Serendipitous Discovery ..... 34

3.3. Ambident Reactivity of Ketones ..... 39

3.4. Barrier to Rotation of **165** ..... 42

3.5. Synthesis of a More Hindered Substrate ..... 44

3.6. Optimization of Asymmetric Reaction Conditions ..... 47

3.7. Oxidation to Orthogonally Protected BINOL and Absolute Configuration ..... 57

3.8. Barrier to Rotation of **166** ..... 59

3.9. Substrate Synthesis ..... 60

*3.9.1. Synthesis of Substituted 1-Tetralones* ..... 60

*3.9.2. Synthesis of Substituted 1-Bromo-2-Methoxynaphthalenes* ..... 64

*3.9.3. Synthesis of Substituted Dihydronaphthalenes* ..... 66

*3.9.4. Synthesis of Substituted 2-Tetralones* ..... 70

3.10. Substrate Scope ..... 73
3.11. Gram Scale Reaction and Absolute Configuration ..... 76
3.12. Deprotection and Derivatization ..... 78
**4. Mechanistic Proposal ..... 85**
4.1. Introduction ..... 85
4.2. Mechanism A: Rate Difference in Ammonium Enolate Alkylation ..... 87
4.3. Mechanism B: Kinetic Counterion-Metathesis ..... 88
4.3. Mechanism C: Equilibration of Ammonium Enolates ..... 89
4.4. Experiments Concerning the Mechanistic Proposal ..... 90
4.5. Proposed Catalyst Substrate Interaction ..... 96
**5. Kinetic Resolution of MeBINOL ..... 102**
5.1. Reaction Optimization ..... 102
5.2. Substrate Synthesis ..... 110
5.3. Dynamic Kinetic Resolution? ..... 111
**6. Conclusions and Future Work ..... 116**
6.1. Conclusion ..... 116
6.2. Future Work ..... 118
**7. Experimental ..... 120**
7.1. General Information ..... 120
*7.1.1. Naming and Numbering* ..... 120
*7.1.2. Reaction Conditions* ..... 120
*7.1.3. Solvents* ..... 120
*7.1.4. Reagents* ..... 120
*7.1.5. Chromatography* ..... 121
*7.1.6. Nuclear Magnetic Resonance Spectrometry* ..... 121
*7.1.7. Infrared Spectroscopy* ..... 121
*7.1.8. Mass Spectrometry* ..... 122
*7.1.9. Polarimetry* ..... 122
*7.1.10. Melting Points* ..... 122
*7.1.11. HPLC* ..... 122
*7.1.12. X-ray Crystallography* ..... 122

7.2. General Experimental Procedures ..... 123
*7.2.1. General Procedure A: Grignard Addition and Elimination* ..... 123
*7.2.2. General Procedure B: Epoxidation and Rearrangement* ..... 123
*7.2.3. General Procedure C: Asymmetric Phase-Transfer Catalyzed Alkylation Followed by DDQ Oxidation* ..... 124
*7.2.4. General Procedure D: Racemic Phase-Transfer Catalyzed Alkylation followed by DDQ Oxidation* ..... 125
7.3. Experimental Procedures ..... 126
**8. Appendices ..... 323**
8.1. Barriers to Rotation ..... 323
*8.1.1. Barrier to Rotation of **165*** ..... 323
*8.1.2. Barrier to Rotation of **166*** ..... 324
8.2. Extended Optimization Tables ..... 325
*8.2.1. Index of Phase-transfer Catalysts* ..... 325
*8.2.2. Optimization Table for the Atropselective O-alkylation of **169*** ..... 327
*8.2.3. Optimizations Tables for the Kinetic Resolution of MeBINOL **281*** ..... 332
8.3. Absolute Configuration ..... 338
*8.3.1. Absolute Configuration of MeBnBINOL **167*** ..... 338
*8.3.2. Absolute Configuration of **275*** ..... 339
*8.3.3. Absolute Configuration of BINOL **168*** ..... 341
*8.3.4. Absolute Configuration of MeBINOL **281*** ..... 342
*8.3.5. Absolute Configuration of **174*** ..... 343
8.4. Deuterium Cross-over Experiment ..... 345
8.5. X-ray Crystallographic Data ..... 346
*8.5.1. X-ray Crystallographic Data and Structure Refinement for **118*** ..... 346
*8.5.2. X-ray Crystallographic Data and Structure Refinement for **129*** ..... 347
*8.5.3. X-ray Crystallographic Data and Structure Refinement for **275*** ..... 348
*8.5.4. X-ray Crystallographic Data and Structure Refinement for **174*** ..... 349
*8.5.5. Crystallographic Information files* ..... 351
**9. References ..... 353**

# 1. Introduction

## 1.1. Atropisomerism

Atropisomerism (from the Greek *atropos*, meaning "not turning") arises when restricted rotation about a single bond results in the formation of two distinct stereoisomers. Compounds are deemed to be atropisomeric if their half-life with respect to racemization, *i.e.* the time it takes for the bulk material to reach 50% *e.e.*, is greater than 1000 s at this temperature. At 300 K this corresponds to a barrier to rotation ($\Delta G^{\ddagger}_{rac}$) of approximately 23.3 kcal mol$^{-1}$.[1]

Atropisomerism is a key feature in many natural products, chiral catalysts, pharmaceuticals; and in recent years has gained increasing importance in these fields (**Figure 1.1.**).

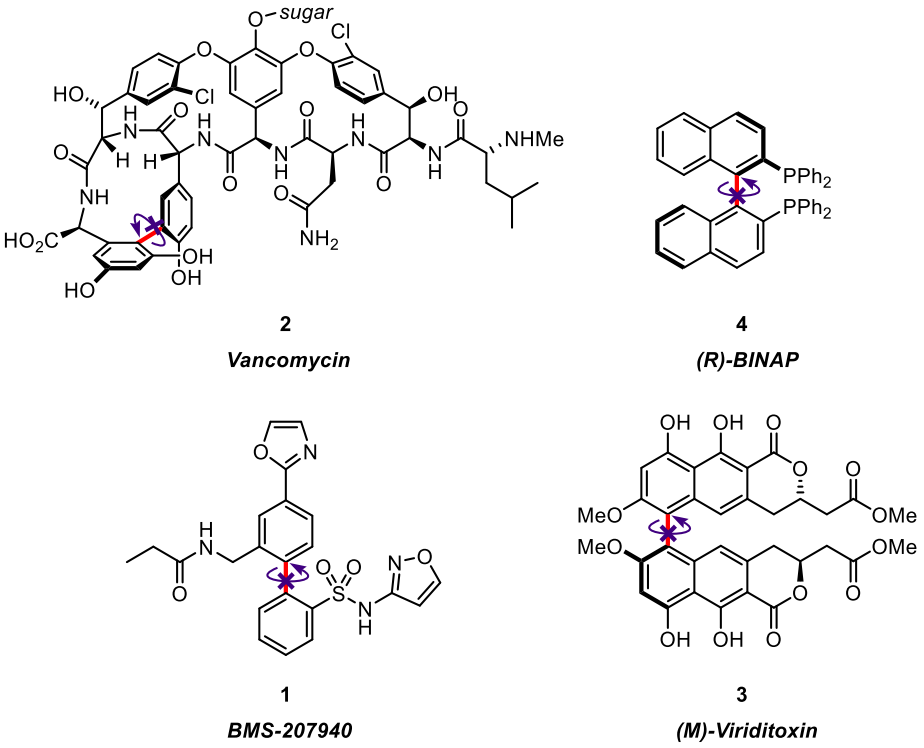



**Figure 1.1.** Atropisomeric natural products, pharmaceuticals and catalysts.

For example, BMS-207940 **1** was an experimental drug that functions as an oral endothelin antagonist for the potential treatment of congestive heart failure and pulmonary hypertension.[2] An example of an atropisomeric natural product is vancomycin **2**, an antibiotic for gram-positive

bacteria, which is produced by the soil bacterium *amycolatopsis orientalis* and has been synthesized *via* total synthesis.[3] Viriditoxin **3**, which was first isolated from the fungus *Aspergillus viridinutans*,[4] possesses hindered rotation about a biaryl axis which is reminiscent of BINAP **4**. The archetypal chiral bidentate bis-phosphine ligand BINAP **4**, has found application in asymmetric hydrogenation and its derivatives are used in a large variety of asymmetric processes.[5]

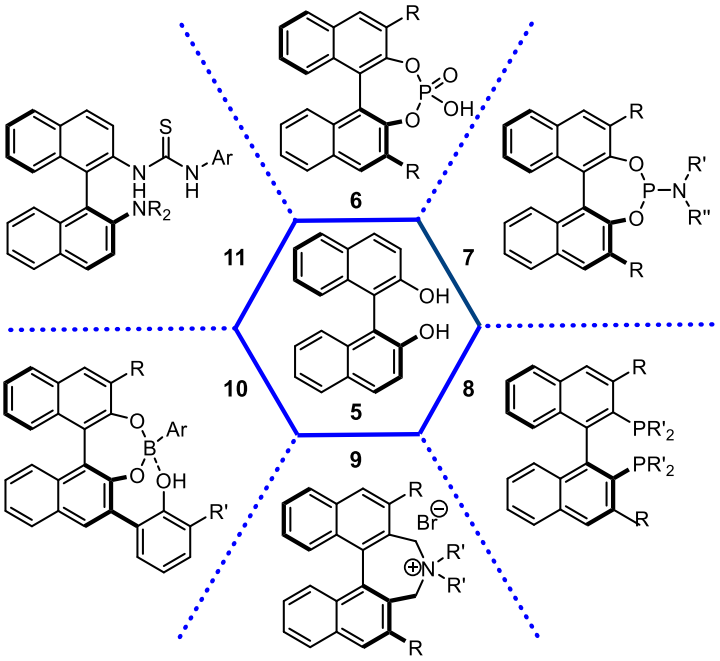


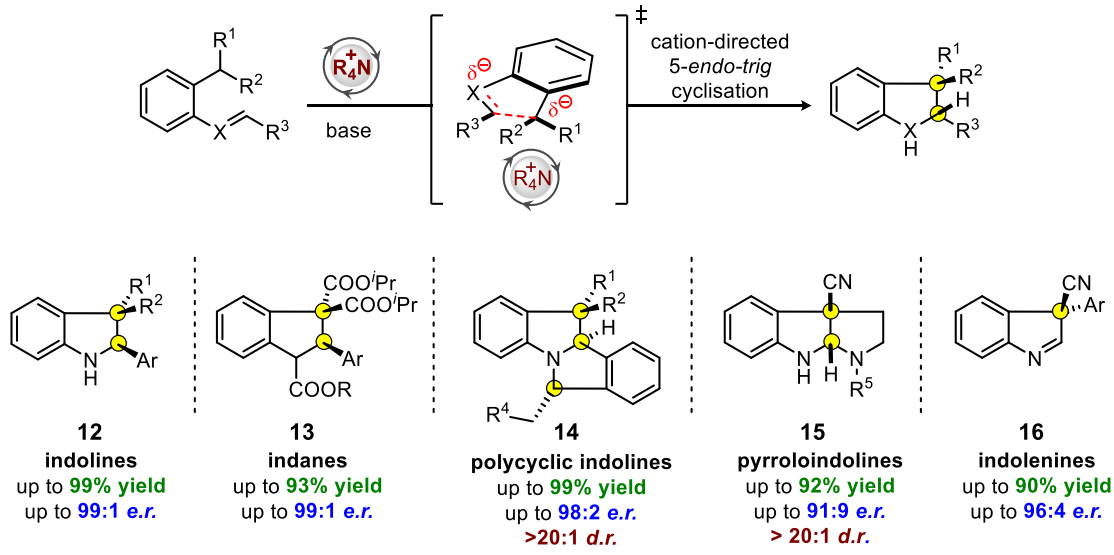

**Figure 1.2.** Chiral catalysts bearing a BINOL backbone.

BINAP **4**, and a number of axially chiral catalysts, can be accessed from BINOL **5**, which possesses hindered rotation about the binaphthyl bond. Chiral catalysts bearing a BINOL backbone **4** have proved to be highly effective (**Figure 1.2.**). The binaphthyl moiety introduces a rigid chiral backbone to the catalyst which can result in a structurally well-defined transition state and aid enantioinduction. A plethora of asymmetric processes have been achieved using BINOL derived catalysts, such as chiral Brønsted acid catalysis (**6**),[6] transition metal catalysis employing phosphoramidite (**7**)[7] and phosphine ligands (**8**),[5] phase transfer catalysis (**9**),[8] Lewis acid catalysis (**10**),[9] and hydrogen bonding catalysis (**11**).[10]

Due to the importance of atropisomerism in the fields mentioned above, atropselective synthesis of biaryls has been a major focus of many research groups. The next part of this introduction will focus on key concepts in atropselective synthesis, and where applicable, examples of where asymmetric phase-transfer catalysis has been applied to the enantioselective synthesis of atropisomers.

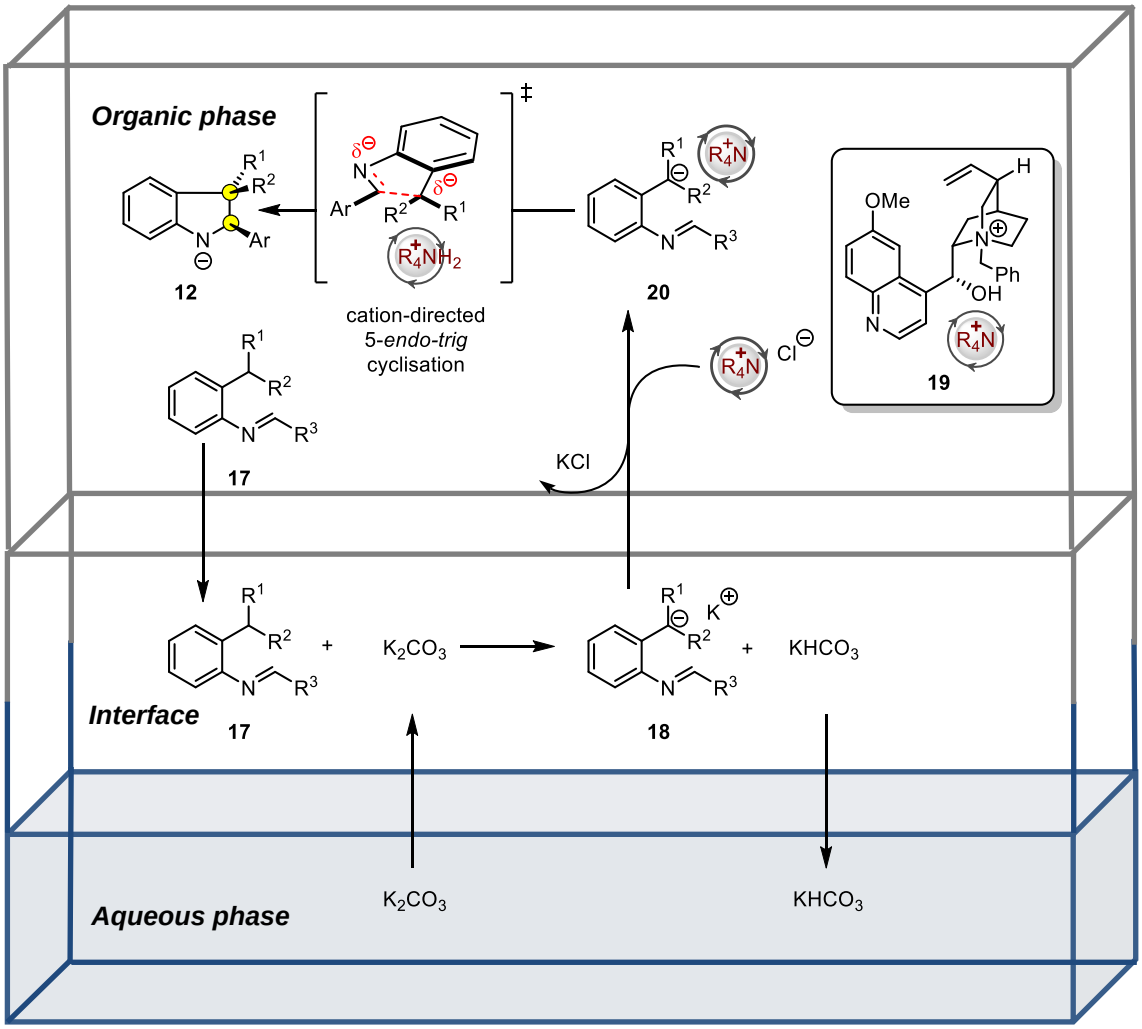
### 1.2. Asymmetric Phase-Transfer Catalysis

Asymmetric phase-transfer catalysis (PTC) has been applied in many enantioselective processes.[8] The Smith group has focussed particularly on enantioselective 5-*endo-trig* cyclizations (**Scheme 1.3.**). In these reactions, a chiral ammonium species preferentially binds to one "face" of an anionic substrate, which results in preferential cyclization to yield one enantiomer of the product. The group has applied this methodology to the enantioselective syntheses of indolines **12**,[11] indanes **13**,[12] polycyclic indolines **14**,[13] pyrroloindolines **15**[14] and indolenines **16**.[15]




**Scheme 1.3.** Phase-transfer catalyzed 5-*endo*-trig cyclizations developed in the Smith group.

To illustrate one possible mechanism of phase-transfer catalyzed reactions, the group's work on the asymmetric synthesis of indolines **12** will be used as an example (**Scheme 1.4.**).[16]

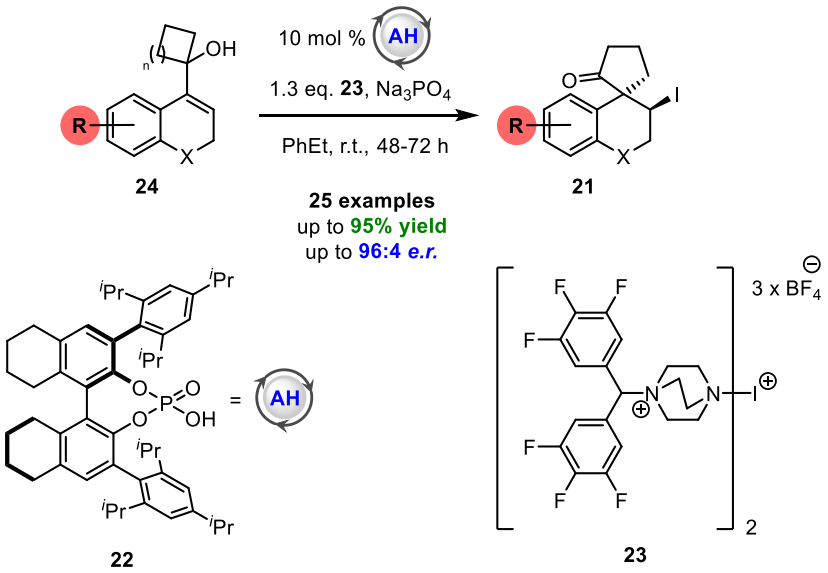



**Scheme 1.4.** Mechanism of phase-transfer catalyzed reaction towards **12**.

First, potassium carbonate enters the interface from the aqueous phase, and aldimine **17** enters from the organic phase. Next, deprotonation of **17** by potassium carbonate occurs to generate a potassium salt **18**, which then undergoes counterion metathesis at the interface with the chiral quinine-derived ammonium salt **19**. The thus formed ammonium salt of **17** then enters the organic phase. Once in the organic phase, **20** cyclizes to **12** *via* a 5-*endo-trig* cyclization to furnish **12** with excellent stereocontrol.

The phase-transfer reactions illustrated in **Scheme 1.3.** all employ chiral cations. However, phase-transfer catalysis is not limited to the use of chiral cations and has also been performed with chiral anions as chiral catalysts. For example, Alexakis and co-workers have employed

anionic phase-transfer catalysis to synthesize spiroketones **21** *via* an iodination-initiated Wagner-Meerwein rearrangement (**Scheme 1.5.**).[17]



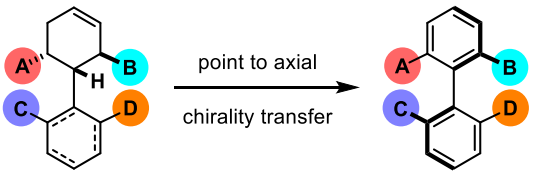

**Scheme 1.5.** An iodination-initiated Wagner-Meerwein rearrangement

In this reaction, chiral phosphoric acid **22** acts as the phase-transfer catalyst. Upon deprotonation by sodium phosphate it can transport iodinating reagent **23**, which by itself is insoluble in ethyl benzene, to the organic phase. A tight ion pair between **22** and **23** is thus formed in the organic phase, which acts as a chiral iodinating reagent in the Wagner-Meerwein rearrangement of cycloalkanols **24** to spiroketones **21**.

### 1.3. Atropselective Synthesis of Biaryls

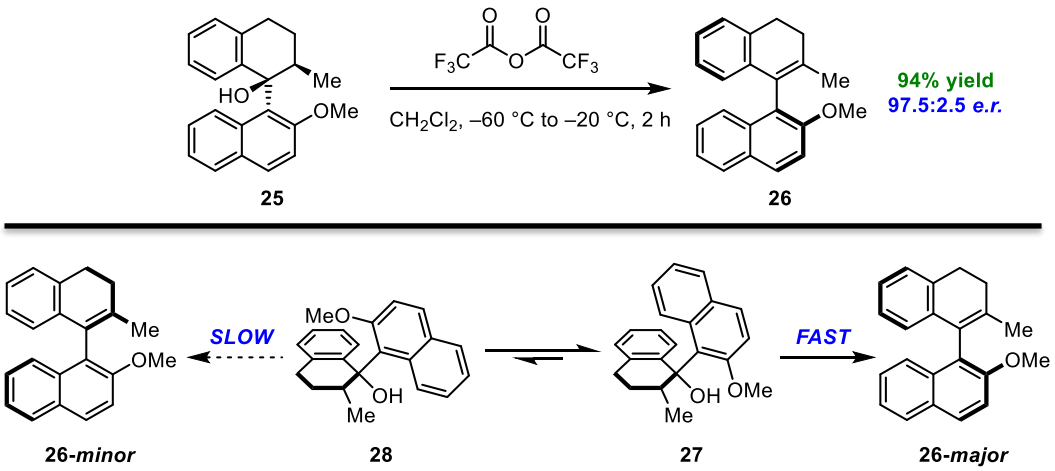
There are many both creative and effective solutions to the challenges of atropselective synthesis, which have been beautifully illustrated in comprehensive reviews by Bringmann, Kaneko and Colobert and respective co-workers.[18-20] This chapter will illustrate, using selected examples, what we consider to be the six most common methods to enantioselectively synthesize axially chiral biaryls, focusing mainly on organocatalytic and phase-transfer methods, where applicable.

### *1.3.1. Method A: Point to Axial Chirality Transfer*




**Scheme 1.6.** Method A: Point to axial chirality transfer

The first method relies on the conversion of point chiral molecules into axially chiral molecules without erosion in enantiopurity (**Scheme 1.6.**). This approach can be highly effective and in fact, point to axial chirality transfer is prevalent in several examples for the latter 5 methods of atropselective synthesis. To achieve effective communication of chiral information, the chiral centre is classically placed in close proximity to where the biaryl axis will be formed. For example, tertiary alcohol **25** undergoes $E_1$ elimination to afford **26** with good point to axial chirality transfer in the presence of trifluoroacetic anhydride in dichloromethane (**Scheme 1.7.**).[21] The authors suggest that the tertiary alcohol exists as a mixture of rotamers, whose ratio has been determined by $^1$H NMR spectroscopy to be approximately 6.3:1 (**27**:**28**).



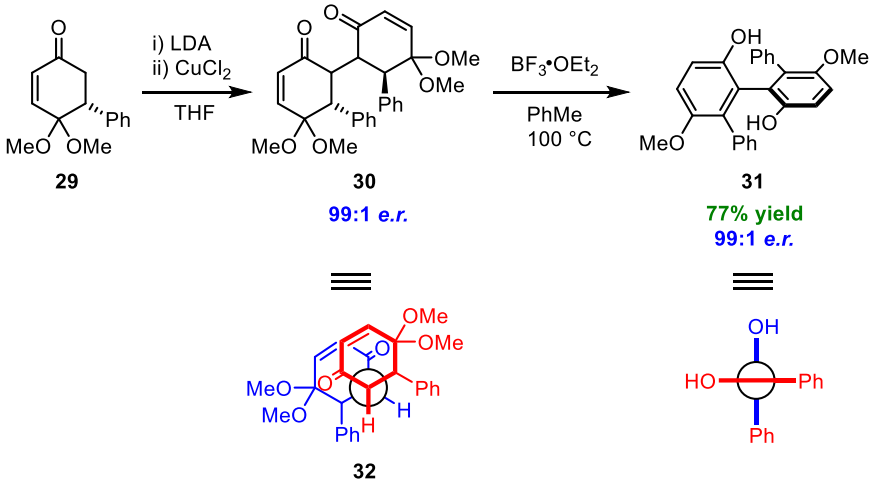

**Scheme 1.7.** $E_1$ Elimination with point to axial chirality transfer.

It is proposed that elimination from conformer **27** to **26-*major*** is faster than the elimination from conformer **28** to **26-*minor***. Overall, a combination of these two effects results in efficient point to axial chirality transfer.

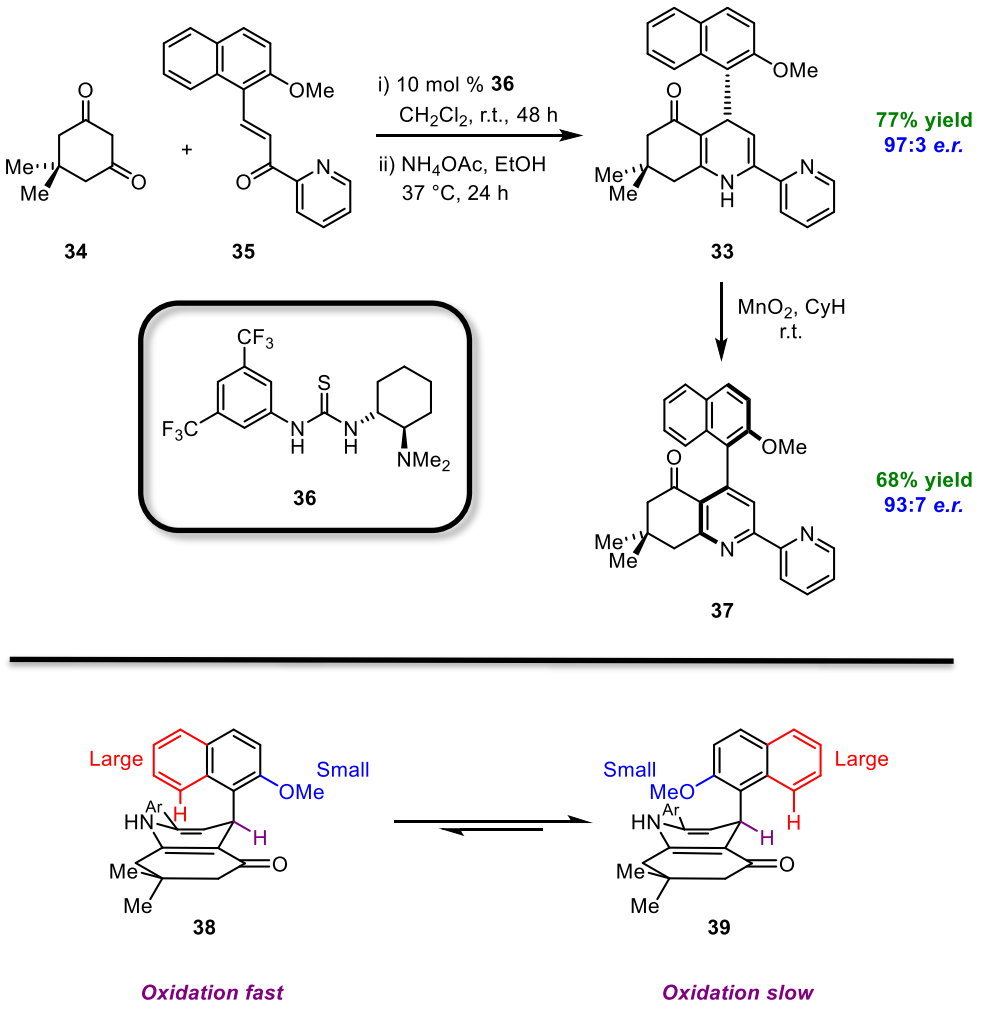
Thomson and co-workers have reported a copper(II)-mediated diastereoselective oxidative dimerization of enantiopure enone **29** to furnish diketone **30** (**Scheme 1.8.**).[22] Upon treatment with a Lewis acid, the diketone aromatizes to **31** with complete point to axial chirality transfer.

The lowest energy conformation of diketone **30** is shown in Newman projection **32**, which the authors also observed in the crystal structure of **30**. Re-aromatization from conformer **32** is consistent with the absolute configuration of biaryl **31**.

An example of point chirality being installed organocatalytically was demonstrated in the work by Rodriguez *et al.* (**Scheme 1.9.**).[23] First, a dihydropyridine **33** is enantioselectively formed *via* an organocatalytic Hantzsch-type reaction, wherein 1,3-dicarbonyl **34** undergoes an enantioselective Michael addition with **35**, catalyzed by thiourea **36**. Subsequent condensation with ammonium acetate furnishes dihydropyridine **33** with good enantioselectivity. Oxidation of dihydopyridine **33** with manganese dioxide in cyclohexane results in aromatization of the dihydropyridine moiety to generate axially chiral biaryl **37** with good point to axial chirality transfer.



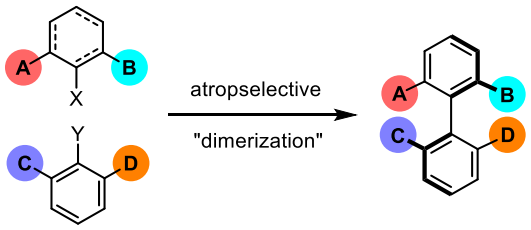

**Scheme 1.8.** Oxidative dimerization followed by point to axial chirality transfer.




**Scheme 1.9.** Enantioselective Hantzsch pyridine synthesis followed by point to axial chirality transfer.

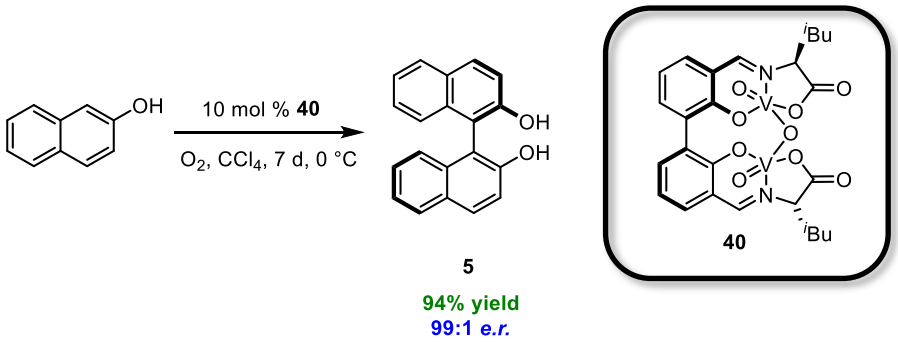
In analogy to the process illustrated in **Scheme 1.7.**, slow rotation about the pro-biaryl axis results in two distinct conformers (**38** and **39**). Whilst conformer **39** is the lowest energy conformation owing to minimized steric repulsion between the 2-methoxynaphthalene and the dihydropyridine moieties, the oxidation of conformer **39** is proposed to be relatively slow due to increased steric bulk about the aliphatic dihydropyridine hydrogen. Conformer **38**, though higher in energy, possesses less steric bulk about the aliphatic dihydropyridine hydrogen and therefore oxidation of conformer **38** is proposed to be faster, resulting in the observed absolute configuration.

### *1.3.2. Method B: Atropselective Biaryl Bond Formation*



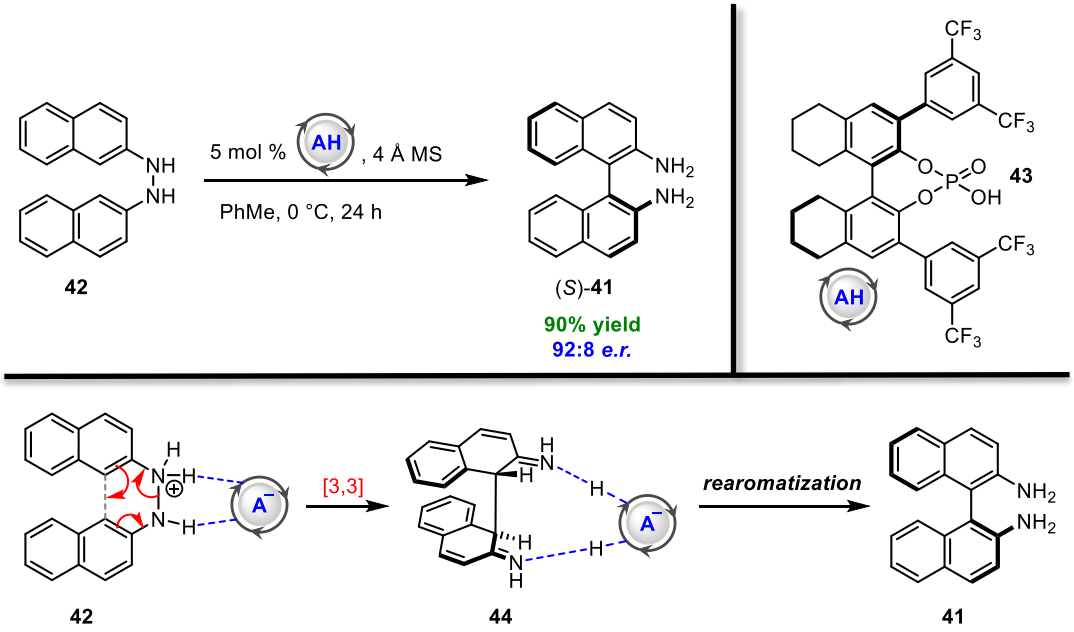

**Scheme 1.10.** Method B: atropselective bond formation

In the second method, the bond about which restricted rotation of the biaryl product exists is formed enantioselectively in the key step of the reaction. This usually involves the atropselective "dimerization" of two formal coupling partners. BINOL **5** itself can be prepared *via* an atropselective oxidative dimerization of 2-naphthol (**Scheme 1.11.**).[24] In this reaction, vanadium complex **40** acts as a chiral oxidant. Following the dimerization of 2-naphthol, the catalyst is turned over *via* re-oxidation with molecular oxygen.



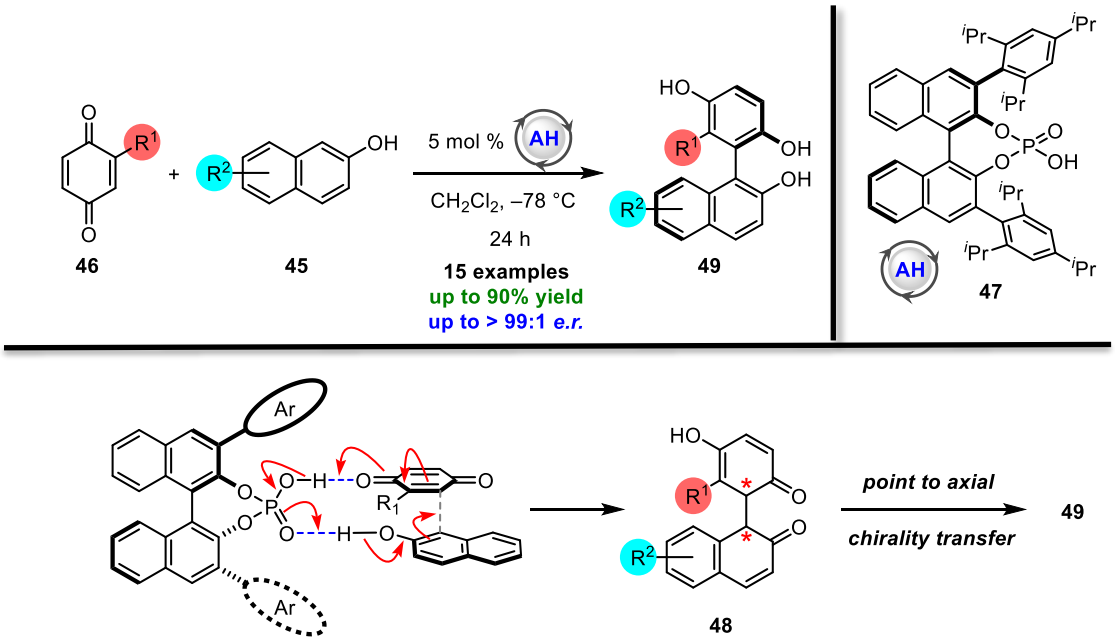

**Scheme 1.11.** Enantioselective oxidative dimerization of 2-naphthol.

List and Kürti, and respective co-workers, simultaneously reported atropselective syntheses of (*S*)-BINAM **41**, an amine derivative of BINOL **5**, *via* a [3,3]-sigmatropic rearrangement of 2,2'-hydrazonaphthalene **42** catalyzed by chiral phosphoric acid **43** (**Scheme 1.12.**).[25-26] First, a point chiral intermediate **44** is formed by a chiral phosphoric acid promoted [3,3]-sigmatropic rearrangement of **42**, which then rearomatizes to (*S*)-BINAM **41** with point to axial chirality transfer.




**Scheme 1.12.** Chiral Brønsted acid catalyzed [3,3]-sigmatropic rearrangement.

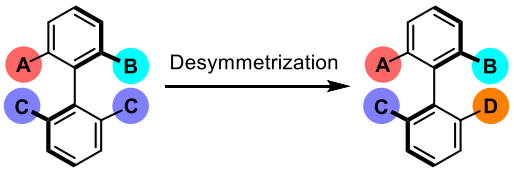
The authors suggest that hydrogen bonding of the chiral intermediate **44** to the chiral phosphoric **43** imposes a conformational bias for the rearomatization of **44** to BINAM **41**, preventing any erosion in stereochemical integrity during the aromatization process *via* rotation about the pro-biaryl bond.




**Scheme 1.13.** Chiral Brønsted acid catalyzed Michael addition.

A further example of chiral Brønsted acid-mediated atropselective synthesis is shown in **Scheme 1.3.** It involves a dearomatizing enantioselective Michael addition of 2-naphthols **45** to quinone methides **46**, mediated by chiral phosphoric acid **47**.[27] The diketone products **48** of the Michael additions are point chiral and rearomatize to axially chiral triols **49** with good point to axial chirality transfer, likely occurring in an analogous fashion to **44**.

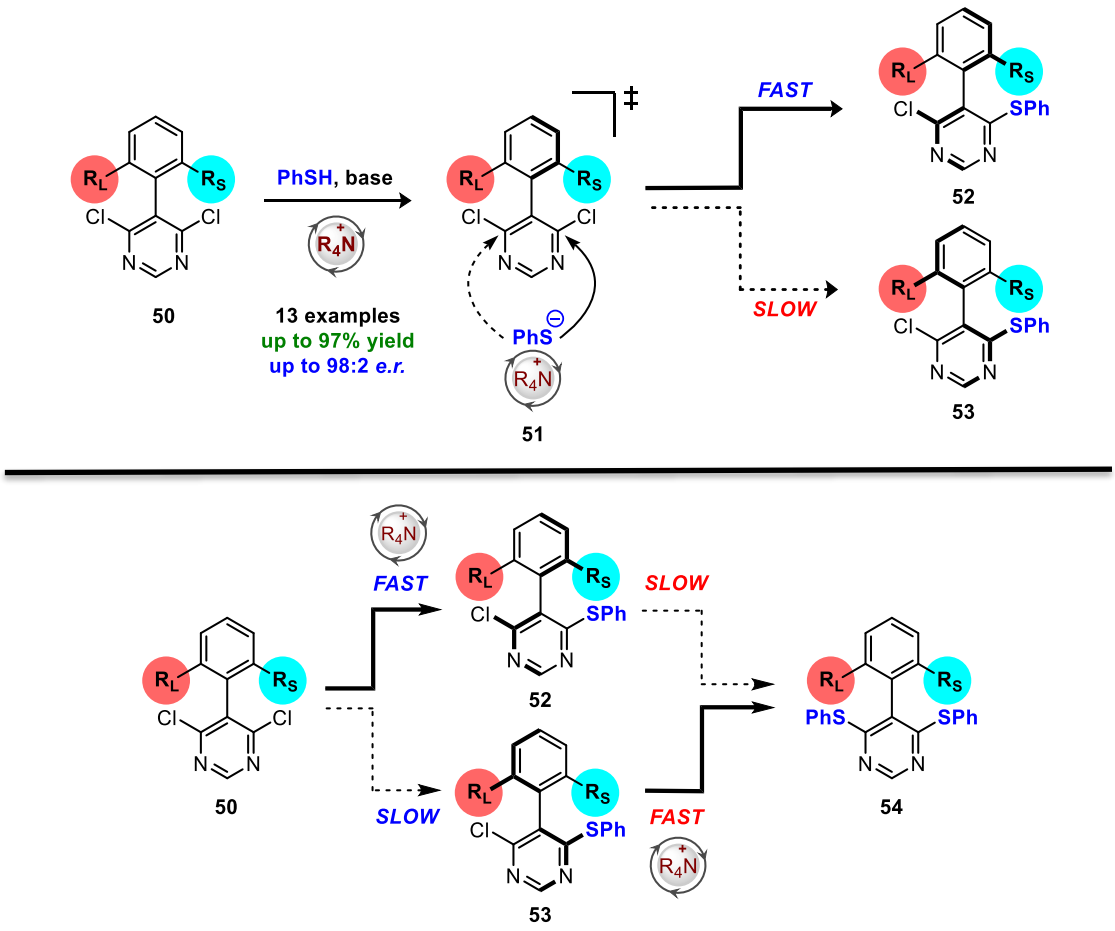
### *1.3.3. Method C: Desymmetrization of Prochiral Biaryls*




**Scheme 1.14.** Desymmetrization of prochiral biaryls.

In the third approach, the starting material already exhibits hindered rotation about the biaryl bond and possesses a plane of symmetry. The product can be furnished enantioselectively by removing the plane of symmetry. For example, in **Scheme 1.14.** a prochiral biaryl contains two identical substituents "*C*". In an enantioselective reaction, only one of the prochiral substituents "*C*" would react with the other remaining unchanged.

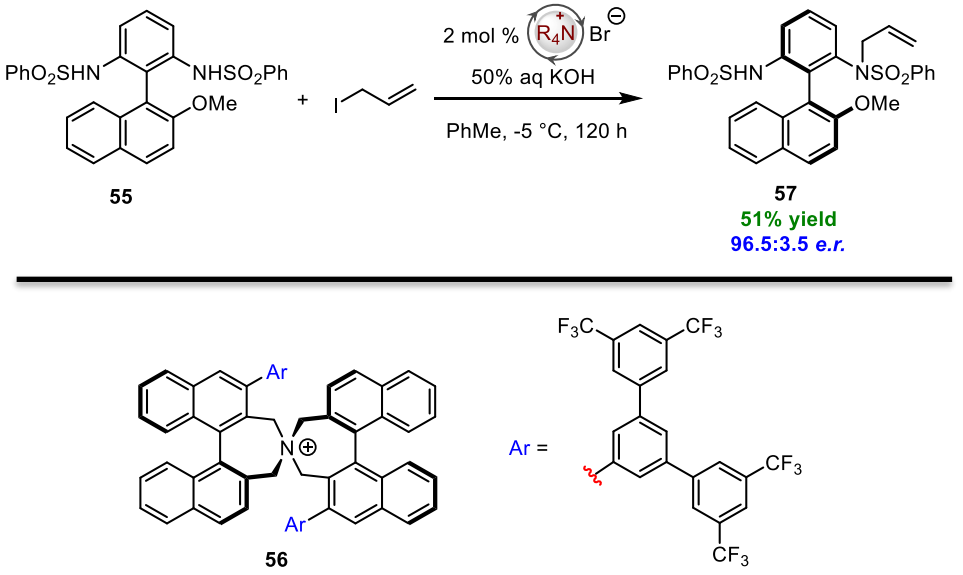
An example of an atropselective synthesis *via* atropselective desymmetrization was developed by Dr Roland J. Armstrong, a former DPhil student in the Smith group, who also contributed to the project which is the primary focus of this thesis (See **chapter 3.9.**).[28] The prochiral biaryl in this case is dichloropyrimidine **50** (**Scheme 1.15.**). Under phase-transfer catalysis, thiophenolate-ammonium ion pair **51**, preferentially directs the thiol nucleophile to one "face" of the dichloropyrimidine. A desymmetrizing nucleophilic aromatic substitution then furnishes the chiral biaryls **52** in good yields and enantioselectivities. Interestingly, when the thiol loading was increased, an increase in *e.r.* of product **52** was observed. This was attributed to the thiophenol-ammonium ion **51** pair reacting preferentially with the minor enantiomer of product **53**.




**Scheme 1.15.** A desymmetrizing $S_NAr$ reaction developed in the Smith group.

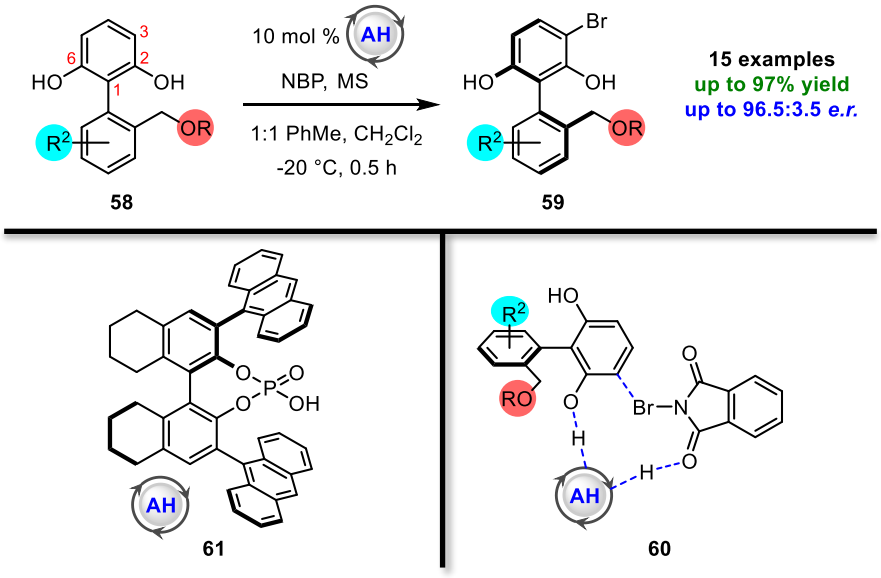
In other words, a "proofreading" process of the product occurs wherein the minor enantiomer **53** is removed by kinetic resolution. This effect has also been observed by Hayashi *et al.* and Akiyama *et al.* in the desymmetrizations of analogous biaryls.[29-32]

Maruoka and co-workers have disclosed a similar desymmetrization which also employs asymmetric phase-transfer catalysis (**Scheme 1.16.**).[33] Here, however, the polarity is reversed and the prochiral biaryl is the nucleophile reacting with an achiral electrophile. The prochiral biaryl **55** bears two sulphonamides which are identical by symmetry and are both reversibly protonated and deprotonated under phase-transfer conditions. Subsequently, counterion metathesis with a chiral ammonium salt **56** occurs at the interface analogously to **Scheme 1.14.** Following this, one diastereomer of the thus formed ammonium sulphonamide ion pair is preferentially alkylated to furnish axially chiral sulphonamide **57**.

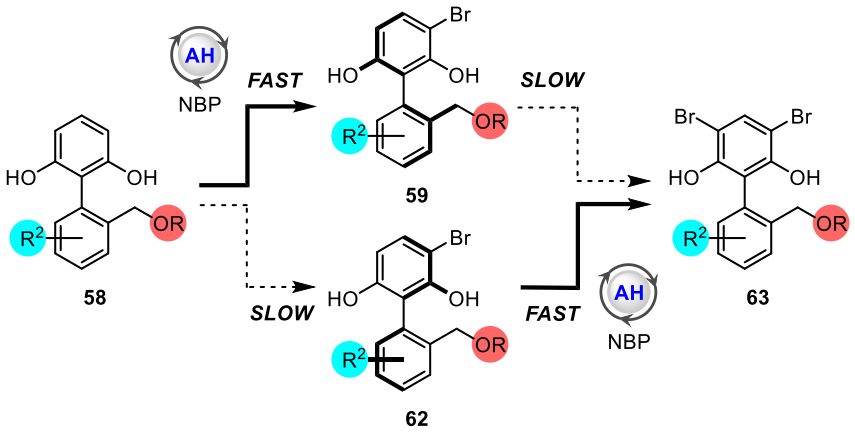



**Scheme 1.16.** A desymmetrizing phase-transfer catalyzed allylation.

A final example of an atropselective desymmetrization is the work of Akiyama *et al.* which employs chiral Brønsted acid catalysis (**Scheme 1.17.**).[32] In this reaction, the prochiral biaryl **58** contains a symmetrical 2,6-dihydroxy arene moiety which is then desymmetrized by selective bromination at *C*-3 to furnish **59**. The authors propose triad **60** as a possible intermediate, formed by hydrogen bonding between **58**, NBP and the chiral phosphoric acid **61**.



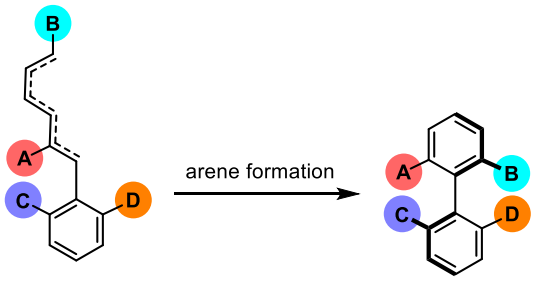

**Scheme 1.17.** A chiral Brønsted acid catalyzed desymmetrizing atropselective bromination.




**Scheme 1.18.** A tandem desymmetrization/kinetic resolution

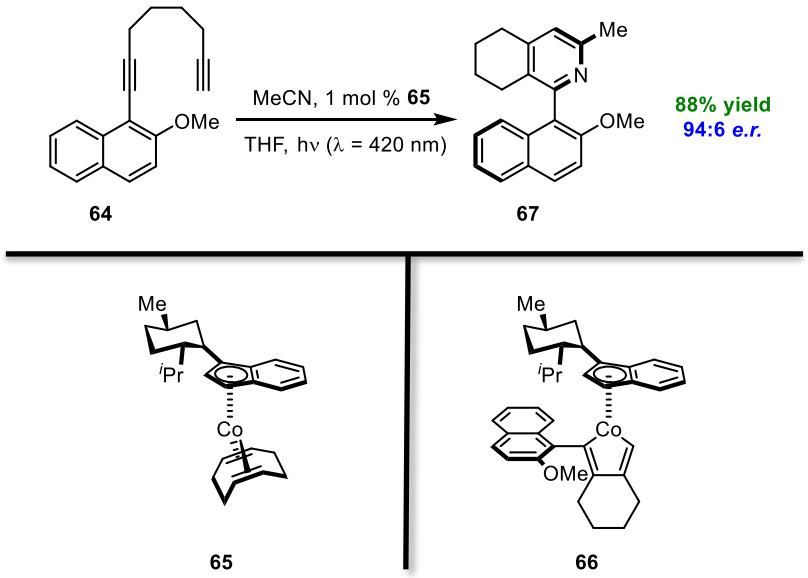
As mentioned above, this reaction also proceeds *via* a tandem desymmetrization/kinetic resolution process (**Scheme 1.18.**). Here, the minor enantiomer **62** of the product is brominated at a faster rate than the major product to generate achiral dibromoarene **63**. Overall, this results in a "proofreading" process of the monobromoarene product **59**, resulting in further enantioenrichment.

### *1.3.4. Method D: De-Novo Construction of an Aromatic Ring*




**Scheme 1.19.** Atropselective *de-novo* construction of an aromatic ring

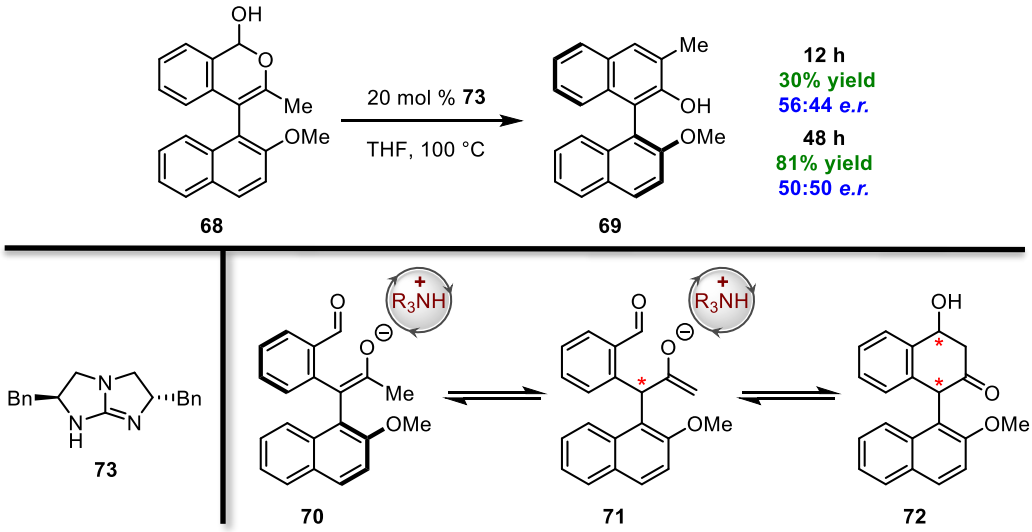
The fourth method involves the construction of one of the aromatic rings of the biaryl product, while simultaneously installing the hindered rotation about the biaryl axis atropselectively (**Scheme 1.19.**). The *de-novo* construction of an aromatic ring is a remarkable feat on its own, thus achieving this with atropselectivity has made this approach an attractive challenge to many research groups.




**Scheme 1.20.** Atropselective [2+2+2] cycloaddition.

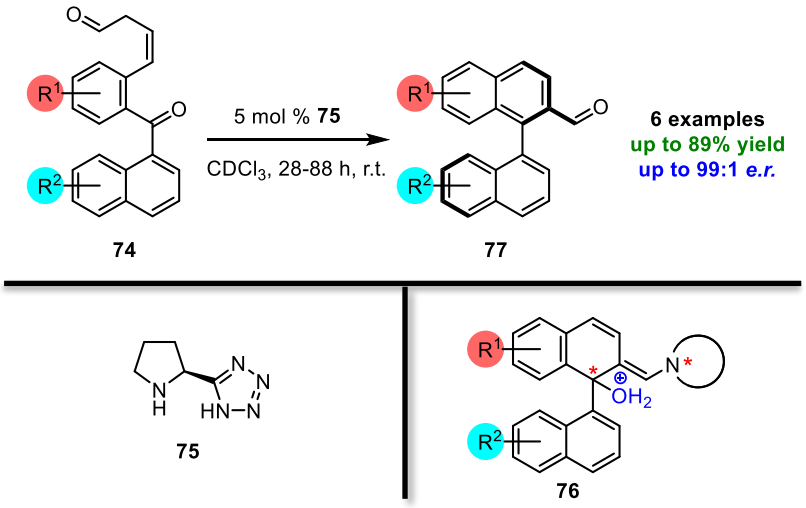
A very elegant solution to this problem is the work by Gutnov and Heller *et al.* (**Scheme 1.20.**).[34] When diyne **64** is treated with chiral cobalt(I) complex **65**, a diastereoselective oxidative coupling occurs to furnish axially chiral cobaltacyclopentadiene **66**. The chiral cobalt(III) metallocycle **66** then forms a $\pi$-complex with acetonitrile. Following two sequential carbometallations and a reductive elimination, tetrahydroisoquinoline **67** is furnished in excellent yield and enantioselectivity. The authors suggest the enantiodetermining step to be the diastereoselective formation of the cobaltacyclopentadiene **66**, and that the following carbometallations and reductive elimination occur without rotation about the biaryl bond.

An organocatalytic example of an atropselective arene formation is the work by Terada and Dan (**Scheme 1.21.**).[35] It involves a chiral Brønsted base-mediated Ferrier-type rearrangement of hemiacetal **68** to BINOL derivative **69**, albeit with low enantioselectivity. The authors suggest the first step to be deprotonation of acetal **68** to generate enolate **70**. Following tautomerization to enolate **71**, an intramolecular aldol reaction is proposed to furnish point chiral intermediate **72**. Subsequently, the β-hydroxy ketone **72** is suggested to undergo dehydration and tautomerization. The authors do not offer any insight into what they believe to be the enantiodetermining step.



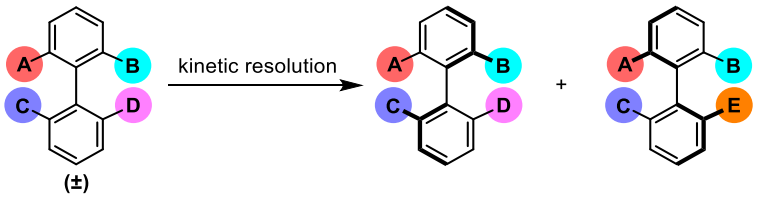

**Scheme 1.21.** Atropselective Ferrier-type carbocyclization.

A conceptually similar approach was reported by Link and Sparr (**Scheme 1.22.**).[36] Here, atropselective arene formation was also achieved *via* an intramolecular aldol condensation. First, aldehyde **74** is proposed to form an enamine upon treatment with chiral secondary amine catalyst **75**. Next, an intramolecular enamine-aldol addition to the ketone occurs to furnish a tertiary alcohol. Upon protonation, the tertiary alcohol **76** possibly undergoes dehydration with point to axial chirality transfer to furnish **77** in an analogous fashion to the reaction illustrated in **Scheme 1.7.** Overall, this reaction proceeds with excellent yields and enantioselectivities.




**Scheme 1.22.** Atropselective intramolecular aldol condensation.

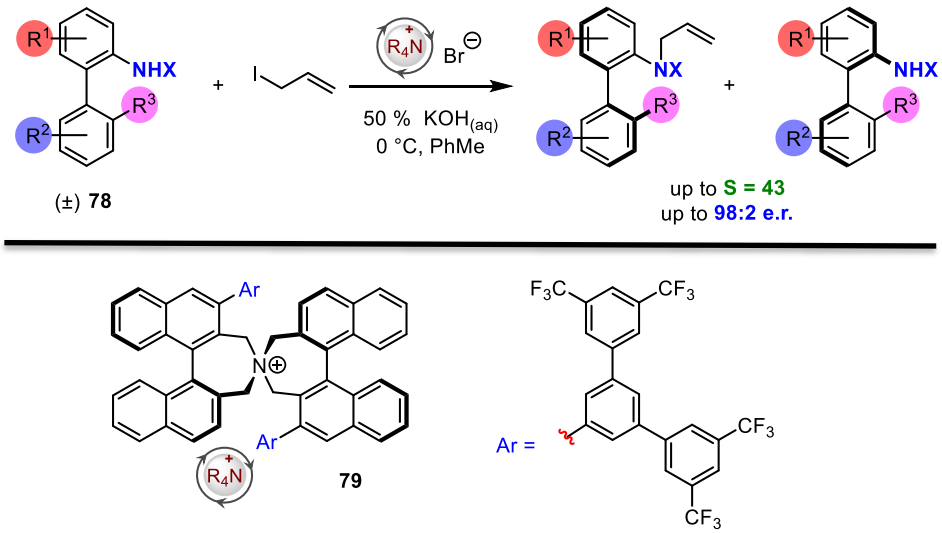
### *1.3.5. Method E: Kinetic Resolution of Axially Chiral Biaryls*



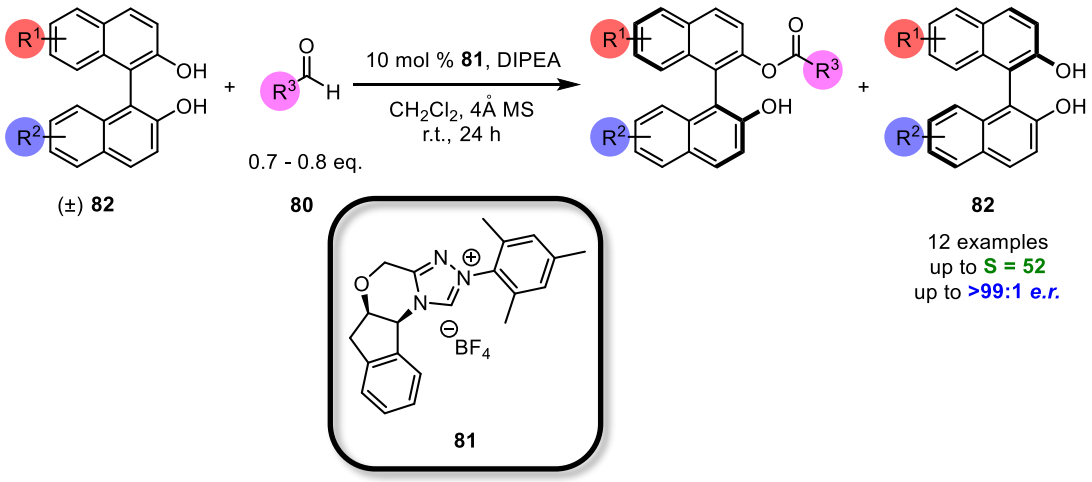

**Scheme 1.23.** Atropselective kinetic resolution of axially chiral biaryls.

The fifth method achieves atropselectivity *via* kinetic resolution of a chiral but racemic biaryl. Here, one enantiomer of the racemic starting material is selectively chemically modified, thus enantioenriching the starting material and furnishing the enantioenriched axially chiral product.

An asymmetric phase-transfer catalyzed approach to the kinetic resolution of biaryls was reported by Maruoka *et al.* (**Scheme 1.24.**).[33] The axially chiral but racemic starting material **78** bears an acidic *N*-H proton. Upon interfacial deprotonation and subsequent counterion-metathesis with the BINOL derived ammonium salt **79**, one diastereomer of the thus formed ammonium anilide is preferentially alkylated. Including other axially chiral anilines, the group has applied this kinetic resolution approach to the enantioselective synthesis of BINAM and NOBIN.

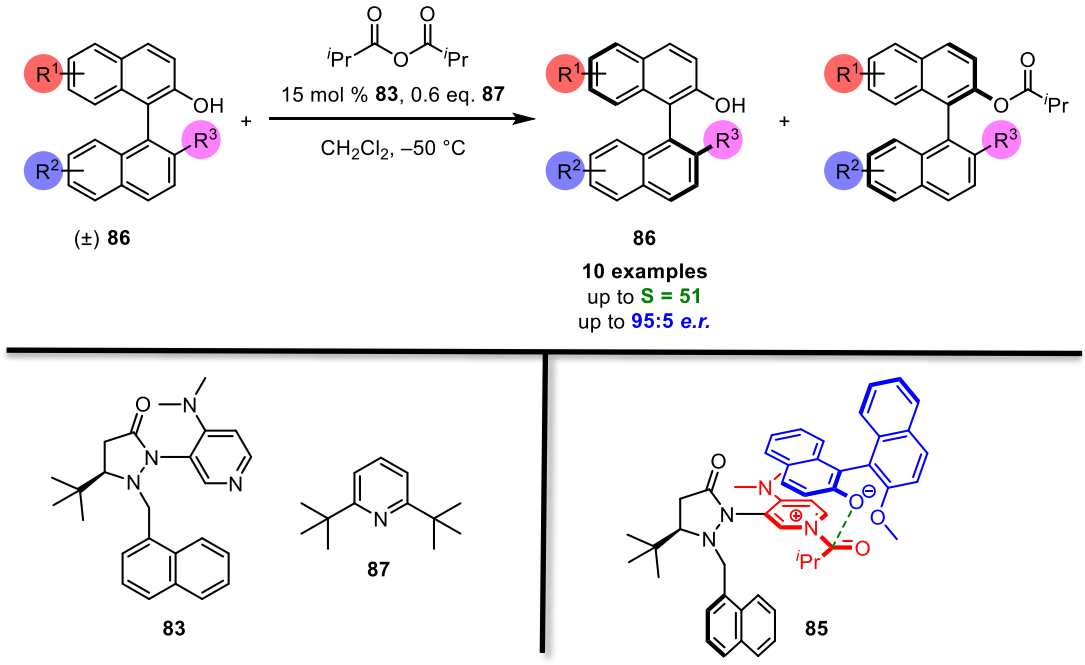



**Scheme 1.24.** Asymmetric phase-transfer catalyzed kinetic resolution of axially chiral anilines.




**Scheme 1.25.** NHC catalyzed kinetic resolution of BINOL derivatives.

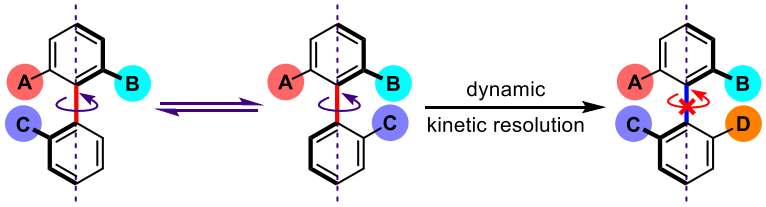
A more common approach to the kinetic resolution of axially chiral biaryls is the *in situ* generation of a chiral reagent which reacts faster with one enantiomer of the chiral but racemic starting material. An example of this approach is the work by Zhao *et al.* (**Scheme 1.25.**).[37] It involves the formation of a chiral azolium intermediate from aldehyde **80** and an *in situ* generated NHC from **81**. The chiral azolium then acts as a chiral acylating reagent which preferentially reacts with one enantiomer of a chiral but racemic BINOL derivative **82**.




**Scheme 1.26.** Chiral DMAP catalyzed kinetic resolution of BINOL derivatives.

Another method which involves the *in situ* formation of a chiral acylating reagent is the work by Sibi *et al.* (**Scheme 1.26.**).[38] Here a chiral DMAP catalyst **83** reacts with anhydride **84** to generate the chiral acylating reagent *in situ*. The authors propose transition state **85** as the most favoured approach of a BINOL derivative **86** and the origin of enantioselectivity. Following acylation of the BINOL derivative **86**, catalyst **83** is regenerated by deprotonation with a non-nucleophilic Brønsted base **87**.

### *1.3.6. Method F: Dynamic Kinetic Resolution of Biaryls*

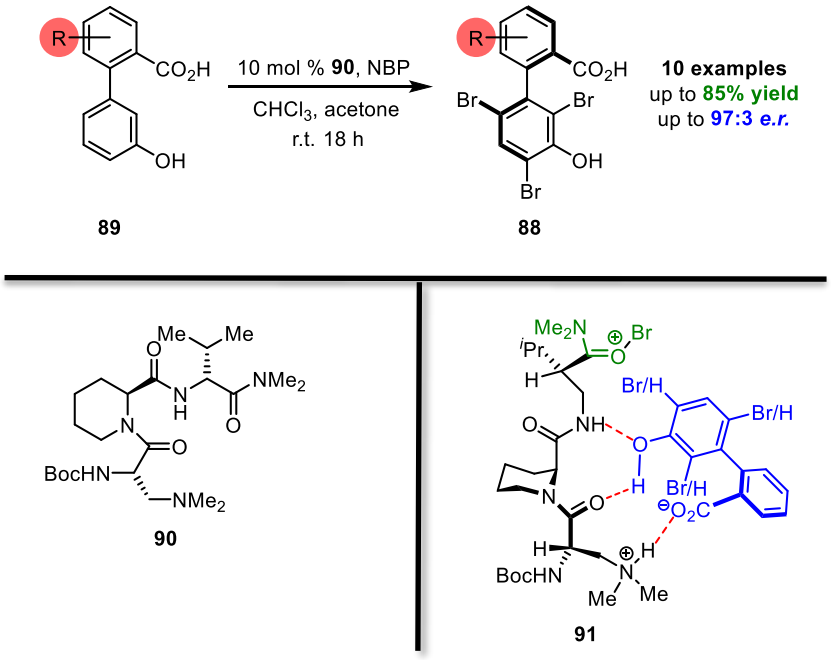



**Scheme 1.27.** Dynamic kinetic resolution of biaryls.

The previous approach involved the enantioselective transformation of one enantiomer of an axially chiral but racemic starting material where the hindered rotation about the biaryl axis is already in place. The final method also selectively transforms one enantiomer of the chiral biaryl starting material, however, here the barrier to rotation about the biaryl bond in the starting material is intrinsically low enough, or is reduced following a chemical transformation, to allow interconversion between the enantiomers of the starting material. It is crucial that the reaction in question results in a product-barrier to rotation significantly high enough to prevent any erosion in stereochemical integrity of the product *via* rotation about the biaryl bond. Overall this process achieves the atropselective synthesis of biaryls by dynamic kinetic resolution.

Miller *et al.* have succeeded in applying this approach to the atropselective synthesis of tribromobiaryls of type **88** (**Scheme 1.28.**).[39] The starting material **89** bears a 3-hydroxyphenyl and a 2-carboxyl moiety as the aryl components. The barrier to rotation about the biaryl bond is approximately 7 kcal $mol^{-1}$ and therefore this compound is not atropisomeric at room

temperature. A chiral peptide catalyst **90** subsequently facilitates an atropselective tri-bromination. The bromination *para* to the biaryl bond is unlikely to have any significant impact on the barrier to rotation, however each *ortho*-bromination with respect to the biaryl bond significantly increases the barrier to rotation of the resulting biaryl, with the tribromoarene product **88** possessing a sufficiently high barrier to rotation to preclude any racemization at room temperature. As a model for enantioinduction, the authors propose transition state **91**. The peptide catalyst deprotonates the carboxylic acid moiety of **89**, and a hydrogen bond between the resulting ammonium and carboxylate is thus formed. Additional hydrogen bonding is proposed between the phenolic oxygen with an amide *N*-H, and the phenolic hydrogen with an amide oxygen. Overall, these three hydrogen bonds are proposed to conformationally lock the biaryl, with the bromonium ion being delivered by the catalyst from an *O*-brominated amide oxygen on the catalyst.

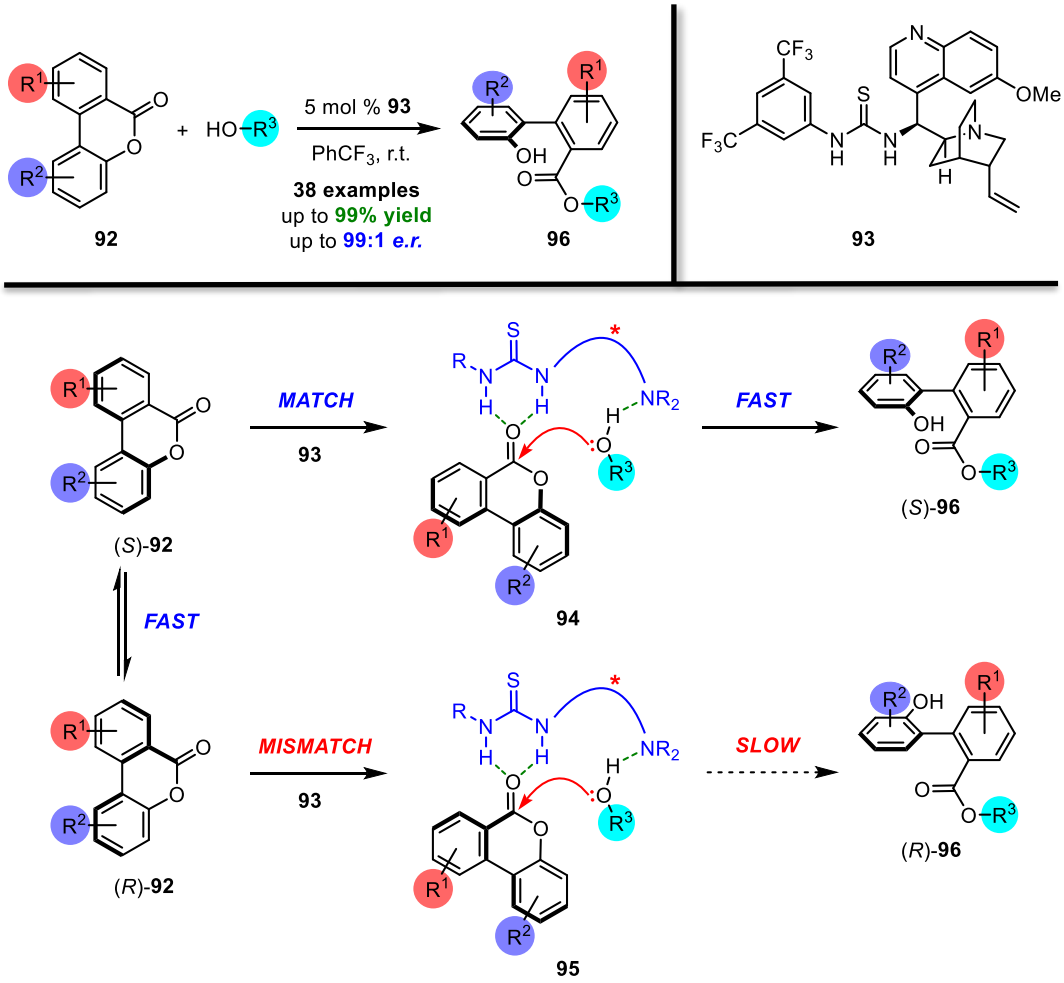



**Scheme 1.28.** Peptide-catalyzed asymmetric bromination.

The work by Miller *et al.* achieved an increase in barrier to rotation about the biaryl bond from starting material to product, by sequentially introducing *ortho* substituents. In the second example, both product and starting material possess an equal number of ortho substituents,

but in the starting material two of the *ortho* substituents are linked resulting in the formation of an almost planar product containing a usually six-membered strained ring. Here, interconversion between the two atropisomers occurs *via* a ring flip. If the tether is removed in only one conformer of the strained ring, the product can be enantioselectively generated *via* dynamic kinetic resolution. With the tether removed, the barrier to rotation about the biaryl bond is high enough to prevent racemization at room temperature. Bringmann *et al.* have pioneered this approach with the enantioselective transformation of 6-membered lactones of type **92**.[40-43]

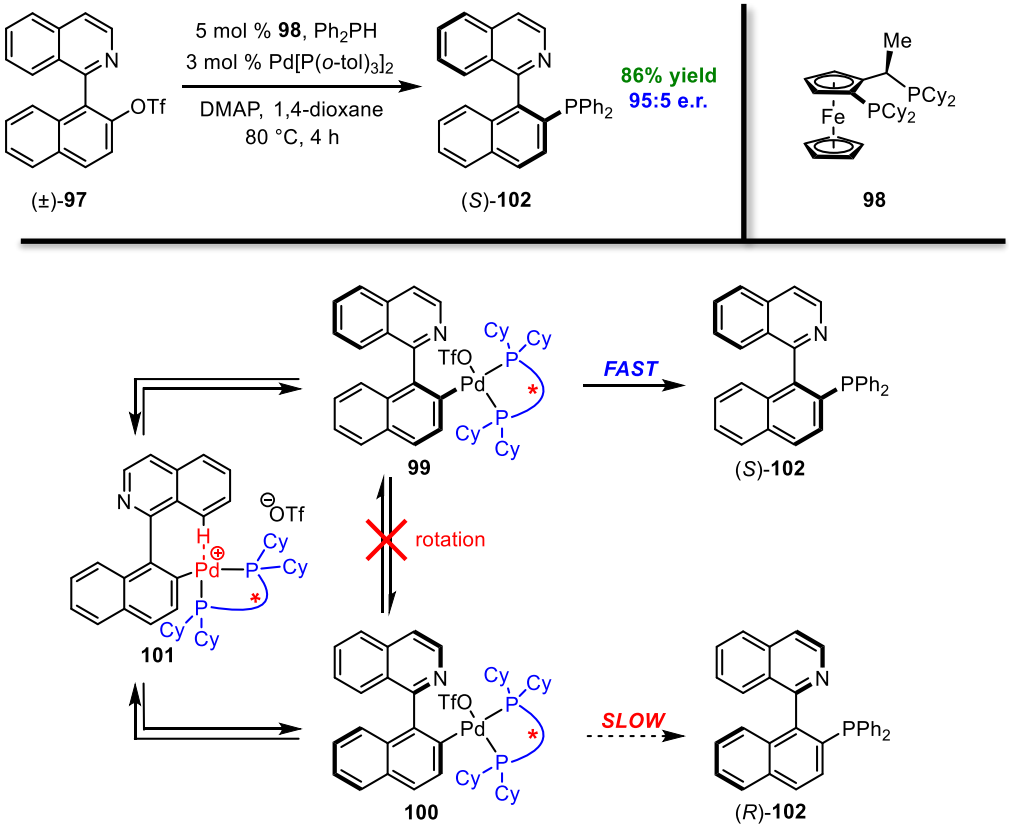
A recent organocatalytic implementation of this approach is the work by Wang et al (**Scheme 1.29.**).[44] Here, the lactone **92** is opened *via* a chiral thiourea **93** catalyzed transesterification with an alcohol.




**Scheme 1.29.** Thiourea catalyzed atropselective transesterification.

In analogy to the seminal work by Bringmann et al., the authors propose that the atropisomers of lactone **92** undergo rapid interconversion. The lactone oxygen hydrogen bonds to the thiourea of **93**, and the quinuclidine nitrogen of **93** hydrogen bonds to the alcohol. In the matched case **94**, the lactone is readily opened by the alcohol, whereas in the mismatched case **95**, the authors propose that the catalyst **93** is unable to direct the alcohol to the lactone.

The final example also relies on atropisomeric interconversion *via* a strained bridge, however here, the bridge is not present in the starting material and is introduced as a temporary tether during the reaction (**Scheme 1.30.**).[45]




**Scheme 1.30.** Atropselective synthesis of QUINAP *via* dynamic kinetic resolution

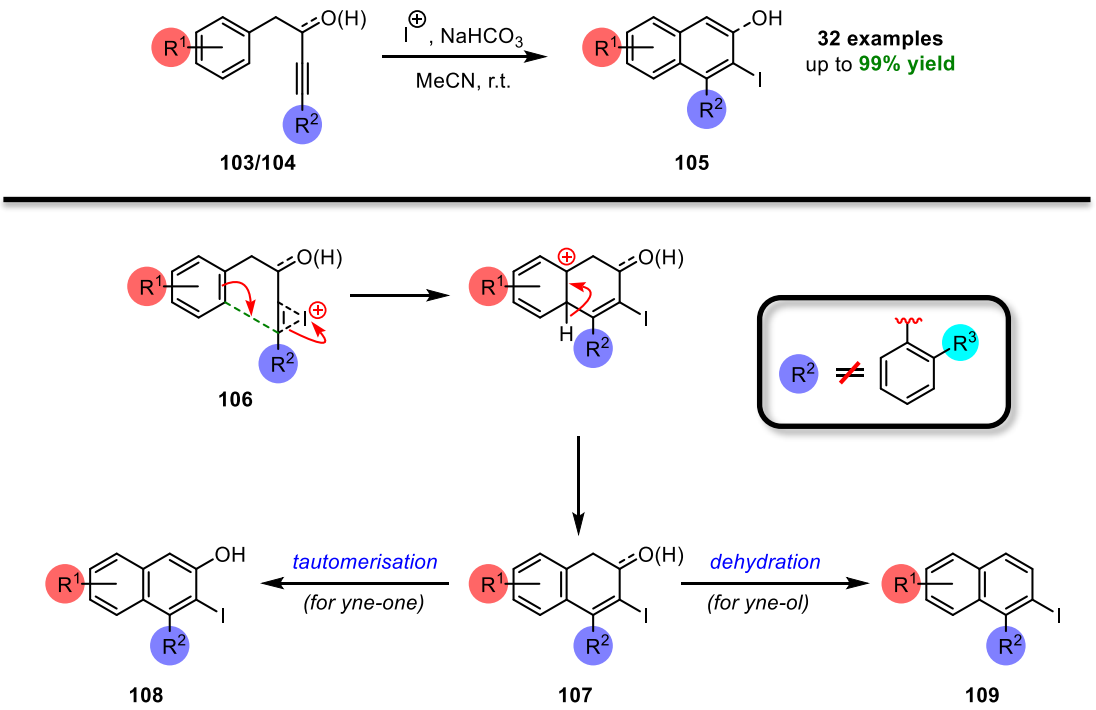
The starting material isoquinoline **97** is atropisomeric. Upon oxidative addition by a palladium complex with chiral ligand **98**, two diastereomeric palladium complexes (**99** and **100**) are formed. These are proposed to interconvert *via* intermediate **101**, where an agostic interaction between palladium and a quinoline *C-H* results in the isoquinoline and naphthyl moieties being

coplanar. A coupling partner is then added dropwise to the reaction mixture to prevent competitive reductive elimination proceeding at a greater rate than atropisomeric interconversion. The authors have successfully implemented this dynamic kinetic resolution protocol to the enantioselective synthesis of the ligand QUINAP **102** with good yield and enantioselectivity.

## 2. Binaphthyl Synthesis by Iodocyclization of Yne-ones and Yne-ols

### 2.1. Background and Project Aims

With the group having had success in desymmetrizations of biaryls (**Scheme 1.15.**),[28] we were interested in atropselective methods where hindered rotation about the biaryl axis is not present in the starting material. The *de novo* construction of an aromatic ring (Method D) appealed to us in particular.




**Scheme 2.1.** An iodocyclization approach to the synthesis of 2-iodonaphtalene derivatives.

As a starting point, we researched the literature for reactions which generate naphthalenes, and could possibly be applied to atropselective synthesis. Larock and co-workers reported an iodocyclization approach utilizing yne-ones **103** and yne-ols **104** in the synthesis of 2-iodonaphthalene derivatives **105** (**Scheme 2.1.**).[46] As a mechanistic proposal the authors suggest that initially a cyclic iodonium species **106** is formed, which is immediately ring-opened *via* a Friedel-Crafts type electrophilic aromatic substitution by the aromatic ring. Intermediate **107** can then tautomerize to naphthol **108** if an yne-one was used as the starting material, or

naphthalene **109** can be furnished by dehydration if an yne-ol was used as the starting material. It is worth noting that no *ortho*-substituted aryl substituents for $R^2$ were reported. If $R^2$ was indeed *ortho*-substituted, for example 1-naphthyl, then the resulting products would be atropisomeric.[47] More importantly, could this transformation be achieved enantioselectively with a chiral iodonium source such as the anionic phase-transfer iodination mentioned in **Scheme 1.5.** (**Figure 2.2.**)?

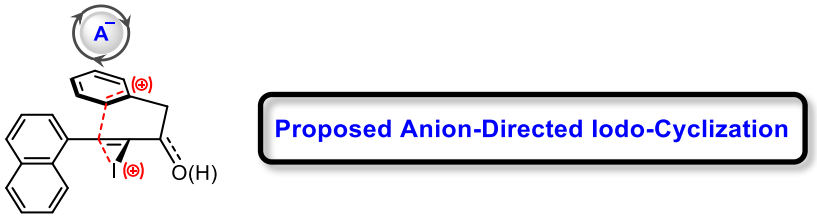
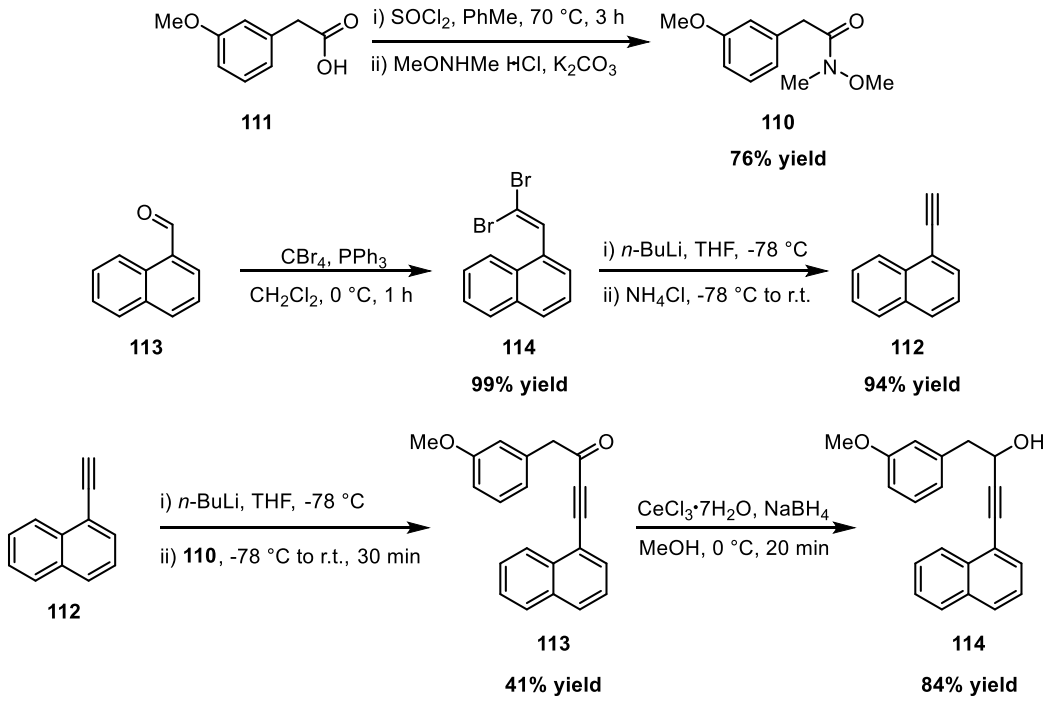



**Figure 2.2.** Potential atropselective synthesis of iodobinaphthalenes.

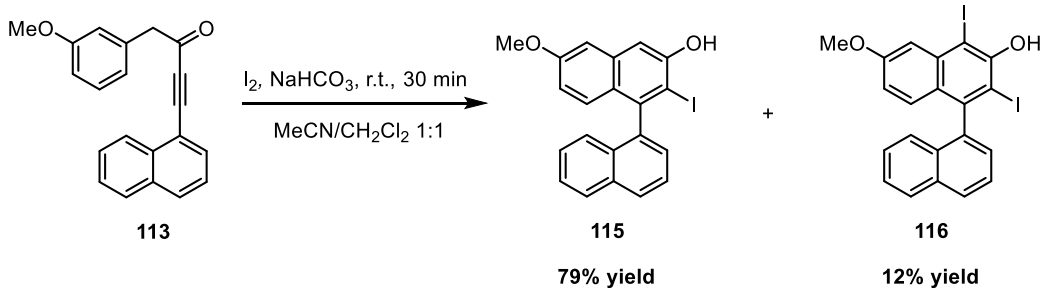
## 2.2. Substrate Synthesis and Racemic Reaction

To probe the feasibility of this concept, we set out to synthesize a model substrate to investigate whether the iodocyclization proceeds with $R^2$ = *ortho*-substituted arenes, and whether the reaction can be performed asymmetrically using established asymmetric iodination protocols.



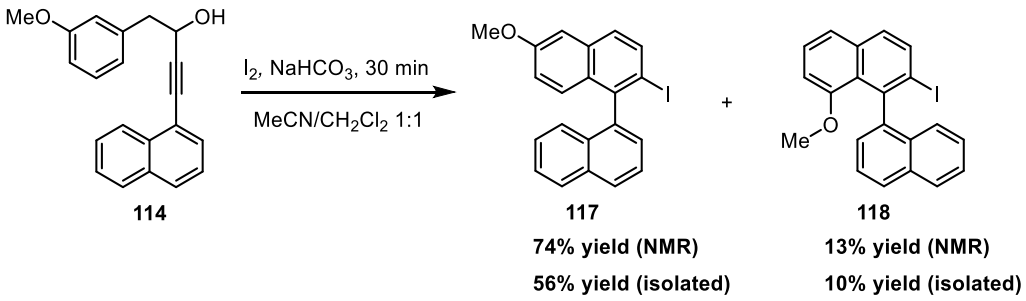

**Scheme 2.3.** Starting material synthesis.

In analogy to the seminal work by Larock et al,[46] we were able to prepare 1-naphthyl analogues of yne-one **103** and yne-ol **104** (**Scheme 2.3.**). Weinreb amide **110** was prepared from commercially available carboxylic acid **111**. 1-Ethynyl-naphthalene **112** is commercially available, though it is somewhat expensive. It was therefore prepared on multi-gram scale from 1-naphthaldehyde **113** by a Corey-Fuchs reaction *via* intermediate dibromo olefin **114**. Deprotonation with *n*-BuLi and addition to Weinreb amide **110** furnished yne-one **113** in good yield. A subsequent Luche reduction of yne-one **113** proceeded smoothly to yne-ol **114**.




**Scheme 2.4.** Iodocyclization of yne-one **113**.

With substrates **113** and **114** in hand, we proceeded to investigate whether the iodocyclizations would proceed if $R^2$= 1-naphthyl. Pleasingly, the iodocyclization of yne-one **113** proceeded smoothly to the anticipated binaphthyl derivative **113** (**Scheme 2.4.**). A 1:1 mixture of acetonitrile/dichloromethane was employed due to solubility issues of the starting material in acetonitrile. Product **116** was afforded as a minor by-product, presumably due to iodination of product **115** under the reaction conditions.




**Scheme 2.5.** Iodocyclization of yne-ol **114**.

The iodocyclization of yne-ol **114** proceeded with good conversion, however separation of the regio-isomeric products **117** and **118** by column chromatography proved to be challenging (**Scheme 2.5.**). We were pleased to be able to confirm the structure of **118** by single crystal X-ray diffraction (**Figure 2.6.**).

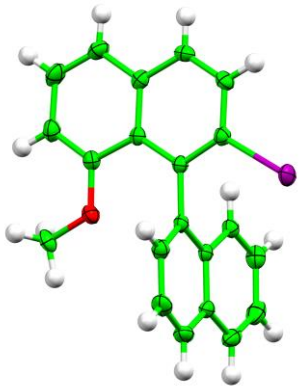
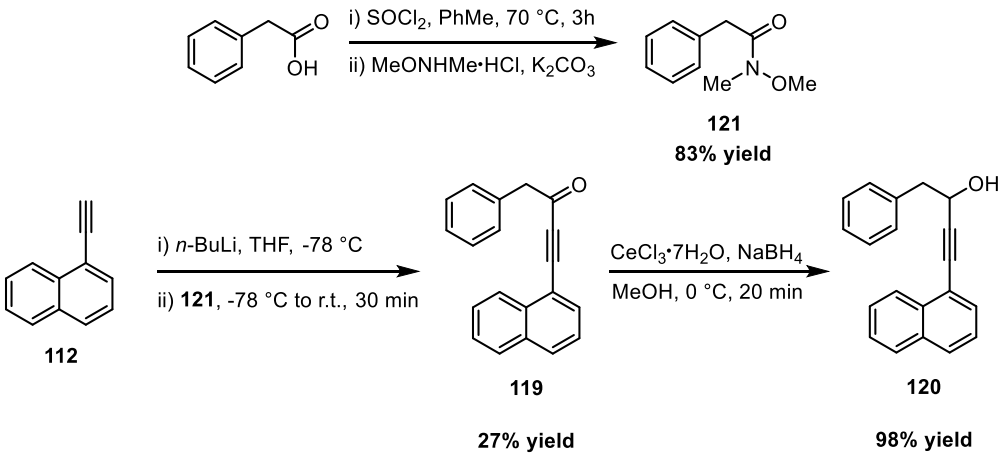


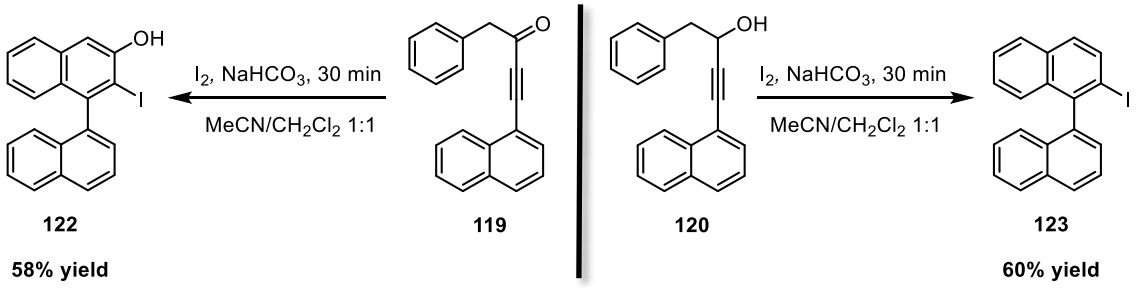
**Figure 2.6.** Crystal structure **118** of with ADP at 50% probability.

Next, we sought to establish whether the iodocyclization would proceed without the electron donating methoxy substituent. To this end, we prepared unsubstituted yne-one **119** and yne-ol **120** using the same methodology as before (**Scheme 2.7.**). Whilst the organolithium addition of **112** to **121** did not result in a high yield of **119**, the Luche reduction of **119** to **120** proceeded smoothly.



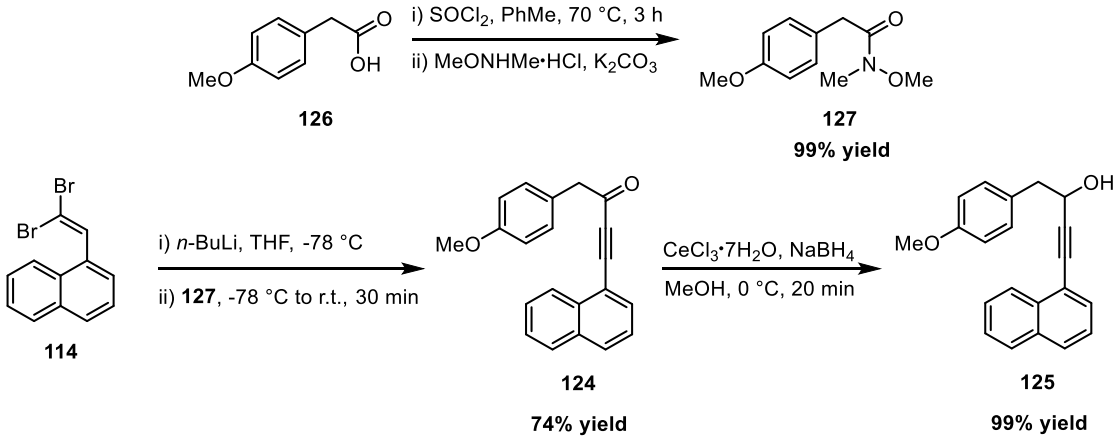

**Scheme 2.7.** Second substrate synthesis.

With these substrates in hand, we subjected them to the iodocyclization conditions (**Scheme 2.8.**). The iodocyclization of yne-one **119** only yielded mono-iodonated product **122** in a moderate yield. The cyclization of yne-ol **120** also resulted in a lower yield of **123**. Presumably this is due to a reduction in rate of the Friedel-Crafts cyclization, owing to less electron rich arene moieties in **119** and **120**.

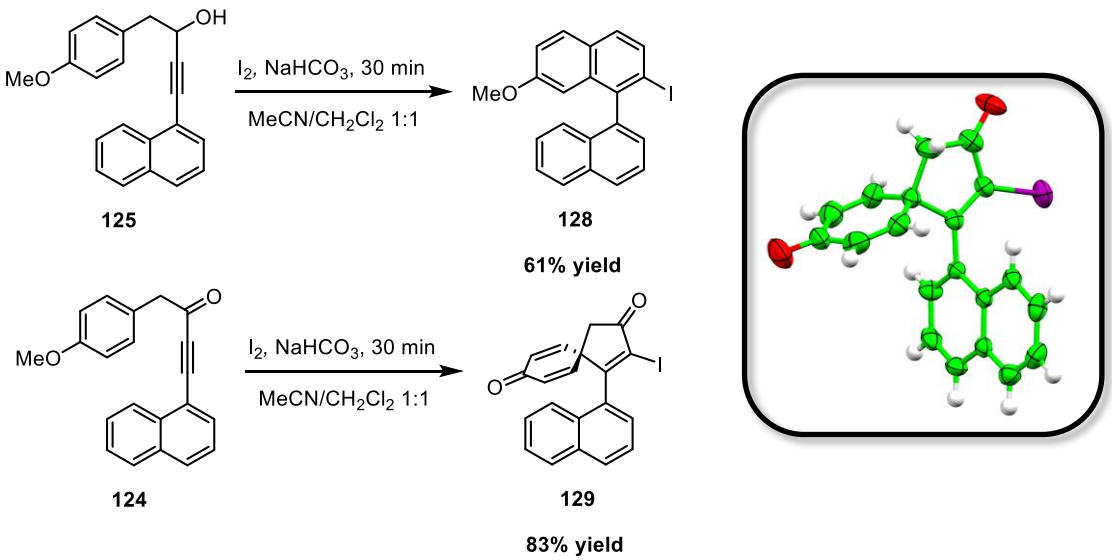



**Scheme 2.8.** Iodocyclizations of **119** and **120**.

Since it became apparent that an electron rich arene was beneficial for the reaction, we decided to synthesize yne-one **124** and yne-ol **125** (**Scheme 2.9.**). Here the methoxy group is in the para-position, which we hoped would circumvent the issues we experienced previously with respect to regioselectivity. In analogy to recent work by a former DPhil student in the group (Dr Craig Johnston),[12] we generated the anion of **112** for the organolithium addition to **127** in situ from **114**. Pleasingly, this approach afforded yne-one **124** in good yield. As before, Luche reduction of **124** afforded yne-ol **125** in excellent yield.



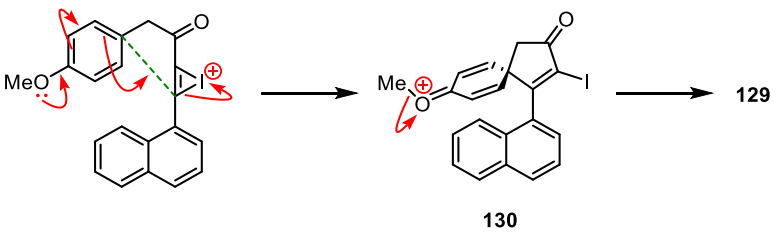

**Scheme 2.9.** Third substrate synthesis.




**Scheme 2.10.** Iodocyclizations of **124** and **125** and X-ray structure of **129** with ADP at 50% probability.

The iodo cyclization of yne-ol **125** resulted in a moderate yield of **128** (**Scheme 2.10.**). The iodocyclization of yne-one **124**, however, did not yield a binaphthyl product. Instead, spirocycle **129** was formed in good yield. This was also observed in the seminal work and a later publication by Larock *et al.*,[46, 48] where $R^2$ = Ph. It is proposed that the spirocycle is formed *via* an intermediate quinone methide **130**, which is subsequently dealkylated (**Scheme 2.11.**).

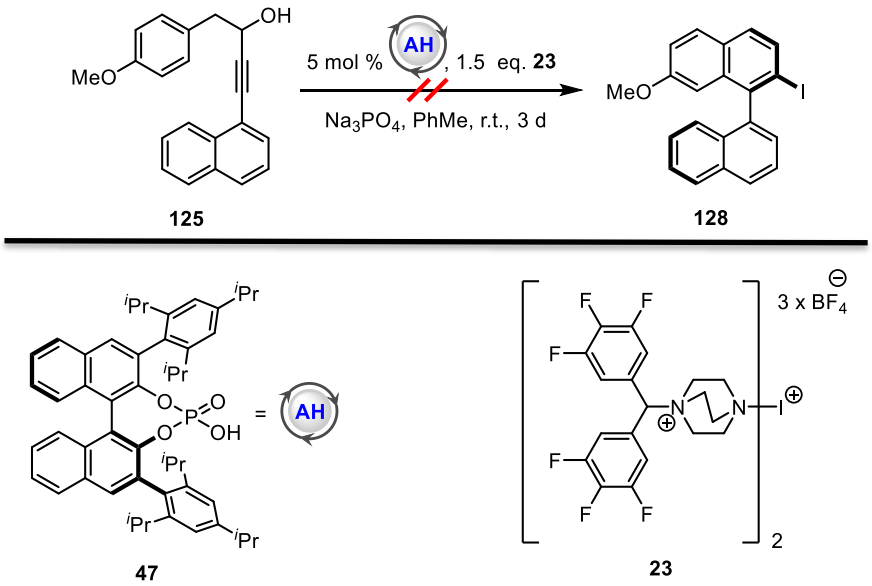
We were able to confirm the structure of spirocycle **129** by single crystal X-ray diffraction. Due to a temporary cryo-stream malfunction, the diffraction experiment was carried out at room temperature, rather 150 K, with the single crystal being affixed with nail varnish rather than by vitrification in fomblin oil. Therefore, the thermal ellipsoids are slightly enlarged.




**Scheme 2.11.** Proposed mechanism for the formation of **129**.

## 2.3. Attempted Enantioselective Iodocyclizations

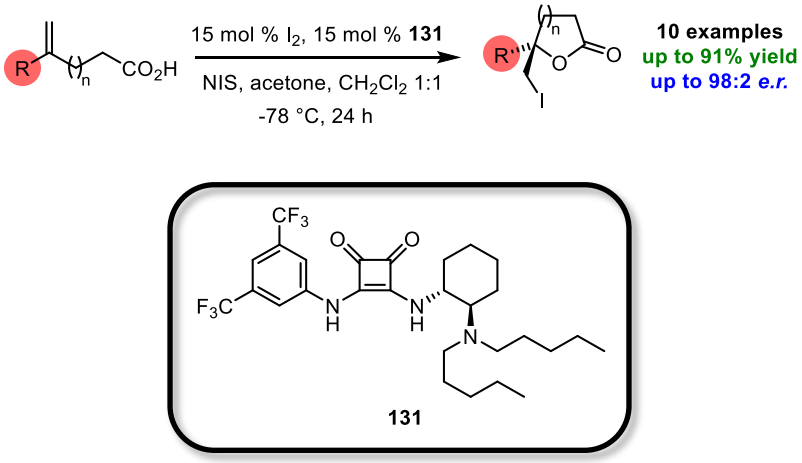
Having established the desired reactivity in a racemic fashion, we set out to develop an enantioselective variant of the aforementioned iodocyclizations. To this end, we prepared iodonating reagent **23** and chiral phosphoric acid (*S*)-TRIP **47** according to established literature procedures (see experimental section for full details).[17, 49-50]




**Scheme 2.12.** Attempted asymmetric phase-transfer iodination of **125**.

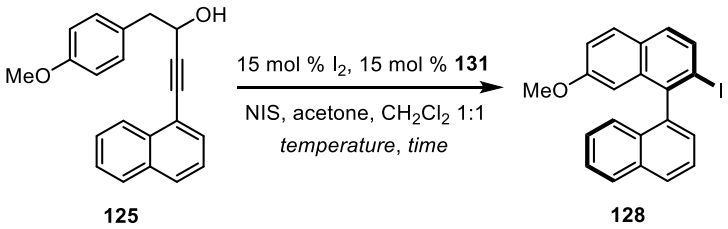
With catalyst **47** and iodinating reagent **23** in hand, we employed the reaction conditions reported for the asymmetric Wagner-Meerwein rearrangement in **Scheme 1.5.**[17] Unfortunately, we were unable to observe any conversion after three days (**Scheme 2.12.**). A potential rationalization for this could be the need of a polar solvent for the iodocyclization to proceed. To this end, we sought out an asymmetric iodination protocol which employed more polar solvents.

Hansen et al. reported an asymmetric iodolactonization,[51] catalyzed by chiral squaramide **131** (**Scheme 2.13.**). Their reaction conditions appealed to us, since they employed considerably more polar solvents than toluene. To this end we prepared chiral squaramide **131** according to the procedure by Hansen *et al.* (See experimental section for full details).[51]




**Scheme 2.13.** Squaramide catalyzed iodolactonization.

With squaramide **131** in hand, we subjected yne-ol **125** to these asymmetric iodination conditions (**Table 2.14.**). Unfortunately, neither at -78 °C nor -50 °C could any conversion to binaphthalene **128** be observed. Increasing the temperature to ambient temperature did result in some conversion to the desired binaphthalene **128**, but the product obtained was racemic.

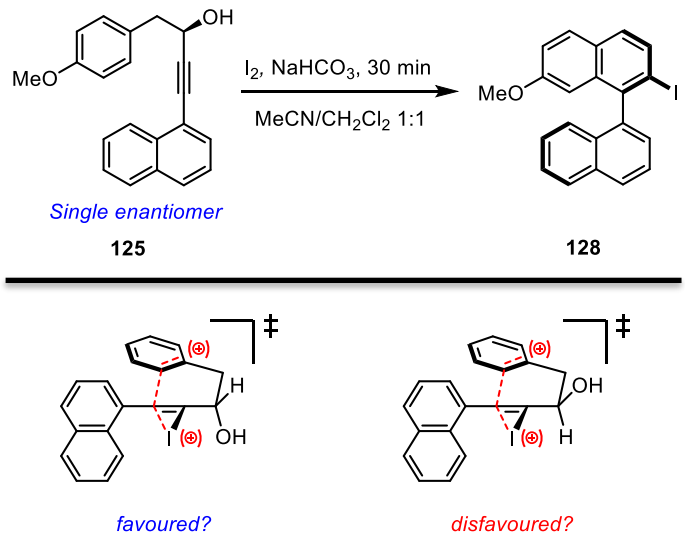



| Entry | Time/h | Temperature | Conversion[a] | *e.r.* [b] |
|---|---|---|---|---|
| **1** | 24 | –78 °C | <5% | N/A |
| **2** | 18 | –50 °C | <5% | N/A |
| **3** | 24 | r.t. | 8% | 50:50 |

[a] Conversion determined by $^{1}$H NMR spectroscopy; [b] determined by chiral stationary phase HPLC.

**Table 2.14.** Attempted asymmetric iodination of **125**.

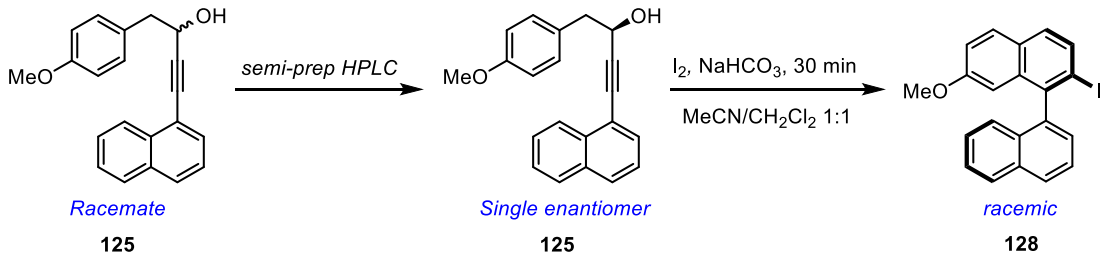
## 2.4. Attempted Point to Axial Chirality Transfer




**Scheme 2.15.** Hypothesized point to axial chirality transfer.

Having had no success in developing a catalytic asymmetric variant for the iodocyclization of **125** to **128**, we envisaged an alternative method for the atropselective synthesis of **128**. We speculated whether point to axial chirality transfer could be achieved if a single enantiomer of **125** was used in the reaction (**Scheme 2.15.**).

To this end, we isolated an analytical amount of enantiopure yne-ol **125** by semi-preparative HPLC. Subjecting enantiopure **125** to the iodocyclization conditions unfortunately led to racemic product **128** (**Scheme 2.16**).

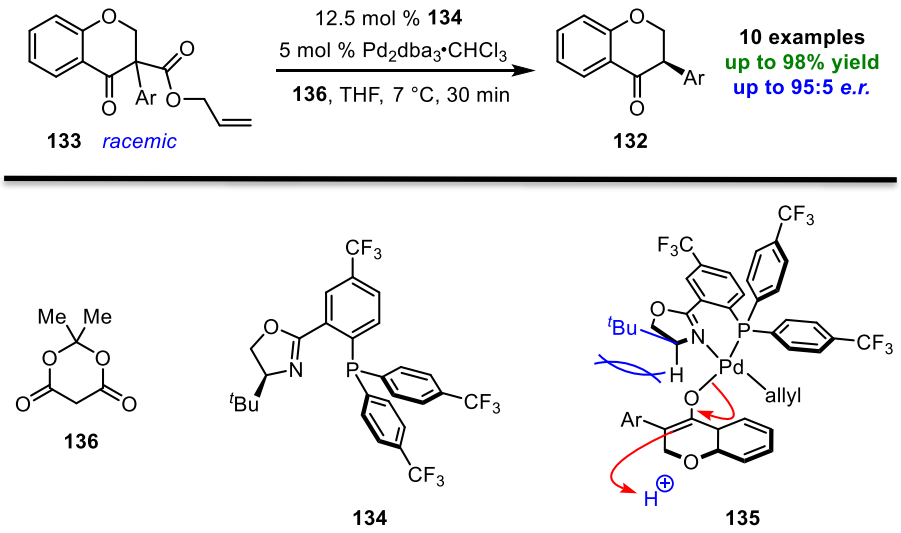



**Scheme 2.16.** Attempted point to axial chirality transfer.

Whilst we had no success achieving point to axial chirality transfer by iodocyclization, we were still determined to develop a system which achieves point to axial chirality transfer.

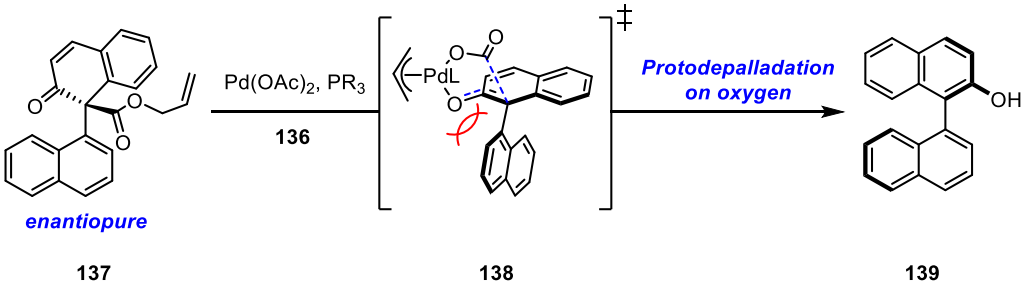
# 3. Binaphthyl Synthesis by Atropselective Ketone *O*-Alkylation

## 3.1. Background and Project Aims




**Scheme 3.1.** Decarboxylative enantioselective protonation.

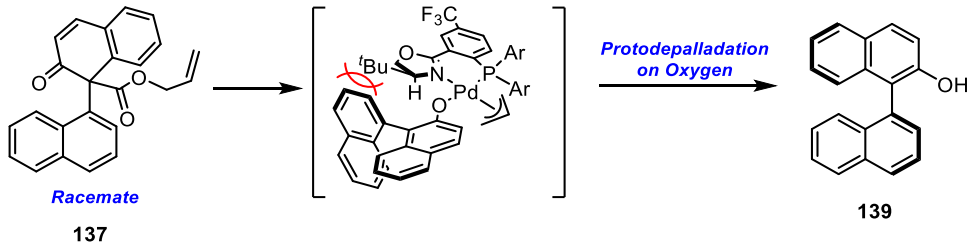
Guiry and co-workers have reported an asymmetric protonation approach to the enantioselective synthesis of isoflavanone derivatives **132** (**Scheme 3.1.**).[52] Here, a racemic quaternary allyl substituted β-keto ester **133** is proposed to undergo initial π-coordination to a $Pd^0$ complex bearing chiral ligand **134**. After oxidation and decarboxylation, a palladium enolate **135** is generated. It is suggested that the large *t*-butyl group of ligand **134** blocks the "top" face of the palladium enolate and that the subsequent protodepalladation occurs on the "lower" face.




