Harnessing Triaryloxonium Ions for Aryne Generation and Stereogenic Control of Oxygen

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Declaration

This dissertation describes work carried out in the Chemistry Research Laboratory at the University of Oxford between October 2020 and April 2024. The dissertation is the product of my own work and includes no results obtained through collaboration, except where specifically indicated in the text.

Madeleine Hindson

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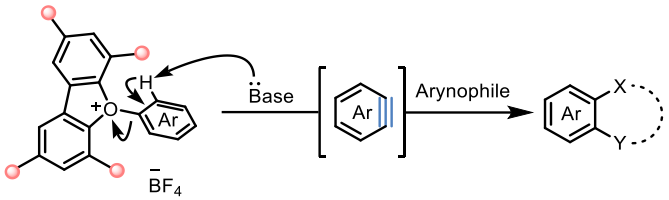
Abbreviations

Ac	acetyl
acac	acetylacetone
APCI	Atmospheric Pressure Chemical Ionisation
aq	aqueous
Ar	aryl
atm	atmospheres
BINOL	1,1'-bi-2-naphthol
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bu	butyl
Conc.	concentration
d.e.	diastereomeric excess
d.r.	diastereomeric ration
DIBAL	diisopropylethylamine
DME	dimethoxyethane
DMF	*N*,*N*-Dimethylformamide
DMI	1,3-Dimethyl-2-imidazolidinone
dppf	1,1'-ferrocenediyl-bis(diphenylphosphine)
e.e.	enantiomeric excess
e.r.	enantiomeric ratio
EI	Electron Ionisation
ent	enantiomerisation
eq.	equivalents
ESI	Electrospray Ionisation
Et	ethyl
FVT	Flow Vacuum Thermolysis
HDDA	hexadehydro-Diels–Alder
HFIP	hexafluoroisopropanol
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
inv	inversion
IPA	isopropyl alcohol
IR	Infrared
IUPAC	International Union of Pure and Applied Chemistry
m-CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
min	minutes
NMP	*N*-Methyl-2-pyrrolidone
NMR	Nuclear Magnetic Resonance
Nu	nucleophile
Ph	phenyl

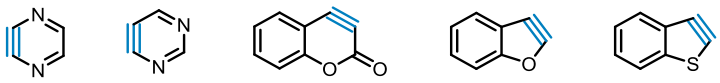
Pin	pinacolato
Pr	Propyl
qNMR	Quantitative Nuclear Magnetic Resonance
r.t.	room temperature
rac	racemisation
RBF	Round Bottom Flask
sat.	saturated
TBAB	tetra-*n*-butylammonium bromide
TBS	tert-butyldimethylsilyl
Temp.	temperature
Tf	trifluoromethanesulfonate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMP	2,2,6,6-tetramethylpiperidine
TPP	thiamine pyrophosphate
Ts	*para*-toluenesulfonyl
UHP	Urea Hydrogen Perioxide
VT	Variable Temperature
w/w	weight by weight
wt%	percent by weight

Abstract

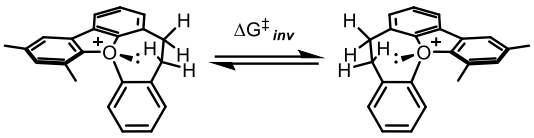
Oxonium ions are perceived to be highly reactive electrophiles, thus, triaryloxonium ions have been underutilised in synthesis despite their remarkable stability. This body of work explores novel applications of triaryloxonium ions. Chapter 1 demonstrates their utility as benzyne precursors, activated with weak bases to achieve broad functional group tolerance, offering a complementary approach to alternative aryne-generating methods. This is further illustrated by their compatibility with a diverse range of arynophiles.



Inspired by these findings, Chapter 2 assesses their potential application as hetaryne precursors. Synthetic routes towards heteroaromatic-containing triaryloxonium ions as well as methods to enhance their stability are evaluated. Various heteroaromatic triaryloxonium ions exhibit aryne-like reactivity in the presence of base and arynophiles, including the five-membered hetaryne, 2,3-benzothiophyne.



Beyond aryne generation, the Smith group has harnessed triaryloxonium ions to generate the first chiral, non-racemic, and configurationally stable molecule in which the oxygen atom is the sole stereogenic centre. This work probes the configurational stability of this oxonium ion by conducting kinetic analysis of the enantioenriched oxonium to measure the inversion barrier of the stereogenic oxygen centre.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Contents

1 Chapter 1: Aryne Generation from Triaryloxonium Ions 1

1.1 Introduction 1

1.1.1 Trialkyloxonium ions 1

1.1.2 Triaryloxonuim ions 1

1.1.3 Arynes 2

1.1.4 Aryne generation 3

1.1.4.1 Deprotonation of aryl halides 3

1.1.4.2 Benzenediazonium carboxylates 4

1.1.4.3 Aminobenzotriazoles 5

1.1.4.4 The Kobayashi method 5

1.1.4.5 Hexadeyhdro Diels-Alder reaction 6

1.1.4.6 Pd(II)-catalysed C-H activation of benzoic acid 7

1.1.4.7 Onium salts: λ^3-bromanes, -chloranes, and iodanes 7

1.1.5 Aryne generation from triaryloxonium ions 9

1.1.6 Previous work within the group 11

1.1.7 Project aims 13

1.2 Results and discussions 13

1.2.1 Synthesis of bis(aryl) ethers 13

1.2.2 Triaryloxonium salt synthesis 15

1.2.3 Arynes scope 18

1.2.4 Arynophile scope 21

1.3 Conclusion 23

2 Chapter 2: Hetaryne Generation from Triaryloxonium Ions 24

2.1 Introduction 24

2.1.1 Computational model for hetaryne energy 24

2.1.2 Experimental evidence for hetaryne generation 26

2.1.2.1 2,3-Benzofuryne 27

2.1.2.2 Cumulenes: 3,4-thiophyne, 3,4-pyrrolyne, and 3,4-furyne 28

2.1.2.3 2,3-Thiophyne and 2,3-benzothiophyne 29

2.1.2.4 4,5-Pyrimidyne 32

2.1.2.5 2,3- and 3,4-Pyridyne 34

2.1.2.6 Arynes fused to a heteroatom-containing ring 35

2.1.3 Project aims 36

2.2 Results and discussion 36

2.2.1 2,3-Pyrazyne 36

2.2.2 4,5-Pyrimidyne 39

2.2.2.1 Triaryloxonium salt synthesis 40

2.2.2.2 4,5-Pyrimidyne generation 45

2.2.3 3,4-Coumaryne 47

2.2.3.1 Triaryloxonium salt synthesis 48

2.2.3.2 Stability of the coumarin-containing triaryloxonium salts 50
2.2.3.2.1 NMR study 51
2.2.3.2.2 Counterion effect 54
2.2.3.2.3 Substituent effect 57
2.2.3.3 Triaryloxonium salt synthesis 62
2.2.3.4 3,4-Coumaryne generation 66
2.2.4 Five-membered hetaryne generation 67
2.2.4.1 2,3-Benzofuryne 68
2.2.4.1.1 Triaryloxonium salt synthesis 68
2.2.4.1.2 2,3-Benzofuryne generation 71
2.2.4.2 2,3-Benzothiophyne 72
2.2.4.2.1 Synthetic routes to triaryloxonium salts 72
2.2.4.2.2 2,3-Benzothiophyne generation 81
2.2.4.2.3 Triaryloxonium salt synthesis 84
2.2.4.2.4 2,3-Benzothiophynes scope 88
2.2.4.2.5 Arynophile scope 89
2.2.4.3 Conclusion 93
3 Chapter 3: Chiral Triaryloxonium Ions 94
3.1 Introduction 94
3.1.1 Pyramidal inversion of trivalent compounds 94
3.1.2 Pyramidal inversion of oxoniums 95

3.1.3 Oxonium atropisomers 96

3.1.4 Measuring configurational stability 97

3.1.4.1 Kinetic analysis of the racemisation of an enantioenriched sample 98

3.1.4.2 Dynamic HPLC 99

3.1.4.3 Variable temperature NMR 99

3.1.5 Previous work within the group 99

3.1.6 Project aims 102

3.2 Results and discussions 103

3.2.1 Diastereomerisation barrier 103

3.2.2 Resolution 106

3.2.3 Enantiomerisation barrier 108

3.2.4 Conclusion 109

4 Supporting Information 110

4.1 General Information 110

4.1.1 Naming and Numbering 110

4.1.2 Reaction Conditions 110

4.1.3 Solvents and Reagents 110

4.1.4 Chromatography 110

4.1.5 NMR Spectroscopy 111

4.1.6 Infrared Spectroscopy 111

4.1.7 Mass Spectrometry 111

4.1.8 Melting Points 111

4.2 General Procedures 112

4.3 Experimental Data 122

4.4 Inversion Barrier Measurements 304

4.4.1 Equilibration of 11,13-Dimethyl-4,5-dihydrobenzo[*b*]benzo[6,7]oxepino[3,2,1-*hi*]benzofuran-10-ium, [*P*, $(R)_O$]-bis-(*R*)-BINOL borate, 462: 304

4.4.2 Enantiomeric ratio erosion study of 11,13-dimethyl-4,5-dihydrobenzo[b]benzo[6,7]oxepino[3,2,1-hi]benzofuran-10-ium hexafluorophosphate, enantioenriched-[*M*, $(S)_O$]-464: 308

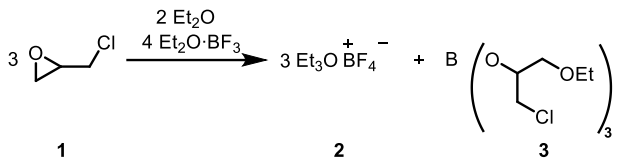
5 Bibliography 310

1 Chapter 1: Aryne Generation from Triaryloxonium Ions

1.1 Introduction

1.1.1 Trialkyloxonium ions

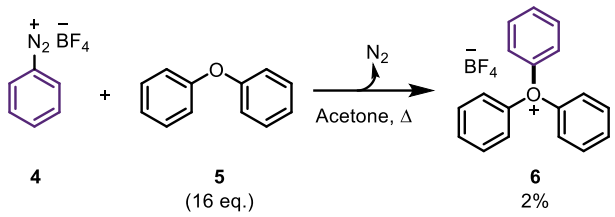
Oxonium ions are highly reactive electrophilic species and therefore often only exist as fleeting intermediates.[1] However, trialkyloxonium ions, known as Meerwein's salts, are kinetically stable and are amongst the most powerful alkylating reagents known.[2,3] Meerwein's reagent refers to triethyloxonium tetrafluoroborate **2** which is readily prepared from diethyl ether, $Et_2O{\cdot}BF_3$, and epichlorohydrin **1** (**Scheme 1**).[4] Meerwein salts are highly electrophilic and alkylate even weak nucleophiles, however, this reactivity also limits their utility in the synthesis of functionalised molecules.



Scheme 1: Synthesis of Meerwein's reagent **2**.

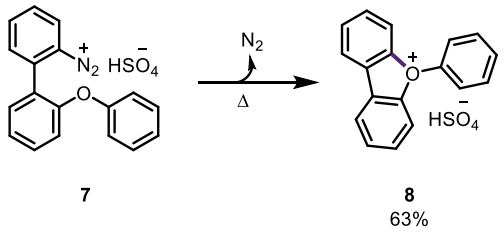
1.1.2 Triaryloxonuim ions

Triaryloxonium ions, first reported by Nesmeyanov and coworkers in 1957, were generated from *O*-arylation of diphenyl ether **5** with phenyl diazonium salts **4**, *via* the loss of N_2, in very low yields (2%).[5,6] The resulting triaryloxonium salts exhibited significantly higher decomposition temperatures (>150 °C) compared to their alkyl counterparts, as well as stability towards weak nucleophiles such as H_2O (**Scheme 2**).



Scheme 2: Intermolecular synthesis of triphenyloxonium tetrafluoroborate **6** *via* *O*-arylation of diphenyl ether **5** with phenyl diazonium salts **4**.

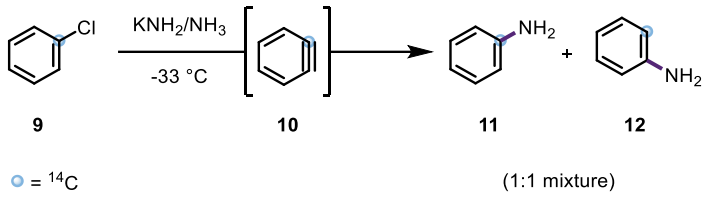
Two years later, Nesmeyanov and coworkers demonstrated that triaryloxonium ions containing a dibenzofuran scaffold could be readily made with significantly higher yield *via* intramolecular *O*-arylation.[7] A similar observation was made by Hellwinkel and coworkers in 1972 (**Scheme 3**).[8]



Scheme 3: Intramolecular *O*-arylation to afford triaryloxonium salt **8**.

1.1.3 Arynes

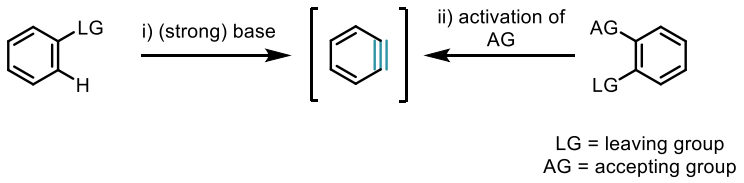
Arynes are highly reactive intermediates generated by the removal of two substituents on an aromatic ring. Despite being proposed more than a century ago by Stoermer and Kahlert,[9] their existence was not experimentally validated until 1953 where Roberts and coworkers performed a ^{14}C labelling experiment.[10] ^{14}C Labelled chlorobenzene **9** was treated with potassium amide in ammonia to give a 1:1 mixture of the *ipso*- and *ortho*-substituted anilines, **11** and **12** respectively, providing evidence for the electronically neutral and symmetrical aryne intermediate **10** (**Scheme 4**).



Scheme 4: ^{14}C labelling experiment to probe the existence of benzyne **10**.

1.1.4 Aryne generation

In general, the synthesis of *ortho*-aryne intermediates requires the removal of two vicinal substituents on an aromatic ring. This can be achieved by i) deprotonation *ortho* to a leaving group, or ii) concurrent elimination of a neighbouring accepting group and a leaving group (**Scheme 5**). Typically, monosubstituted precursors, which are activated by deprotonation, are more readily synthesised and provide better atom economy whereas 1,2-disubstituted precursors are activated under milder conditions.

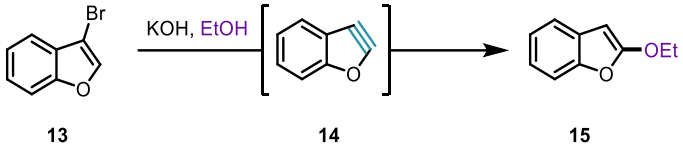


Scheme 5: General approaches to *ortho*-aryne synthesis from i) monosubstituted precursors ii) 1,2-disubstituted precursors.

1.1.4.1 Deprotonation of aryl halides

The earliest postulated arynes were reported to be generated from monosubstituted aryl halides *via ortho*-deprotonation with strong base, as demonstrated in the labelling experiment described in section **1.1.3** (**Scheme 4**). In 1902, Stoermer and Kahlert first proposed the existence of 2,3-benzofuryne **14** after observing the formation of 2-ethoxybenzofuran **15** when 3-bromobenzofuran **13** was heated in the presence of base and ethanol (**Scheme 6**).[9] The existence

of this intermediate has since been brought into question,[11–13] however, its significance within aryne chemistry persists.

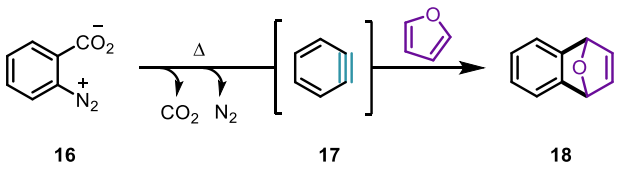


Scheme 6: The first postulated aryne **14**, generated from 3-bromobenzofuran **13**.

Requiring strong bases to generate the arynes restrict the functional group compatibility of this precursor, prompting the development of milder methods for aryne generation to enhance its utility in organic synthesis. Therefore, the subsequent generation of aryne precursors shifted focus to the 1,2-disubstituted variant to reduce the reliance on strong bases.

1.1.4.2 Benzenediazonium carboxylates

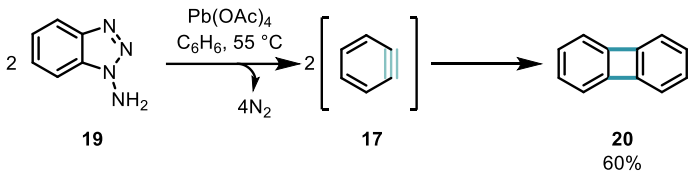
For instance, in 1960 Stiles and Miller demonstrated that benzenediazonium carboxylate **16** decomposed to generate benzyne **17** *via* the evolution of CO_2 and N_2.[14] Heating the precursor in the presence of furan yielded the corresponding [4+2] cycloaddition product **18** indicating the formation of an aryne intermediate **17** (**Scheme 7**). However, the explosive nature of the precursor imposes some limits on its practical utility.



Scheme 7: The generation and trapping with furan of benzyne **17** from benzenediazonium carboxylate **16**.

1.1.4.3 Aminobenzotriazoles

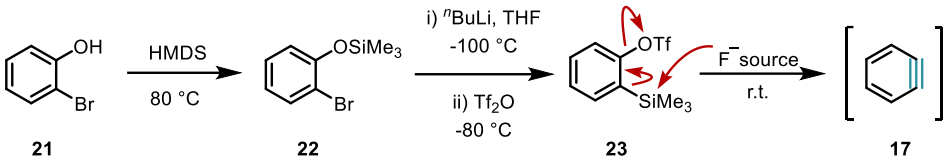
The generation of arynes from aminobenzotirazoles is also driven by the evolution of gas.[15] Campbell and Rees reported that upon treatment with $Pb(OAc)_4$, 2-aminobenzotriazole **19** is oxidised and subsequently fragments with the loss of two molecules of N_2 to afford benzyne **17** (**Scheme 8**). In the absence of an alternative trapping agent, benzyne **17** dimerises to afford biphenylene **20** in good yield (60%). However, the explosive nature of the precursor, along with the toxicity of the oxidising agent, limits the practicality of this method.



Scheme 8: Generation and dimerization of benzyne **17** from 2-aminobenzotrizaole **19**.

1.1.4.4 The Kobayashi method

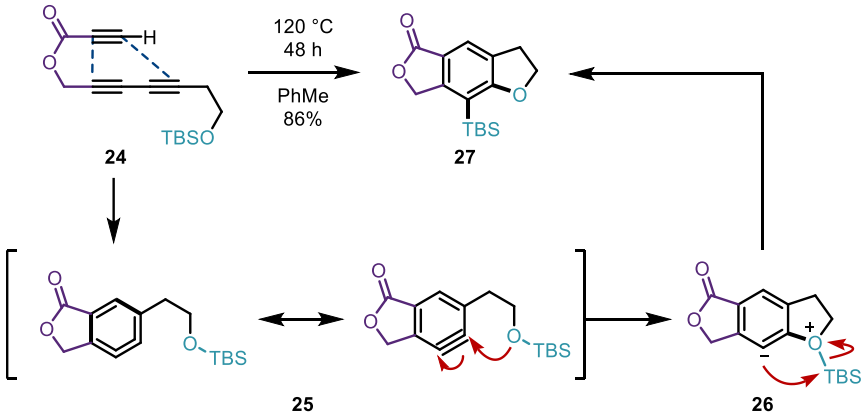
The fluoride mediated aryne generation method from *ortho*-silyl aryl triflates reported by Kobayashi and coworkers in 1983 represented a significant development in the chemistry available for aryne generation.[16] The precursor can be readily prepared from 2-bromophenol **21** and the use of fluoride for activation of the precursor **23** allowed for compatibility with a much broader array of trapping agents, thereby accelerating the incorporation of arynes into modern organic synthesis (**Scheme 9**).[17] However, the synthesis of the precursor requires organometallic regents, limiting the versatility of accessible arynes from this precursor.



Scheme 9: Synthesis of Kobayashi precursor **23** and the generation of benzyne **17** using a fluoride source.

1.1.4.5 Hexadeyhdro Diels-Alder reaction

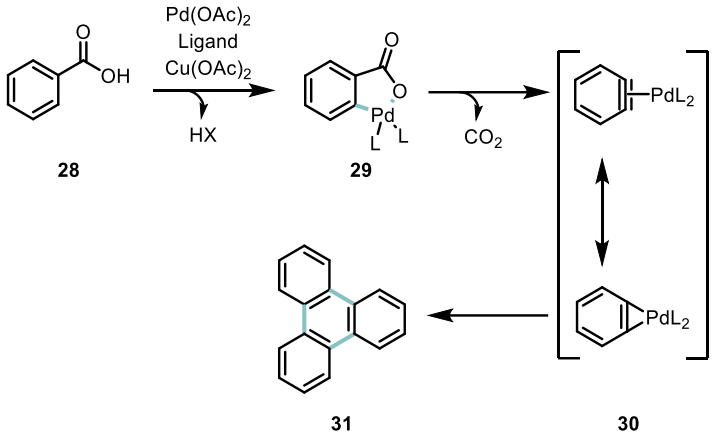
More recently in 2012, Hoye and coworkers developed a 'reagent free' method for aryne generation *via* an intramolecular Hexadehydro Diels-Alder (HDDA) reaction[18] which built on early reports from both Johnson and coworkers[19] and Ueda and coworkers[20] in 1997. The reaction proceeds *via* a [4+2] cycloaddition between a 1,3-diyne tethered to an alkyne to give an *ortho*-benzyne which is subsequently trapped by an appropriate trapping agent (**Scheme 10**). This methodology gives access to a diverse range of complex benzenoid products.[18] While no external reagent is required to activate the reaction, the incorporation of the tether in the final product/subsequent steps to remove it imposes some limitations to this methodology.



Scheme 10: HDDA aryne generation and intramolecular trapping *via* insertion into the O-Si Bond.

1.1.4.6 Pd(II)-catalysed C-H activation of benzoic acid

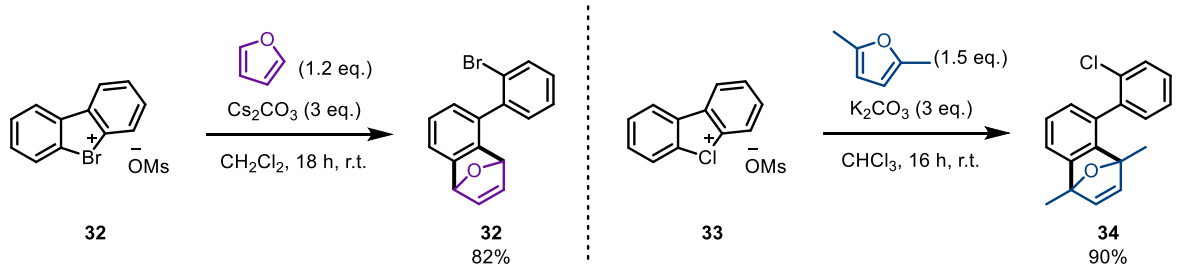
Greaney and coworkers developed a method to generate arynes using Pd(II)-catalysed C-H activation from readily available monosubstituted benzoic acids.[21] *Ortho*-C-H activation of **28** generates oxapalladacycle **29** and subsequent decarboxylation yields palladium coordinated aryne/metallocyclopropene **30** which trimerized to form triphenylene **31** (**Scheme 11**).



Scheme 11: The Pd(II)-catalysed C-H activation of benzoic acid **28** to generate coordinated aryne **30** and its [2+2+2] trimerisation product **31**.

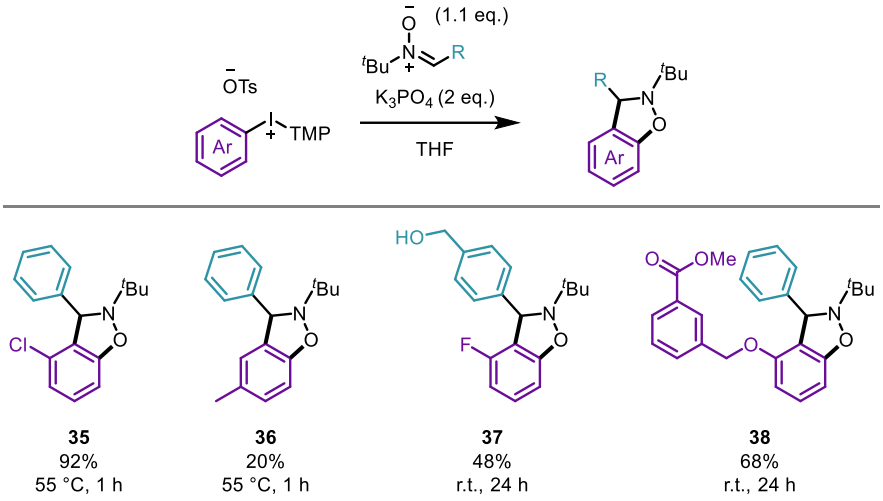
1.1.4.7 Onium salts: λ^3-bromanes, -chloranes, and iodanes

A recent resurgence in the field of onium chemistry, in particular hypervalent λ^3-bromanes, -chloranes, and -iodanes has led to an increase in the development of monosubstituted aryne precursors under milder conditions. The excellent leaving group ability of hypervalent halogens facilitates aryne generation using considerably weaker base than those required for the corresponding aryl halides. Wencel-Delord and coworkers have pioneered the use of cyclic diaryl λ^3-bromanes[22,23] and λ^3-chloranes[24] to generate arynes using weak base (**Scheme 12**). While the milder conditions allow the potential to have a broader range of substituents on the aryl ring, the resultant aryne incorporates the halogenated biaryl moiety. Thus, simple monoaryl arynes are not readily accessible from these precursors.



Scheme 12: The generation of arynes from cyclic biaryl λ³-bromanes and λ³-chloranes.

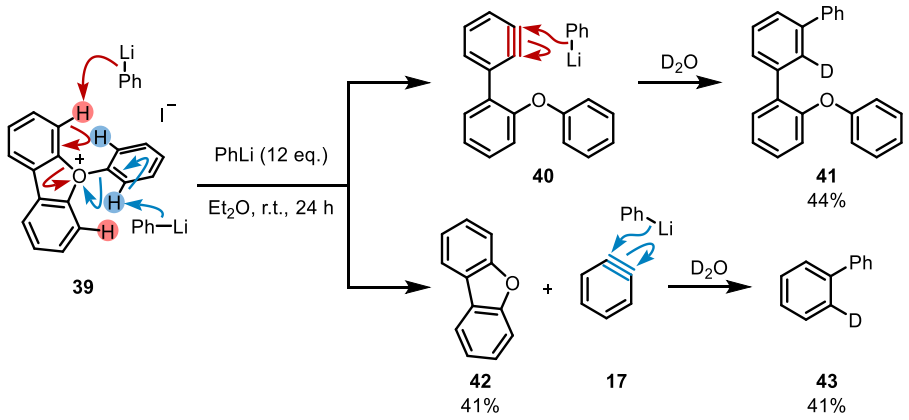
Unlike λ³-bromanes and λ³-chloranes, λ³-iodanes have had widespread use in organic synthesis.[25] However, their use as aryne precursors had been limited until the disclosure of publications from Li,[26] Han,[27] and Stuart[28–30] demonstrating the generation of arynes from iodonium salts using mild bases. Stuart and coworkers reported the broadest functional group tolerance for arynes using aryl(TMP)iodonium salts, enabled using weak base, potassium phosphate (**Scheme 13**). However, the efficient generation of aryne requires the presence of a *meta*-substituted inductively withdrawing group. Additionally, the incorporation of sensitive functional groups, such as an alcohol **37** or an ester **38**, occurs through tethered aryl moieties, rather than direct attachment to the aryne, thereby limiting the range of functionality directly on the aryne ring.



Scheme 13: Aryne generation and trapping from aryl(TMP)iodonium salts.

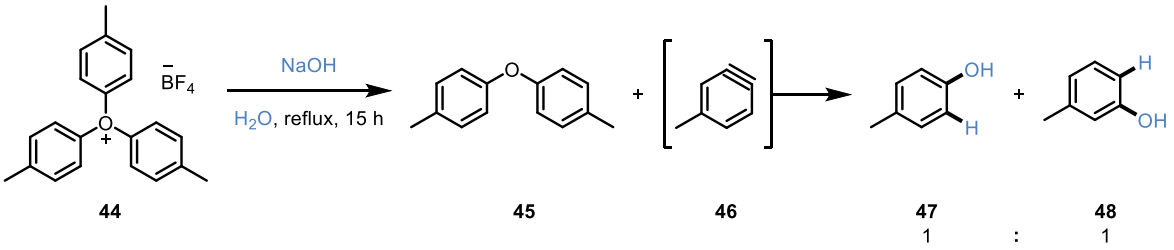
1.1.5 Aryne generation from triaryloxonium ions

In 1972, Hellwinkel and Seifert treated triaryloxonium salt **39** with excess PhLi in the presence of D_2O to yield products, **41** and **43**, which were consistent with trapping of aryne intermediates, **40** and **17** respectively (**Scheme 14**).[31] The two proposed aryne intermediates were likely generated *via* deprotonation *ortho* to the positively charged oxygen followed by cleavage of the neighbouring C-O bond. Subsequent nucleophilic attack of phenylate and quenching with D_2O afforded the trapped aryne products in a 1.07:1 (**41**:**43**) distribution demonstrating poor selectivity in the deprotonation step.



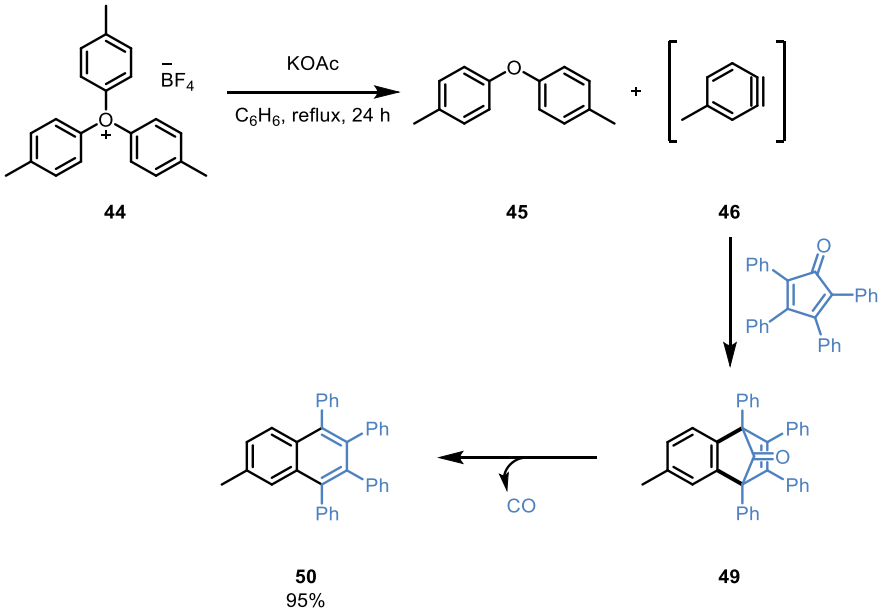
Scheme 14: Generation of arynes **40** and **17** from triaryloxonium salt **39** using PhLi.

Over a decade later, Tolstaya and coworkers provided further evidence in support of aryne generation from triaryloxonium ions.[32] Tri-*para*-tolyloxonium tetrafluoroborate salt **44** was refluxed in the presence of sodium hydroxide in water to yield bis(aryl) ether **45** and a 1:1 mixture of *para*- and *meta*-cresols, **47** and **48** respectively (**Scheme 15**). The distribution of products was consistent with trapping electronically neutral aryne intermediate **46** with water.



Scheme 15: Aryne generation from tri-*para*-tolyloxonium tetrafluoroborate salt **44** and its trapped products, **47** and **48**, with H_2O.

Furthermore, triaryloxonium salt **44** was refluxed in benzene in the presence of weak base, potassium acetate, and tetraphenylcyclopentadienone to afford tetraphenylnaphthalene **49** in excellent yield (95%) (**Scheme 16**).[32] This reaction was proposed to proceed *via* a [4+2] cycloaddition between an aryne intermediate **46** and the diene followed by rearomatisation by extrusion of carbon monoxide.

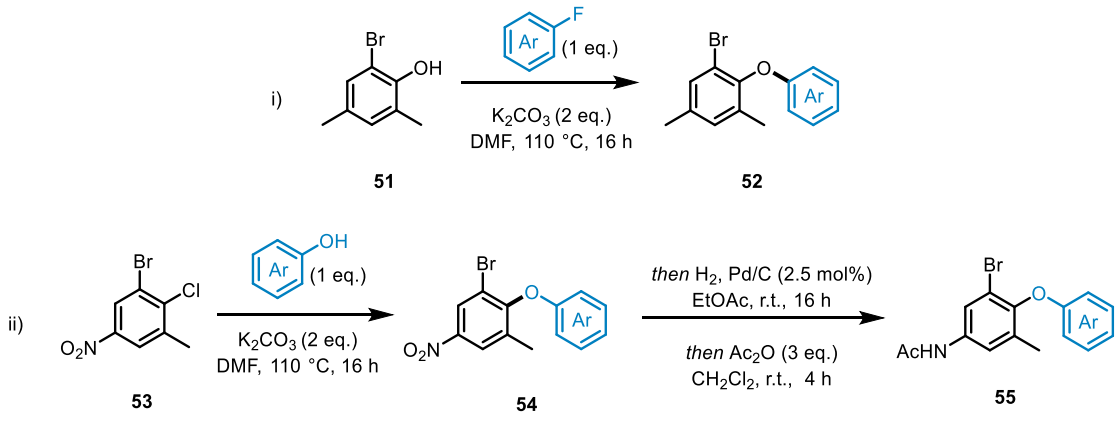


Scheme 16: Aryne generation from tri-*para*-tolyloxonium tetrafluoroborate salt **44** and trapping with tetraphenylcyclopentadienone followed by loss of CO.

1.1.6 Previous work within the group

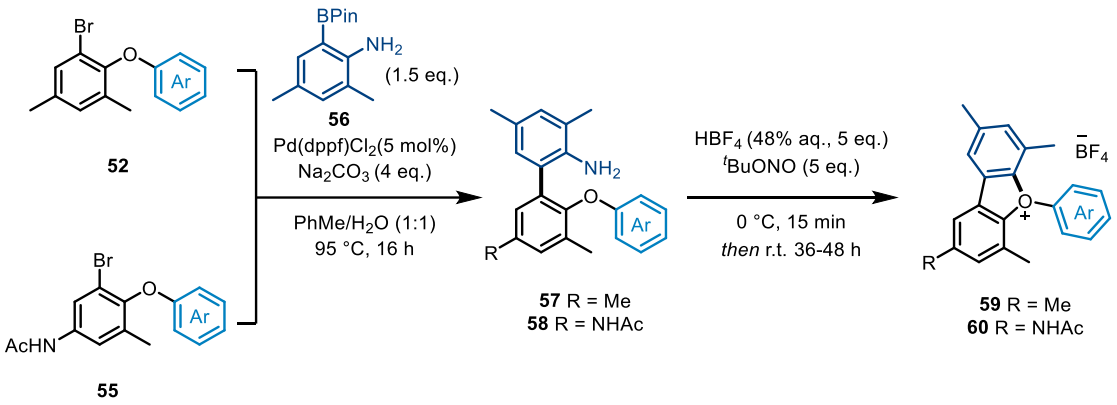
Since these reports over 20 years ago, triaryloxoniums salts have been absent in modern aryne synthesis. It was postulated that given their remarkable stability,[6] along with the potential to generate arynes using mild base,[32] triaryloxonium ions could be harnessed as mild aryne precursors to broaden the scope of synthetically accessible arynes.

To achieve this, a synthetic route was developed in the Smith group by Owen Smith to generate triaryloxonium ions from commercially available building blocks.[33] *O*-Arylation is achieved *via* an S_NAr reaction where the desired aryl group can be incorporated either: i) within an aryl fluoride bearing an electron-withdrawing group or ii) within a phenol (**Scheme 17**). It was observed that the presence of a strong electron withdrawing group *para* to the oxygen prevented oxonium formation. Therefore, when the *O*-arylation was achieved using **53**, hydrogenation and acetylation of the nitro group was required to facilitate subsequent oxonium formation. In addition, blocking methyl groups were strategically installed to ensure selective deprotonation of the pendent aryl rather than the C-H bonds on the dibenzofuran core.



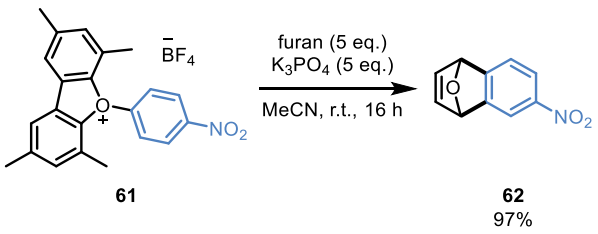
Scheme 17: *O*-arylation *via* S_NAr with i) an aryl fluoride bearing an electron withdrawing group or ii) a phenol.

The biaryl bond, which connects the aniline moiety, is then installed *via* a Suzuki-Miyaura coupling with aniline containing pinacol borane **56**.[34] The key bond disconnection to generate the oxonium tetrafluoroborate salt, **59** or **60**, can be achieved by diazotisation of the aniline, **57** or **58**, followed by loss of N_2 and intramolecular *O*-arylation (**Scheme 18**).[7,8]



Scheme 18: Synthetic route to triaryloxonium salts from bis(aryl) ethers.

Furthermore, an optimised set of conditions to generate arynes under mild conditions was developed. Upon treatment with a weak base, potassium phosphate, in acetonitrile triaryloxonium salt **61** generated an aryne which was subsequently trapped by furan to give **62** in excellent yield (97%) (**Scheme 19**). Notably, the use of weak base allows the reaction to proceed under air without additional drying of the solvent making it operationally simple.



Scheme 19: The generation and trapping of a benzyne from triaryloxonium salt **61** with furan.