**Scheme 3.2.** Proposed point to axial chirality transfer.

Inspired by this work, we proposed a system with the potential for point to axial chirality transfer (**Scheme 3.2.**). β-Keto ester **137** would then undergo π-coordination to an achiral $Pd^0$

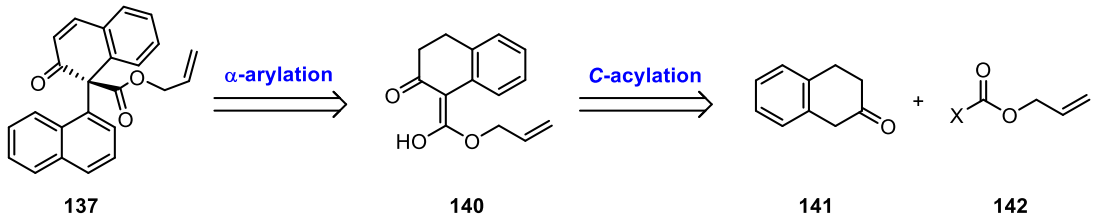
complex followed by oxidative addition. The decarboxylation of **138** would then occur with point to axial chirality transfer to generate an axially chiral palladium *O*-naphtholate which would subsequently protodepalladate on oxygen to furnish BINOL derivative **139**.




**Scheme 3.3.** Ligand controlled atropselective protodepalladation.

If the point to axial chirality transfer proved to be unsuccessful, we reasoned that it may be possible to synthesize BINOL derivative **139** from racemic β-Keto ester **137** and control the absolute stereochemistry of the product by use of a chiral ligand in analogous fashion to Guiry *et al.* (**Scheme 3.3.**).

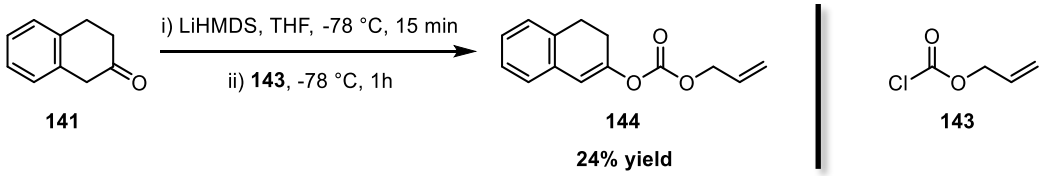
### 3.2. Substrate Synthesis and a Serendipitous Discovery




**Scheme 3.4.** Proposed disconnection for the synthesis of **137**.

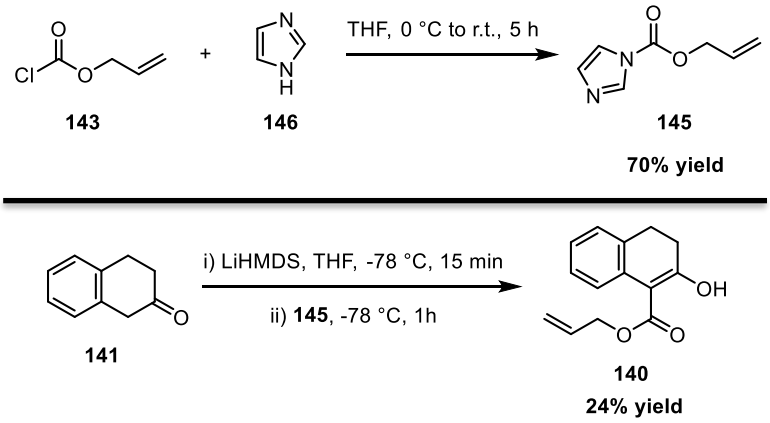
Our first task was to synthesize starting material **137**. We reasoned it may be possible to access **137** via α-arylation of β-keto ester **140** and subsequent oxidation (**Scheme 3.4.**). β-Keto ester **140** would originate via *C*-acylation of commercially available 2-tetralone **141** with an acylating agent **142**.

Our first attempt to synthesize **140** involved treatment of the lithium enolate of 2-tetralone with allyl chloroformate **143** (**Scheme 3.5.**).



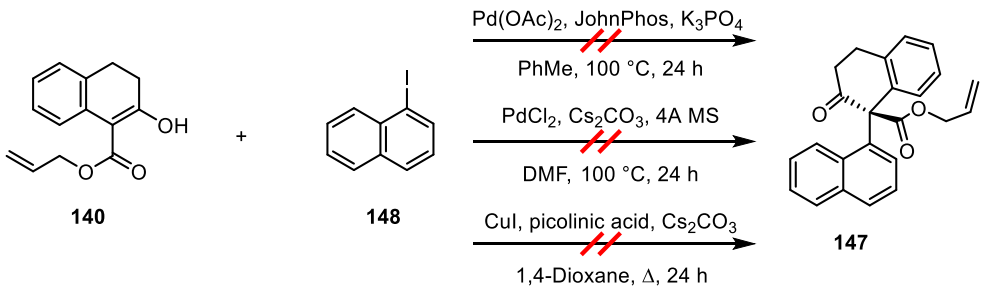

**Scheme 3.5.** *O*-acylation of **141**.

This reaction did not result in the desired *C*-acylation but afforded *O*-acylated enol carbonate **144** as the only product. In hindsight, this result was not very surprising. It is very well documented in the literature that first row metal ketone enolates generally undergo *O*-acylation with chloroformates.[53-55] A known method to achieve ketone *C*-acylation, is the use of an imidazolide as the acylating agent rather than a chloroformate.[56] Allyl imidazolide **145** was not commercially available, therefore it was prepared from allyl chloroformate **143** and imidazole **146** (**Scheme 3.6**).[57] Pleasingly when imidazolide **145** was employed as the acylating reagent, we were able to obtain the desired β-keto ester product **140**.



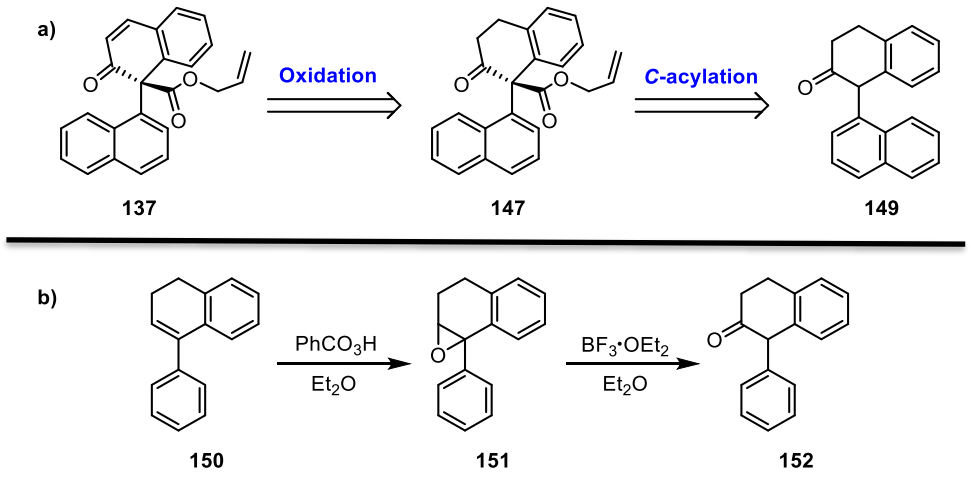

**Scheme 3.6.** *C*-acylation of **141**.

With β-keto ester **140** in hand, our next step was to synthesize **147** by α-arylation (**Scheme 3.7.**). We attempted palladium catalyzed α-arylation of β-keto ester **140** with 1-iodonaphthalene **148**.[58-59] Unfortunately, neither sets of conditions resulted in the desired product, and merely starting material decomposition was observed. We therefore attempted to employ copper catalyzed α-arylation conditions.[60] These conditions however, also resulted in starting material decomposition and no conversion to the desired product **147**.



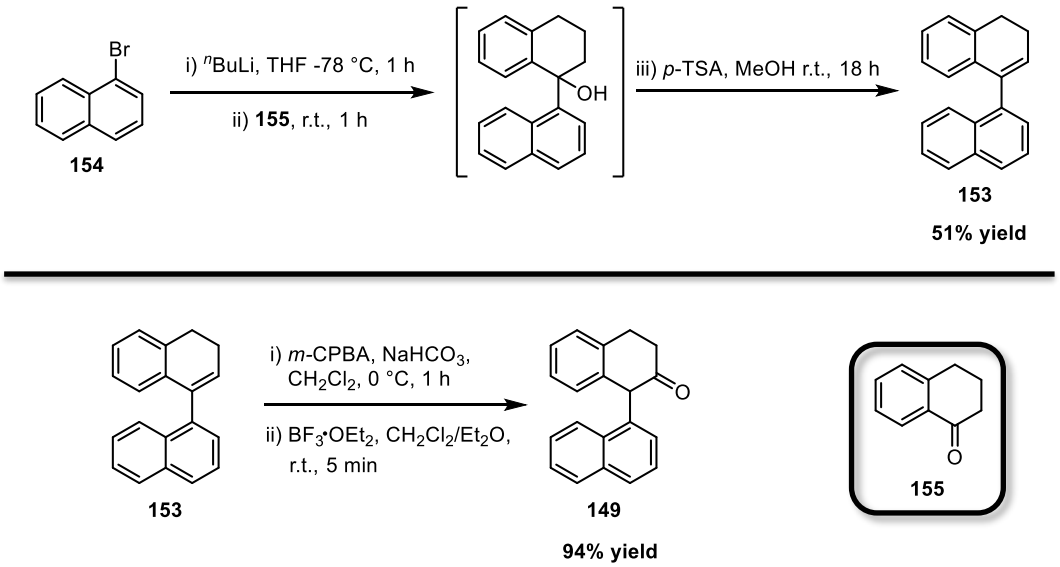

**Scheme 3.7.** Attempted α-arylations of **140**.

At this stage, we sought to access **147** *via* a different approach (**Scheme 3.8.a**). We decided to reverse the order in which the acylation and arylation steps were performed. 1-naphthyl-2-tetralone **149** would be *C*-acylated and subsequently oxidised to the desired product **137**. Since transition metal mediated ketone α-arylation had proven challenging for the previous disconnection, we chose to access ketone **149** by other means.




**Scheme 3.8.** New proposed route to **137**.

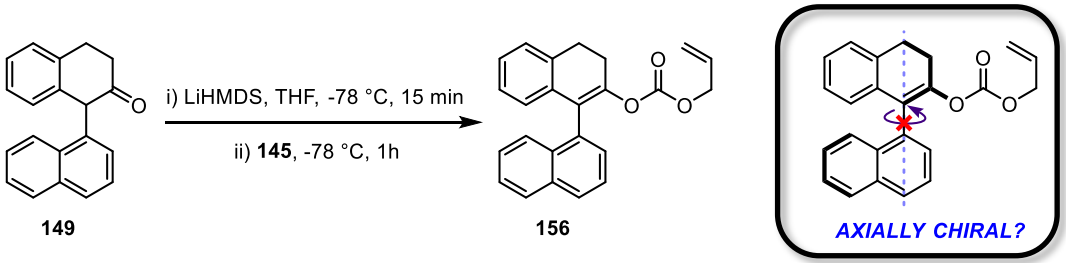
Mills and Schofield reported a synthesis of 1-phenyl-2-tetralone which did not rely on transition metal mediated α-arylation (**Scheme 3.8.b**).[61] Here, an alkene **150** is first treated with perbenzoic acid to furnish an intermediate epoxide **151**. Treatment of the epoxide with a Lewis-acid results in a Meinwald rearrangement *via* a 1,2-Hydride shift to the desired ketone **152**. We reasoned this approach could suitably modified to synthesize the desired 2-tetralone **149**.




**Scheme 3.9.** Synthesis of 2-tetralone **149**.

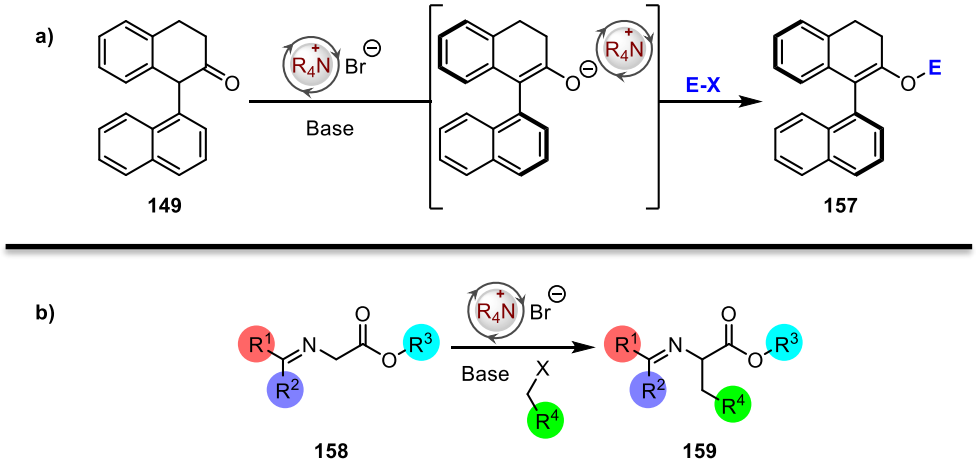
As a starting point, we set out to synthesize dihydrobinaphthalene **153**. First, 1-naphthyllithium was generated by lithium halogen exchange from 1-bromonaphthalene **154** and *n*-BuLi (**Scheme 3.9.**). Subsequent addition to 1-tetralone **155** furnished an intermediate tertiary alcohol which we were unable to isolate by chromatography. Therefore, the crude reaction mixture was used without any further purification and pleasingly, treatment with *p*-toluenesulfonic acid resulted in precipitation of **153** which could be isolated by a simple filtration.

The experimental details for the Meinwald rearrangement of **150** to **152** reported by Mills and Schofield were somewhat vague, consequently we employed reaction conditions employed by Tian *et al.* for a related ketone synthesis.[62] Pleasingly this approach enabled us to synthesize the desired ketone **149** on a multi-gram scale.



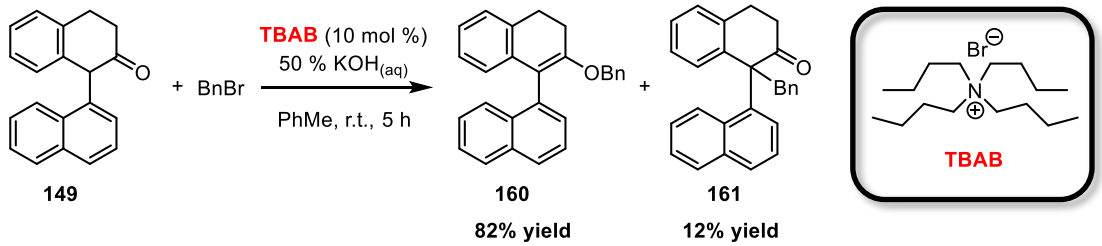

**Scheme 149.** Attempted *C*-acylation of **149**.

We then attempted to synthesize β-keto ester **147** by *C*-acylation using imidazolide **145** as before (**Scheme 1.10.**). The reaction gave a very complex mixture, and by crude $^{1}$H NMR analysis the only species we could identify appeared to be *O*-acylated enol carbonate product **156**. Then, however, it occurred to us that enol carbonate **156** might be axially chiral. More importantly, with this result in hand, we hypothesized that **149** could be trapped exclusively on oxygen with an electrophile using asymmetric phase-transfer catalysis to afford an atropisomeric enol ether **157** (**Scheme 3.11.a**).




**Scheme 3.11. a)** Proposed atropselective enol ether synthesis **b)** Asymmetric PTC *C*-alkylation of **158**.

To the best of our knowledge, enantioselective *C*-acylation by asymmetric phase-transfer catalysis has only been achieved intra- but not intermolecularly.[63] There are however, many reports of asymmetric phase-transfer catalysis being applied to the enantioselective *C*-alkylation of ketones, esters and amides.[64] For example, there are many examples of glycine Schiff bases of type **158** being *C*-alkylated with alkyl halides enantioselectively using asymmetric phase-transfer catalysis to furnish amino acid derivatives **159** (**Scheme 3.11.b**)[65-71]




**Scheme 3.12.** Phase-transfer catalyzed alkylation of **149**.

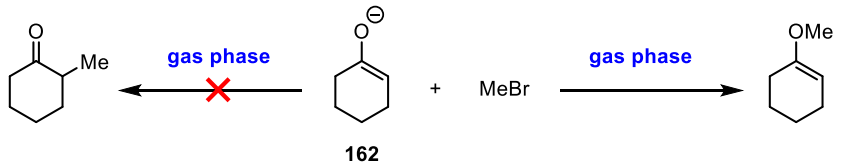
Considering this, we subjected ketone **149** to phase-transfer conditions using benzyl bromide as the alkylating agent, toluene as a solvent, tetrabutylammonium bromide (TBAB) as an achiral phase-transfer catalyst and 50% aqueous potassium hydroxide as the base (**Scheme 3.12.**). Pleasingly we observed mainly *O*-alkylation to furnish enol ether **160** alongside *C*-benzylated ketone **161** as a minor by-product.

### 3.3. Ambident Reactivity of Ketones

At this stage, we considered why the *O*-alkylation of **149** is favoured over the *C*-alkylation of **149**. This chapter will give a short review about what is known about the ambident reactivity of ketones to give some explanation towards the observed preferential *O*-alkylation of **149**.

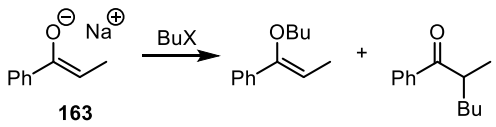
A simple explanation may be derived from HSAB theory, however a very comprehensive review on the ambident reactivity of amphiphiles by Mayr *et al.* states that HSAB theory fails to accurately describe ambident reactivity.[72] The authors appear to be confident about this since the title of the review is *"Farewell to the HSAB Treatment of Ambident Reactivity*" and the first line of the review is a quote by Albert Einstein: *"Mache die Dinge so einfach wie möglich – aber nicht einfacher*", which loosely translates to: *"Make things simple – but no simpler*".

It is important to note that the intrinsic barrier to ketone *O*-alkylation is significantly lower than that of *C*-alkylation. This has been experimentally demonstrated by the reaction of a cyclohexanone enolate **162** with methyl bromide (**Scheme 3.13.**),[72] and in computational studies by Houk and Bertran and respective co-workers.[73-74]




**Scheme 3.13.** *O*-Methylation of **162** in the gas phase.

If *C*-alkylation is intrinsically disfavoured, then why is it often observed? The truth is that there is no single answer to this and that a variety of factors influence *O*- vs. *C*-alkylation, many of which require an in depth understanding of theoretical chemistry to appreciate. There are however certain trends that have been observed that may offer some explanation to the ambident reactivity of **149**.




**163**

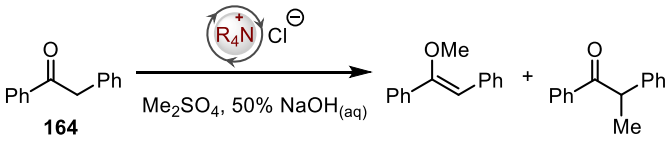
**% *O*-alkylation in selected Solvents**

| X | HMPA | DMSO | $Et_2O$ |
|---|---|---|---|
| **I** | 15 | 10 | 1 |
| **Br** | 40 | 23 | 5 |
| **Cl** | 67 | 46 | 18 |
| **OMs** | 83 | N/A | 11 |
| **OTs** | 85 | 44 | 20 |
| **F** | 96 | N/A | N/A |

**Table 3.14.** Solvent and leaving group effects on the ambident reactivity of **163**.

A publication by Wagner and co-workers illustrates the influence of solvent and electrophile leaving group on *O*- vs *C*-butylation ratios of **163** (**Table 3.14.**).[75] More electronegative leaving groups appear to yield higher *O*-alkylation ratios whereas less polar electrophiles result in more *C*-alkylation. In less polar solvents, such as diethyl ether, *O*-alkylation is disfavoured while in highly polar solvents such as HMPA *C*-alkylation is disfavoured. One rationale for this is that in less polar solvents a tighter ion pairing occurs between the sodium cation and the enolate anion occurs, effectively "shielding" the enolate oxygen from *O*-alkylation. In polar solvents, the

enolate is more solvated and could be seen as a more "naked" anion which reacts readily with butyl bromide on the enolate oxygen. The effect of a "naked" enolate has also been proposed for ketone alkylations under phase-transfer catalysis by Schrader and Dehmlow.[76] They investigated the effect of counterion size of the ammonium cation on the *O*- vs *C*- methylation of deoxybenzoin **164** under phase-transfer catalysis (**Table 3.15.**).




| $R_4N^+$ | % *O*-alkylation |
|---|---|
| $NMe_4^+$ | 55 |
| $NEt_4^+$ | 82 |
| $NPr_4^+$ | 93 |
| $NBu_4^+$ | 94 |

**Table 3.15.** Counterion effects on the ambident reactivity of **164**.

The phase-transfer catalysts employed in this study were tetra-alkyl ammonium chloride salts. When the chain length of the catalyst-alkyl substituent is increased, a higher *O*-alkylation ratio is observed. This is attributed to the enolate anion being able to bind less tightly to the ammonium counterion which results in a less *O*-bound ion pair.

An additional factor that may decrease the level of *C*-alkylation for **149** is the increase of steric bulk about the enolate carbon, owing to the large α-naphthyl substituent (**Figure 3.16.**). In summary, increased steric bulk about the enolate carbon and a "naked enolate" may be some of the factors that offer some explanation to the preference for *O*-alkylation for **149**.

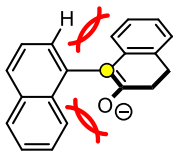
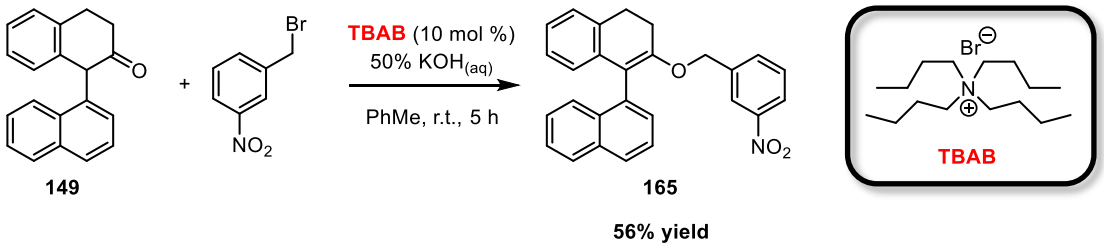



**Figure 3.16.** Increased steric bulk about enolate carbon of **149**.

### 3.4. Barrier to Rotation of 165




**Scheme 3.17.** Synthesis of more polar enol ether **165**.

To establish whether ketone **149** would be a suitable substrate for atropselective *O*-alkylation, we needed to ensure the barrier to rotation for enol ether **160** was sufficiently high enough to preclude any erosion in *e.r.* over the timescale of the reaction. We were unable to separate the enantiomers of **160** on any of the chiral stationary phases available to us, consequently we prepared enol ether **165** with a 3-nitro substituent on the benzyl moiety as a "polar handle" (**Scheme 3.17.**). The enantiomers of **165** were separable on a chiral stationary phases and we were able to obtain a enantioenriched sample of **165** *via* semi-preparative chiral HPLC (> 99:1 *e.r.*) as a solution in IPA/hexane. Through HPLC analysis of aliquots removed over the course of 9 days, we monitored the erosion in *e.r.* of **165** in solution (**Figure 3.18.**).

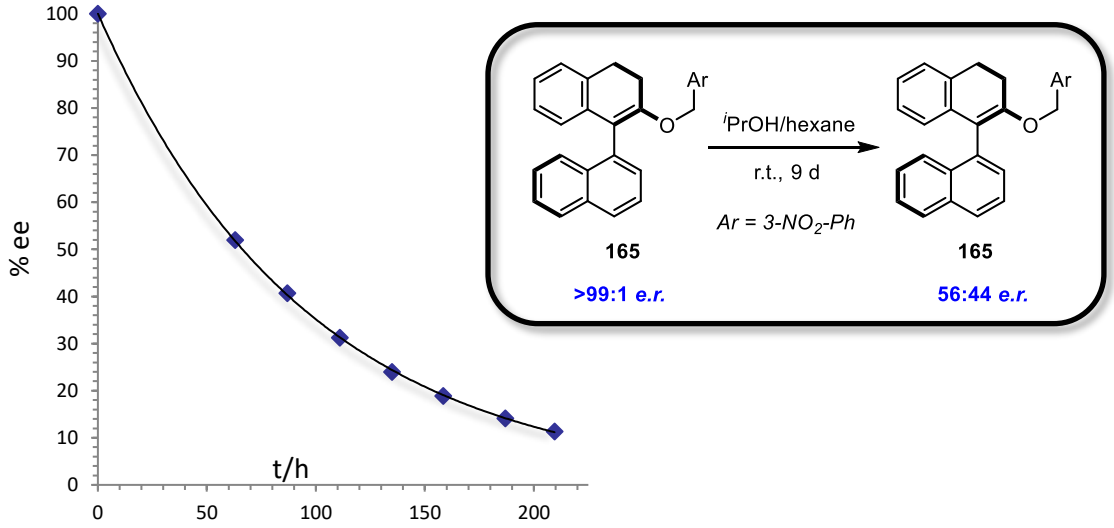



**Figure 3.18.** Erosion in *e.r.* of **165** over time.

After 9 days, the enantiomeric ratio had eroded to 56:44, suggesting the *e.r.* of enol ether **165** would erode over the timescale of an asymmetric phase-transfer reaction. Since the erosion in *e.r.* of showed a first order decay, a plot of ln(1/*e.e.*) against time should give a straight line (Figure, see **Appendix 8.1.1.** for derivation of equation).

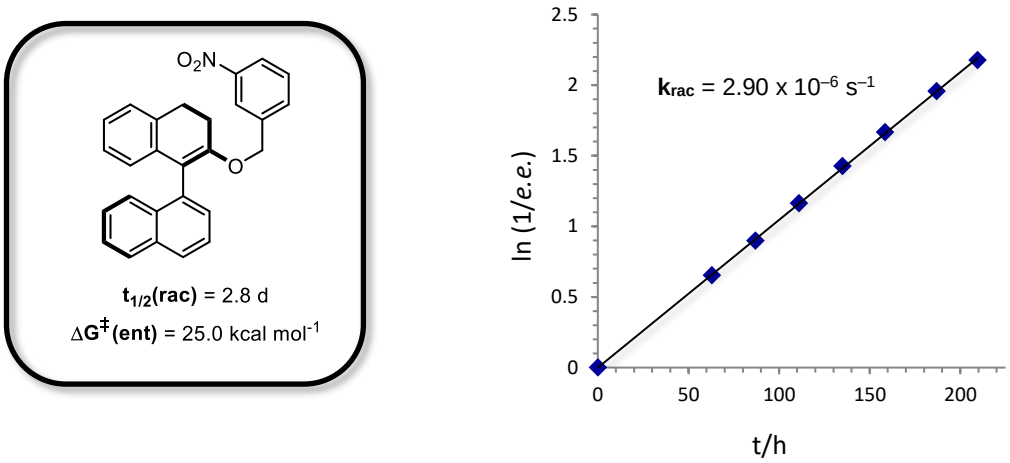
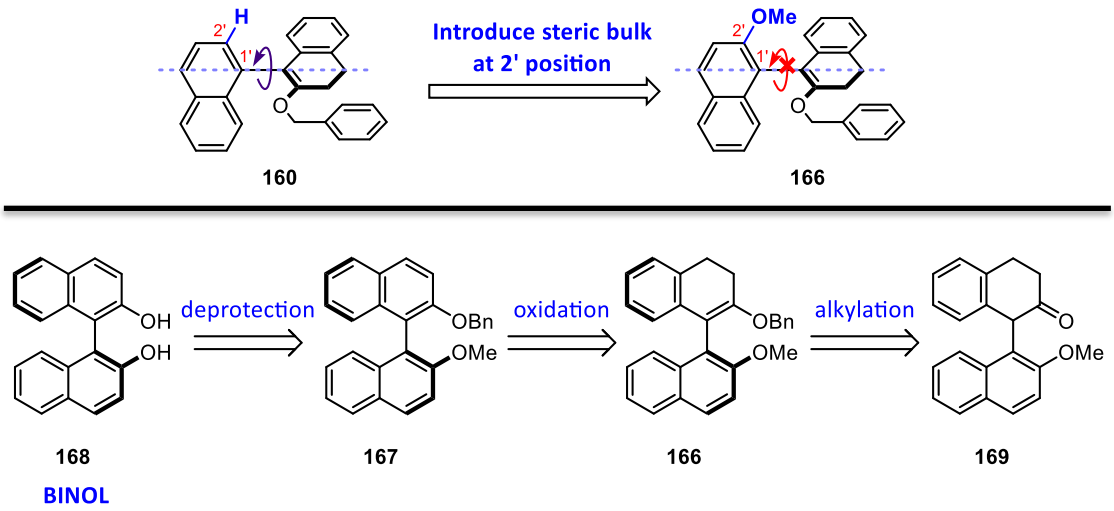



**Figure 3.19.** Erosion in *e.r.* of **165** over time.

The slope of the straight line is the rate constant to racemization ($k_{rac}$). Using $k_{rac}$ the half-life with respect to racemization ($t_{1/2}$(rac)) of **165** can be calculated to be 2.8 days, and the barrier to rotation ($\Delta G^{\ddagger}$(ent)) of **165** to be 25.0 kcal $mol^{-1}$ (See **Appendix 8.1.1.** for derivation of equations and full calculations).

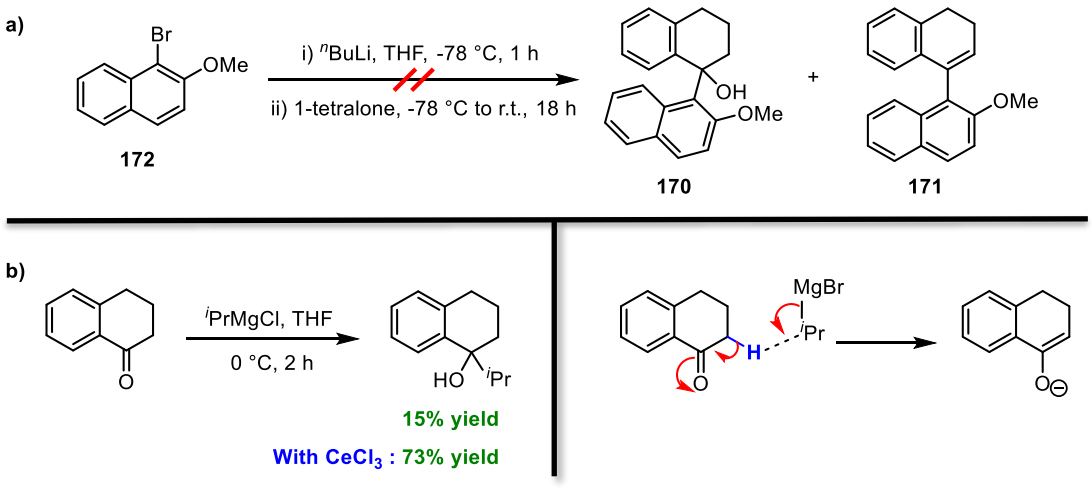
### 3.5. Synthesis of a More Hindered Substrate




**Scheme 3.20.** More hindered enol ether **166** as a BINOL precursor.

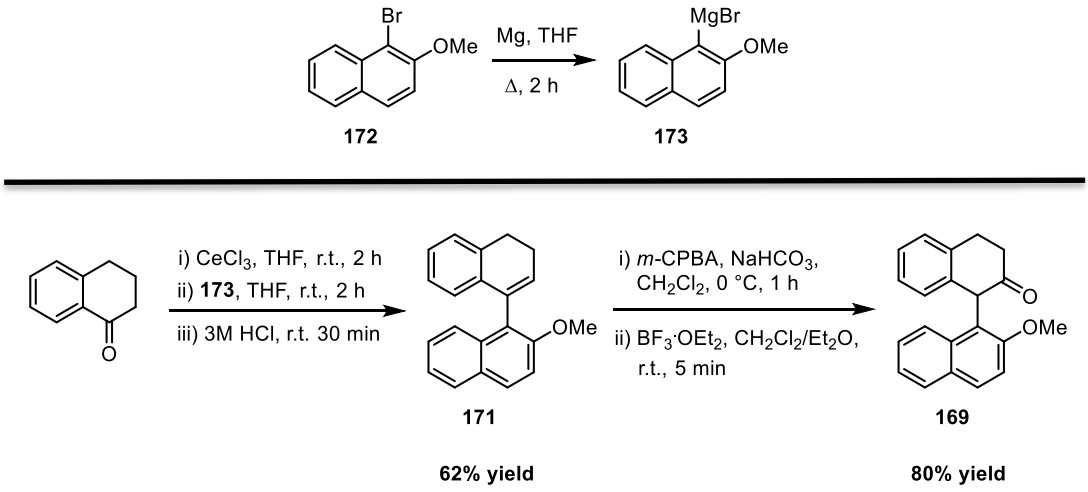
We reasoned that the barrier to rotation of enol ether **160** could be increased by introducing steric bulk at the *C*-2' position (**Scheme 3.20**). If the substituent at *C*-2' was a Methoxy group then oxidation of enol ether **366** could afford orthogonally protected BINOL **167**, which in turn could be deprotected to BINOL **168**. To the best of our knowledge this would be the first organocatalytic enantioselective synthesis of BINOL (other than a kinetic resolution).[37-38]

We attempted to synthesize 2-tetralone **169** using the same method as for **149**. Unfortunately, we were unable to detect any conversion to tertiary alcohol **170** or alkene **171** (**Scheme 3.21.a**).



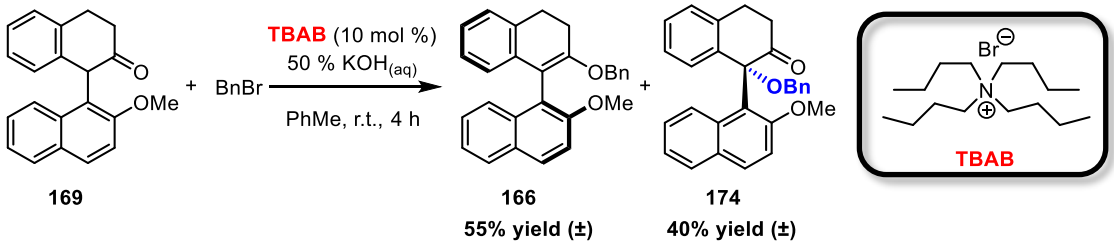

**Scheme 3.21.** Addition of hindered organometallics to 1-tetralone

After closer inspection of the literature, we concluded that this could be rationalized by α-deprotonation of 1-tetralone by the sterically encombered organolithium.[21, 77] Imamoto and co-workers reported that α-deprotonation of 1-tetralone could be minimised by the use of anhydrous cerium (III) chloride in the addition of $^{i}$PrMgBr to 1-tetralone (**Scheme 3.21.b**).[77]




**Scheme 3.22.** Synthesis of 2-tetralone **169**.

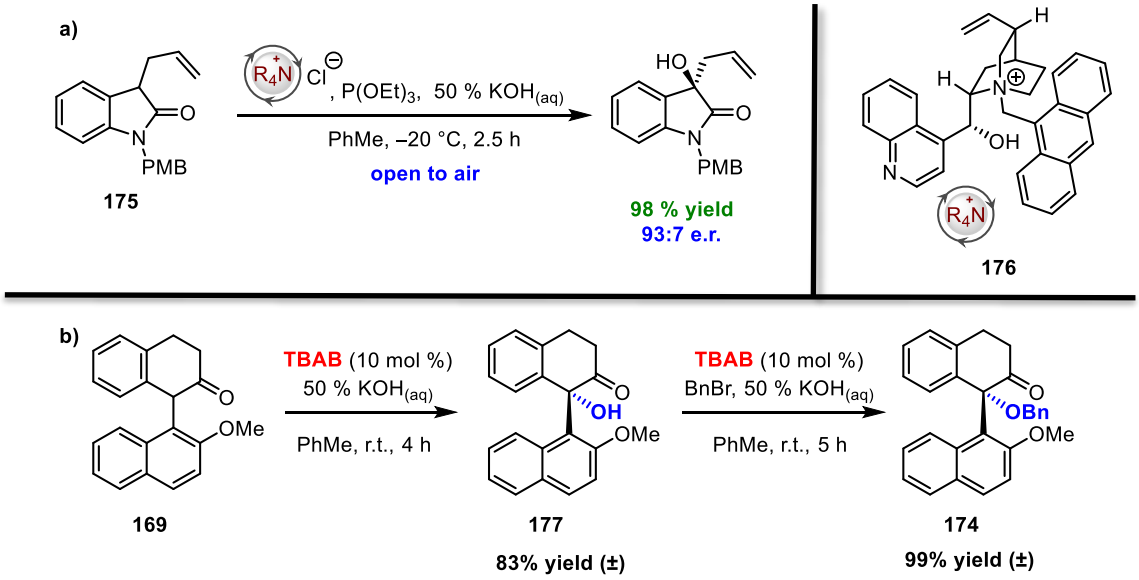
The cerium(III) chloride mediated addition of Grignard reagent **173**, derived from commercially available bromoarene **172**, to 1-tetralone afforded alkene **171** in a reasonable yield after acidic workup (**Scheme 3.22.**). After epoxidation of alkene **171** with *m*-CPBA, a Lewis acid-mediated Meinwald rearrangement of the intermediate epoxide afforded the desired 2-tetralone **169** in good yield.




**Scheme 3.23.** *O*-alkylation of ketone **169**.

With the starting material **169** in hand, we proceeded to subject ketone **169** to the racemic phase-transfer conditions (**Scheme 3.23.**). The desired enol ether **166** was afforded alongside

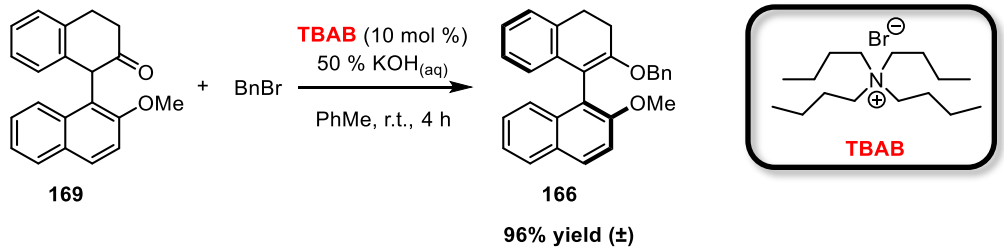
α-benzyloxy ketone **174**. Interestingly, no *C*-alkylation was observed, presumably due to increased steric bulk about the enolate carbon. We rationalized that **174** could have been formed by α-hydroxylation of ketone **169** by adventitious oxygen and subsequent benzylation of the hydroxyl group. α-Hydroxylation of carbonyl compounds under phase-transfer conditions is well precedented and has been achieved enantioselectively, e.g. by Itoh et al. (**Scheme 3.24.a**).[78]




**Scheme 3.24.** Phase-transfer mediated α-hydroxylation.

Here, oxindole **175** is α-hydroxylated enantioselectively by adventitious oxygen under phase-transfer conditions using a cinchonidine derived ammonium salt **176** as chiral phase-transfer catalyst. To test our hypothesis, we subjected ketone **169** to the racemic phase-transfer conditions in the absence of benzyl bromide (**Scheme 3.24.b**). After four hours, complete conversion to α-hydroxy ketone **177** was observed, which could be subsequently benzylated under phase-transfer conditions to ketone **174**.

We were able to supress the α-hydroxylation of **169** by performing the phase-transfer benzylation of **169** under anaerobic conditions with freeze-pump-thawed solvents and an argon atmosphere, to afford the desired enol ether in excellent yield (**Scheme 3.25.**).

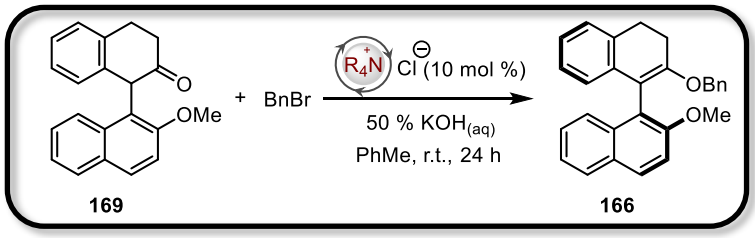


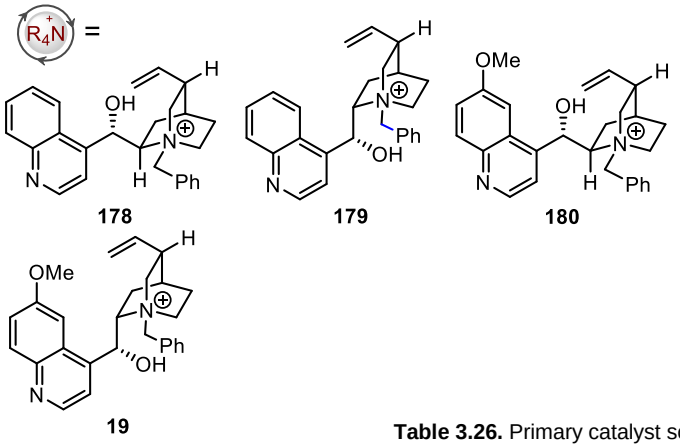

**Scheme 3.25.** *O*-alkylation of ketone **169** under anaerobic conditions.

Next, we sought to establish whether the barrier to rotation of enol ether **166** was sufficiently high to preclude any racemization at room temperature on the timescale of the reaction conditions. To this end, we isolated an analytical amount of enantiopure **166** by semi-preparative HPLC as a solution in IPA/hexane. After two weeks, no erosion in *e.r.* for **166** could be observed, thus excluding any room temperature racemization.

### 3.6. Optimization of Asymmetric Reaction Conditions

With the racemic reaction in hand, our next task was to develop a reaction protocol which could synthesize enol ether **166** enantioselectively using a chiral phase-transfer catalyst. This chapter will illustrate key results. For a full account of the optimization process, see **Appendix 8.2.2**. In all experiments, enantiomeric ratios were determined by chiral stationary phase HPLC.



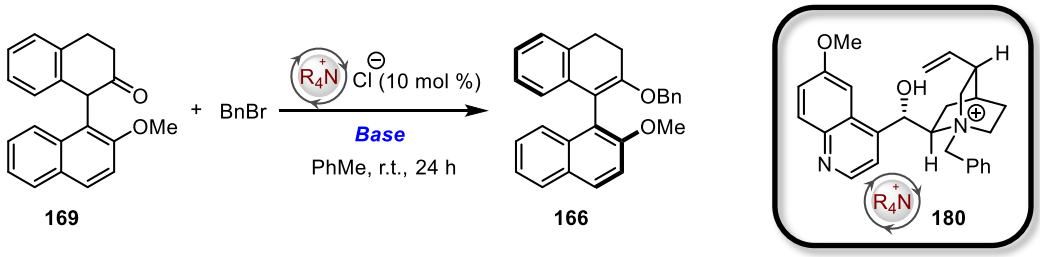




| Entry | Catalyst | *e.r.* |
|---|---|---|
| 1 | **178** | 58:42 |
| 2 | **179** | 43:57 |
| 3 | **180** | 60:40 |
| 4 | **19** | 44:56 |

**Table 3.26.** Primary catalyst screen.

As a starting point, we investigated the four simplest commercially available cinchona alkaloid derived ammonium salts (**Table 3.26.**). We were pleased to observe that in all cases enol ether **166** was non-racemic. Using *N*-benzyl-quinidinium bromide we were able to obtain the enol ether in a promising 60:40 *e.r.* (**Table 3.26.**, entry 3).

At this stage, we decided to screen a small number bases in the phase-transfer reaction catalyzed by **180** (**Table 3.27.**). Our aim was to increase enantioselectivity further to better evaluate the efficacy of selected chiral ammonium salts as asymmetric phase-transfer catalysts in a subsequent catalyst screen.




169 166 180

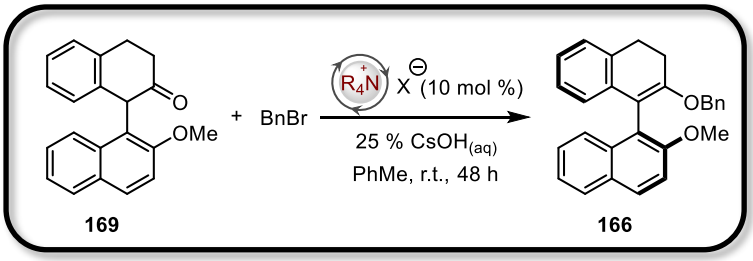
| Entry | Base (eq.) | *e.r.* |
|---|---|---|
| **1** | 50% $KOH_{(aq)}$(5) | 60:40 |
| **2** | 50% $K_2CO_{3(aq)}$ (5) | 71:29 [a] |
| **3** | 50% $Cs_2CO_3$ (5) | 72:28 |
| **4** | KOH (1.5) | 54:46 |
| **5** | $CsOH•OH_2$ (5) | 51:49 |
| **6** | 25% $CsOH•OH_2$ (5) | 73:27 |

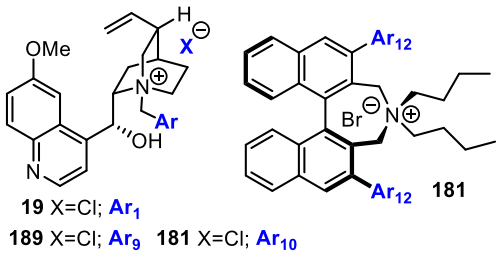
[a] Poor conversion

**Table 3.27.** Primary base screen.

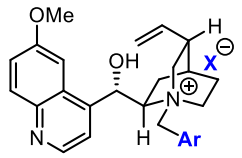
Changing the base from aqueous potassium hydroxide to aqueous potassium carbonate significantly improved the enantioselectivity to 71:29 *e.r.*, however the conversion was very poor (**Table 3.27.**, entry 2). The use of aqueous cesium carbonate resulted in better conversion and similar levels of enantioinduction (**Table 3.27.**, entry 3). All tested solid hydroxide bases gave poor levels of enantioinduction (**Table 3.27.**, entries 4-5). Pleasingly, employing aqueous

cesium hydroxide as a base produced enol ether **169** with an *e.r.* of 73:27 (**Table 3.27.**, entry 6). At this stage, we were confident that we had sufficiently improved the enantioselectivity to effectively examine the efficacy of various ammonium salts as chiral phase-transfer catalysts (**Table 3.28.**).

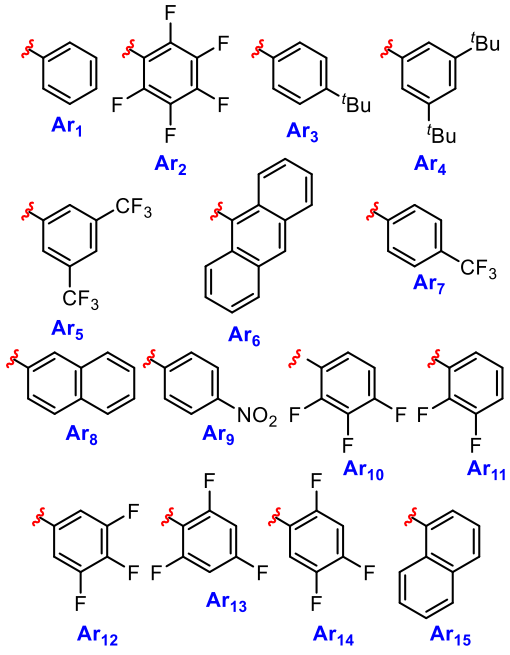



**19** X=Cl; $Ar_1$
**189** X=Cl; $Ar_9$ **181** X=Cl; $Ar_{10}$




**180** X=Cl; $Ar_1$
**182** X=Br; $Ar_2$
**183** X=Br; $Ar_3$
**184** X=Br; $Ar_4$
**185** X=Br; $Ar_5$
**186** X=Br; $Ar_6$ **187** X=Br; $Ar_7$ **188** X=Br; $Ar_8$
**191** X=Br; $Ar_{11}$ **192** X=Br; $Ar_{10}$ **193** X=Br; $Ar_{12}$
**194** X=Br; $Ar_{13}$ **195** X=Br; $Ar_{14}$ **196** X=Br; $Ar_{15}$



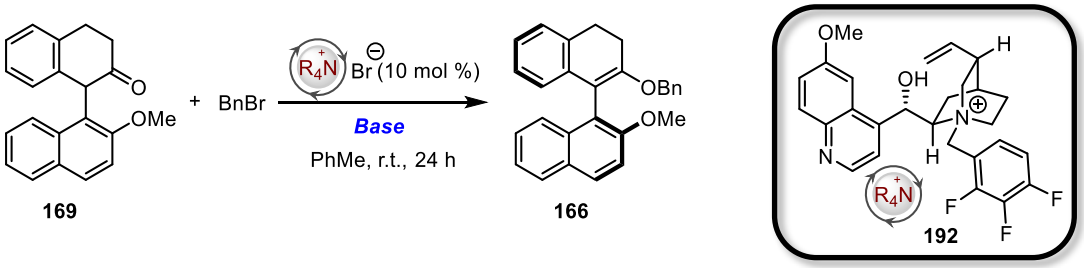

| Entry | Catalyst | *e.r.* |
|---|---|---|
| 1 | 180 | 73:27 |
| 2 | 19 | 40:60 |
| 3 | 181 | 53:47 |
| 4 | 182 | 74:26 |
| 5 | 183 | 74:26 |
| 6 | 184 | 64:36 |
| 7 | 185 | 80:20 |
| 8 | 186 | 81:19 |
| 9 | 187 | 75:25 |
| 10 | 188 | 83:17 |
| 11 | 189 | 31:69 |
| 12 | 190 | 18:82 |
| 13 | 191 | 86:14 |
| 14 | 192 | 88:12 |
| 15 | 193 | 73:27 |
| 16 | 194 | 74:26 |
| 17 | 195 | 83:17 |
| 18 | 196 | 73:27 |

**Table 3.28.** Secondary catalyst screen.

Ammonium salts bearing a BINOL backbone, pioneered by Maruoka et al.,[69] such as **181** resulted in poor enantioinduction, therefore this class of phase-transfer catalyst was not investigated any further (**Table 3.28.**, entry 3). The preliminary catalyst screen indicated that catalysts based on a quinidine architecture were most proficient (**Table 3.28.**, entries 1-2). Consequently, a series of quininium and quinidinium phase-transfer catalysts with a range of *N*-benzyl aryl moieties (**Table 3.28.**, entries 4-18) were investigated. Electron rich arenes failed to increase, or deteriorated enantioselectivity (**Table 3.28.**, entries 5-6). Polycyclic and electron poor arenes improved enantioselectivity (**Table 3.28.**, entries 7-12). After the preliminary catalyst screen, it appeared that quinidinium catalysts performed slightly better than the pseudo-enantiomeric quininium catalysts. Bearing this in mind, we were very pleased to observe a significant improvement in enantioinduction with a quininium derived 2,3,4-trifluoro benzyl catalyst **190** (**Table 3.28.**, entry 12). Consequently, we investigated a series of trifluoro-substituted quinidinium catalysts (**Table 3.28.**, entries 13-18). We were delighted to observe that 2,3,4-trifluorobenzyl quinidinium bromide **192** was able to induce high levels of enantioselectivity at 88:12 *e.r.* (**Table 3.28.**, entry 14). Confident that we had found the optimal phase-transfer catalyst for this reaction, we proceeded to investigate the effects of various bases on enantioselectivity (**Table 3.29.**).

Aqueous sodium and potassium hydroxide led to a deterioration in enantioselectivity, whilst aqueous rubidium hydroxide proved to be equally as effective as aqueous cesium hydroxide (**Table 3.29.**, entries 1-4). Solid sodium carbonate did not result in any conversion and aqueous sodium carbonate improved enantioselectivity slightly, albeit with very low conversion (**Table 3.29.**, entries 5-6). Both solid and aqueous potassium carbonate resulted in a minor improvement in enantioselectivity, however also with very poor conversion (**Table 3.29.**, entries 7-8). Whilst cesium carbonate did improve conversion, the enantioselectivity deteriorated (**Table 3.29.**, entries 9-10). We were very pleased to observe that potassium phosphate bases

led to both good conversion and enantioselectivity with solid potassium phosphate inducing the highest level of enantioinduction at 90:10 *e.r.* observed so far (**Table 3.29.**, entries 11-12).



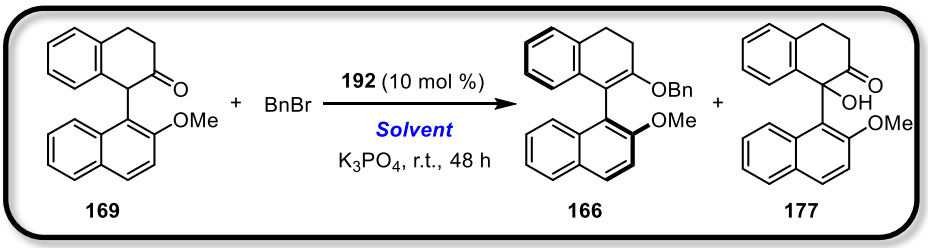

| Entry | Base (eq.) | *e.r.* |
|---|---|---|
| **1** | 25% $NaOH_{(aq)}$(2.5) | 86:14 |
| **2** | 25% $KOH_{(aq)}$(2.5) | 87:13 |
| **3** | 25% $RbOH•OH_2$ (2.5) | 88:12 |
| **4** | 25% $CsOH•OH_2$ (2.5) | 88:12 |
| **5** | $Na_2CO_3$ (5) | N/A[a] |
| **6** | 2M $Na_2CO_{3\,(aq)}$ (5) | 89:11[b] |
| **7** | $K_2CO_3$ (5) | 89:11[b] |
| **8** | 50% $K_2CO_{3\,(aq)}$ (5) | 89:11[b] |
| **9** | $Cs_2CO_3$ (1.5) | 87:13 |
| **10** | 50% $Cs_2CO_{3\,(aq)}$ (5) | 87:13 |
| **11** | $K_3PO_4$ (5) | 90:10 |
| **12** | 50% $K_3PO_{4\,(aq)}$ (5) | 89:11 |

[a] No conversion; [b] Poor conversion.

**Table 3.29.** Secondary base screen.

With an optimal base in hand, we proceeded to investigate the influence of the solvent on enantioselectivity (**Table 3.30.**). Halogenated solvents resulted in a slight decrease in enantioselectivity (**Table 3.30.**, Entries 5-9). In previous asymmetric phase-transfer catalyzed reactions in the group a severe decrease in enantioselectivity has often been observed when halogenated solvents were employed. This has been attributed to a looser pairing in a more

polar solvent. We were therefore delighted to observe that enol ether **166** could be generated in high enantiomeric ratios when halogenated solvents were employed. Ether solvents resulted in both poor enantioselectivity and conversion (**Table 3.30.**, entries 10-12). Aromatic solvents appeared to have the greatest effect on enantioselectivity. Whilst *m*-xylene and *p*-xylene gave both poor conversion and enantioselectivity (**Table 3.30.**, entries 3-4), we were pleased to observe that the use of benzene as the solvent gave the highest enantiomeric ratio for **166** at 92:8 *e.r.* ( **Table 3.30.**, entry 2).




| Entry | Solvent | *e.r.* | 166 : 177 [a] |
|---|---|---|---|
| **1** | Toluene | 90:10 | 1.0:1.2 |
| **2** | Benzene | 92:8 | 1.0:1.4 |
| **3** | *m*-Xylene | 85:15[b] | N/A |
| **4** | *p*-Xylene | 85:15[b] | N/A |
| **5** | trichloroethylene | 88:12 | 1.0:1.3 |
| **6** | 1,2-Dichloroethane | 86:14[b] | N/A |
| **7** | $CCl_4$ | 84:16[b] | N/A |
| **8** | Chloroform | 88:12 | 1.0:0.3 |
| **9** | Dichloromethane | 87:13 | 1.0:0.2 |
| **10** | $Et_2O$ | 82:12[b] | N/A |
| **11** | TBME | 77:23[b] | N/A |
| **12** | $^{i}Pr_2O$ | 60:40[b] | N/A |

[a] Determined by $^{1}H$ NMR spectroscopy; [b] Poor conversion.

**Table 3.30.** Influence of solvent on enantioselectivity and α-hydroxylation.

It is important to note that during the solvent screen we observed different levels of α-hydroxylation of the ketone starting material **169** to furnish α-hydroxy ketone **177**. α-Hydroxylation was the most severe in benzene whereas in dichloromethane it was suppressed significantly. The extent of α-hydroxylation is unlikely to be caused by a difference in oxygen solubility in different solvents. A publication by Yamamoto *et al.* reports that there is no difference in oxygen solubility between benzene and dichloromethane.[79] We propose that, for reasons unknown to us, the solvent affects the relative rates of ketone *O*-alkylation and ketone α-hydroxylation with the rate for α-hydroxylation being the slowest in dichloromethane and the fastest in benzene.

It was at this stage that Dr Roland Armstrong joined this project and I would like to express my sincere gratitude for his valuable practical and theoretical contributions to this work. Any compounds synthesized by Dr Roland Armstrong will be denoted as **RJAXY**, to distinguish between respective contributions to this work.

Confident that, in benzene, we had found the optimal solvent for the enantioselective *O*-alkylation of ketone **169**, we proceeded to investigate the influence of the electrophile on enantioselectivity (**Table 3.32.**). Dr Roland Armstrong synthesized enol ethers **RJA1** to **RJA8** as reference samples for racemic HPLC traces (**Figure 3.31.**).

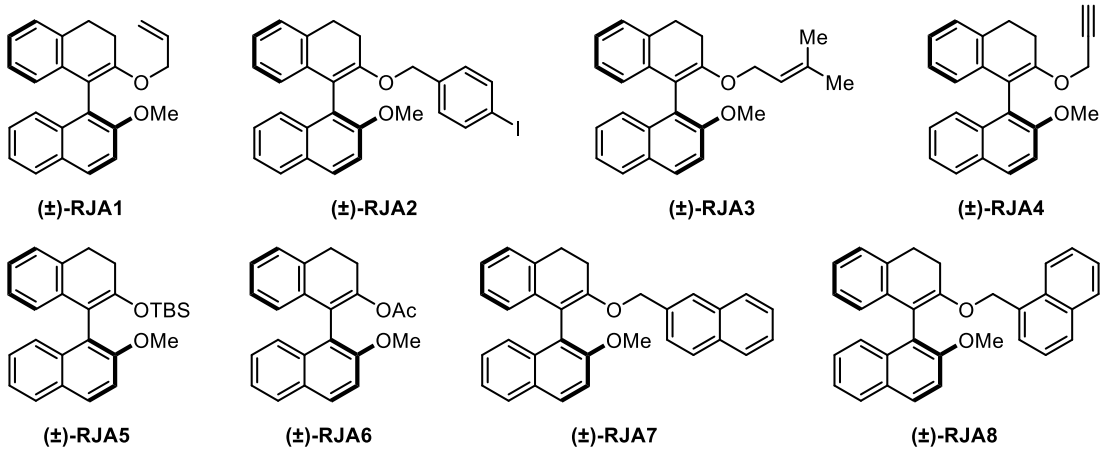
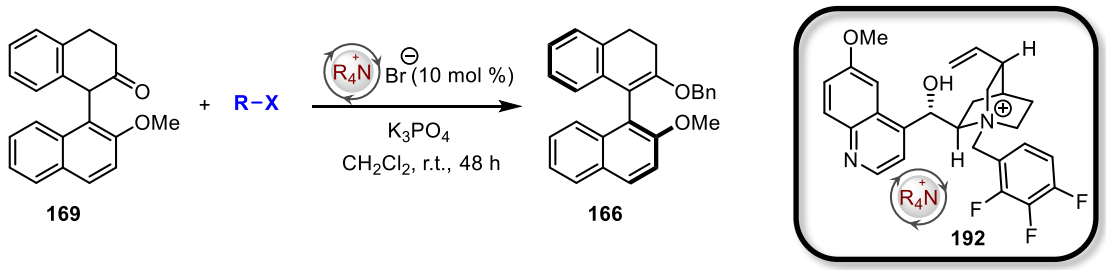



**Figure 3.31.** Influence of solvent on enantioselectivity and α-hydroxylation.



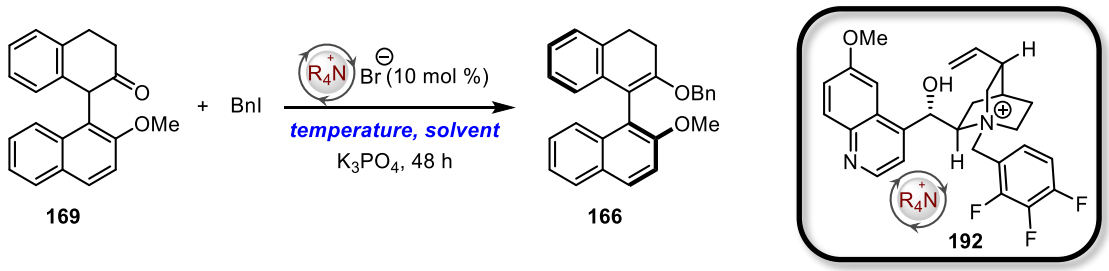

| Entry | Electrophile | *e.r.* |
|---|---|---|
| **1** | $Ac_2O$ | 50:50 |
| **2** | AcCl | N/A[a] |
| **3** | TBDPS-Cl | 50:50 |
| **4** | 1-(Bromomethyl)naphthalene | 79:21 |
| **5** | 2-(Bromomethyl)naphthalene | 79:21 |
| **6** | 4-Iodobenzyl bromide | 85:15 |
| **7** | Prenyl bromide | 80:20 |
| **8** | Propargyl bromide | 72:28 |
| **9** | Methyl iodide | 58:42[b] |
| **10** | Allyl bromide | 79:21 |
| **11** | Allyl iodide | 88:12 |
| **12** | Benzyl chloride | N/A[a] |
| **13** | Benzyl bromide | 87:13 |
| **14** | Benzyl iodide | 91:9 |
| **15** | Benzyl iodide | 94:6[c] |

[a] No conversion; [b] The enantiomers of the enol ether were not separable on any chiral stationary phases available to us, therefore the product was oxidised with DDQ to dimethyl-BINOL; [c] Reaction performed in benzene.

**Table 3.32.** Electrophile screen.

In order to suppress α-hydroxylation of ketone **169**, the electrophile screen was carried out using dichloromethane as the solvent. Acylating and silylating reagents as electrophiles gave racemic enol ethers (**Table 3.32.**, entries 1-3). Next, we investigated different benzyl bromide derivatives where the arene moiety was varied. Unfortunately, no improved enantioselectivity was observed (**Table 3.32.**, entries 4-6). We therefore turned our attention to different alkyl

bromides as electrophiles (**Table 3.32.**, entries 7-10). Again, no increase in enantioselectivity was observed. Interestingly, when allyl iodide was used instead of allyl bromide an increase from 79:21 *e.r.* to 88:12 *e.r.* was observed (**Table 3.32.**, entries 10-11). Consequently, we investigated the nature of the halide leaving group in benzylating reagents (**Table 3.32.**, entries 12-14). Whilst no conversion was observed with benzyl chloride, benzyl iodide gave enol ether in an improved 91:9 *e.r.* We were pleased to observe that carrying out the *O*-alkylation with benzyl iodide in benzene gave enol ether in 94:6 *e.r.* (**Table 3.32.**, entry 15).




| Entry | Temperature | Solvent | yield[a] | *e.r.* |
|---|---|---|---|---|
| **1** | 0 °C | Benzene | N/A[b] | N/A[b] |
| **2** | 0 °C | $CH_2Cl_2$/PhH 1:1 | 99% | 95:5 |
| **3** | 0 °C | $CH_2Cl_2$/PhH 9:1 | 83% | 96:4 |
| **4** | 0 °C | $CH_2Cl_2$/PhH 4:1 | 99% | 96:4 |
| **5** | –10 °C | $CH_2Cl_2$/PhH 9:1 | 40% | 97:3 |

[a] isolated yield; [b] reaction mixture froze.

**Table 3.33.** Optimization of reaction temperature.

Next, we endeavoured to investigate the effect of temperature on both conversion and enantioselectivity (**Table 3.33.**). Carrying out the reaction at 0 °C resulted in no conversion to enol ether **169**, due to the reaction mixture freezing (**Table 3.33.**, entry 1). Consequently, we investigated various dichloromethane/benzene solvent mixtures. We began our investigations with a 1:1 mixture of dichloromethane/benzene at 0 °C. Whilst enantioselectivity was reproducible, we were unable to generate reproducible yields. This perplexed us initially, then however, it occurred to us that the agitation of the base might be important. Deprotonation of

the starting material likely occurs at the solid liquid interface (the mechanism of the reaction will be discussed in more detail in **chapter 4**). Therefore, the rate of deprotonation is likely to depend on the available potassium phosphate surface area, i.e. stirring speed. Since the reaction is sensitive to α-hydroxylation by adventitious oxygen, the reaction ought to be performed under an inert atmosphere. In a long and thin Schlenk tube, the base cannot be sufficiently agitated due to too small a stirrer bar being used (**Figure 3.34.**). In a short and wide Schlenk tube we observed that the reaction mixture encrusted the interior of the Schlenk tube, effectively prohibiting agitation since there was nothing left to agitate. In a round bottomed Schlenk tube the reaction sufficient agitation can be achieved, whilst minimizing the amount of reaction mixture becoming distributed to the neck of the Schlenk tube. It is worth noting that this is only an issue on a small to medium scale (0.5-2.0 mmol) and is not an issue on a large scale (see **chapter 3.11.**).

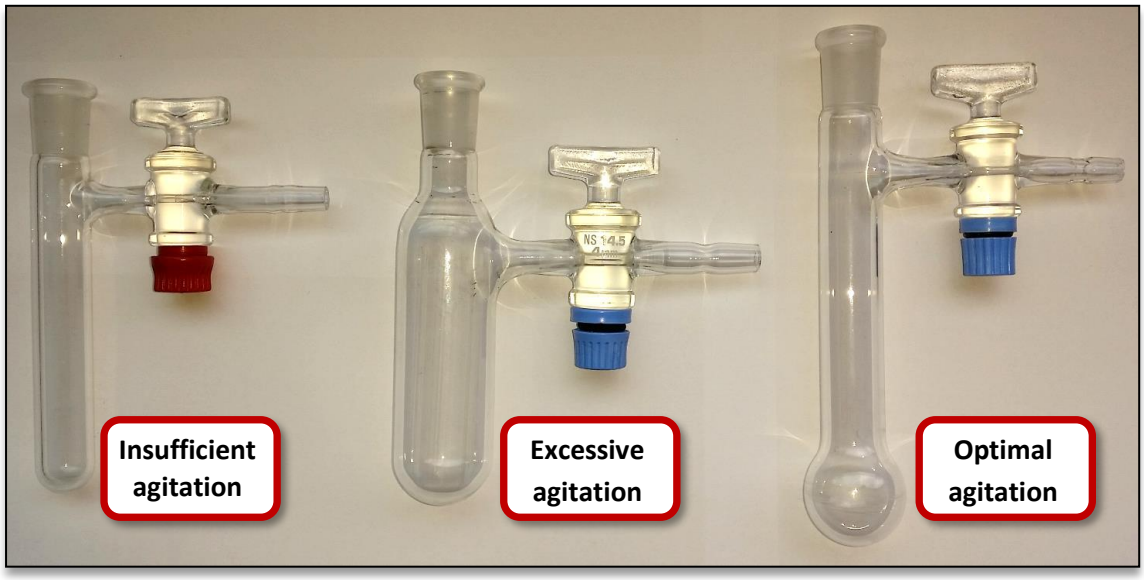
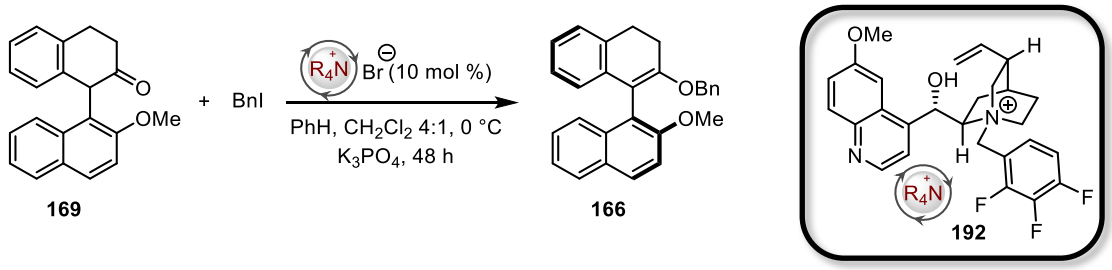



**Figure 3.34.** The importance of the reaction vessel.

Performing the reaction in a round bottomed Schlenk tube gave both reproducible yields and enantioselectivities. We were able to improve the enantioselectivity to 95:5 *e.r.* when using a 1:1 mixture of benzene/dichloromethane with 99% yield (**Table 3.33.**, entry 2). A mixture of 9:1 benzene/dichloromethane did not give full conversion, however a 4:1 mixture gave 94:6 *e.r.* and 99% yield (**Table 3.33.**, entries 3-4). Lowering the temperature to -10 °C did increase

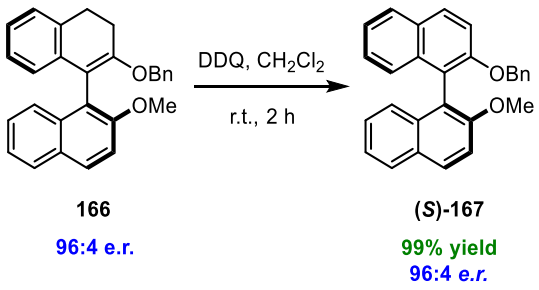
enantioselectivity to 97:3 e.r., albeit with poor conversion (**Table 3.33.**, entry 5). At 96:4 *e.r.* we were confident that we had arrived at the optimal reaction conditions for the atropselective *O*-benzylation of ketone **169** (**Scheme 3.35.**).




**Scheme 3.35.** Optimized reaction conditions.

### 3.7. Oxidation to Orthogonally Protected BINOL and Absolute Configuration

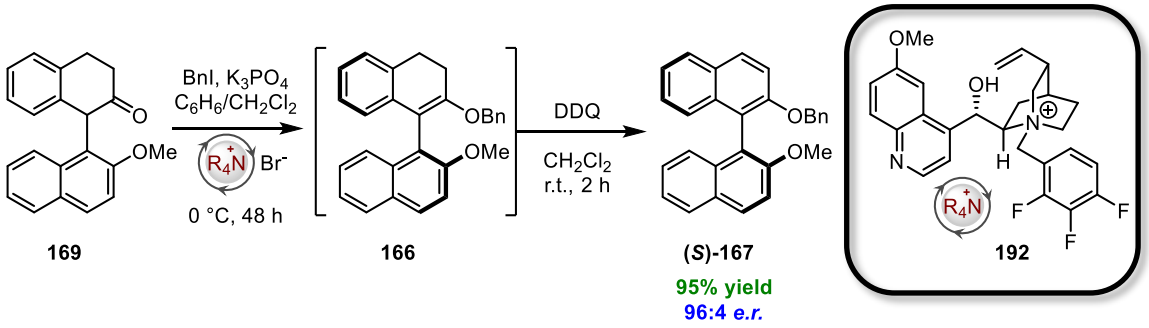
Next, we to turned our attention to the oxidation of enol ether **166** to orthogonally protected BINOL **167**. Pleasingly, oxidation of enol ether **166** with DDQ in dichloromethane afforded BINOL **169** in quantitative yield with no erosion in stereochemical integrity (**Scheme 3.36.**). We were able to establish the absolute configuration of the BINOL derivative to be (*S*)- by direct comparison to an authentic sample prepared from commercially available (*S*)-BINOL (See **Appendix 8.3.1.**).




**Scheme 3.36.** Oxidation to orthogonally protected BINOL.

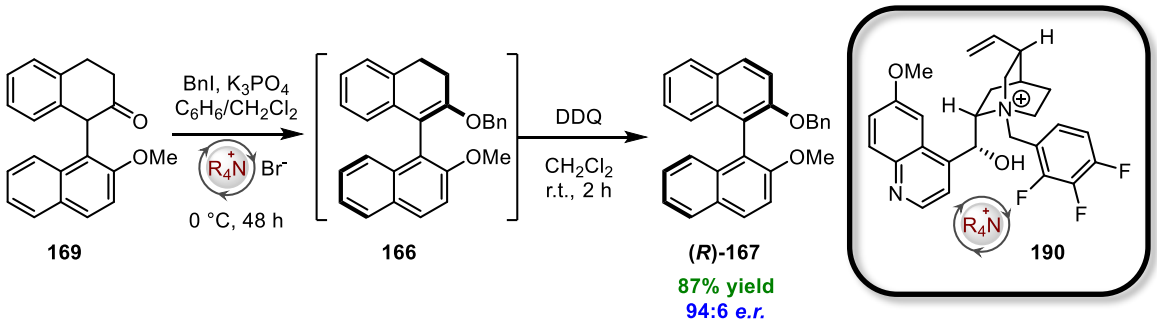
We then sought to establish whether it was possible to carry out the oxidation in a one-pot procedure. Therefore, DDQ was added to the reaction mixture at room temperature once complete starting material consumption had occurred. Unfortunately, the oxidation was very slow and conversion was not always reproducible. Consequently, we investigated whether the

oxidation of the enol ether could be performed on the crude reaction mixture after a solvent switch to dichloromethane (**Scheme 3.37.**).




**Scheme 3.37.** Sequential alkylation/oxidation procedure.

Fortunately, this approach yielded (*S*)-BINOL derivative **167** in good yield and enantioselectivity. More importantly the oxidation was reproducibly complete within two hours at room temperature. Using the pseudo-enantiomeric catalyst *N*-2,3,4-trifluorobenzyl-quininium bromide **190**, we were able to synthesize orthogonally protected (*R*)-BINOL **167**, albeit in slightly lower yield and enantioselectivity (**Scheme 3.38.**).




**Scheme 3.38.** Synthesis of orthogonally protected (*R*)-BINOL.

### 3.8. Barrier to Rotation of 166

As an aside, we were interested in the barrier to rotation of enol ether **166**. To this end, we monitored the *e.r.* of enol ether **166** in a solution of refluxing *m*-xylene over time (**Figure 3.39.**).

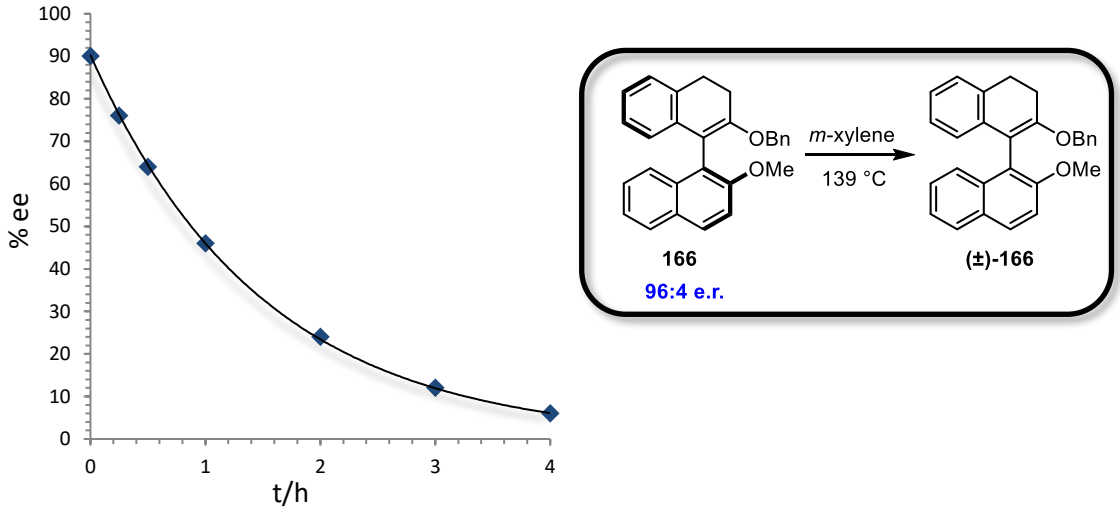



**Figure 3.39.** Erosion in *e.r.* of **166** over time.

After four hours, the enantiomeric ratio had decreased from 95:5 *e.r.* to 53:47 *e.r.* As before, a plot of ln(1/*e.e.*) against time gave a straight line (**Figure 3.40.**). From this we were able to determine the rate constant for racemization ($k_{rac}$). Using $k_{rac}$ we calculated the half-life with respect to racemization ($t_{1/2}$rac) to be 64 minutes at 139 °C and the barrier to rotation ($\Delta G^{\ddagger}$(ent)) to be 32.0 kcal mol $^{-1}$ (See **Appendix 8.1.2.** for derivation of equations and full calculations).

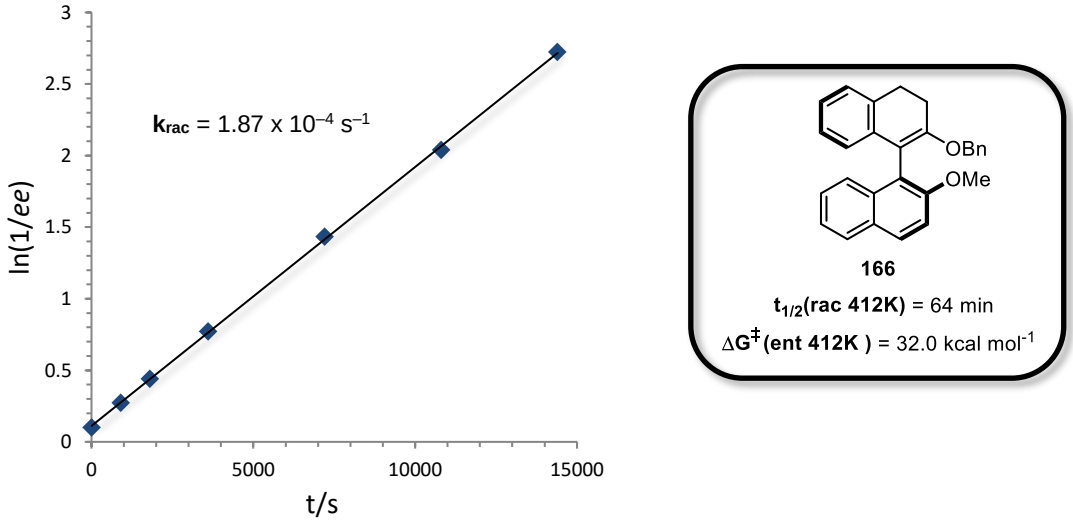
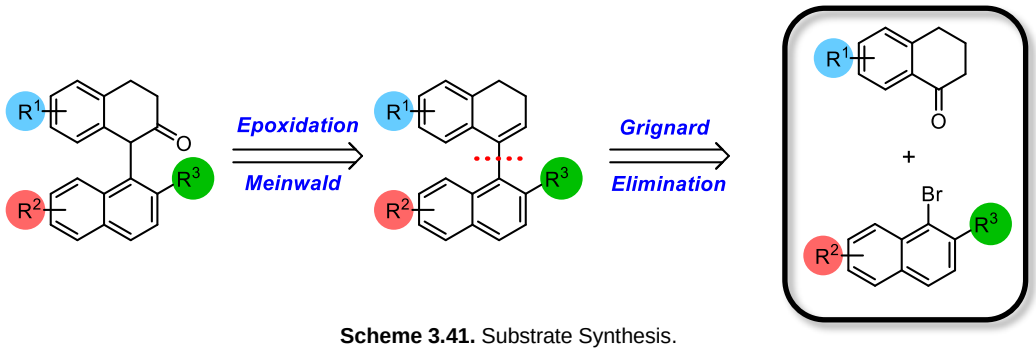



**Figure 3.40.** Erosion in *e.r.* of **166** over time.

### 3.9. Substrate Synthesis

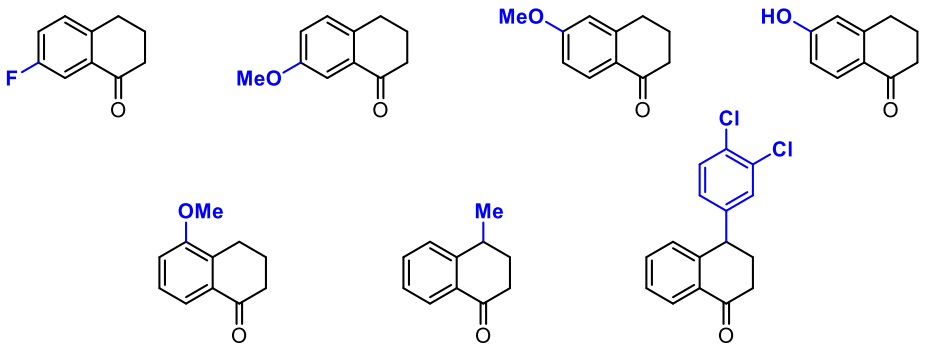



**Scheme 3.41.** Substrate Synthesis.

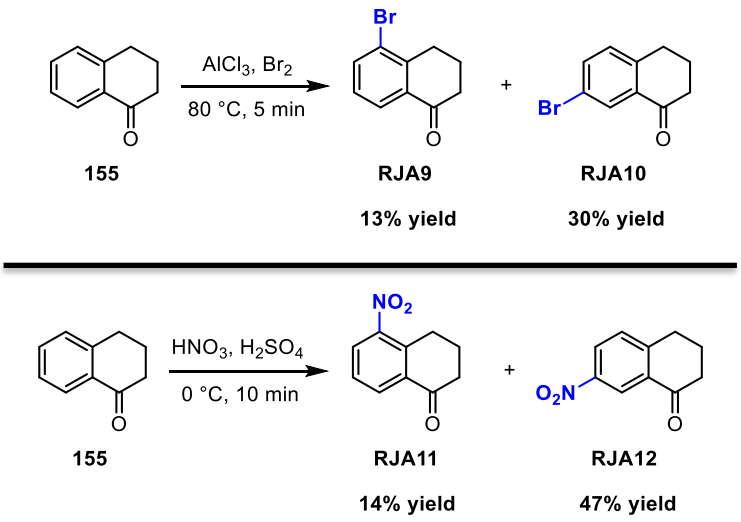
Next, we proceeded to investigate what effect substituted 2-tetralone starting materials would have on both enantioselectivity and conversion. To this end, a library of substituted 2-tetralones was required. Our strategy was to introduce substitution by combining substituted 1-tetralones with substituted methoxynaphthalenes (**Scheme 3.41.**). The work described in this chapter was done largely in collaboration with Dr Roland Armstrong. As mentioned before, compounds synthesized by Dr Roland Armstrong will be denoted by a separate compound identification code **RJAXY**.

#### *3.9.1. Synthesis of Substituted 1-Tetralones*

The first part of this chapter will describe the synthesis of substituted 1-tetralones. Fortunately, selected 1-tetralones were commercially available and did not have to be synthesized (**Scheme 3.42.**).

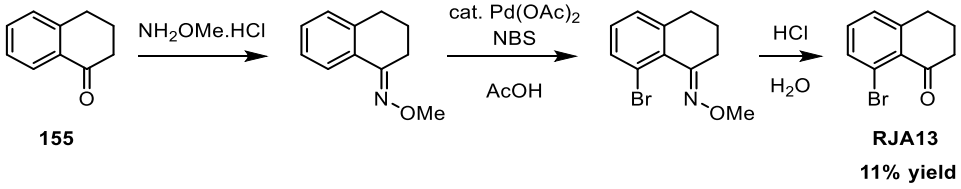



**Scheme 3.42.** Commercially available 1-tetralones.



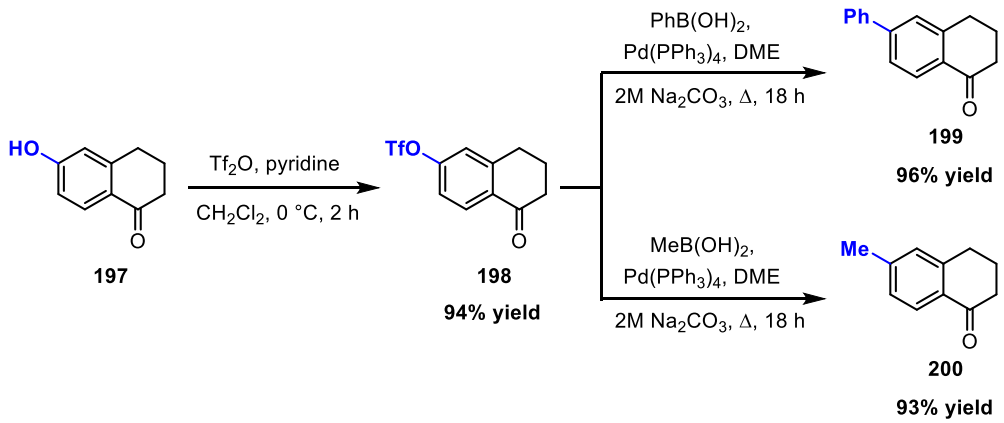

**Scheme 3.43.** Derivatization of 1-tetralone.

Most substituted 1-tetralones, however, were synthesized. For example, substituted 1-tetralones could be accessed by direct derivatization of 1-tetralone (**Scheme 3.43.**). Bromination of 1-tetralone with bromine and aluminium trichloride afforded 5-bromo-1-tetralone **RJA9** and 7-bromo-bromo-1-tetralone **RJA10**.[80] Analogously, 5-nitro-1-tetralone **RJA11** and 7-nitro-1-tetralone **RJA12** could be accessed by nitration of 1-tetralone.[81] Bromination at *C*-8 was achieved using established *C*-H activation methodology (**Scheme 3.44.**).[82]



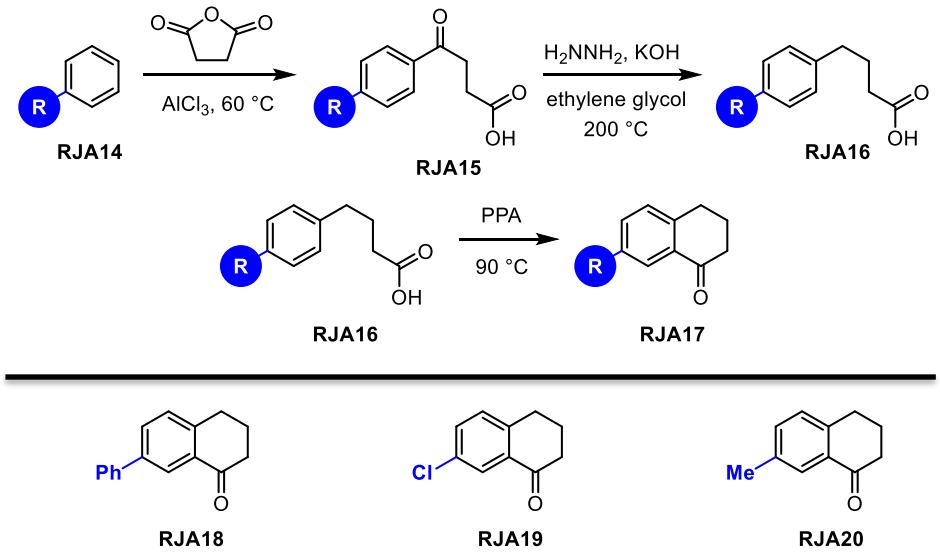

**Scheme 3.44.** Synthesis of 8-bromo-1-tetralone by *C*-H activation.

Triflation of commercially available 6-hydroxy-1-tetralone **197** afforded **198**, which could be further elaborated to 6-phenyl-1-tetralone **199** and 6-methyl-1-tetralone **200** by subsequent Suzuki coupling with phenylboronic acid and methylboronic acid respectively (**Scheme 3.45.**).

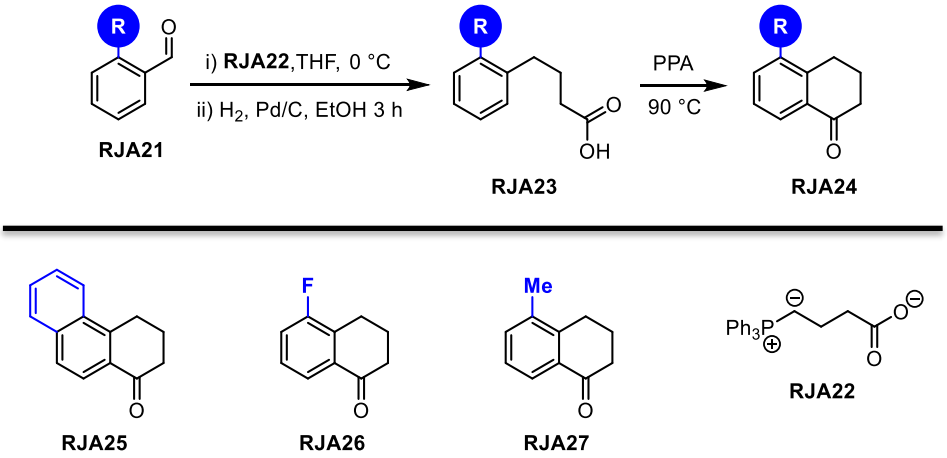



**Scheme 3.45.** Derivatization of 6-hydroxy-1-tetralone **197**.

Substitution at *C*-7 could be introduced according to established literature protocols (**Scheme 3.46.**). [83-85] A substituted arene **RJA14** was acylated under Friedel-Crafts conditions with succinic anhydride to afforded a ketone **RJA15**, which was then converted to a carboxylic acid **RJA16** *via* a Wolff-Kishner reduction. Finally, an intramolecular Friedel-Crafts cyclization of **RJA16** with polyphosphoric acid afforded the desired 7-substituted 1-tetralones **RJA17**. Using this strategy, 7-Phenyl-1-tetralone **RJA18**, 7-Chloro-1-tetralone **RJA19** and 7-Phenyl-1-tetralone **RJA20** were prepared.

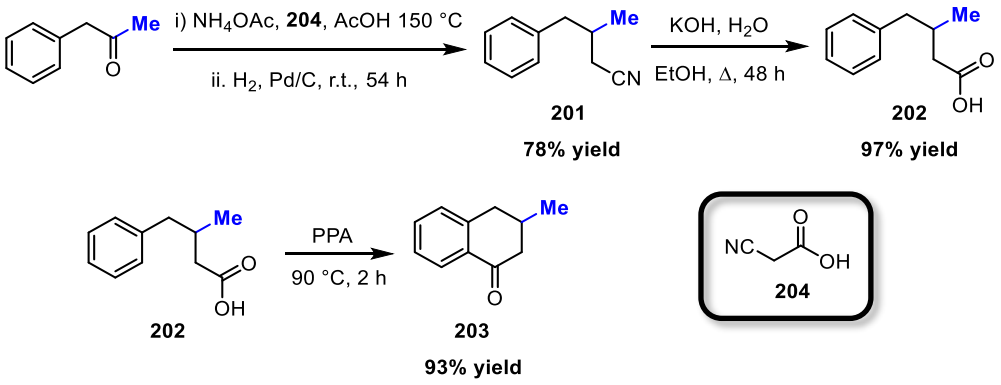



**Scheme 3.46.** Synthesis of 7-substituted 1-tetralones.




**Scheme 3.47.** Synthesis of 5-substituted 1-tetralones.

Employing a similar approach, it was possible to introduce substitution at *C*-5 (**Scheme 3.47.**).[86] First an *ortho*-substituted benzaldehyde **RJA21** was treated with Wittig reagent **RJA22** to afford an intermediate alkene, which was immediately reduced to a carboxylic acid **RJA23** by hydrogenolysis with palladium on carbon. As before, an intramolecular Friedel-Crafts cyclization of **RJA23** with polyphosphoric acid afforded the desired 5-substituted 1-tetralones **RJA24**. Phenanthryl-1-tetralone **RJA25**, 5-Fluoro-1-tetralone **RJA26** and 5-methyl-1-tetralone **RJA27** were synthesized using this methodology.



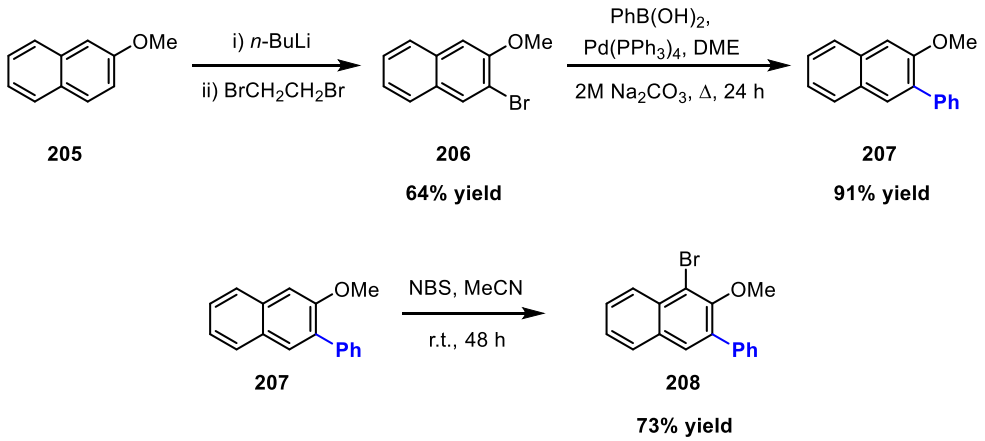

**Scheme 3.48.** Synthesis of 3-methyl-1-tetralone **203**.

3-Methyl-1-tetralone could be synthesized according to an established literature protocol (**Scheme 3.48.**).[87] A Knoevenagel condensation of phenyl acetone with cyanoacetic acid and a subsequent decarboxylation afforded an intermediate alkene, which was immediately reduced

by hydrogenolysis with palladium on carbon to afford nitrile **201**. Hydrolysis of nitrile **201** to carboxylic acid **202**, followed by intramolecular Friedel-Crafts cyclization afforded the desired 3-methyl-1-tetralone **203**.

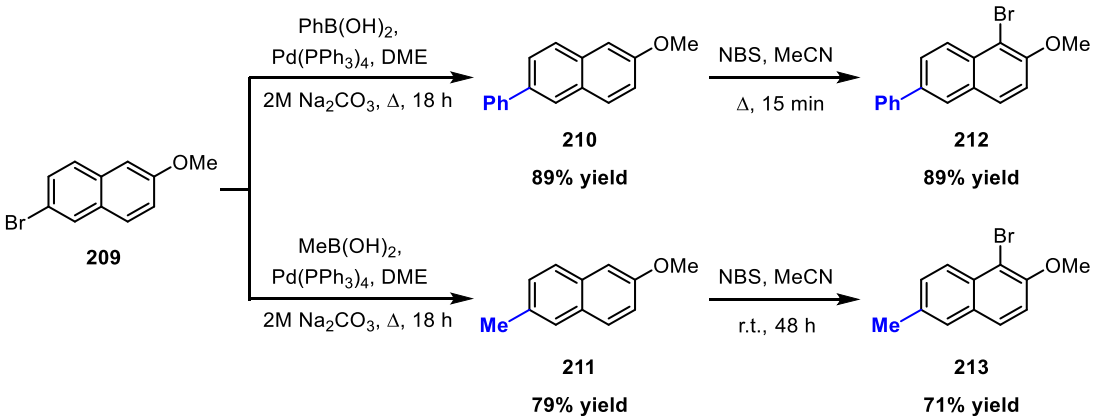
### *3.9.2. Synthesis of Substituted 1-Bromo-2-Methoxynaphthalenes*

With a library of substituted 1-tetralones in hand, we turned our attention to creating a library of substituted 1-bromo-2-methoxynaphthalenes. As a starting point, we sought to introduce substitution at *C*-3 (**Scheme 3.49.**). *Ortho*-lithiation of 2-methyoxynaphthalene **205** and subsequent bromination with 1,2-dibromoethane afforded 3-bromo-2-methoxynaphthalene **206** which could be further elaborated to 3-phenyl-2-methoxynaphthalene **207** in a subsequent Suzuki coupling with phenylboronic acid.[88] Finally, regioselective bromination with NBS afforded the desired aryl bromide **208**.



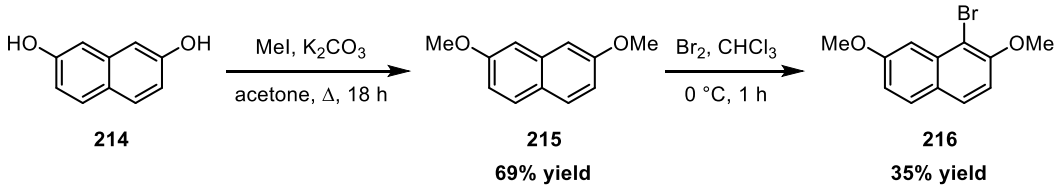

**Scheme 3.49.** Introducing substitution at *C*-3.

Substitution at *C*-6 could be introduced by derivatizing commercially available aryl bromide **209** (**Scheme 3.50.**). A Suzuki coupling with phenyl- or methylboronic acid afforded methoxy-naphthalenes **210** and **211**. Subsequent bromination with NBS in acetonitrile afforded the desired aryl bromides **212** and **213** with phenyl and methyl substituents at *C*-6 respectively.



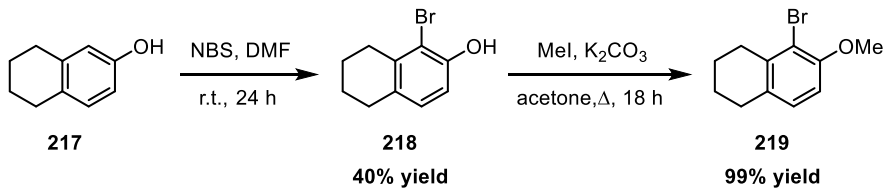

**Scheme 3.50.** Introducing substitution at *C*-6.

Methylation of commercially available dihydroxyarene **214** and subsequent bromination furnished methoxynaphthyl derivative **215** with a methoxy substituent at *C*-7 (**Scheme 3.51.**).




**Scheme 3.51.** Introducing substitution at *C*-7.

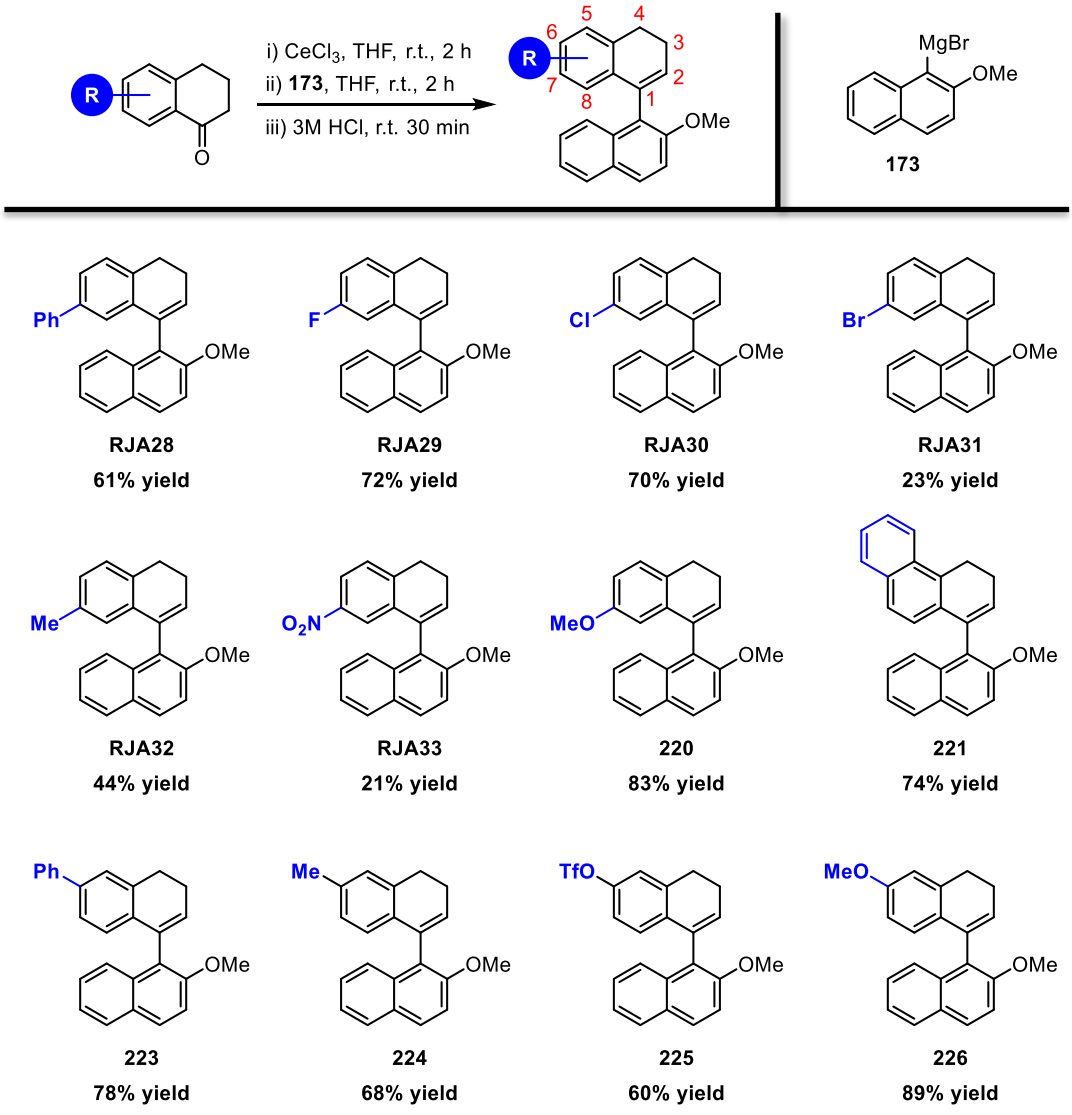
Finally, we sought to prepare a substrate with a saturated backbone (**Scheme 3.51.**). To this end, commercially available tetrahydro-2-naphthol **217** was brominated with NBS in DMF. Methylation with methyl iodide and potassium carbonate afforded the desired tetrahydro-1-bromo-2-methoxynaphthalene **219** in excellent yield.




**Scheme 3.52.** Introduction of a saturated backbone.

### *3.9.3. Synthesis of Substituted Dihydronaphthalenes*

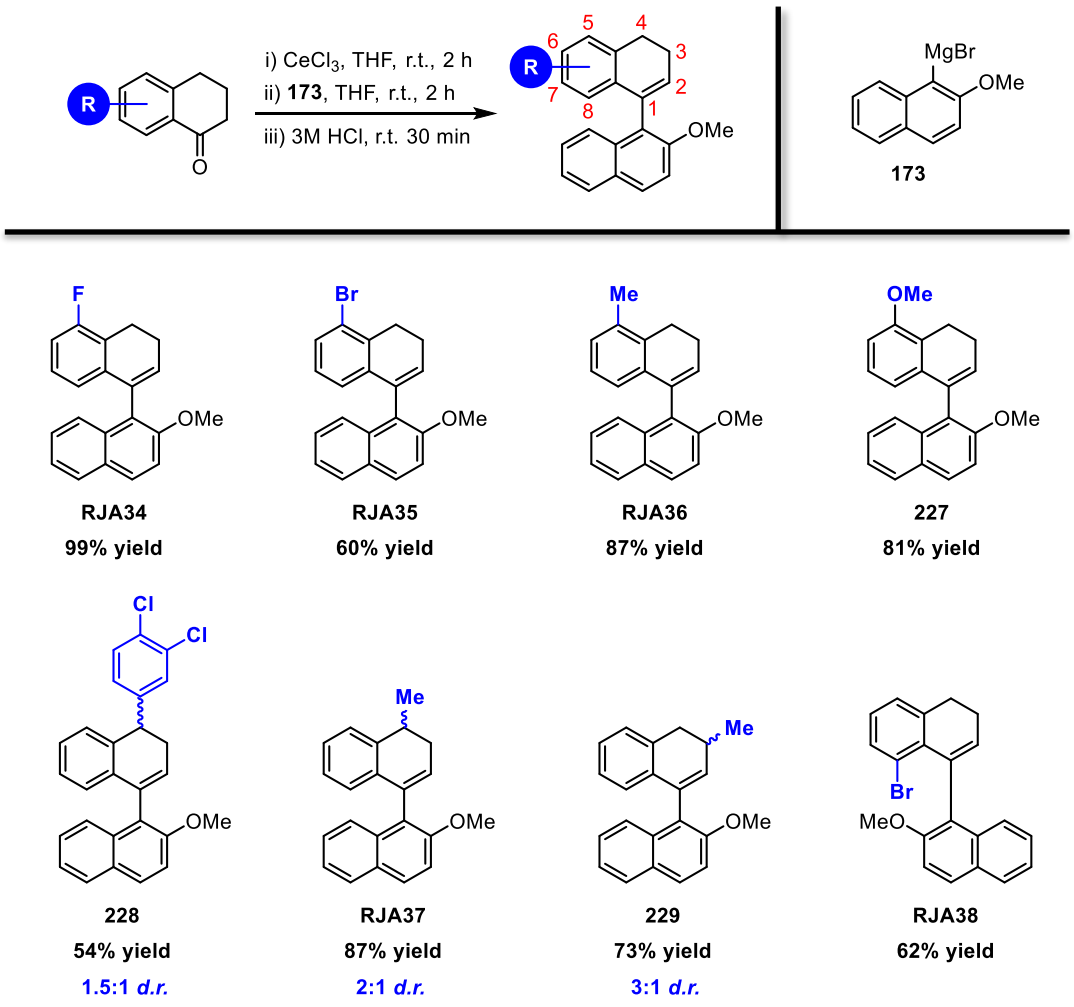
With a library of substituted 1-tetralones and 1-bromo-2-methoxynaphthalenes in hand, we proceeded to synthesize a library of substituted dihydronaphthalenes. It is important to note that in all cases the yields are unoptimized and the reactions were usually performed on gram scale (c.a. 5-10 mmol). First, Grignard reagent **173** was added to substituted 1-tetralones to afford the desired dihydronaphthalenes upon acidic workup (**Schemes 3.53.** and **3.54.**).




**Scheme 3.53.** Synthesis of substituted dihydronaphthalenes, part i).

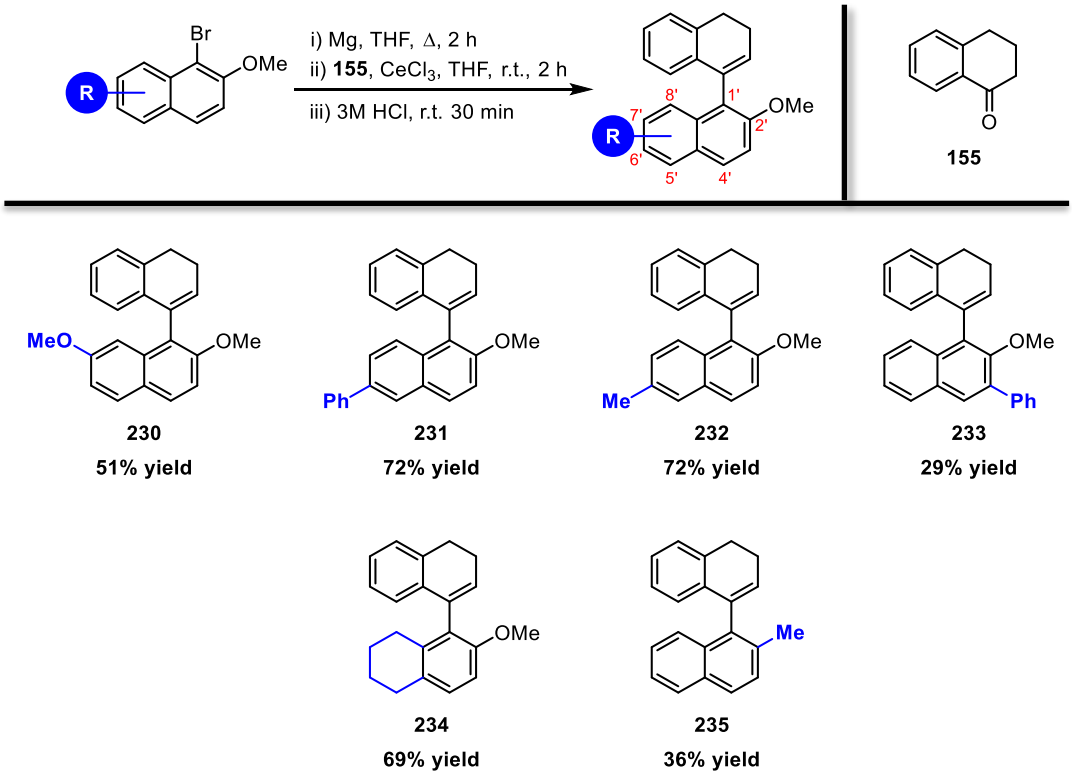
Dihydronaphthalenes bearing halide, phenyl, methyl, nitro and methoxy substituents at *C*-7 could be synthesized from the respective substituted 1-tetralone precursors. We were pleased

to observe that the Grignard addition/elimination sequence proceeded smoothly with phenanthryl-1-tetralone **RJA25** to furnish dihydro phenanthrene **221**. Introduction of methyl, phenyl methoxy and triflate substituents at *C*-6 also proved to be successful. At *C*-3 we were able to introduce fluoro, bromo, methyl and methoxy substituents. At *C*-4 3,4-dichlorophenyl and methyl substituents could be introduced and at *C*-3 it was possible to introduce a methyl group. It is worth noting that the alkenes appear to be atropisomeric since **228**, **RJA37** and **229** were afforded as a mixture of diastereomers. Variable temperature $^{1}$H NMR spectroscopy at high temperature did not result in coalescence of the diastereomeric signals. We were pleased to observe that the Grignard addition of **173** to **RJA13** proceeded despite the increased steric bulk about ketone **RJA13** introduced by the *peri*-bromo substituent at *C*-8.




**Scheme 3.54.** Synthesis of substituted dihydronaphthalenes part ii).

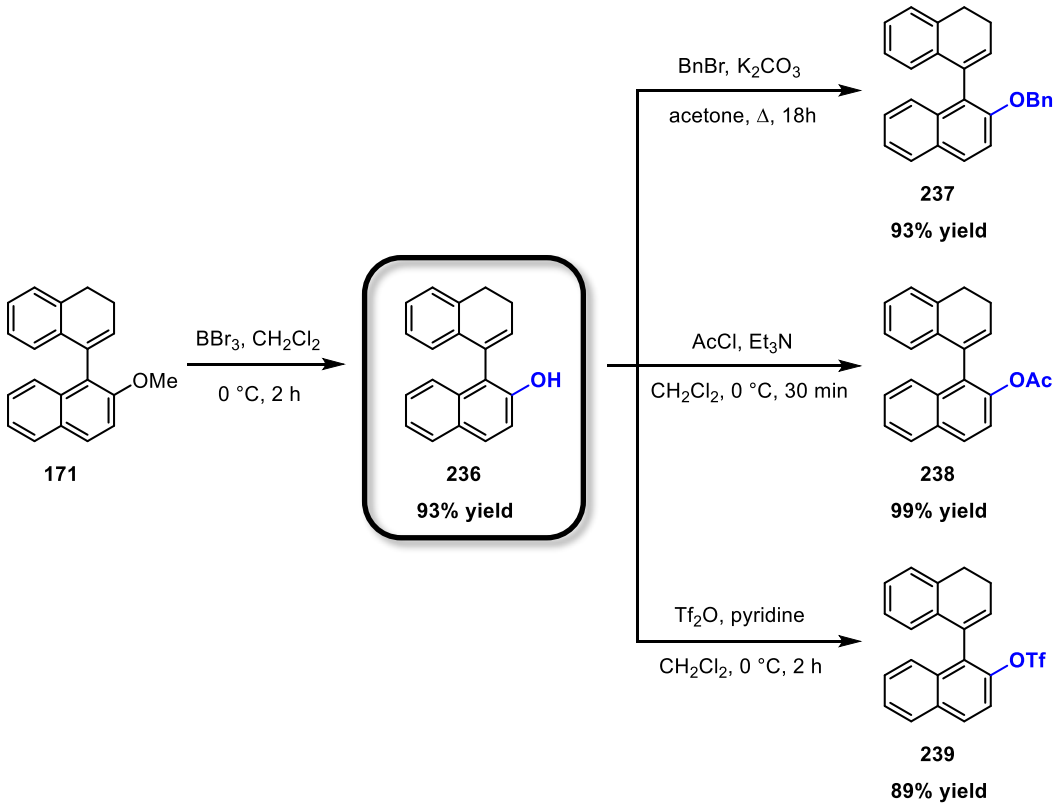
Having successfully generated a library of dihydronaphthalenes with substitution ranging from *C*-3 to *C*-8 we proceeded introduce substitution on the lower aromatic ring by use of the library of substituted aryl bromides in the Grignard additions to 1-tetralone (**Scheme 3.55.**).