1.1.7 Project aims

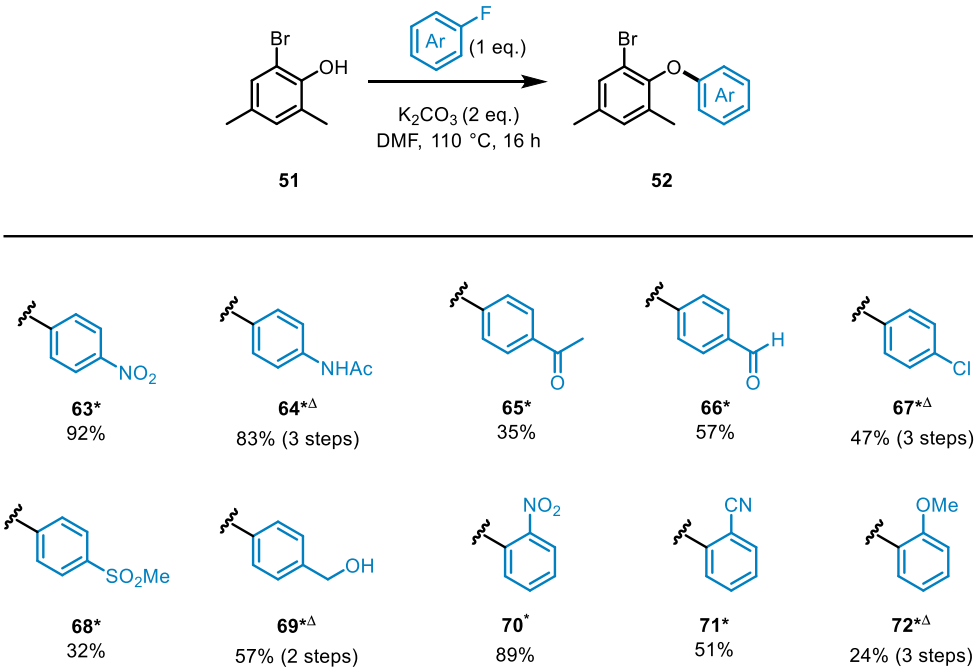
This project aimed to use the synthetic routes developed within the group to generate a broad range of triaryloxonium salts. Subsequently, we would assess their potential to generate the corresponding arynes under the ambient conditions outlined in **Scheme 19**. It was envisioned that this might develop a method complementary to existing aryne literature, benefitting from the mild conditions employed for both oxonium synthesis and aryne generation. This approach aimed to accommodate sensitive functional groups, addressing limitations present in other aryne generation methods.

1.2 Results and discussions

1.2.1 Synthesis of bis(aryl) ethers

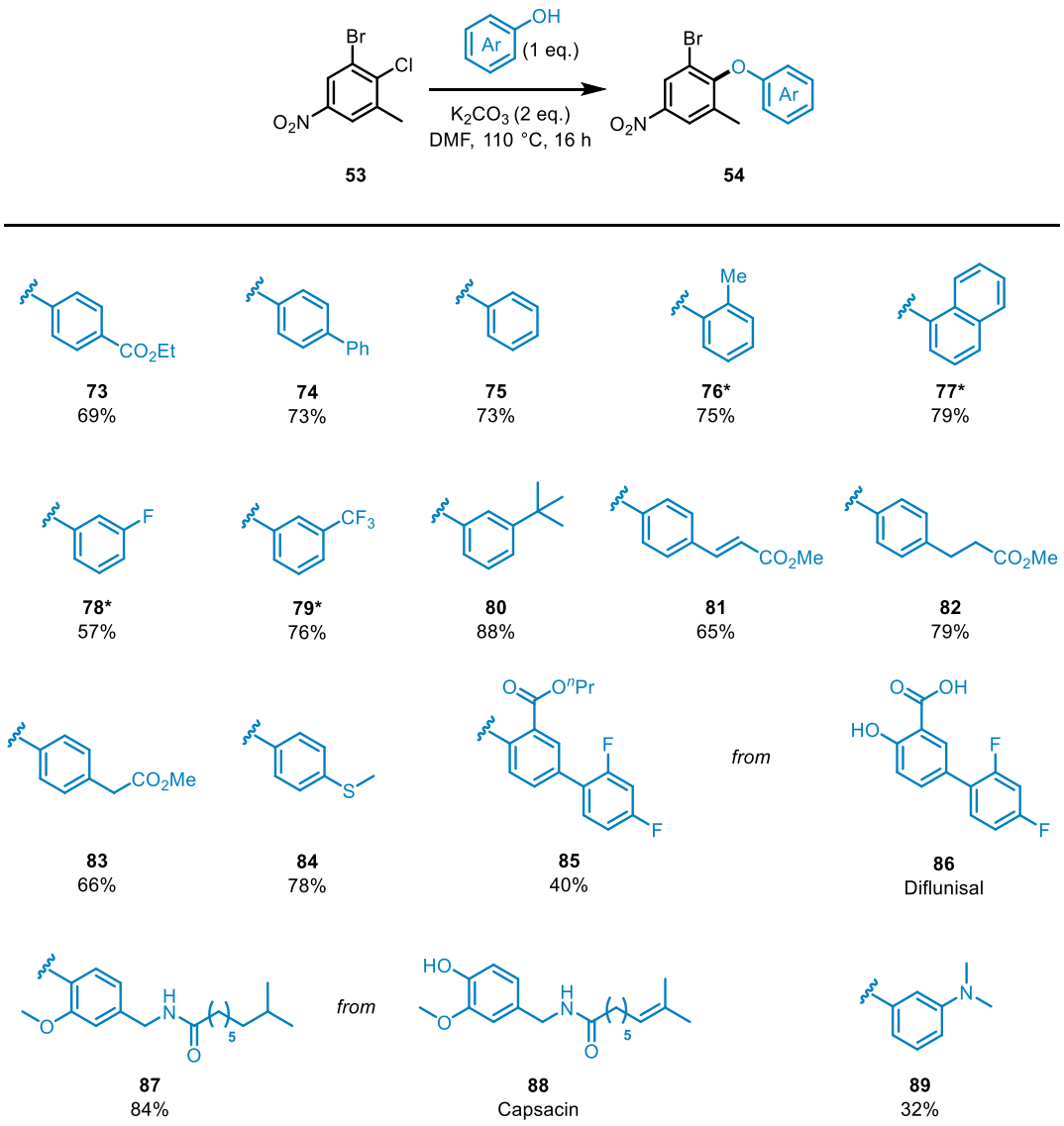
To achieve this goal, we initially set out to synthesise bis(aryl) ethers using the two synthetic routes described in section **1.1.6**.[*] Pleasingly, a broad range of aryl fluorides bearing *ortho*- and *para*-substituted electron withdrawing groups afforded the corresponding bis(aryl) ethers in moderate to good yield (**Scheme 20**).

[*] The full scope has been added for completeness and substrates synthesised by Owen Smith are labelled within schemes. Full details of their synthesis will not be included in the supporting information.



Scheme 20: Synthesis of bis(aryl) ethers from electron deficient aryl fluorides. *Synthesised by Owen Smith. ΔSynthesised using a modified procedure.

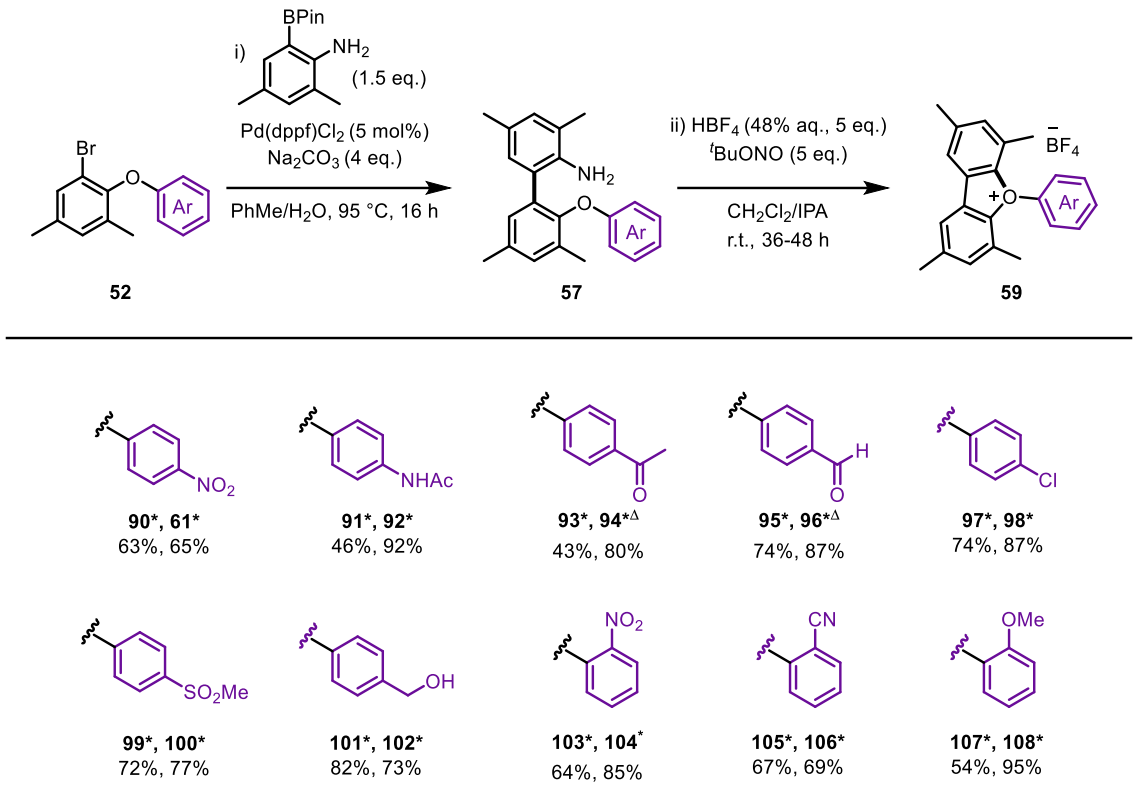
Furthermore, a range of *ortho*-, *meta*-, and *para*-substituted phenols reacted with S_NAr precursor **53** under basic conditions to generate nitro-containing bis(aryl) ethers in moderate to very good yield (**Scheme 21**). To further demonstrate the broad applicability of the route to triaryloxonium salts, we subjected the anti-inflammatory drug Diflunisal **86** and natural product Capsaicin **88** to the synthetic route and to afford the corresponding bis(aryl) ethers, **85** (40%) and **87** (84%) respectively. The diflunisal adduct was modified by esterification of the carboxylic acid to prevent deprotonation upon treatment with potassium phosphate.[35]



Scheme 21: Synthesis of bis(aryl) ether oxonium ion precursors from the corresponding phenols. *Synthesised by Owen Smith

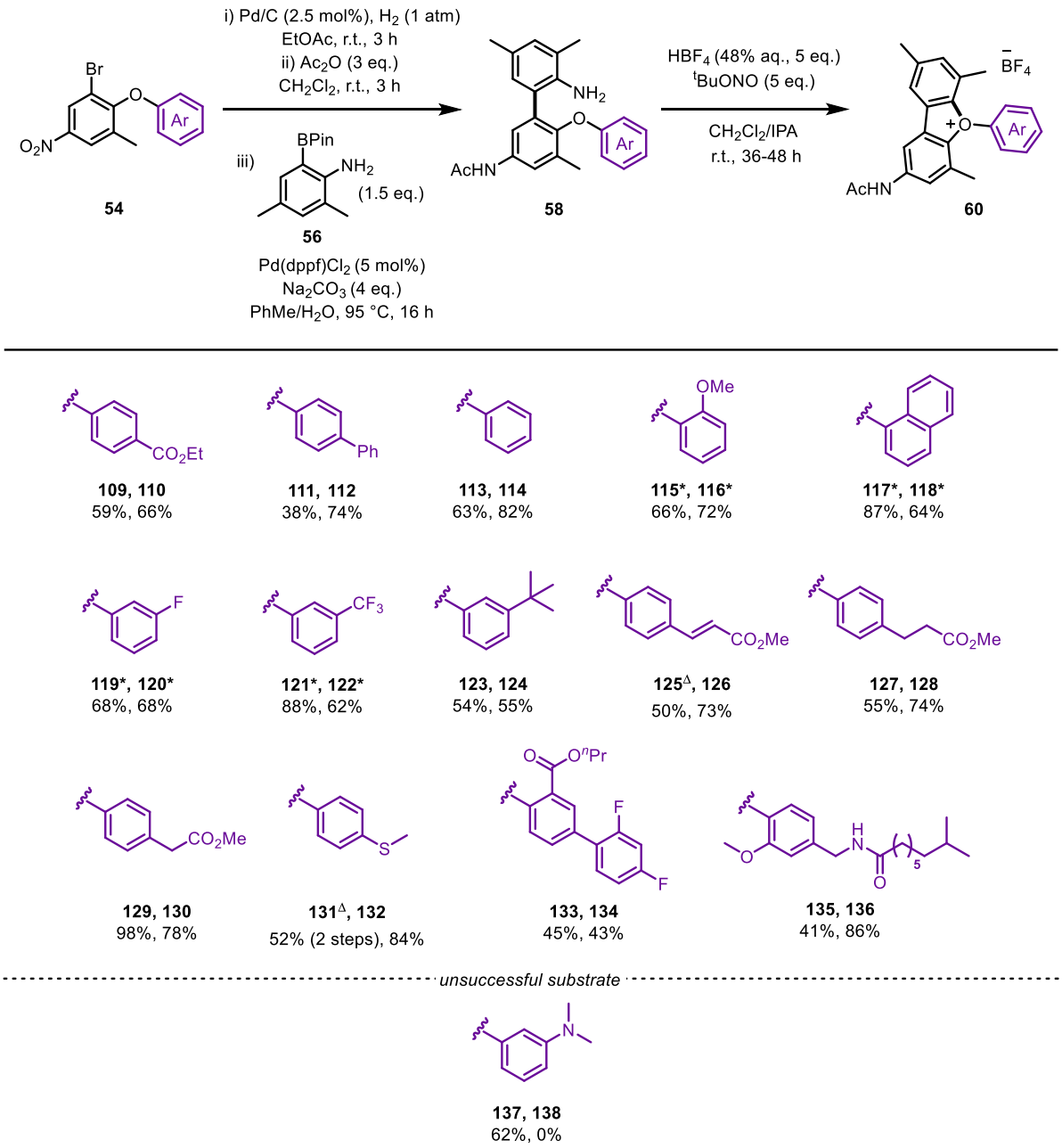
1.2.2 Triaryloxonium salt synthesis

The bis(aryl) ethers were then subjected to Suzuki-Miyaura coupling followed by diazotisation to generate the triaryloxonium salts. Using the bis(aryl) ethers derived from aryl fluorides, the cross-coupling reactions proceeded in moderate to very good yield (46%-82%) while the oxonium formation from the aniline intermediates was generally achieved in higher yield (65%-95%) (**Scheme 22**).



Scheme 22: Synthesis of triaryloxonium tetrafluoroborate salts. Yields are denoted X% (Suzuki-Miyaura coupling), X% (oxonium formation) *Synthesised by Owen Smith. ΔGenerated *via* a triazine to prevent condensation of the aniline moiety with the carbonyl groups.

The modified route containing additional steps to transform a nitro group into a *N*-acetyl group was applied to the bis(aryl) ethers generated from phenolic starting materials (**Scheme 23**). Smooth reduction of the nitro groups to the corresponding anilines followed by acetylation was observed for all the substrates and resultant amides were used crude without further purification in the Suzuki-Miyaura coupling. Therefore, the yield for the aniline formation is reported over three steps.



Scheme 23: Synthesis of triaryloxonium tetrafluoroborate salts. Yields are denoted X% (yield over three steps, i, ii, iii), X% (oxonium formation). *Synthesised by Owen Smith. Δ Generated using a modified procedure.

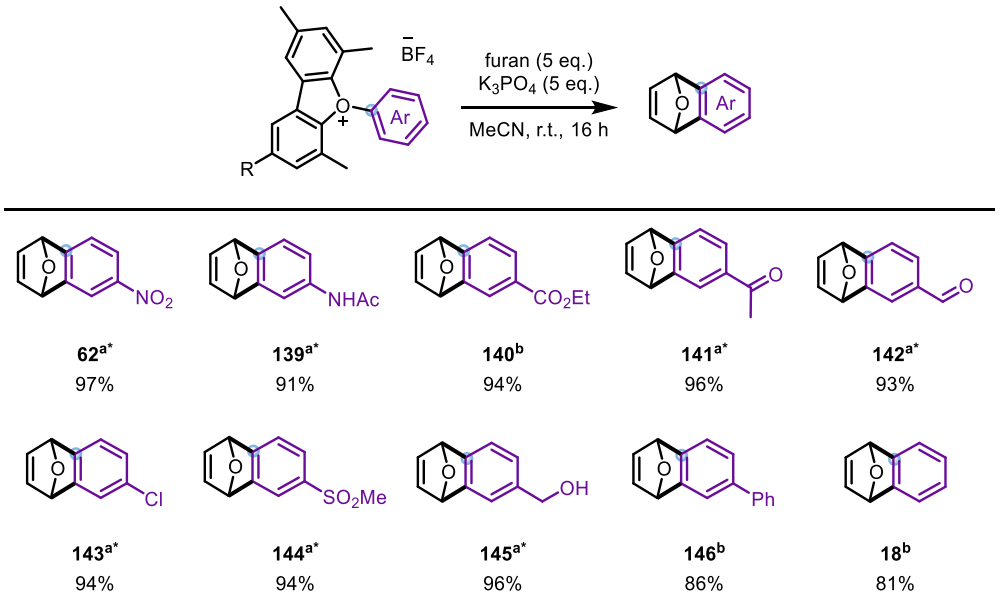
All the bis(aryl) ethers, with the exception of **89**, formed the corresponding anilines and subsequently oxonium salts in moderate to very good yield (**Scheme 23**). On average, oxonium formation proceeded in slightly lower yield compared to those derived from aryl fluorides. A modified procedure *via* an iron mediated reduction of **81** was required to ensure selective reduction

of the nitro group.[36] Furthermore, to prevent sulfur poisoning of the palladium catalyst,[37] the reduction of **84** was also achieved using iron instead of palladium. The aniline derived from 3-(dimethylamino)phenol **137** was unsuccessful in forming the corresponding triaryloxonium salt **138** upon diazotization. This could be a result of the nucleophilic nitrogen lone pair reacting with the diazonium.

1.2.3 Arynes scope

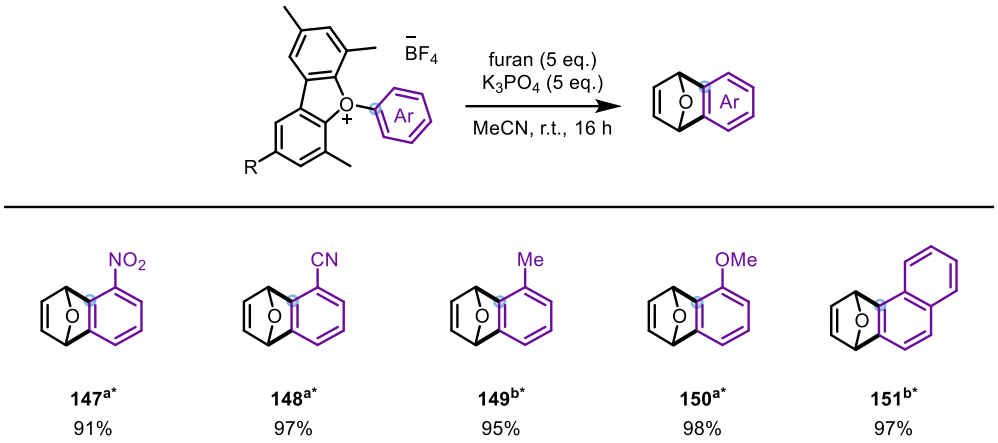
Having synthesised a broad range of triaryloxonium salts, we subjected them to the optimised aryne trapping conditions developed using the *para*-nitro oxonium **61** with furan as the model arynophile (**Scheme 24**). Pleasingly, almost all the substrates gave the desired furan [4+2] adducts in excellent yield.

Several tricycles containing *para*-substituted carbonyl containing functional groups were afforded including amide **139** (91%), ester **140** (94%), ketone **141** (96%), and aldehyde **142** (93%) respectively. The chloro **143** (94%) and sulfoxide **144** (94%) products were also obtained in very good yield. The use of weak base facilitated the generation and trapping of an aryne with furan bearing a free OH group to give **145** in excellent yield (96%). The tricycle with a pendent aryl group **146** was also obtained (86%). The unsubstituted variant **18** was generated with a slightly lower isolated yield (81%) due to the volatility of the product.



Scheme 24: The generation and trapping of benzynes with furan from triaryloxonium salts. [a]Generation from oxoniums where R = Me. [b]Generation from oxoniums where R = NHAc. *Synthesised by Owen Smith.

A range of *ortho*-substituted arynes were also compatible with the conditions (**Scheme 25**). Notably, *ortho*-nitro [4+2] adduct **147** was obtained in very good yield (91%), where the corresponding *ortho*-silyl triflate precursor undergoes a *thia*-Fries rearrangement upon treatment with fluoride.[38] In the presence of potassium phosphate and furan the *ortho*-cyano **147** (97%), methyl **149** (95%), methoxy **150** (98%), and naphthyl **151** (97%) products were isolated in excellent yield.

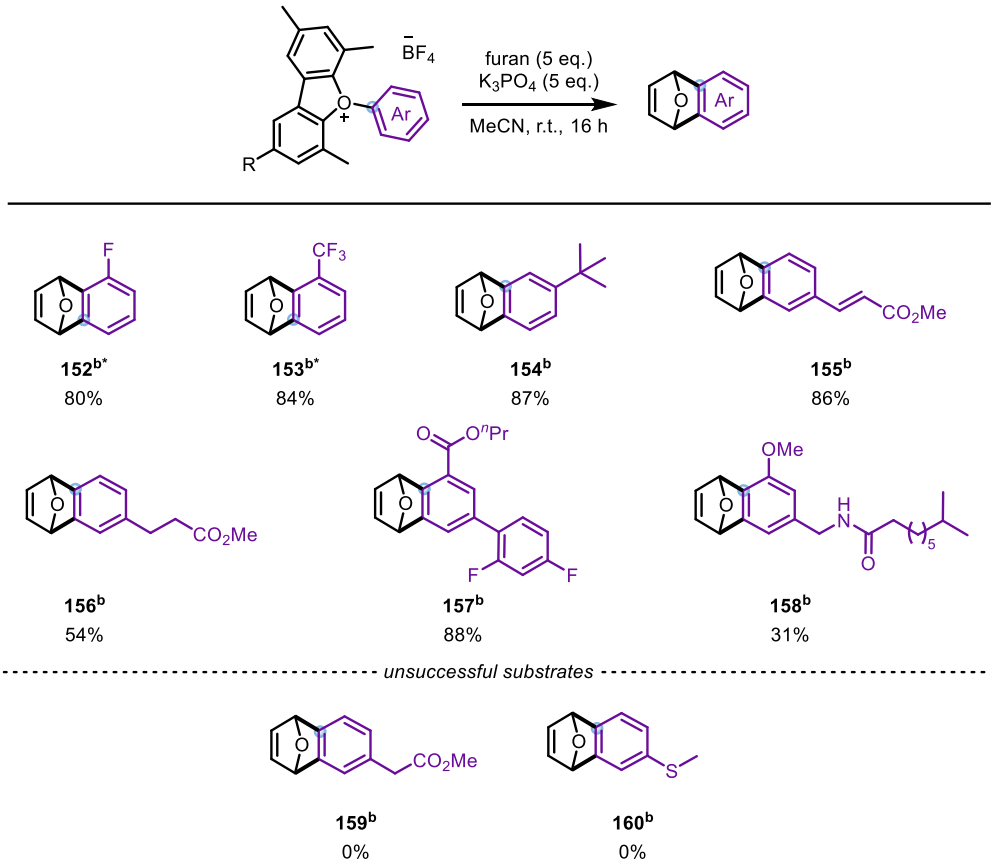


Scheme 25: The generation and trapping of benzynes with furan from triaryloxonium salts. [a]Generation from oxoniums where R = Me. [b]Generation from oxoniums where R = NHAc. *Synthesised by Owen Smith.

Several *meta*-substituted oxoniums probed the regioselectivity of the reaction. The fluoro and CF_3 oxoniums, **120** and **122** respectively, exclusively gave the cycloaddition products **152** (80%) and **153** (84%). The reverse regiochemistry was observed for the oxonium bearing a *meta-tert*-butyl group **124** to give **154** (87%) (**Scheme 26**).

The more densely functionalised Diflunisal and Capsaicin derived oxoniums, **134** and **136** respectively, also proceeded to form the desired products **157** (88%) and **158** (31%). Difficulties in purification were attributed to the lower isolated yield for **158**.

The oxonium bearing a *para*-CH_2CO_2Me group **130** was unsuccessful in generating the corresponding tricycle **159**. This is likely due to preferential deprotonation at the benzylic position. The analogous oxonium with an additional CH_2 unit separating the ester and aryl group **128** successfully gave the desired product **156** in 54% yield. Additionally, the oxonium containing the nucleophilic *para*-SMe group **132** also failed to generate the corresponding tricycle **160**. This is potentially attributed to preferential reactivity of the sulfide with the aryne.[39]



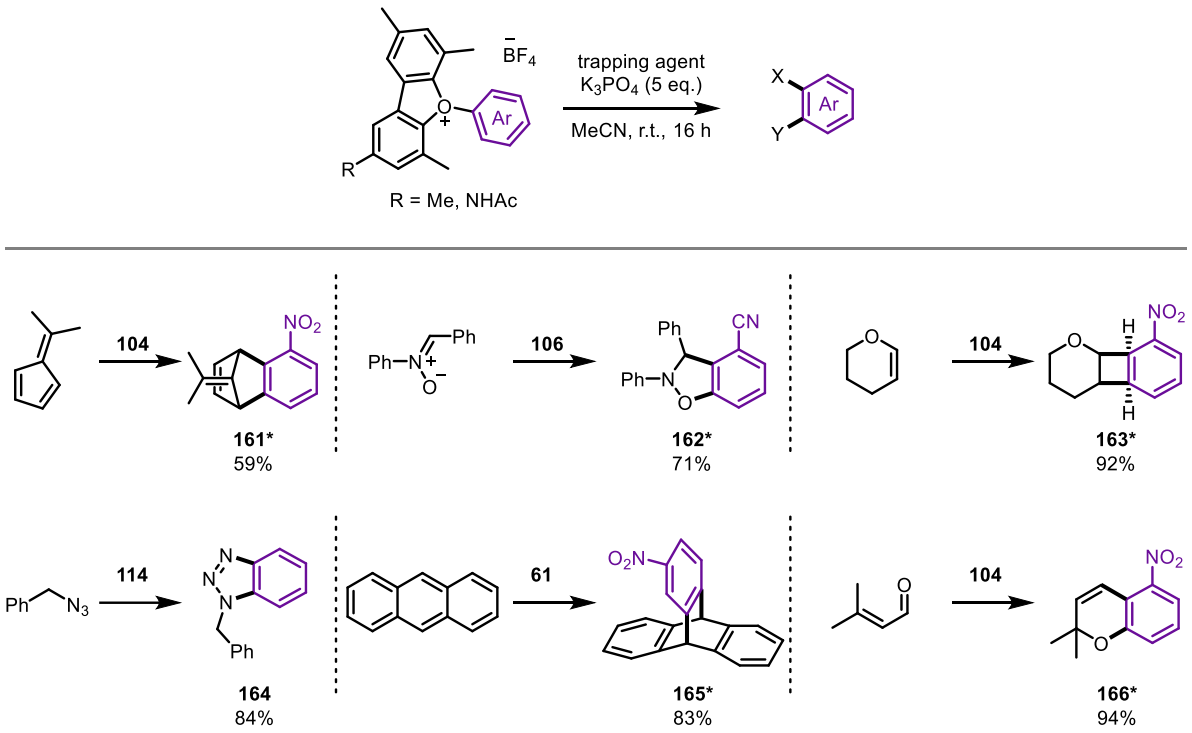
Scheme 26: The generation and trapping of benzynes with furan from triaryloxonium salts. [a]Generation from oxoniums where R = Me. [b]Generation from oxoniums where R = NHAc. *Synthesised by Owen Smith.

1.2.4 Arynophile scope

We then sought to explore the versatility of these aryne precursor by varying the nature of the arynophile. A range of trapping agents successfully yielded the corresponding trapped products upon treatment with oxoniums in the presence of potassium phosphate in acetonitrile.

6,6-Dimethylfulvene underwent a [4+2] cycloaddition with *ortho*-nitro oxonium **104** to give the tricycle **161** (59%).[40] *N*-Diphenylnitrone reacted with *ortho*-cyano oxonium **106** *via* a [3+2] cycloaddition to yield bicycle **162** (71%).[41] 3,4-Dihydro-*2H*-pyran reacted *via* a formal [2+2] cycloaddition with *ortho*-nitro oxonium **104** to afford **163** in excellent yield (92%).[42] Benzyl azide underwent a [3+2] cycloaddition with oxonium **114** to give **164** in 84% yield.[43] Anthracene reacted

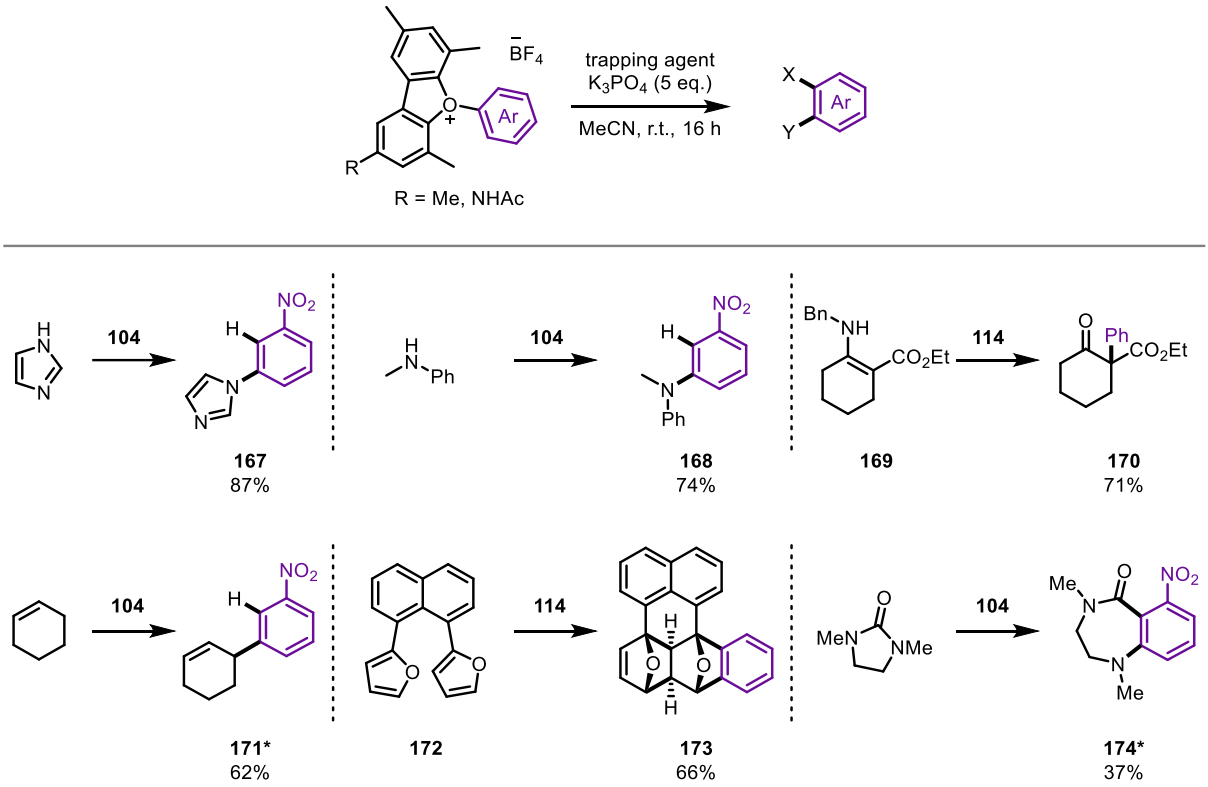
with the precursor **61** *via* a [4+2] cycloaddition to give nitro-substituted Triptycene **165** (83%) (**Scheme 27**).[44]



Scheme 27: Trapping of arynes generated from triaryloxonium salts with trapping agents. *Synthesised by Owen Smith.

Ortho-nitro oxonium **104** also reacted with nucleophiles imidazole and *N*-methylaniline to exclusively give *meta*-substituted regioisomers **167** (87%) and **168** (74%) respectively. Furthermore, oxonium **114** reacted with enamine **169** to form an imine which, upon hydrolysis, yields cyclohexanone **170** containing a quaternary stereocenter in 71% yield.[45] Cyclohexene underwent an Alder-Ene reaction with oxonium **104** to yield **171** (62%) (**Scheme 28**).[46]

The aryne generated from **114** reacted with bisfuran **172** *via* a tandem [4+2]/[4+2] cycloaddition to give *exo*,*exo*-polycycle **173** (47%).[47] 1,3-Dimethyl-2-imidazolidinone (DMI) reacted with oxonium **104** to give sigma bond insertion reaction product **174** in moderate yield (37%) (**Scheme 28**).[48]



Scheme 28: Trapping of arynes generated from triaryloxonium salts with trapping agents. *Synthesised by Owen Smith. See supplementary information for the synthesis of **169** and **172**.

1.3 Conclusion and future work

Two routes developed within the group have been applied to a broad range of phenols and aryl fluorides bearing electron withdrawing groups to generate triaryloxonium salts in good yield. Through treatment with weak base, these oxoniums serve as excellent aryne precursors, exemplified by their efficient trapping with a broad range of arynophiles. This method demonstrates tolerance for a broad spectrum of functionalised arynes, beyond that of any existing method in the literature, and thereby expanding the synthetic potential of arynes. Future work would look to develop a more convergent synthetic route to the aryne precursors along with determining whether other hetaryne are accessible using this methodology.

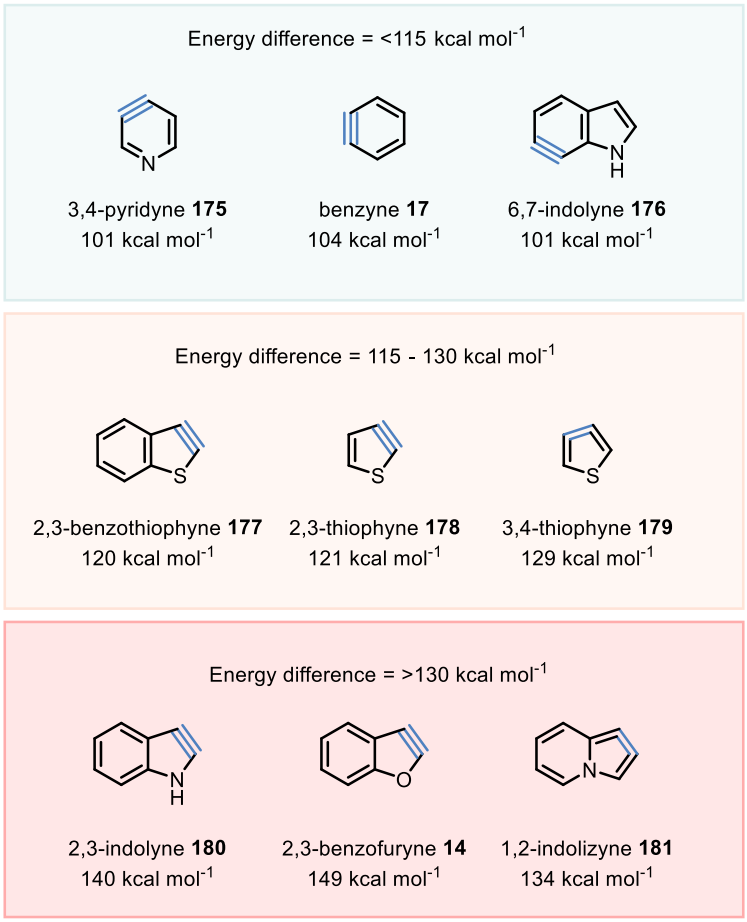
2 Chapter 2: Hetaryne Generation from Triaryloxonium Ions

2.1 Introduction

Hetarynes describe *ortho*-dehydroaromatic compounds containing a heteroatom in the aromatic ring. Compared to arynes, hetaryne generation poses a greater challenge due to enhanced ring strain, side reactions with nucleophilic heteroatoms, and increased complexity in synthesis of their precursors, thereby limiting their development and practical utility.[12] Nonetheless, new methodologies in aryne generation throughout the last century has enabled the synthesis of a variety of hetarynes.

2.1.1 Computational model for hetaryne energy

In 2012, Paton, Houk, Garg, and coworkers conducted a computational study to predict the synthetic utility of hetarynes by calculating arene dehydrogenation energies.[49] Upon comparison with experimentally validated hetarynes, a useful model for predicting the feasibility of generating various hetarynes was established (**Scheme 29**). When the calculated energy was less than 115 kcal mol^{-1} the aryne was readily generated. An energy difference of 115 - 130 kcal mol^{-1} suggested aryne generation is possible but challenging. An energy difference greater than 130 kcal mol^{-1} was indicative of an energetically inaccessible aryne.



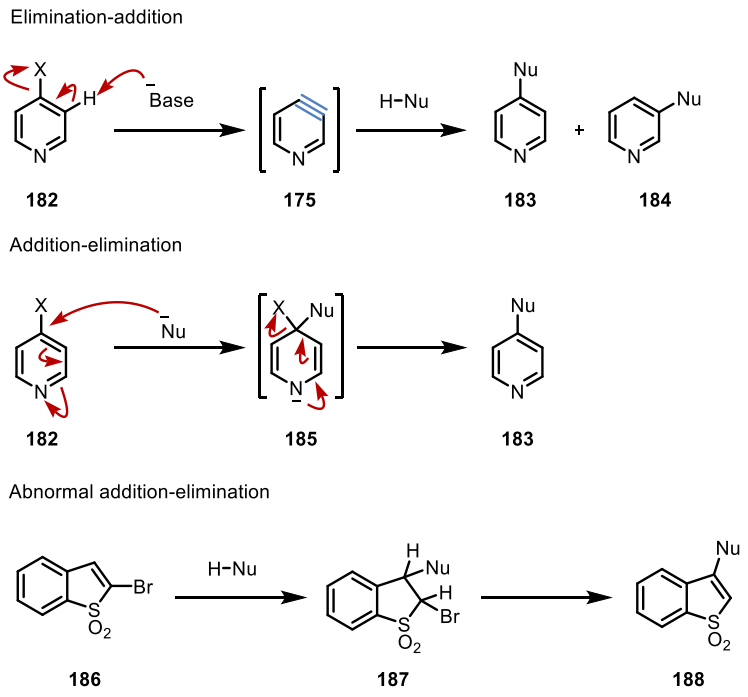
Scheme 29: Examples of calculated dehydrogenation energy of various hetarynes from a computational study. Energy of dehydrogenation = (energy of aryne + energy of H_2) – (energy of parent arene).

In general, the model predicts six-membered hetarynes, such as 3,4-pyridyne **175** and 6,7-indolyne **176**, to be energetically accessible (<115 kcal mol^{-1}) while five-membered hetarynes, for example 2,3-indolyne **140** and 2,3-benzofuryne **149**, typically fall within the energetically inaccessible region (>130 kcal mol^{-1}). However, the five-membered thiophynes, **177**, **178**, and **179**, are predicted to be accessible but challenging to form (115-130 kcal mol^{-1}). This is likely due to the longer C-S bond length providing a degree of relief in ring strain.

2.1.2 Experimental evidence for hetaryne generation

The inherent reactivity of hetarynes means observing these species, and therefore proving their formation, is challenging.[12] Determining whether a reaction proceeds *via* a hetaryne is typically looked for in the distribution of products it forms with trapping agents whose reactivity with arynes is known. However, interpreting these results requires caution, as products may also arise through alternative mechanisms.