**Scheme 3.55.** Synthesis of substituted dihydronaphthalenes part iii).

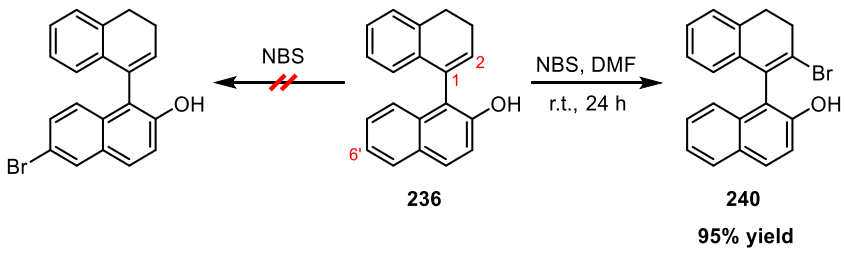
We were pleased to observe that our library of synthesized aryl bromides could be successfully converted to Grignard reagents, and, using the previously established protocol for dihydronaphthalene synthesis, furnish the corresponding dihydronaphthalenes on gram scale. A methoxy group could be introduced at *C*-7', phenyl and methyl groups at *C*-6', and a phenyl substituent at *C*-3'. The synthesis of partially saturated dihydronaphthalene **234** also proceeded smoothly. Using commercially available 1-bromo-2-methyl naphthalene, we synthesized dihydronaphthalene **235**, where the methoxy group at *C*-2' is exchanged for a methyl substituent.

We rationalized that it may be possible to access dihydronaphthalenes with different substituents at *C*-2' by derivatization of the parent dihydronaphthalene **171** (**Scheme 3.56.**).




**Scheme 3.56.** Introduction of substitution at *C*-2.

First, methoxyarene **171** was demethylated with $BBr_3$ to furnish naphthol **236** in excellent yield. We then proceeded to treat naphthol **236** with a series of electrophiles. Naphthol **236** was benzylated with benzyl bromide and potassium carbonate to give **237**, acylated with acetyl chloride and triethylamine to give **238**, and triflated with triflic anhydride and pyridine to furnish dihydronaphthalene **239**.




**Scheme 3.57.** Unexpected regioselectivity in the bromination of naphthol **236**.

Since 1-substituted 2-naphthols generally undergo electrophilic aromatic substitution at *C*-6,[89] we reasoned it may be possible to brominate naphthol **236** at C-6' (**Scheme 3.57.**). Interestingly, bromination does not occur at *C*-6' but at *C*-2. Presumably this occurs by formation of a cyclic bromonium ion which can be cleaved to a benzylic cation, which in turn furnishes naphthol **240** upon deprotonation.

### *3.9.4. Synthesis of Substituted 2-Tetralones*

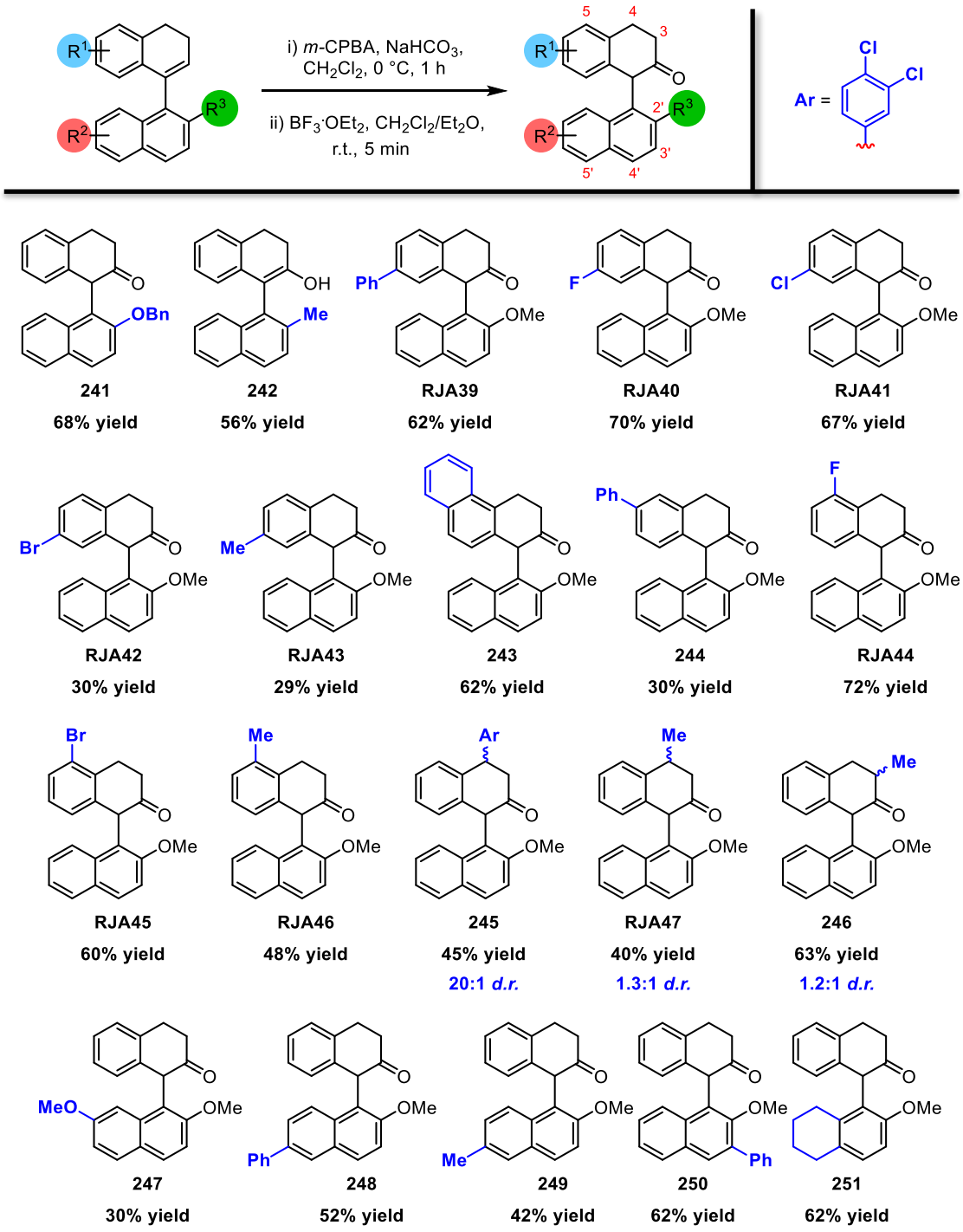
Having established a library of substituted dihydronaphthalenes, our next task was to synthesize a library of substituted 2-tetralones *via* an epoxidation/Meinwald sequence (**Scheme 3.58.**). It should be noted that in all cases the yields are unoptimized and the reactions were usually performed on gram scales (c.a. 5-10 mmol).

The low to medium yields reported are not due to incomplete consumption of starting material, but a result of low yielding purifications of the substituted 2-tetralones. To quote from a review by Lenardão *et al.* on the synthesis of 2-tetralones:[90]

*"However, unlike their congeners the 1-tetralones, which are inexpensive substances, the 2-tetralones are usually more difficult to synthesize and some of them are highly unstable, requiring proper storage conditions, such as freezing, for their long-time preservation. In addition, preparation of 2-tetralones has long been hampered either by poor yields or difficulty in accessing starting materials"*

In almost all cases, the purification of the desired 2-tetralone involved triethylamine buffered column chromatography followed by recrystallization, which is why these reactions were performed on gram scales. Once crystalline, however, all substituted 2-tetralones were bench-stable and we were unable to detect any decomposition after several months.

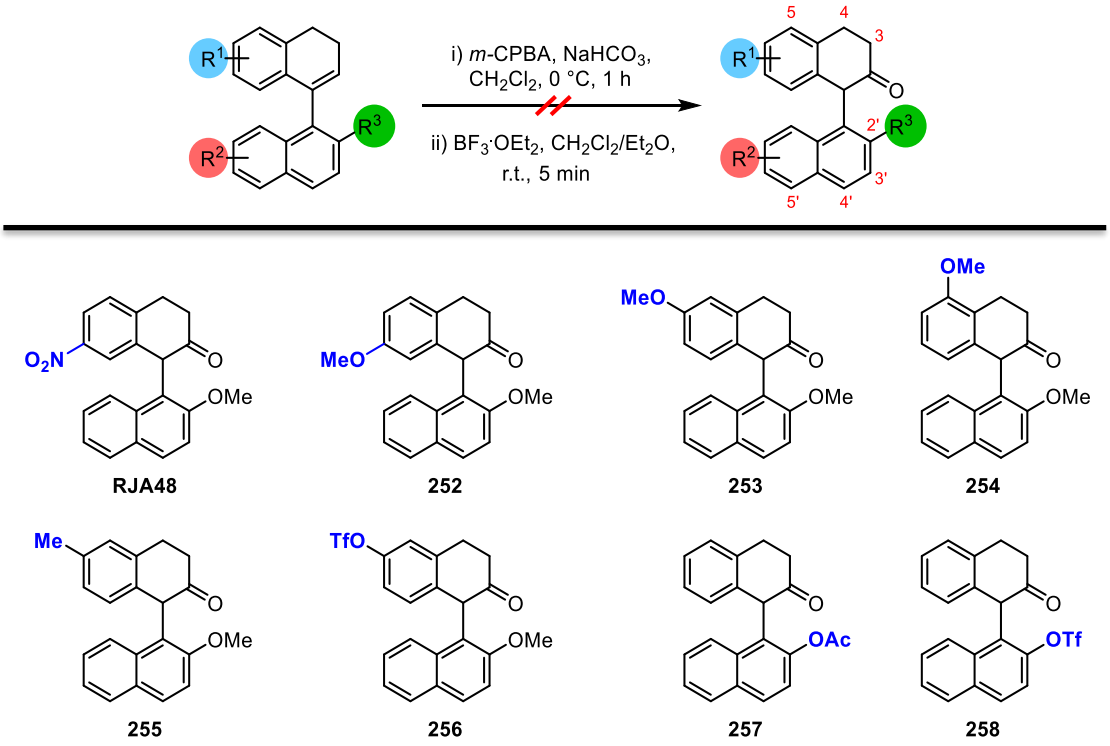
First, this chapter will illustrate where the 2-tetralone synthesis was successful (**Scheme 3.58.**), and then demonstrate the limitations of the epoxidation/Meinwald sequence (**Scheme 3.59.**).




**Scheme 3.58.** Synthesis of substituted 2-tetralones.

At the *C*-2' position, benzyloxy and methyl groups were tolerated. Interestingly 2'-methyl tetralone **242** was exclusively observed as the enol tautomer by $^{1}$H NMR spectroscopy whereas all remaining 2-tetralones were exclusively observed as keto tautomers. Phenyl, halide and methyl groups could be incorporated at *C*-7. At *C*-6, installation of a phenyl substituent and an

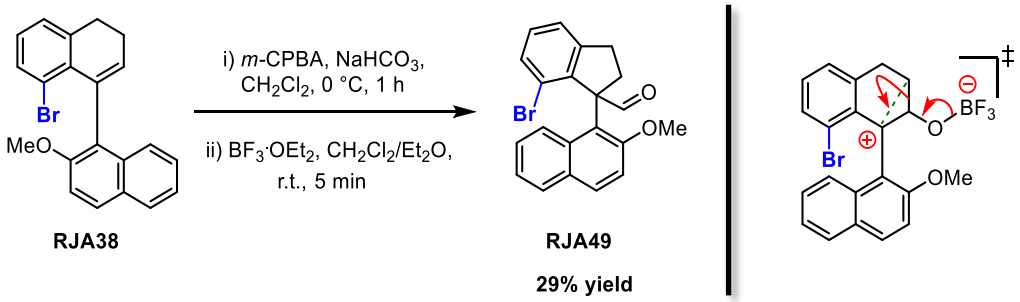
additional aromatic ring (**243**) could be carried out. Halides and a methyl substituent were tolerated at *C*-5. Pleasingly, all dihydronaphthalenes with substitution at *C*-4, *C*-3, *C*-7', *C*-6' and *C*-3' positions were successfully converted to their corresponding 2-tetralones. The conversion of dihydronaphthalene **234**, bearing a saturated backbone, to the corresponding 2-tetralone **251** also proved to be successful.




**Scheme 3.59.** Limitations of the epoxidation/Meinwald sequence.

Highly electron donating or electron withdrawing groups such as methoxy- or nitro-groups were not tolerated. Whilst the epoxidation/Meinwald sequence initially appeared to be successful, in our hands the products proved to be highly unstable and decomposed rapidly during attempted purifications. We were unable to purify tetralones **255** and **256** as they proved to be, at least in our hands, uncrystalline. We were also unable to crystallise tetralones **257** and **258**. Carrying out the phase-transfer alkylation on the crude reaction mixtures of **257** and **258** did also not yield any of the desired enol ethers. Interestingly, when the epoxidation/Meinwald protocol was carried out on dihydronaphthalene **RJA38** we did not observe a 2-tetralone product, but instead aldehyde **RJA49** was formed (**Scheme 3.60.**).

Presumably, this occurs by the Meinwald rearrangement occurring with a 1,2-*C* shift and not a 1,2-*H* shift, resulting in a ring contraction to 5-membered ring product **RJA49** bearing an aldehyde moiety.

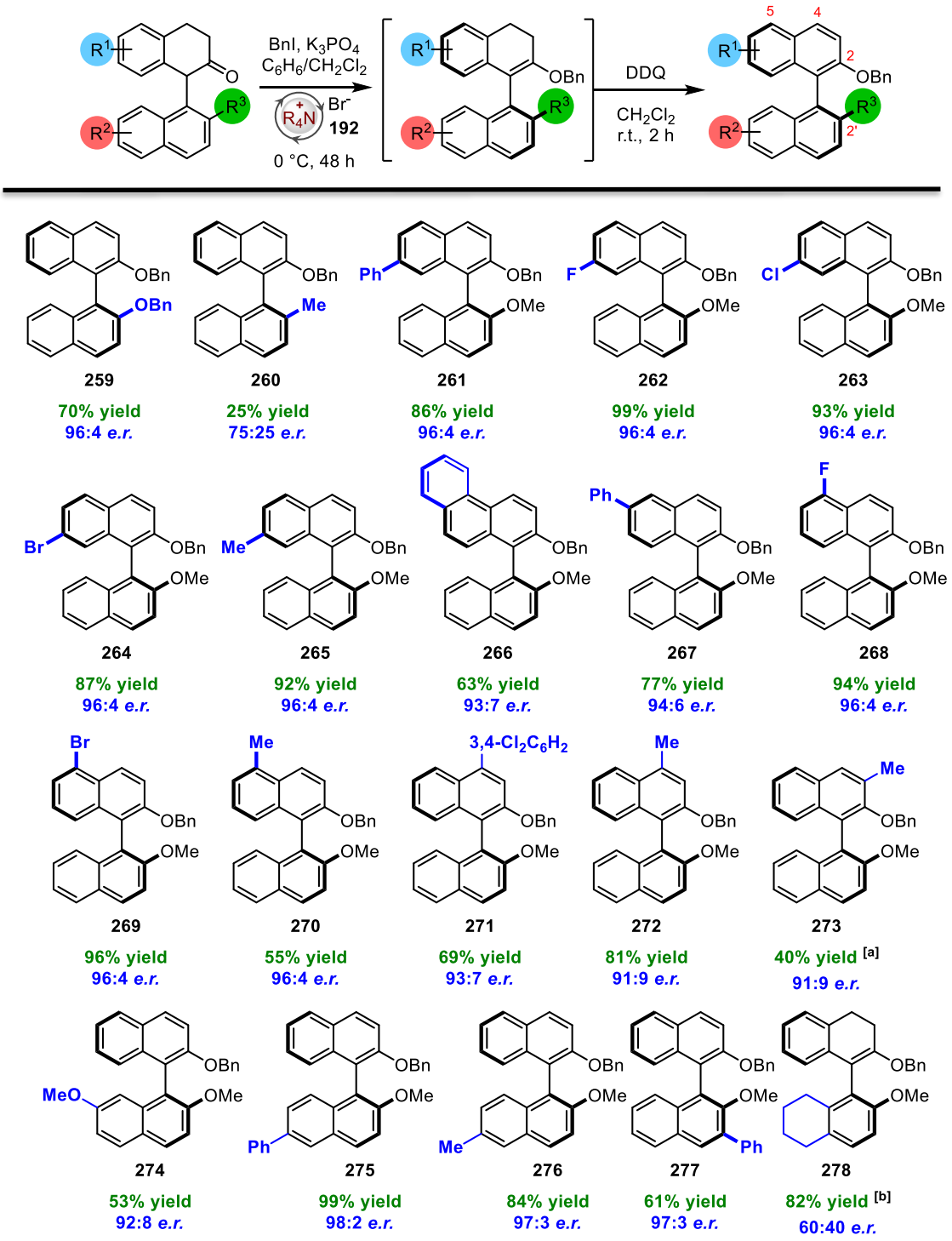



**Scheme 3.60.** 1,2-*C* shift to furnish **RJA49**.

### 3.10. Substrate Scope

With a library of substituted 2-tetralones in hand, our next task was to subject these to the reaction conditions for atropselective *O*-alkylation/oxidation, to investigate substituent effects on both conversion and enantioselectivity (**Scheme 3.61.**). The reactions were carried out on a 0.1-0.2 mmol scale.

Exchange of the methyl ether at the *C*-2' position to a benzyl ether did not affect the enantioselectivity of the alkylation/oxidation protocol (**259**, 70% yield, 96:4 *e.r.*). However, with a methyl group at *C*-2' a considerable decrease in both enantioselectivity and conversion was observed (**260**, 25% yield, 75:25 *e.r.*) This suggests that the presence of an alkoxy substituent at *C*-2' is crucial for both conversion and enantioselectivity (See **chapter 4.5.** for a possible explanation). A phenyl group at *C*-7 did not impact enantioselectivity and only a minor decrease in yield was observed (**261**, 96% yield, 96:4 *e.r.*), suggesting that steric bulk at *C*-7 does not affect the overall process. Fluoro-(**262**, 99% yield, 96:4 *e.r.*), chloro-(**263**, 93% yield, 96:4 *e.r.*), bromo-(**264**, 87% yield, 96:4 *e.r.*) and methyl-(**265**, 92% yield, 96:4 *e.r.*) substituents also support this hypothesis. Introduction of a phenyl group at *C*-6 resulted in a small decrease in enantioselectivity and yield (**267**, 77% yield, 94:6 *e.r.*).




**Scheme 3.61.** Substrate scope of *O*-alkylation; [a] DDQ oxidation carried out for 24 h; [b] DDQ oxidation omitted.

Pleasingly, we were able to synthesize phenanthryl derivative **266**, albeit in slightly decreased yield and enantioselectivity, suggesting that introduction of sterically demanding substituents at *C*-6 and *C*-5 is possible (**266**, 77% yield, 94:6 *e.r.*). This is supported by the introduction of fluoro-(**268**, 94% yield, 96:4 *e.r.*), bromo-(**269**, 96% yield, 96:4 *e.r.*) and methyl-(**270**, 55% yield,

96:4 *e.r.*) substituents at *C*-5 not impacting the enantioselectivity of the process. A decrease in enantioselectivity was observed for substrates with methyl-(**272**, 81% yield, 91:9 *e.r.*) and 3,4-dichlorophenyl (**271**, 69% yield, 93:7 *e.r.*) substituents at *C*-4 and methyl-(**273**, 40% yield, 91:9 *e.r.*) at *C*-3. Presumably the decrease in *e.r.* is due to a steric clash between the catalyst and substrate substituent (see **chapter 4.5.**). Interestingly, DDQ oxidation of the enol ether intermediate for the synthesis of **273** only fully consumed one of the diastereomers of the enol ether **279** after two hours. Therefore, the reaction time for the DDQ oxidation had to be prolonged by 22 hours for **246**. We propose that the DDQ oxidation likely proceeds by a concerted suprafacial mechanism as reported by Müller and Joly (**Figure 3.62.**).[91]

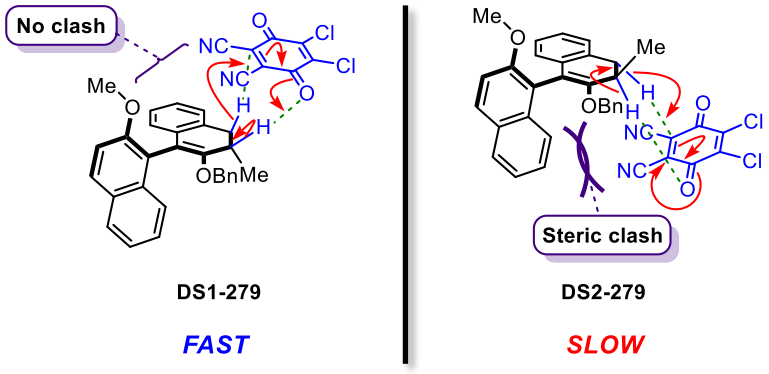


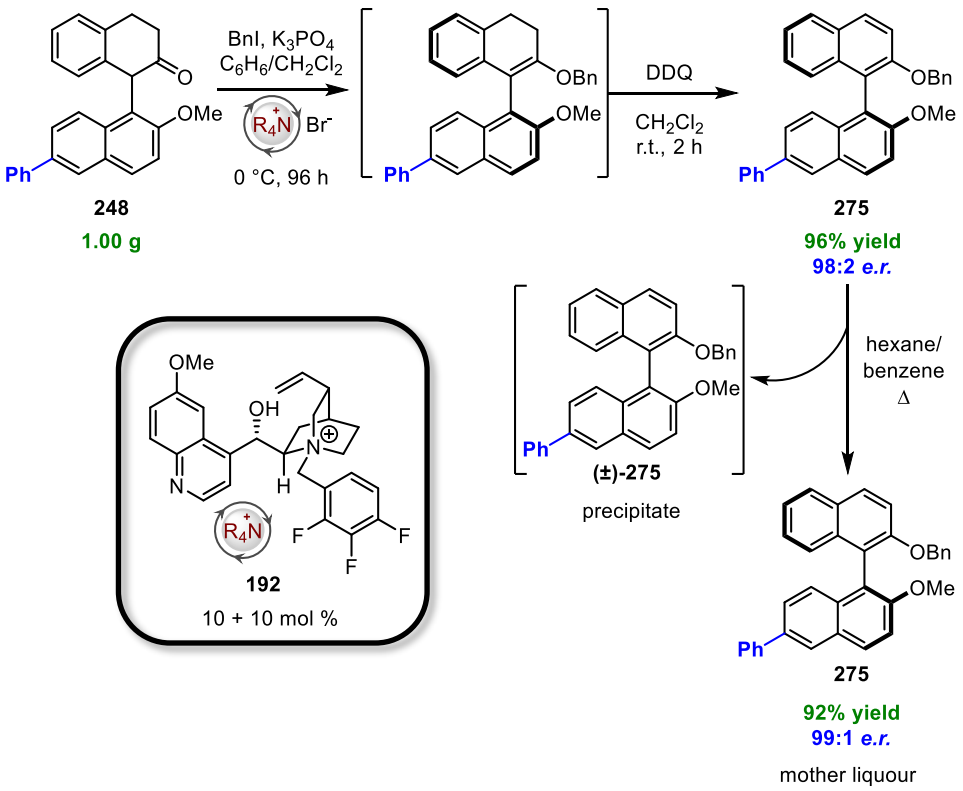

**Figure 3.62.** Proposed mechanism of DDQ oxidation.

Here, the hydrogen atoms which are eliminated from enol ether **279** must be on the same face for the oxidation to proceed. In the first diastereomer **DS1-279** there would be reduced clash between the substrate and DDQ, whereas in the second diastereomer **DS2-279** a steric clash between the aryl moiety of the 2-methoxynaphthyl substituent and DDQ would occur, thus slowing down the oxidation of **DS2-279** relative to **DS1-279**. Before the DDQ oxidation of **279** to **273** we observed full conversion from **246** to enol ether **279** by $^{1}$H NMR spectroscopy. However, after oxidation, we observed 2-tetralone **246** and what we believe to be debenzylated **273** (**280**) (**246** and **280** were isolated as an inseparable mixture) We propose that during the prolonged reaction time for the DDQ oxidation, DDQ-mediated debenzylation of the intermediate enol ether **279** and the product occurs, decreasing the overall yield of **273**.

Varying substitution about the 2-methoxy moiety significantly affected enantioselectivity (See **chapter 4.5.** for a possible explanation). At *C*-7' a methoxy group led to a decrease in enantioselectivity (**274**, 53% yield, 92:8 *e.r.*), whilst at *C*-6' phenyl-(**275**, 99% yield, 99:2 *e.r.*) and methyl-(**276**, 84% yield, 97:3 *e.r.*) groups improved enantioselectivity. Pleasingly, we also observed good enantioselectivity with a phenyl group at *C*-3' (**277**, 61% yield, 97:3 *e.r.*). We were unable to oxidise enol ether **278** selectively without oxidising the tetrahydronaphthyl substituent. We observed a significant decrease in enantioselectivity for the atropselective *O*-alkylation of **251** (**278**, 61% yield, 97:3 *e.r.*; see **chapter 4.5.** for a possible explanation).

### 3.11. Gram Scale Reaction and Absolute Configuration

Next, we sought to establish whether the protocol for atropselective *O*-alkylation/oxidation could be carried out successfully on a gram scale. To this end we subjected 2-tetralone **248** to the previously established reaction conditions for atropselective *O*-alkylation (**Scheme 3.63.**).




**Scheme 3.63.** Gram scale atropselective *O*-alkylation/oxidation.

After 48 h, 65% conversion was observed. We reasoned that due to the increased surface area of potassium phosphate in the heterogeneous reaction mixture, the rate of catalyst decomposition by Hofmann elimination had increased,[92] ultimately leading to complete catalyst decomposition before all the starting material **248** had been consumed. Therefore, an additional 10 mol % of catalyst **192** was added and the reaction mixture stirred for a further 48 hours at 0 °C. We were pleased to observe that after this time complete consumption of the starting material had occurred. Oxidation of the enol ether afforded the desired BINOL **275** in good yield and unchanged enantioselectivity.

We were able to further enantioenrich BINOL **275** by a serendipitously discovered procedure. We were attempting to achieve enantioenrichment of **275** by recrystallization. We suspended **275** at 98:2 *e.r.* in refluxing hexane and added benzene until complete dissolution had occurred. Upon cooling to room temperature, we did not observe crystallization of **275**, but a small amount of precipitate was observed. After isolating the precipitate by filtration, we were able to establish that the precipitate was racemic **275**. Due to racemic **275** precipitating out, the mother liquor was enantioenriched, in this case to 99:1 *e.r.* Interestingly when inspecting HPLC samples of the BINOL derivatives shown in **Scheme 3.61.**, crystallization for most racemic samples was observed but not for enantioenriched samples. This suggests that formation of the centrosymmetric racemic unit cell, and/or its propagation to a crystal lattice, is more facile than for the enantiopure non-centrosymmetric unit cell of MeBnBINOLs.

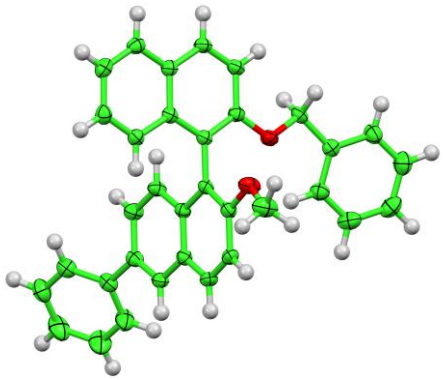
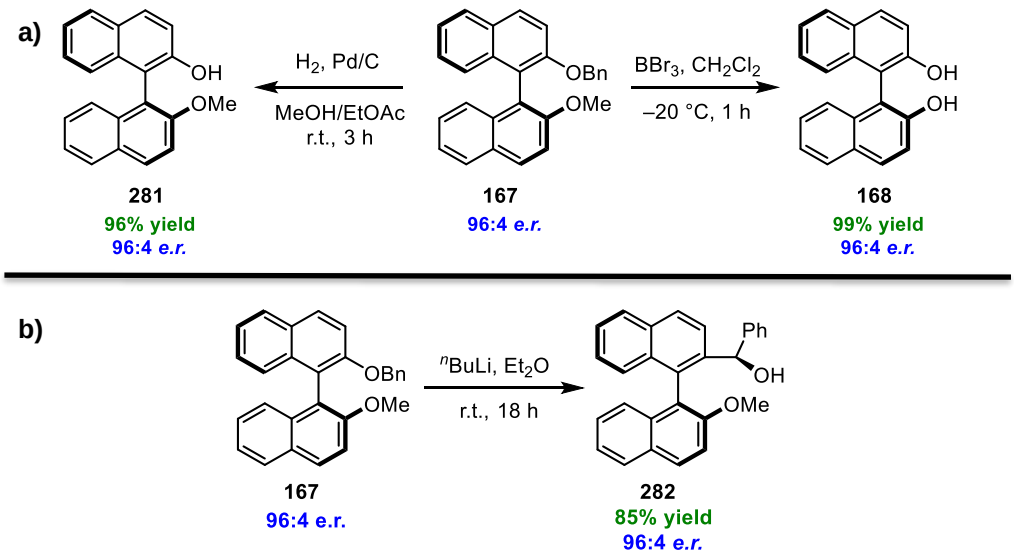


**Figure 3.64.** X-ray structure of **275** with ADP at 50% probability.

The absolute configuration of **275** could be established as (*S*)- by single crystal X-ray diffraction (See **Appendix 8.3.2.** for full details; **Figure 3.64.**). As the same absolute configuration was observed as for BINOL **167**, we assigned the absolute configuration of all other BINOL derivatives depicted in **Scheme 3.61.** as the same by analogy.

### 3.12. Deprotection and Derivatization

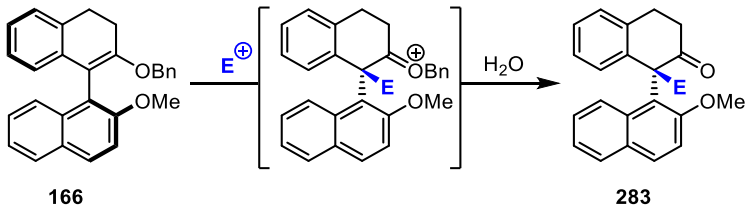
Next, we focused our investigations on possible transformations that could be achieved on MeBnBINOL **167** without eroding stereochemical integrity (**Scheme 3.65.**).




**Scheme 3.65.** Derivatization of MeBnBINOL **167**.

Global deprotection with boron tribromide yielded (*S*)-BINOL **168** in near quantitative yield and debenzylation by hydrogenolysis with palladium on carbon afforded (*S*)-MeBINOL **281** in excellent yield (**Scheme 3.65.a**). In both cases, no erosion in stereochemical integrity was observed. The optical rotation values were consistent with those reported for (*S*)-BINOL **168** and (*S*)-MeBINOL **281** respectively, and the retention times of the major enantiomers matched those of authentic samples of (*S*)-BINOL **168** and (*S*)-MeBINOL **281** respectively (See **Appendices 8.3.3.** and **8.3.4.** for full details).

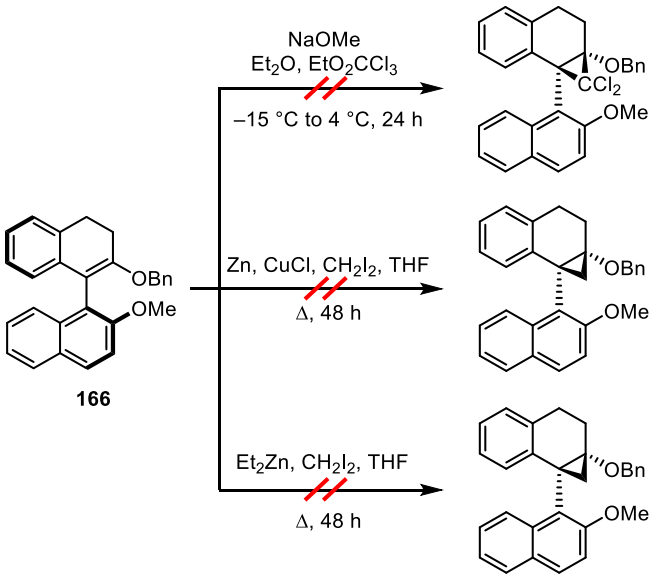
In analogy to seminal work by Xu and co-workers, a *n*-BuLi mediated [1,2]-Wittig rearrangement of **167** could be carried to furnish **282** in good yield without loss in *e.r.* (Scheme **3.65.b**).[93]




**Scheme 3.66.** Proposed axial to point chirality transfer.

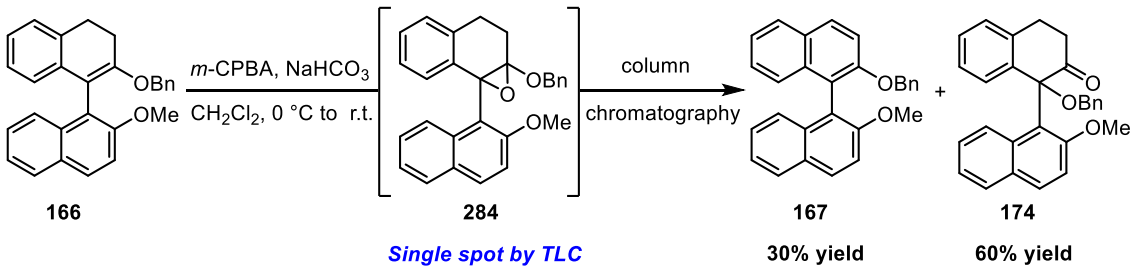
Next, we sought to establish whether enol ether **166** could react diastereoselectively with an electrophile to generate a point chiral ketone **283** with axial to point chirality transfer (**Scheme 3.66.**).

We began our investigations with the aim of cyclopropanating enol ether **166** (**Scheme 3.67.**). Unfortunately, subjecting enol ether to a dichlorocarbene, heterogeneous or homogeneous Simmons-Smith conditions yielded only unreacted starting material.[94-96] Therefore cyclopropanations of **166** were not investigated any further.



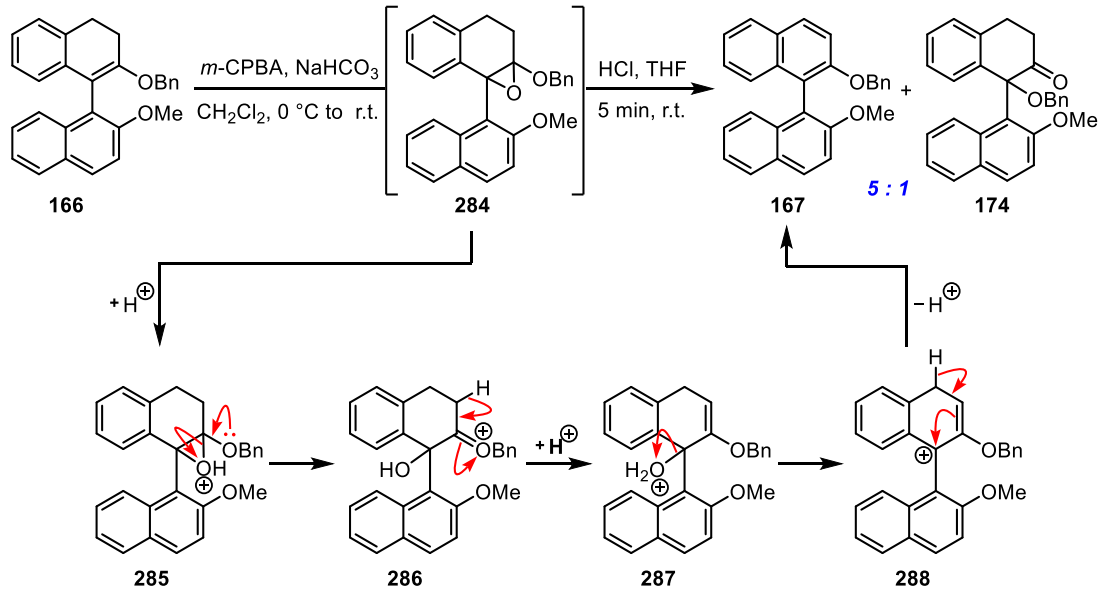

**Scheme 3.67.** Attempted cyclopropanations.

Next, we turned our attention to treating enol ether **166** with *m*-CPBA as the electrophile (**Scheme 3.68.**). Full consumption of starting material was observed after one hour and a single spot could be seen by TLC, which we believe to be epoxyether **284**.




**Scheme 3.68.** Epoxidation of enol ether **166**.

However, following purification by column chromatography two familiar products were isolated with the first product being MeBnBINOL **167** and the second product being α-benzyloxy-2-tetralone **174**. Using silica as a reagent to facilitate the rearrangement of epoxyether **284** proved to be capricious and irreproducible. Therefore, we sought to facilitate the rearrangement by either Brønsted or Lewis acid catalysis, with the aim of favouring the formation of **174** over **167**. First, we treated the intermediate epoxyether **284** with hydrochloric acid (**Scheme 3.69.**).

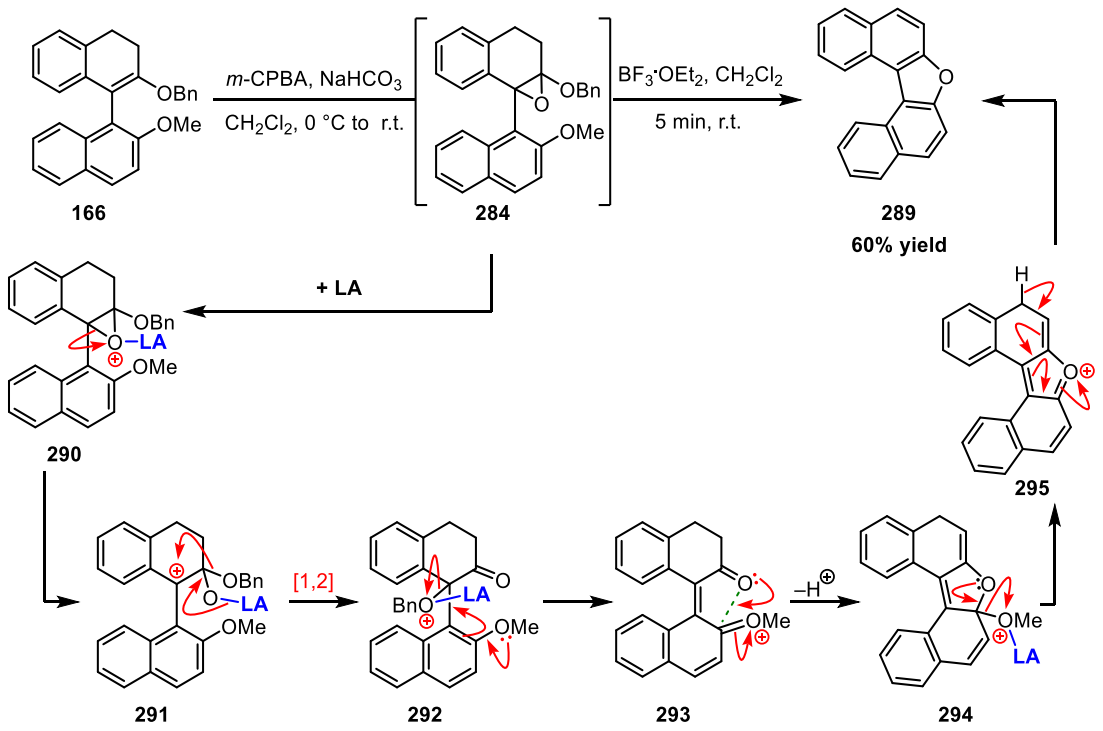



**Scheme 3.69.** Brønsted acid-mediated rearrangement of epoxyether **284**.

These reaction conditions however, favoured the formation of MeBnBINOL **167**. As a plausible mechanism for the formation of **167** we propose that epoxyether **284** is first *O*-protonated on the epoxide moiety to give **285**, which rearranges to oxonium **286**. Next, following

tautomerization and protonation, water is eliminated from **287**. Finally, vinylogous deprotonation of carbo-cation **288** furnishes MeBnBINOL **167**.

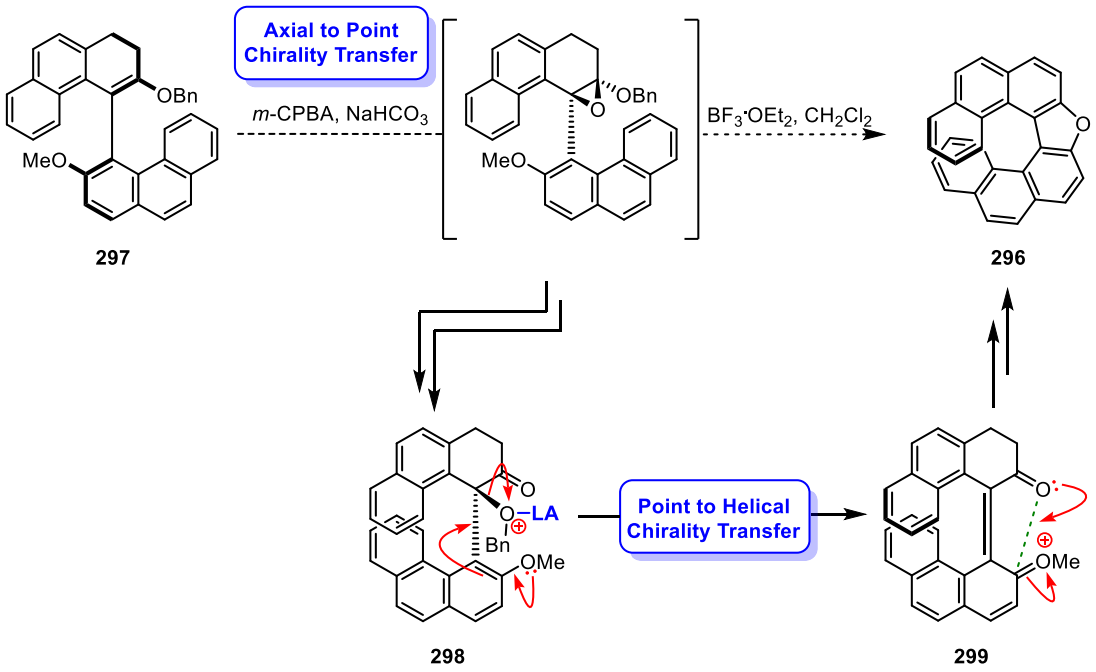
We then investigated whether the Lewis acidic reaction conditions employed in the Meinwald rearrangement for the tetralone synthesis of **169** could be employed to selectively furnish ketone **174** (**Scheme 3.70.**).




**Scheme 3.70.** Proposed mechanism for the rearrangement to dinaphthofuran.

Surprisingly, no MeBnBINOL **167** or **174** was observed. Instead the only isolated product was dinaphthofuran **289**. We propose that the Lewis acid coordinates to the epoxide oxygen to furnish **290**, which then rearranges to benzylic cation **291**. Analogous to the Meinwald rearrangement a [1,2]-benzyloxide shift occurs to furnish **292**, which can undergo elimination to generate quinone methide **293**. Reminiscent of the Paal-Knorr furan synthesis, acetal **294** is then formed which upon elimination generates oxonium **295**. Finally, rearomatization furnishes dinaphthofuran **289**.

Whilst dinaphthofuran **289** is achiral, we wondered whether it would be possible to generate a helically chiral furan such as diphenanthrofuran **296** from a more hindered enol ether **297** (**Scheme 3.71.**).

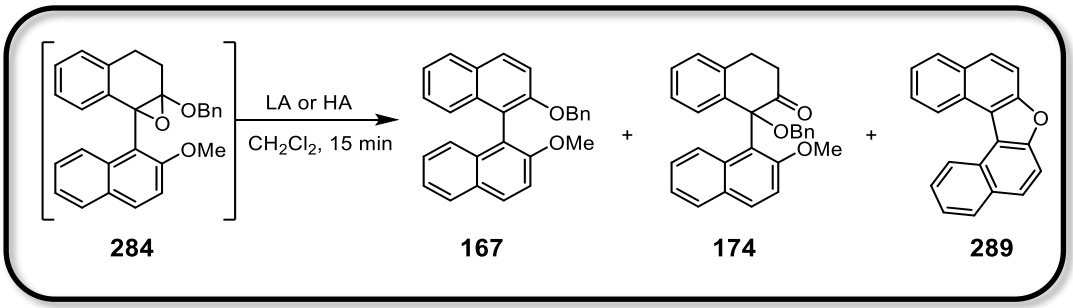



**Scheme 3.71.** Proposed synthesis of helicene **296** with axial to point to helical chirality transfer.

Here, the elimination from point chiral **298** to quinone methide **299** could occur with point to helical chirality transfer. If quinone methide **299** is indeed helically chiral, then furan formation to diphenanthrofuran **296** may occur without loss of stereochemical integrity. Jack Sutro, a Masters student in the Smith group, is currently working on this approach to helically chiral furans as part of his Masters project.

Next, we investigated a series of Brønsted and Lewis acids as potential catalysts to selectively furnish **174** (**Table 3.72.**). Acetic acid did not facilitate any rearrangement of epoxide **284** (**Table 3.72.**, entry 1). Consequently, we investigated more electron withdrawing acetic acid derivatives with lower $pK_a$s. Tribromoacetic acid and dichloroacetic acid did not yield **174** more than hydrochloric acid (**Table 3.72.**, entries 2-3), whereas difluoroacetic acid yielded **174** in 74% yield (**Table 3.72.**, entry 4). Use of camphor sulfonic acid and diphenyl phosphate resulted in

preferential formation of BINOL **167** over the desired product **174** (**Table 3.72.**, entries 5-6). We were pleased to observe that employing Lewis acids ytterbium and cerium triflate yielded exclusively the desired α-alkoxy ketone **174** (**Table 3.72.**, entries 7-8).

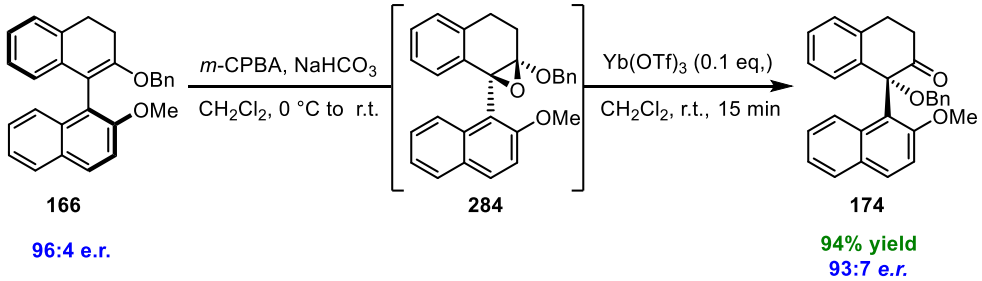



| Entry | Catalyst (10 mol %) | 167[a] | 174[a] | 289[a] |
|---|---|---|---|---|
| **1** | AcOH | <5% | <5% | <5% |
| **2** | $Br_3CCO_2H$ | 41% | 59% | <5% |
| **3** | $Cl_2HCCO_2H$ | 39% | 60% | <5% |
| **4** | $F_2HCCO_2H$ | 20% | 74% | <5% |
| **5** | CSA | 55% | 40% | 5% |
| **6** | $(PhO)_2P(O)OH$ | 48% | 43% | <5% |
| **7** | $Ce(OTf)_3$ | <5% | >95% | <5% |
| **8** | $Yb(OTf)_3$ | <5% | >95% | <5% |

[a] Determined by $^1$H NMR spectroscopy.

**Table 3.72.** Catalyst screen to bias the formation of **174**.

Having identified an appropriate Lewis acid to bias the formation of **174**, we subjected an enantioenriched sample of enol ether **166** at 96:4 *e.r.* to the epoxidation/rearrangement protocol (**Scheme 3.73.**).




**Scheme 3.73.** Catalyst screen to bias the formation of **174**.

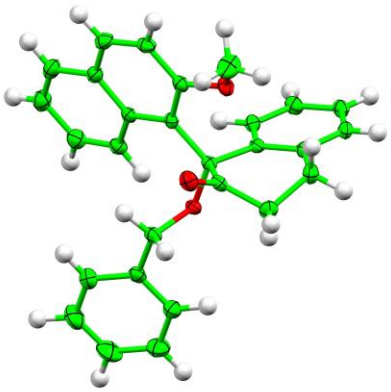
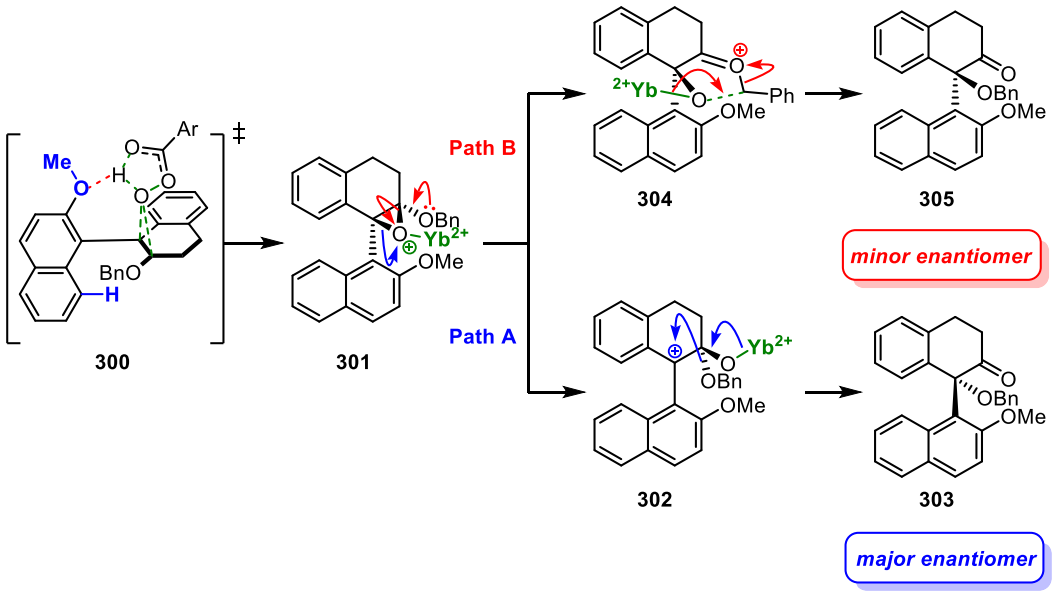


**Figure 3.74.** X-ray structure of **174** with ADP at 50% probability.

We were pleased to observe that employing ytterbium triflate as a Lewis acid catalyst for the rearrangement of epoxy ether **284**, the desired α-benzyloxy ketone **174** was furnished in 94% yield with good axial to point chirality transfer (93:7 *e.r.*). The absolute stereochemistry of **174** was confirmed by single crystal X-ray diffraction (See **Appendix 8.3.5.** for full details; **Figure 3.74**).



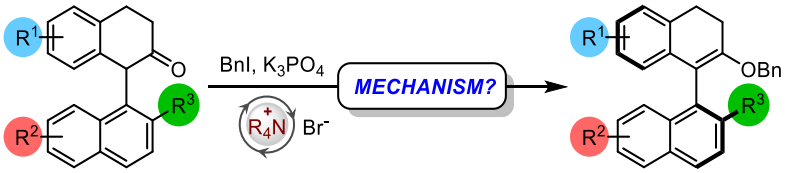

**Scheme 3.75.** Proposed mechanism rationalising the absolute stereochemistry of **174**.

We propose the following mechanism which rationalizes the absolute stereochemistry observed for **174** (**Scheme 3.75.**): First, the enol ether is epoxidized on the *re*-face (**300**). We imagine this could be mainly due to increased steric hindrance on the *si*-face by the aryl moiety of the

2-methoxynaphthyl moiety. It may also be possible that the methoxy group hydrogen bonds to the peracid, although to the best of our knowledge there are no examples of an aromatic alkoxy group acting as a directing group in a diastereoselective epoxidation. Next, epoxyether **301** rearranges to benzylic cation **302** and a subsequent 1,2-alkoxide shift furnishes the major enantiomer **303** (Path A, blue arrows). There are two explanations that may rationalize the imperfect axial to point chirality transfer. Either the epoxidation is not entirely diastereoselective, or a competing mechanism may produce the minor enantiomer **305** (Path B, red arrows). Here, Epoxyether **301** rearranges to oxonium **304** and then an intramolecular $S_N2$ reaction generates the minor enantiomer **305**.

# 4. Mechanistic Proposal

## 4.1. Introduction

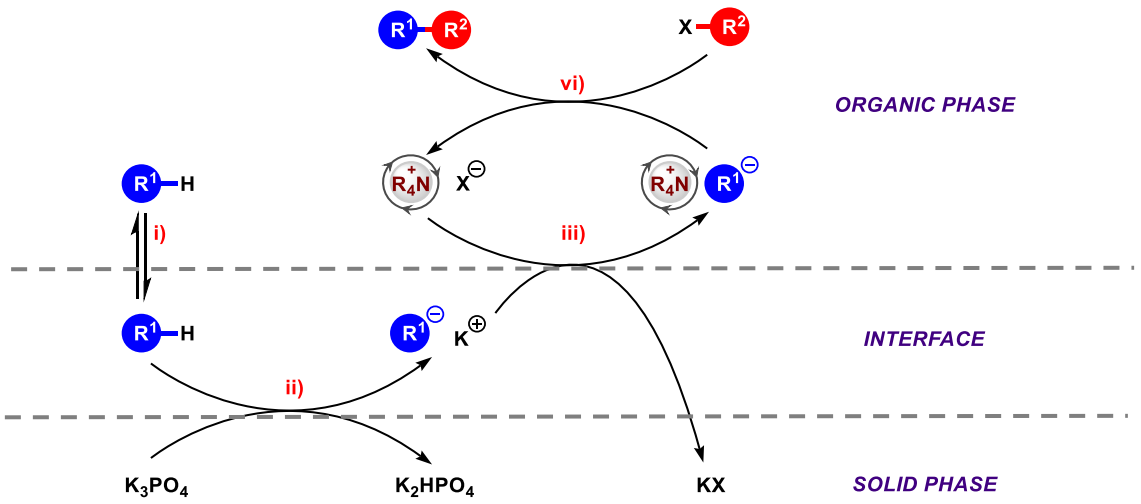



**Scheme 4.1.** Mechanism of atropselective *O*-alkylation?

In this chapter, we shall propose what we believe to be the mechanism for our atropselective ketone *O*-alkylation reaction, with experimental results to support our proposals (**Scheme 4.1.**).

Sasson and co-workers have reported that phase-transfer catalyzed alkylations of acidic methylenes with alkyl halides as electrophiles and potassium phosphate as the base generally proceed by an interfacial mechanism as first proposed by Mąkosza *et al*.[97-98]

**Scheme 4.2.** illustrates a generic phase-transfer catalyzed alkylation of a substrate $R^1$-H bearing an acidic proton with an alkyl halide $R^2$-X with potassium phosphate as the base and an ammonium salt as the phase-transfer catalyst.



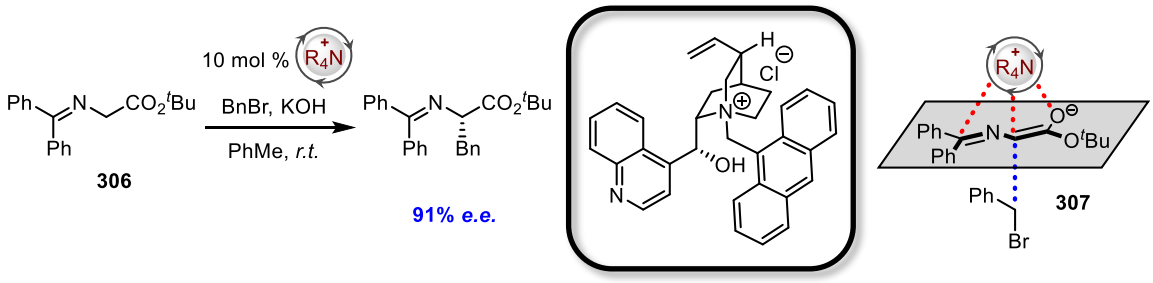

**Scheme 4.2.** Interfacial mechanism for phase-transfer alkylations with potassium phosphate.

i) The substrate enters the interface from the organic phase.

ii) Deprotonation of $R^1$-H occurs by potassium phosphate at the solid-liquid interface to generate the potassium salt of $R^1$.

iii) The potassium salt of $R^1$ undergoes counterion metathesis with the ammonium halide at the interface. A potassium halide precipitates out to the solid phase and the ammonium salt of $R^1$ enters the organic phase.

iv) The ammonium salt of $R^1$ undergoes an $S_N2$ reaction with the alkyl halide to generate $R^1$-$R^2$. The leaving group halide reforms the ammonium halide to turn over the catalytic cycle.




**Scheme 4.3.** Phase-transfer alkylation of a glycine immine.

An example of where asymmetric phase-transfer catalysis proceeds by an interfacial mechanism is the alkylation of glycine Schiff bases **306** (**Scheme 4.3.**).[65] Here, the enantiodetermining step is the alkylation of the ammonium enolate **3.7.** (**Scheme 4.2.**, step iv). Enantioinduction is

achieved by the catalyst preferentially binding to one face of the enolate, therefore favouring alkylation on one face of the enolate.

We sought to establish what the enantiodetermining step in the atropselective *O*-alkylation of ketone **169** is and how the catalyst induces enantioselectivity. Here, the enolate is likely to be axially chiral (**Figure 4.4.**). In the next three sections, we will put forward three possible mechanistic extremes by which the atropselective *O*-alkylation may operate (or by a combination of two, or all three). All three mechanisms are proposed to be interfacial, therefore steps i) to iv) of **Scheme 4.2.** will be incorporated in the proposals.

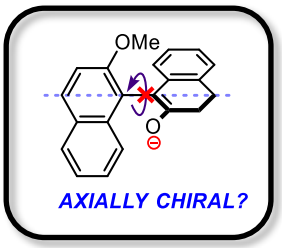
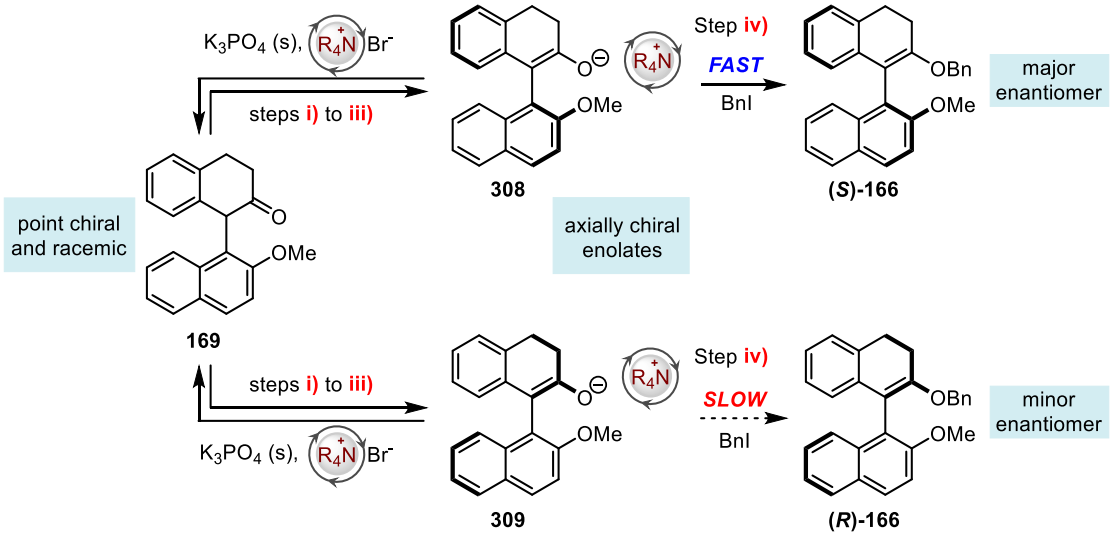



**Figure 4.4.** Axially chiral enolate?

## 4.2. Mechanism A: Rate Difference in Ammonium Enolate Alkylation




**Scheme 4.5.** Different rates of enolate *O*-alkylation.

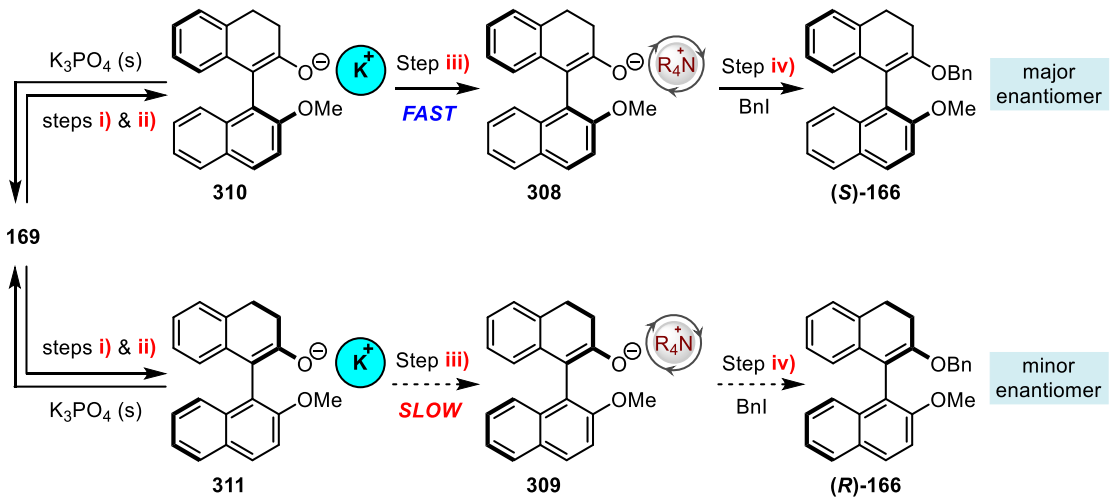
First, tetralone is deprotonated at the interface (steps i and ii) and after counterion metathesis two diastereomeric ammonium enolates **308** and **309** are formed in solution (**Scheme 4.5.**).

Interconversion of one ammonium enolate to the other is unlikely to proceed by rotation about the biaryl bond. Instead, we propose that these interconvert by reversible deprotonation and counterion metathesis at the interface.

Next, ammonium enolate ion pair **308** is alkylated faster than **309**. With the ammonium enolates **308** and **309** being in equilibrium with each other, **308** can be replenished by protonation of **309** to generate **169** which in turn after steps i) to iii) can generate ammonium enolate **308**. Since 2-tetralone **169** and its enolate are chiral, this process can be described as a dynamic kinetic resolution. The crucial step for enantioselectivity is a difference in alkylation rates for ammonium enolates **308** and **309**.

### 4.3. Mechanism B: Kinetic Counterion-Metathesis

It has been demonstrated that ammonium salts of cinchona alkaloids can selectively transport one enantiomer of a chiral anionic substrate from the aqueous phase to the organic phase by "enantioselective liquid-liquid extraction".[99-100] In the second mechanistic proposal, the selective transport of one enantiomer to the organic phase is incorporated (**Scheme 4.6.**).



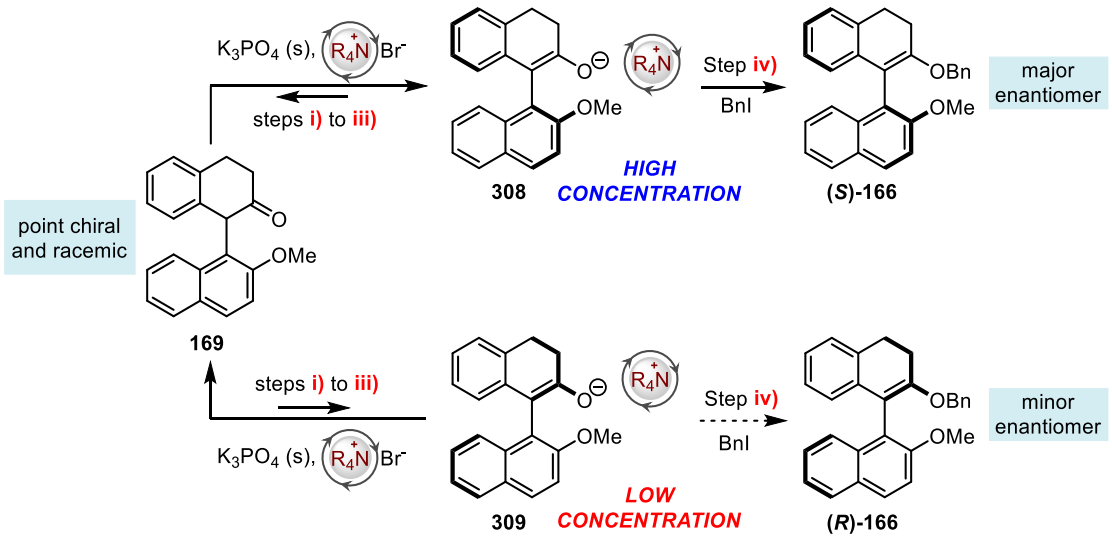

**Scheme 4.6.** Kinetic counterion metathesis.

As with the first mechanism, we propose a fast and reversible deprotonation of **169** by potassium phosphate at the interface to generate two axially chiral potassium enolates **310** and

**311** (Steps i and ii). In step iii), potassium enolate **310** undergoes counterion metathesis with the ammonium salt at a greater rate than **311**. This results in a higher concentration of ammonium enolate **308**. Here, the difference in rate of alkylation of ammonium enolates **308** and **309** is not important and enantioinduction is achieved by "kinetic counterion metathesis" to bias the formation of only one ammonium enolate in the organic phase. Overall this process can also be described as a dynamic kinetic resolution.

### 4.3. Mechanism C: Equilibration of Ammonium Enolates

In the third proposed mechanism, enantioinduction is also achieved by a higher concentration of one ammonium enolate in the organic phase (**Scheme 4.7.**). Here however, a higher concentration is not achieved by kinetic counterion metathesis, but by a biased equilibration to **308**. This could occur, for example, by a favoured interaction between catalyst and enolate in **308** and a disfavoured interaction between catalyst and enolate in **309**. Since interconversion between **308** and **309** is fast and reversible this process is once again a dynamic kinetic resolution.




**Scheme 4.7.** Ammonium enolate equilibration.

### 4.4. Experiments Concerning the Mechanistic Proposal

Next, we sought to support our proposals with experimental evidence. In all three mechanisms, deprotonation of **169** is fast and reversible. Bearing this in mind, we expected the rate of alkylation (step iv) to be several orders of magnitude lower than ammonium enolate formation (steps i to iii). Therefore, the *e.r.* of the enol ether should remain constant throughout the reaction and should not be affected by a change in concentration of the electrophile. To probe whether this assumption was correct, we measured the *e.r.* of **166** over time (**Figure 4.8.**), and carried out the atropselective *O*-alkylation at different concentrations of benzyl iodide (**Figure 4.9.**).

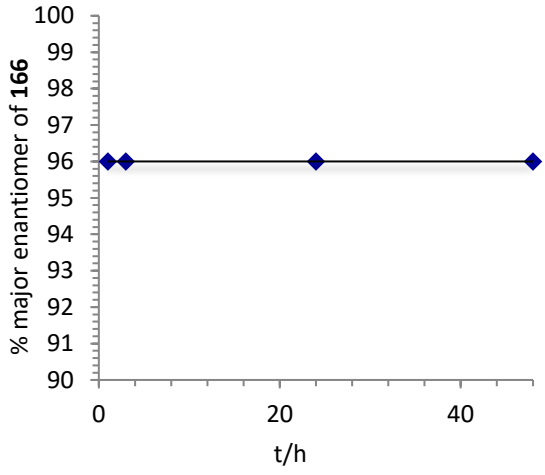



**Figure 4.8.** *e.r.* vs. time.

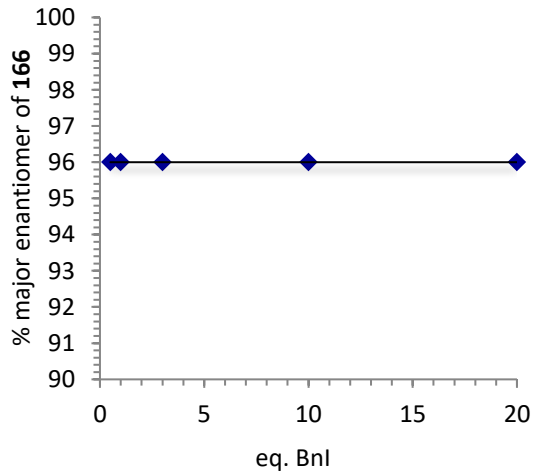
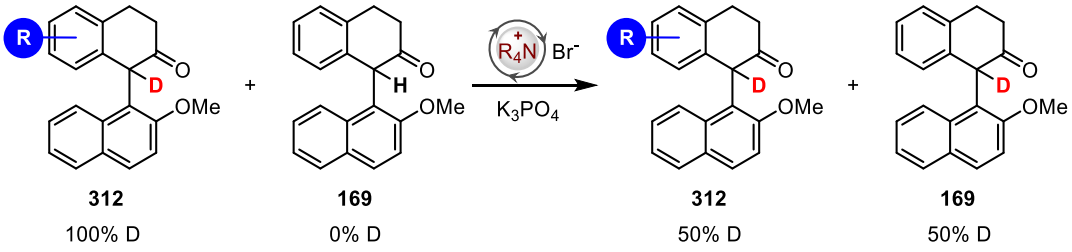



**Figure 4.9.** *e.r.* vs. eq. benzyl iodide.

Consistent with our proposal, we observed no change in *e.r.* over time. The reaction was performed at different concentrations of benzyl iodide by varying the equivalents of benzyl iodide. The same *e.r.* was observed at each concentration – even when 20 equivalents of benzyl iodide were employed.

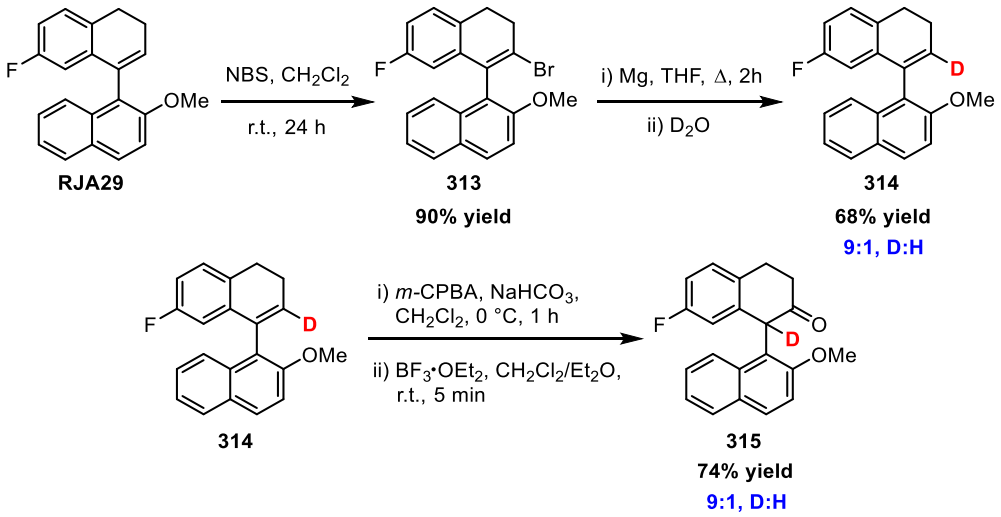
Next, we sought to establish whether the deprotonation of tetralone **169** was indeed reversible. We reasoned that this could be achieved by a double label deuterium cross over experiment. In such a scenario a labelled 2-tetralone **312** which is deuterated at *C*-1, would be subjected to the

reaction conditions for atropselective *O*-alkylation in the presence of **169**, and benzyl iodide omitted from the reaction mixture (**Scheme 4.10.**). If the deprotonation of **169** was indeed reversible, one would expect an equal distribution of the deuterium label across both 2-tetralones.




**Scheme 4.12.** Proposed deuterium cross-over experiment.

Consequently, our first task was to synthesize a double labelled 2-tetralone of type **312** (**Scheme 4.11.**). First, alkene **RJA29** was brominated with NBS to afford vinyl bromide **313**. Alkene **313** was then treated with magnesium to form a Grignard reagent which was subsequently quenched with $D_2O$ to afford deuterated alkene **314**.



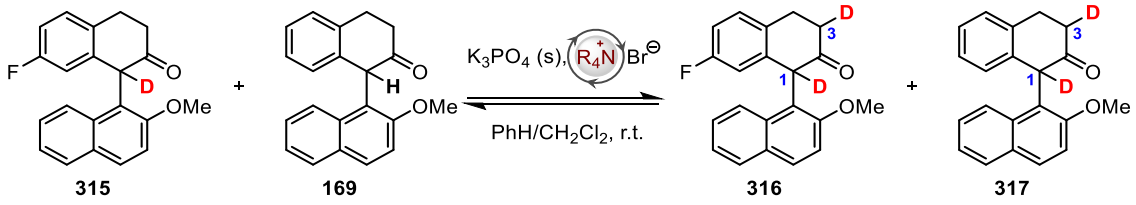

**Scheme 4.11.** Synthesis of deuterated double labelled 2-tetralone **315**.

It should be noted that the low yield for this step is due to a reaction vessel perforation by a rogue stirrer bar which necessitated a paper towel extraction of the fumehood interior.

Subjecting deuterated alkene **314** to the epoxidation/Meinwald protocol afforded the desired α-deuterated 2-tetralone **315** with *c.a.* 90 % deuterium incorporation after a 1,2-deuteride shift.

With deuterium incorporated 2-tetralone **315** in hand, we subjected **315** to the reaction conditions for atropselective *O*-alkylation in the presence of unlabelled ketone **169**, while omitting benzyl iodide (**Scheme 4.12.**; see **Appendix 8.4.** for full experimental procedure). At this point, it is important to acknowledge Dr James Wickens and Dr Barbara Odell for their help and insight with analytical techniques and subsequent data analyses, without them we would not have been able to appropriately analyse and interpret the results of this experiment.

First, we will present how the regiochemistry of deuteration was elucidated. Following this, we will demonstrate how the levels of deuterium incorporation for **316** and **317** were determined.




**Scheme 4.12.** Deuterium crossover experiment.

The regiochemical distribution of deuterium across **316** and **317** were determined by a combination of $^{1}H$, $^{2}H$ and $^{13}C$ NMR spectroscopy (**Figure 4.13.**). **Figure 4.13.a** shows the $^{1}H$ NMR spectrum of a 3:1 mixture of **315** and **169** prior to being subjected to phase-transfer conditions. **Figure 4.13.b** shows the $^{2}H$ NMR spectrum of **315** and **169** at t = 0, where the only peak observed is due to the deuterium at *C*-1 of **315**. **Figure 4.13.c** depicts the $^{2}H$ NMR spectrum after **315** and **169** were subjected to phase transfer conditions. Admittedly, we expected deuterium exchange only to occur from *C*1-(**315**) to *C*-1(**169**). However, it can be seen that the majority of deuterium is incorporated at *C*-3. We reasoned that this could be explained by a kinetic isotope effect when *C*-3 deuterated ketone **318** is deprotonated (**Scheme 4.17.**).

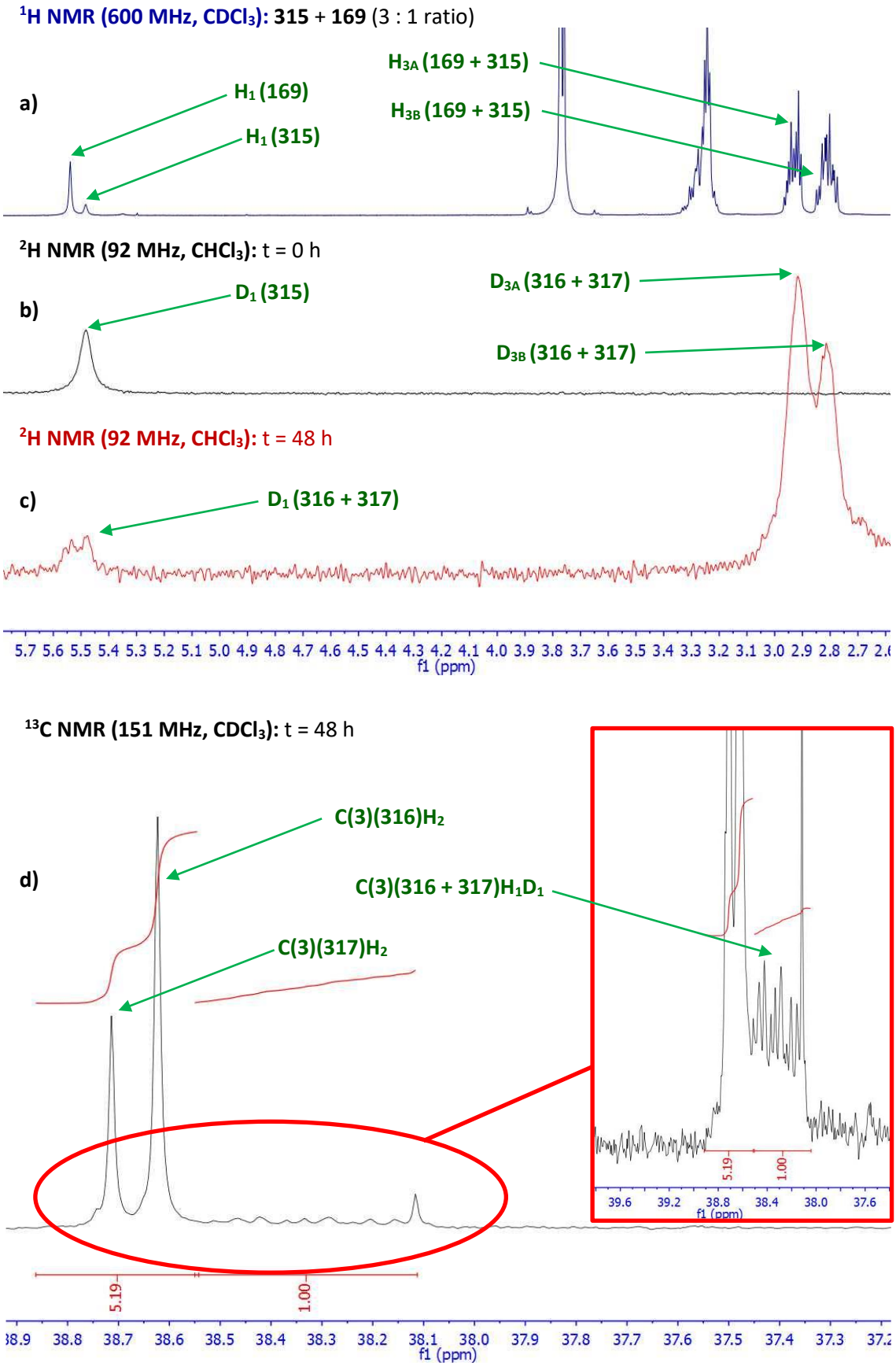



**Figure 4.13.** $^{1}$H, $^{2}$H and $^{13}$C NMR data for the deuterium crossover experiment.

For example, when ketone **318** is treated with potassium phosphate, deprotonation to enolate **319** is fast, whereas due to a kinetic isotope effect dedeuteration to enolate **320** is slow. Consequently, once **316** or **317** is deuterated at *C*-3, the deuterium would become "locked in".

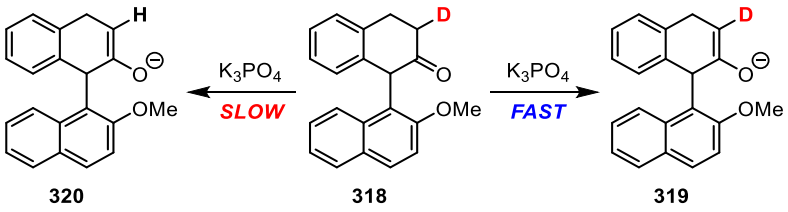



**Figure 4.17.** Kinetic isotope effect as an explanation for increased *C*-3 deuteration.

The $^{13}C$ NMR spectrum also indicates mainly *C*-3 deuteration (**Figure 4.13.d**). If one assumes a negligible difference in T1 relaxation times between T1 ($^{13}CH_2$) and T1 ($^{13}CHD$), then the total level of deuterium incorporation across **316** and **317** can be approximated to be 5:1 H:D by integration.

Whilst having approximated the total level of deuterium incorporation across **316** and **317**, the individual levels of deuterium incorporation for **316** and **317** were still unknown. We were not able to determine these by NMR spectroscopy, therefore these were approximated by high resolution mass spectroscopy (**Figure 4.18.**). Low resolution mass spectroscopy would not have sufficed, since the masses of a deuterated substrate and a substrate, where one $C^{12}$ is exchanged for a $C^{13}$, are too similar to be appropriately distinguished by LRMS.

**Figure 4.18.a** first shows the positive electrospray HRMS signals for deuterated **317** and non-deuterated with one $^{13}C$ atom present. A simulation of a 1:5 deuterium incorporation is consistent with the experimentally obtained results. Pleasingly, a simulation of a 1:5 deuterium incorporation for **316** is also consistent with the experimentally obtained electrospray HRMS results (**Figure 4.18.b**).

Bearing the results of these experiments in mind, we are confident that deprotonation of **169** is fast and reversible and the alkylation of the ammonium enolates is orders of magnitude slower.

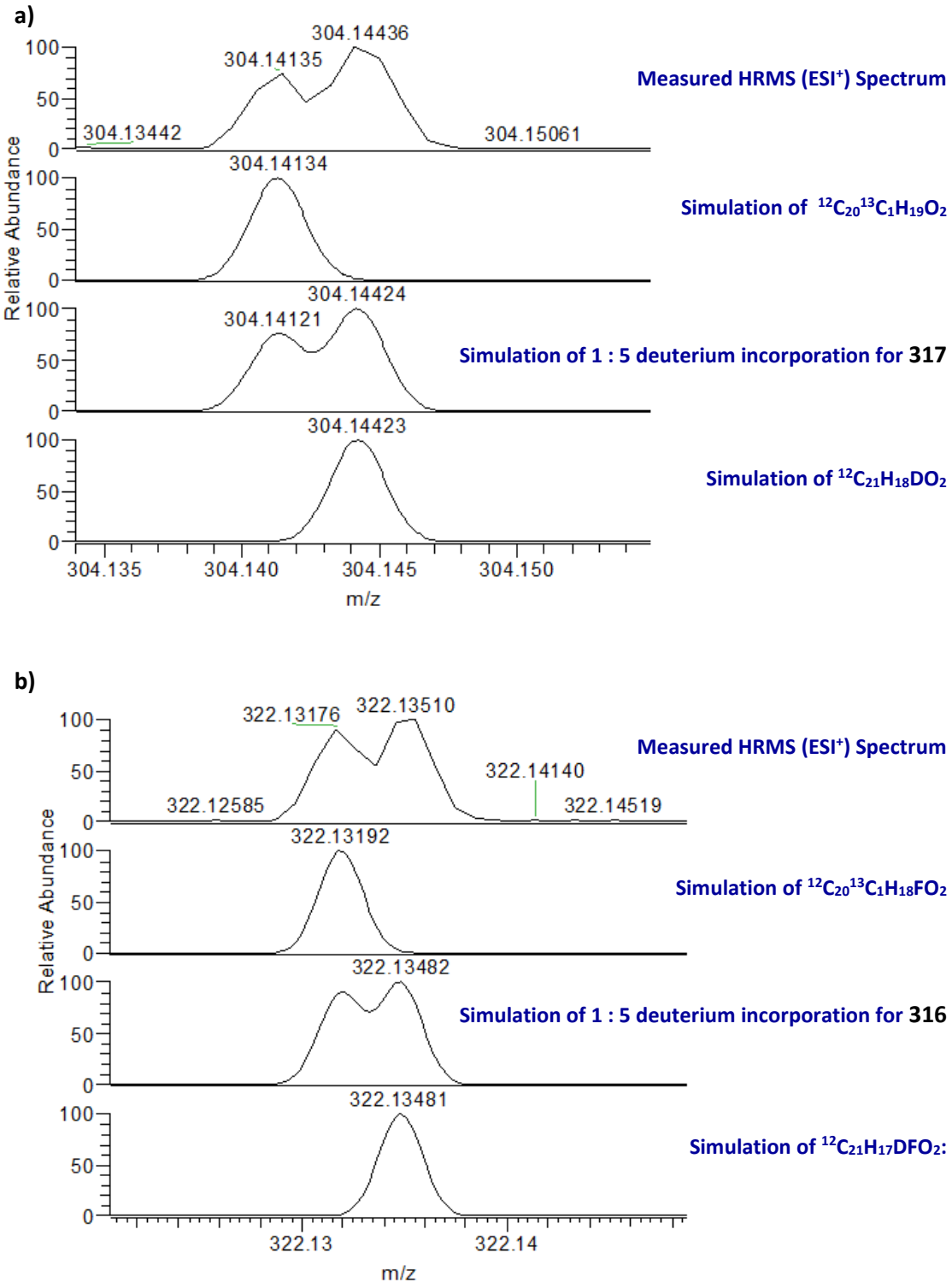



**Figure 4.18.** HRMS (ESI+) data for the deuterium crossover experiment.

### 4.5. Proposed Catalyst Substrate Interaction

Next, we sought to better understand how catalyst **192** induces enantioselectivity. In mechanisms B and C, a higher concentration of ammonium enolate **308** than **309** results in preferential alkylation to one absolute configuration of enol ether. A possible explanation could be a favoured interaction between the (*S*)-enolate of **169** and catalyst **192**, whereas the interaction between the (*R*)-enolate **169** of and catalyst **192** could be disfavoured. At this point, it is important to discuss what is known in the literature about the interaction of ammonium salts with anions.

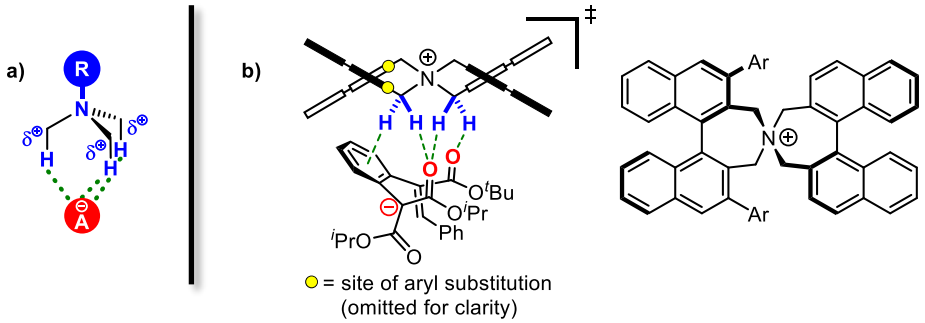



**Figure 4.19. a)** Charge distribution in ammonium salts; **b)** Interaction of an ammonium salt with an anionic substrate.

It has been demonstrated that the positive charge of quaternary ammonium salts does not reside on the tetravalent nitrogen, but is distributed across the benzylic α-carbon atoms and their attached hydrogen atoms (**Figure 4.19.a**).[101-102] This in turn increases the acidity of the benzylic α-hydrogens, which can form hydrogen bonds to an anionic substrate.

These hydrogen bonds are the key interaction between a chiral ammonium salt and an anionic substrate/ transition state. In a recent publication by the Smith group on 5-endo trig cyclizations towards indanes (**Scheme 163**), the interaction between the chiral ammonium salt and the transition state was calculated by DFT (**Figure 4.19.b**).[12] The key interactions are hydrogen bonds between the benzylic hydrogens of the ammonium salt and carbonyl oxygens on the transition state. Based on these reports, we set out to put forward a model for how catalyst

**192** interacts with the (*S*)-enolate of **169** (**Figure 4.20.**). It should be noted that the 3D model has only been included for clarity and has not been calculated using any computational methods such as DFT or UFF.

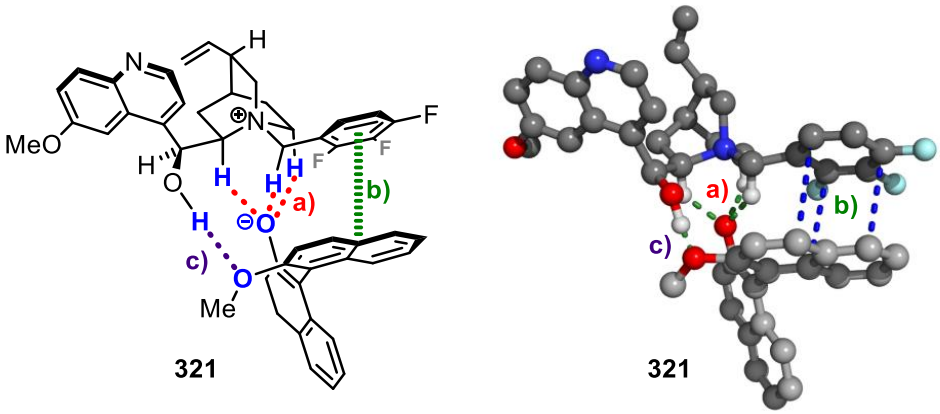
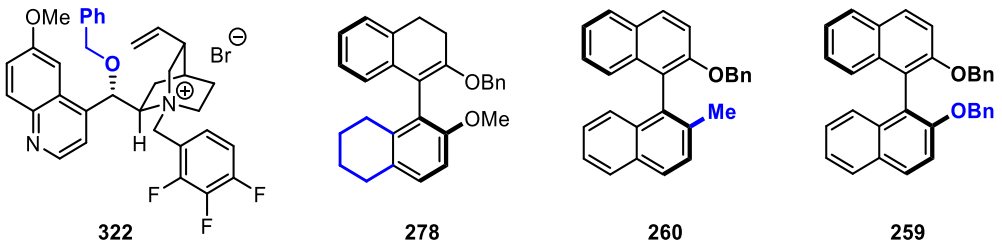



**Figure 4.20.** Proposed catalyst-substrate interaction.

We propose that the benzylic hydrogens of the catalyst hydrogen bond to the enolate oxygen (**Figure 4.20.a**). During the catalyst optimization (**Table 3.28.**) it became evident that the aromatic substituent of the benzyl group of catalyst **192** was crucial for enantioinduction. We reasoned this could potentially be due to a π-π stacking interaction between the catalyst and the substrate. Here, we propose that the catalyst-trifluoroarene π-π stacks with the aryl moiety of the 2-methoxy naphthyl substituent of the enolate (**Figure 4.20.b**). This could be a potential explanation for why poor enantioinduction was observed for **278**, since here, π-π stacking would not be possible due to the saturated backbone (**Figure 4.21.**).




**322**
66:34 *e.r.*

**278**
82% yield
60:40 *e.r.*

**260**
25% yield
75:25 *e.r.*

**259**
70% yield
96:4 *e.r.*

**Figure 4.21.** Experimental results consistent with proposed catalyst-substrate interaction.

Weaker π-π stacking may be an explanation why poor enantioinduction was observed for **260**, since the 2-methylnaphthalene substituent is less electron rich than a 2-methoxynaphthalene substituent, potentially weakening the π-π stacking interaction between catalyst and substrate.

When carrying out the reaction with an *O*-capped catalyst **322**, a severe drop in enantioselectivity was observed. It could be possible that the catalyst O-*H* acts as a hydrogen bond acceptor to form a hydrogen bond with the alkoxy group on the substrate (**Figure 4.20.c**), which would also explain the decrease in enantioinduction for **260**. Increasing the size of the alkoxy substituent, as in **259**, does not impact enantioselectivity and this agrees with the proposed model. More importantly, substitution at *C-5* to *C*-7 about the substrate would also not result in a steric clash with the catalyst, which is consistent with our experimental results where we observe little change in enantioselectivity at these positions (**Scheme 3.61.**).

Apart from a computational calculation of the catalyst-substrate interaction, it would be beneficial to obtain a crystal structure of the ammonium enolate (assuming the same catalyst-substrate interactions occur in the solid state). However, ammonium enolates are notoriously difficult to crystallize and to the best of our knowledge only one example of a crystal structure of an ammonium enolate has been reported by Reetz and co-workers.[103] The authors report a very detailed procedure for growing crystals of the ammonium enolate suitable for single crystal X-ray diffraction:

*"A 250 mL three-necked flask equipped with a 100 mL dropping funnel and a connection to a membrane pump was charged with dry toluene (50 mL) and a methanol solution of tetrabutylammonium hydroxide (20 mL of a 1 M solution, Aldrich). In order to remove the methanol, dry toluene (20 mL) was added and most of the solvents removed in vacuo at 15-19 Torr. In doing so, the total volume was not allowed to fall below 70 mL. The process was repeated 5 more times. Following the addition of toluene (50 mL), acetophenone (5.5 mL, 47 mmol) in toluene (60 mL) was slowly added, during which the reaction mixture was kept under vacuum in*

*order to remove toluene and water azeotropically. The total volume of the yellow solution was not allowed to fall below 100 mL. The total time for addition of acetophenone was about 2.5 h. The total volume was then reduced to about 50 mL and the concentrated mixture was transferred into a Schlenk tube under argon. High vacuum was then applied until the mixture had turned into a thick paste. (If this drying phase is too long, partial decomposition of the desired product sets in.) Under an atmosphere of dry argon a small amount of dry dimethylformamide (DMF) was added. The orange solution was then kept at -60°C for two days, resulting in the formation of gold-yellow crystals of 4. The solvent was removed under vacuum, and the crystals were washed with dry ether and dried in vacuo. The yield was 20% (in some runs higher).”* [103]

Bearing this in mind, it became evident that growing crystals of ammonium enolate **308** or **309** suitable for single crystal X-ray diffraction may prove challenging. There are however, reports of cinchona alkaloid derived ammonium phenolates acting as chiral Brønsted bases, implying that these are stable and isolable.[104] More importantly Corey and co-workers have reported a crystal structure of a cinchona alkaloid derived ammonium salt with a phenolate counterion.[68]

We sought to establish whether (*S*)-MeBINOL **281** could be used as a model substrate for deprotonated ketone **169**, and therefore obtain an X-ray structure of catalyst **192** with the anion of (*S*)-MeBINOL **281** as the counterion (**Figure 4.22.**).

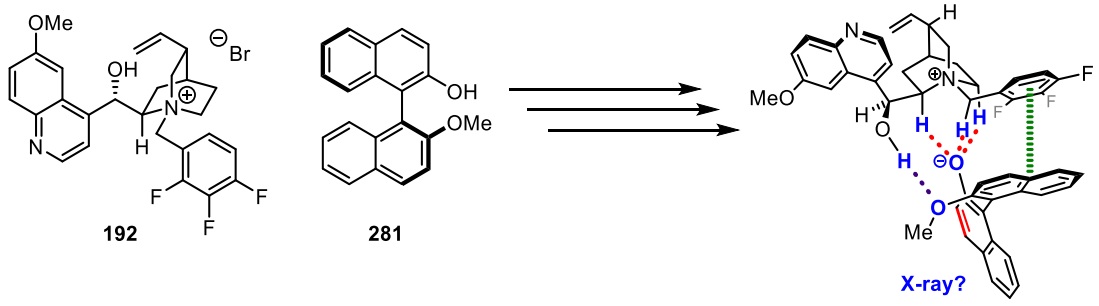
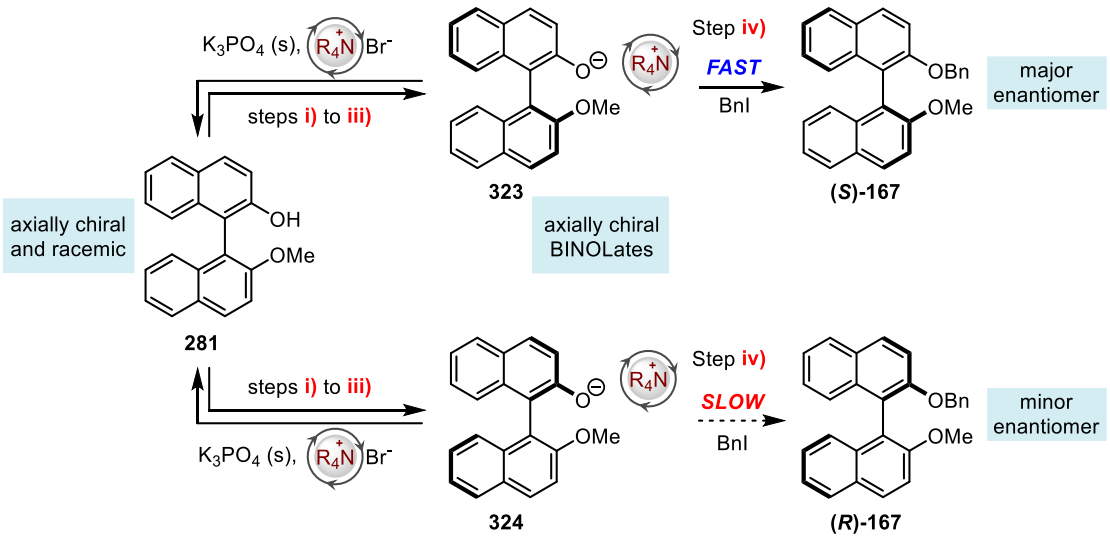


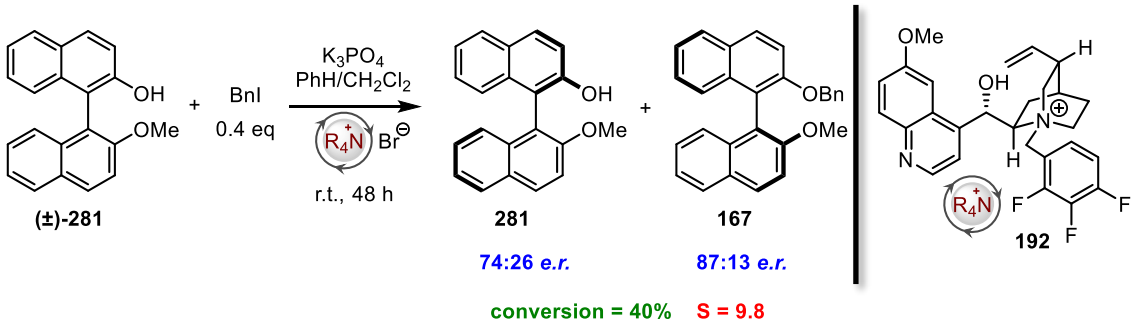

**Figure 4.22.** MeBINOL as a model substrate for ketone **169**.

Our first task was to establish whether MeBINOL **281** was an appropriate model substrate for ketone **169**. Since (*R*)-MeBINOL **281** cannot interconvert to (*S*)-BINOL **281** under the reaction conditions for atropselective *O*-alkylation either by protonation/deprotonation or rotation about the biaryl bond, *O*-alkylation of racemic MeBINOL **281** with a stoichiometric amount of benzyl iodide would lead to racemic MeBnBINOL **167**. However, if a substoichiometric amount of the alkylating agent was employed, MeBnBINOL could be synthesized enantioselectively by kinetic resolution (**Scheme 4.23.**; mechanism A shown here, B and C could also apply).




**Scheme 4.23.** Proposed kinetic resolution of MeBINOL.

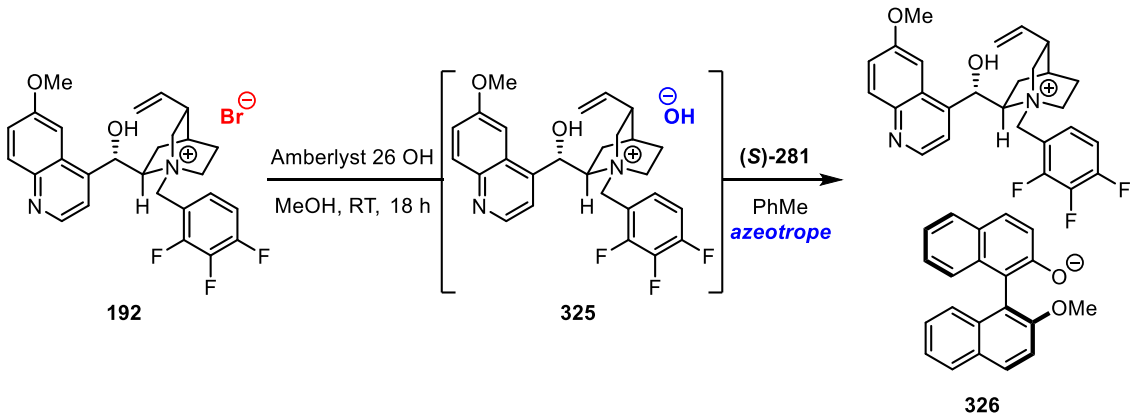
Consequently, we subjected racemic MeBINOL to the reaction conditions for atropselective *O*-alkylation, while employing a substroichiometric amount of benzyl iodide (**Scheme 4.24.**). We were pleased to observe that kinetic resolution of MeBINOL did indeed occur.




**Scheme 4.24.** Kinetic resolution of MeBINOL.

More importantly, the same absolute configuration of MeBnBINOL **167** was observed, implying that the catalyst-substrate interaction may be similar to **321**, suggesting MeBINOL may be a suitable model substrate to obtain a crystal structure of the catalyst-substrate complex. The selectivity factor for this process was approximately 10, meaning that (*S*)-MeBINOL is alkylated at a rate 10 times faster than (*R*)-BINOL.

Having established MeBINOL as a suitable model substrate, we set out to obtain a crystal structure of catalyst **192** with the anion of MeBINOL **281** as the counterion. To this end, an amberlyst resin-mediated ion exchange was performed to generate ammonium hydroxide **325** *in situ*.[104] Following this (*S*)-MeBINOL was added. After azeotropic removal of water, we attempted to crystallize **326** (**Scheme 4.25.**). So far our efforts have not been successful, however our endeavour to crystallize **326** is still ongoing.




**Scheme 4.25.** Attempted crystallization of ammonium salt **326**.

# 5. Kinetic Resolution of MeBINOL

## 5.1. Reaction Optimization

Next we sought to develop a more efficient protocol for the kinetic resolution of MeBINOL **281**. Whilst the reaction conditions for atropselective ketone *O*-alkylation achieved the kinetic resolution of MeBINOL **281** with a S-factor of 10, more optimized reaction conditions may exist. Therefore, we set out to optimize the kinetic resolution, using the same process as before. To establish the efficiency of specific reaction conditions, the S-factor needed to be determined for each reaction, which can be calculated using **equation 1** (**Figure 5.1.**).[105]

$$\textbf{\textit{Equation 1}}\text{: } S = \frac{k_{major}}{k_{minor}} = \frac{\ln(1 - conversion)(1 - e.e._{starting\ material})}{\ln(1 - conversion)(1 + e.e._{starting\ material})}$$

$$\textbf{\textit{Equation 2}}\text{: } Conversion = \frac{e.e._{starting\ material}}{e.e._{starting\ material} + e.e._{product}}$$

**Figure 5.1.** Equations for selectivity factor and conversion in kinetic resolutions.

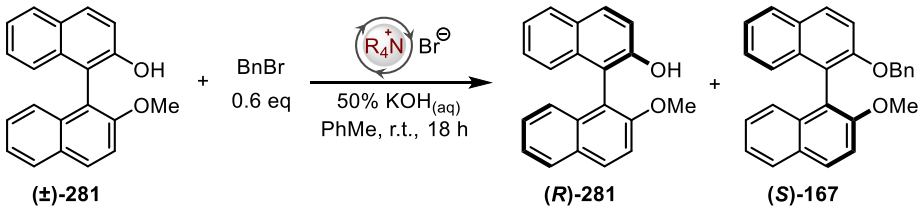
It is possible to calculate the conversion of a kinetic resolution from the enantiomeric rations of the products and starting materials using **equation 2**.[105] The group of Dr Jonathan Goodman (Cambridge) have developed a web applet where one simply can input conversion and enantiomeric ratios to calculate the S-factor:

http://www-jmg.ch.cam.ac.uk/tools/magnus/KinRes.html

It should be noted that this chapter discusses the main findings of the optimization process. For a full account see **Appendix 8.2.3.**

As before, we began the optimization process with investigating which of the four commercially available cinchona alkaloid derived ammonium salts was able to induce the highest level of enantioselectivity (**Table 5.2.**). In all cases, the observed selectivity factors were very low, presumably due to a competing background reaction where the potassium naphtholate is alkylated at the interface in the absence of the phase-transfer catalyst. Nevertheless, as

observed for the ketone *O*-alkylation of, *N*-benzylquinidinium chloride proved to be the most proficient asymmetric phase-transfer catalyst of the four (**Table 5.2.**, entry 4).




| Entry | Catalyst | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | **178** | 55% | 52.5:47.5 | 52:48 | 1.1 |
| **2** | **179** | 50% | 51.5:48.5 | 51.5:48.5 | 1.1 |
| **3** | **180** | 42% | 52.5:47.5 | 52.5:47.5 | 1.2 |
| **4** | **19** | 50% | 51:49 | 51:49 | 1.1 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

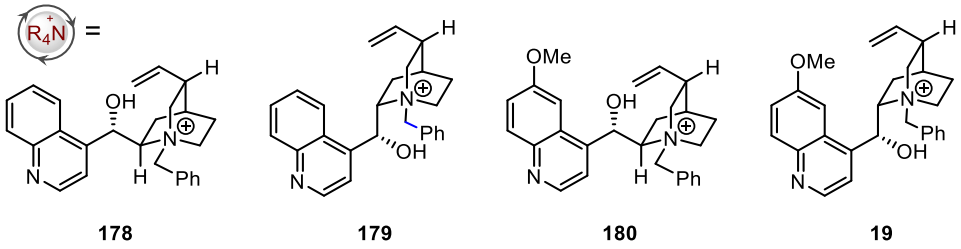
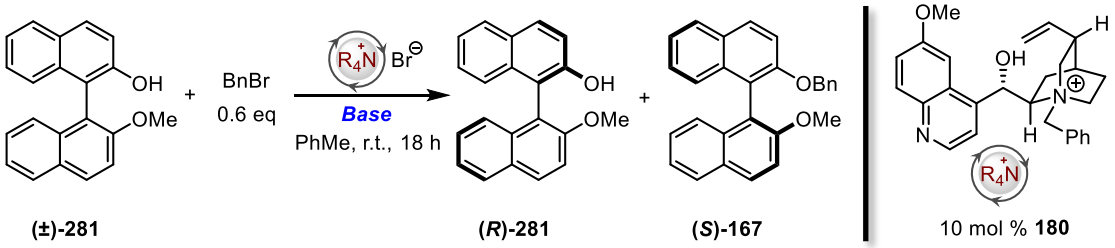



**Table 5.2.** Primary catalyst screen.

Our next task was to identify a base which would sufficiently improve the selectivity factor of the kinetic resolution to be able to identify a more efficient phase-transfer catalyst in a subsequent catalyst screen (**Table 5.3.**). We decided to focus our attention on aqueous bases, since these can be administered rapidly to multiple reaction vessels using an Eppendorf Pipette.

Aqueous hydroxides bases did give good conversion, but no improvement in selectivity factor was observed (**Table 5.3.**, entries 1-3). Aqueous carbonates bases did improve the selectivity, however here a much lower conversion was observed (**Table 5.3.**, entries 5-6). We were pleased to observe that aqueous potassium phosphate led to a significant improvement in selectivity

factor, albeit with low conversion. Hence, subsequent screening reactions were carried out for 48 hours at room temperature.




| Entry | Base (eq.) | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | 25% $NaOH_{(aq)}$ (5) | 36% | 52:48 | 53.5:46.5 | 1.2 |
| **2** | 25% $RbOH{\bullet}OH_{2(aq)}$ (5) | 35% | 55.5:44.5 | 51.5:48.5 | 1.3 |
| **3** | 25% $CsOH{\bullet}OH_{2\,(aq)}$ (5) | 42% | 52.5:47.5 | 53.5:46.5 | 1.2 |
| **4** | 50% $K_2CO_{3(aq)}$ (5) | 12% | 53:47 | 72:28 | 2.7 |
| **5** | 50% $Cs_2CO_{3(aq)}$ (5) | 13% | 53:47 | 71:29 | 2.5 |
| **6** | 50% $K_3PO_{4(aq)}$ (5) | 13% | 53:47 | 73.5:26.5 | 3.1 |

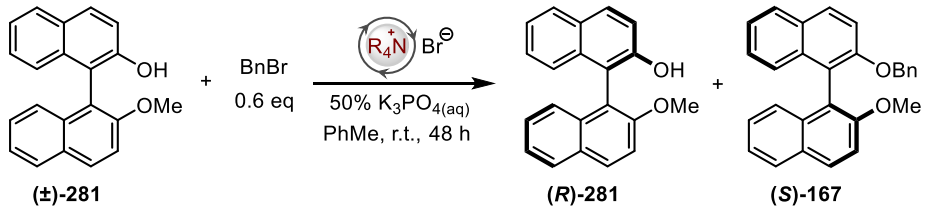
[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Table 5.3.** Primary base screen.