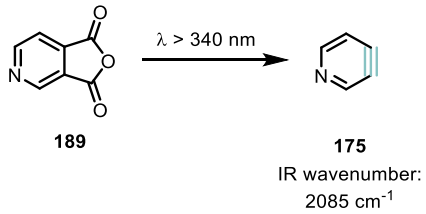
For example, the nucleophilic substitution of heteroaromatics can proceed *via* three main mechanisms. Firstly, the elimination-addition mechanism, which proceeds *via* a hetaryne intermediate **175** to give a mixture of regioisomers, **183** and **184** (**Scheme 30**).[12,50,51] Alternatively **183** can be formed through an addition-elimination reaction *via* an anionic intermediate **185** (**Scheme 30**).[12,50,51] Nucleophilic substitution can also occur through an abnormal addition-elimination mechanism where a nucleophile adds *cine* to a leaving group, followed by *cine* elimination to afford the product **188** (**Scheme 30**).[12,52]



Scheme 30: Mechanisms for nucleophilic substitution of heteroaromatic compounds.

Therefore, observation of the expected product of a nucleophilic substitution reaction of a hetaryne is not considered sufficient evidence of the reaction proceeding *via* an aryne intermediate. Both cycloaddition reactions with conjugated dienes and isotopic labelling experiments are more informative, though not without their own limitations.

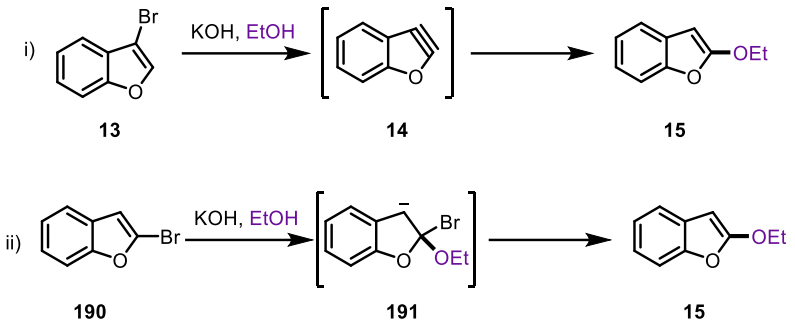
Efforts to directly observe hetarynes have been made. Nam and Leroi provided evidence for 3,4-pyridyne **175** generation when they irradiated 3,4-pyridine dicarboxylic anhydride **189** in a N_2 matrix.[53] The resulting IR spectrum showed a peak at 2085 cm^{-1}, characteristic of an aryne C-C triple bond (**Scheme 31**).[54]



Scheme 31: Irradiation of **189** led to observation of a peak at 2085 cm^{-1} in the resulting IR spectrum, suggested to be due to the proposed hetaryne intermediate **175.**

2.1.2.1 2,3-Benzofuryne

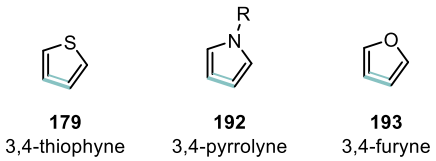
As discussed in **Chapter 1**, the first proposed aryne intermediate was 2,3-benzofuryne **14** when Stoermer and Kahlert observed the formation of 2-ethoxybenzofuran **15** after heating 3-bromobenzofuran **13** in the presence of hydroxide in ethanol (**Scheme 32**, i).[9] However, the existence of this high energy intermediate **14** has been disputed and an alternative route *via* an addition-elimination reaction with trace 2-bromobenzofuran **190** has been proposed (**Scheme 32**, ii).[11] Furthermore, the calculated energy of dehydrogenation to form **14** was reported to be 149 kcal mol^{-1}, supporting the unlikelihood of its generation and trapping from **13**.[49]



Scheme 32: i) The first postulated aryne, generated from 3-bromobenzofuran **13** and ii) a proposed alternative addition-elimination pathway from 2-bromobenzofuran **190** to explain the observed reactivity.

2.1.2.2 Cumulenes: 3,4-thiophyne, 3,4-pyrrolyne, and 3,4-furyne

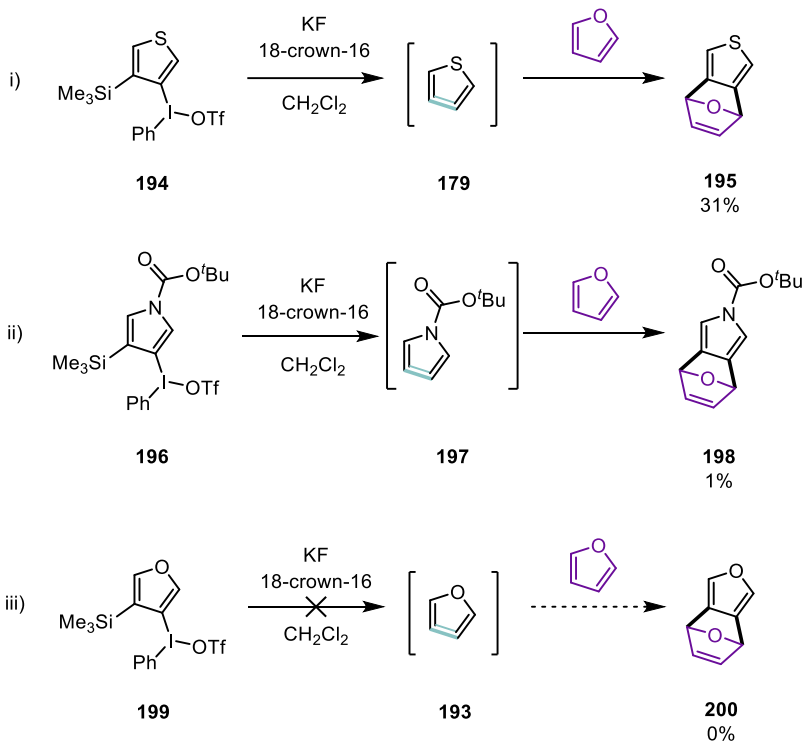
The generation of 3,4-thiophyne **179**, 3,4-pyrrolyne **192**, and 3,4-furyne **193**, requires the removal of *ortho*-substituents around a single bond, leading to the formation of cyclic cumulenes (**Scheme 33**). These intermediates, characterised by three consecutive double bonds, and are isoelectronic with the corresponding 2,3-hetarynes and are often collectively referred to as hetarynes.



Scheme 33: Cumulenes: 3,4-thiophyne **179**, 3,4-pyrrolyne **182**, and 3,4-furyne **193**.

In studies by Wong and coworkers, the generation of 3,4-hetarynes from *ortho*-silyl aryl iodonium triflates was investigated. The precursor for 3,4-thiophyne **194** was treated with potassium fluoride, and in the presence of a large excess of arynophiles such as furan, the corresponding trapped aryne products were formed, albeit in low to moderate yield (7-31%) (**Scheme 34**, i).[55] This outcome indicated the presence of 3,4-thiophyne **179** as a reactive intermediate. Similarly, the precursor for *N*-Boc protected 3,4-pyrrolyne **196**, in the presence of potassium fluoride and excess arynophiles,

formed products consistent with a 3,4-pyrrolyne intermediate **179**, however in very low yield (1-2%) (**Scheme 34**, ii).[56] When the equivalent precursor for 3,4-furyne **199** was subjected to similar conditions in the presence of dienes, none of the desired Diels-Alder products were observed (**Scheme 34**, iii).[57]



Scheme 34: Studies into the generation and trapping with furan of i) 3,4-thiophyne **179** ii) *N*-Boc protected 3,4-pyrrolyne **197** and iii) 3,4-furyne **193**.

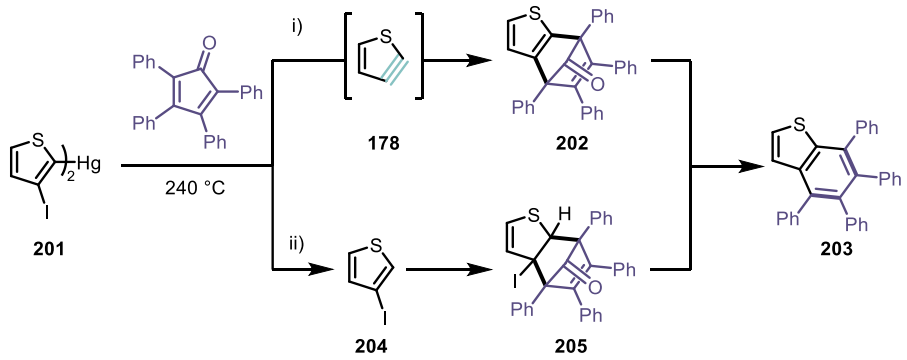
The trend of reactivity is consistent with the calculated energy to generate each hetaryne,[49] which in turn, reflects the ring strain and C-heteroatom bond lengths in the parent hetaryl compounds.[58]

2.1.2.3 2,3-Thiophyne and 2,3-benzothiophyne

Several attempts have been made to generate and trap 2,3-thiophyne **178** and 2,3-benzothiophyne **177** intermediates. However in some instances, mechanistic studies on reactions yielding products

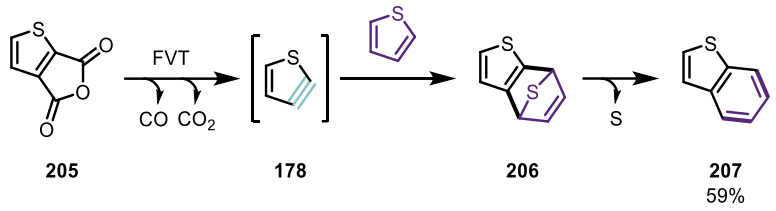
consistent with hetaryne intermediates have revealed alternative pathways responsible for the observed reactivity.

For instance in 1961, Wittig and coworkers heated bis(3-iodothiophen-2-yl)mercury **201** with tetraphenylcyclopentadienone to form tetraphenylbenzothiophene **203** (**Scheme 35**).[59] Initially, a Diels-Alder cycloaddition with 2,3-thiophyne **178** and tetraphenylcyclopentadienone followed by elimination of carbon monoxide was proposed as a potential mechanism (**Scheme 35**, i). However, a mechanistic investigation indicated that the more likely pathway involved the thermal decomposition of **201** to 3-iodothiophene **204**, followed by a [4+2] cycloaddition with 3-iodothiophene **204** (**Scheme 35**, ii).[60]



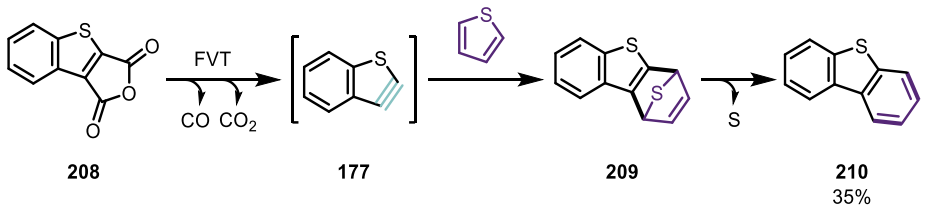
Scheme 35: Proposed mechanistic pathways for the transformation of **201** to **203** *via* i) 2,3-thiophyne **178** and ii) 3-iodothiophene **204**.

In 1976 Reinecke and coworkers proposed the generation of 2,3-thiophyne **178** from the thiophene cyclic anhydride **205** (**Scheme 36**).[61] In a flow vacuum thermolysis reaction (FVT) in the presence of a large excess of thiophene, benzothiophene **207** is obtained in 59% yield which was proposed to form *via* a [4+2] cycloaddition with **178** followed by elimination of sulfur. Other trapping agents were also successfully converted to corresponding products under similar conditions to give the desired aryne trapped products in very low to moderate yield (1-32%).



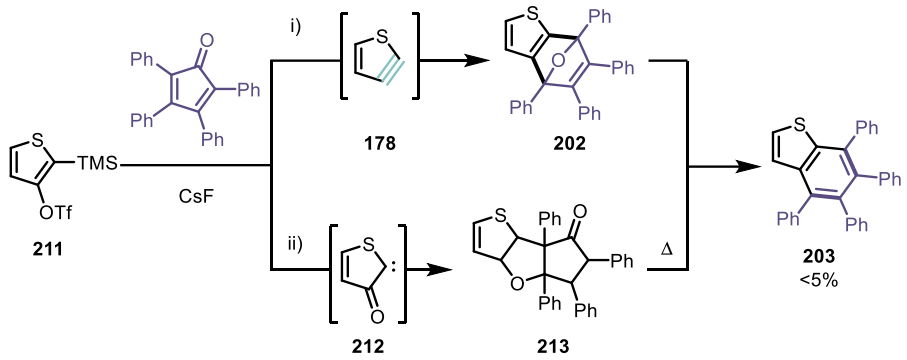
Scheme 36: Generation and trapping with thiophene of 2,3-thiophyne **178** from **205**.

In 1981 Reinecke and coworkers conducted a similar study in which benzothiophene cyclic anhydride **208** underwent a flow vacuum thermolysis reaction with thiophene to give dibenzothiophene **210** in 35% yield.[62]



Scheme 37: Generation and trapping with thiophene of 2,3-benzothiophyne **177** from **208**.

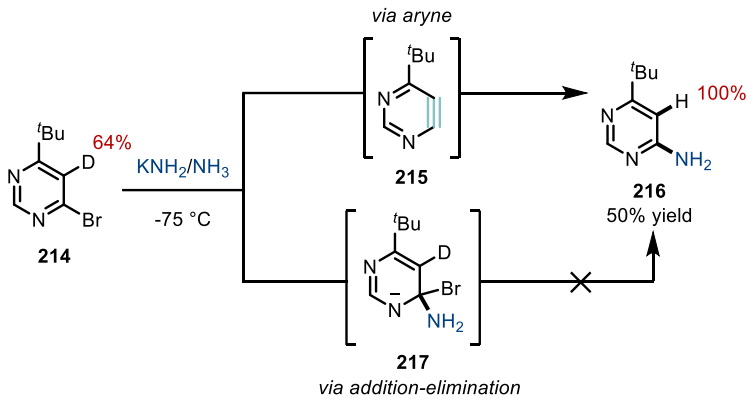
Recently in 2013, Perez and coworkers attempted to generate 2,3-thiophyne **178** using *ortho*-silyl aryl triflate precursor **211** (**Scheme 38**).[63] Treatment of **211** with caesium fluoride in the presence of tetraphenylcyclopentadienone afforded tetraphenylbenzothiophene **203**. While the formation of **203** was consistent with the generation of 2,3-thiophyne **178**, a detailed mechanistic investigation proposed a more likely pathway involving a ketocarbene intermediate **212**. Furthermore, when **211** was treated with caesium fluoride in the presence of other dienes, the cycloaddition products, typical of proceeding *via* an aryne intermediate, were not observed.



Scheme 38: Proposed mechanistic pathways for the transformation of **211** to **203** *via* i) 2,3-thiophyne **178** and ii) the ketocarbene **212**.

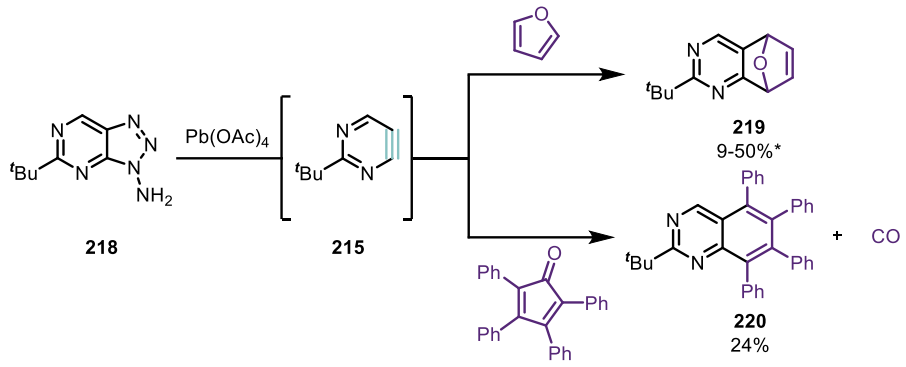
2.1.2.4 4,5-Pyrimidyne

Similarly to thiophynes, there has been limited research into the existence and reactivity of pyrimidynes. In 1968, Van Der Plas and coworkers conducted a deuterium labelling experiment to explore whether 4,5-pyrimidyne intermediate **215** was generated in the amination of bromo-pyrimidine **214** using potassium amide in ammonia (**Scheme 39**).[64] If the reaction proceeds *via* an aryne, deuterium should not be incorporated in the aminated product while an addition-elimination mechanism *via* **217**, should result in deuterium incorporation. Therefore, the complete absence of deuterium in the product **216** suggested the aryne pathway was more likely.



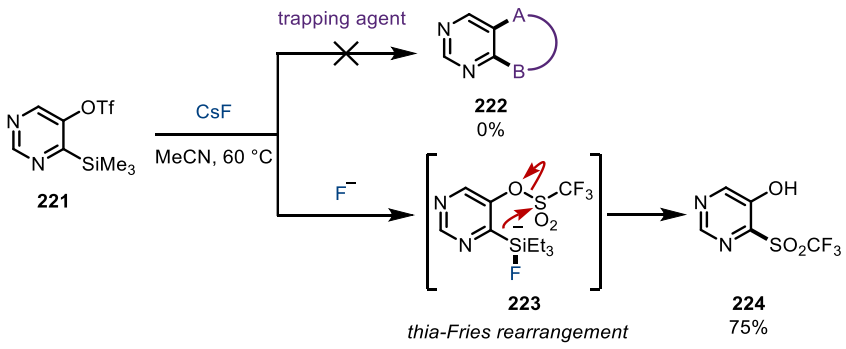
Scheme 39: Proposed mechanistic pathways for the amination of **214** with KNH_2/NH_3.

In 1992, Promel and coworkers also reported the generation of 4,5-pyrimidyne intermediate **215** *via* the oxidation of tetrazole **218** using lead tetraacetate (**Scheme 40**).[65] This was evidenced by the formation of Diels-Alder cycloaddition products, **219** and **220**, in the presence of dienes, furan and tetraphenylcyclopentadienone respectively. Analogous to the trapping of 2,3-thiophyne **178** and 2,3-benzothiophyne **177**,[61,62] achieving moderate yields of the desired products required a substantial excess of trapping agent, indicative of 4,5-pyrimidynes being high energy hetarynes.



Scheme 40: Generation and trapping of 4,5-pyrimidyne **215** from **218** using $Pb(OAc)_4$. *Variation of yield based on the eq. of furan.

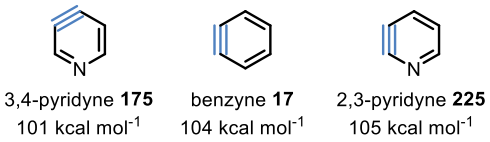
Garg and coworkers attempted to generate 4,5-pyrimidyne from *ortho*-silyl aryl triflate **221** upon treatment with a fluoride source (**Scheme 41**).[66] However, **221** readily underwent a *thia*-Fries rearrangement in the presence of fluoride to afford **224** and no products consistent with formation of an aryne intermediate were observed.



Scheme 41: Attempted 4,5-pyrimidyne generation from **221** and the observed *thia*-Fries rearrangement.

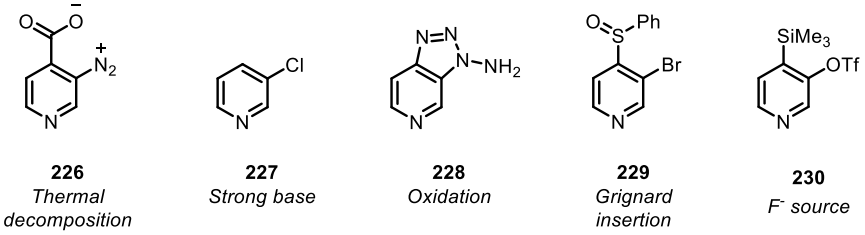
2.1.2.5 2,3- and 3,4-Pyridyne

In the computational study by Paton, Houk, Garg, and coworkers, 3,4-pyridyne **175** and 2,3-pyridyne **225** were the only hetarynes (where the heteroatom resides in the same ring as the arynic bond) predicted to be readily generated.[49] Notably, 3,4-pyridyne **175** (101 kcal mol^{-1}) was calculated to be slightly lower in energy than benzyne **17** (101 kcal mol^{-1}), whereas 2,3-pyridyne **225** was calculated to be slightly higher (105 kcal mol^{-1}) (**Scheme 42**). These calculations are reflected by the extensive studies exploring the synthetic utility of pyridynes, as well as their reported formation *via* a broad range of aryne generating methods.



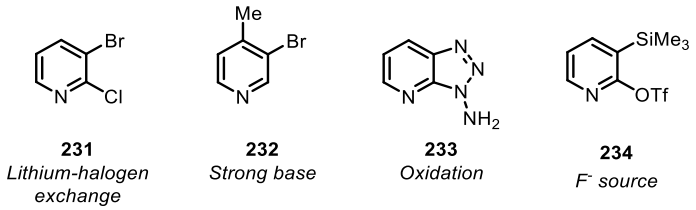
Scheme 42: Calculated energies of dehydrogenation of 3,4-pyridyne **175**, benzyne **17**, and 2,3-pyridyne **225**.

3,4-Pyridyne **175** can be generated from a range of methods for example: the thermal decomposition of diazonium carboxylates **226**,[67] treatment of 3-halopyridine **227** with strong base,[68] the oxidation of *N*-aminotriazole-pyridine **228** with lead tetraacetate,[69] Grignard exchange and elimination using 3-bromo-4-(phenylsulfinyl)pyridine **229**,[70] and the fluoride-mediated elimination of *ortho*-silyl pyridine triflates **230** (**Scheme 43**).[71]



Scheme 43: Examples of 3,4-pyridyne precursors and their methods of activation.

Furthermore, 2,3-pyridyne **225** has also been reportedly formed from a variety of precursors such as lithium halogen exchange using a 2,3-dihalide pyridine **231**,[72] deprotonation of 3-halopyridines **232** (with strategic blocking groups to prevent 3,4-pyridyne generation),[12] oxidation of *N*-aminotriazole-pyridine **233** with lead tetraacetate,[69] and fluoride-induced elimination of *ortho*-silyl pyridine triflates, **234** (**Scheme 44**).[73]



Scheme 44: Examples of 3,4-pyridyne **225** precursors and their methods of activation.

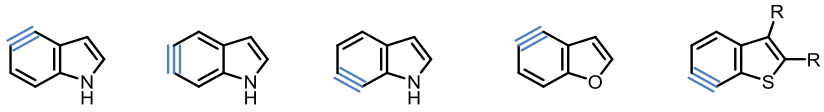
Notably, the *ortho*-silyl pyridine triflate precursors **230** and **234** are commercially available due to their broad functional group tolerance,[74] resulting in their application in the synthesis of complex molecules.[49]

2.1.2.6 Arynes fused to a heteroatom-containing ring

Arynes in which the triple bond resides in a ring fused to a heteroatom-containing ring are commonly categorised as hetarynes. The effect of the heteroatom on the energy of the hetaryne is diminished when it is located outside the ring containing the arynic bond.[49] This facilitates the efficient generation and trapping of these hetarynes, eliminating the need for a substantial excess of trapping agent and expanding their synthetic utility.

In this domain, 4,5-, 5,6-, and 6,7-indolynes, **235**, **236**, and **176** respectively, have emerged as the most extensively employed hetarynes (**Scheme 45**) and early reports provided experimental evidence for the formation of these intermediates.[75,76] Garg's advancement of the Kobayashi-type precursors significantly enhanced their efficiency, rendering them valuable intermediates in the

total synthesis of complex molecules.[77–84] Garg and coworkers also developed *ortho*-silyl aryl triflates which serve as efficient 4,5-benzofuryne **237** and 6,7-thiophyne **238** precursors.[85,86]



235 4,5-indolyne | **236** 5,6-indolyne | **176** 6,7-indolyne | **237** 4,5-benzofuryne | **238** 6,7-thiophyne

Scheme 45: Arynes fused to a heteroatom-containing rings.

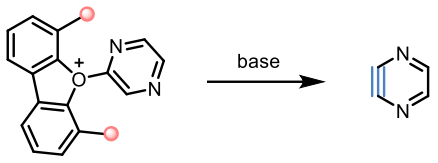
2.1.3 Project aims

Having established triaryloxonium ions as excellent mild aryne precursors, our next endeavour aimed to explore their potential utility as hetaryne precursors. Heterocyclic compounds are present in more than 90% of new drugs,[87] therefore, unlocking the unique reactivity offered by aryne intermediates could prove invaluable in devising new approaches to functionalise heterocycles. We proposed leveraging triaryloxonium ions' compatibility in forming arynes with diverse functional groups to improve the efficiency of hetaryne generation and to access novel hetarynes.

2.2 Results and discussion

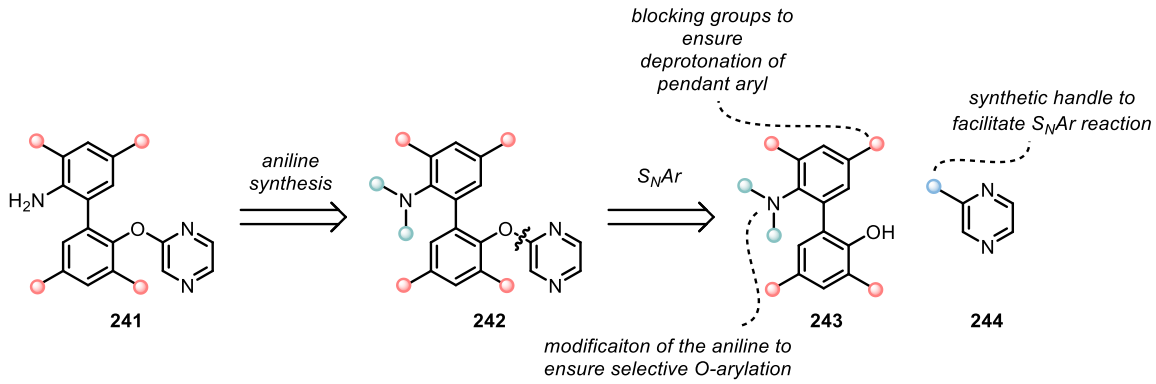
2.2.1 2,3-Pyrazyne

In the pursuit of generating novel hetarynes, 2,3-pyrazyne **240** was initially targeted as a potential aryne that could be accessible from triaryloxonium ions (**Scheme 46**). Pyrazines have been extensively used across various industrial sectors, including pesticides, insecticides, dyes, and pharmaceuticals.[88] Hence, devising new methodologies to functionalise pyrazines could hold significant synthetic value.



Scheme 46: Target 2,3-pyrazyne **240** generation from oxonium ions.

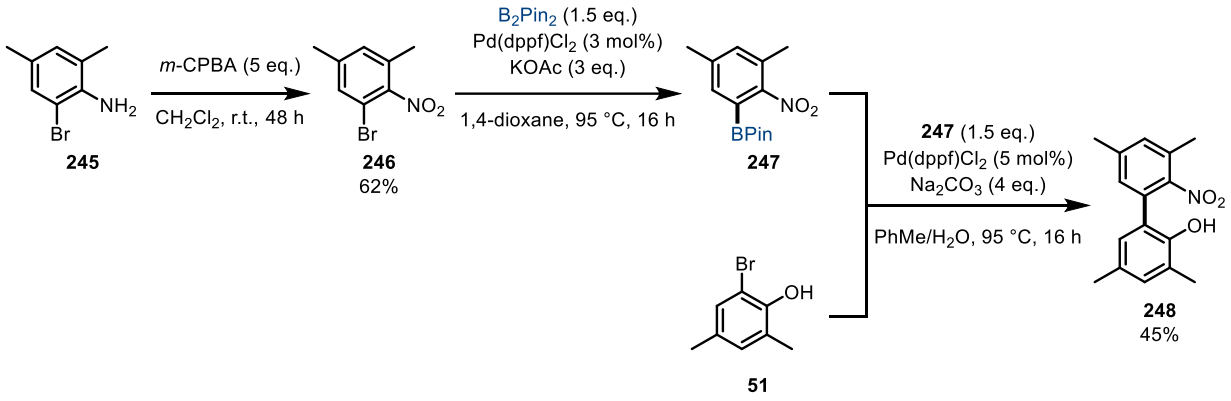
A route was devised to generate the target pyrazine triaryloxonium ion **241** using a pre-functionalised biaryl precursor **243** (**Scheme 47**). Utilising the reactivity of chloro/fluoro-pyrazines with nucleophiles *via* S_NAr reactions,[89] *O*-arylation might be achieved using a phenolic precursor **243**. However, modification of the aniline functional group to prevent *N*-arylation was therefore also necessary. Similarly to the benzyne precursors, methyl blocking groups were introduced for selective deprotonation of the pendant aryl. We proposed that, if an appropriate precursor could be synthesised on scale, triaryloxonium ions could be synthesised *via* a more convergent route potentially increasing their practicality as aryne precursors.



Scheme 47: Design of a convergent synthetic route towards pyrazine triaryloxonium ion precursor **241**.

A nitro-group was chosen as an appropriate functional group that could undergo an S_NAr reaction without reacting with the electrophilic heterocycle and could be readily reduced to the desired aniline following *O*-arylation. Nitro-phenol **248** was synthesised by oxidation of bromo-aniline **245**

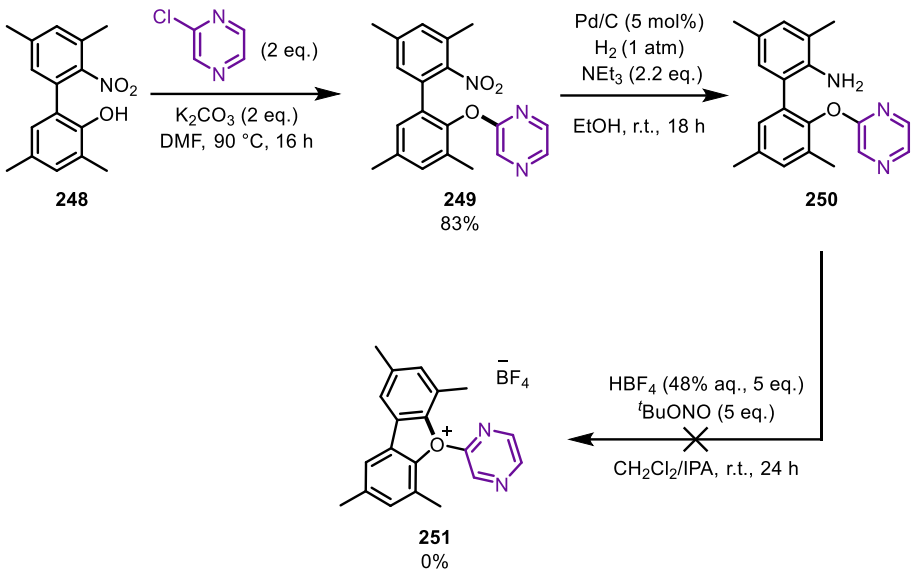
using *m*-CPBA to afford nitro-benzene **246** in 62% yield.[90] Pinacol borane **247** was then generated *via* a Suzuki-Miyaura coupling and used crude assuming full conversion in the cross-coupling reaction with phenol **248** to give the target molecule **248** in 45% yield (**Scheme 48**).[34]



Scheme 48: Synthesis of biaryl **248.**

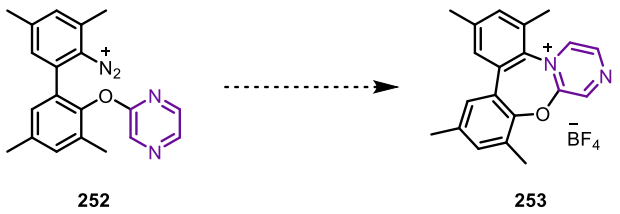
The modification of the aniline moiety reduces the overall yield of **248**. Therefore, pursuing a convergent pathway through this precursor was unlikely to enhance the efficiency of triaryloxonium synthesis. Nevertheless, **248** was used in subsequent steps towards the target oxonium **251** (**Scheme 49**).

Phenol **248** was treated with base and excess 2-chloropyrazine to give the bis(aryl) ether **249** in 83% yield. Smooth reduction of the nitro group using palladium on carbon and hydrogen gas afforded the aniline **250** which was used crude assuming full conversion. To determine whether pyrazine oxonium formation was viable, **250** was diazotised and monitored by ^{1}H NMR for 24 h, however, the desired oxonium **251** was not observed.



Scheme 49: Attempted synthesis of the pyrazine oxonium salt **251**.

We hypothesised that the absence of oxonium generation might be attributed to the reactivity of the *ortho*-nitrogen on the pyrazine with the diazonium where a potential pathway is depicted in **Scheme 50**. Therefore, we turned our attention to heterocycles where *O*-arylation could occur at the *meta*- or *para*-position relative to the heteroatom.

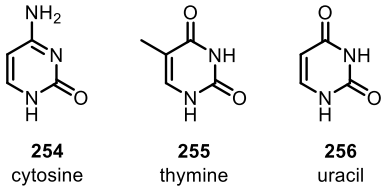


Scheme 50: Potential reactivity of diazonium **252**.

2.2.2 4,5-Pyrimidyne

Pyrimidine, an isomeric diazine to pyrazine, is present in three nucleobases: cytosine **254**, thymine **255**, and uracil **256** (**Scheme 51**). Pyrimidine derivatives have exhibited diverse biological activities, including antimicrobial,[91] anticancer,[92] anti-HIV,[93] and antithyroid effects,[94] amongst others. Due

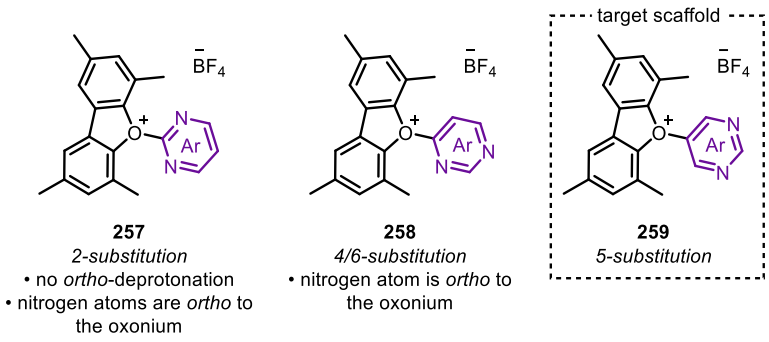
to the medicinal significance of pyrimidines, pyrimidynes were selected as target hetarynes to generate from triaryloxonium ions.



Scheme 51: Nucleobases containing pyrimidines.

2.2.2.1 Triaryloxonium salt synthesis

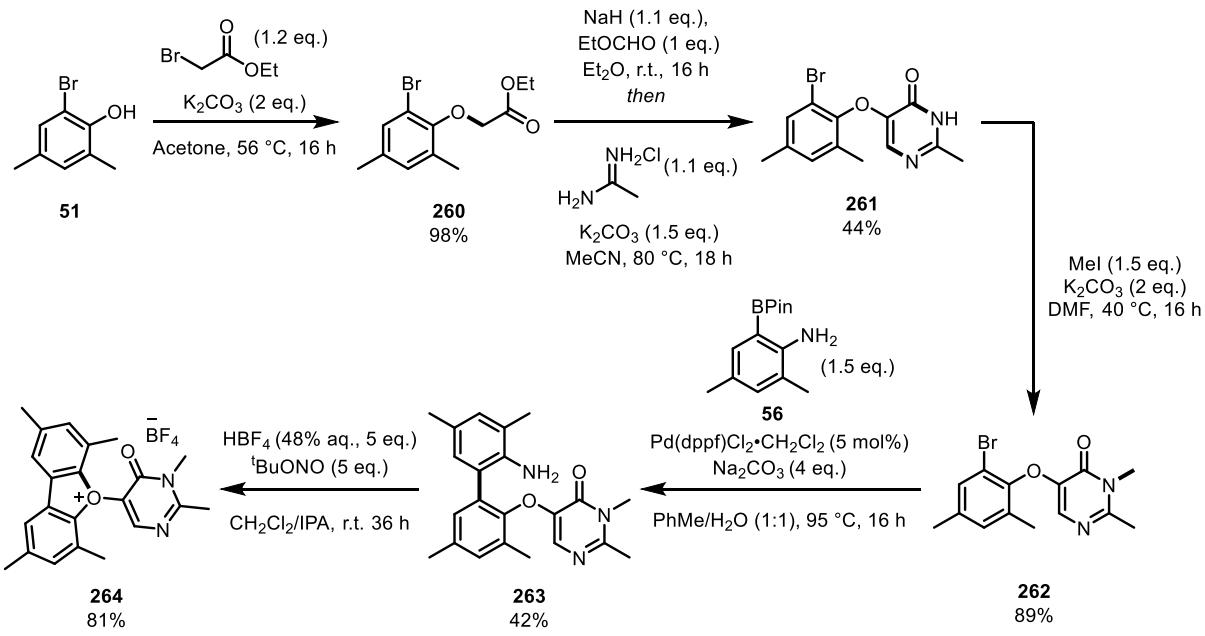
Potential *O*-substitutions on pyrimidine were considered and 5-substitution **259**, where both the nitrogen atoms are situated *meta* to the pyrimidine-oxonium bond, was identified as the optimum target scaffold (**Scheme 52**).



Scheme 52: Potential pyrimidine oxonium scaffolds.

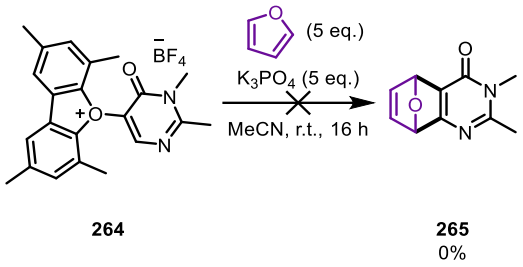
The established S_NAr route used to generate benzyne precursors could not be employed to achieve *O*-arylation at the 5-position of the pyrimidine. Therefore, an alternative synthetic route was designed according to a patent in which the pyrimidine was constructed onto a preformed aryl ether.[95]

Firstly, phenol **51** underwent an S_N2 reaction with ethyl 2-bromoacetate to give ethyl phenoxyacetate **260** in excellent yield (98%). Compound **260** was then deprotonated with sodium hydride and treated with ethyl formate to afford a salt which was subsequently refluxed with a methyl amidinium chloride and potassium carbonate to generate pyrimidone **261**.[95] To prevent deprotonation of the pyrimidone N-H in the aryne generating step, **261** was methylated *via* gentle heating in the presence of iodomethane and potassium carbonate to give *N*-methylated pyrimidone **262**. Under the standard cross-coupling conditions,[34] aniline **263** was formed in 42% yield, which, upon diazotisation gave the desired oxonium salt **264** in 81% yield (**Scheme 53**).