Next, we investigated the effect of aryl substitution about the catalyst benzyl moiety on conversion and selectivity factor (**Table 5.4.**). Electron donating groups had a negative impact on selectivity (**Table 5.4.**, entries 1-2). While naphthyl (**Table 5.4.**, entry 3) and trifluoromethylarenes improved the selectivity of the process (**Table 5.4.**, entries 4-5). Further improvement could be observed with trifluoroarenes, with 2,3,4-trifuorophenyl giving the highest selectivity factor observed so far (**Table 5.4.**, entries 6-7), albeit in poor conversion. We were pleased to observe that pentafluorophenyl substituted catalyst **182**, led to an improvement in both selectivity factor and conversion (**Table 5.4.**, entry 8). Interestingly, when using catalysts based on dihydroquinidine, where the vinyl group is substituted for an ethyl

group, a significant increase in selectivity factor could be observed, with catalyst **328** giving the highest S-factor and conversion (**Table 5.4.**, entries 9-10).




| Entry | Catalyst | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | **184** | 18% | 53:47 | 64:36 | 1.9 |
| **2** | **183** | 16% | 53.5:46.5 | 68.5:31.5 | 2.3 |
| **3** | **188** | 29% | 62.5:37.5 | 80:20 | 5.3 |
| **4** | **187** | 4% | 51:49 | 76:24 | 2.9 |
| **5** | **185** | 3% | 51:49 | 79.5:20.5 | 4.8 |
| **6** | **193** | 13% | 55:45 | 83:17 | 5.6 |
| **7** | **192** | 5% | 52:48 | 91:9 | 7.6 |
| **8** | **182** | 24% | 62:38 | 89:11 | 9.3 |
| **9** | **327** | 6% | 52.5:47.5 | 90.5:9.5 | 8.9 |
| **10** | **328** | 27% | 65:35 | 90:10 | 13 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

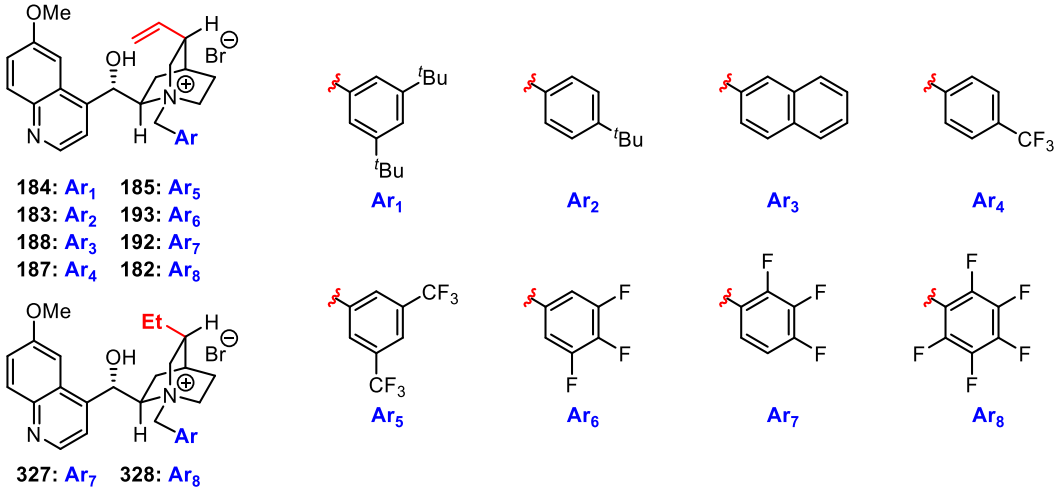
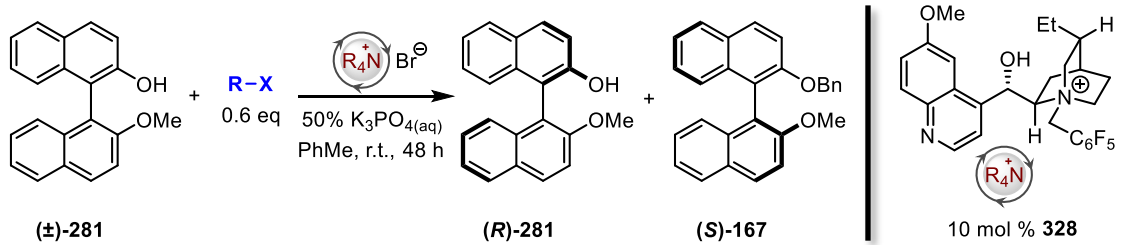



**Table 5.4.** Secondary catalyst screen.

Whilst catalyst **328** did improve the selectivity factor, the conversion was still low. We reasoned that conversion could be increased by employing a more reactive electrophile. Consequently, we investigated selected alkyl halides as electrophiles for the kinetic resolution of MeBINOL **281** (**Table 5.5.**). Whilst no electrophile improved the selectivity factor, we observed improved conversion with allyl iodide and benzyl iodide, with benzyl iodide giving the highest selectivity factor (**Table 5.5.**, entries 2 and 5).




| Entry | Electrophile | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | Allyl bromide | 13% | 55:45 | 85:15 | 7.2 |
| **2** | Allyl iodide | 35% | 68:32 | 83:17 | 7.1 |
| **3** | Methyl iodide | 19% | 56:44 | 76:24 | 3.5 |
| **4** | Benzyl bromide | 27% | 65:35 | 90:10 | 13 |
| **5** | Benzyl iodide | 35% | 89:11 | 71:29 | 12 |

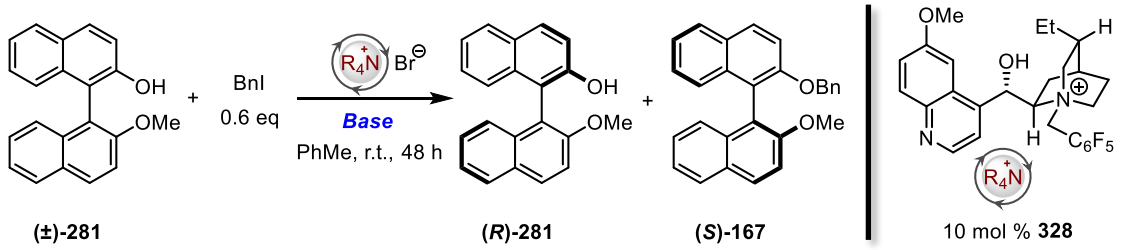
[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Table 5.5.** Electrophile Screen.

Having achieved some improvement in conversion without deteriorating the S-factor, we were confident that further improvements could be made by varying the base and/or base stoichiometry. Consequently, we again investigated a series of bases for the kinetic resolution of MeBINOL **281** using catalyst **328** (**Table 5.6.**). Good conversion was observed for aqueous cesium hydroxide, albeit with a very poor S factor (**Table 5.6.**, entry 1). Both solid and aqueous potassium carbonate gave poor conversion and no improvement in S factor (**Table 5.6.**, entries 2-3). Cesium carbonate bases gave better conversion but worse selectivity factors (**Table 5.6.**, entries 4-6). Aqueous sodium phosphate gave poor selectivity, whereas aqueous potassium

phosphate gave good selectivity (**Table 5.6.**, entries 6 & 8). The selectivity for aqueous potassium phosphate was slightly lower than before. Selectivity factors are very sensitive to a small change in conversion therefore we believe this result to be within the error of the experiment. Surprisingly, solid potassium phosphate performed very poorly (**Table 5.6.**, entry 7). We speculated that base effectiveness had a strong solvent dependence with respect to selectivity factor and conversion. Consequently, we investigated a series of solvents using aqueous potassium phosphate as a base, before reinvestigating selected base-solvent combinations (**Table 5.7.**).




| Entry | Base (eq.) | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | 25% $CsOH_{(aq)}$ (5) | 60% | 78.5:21.5 | 69:31 | 3.8 |
| **2** | $K_2CO_3$ (5) | 11% | 55:45 | 89:11 | 8.8 |
| **3** | 50% $K_2CO_{3(aq)}$ (5) | 12% | 55.5:44.5 | 91.5:8.5 | 12 |
| **4** | $Cs_2CO_3$ (2) | 39% | 56.5:43.5 | 60:40 | 1.7 |
| **5** | 50% $Cs_2CO_{3(aq)}$ (5) | 26% | 62.5:37.5 | 86.5:13.5 | 8.2 |
| **6** | 15% $Na_3PO_{4(aq)}$ (5) | 42% | 71.5:28.5 | 80:20 | 6.1 |
| **7** | $K_3PO_4$ (5) | 44% | 70:30 | 75:25 | 4.4 |
| **8** | 50% $K_3PO_{4(aq)}$ (5) | 40% | 74.5:25.5 | 87.5:12.5 | 11 |

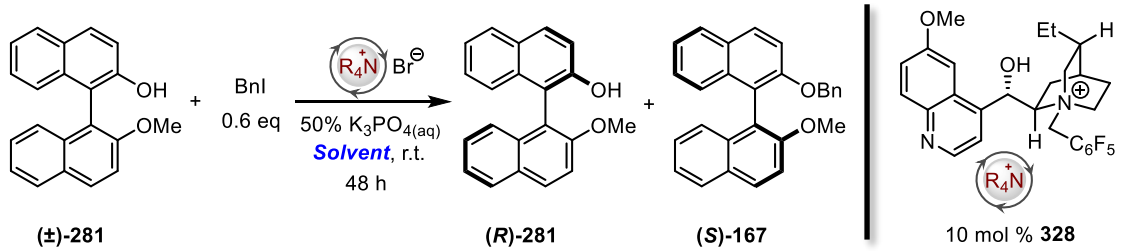
[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Table 5.6.** Secondary base screen.

Ethereal solvents performed poorly (**Table 5.7.**, entries 1-2) and observed that mesityl oxide was not an effective solvent (**Table 5.7.**, entry 3). It should be noted that we observed conversions above 60% in some cases. Presumably this is a result of more than 0.6 equivalents

of benzyl iodide having been added to the reaction mixture as a consequence of human error in stock solution preparation and/or administering.




(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Solvent | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | Diethyl ether | 34% | 68:32 | 84.5:15.5 | 7.7 |
| **2** | TBME | 42% | 69.5:30.5 | 76.5:23.5 | 4.7 |
| **3** | Mesityl oxide | 73% | 76.5:23.5 | 60:40 | 2.4 |
| **4** | Dichloromethane | 68% | 97:3 | 72:28 | 8.2 |
| **5** | Chloroform | 57% | 91:9 | 79.5:20.5 | 10 |
| **6** | Toluene | 44% | 78.5:21.5 | 86:14 | 11 |
| **7** | Benzene | 53% | 90:10 | 85:15 | 14 |
| **8** | Trifluoromethylbenzene | 43% | 62:38 | 66:34 | 2.4 |
| **9** | *m*-Xylene | 10% | 55:45 | 93:17 | 15 |
| **10** | *p*-Xylene | 7% | 53:47 | 92.5:7.5 | 13 |

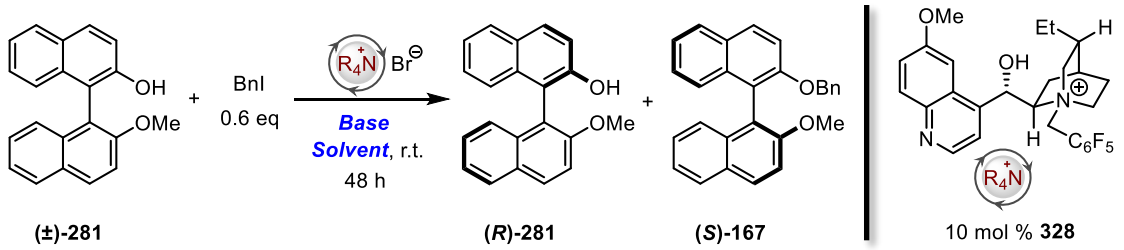
[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Table 5.7.** Solvent screen.

We observed a decrease in selectivity with halogenated solvents, however the conversion was vastly improved resulting in excellent enantioselectivities of the starting material, e.g. at 97:3 *e.r.* for dichloromethane (**Table 5.7.**, entries 4-5). Good conversion and selectivity was observed for benzene, whereas trifluoromethylbenzene performed very poorly (**Table 5.7.**, entries 7-8). Xylenes gave poor conversions with apparent excellent selectivity factors (**Table 5.7.**, entries 9-10). It should be noted that at low conversion the selectivity factor is very sensitive to small changes in conversion therefore these results should be interpreted with

caution. Having eliminated “poor solvents” and “poor bases” we proceeded to investigate the effect of selected solvents on selectivity and conversion with different stoichiometries of either solid or liquid potassium phosphate at room temperature or 0 ° C (**Table 5.8.**).




(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Solvent | Base (eq.) | Conv.[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|---|
| **1** | PhH | $K_3PO_4$ (5) | 65% | 97:3 | 75.5:24.5 | 10 |
| **2** | PhH | $K_3PO_{4(aq)}$ (5) [d] | 50% | 85.5:14.5 | 86:14 | 13 |
| **3** | *m*-Xylene | $K_3PO_4$ (5) | 52% | 73.5:26.5 | 72:28 | 4.0 |
| **4** | *m*-Xylene | $K_3PO_{4(aq)}$ (10) [d] | 11% | 55.5:44.5 | 93:7 | 15 |
| **5** | PhH/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (5) [d] | 54% | 89:11 | 83:17 | 11 |
| **6** | PhH/$CHCl_3$ 9:1 | $K_3PO_4$ (5) | 62% | 96.5:3.5 | 79:21 | 12 |
| **7** | *m*-Xylene/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (5) [d] | 57% | 89:11 | 80:20 | 9.2 |
| **8** | *m*-Xylene/$CHCl_3$ 9:1 | $K_3PO_4$ (5) | 74% | 98.5:1.5 | 67:33 | 7.3 |
| **9** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_{4(aq)}$ (10) [d] | 11% | 55:45 | 91.5:8.5 | 11 |
| **10** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_4$ (5) | 12% | 55.5:44.5 | 92.5:7.5 | 13 |
| **11** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_4$ (10) | 28% | 64.5:35.5 | 88:12 | 10 |
| **12** | *m*-xylene/PhH 4:1 | $K_3PO_{4(aq)}$ (10) [d] | 37% | 88:12 | 72:28 | 11 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet; [d] 50% aqueous w/w; [e] Reaction carried out at 0 °C.

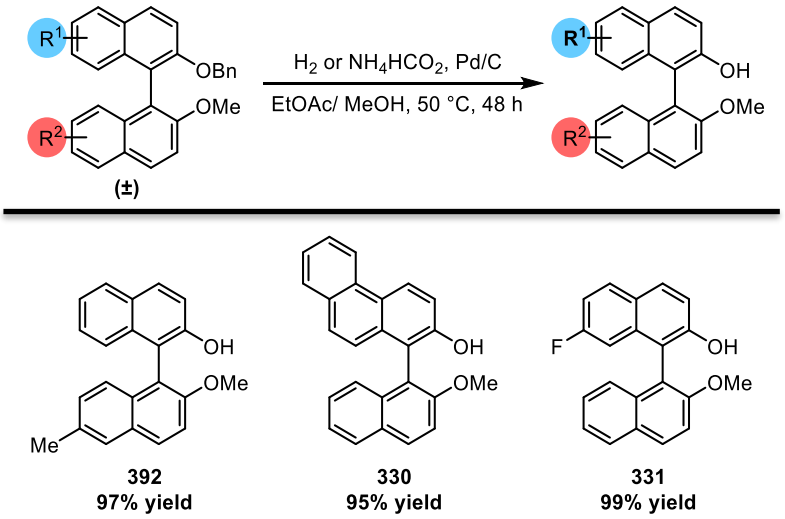
**Table 5.8.** Solvent and base combinations.

Interestingly, in benzene, solid potassium phosphate did perform well in comparison *m*-xylene where poor selectivity was observed (**Table 5.8.**, entries 1-3), supporting our hypothesis that phosphate bases exhibit a strong solvent dependence for this reaction. We reasoned that the conversion may be increased in *m*-xylene by employing a greater excess of aqueous base,

however this did not prove to be the case (**Table 5.8.**, entry 4). Next, we investigated the effect of chloroform as a co-solvent for benzene and *m*-xylene (**Table 5.8.**, entries 5-8). No improvements were observed for xylene, however in a 9:1 benzene chloroform mixture with solid potassium phosphate, MeBINOL **281** was furnished in excellent enantioselectivity at 96.5:3.5 e.r. with full conversion and a good S-factor of 12 (**Table 5.8.**, entry 6). Carrying out the reaction at 0 °C did not improve selectivity and in all cases the conversion was poor (**Table 5.8.**, entries 9-11). A benzene-xylene mixture was also investigated, but to no avail (**Table 5.8.**, entries 9-11). Whilst there is likely still some room for improvement, we are confident that we are approaching fully optimized conditions with the conditions employed in **Table 5.8.**, entry 6 being particularly encouraging.

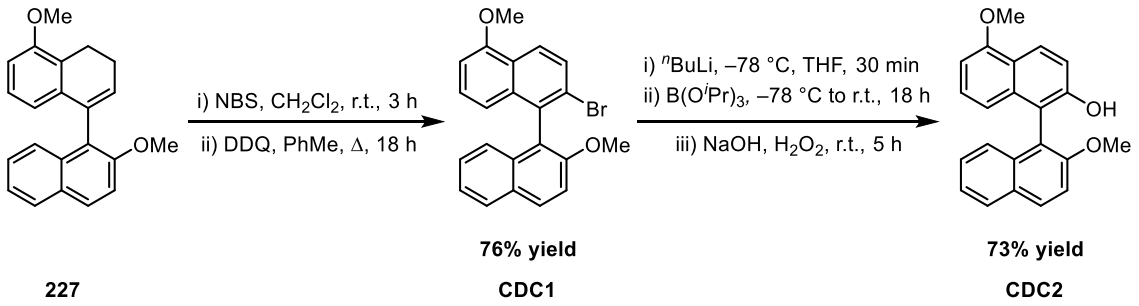
## 5.2. Substrate Synthesis

Next, we sought to synthesize a library of racemic MeBINOLs to investigate the effect of substitution about the MeBINOL starting materials on selectivity and conversion. We reasoned that substituted MeBINOLs could be accessed by debenzylation of the racemic reference samples for the ketone *O*-alkylation work. This is still an ongoing process, and so far we have synthesized three substituted MeBINOLs using this approach (**Scheme 5.9.**).




**Scheme 5.9.** Debenzylation of BnMeBINOLs.

We sought to explore electron rich and electron withdring substrates, since we were unable to investigate these in the ketone *O*-alkylation work. Dr Craig Campbell (CDC) has shown that a methoxy substituted BINOL can be accessed from alkene **227** (**Scheme 5.10.**).

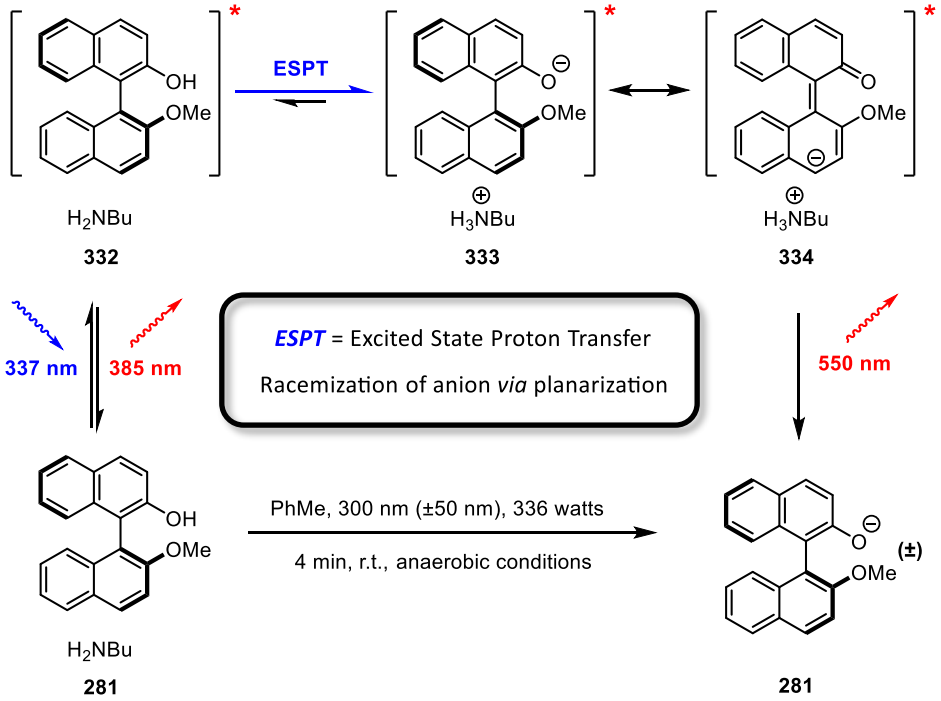



**Scheme 5.10.** Synthesis of an electron rich MeBINOL.

First, alkene was brominated to a vinyl bromide which was then oxidised with DDQ to bromoarene **CDC1**. Following lithium-halogen exchange, borylation, and rearrangement with hydrogen peroxide, racemic methoxy substituted MeBINOL **CDC2** was afforded in good yield. Using this approach, we intend to synthesize a library of MeBINOLS with highly electron withdrawing and donating substituents.

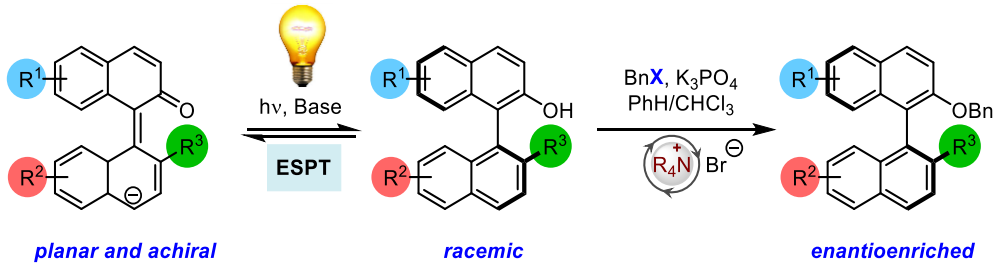
### 5.3. Dynamic Kinetic Resolution?

Next, we sought to establish whether it was possible to turn our protocol for the kinetic resolution of MeBINOL into a dynamic kinetic resolution. Therefore, it was crucial to develop a method which would rapidly interconvert the enantiomers of the racemic starting material. For example, this could occur by rotation about the biaryl bond. Achieving this under thermal conditions is unlikely to be compatible with enantioselective organocatalysis due to the high temperatures required to bring about biaryl bond rotation. There are however, reports in the literature which describe a photochemical approach to the room temperature racemization of MeBINOL (**Scheme 5.11.**).[106] Here, MeBINOL undergoes photoexcitation by irradiation with UV light. Subsequently the excited state **332** is deprotonated by an amine. This process is known as excited state proton transfer. Crucially, the excited state anion **333** is proposed to be planar and therefore achiral (**334**).




**Scheme 5.11.** Photoracemization of MeBINOL.

According to the authors complete photoracemization occurs within five minutes. Importantly, the authors report that doubly alkylated BINOL does not photo-racemize under these conditions. If the photoracemization process outlined above was coupled with our protocol for the kinetic resolution of MeBINOL then it is feasible that a dynamic kinetic resolution of MeBINOL could be achieved, if a stoichiometric amount of a benzylating agent was employed (**Scheme 5.12.**). In this scenario, the enantiomers of the starting material MeBINOL would rapidly interconvert by photoracemization.




**Scheme 5.12.** Proposed photo-mediated dynamic kinetic resolution of MeBINOL.

In a subsequent alkylation, only one enantiomer of MeBINOL would be preferentially alkylated. Crucially once alkylated, MeBnBINOL would photoracemize under these conditions. It should be

noted that benzyl iodide may not be compatible with this process due to photo-mediated homolytic cleavage of the *C-I* bond, which in turn could lead to deleterious radical side reactions. Therefore, alkylating agents such as dibenzyl sulfate, or benzyl tosylate may be more appropriate.

As a starting point, we sought to establish whether photoracemization of MeBINOL could be achieved under phase-transfer conditions. Unfortunately, the only UV Lamp available to us did not possess an emission maximum at or near 337 nm (**Figure 5.13.**).

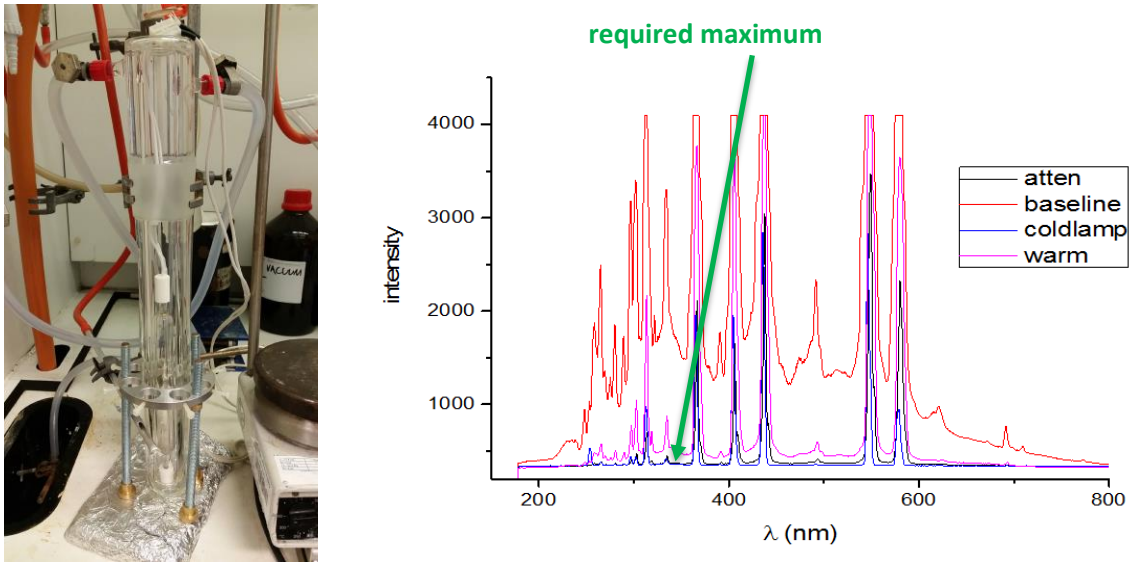
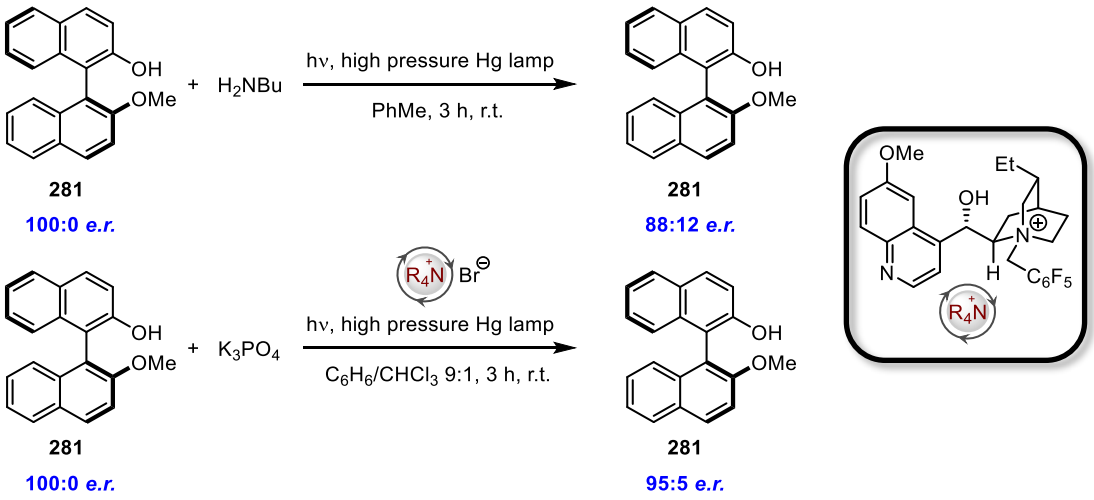


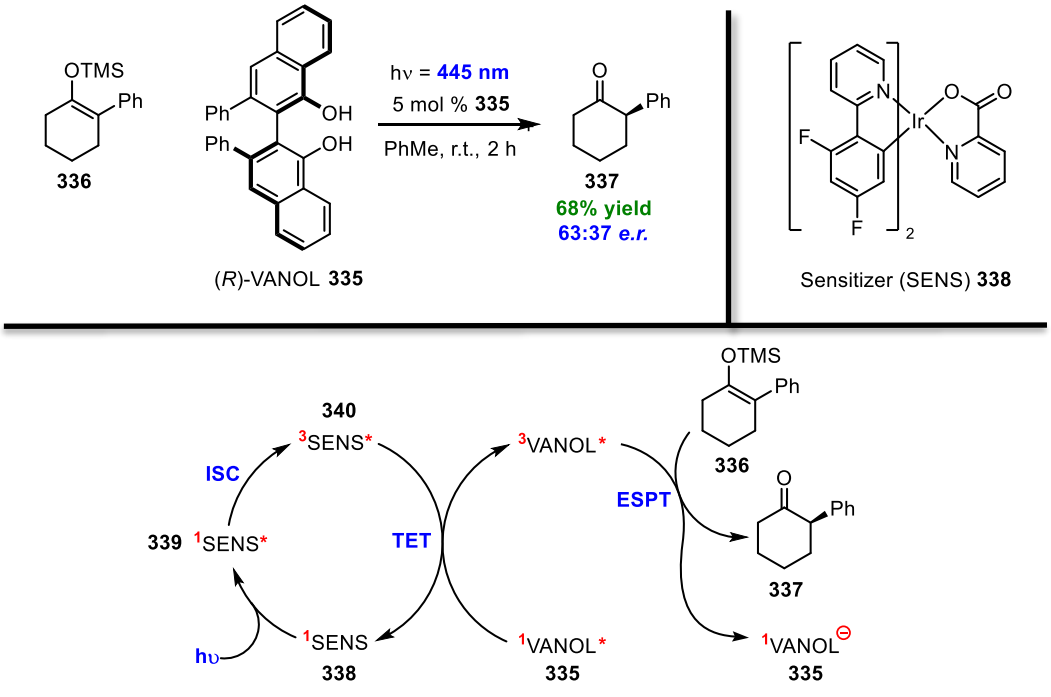

**Figure 5.13.** Available photo-reactor.

Nevertheless, we subjected enantiopure (*S*)-MeBINOL **281** to the conditions in **Scheme 5.11.**, and our reaction conditions for kinetic resolution, omitting benzyl iodide (**Scheme 5.14.**). We were pleased to observe some photoracemization under the literature conditions, albeit at a decreased rate. More importantly, we observed an erosion in *e.r.* while irradiating **281** under phase-transfer conditions. Whilst the rate of racemization is still too slow to be compatible with a dynamic kinetic resolution, the rate of racemization should increase when a photoreactor with an emission maximum closer to 337 nm is employed. It may also be beneficial to use aqueous base instead of solid base to minimise any photon attenuation by the solid base.




**Scheme 5.14.** Photoracemization of MeBINOL.

In an ideal scenario, the photoracemization of MeBINOL would be achieved with visible light, since UV light can have mutagenic effects and thus often requires elaborate shielding of the reaction setup. Since visible light is insufficient to photoexcite MeBINOL, an alternative method to promote MeBINOL to its excited state would be required.

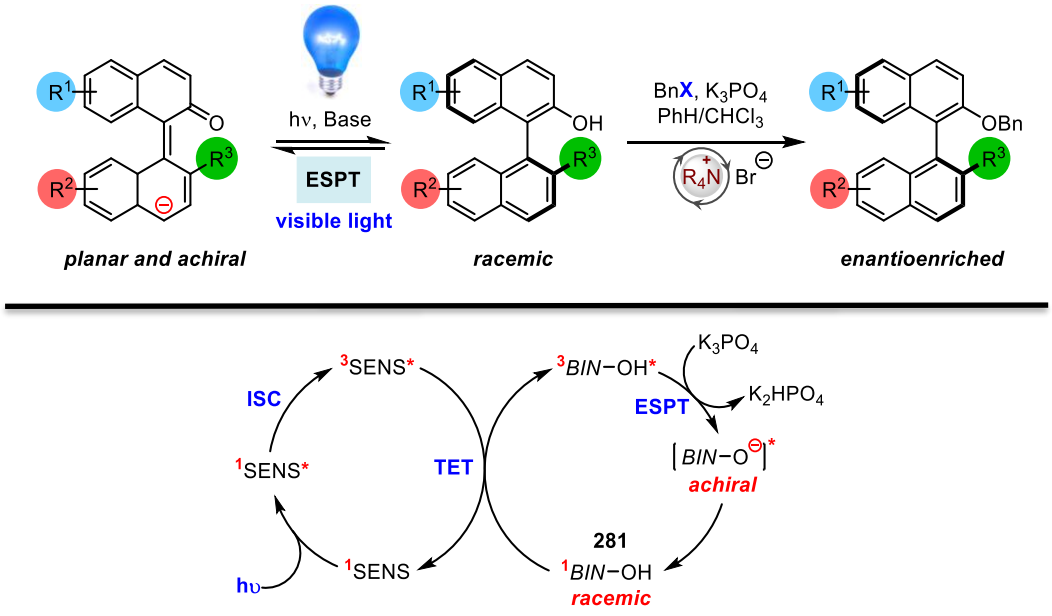



**Scheme 5.15.** Excited state proton transfer by triplet state energy transfer.

A publication by Hanson *et al*. employs ESPT to enantioselectively protonate a silyl enol ether (**Scheme 5.15.**).[107] The excited triplet state of the axially chiral diol VANOL **335** preferentially

protonates one face of silyl enol ether **336** to furnish ketone **337**. The triplet state of VANOL is not accessed by irradiative singlet excitation and subsequent intersystem crossing (ISC). Rather it is promoted to its triplet state by triplet energy transfer (TET) from a sensitizer **338**. First, sensitizer **338** is irradiated with visible light to promote it to its singlet excited state **339**. Subsequently ISC occurs to furnish the triplet state **340**. Triplet state **340** can then return to the singlet ground state **338** by TET to VANOL **335**, thus turning over the photo-catalyst **338**. The authors attempted to employ a catalytic amount of diol, however every sacrificial proton source to protonate **336** also protonated silyl enol ether non-enantioselectively. Interestingly, the authors observed no enantioselectivity when BINOL **168** was employed as the proton source. More importantly they attribute this to photoracemization of BINOL **168** *via* ESPT.

Consequently, we propose that a photo-mediated dynamic kinetic resolution of MeBINOL using visible light could be achieved by use of a photoredox catalyst to access the triplet state of MeBINOL *via* TET, which in turn can photoracemize by ESPT (**Scheme 5.16.**). Alternatively, the photoracemization process could be coupled with established protocols for the kinetic resolution of BINOL derivatives (**Schemes 1.25.** and **1.26.**).



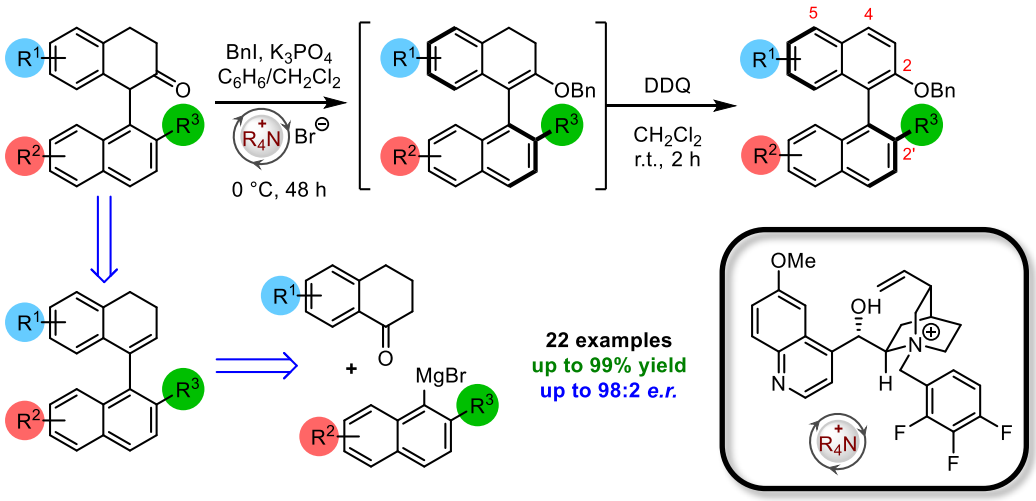

**Scheme 5.16.** Proposed photo-mediated dynamic kinetic resolution involving TET induced ESPT photoracemization.

# 6. Conclusions and Future Work

## 6.1. Conclusion

The thesis has focused on the development of cation-directed approaches to the atropselective synthesis of BINOL derivatives.

The first approach, described in chapter three, involved the phase-transfer mediated atropselective *O*-alkylation of ketones to furnish axially chiral enol ethers which in turn were oxidised to BINOL derivatives without compromising yield or enantioselectivity (**Scheme 6.1.**). A quinidine derived ammonium salt was employed as a chiral phase-transfer catalyst and 22 BINOL derivatives were synthesized in enantiomeric ratios of up to 98:2 and yields of up to 99%.

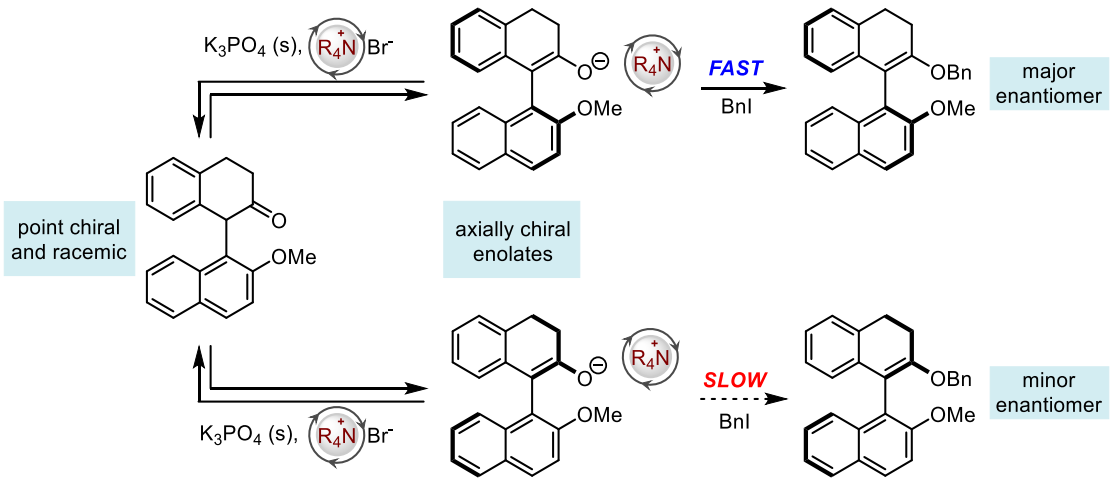



**Scheme 6.1.** Organocatalytic enantioslective synthesis of BINOL derivatives by *O*-alkylation of Ketones.

The prerequisite 2-tetralones were accessed from intermediate alkenes by an epoxidation/Meinwald rearrangement sequence. The alkenes in turn could be synthesized by additions of naphthyl derived Grignard reagents to 1-tetralones, to furnish a tertiary alcohol, which subsequently eliminated to the desired alkenes upon acidic workup.

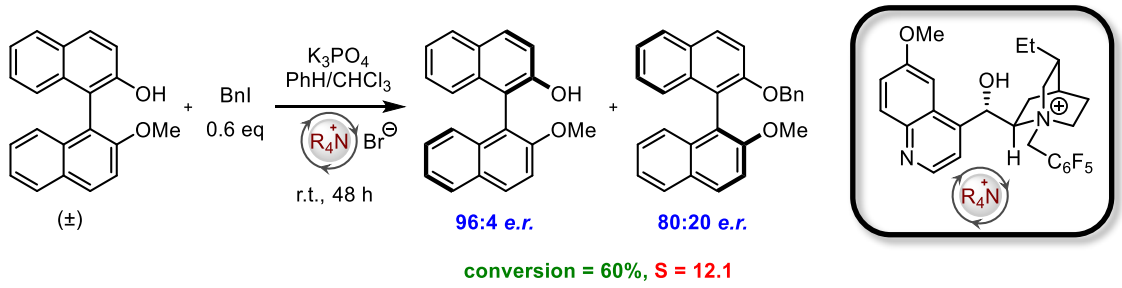
We have demonstrated that the products could be selectively mono- or globally deprotected. In addition to this, we carried out diastereoselective derivatization of the products including a transformation with axial to point chirality transfer.

In chapter four the mechanistic possibilities of the atropselective *O*-alkylation were explored. The reaction likely proceeds by a dynamic kinetic resolution of diastereomeric ammonium enolates (**Scheme 6.2.**). We were also able to demonstrate experimentally that the enolates undergo rapid interconversion by protonation-deprotonation at a rate orders of magnitude faster than alkylation of the enolate.




**Scheme 6.2.** Dynamic kinetic resolution of ammonium enolates.

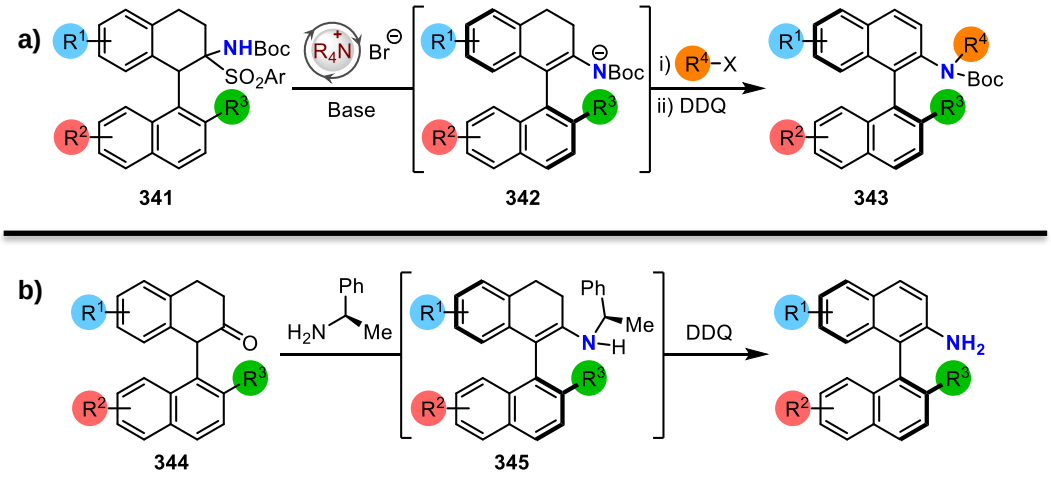
In chapter five, we demonstrated that by employing a substoichiometric amount of alkylating agent the reaction conditions for atropselective ketone *O*-alkylation can be employed to achieve the kinetic resolution of mono-methylated BINOL (**Scheme 6.3.**). After optimising the reaction conditions, we established a reaction protocol which furnishes MeBINOL with very good enantioselectivity. Finally, we have outlined how we intend to achieve a dynamic kinetic resolution of MeBINOL by photochemical means.




**Scheme 6.3.** Kinetic resolution of MeBINOL.

## 6.2. Future Work

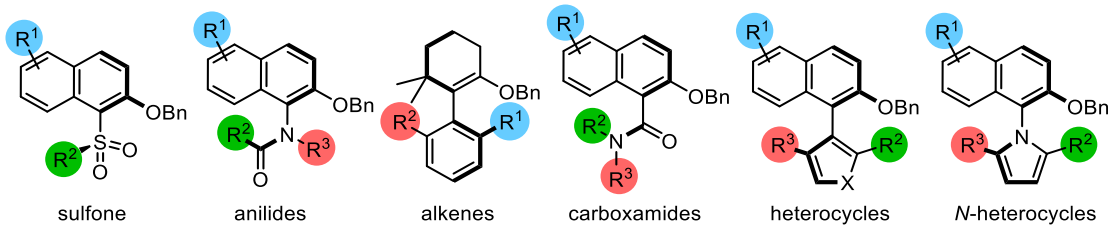
Whilst this thesis has focused on the atropselective synthesis of BINOL derivatives, it would be valuable to establish whether our methodology can be applied to the syntheses of NOBIN and BINAM derivatives by atropselective *N*-alkylation (**Scheme 6.4.a**). Synthesizing and isolating the requisite imine may prove challenging, however it is possible to generate an imine *in situ* under phase-transfer conditions by use of a sulfonyl imine **341**.[108-109] Under phase-transfer conditions **341** would be deprotonated twice to furnish axially chiral enamide **342** which could be atropselectively *N*-alkylated. Oxidation with DDQ would furnish the desired BINAM or NOBIN derivatives **343**.




**Scheme 6.4.** Atropselective synthesis of BINAM and NOBIN.

An alternate approach to the atropselective synthesis of NOBINs and BINAMS may be achievable by stochiometrically employing a chiral amine (**Scheme 6.4.b**). Here a chiral amine such as α-methyl benzylamine could diastereoselectively form enamine **345** from **344**, which could be subsequently oxidized and deprotected with DDQ to the corresponding NOBINs and BINAMS.

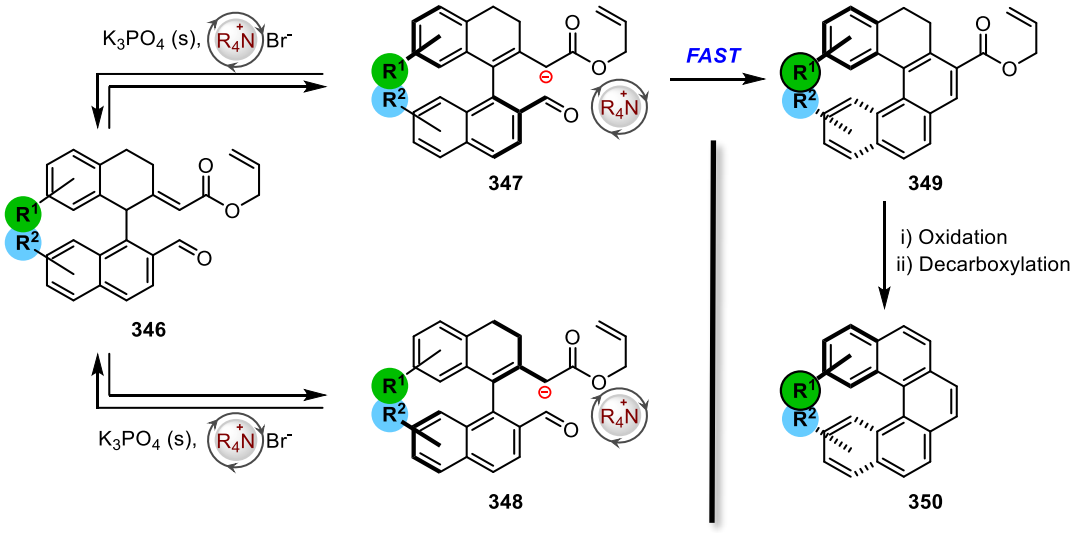
It would be important to establish whether atropselective *O*-alkylation could be employed to synthesize nonbiaryl and heterobiaryl atropisomers (**Scheme 6.5.**). Here the 2-methoxynaphthyl moiety would be substituted for a heteroaryl or non-aromatic group.




**Scheme 6.5.** Non-biaryl and heterobiaryl atropisomers as candidates for atropselective *O*-alkylation.

For these non-biaryl atropisomers it is likely that a different catalyst substrate interaction will be required to achieve high levels of enantioinduction and would therefore require extensive optimization for each new non-biaryl substrate.

In addition to the work currently being carried out by Jack Sutro (**Scheme 3.71.**), it would be interesting to see whether our methodology could be applied to install helical chirality (**Scheme 6.6.**).




**Scheme 6.6.** Atropselective synthesis of helicenes by intramolecular arene formation.

Inspired by Terada's and Sparr's work,[35-36] we propose that, upon γ-deprotonation, allyl ester **346** could form two diastereomeric ammonium enolates **347** and **348**. The counterion would then preferentially facilitate the intramolecular aldol condensation to **349**, which in turn could be oxidised and decarboxylated to helicene **350**.

# 7. Experimental

## 7.1. General Information

### *7.1.1. Naming and Numbering*

Compounds were named according to IUPAC nomenclature recommendations or according to known trivial names where appropriate.

IUPAC recommendations were not adhered to when numbering compounds, but a uniform numbering system was employed to allow the consistent assignment of spectra.

### *7.1.2. Reaction Conditions*

Reactions were carried out in flame-dried glassware under an atmosphere of argon unless stated otherwise. Room temperature refers to 20-25 °C. Temperatures of 0 °C were obtained using an ice/water bath. Temperatures of -78 °C were obtained using a dry ice/acetone bath. Reflux conditions were obtained using an oil bath or a Drysyn® heating block equipped with a contact thermometer. Temperatures of 0 °C or below which had to be maintained for extended periods of time were obtained using a Julabo FT902 immersion cooler.

### *7.1.3. Solvents*

Acetonitrile, dichloromethane, diethyl ether, methanol and tetrahydrofuran were purified by filtration through activated alumina columns employing the method of Grubbs *et al*.[110] Dimethylsulfoxide was purchased as an anhydrous solvent in a Sure/Seal™ bottle from Sigma-Aldrich. All other solvents were used as supplied without prior purification. Solvents for phase-transfer catalyzed reactions were degassed by freeze-pump-thawing as described by Perrin and Armarego.[111]

### *7.1.4. Reagents*

Anhydrous cerium(III) chloride was obtained by vigorously stirring cerium(III) chloride heptahydrate (purchased from Acros Organics) at 150 °C for 6 hours under vacuum (*c.a.*

0.1 mbar). $K_3PO_4$ was ground with a pestle and mortar prior to use in phase-transfer catalyzed reactions. Benzyl iodide was prepared according to the method of Kouklosky *et al*.[112] All other reagents were used directly as supplied by major chemical suppliers, or following purification procedures described by Perrin and Armarego.[111]

### *7.1.5. Chromatography*

Thin layer chromatography was performed on Merck Merck Kieselgel 60 $F_{254}$ 0.25 mm precoated aluminium plates. Product spots were visualized under UV light (λ = 254 nm) and/or by staining with potassium permanganate solution or vanillin solution. Flash chromatography was performed using VWR silica gel 60 (40-63 μm particle size) using head pressure by means of a nitrogen line.

### *7.1.6. Nuclear Magnetic Resonance Spectrometry*

NMR spectroscopy was carried out using Bruker Avance spectrometers in the deuterated solvent stated, using the residiual non-deuterated solvent signal as an internal reference. Chemical shifts are quoted in ppm with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (qn), sextet (sex), septet (sept), octet (oct), nonet (non) and multiplet (m). The abbreviation br. is to denote broad and app. to denote apparent. Coupling constants, *J*, are measured to the nearest 0.1 Hz and are presented as observed. All $^{19}$F-NMR spectra are proton decoupled unless stated otherwise. Assignment of spectra was assisted by the results of DEPT, COSY, HSQC and HMBC experiments.

### *7.1.7. Infrared Spectroscopy*

Infrared spectra were recorded neat on a Bruker Tensor 27 FTIR spectrometer equipped with an attenuated total reflectance attachment with internal calibration. Absorption maxima ($\lambda_{max}$) are quoted in wavenumbers ($cm^{-1}$).

### *7.1.8. Mass Spectrometry*

Low resolution mass spectra were recorded on a Micromass LCT Premier spectrometer under conditions of electrospray ionization (ESI). High resolution mass spectra were carried out using Bruker MicroTOF and Micromass GCT spectrometers under conditions of electrospray ionization (ESI), field ionization (FI) and chemical ionization (CI).

### *7.1.9. Polarimetry*

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). Concentrations are reported in g/100 mL. Temperatures are reported in °C.

### *7.1.10. Melting Points*

Melting points were determined using a Reichert melting point apparatus and are uncorrected.

### *7.1.11. HPLC*

Chiral HPLC was performed on a Dionex UltiMate 3000 system comprising a Dionex LPG-3400A pump, WPS-3000SL autosampler, TCC-3000SD column compartment, DAD-3000 diode-array detector, fitted with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm ø x 25 cm) and corresponding guard column (0.4 cm ø x 1 cm). Wavelengths (λ) are reported in nm, retention times ($t_R$) are reported in minutes and solvent flow rates are reported in mL $min^{-1}$.

### *7.1.12. X-ray Crystallography*

Single crystal X-ray diffraction experiments were carried out by myself under the supervision of Dr Amber Thompson and Dr Russel Driver on Oxford Diffraction Supernova and Nonius KappaCCD diffractometers in the Oxford Chemical Crystallography suite.

## 7.2. General Experimental Procedures

### *7.2.1. General Procedure A: Grignard Addition and Elimination*

According to modified literature procedures,[21, 113] a solution of the appropriate 1-tetralone (1.0 eq.) and anhydrous cerium chloride (2.0 eq.) in THF (10 mL $mmol^{-1}$ tetralone) was stirred at room temperature for 2 hours. After this time, a solution of the appropriate Grignard reagent (0.5 M in THF, 0.8-1.5 eq.) was added in one portion. The resulting mixture was stirred at room temperature for 2 hours and then 3M HCl (10 mL $mmol^{-1}$ tetralone) was added and the resulting mixture was stirred at room temperature for 30 minutes. The majority of the THF was removed under reduced pressure, and the remaining aqueous mixture was extracted three times with dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography (see experimental methods section for specific details) afforded the corresponding alkene product.

### *7.2.2. General Procedure B: Epoxidation and Rearrangement*

According to modified literature procedures,[62, 113] a stirred solution of alkene (1.0 eq.) in dichloro-methane (10 mL/mmol alkene) was cooled to 0 °C and sodium bicarbonate (2.5 eq.) and *meta*-chloroperbenzoic acid (75 % w/w, 2.0 eq.) were added sequentially. The resulting mixture was stirred at 0 °C for 1 hour and then saturated aqueous sodium thiosulfate was added. The organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed twice with saturated aqueous sodium thiosulfate, dried over anhydrous magnesium sulfate, filtered and the solution was concentrated until *c.a.* 5 mL of solvent remained. The residue was dissolved in 1:1 diethyl ether/dichloromethane (20 mL/mmol alkene) and boron trifluoride diethyl etherate (1.6 eq.) was added. The resulting solution was stirred at room temperature for 5 minutes and then saturated aqueous sodium bicarbonate was added. The organic phase was separated and the

aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed twice with saturated aqueous sodium bicarbonate, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography and/or recrystallization (see experimental methods section for specific details) afforded the corresponding 1-aryl-2-tetralone product.

### *7.2.3. General Procedure C: Asymmetric Phase-Transfer Catalyzed Alkylation Followed by DDQ Oxidation*

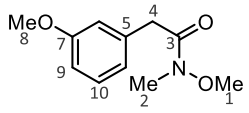
A Schlenk tube was sequentially charged with *N*-(2,3,4-trifluorobenzyl)quinidinium bromide **6** (0.10 eq.), *the appropriate 1-aryl-2-tetralone* (1.0 eq.) and $K_3PO_4$ (10 eq.). The atmosphere was evacuated and backfilled with argon three times. Dichloromethane (2 mL/mmol 1-aryl-2-tetralone) and benzene (3 mL/mmol 1-aryl-2-tetralone) were added. The suspension was cooled to 0 °C and stirred for 5 minutes. A solution of benzyl iodide in benzene (0.6 M, 3 eq.) was added and the suspension was stirred rapidly at a rate of 1000-1400 rpm in the dark at 0 °C for 48 hours. The crude reaction mixture was then filtered through a plug of celite which was subsequently washed with dichloromethane. The filtrate was concentrated under reduced pressure and dissolved in dichloromethane (10 mL/mmol 1-aryl-2-tetralone) and DDQ (3.0 eq.) was subsequently added. After stirring at room temperature for 2 hours, saturated aqueous sodium thiosulfate and ethyl acetate were added. The aqueous later was separated and the organic layer was washed twice with saturated aqueous sodium bicarbonate. The organic layer was then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residiue *via* column chromatography (see experimental methods section for specific details) afforded the corresponding enantioenriched BINOL derivative.

### *7.2.4. General Procedure D: Racemic Phase-Transfer Catalyzed Alkylation followed by DDQ Oxidation*

*The appropriate 1-aryl-2-tetralone* (1.0 eq.) and tetrabutylammonium bromide (0.10 eq.) were dissolved in dichloromethane (10 mL/mmol 1-aryl-2-tetralone) and benzyl bromide (3.0 eq.) and $K_3PO_4$ (10 eq.) were added sequentially. The suspension was stirred rapidly at a rate of 1000-1400 rpm for 18 hours. The crude reaction mixture was then filtered through a plug of celite which was subsequently washed with dichloromethane. The filtrate was concentrated under reduced pressure and dissolved in dichloromethane (10 mL/mmol 1-aryl-2-tetralone) and DDQ (3.0 eq.) was subsequently added. After stirring at room temperature for 2 hours, saturated aqueous sodium thiosulfate and ethyl acetate were added. The aqueous layer was separated and the organic layer was washed twice with saturated aqueous sodium bicarbonate. The organic layer was then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residiue *via* column chromatography (see experimental methods section for specific details) afforded the corresponding racemic BINOL derivative.

## 7.3. Experimental Procedures

### *N*-Methoxy-2-(3-methoxyphenyl)-*N*-methylacetamide, 110




**110**

According to a modified literature procedure,[114] DMF (52 µL, 0.50 mmol) was added to a solution of 3-methoxyphenylacetic acid (1.80 g, 10.0 mmol) in anhydrous toluene (20 mL) at 70 °C. Following this, thionyl chloride (0.88 mL, 12 mmol) was added and the reaction mixture was stirred for 3 h. After cooling to 0 °C, *N*,*O*-dimethylhydroxylamine hydrochloride (1.46 g, 15.0 mmol) was added. A solution of potassium carbonate (5.53 g, 40.0 mmol) in $H_2O$ (10 mL) was then added dropwise over 30 minutes. After the reaction mixture was allowed to warm to room temperature overnight, 2M HCl was added **CAREFULLY** in such a manner that effervescence was kept to a minimum. The biphasic mixture was then extracted twice with diethyl ether and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:3 ethyl acetate/petrol 40-60 afforded the title compound **110** as a yellow oil (1.58 g, 76 %). The spectral data matched that previously reported in the literature.[114]

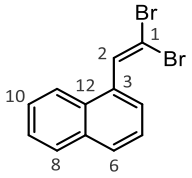
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.22 (dd, *J* = 7.9 Hz, 1H, $H_{10}$), 6.90-6.84 (m, 2H, $H_6$ and $H_{11}$), 6.79 (ddd, *J* = 8.3, 2.5, 0.8 Hz, 1H, $H_9$), 3.79 (s, 3H, $H_8$), 3.74 (s, 2H, $H_4$), 3.60 (s, 3H, $H_1$), 3.19 (s, 3H, $H_2$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 172.4 (Quat, $C_3$), 159.8(Quat, $C_7$), 136.5(Quat, $C_5$), 129.5 (CH, $C_{10}$), 121.8 (CH, $C_{11}$), 114.9 (CH, $C_6$), 112.5 (CH, $C_9$), 61.4 ($CH_3$, $C_8$), 55.3 ($CH_3$, $C_1$), 39.5($CH_2$, $C_4$), 32.3($CH_3$, $C_2$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3000, 2939, 2836, 1657, 1598, 1585, 1491, 1455, 1437, 1415, 1381, 1314, 1258, 1150, 1047, 1005;

LRMS (ESI$^+$): calculated for $C_{11}H_{16}NO_4^+$ = 210, mass found = 210.

**1-(2,2-Dibromovinyl)naphthalene, 114**




**114**

According to a modified literature procedure,[115] triphenylphosphine (8.20 g, 31.3 mmol) was added in portions over 5 minutes to a solution of carbon tetrabromide (5.20 g, 15.7 mmol) in anhydrous dichloromethane (30 mL) at 0 °C. Following this, the reaction mixture was stirred for 30 minutes and 1-naphthaldehyde (2.00 g, 12.8 mmol) was subsequently added. After stirring for 1 h at 0 °C, water (20 mL) and brine (20 mL) were added sequentially. The biphasic mixture was extracted three times with dichloromethane and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 0:1 dichloromethane/petrol 40-60 to 1:0 dichloromethane/petrol 40-60 afforded the title compound **114** as an off-white solid (4.01g, 99 %). The spectral data matched that previously reported in the literature. [115]

Melting point: 54-55 °C (petrol 40-60);

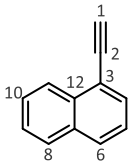
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.95-7.84 (m, 4H, $H_{Ar}$), 7.63-7.59 (m, 1H, $H_{Ar}$), 7.59-7.47 (m, 3H, $H_{Ar}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 136.0 (CH, $C_{Ar}$), 133.6 (Quat, $C_{Ar}$), 133.4 (Quat, $C_{Ar}$), 130.8 (Quat, $C_{Ar}$), 129.0 (CH, $C_{Ar}$), 128.7 (CH, $C_{Ar}$), 126.9 (CH, $C_{Ar}$), 126.7 (CH, $C_{Ar}$), 126.4 (CH, $C_{Ar}$), 125.4 (CH, $C_{Ar}$), 124.3 (CH, $C_{Ar}$), 93.1 (Quat, $C_1$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3057, 3008, 1593, 1506, 1394, 1277, 1251, 1237, 1212, 1015;

HRMS (EI$^+$): calculated for $C_{12}H_8Br_2^+$ = 309.8987, mass found = 309.8987.

**1-Ethynylnaphthalene, 112**




**112**

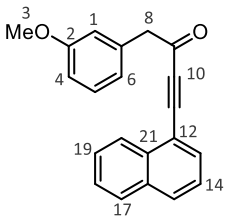
In analogy to a modified literature procedure,[116] *n*-butyllithium (1.6 M solution in hexanes, 9.6 mL, 15 mmol) was added dropwise over a period of 30 minutes *via* syringe pump to a solution of **114** (2.18 g, 7.00 mmol) in THF (20 mL) at -78 °C. After stirring for 45 minutes, the reaction mixture was warmed to 0 °C and stirred for 45 minutes. The reaction mixture was then re-cooled to -78 °C and saturated aqueous ammonium chloride (20 mL) was added dropwise over 10 minutes. After warming to room temperature, the biphasic mixture was extracted three times with diethyl ether. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to afford the title compound **112** as a yellow oil (1.14 g, 94 %). The spectral data matched that previously reported in the literature.[117]

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.38 (d, *J* = 8.4 Hz, 1H, $H_{11}$), 7.90-7.84 (m, 2H, $H_6$ and $H_8$), 7.76 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_4$), 7.60 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H, $H_{10}$), 7.54 (ddd, *J* = 8.1, 6.8, 1.4 Hz, 1H, $H_9$), 7.44 (dd, *J* = 8.3, 7.1 Hz, 1H, $H_5$), 3.49 (s, 1H, $H_1$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 133.6 (Quat, $C_{12}$ or $C_7$), 133.2 (Quat, $C_{12}$ or $C_7$), 131.4 (CH, $C_4$), 129.4 (CH, $C_6$), 128.4 (CH, $C_8$), 127.1 (CH, $C_{10}$), 126.6 (CH, $C_9$), 126.2 (CH, $C_{11}$), 125.2 (CH, $C_5$), 119.9 (Quat, $C_3$), 82.1 (CH, $C_1$), 81.9 (Quat, $C_2$);

FTIR (neat) $\nu/cm^{-1}$ = 3292, 3059, 3047, 3010, 2955, 2929, 2870, 2857, 2363, 2341, ,1587, 1509, 1458, 1419, 1376, 1301, 1217, 1206, 1168, 1069.

**1-(3-Methoxyphenyl)-4-(naphthalen-1-yl)but-3-yn-2-one, 113**




**113**

In analogy to a modified literature procedure,[114] *n*-butyllithium (1.6 M solution in hexanes, 4.43 mL, 7.10 mmol) was added to a solution of **112** (1.14 g, 6.60 mmol) in THF (30 mL) at -78 °C. The reaction mixture was stirred for 5 minutes and then subsequently stirred for an additional 45 minutes at room temperature. After cooling to -78 °C, a solution of **110** (1.06 g, 5.7 mmol) in THF (20 ml) was added over a period of 30 minutes *via* syringe pump. The reaction mixture was then warmed to 0 °C and stirred for 30 minutes. Following this, the reaction mixture was quenched with saturated aqueous ammonium chloride and extracted twice with diethyl ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:10 ethyl acetate/petrol 40-60 afforded the title compound **113** as an off-white solid (628 mg, 41 %).

Melting point: 56-58 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.96-7.90 (m, 2H, $H_{15}$ and $H_{20}$), 7.88-7.82 (m, 1H, $H_{17}$), 7.75 (dd, *J* = 7.2, 1.1 Hz, 1H, $H_{13}$), 7.56-7.51 (m, 2H, $H_{18}$ and $H_{19}$), 7.44 (dd, *J* = 8.3, 7.2 Hz, 1H, $H_{14}$), 7.34 (t, *J* = 7.9 Hz, 1H, $H_5$), 6.99 (d, *J* = 7.6 Hz, 1H, $H_6$), 6.96-6.93 (m, 1H, $H_1$), 6.92 (dd, *J* = 8.2, 2.4 Hz, 1H, $H_4$), 3.99 (s, 2H, $H_8$), 3.82 (s, 3H, $H_3$);

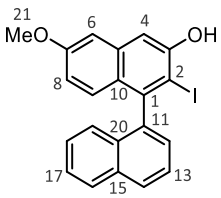
$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 185.3 (Quat, $C_9$), 160.1 (Quat, $C_2$), 134.9 (Quat, $C_7$), 133.7 (Quat, $C_{21}$), 133.6 (CH, $C_{13}$), 133.1 (Quat, $C_{16}$), 131.7 (CH, $C_{15}$), 130.0 (CH, $C_5$), 128.5 (CH, $C_{17}$), 127.7 (CH, $C_{19}$), 127.0 (CH, $C_{18}$), 125.9 (CH, $C_{20}$), 125.3 (CH, $C_{14}$), 122.5 (CH, $C_6$), 117.5 (Quat, $C_{12}$), 115.6 (CH, $C_1$), 113.3 (CH, $C_4$), 92.5 (Quat, $C_{10}$), 91.4 (CH, $C_{11}$), 55.4 ($CH_3$, $C_3$), 52.4 ($CH_2$, $C_8$);

FTIR (neat) $\nu/cm^{-1}$ = 3057, 3003, 2957, 2938, 2918, 2835, 2912, 1661, 1598, 1509, 1465, 1435, 1374, 1289, 1201, 1150, 1091, 1038, 1015;

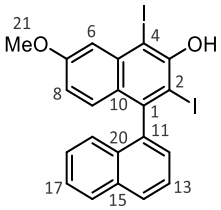
HRMS ($FI^+$): calculated for $C_{21}H_{16}O_2^+$ = 300.1150, mass found = 300.1152.

**2-Iodo-6-methoxy-[1,1'-binaphthalen]-3-ol, 115 &**

**2,4-Diiodo-6-methoxy-1,1'-binaphthalen]-3-ol, 116**




**115**




**116**

In analogy to a modified literature procedure,[46] sodium bicarbonate (126 mg, 1.5 mmol) and iodine (228 mg, 0.900 mmol) were sequentially added to a solution of **113** (91 mg, 0.30) in 1:1 dichloromethane/acetonitrile (3 mL). After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl

acetate/petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 afforded **115** as a white solid (101 mg, 79 %) along with **116** as a yellow solid (20.0 mg, 12 %).

Data for **115**:

Melting point: 157-159 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (dd, *J* = 8.3, 1.0 Hz, 1H, $H_{14}$), 7.97 (dt, *J* = 8.3, 0.9 Hz, 1H, $H_{16}$), 7.63 (dd, *J* = 8.3, 7.0 Hz, 1H, $H_{13}$), 7.50 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1H, $H_{17}$), 7.44 (s, 1H, $H_4$), 7.35 (dd, *J* = 7.0, 1.2 Hz, 1H, $H_{12}$), 7.31 (ddd, *J* = 8.1, 7.0, 1.4 Hz, 1H, $H_{18}$), 7.19 (dd, *J* = 8.5, 1.1 Hz, 1H, $H_{19}$), 7.08 (d, *J* = 2.6 Hz, 1H, $H_6$), 6.98 (d, *J* = 9.2 Hz, 1H, $H_9$), 6.74 (dd, *J* = 9.3, 2.6 Hz, 1H, $H_8$), 5.68 (s, 1H, O*H*), 3.91 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.7 (Quat, $C_7$), 151.9 (Quat, $C_3$), 144.5 (Quat, $C_1$), 141.0 (Quat, $C_{11}$), 136.2 (Quat, $C_{Ar}$), 133.8 (Quat, $C_{Ar}$), 131.7 (Quat, $C_{Ar}$), 129.1 (CH, $C_9$), 128.6 (CH, $C_{14}$), 128.5 (CH, $C_{16}$), 127.8 (CH, $C_{12}$), 126.6 (CH, $C_{18}$), 126.3 (CH, $C_{17}$), 125.7 (CH, $C_{13}$), 125.7 (CH, $C_{19}$), 125.0 (Quat, $C_{10}$), 117.3 (CH, $C_8$), 108.6 (CH, $C_4$), 104.6 (CH, $C_6$), 94.3 (Quat, $C_2$), 55.5 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3461, 3056, 3006, 2957, 2935, 2832, 1703, 1619, 1499, 1433, 1403, 1381, 1230, 1200, 1131, 1031;

HRMS ($EI^+$): calculated for $C_{21}H_{15}IO_2^+$ = 426.0111, mass found = 426.0115.

Data for **116**:

Melting point: dec. > 165 °C (ethyl acetate/petrol 40-60);

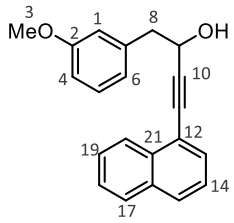
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.97 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.63 (dd, *J* = 8.2, 7.0 Hz, 1H, $H_{13}$), 7.50 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H, $H_{17}$), 7.45 (d, *J* = 2.5 Hz, 1H, $H_6$), 7.35-7.29 (m, 2H, $H_{12}$ and $H_{18}$), 7.17 (d, *J* = 8.4 Hz, 1H, $H_{19}$), 6.98 (d, *J* = 9.2 Hz, 1H, $H_9$), 6.74 (dd, *J* = 9.2, 2.5 Hz, 1H, $H_8$), 6.33 (s, 1H, O*H*), 3.97 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 160.4 (Quat, $C_7$), 151.7 (Quat, $C_3$), 145.7 (Quat, $C_1$), 140.6 (Quat, $C_{11}$), 136.7 (Quat, $C_5$), 133.8 (Quat, $C_{15}$), 131.6 (Quat, $C_{20}$), 130.2 (CH, $C_9$), 128.8 (CH, $C_{14}$), 128.5 (CH, $C_{16}$), 127.9 (CH, $C_{12}$), 126.8 (CH, $C_{18}$), 126.4 (CH, $C_{17}$), 125.7 (CH, $C_{13}$), 125.7 (CH, $C_{19}$), 125.1 (Quat, $C_{10}$), 117.5 (CH, $C_8$), 110.3 (CH, $C_6$), 89.9 (Quat, $C_2$), 82.4 (Quat, $C_4$), 55.6 ($CH_3$, $C_{21}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3444, 3056, 3005, 2956, 2917, 2849, 1699, 1615, 1498, 1462, 1372, 1354, 1258, 1237, 1222, 1132, 1036, 1021;

HRMS ($EI^+$): calculated for $C_{21}H_{14}I_2O_2^+$ = 551.9078, mass found = 551.9083.

**1-(3-Methoxyphenyl)-4-(naphthalen-1-yl)but-3-yn-2-ol, 114**




**114**

In analogy to a modified literature procedure,[118] sodium borohydride (152 mg, 4.00 mmol) was added to a solution of cerium(III) chloride heptahydrate (745 mg, 2.00 mmol) and **113** (300 mg, 1.00 mmol) in methanol (30 mL) at 0 °C. After stirring for 20 minutes at 0 °C, the reaction mixture was quenched **CAREFULLY** with saturated aqueous ammonium chloride. The reaction mixture was warmed to room temperature and the majority of methanol removed under reduced pressure. The biphasic mixture was then extracted three times with chloroform, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:5 ethyl acetate/petrol 40-60 afforded the title compound **114** as an off-white solid (285 mg, 84%).

Melting point: 60-62 °C (ethyl acetate/petrol 40-60);

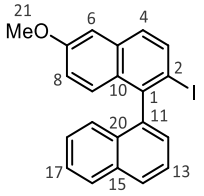
$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 8.18-8.13 (m, 1H, $H_{20}$), 7.87-7.80 (m, 2H, $H_{15}$ and $H_{17}$), 7.65 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_{13}$), 7.55-7.49 (m, 2H, $H_{18}$ and $H_{19}$), 7.41 (dd, *J* = 8.3, 7.1 Hz, 1H, $H_{14}$), 7.29 (dd, *J* = 8.3, 7.5 Hz, 1H, $H_5$), 6.99 (dt, *J* = 7.5, 1.2 Hz, 1H, $H_6$), 6.96 (dd, *J* = 2.6, 1.6 Hz, 1H, $H_1$), 6.86 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H, $H_4$), 5.00 (q, *J* = 6.0 Hz, 1H, $H_9$), 3.77 (s, 3H, $H_3$), 3.20 (d, *J* = 6.3 Hz, 2H, $H_8$), 2.20 (d, *J* = 5.1 Hz, 1H, O*H*);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 159.8 (Quat, $C_2$), 138.2 (Quat, $C_7$), 133.3 (Quat, $C_{16}$ or $C_{21}$), 133.2 (Quat, $C_{16}$ or $C_{21}$), 130.7 (CH, $C_{13}$), 129.6 (CH, $C_5$), 129.1 (CH, $C_{17}$), 128.3 (CH, $C_{15}$), 126.9 (CH, $C_{19}$), 126.5 (CH, $C_{18}$), 126.3 (CH, $C_{20}$), 125.3 (CH, $C_{14}$), 122.4 (CH, $C_6$), 120.2 (Quat, $C_{12}$), 115.6 (CH, $C_1$), 112.7 (CH, $C_4$), 94.4 (Quat, $C_{10}$), 84.1 (Quat, $C_{11}$), 64.0 (CH, $C_9$), 55.3 ($CH_3$, $C_3$), 44.4 ($CH_2$, $C_8$);

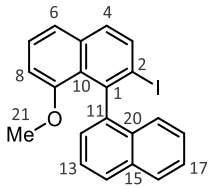
FTIR (neat) $\nu$/cm$^{-1}$ = 3395, 3057, 2950, 2937, 2924, 2835, 2378, 1601, 1585, 1507, 1490, 1464, 1454, 1436, 1377, 1334, 1316, 1258, 1218, 1190, 1053, 1040;

HRMS (EI$^+$): calculated for $C_{21}H_{18}O_2^+$ = 302.1301, mass found = 302.1307.

**2-Iodo-6-methoxy-1,1'-binaphthalene, 117 & 2-Iodo-8-methoxy-1,1'-binaphthalene, 118**




**117**




**118**

In analogy to a modified literature procedure,[46] sodium bicarbonate (34 mg, 0.40 mmol) and iodine (152 mg, 0.600 mmol) were sequentially added to a solution of **114** (60.4 mg, 0.200 mmol) in 1:1 dichloromethane/acetonitrile (2 mL). After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:19

dichloromethane/petrol 40-60 afforded **117** as a white solid (46.1 mg, 56 %) along with **118** as a white solid (9.4 mg, 10 %).

Data for **117**:

Melting point: 184-186 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (500 MHz, $C_6D_6$) $\delta_H$ = 7.95 (d, *J* = 8.7 Hz, 1H, $H_4$), 7.74 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.72 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.37 (dd, *J* = 7.8, 0.7 Hz, 1H, $H_{19}$), 7.35 (dd, *J* = 8.2, 7.0 Hz, 1H, $H_{13}$), 7.25 (d, *J* = 8.7 Hz, 1H, $H_3$), 7.23-7.19 (m, 2H, $H_{12}$ and $H_{17}$), 7.13 (d, *J* = 9.3 Hz, 1H, $H_9$), 7.05 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H, $H_{18}$), 6.88 (d, *J* = 2.6 Hz, 1H, $H_6$), 6.74 (dd, *J* = 9.3, 2.7 Hz, 1H, $H_8$), 3.32 (s, 3H, $H_{21}$);

$^{13}$C NMR (126 MHz, $C_6D_6$) $\delta_C$ = 158.4 (Quat, $C_7$), 143.4 (Quat, $C_1$), 141.5 (Quat, $C_{11}$), 136.5 (CH, $C_4$), 134.7 (Quat, $C_{10}$), 134.3 (Quat, $C_{20}$), 132.5 (Quat, $C_{15}$), 130.2 (Quat, $C_5$), 129.6 (CH, $C_9$), 128.7 (CH, $C_{14}$ or $C_{16}$), 128.6 (CH, $C_{14}$ or $C_{16}$), 128.6 (CH, $C_3$), 128.4 (CH, $C_{12}$ or $C_{17}$), 126.8 (CH, $C_{18}$), 126.4 (CH, $C_{19}$), 126.3 (CH, $C_{12}$ or $C_{17}$), 125.9 (CH, $C_{13}$), 119.9 (CH, $C_8$), 106.3 (CH, $C_6$), 96.6 (Quat, $C_2$), 54.8 ($CH_3$, $C_{21}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3056, 3007, 2962, 2943, 2924, 2844, 1638, 1615, 1583, 1563, 1467, 1458, 1413, 1388, 1371, 1365, 1313, 1226, 1178, 1130, 1066, 1023;

HRMS ($FI^+$): calculated for $C_{21}H_{15}OI^+$ = 410.0168, mass found = 410.0165.

Data for **118**:

Melting point: 123-125 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (500 MHz, $C_6D_6$) $\delta_H$ = 7.97 (d, *J* = 8.7 Hz, 1H, $H_4$), 7.76 (d, *J* = 7.2 Hz, 1H, $H_{16}$), 7.75 (d, *J* = 7.3 Hz, 1H, $H_{14}$), 7.40 (dd, *J* = 8.3, 1.1 Hz, 1H, $H_{19}$), 7.38 (dd, *J* = 8.2, 7.0 Hz, 1H, $H_{13}$), 7.28 (dd, *J* = 8.2, 1.1 Hz, 1H, $H_6$), 7.24 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H, $H_{17}$), 7.22 (d, *J* = 8.7 Hz, 1H, $H_3$), 7.18 (dd, *J* = 7.0, 1.2 Hz, 1H, $H_{12}$), 7.14 (dd, *J* = 8.2, 8.0 Hz, 1H, $H_7$), 7.06 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H, $H_{18}$), 6.25 (dd, *J* = 7.7, 1.1 Hz, 1H, $H_8$), 2.52 (s, 3H, $H_{21}$);

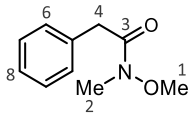
$^{13}$C NMR (126 MHz, $C_6D_6$) $\delta_C$ = 156.2 (Quat, $C_9$), 146.8 (Quat, $C_{11}$), 141.2 (Quat, $C_1$), 136.9 (CH, $C_4$), 135.6 (Quat, $C_{10}$), 133.7 (Quat, $C_{20}$), 132.9 (Quat, $C_{15}$), 129.5 (CH, $C_3$), 127.1 (CH, $C_{14}$), 127.1 (CH, $C_7$), 126.6 (Quat, $C_5$), 126.4 (CH, $C_{12}$), 126.3 (CH, $C_{18}$), 126.0 (CH, $C_{19}$), 125.7 (CH, $C_{17}$), 125.5 (CH, $C_{13}$), 121.3 (CH, $C_6$), 107.2 (CH, $C_8$), 102.4 (Quat, $C_2$), 55.2 ($CH_3$, $C_{21}$);

$C_{16}$ was not observed due to overlap with the residual solvent peak;

FTIR (neat) $\nu$/cm$^{-1}$ = 3051, 3002, 2955, 2930, 2831, 1613, 1592, 1580, 1558, 1506, 1452, 1430, 1422, 1395, 1346, 1310, 1260, 1172, 1104, 1016;

HRMS (FI$^+$): calculated for $C_{21}H_{15}OI^+$ = 410.0168, mass found = 410.0168.

**_N_-Methoxy-_N_-methyl-2-phenylacetamide, 121**




**121**

According to a modified literature procedure,[114] DMF (0.11 mL, 1.00 mmol) was added to a solution of phenylacetic acid (2.73 g, 20.0 mmol) in anhydrous toluene (40 mL) at 70 °C. Following this, thionyl chloride (1.75 mL, 24.0 mmol) was added and the reaction mixture was stirred for 3 h. After cooling to 0 °C, *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) was added. A solution of potassium carbonate (11.1 g, 80.0 mmol) in $H_2O$ (20 mL) was then added dropwise over 30 minutes. After the reaction mixture was allowed to warm to room temperature overnight, 2M HCl was added **CAREFULLY** in such a manner that effervescence was kept to a minimum. The biphasic mixture was then extracted twice with diethyl ether and the combined organic extracts dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:2 ethyl acetate/petrol 40-60 to 1:0 ethyl

acetate/petrol 40-60 afforded the title compound **121** as a yellow oil (3.26 g, 83 %). The spectral data matched that previously reported in the literature.[119]

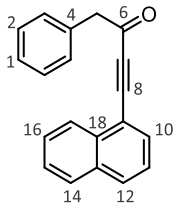
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.35-7.27 (m, 4H, $H_6$ and $H_7$), 7.26-7.21 (m, 1H, $H_8$), 3.77 (s, 2H, $H_4$), 3.60 (s, 3H, $H_1$), 3.19 (s, 3H, $H_2$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 172.5 (Quat, $C_3$), 135.0 (Quat, $C_5$), 129.4 (CH, $C_6$ or $C_7$), 128.6 (CH, $C_6$ or $C_7$), 126.9 (CH, $C_8$), 61.4 ($CH_3$, $C_1$), 39.5 ($CH_2$, $C_4$), 32.3 ($CH_3$, $C_2$);

FTIR (neat) $\nu$/cm$^{-1}$ =3087, 3063, 3030, 3002, 2970, 2938, 2904, 2821, 1656, 1603, 1584, 1496, 1455, 1382, 1173, 1097, 1030, 1000;

LRMS (ESI$^+$): calculated for $C_{10}H_{14}NO_2^+$ = 180, mass found = 180.

**4-(Naphthalen-1-yl)-1-phenylbut-3-yn-2-one, 119**




**119**

In analogy to a modified literature procedure,[114] *n*-butyllithium (1.6 M solution in hexanes, 3.60 mL, 5.70 mmol) was added to a solution of **112** (866 mg, 5.23 mmol) in THF (30 mL) at -78 °C. The reaction mixture was stirred for 5 minutes and then subsequently stirred for an additional 45 minutes at room temperature. After cooling to -78 °C, a solution of **121** (851 mg, 4.75 mmol) in THF (20 ml) was added over a period of 30 minutes *via* syringe pump. The reaction mixture was then warmed to 0 °C and stirred for 30 minutes. Following this, the reaction mixture was quenched with saturated aqueous ammonium chloride and extracted twice with diethyl ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the

residue *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **119** as a yellow oil (351 mg, 27 %). The spectral data matched that previously reported in the literature.[120]

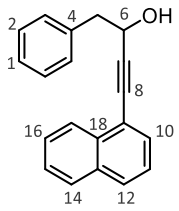
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.93 (d, *J* = 8.3 Hz, 1H, $H_{12}$), 7.91-7.83 (m, 2H, $H_{14}$ and $H_{17}$), 7.74 (dd, *J* = 7.2, 1.2 Hz, 1H, $H_{10}$), 7.56-7.50 (m, 2H, $H_{15}$ and $H_{16}$), 7.47-7.34 (m, 6H, $H_1$, $H_2$, $H_3$ and $H_{11}$), 4.02 (s, 2H, $H_5$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 185.5 (Quat, $C_6$), 133.7 (Quat, $C_{Ar}$), 133.5 (Quat, $C_{Ar}$), 133.5 (CH, $C_{10}$), 133.1 (Quat, $C_{Ar}$), 131.7 (CH, $C_{12}$), 130.2 (CH, $C_3$), 129.0 (CH, $C_2$), 128.6 (CH, $C_{14}$), 127.7 (CH, $C_{15}$ or $C_{16}$), 127.6 (CH, $C_1$), 127.0 (CH, $C_{15}$ or $C_{16}$), 125.9 (CH, $C_{17}$), 125.3 (CH, $C_{11}$), 117.5 (CH, $C_9$), 92.5 (Quat, $C_7$ or $C_8$), 91.5 (Quat, $C_7$ or $C_8$), 52.4 ($CH_2$, $C_5$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 3030, 2192, 2171, 1659, 1600, 1585, 1575, 1509, 1496, 1454, 1374, 1336, 1291, 1251, 1193, 1114, 1064, 1015, 1003;

LRMS (ESI$^+$): calculated for $C_{20}H_{15}O^+$ = 271, mass found = 271.

**4-(Naphthalen-1-yl)-1-phenylbut-3-yn-2-ol, 120**




**120**

In analogy to a modified literature procedure,[118] sodium borohydride (152 mg, 4.00 mmol) was added to a solution of cerium(III) chloride heptahydrate (745 mg, 2.00 mmol) and **119** (270 mg, 1.00 mmol) in 9:1 methanol/dichloromethane (30 mL) at 0 °C. After stirring for 20 minutes at 0 °C, the reaction mixture was quenched **CAREFULLY** with saturated aqueous ammonium chloride. The reaction mixture was warmed to room temperature and the majority of methanol

removed under reduced pressure. The biphasic mixture was then extracted three times with chloroform, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure affording the title compound **120** as a yellow solid (268 mg, 98%).

Melting point: 79-80 °C (methanol/chloroform);

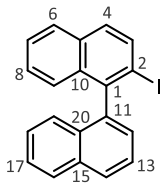
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.19-8.09 (m, 1H, $H_{17}$), 7.87-7.81 (m, 2H, $H_{12}$ and $H_{14}$), 7.65 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_{10}$), 7.55-7.49 (m, 2H, $H_{15}$ and $H_{16}$), 7.45-7.35 (m, 5H, $H_2$, $H_3$ and $H_{11}$), 7.34-7.29 (m, 1H, $H_1$), 5.00 (q, *J* = 6.0 Hz, 1H, $H_6$), 3.23 (d, *J* = 6.4 Hz, 2H, $H_5$), 2.18 (d, *J* = 5.7 Hz, 1H, O*H*);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 136.7 (Quat, $C_4$), 133.3 (Quat, $C_{13}$ or $C_{18}$), 133.2 (Quat, $C_{13}$ or $C_{18}$), 130.6 (CH, $C_{10}$), 130.1 (CH, $C_3$), 129.0 (CH, $C_{12}$ or $C_{14}$), 128.6 (CH, $C_2$), 128.3 (CH, $C_{12}$ or $C_{14}$), 127.1 (CH, $C_1$), 126.9 (CH, $C_{15}$ or $C_{16}$), 126.5 (CH, $C_{15}$ or $C_{16}$), 126.3 (CH, $C_{17}$), 125.3 (CH, $C_{11}$), 120.2 (Quat, $C_9$), 94.3 (Quat, $C_7$), 84.1 (Quat, $C_8$), 64.1 (CH, $C_6$), 44.4 ($CH_2$, $C_5$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3511, 3344, 3059, 3046, 3030, 2949, 2924, 2858, 2223, 1602, 1586, 1507, 1454, 1434, 1396, 1377, 1276, 1242, 1206, 1178, 1144, 1100, 1031;

HRMS (EI$^+$): calculated for $C_{20}H_{16}O^+$ = 272.1196, mass found = 272.1201.

**2-Iodo-1,1'-binaphthalene, 123**




**123**

In analogy to a modified literature procedure,[46] sodium bicarbonate (33.6 mg, 0.400 mmol) and iodine (152 mg, 0.600 mmol) were sequentially added to a solution of **120** (54.5 mg, 0.200 mmol) in 1:1 dichloromethane/acetonitrile (2 mL). After stirring at room temperature for

1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:19 dichloromethane/petrol 40-60 afforded **123** as a white solid (45.3 mg, 60 %). The spectral data matched that previously reported in the literature.[121]

Melting point: 118-120 °C (dichloromethane/petrol 40-60);

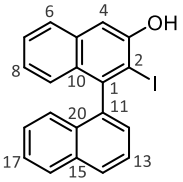
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.83 (d, *J* = 8.7 Hz, 1H, $H_4$), 7.79 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.76 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.68 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.46 (d, *J* = 8.7 Hz, 1H, $H_3$), 7.42 (dd, *J* = 8.3, 7.0 Hz, 1H, $H_{13}$), 7.31-7.23 (m, 2H, $H_7$ and $H_{17}$), 7.16 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_{12}$), 7.10 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_8$), 7.06-6.94 (m, 3H, $H_9$, $H_{18}$, $H_{19}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 142.9 (Quat, $C_1$ or $C_{11}$), 141.0 (Quat, $C_1$ or $C_{11}$), 135.7 (CH, $C_4$), 134.1 (Quat, $C_{10}$ or $C_{20}$), 133.8 (Quat, $C_{10}$ or $C_{20}$), 132.9 (Quat, $C_5$ or $C_{15}$), 131.9 (Quat, $C_5$ or $C_{15}$), 129.4 (CH, $C_3$), 128.5 (CH, $C_6$ or $C_{14}$), 128.5 (CH, $C_6$ or $C_{14}$), 128.1 (CH, $C_{12}$ or $C_{16}$), 128.0 (CH, $C_{12}$ or $C_{16}$), 127.4 (CH, $C_{Ar}$), 127.0 (CH, $C_{Ar}$), 126.5 (CH, $C_{Ar}$), 126.4 (CH, $C_{Ar}$), 126.2 (CH, $C_{Ar}$), 125.9 (CH, $C_{Ar}$), 125.7 (CH, $C_{Ar}$), 99.8 (CH, $C_{13}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3054, 2924, 2852, 1615, 1592, 1561, 1499, 1421, 1403, 1337, 1308, 1272, 1233, 1212, 1181, 1161, 1144, 1133, 1104, 1040, 1016;

HRMS (EI$^+$): calculated for $C_{20}H_{13}I^+$ = 380.0056, mass found = 380.0050.

**2-Iodo-[1,1'-binaphthalen]-3-ol, 122**




**122**

In analogy to a modified literature procedure,[46] sodium bicarbonate (126 mg, 1.50 mmol) and iodine (254 mg, 1.00 mmol) were sequentially added to a solution of **119** (134 mg, 0.500 mmol) in 1:1 dichloromethane/acetonitrile (2 mL). After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:5 ethyl acetate/petrol 40-60 afforded **122** as a white solid (115 mg, 58 %).

Melting point: 59-60 °C (ethyl acetate/petrol 40-60);

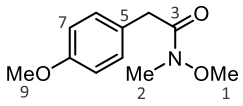
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.03 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.98 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.80 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.64 (dd, *J* = 8.3, 7.0 Hz, 1H, $H_{13}$), 7.54 (s, 1H, $H_4$), 7.50 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H, $H_{17}$), 7.44 (ddd, *J* = 8.2, 4.6, 3.3 Hz, 1H, $H_7$), 7.37 (dd, *J* = 7.0, 1.2 Hz, 1H, $H_{12}$), 7.32 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_{18}$), 7.19 (dd, *J* = 8.5, 0.9 Hz, 1H, $H_8$), 7.11-7.08 (m, 2H, $H_{19}$ and $H_9$), 5.72 (s, 1H, O*H*);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 151.3 (Quat, $C_3$), 144.8 (Quat, $C_{Ar}$), 141.0 (Quat, $C_{Ar}$), 134.7 (Quat, $C_{Ar}$), 133.8 (Quat, $C_{Ar}$), 131.7 (Quat, $C_{Ar}$), 129.3 (Quat, $C_{Ar}$), 128.7 (CH, $C_{14}$ or $C_{16}$), 128.5 (CH, $C_{14}$ or $C_{16}$), 127.9 (CH, $C_{12}$), 127.5 (CH, $C_8$ or $C_9$), 127.3 (CH, $C_7$), 126.8 (CH, $C_6$), 126.7 (CH, $C_{18}$), 126.3 (CH, $C_{17}$), 125.7 (CH, $C_{13}$), 125.7 (CH, $C_{19}$), 124.6 (CH, $C_8$ or $C_9$), 109.3 (CH, $C_4$), 98.0 (Quat, $C_2$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3463, 3056, 3010, 2928, 1703, 1663, 1616, 1562, 1505, 1463, 1444, 1374, 1329, 1256, 1230, 1174, 1072, 1016, 1004;

HRMS (ESI$^-$): calculated for $C_{20}H_{12}IO^-$ = 394.9938, mass found = 394.9936.

**_N_-Methoxy-2-(4-methoxyphenyl)-_N_-methylacetamide, 127**




**127**

According to a modified literature procedure,[114] DMF (0.11 mL, 1.0 mmol) was added to a solution of 4-methoxyphenylacetic acid (3.60 g, 20.0 mmol) in anhydrous toluene (40 mL) at 70 °C. Following this, thionyl chloride (1.75 mL, 24.0 mmol) was added and the reaction mixture was stirred for 3 h. After cooling to 0 °C, *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol) was added. A solution of potassium carbonate (11.1 g, 80.0 mmol) in $H_2O$ (20 mL) was then added dropwise over 30 minutes. After the reaction mixture was allowed to warm to room temperature overnight, 2M HCl was added **CAREFULLY** in such a manner that effervescence was kept to a minimum. The biphasic mixture was then extracted twice with diethyl ether and the combined organic extracts dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure affording the title compound **127** as an off-white solid (4.18 g, 99 %). The spectral data matched that previously reported in the literature.[122]

Melting point: 47-49 °C (ethyl acetate/petrol 40-60);

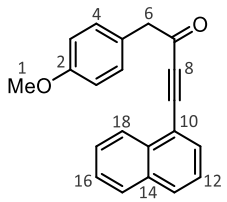
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.24-7.18 (m, 2H, $H_6$), 6.88-6.82 (m, 2H, $H_7$), 3.78 (s, 3H, $H_9$), 3.70 (s, 2H, $H_4$), 3.61 (s, 3H, $H_1$), 3.18 (s, 3H, $H_2$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 172.8, (Quat, $C_3$), 158.6 (Quat, $C_8$), 130.4 (CH, $C_6$), 127.1 (Quat, $C_5$), 114.0 (CH, $C_7$), 61.4 ($CH_3$, $C_9$), 55.4 ($CH_3$, $C_1$), 38.6 ($CH_2$, $C_4$), 32 ($CH_3$, $C_2$).

FTIR (neat) $\nu$/cm$^{-1}$ = 2998, 2938, 2836, 1656, 1612, 1585, 1511, 1462, 1441, 1411, 1381, 1301, 1245, 1110, 1032, 1003;

LRMS (ESI$^+$): calculated for $C_{11}H_{16}NO_3^+$ = 210, mass found = 210.

**1-(4-Methoxyphenyl)-4-(naphthalen-1-yl)but-3-yn-2-one, 124**




**124**

In analogy to a modified literature procedure,[114] *n*-butyllithium (1.6 M solution in hexanes, 7.80 mL, 12.5 mmol) was added to a solution of **114** (1.56 g, 5.00 mmol) in THF (10 mL) at -78 °C. The reaction mixture was stirred for 5 minutes and then subsequently stirred for an additional 45 minutes at 0 °C. After cooling to -78 °C, a solution of **127** (1.67 g, 8.00 mmol) in THF (15 ml) was added over a period of 30 minutes *via* syringe pump. The reaction mixture was then warmed to 0 °C and stirred for 30 minutes. Following this, the reaction mixture was quenched with saturated aqueous ammonium chloride and extracted twice with diethyl ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 1:5 ethyl acetate/petrol 40-60 afforded the title compound **124** as an off-white solid (1.11 g, 74 %).

Melting point: 65-66 °C (ethyl acetate/petrol 40-60);

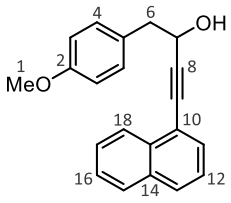
$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.93 (dd, *J* = 8.2, 1.1 Hz, 1H, $H_{13}$), 7.91-7.88 (m, 1H, $H_{18}$), 7.87-7.83 (m, 1H, $H_{15}$), 7.75 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_{11}$), 7.57-7.49 (m, 2H, $H_{16}$ and $H_{17}$), 7.44 (dd, *J* = 8.3, 7.2 Hz, 1H, $H_{12}$), 7.34-7.28 (m, 2H, $H_4$), 7.00-6.91 (m, 2H, $H_3$), 3.96 (s, 2H, $H_6$), 3.83 (s, 3H, $H_1$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 185.9 (Quat, $C_7$), 159.2 (Quat, $C_2$), 133.7 (Quat, $C_{19}$), 133.5 (CH, $C_{11}$), 133.1 (Quat, $C_{14}$), 131.7 (CH, $C_{13}$), 131.2 (CH, $C_4$), 128.5 (CH, $C_{15}$), 127.6 (CH, $C_{16}$ or $C_{17}$), 127.0 (CH, $C_{16}$ or $C_{17}$), 125.9 (CH, $C_{18}$), 125.6 (Quat, $C_5$), 125.3 (CH, $C_{12}$), 117.6 (Quat, $C_{10}$), 114.5 (CH, $C_3$), 92.5 (Quat, $C_8$), 91.3 (Quat, $C_9$), 55.4 ($CH_3$, $C_1$), 51.5 ($CH_3$, $C_6$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3002, 2955, 2934, 2906, 2835, 2191, 1660, 1611, 1510, 1463, 1422, 1374, 1291, 1177, 1115, 1032;

HRMS (EI$^+$): calculated for $C_{21}H_{16}O_2^+$ = 300.1145, mass found = 300.1142.

**1-(4-Methoxyphenyl)-4-(naphthalen-1-yl)but-3-yn-2-ol, 125**




**125**

In analogy to a modified literature procedure,[118] sodium borohydride (152 mg, 4.00 mmol) was added to a solution of cerium(III) chloride heptahydrate (745 mg, 2.00 mmol) and **124** (300 mg, 1.00 mmol) in 9:1 methanol/dichloromethane (30 mL) at 0 °C. After stirring for 20 minutes at 0 °C, the reaction mixture was quenched **CAREFULLY** with saturated aqueous ammonium chloride. The reaction mixture was warmed to room temperature and the majority of methanol removed under reduced pressure. The biphasic mixture was then extracted three times with chloroform, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure affording the title compound **125** as an off-white solid (302 mg, 99%). An analytical amount of enantiopure **125** was obtained via semi-preparative chiral HPLC.

Melting point: 48-50 °C (methanol/chloroform);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.22-8.14 (m, 1H, $H_{18}$), 7.90-7.78 (m, 2H, $H_{13}$ and $H_{15}$), 7.66 (dd, *J* = 7.2, 1.2 Hz, 1H, $H_{11}$), 7.58-7.49 (m, 2H, $H_{17}$ and $H_{16}$), 7.42 (dd, *J* = 8.3, 7.1 Hz, 1H, $H_{12}$), 7.38-7.29 (m, 2H, $H_4$), 6.95-6.88 (m, 2H, $H_3$), 4.97 (t, *J* = 6.3 Hz, 1H, $H_7$), 3.81 (s, 3H, $H_1$), 3.18 (d, *J* = 6.3 Hz, 2H, $H_6$), 2.52 (br s, 1H, O*H*);

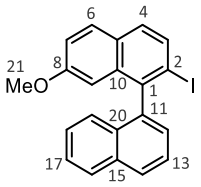
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.7 (Quat, $C_2$), 133.3 (Quat, $C_{14}$ or $C_{19}$), 133.1 (Quat, $C_{14}$ or $C_{19}$), 131.0 (CH, $C_4$), 130.6 (CH, $C_{11}$), 128.9 (CH, $C_{13}$), 128.7 (Quat, $C_5$), 128.3 (CH, $C_{15}$), 126.8 (CH, $C_{16}$ or $C_{17}$), 126.5 (CH, $C_{16}$ or $C_{17}$), 126.3 (CH, $C_{18}$), 125.2 (CH, $C_{12}$), 120.3 (Quat, $C_{10}$), 114.0 (CH, $C_3$), 94.6 (Quat, $C_8$), 83.9 (Quat, $C_9$), 64.1 (CH, $C_7$), 55.3 ($CH_3$, $C_1$), 43.4 ($CH_2$, $C_6$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3386, 3058, 3001, 2951, 2920, 2850, 2223, 1709, 1612, 1585, 1510, 1420, 1378, 1275, 1178, 1109, 1032;

HRMS (EI$^+$): calculated for $C_{21}H_{18}O_2^+$ = 302.1301, mass found = 302.1306;

Chiral HPLC: (Chiral-amylose-SA, 25 x 10 mm, 20 % $^i$PrOH, 80 % hexane, 5.0 mL min$^{-1}$, $\lambda$ = 300 nm, 100 $\mu$L injection), $\tau_R$ (enantiomer A) = 17.5 min, $\tau_R$ (enantiomer B) = 20.4 min.

**2-Iodo-7-methoxy-1,1'-binaphthalene, 128**




**128**

In analogy to a modified literature procedure,[46] sodium bicarbonate (18.5 mg, 0.22 mmol) and iodine (51 mg, 0.20 mmol) were sequentially added to a solution of **125** (30.2 mg, 0.100 mmol) in 1:1 dichloromethane/acetonitrile (1 mL). After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:5 ethyl acetate/petrol 40-60 afforded **128** as a white solid (25.2 mg, 61 %).

Melting point: 92-93 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 8.00 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.97 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.92 (d, *J* = 8.6 Hz, 1H, $H_4$), 7.80 (d, *J* = 8.9 Hz, 1H, $H_6$), 7.64 (dd, *J* = 8.3, 7.0 Hz, 1H, $H_{13}$), 7.59 (d, *J* = 8.6 Hz, 1H, $H_3$), 7.50 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{17}$), 7.39 (dd, *J* = 7.0, 1.2 Hz, 1H, $H_{12}$), 7.33 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H, $H_{18}$), 7.24 (dd, *J* = 8.5, 1.2 Hz, 1H, $H_{19}$), 7.14 (dd, *J* = 8.9, 2.5 Hz, 1H, $H_7$), 6.47 (d, *J* = 2.5 Hz, 1H, $H_9$), 3.46 (s, 3H, $H_{21}$);

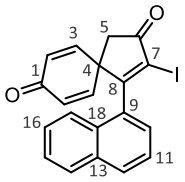
$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 158.3 (Quat, $C_8$), 141.4 (Quat, $C_{11}$), 141.2 (Quat, $C_1$), 135.3 (Quat, $C_{10}$), 133.9 (Quat, $C_{15}$), 133.5 (CH, $C_4$), 131.8 (Quat, $C_{20}$), 129.6 (CH, $C_6$), 129.1 (CH, $C_3$), 128.5 (CH, $C_{14}$), 128.5 (Quat, $C_5$), 128.5 (CH, $C_{16}$), 128.0 (CH, $C_{12}$), 126.5 (CH, $C_{18}$), 126.2 (CH, $C_{17}$), 125.8 (CH, $C_{19}$), 125.7 (CH, $C_{13}$), 118.8 (CH, $C_7$), 106.3 (CH, $C_9$), 100.6 (Quat, $C_2$), 55.2 ($CH_3$, $C_{21}$);

FTIR (neat) $\nu/cm^{-1}$ = 3045, 3002, 2957, 2933, 2835, 1619, 1581, 1563, 1462, 1436, 1383, 1296, 1275, 1256, 1201, 1180, 1129, 1064, 1030;

HRMS ($EI^+$): calculated for $C_{21}H_{15}IO^+$ = 410.0168, mass found = 410.0165;

Chiral HPLC: (Chiralpak ODH, 1 % $^{i}$PrOH, 99 % hexane, 0.5 mL $min^{-1}$, $\lambda$ = 254 nm, 10 $\mu$L injection) $\tau_R$ (enantiomer 1) = 7.4 min, $\tau_R$ (enantiomer 2) = 8.5 min.

**3-Iodo-4-(naphthalen-1-yl)spiro[4.5]deca-3,6,9-triene-2,8-dione, 129**




**129**

In analogy to a modified literature procedure,[46] sodium bicarbonate (18.5 mg, 0.22 mmol) and iodine (51 mg, 0.20 mmol) were sequentially added to a solution of **124** (30.3 mg, 0.100 mmol) in 1:1 dichloromethane/acetonitrile (1 mL). After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous sodium thiosulfate and the biphasic mixture was then extracted three times with dichloromethane. The combined organic extracts

were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:3 ethyl acetate/petrol 40-60 to 1:2 ethyl acetate/petrol 40-60 afforded **129** as a purple solid (34.3 mg, 83 %).

Melting point: 182-184 °C (ethyl acetate/petrol 40-60);

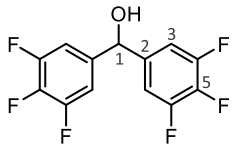
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94-7.84 (m, 2H, $H_{12}$ and $H_{14}$), 7.61-7.48 (m, 3H, $H_{15}$, $H_{16}$, $H_{17}$), 7.43 (dd, *J* = 8.3, 7.1 Hz, 1H, $H_{11}$), 7.11 (dd, *J* = 7.2, 1.2 Hz, 1H, $H_{10}$), 6.94 (dd, *J* = 9.9, 3.1 Hz, 1H, $H_{2A}$), 6.80 (dd, *J* = 10.0, 3.1 Hz, 1H, $H_{2B}$), 6.44 (dd, *J* = 9.9, 1.8 Hz, 1H, $H_{3A}$), 5.97 (dd, *J* = 10.0, 1.8 Hz, 1H, $H_{3B}$), 3.11 (s, 2H, $H_5$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 199.5 (Quat, $C_6$), 184.2 (Quat, $C_1$), 177.0 (Quat, $C_8$), 148.1 (CH, $C_{2A}$), 147.7 (CH, $C_{2B}$), 133.5 (Quat, $C_9$), 131.2 (CH, $C_{3A}$), 131.0 (Quat, $C_{13}$), 130.6 (CH, $C_{3B}$), 130.3 (CH, $C_{12}$ or $C_{14}$), 129.3 (CH, $C_{12}$ or $C_{14}$), 128.5 (Quat, $C_{18}$), 127.2 (CH, $C_{Ar}$), 126.6 (CH, $C_{Ar}$), 124.7 (CH, $C_{Ar}$), 124.6 (CH, $C_{10}$), 124.6 (CH, $C_{11}$), 110.2 (Quat, $C_7$), 55.7 (Quat, $C_4$), 43.3 ($CH_2$, $C_5$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3038, 3000, 2970, 2916, 1715, 1662, 1626, 1606, 1586, 1503, 1456, 1405, 1334, 1233, 1200, 1165, 1101, 1047, 1012;

HRMS (ESI$^+$): calculated for $C_{20}H_{13}IO_2^+$ = 411.9955, mass found = 411.9950.

**Bis(3,4,5-trifluorophenyl)methanol, 351**




**351**

According to a modified literature procedure,[17] *n*-butyllithium (1.6 M solution in hexanes, 10.9 mL, 17.4 mmol) was added to a solution of 1-bromo-3,4,5-trifluorobenzene (2.00 mL, 16.6 mmol) in diethyl ether (30 mL) at -78 °C. The reaction mixture was then stirred for

30 minutes. Following this a solution of freshly distilled ethyl formate[111] (668 µL, 8.30 mmol) in diethyl ether (10 mL) was added dropwise over one hour *via* syringe pump. After allowing the reaction mixture to warm to room temperature over-night, the reaction mixture was quenched with 1M HCl. The biphasic mixture was extracted three times with diethyl ether and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:19 diethyl ether/petrol 40-60 to 1:4 diethyl ether/petrol 40-60 afforded the title compound **351** as a white solid (1.75 g, 72 %). The spectral data matched that previously reported in the literature.[17]

Melting point: 84-85 °C (diethyl ether/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.02-6.93 (m, 4H, $H_3$), 5.68 (d, *J* = 3.3 Hz, 1H, $H_1$), 2.46 (d, *J* = 3.4 Hz, 1H, O*H*);

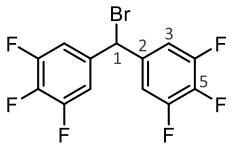
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.1-149.8 (Quat, m, $C_4$), 141.4-138.1 (Quat, m, $C_5$), 138.9-138.5 (Quat, m, $C_2$), 110.8-110.5 (CH, m, $C_2$), 73.7 (CH, $C_1$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –132.7 (d, *J* = 20.6 Hz, $F_4$), –160.5 (t, *J* = 20.5 Hz, $F_5$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3321, 3100, 2887, 2364, 1622, 1525, 1453, 1346, 1301, 1236, 1204, 1034;

LRMS (ESI$^-$): calculated for $C_{13}H_5F_6O^-$ = 291, mass found = 291.

**5,5'-(Bromomethylene)bis(1,2,3-trifluorobenzene), 352**




**352**

According to a modified literature procedure,[17] triphenylphosphine (2.33 g, 8.88 mmol) was added to a solution of **351** (1.73 g, 5.92 mmol) and carbon tetrabromide (2.79 g, 8.88 mmol) in acetonitrile (18 mL). After stirring over-night, the reaction mixture was diluted with diethyl ether and filtered through celite. The filtrate was then concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with petrol 40-60 afforded the title compound **352** as a brown oil (1.84 g, 88 %). The spectral data matched that previously reported in the literature.[17]

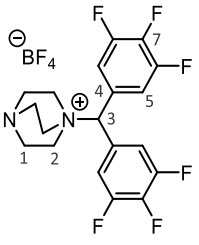
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.10-6.98 (m, 4H, $H_3$), 5.99 (s, 1H, $H_1$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ =151.3 (Quat, ddd, *J* = 252.2, 10.1, 4.0 Hz, $C_4$), 141.4-138.1 (Quat, m, $C_5$), 136.3-135.9 (Quat, m, $C_2$), 113.0-112.7 (CH, m, $C_3$), 50.2 (CH, $C_1$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –132.0 (d, *J* = 20.7 Hz), –158.8 (t, *J* = 20.4 Hz);

FTIR (neat) $\nu$/cm$^{-1}$ = 3057, 1624, 1598, 1528, 1442, 1361, 1349, 1294, 1267, 1202, 1168, 1138, 1114, 1048, 1001;

**1-(Bis(3,4,5-trifluorophenyl)methyl)-1,4-diazabicyclo[2.2.2]octan-1-ium tetrafluoroborate, 353**




**353**

According to a modified literature procedure,[17] anhydrous DABCO (2.88 g, 25.7 mmol) was added to a solution of **352** (1.82 g, 5.13 mmol) in diethyl ether. After stirring at reflux for 3 d, the reaction mixture was filtered and the precipitate washed with ice cold diethyl ether. The precipitate was then dissolved in dichloromethane (10 mL) and sodium tetrafluoroborate

(2.82g, 25.7 mmol) was subsequently added. The resulting suspension was stirred vigorously for 24 h and following this, water was added. The biphasic mixture was extracted twice with dichloromethane. The combined organic extracts were dried over sodium sulfate, filtered and concentrated under reduced pressure to afford the title compound **353** as a white solid (1.49 g, 61 %). The spectral data matched that previously reported in the literature.[17]

Melting point: >200 °C (dichloromethane);

$^{1}$H NMR (400 MHz, acetone-$d_6$) $\delta_H$ = 7.93 (dd, $J$ = 8.8, 6.4 Hz, 4H, $H_5$), 6.03 (s, 1H, $H_3$), 3.74 (t, $J$ = 7.4 Hz, 6H, $H_2$), 3.26 (t, $J$ = 7.3 Hz, 6H, $H_1$);

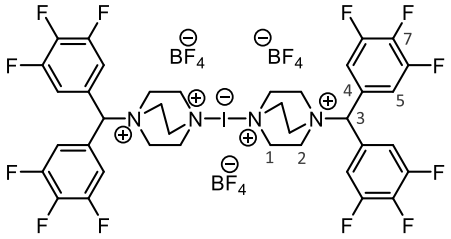
$^{13}$C NMR (101 MHz, acetone-$d_6$) $\delta_C$ = 152.2 (Quat, ddd, $J$ = 249.8, 9.7, 4.0 Hz, $C_6$), 143.4-140.0 (Quat, m, $C_7$), 129.0-128.1 (Quat, m, $C_4$), 118.2-117.5 (CH, m, $C_5$), 79.6 (CH, $C_3$), 52.6 ($CH_2$, $C_2$), 46.3 ($CH_2$, $C_1$);

$^{19}$F NMR (376 MHz, acetone-$d_6$) $\delta_F$ = –133.8 (d, $J$ = 20.5 Hz, $F_6$), –149.7 (s, $BF_4^-$), –159.7 (t, $J$ = 20.7 Hz, $F_7$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3054, 2972, 2898, 1623, 1536, 1489, 1451, 1409, 1374, 1346, 1286, 1242, 1157, 1132, 1057;

LRMS (ESI$^+$): calculated for $C_{19}H_{17}F_6N_2^+$ = 387, mass found = 387.