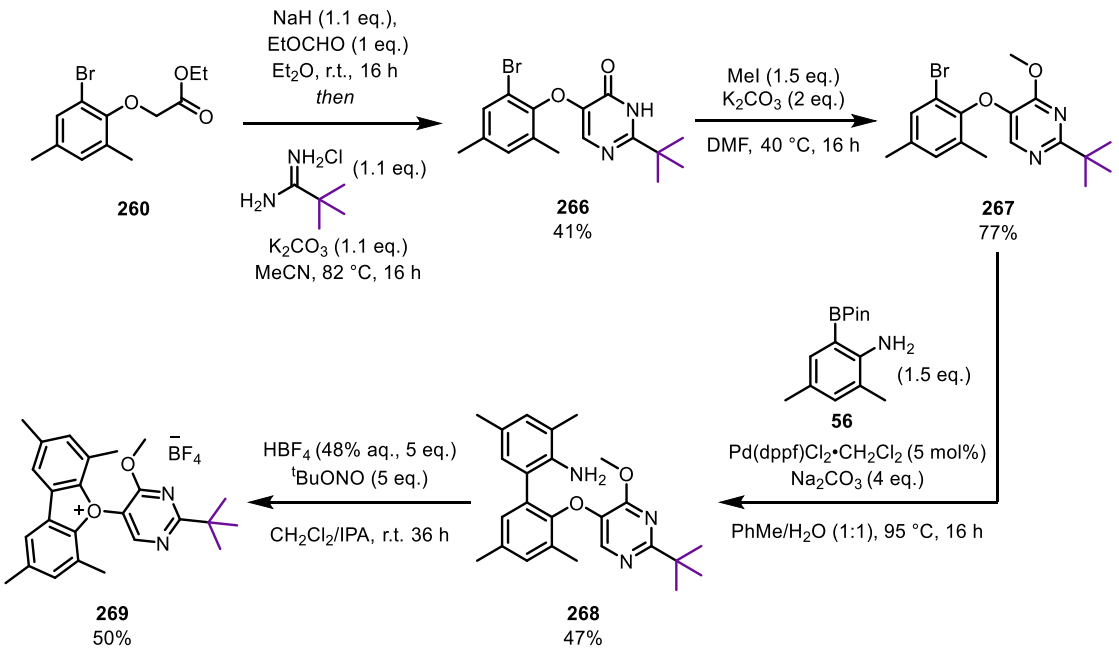
Scheme 53: Synthesis of pyrimidine oxonium salt **264**.

Oxonium salt **264** was then subjected to the oxonium generating and trapping conditions using furan. Unfortunately, a complex reaction mixture was obtained and none of the desired cycloaddition product **265** was observed (**Scheme 54**).



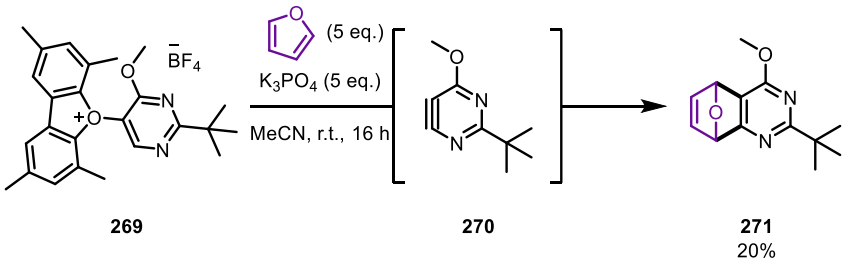
Scheme 54: Attempted 4,5-pyrimidyne generation and trapping with furan from **264**.

4,5-Pyrimidyne **215**, reportedly generated by both Van Der Plas and coworkers Promel and coworkers,[64,65] contained a *tert*-butyl group positioned between the two nitrogen atoms (**Scheme 39** and **40**). It was hypothesised that the steric hinderance imposed by the *tert*-butyl group could impede the reactivity of the hetaryne's nitrogen lone pairs. Therefore, the synthetic route was modified by exchanging the methyl amidinium chloride for a *tert*-butyl amidinium chloride, to afford *tert*-butyl pyrimidone **266** in 41% yield (**Scheme 55**). Interestingly, employing the same methylation conditions resulted in *O*-methylation rather than *N*-methylation of pyrimidone **266** to give **267** in 77% yield. The standard cross-coupling conditions afforded aniline **268** (47%) and, upon diazotization, oxonium salt **269** was isolated in 50% yield.



Scheme 55: Synthesis of the pyrimidine oxonium salt **270**.

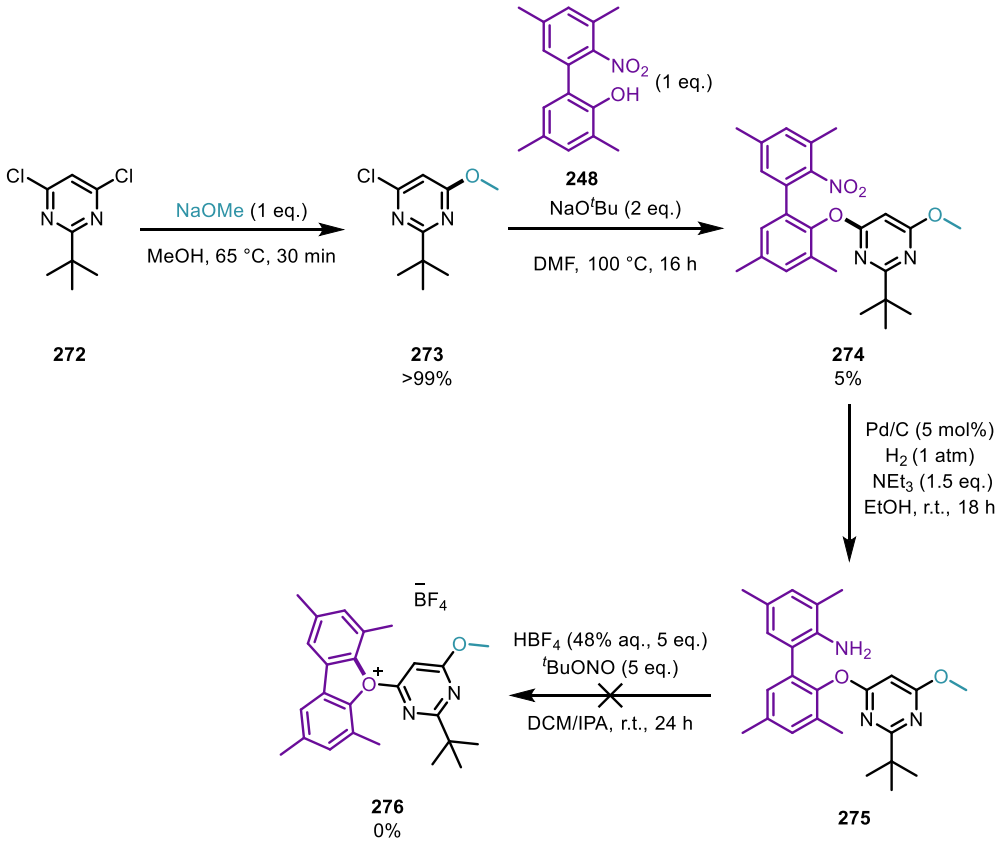
Pleasingly, when the oxonium **269** was stirred in the presence of furan and potassium phosphate, the desired [4+2] cycloaddition product **271** was obtained in 20% yield, consistent with the generation of 4,5-pyrimidyne intermediate **270** (**Scheme 56**). The discrepancy in the reactivity of the oxoniums, **264** and **269**, could be a consequence of the relative energies of the corresponding hetarynes or the steric blocking of the nucleophilic nitrogen atoms imposed by the *tert*-butyl group in **270**.



Scheme 56: Generation of 4,5-pyrimidyne **270** and its trapping with furan.

While this result was promising, synthesising 5-substituted pyrimidine oxoniums was practically challenging. Therefore, recognising *tert*-butyl pyrimdyne **270** was likely accessible, we aimed to synthesise the alternative precursor **277** wherein the oxonium is substituted at the 4-position rather than the 5-position of the pyrimidine (**Scheme 57**). Synthesis of this precursor could offer a more efficient route to the desired hetaryne and test whether triaryloxonium ions bearing *ortho*-substituted heteroatoms are accessible.

To achieve this, 4,6-dichloropyrimidine **272** underwent an S_NAr reaction with sodium methoxide yielding the 4-chloro-6-methoxypyrimidine **273** in quantitative yield (**Scheme 57**).[96] Compound **273** was subsequently heated with phenol **248** and sodium *tert*-butoxide, however, the product was only obtained in 5% yield, with 90% of the starting material **273** recovered. The presence of the mesomerically donating methoxy group likely decreases the rate at which **273** undergoes nucleophilic attack, accounting for the poor yield. Compound **248** was then reduced to give aniline **275** and used crude assuming full conversion. Compound **275** was treated with HBF_4 and ^{t}BuONO and monitored by ^{1}H NMR. Clean conversion to the diazonium was observed. However, a complex reaction mixture was obtained in which the desired oxonium salt **276** could not be detected.

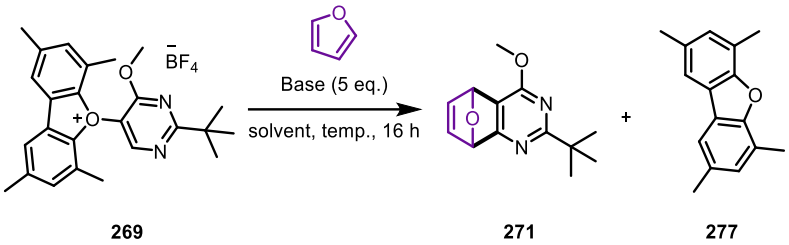


Scheme 57: Attempted synthesis of pyrimidine oxonium salt **276**.

2.2.2.2 4,5-Pyrimidyne generation

Having established that **276** was not a viable precursor to hetaryne **270**, we focused our efforts on optimising the generation and trapping of pyrimidyne **271** from oxonium salt **269** (**Scheme 58**). Changing the solvent from acetonitrile to dichloromethane resulted in a complete shut down in reactivity due to the insolubility of **269** (**Entry 2**). Increasing the amount of furan from 5 eq. to 0.02 M gave the biggest increase in yield from 23% to 71% (**Entry 1-5**). Conducting the reaction at an elevated temperature (30 °C) (**Entry 6**), or a reduced temperature (10 °C) (**Entry 7**), both variations led to reductions in the yield, 68% and 51% respectively. Switching to a weaker base, potassium carbonate (**Entry 8**) or a stronger base, sodium *tert*-butoxide (**Entry 9**) led to reductions in the yield in both instances, 24% and 48% yield respectively. In all the reactions, the oxonium

was completely consumed, and we were unable to identify for any side products other than dibenzofuran **277**.

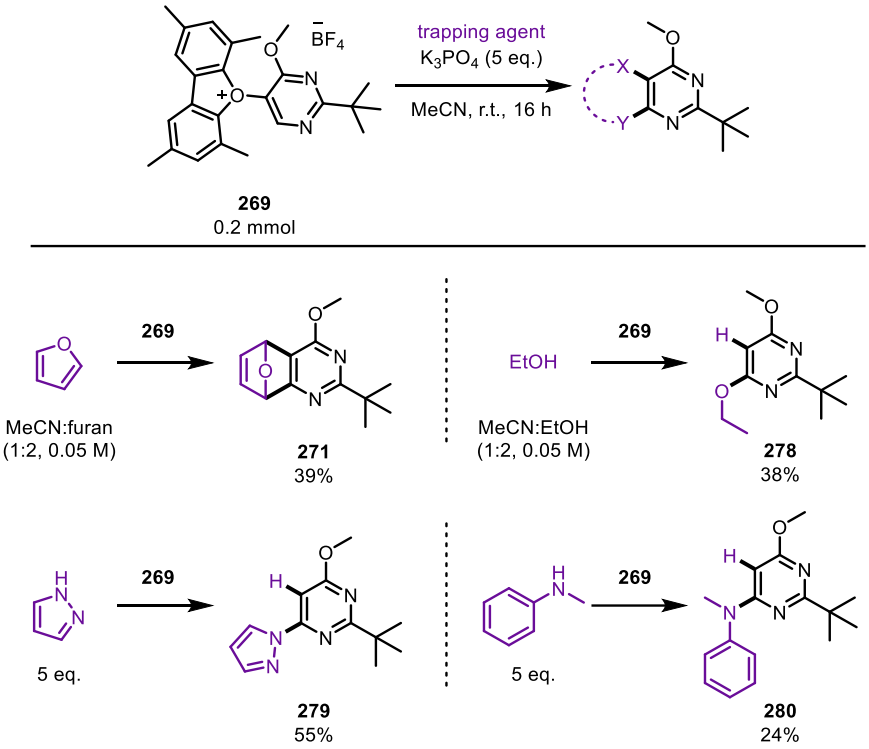


Entry	Solvent	Furan	Conc. (M)	Base	Temp.	Yield* 271
1	MeCN	5 eq.	0.05	K_3PO_4	r.t.	23%
2	CH_2Cl_2	5 eq.	0.05	K_3PO_4	r.t.	0%
3	MeCN	20 eq.	0.05	K_3PO_4	r.t.	40%
4	MeCN	furan:MeCN(1:2)	0.03	K_3PO_4	r.t.	58%
5	**MeCN**	**furan:MeCN(2:1)**	**0.03**	**K_3PO_4**	**r.t.**	**71%**
6	MeCN	furan:MeCN(2:1)	0.03	K_3PO_4	30 °C	68%
7	MeCN	furan:MeCN(2:1)	0.03	K_3PO_4	10 °C	51%
8	MeCN	furan:MeCN(2:1)	0.03	K_2CO_3	r.t.	24%
9	MeCN	furan:MeCN(2:1)	0.03	NaO^{t}Bu	r.t.	47%

Scheme 58: Optimisation of the generation of 4,5-pyrimidyne from **269** and its trapping with furan. *By ^{1}H qNMR using dibromomethane as an internal standard.

The conditions used in **Entry 5** afforded the highest ^{1}H qNMR yield therefore, the reaction was performed on a 0.2 mmol scale, resulting in the isolation of **271** in 39% yield (**Scheme 59**). Notably, the isolated yield was significantly lower than the NMR yield observed in the optimisation however, generating sufficient oxonium **269** to further optimise this reaction was practically challenging. Consequently, the synthesis of pyrimidine triaryloxonium ions was no longer pursued.

A small scope exploring the reactivity of **269** with potassium phosphate and nucleophilic trapping agents was conducted. Pleasingly, ethanol, imidazole, and *N*-methylaniline all reacted with **269** to generate the desired products in moderate yield (**Scheme 59**).

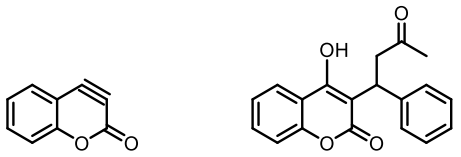


Scheme 59: Scope for the reactivity of **269** with a range of nucleophilic trapping agents.

Future investigations would look to explore alternative heteroaromatic triaryloxonium ions that can be readily synthesised and serve as efficient hetaryne precursors.

2.2.3 3,4-Coumaryne

Similarly to 2,3-pyrazines, 3,4-coumarynes have not been reported in the literature. Coumarin is a natural product renowned for its sweet odour. Its derivatives have demonstrated diverse pharmacological activities, including anti-cancer,[97] anti-HIV,[98] anticoagulant (**Scheme 60**),[99] antibacterial,[100] and anti-inflammatory properties.[101] We aimed to employ triaryloxonium ions to generate 3,4-coumarynes as a novel approach for coumarin functionalisation.



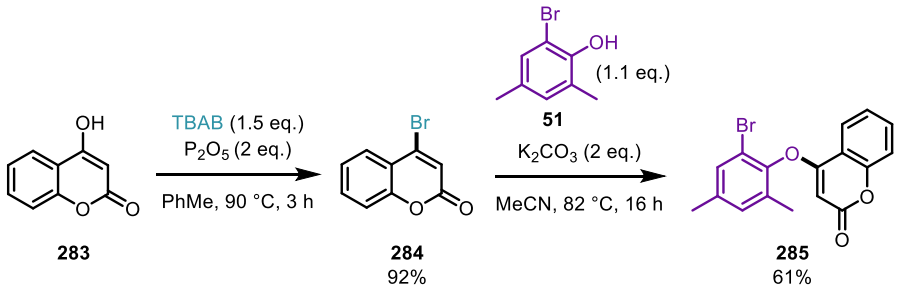
281
3,4-coumaryne

282
Warfarin - anticoagulant drug

Scheme 60: 3,4-Coumaryne **283** and the anticoagulant coumarin-containing drug, Warfarin **284**.

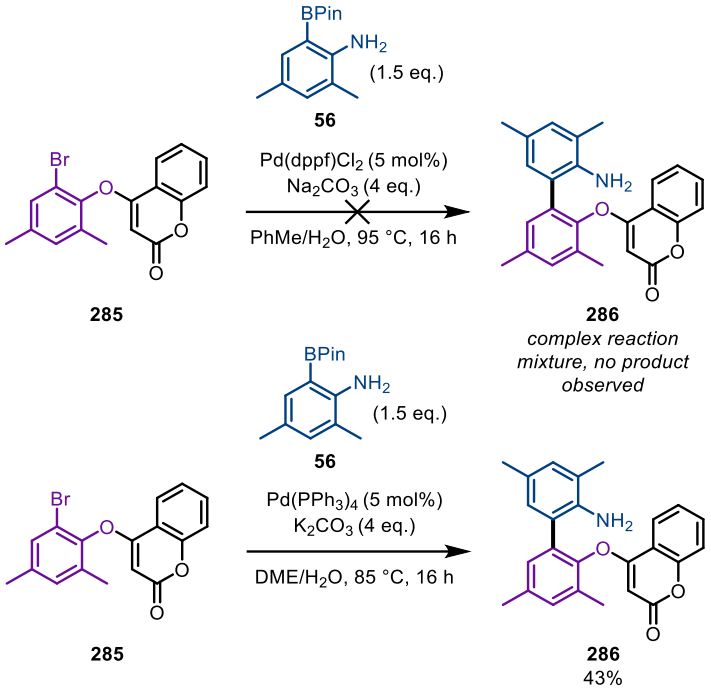
2.2.3.1 Triaryloxonium salt synthesis

4-Bromocoumarins readily undergo S_NAr reactions with phenols which served as a good starting point to synthesise the bis(aryl) ether moiety **285**.[102] Commercially available 4-hydroxycoumarin **283** was brominated using tetrabutylammonium bromide and phosphorous pentoxide to yield 4-bromocoumarin **284** in 92% yield.[103] Subsequently, refluxing **284** with phenol **51** and potassium carbonate gave **285** in good yield (61%) (**Scheme 61**).[104]



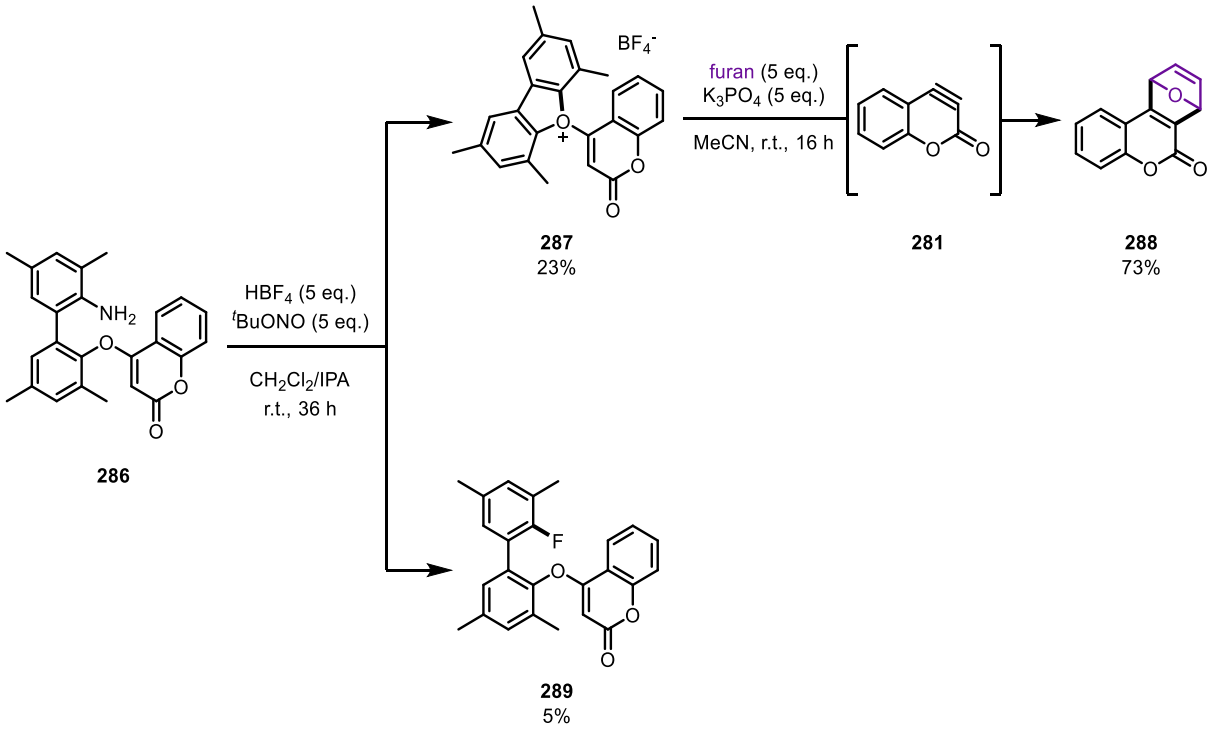
Scheme 61: Synthesis of the bis(aryl) ether **285** from 4-hydroxycoumarin **283**.

The Suzuki-Miyaura coupling conditions used in prior syntheses of triaryloxonium ions using $Pd(dppf)Cl_2$ were applied to **285** (**Scheme 62**).[34] However, the desired aniline **286** was not observed. Therefore, alternative conditions reported by Kwon and co-workers using $Pd(PPh_3)_4$ were employed and pleasingly **286** was afford in 43% yield.[105]



Scheme 62: Cross-coupling reactions to generate **286** from **285**.

Aniline **286** was then treated with HBF_4 and ^tBuONO and maintained at room temperature for 36 h. Purification by trituration afforded triaryloxonium salt **287** in 23% yield and analysis of the filtrate obtained in the trituration found a complex mixture containing the aryl fluoride **289** as the major component which was isolated in 5% yield (**Scheme 63**). The optimised trapping conditions using furan as the arynophile were then applied to the **287**. The desired [4+2] cycloaddition product **288**, consistent with the generation of 3,4-coumaryne intermediate **281**, was afforded in good yield (73%).

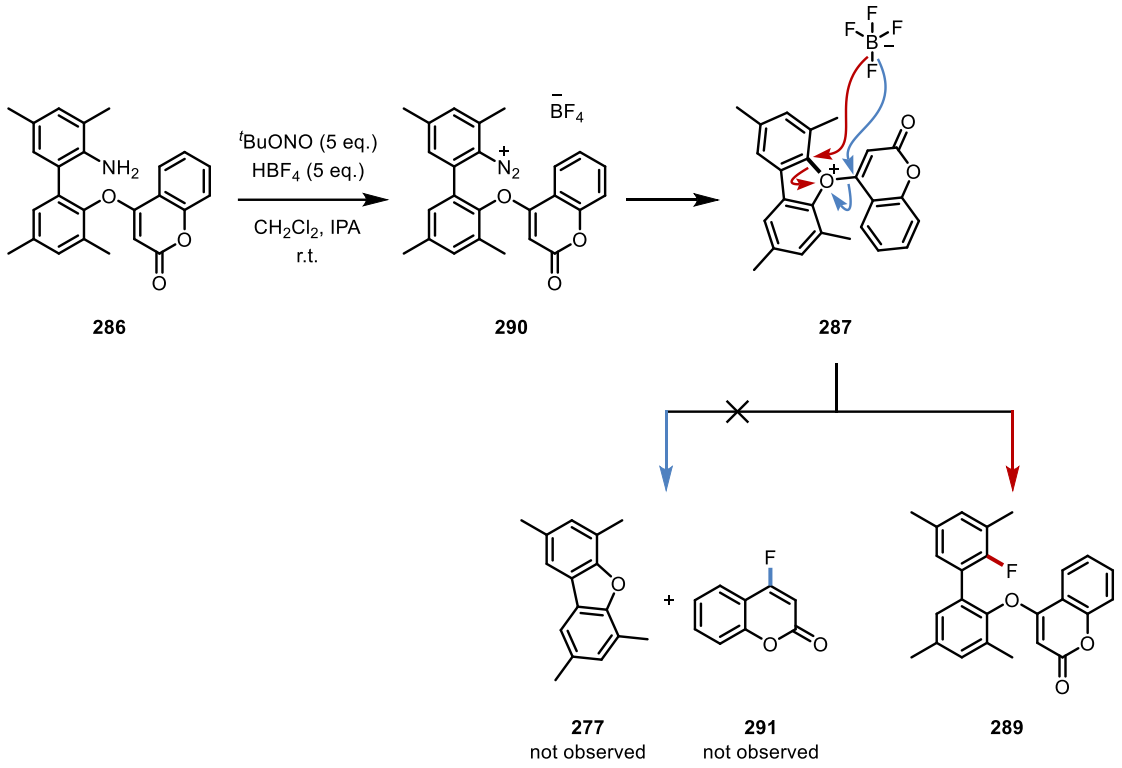


Scheme 63: Triaryloxonium salt **287** formation and generation of 3,4-coumaryne **281** and its trapping with furan to give **288**.

With this result in hand, our focus shifted to optimising the synthesis of the coumarin triaryloxonium salt **287** to establish a practical method for generating 3,4-coumarynes.

2.2.3.2 Stability of the coumarin-containing triaryloxonium salts

When stored as a solid at room temperature, coumarin-containing triaryloxonium salt **287** was stable for over one week. However, in solution **287** slowly degrades to give a complex reaction mixture. The major degradation product was identified as the aryl fluoride **289**, which likely formed *via* nucleophilic attack from the tetrafluoroborate counterion onto the dibenzofuran core (**Scheme 64**). Notably, the alternative aryl fluoride **291** and the dibenzofuran **277**, which would result from nucleophilic attack on the pendant coumarin, were not observed (**Scheme 64**).



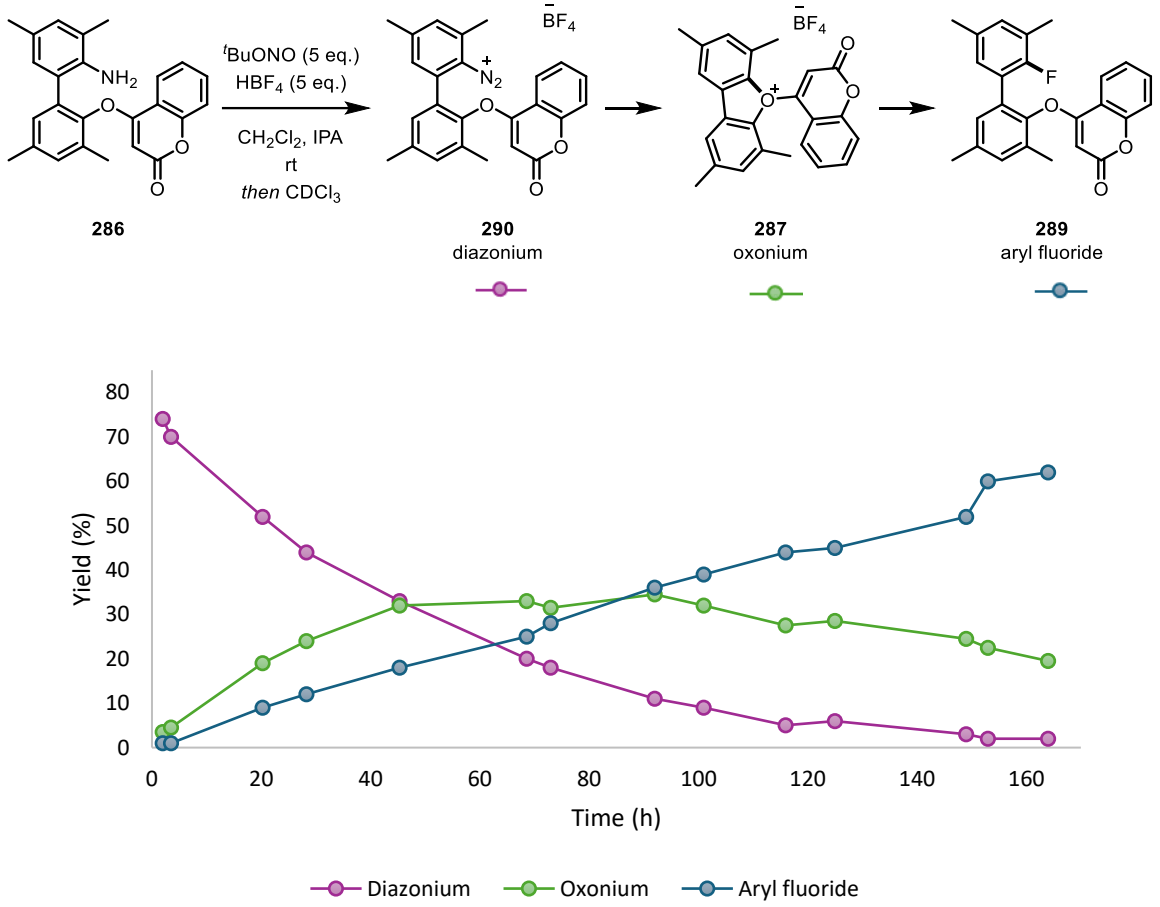
Scheme 64: Synthetic routes to aryl fluorides **289** and **291** from aniline **286**.

2.2.3.2.1 NMR study

To investigate the generation and degradation of **287**, an NMR study was conducted to monitor the yields of the components of the reaction at over time (**Scheme 65**). Aniline **286** was treated with HBF_4 and ^tBuONO to afford diazonium **290** which was dissolved in $CDCl_3$ and maintained at room temperature in an NMR tube. The yields of diazonium **290**, oxonium **287**, and aryl fluoride **289** were monitored by ^1H qNMR.

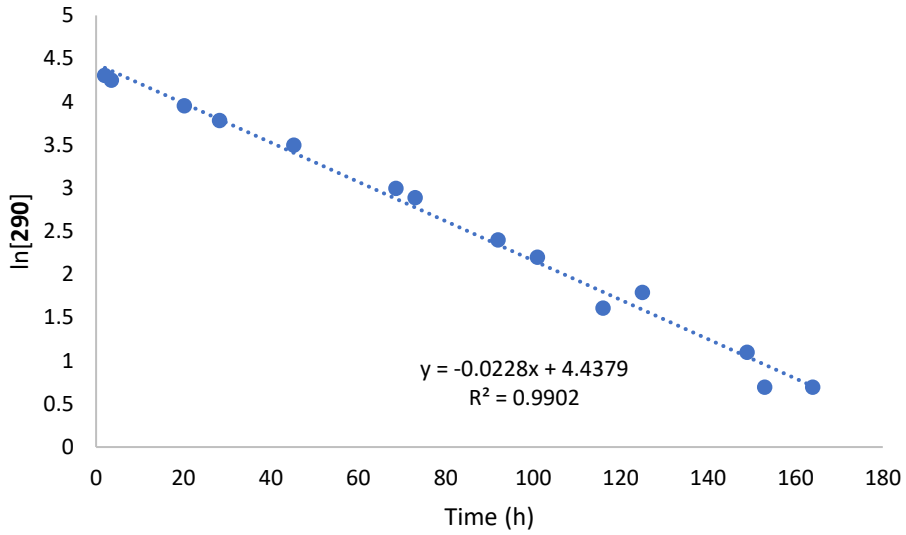
The initial measurement at 2 h showed aniline **286** was fully consumed with the major component being diazonium **290** (77%). Oxonium **287** and aryl fluoride **289** were also present in 7% and 1% yield respectively. Diazonium **290** was gradually consumed as oxonium **287** and aryl fluoride **289** were generated. Between 45-100 h the yield of oxonium **287** remained between 30-35% suggesting the rate of formation and consumption of **287** were comparable. The yield of oxonium **287** then

gradually decreased while the yield of aryl fluoride **289** continued to increase for the duration of the experiment (**Scheme 65**).



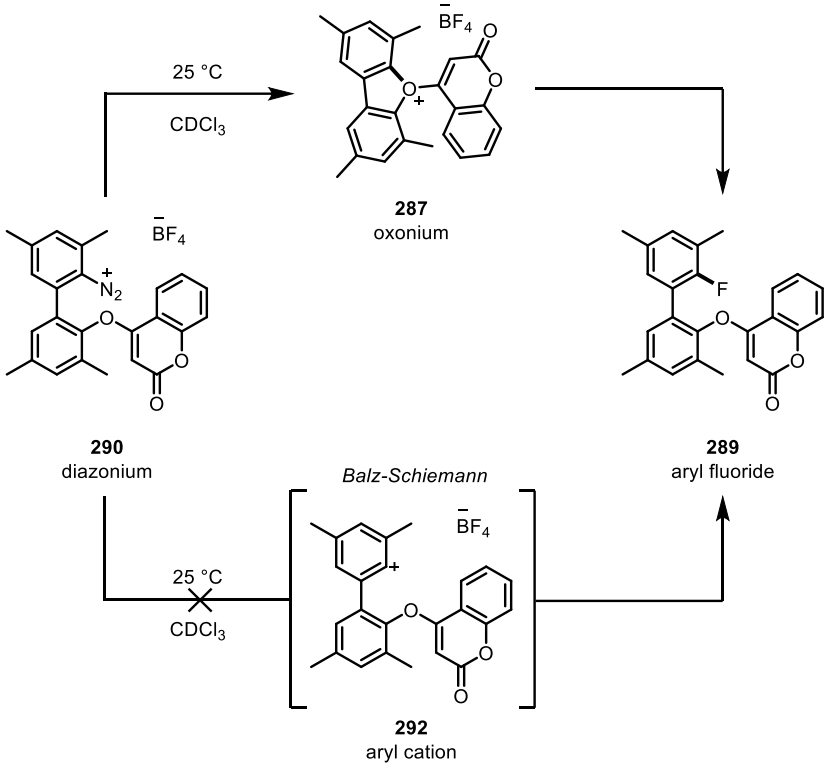
Scheme 65: ^{1}H NMR experiment showing the yields of the components of the reaction over time. Yields are measured by ^{1}H qNMR using dibromomethane as an internal standard. T = 0 h corresponds to the time at which the ^{t}BuONO was added to the reaction.

Plotting ln[**290**] as a function of time give a straight line (**Scheme 66**) indicting that the decay of **290** is a 1st order process which is consistent with the oxonium formation being an intramolecular process. The gradient of the line, -0.0228 s^{-1}, corresponds to the rate constant of the reaction.[106]



Scheme 66: The correlation between ln[**290**] and time.

The Balz-Schiemann reaction is a process wherein an aryl fluoride is generated from an aryl diazonium tetrafluoroborate.[107] This occurs through either thermal or photochemical decomposition of the aryl diazonium tetrafluoroborate to the aryl cation, followed by nucleophilic addition from the tetrafluoroborate counterion to produce the aryl fluoride (**Scheme 267**). Thermal decomposition for this reaction typically proceeds elevated temperatures (110 – 170 °C), however,[108] we have demonstrated that triaryloxonium formation is possible at ambient temperature.[109] Therefore, we reasoned that we reasoned that aryl fluoride formation at room temperature is likely attributed exclusively to nucleophilic attack of oxonium **287**, as opposed to the Balz-Schiemann reaction pathway (**Scheme 67**).



Scheme 67: Proposed mechanistic pathways to generate aryl fluoride **289** from the aryl diazonium tetrafluoroborate **290**.

The maximum observed yield for oxonium **287** was 35%, making this method impractical for efficient generation of 3,4-coumarynes. As a result, we turned our attention to strategies aimed at enhancing the stability of the oxonium.

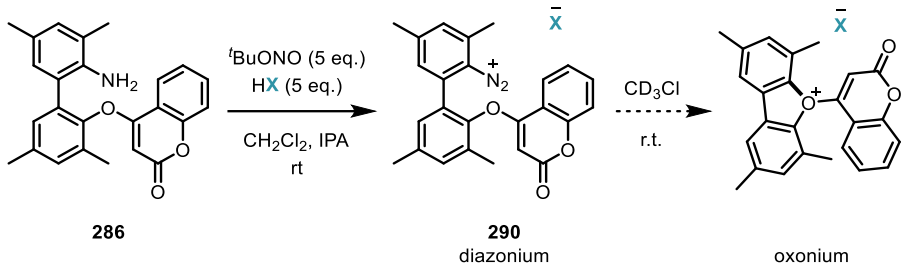
2.2.3.2.2 Counterion effect

Having established the role of the tetrafluoroborate counterion in the degradation of oxonium salt **287**, it was proposed that an alternative the counterion might improve the stability of the oxonium ion. To investigate this, a screen of commercially available acids containing alternative counterions was conducted.

The diazonium salts were generated through treatment with the appropriate acid and ^{t}BuONO. The salts were isolated, dissolved in $CDCl_3$, and their conversion was monitored by ^{1}H and ^{19}F

NMR spectroscopy. Oxonium formation can be identified by a characteristic change in the ^{1}H NMR spectrum: the four methyl resonances in the diazonium ^{1}H NMR spectrum merge into two, indicating that the two *ortho*-methyl groups and two *para*-methyl groups were now in the same chemical and magnetic environment. Additionally, a new ^{19}F NMR peak at approximately -150 ppm, corresponding to the tetrafluoroborate ion, is observed upon oxonium formation.

To ascertain the potential formation and stability of each triaryloxonium salt, we looked for evidence of oxonium formation and its stability in solution by closely monitoring the corresponding ^{1}H and ^{19}F NMR spectra (**Scheme 68**). Unfortunately, none of the counterions were successful in generating a stable coumarin triaryloxonium salt. Given tetrafluoroborate and hexafluorophosphate are weakly coordinating anions,[110] we reasoned that a weaker coordinating counterion would be necessary to prevent reactivity with the oxonium ion.