**Bis(4-(bis(3,4,5-trifluorophenyl)methyl)-1,4-diazabicyclo[2.2.2]octan-1,4-diium-1-yl)iodate(I) tri-tetrafluoroborate salt, 23**



**23**

According to a modified literature procedure,[17] silver tetrafluoroborate (107 mg, 0.55 mmol) was added to a solution of **353** in anhydrous acetonitrile (40 mL). After cooling to -40 °C, a solution of iodine (152 mg, 0.600 mmol) in anhydrous acetonitrile (4 mL) was added. The reaction mixture was stirred for one hour and then slowly warmed to room temperature over the period of one hour. The reaction mixture was filtered and the filter cake washed with acetonitrile. Following this, the reaction mixture was triturated with dichloromethane/hexane and the resulting suspension was sonicated for 5 minutes. The precipitate was isolated *via* filtration, dissolved in nitromethane and re-precipitated *via* addition of dichloromethane/ hexane. After sonicating the resulting suspension for 5 minutes, the precipitate was isolated *via* filtration to afford the title compound **23** as a white solid (228 mg, 40 %). The spectral data matched that previously reported in the literature.[17]

Melting point: dec > 90 °C (dichloromethane/hexane);

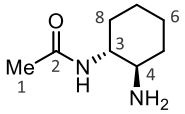
$^{1}$H NMR (400 MHz, acetone-*d*$_6$) $\delta_H$ = 7.94 (dd, *J* = 8.7, 6.4 Hz, 8H, $H_5$), 6.14 (s, 2H, $H_3$), 4.05 (t, *J* = 7.4 Hz, 12H, $H_2$), 3.73 (t, *J* = 7.4 Hz, 12H, $H_1$);

$^{13}$C NMR (101 MHz, acetone-*d*$_6$) $\delta_C$ = 153.82-150.69 (Quat, m, $C_6$), 142.60-139.63 (Quat, m, $C_7$), 128.13-127.00 (Quat, m, $C_4$), 118.26-117.67 (CH, m, $C_5$), 80.1 (CH, $C_3$), 51.9 ($CH_2$, $C_2$), 46.1 ($CH_2$, $C_1$);

$^{19}$F NMR (376 MHz, acetone-*d*$_6$) $\delta_F$ = –130.04 (d, *J* = 20.6 Hz, $F_6$), –146.80 (s, –155.70, B$F_4^-$) (t, *J* = 20.5 Hz, $F_7$);

FTIR (neat) $\nu$/cm$^{-1}$ =3569, 3059, 2928, 1706, 1624, 1535, 1506, 1417, 1367, 1347, 1257, 1055;

**_N_-((1_R_,2R)-2-aminocyclohexyl)acetamide, 354**




**354**

According to a modified literature procedure,[123] (1*R*,2*R*)-(-)-1,2-diaminocyclohexane (1.15 g, 10.0 mmol) was added to a solution of ethyl acetimidate hydrochloride (2.26 g, 18.3 mmol) in ethanol (25 mL). After stirring at room temperature for 12 hours, the reaction mixture was concentrated under reduced pressure. 1M NaOH (75 mL) was added and the mixture stirred for one hour. Following this the reaction mixture was extracted five times with dichloromethane and the combined organic extracts were concentrated under reduced pressure. The crude residue was then dissolved in 1:2 ethanol/water (50 mL) and following this, the reaction mixture was stirred at reflux for 12 hours. After cooling to room temperature, the majority of ethanol was removed under reduced pressure and the reaction mixture was then extracted three times with chloroform. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford the title compound **354** as a white solid (702 mg, 45 %). The spectral data matched that previously reported in the literature.[123]

Melting point: 105-107 °C ($CHCl_3$);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 5.73 (d, *J* = 4.4 Hz, 1H, N*H*), 3.47 (dddd, *J* = 11.4, 9.9, 8.7, 4.0 Hz, 1H, $H_3$), 2.34 (td, *J* = 10.4, 4.0 Hz, 1H, $H_4$), 2.03-1.87 (m, 5H, $H_1$, $H_{5A}$ and $H_{8A}$), 1.77-1.62 (m, 2H, $H_{6A}$ and $H_{7A}$), 1.45 (br s, 2H, N$H_2$), 1.35-1.01 (m, 4H, $H_{5B}$, $H_{6B}$, $H_{7B}$ and $H_{8B}$,);

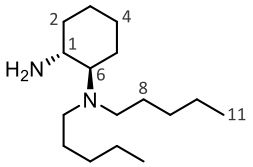
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 170.4 (Quat, $C_2$), 56.2 (CH, $C_3$), 55.6 (CH, $C_4$), 35.7 ($CH_2$, $C_5$ or $C_8$), 32.7 ($CH_2$, $C_5$ or $C_8$), 25.2 ($CH_2$, $C_6$ or $C_7$), 25.1 ($CH_2$, $C_6$ or $C_7$), 23.7 ($CH_3$, $C_1$);

FTIR (neat) $\nu$/cm$^{-1}$ =3363, 3277, 2080, 2926, 2857, 1635, 1597, 1552, 1447, 1371, 1341, 1282, 1243, 1147, 1127, 1085, 1040;

LRMS (ESI$^+$): calculated for $C_8H_{17}N_2O^+$ = 157, mass found = 157;

$[\alpha]_D^{25}$ = –15.4 (*c* = 1.00, $CHCl_3$).

**(1*R*,2*R*)-*N*$^1$,*N*$^1$-dipentylcyclohexane-1,2-diamine, 355**




**355**

According to a modified literature procedure,[51] water (1.2 mL) was added to a solution of **354** (674 mg, 4.31 mmol) in acetonitrile (25 mL). Following this, valeraldehyde (2.29 mL, 21.6 mmol) was added. After stirring at room temperature for 5 minutes, sodium cyanoborohydride (569 mg, 9.05 mmol) was added. The reaction mixture was stirred for 15 minutes and then acetic acid (1.2 mL) was added. The majority of acetonitrile was removed under reduced pressure and following this ethyl acetate and 1M NaOH were added. The organic layer was washed three times with 1M NaOH and then with brine. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. After this, 4 M HCl (25 mL) was added and the reaction mixture was then stirred at reflux for 12 hours. After cooling to room temperature, the reaction mixture was basified **CAREFULLY** *via* dropwise addition of 4 M NaOH. The mixture was extracted three times with dichloromethane and the combined organic extracts were then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford the title compound **355** as a brown oil (1.01 g, 92 %). The spectral data matched that previously reported in the literature.[51]

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ =2.52 (td, *J* = 10.3, 4.2 Hz, 1H, $H_6$), 2.42 (ddd, *J* = 12.9, 8.6, 7.3 Hz, 2H, $H_{7A}$), 2.26 (ddd, *J* = 12.9, 8.1, 4.8 Hz, 2H, $H_{7B}$), 2.05 (ddd, *J* = 11.0, 9.8, 3.1 Hz, 1H, $H_1$), 2.01-1.92 (m, 1H, C*H*$_2$), 1.92-1.58 (m, 5H, N*H*$_2$ and C*H*$_2$), 1.48-0.99 (m, 16H, C*H*$_2$), 0.88 (t, *J* = 7.0 Hz, 6H, $H_{11}$);

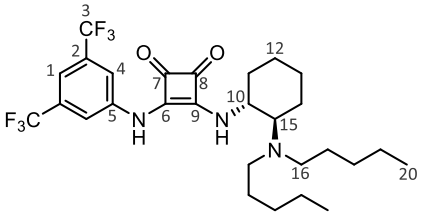
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 67.0 (CH, $C_1$), 51.5 (CH, $C_6$), 50.2 ($CH_2$, $C_7$), 35.3 ($CH_2$), 29.9 ($CH_2$), 29.3 ($CH_2$), 26.2 ($CH_2$), 25.3 ($CH_2$), 23.0 ($CH_2$), 22.8 ($CH_2$), 14.3 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3356, 2953, 2926, 2856, 2810, 1670, 1582, 1463, 1449, 1377, 1290, 1212, 1166, 1082;

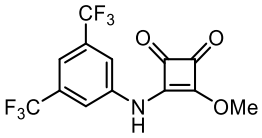
LRMS (ESI$^+$): calculated for $C_{16}H_{35}N_2^+$ = 255, mass found = 255;

$[\alpha]_D^{25}$ = –84.7 (*c* = 1.00, $CHCl_3$).

**3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*R*,2*R*)-2-(dipentylamino)cyclohexyl)amino) cyclobut-3-ene-1,2-dione, 131**



**131**



**CPJ1**

According to a modified literature procedure,[51] **CPJ1** (*synthesised and provided by Dr Craig P. Johnston*, 1.32 g, 3.89 mmol) was added to a solution of **355** (990 mg, 3.89 mmol) in methanol (60 mL). After stirring at room temperature for 24 h, the resulting precipitate was isolated *via* filtration and subsequently washed with ice-cold methanol to afford the title compound **131** as a white solid (1.54 g, 70 %).

Melting point: 194-196 °C (MeOH);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (s, 2H, $H_4$), 7.46 (s, 1H, $H_1$), 4.22-4.08 (m, 1H, $H_{10}$), 2.71-2.54 (m, 1H, $H_{15}$), 2.50-2.22 (m, 4H, $H_{16}$), 2.18-1.65 (m, 4H, C$H_2$), 1.65-1.46 (m, 2H, C$H_2$), 1.43-0.92 (m, 16H, C$H_2$), 0.70 (t, *J* = 6.7 Hz, 6H, $H_{20}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 184.3 (Quat, $C_7$ or $C_8$), 180.3 (Quat, $C_7$ or $C_8$), 170.2 (Quat, $C_6$ or $C_9$), 161.6 (Quat, $C_6$ or $C_9$), 140.3 (Quat, $C_5$), 132.6 (Quat, q, *J* = 33.3 Hz, $C_2$), 123.2 (Quat, q, *J* = 272.9 Hz, $C_3$), 119.4-119.0 (CH, m, $C_4$), 116.7-116.2 (CH, m, $C_1$), 64.1 (CH, $C_{15}$), 56.9 (CH, $C_{10}$),

50.0 ($CH_2$, $C_{16}$), 33.9 ($CH_2$), 29.8 ($CH_2$), 29.2 ($CH_2$), 25.3 ($CH_2$), 25.0 ($CH_2$), 24.6 ($CH_2$), 22.8 ($CH_2$), 14.2 ($C_{20}$);

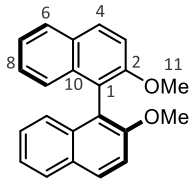
$^{19}F$ NMR (376 MHz, $CDCl_3$) $\delta_F$ = –63.2;

FTIR (neat) $\nu/cm^{-1}$ = 3243, 3158, 3084, 2932, 2860, 2813, 1796, 1681, 1625, 1592, 1548, 1458, 1379, 1279, 1182, 1120, 1087;

LRMS ($ESI^+$): calculated for $C_{28}H_{38}F_6N_3O_2^+$ = 562, mass found = 562;

$[\alpha]_D^{25}$ = –141.2 (*c* = 1.00, $CHCl_3$).

**(*S*)- 2,2'-Dimethoxy-1,1'-binaphthalene, 356**




**356**

According to a literature procedure,[49] Potassium carbonate (22.8 g, 166 mmol) and iodomethane (18.4 mL, 293 mmol) were added to a solution of (*S*)-BINOL (14.0 g, 49.0 mmol) in acetone (200 mL). The suspension was then stirred at reflux for 24 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure to approximately a total volume of 50 mL. $H_2O$ (500 mL) was added, and the mixture stirred for 8 h at room temperature. The precipitate was isolated by filtration and subsequently washed three times with water to afford the title compound **356** as a white solid (14.9 g, 96%). The spectral data matched that previously reported in the literature.[49]

Melting point: > 200 °C (water/acetone);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.99 (d, *J* = 9.0 Hz, 2H, $H_4$), 7.88 (d, *J* = 8.2 Hz, 2H, $H_9$), 7.47 (d, *J* = 9.0 Hz, 2H, $H_3$), 7.33 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 2H, $H_8$), 7.23 (ddd, *J* = 8.1, 7.3, 4.0 Hz, 2H, $H_7$), 7.13 (dd, *J* = 8.5, 0.6 Hz, 2H, $H_6$), 3.78 (s, 6H, $H_{11}$);

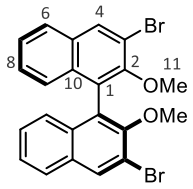
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$), 134.2 (Quat, $C_{10}$), 129.5 (CH, $C_4$), 129.4 (Quat, $C_5$), 128.1 (CH, $C_9$), 126.4 (CH, $C_7$), 125.4 (CH, $C_6$), 123.6 (CH, $C_8$), 119.7 (Quat, $C_1$), 114.4 (CH, $C_3$), 57.0 ($CH_3$, $C_{11}$).

FTIR (neat) $\nu$/cm$^{-1}$ = 3048, 2956, 2934, 2837, 1619, 1591, 1475, 1429, 1354, 1250, 1020;

LRMS (ESI$^+$): calculated for $C_{22}H_{19}O_2^+$ = 315, mass found = 315;

$[\alpha]_D^{25}$ = –57.1 (*c* = 1.00, $CHCl_3$).

**(*S*)-3,3'-Dibromo-2,2'-dimethoxy-1,1'-binaphthalene, 357**




**357**

According to a modified literature procedure,[49] To a stirred solution of tetramethylenediamine (5.27 mL, 35.2 mmol) in diethyl ether (250 mL) was slowly added *n*-butyllithium (1.6 M solution in hexanes, 35 mL, 56 mmol). The reaction mixture was then stirred for one hour and **356** (5.03 g, 16.0 mmol) was added. After cooling to -78 °C, bromine (4.1 mL, 80 mmol) was added. The reaction mixture was allowed to warm to room temperature and was subsequently stirred for 20 h. Saturated aqueous sodium sulphite was added, and the biphasic mixture was then stirred for 1 h. The aqueous phase was extracted with three times with diethyl ether and the combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/ petrol 40-60 to 1:49 ethyl

acetate/ petrol 40-60 afforded the title compound **357** as a white solid (4.25 g, 56%). The spectral data matched that previously reported in the literature.[49]

Melting point: 175-179 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.29 (s, 2H, $H_4$), 7.85 (d, *J* = 8.2 Hz, 2H, $H_9$), 7.45 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 2H, $H_8$), 7.29 (ddd, *J* = 8.2, 5.2, 1.2 Hz, 1H, $H_7$), 7.10 (d, *J* = 7.9 Hz, 1H, $H_6$), 3.53 (s, 6H, $H_{11}$);

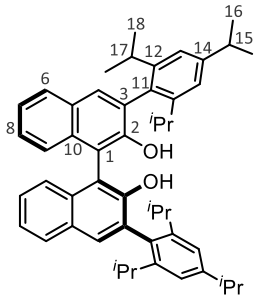
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 152.7 (Quat, $C_2$), 133.2 (Quat, $C_{10}$), 133.1 (CH, $C_4$), 131.6 (Quat, $C_5$), 127.3 (CH, $C_9$), 127.0 (CH, $C_7$), 126.7 (Quat, $C_1$), 126.0 (CH, $C_8$), 125.9 (CH, $C_6$), 117.7 (Quat, $C_3$), 61.3 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3057, 3005, 2938, 2849, 1652, 1575, 1493, 1458, 1400, 1350, 1328, 1201, 1015;

LRMS (ESI$^+$): calculated for $C_{22}H_{16}O_2Na^+$ = 493, mass found = 493;

$[\alpha]_D^{25}$ = –14.6 (*c* = 1.00, $CHCl_3$).

**(1*S*,3's)-3,3'-bis(2,4,6-triisopropylphenyl)-[1,1'-binaphthalene]-2,2'-diol, 358**




**358**

According to a modified literature procedure,[50] to a suspension of mechanically-activated magnesium turnings (1.26 g, 52 mmol) in diethyl ether (3 mL) was added a single crystal of iodine and a solution of 2-bromo-1,3,5-triisopropylbenzene (6.9 mL, 26 mmol) and 1,2-dibromoethane (0.1 mL) in diethyl ether (35 mL) in such a manner that the exothermic reaction was maintained.

The suspension was heated to reflux and stirred vigorously for 24 h. After cooling to room temperature, the Grignard solution was filtered through a short pad of cotton wool and added drop wise to a stirred suspension of bromoarene **357** and bis(triphenylphosphine)nickel(II) chloride (277 mg, 0.42 mmol) in diethyl ether (25 mL). Following this, the reaction mixture was stirred at reflux for 6 h. After cooling to room temperature, 1M HCl was added and the aqueous layer was subsequently extracted three times with diethyl ether. The combined organic layers ware dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude residue was dissolved in dichloromethane (100 mL) and cooled to 0 °C. $BBr_3$ (1.0 M in dichloromethane, 30 mL, 30 mmol) was then added drop wise. After warming to room temperature, the solution was stirred for a further 24 h. Following this, the reaction mixture was cooled to 0 °C and the reaction was **CAREFULLY** quenched *via* dropwise addition of $H_2O$ (40 mL). The biphasic mixture was then extracted three times with dichloromethane. Following this, the combined organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:99 ethyl acetate/petrol 40-60 and subsequent trituration with hexane afforded the title compound **358** as a white solid (883 mg, 30 %). The spectral data matched that previously reported in the literature.[50]

Melting point: >200 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.89 (d, *J* = 7.9 Hz, 2H, $H_9$), 7.79 (s, 2H, $H_4$), 7.40 (ddd, *J* = 8.1, 6.2, 1.9 Hz, 2H, $H_8$), 7.37-7.29 (m, 4H, $H_6$ and $H_7$), 7.16 (d, *J* = 1.5 Hz, 2H, $H_{13A}$), 7.14 (d, *J* = 1.5 Hz, 2H, $H_{13B}$), 4.94 (s, 2H, O*H*), 2.98 (hept, *J* = 6.9 Hz, 2H, $H_{15}$), 2.87 (hept, *J* = 6.9 Hz, 2H, $H_{17A}$), 2.71 (hept, *J* = 6.7 Hz, 2H, $H_{17B}$), 1.33 (d, *J* = 6.9 Hz, 12H, $H_{16}$), 1.22 (d, *J* = 6.8 Hz, 6H, $H_{18A}$), 1.13 (d, *J* = 6.9 Hz, 6H, $H_{18B}$), 1.11 (d, *J* = 6.9 Hz, 6H, $H_{18C}$), 1.05 (d, *J* = 6.9 Hz, 6H, $H_{18D}$);

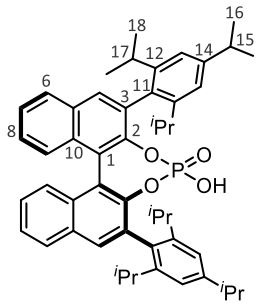
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 150.8 (Quat, $C_2$), 149.3 (Quat, $C_{14}$), 147.9 (Quat, $C_{12A}$), 147.9 (Quat, $C_{12B}$), 133.6 (Quat, $C_{Ar}$), 130.8 (CH, $C_4$), 130.5 (Quat, $C_{Ar}$), 129.3 (Quat, $C_{Ar}$), 129.2 (Quat, $C_{Ar}$),

128.4 (Quat, $C_9$), 126.8 (CH, $C_{Ar}$), 124.7 (CH, $C_{Ar}$), 123.9 (CH, $C_7$), 121.4 (CH, $C_{13A}$), 121.3 (CH, $C_{13B}$), 113.2 (Quat, $C_1$), 34.5 (CH, $C_{15}$), 31.0 (CH, $C_{17A}$), 31.00 (CH, $C_{17B}$), 24.5 (C$H_3$), 24.4 (C$H_3$), 24.2 (C$H_3$), 24.2 (C$H_3$), 24.1 (C$H_3$), 23.9 (C$H_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3056, 2960, 2929, 2869, 1605, 1568, 1498, 1459, 1422, 1383, 1256, 1172, 1067;

$[\alpha]_D^{25}$ = –82.3 (*c* = 1.00, $CHCl_3$).

**(*S*)-TRIP, 47**




**47**

According to a modified literature procedure,[50] Phosphorus(V) oxychloride (0.28 mL, 3.0 mmol) was added to a stirred solution of diol **358** (691 mg, 1.00 mmol ) in pyridine (2 mL). Following this, the reaction mixture was stirred at reflux for 18 h. After cooling to room temperature, $H_2O$ (20 mL) was added. The reaction mixture was then stirred vigorously at reflux for 3 h. After cooling to room temperature, the reaction mixture was extracted three times with dichloromethane and the combined organic extracts were washed with 3 M HCl, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to afford (*S*- TRIP **47** as a white solid (739 mg, 98%). The spectral data matched that previously reported in the literature.[50]

Melting point: >200 °C (dichloromethane);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.89 (d, *J* = 8.2 Hz, 2H, $H_9$), 7.80 (s, 2H, $H_4$), 7.50 (ddd, *J* = 8.1, 6.0, 1.9 Hz, 2H, $H_8$), 7.37-7.29 (m, 4H, $H_6$ and $H_7$), 6.94 (d, *J* = 1.5 Hz, 2H, $H_{12A}$), 6.91 (d, *J* = 1.5 Hz, 2H, $H_{12B}$), 5.79 (s, 1H, O*H*), 2.83 (hept, *J* = 6.9 Hz, 2H, $H_{15}$), 2.59 (hept, *J* = 6.8 Hz, 2H, $H_{17A}$), 2.50 (hept, *J* = 6.7 Hz, 2H, $H_{17B}$), 1.23 (d, *J* = 6.9 Hz, 6H, $H_{16A}$), 1.22 (d, *J* = 6.9 Hz, 6H, $H_{16B}$), 1.00 (d, *J* = 7.2 Hz, 7H, $H_{18A}$), 0.98 (d, *J* = 7.1 Hz, 6H, $H_{18B}$), 0.90 (d, *J* = 6.8 Hz, 6H, $H_{18C}$), 0.66 (d, *J* = 6.6 Hz, 6H, $H_{18D}$);

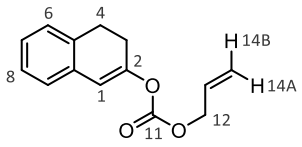
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 148.5 (Quat, $C_{Ar}$), 148.1 (Quat, $C_{Ar}$), 147.5 (Quat, $C_{Ar}$), 146.0 (Quat, d, *J* = 9.5 Hz, $C_2$), 133.0 (Quat, $C_{Ar}$), 132.4 (CH, $C_4$), 132.4 (Quat, d, *J* = 3.1 Hz, $C_3$), 131.4 (Quat, $C_{Ar}$), 131.1 (Quat, $C_{Ar}$), 128.3 (CH, $C_9$), 127.5 (CH, $C_{Ar}$), 126.3 (CH, $C_{Ar}$), 125.7 (CH, $C_8$), 122.2 (Quat, d, *J* = 1.9 Hz, $C_1$), 121.2 (CH, $C_{13A}$), 120.4 (CH, $C_{13B}$), 34.4 (CH, $C_{15}$), 31.1 (CH, $C_{15A}$), 30.8 (CH, $C_{15B}$), 26.4 ($CH_3$, $C_8$), 25.1 (C 18), 24.3 ($CH_3$, $C_{16A}$), 24.0 ($CH_3$, $C_{16B}$), 23.4 ($CH_3$, $C_{18A}$), 23.0 ($CH_3$, $C_{18B}$);

$^{31}$P NMR (162 MHz, $CDCl_3$) $\delta_P$ = 2.42;

FTIR (neat) $\nu$/cm$^{-1}$ = 3567, 3054, 2960, 2870, 1607, 1568, 1497, 1446, 1383, 1315, 1281, 1238, 1150, 1021;

$[\alpha]_D^{25}$ = +33.4 (*c* = 1.00, $CHCl_3$).

**Allyl (3,4-dihydronaphthalen-2-yl) carbonate, 144**




**144**

In analogy to a modified literature procedure,[124] *n*-butyllithium (2.5 M solution in hexanes, 1.7 mL, 4.2 mmol) was added to a solution of hexamethyldisilazane (918 µL, 4.4 mmol) in THF (10 mL) at -40 °C. After stirring for 15 minutes the solution was cooled to -78 °C. The LiHMDS solution was then cannulated to a solution of 2-tetralone (292 mg, 2.00 mmol) in THF (10 mL) at -78 °C. The reaction mixture was stirred for 15 minutes and allyl chloroformate (230 µL,

2.2 mmol) was subsequently added. After stirring for 1 hour, the reaction mixture was quenched with saturated aqueous ammonium chloride and subsequently warmed to room temperature. 1 M HCl was added and the biphasic mixture was then extracted three times with diethyl ether. The combined organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 3:97 ethyl acetate/petrol 40-60 afforded the title compound **144** as a colourless oil (111 mg, 24 %). The spectral data matched that previously reported in the literature.[125]

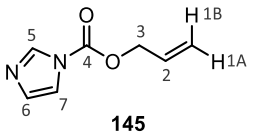
$^{1}$H NMR (400 MHz, $C_6D_6$) $\delta_H$ = 7.01-6.90 (m, 2H, $H_{Ar}$), 6.86-6.73 (m, 2H, $H_{Ar}$), 6.29 (s, 1H, $H_1$), 5.66 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H, $H_{13}$), 5.12 (dq, *J* = 17.2, 1.5 Hz, 1H, $H_{14A}$), 4.95 (dq, *J* = 10.5, 1.3 Hz, 1H, $H_{14B}$), 4.39 (dt, *J* = 5.7, 1.4 Hz, 2H, $H_{12}$), 2.61 (t, *J* = 8.3 Hz, 2H, $H_4$), 2.35 (td, *J* = 8.3, 1.1 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $C_6D_6$) $\delta_C$ = 153.1 (Quat, $C_2$) 151.4 (Quat, $C_{11}$), 133.4 (Quat, $C_5$ or $C_{10}$), 133.4 (Quat, $C_5$ or $C_{10}$), 131.8 (CH, $C_{13}$), 127.5 (CH, $C_{Ar}$), 127.2 (CH, $C_{Ar}$), 126.9 (CH, $C_{Ar}$), 126.8 (CH, $C_{Ar}$), 118.7 ($CH_2$, $C_{14}$), 114.8 (CH, $C_1$), 68.7 ($CH_2$, $C_{12}$), 28.8 ($CH_2$, $C_4$), 26.2 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3064, 3019, 2944, 2891, 2836, 1755, 1667, 1650, 1573, 1487, 1426, 1320, 1271, 1223, 1145, 1091, 1034;

HRMS (EI$^+$): calculated for $C_{14}H_{14}O_3^+$ = 230.0937, mass found = 230.0936.

**Allyl 1*H*-imidazole-1-carboxylate, 145**




**145**

According to a modified literature procedure,[57] allyl chloroformate (2.98 mL, 28.0 mmol) was added dropwise over 30 minutes *via* syringe pump to a solution of imidazole (3.75 g, 55 mmol) in THF (50 mL) at 0 °C. The resulting suspension was stirred for 1h and then stirred for an

additional 4 h at room temperature. Following this, the suspension was filtered and the filter cake washed with diethyl ether. The filtrate was then concentrated under reduced pressure and subsequently dissolved in diethyl ether (50 mL). The mixture was washed three times with water and the organic layer was then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to afford the title compound **145** as a yellow oil (2.99 g, 70 %). The spectral data matched that previously reported in the literature.[57]

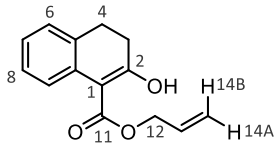
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.14 (t, *J* = 1.1 Hz, 1H, $H_5$), 7.42 (t, *J* = 1.5 Hz, 1H, $H_7$), 7.06 (dd, *J* = 1.7, 0.9 Hz, 1H, $H_6$), 6.00 (ddt, *J* = 17.2, 10.4, 6.0 Hz, 1H, $H_2$), 5.44 (dq, *J* = 17.2, 1.4 Hz, 1H, $H_{1B}$), 5.37 (dq, *J* = 10.4, 1.1 Hz, 1H, $H_{1A}$), 4.87 (dt, *J* = 6.0, 1.3 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 148.6 (Quat, $C_4$), 137.2 (CH, $C_5$), 130.8 (CH, $C_6$), 130.5 (CH, $C_2$), 120.5 ($CH_2$, $C_1$), 117.2 (CH, $C_7$), 68.7 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3132, 2989, 2953, 1757, 1650, 152, 1473, 1425, 1392, 1368, 1316, 1280, 1238, 1173, 1096, 1059;

LRMS (ESI$^+$): calculated for $C_7H_9N_2O_2^+$ = 153, mass found = 153.

**Allyl 2-hydroxy-3,4-dihydronaphthalene-1-carboxylate, 140**




**140**

In analogy to a modified literature procedure,[124] *n*-butyllithium (2.5 M solution in hexanes, 4.80 mL, 12.0 mmol) was added to a solution of hexamethyldisilazane (2.71 mL, 13.0 mmol) in THF (50 mL) at -40 °C. After stirring for 15 minutes the solution was cooled to -78 °C. The LiHMDS solution was then cannulated to a solution of 2-tetralone (1.59 mL, 12.0 mmol) in THF (50 mL) at -78 °C. The reaction mixture was stirred for 15 minutes and a solution of **145** (1.52 g,

10.0 mmol) in THF (25 mL) was subsequently added. After stirring for 1 hour, the reaction mixture was quenched with saturated aqueous ammonium chloride and subsequently warmed to room temperature. 1 M HCl was added and the biphasic mixture was then extracted three times with diethyl ether. The combined organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:49 ethyl acetate/petrol 40-60 afforded the title compound **140** as a colourless oil (1.42 g, 62 %).

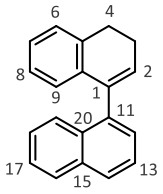
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 13.33 (br s, 1H, O*H*), 7.74 (dd, *J* = 7.9, 1.2 Hz, 1H, $H_9$), 7.20 (td, *J* = 7.6, 1.7 Hz, 1H, $H_8$), 7.14 (dd, *J* = 7.3, 1.5 Hz, 1H, $H_6$), 7.07 (td, *J* = 7.3, 1.3 Hz, 1H, $H_7$), 6.05 (ddt, *J* = 17.2, 10.4, 5.6 Hz, 1H, $H_{13}$), 5.42 (dq, *J* = 17.3, 1.6 Hz, 1H, $H_{14A}$), 5.31 (dq, *J* = 10.4, 1.3 Hz, 1H, $H_{14B}$), 4.84 (dt, *J* = 5.6, 1.4 Hz, 2H, $H_{12}$), 2.86-2.79 (m, 2H, $H_4$), 2.55 (dd, *J* = 8.4, 6.6 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 178.9 (Quat, $C_2$), 171.8 (Quat, $C_{11}$), 133.3 (Quat, $C_5$), 131.9 (CH, $C_{13}$), 131.5 (Quat, $C_{10}$), 127.3 (CH, $C_6$), 126.5 (CH, $C_8$), 126.1 (CH, $C_9$), 125.1 (CH, $C_7$), 118.8 ($CH_2$, $C_{14}$), 100.0 (Quat, $C_1$), 65.7 ($CH_2$, $C_{12}$), 29.7($CH_2$, $C_3$), 27.9($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3066, 3024, 2952, 2894, 2838, 1719, 1633, 1597, 1567, 1488, 1454, 1422, 1394, 1360, 1333, 1275, 1216, 1160, 1119, 1092;

HRMS (ESI$^-$): calculated for $C_{14}H_{13}O_3^-$ = 229.0870, mass found = 229.0869.

**3,4-Dihydro-1,1'-binaphthalene, 153**




**153**

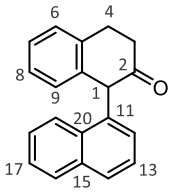
According to a modified literature procedure,[126] *n*-butyllithium (2.5 M solution in hexanes, 5.6 mL, 14 mmol) was added to a solution of 1-bromonaphthalene (3.11 g, 15.0 mmol) in THF (100 mL) at -78 °C. After stirring for 3 h at -78 °C, 1-tetralone (1.33 mL, 10.0 mmol) was added. Following this, the reaction was warmed to room temperature and stirred for 1 h. The reaction mixture was quenched with saturated aqueous ammonium chloride and the majority of THF was subsequently removed under reduced pressure. The mixture was extracted three times with dichloromethane and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude reaction mixture was dissolved in methanol (25 mL) and *p*-toluenesulfonic acid monohydrate was subsequently added (95 mg, 0.5 mmol). After stirring the reaction mixture over night, the resulting precipitate was isolated *via* filtration. The precipitate was washed with ice-cold methanol. After drying the precipitate under reduced pressure (c.a. 0.1 mbar) for 3 h, the title compound **153** was obtained as a white solid (1.32 g, 51 %). The spectral data matched that previously reported in the literature.[127]

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 8.4 Hz, 1H, $H_{16}$), 7.90 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.80 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.56 (dd, *J* = 8.2, 7.0 Hz, 1H, $H_{13}$), 7.50 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H, $H_{17}$), 7.46 (dd, *J* = 6.9, 1.2 Hz, 1H, $H_{12}$), 7.39 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_{18}$), 7.28 (d, *J* = 7.2 Hz, 1H, $H_6$), 7.17 (td, *J* = 7.4, 1.1 Hz, 1H, $H_7$), 6.99 (t, *J* = 7.5 Hz, 1H, $H_8$), 6.59 (d, *J* = 7.6 Hz, 1H, $H_9$), 6.19 (dd, *J* = 4.6, 4.5 Hz, 1H, $H_2$), 3.11 (ddd, *J* = 15.4, 11.3, 7.4 Hz, 1H, $H_{4A}$), 3.06-2.96 (m, 1H, $H_{4B}$), 2.66-2.51 (m, 2H, $H_3$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 138.9 (Quat, $C_{11}$), 138.5 (Quat, $C_1$), 136.0 (Quat, $C_{10}$), 135.7 (Quat, $C_5$), 133.7 (Quat, $C_{15}$), 132.4 (Quat, $C_{20}$), 129.4 (CH, $C_2$), 128.3 (CH, $C_{16}$), 127.8 (CH, $C_{14}$), 127.6 (CH, $C_6$), 127.3 (CH, $C_{12}$), 127.1 (CH, $C_8$), 126.6 (CH, $C_{19}$), 126.5 (CH, $C_7$), 125.9 (CH, $C_{18}$), 125.8 (CH, $C_{17}$), 125.8 (CH, $C_{13}$), 125.7 (CH, $C_9$), 28.4 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

HRMS ($EI^+$): calculated for $C_{20}H_{16}^+$ = 256.1247, mass found = 256.1244.

**3,4-Dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 149**




**149**

According to **General Procedure B** with **153** (256 mg, 1.00 mmol), dichloromethane (10 mL), sodium bicarbonate (210 mg, 2.50 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 460 mg, 2.0 mmol); then 1:1 diethyl ether/dichloromethane (20 mL), boron trifluoride diethyl etherate (0.20 mL, 1.6 mmol). Purification *via* column chromatography eluting with a gradient from 5:94:1 ethyl acetate/petrol 40-60/triethylamine to 10:89:1 ethyl acetate/petrol 40-60/triethylamine afforded the title compound **149** as an off white solid (258 mg, 94 %).

Melting point: 104-106 °C (ethyl acetate/petrol 40-60/triethylamine);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.96-7.87 (m, 2H, $H_{16}$ and $H_{19}$), 7.84 (d, *J* = 8.2 Hz, 1H, $H_{14}$), 7.52 7.41 (m, 3H, $H_{13}$, $H_{17}$ and $H_{18}$), 7.35 (d, *J* = 7.6 Hz, 1H, $H_6$), 7.27 (t, *J* = 7.4 Hz, 1H, $H_7$), 7.17 (dd, *J* = 7.1, 1.2 Hz, 1H, $H_{12}$), 7.12 (td, *J* = 7.6, 1.4 Hz, 1H, $H_8$), 6.77 (d, *J* = 7.7 Hz, 1H, $H_9$), 5.40 (s, 1H, $H_1$), 3.40-3.22 (m, 2H, $H_4$), 2.93-2.71 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 209.3 (Quat, $C_2$), 137.5 (Quat, $C_5$), 136.5 (Quat, $C_{20}$), 134.8 (Quat, $C_{10}$), 134.3 (Quat, $C_{11}$), 131.9 (Quat, $C_{15}$), 129.2 (CH, $C_9$), 129.0 (CH, $C_{16}$), 128.8 (CH, $C_{12}$), 128.5

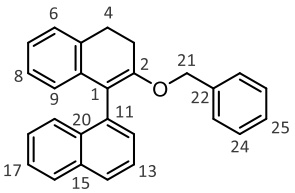
(CH, $C_{19}$), 127.9 (CH, $C_6$), 127.3 (CH, $C_8$), 127.1 (CH, $C_7$), 126.4 (CH, $C_{17}$ or $C_{18}$), 125.8 (CH, $C_{17}$ or $C_{18}$), 125.5 (CH, $C_{13}$), 125.1 (CH, $C_{14}$), 57.7 (CH, $C_1$), 37.3 ($CH_2$, $C_3$), 29.1 ($CH_2$, $C_4$);

FTIR (neat) $\nu/cm^{-1}$ = 3062, 2950, 2905, 2847, 1716, 1654, 1636, 1597, 1559, 1510, 1486, 1396, 1347, 1330, 1304, 1275, 1235, 1124, 1020;

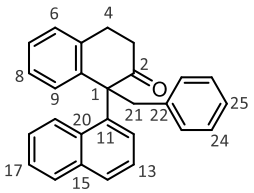
HRMS ($ESI^+$): calculated for $C_{20}H_{16}ONa^+$ = 295.1093, mass found = 295.1093.

**2-(Benzyloxy)-3,4-dihydro-1,1'-binaphthalene, 160 &**

**1-benzyl-3,4-dihydro-1,1'-binaphthalen]-2(1*H*)-one, 161**




**160**




**161**

A 14 mL vial was sequentially charged with tetrabutylammonium bromide (16 mg, 0.050 mmol) and **149** (136 mg, 0.500 mmol). Toluene (5.0 ml) and benzyl bromide (89 μL, 0.75 mmol) were added and the reaction mixture was then stirred for 5 minutes. After the addition of 50 % aqueous potassium hydroxide (84 μL, 0.75 mmol) the reaction mixture was stirred rapidly at a rate of 1000-1400 rpm at room temperature for 5 hours. Water and dichloromethane were added and the organic layer was separated. The aqueous layer was then extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:2 dichloromethane/petrol 40-60 to 2:1 dichloromethane/petrol 40-60 afforded **160** as white solid (149 mg, 82 %) along with **161** as a white solid (21.8 mg, 12 %).

Data for **160**:

Melting point: 81-82 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.91 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.88 (d, *J* = 8.3 Hz, 1H, $H_{14}$), 7.78-7.75 (m, 1H, $H_{19}$), 7.54 (dd, *J* = 8.2, 7.0 Hz, 1H, $H_{13}$), 7.47 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H, $H_{17}$), 7.37 (dd, *J* = 6.8, 1.4 Hz, 1H, $H_{18}$), 7.34 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H, $H_{12}$), 7.21-7.14 (m, 3H, $H_6$, $H_{24}$ and $H_{25}$), 7.02 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.96-6.86 (m, 3H, $H_8$ and $H_{23}$), 6.40 (dd, *J* = 7.8, 1.3 Hz, 1H, $H_9$), 4.75 (d, *J* = 12.4 Hz, 1H, $H_{21A}$), 4.71 (d, *J* = 12.4 Hz, 1H, $H_{21B}$), 3.19-3.00 (m, 2H, $H_4$), 2.79-2.65 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.2 (Quat, $C_2$), 137.4 (Quat, $C_{Ar}$), 137.3 (Quat, $C_{Ar}$), 135.0 (Quat, $C_{Ar}$), 133.9 (Quat, $C_{Ar}$), 132.9 (Quat, $C_{Ar}$), 132.4 (Quat, $C_{Ar}$), 128.5 (CH, $C_{12}$), 128.3 (CH, $C_{16}$), 128.3 (CH, $C_{24}$), 127.8 (CH, $C_{25}$), 127.6 (CH, $C_{23}$), 127.5 (CH, $C_{14}$), 126.9 (CH, $C_8$), 126.6 (CH, $C_6$), 126.4 (CH, $C_{19}$), 125.9 (CH, $C_{18}$), 125.8 (CH, $C_{13}$), 125.7 (CH, $C_{17}$), 125.2 (CH, $C_7$), 124.8 (CH, $C_9$), 118.1 (Quat, $C_1$), 70.3 ($CH_2$, $C_{21}$), 29.2 ($CH_2$, $C_4$), 25.0 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3054, 3029, 3010, 2960, 2880, 2829, 1638, 1594, 1567, 1505, 1483, 1432, 1364, 1223, 1014;

HRMS (EI$^+$): calculated for $C_{27}H_{22}O^+$ = 362.1665, mass found = 362.1664;

Data for **161**:

Melting point: 156-159 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.05 (dd, *J* = 7.5, 1.1 Hz, 1H, $H_{12}$), 7.85 (d, *J* = 8.2 Hz, 1H, $H_{14}$), 7.82 (dd, *J* = 8.1, 1.3 Hz, 1H, $H_{16}$), 7.60 (dd, *J* = 8.2, 7.4 Hz, 1H, $H_{13}$), 7.41 (dd, *J* = 8.8, 1.0 Hz, 1H, $H_{19}$), 7.31 (ddd, *J* = 8.0, 6.8, 1.1 Hz, 1H, $H_{17}$), 7.25-7.19 (m, 1H, $H_{25}$), 7.16 (td, *J* = 7.3, 1.3 Hz, 1H, $H_{18}$), 7.14-7.07 (m, 3H, $H_7$ and $H_{24}$), 7.07-7.01 (m, 2H, $H_6$ and $H_8$), 6.83 (dd, *J* = 8.3, 1.4 Hz, 1H, $H_9$), 6.65-6.59 (m, 2H, $H_{23}$), 4.10 (d, *J* = 11.5 Hz, 1H, $H_{21A}$), 3.47 (d, *J* = 11.5 Hz, 1H, $H_{21B}$), 2.93 (ddd,

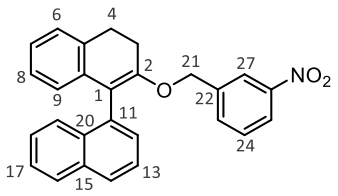
*J* = 18.0, 11.7, 7.9 Hz, 1H, $H_{3A}$), 2.72 (ddd, *J* = 16.5, 7.9, 2.9 Hz, 1H, $H_{4A}$), 2.40 (ddd, *J* = 18.0, 6.9, 2.9 Hz, 1H, $H_{3B}$), 1.49 (ddd, *J* = 17.5, 11.7, 6.9 Hz, 1H, $H_{4B}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 213.8 (Quat, $C_2$), 141.2 (Quat, $C_{Ar}$), 140.7 (Quat, $C_{Ar}$), 136.2 (Quat, $C_{Ar}$), 135.4 (Quat, $C_{Ar}$), 135.0 (Quat, $C_{Ar}$), 131.1 (Quat, $C_{Ar}$), 131.1 (CH, $C_{24}$), 129.4 (CH, $C_{16}$), 128.8 (CH, $C_{14}$), 128.4 (CH, $C_9$), 128.0 (CH, $C_{23}$), 128.0 (CH, $C_6$ or $C_8$), 127.3 (CH, $C_6$ or $C_8$), 127.1 (CH, $C_{25}$), 126.9 (CH, $C_{15}$), 126.0 (CH, $C_{12}$), 125.6 (CH, $C_{19}$), 125.5 (CH, $C_7$), 125.2 (CH, $C_{13}$), 125.1 (CH, $C_{17}$), 61.1 (Quat, $C_1$), 50.0 ($CH_2$, $C_{21}$), 38.2 ($CH_2$, $C_3$), 26.5 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3025, 2921, 2864, 1695, 1599, 1579, 1510, 1452, 1398, 1311, 1286, 1202, 1142, 1076, 1030, 1007;

HRMS (EI$^+$): calculated for $C_{27}H_{22}O^+$ = 362.1665, mass found = 362.1665.

**2-((3-nitrobenzyl)oxy)-3,4-dihydro-1,1'-binaphthalene, 165**




**165**

A 14 mL vial was sequentially charged with tetrabutylammonium bromide (16 mg, 0.050 mmol) and **149** (136 mg, 0.500 mmol). Toluene (5.0 ml) and 3-nitrobenzyl bromide (162 mg, 0.75 mmol) were added and the reaction mixture was then stirred for 5 minutes. After the addition of 50 % aqueous potassium hydroxide (84 μL, 0.75 mmol) the reaction mixture was stirred rapidly at a rate of 1000-1400 rpm at room temperature for 5 hours. Water and dichloromethane were added and the organic layer was separated. The aqueous layer was then extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:3

dichloromethane/petrol 40-60 to 1:1 dichloromethane/petrol 40-60 afforded **165** as white solid (113 mg, 56 %).

Melting point: 166-167 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.98 (ddd, *J* = 8.1, 2.4, 1.1 Hz, 1H, $H_{25}$), 7.89 (d, *J* = 7.7 Hz, 1H, $H_{16}$), 7.88 (d, *J* = 7.9 Hz, 1H, $H_{14}$), 7.72 (t, *J* = 2.0 Hz, 1H, $H_{27}$), 7.68 (dd, *J* = 8.4, 1.1 Hz, 1H, $H_{19}$), 7.54 (dd, *J* = 8.3, 7.0 Hz, 1H, $H_{13}$), 7.44 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_{17}$), 7.35 (dd, *J* = 7.0, 1.2 Hz, 1H, $H_{12}$), 7.32 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_{18}$), 7.24 (t, *J* = 7.9 Hz, 1H, $H_{24}$), 7.19 (dd, *J* = 7.5, 1.2 Hz, 1H, $H_6$), 7.11 (d, *J* = 7.7 Hz, 1H, $H_{23}$), 7.04 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.91 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.42 (dd, *J* = 7.7, 1.2 Hz, 1H, $H_9$), 4.79 (d, *J* = 12.7 Hz, 1H, $H_{21A}$), 4.75 (d, *J* = 12.7 Hz, 1H, $H_{21B}$), 3.21-3.08 (m, 2H, $H_4$), 2.84-2.69 (m, 2H, $H_3$);

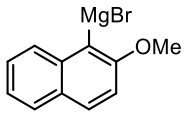
$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 153.4 (Quat, $C_2$), 148.1 (Quat, $C_{26}$), 139.4 (Quat, $C_{22}$), 136.8 (Quat, $C_{10}$), 134.4 (Quat, $C_{15}$), 133.9 (Quat, $C_{11}$), 133.2 (CH, $C_{23}$), 132.7 (Quat, $C_{20}$), 132.4 (Quat, $C_5$), 129.2 (CH, $C_{24}$), 128.5 (CH, $C_{16}$), 128.4 (CH, $C_{12}$), 127.8 (CH, $C_{14}$), 127.0 (CH, $C_6$), 126.7 (CH, $C_8$), 126.0 (CH, $C_{18}$ or $C_{19}$), 126.0 (CH, $C_{18}$ or $C_{19}$), 125.8 (CH, $C_{17}$), 125.8 (CH, $C_{13}$), 125.7 (CH, $C_7$), 125.1 (CH, $C_9$), 122.7 (CH, $C_{25}$), 122.2 (CH, $C_{27}$), 119.2 (Quat, $C_1$), 69.3 ($CH_2$, $C_{21}$), 29.2 ($CH_2$, $C_4$), 25.1 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3057, 3042, 2941, 2882, 2832, 1636, 1591, 1570, 1528, 1483, 1348, 1182, 1159, 1016;

HRMS (EI$^+$): calculated for $C_{27}H_{21}NO_3^+$ = 407.1516, mass found = 407.1522;

Chiral HPLC: (Chiralpak ADH, 5 % $^i$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 273 nm, 10 $\mu$L injection) $\tau_R$ (enantiomer 1) = 15.2 min, $\tau_R$ (enantiomer 2) = 17.1 min.

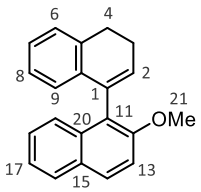
**(2-Methoxynaphthalen-1-yl)magnesium bromide solution (0.5 M in THF), 173**




**173**

Magnesium turnings (729 mg, 30 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature, THF (10 mL) followed by a solution of 1-bromo-2-methoxynaphthalene (5.46g, 20 mmol) in THF (30 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.2 mL) and subsequently stirred at reflux for 2 hours. The suspension was decanted *via* cannulation under inert atmosphere and diluted to a volume of 40 mL. The resulting solution of (2-methoxynaphthalen-1-yl)magnesium bromide **173** was then used immediately in subsequent additions to 1-tetralones.

**2'-Methoxy-3,4-dihydro-1,1'-binaphthalene, 171**




**171**

According to **General Procedure A** with 1-tetralone (6.43 g, 44 mmol), anhydrous cerium chloride (21.7 g, 88.0 mmol), THF (440 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 80 mL, 40.0 mmol), 3 M HCl (440 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 30-40 to 1:4 dichloromehtane/petrol 30-40 afforded the title compound **171** as a colourless gum (7.09 g, 62 %).

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.89 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.86-7.81 (m, $H_{16}$), 7.79-7.73 (m, 1H, $H_{19}$), 7.38 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.37-7.32 (m, 2H, $H_{17}$ and $H_{18}$), 7.24 (dd, *J* = 7.4, 1.2 Hz, 1H, $H_6$),

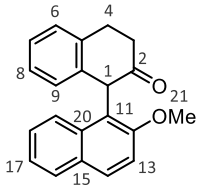
7.12 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.96 (td, *J* = 7.5, 1.4 Hz, 1H, $H_8$), 6.52 (dd, *J* = 7.6, 1.2 Hz, 1H, $H_9$), 6.06 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.85 (s, 3H, $H_{21}$), 3.11-3.00 (m, 2H, $H_4$), 2.60 (ddd, *J* = 9.3, 7.3, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 154.5 (Quat, $C_{12}$), 135.9 (Quat, $C_5$), 135.6 (Quat, $C_{10}$), 134.0 (Quat, $C_{20}$), 133.7 (Quat, $C_1$), 130.0 (CH, $C_2$), 129.3 (Quat, $C_{15}$), 129.1 (CH, $C_{14}$), 127.9 (CH, $C_{16}$), 127.6 (CH, $C_6$), 126.9 (CH, $C_7$), 126.5 (CH, $C_8$), 126.4 (CH, $C_{18}$), 125.5 (CH, $C_{19}$), 124.7 (CH, $C_9$), 123.7 (Quat, $C_{11}$), 123.7 (CH, $C_{17}$), 114.2 (CH, $C_{13}$), 57.1 ($CH_3$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3064, 3014, 2932, 2882, 2834, 1621, 1593, 1507, 1388, 1121, 1085;

HRMS (ESI$^+$): calculated for $C_{21}H_{19}O^+$ = 287.1430, mass found = 287.1432.

**2'-Methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 169**




**169**

According to **General Procedure B** with **171** (3.16 g, 11.0 mmol), dichloromethane (110 mL), sodium bicarbonate (2.31 g, 27.5 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 5.06 g, 22.0 mmol); then 1:1 diethyl ether/dichloromethane (220 mL), boron trifluoride diethyl etherate (2.17 mL, 17.6 mmol). Purification *via* column chromatography eluting with 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **169** as a white solid (2.67 g, 80 %).

Melting point: 146-148 °C (ethyl acetate/hexane);

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.89 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.86 (dd, *J* = 8.0, 1.5 Hz, 1H, $H_{16}$), 7.56 (d, *J* = 7.3 Hz, 1H, $H_{19}$), 7.39 (ddd, *J* = 8.4, 6.7, 1.5 Hz, 1H, $H_{18}$), 7.37-7.29 (m, 3H, $H_6$, $H_{13}$ and $H_{17}$),

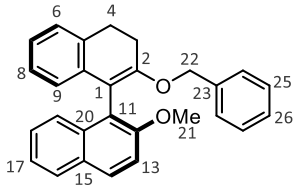
7.17 (tt, *J* = 7.4, 1.2 Hz, 1H, $H_7$), 6.98 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.55 (d, *J* = 7.8 Hz, 1H, $H_9$), 5.55 (s, 1H, $H_1$), 3.77 (s, 3H, $H_{21}$), 3.30 (dt, *J* = 11.5, 5.5 Hz, 2H, $H_4$), 2.95 (dt, *J* = 16.2, 5.4 Hz, 1H, $H_{3B}$), 2.83 (ddd, *J* = 16.2, 10.2, 6.0 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 210.6 (Quat, $C_2$), 154.8 (Quat, $C_{12}$), 137.6 (Quat, $C_{10}$), 136.2 (Quat, $C_5$), 133.4 (Quat, $C_{20}$), 129.8 (CH, $C_{14}$), 129.8 (Quat, $C_{15}$), 128.9 (CH, $C_{16}$), 127.6 (CH, $C_6$), 127.4 (CH, $C_9$), 126.9 (CH, $C_{18}$), 126.8 (CH, $C_8$), 126.4 (CH, $C_7$), 123.7 (CH, $C_{19}$), 123.6 (CH, $C_{17}$), 121.4 (CH, $C_{11}$), 114.0 (CH, $C_{13}$), 56.6 ($CH_3$, $C_{21}$), 50.4 (CH, $C_1$), 38.8 ($CH_2$, $C_3$), 28.7 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3068, 2962, 2904, 2840, 1713, 1624, 1597, 1512, 1306, 1009;

HRMS (ESI$^+$): calculated for $C_{21}H_{19}O_2^+$ = 303.1380, mass found = 303.1381.

**(*S*)-2-(Benzyloxy)-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, 166**




**166**

**Asymmetric:** A Schlenk tube was sequentially charged with *N*-(2,3,4-trifluorobenzyl)quinidinium bromide **192** (11 mg, 0.020 mmol), 2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one **169** (60.5 mg*, 0.200* mmol) and $K_3PO_4$ (425 mg, 2.00 mmol). The atmosphere was evacuated and backfilled with argon three times. Dichloromethane (0.40 mL) and benzene (0.60 mL) were added. The suspension was cooled to 0 °C and stirred for 5 minutes. A solution of benzyl iodide (131 mg) in benzene (1.0 mL) was added and the suspension was stirred rapidly at a rate of 1000-1400 rpm in the dark at 0 °C for 48 hours. The crude reaction mixture was then filtered through a plug of celite which was subsequently washed with dichloromethane. The filtrate was concentrated under reduced pressure and subsequent purification of the residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl

acetate/petrol 40-60 afforded the title compound **166** as thick colourless oil (78.1 mg, 99 %, 96:4 *e.r.*).

**Racemic:** A Schlenk tube was sequentially charged with tetrabutylammonium bromide (6.4 mg, 0.020 mmol) and 2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one **169** (60.5 mg, 0.200 mmol). The atmosphere was evacuated and backfilled with argon three times. Toluene (2.0 ml) and benzyl bromide (36 μL, 0.30 mmol) were added and the reaction mixture was then stirred for 5 minutes. After the addition of degassed 50 % aqueous potassium hydroxide (112 μL, 1.00 mmol) the reaction mixture was stirred rapidly at a rate of 1000-1400 rpm at room temperature for 4 hours. Water and dichloromethane were added and the organic layer was separated. The aqueous layer was then extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **166** as a thick colourless oil (75.1 mg, 96 %).

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.87-7.83 (m, 1H, $H_{16}$), 7.69-7.64 (m, 1H, $H_{19}$), 7.39 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.35-7.30 (m, 2H, $H_{17}$ and $H_{18}$), 7.20-7.12 (m, 4H, $H_{6,}$ , $H_{25}$ and $H_{26}$), 7.01 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.97-6.93 (m, 2H, $H_{24}$), 6.91 (td, *J* = 7.7, 1.2 Hz, 1H, $H_8$), 6.40 (dd, *J* = 7.8, 1.3 Hz, 1H, $H_9$), 4.76 (d, *J* = 12.3 Hz, 1H, $H_{22A}$), 4.72 (d, *J* = 12.3 Hz, 1H, $H_{22B}$), 3.84 (s, 3H, $H_{21}$), 3.15-3.10 (m, 2H, $H_4$), 2.81-2.68 (m, 2H, $H_3$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 154.9 (Quat, $C_{12}$), 154.7 (Quat, $C_2$), 137.9 (Quat, $C_{23}$), 136.8 (Quat, $C_{10}$), 133.9 (Quat, $C_{20}$), 132.6 (Quat, $C_5$), 129.3 (Quat, $C_{15}$), 129.0 (CH, $C_{14}$), 128.2 (CH, $C_{25}$), 128.0 (CH, $C_{16}$), 127.5 (CH, $C_6$), 127.3 (CH, $C_{24}$), 126.9 (CH, $C_{26}$), 126.6 (CH, $C_8$), 126.4 (CH, $C_{18}$), 125.6 (CH, $C_{19}$), 125.0 (CH, $C_7$), 124.1 (CH, $C_9$), 123.5 (CH, $C_{17}$), 120.0 (Quat, $C_{11}$), 114.0 (CH, $C_{13}$), 113.3 (Quat, $C_1$), 70.1 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$), 29.3 ($CH_2$, $C_4$), 25.2 ($CH_2$, $C_3$);

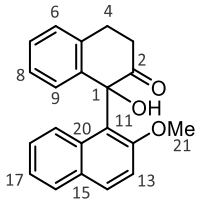
FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 2937, 2886, 2834, 1637, 1539, 1568, 1507, 1484, 1332, 1264, 1204;

HRMS (Cl$^{+}$): calculated for $C_{28}H_{24}O_2^{+}$ = 393.1849, mass found = 393.1852;

$[\alpha]_D^{25}$ = –100 (*c* = 1.00, $CHCl_3$);

Chiral HPLC**:** (Chiralpak ADH, 1 % $^{i}$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 5 μL injection) $\tau_R$ (major) = 14.9 min, $\tau_R$ (minor) = 18.1 min.

**1-Hydroxy-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1H)-one, 177**




**177**

A 7ml vial tube was sequentially charged with tetrabutylammonium bromide (6.4 mg, 0.020 mmol) and 2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one **169** (60.5 mg, 0.200 mmol). Toluene (2.0 ml) was added and the reaction mixture was then stirred for 5 minutes. After the addition of 50 % aqueous potassium hydroxide (112 μL, 1.00 mmol) the reaction mixture was stirred rapidly at a rate of 1000-1400 rpm open to air at room temperature for 4 hours. Water and dichloromethane were added and the organic layer was separated. The aqueous layer was then extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 15:85 ethyl acetate/petrol 40-60 afforded the title compound **177** as a thick colourless oil (53.1 mg, 83 %).

Melting point: 67-70 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.13 (d, *J* = 8.7 Hz, 1H, $H_9$), 8.08 (dd, *J* = 7.8, 1.3 Hz, 1H, $H_{19}$), 7.83 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.73 (dd, *J* = 8.0, 1.7 Hz, 1H, $H_{16}$), 7.37 (td, *J* = 7.6, 1.3 Hz, 1H, $H_{17}$), 7.30-7.17

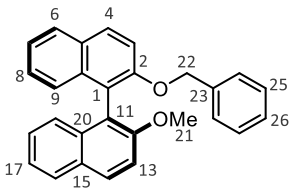
(m, 4H, $H_{13}$, $H_7$, $H_8$, and $H_{18}$), 7.05 (d, *J* = 7.4 Hz, 1H, $H_6$), 4.86 (s, 1H, O*H*), 3.78 (s, 3H, $H_{21}$), 2.94 (ddd, *J* = 17.2, 5.5, 3.3 Hz, 1H, $H_{3A}$), 2.78-2.63 (m, 2H, $H_4$), 2.51 (ddd, *J* = 17.1, 10.0, 6.9 Hz, 1H, $H_{3B}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 208.0 (Quat, $C_2$), 155.1 (Quat, $C_{12}$), 140.5 (Quat, $C_{Ar}$), 138.0 (Quat, $C_{Ar}$), 133.0 (Quat, $C_{Ar}$), 131.8 (CH, $C_{14}$), 130.9 (Quat, $C_{Ar}$), 128.7 (CH, $C_{16}$), 128.2 (CH, $C_{19}$), 127.6 (CH, $C_{Ar}$), 127.6 (CH, $C_{Ar}$), 126.8 (CH, $C_{17}$), 126.3 (CH, $C_{Ar}$), 124.8 (CH, $C_9$), 123.9 (CH, $C_{Ar}$), 122.1 (Quat, $C_{11}$), 115.0 (CH, $C_{13}$), 80.3 (Quat, $C_1$), 57.5 ($CH_3$, $C_{21}$), 34.9 ($CH_2$, $C_4$), 28.0 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3426, 3058, 2939, 2927, 1711, 1621, 1598, 1469, 1410, 1324, 1271, 1251, 1209, 1151, 1108, 1026;

LRMS (ESI$^+$): calculated for $C_{21}H_{18}O_3Na^+$ = 341.1148, mass found = 314.1144.

**(*S*)-2-(Benzyloxy)-2'-methoxy-1,1'-binaphthalene, 167**




**167**

**Asymmetric:** According to **General Procedure C** with **169** (60.5 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **167** as a white solid (74.4 mg, 95 %, 96:4 *e.r.*). The spectral data matched that previously reported in the literature.[128]

**Racemic:** According to **General Procedure D** with **169** (227 mg, 0.750 mmol), tetrabutylammonium bromide (24 mg, 0.075 mmol), $K_3PO_4$ (1.59 g, 7.5 mmol), dichloromethane

(7.5 mL), benzyl bromide (268 μL, 2.25 mmol); then dichloromethane (7.5 mL), DDQ (511 mg, 2.25 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **167** as a white solid (281 mg, 96 %). The spectral data matched that previously reported in the literature.[128]

Melting point: 128-129 °C (ethyl acetate/ petrol 40-60);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.93 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.90 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.87 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.47 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.44 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.37-7.30 (m, 2H, $H_7$ and $H_{17}$), 7.27-7.19 (m, 3H, $H_8$, $H_{18}$ and $H_{26}$), 7.18-7.13 (m, 4H, $H_9$, $H_{19}$ and $H_{25}$), 7.03-6.98 (m, 2H, $H_{24}$), 5.09 (d, *J* = 12.6 Hz, 1H, $H_{22B}$), 5.05 (d, *J* = 12.6 Hz, 1H, $H_{22A}$), 3.77 (s, 3H, $H_{21}$);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$), 154.2 (Quat, $C_{12}$), 137.7 (Quat, $C_{23}$), 134.2 (Quat, $C_{10}$ or $C_{20}$), 134.2 (Quat, $C_{10}$ or $C_{20}$), 129.6 (Quat, $C_5$), 129.5 (CH, $C_{14}$), 129.4 (CH, $C_4$), 129.3 (Quat, $C_{15}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 128.0 (CH, $C_6$), 127.4 (CH, $C_{26}$), 126.9 (CH, $C_{24}$), 126.5 (CH, $C_8$ or $C_{18}$), 126.4 (CH, $C_8$ or $C_{18}$), 125.6 (CH, $C_9$ or $C_{19}$), 125.5 (CH, $C_9$ or $C_{19}$), 123.9 (CH, $C_7$ or $C_{17}$), 123.6 (CH, $C_7$ or $C_{17}$), 121.0 (Quat, $C_1$), 119.6 (Quat, $C_{11}$), 116.3 (CH, $C_3$), 114.0 (CH, $C_{13}$), 71.4 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$);

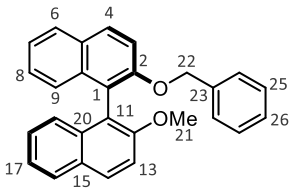
FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 2935, 2837, 1621, 1592, 1507, 1467, 1431, 1355, 1330, 1263, 1249, 1219, 1133, 1090;

HRMS (ESI$^+$): calculated for $C_{28}H_{23}O_2^+$ = 391.1693, mass found = 391.1699;

$[\alpha]_D^{25}$ = –55.2 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 1 % $^i$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 337 nm, 5 μL injection) $\tau_R$ (major) = 9.3 min, $\tau_R$ (minor) = 13.5 min.

**(*R*)-2-(Benzyloxy)-2'-methoxy-1,1'-binaphthalene, 167**



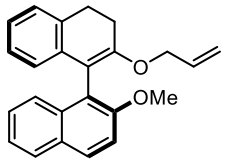

**167**

**Asymmetric:** According to **General Procedure C** with **169** (60.5 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quininium bromide **190** (11 mg, 0.020 mmol),[129] $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **167** as a white solid (68.1 mg, 87 %, 94:6 *e.r.*). The spectral data matched that obtained previously.

$[\alpha]_D^{25}$ = +51.5 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 1 % $^i$PrOH, 99 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 337 nm, 5 μL injection) $\tau_R$ (minor) = 9.3 min, $\tau_R$ (major) = 13.5 min.

**2-(Allyloxy)-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA1**




**RJA1**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), allyl bromide (34 μL, 0.40 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room

temperature for 3 h. Purification *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA1** as a white solid (58 mg, 85 %).

**Asymmetric with allyl bromide**: According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), allyl bromide (13 µL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA1** for HPLC analysis was obtained *via* preparative thin layer chromatography.

**Asymmetric with allyl iodide**: According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), allyl iodide (14 µL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA1** for HPLC analysis was obtained *via* preparative thin layer chromatography.

Melting point: 98-100 °C (petrol 40-60/ethyl acetate);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H), 7.76-7.70 (m, 1H), 7.60-7.55 (m, 1H), 7.29 (d, *J* = 9.0 Hz, 1H), 7.27-7.19 (m, 2H), 7.09 (dd, *J* = 7.4, 0.7 Hz, 1H), 6.91 (td, *J* = 7.4, 1.3 Hz, 1H), 6.80 (td, *J* = 7.6, 1.1 Hz, 1H), 6.26 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.56 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 4.97-4.87 (m, 2H), 4.14 (ddt, *J* = 13.4, 5.4, 1.5 Hz, 1H), 4.09 (ddt, *J* = 13.4, 5.2, 1.6 Hz, 1H), 3.76 (s, 3H), 3.13-2.98 (m, 2H), 2.71-2.57 (m, 2H);

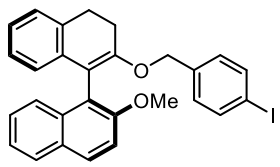
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.8, 154.4, 136.7, 134.5, 133.8, 132.5, 129.2, 128.9, 127.9, 126.8, 126.5, 126.2, 125.5, 124.9, 123.9, 123.4, 120.0, 116.5, 113.9, 112.7, 68.7, 56.7, 29.1, 24.9;

FTIR (neat) $\nu$/cm$^{-1}$ = 2936, 2835, 1637, 1593, 1508, 1485, 1463, 1332, 1264, 1247, 1184, 1087, 1057, 1019;

HRMS (ESI$^+$) calculated for $C_{24}H_{22}O_2Na^+$ = 365.1512, mass found = 365.1515;

Chiral HPLC: (Chiralpak ADH, 1 % $^{i}$PrOH, 99 % hexane, 0.5 mL min$^{-1}$, $\lambda$ = 280 nm, 10 μL injection) $\tau_R$ (major) = 16.3 min, $\tau_R$ (minor) = 14.1 min.

**2-((4-Iodobenzyl)oxy)-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA2**




**RJA2**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2.0 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), 4-iodobenzyl bromide (88 mg, 0.30 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room temperature for 8 hours. Purification *via* column chromatography eluting with 1:10 ethyl acetate/petrol 40-60 afforded the title compound **RJA2** as a white solid (64 mg, 62 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), 4-iodobenzyl bromide (45 mg, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA2** for HPLC analysis was obtained *via* preparative thin layer chromatography.

Melting point: 133-135 °C (petrol 40-60/ethyl acetate);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H), 7.73 (dd, *J* = 7.0, 1.7 Hz, 1H), 7.51-7.48 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 9.1 Hz, 1H), 7.25-7.17 (m, 2H), 7.07 (dd, *J* = 7.5, 0.8 Hz, 1H), 6.91 (td, *J* = 7.4, 1.3 Hz, 1H), 6.80 (td, *J* = 7.5, 1.2 Hz, 1H), 6.50 (d, *J* = 8.5 Hz, 2H), 6.29 (dd, *J* = 7.7, 1.0 Hz, 1H), 4.58 (d, *J* = 13.2 Hz, 1H), 4.54 (d, *J* = 13.2 Hz, 1H), 3.71 (s, 3H), 3.02 (t, *J* = 8.1 Hz, 2H), 2.65-2.59 (m, 2H);

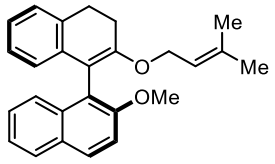
$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.8, 154.1, 137.4, 137.1, 136.5, 133.7, 132.5, 129.2, 129.1, 129.0, 127.9, 126.9, 126.6, 126.4, 125.4, 125.1, 124.1, 123.5, 119.7, 113.8, 113.8, 93.0, 69.3, 56.7, 29.1, 25.0;

FTIR (neat) $\nu/cm^{-1}$ = 2936, 2834, 1638, 1592, 1507, 1484, 1462, 1332, 1264, 1247, 1180, 1159, 1088, 1058, 1020, 1006;

HRMS ($ESI^+$) calculated for $C_{28}H_{23}O_2INa^+$ = 541.0635, mass found = 541.0635;

Chiral HPLC: (Chiralpak ADH, 20 % $^i$PrOH, 80 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 280 nm, 10 μL injection) $\tau_R$ (major) = 4.5 min, $\tau_R$ (minor) = 5.2min.

**2'-Methoxy-2-((3-methylbut-2-en-1-yl)oxy)-3,4-dihydro-1,1'-binaphthalene, RJA3**




**RJA3**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2.0 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), prenyl bromide (46 μL, 0.40 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room temperature for 20 hours. Purification *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA3** as a colourless gum (49 mg, 67 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), prenyl bromide (18 μL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA3** for HPLC analysis was obtained *via* preparative thin layer chromatography.

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.78 (d, *J* = 9.1 Hz, 1H), 7.74-7.69 (m, 1H), 7.61-7.55 (m, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.25-7.18 (m, 2H), 7.08 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.90 (td, *J* = 7.4, 1.3 Hz, 1H), 6.79 (td, *J* = 7.7, 1.3 Hz, 1H), 6.25 (dd, *J* = 7.7, 1.1 Hz, 1H), 5.00-4.94 (m, 1H), 4.12 (dd, *J* = 12.2, 7.1 Hz, 1H), 4.02 (dd, *J* = 12.1, 6.5 Hz, 1H), 3.76 (s, 3H), 3.04 (t, *J* = 8.0 Hz, 2H), 2.68-2.55 (m, 2H), 1.49 (d, *J* = 0.8 Hz, 3H), 1.28 (d, *J* = 0.8 Hz, 3H);

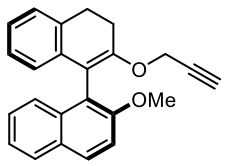
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.8, 154.8, 136.9, 136.7, 133.9, 132.6, 129.2, 128.8, 127.8, 126.8, 126.5, 126.2, 125.6, 124.8, 123.9, 123.4, 121.1, 120.3, 113.9, 112.9, 64.8, 56.8, 29.3, 25.7, 25.2, 17.7;

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3013, 2934, 2835, 1672, 1636, 1623, 1593, 1568, 1484, 1463, 1451, 1432, 1358, 1264, 1204, 1157, 1117, 1017;

HRMS (EI$^+$) calculated for $C_{26}H_{26}O_2^+$ = 370.1972, mass found = 390.1942;

Chiral HPLC: (Chiralpak IC, 1 % $^{i}$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (major) = 10.2 min, $\tau_R$ (minor) = 15.0 min.

**2'-Methoxy-2-(prop-2-yn-1-yloxy)-3,4-dihydro-1,1'-binaphthalene, RJA4**




**RJA4**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2.0 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), propargyl bromide (44 μL, 0.40 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room temperature for 2 hours. Purification *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA4** as a colourless gum (59 mg, 87 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), propargyl bromide (22 μL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA4** for HPLC analysis was obtained *via* preparative thin layer chromatography.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.79 (d, *J* = 9.0 Hz, 1H), 7.75-7.69 (m, 1H), 7.62-7.57 (m, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.24-7.19 (m, 2H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.92 (t, *J* = 7.4 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 7.6 Hz, 1H), 4.24 (dd, *J* = 16.0, 2.4 Hz, 1H), 4.13 (dd, *J* = 16.1, 2.5 Hz, 1H), 3.75 (s, 3H), 3.15-3.00 (m, 2H), 2.72 (t, *J* = 8.0 Hz, 2H), 2.26 (t, *J* = 2.4 Hz, 1H);

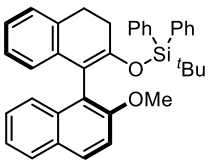
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.8, 153.7, 136.4, 133.7, 132.8, 129.2, 129.2, 127.9, 126.9, 126.5, 126.3, 125.6, 125.3, 124.2, 123.6, 119.4, 114.0, 114.0, 79.7, 74.9, 56.8, 55.8, 29.1, 24.8;

FTIR (neat) $\nu$/cm$^{-1}$ = 3275, 2935, 2835, 1642, 1621, 1593, 1508, 1484, 1451, 1429, 1332, 1264, 1246, 1179, 1159, 1117, 1087, 1058;

HRMS (ESI$^+$) calculated for $C_{24}H_{20}O_2Na^+$ = 363.1356, mass found = 363.1355;

Chiral HPLC: (Chiralpak ADH, 1 % $^i$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (major) = 30.2 min, $\tau_R$ (minor) = 28.6 min.

### *tert*-Butyl((2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2-yl)oxy)diphenylsilane, RJA5




**RJA5**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (40 mg, 0.13 mmol), dichloromethane (1.3 mL),

tetrabutylammonium hydrogensulfate (4 mg, 0.013 mmol), tert-butyl(chloro)diphenylsilane (103 μL, 0.40 mmol), $K_3PO_4$ (280 mg, 1.3 mmol). Reaction conditions: room temperature for 20 hours. Purification *via* column chromatography eluting with a gradient from petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **RJA5** as a white solid (27 mg, 38 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), tert-butyl(chloro)diphenylsilane (37 μL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA5** for HPLC analysis was obtained *via* preparative thin layer chromatography.

Melting point: 66-68 °C (petrol 40-60/ethyl acetate);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.81 (d, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.60 (dt, *J* = 6.5, 1.4 Hz, 2H), 7.51 (dt, *J* = 6.8, 1.4 Hz, 2H), 7.37-7.21 (m, 9H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.86 (td, *J* = 7.4, 1.5 Hz, 1H), 6.82 (td, *J* = 7.4, 1.4 Hz, 1H), 6.39 (dd, *J* = 7.5, 1.5 Hz, 1H), 3.79 (s, 3H), 2.74-2.57 (m, 2H), 2.28-2.14 (m, 2H), 0.33 (s, 9H);

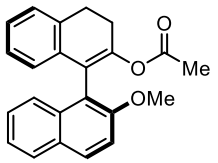
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.9, 151.1, 137.2, 135.2, 135.2, 134.0, 133.8, 133.7, 132.2, 129.8, 129.7, 129.3, 128.7, 127.9, 127.6, 127.6, 126.7, 126.4, 126.1, 125.7, 124.4, 123.8, 123.3, 120.3, 113.7, 112.6, 56.4, 29.6, 28.9, 25.4, 18.7;

FTIR (neat) $\nu$/cm$^{-1}$ = 2931, 2857, 1637, 1592, 1508, 1486, 1428, 1361, 1333, 1265, 1247, 1192, 1115, 1088, 1008;

HRMS (ESI$^+$) calculated for $C_{37}H_{36}O_2NaSi^+$ = 563.2377, mass found = 563.2374;

Chiral HPLC: (Chiralpak ADH, 1 % $^i$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (enantiomer 1) = 4.5 min, $\tau_R$ (enantiomer 2) = 4.9 min.

**2'-Methoxy-3,4-dihydro-[1,1'-binaphthalen]-2-yl acetate, RJA6**




**RJA6**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (20 mg, 0.066 mmol), dichloromethane (0.7 mL), tetrabutylammonium hydrogensulfate (2 mg, 0.006 mmol), acetic anhydride (31 μL, 0.33 mmol), $K_3PO_4$ (140 mg, 0.66 mmol). Reaction conditions: room temperature for 20 hours. Purification *via* column chromatography eluting with a gradient from petrol 40-60 to 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA6** as a colourless gum (26 mg, 99 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), acetic anhydride (14 μL, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA6** for HPLC analysis was obtained *via* preparative thin layer chromatography.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H), 7.75-7.69 (m, 1H), 7.59-7.52 (m, 1H), 7.27 (d, *J* = 9.0 Hz, 1H), 7.26-7.22 (m, 2H), 7.13 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.00 (td, *J* = 7.4, 1.3 Hz, 1H), 6.83 (td, *J* = 7.5, 0.9 Hz, 1H), 6.35 (dd, *J* = 7.7, 1.1 Hz, 1H), 3.75 (s, 3H), 3.22-3.03 (m, 2H), 2.82-2.66 (m, 2H), 1.64 (s, 3H);

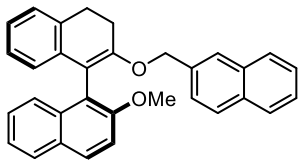
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 168.5, 154.6, 148.6, 135.0, 133.9, 133.2, 129.5, 129.1, 127.8, 127.2, 126.6, 126.5, 126.5, 125.3, 125.1, 123.7, 120.6, 118.1, 113.8, 56.9, 28.9, 27.1, 20.7;

FTIR (neat) $\nu$/cm$^{-1}$ = 2937, 2837, 1755, 1622, 1593, 1508, 1266, 1248, 1204, 1176, 1149;

HRMS (ESI$^+$) calculated for $C_{23}H_{20}O_3Na^+$ = 367.1305, mass found = 367.1303;

Chiral HPLC: (Chiralpak ADH, 1 % $^{i}$PrOH, 99 % hexane, 0.5 mL min$^{-1}$, $\lambda$ = 273 nm, 10 μL injection) $\tau_R$ (enantiomer 1) = 29.9 min, $\tau_R$ (enantiomer 2) = 31.0 min.

**2'-Methoxy-2-(naphthalen-2-ylmethoxy)-3,4-dihydro-1,1'-binaphthalene, RJA7**




**RJA7**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2.0 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), 2-(bromomethyl)naphthalene (88 mg, 0.40 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room temperature for 2 hours. Purification *via* column chromatography eluting with a gradient from petrol 40-60 to 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA7** as a colourless gum (91 mg, 99 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), 2-(bromomethyl)naphthalene (32 mg, 0.15 mmol); omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA7** for HPLC analysis was obtained *via* preparative thin layer chromatography.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H), 7.75-7.72 (m, 1H), 7.63-7.58 (m, 1H), 7.57-7.53 (m, 1H), 7.49-7.43 (m, 2H), 7.31-7.27 (m, 2H), 7.25 (d, *J* = 9.0 Hz, 1H), 7.23-7.17 (m, 2H), 7.15 (ddd, *J* = 8.2, 6.7, 1.6 Hz, 1H), 7.05 (dd, *J* = 7.3, 0.7 Hz, 1H), 6.91-6.85 (m, 2H), 6.78 (td, *J* = 7.5, 1.2 Hz, 1H), 6.30 (dd, *J* = 7.7, 1.0 Hz, 1H), 4.79 (d, *J* = 12.5 Hz, 1H), 4.75 (d, *J* = 12.5 Hz, 1H), 3.66 (s, 3H), 3.00 (t, *J* = 8.1 Hz, 2H), 2.73-2.59 (m, 2H);

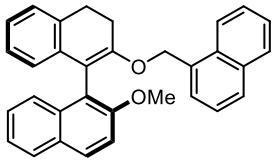
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.9, 154.5, 136.7, 135.3, 133.9, 133.2, 132.9, 132.6, 129.3, 129.0, 128.0, 128.0, 127.8, 127.6, 126.9, 126.6, 126.4, 125.9, 125.9, 125.8, 125.6, 125.2, 125.0, 124.1, 123.5, 120.0, 114.0, 113.5, 70.1, 56.7, 29.2, 25.1;

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 2934, 2835, 1638, 1593, 1508, 1484, 1465, 1361, 1332, 1264, 1246, 1182, 1147, 1088, 1058, 1019;

HRMS (ESI$^+$) calculated for $C_{32}H_{26}O_2Na^+$ = 465.1825, mass found = 465.1821;

Chiral HPLC: (Chiralpak ADH, 1 % $^i$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (major) = 37.6 min, $\tau_R$ (minor) = 24.7 min.

**2'-Methoxy-2-(naphthalen-1-ylmethoxy)-3,4-dihydro-1,1'-binaphthalene, RJA8**




**RJA8**

**Racemic**: *This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure D** with **169** (60 mg, 0.20 mmol), dichloromethane (2.0 mL), tetrabutylammonium hydrogensulfate (7 mg, 0.02 mmol), 1-(bromomethyl)naphthalene (88 mg, 0.40 mmol), 50 % w/w aqueous potassium hydroxide (56 μL, 1.0 mmol). Reaction conditions: room temperature for 2 hours. Purification *via* column chromatography eluting with a gradient from petrol 40-60 to 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA8** as a colourless gum (89 mg, 99 %).

**Asymmetric:** According to **General Procedure C** with **169** (15.1 mg, 0.0500 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (2.8 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), 1-(bromomethyl)naphthalene (32 mg, 0.15 mmol);

omitting the DDQ oxidation. An analytical amount of enantioenriched **RJA8** for HPLC analysis was obtained *via* preparative thin layer chromatography.

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.77 (d, *J* = 9.0 Hz, 1H), 7.73-7.69 (m, 1H), 7.63-7.59 (m, 1H), 7.58-7.53 (m, 2H), 7.26-7.10 (m, 7H), 7.07 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.00 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 6.90 (td, *J* = 7.4, 1.3 Hz, 1H), 6.79 (td, *J* = 7.6, 1.1 Hz, 1H), 6.29 (dd, *J* = 7.7, 1.0 Hz, 1H), 5.00 (d, *J* = 12.8 Hz, 1H), 4.97 (d, *J* = 12.7 Hz, 1H), 3.61 (s, 3H), 3.08-3.00 (m, 2H), 2.71-2.66 (m, 2H);

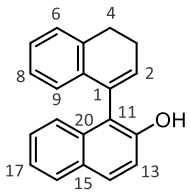
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.9, 154.8, 136.7, 134.0, 133.5, 133.3, 132.8, 131.4, 129.2, 129.0, 128.6, 128.2, 127.9, 126.9, 126.5, 126.4, 126.1, 125.9, 125.6, 125.4, 125.1, 125.1, 124.2, 123.7, 123.5, 119.9, 114.0, 113.8, 68.9, 56.6, 29.3, 25.6;

FTIR (neat) $\nu$/cm$^{-1}$ = 2934, 2835, 1640, 1621, 1594, 1508, 1484, 1358, 1332, 1264, 1246, 1183, 1147, 1088, 1057, 1018;

HRMS (ESI$^+$) calculated for $C_{32}H_{26}O_2Na^+$ = 465.1825, mass found = 465.1823;

Chiral HPLC: (Chiralpak ADH, 1 % $^i$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (major) = 23.2 min, $\tau_R$ (minor) = 18.7 min.

**3',4'-Dihydro-[1,1'-binaphthalen]-2-ol, 236**




**236**

A solution of **171** (5.73 g, 20 mmol) in dichloromethane (200 mL) was cooled to 0 °C. Boron tribromide (3.9 mL, 40 mmol) was added and the resulting solution was stirred for 15 minutes at 0 °C. After warming to room temperature, the reaction mixture was stirred for a further 2 hours. The solution was then re-cooled to 0 °C and $H_2O$ (200 mL) was added carefully at such a rate that effervescence was kept to a minimum. The mixture was extracted with

dichloromethane twice and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:3 dichloromethane/petrol 40-60 afforded the title compound **236** as a white solid (5.03g, 93 %).

Melting point: 122-124 °C (dichloromethane/petrol 40-60);

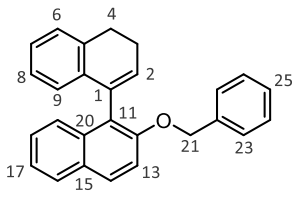
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.87-7.76 (m, 2H, $H_{14}$ and $H_{16}$), 7.57-7.51 (m, 1H, $H_{19}$), 7.36-7.31 (m, 2H, $H_{17}$ and $H_{18}$), 7.29 (d, *J* = 8.9 Hz, 1H, $H_{13}$), 7.26 (dd, *J* = 7.5, 1.2 Hz, 1H, $H_6$), 7.18 (td, *J* = 7.5, 1.3 Hz, 1H, $H_7$), 6.98 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.58 (d, *J* = 7.6 Hz, 1H, $H_9$), 6.28 (t, *J* = 4.5 Hz, 1H, $H_2$), 5.46 (s, 1H, O*H*), 3.13 (dt, *J* = 15.8, 9.0 Hz, 1H, $H_{4B}$), 3.02 (dt, *J* = 15.3, 7.2 Hz, 1H, $H_{4A}$), 2.67-2.60 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 150.8 (Quat, $C_{12}$), 136.0 (Quat, $C_5$), 134.0 (Quat, $C_{10}$), 133.4 (Quat, $C_{20}$), 133.0 (CH, $C_2$), 132.4 (Quat, $C_1$), 129.5 (CH, $C_{14}$), 129.0 (Quat, $C_{15}$), 128.2 (CH, $C_{16}$), 128.0 (CH, $C_6$), 127.9 (CH, $C_7$), 127.0 (CH, $C_8$), 126.6 (CH, $C_{18}$), 125.2 (CH, $C_9$), 125.0 (CH, $C_{19}$), 123.4 (CH, $C_{17}$), 118.8 (Quat, $C_{11}$), 117.4 (CH, $C_{13}$), 28.1 ($CH_2$, $C_4$), 23.8($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3517, 3058, 3016, 2933, 2883, 2829, 1620, 1596, 1390, 1271, 1374;

HRMS (ESI$^-$): calculated for $C_{20}H_{15}O^-$ = 271.1128, mass found = 271.1133.

**2'-(Benzyloxy)-3,4-dihydro-1,1'-binaphthalene, 237**




**237**

To a solution of **236** (2.04 g, 7.5 mmol) and benzyl bromide (2.68 mL, 22.5 mmol) in acetone (70 mL) was added potassium carbonate (5.18 g, 37.5 mmol). The resulting suspension was

stirred at reflux for 18 h and then cooled to room temperature. The crude reaction mixture was filtered through a plug of celite which was subsequently washed with ethyl acetate. The filtrate was then concentrated under reduced pressure. Purification of the crude residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **237** as a colourless gum (2.70 g, 99 %).

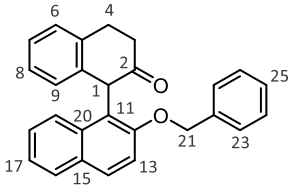
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.86 (d, *J* = 9.2 Hz, 1H, $H_{14}$), 7.84-7.79 (m, 2H, $H_{16}$ and $H_{19}$), 7.41-7.34 (m, 3H, $H_{13}$, $H_{17}$, and $H_{18}$), 7.27-7.21 (m, 4H, $H_6$, $H_{24}$, and $H_{25}$), 7.17-7.10 (m, 3H, $H_7$ and $H_{23}$), 6.97 (td, *J* = 7.6, 1.4 Hz, 1H, $H_8$), 6.57 (dd, *J* = 7.7, 1.2 Hz, 1H, $H_9$), 6.06 (t, *J* = 4.5 Hz, 1H, $H_2$), 5.15 (d, *J* = 12.0 Hz, 1H, $H_{21B}$), 5.06 (d, *J* = 12.0 Hz, 1H, $H_{21A}$), 3.06-2.96 (m, 2H, $H_4$), 2.67-2.48 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.5 (Quat, $C_{12}$), 137.5 (Quat, $C_{22}$), 136.1 (Quat, $C_5$), 135.9 (Quat, $C_{10}$), 134.1 (Quat, $C_{20}$), 133.8 (Quat, $C_1$), 130.0 (CH, $C_2$), 129.6 (Quat, $C_{15}$), 128.9 (CH, $C_{14}$), 128.3 (CH, $C_{24}$), 128.0 (CH, $C_6$), 127.6 (CH, $C_7$), 127.5 (CH, $C_{25}$), 127.2 (CH, $C_{23}$), 126.9 (CH, $C_{16}$), 126.6 (CH, $C_8$), 126.4 (CH, $C_{18}$), 125.6 (CH, $C_{19}$), 125.0 (Quat, $C_{11}$), 124.8 (CH, $C_9$), 123.9 (CH, $C_{17}$), 116.0 (CH, $C_{13}$), 71.6 ($CH_2$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.7 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3029, 2932, 2881, 2828, 1621, 1590, 1507, 1332, 1178;

HRMS (ESI$^+$): calculated for $C_{27}H_{22}ONa^+$ = 385.1563, mass found = 385.1562.

**2'-(Benzyloxy)-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 241**




**241**

According to **General Procedure B** with **237** (2.70 g, 7.45 mmol), dichloromethane (75 mL), sodium bicarbonate (1.56 g, 18.6 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 3.43 g,

19.9 mmol); then 1:1 diethyl ether/dichloromethane (150 mL), boron trifluoride diethyl etherate (1.47 mL, 11.9 mmol). Recrystallization from hexane/ethyl acetate afforded the title compound **241** as a white solid (2.67 g, 68 %).

Melting point: 170-172 °C (ethyl acetate/hexane);

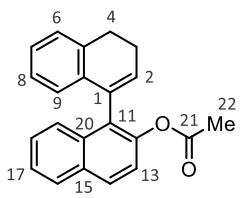
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92-7.82 (m, 2H, $H_{14}$ and $H_{16}$), 7.69 (d, *J* = 8.3 Hz, 1H, $H_{19}$), 7.43 (t, *J* = 7.3 Hz, 1H, $H_{18}$), 7.37 (d, *J* = 7.3 Hz, 1H, $H_{17}$), 7.34 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.30-7.22 (m, 4H, $H_6$, $H_7$ and $H_{24}$), 7.20 (t, *J* = 7.4 Hz, 1H, $H_{25}$), 7.07-6.94 (m, 3H, $H_8$ and $H_{23}$), 6.56 (d, *J* = 7.7 Hz, 1H, $H_9$), 5.52 (s, 1H, $H_1$), 5.05 (d, *J* = 11.4 Hz, 1H, $H_{21B}$), 4.96 (d, *J* = 11.4 Hz, 1H, $H_{21A}$), 3.16 (ddd, *J* = 15.8, 11.0, 5.1 Hz, 1H, $H_{4B}$), 3.00 (dt, *J* = 15.5, 5.5 Hz, 1H, $H_{4A}$), 2.78 (dt, *J* = 16.2, 5.3 Hz, 1H, $H_{3B}$), 2.49 (ddd, *J* = 16.3, 10.9, 5.5 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = = 210.5 (Quat, $C_2$), 153.7 (Quat, $C_{12}$), 137.9 (Quat, $C_{10}$), 136.6 (Quat, $C_{22}$), 136.3 (Quat, $C_5$), 133.8 (Quat, $C_{20}$), 129.7 (Quat, $C_{15}$), 129.7 (CH, $C_{14}$), 129.0 (CH, $C_{16}$), 128.5 (CH, $C_{24}$), 128.1 (CH, $C_6$), 127.9 (CH, $C_{23}$), 127.6 (CH, $C_7$), 127.3 (CH, $C_8$), 127.0 (CH, $C_9$), 126.8 (CH, $C_{18}$), 126.3 (CH, $C_{25}$), 123.7 (CH, $C_{17}$), 123.3 (CH, $C_{19}$), 121.8 (CH, $C_{11}$), 114.7 (CH, $C_{13}$), 71.3 ($CH_2$, $C_{21}$), 50.5 (CH, $C_1$), 38.6 ($CH_2$, $C_3$), 28.5 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3032, 2945, 2848, 1714, 1624, 1595, 1486, 1348, 1254, 1180;

HRMS (ESI$^+$): calculated for $C_{27}H_{22}O_2Na^+$ = 401.1512, mass found = 401.1507.

**3',4'-Dihydro-[1,1'-binaphthalen]-2-yl acetate, 238**




**238**

In analogy to a modified literature procedure,[130] acetyl chloride (0.28 mL, 4.0 mmol) was added to a solution of **236** (545 mg, 2.00 mmol) in anhydrous dichloromethane (5 mL). After cooling to 0 °C, triethylamine (0.42 mL, 3.0 mmoL) was added. Following this, the reaction mixture was stirred for 10 minutes and an additional 20 hours at room temperature. The reaction mixture was then quenched with 1 M HCl and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:19 ethyl acetate/petrol 40-60 afforded the title compound **238** as a colourless gum (639 mg, 99%).

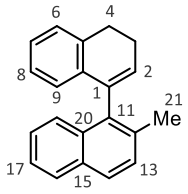
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.90 (d, *J* = 8.8 Hz, 1H, $H_{14}$), 7.89 (dd, *J* = 7.8, 1.5 Hz, 1H, $H_{16}$), 7.79 (dd, *J* = 8.4, 1.5 Hz, 1H, $H_{19}$), 7.47 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H, $H_{17}$), 7.40 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H, $H_{18}$), 7.30 (d, *J* = 8.9 Hz, 1H, $H_{13}$), 7.23 (dd, *J* = 7.5, 1.3 Hz, 1H, $H_6$), 7.13 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.97 (td, *J* = 7.6, 1.5 Hz, 1H, $H_8$), 6.51 (dd, *J* = 7.6, 1.2 Hz, 1H, $H_9$), 6.08 (t, *J* = 4.6 Hz, 1H, $H_2$), 3.10-2.87 (m, 2H, $H_4$), 2.65-2.44 (m, 2H, $H_3$), 2.09 (s, 3H, $H_{22}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 170.0 (Quat, $C_{21}$), 146.2 (Quat, $C_{12}$), 135.6 (Quat, $C_{Ar}$), 134.9 (Quat, $C_{Ar}$), 133.6 (Quat, $C_{Ar}$), 132.8 (Quat, $C_{Ar}$), 132.0 (Quat, $C_{Ar}$), 130.5 (CH, $C_2$), 129.2 (Quat, $C_{Ar}$), 128.9 (CH, $C_{14}$), 128.2 (CH, $C_{16}$), 127.5 (CH, $C_6$), 127.2 (CH, $C_7$), 126.7 (CH, $C_8$), 126.6 (CH, $C_{18}$), 126.3 (CH, $C_{19}$), 125.7 (CH, $C_{17}$), 125.1 (CH, $C_9$), 121.9 (CH, $C_{13}$), 28.3 ($CH_2$, $C_4$), 23.7 ($CH_2$, $C_3$), 20.9 ($CH_2$, $C_{22}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3019, 2935, 2882, 2829, 1760, 1622, 1594, 1510, 1485, 1450, 1427, 1392, 1270, 1157, 1074, 1012;

LRMS (ESI$^+$): calculated for $C_{22}H_{18}O_2Na^+$ = 337.1199, mass found = 337.1198.

**2'-Methyl-3,4-dihydro-1,1'-binaphthalene, 235**




**235**

Magnesium turnings (365 mg, 15.0 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of 1-bromo-2-methylnaphthalene (2.21 g, 10.0 mmol) in THF (20 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 2 hours. The resulting Grignard reagent was then used immediately according to **General Procedure A** with 1-tetralone (1.6 mL, 12 mmol), anhydrous cerium chloride (5.92 g, 24.0 mmol), THF (75 mL) and 3M HCl (75 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:3 dichloromethane/petrol 40-60 afforded the title compound **235** as a white solid (983 mg, 36 %).

Melting point: 94-96 °C (dichloromethane/petrol 40-60);

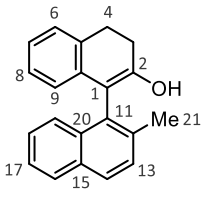
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.85 (d, *J* = 7.8 Hz, 1H, $H_{14}$), 7.82-7.77 (m, 2H, $H_{16}$ and $H_{19}$), 7.44 (d, *J* = 8.5 Hz, 1H, $H_{13}$), 7.44-7.34 (m, 2H, $H_{17}$ and $H_{18}$), 7.26 (d, *J* = 7.3 Hz, 1H, $H_6$), 7.14 (td, *J* = 7.5, 1.3 Hz, 1H, $H_7$), 6.96 (td, *J* = 7.5, 1.3 Hz, 1H, $H_8$), 6.45 (d, *J* = 7.6 Hz, 1H, $H_9$), 6.01 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.14-2.98 (m, 2H, $H_4$), 2.68-2.52 (m, 2H, $H_3$), 2.35 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 136.7 (Quat, $C_{12}$), 136.3 (Quat, $C_{Ar}$), 136.0 (Quat, $C_{Ar}$), 135.3 (Quat, $C_{Ar}$), 133.9 (Quat, $C_{Ar}$), 133.2 (Quat, $C_{Ar}$), 132.2 (Quat, $C_{Ar}$), 129.3 (CH, $C_2$), 128.8 (CH, $C_{13}$), 127.9 (CH, $C_{14}$), 127.6 (CH, $C_6$), 127.2 (CH, $C_7$), 127.1 (CH, $C_8$), 126.7 (CH, $C_{18}$), 126.1 (CH, $C_{16}$ or $C_{19}$), 126.0 (CH, $C_{16}$ or $C_{19}$), 124.9 (CH, $C_9$ or $C_{17}$), 124.9, 28.4 ($CH_2$, $C_4$), 23.7 ($CH_2$, $C_3$), 20.4 ($CH_3$, $C_{21}$);

FTIR (neat) $\nu/cm^{-1}$ = 3054, 3017, 2931, 2881, 2828, 1597, 1507, 1483, 1438, 1378, 1326, 1039, 1028, 1020;

HRMS ($EI^+$): calculated for $C_{21}H_{19}^+$ = 271.1481, mass found = 271.1492.

**2'-methyl-3,4-dihydro-[1,1'-binaphthalen]-2-ol, 242**




**242**

According to **General Procedure B** with **235** (927 mg, 3.43 mmol), dichloromethane (35 mL), sodium bicarbonate (719 mg, 8.56 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.58 g, 6.86 mmol); then 1:1 diethyl ether/dichloromethane (70 mL), boron trifluoride diethyl etherate (0.68 mL, 5.5 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **242** as an off white solid (546 mg, 56 %).

Melting point: 169-171 °C (ethyl acetate/hexane);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.88 (d, *J* = 8.2 Hz, 1H, $H_{14}$), 7.85 (d, *J* = 8.5 Hz, 1H, $H_{16}$), 7.77 (d, *J* = 8.3 Hz, 1H, $H_{19}$), 7.49 (d, *J* = 8.2 Hz, 1H, $H_{13}$), 7.46-7.38 (m, 3H, $H_{17}$ and $H_{18}$), 7.22 (d, *J* = 7.3 Hz, 1H, $H_6$), 7.02 (t, *J* = 7.3 Hz, 1H, $H_7$), 6.91 (t, *J* = 7.5 Hz, 1H, $H_8$), 6.24 (d, *J* = 7.6 Hz, 1H, $H_9$), 4.63 (br s, 1H, O*H*), 3.25-3.09 (m, 2H, $H_4$), 2.84-2.63 (m, 2H, $H_3$), 2.35 (s, 3H, $H_{21}$);

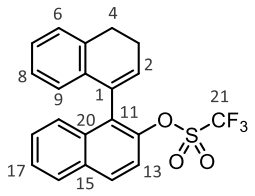
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 151.8 (Quat, $C_2$), 137.1 (Quat, $C_{12}$), 136.1 (Quat, $C_{Ar}$), 133.1 (Quat, $C_{Ar}$), 132.7 (Quat, $C_{Ar}$), 132.2 (Quat, $C_{Ar}$), 129.1 (CH, $C_{13}$), 129.1 (Quat, $C_{Ar}$), 128.6 (CH, $C_{16}$), 128.3

(CH, $C_{14}$), 127.2 (CH, $C_6$), 126.8 (CH, $C_{18}$), 126.7 (CH, $C_8$), 125.5 ($C_{17}$ or $C_{19}$), 125.5 (CH, $C_{17}$ or $C_{19}$), 124.6 (CH, $C_7$), 123.2 (CH, $C_9$), 108.1 (Quat, $C_1$), 28.8 ($CH_2$, $C_4$), 26.3 ($CH_2$, $C_3$), 20.1 ($CH_3$, $C_{21}$);

FTIR (neat) $\nu/cm^{-1}$ = 3466, 3406, 3055, 3014, 2942, 2888, 2834, 1714, 1645, 1596, 1569, 1484, 1484, 1394, 1314, 1280, 1219, 1180, 1110, 1028;

HRMS ($ESI^+$): calculated for $C_{21}H_{19}O^+$ = 287.1430, mass found = 287.1426.

**3',4'-Dihydro-[1,1'-binaphthalen]-2-yl trifluoromethanesulfonate, 239**




**239**

In analogy to a modified literature procedure,[131] pyridine (0.80 mL, 9.8 mmol) was added to a solution of **236** (1.34 g, 4.92 mmol) in dichloromethane (5 mL). After cooling to 0 °C triflic anhydride (1.00 mL, 5.90 mmol) was added dropwise over a period of 10 minutes. The reaction mixture was stirred for 2 hours at 0 °C and then warmed to room temperature. The crude reaction mixture was diluted with ethyl acetate and quenched with 1 M aqueous HCl. The aqueous layer was separated and the organic layer was washed with 1M HCL, saturated aqueous $NaHCO_3$ and brine. The organic layer was then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with petrol 40-60 afforded the title compound **239** as a colourless gum (1.77 g, 89 %).

$^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.95 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.93 (d, *J* = 8.0 Hz, 1H, $H_{16}$), 7.85 (dd, *J* = 8.5, 1.2 Hz, 1H, $H_{19}$), 7.56 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, $H_{17}$), 7.51-7.45 (m, 1H, $H_{18}$), 7.45 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.26-7.23 (m, 1H, $H_6$), 7.15 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.95 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.39 (dd, *J* = 7.7, 1.2 Hz, 1H, $H_9$), 6.23 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.15-2.95 (m, 2H, $H_4$), 2.66-2.56 (m, 2H, $H_3$);

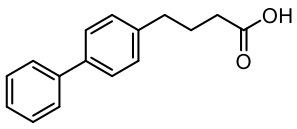
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 144.9 (Quat, $C_{12}$), 135.9 (Quat, $C_{Ar}$), 134.3 (Quat, $C_{Ar}$), 133.6 (Quat, $C_{Ar}$), 132.9 (CH, $C_2$), 132.7 (Quat, $C_{Ar}$), 131.3 (Quat, $C_{Ar}$), 131.2 (Quat, $C_{Ar}$), 130.1 (CH, $C_{14}$), 128.3 (CH, $C_{16}$), 127.8 (CH, $C_6$), 127.6 (CH, $C_7$ or $C_{18}$), 127.6 (CH, $C_7$ or $C_{18}$), 127.1 (CH, $C_{17}$), 127.0 (CH, $C_{19}$), 126.6 (CH, $C_8$), 124.9 (CH, $C_9$), 119.5 (CH, $C_{13}$), 118.6 (Quat, q, *J* = 320.0 Hz, $C_{21}$), 27.8 ($CH_2$, $C_4$), 23.7 ($CH_2$, $C_3$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –74.4;

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3022, 2938, 2833, 1621, 1593, 1509, 1486, 1451, 1357, 1323, 1270, 1249, 1174, 1121, 1022;

HRMS (ESI$^+$): calculated for $C_{21}H_{16}F_3O_3S^+$ = 405.0767, mass found = 405.0769.

**4-([1,1'-Biphenyl]-4-yl)butanoic acid, RJA50**




**RJA50**

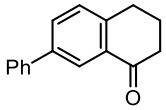
*This compound was synthesised and analysed by Dr Roland Armstrong* according to a modified literature procedure,[84] a stirred suspension of Fenbufen (5.00 g, 19.7 mmol), hydrazine monohydrate (98 %, 1.96 mL, 40.4 mmol) and powdered potassium hydroxide (4.74 g, 84.7 mmol) in ethylene glycol (60 mL) was heated to 120 °C for 1 hour. After this time the reaction mixture was heated at reflux for a further 3 hours and then cooled to room temperature and acidified by dropwise addition of concentrated HCl (pH 1-2). The mixture was diluted with water and extracted three times with ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:4 ethyl acetate/toluene afforded the title compound **RJA50** as a white solid (2.35 g, 50 %). The spectral data matched that previously reported in the literature. [132]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 11.13 (br s, COO*H*), 7.50-7.46 (m, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.22 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.90 (qn, *J* = 7.5 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 180.3, 141.1, 140.4, 139.1, 129.0, 128.8, 127.2, 127.2, 127.1, 34.7, 33.5, 26.2;

LRMS ($ESI^+$) calculated for $C_{16}H_{16}O_2Na^+$ = 263, mass found = 263.

**7-Phenyl-3,4-dihydronaphthalen-1(2*H*)-one, RJA18**




**RJA18**

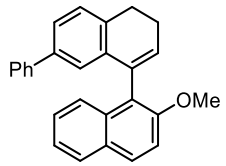
*This compound was synthesised and analysed by Dr Roland Armstrong* by analogy to a modified literature procedure,[85] a mechanically stirred suspension of **RJA50** (500 mg, 2.08 mmol) in polyphosphoric acid (2.1 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/toluene afforded the title compound **RJA18** as a white solid (440 mg, 95 %). The spectral data matched that previously reported in the literature.[133]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.20 (d, *J* = 2.0 Hz, 1H), 7.62 (dd, *J* = 7.9, 2.1 Hz, 1H), 7.55-7.51 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.29-7.21 (m, 2H), 2.90 (t, *J* = 6.1 Hz, 2H), 2.60 (t, *J* = 6.6 Hz, 2H), 2.07 (qn, = 6.3 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ =198.4, 143.4, 140.0, 139.6, 132.9, 131.9, 129.4, 128.9, 127.6, 127.0, 125.5, 39.3, 29.4, 23.3;

LRMS ($ESI^+$) calculated for $C_{16}H_{14}ONa^+$ = 245, mass found = 245.

**2'-Methoxy-7-phenyl-3,4-dihydro-1,1'-binaphthalene, RJA28**




**RJA28**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA18** (1.00 g, 4.50 mmol), anhydrous cerium chloride (2.22 g, 9.00 mmol), THF (45 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 10.8 mL, 5.40 mmol), 3M HCl (45 mL). Purification *via* column chromatography eluting with a gradient from 3:17 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 afforded the title compound **RJA28** as a white solid (988 mg, 61 %).

Melting point: 64-65 °C (dichloromethane/petrol 40-60);

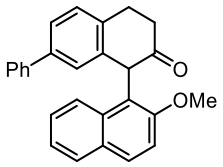
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H), 7.90-7.83 (m, 2H), 7.46-7.22 (m, 10H), 6.81 (d, *J* = 1.5 Hz, 1H), 6.15 (t, *J* = 4.5 Hz, 1H), 3.91 (s, 3H), 3.14 (t, *J* = 8.1 Hz, 2H), 2.68 (td, *J* = 8.1, 4.6 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 141.5, 139.5, 135.9, 135.1, 134.0, 133.7, 130.5, 129.2, 129.1, 128.5, 127.9, 127.9, 127.0, 126.8, 126.4, 125.7, 125.4, 123.6, 123.4, 123.4, 114.0, 57.0, 28.0, 23.8;

FTIR (neat) $\nu$/cm$^{-1}$ = 2933, 2833, 1592, 1507, 1481, 1333, 1253, 1087, 1058, 1020;

HRMS ($ESI^+$) calculated for $C_{27}H_{23}O^+$ = 363.1743, mass found = 363.1743.

**2'-Methoxy-7-phenyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA39**




**RJA39**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA28** (980 mg, 2.70 mmol), dichloromethane (27 mL) sodium bicarbonate (567 mg, 6.75 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.24 g, 5.40 mmol); then 1:1 diethyl ether/dichloromethane (54 mL), boron trifluoride diethyl etherate (0.53 mL, 4.32 mmol). Purification *via* recrystallization from petrol 60-80/ethyl acetate afforded the title compound **RJA39** as a white solid (634 mg, 62 %).

Melting point: 115-116 °C (ethyl acetate/petrol 60-80);

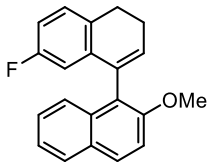
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.93 (d, *J* = 8.9 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 6.45 (d, *J* = 7.5 Hz, 1H), 7.48-7.33 (m, 5H), 7.32-7.21 (m, 5H), 6.82 (s, 1H), 5.67 (s, 1H), 3.81 (s, 3H), 3.44-3.30 (m, 2H), 3.02 (dtd, *J* = 16.3, 5.4, 1.6 Hz, 1H), 2.89 (dddd, *J* = 16.3, 8.9, 7.2, 2.0 Hz, 1H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.3, 154.8, 140.9, 139.8, 138.1, 135.3, 133.4, 129.8, 129.7, 128.9, 128.6, 128.0, 127.0, 127.0, 126.9, 126.0, 125.2, 123.5, 123.5, 121.0, 113.8, 56.5, 50.5, 38.8, 28.3;

FTIR (neat) $\nu$/cm$^{-1}$ = 2939, 2840, 1714, 1624, 1596, 1512, 1483, 1252, 1147, 1080, 1025;

HRMS (ESI$^+$) calculated for $C_{27}H_{23}O_2^+$ = 379.1693, mass found = 379.1692.

**7-Fluoro-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA29**




**RJA29**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with 7-fluoro-1-tetralone (821 mg, 5.00 mmol), anhydrous cerium chloride (2.47 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA29** as a colourless oil which solidified to a white solid upon standing (1.09 g, 72 %).

Melting point: 90-92 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H), 7.90-7.85 (m, 1H), 7.78-7.74 (m, 1H), 7.45-7.36 (m, 3H), 7.20 (dd, *J* = 8.2, 5.7 Hz, 1H), 6.84 (td, *J* = 8.5, 2.8 Hz, 1H), 6.28 (dd, *J* = 10.1, 2.6, 1H), 6.15 (t, *J* = 4.5 Hz, 1H), 3.90 (s, 3H), 3.04 (t, *J* = 8.1 Hz, 2H), 2.63 (td, *J* = 8.2, 4.5 Hz, 2H);

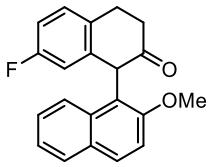
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 161.9 (d, *J* = 242.4), 154.4, 137.4 (d, *J* = 7.9 Hz), 133.8, 133.1 (d, *J* = 2.4 Hz), 131.2 (d, *J* = 3.2 Hz), 131.1, 129.3, 129.2, 128.4 (d, *J* = 7.9 Hz), 128.0, 126.5, 125.0, 123.7, 122.7, 113.8, 113.0 (d, *J* = 21.5 Hz), 111.5 (d, *J* = 23.0 Hz), 56.8, 27.4, 23.8;

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –117.1;

FTIR (neat) $\nu$/cm$^{-1}$ = 2935, 2835, 1593, 1578, 1507, 1487, 1466, 1430, 1332, 1256, 1237, 1082, 1056, 1020;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}OF^+$ = 305.1336, mass found = 305.1337.

**7-Fluoro-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA40**




**RJA40**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA29** (1.01 g, 3.32 mmol), dichloromethane (33 mL), sodium bicarbonate (697 mg, 8.30 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.53 g, 6.64 mmol); then 1:1 diethyl ether/dichloromethane (66 mL), boron trifluoride diethyl etherate (0.66 mL, 5.35 mmol). Purification *via* recrystallization from petrol 60-80/ethyl acetate afforded the title compound **RJA40** as a white solid (744 mg, 70 %).

Melting point: 104-105 °C (ethyl acetate/petrol 60-80);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H), 7.90 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.63-7.50 (m, 1H), 7.45 (ddd, *J* = 7.8, 6.7, 1.1 Hz, 1H), 7.39 (ddd, *J* = 8.0, 7.0, 1.3 Hz, 1H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.28 (dd, *J* = 8.3, 5.7 Hz, 1H), 6.89 (tdd, *J* = 8.4, 2.6, 0.6 Hz, 1H), 6.28 (dd, *J* = 10.0, 2.5, 1H), 5.54 (s, 1H), 3.81 (s, 3H), 3.35-3.22 (m, 2H), 2.97 (dt, *J* = 16.3, 5.2 Hz, 1H), 2.84 (ddd, *J* = 16.3, 9.6, 6.8 Hz, 1H);

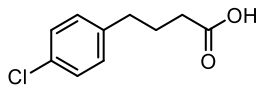
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 209.6, 161.9 (d, *J* = 243.2 Hz), 154.7, 139.9 (d, *J* = 7.2 Hz), 133.1, 131.8 (d, *J* = 3.2 Hz), 130.0, 129.7, 129.0, 128.8 (d, *J* = 7.9 Hz), 127.0, 123.6, 123.2, 120.5, 114.2 (d, *J* = 22.3 Hz), 113.7, 113.1 (d, *J* = 21.5 Hz), 56.4, 50.2, 38.6, 27.9;

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –116.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 2941, 2842, 1714, 1613, 1593, 1512, 1493, 1470, 1258, 1146, 1103, 1077, 1024;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}O_2F^+$ = 321.1285, mass found = 321.1286.

**4-(4-Chlorophenyl)butanoic acid, RJA51**




**RJA51**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a literature procedure, [83] a stirred solution of succinic anhydride (4.00 g, 40.0 mmol) in chlorobenzene (40 mL) was cooled to 0 °C and aluminium trichloride (10.6 g, 80.0 mmol) was added in four portions over 10 minutes. The resulting solution was heated to 65 °C for three hours and then cooled to room temperature. 15 % HCl (30 mL) was added and the majority of the volatile organics were removed under reduced pressure. The remaining mixture was diluted with 15 % HCl (30 mL) and heated to 80 °C for 20 minutes and then cooled to room temperature. The solid was collected by vacuum filtration and the filter cake was washed with water and hexane and dried under high vaccuum for several hours to afford the crude product as a beige solid (7.46 g, 88 %) which was used without further purification in the subsequent step.

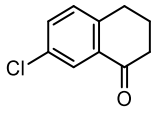
According to a modified literature procedure,[84] a mixture of the crude Friedel-Crafts acylation product (5.00 g, 23.5 mmol), hydrazine monohydrate (98 %, 2.33 mL, 48.0 mmol), powdered potassium hydroxide (5.66 g, 101 mmol) and ethylene glycol (72 mL) was heated to 120 °C for 1 hour. After this time the resulting mixture was heated to reflux for 2 hours and then cooled to room temperature and diluted with water and then acidified by dropwise addition of concentrated HCl (pH 1-2) resulting in the formation of a beige solid. The solid was collected by vacuum filtration and the filter cake was washed with water and hexane and dried under high vaccuum for several hours. Purification *via* column chromatography eluting with 1:4 ethyl acetate/toluene afforded the title compound **RJA51** as a white solid (750 mg, 14 % for 2 steps). The spectral data matched that previously reported in the literature.[134]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 11.35 (br s, 1H. COO*H*), 7.29 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 2.68 (t, *J* = 7.5 Hz, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 1.98 (qn, *J* = 7.5 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 179.9, 139.6, 131.8, 129.8, 128.5, 34.3, 33.2, 26.1;

LRMS ($ESI^+$) calculated for $C_{10}H_{11}ClO_2Na^+$ = 221, mass found = 221.

**7-Chloro-3,4-dihydronaphthalen-1(2*H*)-one, RJA19**




**RJA19**

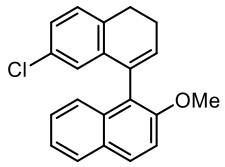
*This compound was synthesised and analysed by Dr Roland Armstrong* according to a modified literature procedure,[85] a mechanically stirred suspension of **RJA51** (696 mg, 3.50 mmol) in polyphosphoric acid (3.5 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/toluene afforded the title compound **RJA19** as a white solid (543 mg, 86 %). The spectral data matched that previously reported in the literature.[135]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 2.2 Hz, 1H), 7.44 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.23 (d, *J* = 8.1 Hz, 1H), 2.96 (t, *J* = 6.1 Hz, 2H), 2.67 (t, *J* = 6.6 Hz, 2H), 2.19-2.12 (m, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 197.1, 142.7, 133.8, 133.3, 132.8, 130.4, 126.9, 38.8, 29.1, 23.0;

LRMS ($ESI^+$) calculated for $C_{10}H_9ClONa^+$ = 203, mass found = 203.

**7-Chloro-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA30**




**RJA30**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA19** (500 mg, 2.77 mmol), anhydrous cerium chloride (1.36 g, 5.52 mmol), THF (28 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 6.70 mL, 3.35 mmol), 3M HCl (28 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA30** as a white solid (622 mg, 70 %).

Melting point: 93-94 °C (dichloromethane/petrol 40-60);

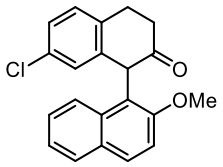
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H), 7.76-7.71 (m, 1H), 7.63-7.58 (m, 1H), 7.29-7.22 (m, 3H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.98 (dd, *J* = 7.8, 2.2 Hz, 1H), 6.39 (d, *J* = 2.2 Hz, 1H), 5.99 (t, *J* = 4.5 Hz, 1H), 3.75 (s, 3H), 2.89 (t, *J* = 8.1 Hz, 2H), 2.51-2.44 (m, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 137.3, 134.2, 133.8, 133.0, 132.1, 131.3, 129.3, 129.2, 128.7, 128.0, 126.6, 126.5, 125.0, 124.4, 123.7, 122.6, 113.8, 56.8, 27.6, 23.6;

FTIR (neat) $\nu$/cm$^{-1}$ = 2934, 2834, 1622, 1593, 1508, 1479, 1401, 1332, 1254, 1085, 1057, 1021;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}OCl^+$ = 321.1041, mass found = 321.1043.

**7-Chloro-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA41**




**RJA41**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA30** (572 mg, 1.78 mmol), dichloromethane (18 mL), sodium bicarbonate (374 mg, 4.45 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 821 mg, 3.57 mmol); then 1:1 diethyl ether/dichloromethane (36 mL), boron trifluoride diethyl etherate (0.35 mL, 2.85 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **RJA41** as a white solid (404 mg, 67 %).

Melting point: 148-149 °C (hexane/ethyl acetate);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.83 (d, *J* = 9.0 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.46 (br s, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 9.0 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.06 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.44-6.43 (m, 1H), 5.39 (s, 1H), 3.69 (s, 3H), 3.22-3.13 (m, 2H), 2.84 (dt, *J* = 16.2, 5.4 Hz, 1H), 2.72 (ddd, *J* = 16.2, 9.0, 7.2 Hz, 1H);

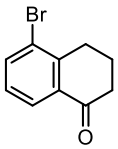
$^{13}$C NMR (121 MHz, $CDCl_3$) $\delta_C$ = 208.3, 153.6, 138.6, 133.5, 132.1, 131.5, 129.0, 128.6, 127.9, 127.8, 126.1, 126.1, 125.4, 122.6, 122.0, 119.3, 112.6, 55.3, 49.0, 37.4, 27.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 2941, 2841, 1717, 1624, 1596, 1513, 1480, 1254, 1147, 1090;

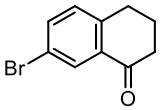
HRMS (ESI$^+$) calculated for $C_{21}H_{17}O_2ClNa^+$ = 359.0809, mass found = 359.0810.

**5-Bromo-3,4-dihydronaphthalen-1(2*H*)-one, RJA9 &**

**7-bromo-3,4-dihydronaphthalen-1(2*H*-one, RJA10**




**RJA9**




**RJA10**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a modified literature procedure,[80] solid aluminium trichloride (16.6 g, 125 mmol) was stirred vigorously at room temperature and 1-tetralone (6.64 mL, 50.0 mmol) was added over 3 minutes. Bromine (3.07 mL, 60.0 mmol) was added over 10 minutes [CARE-evoloution of bromine vapours] and the resulting viscous mixture was heated to 80 °C for 5 minutes. Whilst still molten, the reaction mixture was poured onto crushed ice (150 g) containing 20 mL of 12 M HCl [CARE-evolution of gaseous HCl]. The resulting mixture was allowed to warm to room temperature and extracted twice with diethyl ether. The combined organic extracts were washed with saturated aqueous sodium thiosulfate, dried over anhydrous magneisum sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with 1:19 THF/hexane afforded **RJA9** (the columned material was recrystallized from hexane to give **RJA9** as an off white solid: 1.51 g, 13 %) along with **RJA10** (the columned material was recrystallized from hexane to give **RJA10** as a brown solid: 3.33 g, 30 %). The spectral data for both **RJA9** and **RJA10** matched that previously reported in the literature.[136-137]

Data for **RJA9**:

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.03 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 3.03 (t, *J* = 6.2 Hz, 2H), 2.67 (t, *J* = 6.6 Hz, 2H), 2.18 (qn, *J* = 6.4 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 197.4, 143.4, 137.3, 134.6, 127.7, 126.5, 124.8, 38.2, 30.0, 22.3;

LRMS (ESI$^+$) calculated for $C_{10}H_9BrNaO^+$ = 247, mass found = 247.

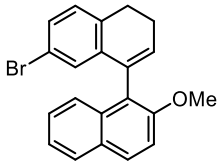
Data for **RJA10**:

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.15 (d, *J* = 1.8 Hz, 1H), 7.57 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 2.93 (t, *J* = 6.1 Hz, 2H), 2.66 (t, *J* = 6.5 Hz, 2H), 2.15 (qn, *J* = 6.3 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 197.0, 143.1, 136.1, 134.1, 130.6, 130.0, 120.6, 38.8, 29.2, 23.0;

LRMS (ESI$^+$) calculated for $C_{10}H_9BrNaO^+$ = 247, mass found = 247.

**7-Bromo-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA31**




**RJA31**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA10** (1.00 g, 4.44 mmol), anhydrous cerium chloride (2.19 g, 8.88 mmol), THF (44 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 10.7 mL, 5.35 mmol), 3M HCl (44 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA31** as a colourless gum (375 mg, 23 %).

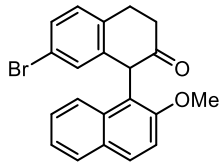
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H), 7.90-7.85 (m, 1H), 7.78-7.73 (m, 1H), 7.44-7.36 (m, 3H), 7.28 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 6.12 (t, *J* = 4.5 Hz, 1H), 3.89 (s, 3H), 3.02 (t, *J* = 8.1 Hz, 2H), 2.62 (td, *J* = 8.1, 4.5 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.3, 137.6, 134.7, 133.8, 132.9, 131.3, 129.6, 129.4, 129.2, 129.1, 128.0, 127.2, 126.5, 125.0, 123.7, 122.5, 120.2, 113.8, 56.8, 27.7, 23.5;

FTIR (neat) $\nu$/cm$^{-1}$ = 2932, 2835, 1622, 1592, 1508, 1476, 1333, 1254, 1147, 1088, 1057, 1021;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}OBr^+$ = 365.0536, mass found = 365.0537.

**7-Bromo-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA42**




**RJA42**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA31** (355 mg, 0.972 mmol), dichloromethane (10 mL), sodium bicarbonate (204 mg, 2.43 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 447 mg, 1.94 mmol); then 1:1 diethyl ether/dichloromethane (20 mL), boron trifluoride diethyl etherate (191 μL, 1.56 mmol). Purification *via* column chromatography on neutral alumna eluting with 1:1 dichloromethane/petrol 40-60 followed by recrystallization from hexane/ethyl acetate afforded the title compound **RJA42** as a white solid (111 mg, 30 %).

Melting point: 129-131 °C (ethyl acetate/hexane);

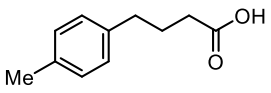
$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.93 (d, *J* = 9.1 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.57 (br s, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.33-7.30 (m, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 6.69 (m, 1H), 5.50 (s, 1H), 3.79 (s, 3H), 3.25 (dd, *J* = 8.0, 5.6 Hz, 2H), 2.74 (dt, *J* = 16.2, 5.5 Hz, 1H), 2.82 (dt, *J* = 16.2, 8.1 Hz, 1H);

$^{13}$C NMR (121 MHz, $CDCl_3$) $\delta_C$ = 209.3, 154.6, 140.1, 135.1, 133.2, 130.1, 130.0, 129.7, 129.4, 129.2, 129, 127.1, 123.6, 123.0, 120.6, 120.3, 113.7, 56.4, 50.0, 38.4, 28.2;

FTIR (neat) $\nu$/cm$^{-1}$ = 2940, 2840, 1717, 1624, 1595, 1513, 1475, 1267, 1254, 1082;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}O_2Br^+$ = 381.0485, mass found = 381.0486.

**4-(*p*-Tolyl)butanoic acid, RJA52**




**RJA52**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a literature procedure,[83] a stirred solution of succinic anhydride (4.00 g, 40.0 mmol) in toluene (60 mL) was cooled to 0 °C and aluminium trichloride (10.6 g, 80.0 mmol) was added in four portions over 10 minutes. The resulting solution was heated to 65 °C for three hours and then cooled to room temperature. 15 % HCl (30 mL) was added and the majority of the volatile organics were removed under reduced pressure. The remaining mixture was diluted with 15 % HCl (30 mL) and heated to 80 °C for 20 minutes and then cooled to room temperature. The resulting suspension was filtered and the solid obtained was dissolved in 15 % aqueous sodium hydroxide (70 mL) and heated to reflux for 15 minutes. The solution was cooled to room temperature and then filtered. The filtrate was acidified (pH 1-2) by addition of 15 % HCl resulting in precipitation of a solid, which was collected by vacuum filtration and dried under high vaccuum for several hours to afford the crude product (6.08 g) as a beige solid which was used without further purifiaction in the subsequent step.

By analogy to a modified literature procedure,[138] a three-necked round bottomed flask equipped with a Liebig condenser, thermometer and glass stopper was charged with the crude Friedel-Crafts acylation product (5.00 g, 26.0 mmol), hydrazine monohydrate (98 %, 2.6 mL, 53.4 mmol), powdered potassium hydroxide (6.26 g, 111.8 mmol) and ethylene glycol (80 mL). The resulting mixture was heated to 120 °C for 1 hour. After this time glass stopper was exchanged for a short path distillation apparatus and the reaction mixture was heated to reflux. During this time a distillate was collected and the internal temperature of the reaction mixture rose to *c.a.* 205 °C. The glass stopper was replaced and the solution was refluxed for a further

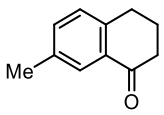
3 hours and then cooled to room temperature and diluted with water and then acidified by dropwise addition of concentrated HCl (pH 1-2). The mixture was diluted with water and extracted three times with ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:4 ethyl acetate/toluene afforded the title compound **RJA52** as a white solid (1.60 g, 27 % for 2 steps). The spectral data matched that previously reported in the literature.[139]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 11.23 (br s, 1H, COO*H*), 7.17-7.10 (m, 4H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.37 (s, 3H), 2.00 (qn, *J* = 7.5 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 180.1, 138.1, 135.5, 129.1, 128.4, 34.6, 33.4, 26.3, 21.0;

LRMS ($ESI^-$) calculated for $C_{11}H_{13}O_2^-$ = 177, mass found = 177.

**7-Methyl-3,4-dihydronaphthalen-1(2*H*)-one, RJA20**




**RJA20**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a modified literature procedure,[85] a mechanically stirred suspension of **RJA52** (1.20 g, 6.73 mmol) in polyphosphoric acid (6.7 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/toluene afforded the title

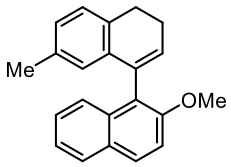
compound **RJA20** as a white solid (831 mg, 77 %). The spectral data matched that previously reported in the literature.[140]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.84 (d, *J* = 1.6 Hz, 1H), 7.28 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 2.92 (t, *J* = 6.1 Hz, 2H), 2.63 (t, *J* = 6.4 Hz, 2H), 2.35 (s, 3H), 2.11 (qn, *J* = 6.3 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.7, 141.6, 136.3, 134.4, 132.4, 128.7, 127.3, 39.2, 29.3, 23.4, 21.0;

LRMS ($ESI^+$) calculated for $C_{11}H_{12}ONa^+$ = 183, mass found = 183.

**2'-Methoxy-7-methyl-3,4-dihydro-1,1'-binaphthalene, RJA32**




**RJA32**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA20** (733 mg, 4.58 mmol), anhydrous cerium chloride (2.26 g, 9.15 mmol), THF (46 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 11.0 mL, 5.50 mmol), 3M HCl (46 mL). Purification *via* column chromatography eluting with a gradient from 3:17 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 afforded the title compound **RJA32** as a colourless gum (610 mg, 44 %).

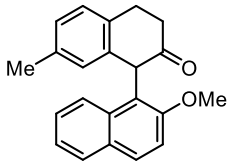
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.91 (d, *J* = 9.0 Hz, 1H), 7.88-7.82 (m, 1H), 7.81-7.74 (m, 1H), 7.43-7.33 (m, 3H), 7.15 (d, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.37 (s, 1H), 6.06-6.02 (m, 1H), 3.87 (s, 3H), 3.02 (t, *J* = 7.8 Hz, 2H), 2.62-2.54 (m, 2H), 2.09 (s, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 135.8, 135.4, 134.0, 133.8, 132.9, 130.0, 129.2, 128.9, 127.8, 127.5, 127.4, 126.3, 125.5, 125.3, 123.9, 123.6, 114.2, 57.0, 27.9, 23.9, 21.2;

FTIR (neat) $\nu$/cm$^{-1}$ = 2933, 2834, 1622, 1592, 1507, 1463, 1333, 1270, 1255, 1237, 1147, 1086, 1058, 1020;

HRMS (ESI$^+$) calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1587.

**2'-Methoxy-7-methyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA43**




**RJA43**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA32** (610 mg, 2.03 mmol), dichloromethane (20 mL) sodium bicarbonate (426 mg, 5.08 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 934 mg, 4.06 mmol); then 1:1 diethyl ether/dichloromethane (40 mL), boron trifluoride diethyl etherate (0.40 mL, 3.25 mmol). Purification *via* column chromatography eluting with 15:84:1 ethyl acetate/petrol 40-60/ triethyl-amine followed by recrystallization from petrol 60-80/ethyl acetate afforded the title compound **RJA43** as a white solid (187 mg, 29 %).

Melting point: 148-150 °C (ethyl acetate/petrol 60-80);

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.0 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.43 (ddd, *J* = 7.9, 6.7, 1.0 Hz, 1H), 7.38 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.40 (s, 1H), 5.54 (s, 1H), 3.80 (s, 3H), 3.30-3.25 (m, 2H), 2.95 (dt, *J* = 16.0, 5.6 Hz, 1H), 2.84 (ddd, *J* = 16.0, 8.8, 7.1 Hz, 1H), 2.09 (s, 3H);

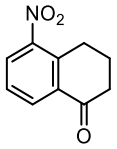
$^{13}$C NMR (121 MHz, $CDCl_3$) $\delta_C$ = 210.7, 154.7, 137.4, 136.3, 133.4, 133.0, 129.7, 129.6, 128.8, 127.9, 127.4, 127.1, 126.8, 123.6, 123.5, 121.5, 113.9, 56.5, 50.2, 39.0, 28.3, 21.1;

FTIR (neat) $\nu$/cm$^{-1}$ = 2939, 2841, 1714, 1623, 1596, 1512, 1469, 1260, 1147, 1054;

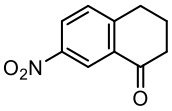
HRMS (ESI$^+$) calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1537.

**5-nitro-3,4-dihydronaphthalen-1(2H)-one, RJA11 &**

**7-nitro-3,4-dihydronaphthalen-1(2H)-one, RJA12**




**RJA11**




**RJA12**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a literature procedure,[81] a stirred solution of $\alpha$-Tetralone (5.00 g, 34.2 mmol) in concentrated sulfuric acid (75 mL) was and cooled to 0 °C. A mixture of concentrated nitric acid (2.15 mL) and concentrated sulfuric acid (12.5 mL) was added over 10 minutes and the resulting solution was stirred for 1 hour at 0 °C and then poured onto crushed ice. The mixture was allowed to warm to room temperature and extracted three times with ethyl acetate. The combined organic extracts were washed with brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:4 ethyl acetate/petrol 40-60 afforded **RJA11** as an off white solid (910 mg, 14 %) along with **RJA12** as an off white solid (3.10 g, 47 %). The spectral data for both **RJA11** and **RJA12** matched that previously reported in the literature.[81]

Data for **RJA11**:

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.27 (d, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 3.14 (t, *J* = 6.1 Hz, 2H), 2.65 (t, *J* = 6.6 Hz, 2H), 2.10 (qn, *J* = 6.4 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 196.0, 149.4, 138.5, 134.5, 132.1, 128.8, 127.0, 38.2, 26.4, 22.2;

LRMS ($FI^+$) calculated for $C_{10}H_9NO_3^+$ = 191, mass found = 191.

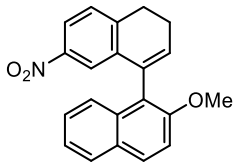
Data for **RJA12**:

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.74 (d, *J* = 2.0 Hz, 1H), 8.20 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 3.01 (t, *J* = 6.1 Hz, 2H), 2.66 (t, *J* = 6.5 Hz, 2H), 2.14 (qn, *J* = 6.3 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 196.0, 151.0, 147.0, 133.4, 130.3, 127.1, 122.5, 38.6, 29.8, 22.5;

LRMS ($ESI^+$) calculated for $C_{10}H_9NO_3Na^+$ = 214, mass found = 214.

**2'-Methoxy-7-nitro-3,4-dihydro-1,1'-binaphthalene, RJA33**




**RJA33**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA12** (956 mg, 5.00 mmol), anhydrous cerium chloride (2.47 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 3:17 ethyl acetate/petrol 40-60 afforded the title compound **RJA33** as a yellow gum (346 mg, 21 %).

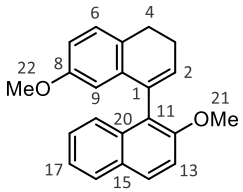
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.88 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.78-7.73 (m, 1H), 7.62-7.57 (m, 1H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.29-7.23 (m, 4H), 6.10 (t, *J* = 4.4 Hz, 1H), 3.76 (s, 3H), 3.03 (t, *J* = 8.2 Hz, 2H), 2.55 (td, *J* = 8.2, 4.5 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 147.3, 143.5, 136.8, 133.6, 132.6, 132.4, 129.8, 129.3, 128.2, 128.2, 126.7, 124.5, 123.7, 121.8, 121.4, 119.1, 113.6, 56.7, 28.3, 23.1;

FTIR (neat) $\nu$/cm$^{-1}$ = 2937, 2837, 1621, 1593, 1574, 1514, 1465, 1341, 1549, 1104, 1080, 1057, 1021;

HRMS (ESI$^+$) calculated for $C_{21}H_{17}O_3NNa^+$ = 354.1101, mass found = 354.1100.

**2',7-Dimethoxy-3,4-dihydro-1,1'-binaphthalene, 220**




**220**

According to **General Procedure A** with 7-methoxy-1-tetralone (881 mg, 5.00 mmol), anhydrous cerium chloride (2.47 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:4 dichloromethane/petrol 40-60 to 1:2 dichloromethane/petrol 40-60 afforded the title compound **220** as a white solid (1.31 g, 83 %).

Melting point: 108-109 °C (dichloromethane/petrol 40-60);

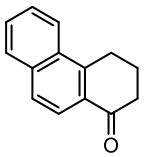
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.87 (d, *J* = 9.1 Hz, 1H, $H_{14}$), 7.84-7.80 (m, 1H, $H_{16}$), 7.76-7.71 (m, 1H, $H_{19}$), 7.39-7.30 (m, 3H, $H_{13}$, $H_{17}$ and $H_{18}$), 7.15 (dd, *J* = 8.2, 0.9 Hz, 1H, $H_6$), 6.67 (dd, *J* = 8.2, 2.7 Hz, 1H, $H_7$), 6.13 (d, *J* = 2.7 Hz, 1H, $H_9$), 6.07 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.85 (s, 3H, $H_{21}$), 3.56 (s, 3H, $H_{22}$), 2.98 (t, *J* = 8.0 Hz, 2H, $H_4$), 2.57 (ddd, *J* = 8.9, 7.4, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.4 (Quat, $C_8$), 154.5 (Quat, $C_{12}$), 136.8 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 133.7 (Quat, $C_{Ar}$), 130.7 (CH, $C_2$), 129.3 (Quat, $C_{Ar}$), 129.1 (CH, $C_{14}$), 128.3 (Quat, $C_{Ar}$), 128.1 (CH, $C_6$), 127.9 (CH, $C_{16}$), 126.4 (CH, $C_{17}$ or $C_{18}$), 125.4 (CH, $C_{19}$), 123.6 (CH, $C_{17}$ or $C_{18}$), 123.5 (Quat, $C_{11}$), 114.1 (CH, $C_{13}$), 111.7 (CH, $C_7$), 110.9 (CH, $C_9$), 57.1 ($CH_3$, $C_{21}$), 55.2 ($CH_3$, $C_{22}$), 27.4 ($CH_2$, $C_4$), 24.2 ($CH_2$, $C_3$);

FTIR (neat) $\nu/cm^{-1}$ = 3056, 2999, 2933, 2832, 1593, 1569, 1507, 1464, 1442, 1421, 1355, 1301, 1271, 1242, 1200, 1179, 1030, 1044, 1020;

HRMS ($ESI^+$): calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1537.

**3,4-Dihydrophenanthren-1(2*H*)-one, RJA25**



**RJA25**

*This compound was synthesised and analysed by Dr Roland Armstrong* by analogy to a modified literature procedure,[86] a stirred solution of 1-naphthaldehyde (2.70 g, 17.3 mmol) and (2-carboxyethyl)triphenylphosphonium chloride[141] (6.60 g, 17.8 mmol) in a 1:1 mixture of THF/DMSO (50 mL) was cooled to 0 °C and sodium hydride (60 % w/w in mineral oil, 1.42 g, 35.6 mmol) was added in a single portion. The resulting mixture was warmed to room temperature and stirred for 20 hours. The mixture was then cooled to 0 °C and water was added. The resulting aqueous solution was washed three times with diethyl ether. The aqueous phase was then acidified to pH 1-2 by addition of concentrated HCl and extracted three times with diethyl ether. The combined organic extracts were washed with brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure.

The crude residue thus obtained was dissolved in ethanol (100 mL). The solution was transferred into a pressure tube and Pd/C (270 mg, 10 wt. %) was added. The resulting suspension was stirred under an atmosphere of hydrogen (5 bar) for 2 hours. The reaction mixture was filtered through a plug of celite, which was subsequently washed with dichloromethane and the filtrate was then concentrated under reduced pressure to afford the crude carboxylic acid as a yellow oil (2.57 g) which was used without further purification in the subsequent step.

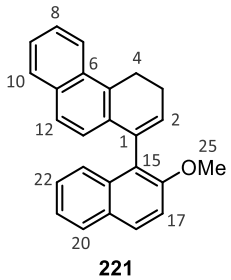
According to a modified literature procedure,[85] a mechanically stirred suspension of the crude carboxylic acid (2.57 g) in polyphosphoric acid (10 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/toluene afforded the title compound **RJA25** as a white solid (1.29 g, 38 % for 3 steps). The spectral data matched that previously reported in the literature.[142]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.18-8.11 (m, 2H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.66-7.58 (m, 2H), 3.40 (t, *J* = 6.2 Hz, 2H), 2.76 (t, *J* = 6.6 Hz, 2H), 2.32 (qn, *J* = 6.4 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.6, 142.9, 135.7, 131.4, 130.0, 128.8, 128.3, 126.9, 126.7, 124.8, 122.8, 38.4, 25.6, 22.8;

LRMS ($ESI^+$) calculated for $C_{14}H_{12}ONa^+$ = 219, mass found = 219.

**1-(2-Methoxynaphthalen-1-yl)-3,4-dihydrophenanthrene, 221**




**221**

According to **General Procedure A** with **RJA25** (981 mg, 5.00 mmol), anhydrous cerium chloride (2.56 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.0 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with

a gradient from 3:17 dichloromethane/petrol 40-60 to 15:85 dichloromethane/petrol 40-60 afforded the title compound **221** as a white solid (1.24 g, 74 %).

Melting point: 153-154 °C (dichloromethane/petrol 40-60);

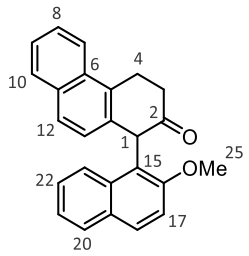
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.19 (dd, *J* = 8.7, 1.0 Hz, 1H, $H_7$), 7.92 (d, *J* = 9.0 Hz, 1H, $H_{18}$), 7.88-7.82 (m, 1H, $H_{20}$), 7.81-7.71 (m, 2H, $H_{10}$ and $H_{23}$), 7.54 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H, $H_8$), 7.46 (d, *J* = 9.0 Hz, 1H, $H_{12}$), 7.44-7.38 (m, 2H, $H_9$ and $H_{17}$), 7.38-7.31 (m, 2H, $H_{21}$ and $H_{22}$), 6.75 (d, *J* = 8.5 Hz, 1H, $H_{13}$), 6.17 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.84 (s, 3H, $H_{25}$), 3.49 (t, *J* = 8.6 Hz, 2H, $H_4$), 2.75 (ddd, *J* = 9.6, 7.9, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.6 (Quat, $C_{16}$), 134.1 (Quat, $C_{Ar}$), 134.1 (Quat, $C_{Ar}$), 133.2 (Quat, $C_{Ar}$), 132.9 (Quat, $C_{Ar}$), 131.6 (Quat, $C_{Ar}$), 130.9 (Quat, $C_{Ar}$), 129.5 (CH, $C_2$), 129.3 (Quat, $C_{19}$), 129.1 (CH, $C_{18}$), 128.6 (CH, $C_{Ar}$), 128.0 (CH, $C_{20}$), 126.5 (CH, $C_{Ar}$), 126.2 (CH, $C_{12}$), 126.0 (CH, $C_8$), 125.5 (CH, $C_{Ar}$), 125.0 (CH, $C_{Ar}$), 124.0 (Quat, $C_{15}$), 123.9 (CH, $C_{Ar}$), 123.8 (CH, $C_{Ar}$), 123.7 (CH, $C_{Ar}$), 114.2 (CH, $C_{17}$), 57.1 ($CH_3$, $C_{25}$), 23.6 ($CH_3$, $C_3$), 23.2 ($CH_3$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3054, 3004, 2934, 2877, 2834, 1620, 1592, 1507, 1253, 1113;

HRMS (ESI$^+$): calculated for $C_{25}H_{21}O^+$ = 337.1587, mass found = 337.1587.

**1-(2-Methoxynaphthalen-1-yl)-3,4-dihydrophenanthren-2(1*H*)-one, 243**




**243**

According to **General Procedure B** with **221** (1.18 g, 3.51 mmol), dichloromethane (35 mL), sodium bicarbonate (738 mg, 7.02 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.62 g,

7.02 mmol); then 1:1 diethyl ether/dichloromethane (70 mL), boron trifluoride diethyl etherate (0.69 mL, 5.6 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **243** as a white solid (569 mg, 46 %).

Melting point: 204-206 °C (ethyl acetate/hexane);

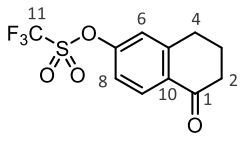
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.17 (d, *J* = 8.5 Hz, 1H, $H_7$), 7.91-7.84 (m, 2H, $H_{18}$ and $H_{20}$), 7.77 (d, *J* = 8.1 Hz, 1H, $H_{10}$), 7.72 (d, *J* = 8.6 Hz, 1H, $H_{23}$), 7.59 (ddd, *J* = 8.5, 6.7, 1.4 Hz, 1H, $H_8$), 7.52-7.45 (m, 2H, $H_9$ and $H_{12}$), 7.42 (t, *J* = 7.5 Hz, 1H, $H_{21}$), 7.36 (t, *J* = 7.3 Hz, 1H, $H_{22}$), 7.30 (d, *J* = 9.0 Hz, 1H, $H_{17}$), 6.81 (d, *J* = 8.6 Hz, 1H, $H_{13}$), 5.79 (s, 1H, $H_1$), 3.86-3.76 (m, 1H, $H_{4B}$), 3.74 (s, 3H, $H_{25}$), 3.72-3.63 (m, 1H, $H_{4A}$), 3.15-2.96 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.1 (Quat, $C_2$), 154.9 (Quat, $C_{12}$), 135.4 (Quat, $C_{Ar}$), 133.5 (Quat, $C_{Ar}$), 132.3 (Quat, $C_{Ar}$), 131.3 (Quat, $C_{Ar}$), 130.8 (Quat, $C_{Ar}$), 129.8 (CH, $C_{Ar}$), 129.8 (Quat, $C_{Ar}$), 129.0 (CH, $C_{Ar}$), 128.7 (CH, $C_{Ar}$), 127.2 (CH, $C_{Ar}$), 127.1 (CH, $C_{Ar}$), 126.5 (CH, $C_8$), 126.1 (CH, $C_{13}$), 125.5 (CH, $C_{Ar}$), 123.6 (CH, $C_{22}$), 123.4 (CH, $C_{23}$), 123.2 (CH, $C_7$), 122.0 (CH, $C_{15}$), 113.9 (CH, $C_{17}$), 56.6 (CH, $C_{25}$), 50.1 (CH, $C_1$), 38.9 (CH, $C_3$), 24.5 (CH, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3046, 2996, 2960, 2840, 1716, 1622, 1595, 1510, 1471, 1263, 1091;

HRMS ($Cl^+$): calculated for $C_{25}H_{21}O_2^+$ = 353.1536, mass found = 353.1536.

**5-Oxo-5,6,7,8-tetrahydronaphthalen-2-yl trifluoromethanesulfonate, 198**




**198**

By analogy to a modified literature procedure,[131] pyridine (3.24 mL, 40.0 mmol) was added to a solution of 6-hydroxy-1-tetralone (3.24 g, 20.0 mmol) in dichloromethane (15 mL). After cooling to 0 °C triflic anhydride (4.04 mL, 24.0 mmol) was added dropwise over a period of 10 minutes.

The reaction mixture was stirred for 2 hours at 0 °C and then warmed to room temperature. The crude reaction mixture was diluted with ethyl acetate and quenched with 1M aqueous HCl. The aqueous layer was separated and the organic layer was washed with 1M HCL, saturated aqueous $NaHCO_3$ and brine. The organic layer was then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 afforded the title compound **198** as a yellow oil (5.53 g, 94 %). The spectral data matched that previously reported in the literature.[143]

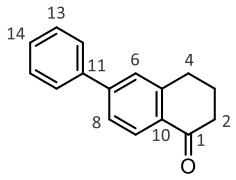
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.13 (d, *J* = 8.4 Hz, 1H, $H_9$), 7.22-7.17 (m, 2H, $H_8$ and $H_6$), 3.02 (t, *J* = 6.1 Hz, 2H, $H_4$), 2.68 (dd, *J* = 7.3, 5.8 Hz, 2H, $H_2$), 2.18 (tt, *J* = 6.6, 5.6 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 196.6 (Quat, $C_1$), 152.5 (Quat, $C_7$), 147.2 (Quat, $C_{Ar}$), 132.5 (Quat, $C_{Ar}$), 130.2 (CH, $C_5$), 121.5 (CH, $C_{Ar}$), 119.8 (CH, $C_{Ar}$), 118.80 (q, *J* = 320.7 Hz, Quat, $C_{11}$), 38.9 ($CH_2$, $C_2$), 29.9 ($CH_2$, $C_4$), 23.1 ($CH_2$, $C_3$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –72.8;

FTIR (neat) $\nu$/cm$^{-1}$ = 2951, 2876, 1690, 1605, 1579, 1482, 1457, 1421, 1208, 1139, 942.

**6-Phenyl-3,4-dihydronaphthalen-1(2*H*)-one, 199**




**199**

By analogy to a modified literature procedure,[144] degassed 2 M aqueous $Na_2CO_3$ (12.5 mL, 25 mmol) was added to a suspension of **198** (1.47g, 5.0 mmol), phenylboronic acid (1.07 g, 8.75 mmol) and $Pd(PPh_3)_4$ (578 mg, 0.5 mmol) in degassed 1,2-dimethoxyethane (50 mL). The reaction mixture was then stirred at reflux for 18 h. After cooling to room temperature, the

reaction was quenched with saturated aqueous ammonium chloride and the majority of 1,2-dimethoxyethane was removed under reduced pressure. Ethyl acetate was added and the aqueous layer was separated. The organic layer was washed with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with a gradient from 1:19 ethyl acetate/petrol 40-60 to 1:9 ethyl acetate/petrol 40-60 afforded the title compound **199** as a white solid (1.07 g, 96 %). The spectral data matched that previously reported in the literature.[142]

Melting point: 108-109 °C (ethyl acetate/hexane);

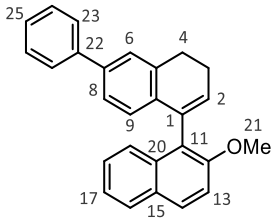
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.11 (d, *J* = 8.1 Hz, 1H, $H_9$), 7.64-7.60 (m, 2H, $H_{12}$), 7.54 (dd, *J* = 8.2, 1.8 Hz, 1H, $H_8$), 7.50-7.44 (m, 3H, $H_6$ and $H_{13}$), 7.43-7.37 (m, 1H, $H_{14}$), 3.03 (t, *J* = 6.1 Hz, 2H, $H_4$), 2.74-2.64 (m, 2H, $H_2$), 2.23-2.13 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.2 (Quat, $C_1$), 146.1 (Quat, $C_{Ar}$), 145.0 (Quat, $C_{Ar}$), 140.1 (Quat, $C_{Ar}$), 131.6 (Quat, $C_{Ar}$), 129.0 (CH, $C_{13}$), 128.3 (CH, $C_{14}$), 127.9 (CH, $C_9$), 127.4 (CH, $C_6$), 127.4, (CH, $C_{12}$) 125.6 (CH, $C_8$), 39.3 ($CH_2$, $C_2$), 30.1 ($CH_2$, $C_3$), 23.4 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3031, 2948, 2875, 1674, 1603, 1501, 1477, 1406, 1348, 1278, 1186;

LRMS (ESI$^+$): calculated for $C_{16}H_{15}O^+$ = 223, mass found = 223.

**2'-Methoxy-6-phenyl-3,4-dihydro-1,1'-binaphthalene, 223**




**223**

According to **General Procedure A** with **199** (1.05 g, 4.72 mmol), anhydrous cerium chloride (2.33 g, 9.44 mmol), THF (47 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 11.3 mL, 5.66 mmol), 3M HCl (47 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 30-40 to 1:4 dichloromethane/petrol 30-40 afforded the title compound **223** as a white solid (1.34 g, 78 %).

Melting point: 56-58 °C (dichloromethane/petrol 30-40);

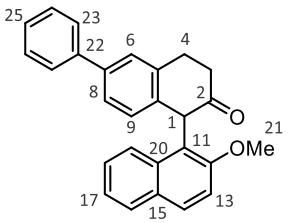
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.1 Hz, 1H, $H_{14}$), 7.88-7.83 (m, 1H, $H_{16}$), 7.82-7.77 (m, 1H, $H_{19}$), 7.61-7.57 (m, 2H, $H_{23}$), 7.49 (d, *J* = 1.8 Hz, 1H, $H_6$), 7.46-7.35 (m, 5H, $H_{13}$, $H_{17}$, $H_{18}$ and $H_{24}$), 7.35-7.29 (m, 1H, $H_{25}$), 7.20 (dd, *J* = 8.0, 2.0 Hz, 1H, $H_8$), 6.60 (d, *J* = 7.9 Hz, 1H, $H_9$), 6.09 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.88 (s, 3H, $H_{21}$), 3.13 (t, *J* = 8.1 Hz, 2H, $H_4$), 2.65 (ddd, *J* = 9.4, 7.2, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.5 (Quat, $C_{12}$), 141.2 (Quat, $C_{Ar}$), 139.7 (Quat, $C_{Ar}$), 136.3 (Quat, $C_{Ar}$), 134.8 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 133.5 (Quat, $C_{Ar}$), 130.1 (CH, $C_2$), 129.3 (Quat, $C_{15}$), 129.1 (CH, $C_{14}$), 128.8 (CH, $C_{24}$), 128.0 (CH, $C_{16}$), 127.1 (CH, $C_{25}$), 127.0 (CH, $C_{23}$), 126.5 (CH, $C_6$), 126.5 (CH, $C_{18}$), 125.4 (CH, $C_{19}$), 125.2 (CH, $C_8$), 125.1 (CH, $C_9$), 123.7 (CH, $C_{17}$), 123.6 (Quat, $C_{11}$), 114.1 (CH, $C_{13}$), 57.1 ($CH_3$, $C_{21}$), 28.5 ($CH_3$, $C_4$), 23.9 ($CH_3$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3028, 2932, 2834, 1621, 1592, 1482, 1467, 1332, 1234;

HRMS (ESI$^+$): calculated for $C_{27}H_{23}O^+$ = 363.1743, mass found = 363.1743.

**2'-Methoxy-6-phenyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 244**




**244**

According to **General Procedure B** with **223** (1.29 g, 3.56 mmol), dichloromethane (36 mL), sodium bicarbonate (748 mg, 8.90 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.64 g, 7.12 mmol); then 1:1 diethyl ether/dichloromethane (72 mL), boron trifluoride diethyl etherate (0.70 mL, 5.7 mmol). Purification *via* column chromatography eluting with 25:74:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **244** as a white solid (404 mg, 30 %).

Melting point: 172-173 °C (ethyl acetate/hexane);

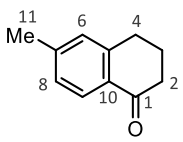
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.88 (dd, *J* = 8.1, 1.4 Hz, 1H, $H_{16}$), 7.64-7.59 (m, 1H, $H_{19}$), 7.59-7.55 (m, 2H, $H_{23}$), 7.55 (d, *J* = 1.8 Hz, 1H, $H_6$), 7.49-7.29 (m, 7H, $H_{13}$, $H_{17}$, $H_{18}$, $H_{24}$ and $H_{25}$), 7.21 (dd, *J* = 8.1, 1.9 Hz, 1H, $H_8$), 6.62 (d, *J* = 8.2 Hz, 1H, $H_9$), 5.59 (s, 1H, $H_1$), 3.80 (s, 3H, $H_{21}$), 3.43-3.29 (m, 2H, $H_4$), 3.00 (dt, *J* = 16.2, 5.3 Hz, 1H, $H_{3B}$), 2.88 (ddd, *J* = 16.2, 9.9, 6.3 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.5 (Quat, $C_2$), 154.8 (Quat, $C_{12}$), 140.8 (Quat, $C_{Ar}$), 139.4 (Quat, $C_{Ar}$), 136.7 (Quat, $C_{Ar}$), 136.6 (Quat, $C_{Ar}$), 133.4 (Quat, $C_{Ar}$), 129.9 (CH, $C_{14}$), 129.8 (Quat, $C_{Ar}$), 129.0 (CH, $C_{16}$), 128.9 (CH, $C_{24}$), 127.9 (CH, $C_9$), 127.3 (CH, $C_{Ar}$), 127.1 (CH, $C_{23}$), 127.0 (CH, $C_{Ar}$), 126.4 (CH, $C_6$), 125.6 (CH, $C_8$), 123.6 (CH, $C_{17}$), 121.3 (CH, $C_{19}$), 114.0 (Quat, $C_{11}$), 56.6 ($CH_3$, $C_{21}$), 50.2 (CH, $C_1$), 38.8 ($CH_2$, $C_3$), 28.8 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 2930, 2903, 2840, 1714, 1624, 1596, 1566, 1381, 1202;

HRMS (ESI$^+$): calculated for $C_{27}H_{23}O_2^+$ = 379.1693, mass found = 379.1688.

**6-Methyl-3,4-dihydronaphthalen-1(2*H*)-one, 200**




**200**

By analogy to a modified literature procedure,[144] degassed 2 M aqueous $Na_2CO_3$ (13 mL, 26 mmol) was added to a suspension of **198** (1.47g, 5.0 mmol), methylboronic acid (600 mg, 10.0 mmol) and $Pd(PPh_3)_4$ (290 mg, 0.25 mmol) in degassed 1,2-dimethoxyethane (50 mL). The reaction mixture was then stirred at reflux for 18 h. After cooling to room temperature, the reaction was quenched with saturated aqueous ammonium chloride and the majority of 1,2-dimethoxyethane was removed under reduced pressure. Ethyl acetate was added and the aqueous layer was separated. The organic layer was washed with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with 1:24 ethyl acetate/petrol 40-60 afforded the title compound **200** as a yellow oil (743 mg, 93 %). The spectral data matched that previously reported in the literature.[143]

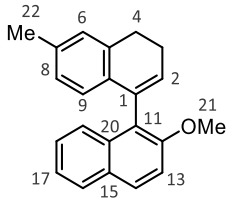
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.93 (d, *J* = 7.9 Hz, 1H, $H_9$), 7.11 (dd, *J* = 8.0, 1.6 Hz, 1H, $H_8$), 7.05 (d, *J* = 1.5 Hz, 1H, $H_6$), 2.91 (t, *J* = 6.1 Hz, 2H, $H_4$), 2.62 (dd, *J* = 7.2, 5.9 Hz, 2H, $H_2$), 2.37 (s, 3H, $H_{11}$), 2.11 (p, *J* = 6.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.3 (Quat, $C_1$), 144.7 (Quat, $C_7$ or $C_{10}$), 144.3 (Quat, $C_7$ or $C_{10}$), 130.4 (Quat, $C_5$), 129.3 (CH, $C_6$), 127.7(CH, $C_8$), 127.4(CH, $C_9$), 39.3($CH_2$, $C_2$), 29.8($CH_2$, $C_4$), 23.5($CH_2$, $C_3$), 21.8($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 2942, 2893, 2867, 2837, 1678, 1631, 1607, 1581, 1512, 1435, 1412, 1380, 1323, 1261, 1236, 1184, 1129, 1073, 1026;

LRMS ($ESI^+$): calculated for $C_{11}H_{13}O^+$ = 161, mass found = 161.

**2'-Methoxy-6-methyl-3,4-dihydro-1,1'-binaphthalene, 224**




**224**

According to **General Procedure A** with **200** (723 mg, 4.51 mmol), anhydrous cerium chloride (2.22 g, 9.02 mmol), THF (45 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 10.8 mL, 5.41 mmol), 3M HCl (45 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 afforded the title compound **224** as a colourless gum (918 mg, 68 %).

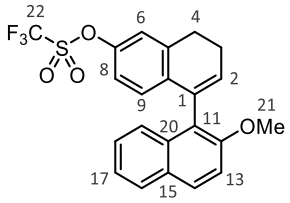
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.88 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.85-7.80 (m, 1H, $H_{16}$), 7.79-7.73 (m, 1H, $H_{19}$), 7.37 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.36-7.31 (m, 2H, $H_{17}$ and $H_{18}$), 7.07 (d, *J* = 0.8 Hz, 1H, $H_6$), 6.77 (dd, *J* = 7.8, 0.8 Hz, 1H, $H_8$), 6.41 (d, *J* = 7.8 Hz, 1H, $H_9$), 5.99 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.85 (s, 3H, $H_{21}$), 3.03 (dt, *J* = 9.6, 6.6 Hz, 2H, $H_4$), 2.59 (ddd, *J* = 9.4, 7.1, 4.5 Hz, 2H, $H_3$), 2.31 (s, 3H, $H_{22}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.5 (Quat, $C_{12}$), 136.6 (Quat, $C_7$), 135.9 (Quat, $C_{Ar}$), 134.1 (Quat, $C_{Ar}$), 133.6 (Quat, $C_{Ar}$), 133.0 (Quat, $C_{Ar}$), 129.3 (Quat, $C_{Ar}$), 129.0 (CH, $C_2$), 128.9 (CH, $C_{14}$), 128.5 (CH, $C_6$), 127.9 (CH, $C_{16}$), 127.1 (CH, $C_8$), 126.4 (CH, $C_{17}$ or $C_{18}$), 125.5 (CH, $C_{19}$), 124.7 (CH, $C_9$), 123.9 (Quat, $C_{11}$), 123.7 (CH, $C_{17}$ or $C_{18}$), 114.2 (CH, $C_{13}$), 57.1 ($CH_3$, $C_{21}$), 28.4 ($CH_2$, $C_4$), 23.9 ($CH_2$, $C_3$), 21.3 ($CH_2$, $C_{22}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 3004, 2932, 2882, 2833, 1621, 1593, 1507, 1463, 1430, 1387, 1350, 1269, 1255, 1198, 1147, 1131, 1059, 1020;

HRMS ($ESI^+$): calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1589.

**2'-Methoxy-3,4-dihydro-[1,1'-binaphthalen]-6-yl trifluoromethanesulfonate, 225**




**225**

According to **General Procedure A** with **198** (1.47 g, 5.00 mmol), anhydrous cerium chloride (2.56 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 30-40 to 1:4 dichloromethane/petrol 30-40 afforded the title compound **225** as a colourless gum (1.31 g, 60 %).

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.91 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.86-7.80 (m, 1H, $H_{16}$), 7.70-7.65 (m, 1H, $H_{19}$), 7.40-7.31 (m, 3H, $H_{13}$, $H_{17}$ and $H_{18}$), 7.13 (d, *J* = 2.6 Hz, 1H, $H_6$), 6.81 (dd, *J* = 8.5, 2.6 Hz, 1H, $H_8$), 6.54 (d, *J* = 8.5 Hz, 1H, $H_9$), 6.11 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.85 (s, 3H, $H_{21}$), 3.06 (dd, *J* = 9.5, 7.6 Hz, 2H, $H_4$), 2.61 (ddd, *J* = 9.5, 7.2, 4.5 Hz, 2H, $H_3$);

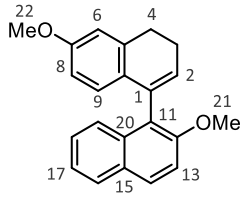
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4 (Quat, $C_{12}$), 148.0 (Quat, $C_7$), 138.5 (Quat, $C_{Ar}$), 135.8 (Quat, $C_{Ar}$), 133.8 (Quat, $C_{Ar}$), 132.6 (Quat, $C_{Ar}$), 131.4 (CH, $C_2$), 129.5 (CH, $C_{14}$), 129.2 (Quat, $C_{Ar}$), 128.1 (CH, $C_{16}$), 126.7 (CH, $C_{17}$ or $C_{18}$), 126.2 (CH, $C_9$), 125.0 (CH, $C_{19}$), 123.8 (CH, $C_{17}$ or $C_{18}$), 122.5 (Quat, $C_{11}$), 120.4 (CH, $C_6$), 119.0 (CH, $C_8$), 118.9 (Quat, q, *J* = 320.6 Hz, $C_{22}$), 113.8 (CH, $C_{13}$), 56.9 ($CH_3$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.3 ($CH_2$, $C_3$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –73.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 2938, 2837, 1621, 1593, 1508, 1468, 1419, 1333, 1271, 1210, 1140, 1113, 1021;

HRMS ($ESI^+$): calculated for $C_{22}H_{18}F_3O_4S^+$ = 435.0872, mass found = 435.0872.

**2',6-Dimethoxy-3,4-dihydro-1,1'-binaphthalene, 226**




**226**

According to **General Procedure A** with 6-methoxy-1-tetralone (881 mg, 5.00 mmol), anhydrous cerium chloride (2.56 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:3 dichloromethane/petrol 40-60 to 1:2 dichloromethane/petrol 40-60 afforded the title compound **226** as a white solid (1.41 g, 89 %).

Melting point: 116-118 °C (dichloromethane/petrol 40-60);

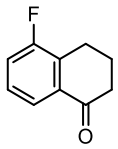
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.88 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.85-7.79 (m, 1H, $H_{16}$), 7.78-7.71 (m, 1H, $H_{19}$), 7.39-7.31 (m, 3H, $H_{13}$, $H_{17}$ and $H_{18}$), 6.81 (d, *J* = 2.5 Hz, 1H, $H_6$), 6.48 (dd, *J* = 8.5, 2.6 Hz, 1H, $H_8$), 6.44 (d, *J* = 8.5 Hz, 1H, $H_9$), 5.92 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.85 (s, 3H, $H_{21}$ or $H_{22}$), 3.77 (s, 3H, $H_{21}$ or $H_{22}$), 3.02 (t, *J* = 7.9 Hz, 2H, $H_4$), 2.58 (ddd, *J* = 9.4, 7.2, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.6 (Quat, $C_7$ or $C_{12}$), 154.4 (Quat, $C_7$ or $C_{12}$), 137.7 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 133.2 (Quat, $C_{Ar}$), 129.3 (Quat, $C_{Ar}$), 129.0 (CH, $C_{14}$), 128.9 (Quat, $C_{Ar}$), 127.9 (CH, $C_{16}$), 127.3 (CH, $C_2$), 126.4 (CH, $C_{17}$ or $C_{18}$), 125.9 (CH, $C_9$), 125.5 (CH, $C_{19}$), 124.0 (Quat, $C_{11}$), 123.7 (CH, $C_{17}$ or $C_{18}$), 114.2 (CH, $C_{13}$), 113.9 (CH, $C_6$), 111.0 (CH, $C_8$), 57.2 ($CH_3$, $C_{21}$ or $C_{22}$), 55.3 ($CH_3$, $C_{21}$ or $C_{22}$), 28.9 ($CH_2$, $C_4$), 23.7 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3056, 3026, 2999, 2934, 2833, 1606, 1593, 1495, 1465, 1387, 1351, 1331, 1271, 1201, 1168, 1149, 1128, 1088, 1021;

LRMS (ESI$^+$): calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1537.

**5-Fluoro-3,4-dihydronaphthalen-1(2*H*)-one, RJA26**




**RJA26**

*This compound was synthesised and analysed by Dr Roland Armstrong* by analogy to a modified literature procedure,[86] a stirred solution of *o*-fluorobenzaldehyde (2.14 g, 17.3 mmol) and (2-carboxyethyl)triphenylphosphonium chloride [141] (6.60 g, 17.8 mmol) in a 1:1 mixture of THF/DMSO (50 mL) was cooled to 0 °C and sodium hydride (60 % w/w in mineral oil, 1.42 g, 35.6 mmol) was added in a single portion. The resulting mixture was warmed to room temperature and stirred for 20 hours. The mixture was then cooled to 0 °C and water was added. The resulting aqueous solution was washed three times with diethyl ether. The aqueous phase was then acidified to pH 1-2 by addition of concentrated HCl and extracted three times with diethyl ether. The combined organic extracts were washed with brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure.

The crude residue thus obtained was dissolved in ethanol (100 mL) and was stirred at room temperature and Pd/C (214 mg, 10 wt. %) was added. The resulting stirred suspension was sparged with hydrogen for 30 minutes and then stirred under an atmosphere of hydrogen (balloon pressure) for 3 hours. The reaction mixture was filtered through a plug of celite, washing with dichloromethane and the filtrate was concentrated under reduced pressure to afford the crude carboxylic acid as a yellow oil (3.08 g) which was used without further purifiaction in the subsequent step.

According to a modified literature procedure,[85] a mechanically stirred suspension of the crude carboxylic acid (1.50 g, 8.23 mmol) in polyphosphoric acid (8.2 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and

dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **RJA26** as a white solid (427 mg, 31 % for 3 steps). The spectral data matched that previously reported in the literature. [145]

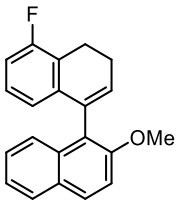
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.90 (d, *J* = 7.7 Hz, 1H), 7.34-7.20 (m, 2H), 2.97 (t, *J* = 6.1 Hz, 2H), 2.68 (t, *J* = 6.5 Hz, 2H), 2.17 (qn, *J* = 6.3 Hz, 2H;

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 197.2 (d, *J* = 2.9 Hz), 160.0 (d, *J* = 245.8 Hz), 134.4 (d, *J* = 3.7 Hz), 131.3 (d, *J* = 17.6 Hz), 127.3 (d, *J* = 8.1 Hz), 122.7 (d, *J* = 3.7 Hz), 119.7 (d, *J* = 22.0 Hz), 38.8, 22.4, 21.9 (d, *J* = 3.7 Hz);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –117.6;

LRMS ($ESI^+$) calculated for $C_{10}H_{10}FO^+$ = 165, mass found = 165.

**5-Fluoro-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA34**




**RJA34**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA26** (357 mg, 2.17 mmol), anhydrous cerium chloride (1.07 g, 4.35 mmol), THF (22 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 6.50 mL, 3.25 mmol), 3M HCl (22 mL). Purification *via* column chromatography eluting with 3:17

dichloromethane/petrol 40-60 afforded the title compound **RJA34** as a white solid (676 mg, 99 %).

Melting point: 120-122 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.78 (d, *J* = 9.0 Hz, 1H), 7.74-7.69 (m, 1H), 7.64-7.59 (m, 1H), 7.28-7.21 (m, 3H), 6.80-6.74 (m, 2H), 6.24-6.18 (m, 1H), 5.98 (t, *J* = 4.5 Hz, 1H), 3.74 (s, 3H), 2.96 (t, *J* = 8.3 Hz, 2H), 2.49 (td, *J* = 8.3, 4.5 Hz, 2H);

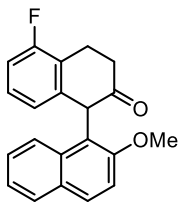
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 159.8 (d, *J* = 242.4 Hz), 154.4, 137.6 (d, *J* = 4.8 Hz), 133.8, 133.1 (d, *J* = 4.0 Hz), 130.7, 129.2, 129.2, 127.9, 126.9 (d, *J* = 8.7 Hz), 126.4, 125.2, 123.7, 123.3, 122.0 (d, *J* = 17.5 Hz), 120.4 (d, *J* = 2.4 Hz), 113.9, 113.9 (d, *J* = 23.0 Hz), 56.9, 22.7, 19.4 (d, *J* = 4.0 Hz);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –120.9;

FTIR (neat) $\nu$/cm$^{-1}$ = 2936, 2836, 1614, 1593, 1507, 1459, 1332, 1257, 1240, 1179, 1147, 1112, 1073, 1020;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}OF^+$ = 305.1336, mass found = 305.1338.

**5-Fluoro-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA44**




**RJA44**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA34** (510 mg, 1.68 mmol), dichloromethane (17 mL), sodium bicarbonate (353 mg, 4.20 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 771 mg, 3.35 mmol); then 1:1 diethyl ether/dichloromethane (34 mL), boron trifluoride diethyl etherate (0.33 mL, 2.69 mmol).

Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **RJA44** as a white solid (387 mg, 72 %).

Melting point: 136-138 °C (hexane/ethyl acetate);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.79 (d, *J* = 9.0 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.50 (br d, *J* = 8.0 Hz, 1H), 7.32 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H), 7.26 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.20 (d, *J* = 9.0 Hz, 1H), 6.86-6.78 (m, 2H), 6.31-6.24 (m, 1H), 5.43 (s, 1H), 3.66 (s, 3H), 3.36 (dt, *J* = 16.1, 6.0 Hz, 1H), 3.09 (ddd, *J* = 16.0, 10.0, 5.8 Hz, 1H), 2.84 (ddd, *J* = 16.1, 6.3, 5.6 Hz, 1H), 2.73 (ddd, *J* = 16.0, 9.9, 5.7 Hz, 1H);

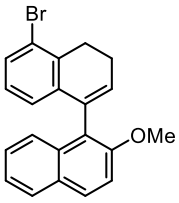
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 209.5, 159.7 (d, *J* = 244.0 Hz), 154.6, 140.5 (d, *J* = 4.0 Hz), 133.2, 129.8, 129.6, 128.9, 127.7 (d, *J* = 7.9 Hz), 127.0, 123.6, 123.2, 123.2 (d, *J* = 18.3 Hz), 123.0 (d, *J* = 3.2 Hz), 121.3, 113.8, 113.0 (d, *J* = 22.3 Hz), 56.4, 49.9 (d, *J* = 1.6 Hz), 37.9, 20.5 (d, *J* = 4.0 Hz);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –119.6;

FTIR (neat) $\nu$/cm$^{-1}$ = 2841, 1715, 1619, 1596, 1583, 1512, 1464, 1248, 1147, 1091, 1071, 1041, 1026;

HRMS (ESI$^+$) calculated for $C_{21}H_{17}O_2FNa^+$ = 343.1105, mass found = 343.1104.

**5-Bromo-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA35**




**RJA35**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA9** (1.04 g, 4.62 mmol), anhydrous cerium chloride (2.28 g, 9.24 mmol), THF (46 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 11.1 mL, 5.55 mmol),

3M HCl (46 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA35** as a colourless oil (1.00 g, 59 %).

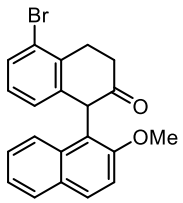
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.90 (d, *J* = 8.8 Hz, 1H), 7.86-7.82 (m, 1H), 7.73-7.68 (m, 1H), 7.40-7.34 (m, 4H), 6.80 (t, *J* = 7.8 Hz, 1H), 6.48 (d, *J* = 7.3 Hz, 1H), 6.08 (t, *J* = 4.5 Hz, 1H), 3.85 (s, 3H), 3.20 (t, *J* = 8.2 Hz, 2H), 2.63 (td, *J* = 8.2, 4.6 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 137.6, 135.1, 133.8, 133.2, 131.1, 130.7, 129.2, 129.1, 127.9, 127.5, 126.5, 125.1, 124.0, 123.9, 123.7, 123.0, 113.9, 56.9, 27.5, 23.3;

FTIR (neat) $\nu$/cm$^{-1}$ = 2933, 2834, 1621, 1592, 1507, 1454, 1434, 1333, 1255, 1088, 1059, 1019;

HRMS (EI$^+$) calculated for $C_{21}H_{17}OBr^+$ = 364.0457, mass found = 364.0464.

**5-Bromo-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA45**




**RJA45**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA35** (950 mg, 2.60 mmol), dichloromethane (26 mL), sodium bicarbonate (546 mg, 6.50 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.20 g, 5.20 mmol); then 1:1 diethyl ether/dichloromethane (52 mL), boron trifluoride diethyl etherate (0.51 mL, 4.13 mmol). Purification *via* recrystallization from petrol 60-80/ethyl acetate afforded the title compound **RJA45** as a white solid (592 mg, 60 %).

Melting point: 184-186 °C (ethyl acetate/petrol 60-80);

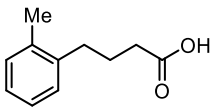
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.1 Hz, 1H), 7.89 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.59 (br d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.45 (ddd, *J* = 8.0, 6.7, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 6.86 (t, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 7.8 Hz, 1H), 5.57 (s, 1H), 3.79 (s, 3H), 3.63 (dt, *J* = 16.4, 5.8 Hz, 1H), 3.33 (ddd, *J* = 16.3, 10.3, 5.6 Hz, 1H), 2.98 (ddd, *J* = 16.3, 5.9, 5.6 Hz, 1H), 2.86 (ddd, *J* = 16.2, 10.3, 5.6 Hz, 1H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 209.5, 154.6, 140.0, 135.6, 133.2, 130.6, 129.9, 129.6, 128.9, 127.9, 127.0, 126.8, 123.8, 123.6, 123.3, 121.0, 113.7, 56.4, 50.1, 38.3, 28.3;

FTIR (neat) $\nu$/cm$^{-1}$ = 2939, 2840, 1716, 1624, 1596, 1561, 1512, 1440, 1259, 1182, 1148, 1122, 1080, 1025;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}O_2Br^+$ = 381.0485, mass found = 381.0487.

**4-(*o*-Tolyl)butanoic acid, RJA53**




**RJA53**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a literature procedure,[86] a stirred solution of *o*-tolualdehyde (2.08 g, 17.3 mmol) and (2-carboxyethyl)triphenylphosphonium chloride[141] (6.60 g, 17.8 mmol) in a 1:1 mixture of THF/DMSO (50 mL) was cooled to 0 °C and sodium hydride (60 % w/w in mineral oil, 1.42 g, 35.6 mmol) was added in a single portion. The resulting mixture was warmed to room temperature and stirred for 20 hours. The mixture was then cooled to 0 °C and water was added. The resulting aqueous solution was washed three times with diethyl ether. The aqueous phase was then acidified to pH 1-2 by addition of concentrated HCl and extracted three times with diethyl ether. The combined organic extracts were washed with brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure.

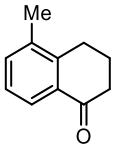
The crude residue thus obtained was dissolved in ethanol (100 mL) and stirred at room temperature. Pd/C (300 mg) was added and the resulting stirred suspension was sparged with hydrogen for 30 minutes and then stirred under an atmosphere of hydrogen (balloon pressure) for 3 hours. The reaction mixture was filtered through a plug of celite, washing with dichloromethane and the filtrate was concentrated under reduced pressure. Purification *via* column chromatography eluting with 1:4 ethyl acetate/toluene afforded the title compound **RJA53** as a white solid (1.40 g, 45 % for 2 steps). The spectral data matched that previously reported in the literature.[86]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 11.4 (br s, 1H, COO*H*), 7.24-7.12 (m, 4H), 2.72 (t, *J* = 7.8 Hz, 2H), 2.49 (t, *J* = 7.3 Hz, 2H), 2.37 (s, 3H), 1.98 (qn, *J* = 7.6 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 180.2, 139.4, 136.0, 130.3, 129.0, 126.2, 126.0, 33.7, 32.4, 25.0, 19.3;

LRMS ($ESI^+$) calculated for $C_{11}H_{14}O_2Na^+$ = 201, mass found = 201.

**5-Methyl-3,4-dihydronaphthalen-1(2*H*)-one, RJA27**




**RJA27**

*This compound was synthesised and analysed by Dr Roland Armstrong* By analogy to a modified literature procedure,[85] a mechanically stirred suspension of **RJA53** (1.09 g, 6.12 mmol) in polyphosphoric acid (6.1 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the

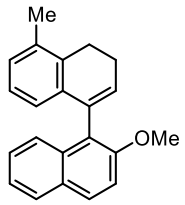
residue *via* column chromatography eluting with 1:9 ethyl acetate/toluene afforded the title compound **RJA27** as a white solid (545 mg, 56 %). The spectral data matched that previously reported in the literature.[145]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 2.86 (t, *J* = 6.1 Hz, 2H), 2.63 (t, *J* = 6.5 Hz, 2H), 2.31 (s, 3H), 2.15 (qn, *J* = 6.3 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.8, 142.8, 136.3, 134.8, 132.8, 126.1, 125.0, 38.7, 26.5, 22.6, 19.5;

LRMS ($ESI^+$) calculated for $C_{11}H_{12}ONa^+$ = 183, mass found = 183.

**2'-Methoxy-5-methyl-3,4-dihydro-1,1'-binaphthalene, RJA36**




**RJA36**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA27** (497 mg, 3.10 mmol), anhydrous cerium chloride (1.53 g, 6.20 mmol), THF (31 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 9.30 mL, 4.65 mmol), 3M HCl (31 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA26** as a colourless gum (814 mg, 87 %).

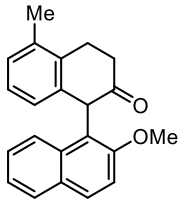
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.0 Hz, 1H), 7.88-7.84 (m, 1H), 7.82-7.77 (m, 1H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.40-7.35 (m, 2H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.43 (d, *J* = 7.6 Hz, 1H), 6.08 (t, *J* = 4.5 Hz, 1H), 3.88 (s, 3H), 3.04 (t, *J* = 8.2 Hz, 2H), 2.64 (td, *J* = 8.2, 4.4 Hz, 2H), 2.43 (s, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.4, 135.3, 134.7, 134.0, 134.0, 133.8, 129.3, 129.2, 129.1, 128.9, 127.8, 126.3, 125.7, 125.5, 124.1, 123.6, 122.8, 114.1, 57.0, 23.9, 23.4, 19.8;

FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 2935, 2833, 1621, 1592, 1507, 1467, 1332, 1257, 1147, 1111, 1086, 1021;

HRMS (ESI$^+$) calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1588.

**2'-Methoxy-5-methyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA46**




**RJA46**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA36** (788 mg, 2.62 mmol), dichloromethane (26 mL), sodium bicarbonate (550 mg, 6.55 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.21 g, 5.25 mmol); then 1:1 diethyl ether/dichloromethane (52 mL), boron trifluoride diethyl etherate (0.52 mL, 4.19 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **RJA46** as a white solid (397 mg, 48 %).

Melting point: 170-171 °C (hexane/ethyl acetate);

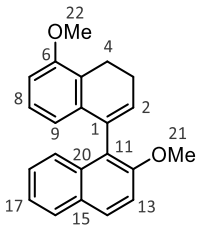
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.78 (d, *J* = 9.1 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.46 (br d, *J* = 8.2 Hz, 1H), 7.28 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1H), 7.23 (ddd, *J* = 8.1, 6.9, 1.4 Hz, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.77 (t, *J* = 7.6 Hz, 1H), 6.33 (d, *J* = 7.7 Hz, 1H), 5.46 (s, 1H), 3.66 (s, 3H), 3.25 (dt, *J* = 15.9, 5.9 Hz, 1H), 3.05 (ddd, *J* = 15.7, 10.2, 5.3 Hz, 1H), 2.85 (ddd, *J* = 16.2, 5.9, 5.3 Hz, 1H), 2.71 (ddd, *J* = 16.0, 10.2, 5.6 Hz, 1H), 2.32 (s, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.7, 154.8, 137.7, 134.8, 134.6, 133.3, 129.7, 129.6, 128.9, 128.1, 126.8, 126.4, 125.4, 123.7, 123.5, 121.6, 113.9, 56.5, 50.4, 38.6, 24.7, 20.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 2941, 2840, 1714, 1624, 1596, 1512, 1468, 1250, 1147, 1086, 1067, 1044, 1025;

HRMS (ESI$^+$) calculated for $C_{22}H_{20}O_2Na^+$ = 339.1356, mass found = 339.1353.

**2',5-Dimethoxy-3,4-dihydro-1,1'-binaphthalene, 227**




**227**

According to **General Procedure A** with 5-methoxy-1-tetralone (881 mg, 5.00 mmol), anhydrous cerium chloride (2.56 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:3 dichloromethane/petrol 40-60 to 1:2 dichloromethane/petrol 40-60 afforded the title compound **227** as a colourless gum (1.31 g, 81 %).

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.88 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.84-7.79 (m, 1H $H_{16}$), 7.77-7.72 (m, 1H $H_{19}$), 7.41-7.29 (m, 3H $H_{13}$, $H_{17}$ and $H_{18}$), 6.91 (t, *J* = 8.0 Hz, 1H $H_8$), 6.76 (dd, *J* = 8.2, 1.1 Hz, 1H $H_7$), 6.18 (dd, *J* = 7.7, 1.0 Hz, 1H $H_9$), 6.05 (t, *J* = 4.5 Hz, 1H $H_2$), 3.88 (s, 3H $H_{21}$ or $H_{22}$), 3.84 (s, 3H $H_{21}$ or $H_{22}$), 3.05 (t, *J* = 8.3 Hz, 2H $H_4$), 2.57 (ddd, *J* = 9.3, 7.7, 4.5 Hz, 2H $H_3$);

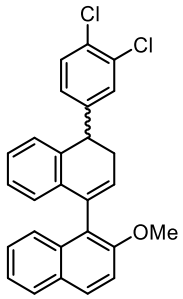
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 156.2 (Quat, $C_6$ or $C_{12}$), 154.5 (Quat, $C_6$ or $C_{12}$), 136.6 (Quat, $C_{Ar}$), 134.1 (Quat, $C_{Ar}$), 133.5 (Quat, $C_{Ar}$), 130.2 (CH, $C_2$), 129.3 (Quat, $C_{Ar}$), 129.0 (CH, $C_{14}$), 127.9 (CH, $C_{16}$), 126.5 (CH, $C_8$), 126.4 (CH, $C_{17}$ or $C_{18}$), 125.5 (CH, $C_{19}$), 124.1 (Quat, $C_5$ or $C_{11}$), 123.7 (Quat,

$C_5$ or $C_{11}$), 123.7 (CH, $C_{17}$ or $C_{18}$), 117.8 (CH, $C_9$), 114.2 (CH, $C_{13}$), 109.7 (CH, $C_7$), 57.1 ($CH_3$, $C_{21}$ or $C_{22}$), 55.7 ($CH_3$, $C_{21}$ or $C_{22}$), 23.2 ($CH_2$, $C_3$), 20.0 ($CH_2$, $C_4$);

FTIR (neat) $\nu/cm^{-1}$ = 3064, 2999, 2935, 2885, 2834, 1621, 1593, 1573, 1507, 1467, 1438, 1387, 1297, 1256, 1240, 1177, 1119, 1077, 1057, 1020;

LRMS ($ESI^+$): calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1537.

**4-(3,4-Dichlorophenyl)-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, 228**




**228**

According to **General Procedure A** with 4-(3,4-dichlorophenyl)-1-tetralone (1.46 g, 5.0 mmol), anhydrous cerium chloride (2.56 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.00 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 30-40 to 1:4 dichloromethane/petrol 30-40 afforded the title compound **228** as a white solid (1.12 g, 54 %, *c.a.*, 1.5:1 *d.r.*).

Melting point: 60-61 °C (dichloromethane/petrol 30-40);

$^1H$ NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 9.0 Hz, $1H_{min}$), 7.92 (d, *J* = 9.0 Hz, $1H_{maj}$), 7.89-7.79 (m, $1H_{maj} + 2H_{min}$), 7.69-7.61 (m, $1H_{maj}$), 7.54 (d, *J* = 2.1 Hz, $1H_{min}$), 7.50-7.46 (m, $1H_{maj} + 1H_{min}$), 7.43-7.32 (m, $3H_{maj} + 3H_{min}$), 7.31 (dd, *J* = 8.3, 2.1 Hz, $1H_{min}$), 7.28-7.24 (m, $2H_{maj}$), 7.18-7.11 (m, $1H_{maj} + 1H_{min}$), 7.10-7.01 (m, $1H_{maj} + 2H_{min}$), 7.00-6.95 (m, $1H_{maj}$), 6.67-6.60 (m, $1H_{maj} + 1H_{min}$), 6.01 (t, *J* = 4.5 Hz, $1H_{maj}$), 5.90 (dd, *J* = 5.6, 3.3 Hz, $1H_{min}$), 4.36 (dd, *J* = 8.9, 7.1 Hz, $1H_{maj}$), 4.30 (dd,

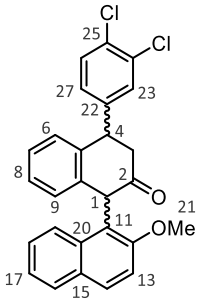
*J* = 7.8, 4.6 Hz, $1H_{min}$), 3.90 (s, $3H_{min}$), 3.87 (s, $3H_{maj}$), 3.17 (ddd, *J* = 17.2, 7.8, 3.4 Hz, $1H_{min}$), 3.02-2.85 (m, $2H_{maj}$), 2.78 (ddd, *J* = 17.2, 5.7, 4.6 Hz, $1H_{min}$);

$^{13}C$ NMR (126 MHz, $CDCl_3$) $\delta_C$ = 154.5 (min), 154.5 (maj), 145.7 (min), 145.1 (maj), 136.8 (maj), 136.5 (min), 135.4 (min), 135.3 (maj), 134.4 (min), 134.2 (maj), 134.0 (min), 132.6 (maj), 132.2 (min), 130.6 (maj), 130.6 (maj), 130.5 (maj), 130.4 (min), 130.3 (min), 130.2 (min), 129.3 (maj), 129.3 (maj), 129.2 (min), 129.2 (min), 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.5, 127.3, 126.8, 126.6 (maj), 126.5 (min), 125.3 (min), 125.3 (maj), 125.2 (min), 123.7 (maj), 123.7 (min), 123.0 (maj), 122.9 (min), 113.9 (maj), 113.6 (min), 57.0 (maj), 56.7 (min), 43.2 (maj), 42.9 (min), 32.0 (min), 31.8 (maj); Peaks corresponding to to the respective diastereomers were assigned only where appropriate. Several $^{13}C$ signals were coincident.

FTIR (neat) $\nu/cm^{-1}$ = 3058, 3026, 2934, 2837; 1621, 1593, 1560, 1509, 1448, 1395, 1350, 1269, 1178, 1174, 1132, 1087, 1029;

HRMS ($EI^+$) calculated for $C_{27}H_{20}O_2Cl_2^+$ = 430.0886, mass found = 430.0893.

**4-(3,4-Dichlorophenyl)-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 245**




**245**

According to **General Procedure B** with **228** (1.08 g, 2.61 mmol), dichloromethane (26 mL), sodium bicarbonate (549 mg, 6.53 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.20 g, 5.22 mmol); then 1:1 diethyl ether/dichloromethane (52 mL), boron trifluoride diethyl etherate (0.52 mL, 4.18 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the

title compound **245** as an off white solid (530 mg, 45 %, *c.a.* 20:1 *d.r.*). The NMR data reported is for the major diastereomer only.

Melting point: 187-188 °C (ethyl acetate/hexane);

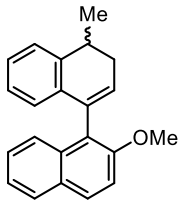
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.89 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.86 (d, *J* = 7.8 Hz, 1H, $H_{16}$), 7.64-7.53 (m, 1H, $H_{19}$), 7.48-7.40 (m, 2H, $H_{26}$ and $H_{18}$), 7.40-7.34 (m, 2H, $H_{17}$ and $H_{23}$), 7.30 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.25-7.18 (m, 2H, $H_6$ and $H_7$), 7.10 (dd, *J* = 8.3, 2.2 Hz, 1H, $H_{27}$), 7.05 (ddd, *J* = 7.8, 6.3, 2.5 Hz, 1H $H_8$), 6.63 (d, *J* = 7.7 Hz, 1H, $H_9$), 5.37 (s, 1H, $H_1$), 4.66 (t, *J* = 5.6 Hz, 1H, $H_4$), 3.73 (s, 3H, $H_{21}$), 3.27 (dd, *J* = 5.6, 1.7 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 208.6 (Quat, $C_2$), 154.5 (Quat, $C_{12}$), 142.6 (Quat, $C_{22}$), 138.0 (Quat, $C_{10}$), 136.8 (Quat, $C_5$), 133.5 (Quat, $C_{20}$), 133.1 (Quat, $C_{15}$), 131.2 (Quat, $C_{24}$ or $C_{25}$), 130.9 (Quat, $C_{24}$ or $C_{25}$), 130.0 (CH, $C_{26}$), 129.9 (CH, $C_{14}$), 129.7 (CH, $C_{23}$), 129.0 (CH, $C_{16}$), 128.5 (CH, $C_6$), 128.1 (CH, $C_9$), 127.8 (CH, $C_8$), 127.3 (CH, $C_{18}$), 127.2 (CH, $C_{27}$), 126.9 (CH, $C_7$), 123.8 (CH, $C_{17}$), 123.1 (CH, $C_{19}$), 121.7 (Quat, $C_{11}$), 114.0 (CH, $C_{13}$), 56.5 ($CH_3$, $C_{21}$), 50.2 (CH, $C_1$), 45.7 ($CH_2$, $C_3$), 44.1 (CH, $C_4$);

FTIR (neat) $\nu/cm^{-1}$ = 3063, 2964, 2938, 2840, 1716, 1624, 1597, 1485, 1435, 1350, 1257, 1184, 1133;

HRMS ($ESI^+$): calculated for $C_{27}H_{21}O_2Cl_2^+$ = 447.0913, mass found = 447.0911.

**2'-Methoxy-4-methyl-3,4-dihydro-1,1'-binaphthalene, RJA37**




**RJA37**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with 4-methyl-1-tetralone (801 mg, 5.00 mmol), anhydrous cerium chloride

(2.47 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 12.0 mL, 6.00 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA37** as a colourless oil (1.30 g, 87 %, *c.a.* 2:1 *d.r.*).

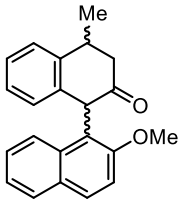
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, $1H_{maj}$ + $1H_{min}$), 7.92-7.87 (m, $1H_{maj}$ + $1H_{min}$), 7.86-7.80 (m, $1H_{maj}$ + $1H_{min}$), 7.46-7.39 (m, $3H_{maj}$ + $3H_{min}$), 7.34 (t, *J* = 6.7 Hz, $1H_{maj}$ + $1H_{min}$), 7.26-7.20 (m, $1H_{maj}$ + $1H_{min}$), 7.02 (t, *J* = 7.6 Hz, $1H_{maj}$ + $1H_{min}$), 6.61 (d, *J* = 7.6 Hz, $1H_{maj}$ + $1H_{min}$), 6.06 (t, *J* = 4.5 Hz, $1H_{maj}$), 6.03 (t, *J* = 4.5 Hz, $1H_{min}$), 3.90 (s, $3H_{maj}$), 3.89 (s, $3H_{min}$), 3.31-3.18 (m, $1H_{maj}$ + $1H_{min}$), 2.87 (ddd, *J* = 6.3, 4.2, 1.9 Hz, $1H_{min}$), 2.82 (ddd, *J* = 6.4, 4.2, 2.0 Hz, $1H_{maj}$), 2.51-2.42 (m, $1H_{maj}$ + $1H_{min}$), 1.56 (d, *J* = 6.8 Hz, $3H_{maj}$), 1.52 (d, *J* = 7.1 Hz, $3H_{min}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.6 (maj), 154.5 (min), 141.0 (min), 140.7 (maj), 134.9 (min), 134.7 (maj), 134.1 (min), 134.1 (maj), 133.3 (min), 133.2 (maj), 129.2 (maj), 129.2 (min), 129.0 (maj), 128.9 (min), 128.7 (maj), 128.1 (min), 127.9 (maj), 127.9 (min), 127.2 (maj), 127.1 (min), 126.4 (maj + min), 126.3 (maj + min), 126.2 (maj + min), 125.5 (maj), 125.4 (min), 124.9 (maj), 124.9 (min), 124.0 (min), 123.7 (maj), 123.6 (min), 123.6 (maj), 114.2 (maj), 114.1 (min), 57.0 (maj), 57.0 (min), 32.6 (min), 32.2 (maj), 31.7 (maj), 31.5 (min), 20.7 (maj), 20.4 (min);

FTIR (neat) $\nu$/cm$^{-1}$ = 2958, 2835, 1621, 1593, 1508, 1462, 1431, 1331, 1257, 1147, 1078, 1052, 1019;

HRMS (ESI$^+$) calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1587.

**2'-Methoxy-4-methyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, RJA47**




**RJA47**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA37** (730 mg, 2.43 mmol), dichloromethane (24 mL), sodium bicarbonate (510 mg, 6.07 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.12 g, 4.87 mmol); then 1:1 diethyl ether/dichloromethane (48 mL), boron trifluoride diethyl etherate (0.48 mL, 3.89 mmol). Purification *via* column chromatography on neutral alumna eluting with 1:1 dichloromethane/petrol 40-60 followed by recrystallization from hexane/ethyl acetate afforded the title compound **RJA47** as a white solid (305 mg, 40 %, *c.a.* 1.3:1 *d.r.*).

Melting point: 125-127 °C (ethyl acetate/hexane);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 8.8 Hz, $1H_{maj}$), 7.91 (d, *J* = 9.1 Hz, $1H_{min}$), 7.90-7.86 (m, $1H_{maj}$ + $1H_{min}$), 7.70 (br d, *J* = 7.3 Hz, $1H_{min}$), 7.48-7.34 (m, $4H_{maj}$ + $3H_{min}$), 7.33 (d, 9.0 Hz, $1H_{min}$), 7.28 (t, 7.5 Hz, $1H_{maj}$), 7.22 (t, *J* = 7.5 Hz, $1H_{min}$), 7.03-6.97 (m, $1H_{maj}$ + $1H_{min}$), 6.57 (d, *J* = 8.0 Hz, $1H_{min}$), 6.49 (d, *J* = 7.6 Hz, $1H_{maj}$), 5.64 (br s, $1H_{maj}$), 5.52 (s, $1H_{min}$), 3.78 (br s, $3H_{maj}$), 3.76 (s, $3H_{min}$), 3.57-3.42 (m, $1H_{maj}$ + $1H_{min}$), 3.12 (dd, *J* = 15.5, 5.4 Hz, $1H_{min}$), 2.97 (dd, *J* = 16.4, 3.9 Hz, $1H_{maj}$), 2.82 (dd, *J* = 15.7, 4.7 Hz, $1H_{min}$), 2.65-2.54 (m, $1H_{maj}$), 1.62 (d, *J* = 6.8 Hz, $3H_{maj}$), 1.50 (d, *J* = 7.3 Hz, $3H_{min}$);

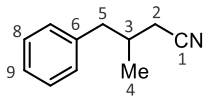
$^{13}$C NMR (121 MHz, $CDCl_3$) $\delta_C$ = 211.0 (min), 210.1 (maj), 154.6 (maj + min), 140.8 (maj), 140.5 (min), 137.2 (min), 137.0 (maj), 133.9 (min), 133.7 (maj), 129.9, 129.8, 129.7, 128.9 (maj), 127.7, 127.1, 127.0, 126.9 (maj), 126.8, 126.6 (maj), 126.6, 124.4, 123.7, 123.6, 123.3, 122.4 (min), 114.1, 56.4 (min), 51.2 (maj), 49.4 (min), 46.6 (maj), 46.0 (min), 34.6 (min), 31.9 (maj), 21.4 (min), 18.6 (maj);

Peaks corresponding to to the respective diastereomers were assigned only where appropriate. Several $^{13}$C signals were coincident.

FTIR (neat) $\nu/cm^{-1}$ = 2961, 2840, 1714, 1624, 1596, 1512, 1463, 1378, 1350, 1258, 1148, 1080, 1024;

HRMS (ESI$^+$) calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1538.

**3-Methyl-4-phenylbutanenitrile, 201**




**201**

According to a literature procedure,[87] a two necked flask equipped with a Dean-Stark apparatus was charged with phenylacetone (32.2 g 240 mmol), benzene (30 mL), acetic acid (20.6 mL, 360 mmol), cyanoacetic acid (21.2 g, 250 mmol) and ammonium acetate (4.1 g, 53 mmol). The reaction mixture was then stirred at reflux for 24 h. After cooling to room temperature, the majority of benzene and acetic acid was removed under reduced pressure. Following this, the reaction mixture was stirred at 150 °C for 3 h and subsequently cooled to room temperature. A mixture of regioisomers of the desired olefin was obtained *via* vacuum distillation (118–125 °C, 0.3 mmHg) as a colourless oil (29.8 g, 79 %) which was used in the next step without any further purification. Pd/C (680 mg, 0.64 mmol) was added to the regioisomeric mixture of the previously obtained olefin (10.0 g, 64.0 mmol). The resulting suspension was subsequently sparged with argon for 30 minutes. Following this, the suspension was stirred under an atmosphere of hydrogen (balloon) for 54 h. The suspension was then filtered through celite and the filter cake was subsequently washed with ethyl acetate. The filtrate was concentrated under reduced pressure to afford the title compound **201** as a colourless oil (10.1 g, 99 %). The spectral data matched that previously reported in the literature.[87]

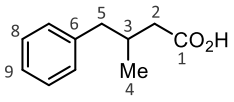
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.37-7.31 (m, 2H, $H_8$), 7.29-7.24 (m, 1H, $H_9$), 7.22-7.17 (m, 2H, $H_7$), 2.69 (dd, *J* = 7.2, 1.7 Hz, 2H, $H_5$), 2.37-2.13 (m, 3H, $H_2$ and $H_3$), 1.15 (d, *J* = 6.6 Hz, 3H, $H_4$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 139.1 (Quat, $C_6$), 129.1 (CH, $C_7$), 128.7 (CH, $C_8$), 126.7 (CH, $C_9$), 118.7 (Quat, $C_1$), 42.1 ($CH_2$, $C_5$), 32.6 ($CH_2$, $C_2$), 23.7 (CH, $C_3$), 19.6 ($CH_3$, $C_4$);

FTIR (neat) $\nu/cm^{-1}$ = 3063, 3028, 2962, 2928, 2874, 2855, 2246, 1604, 1496, 1454, 1383, 1345, 1235, 1130, 1090, 1030;

HRMS ($CI^+$) calculated for $C_{11}H_{13}NNH_4^+$ = 177.1386, mass found = 177.1386.

**3-Methyl-4-phenylbutanoic acid, 202**




**202**

According to a modified literature procedure,[87] potassium hydroxide (85 %, 20.6 g, 312 mmol) was added to a solution of **201** (9.93 g, 62.3 mmol) in 9:1 ethanol/water (125 mL). The solution was stirred at reflux for 48 h and subsequently cooled to room temperature. Following this, the majority of ethanol was removed under reduced pressure and the reaction mixture was subsequently acidified *via* careful dropwise addition of 3M HCl. The mixture was extracted three times with ethyl acetate and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to afford the title compound **202** as a yellow oil (10.8 g, 97%). The spectral data matched that previously reported in the literature.[87]

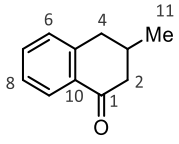
$^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.32-7.25 (m, 2H, $H_8$), 7.24-7.14 (m, 3H, $H_7$ and $H_9$), 2.65 (dd, *J* = 13.4, 6.8 Hz, 1H, $H_{5A}$), 2.53 (dd, *J* = 13.4, 7.3 Hz, 1H, $H_{5B}$), 2.38 (dd, *J* = 14.8, 5.5 Hz, 1H, $H_{2A}$), 2.37-2.21 (m, 1H, $H_3$), 2.18 (dd, *J* = 14.8, 7.9 Hz, 1H, $H_{2B}$), 0.99 (d, *J* = 6.5 Hz, 3H, $H_4$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 179.4 (Quat, $C_1$), 140.2 (Quat, $C_6$), 129.3 (CH, $C_7$), 128.4 (CH, $C_8$), 126.2 (CH, $C_9$), 43.0 ($CH_2$, $C_5$), 40.9 ($CH_2$, $C_2$), 32.2 (CH, $C_3$), 19.7 ($CH_3$, $C_4$);

FTIR (neat) $\nu/cm^{-1}$ = 3085, 3062, 3027, 2961, 2926, 2874, 2854, 1704, 1496, 1454, 1410, 1291, 1230, 1169;

LRMS (ESI$^-$) calculated for $C_{11}H_{13}O_2^-$ = 177, mass found = 177.

**3-Methyl-3,4-dihydronaphthalen-1(2*H*)-one, 203**




**203**

By analogy to a modified literature procedure,[85] a mechanically stirred suspension of **202** (10.8 g, 60.6 mmol) in polyphosphoric acid (60 mL) was heated to 90 °C for 2 h. After this time, the reaction mixture was poured onto a mixture of crushed ice and dichloromethane. Once warmed to room temperature, the organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/ petrol 40-60 afforded the title compound **203** as a yellow oil (9.04 g, 93 %). The spectral data matched that previously reported in the literature.[87]

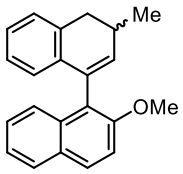
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (dd, *J* = 7.8, 1.5 Hz, 1H, $H_9$), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H, $H_8$), 7.33-7.27 (m, 1H, $H_7$), 7.26-7.21 (m, 1H, $H_6$), 3.02-2.93 (m, 1H, $H_{2A}$), 2.79-2.62 (m, 2H, $H_{2B}$ and $H_{4A}$), 2.39-2.24 (m, 2H, $H_3$ and $H_{4B}$), 1.14 (d, *J* = 6.2 Hz, 3H, $H_{11}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 198.6 (Quat, $C_1$), 143.9 (Quat, $C_5$), 133.6 (CH, $C_8$), 132.3 (Quat, $C_{10}$), 128.9 (CH, $C_6$), 127.1 (CH, $C_9$), 126.7 (CH, $C_7$), 47.3 ($CH_2$, $C_4$), 38.1 ($CH_2$, $C_2$), 30.6 (CH, $C_3$), 21.5 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 2955, 2926, 2872, 2830, 1681, 1602, 1483, 1455, 1434, 1411, 1362, 1332, 1316, 1300, 1259, 1224, 1156, 1119, 1045, 1025;

LRMS (ESI$^+$) calculated for $C_{11}H_{13}O^+$ = 161, mass found = 161.

**2'-Methoxy-3-methyl-3,4-dihydro-1,1'-binaphthalene, 229**




**229**

According to **General Procedure A** with **203** (1.60 g, 10.0 mmol), anhydrous cerium chloride (4.93 g, 20.0 mmol), THF (76 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 24.0 mL, 12.0 mmol), 3M HCl (100 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 afforded the title compound **229** as a colourless gum (2.19 g, 73 %, *c.a.* 3:1 *d.r.*).

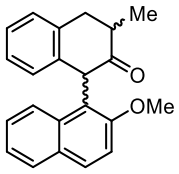
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92-7.88 (m, $1H_{maj}$ + $1H_{min}$), 7.87-7.78 (m, $2H_{maj}$ + $1H_{min}$), 7.75-7.71 (m, $1H_{min}$), 7.42-7.33 (m, $3H_{maj}$ + $3H_{min}$), 7.26-7.21 (m, $1H_{maj}$ + $1H_{min}$), 7.17-7.10 (m, $1H_{maj}$ + $1H_{min}$), 7.00-6.94 (m, $1H_{maj}$ + $1H_{min}$), 6.56-6.49 (m, $1H_{maj}$ + $1H_{min}$), 5.92 (d, *J* = 3.3 Hz, $1H_{min}$), 5.89 (d, *J* = 3.0 Hz, $1H_{maj}$), 3.88 (s, $3H_{min}$), 3.82 (s, $3H_{maj}$), 3.15-3.08 (m, $1H_{min}$), 3.08-3.01 (m, $1H_{maj}$), 2.95-2.79 (m, $2H_{maj}$ + $2H_{min}$), 1.28 (d, *J* = 6.5 Hz, $3H_{min}$), 1.27 (d, *J* = 6.7 Hz, $3H_{maj}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.6 (min), 154.4 (maj), 136.5 (min), 136.4 (maj), 135.6 (maj), 135.5 (maj), 135.4 (min), 135.1 (min), 134.3 (maj), 133.8 (min), 132.8 (maj), 132.5 (min), 129.3 (maj), 129.2 (min), 129.1 (min), 129.0 (maj), 128.0 (maj), 128.0 (min), 127.9 (min), 127.7 (maj), 126.9 (min), 126.8 (maj), 126.5 (min), 126.5 (maj), 126.4 (min), 126.4 (maj), 125.5 (maj), 125.3 (min), 124.7 (min), 124.6 (maj), 123.9 (min), 123.7 (maj), 123.6 (maj), 123.4 (min), 114.5 (maj), 114.1 (min), 57.2 (maj), 57.1 (min), 36.9 (maj), 36.8 (min), 29.7 (maj), 29.6 (min), 20.2 (maj), 20.2 (min);

FTIR (neat) $\nu/cm^{-1}$ = 3058, 3014, 2954, 2927, 2869, 2835, 1621, 1593, 1508, 1485, 1452, 1431, 1386, 1333, 1266, 1252, 1178, 1147, 1123, 1081, 1037, 1020;

HRMS (ESI$^+$) calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1588.

**2'-Methoxy-3-methyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 246**




**246**

According to **General Procedure B** with **229** (2.08 g, 6.92 mmol), dichloromethane (70 mL), sodium bicarbonate (1.45 g, 17.3 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 3.19 g, 13.8 mmol); then 1:1 diethyl ether/dichloromethane (140 mL), boron trifluoride diethyl etherate (1.37 mL, 11.1 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **246** as an off white solid (1.39 g, 63 %, *c.a.* 1.2:1 *d.r.*).

Melting point: 130-133 °C (ethyl acetate/hexane);

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.91 (d, *J* = 9.0 Hz, $1H_{maj}$), 7.89-7.83 (m, $1H_{maj}$ + $2H_{min}$), 7.81-7.62 (br m, $1H_{min}$), 7.57-7.41 (br m, $1H_{maj}$ + $1H_{min}$), 7.40-7.32 (m, $3H_{maj}$ + $2H_{min}$), 7.32-7.24 (m, $1H_{maj}$ + $1H_{min}$), 7.20 (tt, *J* = 7.5, 1.2 Hz, $1H_{maj}$), 7.15 (tt, *J* = 7.5, 1.0 Hz, $1H_{min}$), 7.02- 6.96 (m, $1H_{maj}$ + $1H_{min}$), 6.74 (d, *J* = 7.8 Hz, $1H_{min}$), 6.47 (d, *J* = 7.8 Hz, $1H_{maj}$), 5.67 (br s, $1H_{min}$), 5.52 (br s, $1H_{maj}$), 3.77 (s, $3H_{maj}$), 3.72 (s, $3H_{min}$), 3.33 (dd, *J* = 15.5, 5.8 Hz, $1H_{min}$), 3.26-3.02 (m, $2H_{maj}$ + $2H_{min}$), 2.88-2.78 (m, $1H_{maj}$), 1.39 (d, *J* = 6.8 Hz, $3H_{maj}$), 1.32 (d, *J* = 6.6 Hz, $3H_{min}$).

$^{13}$C NMR (121 MHz, $CDCl_3$) $\delta_C$ = 212.4 (maj), 210.2 (min), 154.9 (maj), 154.4 (min), 138.5, 137.3, 136.3, 135.1, 133.4 (maj), 133.3 (min), 129.7, 129.7, 129.7, 129.4, 128.9, 128.8, 128.0, 127.8, 127.3, 126.8, 126.8, 126.8, 126.6, 126.3, 126.2, 123.7 (min), 123.5 (maj), 123.4 (maj), 123.2

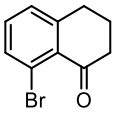
(min), 121.1, 114.0 (min), 113.9 (maj), 56.5, 56.5, 50.0 (maj), 49.8 (min), 43.1 (min), 42.0 (maj), 37.6 (min), 36.6 (maj), 15.3 (maj), 15.3 (min);

Peaks corresponding to to the respective diastereomers were assigned only where appropriate. Two $^{13}C$ signals were coincident.

FTIR (neat) $\nu/cm^{-1}$ = 3063, 3020 ,2965, 2932, 2870, 2834, 1712, 1624, 1596, 1512, 1487, 1455, 1435, 1377, 1350, 1305, 1256, 1212, 1182, 1145, 1110, 1024;

HRMS ($EI^+$) calculated for $C_{22}H_{20}O_2^+$ = 316.1455, mass found = 316.1458.

**8-Bromo-3,4-dihydronaphthalen-1(2H)-one, RJA13**




**RJA13**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to a modified literature procedure,[82] a stirred solution of 1-tetralone (6.50 mL, 48.9 mmol) and methoxyamine hydrochloride (6.55 g, 78.4 mmol) in ethanol (100 mL) was heated at reflux for 1.5 hours. The solution was cooled to room temperature and water and dichloromethane were added. The organic phase was seperated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure.

The crude residue thus obtained was dissolved in glacial acetic acid (350 mL) and stirred at room temperature. N-bromosuccinimide (8.97 g, 50.4 mmol) and palladium acetate (559 mg, 2.49 mmol) were added and the resulting stirred mixture was heated to reflux for 1.5 hours and then cooled to room temperature and poured into a mixture of water and dichloromethane. The organic phase was seperated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed twice with water and twice with

1M aqueous potassium hydroxide and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure.

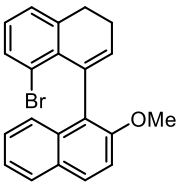
The crude residue thus obtained was dissolved in 1,4 dioxane (120 mL) and stirred at room temperature. 6M aqueous HCl (200 mL) was added and the resulting mixture was heated to reflux for 2.5 hours and then cooled to room temperature and the majority of the volitile organics were removed under reduced pressure. The residue was extracted three times with dichloromethane and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 followed by recrystallization from hexane/ethyl acetate afforded the title compound **RJA13** as a brown solid (1.25 g, 11 % for 3 steps) contaminated by *c.a.* 10 % of an inseperable impurity. The spectral data matched that previously reported in the literature.[146]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.60-7.55 (m, 1H), 7.27-7.20 (m, 2H), 2.99 (t, *J* = 6.1 Hz, 2H), 2.72 (t, *J* = 6.7 Hz, 2H), 2.12 (qn, *J* = 6.4 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 196.7, 147.2, 134.0, 132.8, 131.1, 128.2, 121.9, 40.0, 30.9, 22.5;

LRMS ($ESI^+$) calculated for $C_{10}H_9BrNaO^+$ = 247, mass found = 247.

**8-Bromo-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, RJA38**




**RJA38**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure A** with **RJA13** (1.13 g, 5.00 mmol), anhydrous cerium chloride (2.47 g, 10.0 mmol), THF (50 mL), (2-methoxynaphthalen-1-yl)magnesium bromide (0.5 M in THF, 15.0 mL,

7.50 mmol), 3M HCl (50 mL). Purification *via* column chromatography eluting with 3:17 dichloromethane/petrol 40-60 afforded the title compound **RJA38** as a colourless gum (1.13 g, 62 %).

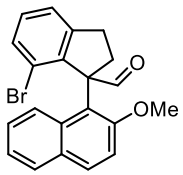
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.74 (d, *J* = 9.0 Hz, 1H), 7.71-7.67 (m, 1H), 7.66-7.62 (m, 1H), 7.28-7.15 (m, 4H), 7.12 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.85 (t, *J* = 7.6 Hz, 1H), 6.23 (t, *J* = 5.0 Hz, 1H), 3.70 (s, 3H), 2.91-2.77 (m, 2H), 2.32 (td, *J* = 7.6, 4.9 Hz, 2H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.1, 140.5, 135.5, 135.3, 133.9, 133.2, 133.2, 129.4, 128.7, 128.0, 127.5, 126.8, 126.1, 125.4, 125.4 , 123.4, 119.8, 114.0, 56.8, 30.3, 23.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 3052, 2936, 2834, 1622, 1592, 1509, 1463, 1439, 1334, 1256, 1094, 1075, 1054, 1022;

HRMS (ESI$^+$) calculated for $C_{21}H_{18}OBr^+$ = 365.0536, mass found = 365.0536.

**7-Bromo-1-(2-methoxynaphthalen-1-yl)-2,3-dihydro-1*H*-indene-1-carbaldehyde, RJA49**




**RJA49**

*This compound was synthesised and analysed by Dr Roland Armstrong* according to **General Procedure B** with **RJA38** (535 mg, 1.46 mmol), dichloromethane (15 mL), sodium bicarbonate (307 mg, 3.65 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 674 mg, 2.93 mmol); then 1:1 diethyl ether/dichloromethane (30 mL), boron trifluoride diethyl etherate (0.29 mL, 2.34 mmol). Purification *via* recrystallization from petrol 40-60/ethyl acetate afforded the title compound **RJA49** as a white solid (163 mg, 29 %).

Melting point: 173-175 °C (petrol 40-60/ethyl acetate);

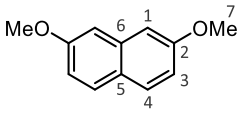
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 9.81 (d, *J* = 1.4 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.24 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.21 (d, *J* = 9.1 Hz, 1H), 7.19 (td, *J* = 7.5, 1.1 Hz, 1H), 7.15-7.03 (m, 3H), 7.00 (ddd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 3.80 (s, 3H), 3.28-3.08 (m, 3H), 2.43-2.31 (m, 1H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 191.0, 154.1, 147.6, 141.3, 132.4, 131.8, 130.7, 130.5, 130.1, 129.2, 126.0, 125.2, 123.7, 123.4, 123.4, 120.6, 115.4, 67.7, 57.7, 32.7, 31.7;

FTIR (neat) $\nu$/cm$^{-1}$ = 2942, 2839, 1713, 1621, 1597, 1562, 1511, 1447, 1270, 1253, 1098;

HRMS (ESI$^+$) calculated for $C_{21}H_{17}O_2BrNa^+$ = 403.0304, mass found = 403.0306.

**2,7-Dimethoxynaphthalene, 215**




**215**

To a solution of 2,7-dihydroxynaphthalene (16.0 g, 100 mmol) in acetone (500 mL) was added $K_2CO_3$ (68.4 g, 400 mmol). Iodomethane (37.4 mL, 600 mmol) was added and the resulting suspension was stirred at reflux for 18 hours. After cooling to room temperature the reaction was quenched with 5 % aqueous ammonia (300 mL) and methanol (50 mL), and stirred for a further 2 hours at room temperature. The majority of the acetone was removed under reduced pressure. Dichloromethane was added and the organic phase was then separated. The aqueous phase was extracted twice with dichloromethane and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* recrystallization from hexane/ethyl acetate afforded the title compound **215** as a white solid (12.9 g, 69 %). The spectral data matched that previously reported in the literature.[147]

Melting point: 132-133 °C (ethyl acetate/hexane);

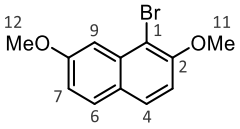
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.67 (d, *J* = 8.8 Hz, 2H, $H_4$), 7.07 (d, *J* = 2.5 Hz, 2H, $H_1$), 7.01 (dd, *J* = 8.9, 2.5 Hz, 2H, $H_3$), 3.92 (s, 6H, $H_7$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.3 (Quat, $C_2$), 136.0 (Quat, $C_6$), 129.3 (CH, $C_4$), 124.4 (Quat, $C_5$), 116.1 (CH, $C_3$), 105.4 (CH, $C_1$), 55.4 ($CH_3$, $C_7$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3059, 3010, 2934, 1626, 1606, 1562, 1512, 1334, 1212, 1166;

LRMS ($ESI^+$): calculated for $C_{12}H_{13}O_2^+$ = 189, mass found = 189.

**1-Bromo-2,7-dimethoxynaphthalene, 216**




**216**

According to a modified literature procedure,[148] a stirred solution of **215** (5.65 g, 30 mmol) in chloroform (75 mL) was cooled to 0 °C. A solution of bromine (1.54 mL, 30 mmol) in chloroform (25 mL) was then added dropwise over a period of one hour. After warming to room temperature the reaction was quenched with saturated aqueous sodium thiosulfate. The organic layer was separated and the aqueous layer was extracted twice with chloroform. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* recrystallization from hexane/ethyl acetate afforded the title compound **216** as a white solid (2.81 g, 35 %).

Melting point: 72-74 °C (ethyl acetate/hexane);

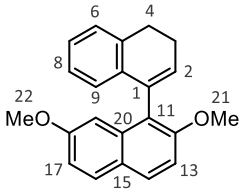
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.73 (d, *J* = 8.9 Hz, 1H, $H_4$), 7.67 (d, *J* = 8.9 Hz, 1H $H_6$), 7.50 (d, *J* = 2.5 Hz, 1H $H_9$), 7.11 (d, *J* = 8.9 Hz, 1H $H_3$), 7.04 (dd, *J* = 8.9, 2.5 Hz, 1H $H_7$), 4.02 (s, 3H, $H_{11}$ or $H_{12}$), 3.97 (s, 3H, $H_{11}$ or $H_{12}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 159.5 (Quat, $C_8$), 154.4 (Quat, $C_2$), 134.7 (Quat, $C_{10}$), 129.9 (CH, $C_6$), 128.7 (CH, $C_4$), 125.3 (Quat, $C_5$), 117.4 (CH, $C_7$), 110.9 (CH, $C_3$), 107.6 (Quat, $C_1$), 104.5 (CH, $C_9$), 57.0 ($CH_3$, $C_{11}$ or $C_{12}$), 55.5 ($CH_3$, $C_{11}$ or $C_{12}$);

FTIR (neat) $\nu/cm^{-1}$ = 3002, 2960, 2840, 1627, 1604, 1510, 1462, 1461, 1317, 1245, 1128;

HRMS ($Cl^+$): calculated for $C_{12}H_{12}BrO_2^+$ = 267.0015, mass found = 267.0012.

**2',7'-Dimethoxy-3,4-dihydro-1,1'-binaphthalene, 230**




**230**

Magnesium turnings (256 mg, 10.5 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of **216** (1.87 g, 7 mmol) in THF (15 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 3 hours. The resulting Grignard reagent was then used immediately according to **General Procedure A** with 1-tetralone (1.12 mL, 8.40 mmol), anhydrous cerium chloride (2.47 g, 16.8 mmol), THF (80 mL) and 3M HCl (80 mL). Purification *via* column chromatography eluting with a gradient from 3:17 dichloromethane/petrol 30-40 to 1:4 dichloromethane/petrol 30-40 afforded the title compound **230** as a colourless gum (1.12 g, 51 %).

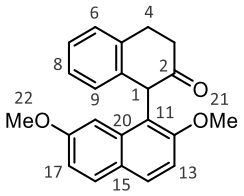
$^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.72 (d, *J* = 8.8 Hz, 1H, $H_{16}$), 7.24-7.19 (m, 2H, $H_6$ and $H_{13}$), 7.12 (td, *J* = 7.4, 1.4 Hz, 1H, $H_7$), 7.04 (d, *J* = 2.6 Hz, 1H, $H_{19}$), 7.01 (dd, *J* = 8.8, 2.5 Hz, 1H, $H_{17}$), 6.96 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.56 (dd, *J* = 7.6, 1.2 Hz, 1H, $H_9$), 6.07 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.83 (s, 3H, $H_{21}$ or $H_{22}$), 3.72 (s, 3H, $H_{21}$ or $H_{22}$), 3.11-2.94 (m, 2H, $H_4$), 2.63-2.54 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.1 (Quat, $C_{12}$ or $C_{18}$), 155.1 (Quat, $C_{12}$ or $C_{18}$), 136.0 (Quat, $C_{Ar}$), 135.5 (Quat, $C_{Ar}$), 135.3 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 129.8 (CH, $C_2$), 129.5 (CH, $C_{16}$), 128.7 (CH, $C_{14}$), 127.5 (CH, $C_6$), 126.9 (CH, $C_7$), 126.5 (CH, $C_8$), 124.8 (Quat, $C_{11}$), 124.7 (CH, $C_9$), 122.6 (Quat, $C_{15}$), 116.2 (CH, $C_{17}$), 111.4 (CH, $C_{13}$), 103.9 (CH, $C_{19}$), 56.9 ($CH_3$, $C_{21}$ or $C_{22}$), 55.2 ($CH_3$, $C_{21}$ or $C_{22}$), 28.4 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 3013, 2934, 2832, 1624, 1600, 1510, 1462, 1354, 1220, 1055;

HRMS (ESI$^+$): calculated for $C_{22}H_{21}O_2^+$ = 317.1536, mass found = 317.1536.

**2',7'-Dimethoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 247**




**247**

According to **General Procedure B** with **230** (1.10 g, 3.48 mmol), dichloromethane (35 mL), sodium bicarbonate (731 mg, 8.70 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.60 g, 6.96 mmol); then 1:1 diethyl ether/dichloromethane (70 mL), boron trifluoride diethyl etherate (0.69 mL, 5.6 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **247** as a white solid (353 mg, 30 %).

Melting point: 156-158 °C (ethyl acetate/hexane);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.74 (d, *J* = 8.9 Hz, 1H, $H_{16}$), 7.30 (d, *J* = 7.4 Hz, 1H, $H_6$), 7.21-7.12 (m, 2H, $H_7$ and $H_{13}$), 7.05-6.96 (m, 2H, $H_8$ and $H_{17}$), 6.81 (s, 1H, $H_{19}$),

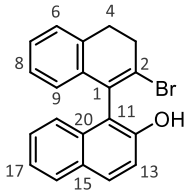
6.61 (d, $J$ = 7.7 Hz, 1H, $H_9$), 5.48 (s, 1H, $H_1$), 3.75 (s, 3H, $H_{21}$ or $H_{22}$), 3.72 (s, 3H, $H_{21}$ or $H_{22}$), 3.37-3.22 (m, 2H, $H_4$), 2.97 (dt, $J$ = 16.0, 5.5 Hz, 1H, $H_{3B}$), 2.82 (ddd, $J$ = 16.0, 9.9, 6.0 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.6 (Quat, $C_2$), 158.6 (Quat, $C_{12}$ or $C_{18}$), 155.4 (Quat, $C_{12}$ or $C_{18}$), 137.6 (Quat, $C_{Ar}$), 136.1 (Quat, $C_{Ar}$), 134.7 (Quat, $C_{Ar}$), 130.5 (CH, $C_{16}$), 129.5 (CH, $C_{14}$), 127.6 (CH, $C_6$ or $C_9$), 127.5 (CH, $C_6$ or $C_9$), 126.9 (CH, $C_8$), 126.4 (CH, $C_7$), 125.3 (Quat, $C_{11}$), 120.5 (Quat, $C_{15}$), 116.2 (CH, $C_{17}$), 111.3 (CH, $C_{13}$), 102.3 (CH, $C_{19}$), 56.4 ($CH_3$, $C_{21}$ or $C_{22}$), 55.2 ($CH_3$, $C_{21}$ or $C_{22}$), 50.5 (CH, $H_1$), 39.0 ($CH_2$, $C_3$), 28.8 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3064, 3002, 2939, 2840, 1712, 1626, 1603, 1579, 1514, 1488, 1387, 1255;

HRMS (ESI$^+$): calculated for $C_{22}H_{21}O_3^+$ = 333.1485, mass found = 333.1482.