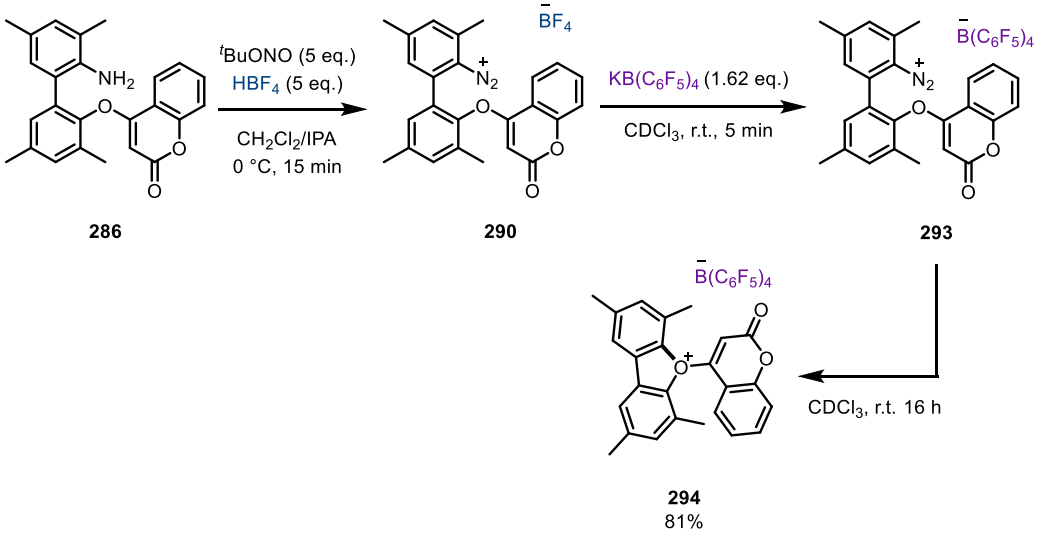


286 **290** diazonium oxonium

X	Stable oxonium formation?
CF_3CO_2	No
CF_3SO_3	No
Cl	No
HSO_4	No
para-TsO	No
PF_6	No

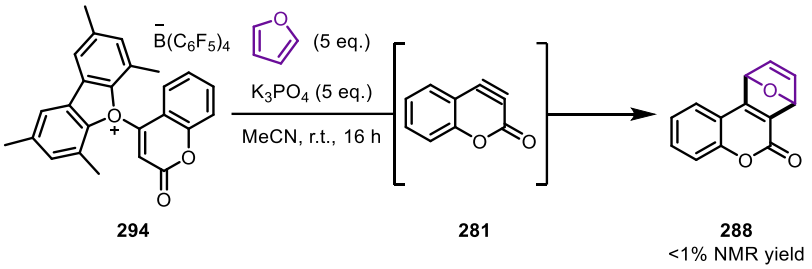
Scheme 68: Screening of counterions to ascertain the stability of the corresponding coumarin-containing triaryloxonium salts.

Fluorinated tetraarylborates are amongst the weakest coordinating anions and have therefore been used to facilitate the study of highly reactive cations.[110,111] Tetrakis(pentafluorophenyl)borate $[B(C_6F_5)_4]^-$,[112] belonging to this class, was tested as a potential non-reactive anion with the electrophilic triaryloxonium ion. To synthesise the desired oxonium salt **294**, tetrafluoroborate diazonium **290** was generated and underwent a counterion metathesis with an excess of $KB(C_6F_5)_4$ to obtain diazonium $[B(C_6F_5)_4]^-$ salt **293** (**Scheme 69**). After 16 h at room temperature, diazonium **293** was fully consumed, yielding the desired oxonium **294** in 81% yield. The tetrafluoroborate resonance was absent in the ^{19}F NMR spectrum and three new resonances were observed corresponding to the fluorinated tetraarylborate anion, indicated complete anion exchange has occurred. Compound **294** was stable in solution for an additional two days, illustrating its enhanced stability compared to tetrafluoroborate oxonium **287**.



Scheme 69: Synthesis of tetrakis(pentafluorophenyl)borate oxonium salt **294**.

We next assessed whether **294** could serve as a 3,4-coumaryne precursor. Compound **294** was subjected to the optimised aryne generating and trapping conditions with furan, however, only a trace of the desired [4+2] cycloaddition product **288** was observed.

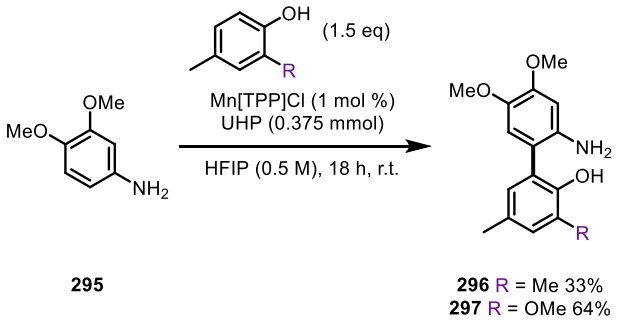


Scheme 70: Attempted 3,4-coumaryne **281** generation and trapping with furan from **294**.

Efforts to improve the stability of the coumarin by modifying the counterion while maintaining its efficiency as a 3,4-coumaryne precursor were unfruitful. Therefore, we next explored modification to the oxonium scaffold in hopes of achieving this goal.

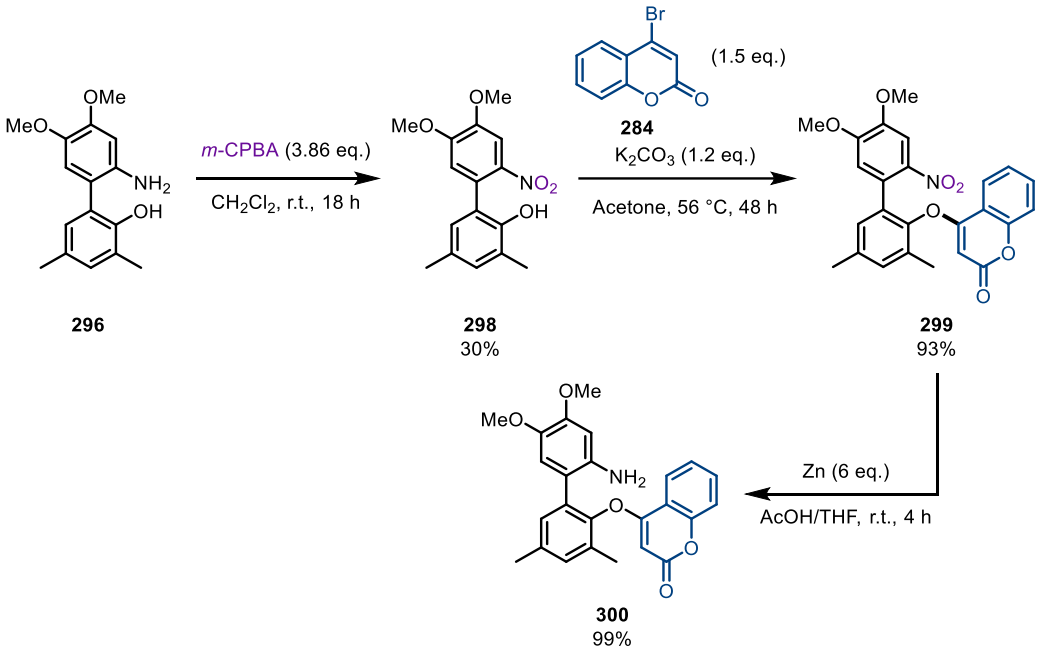
2.2.3.2.3 Substituent effect

We proposed varying the substituents on the backbone of the triaryloxonium could reduce its susceptibility to nucleophilic attack. The methoxy group was chosen as an appropriate substituent to reduce the electrophilicity of the triaryloxonium ion through mesomeric donation of its lone pairs. A synthetic route was devised to generate methoxy-substituted triaryloxonium ions utilising Vershinin, Pappo, and coworkers' manganese-catalysed oxidative cross-coupling of phenols and anilines.[113] Using this procedure, methoxy-substituted biaryls, **296** and **297**, were successfully synthesised in moderate to good yields (44% and 64% respectively) (**Scheme 71**).



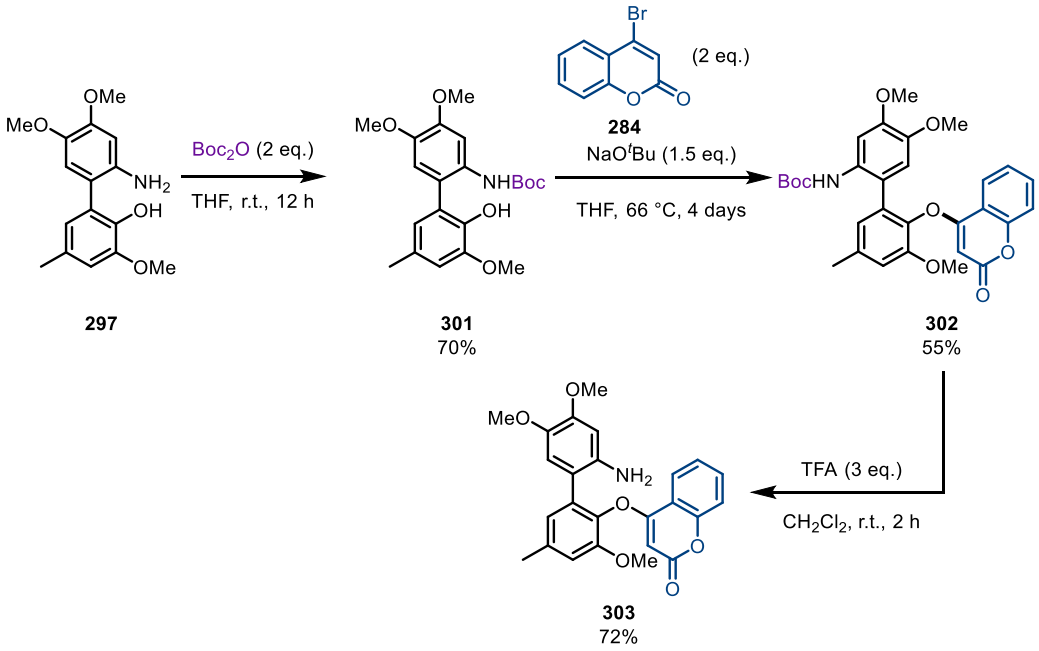
Scheme 71: Synthesis of the methoxy-substituted biaryls **296** and **297**.

Using **296** and **297**, two methods to modify the aniline functional groups to ensure selective *O*-arylation were explored. Firstly, **296** was oxidised using *m*-CPBA in moderate yield (30%) to give **298** (**Scheme 72**). Refluxing **298** with 4-bromocoumarin **284** and potassium carbonate afforded the desired product **299** in very good yield (93%). Finally, the nitro-group was reduced to give aniline **300** in excellent yield (99%).[114]



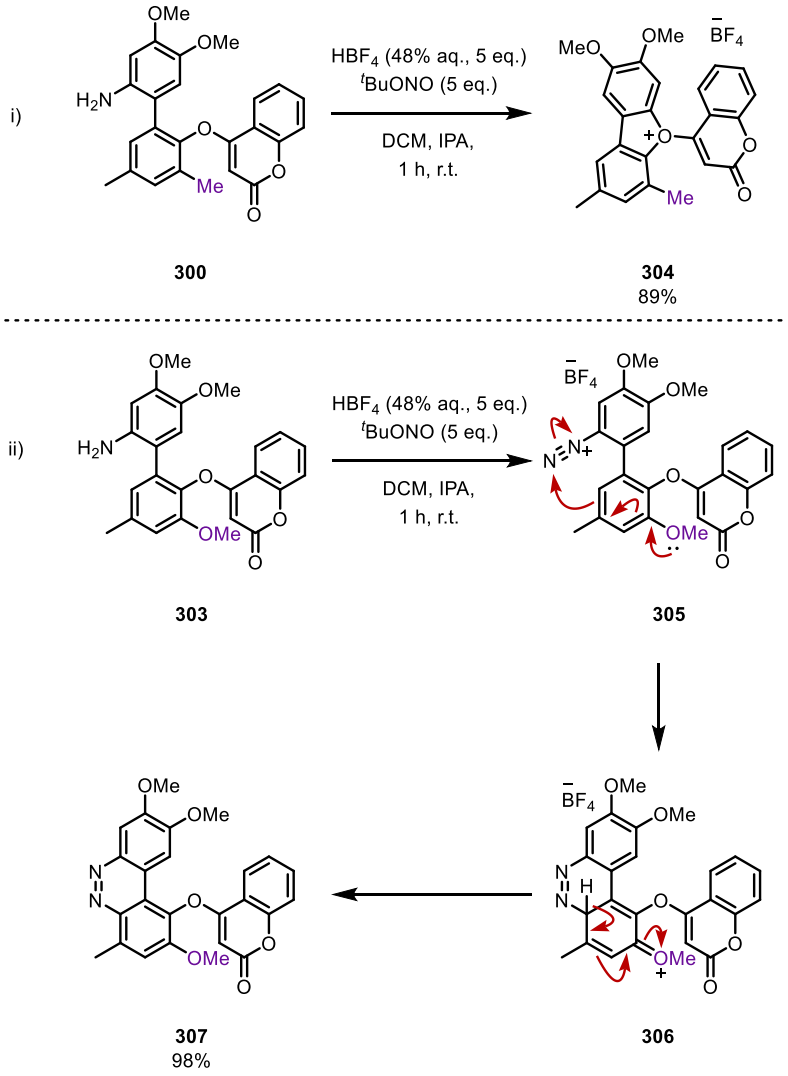
Scheme 72: Synthesis of aniline **300**.

The aniline moiety in biaryl **297** was selectively protected using Boc anhydride generating **301** in 70% yield.[115] Refluxing **301** in the presence of 4-bromocoumarin **284** and sodium *tert*-butoxide generated the desired product **302** in moderate yield (55%). Deprotection of **302** was achieved using TFA yielding **303** in good yield (72%) (**Scheme 73**).[116]



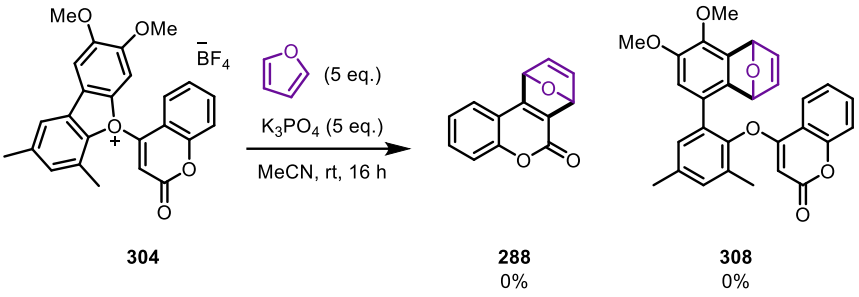
Scheme 73: Synthesis of aniline **303**.

To form the corresponding oxoniums, anilines **300** and **303** were treated with HBF_4 and ^{t}BuONO. For methyl-substituted aniline **300**, within 1 h the diazonium had been consumed and the desired oxonium salt **304** was afforded in good yield (80%) (**Scheme 74**, i). However, methoxy-substituted aniline 3**03** did not yield the target oxonium. Instead, after 1 h the pyridazine **307** was isolated in 98% yield (**Scheme 74**, ii). This transformation likely proceeded *via* nucleophilic attack *para* to the methoxy group onto the terminal nitrogen of the diazonium, followed by rearomatisation by deprotonation.



Scheme 74: i) oxonium salt **304** generation ii) proposed mechanism for pyridazine **307** generation.

Oxonium salt **304** was then subjected to the aryne generating and trapping conditions using furan as the trapping agent. A complex reaction mixture was afforded containing none of the desired cycloaddition product from deprotonation of the pendant coumarin **288** or the dibenzofuran core **308** (**Scheme 75**).

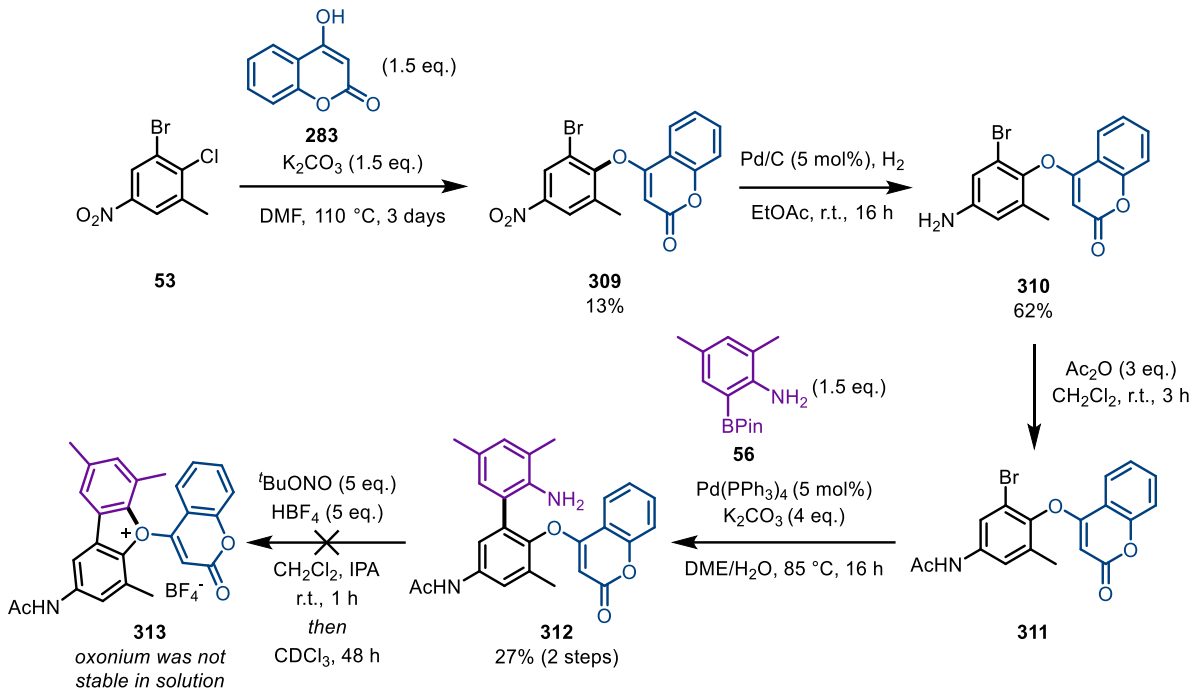


304 **288** 0% **308** 0%

Scheme 75: Attempted aryne generation and trapping from **304**.

To explain this result, we hypothesised that stabilisation from the methoxy-groups reduces the ground state energy of oxonium **304** relative to 3,4-coumaryne intermediate **281**. Thereby increasing barrier to form **281** to where it is no longer energetically feasible. To offset this effect, we proposed using the weaker mesomerically electron-donating group *N*-acetyl group to stabilise the oxonium relative to the tetrafluoroborate anion while maintaining energetic accessibility to 3,4-coumaryne **281**.

A synthetic route to *N*-acetyl-substituted oxonium salt **313** was devised, adopting the protocol used for generating triaryloxonium ions from phenols in section **1.2.1**. 4-Hydroxycoumarin **283** was reacted with 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** and potassium carbonate to afford **309** in poor yield (13%) (**Scheme 76**). The low yield was likely attributed to the poor nucleophilicity of the alcohol group. The *N*-acetyl group was then afforded by reduction and subsequent acetylation of the nitro group. The biaryl bond was installed *via* a Suzuki-Miyaura coupling to give **312** in moderate yield (27%).[105] Aniline **312** was treated with HBF_4 and ^{t}BuONO and the corresponding diazonium was dissolved in $CDCl_3$ and monitored by ^{1}H NMR over two days. The diazonium was consumed to give a complex reaction mixture, inconsistent with the generation of a stable oxonium salt.



Scheme 76: Attempted synthesis of coumarin oxonium salt **313**.

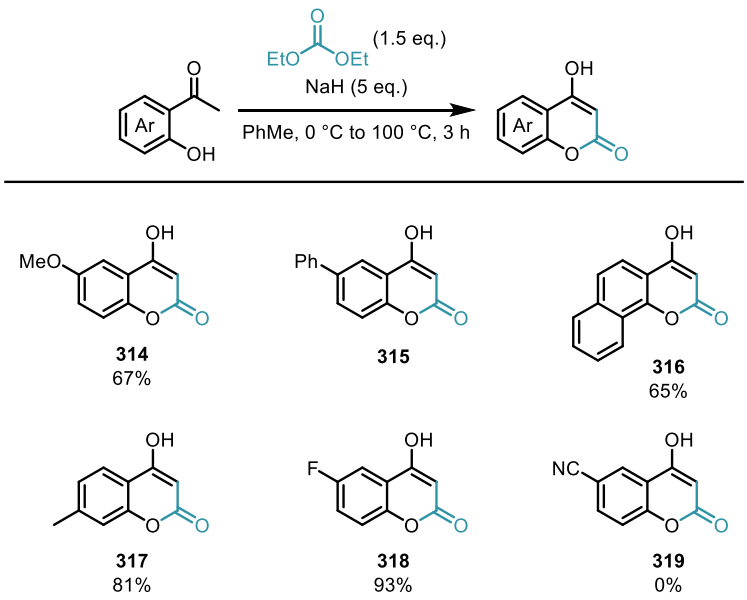
Despite extensive studies towards improving the stability of triaryloxonium salts containing the coumarin moiety while maintaining their utility as 3,4-coumaryne precursors, our efforts were unsuccessful. We therefore shifted our attention back to tetrafluoroborate oxonium salt **287** given its potential as a 3,4-coumaryne precursor, despite its inherent instability.

2.2.3.3 Triaryloxonium salt synthesis

Until this point, the substituents on the dibenzofuran moiety and the nature of the counterion had been varied. Our subsequent goal was to synthesise a variety of tetrafluoroborate coumarin triaryloxonium salts with different substituents on the coumarin backbone. We hoped to understand how these variations affect both the stability of the oxonium and the generation of 3,4-coumaryne.

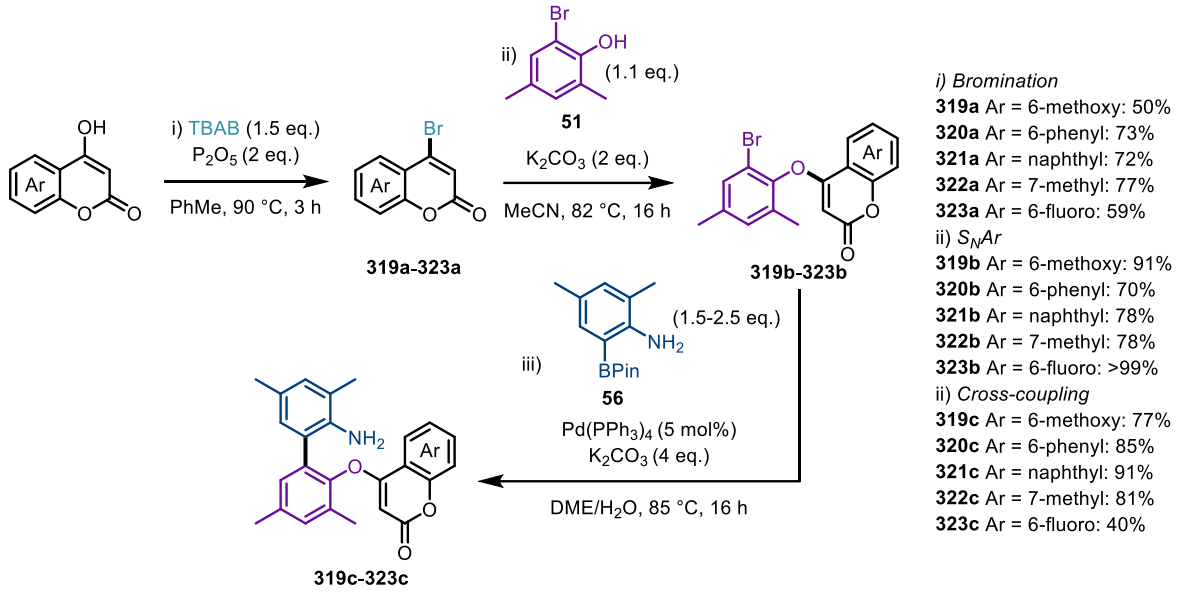
A range of functionalised 4-hydroxycoumarins were synthesised using a method outline by Litinas and co-workers in which *ortho*-hydroxyacetophenones were refluxed in the presence of

diethylcarbonate and sodium hydride to generate the corresponding 4-hydroxycoumarins (**Scheme 77**).[103] All the desired 4-hydroxycoumarins were successfully made in good to very good yield with the exception of the nitrile-substrate **319**. Difficulties in purification meant the phenyl-substrate **315** was carried through as a crude mixture and purified in the subsequent step.



Scheme 77: Synthesis of 4-hydroxycoumarins.

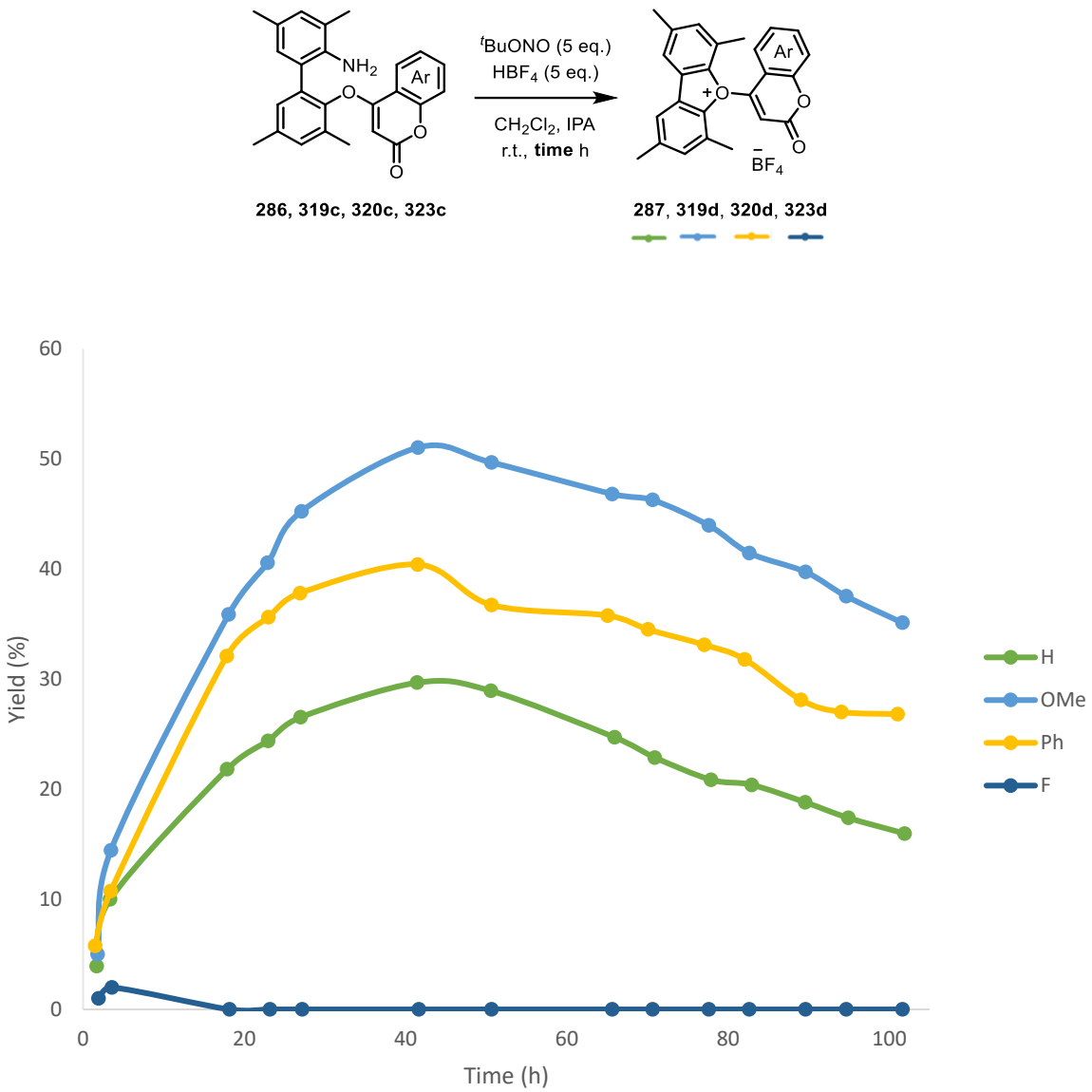
Using the protocol developed to synthesise **286** (**Scheme 61** and **62**), the 4-hydroxycoumarins were converted into the corresponding anilines *via* a bromination,[103] S_NAr reaction with phenol **51**, and Suzuki-Miyaura coupling with aniline-containing pinacol borane **56** (**Scheme 78**).[105]



Scheme 78: Synthesis of coumarin-containing anilines **319c**-**323c**.

A ^{1}H NMR study was then conducted monitoring oxonium formation over time to determine how the maximum oxonium yield, and the time at which this occurred, varies with the electron density of the coumarin. The unsubstituted- **286**, methoxy- **319c**, phenyl- **320c**, and fluoro- **323c** coumarin anilines were diazotised, dissolved in $CDCl_3$, and the yields of the corresponding oxoniums were monitored over time (**Scheme 79**).

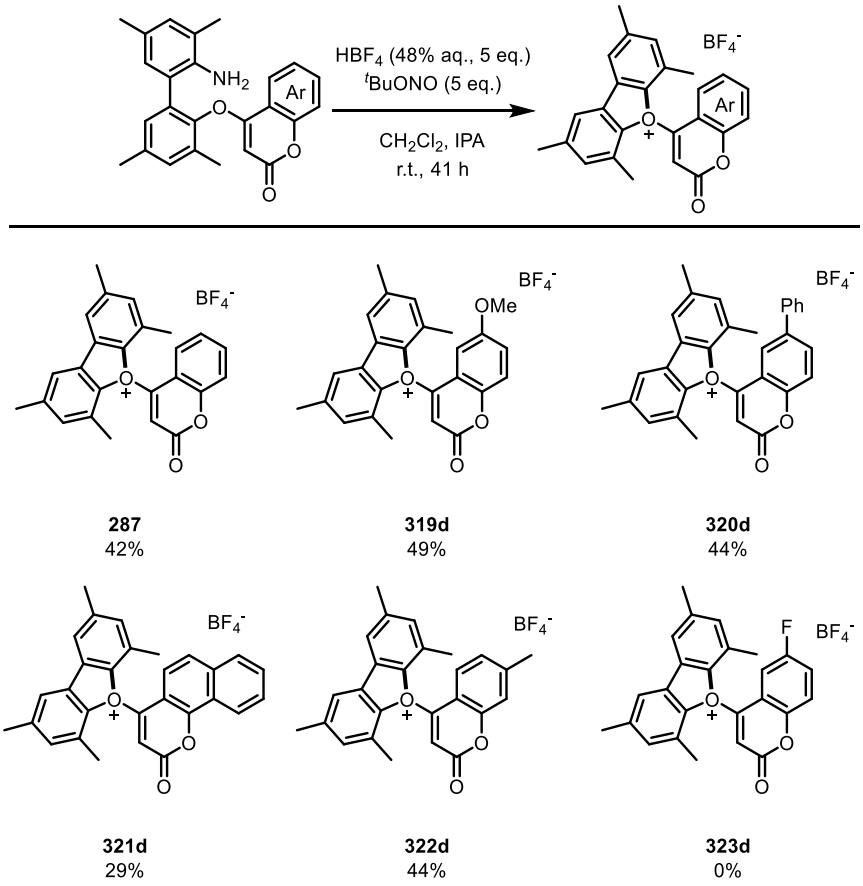
The yields of the unsubstituted- **287**, methoxy- **319d**, and phenyl- **320d** oxoniums exhibited similar trends, reaching a maximum at approximately 41 hours. Methoxy-oxonium **319d** showed the highest yield, reaching 52% at 42 hours. The suspected fluoro-oxonium **323d** appeared briefly, with a yield of 2% after approximately 4 hours, but was no longer detectable by the subsequent measurement at 18 hours. These findings suggest that increased electron density of the oxonium enhances its stability to the tetrafluoroborate anion, consistent with previous substitution studies (section **2.2.3.2.3**) and the proposed mechanism for oxonium degradation *via* nucleophilic attack (**Scheme 64**).



Scheme 79: The yields of oxoniums (**287**, **319d**, **320d**, and **323d**) generated from diazotisation of the corresponding anilines (**286**, **319c**, **320d**, and **323d**) over time. Time = 0 h corresponds to the time at which ^{t}BuONO was added. Yields are measured by ^{1}H qNMR using dibromomethane as an internal standard.

The anilines were then subjected to the oxonium generating conditions and maintained at room temperature for 41 hours. Methoxy-substituted oxonium **319d** was afforded in the highest yield (49%) and as expected none of the electron-deficient fluoro-substituted oxonium **323d** was obtained (**Scheme 80**). The remaining oxoniums, **320d-322d**, were obtained in moderate yield, with the naphthyl-substituted oxonium **321d** being isolated in notably lower yield (29%). Due to

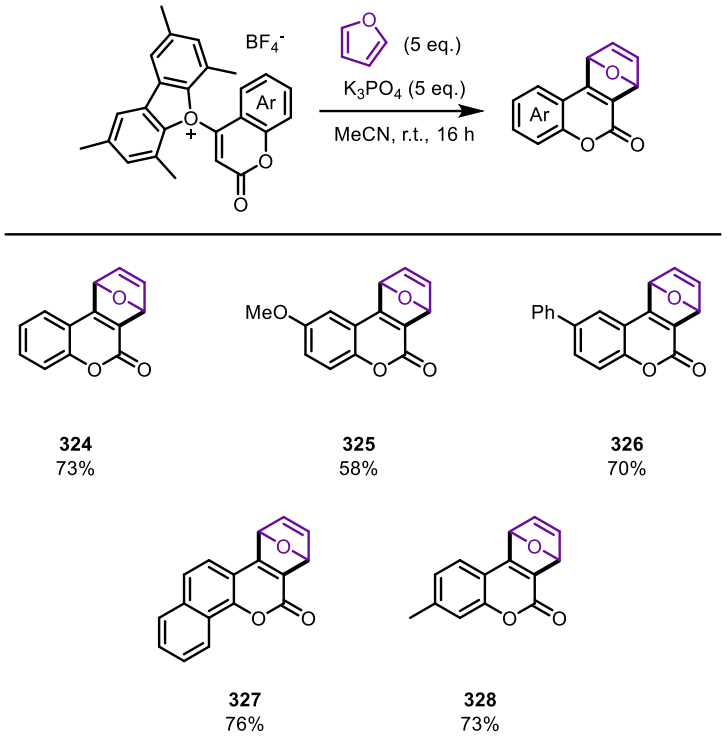
the instability of the oxoniums and the presence of unreacted diazonium, multiple triturations were often required in the purification step, resulting in diminished yields, which could explain the lower isolated yield for **321d**.



Scheme 80: Scope for coumarin-containing triaryloxonium salt formation.

2.2.3.4 3,4-Coumaryne generation

The oxoniums were then subjected to the aryne generating and trapping conditions using furan and pleasingly, all the [4+2] cycloaddition products were generated in good yield (**Scheme 81**).



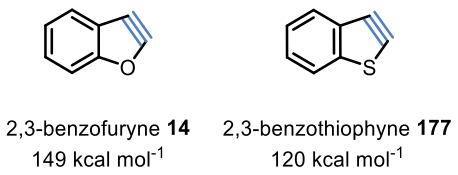
Scheme 81: Scope for generation and trapping of 3,4-coumarynes with furan from oxonium salts.

These results suggest that triaryloxonium ions can effectively serve as 3,4-coumaryne precursors. However, further investigations employing alternative trapping agents and isotopic labelling experiments would offer more definitive insights into whether this reaction proceeds *via* the proposed hetaryne mechanism. While we were encouraged by the reactivity of coumarin oxonium ions, the practical utility of this method is constrained by their inherent instability. Therefore, we continued our efforts focusing on alternative hetaryne targets.

2.2.4 Five-membered hetaryne generation

The generation of five-membered hetarynes presents a significant challenge to chemists due to their strain.[117] Having successfully demonstrated the mild preparation of functionalised benzynes and novel six-membered hetarynes from triaryloxonium ions,[118] we envisioned their potential application in generating five-membered hetarynes.

To test the limits of triaryloxonium ions as hetaryne precursors, we targeted 2,3-benzofuryne **14** and 2,3-benzothiophyne **177** generation *via* oxonium ions (**Scheme 82**). The computational model by Paton, Houk, and Garg predicted 2,3-benzofuryne **14** to be energetically inaccessible (149 kcal mol^{-1}), while the generation of 2,3-benzothiophyne **177** was expected to be potentially viable (120 kcal mol^{-1}).[49]

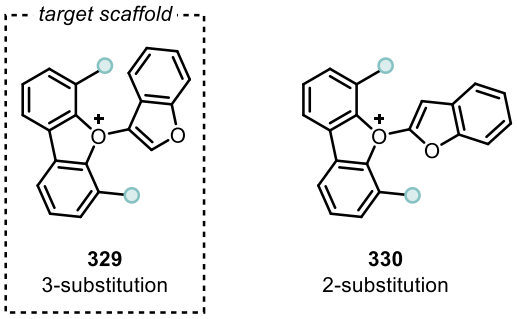


Scheme 82: Calculated dehydrogenation energy of 2,3-benzofuryne **14** and 2,3-benzothiophyne **177**.

2.2.4.1 2,3-Benzofuryne

2.2.4.1.1 Triaryloxonium salt synthesis

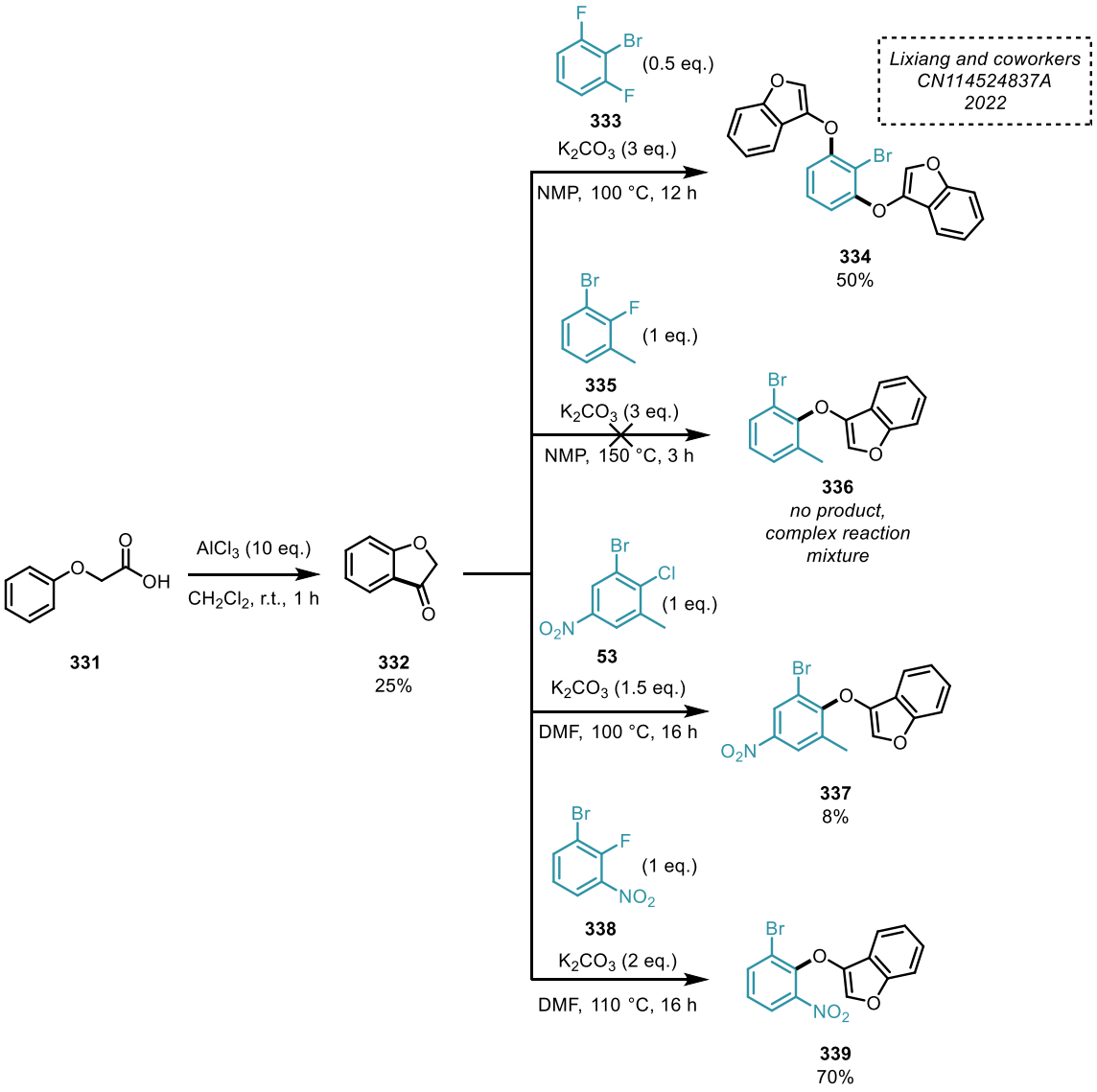
In designing a benzofuran-containing triaryloxonium ion scaffold, we opted for a 3-substituted **329**, rather than 2-substituted **330**, heterocycle to avoid the benzofuran oxygen being positioned *ortho* to the oxonium bond (**Scheme 83**).