**2-Bromo-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, 240**




**240**

In analogy to a modified literature procedure, [149] *N*-bromosuccinimde (196 mg, 1.10 mmol) was added to a stirred solution of **236** (272 mg, 1.00 mmol) in DMF (2 mL). After stirring at room temperature for 24 hours the mixture was quenched with saturated aqueous sodium thiosulfate and the majority of the DMF was removed under reduced pressure. Ethyl acetate was added and the aqueous layer separated. The organic layer was then washed with $H_2O$ three times, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 **240** as a white solid (334 mg, 95 %).

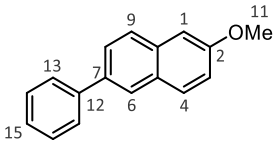
Melting point: dec >50 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.87 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.86-7.83 (m, 1H, $H_{16}$), 7.50-7.45 (m, 1H, $H_{19}$), 7.41-7.32 (m, 2H, $H_{17}$ and $H_{18}$), 7.30 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.23 (dd, *J* = 7.5, 1.4 Hz, 1H, $H_6$), 7.18 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.96 (td, *J* = 7.5, 1.4 Hz, 1H, $H_8$), 6.53 (dd, *J* = 7.8, 1.2 Hz, 1H, $H_9$), 5.15 (s, 1H, O*H*), 3.37-3.05 (m, 4H, $H_3$ and $H_4$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 150.3 (Quat, $C_{12}$), 134.0 (Quat, $C_{Ar}$), 133.9 (Quat, $C_{Ar}$), 132.2 (Quat, $C_{Ar}$), 131.7 (Quat, $C_{Ar}$), 130.2 (CH, $C_{14}$), 129.2 (Quat, $C_{Ar}$), 129.2 (Quat, $C_{Ar}$), 128.4 (CH, $C_{16}$), 128.1 (CH, $C_7$), 127.8 (CH, $C_6$), 127.3 (CH, $C_8$), 127.0 (CH, $C_{17}$ or $C_{18}$), 125.6 (CH, $C_9$), 124.3 (CH, $C_{19}$), 123.7 (CH, $C_{17}$ or $C_{18}$), 118.2 (Quat, $C_2$), 117.6 (CH, $C_{13}$), 35.3 ($CH_2$, $C_4$), 29.6 ($CH_2$, $C_3$);

HRMS ($ESI^+$): calculated for $C_{20}H_{16}BrO^+$ = 351.0379, mass found = 351.0380.

**2-Methoxy-6-phenylnaphthalene, 210**




**210**

By analogy to a modified literature procedure,[144] degassed 2 M aqueous $Na_2CO_3$ (42 mL, 83 mmol) was added to a suspension of 6-bromo-2-methoxynaphthalene (3.80 g, 16.0 mmol), phenylboronic acid (3.90 g, 32.0 mmol) and $Pd(PPh_3)_4$ (925 mg, 0.8 mmol) in degassed 1,2-dimethoxyethane (160 mL). The reaction mixture was then stirred at reflux for 18 hours. After cooling to room temperature, the reaction was quenched with saturated aqueous ammonium chloride and the majority of 1,2-dimethoxyethane was removed under reduced pressure. Ethyl acetate was added and the aqueous layer was separated. The organic layer was washed with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification *via* column chromatography eluting with 1:3 dichloromethane/petrol 40-60 afforded the title compound

**210** as a white solid (3.34 g, 89 %). The spectral data matched that previously reported in the literature.[150]

Melting point: 144-145 °C (dichloromethane/petrol 40-60);

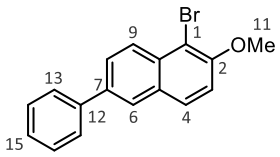
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.00 (d, *J* = 1.8 Hz, 1H, $H_6$), 7.83 (d, *J* = 5.4 Hz, 1H, $H_9$), 7.81 (d, *J* = 5.6 Hz, 1H, $H_4$), 7.77-7.71 (m, 3H, $H_8$ and $H_{13}$), 7.53-7.47 (m, 2H, $H_{14}$), 7.41-7.36 (m, 1H, $H_{15}$), 7.23-7.17 (m, 2H, $H_1$ and $H_3$), 3.96 (s, 3H, $H_{11}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 157.9 (Quat, $C_2$), 141.3 (Quat, $C_{12}$), 136.5 (Quat, $C_{Ar}$), 133.9 (Quat, $C_{Ar}$), 129.8 (CH, $C_4$), 129.3 (Quat, $C_5$), 128.9 (CH, $C_{14}$), 127.4 (CH, $C_9$), 127.3 (CH, $C_{13}$), 127.2 (CH, $C_{15}$), 126.2 (CH, $C_8$), 125.7 (CH, $C_6$), 119.3 (CH, $C_3$), 105.7 (CH, $C_1$), 55.5 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3056, 3005, 2959, 2904, 1625, 1603, 1497, 1451, 1407, 1276, 1249, 1206, 1165, 1031;

LRMS (ESI$^+$): calculated for $C_{34}H_{29}O_2^+$ = 469, mass found = 469.

**1-Bromo-2-methoxy-6-phenylnaphthalene, 212**




**212**

By analogy to a modified literature procedure,[148] a suspension of **210** (3.29 g, 14 mmol) in acetonitrile (70 mL) was stirred at reflux for 10 minutes. *N*-bromosuccinimide (2.74 g, 15.4 mmol) was added and the mixture was stirred at reflux for 15 minutes. After cooling to room temperature, the mixture was filtered and the precipitate washed with acetonitrile. After drying the precipitate under reduced pressure for 4 hours (*c.a.* 0.1 mbar) the title compound **212** was afforded as a white solid (3.92 g, 89 %). The spectral data matched that previously reported in the literature.[151]

Melting point: 166-168 °C (acetonitrile);

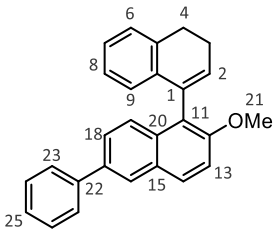
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.29 (d, *J* = 8.9 Hz, 1H, $H_9$), 7.99 (d, *J* = 1.8 Hz, 1H, $H_6$), 7.87 (d, *J* = 9.1 Hz, 1H, $H_4$), 7.84 (dd, *J* = 9.0, 2.0 Hz, 1H, $H_8$), 7.75-7.68 (m, 2H, $H_{13}$), 7.53-7.46 (m, 2H, $H_{14}$), 7.42-7.36 (m, 1H, $H_{15}$), 7.30 (d, *J* = 9.0 Hz, 1H, $H_3$), 4.05 (s, 3H, $H_{11}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.9 (Quat, $C_2$), 140.6 (Quat, $C_{12}$), 137.2 (Quat, $C_{Ar}$), 132.5 (Quat, $C_{Ar}$), 130.2 (Quat, $C_{Ar}$), 129.4 (CH, $C_4$), 129.0 (CH, $C_{14}$), 127.5 (CH, $C_8$ or $C_{15}$), 127.5 (CH, $C_8$ or $C_{15}$), 127.4 (CH, $C_{13}$), 126.9 (CH, $C_9$), 125.9 (CH, $C_6$), 114.1 (CH, $C_1$), 108.7 (CH, $C_3$), 57.2 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 2975, 2846, 1624, 1595, 1492, 1439, 1336, 1250, 1040;

HRMS ($CI^+$): calculated for $C_{17}H_{14}BrO^+$ = 313.0223, mass found = 313.0223.

**2'-Methoxy-6'-phenyl-3,4-dihydro-1,1'-binaphthalene, 231**




**231**

Magnesium turnings (365 mg, 15.0 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of **212** (3.13 g, 10.0 mmol) in THF (20 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 3 hours. The resulting Grignard reagent was then used immediately according to **General Procedure A** with 1-tetralone (1.6 mL, 12 mmol), anhydrous cerium chloride (5.92 g, 24.0 mmol), THF (75 mL) and 3M HCl (75 mL). Purification *via* column chromatography eluting with a gradient from 1:4 dichloromethane/petrol 40-60 to 1:2

dichloromethane/petrol 40-60 afforded the title compound **231** as an off white solid (2.62 g, 72 %).

Melting point: 156-157 °C (dichloromethane/petrol 40-60);

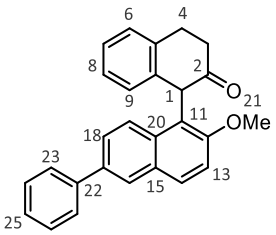
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.04 (d, *J* = 1.9 Hz, 1H, $H_{16}$), 7.95 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.83 (d, *J* = 8.8 Hz, 1H, $H_{19}$), 7.74-7.68 (m, 2H, $H_{23}$), 7.63 (dd, *J* = 8.8, 2.0 Hz, 1H, $H_{18}$), 7.52-7.45 (m, 2H, $H_{24}$), 7.41 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.39-7.34 (m, 1H, $H_{25}$), 7.28-7.23 (m, 1H, $H_6$), 7.14 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.98 (td, *J* = 7.6, 1.4 Hz, 1H, $H_8$), 6.56 (dd, *J* = 7.6, 1.3 Hz, 1H, $H_9$), 6.09 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.87 (s, 3H, $H_{21}$), 3.07 (t, *J* = 8.1 Hz, 2H, $H_4$), 2.62 (ddd, *J* = 9.5, 7.2, 4.5 Hz, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.6 (Quat, $C_{12}$), 141.3 (Quat, $C_{22}$), 136.4 (Quat, $C_{Ar}$), 135.9 (Quat, $C_{Ar}$), 135.6 (Quat, $C_{Ar}$), 133.7 (Quat, $C_{Ar}$), 133.2 (Quat, $C_{Ar}$), 130.1 (CH, $C_2$), 129.5 (Quat, $C_{15}$), 129.4 (Quat, $C_{14}$), 128.9 (CH, $C_{23}$), 127.6 (CH, $C_6$), 127.3 (CH, $C_{24}$), 127.2 (CH, $C_{25}$), 127.0 (CH, $C_7$), 126.6 (CH, $C_8$), 126.1 (CH, $C_{18}$ or $C_{19}$), 126.1 (CH, $C_{18}$ or $C_{19}$), 125.9 (CH, $C_{16}$), 124.7 (CH, $C_9$), 123.6 (Quat, $C_{11}$), 114.5 (CH, $C_{13}$), 57.1 ($CH_3$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 3025, 2934, 2883, 2835, 1623, 1593, 1492, 1461, 1427, 1255, 1176, 1089;

HRMS ($CI^+$): calculated for $C_{27}H_{23}O^+$ = 363.1743, mass found = 363.1743.

**2'-Methoxy-6'-phenyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 248**




**248**

According to **General Procedure B** with **231** (2.52 g, 6.95 mmol), dichloromethane (70 mL), sodium bicarbonate (1.46 g, 17.4 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 3.20 g, 13.9 mmol); then 1:1 diethyl ether/dichloromethane (140 mL), boron trifluoride diethyl etherate (1.37 mL, 11.1 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **248** as a white solid (1.37 g, 52 %).

Melting point: 168-169 °C (ethyl acetate/hexane);

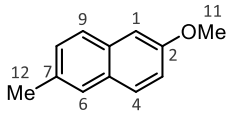
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.06 (d, *J* = 1.8 Hz, 1H, $H_{16}$), 7.95 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.73-7.69 (m, 2H, $H_{23}$), 7.67 (dd, *J* = 8.9, 1.9 Hz, 1H, $H_{18}$), 7.62 (d, *J* = 8.6 Hz, 1H, $H_{19}$), 7.48 (dd, *J* = 8.4, 6.9 Hz, 2H, $H_{24}$), 7.41-7.34 (m, 2H, $H_{13}$ and $H_{25}$), 7.32 (d, *J* = 7.5 Hz, 1H, $H_6$), 7.19 (tt, *J* = 7.5, 1.1 Hz, 1H, $H_7$), 7.01 (td, *J* = 7.7, 1.3 Hz, 1H, $H_8$), 6.61 (d, *J* = 7.8 Hz, 1H, $H_9$), 5.59 (s, 1H, $H_1$), 3.79 (s, 3H, $H_{21}$), 3.39-3.24 (m, 2H, $H_4$), 2.98 (dt, *J* = 16.3, 5.4 Hz, 1H, $H_{3B}$), 2.85 (ddd, *J* = 16.3, 10.1, 6.1 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.5 (Quat, $C_2$), 155.0 (Quat, $C_{12}$), 141.0 (Quat, $C_{22}$), 137.6 (Quat, $C_{Ar}$), 136.3 (Quat, $C_{Ar}$), 136.2 (Quat, $C_{Ar}$), 132.6 (Quat, $C_{Ar}$), 130.1 (CH, $C_{14}$), 130.0 (Quat, $C_{Ar}$), 128.9 (CH, $C_{24}$), 127.6 (CH, $C_6$), 127.4 (CH, $C_9$), 127.3 (CH, $C_{23}$), 127.3 (CH, $C_{25}$), 126.9 (CH, $C_8$), 126.7 (CH, $C_{16}$), 126.6 (CH, $C_7$), 126.5 (CH, $C_{18}$), 124.3 (CH, $C_{19}$), 121.2 (Quat, $C_{11}$), 114.3 (CH, $C_{13}$), 56.6 ($CH_3$, $C_{21}$), 50.5 (CH, $C_1$), 38.8 ($CH_2$, $C_3$), 28.7 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3026, 2904, 2841, 1714, 1625, 1596, 1494, 1456, 1410, 1255, 1084;

HRMS (ESI$^+$): calculated for $C_{27}H_{23}O_2^+$ = 379.1693, mass found = 379.1687.

**2-Methoxy-6-methylnaphthalene, 211**




**211**

By analogy to a modified literature procedure,[144] degassed 2 M aqueous $Na_2CO_3$ (104 mL, 208 mmol) was added to a suspension of 6-bromo-2-methoxynaphthalene (9.5 g, 40.0 mmol), methylboronic acid (4.8 g, 80.0 mmol) and $Pd(PPh_3)_4$ (1.15, 1.00 mmol) in degassed 1,2-dimethoxyethane (400 mL). The reaction mixture was then stirred at reflux for 18 h. After cooling to room temperature, the reaction was quenched with saturated aqueous ammonium chloride and the majority of 1,2-dimethoxyethane was removed under reduced pressure. Ethyl acetate was added and the aqueous layer was separated. The organic layer was washed with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:19 dichloromethane/petrol 40-60 to 1:9 dichloromethane/petrol 40-60 afforded the title compound **211** as a white solid (5.42 g, 79 %). The spectral data matched that previously reported in the literature.[152]

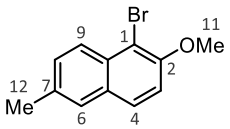
Melting point: 78-79 °C (dichloromethane/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.67 (d, *J* = 8.5 Hz, 1H, $H_4$), 7.66 (d, *J* = 8.2 Hz, 1H, $H_9$), 7.57-7.54 (m, 1H, $H_6$), 7.30 (dd, *J* = 8.4, 1.8 Hz, 1H, $H_8$), 7.17-7.10 (m, 2H, $H_1$ and $H_3$), 3.92 (s, 3H, $H_{11}$), 2.50 (s, 3H, $H_{12}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 157.1 (Quat, $C_2$), 133.1 (Quat, $C_7$ or $C_{10}$), 132.8 (Quat, $C_7$ or $C_{10}$), 129.3 (Quat, $C_5$), 128.8 (CH, $C_4$), 128.7 (CH, $C_8$), 126.8 (CH, $C_6$), 126.7 (CH, $C_9$), 118.7 (CH, $C_3$), 105.8 (CH, $C_1$), 55.4 ($CH_3$, $C_{11}$), 21.6 ($CH_3$, $C_{12}$);

FTIR (neat) $\nu$/cm$^{-1}$ =3054, 3004, 2941, 1632, 1606, 1504, 1483, 1390, 1338, 1229, 1175, 1119;

**1-Bromo-2-methoxy-6-methylnaphthalene, 213**




**213**

By analogy to a modified literature procedure,[148] *N*-bromosuccinimde (3.39 g, 21.7 mmol) was added to a stirred solution of **211** (3.39 g, 19.7 mmol) in acetonitrile (100 mL). After stirring at room temperature for 2 hours the mixture was quenched with saturated aqueous sodium thiosulfate and the majority of the acetonitrile was removed under reduced pressure. Ethyl acetate was added and the aqueous layer separated. The organic layer was then washed with $H_2O$ three times, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 and subsequent recrystallization from hexane afforded the title compound **213** as a white solid (3.52 g, 71 %).

Melting point: 58-59 °C (hexane);

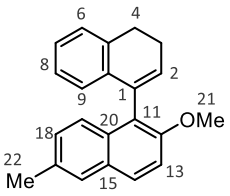
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.11 (d, *J* = 8.7 Hz, 1H, $H_9$), 7.72 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.55 (s, 1H, $H_6$), 7.40 (dd, *J* = 8.7, 1.7 Hz, 1H, $H_8$), 7.24 (d, *J* = 9.0 Hz, 1H, $H_3$), 4.02 (s, 3H, $H_{11}$), 2.50 (s, 3H, $H_{12}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.2 (Quat, $C_2$), 134.0 (Quat, $C_7$ or $C_{10}$), 131.5 (Quat, $C_7$ or $C_{10}$), 130.2 (CH and Quat, $C_5$ and $C_8$), 128.3 (CH, $C_4$), 127.0 (CH, $C_6$), 126.1 (CH, $C_9$), 113.8 (CH, $C_3$), 108.8 (Quat, $C_1$), 57.2 ($CH_3$, $C_{11}$), 21.4 ($CH_3$, $C_{12}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3004, 2965, 2916, 2841, 1603, 1558, 1498, 1461, 1379, 1268, 1251, 1141, 1068;

HRMS ($CI^+$): calculated for $C_{12}H_{11}BrONH_4^+$ = 268.0332, mass found = 268.0328.

**2'-Methoxy-6'-methyl-3,4-dihydro-1,1'-binaphthalene, 232**




**232**

Magnesium turnings (365 mg, 15.0 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of **213** (2.51 g, 10.0 mmol) in THF (20 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 2 hours. The resulting Grignard reagent was then used immediately according to **General Procedure A** with 1-tetralone (1.6 mL, 12 mmol), anhydrous cerium chloride (5.92 g, 24.0 mmol), THF (75 mL) and 3M HCl (75 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:3 dichloromethane/petrol 40-60 afforded the title compound **232** as a colourless gum (2.62 g, 72 %).

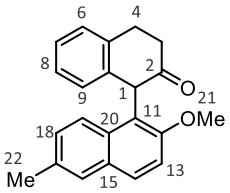
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.66 (d, *J* = 8.7 Hz, 1H, $H_{19}$), 7.61 (s, 1H, $H_{16}$), 7.35 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.25-7.22 (m, 1H, $H_6$), 7.20 (dd, *J* = 8.7, 1.8 Hz, 1H, $H_{18}$), 7.12 (td, *J* = 7.4, 1.3 Hz, 1H, $H_7$), 6.96 (td, *J* = 7.6, 1.4 Hz, 1H, $H_8$), 6.52 (dd, *J* = 7.7, 1.2 Hz, 1H, $H_9$), 6.05 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.83 (s, 3H, $H_{21}$), 3.08-3.02 (m, 2H, $H_4$), 2.60 (ddd, *J* = 9.3, 7.2, 4.5 Hz, 2H, $H_3$), 2.48 (s, 3H, $H_{22}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.9 (Quat, $C_{12}$), 135.9 (Quat, $C_{Ar}$), 135.7 (Quat, $C_{Ar}$), 133.8 (Quat, $C_{Ar}$), 133.1 (Quat, $C_{Ar}$), 132.2 (Quat, $C_{Ar}$), 129.8 (CH, $C_2$), 129.5 (Quat, $C_{15}$), 128.7 (CH, $C_{18}$), 128.3 (CH, $C_{14}$), 127.5 (CH, $C_6$), 126.9 (CH, $C_7$ and $C_{16}$), 126.5 (CH, $C_8$), 125.3 (CH, $C_{19}$), 124.7 (CH, $C_9$), 123.7 (Quat, $C_{11}$), 114.3 (CH, $C_{13}$), 57.2 ($CH_3$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$), 21.5 ($CH_3$, $C_{22}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3021, 2933, 2833, 1595, 1502, 1482, 1461, 1369, 1271, 1254, 1191;

HRMS (ESI$^+$): calculated for $C_{22}H_{21}O^+$ = 301.1587, mass found = 301.1587.

**2'-Methoxy-6'-methyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 249**




**249**

According to **General Procedure B** with **232** (2.31 g, 7.69 mmol), dichloromethane (80 mL), sodium bicarbonate (1.62 g, 19.2 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 3.54 g, 15.4 mmol); then 1:1 diethyl ether/dichloromethane (160mL), boron trifluoride diethyl etherate (1.52 mL, 12.3 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **249** as a white solid (1.02 g, 42 %).

Melting point: 148-149 °C (ethyl acetate/hexane);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.80 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.63 (s, 1H, $H_{16}$), 7.45 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.32-7.27 (m, 2H, $H_6$ and $H_{13}$), 7.23 (dd, *J* = 8.7, 1.8 Hz, 1H, $H_{18}$), 7.17 (tt, *J* = 7.4, 1.1 Hz, 1H, $H_7$), 6.98 (td, *J* = 7.6, 1.3 Hz, 1H, $H_8$), 6.55 (d, *J* = 7.8 Hz, 1H, $H_9$), 5.53 (s, 1H, $H_1$), 3.75 (s, 3H, $H_{21}$), 3.37-3.21 (m, 2H, $H_4$), 2.95 (dt, *J* = 16.2, 5.3 Hz, 1H, $H_{3B}$), 2.83 (ddd, *J* = 16.3, 10.2, 6.1 Hz, 1H, $H_{3A}$), 2.47 (s, 3H, $H_{22}$);

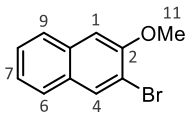
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.7 (Quat, $C_2$), 154.2 (Quat, $C_{12}$), 137.7 (Quat, $C_{Ar}$), 136.2 (Quat, $C_{Ar}$), 133.0 (Quat, $C_{Ar}$), 131.6 (Quat, $C_{20}$), 130.0 (Quat, $C_{15}$), 129.2 (CH, $C_{18}$), 129.0 (CH, $C_{14}$), 127.8,

127.6 (CH, $C_{16}$), 127.4 (CH, $C_6$), 126.8 (CH, $C_9$), 126.4 (CH, $C_8$), 123.6 (CH, $C_7$), 121.3 (CH, $C_{19}$), 114.1 (Quat, $C_{11}$), 56.6 ($CH_3$, $C_{21}$), 50.4 (CH, $C_1$), 38.8 ($CH_2$, $C_3$), 28.7 ($CH_2$, $C_4$), 21.4 ($CH_3$, $C_{22}$);

FTIR (neat) $\nu/cm^{-1}$ = 3065, 3022, 2940, 2916, 2841, 1714, 1601, 1508, 1484, 1455, 1408, 1255, 1158, 1082;

HRMS ($ESI^+$): calculated for $C_{22}H_{20}ONa^+$ = 339.1356, mass found = 339.1352.

**2-Bromo-3-methoxynaphthalene, 206**




**206**

According to a modified literature procedure,[88] *n*-butyllithium (2.5 M solution in hexanes, 19.6 mL, 49.0 mmol) was added dropwise *via* syringe pump over 30 min to a solution of 2-methoxynaphthalene (7.00 g, 44.0 mmol) in THF (60 mL) at room temperature. After cooling to -78 °C, 1,2-dibromoethane (5.7 mL, 66 mmol) was added dropwise *via* syringe pump over one hour. Following this, the reaction mixture was allowed to warm to room temperature overnight. Aqueous sodium hydroxide (1.0 M, 50 mL) was added and the biphasic mixture was subsequently stirred at reflux for one hour. After removing the majority of THF under reduced pressure, the mixture was extracted three times with dichloromethane and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* recrystallization from hexane afforded the title compound **206** as a white solid (6.70 g, 64 %). The spectral data matched that previously reported in the literature.[88]

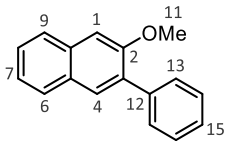
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.06 (s, 1H, $H_4$), 7.73 (d, *J* = 8.3 Hz, 1H, $H_9$), 7.69 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.46 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H, $H_8$), 7.37 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H, $H_7$), 7.16 (s, 1H, $H_1$), 4.00 (s, 3H, $H_{11}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.6 (Quat, $C_2$), 133.6 (Quat, $C_{10}$), 132.4 (CH, $C_4$), 129.5 (Quat, $C_5$), 126.8 (CH, $C_8$), 126.8 (CH, $C_6$), 126.7 (CH, $C_9$), 124.6 (CH, $C_7$), 113.4 (Quat, $C_3$), 106.7 (CH, $C_1$), 56.3 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3055, 3008, 2970, 2943, 2836, 1620, 1587, 1466, 1429, 1382, 1324, 1270, 1249, 1193, 1148, 1041, 1020;

HRMS ($CI^+$): calculated for $C_{11}H_9BrONH_4^+$ = 254.0175, mass found = 254.0171.

**2-Methoxy-3-phenylnaphthalene, 207**




**207**

By analogy to a modified literature procedure,[144] degassed 2 M aqueous $Na_2CO_3$ (39 mL, 78 mmol) was added to a suspension of **206** (3.56 g, 237.1 mmol), phenylboronic acid (3.66 g, 30.0 mmol) and $Pd(PPh_3)_4$ (347 mg, 0.300 mmol) in degassed 1,2-dimethoxyethane (150 mL). The reaction mixture was then stirred at reflux for 18 h. After cooling to room temperature, the reaction was quenched with saturated aqueous ammonium chloride and the majority of 1,2-dimethoxyethane was removed under reduced pressure. Ethyl acetate was added and the aqueous layer was separated. The organic layer was washed with saturated aqueous sodium bicarbonate and brine and then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:19 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 afforded the title compound **207** as a colourless oil (3.19 g, 91 %).

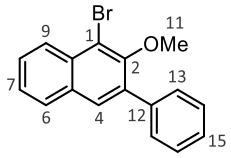
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.86-7.78 (m, 3H, $H_4$, $H_6$ and $H_9$), 7.69-7.63 (m, 2H, $H_{13}$), 7.53-7.47 (m, 3H, $H_8$ and $H_{14}$), 7.45-7.37 (m, 2H, $H_7$ and $H_{15}$), 7.27 (s, 1H, $H_1$), 3.96 (s, 3H, $H_{11}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.4 (Quat, $C_2$), 138.5 (Quat, $C_{12}$), 134.1 (Quat, $C_{10}$), 132.5 (Quat, $C_5$), 130.1 (CH, $C_4$), 129.9 (CH, $C_{13}$), 129.0 (Quat, $C_3$), 128.1 (CH, $C_{14}$), 127.8 (CH, $C_6$), 127.3 (CH, $C_{15}$), 126.5 (CH, $C_8$ or $C_9$), 126.5 (CH, $C_8$ or $C_9$), 124.0 (CH, $C_7$), 105.8 (CH, $C_1$), 55.7 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu/cm^{-1}$ = 3057, 3013, 2941, 2882, 2832, 1636, 1591, 1528, 1483, 1450, 1348, 1221, 1182, 1159, 1016;

HRMS ($CI^+$): calculated for $C_{17}H_{14}O^+$ = = 235.1123, mass found = 235.1117.

**1-Bromo-2-methoxy-3-phenylnaphthalene, 208**




**208**

By analogy to a modified literature procedure,[148] *N*-bromosuccinimde (2.62 g, 14.7 mmol) was added to a stirred solution of **207** (3.13 g, 13.4 mmol) in acetonitrile (70 mL). After stirring at room temperature for 2 hours the mixture was quenched with saturated aqueous sodium thiosulfate and the majority of the acetonitrile was removed under reduced pressure. Ethyl acetate was added and the aqueous layer separated. The organic layer was then washed with $H_2O$ three times, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:19 dichloromethane/petrol 40-60 to 1:4 dichloromethane/petrol 40-60 and subsequent recrystallization from hexane afforded the title compound **208** as a white solid (3.05 g, 73 %).

Melting point: 83-85 °C (hexane);

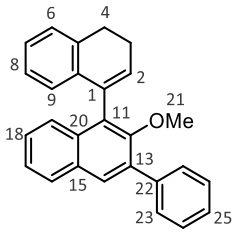
$^1H$ NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.27 (d, *J* = 8.6 Hz, 1H, $H_9$), 7.83 (ddt, *J* = 8.1, 1.2, 0.6 Hz, 1H, $H_6$), 7.81 (s, 1H, $H_4$), 7.71-7.66 (m, 2H, $H_{13}$), 7.60 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H, $H_8$), 7.52-7.45 (m, 3H, $H_7$ and $H_{14}$), 7.45-7.38 (m, 1H, $H_{15}$), 3.53 (s, 3H, $H_{11}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.3 (Quat, $C_2$), 138.0 (Quat, $C_{Ar}$), 135.7 (Quat, $C_{Ar}$), 132.5 (Quat, $C_{Ar}$), 131.6 (Quat, $C_{Ar}$), 129.9 (CH, $C_4$), 129.4 (CH, $C_{13}$), 128.5 (CH, $C_{14}$), 128.3 (CH, $C_6$), 127.8 (CH, $C_{15}$), 127.6 (CH, $C_8$), 126.9 (CH, $C_9$), 126.0 (CH, $C_7$), 116.5 (Quat, $C_1$), 60.6 ($CH_3$, $C_{11}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3055, 2934, 2874, 2835, 1622, 1592, 1557, 1487, 1443, 1409, 1352, 1267, 1214, 1202, 1150, 1040, 1018, 1001;

HRMS ($CI^+$): calculated for $C_{17}H_{13}BrO^+$ = 313.0223, mass found = 313.0222.

**2'-Methoxy-3'-phenyl-3,4-dihydro-1,1'-binaphthalene, 233**




**233**

Magnesium turnings (162 mg, 6.66 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (4 mL) followed by a solution of **208** (1.39 g, 4.44 mmol) in THF (8 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 3 hours. The resulting Grignard reagent was then used immediately according to **General Procedure A** with 1-tetralone (709 µL, 5.33 mmol), anhydrous cerium chloride (2.64 g, 10.7 mmol), THF (33 mL) and 3M HCl (45 mL). Purification *via* column chromatography eluting with a gradient from 1:9 dichloromethane/petrol 40-60 to 1:3 dichloromethane/petrol 40-60 afforded the title compound **233** as a white solid (486 mg, 29 %).

Melting point: 140-141 °C (dichloromethane/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.89 (s, 1H, $H_{14}$), 7.88 (d, *J* = 7.9 Hz, 1H, $H_{16}$), 7.80-7.72 (m, 3H, $H_{19}$ and $H_{23}$), 7.52-7.35 (m, 5H, $H_{17}$, $H_{18}$, $H_{24}$ and $H_{25}$), 7.28-7.24 (m, 1H, $H_6$), 7.15 (td, *J* = 7.4,

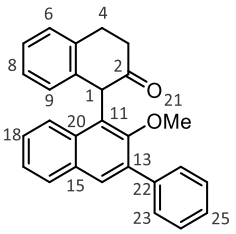
1.3 Hz, 1H, $H_7$), 7.01 (td, *J* = 7.5, 1.4 Hz, 1H, $H_8$), 6.66 (dd, *J* = 7.7, 1.3 Hz, 1H, $H_9$), 6.18 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.33 (s, 3H, $H_{21}$), 3.11-3.03 (m, 2H, $H_4$), 2.67-2.58 (m, 2H, $H_3$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.4 (Quat, $C_{12}$), 138.9 (Quat, $C_{22}$), 135.9 (Quat, $C_{Ar}$), 135.8 (Quat, $C_{Ar}$), 135.2 (Quat, $C_{Ar}$), 133.9 (Quat, $C_{Ar}$), 133.5 (Quat, $C_{Ar}$), 130.9 (Quat, $C_{Ar}$), 130.0 (CH, $C_2$), 129.9 (CH, $C_{14}$), 129.9 (Quat, $C_{Ar}$), 129.5 (CH, $C_{23}$), 128.4 (CH, $C_{24}$), 128.0 (CH, $C_{Ar}$), 127.6 (CH, $C_6$), 127.4 (CH, $C_{Ar}$), 127.1 (CH, $C_7$), 126.6 (CH, $C_8$), 126.3 (CH, $C_{Ar}$), 125.9 (CH, $C_{Ar}$), 125.2 (CH, $C_{Ar}$), 125.1 (CH, $C_9$), 61.1 ($CH_3$, $C_{21}$), 28.3 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3057, 3022, 2931, 2829, 1600, 1495, 1457, 1404, 1386, 1326, 1297, 1213, 1149, 1139, 1076, 1018;

HRMS ($Cl^+$): calculated for $C_{27}H_{22}O^+$ = 363.1743, mass found = 363.1752.

**2'-Methoxy-3'-phenyl-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 250**




**250**

According to **General Procedure B** with **233** (906 mg, 2.39 mmol), dichloromethane (25 mL), sodium bicarbonate (502 mg, 5.98 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.10 g, 4.78 mmol); then 1:1 diethyl ether/dichloromethane (50mL), boron trifluoride diethyl etherate (0.47 mL, 3.8 mmol). Purification *via* column chromatography eluting with a gradient from 10:89:1 ethyl acetate/petrol 40-60/triethylamine to 20:79:1 ethyl acetate/petrol 40-60/triethylamine followed by recrystallization from hexane/ethyl acetate afforded the title compound **250** as a white solid (556 mg, 62 %).

Melting point: 157-159 °C (ethyl acetate/hexane);

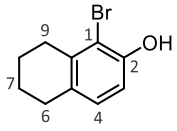
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.91-7.87 (m, 2H, $H_{14}$ and $H_{16}$), 7.74-7.66 (m, 2H, $H_{23}$), 7.52-7.36 (m, 6H, $H_{17}$, $H_{18}$, $H_{19}$, $H_{24}$ and $H_{25}$), 7.34 (d, *J* = 7.6 Hz, 1H, $H_6$), 7.20 (td, *J* = 7.4, 1.2 Hz, 1H, $H_7$), 7.02 (td, *J* = 7.6, 1.4 Hz, 1H, $H_8$), 6.64 (d, *J* = 7.8 Hz, 1H, $H_9$), 5.69 (s, 1H, $H_1$), 3.44-3.25 (m, 2H, $H_4$), 3.10 (s, 3H, $H_{21}$), 3.02 (dt, *J* = 16.4, 5.2 Hz, 1H, $H_{3A}$), 2.86 (ddd, *J* = 16.5, 10.8, 5.9 Hz, 1H, $H_{3B}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 210.3 (Quat, $C_2$), 154.6 (Quat, $C_{12}$), 138.9 (Quat, $C_{22}$), 137.7 (Quat, $C_{Ar}$), 136.0 (Quat, $C_{Ar}$), 134.4 (Quat, $C_{Ar}$), 132.4 (Quat, $C_{Ar}$), 131.4 (Quat, $C_{Ar}$), 131.1 (CH, $C_{14}$), 129.2 (CH, $C_{23}$), 129.0 (CH, $C_{16}$), 128.5 (CH, $C_{24}$), 128.5 (CH, $C_{25}$), 127.8 (CH, $C_6$ or $C_{18}$), 127.7 (CH, $C_9$), 127.5 (CH, $C_6$ or $C_{18}$), 126.9 (CH, $C_8$), 126.6 (CH, $C_{19}$), 126.6 (CH, $C_7$), 124.9 (CH, $C_{17}$), 124.6 (Quat, $C_{11}$), 60.5 ($CH_3$, $C_{21}$), 51.3 ($CH_3$, $C_1$), 38.7 ($CH_2$, $C_3$), 28.7 ($CH_2$, $C_4$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3059, 3025, 2938, 2840, 1714, 1667, 1644, 1600, 1569, 1494, 1444, 1374, 1307, 1247, 1217, 1177, 1152, 1072, 1016.

HRMS ($EI^+$): calculated for $C_{27}H_{22}O_2^+$ = 378.1614, mass found = 378.1607.

**1-Bromo-5,6,7,8-tetrahydronaphthalen-2-ol, 218**




**218**

According to a modified literature procedure,[149] *N*-bromosuccinimde (12.5 g, 70.0 mmol) was added to a stirred solution of 5,6,7,8-tetrahydro-2-naphthol (10.4 g, 70.0 mmol) in DMF (40 mL). After stirring at room temperature for 24 hours the mixture was quenched with saturated aqueous sodium thiosulfate and the majority of the DMF was removed under reduced pressure. Ethyl acetate was added and the aqueous layer separated. The organic layer was then washed with $H_2O$ three times, dried over anhydrous magnesium sulfate, filtered and concentrated under

reduced pressure. Purification of the residue *via* column chromatography eluting with 1:49 ethyl acetate/petrol 40-60 and subsequent recrystallization from hexane afforded the title compound **218** as a white solid (6.41 g, 40 %). The spectral data matched that previously reported in the literature.[149]

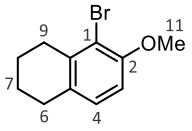
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 6.94 (d, *J* = 8.3 Hz, 1H, $H_4$), 6.82 (d, *J* = 8.3 Hz, 1H, $H_3$), 5.49 (br s, 1H, O*H*), 2.75-2.67 (m, 4H, $H_6$ and $H_9$), 1.86-1.78 (m, 2H, $H_7$ or $H_8$), 1.77-1.69 (m, 2H, $H_7$ or $H_8$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 150.1 (Quat, $C_2$), 136.7 (Quat, $C_{10}$), 131.2 (Quat, $C_5$), 129.3 (CH, $C_4$), 113.6 (Quat, $C_1$), 112.9 (CH, $C_3$), 30.6 ($CH_2$, $C_6$ or $C_9$), 29.4 ($CH_2$, $C_6$ or $C_9$), 23.3 ($CH_2$, $C_7$ or $C_8$), 22.8 ($CH_2$, $C_7$ or $C_8$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3321, 3015, 2928, 2856, 2832, 1601, 1567, 1478, 1356, 1285, 1247, 1228, 1160, 1073, 1009;

LRMS (ESI$^-$): calculated for $C_{10}H_{10}BrO^-$ = 225, mass found = 225.

**5-Bromo-6-methoxy-1,2,3,4-tetrahydronaphthalene, 219**




**219**

To a solution of **218** (6.33 g, 27.9 mmol) in acetone (125 mL) was added $K_2CO_3$ (9.54 g, 55.8 mmol). Iodomethane (5.2 mL, 84 mmol) was added and the resulting suspension was stirred at reflux for 18 h. After cooling to room temperature, the reaction was quenched with 5 % aqueous ammonia (125 mL) and methanol (8mL), and stirred for a further 2 h at room temperature. The majority of the acetone was removed under reduced pressure. Dichloromethane was added and the organic phase was then separated. The aqueous phase was extracted twice with dichloromethane and the combined organic extracts were dried over

anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:49 ethyl acetate/petrol 40-60 afforded the title compound **219** as white solid (6.62 g, 99 %).

Melting point: 36-39 °C (ethyl acetate/petrol 40-60);

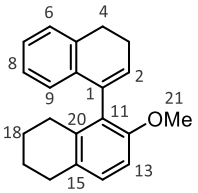
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.00 (d, *J* = 8.4 Hz, 1H, $H_4$), 6.71 (d, *J* = 8.4 Hz, 1H, $H_3$), 3.87 (s, 3H, $H_{11}$), 2.77 (t, *J* = 6.9 Hz, 2H, $H_6$ or $H_9$), 2.73 (t, *J* = 6.4 Hz, 2H, $H_6$ or $H_9$), 1.87-1.77 (m, 2H, $H_7$ or $H_8$), 1.77-1.68 (m, 2H, $H_7$ or $H_8$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.9 (Quat, $C_2$), 138.0 (Quat, $C_{10}$), 131.6 (Quat, $C_5$), 128.5 (CH, $C_4$), 114.8 (Quat, $C_1$), 109.4 (CH, $C_3$), 56.5 ($CH_3$, $C_{11}$), 30.7 ($CH_2$, $C_6$ or $C_9$), 29.6 ($CH_2$, $C_6$ or $C_9$), 23.4 ($CH_2$, $C_7$ or $C_8$), 22.9 ($CH_2$, $C_7$ or $C_8$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3001, 2932, 2857, 2835, 1598, 1561, 1479, 1461, 1438, 1410, 1356, 1319, 1273, 1192, 1162, 1134, 1057;

HRMS (EI$^+$): calculated for $C_{11}H_{13}BrONH_4^+$ = 258.0488, mass found = 258.0489.

**2'-Methoxy-3,4,5',6',7',8'-hexahydro-1,1'-binaphthalene, 234**




**234**

Magnesium turnings (365 mg, 15.0 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of **219** (2.21 g, 10.0 mmol) in THF (20 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 2 hours. The resulting Grignard reagent was then used immediately

according to **General Procedure A** with 1-tetralone (1.6 mL, 12 mmol), anhydrous cerium chloride (5.92 g, 24.0 mmol), THF (75 mL) and 3M HCl (75 mL). Purification *via* column chromatography eluting with 1:4 dichloromethane/petrol 40-60 afforded the title compound **234** as a white solid (1.99 g, 69 %) containing *c.a.* 10 % 6-methoxy-1,2,3,4-tetrahydro-naphthalene.

Melting point: 55-57 °C (dichloromethane/petrol 40-60);

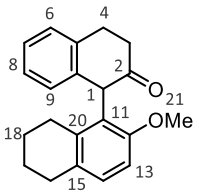
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.18 (dd, *J* = 7.0, 1.0 Hz, 1H, $H_6$), 7.12 (td, *J* = 7.3, 1.4 Hz, 1H, $H_7$), 7.07 (d, *J* = 8.4 Hz, 1H, $H_{14}$), 7.04 (td, *J* = 7.5, 1.4 Hz, 1H, $H_8$), 6.79 (d, *J* = 8.4 Hz, 1H, $H_{13}$), 6.61 (d, *J* = 7.4 Hz, 1H, $H_9$), 5.88 (t, *J* = 4.5 Hz, 1H, $H_2$), 3.69 (s, 3H, $H_{21}$), 2.93 (td, *J* = 8.8, 8.3, 3.5 Hz, 2H, $H_4$), 2.83-2.68 (m, 4H, $H_{16}$ and $H_{19}$), 2.52-2.43 (m, 2H, $H_3$), 1.82-1.57 (m, 4H, $H_{17}$ and $H_{18}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.5 (Quat, $C_{12}$), 137.3 (Quat, $C_{Ar}$), 136.0 (Quat, $C_{Ar}$), 135.1 (Quat, $C_{Ar}$), 134.5 (Quat, $C_{Ar}$), 129.6 (Quat, $C_{Ar}$), 128.7 (CH, $C_{14}$), 128.0 (CH, $C_2$), 127.4 (CH, $C_6$), 126.6 (CH, $C_7$), 126.4 (CH, $C_8$), 124.0 (CH, $C_9$), 111.8 (Quat, $C_{11}$), 108.8 (CH, $C_{13}$), 56.1 ($CH_3$, $C_{21}$), 29.4 ($CH_2$, $C_{16}$ or $C_{19}$), 28.2 ($CH_2$, $C_4$), 27.1 ($CH_2$, $C_{16}$ or $C_{19}$), 23.5 ($CH_2$, $C_3$), 23.3 ($CH_2$, $C_{17}$ or $C_{18}$), 23.1 ($CH_2$, $C_{17}$ or $C_{18}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3015, 1929, 2882, 2856, 2831, 1588, 1501, 1479, 1462, 1450, 1439, 1320, 1264, 1247, 1118, 1046, 1034, 1020;

HRMS (ESI$^+$): calculated for $C_{21}H_{23}O^+$ = 291.1743, mass found = 291.1744.

**2'-Methoxy-3,4,5',6',7',8'-hexahydro-[1,1'-binaphthalen]-2(1*H*)-one, 251**




**251**

According to **General Procedure B** with **234** (1.88 g, 6.47 mmol), dichloromethane (65 mL), sodium bicarbonate (1.36 g, 16.2 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 2.98 g, 12.9 mmol); then 1:1 diethyl ether/dichloromethane (130 mL), boron trifluoride diethyl etherate (1.28 mL, 10.4 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **251** as an off white solid (1.23 g, 62 %).

Melting point: 138-139 °C (ethyl acetate/hexane);

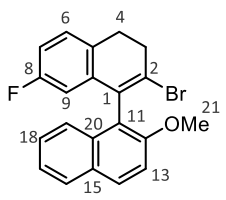
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.29-7.22 (m, 1H, $H_6$), 7.17 (t, *J* = 7.4 Hz, 1H, $H_7$), 7.07 (td, *J* = 7.5, 1.2 Hz, 1H, $H_8$), 7.06 (d, *J* = 8.4 Hz, 1H, $H_{14}$), 6.72 (d, *J* = 8.4 Hz, 1H, $H_{13}$), 6.61 (d, *J* = 7.7 Hz, 1H, $H_9$), 4.94 (s, 1H, $H_1$), 3.54 (s, 3H, $H_{21}$), 3.25-3.09 (m, 2H, $H_4$), 2.90-2.45 (m, 6H, $H_3$, $H_{16}$ and $H_{19}$), 1.82-1.71 (m, 4H, $H_{17}$ and $H_{18}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 211.2 (Quat, $C_2$), 154.8 (Quat, $C_{12}$), 137.7 (Quat, $C_{Ar}$), 137.3 (Quat, $C_{Ar}$), 136.2 (Quat, $C_{Ar}$), 130.3 (Quat, $C_{Ar}$), 129.4 (CH, $C_{14}$), 127.5 (CH, $C_6$), 126.9 (Quat, $C_{11}$), 126.8 (CH, $C_8$), 126.5 (CH, $C_9$), 126.2 (CH, $C_7$), 109.8 (CH, $C_{13}$), 55.8 ($CH_3$, $C_{21}$), 50.9 (CH, $C_1$), 38.6 ($CH_2$, $C_3$), 29.7 ($CH_2$, $C_{16}$ or $C_{19}$), 28.6 ($CH_2$, $C_4$), 27.4 ($CH_2$, $C_{16}$ or $C_{19}$), 23.4 ($CH_2$, $C_{17}$ or $C_{18}$), 22.9 ($CH_2$, $C_{17}$ or $C_{18}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3019, 2932, 2856, 2836, 1714, 1599, 1585, 1481, 1464, 1439, 1408, 1345, 1305, 1201, 1150, 1108, 1084, 1031;

HRMS (ESI$^+$): calculated for $C_{21}H_{23}O_2^+$ = 307.1693, mass found = 307.1693.

**2-Bromo-7-fluoro-2'-methoxy-3,4-dihydro-1,1'-binaphthalene, 313**




**313**

*N*-bromosuccinimide (1.25 g, 7.04 mmol) was added to a stirred solution of **RJA29** (2.04 g, 6.70 mmol) in dichloromethane (70 mL). After stirring at room temperature for 24 hours the mixture was quenched with saturated aqueous sodium thiosulfate. The biphasic mixture was then extracted with dichloromethane three times and following this, the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:4 dichloromethane/petrol 40-60 and subsequent recrystallization from hexane afforded the title compound **313** as a white solid (2.31 g, 90 %).

Melting point: 133-134 °C (hexane);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.96 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.89-7.84 (m, 1H, $H_{16}$), 7.58-7.54 (m, 1H, $H_{19}$), 7.40 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.44-7.35 (m, 2H, $H_{17}$ and $H_{18}$), 7.15 (dd, *J* = 8.2, 5.7 Hz, 1H, $H_6$), 6.82 (td, *J* = 8.4, 2.7 Hz, 1H, $H_7$), 6.18 (dd, *J* = 10.2, 2.7 Hz, 1H, $H_9$), 3.91 (s, 3H, $H_{21}$), 3.21-3.03 (m, 4H, $H_3$ and $H_4$);

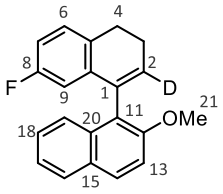
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 162.1 (Quat, d, *J* = 242.6 Hz, $C_8$), 154.2 (Quat, $C_{12}$), 137.0 (d, *J* = 7.8 Hz, $C_{10}$), 133.0 (Quat, d, *J* = 2.1 Hz, $C_1$), 132.3 (Quat, $C_{20}$), 130.1 (CH, $C_{14}$), 129.5 (Quat, d, *J* = 3.1 Hz, $C_5$), 129.2 (Quat, $C_{15}$), 128.6 (CH, d, *J* = 7.9 Hz, $C_6$), 128.3 (CH, $C_{16}$), 127.6 (Quat, $C_{11}$), 127.1 (CH, $C_{18}$), 124.3 (CH, $C_{19}$), 123.9 (CH, $C_{17}$), 121.6 (Quat, $C_2$), 113.8 (CH, $C_{13}$), 113.5 (CH, d, *J* = 21.5 Hz, $C_7$), 112.3 (CH, d, *J* = 23.5 Hz, $C_9$), 56.9 ($CH_3$, $C_{21}$), 35.2 ($CH_2$, $C_3$ or $C_4$), 29.0 ($CH_2$, $C_3$ or $C_4$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –116.4;

FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3007, 2938, 2893, 2837, 1622, 1607, 1594, 1508, 1487, 1463, 1430, 1417, 1383, 1334, 1263, 1249, 1199, 1148, 1089, 1046, 1021;

HRMS ($Cl^+$): calculated for $C_{21}H_{17}BrFO^+$ = 383.0441, mass found = 383.0448.

**7-Fluoro-2'-methoxy-3,4-dihydro-1,1'-binaphthalene-2-*d*, 314**




**314**

In analogy to a modified literature procedure,[153] Magnesium turnings (182 mg, 7.50 mmol) were stirred vigorously under vacuum (*c.a.* 0.1 mbar) at 150 °C for 1 hour. After cooling to room temperature THF (5 mL) followed by a solution of **313** (1.91 g, 5.00 mmol) in THF (5 mL) were added. The reaction mixture was heated to 60 °C. The reaction was then initiated by addition of 1,2-dibromoethane (0.1 mL) and subsequently stirred at reflux for 2 hours. After cooling to room temperature, deuterium oxide (2.7 mL, 150 mmol) was then added *via* an oven dried syringe which was subsequently cooled under an atmosphere of argon. The biphasic mixture was stirred for 1 h at room temperature. The biphasic mixture was filtered, the layers separated and the aqueous layer extracted twice with diethyl ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:4 dichloromethane/petrol 40-60 afforded the title compound **314** as white solid (1.04 g, 68 %) with *c.a.* 90 % deuterium incorporation.

Melting point: 105-107 °C (dichloromethane/petrol 40-60);

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.89-7.86 (m, 1H, $H_{16}$), 7.77-7.74 (m, 1H, $H_{19}$), 7.44-7.37 (m, 3H, $H_{13}$, $H_{17}$ and $H_{18}$), 7.20 (dd, *J* = 8.2, 5.8 Hz, 1H, $H_6$), 6.84 (td, *J* = 8.4, 2.7 Hz, 1H, $H_7$), 6.27 (dd, *J* = 10.2, 2.7 Hz, 1H, $H_9$), 3.89 (s, 3H, $H_{21}$), 3.04 (t, *J* = 8.1 Hz, 2H, $H_4$), 2.64-2.60 (m, 2H, $H_3$);

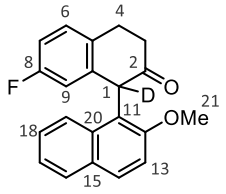
$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 162.0 (Quat, d, *J* = 241.8 Hz, $C_8$), 154.5 (Quat, $C_{12}$), 137.5 (Quat, d, *J* = 7.6 Hz, $C_{10}$), 133.9 (Quat, $C_{20}$), 133.1 (Quat, d, *J* = 2.3 Hz, $C_1$), 131.3 (Quat, d, *J* = 3.0 Hz, $C_5$), 130.9 (CD, t, *J* = 24.0 Hz, $C_2$), 129.4 (CH, $C_{14}$), 129.3 (Quat, $C_{15}$), 128.5 (CH, d, *J* = 7.7 Hz, $C_6$), 128.1 (CH, $C_{16}$), 126.6 (CH, $C_{18}$), 125.1 (CH, $C_{19}$), 123.7 (CH, $C_{17}$), 122.8 (Quat, $C_{11}$), 113.9 (CH, $C_{13}$), 113.1 (CH, d, *J* = 21.3 Hz, $C_7$), 111.6 (CH, d, *J* = 22.7 Hz, $C_9$) 56.9 ($CH_3$, $C_{21}$), 27.5 ($CH_2$, $C_4$), 23.8 ($CH_2$, $C_3$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –117.1;

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3002, 2935, 2887, 2835, 1621, 1611, 1593, 1578, 1508, 1467, 1431, 1417, 1332, 1288, 1263, 1218, 1201, 1163, 1116, 1044, 1021;

HRMS (EI$^+$) calculated for $C_{21}H_{16}DFO^+$ = 305.1321, mass found = 305.1318.

**7-Fluoro-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one-1-*d*, 315**




**315**

According to **General Procedure B** with **314** (974 mg, 3.19 mmol), dichloromethane (32 mL), sodium bicarbonate (670 mg, 7.98 mmol), *meta*-chloroperbenzoic acid (75 % w/w, 1.47 g, 6.38 mmol); then 1:1 diethyl ether/dichloromethane (64 mL), boron trifluoride diethyl etherate (0.63 mL, 5.1 mmol). Purification *via* recrystallization from hexane/ethyl acetate afforded the title compound **315** as an off white solid (756 mg, 74 %) with *c.a.* 90 % deuterium incorporation.

Melting point: 118-120 °C (ethyl acetate/hexane);

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.90 (dd, *J* = 8.0, 1.3 Hz, 1H, $H_{16}$), 7.63-7.50 (m, 1H, $H_{19}$), 7.45 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1H, $H_{18}$), 7.39 (ddd, *J* = 8.0, 6.7, 1.2 Hz, 1H, $H_{17}$), 7.36 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.28 (dd, *J* = 8.3, 5.7 Hz, 1H, $H_6$), 6.89 (td, *J* = 8.4, 2.7 Hz, 1H,

$H_7$), 6.29 (dd, *J* = 10.0, 2.7 Hz, 1H, $H_9$), 3.81 (s, 3H, $H_{21}$), 3.31-3.24 (m, 2H, $H_4$), 2.97 (dt, *J* = 16.2, 5.3 Hz, 1H, $H_{3A}$), 2.84 (ddd, *J* = 16.3, 9.6, 6.8 Hz, 1H, $H_{3B}$);

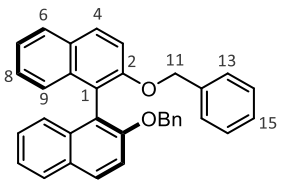
$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 209.7 (Quat, $C_2$), 161.9 (Quat, d, *J* = 243.7 Hz, $C_8$), 154.7 (Quat, $C_{12}$), 139.9 (Quat, d, *J* = 7.4 Hz, $C_{10}$), 133.2 (Quat, $C_{20}$), 131.8 (Quat, d, *J* = 3.2 Hz, $C_5$), 130.1 (CH, $C_{14}$), 129.7 (Quat, $C_{15}$), 129.0 (CH, $C_{16}$), 128.9 (CH, d, *J* = 8.1 Hz, $C_6$), 127.1 (CH, $C_{18}$), 123.7 (CH, $C_{17}$), 123.3 (CH, $C_{19}$), 120.5 (Quat, $C_{11}$), 114.3 (CH, d, *J* = 22.7 Hz, $C_9$), 113.8 (CH, $C_{13}$), 113.2 (CH, d, *J* = 21.4 Hz, $C_7$), 56.5 ($CH_3$, $C_{21}$), 49.9 (CD, t, *J* = 18.1 Hz, $C_1$), 38.7 ($CH_2$, $C_3$), 27.9 ($CH_2$, $C_4$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –116.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3000, 2941, 2906, 2841, 1714, 1614, 1593, 1511, 1492, 1470, 1256, 1149, 1083, 1053, 1025;

HRMS (EI$^+$) calculated for $C_{21}H_{16}DFO_2^+$ = 321.1270, mass found = 321.1272.

**(*S*)-2,2'-Bis(benzyloxy)-1,1'-binaphthalene, 259**




**259**

**Asymmetric:** According to **General Procedure C** with **241** (75.7 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography afforded the title compound **259** as a colourless oil (65.3 mg, 70 %, 96:4 *e.r.*). The spectral data matched that previously reported in the literature.[154]

**Racemic:** Tetrabutylammonium bromide (6.4 mg, 0.020 mmol) and benzyl bromide (144 μL, 1.20 mmol) were sequentially added to a solution of racemic BINOL (57.3 mg, 0.200 mmol) in dichloromethane (2.0 ml) and the reaction mixture was then stirred for 5 minutes. After the addition of 50 % aqueous potassium hydroxide (225 μL, 1.00 mmol) the reaction mixture was stirred rapidly at a rate of 1000-1400 rpm at room temperature for 3 hours. Water and dichloromethane were added and the organic layer was separated. The aqueous layer was then extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:14 ethyl acetate/petrol 40-60 afforded the title compound **259** as a thick colourless oil (91.5 mg, 98 %). The spectral data matched that previously reported in the literature.[154]

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 2H, $H_4$), 7.89 (d, *J* = 8.2 Hz, 2H, $H_6$), 7.43 (d, *J* = 9.0 Hz, 2H, $H_3$), 7.38-7.32 (m, 2H, $H_7$), 7.29-7.20 (m, 4H, $H_8$ and $H_{15}$), 7.18-7.07 (m, 6H, $H_9$ and $H_{14}$), 6.98 (d, *J* = 7.2 Hz, 4H, $H_{13}$), 5.08 (d, *J* = 13.1 Hz, 2H, $H_{11B}$), 5.04 (d, *J* = 13.1 Hz, 2H, $H_{11A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.2 (Quat, $C_2$), 137.7 (Quat, $C_{12}$), 134.3 (Quat, $C_{10}$), 129.6 (Quat, $C_5$), 129.4 (CH, $C_4$), 128.2 (CH, $C_{14}$), 128.0 (CH, $C_6$), 127.4 (CH, $C_{15}$), 126.8 (CH, $C_{13}$), 126.4 (CH, $C_8$), 125.7 (CH, $C_9$), 123.8 (CH, $C_7$), 120.9 (Quat, $C_1$), 116.1 (CH, $C_3$), 71.3 ($CH_2$, $C_{11}$);

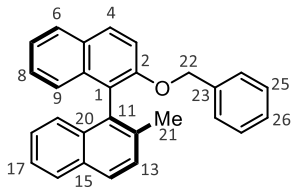
FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 3032, 2932, 2870, 1622, 1591, 1507, 1453, 1431, 1354, 1263, 1178, 1133, 1090;

LRMS (ESI$^+$): calculated for $C_{34}H_{26}O_2Na^+$ = 489, mass found = 489;

$[\alpha]_D^{25}$ = –56.8 (*c* = 1.00, $CH_2Cl_2$);

Chiral HPLC**:** (Chiralpak IA, 5 % $^i$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, λ = 282 nm, 5 μL injection) $\tau_R$ (major) = 6.8 min, $\tau_R$ (minor) = 7.8 min.

**(*S*)- 2-(Benzyloxy)-2'-methyl-1,1'-binaphthalene, 260**




**260**

**Asymmetric:** According to **General Procedure C** with **242** (57.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:49 ethyl acetate/petrol 40-60 afforded the title compound **260** as a white solid (22.1 mg, 30 %, 75:25 *e.r.*).

**Racemic:** According to **General Procedure D** with **242** (57.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **260** as a white solid (72.0 mg, 96 %).

Melting point: 93-95 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.94 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.92-7.86 (m, 3H, $H_6$, $H_{14}$ and $H_{16}$), 7.54 (d, *J* = 8.4 Hz, 1H, $H_{13}$), 7.45 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.41 (ddd, *J* = 8.1, 6.3, 1.5 Hz, 1H, $H_8$), 7.35 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H, $H_7$), 7.27-7.14 (m, 6H, $H_9$, $H_{17}$, $H_{18}$, $H_{25}$ and $H_{26}$), 7.10 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.00-6.94 (m, 2H, $H_{24}$), 5.08 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 5.03 (d, *J* = 12.6 Hz, 1H, $H_{22B}$), 2.13 (s, 3H, $H_{21}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 153.6 (Quat, $C_2$), 137.6 (Quat, $C_{12}$), 135.2 (Quat, $C_{23}$), 133.8 (Quat, $C_{Ar}$), 133.4 (Quat, $C_{Ar}$), 132.5 (Quat, $C_{Ar}$), 132.3 (Quat, $C_{Ar}$), 129.5 (Quat, $C_5$), 129.3 (CH, $C_4$), 128.8 (CH, $C_{13}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{Ar}$), 128.0 (CH, $C_{Ar}$), 127.6 (CH, $C_{Ar}$), 127.5 (CH, $C_{Ar}$), 126.8 (CH, $C_{24}$), 126.7 (CH, $C_{Ar}$), 126.1 (CH, $C_{Ar}$), 126.0 (CH, $C_{Ar}$), 125.3 (CH, $C_{19}$), 124.8 (CH, $C_8$), 124.0 (CH, $C_7$), 123.4 (Quat, $C_1$), 116.0 (CH, $C_3$), 71.1 ($CH_2$, $C_{22}$), 20.5 ($CH_3$, $C_{21}$);

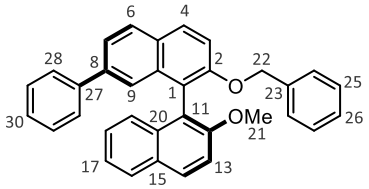
FTIR (neat) $\nu/cm^{-1}$ = 3055, 3009, 2919, 2862, 1621, 1591, 1506, 1454, 1353, 1270, 1263, 1245, 1219, 1177, 1147, 1133, 1086, 1019;

HRMS ($ESI^+$): calculated for $C_{28}H_{23}O^+$ = 375.1743, mass found = 375.1744;

$[\alpha]_D^{25}$ = –9.7 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 1 % $^i$PrOH, 99 % hexane, 0.50 mL $min^{-1}$, $\lambda$ = 282 nm, 5 μL injection) $\tau_R$ (major) = 20.0 min, $\tau_R$ (minor) = 21.4 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-7-phenyl-1,1'-binaphthalene, 261**




**261**

**Asymmetric:** According to **General Procedure C** with **RJA39** (75.7 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **261** as a white solid (80.1 mg, 86 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA39** (75.7 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **261** as a white solid (91.4 mg, 98 %).

Melting point: 64-65 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.95 (d, *J* = 8.7 Hz, 2H, $H_4$ and $H_6$), 7.90 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.61 (dd, *J* = 8.4, 1.8 Hz, 1H, $H_7$), 7.48 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.44 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.42-7.37 (m, 3H, $H_9$ and $H_{28}$), 7.37-7.28 (m, 3H, $H_{29}$ and $H_{30}$), 7.28-7.20 (m, 3H, $H_{17}$, $H_{18}$ and $H_{26}$), 7.20-7.14 (m, 3H, $H_{19}$ and $H_{25}$), 7.03-6.96 (m, 2H, $H_{24}$), 5.10 (d, *J* = 12.6 Hz, 1H, $H_{22B}$), 5.06 (d, *J* = 12.6 Hz, 1H, $H_{22A}$), 3.79 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 154.5 (Quat, $C_2$ or $C_{12}$), 141.6 (Quat, $C_{27}$), 139.1 (Quat, $C_{Ar}$), 137.7 (Quat, $C_{Ar}$), 134.5 (Quat, $C_{10}$ or $C_{20}$), 134.2 (Quat, $C_{10}$ or $C_{20}$), 129.6 (CH, $C_{14}$), 129.3 (Quat, $C_5$ or $C_{15}$), 129.1 (CH, $C_4$), 128.8 (Quat, $C_5$ or $C_{15}$), 128.7 (CH, $C_{29}$), 128.6 (CH, $C_{16}$), 128.3 (CH, $C_{25}$), 128.0 (CH, $C_6$), 127.6 (CH, $C_{28}$), 127.4 (CH, $C_{26}$), 127.1 (CH, $C_{Ar}$), 126.9 (CH, $C_{24}$), 126.5 (CH, $C_{Ar}$), 125.5 (CH, $C_{Ar}$), 123.8 (CH, $C_7$), 123.6 (CH, $C_9$ or $C_{30}$), 123.6 (CH, $C_9$ or $C_{30}$), 121.3 (CH, $C_1$), 119.3 (CH, $C_{11}$), 116.3 (CH, $C_3$), 113.9 (CH, $C_{13}$), 71.3 ($CH_2$, $C_{22}$), 56.7 ($CH_3$, $C_{21}$);

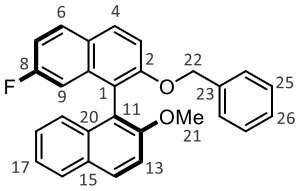
FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 3031, 2935, 2837, 1621, 1593, 1509, 1492, 1454, 1433, 1355, 1322, 1284, 1221, 1093, 1020;

HRMS (ESI$^+$): calculated for $C_{34}H_{26}O_2Na^+$ = 489.1825, mass found = 489.1824;

$[\alpha]_D^{25}$ = +41.5 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 5 % $^{i}$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 257 nm, 5 μL injection) $\tau_R$ (major) = 11.1 min, $\tau_R$ (minor) = 12.7 min.

**(*S*)-2-(Benzyloxy)-7-fluoro-2'-methoxy-1,1'-binaphthalene, 262**




**262**

**Asymmetric:** According to **General Procedure C** with **RJA40** (64.1 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **262** as a white solid (80.9 mg, 99 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA40** (64.1 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **262** as a white solid (77.2 mg, 95 %).

Melting point: 45-47 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.90 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.90 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.83 (dd, *J* = 9.0, 5.8 Hz, 1H, $H_6$), 7.47 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.37 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.37-7.32 (m, 1H, $H_{17}$), 7.25 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{18}$), 7.21-7.10 (m, 4H, $H_{19}$, $H_{25}$

and $H_{26}$), 7.13-7.06 (m, 1H, $H_7$), 7.04-6.97 (m, 2H, $H_{24}$), 6.78 (dd, *J* = 11.4, 2.6 Hz, 1H, $H_9$), 5.10 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.06 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.78 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 161.5 (d, *J* = 244.9 Hz, Quat, $C_8$), 155.0 (Quat, $C_2$ or $C_{12}$), 155.0 (Quat, $C_2$ or $C_{12}$), 137.5 (Quat, $C_{23}$), 135.5 (d, *J* = 9.4 Hz, Quat, $C_{10}$), 134.0 (Quat, $C_{20}$), 130.5 (d, *J* = 9.4 Hz, CH, $C_6$), 129.8 (CH, $C_{14}$), 129.3 (CH and Quat, $C_4$ and $C_{15}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.5 (CH, $C_{26}$), 126.8 (CH, $C_{24}$), 126.6 (CH, $C_{18}$), 126.6 (d, *J* = 6.7 Hz, Quat, $C_5$), 125.2 (CH, $C_{19}$), 123.7 (CH, $C_{17}$), 120.3 (d, *J* = 5.3 Hz, Quat, $C_1$), 118.9 (CH, $C_{11}$), 115.1 (d, *J* = 2.6 Hz, CH, $C_3$), 114.2 (d, *J* = 25.8 Hz, CH, $C_7$), 113.8 (CH, $C_{13}$), 108.8 (d, *J* = 22.0 Hz, CH, $C_9$), 71.1 ($CH_2$, $C_{22}$), 56.7 ($CH_3$, $C_{21}$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –113.9;

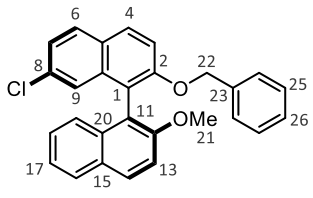
FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 3032, 2937, 2838, 1629, 1593, 1511, 1453, 1385, 1333, 1255, 1178, 1062;

HRMS (ESI$^+$): calculated for $C_{28}H_{21}O_2Na^+$ = 431.1418, mass found = 431.1415;

$[\alpha]_D^{25}$ = –71.3 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak OJH, 5 % $^i$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 331 nm, 5 μL injection) $\tau_R$ (minor) = 13.8 min, $\tau_R$ (major) = 18.0 min.

**(*S*)-2-(Benzyloxy)-7-chloro-2'-methoxy-1,1'-binaphthalene, 263**




**263**

**Asymmetric:** According to **General Procedure C** with **RJA41** (67.4 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg,

2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **263** as a white solid (79.2 mg, 93 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA41** (67.4 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.25 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **263** as a white solid (80.8 mg, 95 %).

Melting point: 130-132 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.89 (d, *J* = 8.5 Hz, 1H, $H_{16}$), 7.87 (d, *J* = 9.2 Hz, 1H, $H_4$), 7.77 (d, *J* = 8.7 Hz, 1H, $H_6$), 7.45 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.39 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.34 (ddd, *J* = 8.1, 6.6, 1.2 Hz, 1H, $H_{17}$), 7.28-7.21 (m, 2H, $H_7$ and $H_{18}$), 7.18-7.13 (m, 4H, $H_9$, $H_{25}$ and $H_{26}$), 7.11 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.00-6.93 (m, 2H, $H_{24}$), 5.07 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.03 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.77 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.0 (Quat, $C_2$ or $C_{12}$), 154.9 (Quat, $C_2$ or $C_{12}$), 137.5 (Quat, $C_{23}$), 135.1 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 132.6 (Quat, $C_{Ar}$), 129.9 (CH, $C_{14}$), 129.7 (CH, $C_6$), 129.3 (Quat, $C_{Ar}$), 129.3 (CH, $C_4$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.7 (Quat, $C_{Ar}$), 127.5 (CH, $C_{26}$), 126.8 (CH, $C_{24}$), 126.6 (CH, $C_{18}$), 125.2 (CH, $C_{19}$), 124.8 (CH, $C_7$), 124.2 (CH, $C_9$), 123.7 (CH, $C_{17}$), 120.3 (Quat, $C_1$), 118.6 (Quat, $C_{11}$), 116.2 (CH, $C_3$), 113.8 (CH, $C_{13}$), 71.1 ($CH_2$, $C_{22}$), 56.7 ($CH_2$, $C_{21}$);

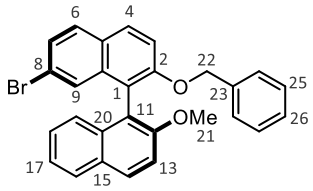
FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 2935, 2838, 1616, 1593, 1499, 1452, 1348, 1315, 1268, 1254, 1222, 1148, 1095, 1075, 1021;

HRMS (ESI$^+$): calculated for $C_{28}H_{21}O_2ClNa^+$ = 447.1122, mass found = 447.1121;

$[\alpha]_D^{25}$ = –43.4 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IA, 1 % $^i$PrOH, 99 % hexane, 0.5 mL min$^{-1}$, $\lambda$ = 287 nm, 5 μL injection) $\tau_R$ (minor) = 48.7 min, $\tau_R$ (major) = 51.4 min.

**(*S*)-2-(Benzyloxy)-7-bromo-2'-methoxy-1,1'-binaphthalene, 264**




**264**

**Asymmetric:** According to **General Procedure C** with **RJA42** (38.1 mg, 0.100 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (5.5 mg, 0.010 mmol), $K_3PO_4$ (412 mg, 1.00 mmol), dichloromethane (0.20 mL), benzene (0.30 mL), benzyl iodide (65 mg, 0.30 mmol) in benzene (0.5 mL); then dichloromethane (1.0 mL), DDQ (38 mg, 0.30 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **264** as a white solid (40.9 mg, 87 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA42** (5.7 mg, 0.015 mmol), tetrabutylammonium bromide (1.0mg, 0.0015 mmol), $K_3PO_4$ (32 mg, 0.15 mmol), dichloromethane (0.5 mL), benzyl bromide (5.4 μL, 0.045 mmol); then dichloromethane (0.5 mL), DDQ (10 mg, 0.045 mmol). An analytical amount of racemic **264** for the generation of a racemic HPLC trace was obtained *via* preparative thin layer chromatography.

Melting point: 49-52 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.02 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.91 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.87 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.71 (d, *J* = 8.7 Hz, 1H, $H_6$), 7.46 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.42 (d, *J* = 8.9 Hz, 1H, $H_3$), 7.40 (dd, *J* = 8.6, 1.9 Hz, 1H, $H_7$), 7.40-7.31 (m, 2H, $H_9$ and $H_{17}$), 7.30-7.21 (m, 1H, $H_{18}$), 7.16 (dd, *J* = 5.0, 1.9 Hz, 3H, $H_{25}$ and $H_{26}$), 7.12 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.01-6.93 (m, 2H, $H_{24}$), 5.08 (d, *J* = 12.8 Hz, 1H, $H_{22B}$), 5.04 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.78 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.0 (Quat, $C_2$ or $C_{12}$), 154.8 (Quat, $C_2$ or $C_{12}$), 137.4 (Quat, $C_{23}$), 135.6 (Quat, $C_{Ar}$), 134.0 (Quat, $C_{Ar}$), 129.9 (CH, $C_{14}$), 129.8 (CH, $C_6$), 129.3 (CH, $C_4$), 129.3 (Quat, $C_{Ar}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.9 (Quat, $C_{Ar}$), 127.5 (CH, $C_9$ or $C_{26}$), 127.5 (CH, $C_9$ or $C_{26}$), 127.3 (CH, $C_7$), 126.8 (CH, $C_{24}$), 126.6 (CH, $C_{18}$), 125.2 (CH, $C_{19}$), 123.7 (CH, $C_{17}$), 121.1 (Quat, $C_8$), 120.2 (Quat, $C_1$), 118.5 (Quat, $C_{11}$), 116.3 (CH, $C_3$), 113.8 (CH, $C_{13}$), 71.1 ($CH_2$, $C_{22}$), 56.7 ($CH_3$, $C_{21}$);

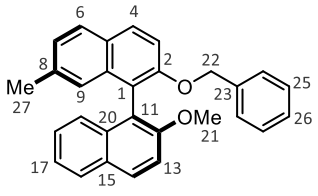
FTIR (neat) $\nu$/cm$^{-1}$ = 3059, 30036, 2935, 2838, 1613, 1594, 1508, 1496, 1463, 1423, 1371, 1315, 1267, 1222, 1178, 1136, 1067;

HRMS (ESI$^+$): calculated for $C_{28}H_{21}O_2BrNa^+$ = 491.0617, mass found = 491.0617;

$[\alpha]_D^{25}$ = –29.3 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 5 % $^i$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 286 nm, 5 $\mu$L injection) $\tau_R$ (minor) = 9.2 min, $\tau_R$ (major) = 10.6 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-7-methyl-1,1'-binaphthalene, 265**




**265**

**Asymmetric:** According to **General Procedure C** with **RJA43** (63.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg,

2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **265** as a white solid (74.4 mg, 92 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA43** (15.8 mg, 0.0500 mmol), tetrabutylammonium bromide (1.6 mg, 0.0050 mmol), $K_3PO_4$ (106 mg, 0.500 mmol), dichloromethane (0.5 mL), benzyl bromide (18 μL, 0.15 mmol); then dichloromethane (0.5 mL), DDQ (34 mg, 0.15 mmol). An analytical amount of racemic **265** for the generation of a racemic HPLC trace was obtained *via* preparative thin layer chromatography.

Melting point: 44-46 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.91 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.87 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.77 (d, *J* = 8.3 Hz, 1H, $H_6$), 7.48 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.35 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.36-7.31 (m, 1H, $H_{17}$), 7.23 (ddd, *J* = 8.0, 6.6, 1.3 Hz, 1H, $H_{18}$), 7.20-7.12 (m, 5H, $H_7$, $H_{19}$, $H_{25}$ and $H_{26}$), 7.02-6.92 (m, 3H, $H_9$ and $H_{24}$), 5.07 (d, *J* = 12.6 Hz, 1H, $H_{22B}$), 5.02 (d, *J* = 12.6 Hz, 1H, $H_{22A}$), 3.77 (s, 3H, $H_{21}$), 2.26 (s, 3H, $H_{27}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 154.3 (Quat, $C_2$ or $C_{12}$), 137.8 (Quat, $C_{23}$), 136.1 (Quat, $C_8$), 134.4 (Quat, $C_{10}$ or $C_{20}$), 134.3 (Quat, $C_{10}$ or $C_{20}$), 129.4 (CH, $C_{14}$), 129.3 (Quat, $C_5$ or $C_{15}$), 129.1 (CH, $C_4$), 128.2 (CH, $C_{25}$), 128.0 (CH, $C_6$ or $C_{16}$), 127.9 (CH, $C_6$ or $C_{16}$), 127.9 (Quat, $C_5$ or $C_{15}$), 127.4 (CH, $C_{26}$), 126.8 (CH, $C_{24}$), 126.4 (CH, $C_7$ or $C_{18}$), 126.3 (CH, $C_7$ or $C_{18}$), 125.6 (CH, $C_{19}$), 124.4 (CH, $C_9$), 123.6 (CH, $C_{17}$), 120.3 (Quat, $C_1$), 119.8 (Quat, $C_{11}$), 115.3 (CH, $C_3$), 114.1 (CH, $C_{13}$), 71.3 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$), 22.1 ($CH_3$, $C_{27}$);

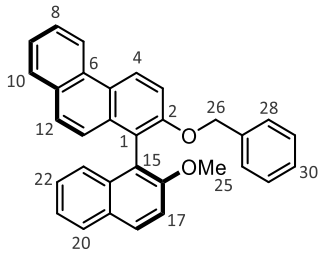
FTIR (neat) $\nu$/cm$^{-1}$ = 3056, 3007, 2936, 2837, 1625, 1594, 1508, 1453, 1372, 1332, 1318, 1250, 1223, 1180, 1136, 1020;

HRMS (ESI$^+$): calculated for $C_{29}H_{25}O_2^+$ = 405.1849, mass found = 405.1848;

$[\alpha]_D^{25}$ = –31.3 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak OJH, 5 % $^i$PrOH, 95 % hexane, 1 mL min$^{-1}$, $\lambda$ = 287 nm, 5 μL injection) $\tau_R$ (minor) = 10.0 min, $\tau_R$ (major) = 14.3 min.

**(*S*)-2-(Benzyloxy)-1-(2-methoxynaphthalen-1-yl)phenanthrene, 266**




**266**

**Asymmetric:** According to **General Procedure C** with **243** (70.5 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **266** as a white solid (55.2 mg, 63 %, 93:7 *e.r.*).

**Racemic:** According to **General Procedure D** with **243** (70.5 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **266** as a white solid (57.3 mg, 65 %).

Melting point: 76-78 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.77 (d, *J* = 9.1 Hz, 1H, $H_4$), 8.68 (d, *J* = 8.3 Hz, 1H, $H_7$), 8.03 (d, *J* = 9.0 Hz, 1H, $H_{18}$), 7.92 (d, *J* = 8.2 Hz, 1H, $H_{20}$), 7.79 (d, *J* = 7.7 Hz, 1H, $H_{12}$), 7.65 (ddd, *J* = 8.5, 7.0, 1.4 Hz, 1H, $H_8$), 7.57-7.46 (m, 4H, $H_3$, $H_9$, $H_{13}$ and $H_{17}$), 7.35 (ddd, *J* = 8.1, 6.5, 1.4 Hz, 1H, $H_{21}$), 7.27-7.13 (m, 6H, $H_{10}$, $H_{22}$, $H_{23}$, $H_{29}$ and $H_{30}$), 7.07-7.00 (m, 2H, $H_{28}$), 5.15 (d, *J* = 12.8 Hz, 1H, $H_{26B}$), 5.11 (d, *J* = 12.8 Hz, 1H, $H_{26A}$), 3.78 (s, 3H, $H_{25}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ and $C_{16}$), 137.7 (Quat, $C_{27}$), 134.3 (Quat, $C_{Ar}$), 133.0 (Quat, $C_{Ar}$), 131.1 (Quat, $C_{Ar}$), 130.8 (Quat, $C_{Ar}$), 129.6 (CH, $C_{18}$), 129.3 (Quat, $C_{Ar}$), 128.6 (CH, $C_{12}$), 128.3 (CH, $C_{29}$), 128.1 (CH, $C_{20}$), 127.6 (CH, $C_{Ar}$), 127.4 (CH, $C_{30}$), 126.8 (CH, $C_{28}$), 126.7 (CH, $C_8$), 126.5 (CH, $C_{13}$), 125.9 (CH, $C_{Ar}$), 125.5 (CH, $C_{Ar}$), 125.3 (Quat, $C_{Ar}$), 124.7 (CH, $C_{Ar}$), 123.9 (CH, $C_4$), 123.6 (CH, $C_{21}$), 122.4 (CH, $C_7$), 122.3 (Quat, $C_1$), 119.7 (Quat, $C_{15}$), 114.7 (CH, $C_3$), 114.0 (CH, $C_{17}$), 70.9 ($CH_2$, $C_{26}$), 56.8 ($CH_3$, $C_{25}$);

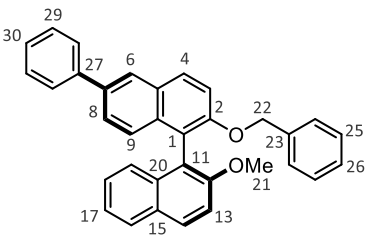
FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 2034, 2934, 2837, 1621, 1606, 1593, 1509, 1475, 1420, 1386, 1332, 1231, 1198, 1027;

HRMS ($ESI^+$): calculated for $C_{32}H_{24}O_2Na^+$ = 463.1669, mass found = 463.1667;

$[\alpha]_D^{25}$ = –46.2 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 10 % $^i$PrOH, 90 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 259 nm, 5 μL injection) $\tau_R$ (minor) = 13.2 min, $\tau_R$ (major) = 14.9 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-6-phenyl-1,1'-binaphthalene, 267**




**267**

**Asymmetric:** According to **General Procedure C** with **244** (75.7 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **267** as a white solid (71.2 mg, 77 %, 94:6 *e.r.*).

**Racemic:** According to **General Procedure D** with **244** (75.7 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **267** as a white solid (76.4 mg, 82 %).

Melting point: 71-73 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.08 (d, *J* = 1.7 Hz, 1H, $H_6$), 8.03 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.98 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.92 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.72-7.66 (m, 2H, $H_{28}$), 7.54-7.43 (m, 5H, $H_3$, $H_8$, $H_{13}$ and $H_{29}$), 7.35 (m, 2H, $H_{17}$ and $H_{18}$), 7.30-7.14 (m, 6H, $H_9$, $H_{19}$, $H_{25}$, $H_{26}$ and $H_{30}$), 7.05-6.99 (m, 2H, $H_{24}$), 5.12 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.07 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.79 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 154.3 (Quat, $C_2$ or $C_{12}$), 141.3 (Quat, $C_{23}$), 137.7 (Quat, $C_7$ or $C_{27}$), 136.6 (Quat, $C_7$ or $C_{27}$), 134.2 (Quat, $C_{10}$ or $C_{20}$), 133.5 (Quat, $C_{10}$ or $C_{20}$), 129.8 (Quat, $C_5$ or $C_{15}$), 129.7 (CH, $C_4$ or $C_{14}$), 129.6 (CH, $C_4$ or $C_{14}$), 129.3 (Quat, $C_5$ or $C_{15}$), 128.9 (CH, $C_{29}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.5 (CH, $C_{Ar}$), 127.4 (CH, $C_{28}$), 127.2 (CH, $C_{18}$), 126.9 (CH, $C_{24}$), 126.5 (CH, $C_{Ar}$), 126.2 (CH, $C_{Ar}$), 126.1 (CH, $C_{Ar}$), 126.0 (CH, $C_{Ar}$), 125.5 (CH, $C_6$), 123.6

(CH, $C_{17}$), 120.8 (Quat, $C_1$), 119.4 (Quat, $C_{11}$), 116.7 (CH, $C_3$), 114.0 (CH, $C_{13}$), 71.3 ($CH_2$, $C_{22}$), 56.8 ($CH_2$, $C_{21}$);

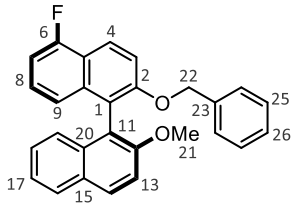
FTIR (neat) $\nu/cm^{-1}$ = 3060, 3030, 2933, 2837, 1622, 1592, 1508, 1493, 1477, 1433, 1349, 1268, 1223, 1180, 1062;

HRMS ($ESI^+$): calculated for $C_{34}H_{27}O_2^+$ = 467.2006, mass found = 467.2006;

$[\alpha]_D^{25}$ = –6.1 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 10 % $^i$PrOH, 90 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 290 nm, 5 μL injection) $\tau_R$ (major) = 5.0 min, $\tau_R$ (minor) = 5.9 min.

**(*S*)-2-(Benzyloxy)-5-fluoro-2'-methoxy-1,1'-binaphthalene, 268**




**268**

**Asymmetric:** According to **General Procedure C** with **RJA44** (64.1 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **268** as a white solid (76.3 mg, 94 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA44** (64.1 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL),

DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **268** as a white solid (64.4 mg, 79 %).

Melting point: 118-120 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.23 (d, *J* = 9.2 Hz, 1H, $H_4$), 8.02 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.92 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.49 (d, *J* = 9.2 Hz, 1H, $H_3$), 7.48 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.36 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{17}$), 7.26 (ddd, *J* = 8.4, 6.7, 1.4 Hz, 1H, $H_{18}$), 7.22-7.12 (m, 5H, $H_8$, $H_{19}$, $H_{25}$ and $H_{26}$), 7.06-6.95 (m, 4H, $H_9$, $H_7$ and $H_{24}$), 5.13 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 5.09 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 3.78 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 159.26 (Quat, d, *J* = 250.9 Hz, $C_6$), 155.0 (Quat, $C_2$ or $C_{12}$), 154.9 (Quat, $C_2$ or $C_{12}$), 137.5 (Quat, $C_{23}$), 136.05 (Quat, d, *J* = 4.3 Hz, $C_{10}$), 134.1 (Quat, $C_{20}$), 129.7 (CH, $C_{14}$), 129.3 (Quat, $C_{15}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.5 (CH, $C_{26}$), 126.8 (CH, $C_{24}$), 126.6 (CH, $C_{18}$), 126.31 (CH, d, *J* = 8.7 Hz, $C_8$), 125.3 (CH, $C_{19}$), 123.7 (CH, $C_{17}$), 122.11 (CH, d, *J* = 5.8 Hz, $C_4$), 121.39 (CH, d, *J* = 3.9 Hz, $C_9$), 120.82 (Quat, d, *J* = 2.8 Hz, $C_1$), 119.81 (CH, d, *J* = 16.7 Hz, $C_5$), 119.1 (Quat, $C_{11}$), 116.24 (CH, d, *J* = 1.3 Hz, $C_3$), 113.9 (CH, $C_{13}$), 107.34 (CH, d, *J* = 19.7 Hz, $C_7$), 71.2 ($CH_2$, $C_{22}$), 56.7 ($CH_3$, $C_{21}$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –123.3;

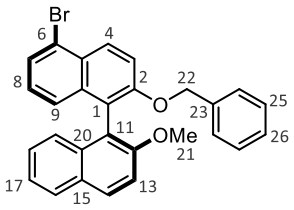
FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3005, 3036, 2838, 1633, 1594, 1508, 1477, 1455, 1414, 1328, 1253, 1221, 1119, 1085, 1021;

HRMS (ESI$^+$): calculated for $C_{28}H_{21}O_2FNa^+$ = 431.1418, mass found = 431.1419;

$[\alpha]_D^{25}$ = –59.0 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 10 % $^i$PrOH, 90 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 285 nm, 5 μL injection) $\tau_R$ (minor) =6.7 min, $\tau_R$ (major) = 8.0 min.

**(*S*)-2-(Benzyloxy)-5-bromo-2'-methoxy-1,1'-binaphthalene, 269**




**269**

**Asymmetric:** According to **General Procedure C** with **RJA45** (76.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **269** as a white solid (90.1 mg, 96 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA45** (76.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **269** as a white solid (84.5 mg, 90 %).

Melting point: 56-58 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.34 (d, *J* = 9.3 Hz, 1H, $H_4$), 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.90 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.62 (dd, *J* = 7.3, 1.1 Hz, 1H, $H_7$), 7.51 (d, *J* = 9.3 Hz, 1H, $H_3$), 7.46 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.34 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{17}$), 7.23 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 1H, $H_{18}$), 7.20-7.13 (m, 4H, $H_9$, $H_{25}$ and $H_{26}$), 7.09 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 7.05 (dd, *J* = 8.4, 7.4 Hz, 1H, $H_8$), 7.02-6.98 (m, 2H, $H_{24}$), 5.12 (d, *J* = 12.8 Hz, 1H, $H_{22B}$), 5.08 (d, *J* = 12.8 Hz, 1H, $H_{22A}$), 3.77 (s, 3H, $H_{21}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 154.7 (Quat, $C_2$ or $C_{12}$), 137.4 (Quat, $C_{23}$), 135.5 (Quat, $C_{10}$), 134.1 (Quat, $C_{20}$), 129.8 (CH, $C_{14}$), 129.3 (Quat, $C_5$), 128.7 (CH, $C_4$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.9 (CH, $C_7$), 127.9 (Quat, $C_{15}$) 127.6 (CH, $C_{26}$), 126.8 (CH, $C_{24}$), 126.8 (CH, $C_{18}$), 126.6 (CH, $C_8$), 125.6 (CH, $C_9$), 125.3 (CH, $C_{19}$), 123.7 (CH, $C_{17}$), 123.0 (Quat, $C_6$), 121.1 (Quat, $C_1$), 119.0 (Quat, $C_{11}$), 117.0 (CH, $C_3$), 113.8 (CH, $C_{13}$), 71.0 (CH, $C_{22}$), 56.7 (CH, $C_{21}$);

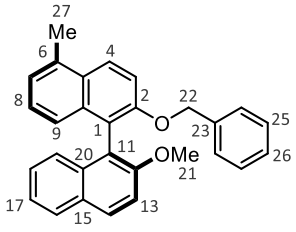
FTIR (neat) $\nu/cm^{-1}$ = 3062, 3033, 3009, 2935, 2837, 1612, 1591, 1498, 1461, 1432, 1395, 1323, 1253, 1191, 1027;

HRMS ($ESI^+$): calculated for $C_{28}H_{21}O_2Br_2Na^+$ = 491.0617, mass found = 491.0617;

$[\alpha]_D^{25}$ = –71.3 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 10 % $^i$PrOH, 90 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 296 nm, 5 μL injection) $\tau_R$ (minor) = 7.0 min, $\tau_R$ (major) = 9.1 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-5-methyl-1,1'-binaphthalene, 270**




**270**

**Asymmetric:** According to **General Procedure C** with **RJA46** (63.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24

ethyl acetate/petrol 40-60 afforded the title compound **270** as a white solid (46.1 mg, 55 %, 96:4 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA46** (76.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **270** as a white solid (62.6 mg, 78 %).

Melting point: 136-137 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.10 (d, *J* = 9.2 Hz, 1H, $H_4$), 8.01 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.90 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.47 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.46 (d, *J* = 9.2 Hz, 1H, $H_3$), 7.33 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{17}$), 7.22 (ddd, *J* = 8.1, 6.6, 1.3 Hz, 1H, $H_{18}$), 7.19-7.14 (m, 5H, $H_8$, $H_{19,}$ $H_{25}$ and $H_{26}$), 7.12 (d, *J* = 6.7 Hz, 1H, $H_9$), 7.07 (d, *J* = 8.4 Hz, 1H, $H_7$), 7.04-6.98 (m, 2H, $H_{24}$), 5.10 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.06 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.77 (s, 3H, $H_{21}$), 2.75 (s, 3H, $H_{27}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 153.9 (Quat, $C_2$ or $C_{12}$), 137.8 (Quat, $C_{23}$), 134.4 (Quat, $C_{Ar}$), 134.4 (Quat, $C_{Ar}$), 134.3 (Quat, $C_{Ar}$), 129.5 (CH, $C_{14}$), 129.3 (Quat, $C_5$ or $C_{15}$), 128.7 (Quat, $C_5$ or $C_{15}$), 128.3 (CH, $C_{25}$), 128.0 (CH, $C_{16}$), 127.4 (CH, $C_{26}$), 126.9 (CH, $C_{24}$), 126.4 (CH, $C_9$ or $C_{18}$), 126.3 (CH, $C_9$ or $C_{18}$), 125.6 (2 x CH, $C_4$ and $C_8$), 124.8 (CH, $C_{19}$), 124.1 (CH, $C_7$), 123.6 (CH, $C_{17}$), 121.4 (Quat, $C_1$), 119.9 (Quat, $C_{11}$), 115.8 (CH, $C_3$), 114.0 (CH, $C_{13}$), 71.2 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$), 19.8 ($CH_3$, $C_{27}$);

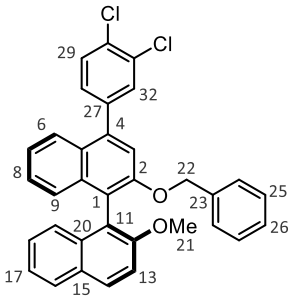
FTIR (neat) $\nu$/cm$^{-1}$ = 3061, 3033, 2935, 2837, 1616, 1593, 1509, 1454, 1432, 1397, 1356, 1253, 1176, 1091;

HRMS (ESI$^+$): calculated for $C_{29}H_{25}O_2^+$ = 405.1849, mass found = 405.1848;

$[\alpha]_D^{25}$ = –62.8 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 5 % $^{i}$PrOH, 95 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 339 nm, 5 μL injection) $\tau_R$ (major) = 4.8 min, $\tau_R$ (minor) = 6.2 min.

**(*S*)-2-(Benzyloxy)-4-(3,4-dichlorophenyl)-2'-methoxy-1,1'-binaphthalene, 271**




**271**

**Asymmetric:** According to **General Procedure C** with **245** (89.5 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **271** as a white solid (73.2 mg, 69 %, 93:7 *e.r.*).

**Racemic:** According to **General Procedure D** with **245** (89.5 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **271** as a white solid (106.5 mg, 99 %).

Melting point: 70-72 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.05 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.93 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.84 (d, *J* = 8.3 Hz, 1H, $H_6$), 7.69 (d, *J* = 2.0 Hz, 1H, $H_{32}$), 7.62 (d, *J* = 8.2 Hz, 1H, $H_{29}$), 7.50 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.43 (dd, *J* = 8.2, 2.0 Hz, 1H, $H_{28}$), 7.40-7.24 (m, 6H, $H_3$, $H_7$, $H_8$, $H_{17}$, $H_{18}$ and $H_{19}$), 7.24-7.14 (m, 4H, $H_9$, $H_{25}$ and $H_{26}$), 6.99 (s, 2H, $H_{24}$), 5.10 (d, *J* = 12.4 Hz, 1H, $H_{22B}$), 5.06 (d, *J* = 12.4 Hz, 1H, $H_{22A}$), 3.82 (s, 3H, $H_{21}$):

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 153.4 (Quat, $C_2$ or $C_{12}$), 140.9 (Quat, $C_4$ or $C_{27}$), 138.8 (Quat, $C_4$ or $C_{27}$), 137.4 (Quat, $C_{23}$), 134.7 (Quat, $C_{10}$ or $C_{20}$), 134.1 (Quat, $C_{10}$ or $C_{20}$), 132.6 (Quat, $C_{30}$ or $C_{31}$), 132.1 (CH, $C_{32}$), 131.8 (Quat, $C_{30}$ or $C_{31}$), 130.4 (CH, $C_{29}$), 129.8 (CH, $C_{14}$), 129.6 (CH, $C_{28}$), 129.3 (Quat, $C_{15}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_{16}$), 127.6 (CH, $C_{26}$), 127.4 (Quat, $C_5$), 127.0 (CH, $C_{24}$), 126.6 (CH, $C_8$ or $C_{18}$), 126.6 (CH, $C_8$ or $C_{18}$), 126.1 (CH, $C_{19}$), 125.6 (CH, $C_9$), 125.4 (CH, $C_6$), 124.4 (CH, $C_7$), 123.7 (CH, $C_{17}$), 121.5 (Quat, $C_1$), 119.1 (Quat, $C_{11}$), 117.7 (CH, $C_3$), 113.9 (CH, $C_{13}$), 71.5 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$);

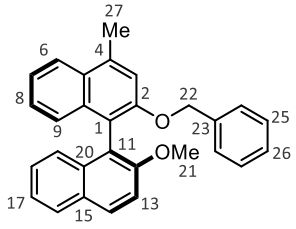
FTIR (neat) $\nu$/cm$^{-1}$ = 3063, 3006, 2935, 2838, 1622, 1592, 1509, 1456, 1422, 1372, 1339, 1252, 1190, 1066, 1027;

HRMS ($CI^+$): calculated for $C_{34}H_{24}Cl_2O_2NH_4^+$ = 552.1492, mass found = 552.1485;

$[\alpha]_D^{25}$ = –54.5 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 10 % $^{i}$PrOH, 90 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 298 nm, 5 μL injection) $\tau_R$ (minor) = 5.8 min, $\tau_R$ (major) = 7.8 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-4-methyl-1,1'-binaphthalene, 272**




**272**

**Asymmetric:** According to **General Procedure C** with **RJA47** (63.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **272** as a white solid (65.6 mg, 81 %, 91:9 *e.r.*).

**Racemic:** According to **General Procedure D** with **RJA47** (63.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:24 ethyl acetate/petrol 40-60 afforded the title compound **272** as a white solid (69.2 mg, 86 %).

Melting point: 133-134 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.02 (d, *J* = 8.4 Hz, 1H, $H_6$), 8.00 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.89 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.46 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.38 (ddd, *J* = 8.3, 6.1, 2.0 Hz, 1H, $H_7$), 7.36-7.30 (m, 2H, $H_3$ and $H_{17}$), 7.29-7.12 (m, 7H, $H_8$, $H_9$, $H_{18}$, $H_{19}$, $H_{25}$ and $H_{26}$), 7.03-6.93 (m, 2H, $H_{24}$), 5.07 (d, *J* = 12.4 Hz, 1H, $H_{22B}$), 5.03 (d, *J* = 12.4 Hz, 1H, $H_{22A}$), 3.76 (s, 3H, $H_{21}$), 2.80 (s, 3H, $H_{27}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.2 (Quat, $C_2$ or $C_{12}$), 153.7 (Quat, $C_2$ or $C_{12}$), 137.8 (Quat, $C_{23}$), 136.0 (Quat, $C_4$), 134.4 (Quat, $C_{10}$ or $C_{20}$), 134.4 (Quat, $C_{10}$ or $C_{20}$), 129.4 (CH, $C_{14}$), 129.3 (Quat, $C_5$ or $C_{15}$), 128.9 (Quat, $C_5$ or $C_{15}$), 128.2 (CH, $C_{25}$), 128.0 (CH, $C_{Ar}$), 127.4 (CH, $C_{Ar}$), 126.9 (CH, $C_{24}$), 126.4 (CH, $C_{Ar}$), 126.2 (CH, $C_{Ar}$), 126.2 (CH, $C_{Ar}$), 125.6 (CH, $C_{Ar}$), 124.3 (CH, $C_6$), 123.7 (CH, $C_7$), 123.5 (CH, $C_{17}$), 119.7 (Quat, $C_1$), 119.1 (Quat, $C_{11}$), 117.5 (CH, $C_3$), 114.0 (CH, $C_{13}$), 71.5 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$), 20.1 ($CH_3$, $C_{27}$);

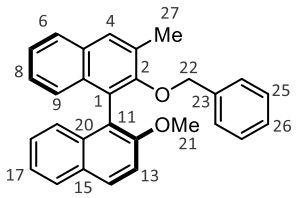
FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 3006, 2936, 2837, 1619, 1593, 1508, 1462, 1378, 1342, 1252, 1168, 1101;

HRMS (ESI$^+$): calculated for $C_{29}H_{25}O_2^+$ = 405.1849, mass found = 405.1850;

$[\alpha]_D^{25}$ = –46.7 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 5 % $^i$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 338 nm, 5 μL injection) $\tau_R$ (major) = 4.6 min, $\tau_R$ (minor) = 5.8 min.

**(*S*)- 2-(Benzyloxy)-2'-methoxy-3-methyl-1,1'-binaphthalene, 273**




**273**

**Asymmetric:** According to **General Procedure C** with **246** (63.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol, 24 h reaction time). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **273** as a white solid (32.4 mg, 40 %, 91:9 *e.r.*).

**Racemic:** According to **General Procedure D** with **246** (63.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol, 24 h reaction time). Purification *via* column chromatography eluting

with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **273** as a white solid (30.3 mg, 37 %).

Melting point: 108-109 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.04 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.91 (d, *J* = 8.1 Hz, 1H, $H_6$), 7.85 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.82 (s, 1H, $H_4$), 7.46 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.39 (ddd, *J* = 8.1, 4.4, 3.5 Hz, 1H, $H_7$), 7.35 (ddd, *J* = 8.2, 6.3, 1.7 Hz, 1H, $H_{17}$), 7.30-7.23 (m, 2H, $H_8$ and $H_{18}$), 7.23-7.20 (m, 2H, $H_9$ and $H_{19}$), 7.19-7.09 (m, 3H, $H_{25}$ and $H_{26}$), 6.78-6.70 (m, 2H, $H_{24}$), 4.58 (d, *J* = 10.7 Hz, 1H, $H_{22A}$), 4.52 (d, *J* = 10.7 Hz, 1H, $H_{22B}$), 3.79 (s, 3H, $H_{21}$), 2.55 (s, 3H, $H_{27}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.1 (Quat, $C_2$ or $C_{12}$), 154.5 (Quat, $C_2$ or $C_{12}$), 137.6 (Quat, $C_{23}$), 134.3 (Quat, $C_{Ar}$), 133.0 (Quat, $C_{Ar}$), 131.8 (Quat, $C_{Ar}$), 131.1 (Quat, $C_{Ar}$), 129.8 (CH, $C_{14}$), 129.5 (CH, $C_4$), 129.2 (Quat, $C_{Ar}$), 128.1 (CH, $C_{25}$), 128.0 (CH, $C_{26}$), 127.9 (CH, $C_{24}$), 127.6 (CH, $C_6$), 127.3 (CH, $C_{16}$), 126.8 (CH, $C_{Ar}$), 125.6 (CH, $C_{Ar}$), 125.5 (CH, $C_{Ar}$), 125.4 (CH, $C_{Ar}$), 125.3 (Quat, $C_1$), 124.8 (CH, $C_7$), 123.7 (CH, $C_{17}$), 119.7 (Quat, $C_{11}$), 113.7 (CH, $C_{13}$), 74.6 ($CH_2$, $C_{22}$), 56.7 ($CH_3$, $C_{21}$), 17.6 ($CH_3$, $C_{27}$);

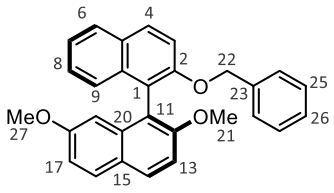
FTIR (neat) $\nu$/cm$^{-1}$ = 3059, 2004, 2931, 2838, 1622, 1593, 1508, 1500, 1458, 1432, 1373, 1265, 1247, 1180, 1147, 1081, 1019;

HRMS ($Cl^+$): calculated for $C_{29}H_{25}O_2^+$ = 405.1849, mass found = 405.1853;

$[\alpha]_D^{25}$ = –76.7 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ODH, 1 % $^{i}$PrOH, 99 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 250 nm, 10 μL injection) $\tau_R$ (major) = 9.0 min, $\tau_R$ (minor) = 11.6 min.

**(*S*)-2'-(Benzyloxy)-2,7-dimethoxy-1,1'-binaphthalene, 274**




**274**

**Asymmetric:** According to **General Procedure C** with **247** (66.5 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **274** as a white solid (44.5 mg, 53 %, 92:8 *e.r.*).

**Racemic:** According to **General Procedure D** with **247** (66.5 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **274** as a white solid (71.8 mg, 86 %).

Melting point: 119-121 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.92 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.91 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.86 (d, *J* = 8.1 Hz, 1H, $H_6$), 7.79 (d, *J* = 8.9 Hz, 1H, $H_{16}$), 7.43 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.36-7.32 (m, 1H, $H_7$), 7.31 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.28-7.20 (m, 2H, $H_8$ and $H_9$), 7.20-7.14 (m, 3H, $H_{25}$ and $H_{26}$), 7.07-6.97 (m, 3H, $H_{17}$ and $H_{24}$), 6.40 (d, *J* = 2.3 Hz, 1H, $H_{19}$), 5.10 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.07 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.75 (s, 3H, $H_{21}$ or $H_{27}$), 3.44 (s, 3H, $H_{21}$ or $H_{27}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 158.2 (Quat, $OC_{Ar}$), 155.7 (Quat, $OC_{Ar}$), 154.1 (Quat, $OC_{Ar}$), 137.8 (Quat, $C_{23}$), 135.6 (Quat, $C_{10}$ or $C_{20}$), 134.1 (Quat, $C_{10}$ or $C_{20}$), 129.6 (Quat, $C_5$), 129.6 (CH, $C_{16}$), 129.3 (CH, $C_{14}$), 129.2 (CH, $C_4$), 128.3 (CH, $C_{25}$), 128.0 (CH, $C_6$), 127.5 (CH, $C_{26}$), 126.9 (CH, $C_{24}$), 126.4 (CH, $C_8$ or $C_9$), 125.6 (CH, $C_8$ or $C_9$), 124.9 (Quat, $C_{15}$), 123.8 (CH, $C_7$), 121.1 (Quat, $C_1$), 118.5 (Quat, $C_{11}$), 116.3 (CH, $C_3$), 116.1 (CH, $C_{17}$), 111.3 (CH, $C_{13}$), 104.0 (CH, $C_{19}$), 71.4 ($CH_2$, $C_{22}$), 56.6 (CH, $C_{21}$ or $C_{27}$), 55 (CH, $C_{21}$ or $C_{27}$);

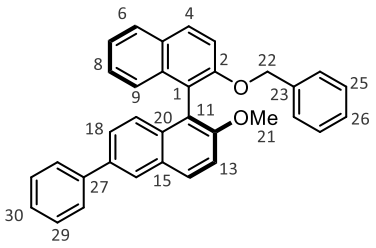
FTIR (neat) $\nu/cm^{-1}$ = 3060, 2936, 2836, 1623, 1592, 1509, 1462, 1426, 1382, 1319, 1221, 1181, 1147, 1093, 1030;

HRMS ($ESI^+$): calculated for $C_{29}H_{25}O_3^+$ = 421.1798, mass found = 421.1795;

$[\alpha]_D^{25}$ = –15.1 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 5 % $^i$PrOH, 95 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 330 nm, 5 μL injection) $\tau_R$ (minor) = 9.0 min, $\tau_R$ (major) = 16.4 min.

**(*S*)-2'-(Benzyloxy)-2-methoxy-6-phenyl-1,1'-binaphthalene, 275**




**275**

**Asymmetric (0.200 mmol scale):** According to **General Procedure C** with **248** (75.7 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol

40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **275** as a white solid (92.8 mg, 99 %, 98:2 *e.r.*).

**Asymmetric (1.00 gram scale):** A Schlenk tube was sequentially charged with *N*-(2,3,4-trifluorobenzyl)quinidinium bromide **192** (145 mg, 0.264 mmol), **248** (1.00 g, 2.64 mmol) and $K_3PO_4$ (5.60 g, 26.4 mmol). The atmosphere was evacuated and backfilled with argon three times. Dichloromethane (2.5 mL) and benzene (10 mL) were added. The suspension was cooled to 0 °C and stirred for 5 minutes. A solution of benzyl iodide in dichloromethane (2.5mL) and benzene (10 mL) was prepared at 0 °C and subsequently added. The resulting suspension was stirred rapidly at a rate of 1000-1400 rpm in the dark at 0 °C for 48 hours. A further catalytic amount of *N*-(2,3,4-trifluorobenzyl)quinidinium bromide **192** (145 mg, 0.264 mmol) was added and the reaction mixture stirred rapidly at a rate of 1000-1400 rpm in the dark at 0 °C for 48 hours. The crude reaction mixture was then filtered through a plug of celite which was subsequently washed with dichloromethane. The filtrate was concentrated under reduced pressure and dissolved in dichloromethane (25 mL) and DDQ (1.80 g, 7.92 mmol) was subsequently added. After stirring at room temperature for 2 hours, saturated aqueous sodium thiosulfate and ethyl acetate were added. The aqueous later was separated and the organic layer was washed twice with saturated aqueous sodium bicarbonate. The organic layer was then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:2 dichloromethane/petrol 40-60 to 1:1 dichloromethane/petrol 40-60 afforded the title compound **275** as a white solid (1.16 g, 96 %, 98:2 *e.r.*). The *e.r.* could be improved *via* the following procedure: A suspension of **275** (1.16 g, 2.49 mmol) in hexane (100 mL) was stirred rapidly at reflux for 5 minutes. Benzene was added dropwise until complete dissolution of the precipitate was observed. The stirrer bar was removed and the solution was allowed to cool to room temperature. The racemic precipitate was isolated *via* filtration and the mother liquor was concentrated under reduced pressure to afford the title compound **275** (1.14 g, 92 %, 99:1 *e.r.*).

**Racemic:** According to **General Procedure D** with **248** (66.5 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.25 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **275** as a white solid (86.1 mg, 92 %).

Melting point: 178-179 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.09 (d, *J* = 1.8 Hz, 1H, $H_{16}$), 8.06 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.93 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.87 (d, *J* = 8.1 Hz, 1H, $H_6$), 7.72-7.66 (m, 2H, $H_{28}$), 7.52-7.41 (m, 5H, $H_3$, $H_{13}$, $H_{18}$ and $H_{29}$), 7.38-7.31 (m, 2H, $H_7$ and $H_{30}$), 7.26 (dd, *J* = 8.5, 1.2 Hz, 1H, $H_9$), 7.24-7.19 (m, 2H, $H_8$ and $H_{19}$), 7.18-7.12 (m, 3H, $H_{25}$ and $H_{26}$), 7.06-6.99 (m, 2H, $H_{24}$), 5.11 (d, *J* = 12.7 Hz, 1H, $H_{22B}$), 5.07 (d, *J* = 12.7 Hz, 1H, $H_{22A}$), 3.78 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.3 (Quat, $C_2$ or $C_{12}$), 154.2 (Quat, $C_2$ or $C_{12}$), 141.4 (Quat, $C_{27}$), 137.7 (Quat, $C_{23}$), 136.3 (Quat, $C_{17}$), 134.2 (Quat, $C_{10}$ or $C_{20}$), 133.5 (Quat, $C_{10}$ or $C_{20}$), 129.9 (CH, $C_{14}$), 129.6 (Quat, $C_5$ or $C_{15}$), 129.5 (Quat, $C_5$ or $C_{15}$), 129.4 (CH, $C_4$), 128.9 (CH, $C_{29}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_6$), 127.5 (CH, $C_{26}$), 127.3 (CH, $C_{28}$), 127.1 (CH, $C_{30}$), 126.9 (CH, $C_{24}$), 126.5 (CH, $C_9$), 126.2 (CH, $C_{Ar}$), 126.1 (CH, $C_{Ar}$), 125.9 (CH, $C_{16}$), 125.5 (CH, $C_{Ar}$), 123.9 (CH, $C_7$), 120.8 (CH, $C_1$), 119.5 (CH, $C_{11}$), 116.3 (CH, $C_3$), 114.4 (CH, $C_{13}$), 71.4 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$);

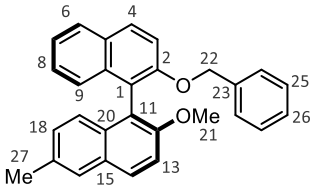
FTIR (neat) $\nu$/cm$^{-1}$ = 3060, 6030, 2934, 2838, 1622, 1592, 1478, 1454, 1330, 1252, 1176, 1093, 1019;

HRMS (EI$^+$): calculated for $C_{34}H_{26}O_2^+$ = 466.1927, mass found = 466.1922;

$[\alpha]_D^{25}$ = –44.3 (*c* = 1.00, $CHCl_3$, at 99:1 *e.r.*);

Chiral HPLC: (Chiralpak ADH, 30 % $^{i}$PrOH, 70 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 256 nm, 5 μL injection) $\tau_R$ (major) = 8.4 min, $\tau_R$ (minor) = 17.4 min.