Scheme 83: Potential substitution patterns of benzofuran-containing triaryloxonium ions.

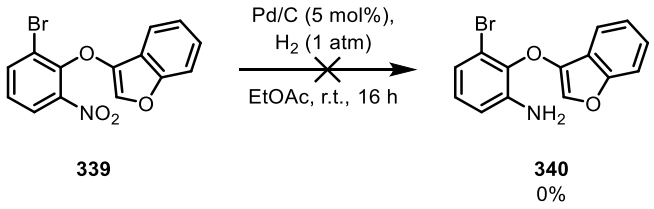
Based on a recent patent,[119] we postulated that oxonium scaffold **329** could be accessed *via* a benzofuran bis(aryl) ether, which could be constructed by the reaction of benzofuranone **332** and a suitable electrophilic aryl reagent (**Scheme 84**).

Benzofuranone **332** was prepared using an $AlCl_3$-promoted intramolecular Friedel-Crafts acylation of 2-phenoxyacetic acid **331**, as outlined by Chae and coworkers (**Scheme 84**).[120] **332** was then heated with commercially available 1-bromo-2-fluoro-3-methylbenzene **333** in the presence of potassium carbonate at high temperature.[119] The desired product **336** was not obtained, which might be attributed to the sterically hindered C-F bond situated between two *ortho*-substituents. We proposed that a more strongly activated electrophile might improve the desired reactivity. Therefore, 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53**, used in prior syntheses, was employed and the desired bis(aryl) ether **337** was obtained in low yield (8%). With this in mind, we turned to the even more activated and commercially available precursor 1-bromo-2-fluoro-3-nitrobenzene **338** and pleasingly the corresponding bis(aryl) ether **339** was afforded in significantly higher yield (70%).



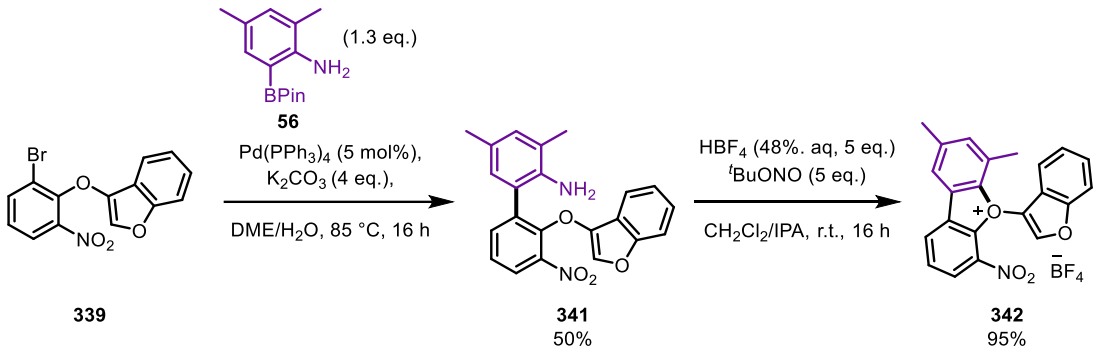
Scheme 84: S_NAr reactions with benzofuranone **332** to generate bis(aryl) ethers.

Anticipating that the electron withdrawing nitro-group may destabilise the oxonium ion derived from **339**, we attempted to moderate its electronic influence by reduction and acetylation. However, when **339** was stirred with palladium on carbon in an atmosphere of hydrogen a complex reaction mixture was obtained and none of the desired aniline **340** was isolated.



Scheme 85: Attempted reduction of **339**.

Therefore, **339** was carried through to the next step to determine whether the reduction and acetylation steps were necessary for this oxonium system. Using the previously employed cross-coupling conditions,[105] aniline **341** was obtained in 50% yield. Aniline **341** was then treated with HBF_4 and ^{t}BuONO and after 16 hours the corresponding oxonium salt **342** was afforded in excellent yield (95%). Interestingly, the nitro-substituent was tolerated in the oxonium generation, unlike the phenyl-containing triaryloxoniums.[109] We reasoned that mesomeric donation by the oxygen lone pair of the enol ether moiety likely contributes to the stability of **342**.

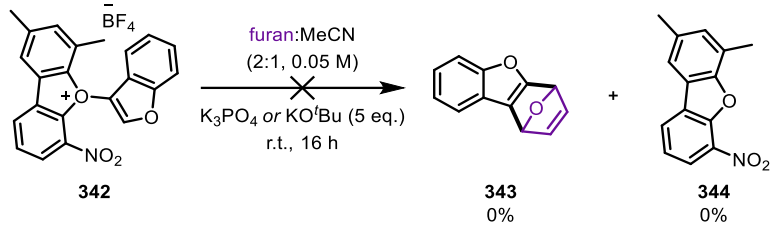


Scheme 86: Synthesis of oxonium salt **342**.

2.2.4.1.2 2,3-Benzofuryne generation

Oxonium salt **342** was then subjected to the trapping conditions developed in section **2.2.2.2** using a large excess of furan and potassium phosphate. After stirring overnight, **342** was consumed to

afford a complex reaction mixture and none of the desired product **343** or dibenzofuran **344** were observed. The same result was obtained where potassium *tert*-butoxide was employed as the base.



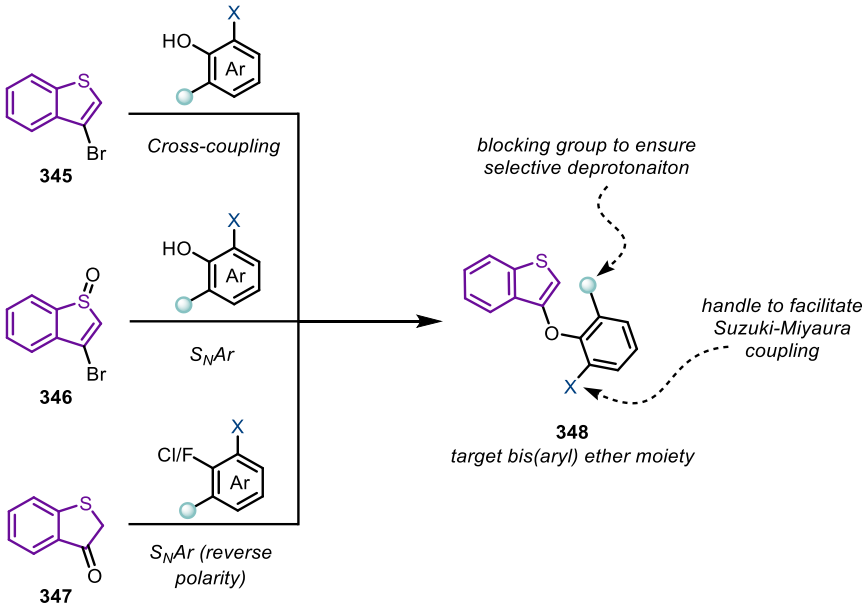
Scheme 87: Attempted 2,3-benzofuryne generation from **342**.

This result is consistent with the prediction that **14** is an energetically inaccessible hetaryne.[49] Therefore, we continued our pursuit of five-membered hetaryne generation focusing on the lower energy hetaryne, 2,3-benzothiophyne **177**.

2.2.4.2 2,3-Benzothiophyne

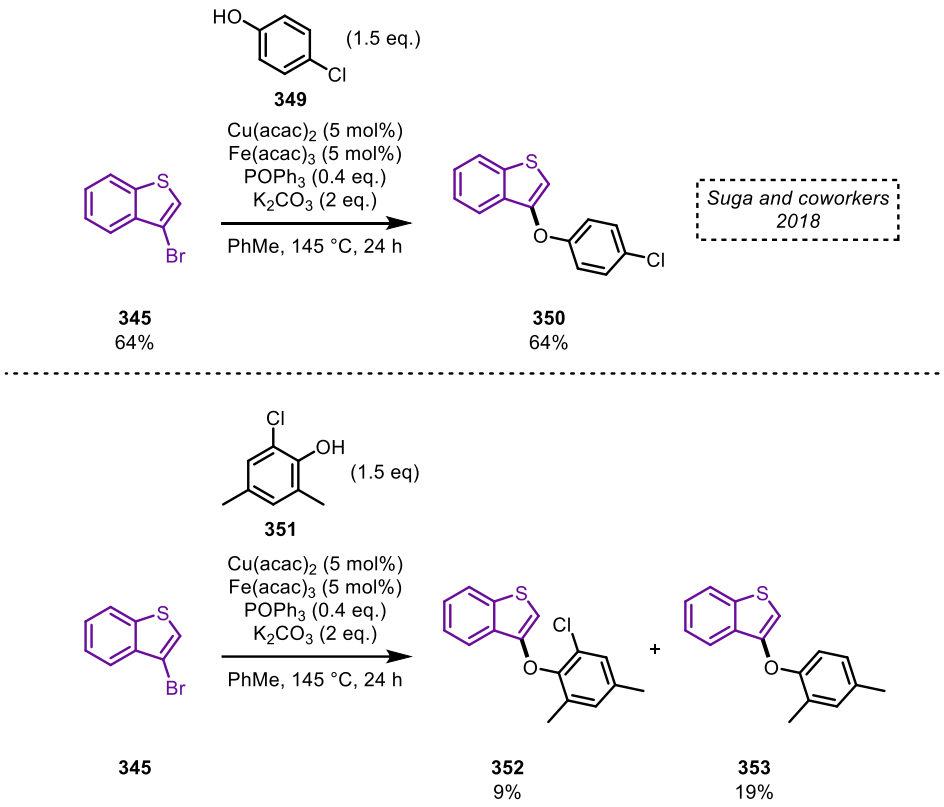
2.2.4.2.1 Synthetic routes to triaryloxonium salts

Following a similar approach to the synthesis of the benzofuran-containing triaryloxoniums, we designed benzothiophene-containing triaryloxoniums wherein the oxonium was substituted at the 3-position of the heterocycle. Various synthetic routes to the target bis(aryl) ether moiety **348** were considered (**Scheme 88**). According to literature precedent, benzothiophene (bis)aryl ethers have been generated *via* copper-catalysed cross-coupling reactions between 3-bromobenzothiophene **345** and phenols (**Scheme 89**).[121,122] Alternatively, oxidation of sulfur to form sulfoxide **346** could facilitate nucleophilic addition from a phenol to install the desired functionality (**Scheme 88**).[123] The bis(aryl) ether might also be generated in a similar fashion to **339** using benzothiophenone **347** and an electron-deficient chloro/fluoro-aryl ether (**Scheme 88**).[124]



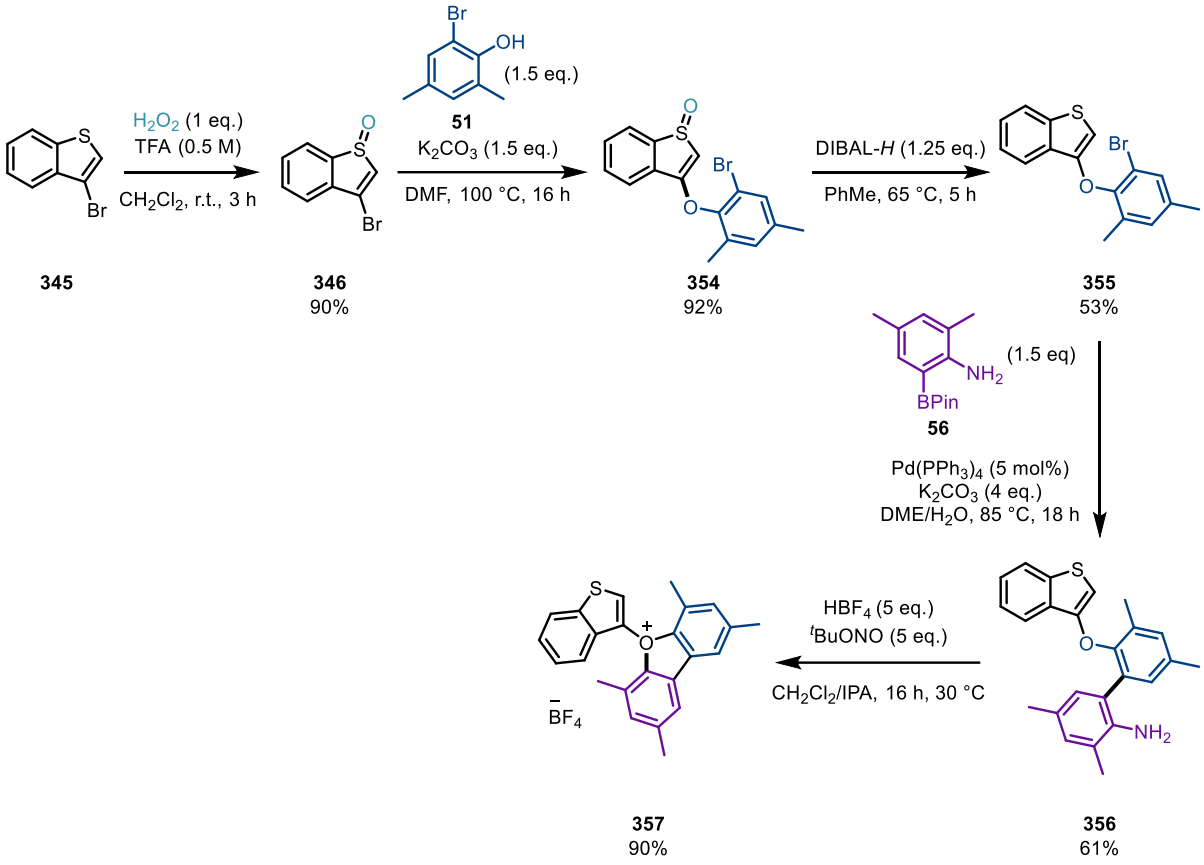
Scheme 88: Proposed synthetic routes to generate the target bis(aryl) ether moiety.

We initially explored the cross-coupling pathway due to the ready availability of the starting materials, involving the coupling of **345** with a suitable phenol bearing a blocking group and a synthetic handle to connect the aniline. These requirements presented two challenges: the generation of a sterically encumbered bis(aryl) ether and the requirement for the cross-coupling to be selective. To address the latter challenge, we were inspired by Suga and coworkers' copper/iron-catalysed etherification of 3-bromobenzothiophene **345** which demonstrated tolerance for selective cross-coupling of 4-chlorophenol **349** to afford bis(aryl) ether **350** (**Scheme 89**).[121] Therefore, we proposed 2-chloro-4,6-dimethylphenol **351** might be tolerated as coupling partner with **345** under this method. However, when **345** and **351** were subjected to Suga and co-workers' optimised conditions the desired product **352** was only obtained in 9% yield (**Scheme 89**).[121] Furthermore, the major product in this case was the dehalogenated product **353**, isolated in 19% yield. The presence of two *ortho*-substituents evidently reduces the efficiency of this reaction - there are no such examples in the original reaction scope.



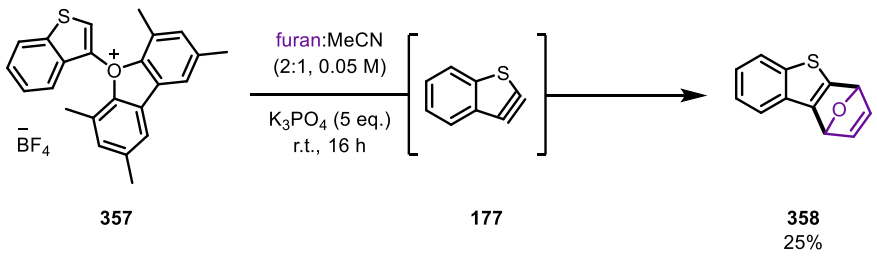
Scheme 89: Synthesis of bis(aryl) ethers *via* copper-catalysed cross-coupling reactions.

The next avenue explored was the addition-elimination of phenol into sulfoxide **346** (**Scheme 91**). Sulfoxide **346** was afforded upon treatment of benzothiophene **345** with H_2O_2 in the presence of TFA in 90% yield.[123] Compound **346** was then heated with phenol **51** in the presence of potassium carbonate to give bis(aryl) ether **354** in very good yield (92%). DIBAL-*H* was then employed to reduce the sulfoxide generating **355** in 53% yield.[123] Suzuki-Miyaura coupling with **56** then gave aniline **356** in 61% yield,[105] which, upon diazotisation and gentle heating for 16 h, afforded the desired oxonium salt **357** in 90% yield.



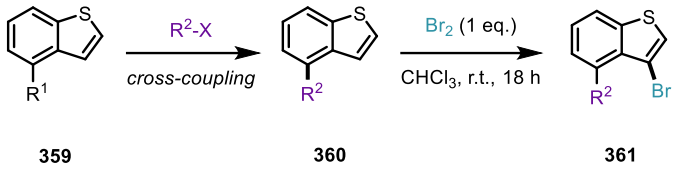
Scheme 90: Synthesis of benzothiophene-containing oxonium salt **357**.

Compound **357** was then stirred with potassium phosphate and a large excess of furan in acetonitrile. Pleasingly, the cycloaddition product **358** was isolated in 25% yield, which was proposed to form *via* the five-membered aryne intermediate **177**.



Scheme 91: Generation and trapping of 2,3-benzothiophyne **177** with furan from **357**.

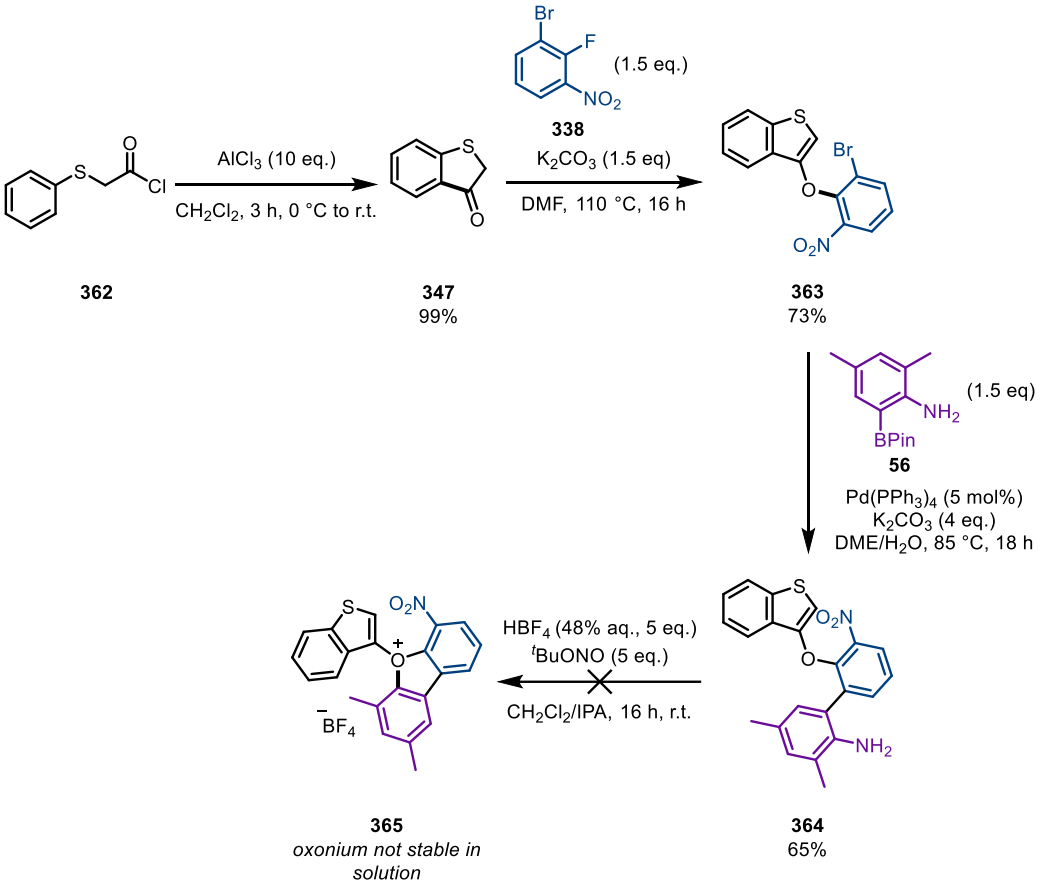
We proceeded to evaluate the feasibility of this synthetic approach with substituted benzothiophenes. 3-Bromobenzothiophenes **361** were synthesised from halogenated benzothiophenes **359**, which underwent cross-coupling reactions to form substituted benzothiophenes **360**, followed by bromination (**Scheme 92**). However, we were unable to reliably obtain pure 3-bromobenzothiophenes **361** due to challenges in purification.



359 **360** **361**

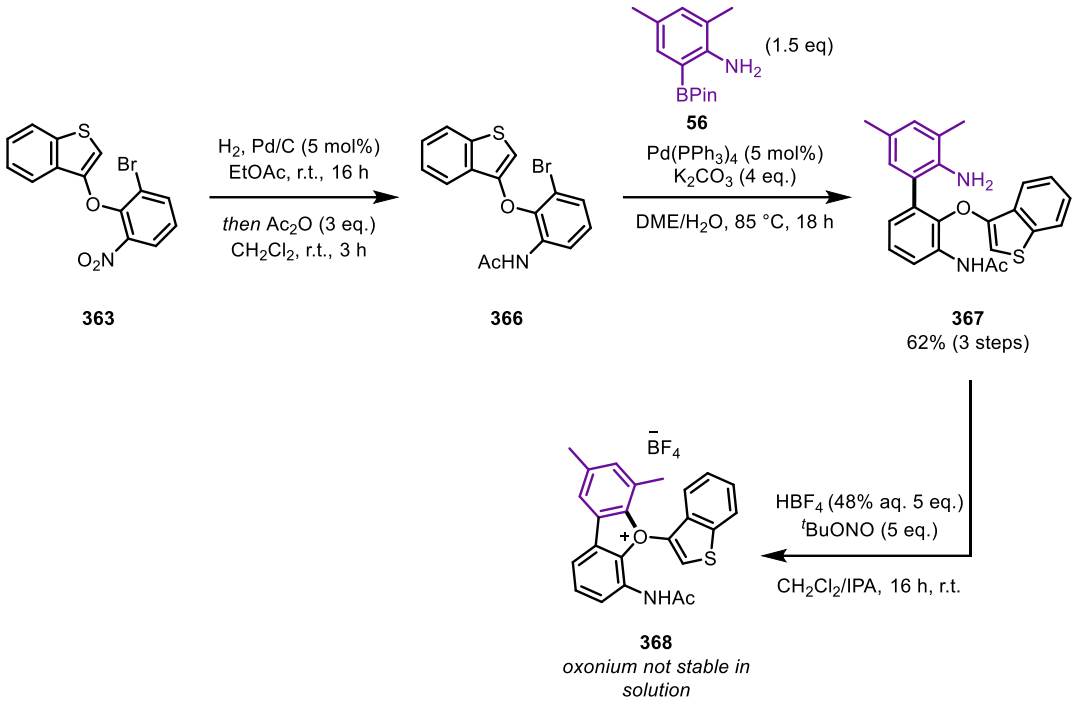
Scheme 92: General synthetic route to substituted 3-bromobenzothiophenes **361**.

Therefore, we investigated the alternative route *via* S_NAr using benzothiophenone **347** and electron deficient chloro/fluoro-aryls (**Scheme 93**). Considering the stability of the nitro-substituted benzofuran-containing oxonium **342**, we were intrigued whether the corresponding benzothiophene-containing oxonium **365** would exhibit similar stability. Benzothiophenone **347** was efficiently generated (99%) *via* an intramolecular Friedel-Crafts acylation of 2-(phenylthio)acetyl chloride **362** with $AlCl_3$ (**Scheme 93**).[125] Subsequent S_NAr reaction with 1-bromo-2-fluoro-3-nitrobenzene **338** afforded bis(aryl) ether **363** in good yield (73%). Employing the standard cross-coupling conditions to **363**,[105] aniline **364** was obtained in 65% yield. Aniline **364** was subjected to the diazotisation conditions and monitored by ^1H NMR. Clean transformation to the corresponding diazonium was observed, however gradual conversion over 48 h to give a complex reaction mixture suggested oxonium salt **365** is unstable in solution.



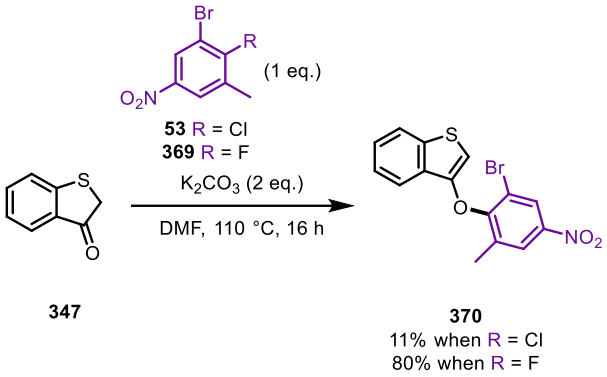
Scheme 93: Attempted synthesis of oxonium salt **365**.

In hopes of generating a stable benzothiophene-containing oxonium salt, we reasoned a less electron withdrawing *N*-acetyl-group could be used. Nitro-aryl ether **363** was reduced and acetylated, and then directly converted into amide **366** without intermediate purification (**Scheme 94**). Aniline **367** was obtained in 62% yield from **366**. Aniline **367** was treated with HBF_4 and ^tBuONO and the resultant diazonium was monitored by ^1H NMR. However, decomposition to a complex mixture was observed over 48 h, suggesting **368** is unstable in solution. We hypothesised that the instability of **368** is likely due to steric repulsion between the *N*-acetyl- and benzothiophene-group.



Scheme 94: Attempted synthesis of oxonium salt **368**.

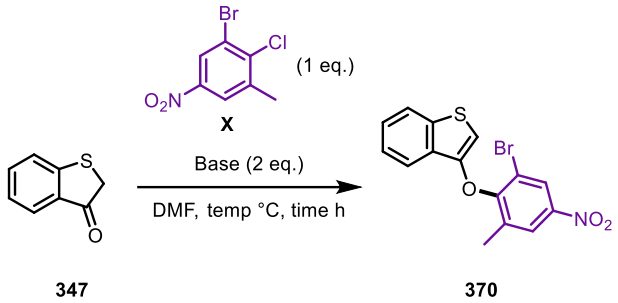
Given efforts to employ the commercially available electrophile 1-bromo-2-fluoro-3-nitrobenzene **338** to construct a stable benzothiophene oxonium were unsuccessful, we explored alternative electrophiles, namely chloro-nitro-benzene **53** and fluoro-nitro-benzene **369**. Heating benzothiophenone **347** with **53** afforded bis(aryl) ether **370** in low yield (11%) while the reaction with **369** generated **370** in significantly higher yield (80%) (**Scheme 95**). Although **369** demonstrated superior efficiency in forming **370**, its synthesis was deemed impractical, requiring heating of a diazonium at 150 °C under reduced pressure. As a result, our focus shifted to optimising the reaction using the chlorinated electrophile **53**.



Scheme 95: S_NAr reactions of benzothiophenone **347** with **53** and **369** to generate bis(aryl) ether **370**.

The S_NAr reaction of benzothiophenone **347** with **53** (**Scheme 96**) was optimised by varying the base, temperature, and duration of reaction. Unfortunately, **53** could not be added in excess because it was challenging to separate from **370**, therefore all the reactions were carried out using one equivalent of **53**. Employing potassium carbonate as the base at 110 °C for 16 hours (**Entry 1**) the desired product was obtained in 11% yield and none of the starting material **347** was recovered. Using a stronger base, sodium *tert*-butoxide, led to a reduction in yield (3%) (**Entry 2**).

Reducing the temperature to 60 °C (**Entry 3**) afforded **370** in 33% yield and reducing it further to 35 °C (**Entry 4**) and then 25 °C (**Entry 5**) reduced the yield of the product, 20% and 15% respectively, but decreased the conversion of benzothiophenone **347**. Therefore, the reaction was maintained at 40 °C until **347** was undetectable by TLC. After 4 days, **347** was fully consumed, and the product was isolated in 45% yield. While reducing the temperature and extending the reaction time would likely further increase the yield, it was deemed impractical to prolong the reaction beyond 4 days.

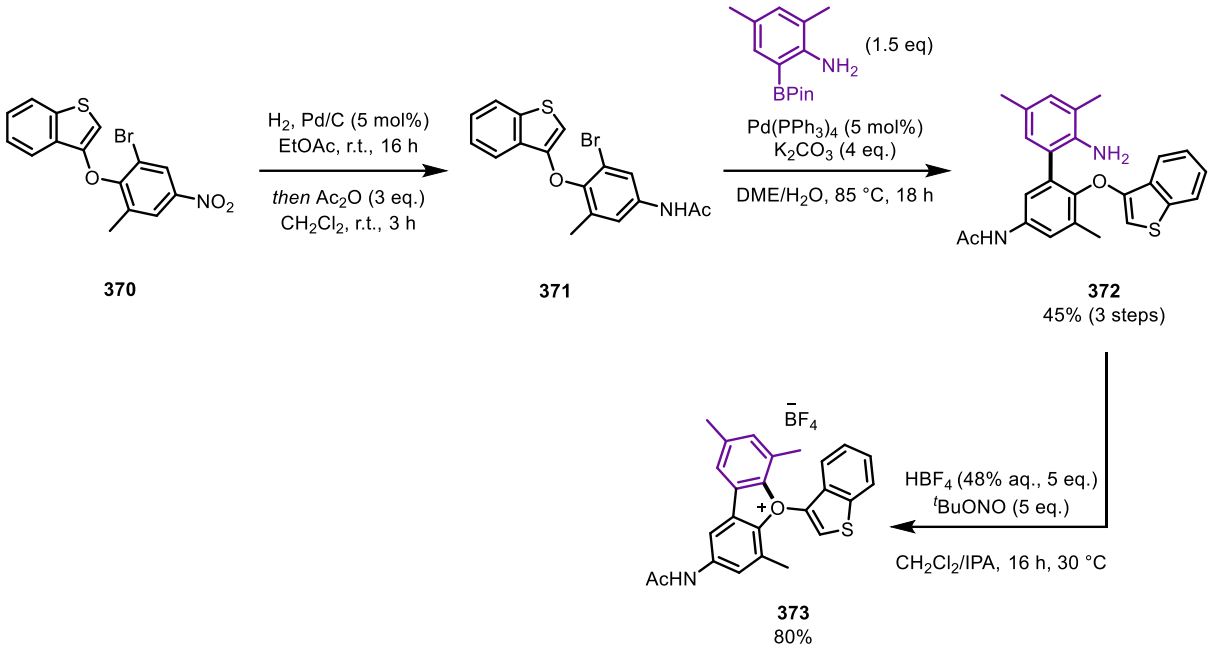


347 370

Entry	Temp (˚C)	Base	Time	Yield 370	Recovered 347
1	110	K_2CO_3	16 h	11%	0%
2	110	NaO^{t}Bu	16 h	3%	0%
3	60	K_2CO_3	16 h	33%	0%
4	35	K_2CO_3	16 h	20%	29%
5	25	K_2CO_3	16 h	15%	75%
6	40	K_2CO_3	4 days	45%	0%

Scheme 96: Optimisation table for the S_NAr reaction between **347** and **53** to afford **370**. Yields are measured by ^1H qNMR using dibromomethane as an internal standard.

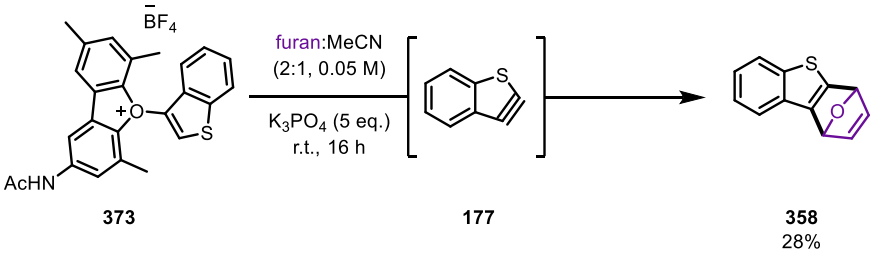
With an improved procedure to synthesise bis(aryl) ether **370**, we then reduced and acetylated the nitro-group followed by installing the aniline to give the oxonium precursor **372** in 45% yield. Subsequent treatment of **372** with HBF_4 and ^{t}BuONO and gentle warming gave the oxonium salt **373** in 80% yield.



Scheme 97: Synthesis of oxonium salt **373**.

2.2.4.2.2 2,3-Benzothiophyne generation

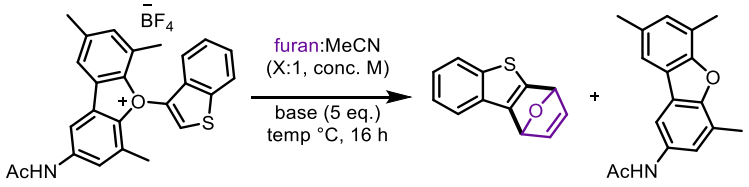
The benzothiophene-containing oxonium salt **373** was subjected to the trapping conditions developed in section **2.2.2.2** and pleasingly, the desired cycloaddition product was obtained in 38% yield (**Scheme 98**).



Scheme 98: Trapping of 2,3-benzothiophyne **177** with furan using **373**.

We then sought to optimise the trapping reaction (**Scheme 99**). Altering the concentration (**Entry 2 and 3**) resulted in diminished yields. Changing the solvent to 1,4-dioxane, toluene, and HFIP

(**Entry 4-6**) similarly decreased the yield of product **358** while using dichloromethane (**Entry 7**) led to a slight increase in yield (31%). Increasing the temperature to 40°C or decreasing it to 0°C both reduced the yield of **358** (**Entry 8 and 9**). Adjusting the furan to dichloromethane ratio to 3:1 marginally increased the yield to 32%, and further adjustment to 9:1 yielded **358** in 30% (**Entry 12-13**). Finally, varying the base using sodium carbonate, sodium *tert*-butoxide, potassium hydroxide, and cesium carbonate (**Entry 15-18**) revealed that using sodium *tert*-butoxide resulted in an increased yield of 37%. These optimised conditions were subsequently employed in further reactions.



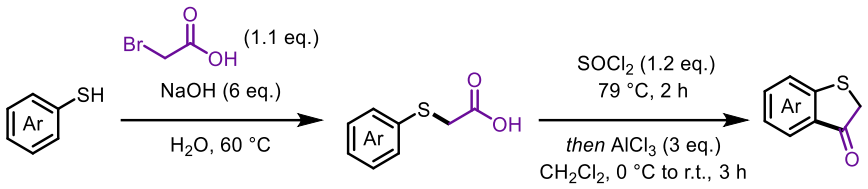
373 358 374

Entry	Base (5 eq.)	Solvent	Conc. (M)	Furan:MeCN *or* eq. of Furan*	temp	Yield 358 (%)	Yield 374 (%)	Conversion (%)
1	K_3PO_4	MeCN	0.05	2:1	r.t.	28	88	100
2	K_3PO_4	MeCN	0.1	2:1	r.t.	22	39	100
3	K_3PO_4	MeCN	0.01	2:1	r.t.	14	16	100
4	K_3PO_4	1,4-dioxane	0.05	2:1	r.t.	27	97	100
5	K_3PO_4	PhMe	0.05	2:1	r.t.	23	77	100
6	K_3PO_4	HFIP	0.05	2:1	r.t.	0	0	34
7	K_3PO_4	CH_2Cl_2	0.05	2:1	r.t.	31	98	100
8	K_3PO_4	CH_2Cl_2	0.05	2:1	40 °C	24	93	100
9	K_3PO_4	CH_2Cl_2	0.05	2:1	0 °C	7	44	100
10	K_3PO_4	CH_2Cl_2	0.05	5 eq.*	r.t.	3	82	100
11	K_3PO_4	CH_2Cl_2	0.05	1:1	r.t.	24	60	100
12	K_3PO_4	CH_2Cl_2	0.05	3:1	r.t.	32	69	100
13	K_3PO_4	CH_2Cl_2	0.05	9:1	r.t.	30	54	100
14	K_2CO_3	CH_2Cl_2	0.05	3:1	r.t.	15	50	100
15	Na_2CO_3	CH_2Cl_2	0.05	3:1	r.t.	0	0	40
16	**NaO^{t}Bu**	**CH_2Cl_2**	**0.05**	**3:1**	**r.t.**	**37**	**97**	**100**
17	KOH	CH_2Cl_2	0.05	3:1	r.t.	32	97	100
18	Cs_2CO_3	CH_2Cl_2	0.05	3:1	r.t.	31	96	100

Scheme 99: Optimisation table for 2,3-benzothiophyne **177** trapping with furan using **373**.

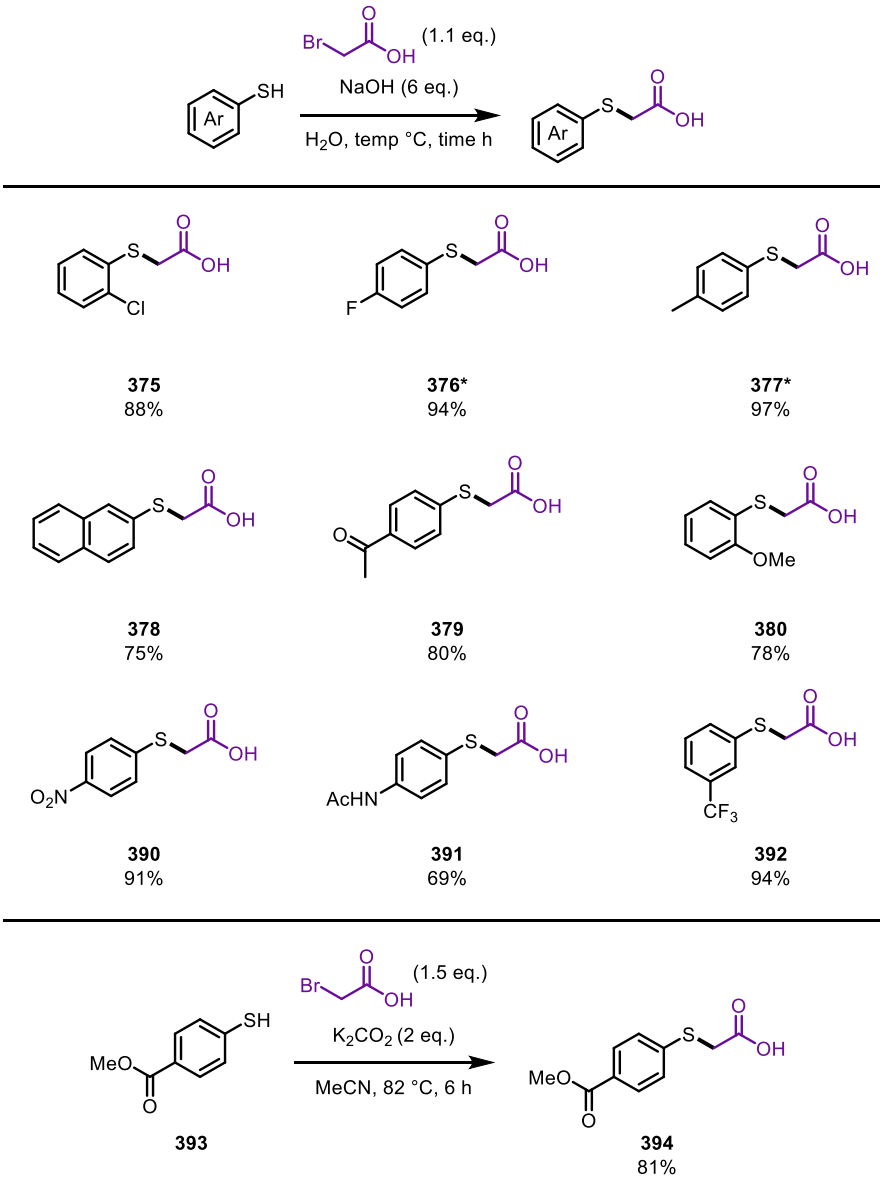
2.2.4.2.3 Triaryloxonium salt synthesis

Having established that **373** is a stable oxonium salt that can potentially serve as a 2,3-benzothiophyne precursor, our next goal was to assess the tolerance of substituted benzothiophenes *via* this synthetic route. Substituted benzothiophenones were synthesised from the corresponding thiophenols according to a literature procedure (**Scheme 100**).[126]



Scheme 100: Synthetic route to benzothiophenones.

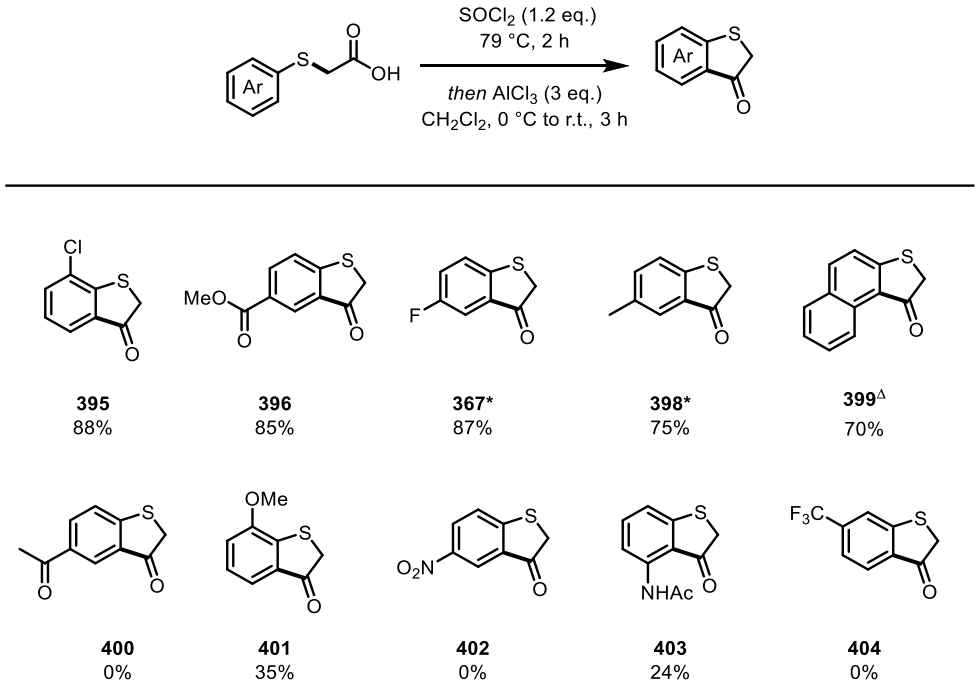
Initially, a range of thiophenols were treated with bromoacetic acid and sodium hydroxide to afford the desired 2-(phenylthio)acetic acids in good to excellent yield (**Scheme 101**). The reaction durations and temperatures were modified according to the solubility of the thiophenols (see supplementary information for full details). To avoid hydrolysis of the ester group, *para*-CO_2Me substrate **394** was synthesised under non-aqueous conditions and using potassium carbonate as the base.



Scheme 101: Scope for the synthesis of 2-(phenylthio)acetic acids. *Synethesised by Dima Petropavlovskikh.

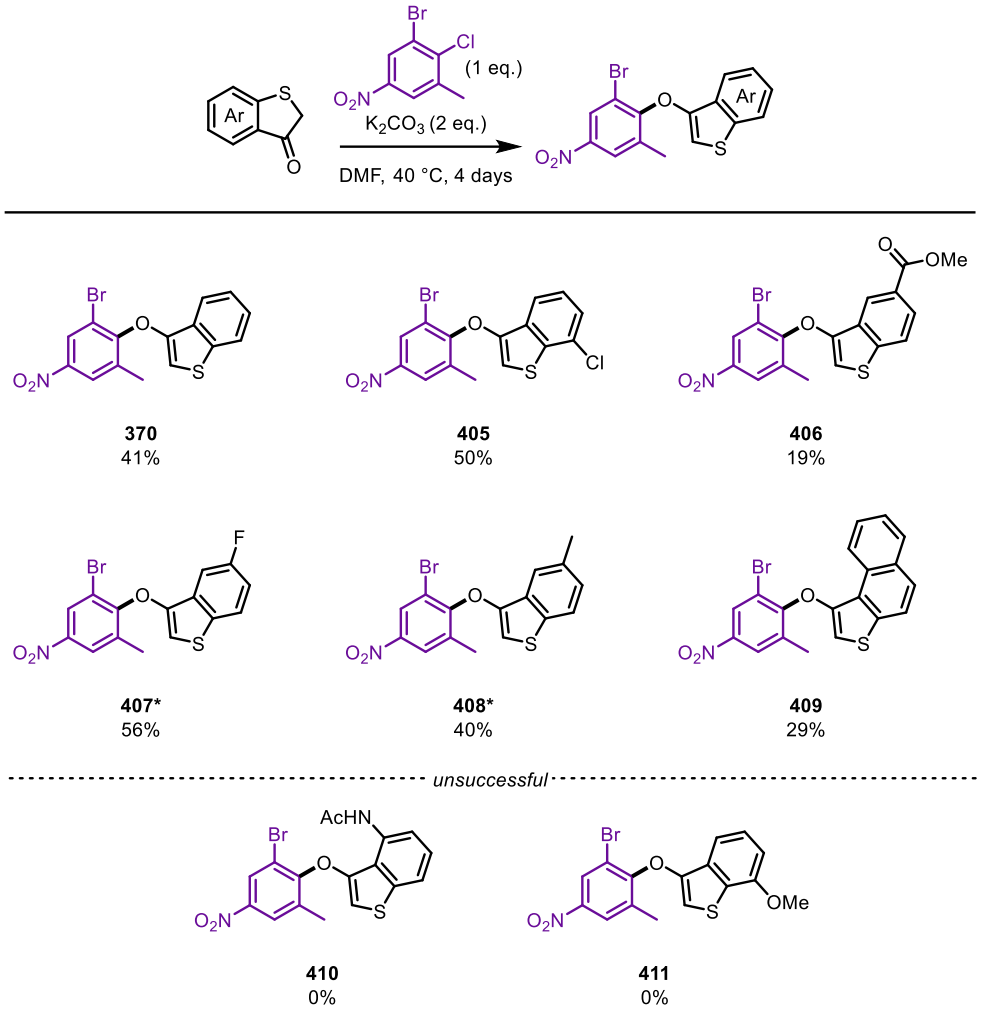
The 2-(phenylthio)acetic acids were then refluxed in thionyl chloride to generate acyl chlorides followed by stirring with $AlCl_3$ to form the corresponding benzothiophenones (**Scheme 102**). Pleasingly, the chloro- **395**, CO_2Me- **396**, fluoro- **367**, methyl- **398**, and naphthyl- 399 benzothiophenones were generated in very good yield. However, benzothiophenones bearing mesomerically electron donating groups, specifically methoxy- **401** and *N*-acetyl- **403** products, were only afforded in moderate yield, 24% and 35% respectively. Furthermore, products

containing the acyl- **400**, nitro- **402**, and CF_3- **404** groups were not obtained. These results were attributed to the electron-withdrawing groups deactivating the aryl ring towards Friedel-Crafts acylation, which proceeds *via* a cationic intermediate.



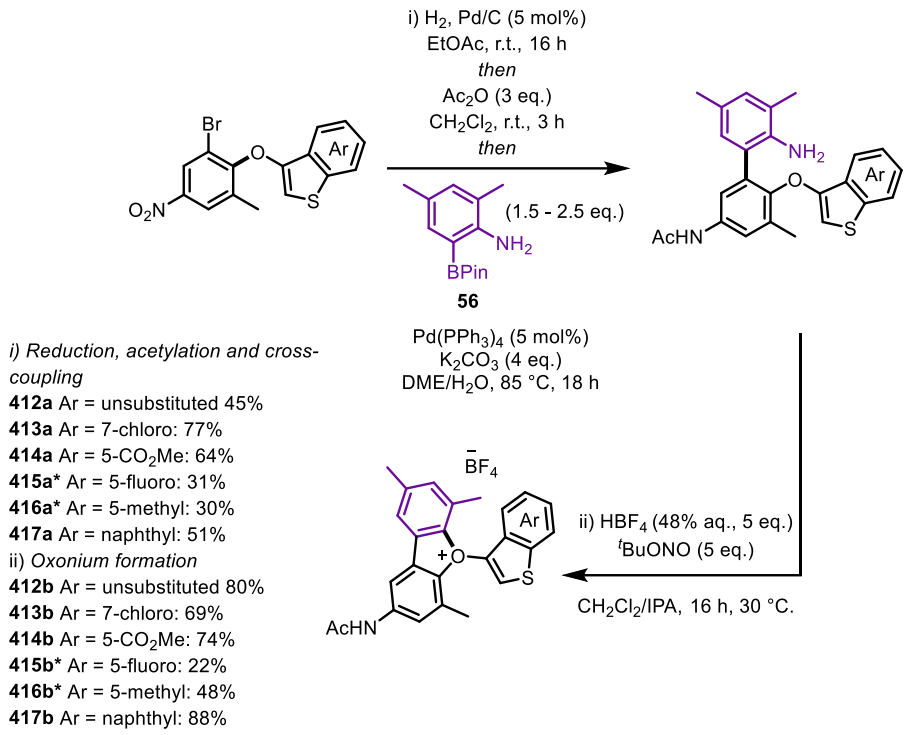
Scheme 102: Scope for the synthesis of benzothiophenones. *Synthesised by Dima Petropavloskikh. ΔGenerated using an alternative procedure.

The benzothiophenones were then subjected to the optimised S_NAr conditions to afford bis(aryl) ethers (**Scheme 103**). The chloro- **405**, CO_2Me- **406**, fluoro- **407**, methyl- **408**, and naphthyl- **409** substituted bis(aryl) ethers were successfully synthesised in low to moderate yield (19-56%). However, the bis(aryl) ethers bearing more strongly mesomerically donating groups, *N*-acetyl **410** and methoxy **411**, were not obtained.



Scheme 103: Scope for the synthesis of bis(aryl) ethers. *Synthesised by Dima Petropavloskikh.

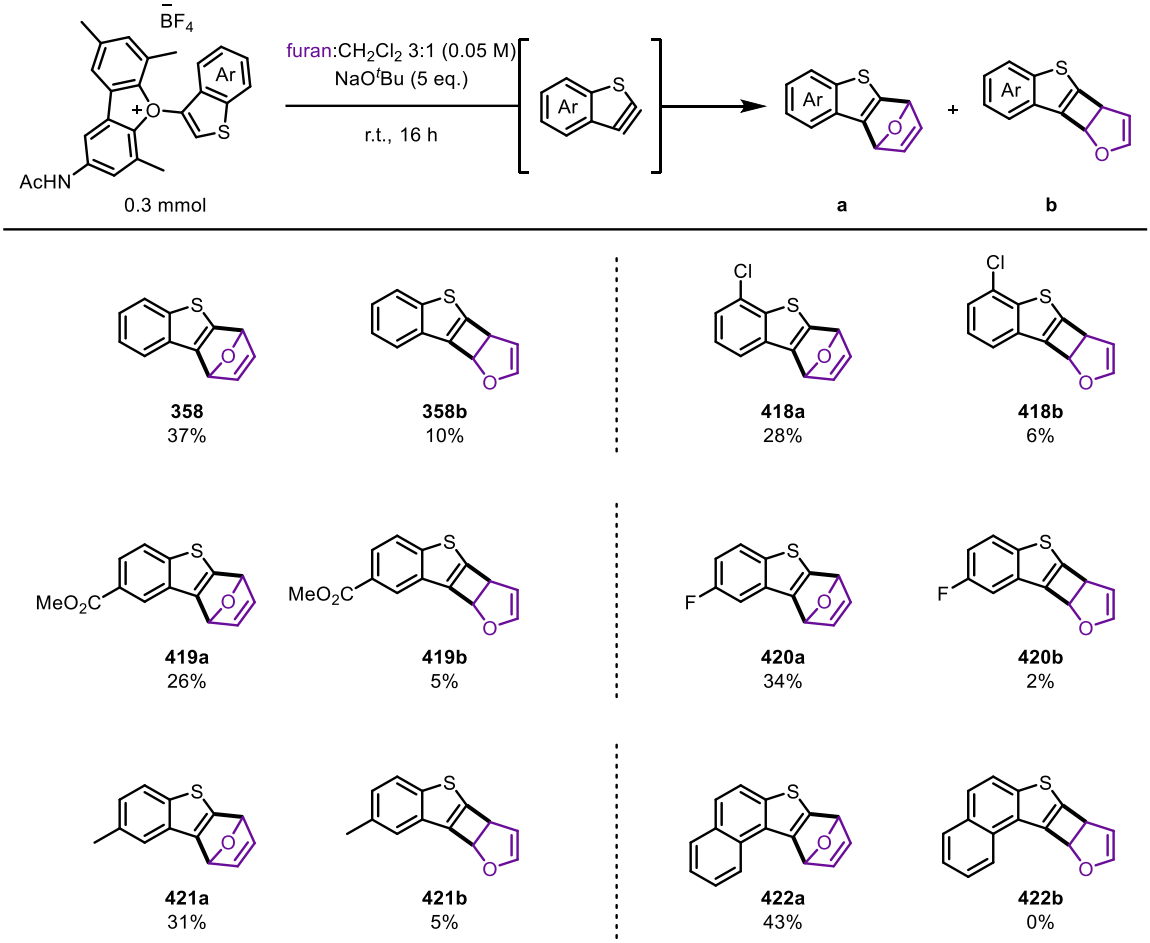
The bis(aryl) ethers were then successfully converted into the corresponding oxonium salts *via* reduction and acetylation of the nitro-group, cross-coupling with the aniline pinacolborane **56**,[105] and diazotization with gentle heating (**Scheme 104**).



Scheme 104: Synthesis of benzothiophene-containing oxoniums salts. *Synthesised by Dima Petropavloskikh. **412a-417a** yields reported over three steps: reduction, acetylation, and cross-coupling. **412b-417b** yields reported for oxonium formation.

2.2.4.2.4 2,3-Benzothiophynes scope

The benzothiophene triaryloxoniums were then subjected to the optimised trapping conditions using sodium *tert*-butoxide and a large excess of furan (**Scheme 105**). All the oxonium salts yielded the corresponding [4+2] cycloaddition products in moderate yield, indicative of the trapping of 2,3-benzothiophyne intermediates. Additionally, the formal [2+2] cycloaddition products were obtained as minor products for all substrates, except for the naphthyl-substrate **422b**. Since pericyclic [2+2] cycloadditions are symmetry forbidden by Woodward-Hoffmann rules, this transformation likely proceeds *via* a stepwise mechanism.[127] The regiochemistry of the [2+2] cycloaddition product is ambiguous from NMR data alone. However, predicted regioisomers have been denoted, considering the observed regioselectivity with alternative arynophiles (see section **2.2.4.2.5**). Trace amounts of the suspected [2+2] cycloaddition minor regioisomer were observed in the ^{1}H NMR. To confirm this, trapping reactions would need to be performed on a larger scale.



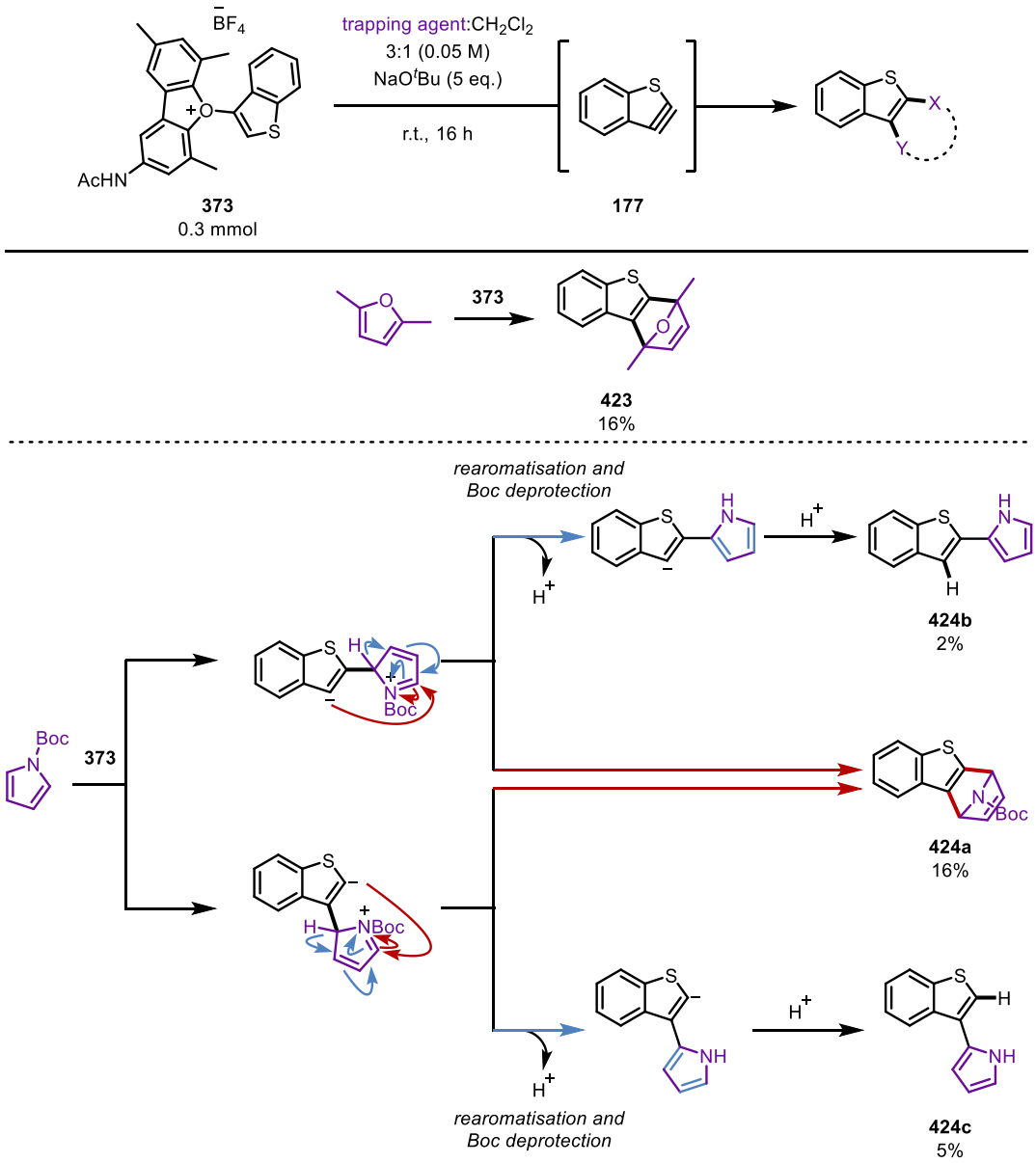
Scheme 105: Trapping scope of 2,3-benzothiophynes with furan.

2.2.4.2.5 Arynophile scope

We next aimed to assess the compatibility of the oxonium salts with alternative arynophiles to provide more conclusive evidence of aryne-like reactivity. To successfully trap 2,3-benzothiophyne with furan, a substantial excess of trapping agent was necessary. Therefore, we directed our attention to arynophiles with sufficiently low boiling points that they can be removed under reduced pressure.

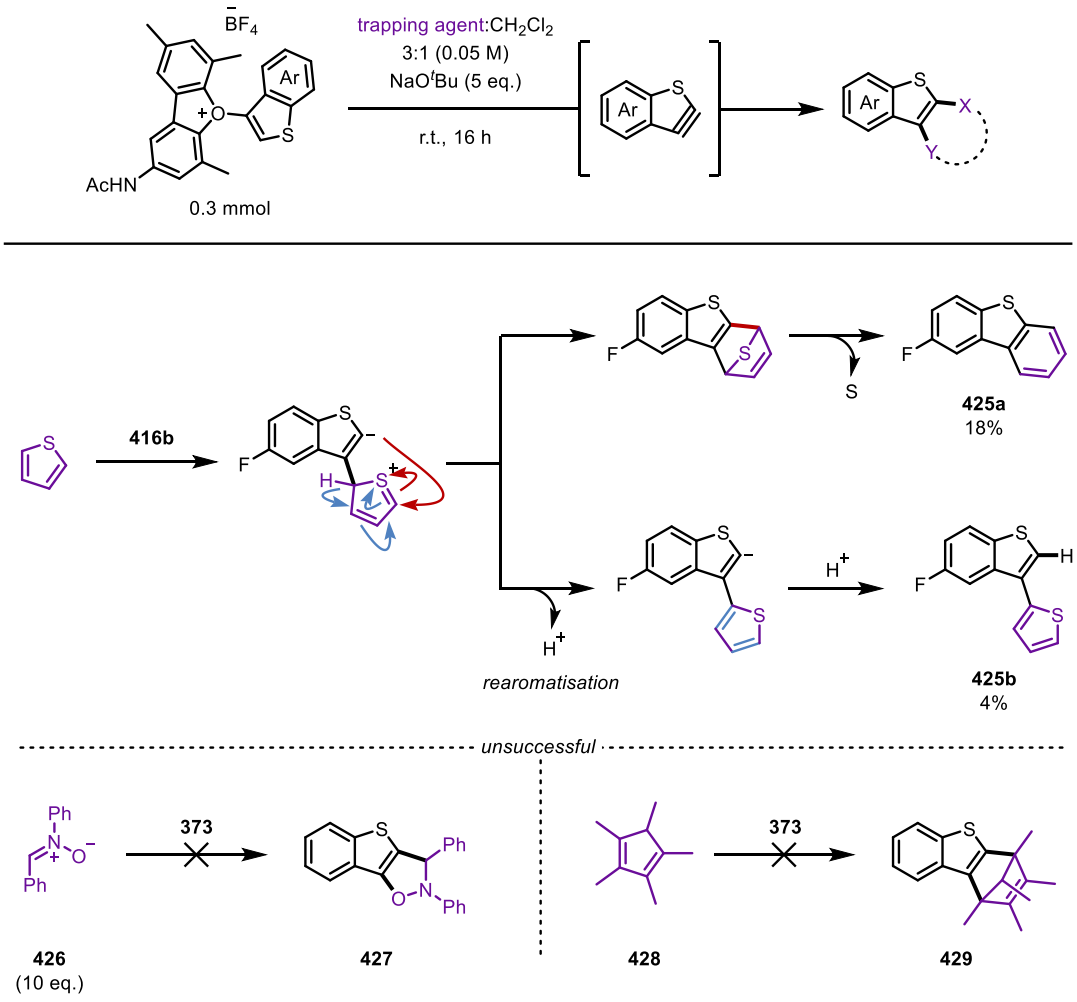
Initially, our focus centred on trapping agents with the potential to undergoing cycloaddition reactions with the proposed hetaryne (**Scheme 106** and **107**). Oxonium **373** reacted with 2,5-dimethylfuran, yielding the [4+2] cycloaddition product **423** in 16% yield (**Scheme 106**).

Treatment of **373** with *N*-Boc-pyrrole yielded tricycle **424a** in 16% yield, along with the 2- **424b** and 3- **424c** pyrrole substituted thiophenes in 2% and 5% yield respectively. A proposed mechanism for the generation of **424b** and **424c** is outlined in **Scheme 106** wherein *N*-Boc-pyrrole undergoes electrophilic addition with 2,3-benzothiophyne at the C2 or C3 position of the hetaryne, followed by rearomatisation of the pyrrole, Boc deprotection, and protonation of the hetaryl. The formation of the pyrrole derivatives **424b** and **424c** is indicative the trapping of an asymmetric hetaryne intermediate.



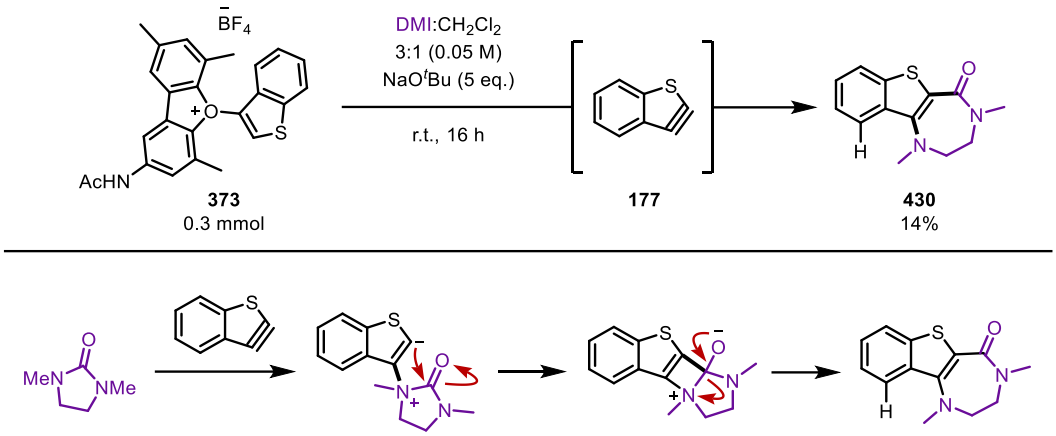
Scheme 106: Trapping reactions of 2,3-benzothiophynes with dienes.

In the presence of thiophene, fluoro-oxonium salt **416b** produced the dibenzothiophene **425a** in 18% yield, likely *via* a [4+2] cycloaddition reaction followed by extrusion of sulfur (**Scheme 107**).[61,62] Additionally, the 3-thiophene-substituted benzothiophene **425b** was isolated in 4% yield, presumably formed similarly to the pyrrole derivative **424c**. Unfortunately, upon treatment of **373** with nitrone **426** and pentamethylcyclopentadiene **428**, we were unable to isolate the any cycloaddition products, **427** and **429** respectively.



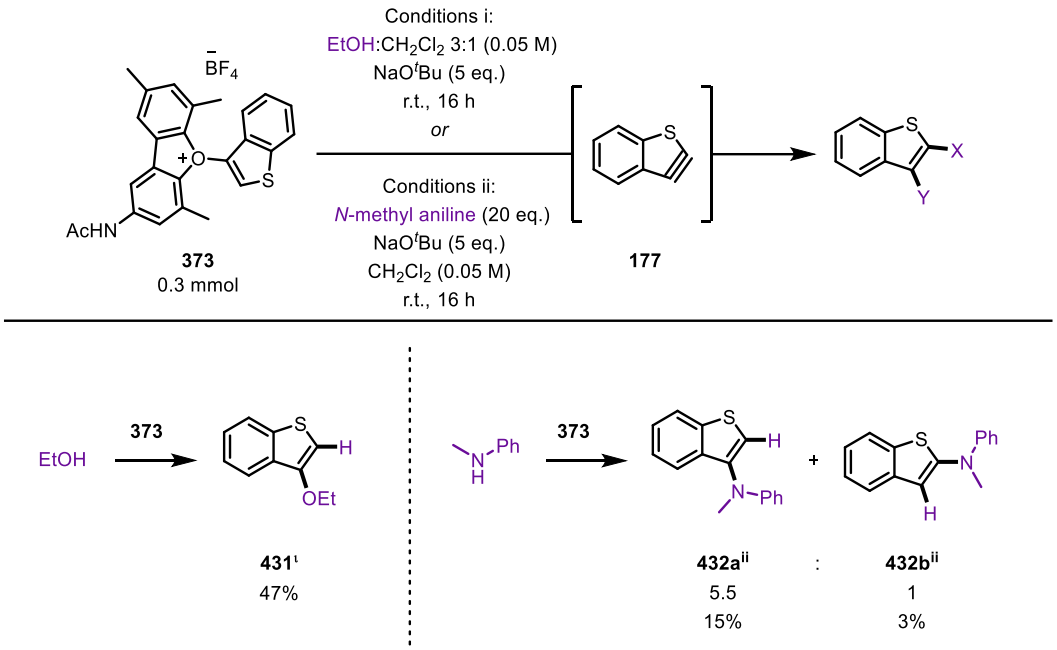
Scheme 107: Trapping reactions of 2,3-benzothiophynes with dienes.

Pleasingly, carrying out the reaction in DMI gave the desired ring expansion product **430** in 14% yield (**Scheme 108**). The regiochemistry of **430** was determined by a ^{1}H-^{1}H NOESY correlation between the non-amide NMe-group and the proximal aromatic hydrogen atom.



Scheme 108: Ring expansion reaction of DMI with the 2,3-benzothiophyne **177**.

The nucleophilic trapping agents ethanol and *N*-methyl aniline also reacted with **373** to afford the trapped products (**Scheme 109**). Ethanol reacted to exclusively give the 3-substituted aryl ether **431** in 47% yield. *N*-methyl aniline was added in a smaller excess, due to its higher boiling point, to give an inseparable mixture of the 3- and 2-substituted *N*-arylated thiophenes, **432a** and **432b**, in 15% and 3% yield respectively. This result is consistent with the trapping of a polarised hetaryne intermediate.



Scheme 109: Trapping reactions of 2,3-benzothiophyne **177** with nucleophilic trapping agents. **i**: synthesised using conditions **i**. **ii**: synthesised using conditions **ii**.

2.2.4.3 Conclusions and future work

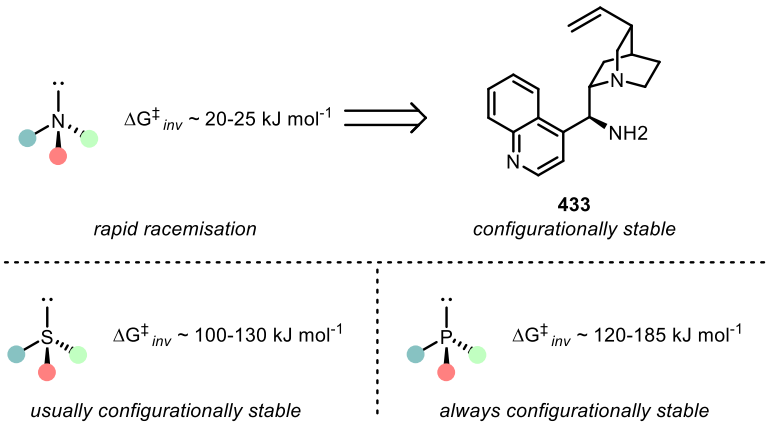
This work provides evidence that benzothiophene triaryloxoniums undergo aryne-like reactivity in the presence of base and trapping agents. The inefficiency of the reaction is consistent with the calculated energy of the hetaryne,[49] likely nearing the synthetically accessible limit for arynes. While acknowledging the method's limitations, it is noteworthy that precedent for generation of five-membered hetarynes is significantly limited. Moreover, there are several examples where conventional aryne precursors fail in producing analogous hetarynes.[59,60,63] Future work would investigate whether the observed regioselectivity is consistent with that predicted by computational calculations. In addition, further investigations would look to determine if the five-membered hetarynes 2,3-thiophyne and 3,4-thiophyne are accessible using this methodology.

3 Chapter 3: Chiral Triaryloxonium Ions

3.1 Introduction

3.1.1 Pyramidal inversion of trivalent compounds

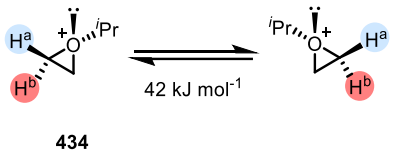
Pyramidal inversion is the process in which pyramidal molecules invert *via* a planar trigonal transition state, effectively turning inside out. The energetic barrier associated with this process has been extensively studied to understand the factors affecting the optical stability of asymmetric trivalent compounds.[128] When the inversion barrier is low, compounds with a stereogenic centre rapidly racemise. However, pyramidal compounds with high inversion barriers, such as phosphines (120-185 kJ mol^{-1})[129] and sulfonium ions (100-130 kJ mol-1),[130–133] can exhibit configurational stability under ambient conditions and therefore can be isolated as single enantiomers. This stability, seen in chiral phosphines and sulfonium ions at room temperature, is harnessed in various applications, including the use of chiral phosphine ligands in asymmetric catalysis.[134] In contrast, amines possess lower inversion barriers (20-25 kJ mol^{-1}) therefore the enantiomers of stereogenic amines rapidly interconvert.[128] However, when constrained within bicyclic scaffolds, as seen in cinchona alkaloids, their conformation can be locked, rendering them configurationally stable and useful in applications such as asymmetric organocatalysis (**Scheme 110**).[135]



Scheme 110: Approximate inversion barriers of trivalent amines, sulfoniums, and phosphines as well as the configurational stability of their enantiomers at room temperature.

3.1.2 Pyramidal inversion of oxoniums

Similarly to amines, oxonium ions generally have low barriers to inversion.[136] However, investigations into the inversion of trivalent oxygen has been limited due to trialkyloxonium ions being highly reactive towards weak nucleophiles. The only measured barrier to inversion of an oxonium ion was reported by Lambert and Johnson using the epoxide derived trialkyloxonium **434**.[136] Using low temperature ^{1}H NMR, the coalescence temperature of the ring hydrogen atoms was determined and from this, the barrier of inversion was calculated to be 42 kJ mol^{-1} (**Scheme 111**).

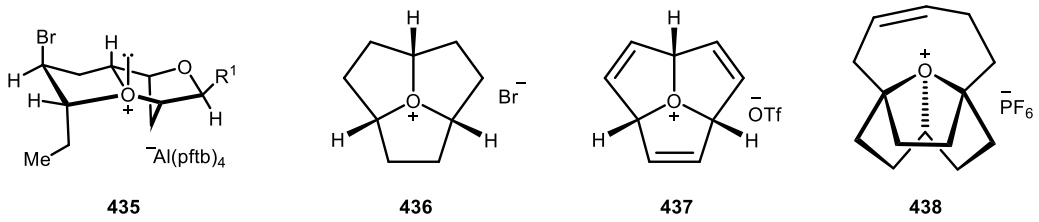


Scheme 111: The measured inversion barrier of **434**.

As well as being powerful alkylating agents, trialkyloxonium ions also exist as reactive intermediates in biological processes. Burton and coworkers synthesised and characterised tricyclic oxonium ion

435 as a likely intermediate in the synthesis of Laurencia natural products (**Scheme 112**).[1] The fused ring system locks the confirmation of the oxonium making the oxygen stereogenic. However, **435** is highly reactive; degrading above -40 °C and requiring the weakly coordinating Krossing's counterion to prevent nucleophilic attack from the counterion.[137]

Mascal and coworkers also generated fused cyclic trialkyloxonium ions oxatriquinane **436** and oxatriquinacene **437**. These oxoniums exhibit remarkable stability towards weak nucleophiles, such as H_2O and alkyl alcohols, which was attributed to the rigid tricyclic framework (**Scheme 112**).[138,139] Introduction of an asymmetric bridge by Reed and coworkers to the oxatriaquinane to form **438** renders the oxygen atom stereogenic.[140]



435 **436** **437** **438**

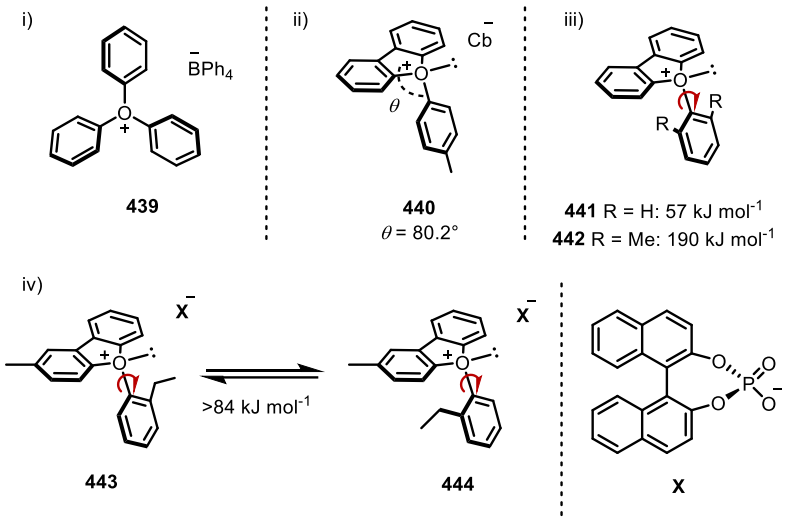
Scheme 112: Fused tricyclic oxonium ions.