**(*S*)-2'-(Benzyloxy)-2-methoxy-6-methyl-1,1'-binaphthalene, 276**




**276**

**Asymmetric:** According to **General Procedure C** with **249** (63.3 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **276** as a white solid (67.8 mg, 84 %, 97:3 *e.r.*).

**Racemic:** According to **General Procedure D** with **249** (63.3 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **276** as a white solid (57.0 mg, 71 %).

Melting point: 98-99 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.93 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.92 (d, *J* = 9.0 Hz, 1H, $H_4$), 7.87 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.68 (s, 1H, $H_{16}$), 7.44 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.43 (d, *J* = 9.0 Hz, 1H, $H_3$), 7.34 (ddd, *J* = 8.1, 6.4, 1.6 Hz, 1H, $H_7$), 7.26-7.15 (m, 5H, $H_8$, $H_9$, $H_{25}$ and $H_{26}$), 7.09-7.05 (m, 2H, $H_{18}$ and

$H_{19}$), 7.05-6.99 (m, 2H, $H_{24}$), 5.09 (d, *J* = 12.6 Hz, 1H, $H_{22B}$), 5.05 (d, *J* = 12.6 Hz, 1H, $H_{22A}$), 3.75 (s, 3H, $H_{21}$), 2.48 (s, 3H, $H_{27}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.6 (Quat, $C_2$ or $C_{12}$), 154.2 (Quat, $C_2$ or $C_{12}$), 137.8 (Quat, $C_{23}$), 134.3 (Quat, $C_{17}$), 133.0 (Quat, $C_{10}$ or $C_{20}$), 132.4 (Quat, $C_{10}$ or $C_{20}$), 129.6 (Quat, $C_5$ or $C_{15}$), 129.5 (Quat, $C_5$ or $C_{15}$), 129.3 (CH, $C_{19}$), 128.8 (2 x CH, $C_4$ and $C_{14}$), 128.3 (CH, $C_{25}$), 128.0 (CH, $C_6$), 127.4 (CH, $C_{26}$), 127.0 (CH, $C_{16}$), 126.9 (CH, $C_{24}$), 126.4 (CH, $C_8$), 125.6 (CH, $C_9$), 125.4 (CH, $C_{18}$), 123.9 (CH, $C_7$), 121.2 (Quat, $C_1$), 119.5 (Quat, $C_{11}$), 116.5 (CH, $C_3$), 114.2 (CH, $C_{13}$), 71.4 ($CH_2$, $C_{22}$), 56.8 ($CH_3$, $C_{21}$), 21.5 ($CH_3$, $C_{27}$);

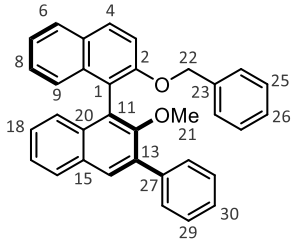
FTIR (neat) $\nu/cm^{-1}$ = 3061, 3032, 2935, 2837, 1621, 1594, 1483, 1434, 1371, 1330, 1263, 1221, 1149;

HRMS ($ESI^+$): calculated for $C_{29}H_{25}O_2^+$ = 405.1849, mass found = 405.1836;

$[\alpha]_D^{25}$ = –37.0 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak IC, 1 % $^i$PrOH, 99 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 337 nm, 5 μL injection) $\tau_R$ (major) = 9.3 min, $\tau_R$ (minor) = 14.6 min.

**(*S*)- 2'-(Benzyloxy)-2-methoxy-3-phenyl-1,1'-binaphthalene, 277**




**277**

**Asymmetric:** According to **General Procedure C** with **250** (75.7 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol)

in benzene (1.0 mL); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **277** as a white solid (56.9 mg, 61 %, 97:3 *e.r.*).

**Racemic:** According to **General Procedure D** with **250** (75.7 mg, 0.200 mmol), tetrabutylammonium bromide (6.4 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 7.5 mmol), dichloromethane (2.0 mL), benzyl bromide (72 μL, 2.3 mmol); then dichloromethane (2.0 mL), DDQ (136 mg, 0.60 mmol). Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **277** as a white solid (79.1 mg, 85 %).

Melting point: 157-159 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.02 (s, 1H, $H_{14}$), 7.98 (d, *J* = 8.9 Hz, 1H, $H_4$), 7.95 (d, *J* = 7.9 Hz, 1H, $H_6$), 7.90 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.82-7.76 (m, 2H, $H_{28}$), 7.53-7.46 (m, 3H, $H_{29}$ and $H_{30}$), 7.46-7.36 (m, 3H, 3 x $H_{Ar}$), 7.35-7.29 (m, 2H, 2 x $H_{Ar}$), 7.26 (td, *J* = 7.1, 1.3 Hz, 1H, $H_{Ar}$), 7.22-7.16 (m, 4H, $H_{25}$, $H_{26}$ and $H_{Ar}$), 7.13-7.04 (m, 2H, $H_{24}$), 5.19 (d, *J* = 12.5 Hz, 1H, $H_{22A}$), 5.12 (d, *J* = 12.5 Hz, 1H, $H_{22B}$), 3.13 (s, 3H, $H_{21}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.3 (Quat, $C_2$ or $C_{12}$), 154.2 (Quat, $C_2$ or $C_{12}$), 139.1 (Quat, $C_{23}$), 137.6 (Quat, $C_{27}$), 135.2 (Quat, $C_{Ar}$), 134.3 (Quat, $C_{Ar}$), 133.6 (Quat, $C_{Ar}$), 131.0 (Quat, $C_{Ar}$), 130.4 (CH, $C_{14}$), 129.6 (CH, $C_4$), 129.5 (CH, $C_{28}$), 129.5 (Quat, $C_{Ar}$), 128.3 (CH, $C_{29}$), 128.3 (CH, $C_{25}$), 128.1 (CH, $C_6$), 128.1 (CH, $C_{16}$), 127.5 (CH, $C_{Ar}$), 127.3 (CH, $C_{Ar}$), 126.9 (CH, $C_{24}$), 126.7 (CH, $C_{Ar}$), 126.2 (CH, $C_{Ar}$), 125.9 (CH, $C_{Ar}$), 125.8 (Quat, $C_1$), 125.6 (CH, $C_{Ar}$), 125.0 (CH, $C_{Ar}$), 123.9 (CH, $C_{Ar}$), 120.9 (CH, $C_{11}$), 115.9 (CH, $C_3$), 71.3 ($CH_2$, $C_{22}$), 60.6 ($CH_3$, $C_{21}$);

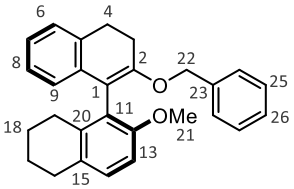
FTIR (neat) $\nu$/cm$^{-1}$ = 3058, 2933, 2868, 2831, 1622, 1592, 1508, 1497, 1444, 1405, 1371, 1266, 1246, 1220, 1147, 1088, 1038, 1018;

HRMS ($EI^+$): calculated for $C_{34}H_{26}O_2^+$ = 466.1927, mass found = 466.1930;

$[\alpha]_D^{25}$ = +1.3 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 30 % $^i$PrOH, 70 % hexane, 1.0 mL $min^{-1}$, $\lambda$ = 281 nm, 10 μL injection) $\tau_R$ (major) = 8.3 min, $\tau_R$ (minor) = 4.3 min.

**(*S*)-2-(Benzyloxy)-2'-methoxy-3,4,5',6',7',8'-hexahydro-1,1'-binaphthalene, 278**




**278**

**Asymmetric:** According to **General Procedure C** with **251** (61.2 mg, 0.200 mmol), *N*-(2,3,4-trifluoro-benzyl) quinidinium bromide **192** (11 mg, 0.020 mmol), $K_3PO_4$ (425 mg, 2.00 mmol), dichloromethane (0.40 mL), benzene (0.60 mL), benzyl iodide (131 mg, 0.60 mmol) in benzene (1.0 mL); omitting the DDQ oxidation. Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **278** as a white solid (56.2 mg, 82 %, 60:40 *e.r.*).

**Racemic:** According to **General Procedure D** with **251** (368 mg, 1.20 mmol), tetrabutylammonium bromide (46 mg, 0.12 mmol), $K_3PO_4$ (2.55 g, 12.0 mmol), dichloromethane (12 mL), benzyl bromide (428 μL, 3.60 mmol); omitting the DDQ oxidation. Purification *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:19 ethyl acetate/petrol 40-60 afforded the title compound **278** as a white solid (389 mg, 82 %).

Melting point: 68-71 °C (ethyl acetate/petrol 40-60);

$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.30-7.20 (m, 3H, $H_6$ and $H_{25}$), 7.16-7.11 (m, 3H, $H_7$ and $H_{24}$), 7.09 (d, *J* = 8.4 Hz, 1H, $H_{14}$), 7.05-6.96 (m, 2H, $H_8$ and $H_{26}$), 6.79 (d, *J* = 8.4 Hz, 1H, $H_{13}$), 6.52 (dd, *J* = 6.9,

2.2 Hz, 1H, $H_9$), 4.81 (d, *J* = 12.3 Hz, 1H, $H_{22A}$), 4.75 (d, *J* = 12.3 Hz, 1H, $H_{22B}$), 3.69 (s, 3H, $H_{21}$), 3.05-2.95 (m, 2H, $H_4$), 2.78 (t, *J* = 6.3 Hz, 2H, $H_{16}$ or $H_{19}$), 2.67-2.53 (m, 3H, $H_{16}$ or $H_{19}$ and $H_{3A}$), 2.32 (dt, *J* = 17.0, 6.1 Hz, 1H, $H_{3B}$), 1.80-1.55 (m, 4H, $H_{17}$ and $H_{18}$);

$^{13}C$ NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.7 (Quat, $C_2$ or $C_{12}$), 153.2 (Quat, $C_2$ or $C_{12}$), 138.3 (Quat, $C_{23}$), 137.9 (Quat, $C_{Ar}$), 136.4 (Quat, $C_{Ar}$), 132.9 (Quat, $C_{Ar}$), 129.6 (Quat, $C_{Ar}$), 128.8 (CH, $C_{14}$), 128.3 (CH, $C_{25}$), 127.5 (CH, $C_6$), 127.3 (CH, $C_{24}$), 126.8 (CH, $C_{Ar}$), 126.6 (CH, $C_{Ar}$), 124.9 (CH, $C_{Ar}$), 124.9 (Quat, $C_1$), 123.5 (CH, $C_9$), 114.5 (Quat, $C_{11}$), 108.5 (CH, $C_{13}$), 70.2 ($CH_2$, $C_{22}$), 55.9 ($CH_3$, $C_{21}$), 29.6 ($CH_2$, $C_{16}$ or $C_{19}$), 29.2 ($CH_2$, $C_4$), 26.9 ($CH_2$, $C_3$), 25.3 ($CH_2$, $C_{16}$ or $C_{19}$), 23.4 ($CH_2$, $C_{17}$ or $C_{18}$), 23.3 ($CH_2$, $C_{17}$ or $C_{18}$);

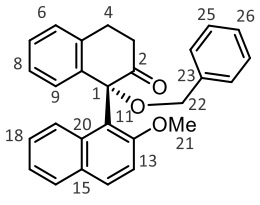
FTIR (neat) $\nu/cm^{-1}$ = 3062, 3029, 2931, 2883, 2857, 2832, 1639, 1592, 1570, 1463, 1423, 1377, 1336, 1277, 1219, 1204, 1158, 1114, 1090, 1046, 1025;

HRMS ($ESI^+$): calculated for $C_{28}H_{28}O_2Na^+$ = 419.1982, mass found = 419.1975;

$[\alpha]_D^{25}$ = –9.1 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ODH, 1 % $^i$PrOH, 99 % hexane, 0.50 mL $min^{-1}$, $\lambda$ = 277 nm, 5 μL injection) $\tau_R$ (major) = 15.8 min, $\tau_R$ (minor) = 14.1 min.

**(*S*)-1-(Benzyloxy)-2'-methoxy-3,4-dihydro-[1,1'-binaphthalen]-2(1*H*)-one, 174**




**174**

**Asymmetric:** Sodium bicarbonate (26.8 mg, 0.320 mmol) was added to a solution of **166** (50.2 mg, 0.128 mmol, 96:4 *e.r.*) in dichloromethane (1.5 mL). After cooling to 0 °C, *meta*-chloroperbenzoic acid (75 % w/w, 58.9 mg, 0.256 mmol) was added and the resulting

suspension was stirred at 0 °C for 1 hour. The reaction was then quenched with saturated aqueous sodium thiosulfate and dichloromethane was subsequently added. The organic layer was separated and the aqueous layer was extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The residue was then dissolved in dichloromethane (1.5 mL) and ytterbium(III) triflate (7.9 mg, 0.013 mmol) was subsequently added. After stirring at room temperature for 15 minutes Merck Kieselgel Silica (1 g) was added. The solvent was removed under reduced pressure and purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/ petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 afforded the title compound **174** as a white solid (49.2 mg, 94 %, 93:7 *e.r.*).

**Racemic:** Sodium bicarbonate (42.0 mg, 0.500 mmol) was added to a solution of **166** (78.5 mg, 0.20 mmol) in dichloromethane (2.0 mL). After cooling to 0 °C, *meta*-chloroperbenzoic acid (75 % w/w, 92.0 mg, 0.400 mmol) was added and the resulting suspension was stirred at 0 °C for 1 hour. The reaction was then quenched with saturated aqueous sodium thiosulfate and dichloromethane was subsequently added. The organic layer was separated and the aqueous layer was extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The residue was then dissolved in dichloromethane (2.0 mL) and ytterbium(III) triflate (12.4 mg, 0.0200 mmol) was subsequently added. After stirring at room temperature for 15 minutes Merck Kieselgel Silica (1 g) was added. The solvent was removed under reduced pressure and purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/ petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 afforded the title compound **174** as a white solid (77.6 mg, 95 %).

Melting point: 103-104 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.78-8.71 (m, 1H, $H_{19}$), 7.89 (d, *J* = 8.9 Hz, 1H, $H_{14}$), 7.83-7.77 (m, 1H, $H_{16}$), 7.52 (dd, *J* = 7.7, 1.3 Hz, 1H, $H_9$), 7.36-7.22 (m, 8H, $H_{13}$, $H_{17}$, $H_{18}$, $H_{24}$, $H_{25}$, $H_{26}$), 7.21 (dd, *J* = 7.2, 1.3 Hz, 1H, $H_6$), 7.19-7.15 (m, 1H, $H_7$), 7.13 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H, $H_8$), 4.70 (d, *J* = 11.3 Hz, 1H, $H_{22B}$), 4.40 (d, *J* = 11.3 Hz, 1H, $H_{22A}$), 3.75 (s, 3H, $H_{21}$), 3.13 (ddd, *J* = 14.9, 7.0, 5.7 Hz, 1H, $H_{4B}$), 2.95 (ddd, *J* = 14.8, 7.4, 5.7 Hz, 1H, $H_{4A}$), 2.86 (ddd, *J* = 16.7, 7.1, 5.7 Hz, 1H, $H_{3B}$), 2.65 (ddd, *J* = 16.7, 7.4, 5.7 Hz, 1H, $H_{3A}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 204.2 (Quat, $C_2$), 155.5 (Quat, $C_{12}$), 139.6 (Quat, $C_{23}$), 138.6 (Quat, $C_5$ or $C_{10}$), 138.2 (Quat, $C_5$ or $C_{10}$), 133.9 (Quat, $C_{20}$), 131.4 (CH, $C_{14}$), 130.4 (Quat, $C_{15}$), 129.0 (CH, $C_9$), 128.6 (CH, $C_{16}$), 128.2 (2 x CH, $C_{24}$ and $C_{25}$), 128.1 (CH, $C_7$), 127.8 (CH, $C_6$), 127.4 (CH, $C_{26}$), 126.6 (CH, $C_8$ or $C_{18}$), 126.6 (CH, $C_8$ or $C_{18}$), 125.9 (CH, $C_{17}$), 123.8 (CH, $C_{19}$), 119.6 (Quat, $C_{11}$), 114.1 (CH, $C_{13}$), 85.3 (CH, $C_1$), 68.1 ($CH_2$, $C_{22}$), 56.2 ($CH_3$, $C_{21}$), 37.2 ($CH_2$, $C_3$), 28.2 ($CH_2$, $C_4$);

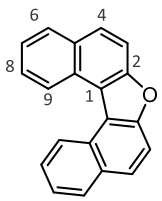
FTIR (neat) $\nu$/cm$^{-1}$ = 3062, 3030, 2939, 2841, 1720, 1621, 1596, 1509, 1454, 1375, 1270, 1213, 1130;

HRMS ($ESI^+$): calculated for $C_{28}H_{24}O_3Na^+$ = 431.1618, mass found = 431.1612;

$[\alpha]_D^{25}$ = +96.9 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 5 % $^{i}$PrOH, 95 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 284nm, 5 $\mu$L injection) $\tau_R$ (minor) = 21.0 min, $\tau_R$ (major) = 23.6 min.

**Dinaphtho[2,1-*b*:1',2'-d]furan 289**




**289**

Sodium bicarbonate (42.0 mg, 0.500 mmol) was added to a solution of **166** (78.5 mg, 0.20 mmol) in dichloromethane (2.0 mL). After cooling to 0 °C, *meta*-chloroperbenzoic acid (75 % w/w, 92.0 mg, 0.400 mmol) was added and the resulting suspension was stirred at 0 °C for 1 hour. The reaction was then quenched with saturated aqueous sodium thiosulfate and dichloromethane was subsequently added. The organic layer was separated and the aqueous layer was extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The residue was then dissolved in dichloromethane (2.0 mL) and boron trifluoride diethyl etherate (40 µL, 0.32 mmol) was subsequently added. After stirring at room temperature for 5 minutes, saturated aqueous sodium bicarbonate was added. The organic phase was separated and the aqueous phase was extracted twice with dichloromethane. The combined organic extracts were washed twice with saturated aqueous sodium bicarbonate, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 dichloromethane/ petrol 40-60 afforded the title compound **289** as a white solid (32.4 mg, 60 %). The spectral data matched that previously reported in the literature.[155]

Melting point: 149-150 °C (dichloromethane/petrol 40-60);

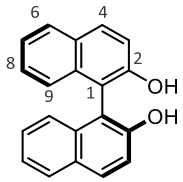
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 9.17 (dd, *J* = 8.5, 1.1 Hz, 2H, $H_9$), 8.08 (dd, *J* = 8.1, 1.3 Hz, 2H, $H_6$), 7.96 (d, *J* = 8.8 Hz, 2H, $H_4$), 7.84 (d, *J* = 8.9 Hz, 2H, $H_3$), 7.76 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 2H, $H_8$), 7.60 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 2H, $H_7$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 154.5 (Quat, $C_2$), 131.3 (Quat, $C_{10}$), 129.6 (CH, $C_6$), 128.7 (Quat, $C_5$), 128.4 (CH, $C_4$), 126.3 (CH, $C_8$), 125.7 (CH, $C_9$), 124.5 (CH, $C_7$), 119.5 (Quat, $C_1$), 112.8 (CH, $C_3$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3051, 3011, 2955, 2924, 2852, 1619, 1579, 1529, 1441, 1383, 1264, 1236, 1154, 1034, 1005;

HRMS ($CI^+$): calculated for $C_{20}H_{12}O^+$ = 269.0961, mass found = 269.0964.

**(*S*)-[1,1'-Binaphthalene]-2,2'-diol, 168**




**168**

**Asymmetric:** In analogy to a modified literature procedure,[156] a solution of **167** (78.1 mg, 0.20 mmol, 96:4 *e.r.*) in anhydrous dichloromethane (3.5 mL) was cooled to –20 °C and stirred for 15 minutes. Subsequently, $BBr_3$ (1.0 M in dichloromethane, 0.80 mL, 0.80 mmol) was added. The reaction mixture was warmed to room temperature and stirred for one hour. After cooling to 0 °C, the reaction was quenched *via* drowise addition of water ensuring that the rate of addition of water was such that effervescence was kept to a minimum. Dichloromethane was then added and the organic layer was separated. The aqueuous layer was subsequently extracted twice with dichloromethane. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 0:1 ethyl acetate/petrol 40-60 to 1:4 ethyl acetate/petrol 40-60 afforded the title compound **168** as a white solid (56.4 mg, 99 %, 96:4 *e.r.*). The spectral data matched that previously reported in the literature and that of commercially available *(S)*-BINOL.[157]

**Racemic:** An authentic sample of racemic BINOL **168** was commercially available from Acros Organics.

Melting point: 199-201 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 7.97 (d, *J* = 9.0 Hz, 2H, $H_4$), 7.89 (dd, *J* = 7.7, 1.4 Hz, 2H, $H_6$), 7.38 (d, *J* = 9.0 Hz, 2H, $H_3$), 7.38 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 2H, $H_7$), 7.31 (ddd, *J* = 8.2, 6.8, 1.4 Hz, 2H, $H_8$), 7.16 (dd, *J* = 8.4, 1.3 Hz, 2H, $H_9$), 5.05 (s, 2H, OH);

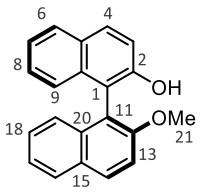
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 152.9 (Quat, $C_2$), 133.5 (Quat, $C_{10}$), 131.6 (CH, $C_4$), 129.6 (Quat, $C_5$), 128.5 (CH, $C_6$), 127.6 (CH, $C_8$), 124.3 (CH, $C_7$), 124.2 (CH, $C_9$), 117.9 (CH, $C_3$), 110.9 (CH, $C_1$);

LRMS ($ESI^-$): calculated for $C_{20}H_{13}O_2^-$ = 285, mass found = 285;

$[\alpha]_D^{25}$ = –31.9 (*c* = 1.00, THF);

Chiral HPLC: (Chiralpak ADH, 40 % $^{i}$PrOH, 60 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 335 nm, 5 μL injection) $\tau_R$ (minor) = 8.9 min, $\tau_R$ (major) = 10.8 min.

**(*S*)-2'-Methoxy-[1,1'-binaphthalen]-2-ol, 281**




**281**

**Asymmetric:** In analogy to a modified literature procedure,[158] a solution of **167** (78.1 mg, 0.20 mmol, 96:4 *e.r.*) in degassed 9:1 methanol/ethyl acetate (1 mL) was added to Pd/C (10 wt %, 28 mg). The reaction mixture was stirred under an atmosphere of hydrogen (balloon) for 3 hours. The reaction mixture was then filtered through a plug of celite which was subsequently washed with ethyl acetate. The filtrate was concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **281** (57.7 mg, 96 %, 96:4 *e.r.*) as a white solid. The spectral data matched that previously reported in the literature.[159]

**Racemic**: In analogy to a modified literature procedure,[158] a solution of **167** (281 mg, 0.720 mmol) in degassed 9:1 methanol/ethyl acetate (1 mL) was added to palladium on carbon (10 wt %, 100 mg). The reaction mixture was stirred under an atmosphere of hydrogen (balloon) for 3 hours. The reaction mixture was then filtered through a plug of celite which was subsequently washed with ethyl acetate. The filtrate was concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with 1:9 ethyl acetate/petrol 40-60 afforded the title compound **281** (204 mg, 94 %) as a white solid. The spectral data matched that previously reported in the literature.[159]

Melting point: 107-108 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.06 (d, *J* = 9.1 Hz, 1H, $H_{14}$), 7.93 (d, *J* = 8.9 Hz, 1H, $H_4$), 7.92 (d, *J* = 8.2 Hz, 1H, $H_{16}$), 7.89 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.49 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.38 (d, *J* = 8.9 Hz, 1H, $H_3$), 7.42-7.23 (m, 4H, $H_7$, $H_8$, $H_{17}$ and $H_{18}$), 7.21 (d, *J* = 8.6 Hz, 1H, $H_9$), 7.08 (d, *J* = 8.4 Hz, 1H, $H_{19}$), 4.96 (s, 1H, OH), 3.81 (s, 3H, $H_{21}$);

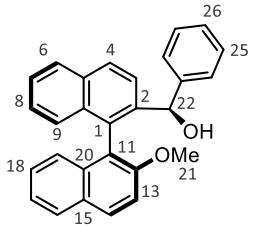
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 156.1 (Quat, $C_{12}$), 151.3 (Quat, $C_2$), 134.1 (Quat, $C_{10}$ or $C_{20}$), 133.9 (Quat, $C_{10}$ or $C_{20}$), 131.2 (CH, $C_{14}$), 129.9 (CH, $C_4$), 129.5 (Quat, $C_5$ or $C_{15}$), 129.2 (Quat, $C_5$ or $C_{15}$), 128.3 (CH, $C_6$ or $C_{16}$), 128.3 (CH, $C_6$ or $C_{16}$), 127.4 (CH, $C_8$ or $C_{18}$), 126.5 (CH, $C_8$ or $C_{18}$), 125.0 (CH, $C_9$ or $C_{19}$), 124.9 (CH, $C_9$ or $C_{19}$), 124.3 (CH, $C_{17}$), 123.3 (CH, $C_7$), 117.6 (CH, $C_3$), 115.4 (Quat, $C_1$ or $C_{11}$), 115.1 (Quat, $C_1$ or $C_{11}$), 113.9 (CH, $C_{13}$), 56.8 ($CH_3$, $C_{21}$);

LRMS ($ESI^-$): calculated for $C_{21}H_{15}O_2^-$ = 299, mass found = 299;

$[\alpha]_D^{25}$ = –44.1 (*c* = 1.00, acetone);

Chiral HPLC: (Chiralpak ADH, 10 % $^{i}$PrOH, 90 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 335 nm, 5 μL injection) $\tau_R$ (major) = 13.1 min, $\tau_R$ (minor) = 19.1 min.

**(*R*)-((*S*)-2'-Methoxy-[1,1'-binaphthalen]-2-yl)(phenyl)methanol, 282**




**282**

**Asymmetric:** In analogy to a modified literature procedure,[93] *n*-butyllithium (2.5 M solution in hexanes, 0.16 mL, 0.40 mmol) was added to a suspension of **167** (78.1 mg, 0.20 mmol, 96:4 *e.r.*) in anhydrous diethyl ether (2 mL). After stirring at room temperature for 18 hours, the reaction mixture was quenched with saturated aqueous ammonium chloride. Dichloromethane and $H_2O$ were added and the organic layer was then separated. The aqueous layer was extracted twice with dichloromethane. Following this, the combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residiue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 1:4 ethyl acetate/ petrol 40-60 afforded the title compound **282** as a white solid (65.8 mg, 85 %, 96:4 *e.r.*).

**Racemic:** In analogy to a modified literature procedure,[93] *n*-butyllithium (2.5 M solution in hexanes, 0.16 mL, 0.40 mmol) was added to a suspension of **167** (78.1 mg, 0.20 mmol) in anhydrous diethyl ether (2 mL). After stirring at room temperature for 18 hours, the reaction mixture was quenched with saturated aqueous ammonium chloride. Dichloromethane and $H_2O$ were added and the organic layer was then separated. The aqueous layer was extracted twice with dichloromethane. Following this, the combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:9 ethyl acetate/petrol 40-60 to 1:4 ethyl acetate/ petrol 40-60 afforded the title compound **282** as a white solid (53.3 mg, 68 %).

Melting point: 73-75 °C (ethyl acetate/petrol 40-60);

$^{1}$H NMR (500 MHz, $CDCl_3$) $\delta_H$ = 8.05 (d, *J* = 9.0 Hz, 1H, $H_{14}$), 7.92 (d, *J* = 8.1 Hz, 1H, $H_{16}$), 7.91 (d, *J* = 8.2 Hz, 1H, $H_6$), 7.89 (d, *J* = 8.2 Hz, 1H, $H_4$), 7.52 (d, *J* = 9.0 Hz, 1H, $H_{13}$), 7.45 (d, *J* = 8.6 Hz, 1H, $H_3$), 7.46-7.43 (m, 1H, $H_7$), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H, $H_{17}$), 7.28-7.14 (m, 7H, $H_8$, $H_{18}$, $H_{24}$, $H_{25}$ and $H_{26}$), 7.13 (d, *J* = 8.4 Hz, 1H, $H_9$), 7.06 (d, *J* = 8.5 Hz, 1H, $H_{19}$), 5.66 (s, 1H, $H_{22}$), 3.82 (s, 3H, $H_{21}$), 2.96 (br s, 1H, OH);

$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta_C$ = 154.6 (Quat, $C_{12}$), 142.7 (Quat, $C_{23}$), 141.1 (Quat, $C_2$), 134.4 (Quat, $C_{20}$), 133.3 (Quat, $C_5$), 132.9 (Quat, $C_{10}$), 132.4 (Quat, $C_1$), 130.3 (CH, $C_{14}$), 129.5 (Quat, $C_{15}$), 128.9 (CH, $C_4$), 128.2 (2 x CH, $C_8$ and $C_{16}$), 128.1 (CH, $C_{25}$), 127.0 (CH, $C_{18}$), 126.8 (CH, $C_9$), 126.8 (CH, $C_{26}$), 126.4 (CH, $C_6$), 126.2 (CH, $C_{24}$), 126.1 (CH, $C_7$), 125.6 (CH, $C_3$), 125.6 (CH, $C_{19}$), 124.2 (CH, $C_{17}$), 121.3 (Quat, $C_{11}$), 113.9 (CH, $C_{13}$), 73.4 (CH, $C_{22}$), 57.1 ($CH_3$, $C_{21}$);

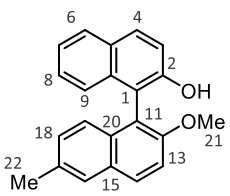
FTIR (neat) $\nu$/cm$^{-1}$ = 3046, 3060, 3028, 2936, 2839, 1621, 1592, 1508, 1493, 1462, 1431, 1395, 1331, 1265, 1120, 1019;

HRMS ($ESI^+$): calculated for $C_{28}H_{22}O_2Na^+$ = 413.1512, mass found = 413.1509;

$[\alpha]_D^{25}$ = +234 (*c* = 1.00, $CHCl_3$);

Chiral HPLC: (Chiralpak ADH, 10 % $^{i}$PrOH, 90 % hexane, 1.0 mL min$^{-1}$, $\lambda$ = 283 nm, 5 μL injection) $\tau_R$ (minor) = 15.4 min, $\tau_R$ (major) = 17.5 min.

**2'-Methoxy-6'-methyl-[1,1'-binaphthalen]-2-ol, 392**




**392**

In analogy to a modified literature procedure,[160] ammonium formate (473 mg, 7.5 mmol) and Pd/C (10 wt %, 40 mg) were added to a solution of **rac-276** (505 mg, 1.25 mmol) in 9:1 ethyl acetate/methanol in a sealed pressure tube. The suspension was then stirred at 50 °C for 24 h. after cooling to room temperature, the reaction mixture was filtered through celite, washing the filtercake with ethyl acetate, and the filtrate was subsequently washed twice with water and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:2 dichloromethane/petrol 40-60 to 1:1 dichloromethane/petrol 40-60 afforded the title compound **392** as a white solid (379 mg, 97 %).

Melting point: 81-82 °C (dichloromethane/petrol 40-60);

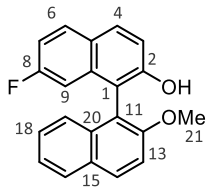
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = .97 (d, *J* = 9.1 Hz, 1H, $H_{14}$), 7.92 (d, *J* = 8.9 Hz, 1H, $H_4$), 7.88 (dd, *J* = 8.1, 0.9 Hz, 1H, $H_6$), 7.69 (d, *J* = 1.8, Hz, 1H, $H_{16}$), 7.45 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.38 (d, *J* = 8.9 Hz, 1H, $H_3$), 7.33 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H, $H_7$), 7.24 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H, $H_8$), 7.14 (dd, *J* = 8.7, 1.7 Hz, 1H, $H_{18}$), 7.12-7.06 (m, 2H, $H_9$ and $H_{19}$), 4.97 (br s, 1H, O*H*), 3.79 (s, 3H, $H_{21}$), 2.49 (s, 3H, $H_{22}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.5 (Quat, $C_{12}$), 151.3 (Quat, $C_2$), 133.9 (Quat, $C_{10}$ or $C_{20}$), 133.9 (Quat, $C_{17}$), 132.3 (Quat, $C_{10}$ or $C_{20}$), 130.4 (CH, $C_{14}$), 129.8 (CH, $C_4$), 129.8 (Quat, $C_5$ or $C_{15}$), 129.7 (CH, $C_{18}$), 129.2 (Quat, $C_5$ or $C_{15}$), 128.2 (CH, $C_6$), 127.2 (CH, $C_{16}$), 126.5 (CH, $C_7$), 125.0 (CH, $C_9$ or $C_{19}$), 124.9 (CH, $C_9$ or $C_{19}$), 123.3 (CH, $C_8$), 117.6 (CH, $C_3$), 115.4 (Quat, $C_1$ or $C_{11}$), 115.3 (Quat, $C_1$ or $C_{11}$), 114.0 (CH, $C_{13}$), 56.8 ($CH_3$, $C_{21}$), 21.5 ($CH_3$, $C_{22}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3490, 3424, 3058, 3017, 2937, 2918, 2839, 1620, 1595, 1515, 1501, 1463, 1379, 1353, 1334, 1300, 1250, 1228, 1147, 1084, 1051;

HRMS (ESI$^-$): calculated for $C_{22}H_{17}O_2^-$ = 313.1234, mass found = 313.1233.

**7-Fluoro-2'-methoxy-[1,1'-binaphthalen]-2-ol, 331**




**331**

In analogy to a modified literature procedure,[158] a solution of **rac-262** (579 mg, 1.42 mmol) in degassed 1:9 methanol/ethyl acetate (1 mL) was added to palladium on carbon (10 wt %, 42 mg). The reaction mixture was stirred under an atmosphere of hydrogen (balloon) for 24 hours. The reaction mixture was then filtered through a plug of celite which was subsequently washed with ethyl acetate. The filtrate was concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:1 dichloromethane/petrol 40-60 to 2:1 dichloromethane/petrol 40-60 afforded the title compound **331** (454 mg, 99 %) as a white solid.

Melting point: 201-202 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.06 (d, *J* = 9.1 Hz, 1H, $H_{14}$), 7.93-7.87 (m, 2H, $H_4$ and $H_{16}$), 7.84 (dd, *J* = 8.9, 5.8 Hz, 1H, $H_6$), 7.48 (d, *J* = 9.1 Hz, 1H, $H_{13}$), 7.39 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H, $H_{17}$), 7.35-7.28 (m, 2H, $H_3$ and $H_{18}$), 7.20-7.15 (m, 1H, $H_{19}$), 7.09 (ddd, *J* = 8.9, 8.3, 2.6 Hz, 1H, $H_7$), 6.67 (dd, *J* = 11.3, 2.6 Hz, 1H, $H_9$), 4.99 (br s, 1H, O*H*), 3.82 (s, 3H, $H_{21}$);

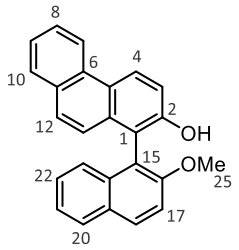
$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 161.7 (Quat, d, *J* = 244.8 Hz, $C_8$), 156.1 (Quat, $C_{12}$), 152.3 (Quat, $C_2$) 135.2 (Quat, d, *J* = 9.4 Hz, $C_{10}$), 133.9 (Quat, $C_{20}$), 131.5 (CH, $C_{14}$), 130.6 (CH, d, *J* = 9.4 Hz, $C_6$), 129.8 (CH, $C_4$), 129.6 (Quat, $C_{15}$), 128.4 (CH, $C_{16}$), 127.6 (CH, $C_{17}$), 126.2 (Quat, $C_5$), 124.7 (CH, $C_{18}$), 124.4 (CH, $C_{19}$), 116.8 (CH, d, *J* = 2.5 Hz, $C_3$), 114.9 (Quat, d, *J* = 5.3 Hz, $C_{11}$), 113.8 (CH, $C_{13}$), 113.5 (CH, d, *J* = 25.4 Hz, $C_7$), 108.5 (CH, d, *J* = 22.1 Hz, $C_9$), 56.7 ($CH_3$, $C_{21}$);

$^{19}$F NMR (376 MHz, $CDCl_3$) $\delta_F$ = –114.0;

FTIR (neat) $\nu$/cm$^{-1}$ = 3492, 3428, 3062, 2840, 1624, 1592, 1508, 1472, 1431, 1378, 1360, 1230, 1200, 1166, 1149, 1135, 1080, 1053, 1021;

HRMS (ESI$^-$): calculated for $C_{21}H_{14}FO_2^-$ = 317.0983, mass found = 317.0981.

**(*S*)-1-(2-Methoxynaphthalen-1-yl)phenanthren-2-ol, 330**




**330**

In analogy to a modified literature procedure,[160] ammonium formate (260 mg, 4.12 mmol) and Pd/C (10 wt %, 105 mg) were added to a solution of **rac-266** (303 mg, 0.687 mmol) in 9:1 ethyl acetate/methanol in a sealed pressure tube. The suspension was then stirred at 50 °C for 48 h. after cooling to room temperature, the reaction mixture was filtered through celite, washing the filtercake with ethyl acetate, and the filtrate was subsequently washed twice with water and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with a gradient from 1:2 dichloromethane/petrol 40-60 to 1:1 dichloromethane/petrol 40-60 afforded the title compound **330** as a white solid (228 mg, 95 %).

Melting point: 123-125 °C (dichloromethane/petrol 40-60);

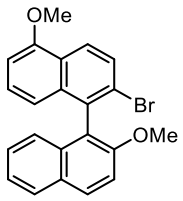
$^1$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.79 (d, *J* = 9.0 Hz, 1H, $H_4$), 8.71 (d, *J* = 8.2 Hz, 1H, $H_7$), 8.08 (d, *J* = 9.1 Hz, 1H, $H_{18}$), 7.93 (dd, *J* = 8.2, 0.9 Hz, 1H, $H_{20}$), 7.81 (dd, *J* = 7.8, 1.3 Hz, 1H, $H_{12}$), 7.67 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H, $H_8$), 7.58-7.47 (m, 4H, $H_3$, $H_9$, $H_{13}$ and $H_{17}$), 7.40 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{21}$), 7.30 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H, $H_{22}$), 7.24-7.18 (m, 1H, $H_{23}$), 7.05 (d, *J* = 9.1 Hz, 1H, $H_{10}$), 4.98 (br s, 1H, O*H*), 3.82 (s, 3H, $H_{25}$);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 156.1 (Quat, $C_{16}$), 152.3 (Quat, $C_2$), 134.2 (Quat, $C_{Ar}$), 132.6 (Quat, $C_{Ar}$), 131.3 (CH, $C_{18}$), 130.9 (Quat, $C_{Ar}$), 130.8 (Quat, $C_{Ar}$), 129.5 (Quat, $C_{Ar}$), 128.6 (CH, $C_{12}$), 128.3 (CH, $C_{20}$), 127.7 (CH, $C_9$), 127.6 (CH, $C_{22}$), 126.8 (CH, $C_8$), 125.7 (CH, $C_{13}$), 124.9 (CH, $C_{23}$), 124.9 (Quat, $C_{Ar}$), 124.5 (CH, $C_4$), 124.4 (CH, $C_{10}$ or $C_{21}$), 124.4 (CH, $C_{10}$ or $C_{21}$), 122.4 (CH, $C_7$), 117.3 (Quat, $C_1$) 116.5 (CH, $C_3$), 115.6 (Quat, $C_{15}$), 113.9 (CH, $C_{17}$), 56.8 ($CH_3$, $C_{25}$);

FTIR (neat) $\nu$/cm$^{-1}$ = 3495, 3424, 3057, 2936, 2839, 1620, 1592, 1529, 1506, 1460, 1431, 1420, 1332, 1306, 1268, 1250, 1214, 1203, 1171, 1146, 1119, 1076, 1057, 1034, 1020;

HRMS (ESI$^-$): calculated for $C_{25}H_{17}O_2^-$ = 349.1234, mass found = 349.1233.

**2-Bromo-2',5-dimethoxy-1,1'-binaphthalene, CDC1**




**CDC1**

*This compound was synthesised and analysed by Dr Craig Campbell*. *N*-bromosuccinimde (522 mg, 2.93 mmol) was added to a stirred solution of **227** (928 mg, 2.93 mmol) in dichloromethane (30 mL). After stirring at room temperature for 3 hours the mixture was quenched with saturated aqueous sodium thiosulfate. The biphasic mixture was then extracted with dichloromethane three times and following this, the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude residue was subsequently dissolved in toluene (30 mL) and DDQ (2.00 g, 8.81 mmol) was then added. After stirring at reflux for 16 h, the reaction mixture was cooled to room temperature and quenched with saturated aqueous sodium thiosulfate. The biphasic mixture was then extracted with dichloromethane three times and following this, the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under

reduced pressure. Purification of the residue *via* column chromatography eluting with 1:3 dichloromethane/petrol 40-60 afforded the title compound **CDC1** as a white solid (836 mg, 73 %).

Melting point: 63-65 °C (dichloromethane/petrol 40-60);

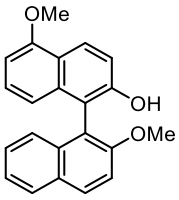
$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.29 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 7.35 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.31-7.23 (m, 1H), 7.18 (t, *J* = 8.1 Hz, 1H), 7.08-7.00 (m, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 4.03 (s, 3H), 3.82 (s, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 155.8, 154.6, 135.4, 134.5, 133.2, 130.1, 129.4, 129.1, 128.1, 127.2, 126.9, 124.8, 124.7, 124.4, 123.9, 123.6, 122.7, 118.8, 114.0, 104.2, 56.9, 55.8;

FTIR (neat) $\nu$/cm$^{-1}$ = 3004, 2957, 2932, 2837, 1618, 1593, 1578, 1509, 1460, 1410, 1357, 1304, 1269, 1221, 1176, 1126, 1076, 1020;

HRMS (ESI$^+$): calculated for $C_{22}H_{18}O_2^+$ = 395.0464, mass found = 395.0459.

**2',5-Dimethoxy-[1,1'-binaphthalen]-2-ol, CDC2**




**CDC2**

*This compound was synthesised and analysed by Dr Craig Campbell*. *n*-Butyllithium (2.5 M solution in hexanes, 0.77 mL, 1.9 mmol) was added to solution of **CDC1** (750 mg, 1.91 mmol) in anhydrous THF (7.5 mL) at -78 °C. After stirring at -78 °C for 30 minutes, triisopropyl borate (0.88 mL, 3.8 mmol) was added. Following this the reaction mixture was allowed to warm to room temperature over night. A solution of sodium hydroxide (2.68 g, 67.0 mmol) in 20%

aqueous hydrogen peroxide (26.5 mL) was subsequently added. After stirring at room temperature for 5 hours, the reaction mixture was quenched with saturated aqueous sodium sulfite. The biphasic mixture was then extracted with dichloromethane three times and following this, the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Purification of the residue *via* column chromatography eluting with dichloromethane afforded the title compound **CDC2** as a white solid (478 mg, 76 %).

Melting point: 80-81 °C (dichloromethane/petrol 40-60);

$^{1}$H NMR (400 MHz, $CDCl_3$) $\delta_H$ = 8.38 (d, *J* = 9.1 Hz, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.97-7.86 (m, 1H), 7.47 (d, *J* = 9.1 Hz, 1H), 7.42-7.32 (m, 2H), 7.29 (ddd, *J* = 8.2, 6.7, 1.4 Hz, 1H), 7.20 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.14 (dd, *J* = 8.5, 7.6 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 1H), 4.93 (s, 1H), 4.02 (s, 3H), 3.81 (s, 3H);

$^{13}$C NMR (101 MHz, $CDCl_3$) $\delta_C$ = 156.0, 155.9, 151.8, 135.0, 134.1, 131.0, 129.4, 128.1, 127.3, 126.7, 125.0, 124.2, 124.0, 121.0, 117.4, 116.4, 115.6, 114.9, 113.8, 101.7, 56.7, 55.5;

FTIR (neat) $\nu$/cm$^{-1}$ = 3493, 3434, 3063, 3003, 2958, 2936, 2838, 1620, 1591, 1464, 1431, 1415, 1333, 1301, 1268, 1252, 1223, 1165, 1149, 1122, 1076, 1052, 1020;

LRMS (ESI$^+$): calculated for $C_{22}H_{19}O_3^+$ = 331.1328, mass found = 331.1328.

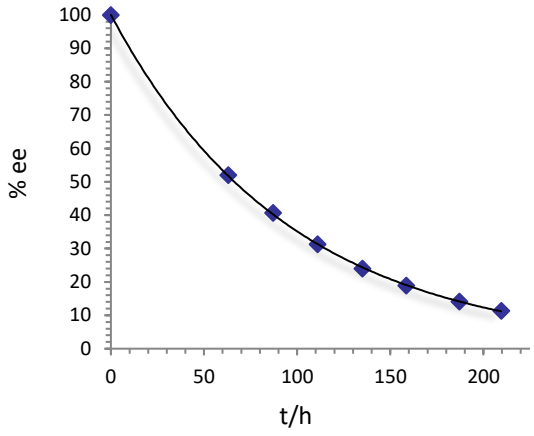
# 8. Appendices

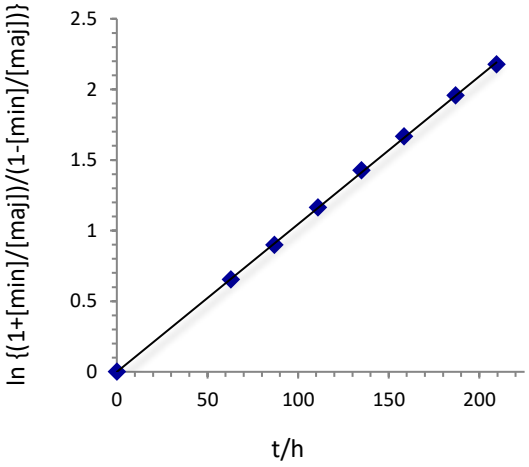
## 8.1. Barriers to Rotation

### *8.1.1. Barrier to Rotation of 165*

An analytical amount of enantiopure **165** was obtained *via* semi-preparative chiral HPLC. The barrier to rotation of **165** was determined according to the literature method ($t_{1/2}^{rac}$ = 2.8 d at 21 °C (294.15 K), hexane/isopropanol (95 : 5); $\Delta G^{\ddagger}$ = 25.0 kcal mol$^{-1}$).[161-164]

| time / h | time / s | % major ent. | % minor ent. | ln [(1+[min]/[maj])/(1-[min]/[maj])] |
|---|---|---|---|---|
| 0 | 0 | 99.99 | 0.00 | 0.000 |
| 63 | 2.27E+05 | 76.04 | 23.96 | 0.654 |
| 87 | 3.13E+05 | 70.36 | 29.64 | 0.898 |
| 111 | 4.00E+05 | 65.63 | 34.37 | 1.16 |
| 135 | 4.86E+05 | 62.07 | 37.93 | 1.43 |
| 158.5 | 5.71E+05 | 59.44 | 40.56 | 1.67 |
| 187 | 6.73E+05 | 57.06 | 42.94 | 1.96 |
| 209.5 | 7.54E+05 | 55.67 | 44.33 | 1.18 |




$$\ln\left(\frac{1+[min]/[maj]}{1-[min]/maj]}\right) = 2k_{ent}t + C$$

Therefore, $k_{ent}$ = ½ slope = 1.45 x 10$^{-6}$ s$^{-1}$

$k_{rac}$ = $2k_{ent}$ = 2.90 x 10$^{-6}$ s$^{-1}$

$t_{1/2}^{rac}$ = ln(2)/$k_{rac}$ = 2.8 days

Employing the Eyring equation:

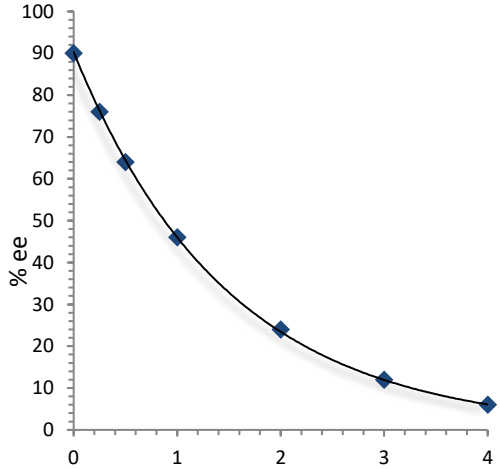
$$\Delta G^{\ddagger} = -RT \ln\left(\frac{k_{ent} \times h}{k_B \times T}\right)$$

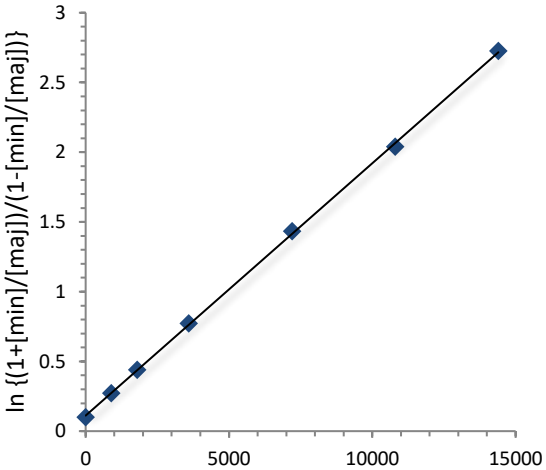
= 25.0 kcal mol$^{-1}$

### *8.1.2. Barrier to Rotation of 166*

The barrier to rotation of **166** was determined according to the literature method ($t_{1/2}^{rac}$ = 63 min at 139 °C (412.15 K), *m*-xylene; $\Delta G^{\ddagger}$ = 32.0 kcal mol$^{-1}$).[161-164]

| time / h | time / s | % major ent. | % minor ent. | ln [(1+[min]/[maj])/(1-[min]/[maj])] |
|---|---|---|---|---|
| 0 | 0 | 95.21 | 4.79 | 0.101 |
| 0.25 | 900 | 88.07 | 11.93 | 0.273 |
| 0.5 | 1800 | 82.19 | 17.81 | 0.440 |
| 1 | 3600 | 73.11 | 26.89 | 0.772 |
| 2 | 7200 | 61.93 | 38.07 | 1.433 |
| 3 | 10800 | 56.28 | 43.27 | 2.04 |
| 4 | 14400 | 53.28 | 46.72 | 2.72 |




$$\ln\left(\frac{1 + [min]/[maj]}{1 - [min]/maj]}\right) = 2k_{ent}t + C$$

Therefore, $k_{ent}$ = ½ slope = 9.37 x 10$^{-5}$ s$^{-1}$

$k_{rac} = 2k_{ent} = 1.87 \times 10^{-4}\ s^{-1}$

$t_{1/2}^{rac} = \ln(2)/k_{rac} = 64$ minutes

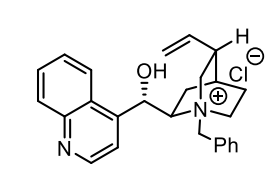
Employing the Eyring equation:

$$\Delta G^{\ddagger} = -RT \ln\left(\frac{k_{ent} \times h}{k_B \times T}\right)$$

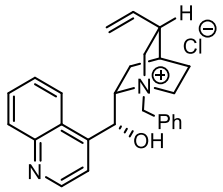
$= 32.0$ kcal mol$^{-1}$

## 8.2. Extended Optimization Tables

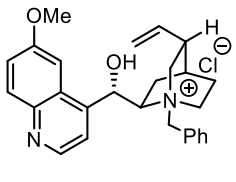
### *8.2.1. Index of Phase-transfer Catalysts*



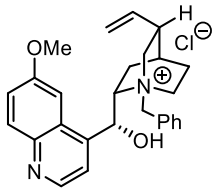
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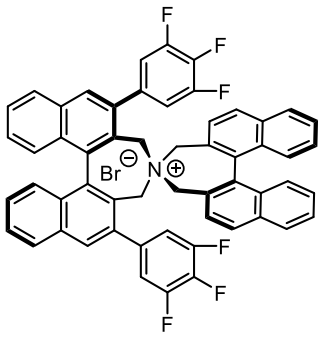
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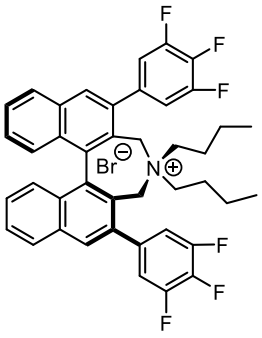
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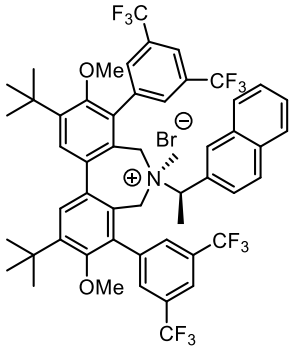
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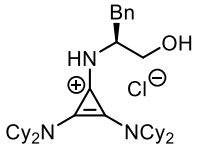
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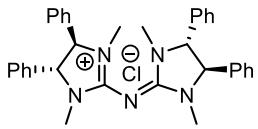
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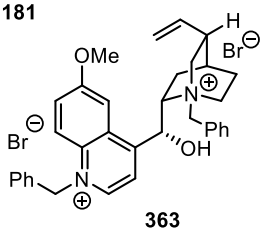
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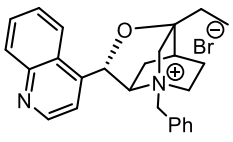
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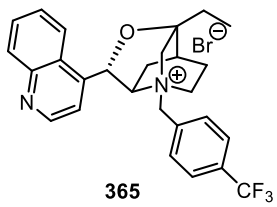
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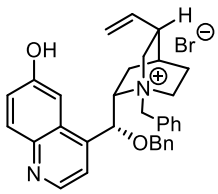
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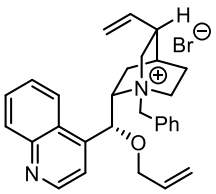
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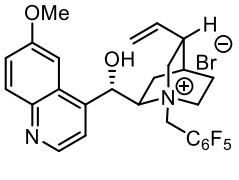
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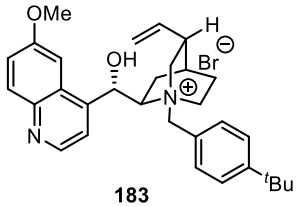
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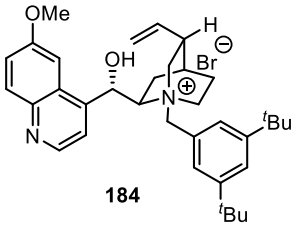
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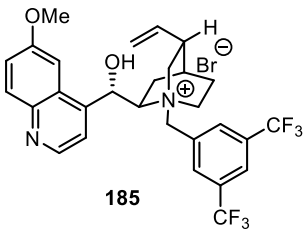
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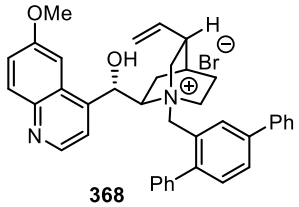
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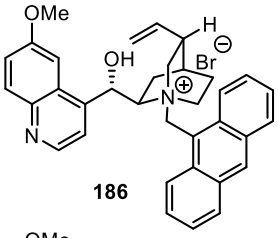
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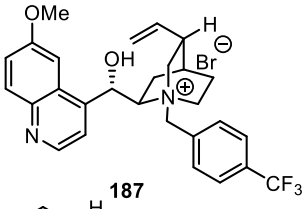
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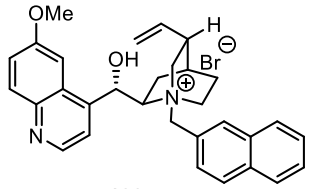
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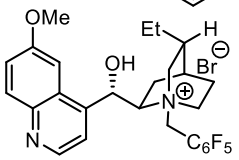
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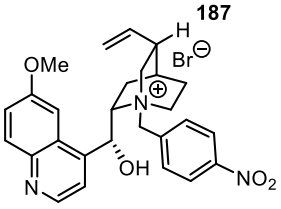
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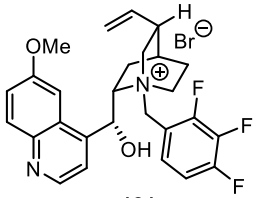
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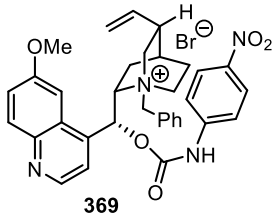
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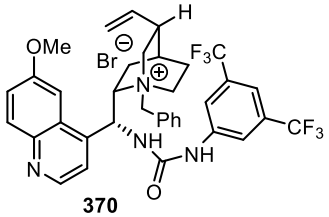
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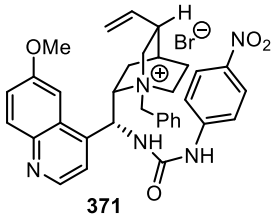
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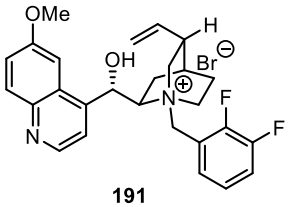
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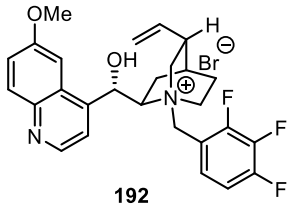
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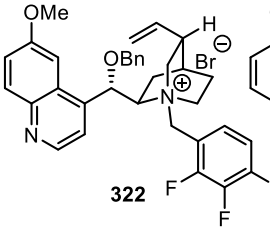
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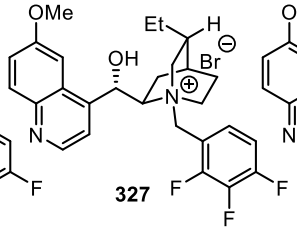
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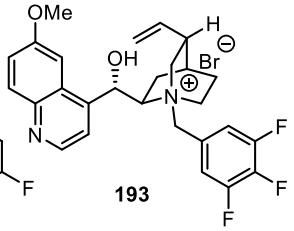
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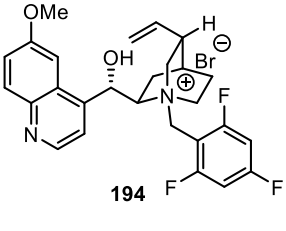
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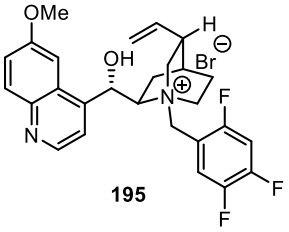
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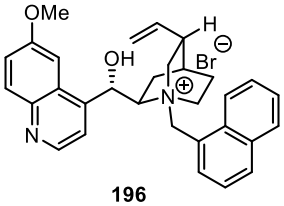
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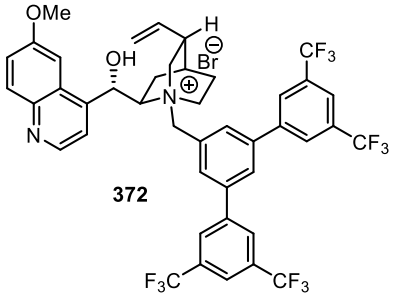
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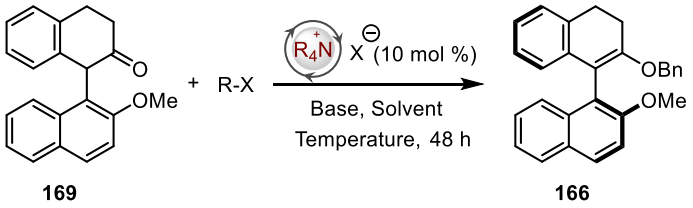


**196**



**372**

### *8.2.2. Optimization Table for the atropselective O-alkylation of 169*

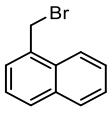
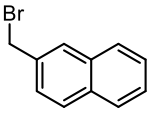
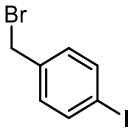
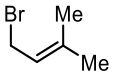



169 166

| Entry | Solvent (M) | Catalyst | Base (eq) | T / °C | R-X | e.r.[a] |
|---|---|---|---|---|---|---|
| **1** | PhMe | $Bu_4NBr$ | KOH (5) (aq) [b] | r.t. | BnBr | 50:50 |
| **2** | PhMe | **178** | KOH (5) (aq) [b] | r.t | BnBr | 53:57 |
| **3** | PhMe | **179** | KOH (5) (aq) [b] | r.t | BnBr | 43:57 |
| **4** | PhMe | **180** | KOH (5) (aq) [b] | r.t. | BnBr | 60:40 |
| **5** | PhMe | **19** | KOH (5) (aq) [b] | r.t. | BnBr | 45:55 |
| **6** | PhMe | **180** | $K_2CO_3$ (5) (aq) [b] | r.t. | BnBr | 71:29 |
| **7** | PhMe | **180** | KOH (1.5) | r.t. | BnBr | 54:46 |
| **8** | PhMe | **180** | $CsOH•OH_2$ (5) | r.t. | BnBr | 51:49 |
| **9** | PhMe | **180** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 73:27 |
| **10** | PhMe | **180** | $Cs_2CO_3$ (5) (aq) [c] | r.t. | BnBr | 72:28 |
| **11** | PhMe | **180** | $Cs_2CO_3$ (1.5) | r.t. | BnBr | 73:27 |
| **12** | PhMe | **359** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 50:50 |
| **13** | PhMe | **181** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 53:47 |
| **14** | PhMe | **360** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 51:49 |
| **15** | PhMe | **361** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 72:28 |
| **16** | PhMe | **362** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 56:44 |
| **17** | PhMe | **363** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 47:53 |
| **18** | PhMe | **364** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 50:50 |
| **19** | PhMe | **365** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 48:52 |

| Entry | Solvent (M) | Catalyst | Base (eq) | T / °C | R-X | e.r.[a] |
|---|---|---|---|---|---|---|
| **20** | PhMe | **366** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 51:49 |
| **21** | PhMe | **367** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 50:50 |
| **22** | PhMe | **182** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 74:26 |
| **23** | PhMe | **183** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 74:26 |
| **24** | PhMe | **184** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 64:36 |
| **25** | PhMe | **185** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 80:20 |
| **26** | PhMe | **186** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 81:19 |
| **27** | PhMe | **187** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 75:25 |
| **28** | PhMe | **188** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 83:17 |
| **29** | PhMe | **328** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 76:24 |
| **30** | PhMe | **189** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 31 :69 |
| **31** | PhMe | **181** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 18:82 |
| **32** | PhMe | **369** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 38:62 |
| **33** | PhMe | **370** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 43:57 |
| **34** | PhMe | **371** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 48:52 |
| **35** | PhMe | **191** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 86:14 |
| **36** | PhMe | **192** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 88:12 |
| **37** | PhMe | **193** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 73:27 |
| **38** | PhMe | **194** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 74:26 |
| **39** | PhMe | **195** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 83:17 |
| **40** | PhMe | **196** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 73:27 |
| **41** | PhMe | **372** | $CsOH•OH_2$ (5) (aq) [c] | r.t. | BnBr | 69:31 |
| **42** | PhMe | **192** | NaOH (5) (aq) [b] | r.t. | BnBr | 70:30 |
| **43** | PhMe | **192** | NaOH (2.5) (aq) [c] | r.t. | BnBr | 86:14 |

| Entry | Solvent (M) | Catalyst | Base (eq) | T / °C | R-X | e.r.[a] |
|---|---|---|---|---|---|---|
| **44** | PhMe | **192** | KOH (5) (aq) [b] | r.t. | BnBr | 77:23 |
| **45** | PhMe | **192** | KOH (2.5) (aq) [c] | r.t. | BnBr | 87:13 |
| **46** | PhMe | **192** | $RbOH•OH_2$ (5) (aq) [b] | r.t. | BnBr | 87:13 |
| **47** | PhMe | **192** | $RbOH•OH_2$(2.5)(aq) [c] | r.t. | BnBr | 88:12 |
| **48** | PhMe | **192** | $CsOH•OH_2$ (5) (aq) [b] | r.t. | BnBr | 85:15 |
| **49** | PhMe | **192** | $CsOH•OH_2$(2.5)(aq) [c] | r.t. | BnBr | 88:12 |
| **50** | PhMe | **192** | $Li_2CO_3$ (5) | r.t. | BnBr | N/A[d] |
| **51** | PhMe | **192** | $Ag_2CO_3$ (5) | r.t. | BnBr | N/A[d] |
| **52** | PhMe | **192** | $Na_2CO_3$ (5) | r.t. | BnBr | N/A[d] |
| **53** | PhMe | **192** | $Na_2CO_3$ (5) (2M aq) | r.t. | BnBr | 89:11[e] |
| **54** | PhMe | **192** | $Cs_2CO_3$ (5) | r.t. | BnBr | 76:24 |
| **55** | PhMe | **192** | $Cs_2CO_3$ (1.5) | r.t. | BnBr | 87:13 |
| **56** | PhMe | **192** | $Cs_2CO_3$ (5) (aq) [b] | r.t. | BnBr | 87:13 |
| **57** | PhMe | **192** | $K_3PO_4$ (5) (aq) [b] | r.t. | BnBr | 89:11 |
| **58** | PhMe | **192** | $K_3PO_4$ (5) | r.t. | BnBr | 90:10 |
| **59** | PhMe | **192** | $Na_3PO_4$ (5) (aq) [f] | r.t. | BnBr | 89:11[e] |
| **60** | PhMe | **192** | $Na_3PO_4$ (5) | r.t. | BnBr | 90:10[e] |
| **61** | PhMe | **192** | $K_2CO_3$ (5) | r.t. | BnBr | 89:11[e] |
| **62** | PhMe | **192** | $K_2CO_3$ (5) (aq) [b] | r.t. | BnBr | 89:11[e] |
| **63** | PhH | **192** | $K_3PO_4$ (5) | r.t | BnBr | 92:8 |
| **64** | $Cl_2CCHCl$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 88:12 |
| **65** | *m*-Xylene | **192** | $K_3PO_4$ (5) | r.t | BnBr | 85:15[e] |
| **66** | $Cl_2CHCHCl_2$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | N/A[d] |
| **67** | *p*-Xylene | **192** | $K_3PO_4$ (5) | r.t | BnBr | 85:15[e] |

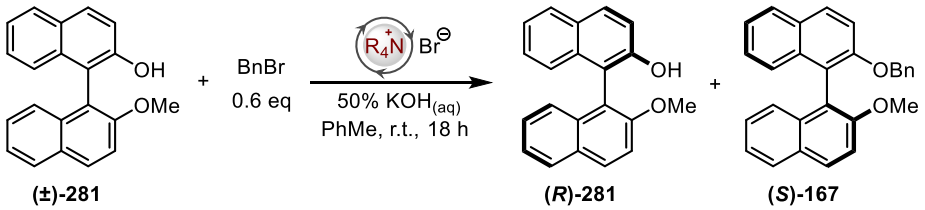
| Entry | Solvent (M) | Catalyst | Base (eq) | T / °C | R-X | e.r.[a] |
|---|---|---|---|---|---|---|
| **68** | $Cl_2HCHCl_2$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 86:14[e] |
| **69** | $CCl_4$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 84:16[e] |
| **70** | $CHCl_3$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 88:12 |
| **71** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 87:13 |
| **72** | $Et_2O$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 82:18[e] |
| **73** | TBME | **192** | $K_3PO_4$ (5) | r.t | BnBr | 77:23[e] |
| **74** | *i*-$Pr_2O$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 60:40[e] |
| **75** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | $Ac_2O$ | 50:50 |
| **76** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | AcCl | N/A[d] |
| **77** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | TBDPS-Cl | 50:50 |
| **78** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. |  | 79:21 |
| **79** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. |  | 79:21 |
| **80** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. |  | 85:15 |
| **81** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. |  | 80:20 |
| **82** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. |  | 72:28 |
| **83** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | MeI | 58:53[g] |
| **84** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | Allyl bromide | 79:21 |
| **85** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | Allyl iodide | 88:12 |
| **86** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | BnCl | N/A[d] |

| Entry | Solvent (M) | Catalyst | Base (eq) | T / °C | R-X | e.r.[a] |
|---|---|---|---|---|---|---|
| **87** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t | BnBr | 87:13 |
| **88** | $CH_2Cl_2$ | **192** | $K_3PO_4$ (5) | r.t. | BnI | 91:9 |
| **89** | PhH | **192** | $K_3PO_4$ (5) | r.t. | BnI | 94:6 |
| **90** | PhH | **192** | $K_3PO_4$ (5) | 0 | BnI | N/A[h] |
| **91** | PhH/$CH_2Cl_2$ (1:1) | **192** | $K_3PO_4$ (5) | 0 | BnI | 94:6 |
| **92** | PhH/$CH_2Cl_2$ (9:1) | **192** | $K_3PO_4$ (5) | 0 | BnI | 96:4[e] |
| **93** | PhH/$CH_2Cl_2$ (4:1) | **192** | $K_3PO_4$ (5) | 0 | BnI | 96:4[e] |
| **94** | PhH/$CH_2Cl_2$ (4:1) | **192** | $K_3PO_4$ (10) | 0 | BnI | 96:4 |
| **95** | PhH/$CH_2Cl_2$ (4:1) | **192** | $K_3PO_4$ (10) | –10 | BnI | 97:3[e] |
| **96** | PhH/$CH_2Cl_2$ (4:1) | **327** | $K_3PO_4$ (10) | 0 | BnI | 96:4 |

[a] e.r. determined by chiral stationary phase HPLC. [b] base: 50% aq., w/w; [c] base: 25% aq., w/w; [d] no conversion; [e] poor conversion; [f] Base: 15% aq., w/w; [g] Enol ether oxidized to dimethyl BINOL [h] reaction mixture froze.

### *8.2.3. Optimizations Tables for the Kinetic Resolution of MeBINOL 281*

**Primary Catalyst Screen:**



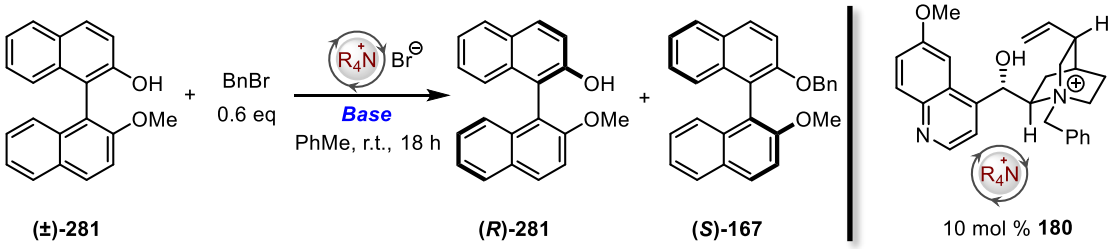

(±)-281 (*R*)-281 (*S*)-167

| Entry | Catalyst | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | **178** | 55% | 52.5:47.5 | 52:48 | 1.1 |
| **2** | **179** | 50% | 51.5:48.5 | 51.5:48.5 | 1.1 |
| **3** | **180** | 42% | 52.5:47.5 | 52.5:47.5 | 1.2 |
| **4** | **19** | 50% | 51:49 | 51:49 | 1.1 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Primary Base Screen:**



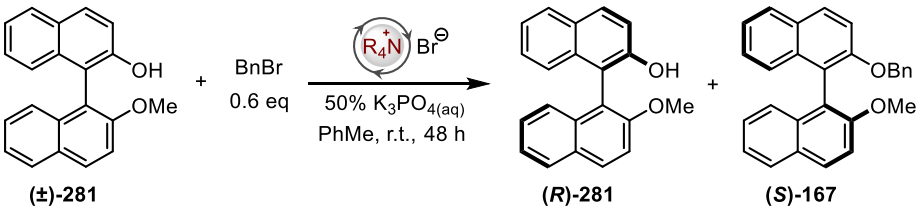

(±)-281 (*R*)-281 (*S*)-167 10 mol % **180**

| Entry | Base (eq.) | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | 25% $NaOH_{(aq)}$ (5) | 36% | 52:48 | 53.5:46.5 | 1.2 |
| **2** | 25% $RbOH{\bullet}OH_{2(aq)}$ (5) | 35% | 55.5:44.5 | 51.5:48.5 | 1.3 |
| **3** | 25% $CsOH{\bullet}OH_{2\,(aq)}$ (5) | 42% | 52.5:47.5 | 53.5:46.5 | 1.2 |
| **4** | 50% $K_2CO_{3(aq)}$ (5) | 12% | 53:47 | 72:28 | 2.7 |
| **5** | 50% $Cs_2CO_{3(aq)}$ (5) | 13% | 53:47 | 71:29 | 2.5 |
| **6** | 50% $K_3PO_{4(aq)}$ (5) | 13% | 53:47 | 73.5:26.5 | 3.1 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Secondary Catalyst Screen:**

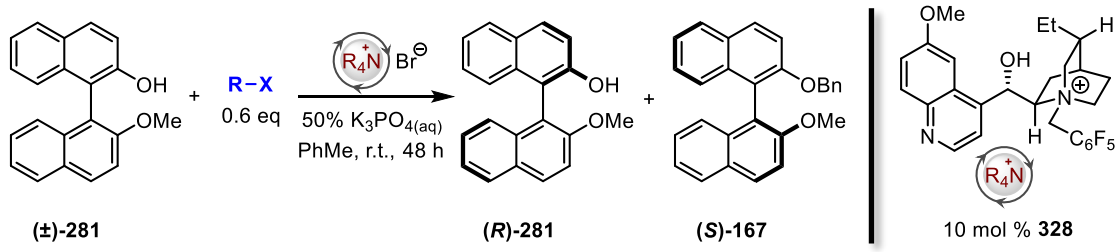



| Entry | Catalyst | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | **184** | 18% | 53:47 | 64:36 | 1.9 |
| **2** | **183** | 16% | 53.5:46.5 | 68.5:31.5 | 2.3 |
| **3** | **188** | 29% | 62.5:37.5 | 80:20 | 5.3 |
| **4** | **187** | 4% | 51:49 | 76:24 | 2.9 |
| **5** | **185** | 3% | 51:49 | 79.5:20.5 | 4.8 |
| **6** | **193** | 13% | 55:45 | 83:17 | 5.6 |
| **7** | **192** | 5% | 52:48 | 91:9 | 7.6 |
| **8** | **182** | 24% | 62:38 | 89:11 | 9.3 |
| **9** | **327** | 6% | 52.5:47.5 | 90.5:9.5 | 8.9 |
| **10** | **328** | 27% | 65:35 | 90:10 | 13 |
| **11** | **368** | 10% | 52.5:47.5 | 73.5:26.5 | 2.8 |
| **12** | **186** | 2% | 51:49 | 74.5:25.5 | 3.0 |
| **13** | **191** | 13% | 55.5:44.5 | 88:12 | 7.3 |
| **14** | **194** | 14% | 56:44 | 87:13 | 7.4 |
| **15** | **322** | N/A | 50:50 | 51:49 | N/A |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Electrophile Screen:**



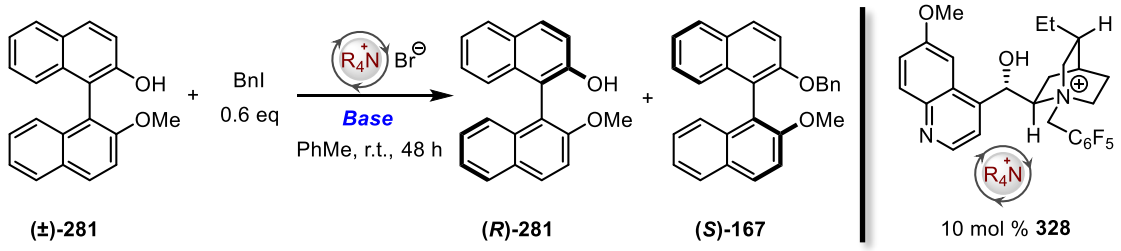

(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Electrophile | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | Allyl bromide | 13% | 55:45 | 85:15 | 7.2 |
| **2** | Allyl iodide | 35% | 68:32 | 83:17 | 7.1 |
| **3** | Methyl iodide | 19% | 56:44 | 76:24 | 3.5 |
| **4** | Benzyl bromide | 27% | 65:35 | 90:10 | 13 |
| **5** | Benzyl iodide | 35% | 89:11 | 71:29 | 12 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Base Screen:**



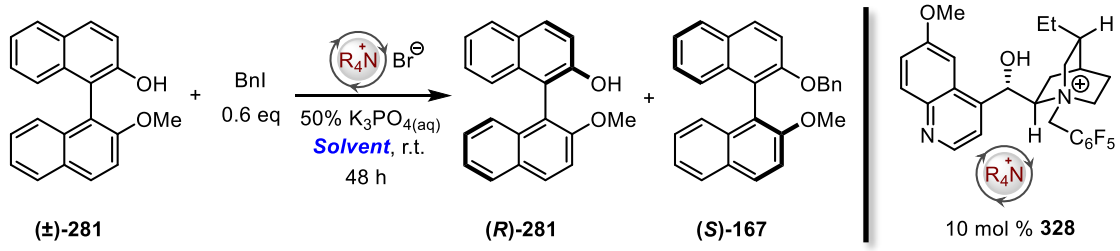

(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Base (eq.) | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | 25% $CsOH_{(aq)}$ (5) | 60% | 78.5:21.5 | 69:31 | 3.8 |
| **2** | $K_2CO_3$ (5) | 11% | 55:45 | 89:11 | 8.8 |
| **3** | 50% $K_2CO_{3(aq)}$ (5) | 12% | 55.5:44.5 | 91.5:8.5 | 12 |
| **4** | $Cs_2CO_3$ (2) | 39% | 56.5:43.5 | 60:40 | 1.7 |
| **5** | 50% $Cs_2CO_{3(aq)}$ (5) | 26% | 62.5:37.5 | 86.5:13.5 | 8.2 |
| **6** | 15% $Na_3PO_{4(aq)}$ (5) | 42% | 71.5:28.5 | 80:20 | 6.1 |
| **7** | $K_3PO_4$ (5) | 44% | 70:30 | 75:25 | 4.4 |
| **8** | $K_3PO_4$ (10) | 55% | 81:29 | 75:25 | 5.5 |
| **9** | $K_3PO_4$ (2) | 45% | 74.5:25.5 | 80:20 | 6.4 |
| **10** | $Na_3PO_4$ (5) | 12% | 55:45 | 88.5:11.5 | 8.5 |
| **11** | $Na_2CO_3$ (5) | N/A | 50:50 | 75:25 | N/A |
| **12** | 2M $Na_2CO_{3(aq)}$ (5) | 9% | 54:46 | 90:10 | 9.7 |
| **13** | 25% $CsOH_{(aq)}$ (5) | 56% | 83.5:16.5 | 76:24 | 6.1 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Solvent Screen:**



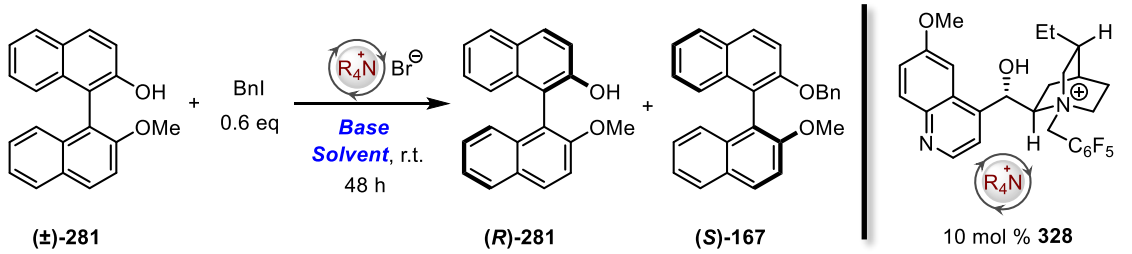

(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Solvent | Conversion[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|
| **1** | Diethyl ether | 34% | 68:32 | 84.5:15.5 | 7.7 |
| **2** | TBME | 42% | 69.5:30.5 | 76.5:23.5 | 4.7 |
| **3** | Mesityl oxide | 73% | 76.5:23.5 | 60:40 | 2.4 |
| **4** | Dichloromethane | 68% | 97:3 | 72:28 | 8.2 |
| **5** | Chloroform | 57% | 91:9 | 79.5:20.5 | 10 |
| **6** | Toluene | 44% | 78.5:21.5 | 86:14 | 11 |
| **7** | Benzene | 53% | 90:10 | 85:15 | 14 |
| **8** | Trifluoromethylbenzene | 43% | 62:38 | 66:34 | 2.4 |
| **9** | *m*-Xylene | 10% | 55:45 | 93:17 | 15 |
| **10** | *p*-Xylene | 7% | 53:47 | 92.5:7.5 | 13 |
| **11** | 1,2-Dichloroethane | 72% | 98:2 | 69:31 | 7.6 |
| **12** | $CCl_4$ | 29% | 65:35 | 86.5:13.5 | 8.6 |
| **13** | 2-Methylfuran | 34% | 69:31 | 87:13 | 9.7 |
| **14** | Diisopropyl ether | 8% | 51.5:48.5 | 67.5:32.5 | 2.1 |
| **15** | THF | 67% | 74.5:25.5 | 62:38 | 2.5 |
| **16** | 1,4-Dioxane | 60% | 88:12 | 75:25 | 6.6 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

[c] Determined using equation **1** with the JMG web applet.

**Solvent and Base Combinations:**




(±)-281 (*R*)-281 (*S*)-167 10 mol % **328**

| Entry | Solvent | Base (eq.) | Conv.[a] | *e.r.* (281) [b] | *e.r.* (167) [b] | S [c] |
|---|---|---|---|---|---|---|
| **1** | PhH | $K_3PO_4$ (5) | 65% | 97:3 | 75.5:24.5 | 10 |
| **2** | PhH | $K_3PO_{4(aq)}$ (5) [d] | 50% | 85.5:14.5 | 86:14 | 13 |
| **3** | *m*-Xylene | $K_3PO_4$ (5) | 52% | 73.5:26.5 | 72:28 | 4.0 |
| **4** | *m*-Xylene | $K_3PO_{4(aq)}$ (10) [d] | 11% | 55.5:44.5 | 93:7 | 15 |
| **5** | PhH/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (5) [d] | 54% | 89:11 | 83:17 | 11 |
| **6** | PhH/$CHCl_3$ 9:1 | $K_3PO_4$ (5) | 62% | 96.5:3.5 | 79:21 | 12 |
| **7** | *m*-Xylene/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (5) [d] | 57% | 89:11 | 80:20 | 9.2 |
| **8** | *m*-Xylene/$CHCl_3$ 9:1 | $K_3PO_4$ (5) | 74% | 98.5:1.5 | 67:33 | 7.3 |
| **9** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_{4(aq)}$ (10) [d] | 11% | 55:45 | 91.5:8.5 | 11 |
| **10** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_4$ (5) | 12% | 55.5:44.5 | 92.5:7.5 | 13 |
| **11** | PhH/$CHCl_3$ 9:1 [e] | $K_3PO_4$ (10) | 28% | 64.5:35.5 | 88:12 | 10 |
| **12** | *m*-xylene/PhH 4:1 | $K_3PO_{4(aq)}$ (10) [d] | 37% | 88:12 | 72:28 | 11 |
| **13** | PhH | $K_3PO_4$ (2) | 50% | 84:16 | 84:16 | 11 |
| **14** | PhH | $K_3PO_4$ (10) | 68% | 98:2 | 72.5:27.5 | 9.3 |
| **15** | PhH | $K_3PO_{4(aq)}$ (10) [d] | 55% | 91:9 | 83:17 | 12 |
| **16** | PhH | $K_3PO_{4(aq)}$ (2) [d] | 36% | 71.5:28.5 | 88:12 | 11 |
| **17** | PhH/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (2) [d] | 30% | 66:44 | 87:13 | 9.1 |
| **18** | PhH/$CHCl_3$ 9:1 | $K_3PO_{4(aq)}$ (10) [d] | 52% | 88.5:11.5 | 85.5:14.5 | 14 |
| **19** | PhH/$CHCl_3$ 9:1 | $K_3PO_4$ (2) | 57% | 93.5:6.5 | 83.5:16.5 | 14 |
| **20** | PhH/$CHCl_3$ 9:1 | $K_3PO_4$ (10) | 66% | 98:2 | 75:25 | 11 |

[a] Determined using equation **2**; [b] Determined by chiral stationary phase HPLC;

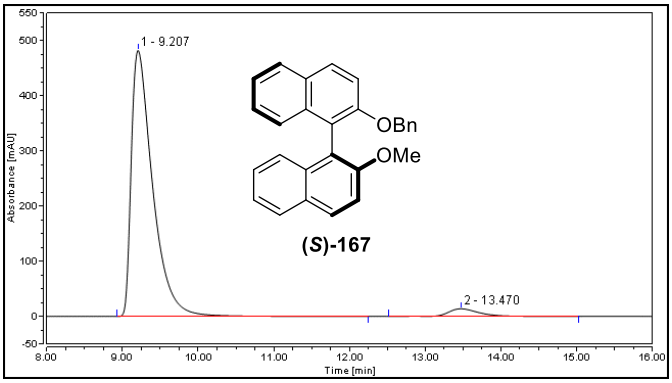
[c] Determined using equation **1** with the JMG web applet; [d] 50% aqueous w/w; [e] Reaction carried out at 0 °C.

## 8.3. Absolute Configuration

### *8.3.1. Absolute Configuration of MeBnBINOL 167*

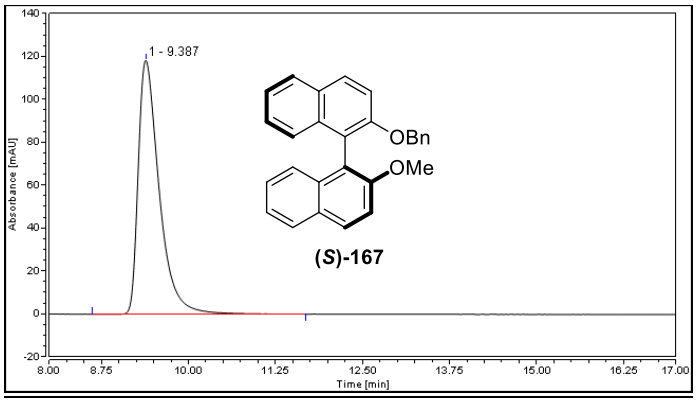
The absolute stereochemistry of **167** was determined by comparing the optical rotation to literature values,[128] and comparing the HPLC traces to authentic samples prepared from commercially available (*S*)-BINOL.[165-166]

**Asymmetric using catalyst 192**




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 9.207 | 157.613 | 482.386 | 95.89 |
| 2 | n.a. | 13.470 | 6.749 | 14.013 | 4.11 |
| **Total:** | | | **164.362** | **496.399** | **100.00** |

**Authentic sample prepared from (*S*)-BINOL**




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 9.387 | 41.379 | 118.340 | 100.00 |
| **Total:** | | | **41.379** | **118.340** | **100.0** |

### *8.3.2. Absolute Configuration of 275*

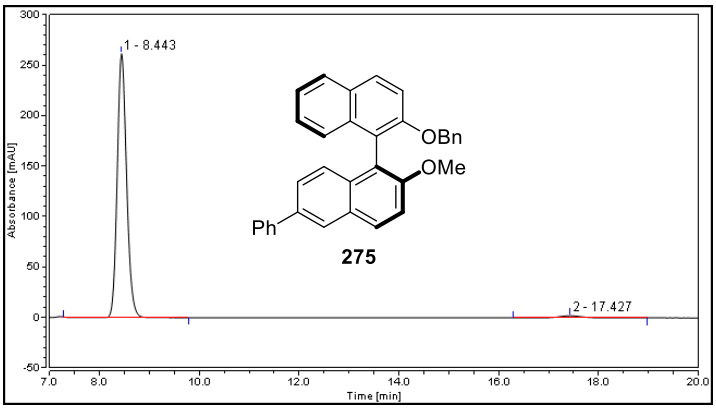
The product **275** was crystallized *via* vapour diffusion by dissolving 5 mg of **275** at 98:2 *e.r.* in benzene (*c.a.* 50 μL) and using pentane as the volatile component. Low temperature[167] single crystal X-ray diffraction studies were carried out at 150 K on **275** using $CuK_{\alpha}$ radiation on an Oxford Diffraction SuperNova diffractometer equipped with an area detector and graphite monochromator, within the University of Oxford Chemistry Department. Raw frame data were reduced using CrysAlisPro(Agilent) and the structures were solved using superflip.[168] Full-matrix least-squares refinement of the structures were carried out using CRYSTALS.[169-170] The Flack x parameter[171-172] refined to -0.04(10) and Bayesian analysis of the Bijvoet pairs[173] gave the Hooft y parameter as 0.03(5) and the probability that the structure was the correct hand of >99.99 % given that the crystal was enantiopure, thus determining the absolute stereochemistry.

After completion of the data collection, the crystal used in the single crystal X-ray diffraction studies was compared to the bulk material by dissolution of the crystal in 1:4 *i*-PrOH/hexane and subsequent analysis *via* chiral HPLC. The observed retention time matched that of the major enantiomer of **275**, thus confirming that the crystal used in the single crystal X-ray diffraction studies comprised of the major enantiomer of **275**.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1476066).

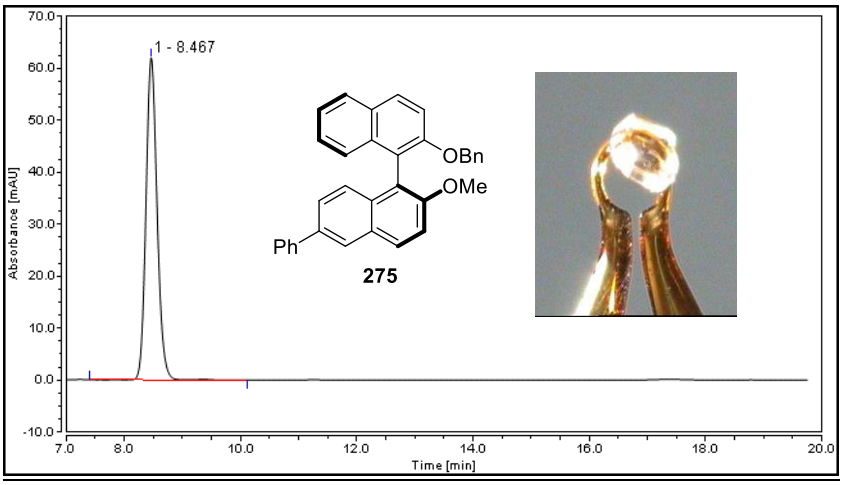
Copies of these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

## Asymmetric at 98:2 *e.r.*




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 8.443 | 56.031 | 261.258 | 98.10 |
| 2 | n.a. | 17.427 | 1.086 | 2.125 | 1.90 |
| **Total:** | | | **57.117** | **263.382** | **100.00** |

## Single crystal used for absolute configuration determination

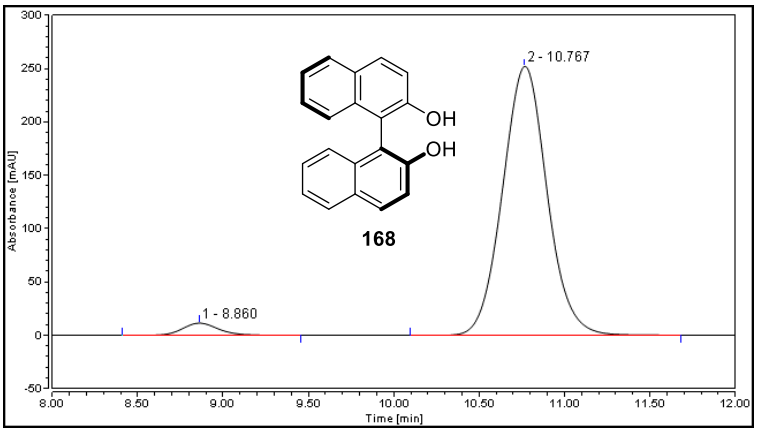



| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 8.467 | 13.706 | 61.998 | 100.00 |
| **Total:** | | | **13.706** | **61.998** | **100.00** |

### *8.3.3. Absolute Configuration of BINOL 168*

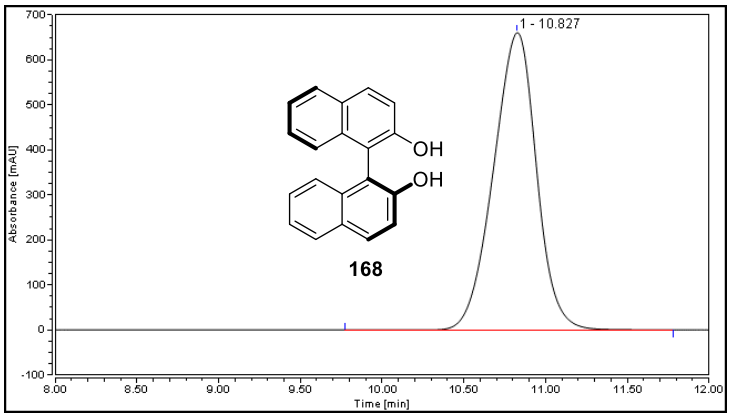
The absolute stereochemistry of **168** was determined by comparing the optical rotation to literature values,[157] and comparing the HPLC traces to commercially available (*S*)-BINOL.

**Asymmetric**




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 8.860 | 3.000 | 11.580 | 3.80 |
| 2 | n.a. | 10.767 | 76.035 | 252.063 | 96.20 |
| **Total:** | | | **79.035** | **263.643** | **100.00** |

**Commercially available (*S*)-BINOL**

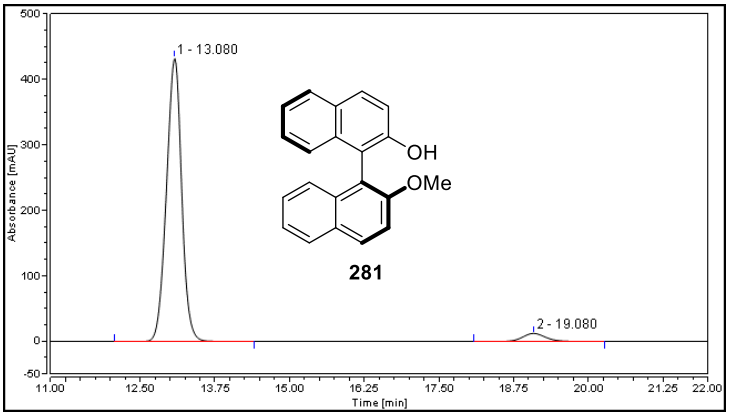



| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 10.827 | 201.399 | 660.246 | 100.00 |
| **Total:** | | | **201.399** | **660.246** | **100.00** |

### *8.3.4. Absolute Configuration of MeBINOL 281*

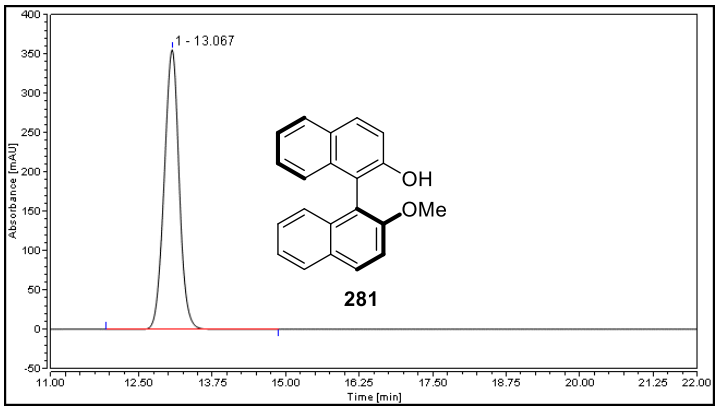
The absolute stereochemistry of **281** was determined by comparing the optical rotation to literature values,[159] and comparing the HPLC traces to authentic samples prepared from commercially available (*S*)-BINOL.[165-166]

**Asymmetric**




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 13.080 | 127.298 | 432.360 | 95.93 |
| 2 | n.a. | 19.080 | 5.395 | 12.236 | 4.07 |
| **Total:** | | | **132.693** | **444.596** | **100.00** |

**Authentic sample prepared from (*S*)-BINOL**




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 13.067 | 104.650 | 355.555 | 100.00 |
| **Total:** | | | **104.650** | **355.555** | **100.00** |

### *8.3.5. Absolute Configuration of 174*

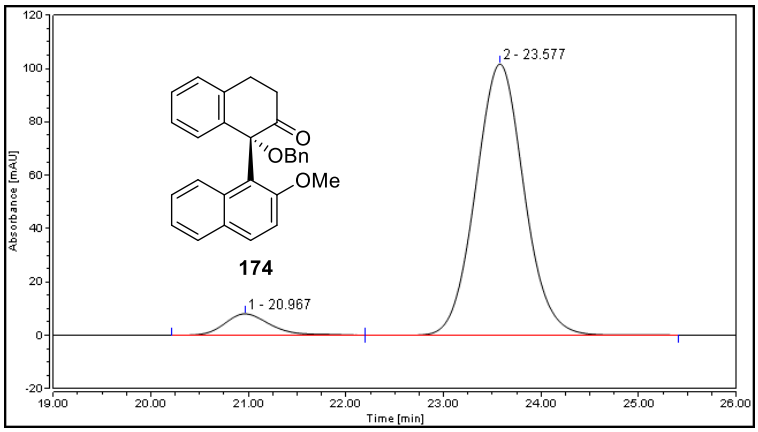
The product **174** was crystallized *via* vapour diffusion by dissolving 5 mg of **174** at 93:7 *e.r.* in benzene (*c.a.* 50 μL) and using pentane as the volatile component. Low temperature[167] single crystal X-ray diffraction studies were carried out at 150 K on **174** using $CuK_{\alpha}$ radiation on an Oxford Diffraction SuperNova diffractometer equipped with an area detector and graphite monochromator, within the University of Oxford Chemistry Department. Raw frame data were reduced using CrysAlisPro(Agilent) and the structures were solved using superflip.[168] Full-matrix least-squares refinement of the structures were carried out using CRYSTALS.[169-170] The Flack x parameter[171-172] refined to 0.01(12) and Bayesian analysis of the Bijvoet pairs[173] gave the Hooft y parameter as 0.03(3) and the probability that the structure was the correct hand of >99.99 % given that the crystal was enantiopure, thus determining the absolute stereochemistry.

After completion of the data collection, the crystal used in the single crystal X-ray diffraction studies was compared to the bulk material by dissolution of the crystal in 1:4 *i*-PrOH/hexane and subsequent analysis *via* chiral HPLC. The observed retention time matched that of the major enantiomer of **174**, thus confirming that the crystal used in the single crystal X-ray diffraction studies comprised of the major enantiomer of **174**.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1476099).

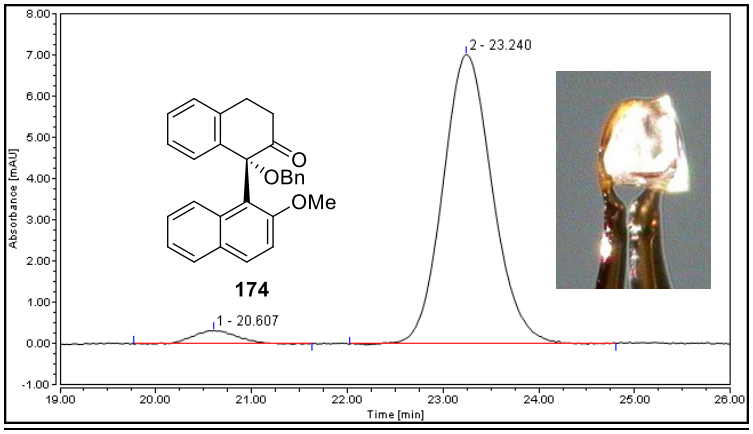
Copies of these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

## Asymmetric



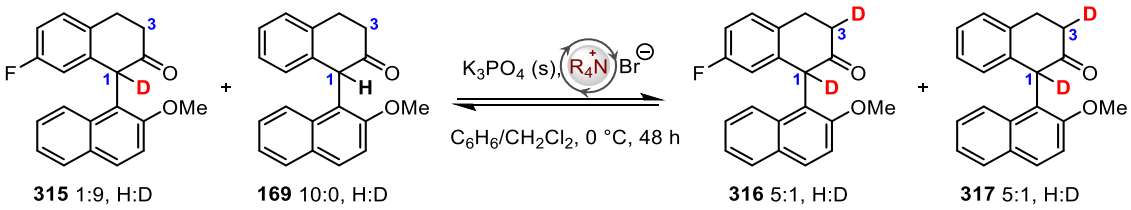

| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 20.967 | 4.331 | 8.013 | 6.91 |
| 2 | n.a. | 23.577 | 58.302 | 101.652 | 93.09 |
| **Total:** | | | **62.633** | **109.665** | **100.00** |

## Single crystal used for absolute configuration determination




| No. | Peak Name | Retention Time | Area | Height | Relative Area |
|---|---|---|---|---|---|
| | | min | mAU*min | mAU | % |
| 1 | n.a. | 20.607 | 0.170 | 0.326 | 3.89 |
| 2 | n.a. | 23.240 | 4.188 | 7.020 | 96.11 |
| **Total:** | | | **4.357** | **7.346** | **100.00** |

### 8.4. Deuterium Cross-over Experiment

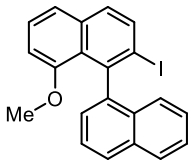



**315** 1:9, H:D **169** 10:0, H:D **316** 5:1, H:D **317** 5:1, H:D

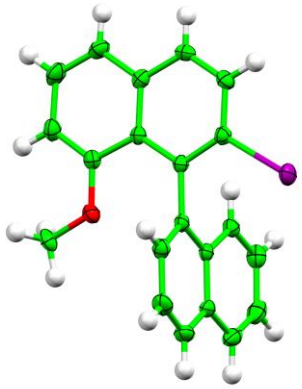
A Schlenk tube was sequentially charged with *N*-(2,3,4-trifluorobenzyl)quinidinium bromide **192** (11 mg, 0.020 mmol), **169** (15.1 mg, 0.0500 mmol), **315** (48.2 mg, 0.150 mmol) and $K_3PO_4$ (425 mg, 2.00 mmol). The atmosphere was evacuated and backfilled with argon three times. Dichloromethane (0.40 mL) and benzene (1.60 mL) were added. The suspension was cooled to 0 °C and stirred rapidly at a rate of 1000-1400 rpm in the dark at 0 °C for 48 hours. The crude reaction mixture was then filtered through a plug of silica which was subsequently washed with dichloromethane. The filtrate was concentrated under reduced pressure and subjected to HRMS ($ESI^+$), $^{13}C$ NMR and $^2H$ NMR analysis.

## 8.5. X-ray Crystallographic Data

### *8.5.1. X-ray Crystallographic Data and Structure Refinement for 118, 021JDJ14*

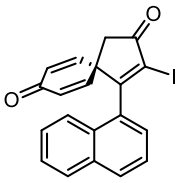



118

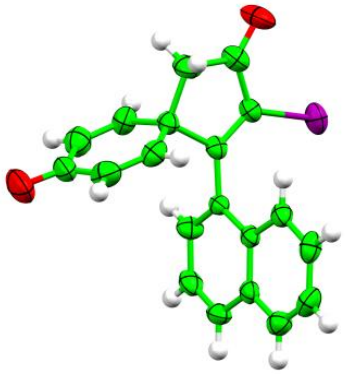


| | | |
|---|---|---|
| **Identification code** | 021JDJ14 | |
| **Empirical formula** | $C_{21}H_{15}IO$ | |
| **Formula weight** | 410.25 | |
| **Temperature** | 150 K | |
| **Wavelength** | 0.71073 Å | |
| **Crystal system** | Triclinic | |
| **Space group** | P -1 | |
| **Unit cell dimensions** | a = 7.6642 Å | α = 93.9142° |
| | b = 10.3427 Å | β = 92.2245° |
| | c = 11.0229 Å | γ = 109.6517 ° |
| **Volume** | 819.180 $Å^3$ | |
| **Z,Z'** | Z: 2 Z': 0 | |
| **Density (calculated)** | 1.66 Mg $m^{-3}$ | |
| **Absorption coefficient** | 1.956 $mm^{-1}$ | |
| **F(000)** | 404.0 | |
| **Crystal size** | 0.19 x 0.21 x 0.21 $mm^3$ | |
| **Theta range for data collection** | 5.249° to 27.440° | |
| **Reflections collected** | 5914 | |
| **Independent reflections** | 3700 | |
| **Absorption correction** | Multi-scan | |
| **Refinement method** | Full-matrix least squares on $F^2$ | |
| **Goodness-of-fit on $F^2$** | 1.004 | |
| **Final R indices [I>2σ(I)]** | $R^1$ = 0.0271, $wR^2$ = 0.0623 | |
| **R indices (all data)** | $R^1$ = 0.0319, $wR^2$ = 0.0642 | |

### *8.5.2. X-ray Crystallographic Data and Structure Refinement for 129, 026JDJ14*

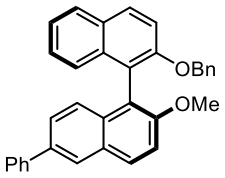



129

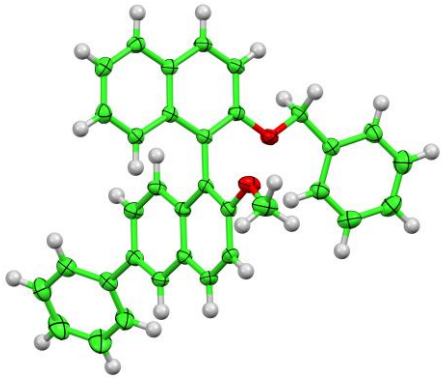


| | | |
|---|---|---|
| **Identification code** | 026JDJ14 | |
| **Empirical formula** | $C_{20}H_{13}IO_2$ | |
| **Formula weight** | 412.23 | |
| **Temperature** | 293 K | |
| **Wavelength** | 0.71073 Å | |
| **Crystal system** | Monoclinic | |
| **Space group** | P $2_1$/n | |
| **Unit cell dimensions** | a = 8.1392 Å | α = 90° |
| | b = 10.7580 Å | β = 92.8829° |
| | c = 18.7004 Å | γ = 90° |
| **Volume** | 1635.36 $Å^3$ | |
| **Z,Z'** | Z: 4 Z': 0 | |
| **Density (calculated)** | 1.67 Mg $m^{-3}$ | |
| **Absorption coefficient** | 1.965 $mm^{-1}$ | |
| **F(000)** | 808.0 | |
| **Crystal size** | 0.20 x 0.30 x 0.30 $mm^3$ | |
| **Theta range for data collection** | 5.277° to 27.505° | |
| **Reflections collected** | 6686 | |
| **Independent reflections** | 6686 | |
| **Absorption correction** | Multi-scan | |
| **Refinement method** | Full-matrix least squares on $F^2$ | |
| **Goodness-of-fit on $F^2$** | 0.978 | |
| **Final R indices [I>2σ(I)]** | $R^1$ = 0.0435, $wR^2$ = 0.0817 | |
| **R indices (all data)** | $R^1$ = 0.0987, $wR^2$ = 0.1155 | |

### *8.5.3. X-ray Crystallographic Data and Structure Refinement for 275, 040JDJ16*

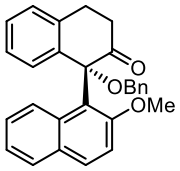



**275**

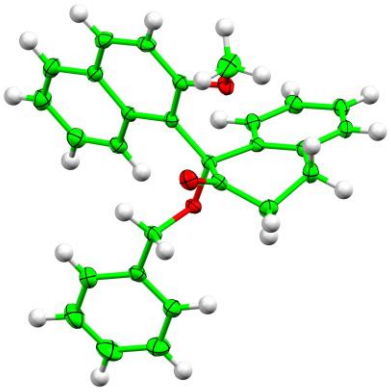


| | | |
|---|---|---|
| **Identification code** | 040JDJ16 | |
| **Empirical formula** | $C_{34}H_{26}O_2$ | |
| **Formula weight** | 466.58 | |
| **Temperature** | 150 K | |
| **Wavelength** | 1.54180 Å | |
| **Crystal system** | Monoclinic | |
| **Space group** | P $2_1$ | |
| **Unit cell dimensions** | a = 8.27430 Å | α = 90° |
| | b = 20.90150 Å | β = 99.5284° |
| | c = 14.42880 Å | γ = 90° |
| **Volume** | 2460.966 $Å^3$ | |
| **Z,Z'** | Z: 4 Z': 0 | |
| **Density (calculated)** | 1.26 Mg $m^{-3}$ | |
| **Absorption coefficient** | 0.598 $mm^{-1}$ | |
| **F(000)** | 984.0 | |
| **Crystal size** | 0.06 x 0.15 x 0.15 mm $^3$ | |
| **Theta range for data collection** | 3.106° to 76.453° | |
| **Reflections collected** | 61230 | |
| **Independent reflections** | 10143 | |
| **Absorption correction** | Multi-scan | |
| **Refinement method** | Full-matrix least squares on $F^2$ | |
| **Goodness-of-fit on $F^2$** | 0.946 | |
| **Final R indices [I>2σ(I)]** | $R^1$ = 0.0267, $wR^2$ = 0.0680 | |
| **R indices (all data)** | $R^1$ = 0.0274, $wR^2$ = 0.0689 | |

### *8.5.4. X-ray Crystallographic Data and Structure Refinement for 174, 094ALT16*




174



| | | |
|---|---|---|
| **Identification code** | 094ALT16 | |
| **Empirical formula** | $C_{28}H_{24}O_3$ | |
| **Formula weight** | 408.50 | |
| **Temperature** | 150 K | |
| **Wavelength** | 1.54180 Å | |
| **Crystal system** | Orthorhombic | |
| **Space group** | P $2_1$ $2_1$ $2_1$ | |
| **Unit cell dimensions** | a = 8.27430 Å | α = 90° |
| | b = 20.90150 Å | β = 99.5284° |
| | c = 14.42880 Å | γ = 90° |
| **Volume** | 2125.015 $Å^3$ | |
| **Z,Z'** | Z: 4 Z': 0 | |
| **Density (calculated)** | 1.28 Mg $m^{-3}$ | |
| **Absorption coefficient** | 0.648 $mm^{-1}$ | |
| **F(000)** | 864.0 | |
| **Crystal size** | 0.12 x 0.12 x 0.15 $mm^3$ | |
| **Theta range for data collection** | 4.280° to 76.135° | |
| **Reflections collected** | 49279 | |
| **Independent reflections** | 4415 | |
| **Absorption correction** | Multi-scan | |
| **Refinement method** | Full-matrix least squares on $F^2$ | |
| **Goodness-of-fit on $F^2$** | 1.043 | |
| **Final R indices [I>2σ(I)]** | $R^1$ = 0.0251, $wR^2$ = 0.0643 | |
| **R indices (all data)** | $R^1$ = 0.0255, $wR^2$ = 0.0646 | |

### *8.5.5. Crystallographic Information files*

The crystallographic information files (.cif) for all X-ray structures in this thesis can be found in the attached CD.

# 9. References


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