3.1.3 Oxonium atropisomers

Atropisomerism arises from restricted rotation about a single bond. When the barrier to rotation is sufficiently high, distinct conformers, known as atropisomers, can be isolated. Oki defined the threshold for a molecule to be atropisomeric as when its conformers interconvert with $t_{rac}^{1/2}$ > 1000 seconds at a specified temperature, equivalent to 92 kJ mol^{-1} at 298 K.[141]

The only cited atropisomeric oxonium ions were documented by Siegel and coworkers using dibenzofuran oxoniums.[142] Olah reported that triphenyloxonium tetraphenylborate **439** showed only slight non planarity about the oxygen (**Scheme 113**, i).[143] However, single X-ray

crystallography studies showed dibenzofuran oxoniums to be pyramidal at the oxygen atom, with **440** possessing a dihedral angle of 80.2° (**Scheme 113**, ii).[142] *Ortho*-substitution of the pendant aryl ring to give **442** was calculated to increase the barrier of rotation about the C-O bond to the point where the conformers would be configurationally stable under ambient laboratory conditions (**Scheme 113**, iii). In the presence of enantioenriched chiral BINOL phosphate counterion, ^{1}H NMR enantiodifferentiation of the oxonium enantiomers **443** and **444** was observed. Using EXSY analysis to measure the rate of exchange of nuclei against an internal rate reference, the barrier to rotation about the C-O bond was measured to be greater than 84 kJ mol^{-1} (**Scheme 113**, iv).



Scheme 113: i) Triphenyloxonium tetraphenylborate salt **439** ii) The measured dihedral angle of **440** using single X-ray crystallography. Cb^{-} = $[CB_{11}H_6Cl_6]^{-}$. iii) The calculated barriers of rotation for **441** and **442**. iv) The minimum measured rotational barrier of **443** using EXSY analysis.

3.1.4 Measuring configurational stability

Three main protocols are employed to determine the configurational stability of chiral molecules that use standard analytical techniques, NMR and HPLC.[144] The suitability of each method depends on the rate of interconversion of the stereoisomers. The below methods measure either

the rate of racemisation† (k_{rac}) or enantiomerisation‡ (k_{ent}). These rates can be used to calculate the racemisation half life ($t_{rac}^{1/2}$)§ and the barrier to enantiomerisation ($\Delta G_{ent}^{\ddagger}$) using the Eyring equation (3). Enantiomerisation converts one enantiomer into the other reducing the enantiomeric excess by two molecules. Therefore, k_{rac} is twice as fast as k_{ent}.

$$(1)\ k_{rac} = 2k_{ent}$$

$$(2)\ t_{rac}^{1/2} = \frac{\ln 2}{k_{rac}}$$

$$(3)\ \Delta G_{ent}^{\ddagger}(T) = RT_c ln\left(\frac{k_B T}{h k_{ent}}\right)$$

$$R = 8.314\ JK^{-1}mol^{-1}, k_B = 1.3806 \times 10^{-23}\ JK^{-1}, h = 6.626 \times\ 10^{-34}\ Js$$

3.1.4.1 Kinetic analysis of the racemisation of an enantioenriched sample

This procedure involves monitoring the enantiomeric ratio (e.r.) of an enantioenriched sample using HPLC over a period of time at a constant temperature.[144] Racemisation is a first order process, therefore, plotting $ln\left(\frac{e.e._0}{e.e._t}\right)$ as a function of time should give a straight line where the gradient is equal to k_{rac}. This method is appropriate when the configurational stability is sufficiently high that several HPLC measurements can be taken. Therefore, $t_{rac}^{1/2}$ needs to be significantly longer than the difference between the retention times.

† Racemisation describes the macroscopic and irreversible process where a bulk enantioenriched sample is converted to a racemic material.

‡ Enantiomerisation is the microscopic and reversible process where enantiomers are interconverted.

§ $t_{rac}^{\frac{1}{2}}$ is the time taken for an enantiopure sample to reach an enantiomeric excess of 50%.

3.1.4.2 Dynamic HPLC

When $t_{rac}^{1/2}$ is comparable to the retention times of the enantiomers, dynamic HPLC can be a useful tool to measure the rate of enantiomerisation.[144] In this scenario, as the enantiomers pass through the column, the enantiomer peaks plateau resulting in a specific peak shape known as the 'Batman effect'. The parameters of this peak can be used to determine the k_{ent} using methods developed by Trapp and coworkers.[145–148]

3.1.4.3 Variable temperature NMR

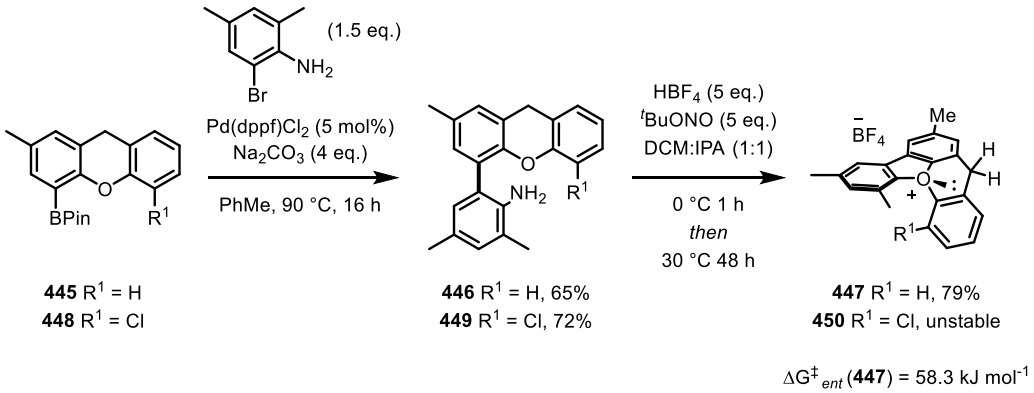
When $t_{rac}^{1/2}$ is significantly shorter than the retention time, variable temperature (VT) NMR can be used to measure the rate of interconversion (k_{ent}) of enantiomers containing diastereotopic groups. The diastereotopic groups are in distinct chemical and magnetic environments, therefore will produce distinct peaks. Enantiomerisation interconverts diastereotopic groups and, when this process occurs at a comparable rate to the ^{1}H NMR timescale, broadening of the resonances is observed to the point where they cannot be distinguished. The temperature at which this occurs is known as the coalescence temperature and can be used to calculate k_{ent}. This method is appropriate for enantiomers with diastereotopic groups and is typically favoured for systems with low barriers to inversion.[144,149]

3.1.5 Previous work within the group

There are no examples of a chiral and non-racemic configurationally stable molecule where oxygen is the sole stereogenic centre. Inspired by Siegel and Mascal's findings,[138,142] it was proposed that linking the dibenzofuran and pendant aryl group to form a bicyclic fused triaryloxonium ion could increase the inversion barrier of the oxonium oxygen. Varying the sterics around the oxygen atom as well as the flexibility of the rings could further elevate the barrier to inversion while maintaining

the ground state stability exhibited by triaryloxonium ions. For the purposes of this study, an enantiomerisation barrier higher than 107 kJ mol^{-1} ($t_{rac}^{1/2}$ = 7 days at 25 °C) was determined to be configurationally stable on a laboratory time scale.[150]

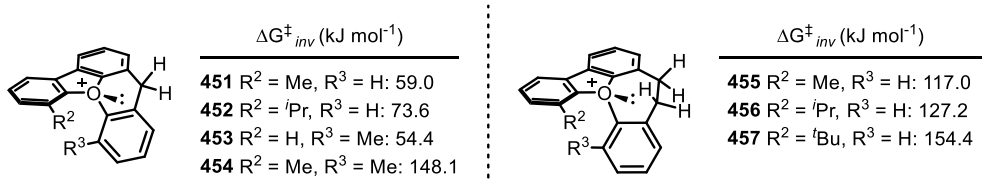
Initial studies carried out by Owen Smith focused on generating the benzofuran-xanthene scaffold, **447**, which was successfully synthesised using an analogous route employed in the synthesis of triaryloxonium benzyne precursors (**Scheme 114**). VT ^{1}H NMR was used to determine the coalescence temperature of the bridged CH_2 protons, from which, the barrier of enantiomerisation was calculated to be 58.3 kJ mol^{-1}.[150] Therefore, **447** is not configurationally stable at room temperature. Furthermore, increasing the steric bulk around the oxygen by substituting the oxonium with a chloro-group destabilised the oxonium **450** (**Scheme 114**).



Scheme 114: Synthesis of xanthene oxoniums **447** and **450**.

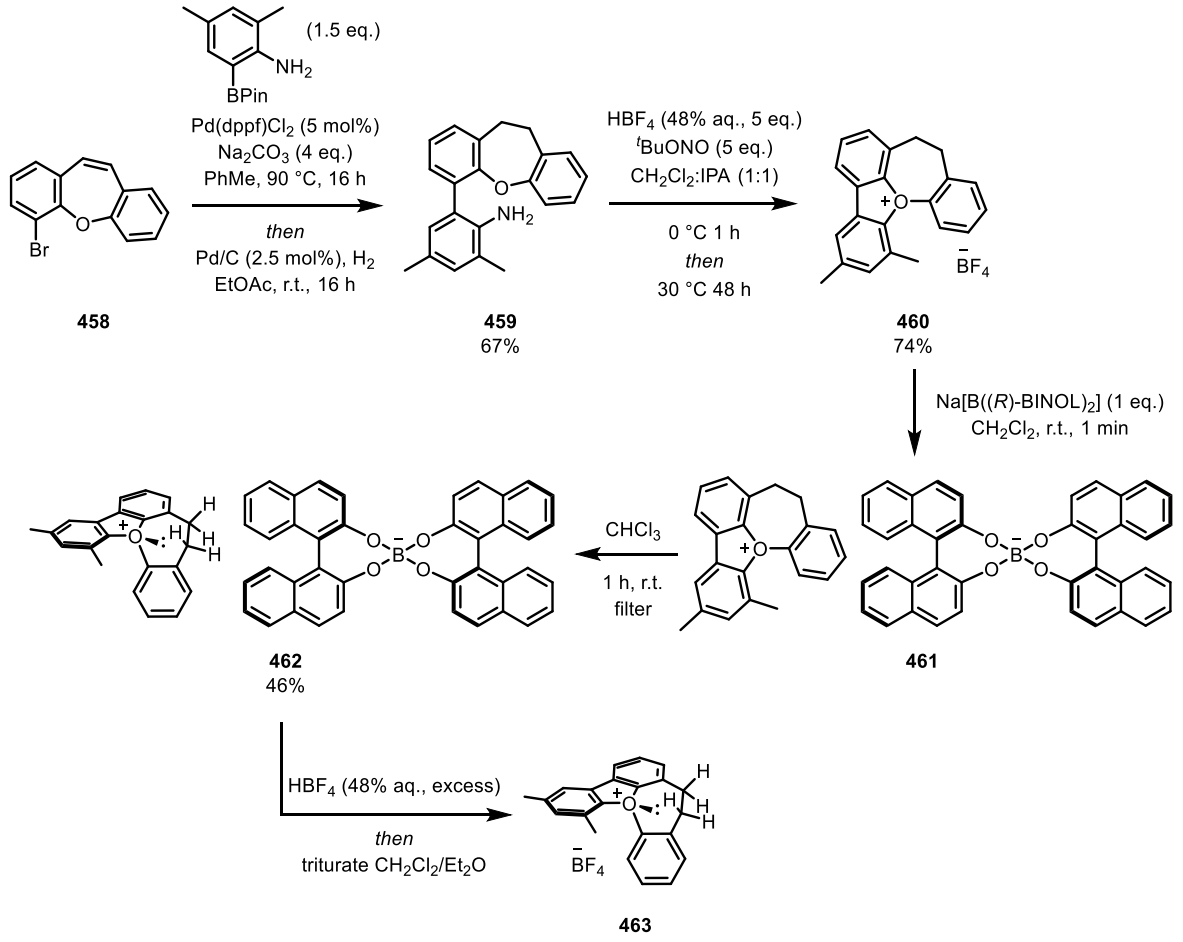
Mihai Popescu performed B3LYP-D3(BJ)/6-31+G(d,p) quantum chemical calculations to assess the impact of varying linker length and substitution patterns of the oxonium ion on the enantiomerisation transition state (**Scheme 115**).[150] Increasing the size of the substituents R^2 and R^3 increased the oxonium inversion barrier however destabilized the ground state of the oxonium, consistent with the instability of the chloro-substituted oxonium **450**. Conversely, elongating the linker between aryl groups to form an oxepin scaffold (**451** vs **455**) raised the inversion barrier to

117 kJ mol^{-1} without significant ground state destabilization, indicating configurational stability at room temperature. Therefore, the oxonium oxepin scaffold was next targeted.



Scheme 115: Calculated barriers to inversion of the xanthene and oxepin oxonium scaffolds.

The oxepin oxonium **460** was generated, yielding a racemic mixture of enantiomeric salts (**Scheme 116**). Through counterion metathesis with chiral sodium bis-(*R*)-BINOL borate, a 1:1 mixture of diastereomeric salts was obtained, **461**. The diastereomeric salts displayed different solubilities in chloroform, enabling the isolation of a diastereomerically enriched salt **462**. Counterion metathesis of the enriched salt with excess HBF_4, followed by crystallization, produced an the enantioenriched salt **463**. The absolute configuration of **463** was determined using single X-ray crystallography (**Scheme 116**).



Scheme 116: Synthesis and structural study of stereogenic-at-oxygen compounds.

3.1.6 Project aims

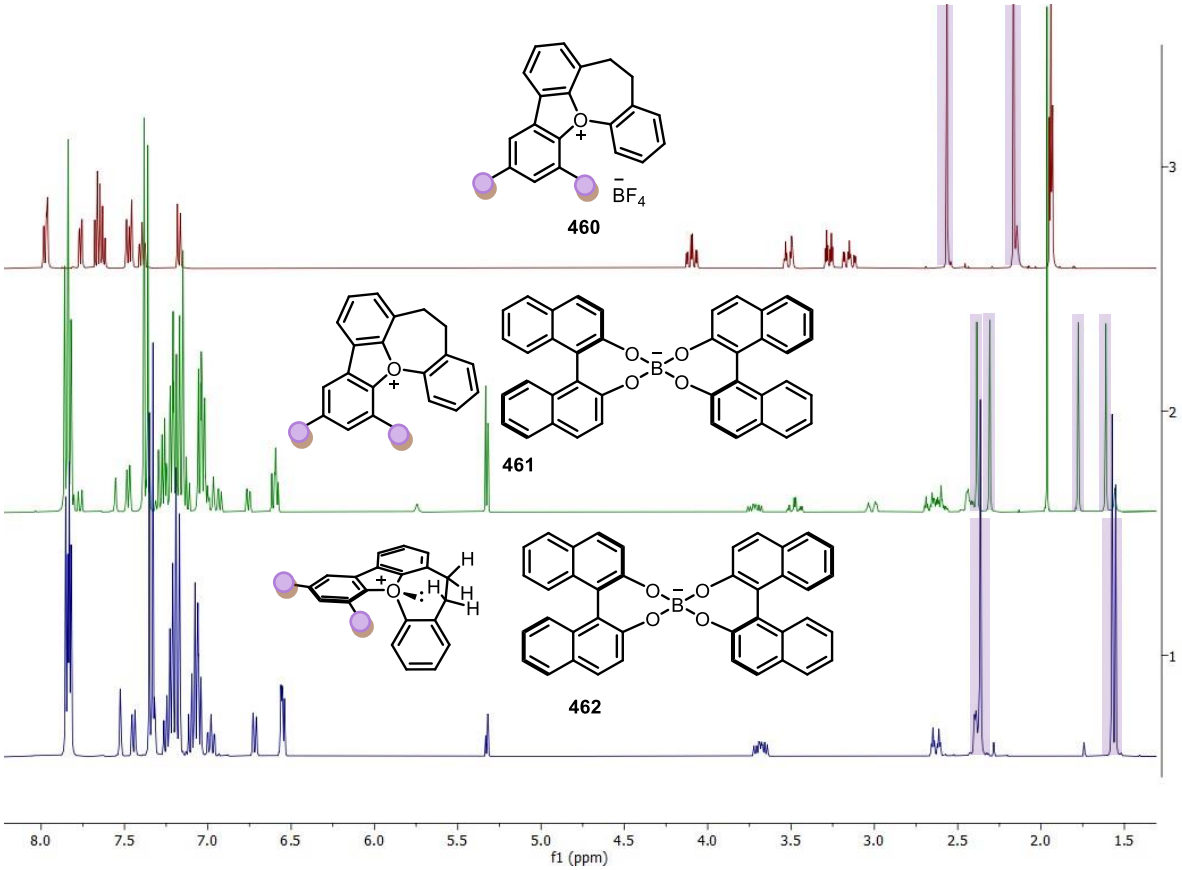
This work aimed to probe the configurational stability of the oxonium **463** by measuring the inversion barrier of the stereogenic oxygen centre. Using the diastereomerically enriched oxonium **461**, we aimed to determine the free energy of diastereomerisation. Furthermore, if sufficient enantioenriched tetrafluoroborate oxonium **463** could be generated, the free energy of enantiomerisation could also be measured using the methodology outlined in section **3.1.4**.

3.2 Results and discussions

3.2.1 Diastereomerisation barrier

In the *rac*-**460** salt, the two oxonium ions exhibit identical ^{1}H NMR spectra. Counterion metathesis of the tetrafluoroborate with the bis-(*R*)-BINOL borate counterion results in the two enantiomers in distinct chemical and environments hence, leading to two diastereomeric oxonium salts. Distinct resonances, corresponding to the CH_2 bridging and methyl groups for the enantiomeric oxonium ions, are observed for the mixture of diastereomers **461**. This indicates that enantiomersation of the oxonium ions occurs at a rate slower than the NMR timescale. Comparison of the top and middle spectra in **Scheme 117** shows splitting of the ^{1}H NMR signals of the enantiomeric oxonium ions in the presence of the bis-(*R*)-BINOL borate counterion, highlighted by the methyl resonances.

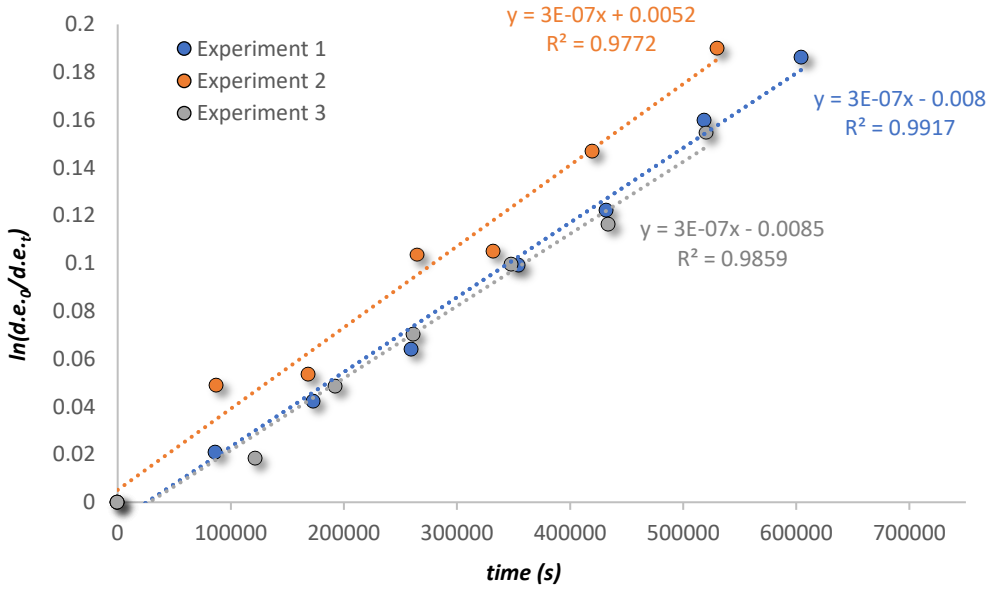
Resolution of the sample in chloroform affords the enriched diastereomer **462** which can be seen in the bottom spectrum ^{1}H NMR spectrum in **Scheme 117**, where the two methyl peaks of the major enantiomer are highlighted. Clear baseline separation between peaks corresponding to the oxonium enantiomers allows us to monitor the diastereomeric ration (d.r.) over time using ^{1}H NMR and, using this data, the free energy of diastereomerisation can be calculated.



Scheme 117: ^{1}H NMR spectra of *rac*-**460** (top), 1:1 mixture of diastereoisomers **461** (middle), and diastereoisomerically enriched **462** (d.r. 94:6, bottom).

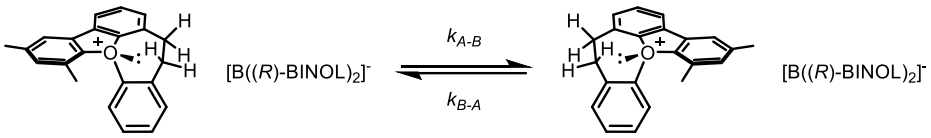
An erosion study of the enriched diastereomer **462** was conducted in which the d.r. was monitored by ^{1}H qNMR by comparing the integrated peaks corresponding to one of the linker C*H* atoms for each diastereomer. An internal standard was added to monitor the sum of the integrals to determine whether degradation of the diastereomers occurred. The sum of the integrals remained constant over the course of the study, indicating that diastereomerisation was the only observable process.

Three inversion barrier experiments were conducted and for each $ln\left(\frac{d.e._0}{d.e._t}\right)$ was plotted against time to give three straight lines (**Scheme 118**), from which the gradient was equal to the rate constant for equilibration of the enriched diastereomer **462**, k_{A-eq}.



Scheme 118: Graphs to show the correlation between ln(d.e.$_0$/d.e.$_t$) and time for inversion barrier experiments 1, 2 and 3 for **462**.

Diastereomers are energetically inequivalent therefore the rate constants for their interconversion are not equal ($k_{A-B} \neq k_{B-A}$). Using the method presented by Schurig,[151] the diastereomerisation constants, k_{A-B} and k_{B-A}, for a diastereotopic AB system can be calculated using the equilibrium constant, K_{eq}, and the rate constant for equilibration, k_{A-eq}, using equation (5). Therefore, to determine K_{eq}, a sample of **462** was left to equilibrate for 5 weeks and the ratio of diastereoisomers was found to be **462**:**463** 1:1.02 by integration of the ^{1}H NMR peaks at 3.70 and 3.44 ppm. Substitution of k_{A-B} and k_{B-A} into the Eyring equation (6) gives the diastereomerisation barriers, $\Delta G^{\ddagger}_{A-to-B}$ and $\Delta G^{\ddagger}_{B-to-A}$, respectively. The free energies are given as an average over three experiments (see supplementary information for full details).



462 463

$$A \leftrightharpoons B$$

$$(4)\ K_{eq} = \frac{k_{A-to-B}}{k_{B-to-A}} = \frac{[B_{eq}]}{[A_{eq}]}$$

$$(5)\ k_{A-to-eq} = k_{A-to-B}\left(1 + \frac{1}{K_{eq}}\right) = k_{B-to-A}(1 + K_{eq})$$

$$(6)\ \Delta G^{\ddagger}_{A-to-B}(T) = RT_c ln\left(\frac{k_B T}{h k_{A-to-B}}\right)$$

$$T\ = 298\ K, R = 8.314\ JK^{-1}mol^{-1},\ k_B = 1.3806 \times 10^{-23}\ JK^{-1}\ and\ h = 6.626 \times\ 10^{-34}\ Js$$

$$\Delta G^{\ddagger}_{A-to-B}(298) = 111.8\ kJ\ mol^{-1}\ , \Delta G^{\ddagger}_{B-to-A}(298) = 111.7\ kJ\ mol^{-1}$$

The barriers for the forward and backwards reactions are close in energy (± 0.1 kcal mol^{-1}) suggesting that the free energy of diastereomerisation serves as a reliable predictor for the free energy of enantiomerisation. Nevertheless, our subsequent objective was to measure the enantiomerisation barrier.

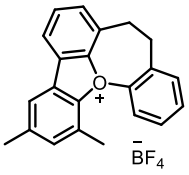
3.2.2 Resolution

We reasoned that, kinetic analysis of the racemisation of an enantioenriched sample would be the most appropriate method to measure the barrier to enantiomerisation. The enantioenriched tetrafluoroborate salt **463** had previously been generated by counterion metathesis of the enriched diastereomer **462** back to the tetrafluroroborate salt and measured using X-ray crystallography. However, **463** it could not be prepared on an appropriate scale for an erosion study *via* this method.

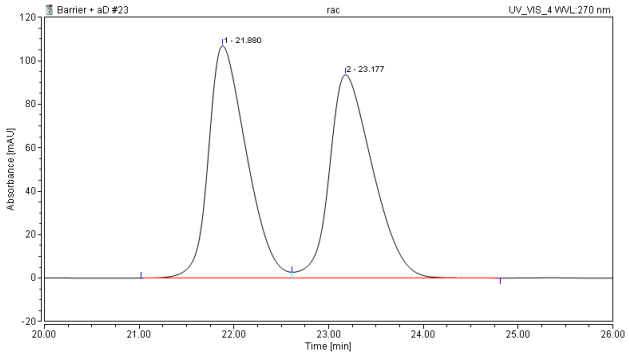
Therefore, the racemic oxonium salt **460** was resolved using chiral stationary phase preparative HPLC to afford the enantioenriched hexafluorophosphate oxonium salt **464** (**Scheme 119**). The enantiomers were separated using the mobile phase; MeOH/H_2O, 10:1, 100mM $NaPF_6$. Therefore, under these conditions, complete counterion metathesis to generate the hexafluorophosphate salts $[PF_6]^-$ was assumed.

The chromatograms depicting the separation of the two enantiomers are shown in **Scheme 119**. Separation of the *rac*-**460** sample is shown in i). The enantioenriched **464** (major enantiomer [*M*, $(S)_O$] after preparative HPLC separation is displayed in ii). The major enantiomer in this 97:3 ratio was correlated with the known absolute configuration of **462** separated in the resolution process. This was achieved by comparing the HPLC retention of the major/minor enantiomers of **464** with that of a sample of highly diastereoenriched **462** under these conditions.

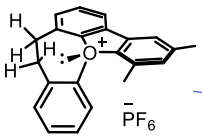
i)



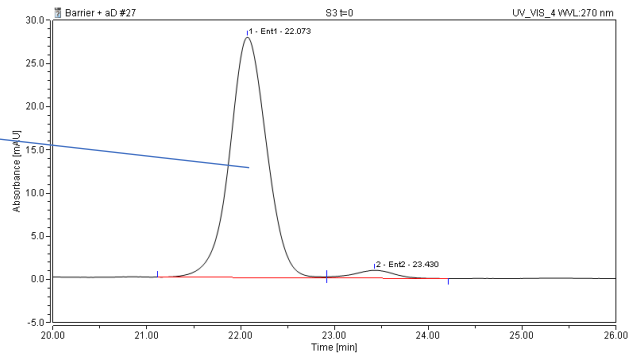
460

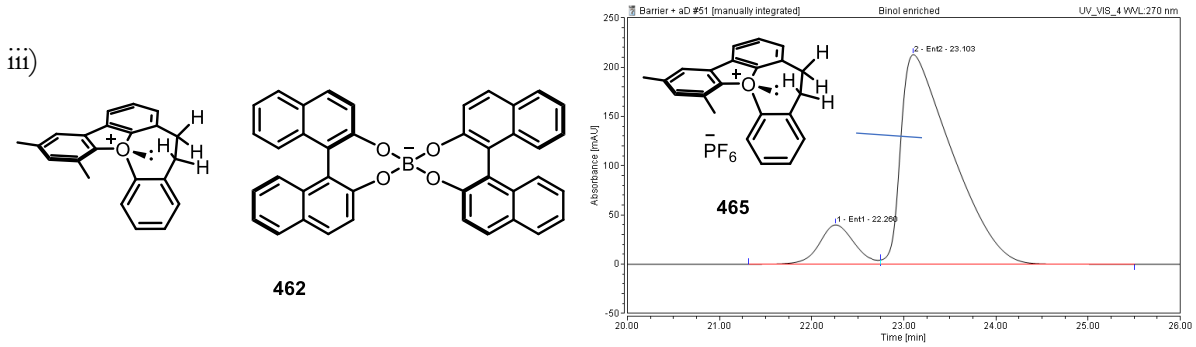


ii)



464

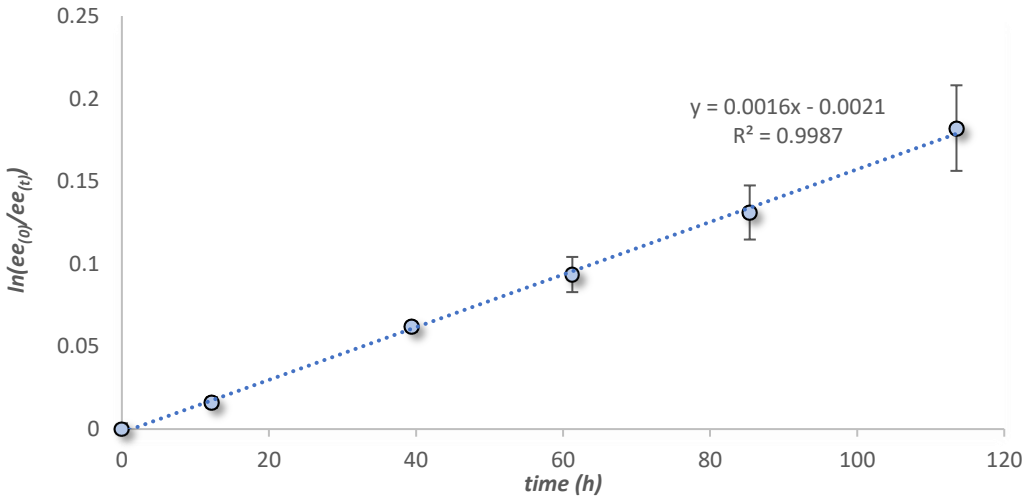




Scheme 119: HPLC chromatograms (2x Chiralpak IC, 95% 100 mM $NaPF_6$ in MeOH, 5% H_2O, 1.0 mL min^{-1}, λ = 270 nm). **i)** racemic **460** after *in-situ* counterion metathesis to $[PF_6]^-$ salt; **ii)** enantioenriched **464** (major enantiomer [*M*, $(S)_O$] after preparative HPLC separation. **iii) 462** after *in-situ* counterion metathesis to enantioenriched $[PF_6]^-$ salt **465** (major enamtiomer [*P*, $(R)_O$]).

3.2.3 Enantiomerisation barrier

Three samples of the same enantioenriched oxonium ion **464** were dissolved in MeOH and maintained at 298 K for 5 days and their enantiomeric ratios were monitored by HPLC. Plotting $ln\left(\frac{e.e._0}{e.e._t}\right)$ against time gave a straight line where the gradient was equal to k_{rac} (**Scheme 120**).



Scheme 120: Graph to show the correlation between $ln(de_0/de_t)$ and time for inversion barrier experiments 1, 2 and 3 for compound **464**.

Using the method outlined in section **3.1.4.1**, the barrier to inversion was measured to be 111.0 $\pm$ 0.1 kJ mol^{-1} (for full data see supporting information). Therefore, **464** is configurationally stable at 298 K with a $t_{rac}^{1/2}$ of 18 days. As predicted, the free energy of enantiomerisation of **464** is very close in energy to the free energy of diastereomerisation of **462** and **463** as well as the calculated enantiomerisation barrier for **455**.

3.2.4 Conclusions and future work

Triaryloxonium ions exhibit enhanced stability compared to their alkyl counterparts. Therefore, synthesis of a triaryloxonium ion within a fused bicyclic system restricts inversion of the lone pair on the oxygen while maintaining ground state stability. Through combined synthesis, computational calculations, and kinetic analysis to probe configurational stability, we have generated the first chiral non-racemic and configurationally stable molecule in which the oxygen atom is the sole stereogenic centre. Future work would attempt to control the stereochemistry of amines and sulfoniums using analogous fused bicyclic systems and explore potential applications of chiral oxonuims in catalysis.

4 Supporting Information

4.1 General Information

4.1.1 Naming and Numbering

Compounds have been named according to IUPAC recommendations or commonly used names where appropriate. The atomic numbering within each compound does not correspond to the IUPAC numbering system, it has been arbitrarily chosen for the purpose of consistent assignment of spectra.

4.1.2 Reaction Conditions

Reactions were carried out under ambient conditions unless specified in the procedure. Glassware for reactions carried out under inert conditions using N_2 or Ar atmospheres was flame dried under vacuum prior to use. Room temperature (r.t.) refers to temperatures between 20-25 °C. Temperatures of 0 °C were obtained using a water/ice bath or using a Polar Bear Plus when greater accuracy was required. Temperatures of -78 °C were obtained using a dry ice/acetone bath. Reactions were heated using a DrySyn® heating block and contact thermometer.

4.1.3 Solvents and Reagents

Anhydrous THF, CH_2Cl_2, MeCN, Et_2O, DMF, and 1,4-dioxane were obtained using an MBraun SPS5 solvent purification system. All other solvents and reagents were used as supplied without further purification.

4.1.4 Chromatography

Thin Layer Chromatography was carried out on Merck Kieselgel 60 F254 0.25 mm precoated aluminium plates. Visualization was achieved by UV light (λ = 254 nm) followed by staining with basic $KMnO_4$ solution. Flash column chromatography was carried out using silica gel 60 (0.043-0.063 nm, VWR) under pressure (0.2-0.4 bar) from the house N_2 supply.

4.1.5 NMR Spectroscopy

Spectra were recorded on Bruker Avance (600, 500 and 400 MHz (^{1}H)) and Bruker Avance NEO (600 MHz (1H)) spectrometers in the deuterated solvent specified. ^{1}H NMR were referenced to the non-deuterated residual solvent peak, ^{13}C NMR were referenced to the residual solvent peak and ^{19}F NMR were referenced externally to $CFCl_3$ = 0 ppm. Chemical shifts are quoted in ppm with splitting assigned as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m) or combinations of the above. Coupling constants, *J*, are measured to the nearest 0.1 Hz and are presented as observed. Spectra were assigned with the aid of COSY, HSQC, HMBC and NOESY experiments.

4.1.6 Infrared Spectroscopy

Infra-red spectra were recorded on a Bruker Tensor 27 FTIR spectrometer equipped with a diamond ATR module. Absorbtion maxima (λ max) are reported in wavenumbers (cm^{-1}).

4.1.7 Mass Spectrometry

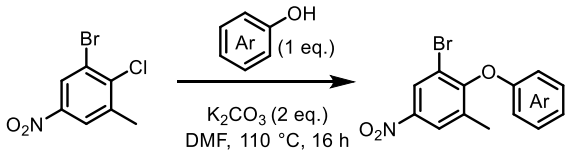
Low-resolution mass spectra were recorded on a Micro Mass LCT Premier spectrometer under conditions of electrospray ionization (ESI). High resolution mass spectra were recorded on a Bruker MicroTOF and Micromass GCT spectrometers under conditions of electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or electron ionization (EI).

4.1.8 Melting Points

Melting points were determined by using Reichert melting point apparatus and are uncorrected. Unless otherwise stated, the solid material is obtained from *in vacuo* removal of the solvent system used for flash column chromatography.

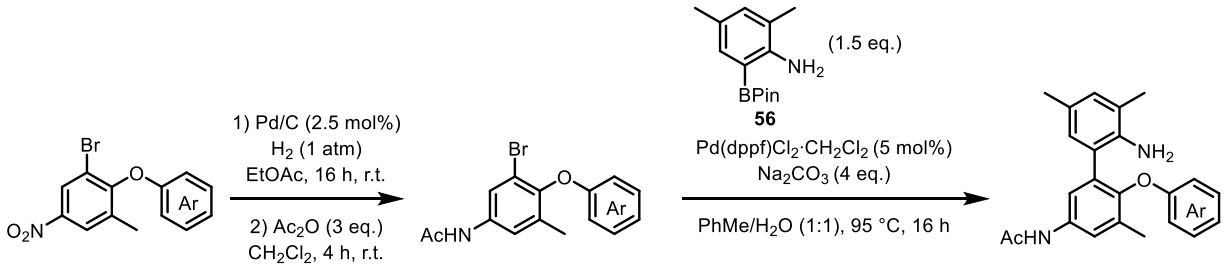
4.2 General Procedures

General Procedure A for S_NAr reaction with phenols:



K_2CO_3 (2 eq.) was added to a solution of *the appropriate phenol* (1 eq.) and 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1 eq.) in DMF (2.5 mL/mmol) and the reaction mixture was heated to 110 °C. After 16 h, the reaction mixture was cooled to r.t., H_2O (5 mL/mmol) was added, and the aqueous layer was extracted with EtOAc (3 × 10 mL/mmol). The combined organic layers were washed with H_2O (10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

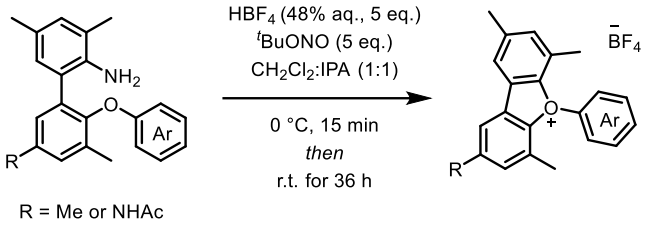
General Procedure B for hydrogenation, acetylation, and cross coupling of aryl bromides:



H_2 was sparged through a solution of *the appropriate aryl bromide* (1 eq.) and Pd/C (10 wt%, 2.5 mol%) and EtOAc (5 mL/mmol) under N_2 for 5 minutes and kept under a H_2 pressure (1 atm). After 16 h, N_2 was sparged through the solution for 10 mins, the reaction was filtered over Celite® and concentrated *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (5 mL/mmol) and Ac_2O (3

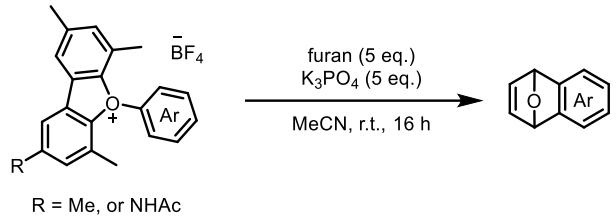
eq.) was added. After 4 h, $NaHCO_3$ (sat. aq., 15 mL/mmol) was added and the mixture was extracted with CH_2Cl_2 (3 × 5 mL/mmol). The combined organic extracts were washed with $NaHCO_3$ (sat. aq., 10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue, 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.5 eq.) as a solution in PhMe (6 mL/mmol), and water (10 mL/mmol) were sequentially added to $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (5 mol%) and Na_2CO_3 (4 eq.) in PhMe (4 mL/mmol) under N_2 at r.t.. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

General Procedure C for formation of oxonium ions:



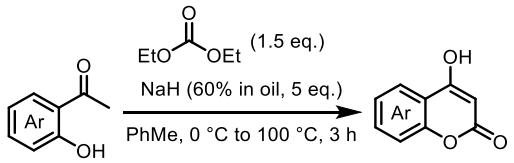
^{t}BuONO (5 eq.) was added to a solution of *the appropriate aniline* (1 eq.) and HBF_4 (48% aq., 5 eq.) in CH_2Cl_2:IPA (1:1, 4 mL/mmol) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (5 mL/mmol), washed with H_2O (2 mL/mmol), and warmed to r.t.. After 36 h, the solvent was removed by a steady stream of N_2 and Et_2O (5 mL/mmol) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® with Et_2O (4 x 1 mL/mmol). The solid was dissolved in MeCN (4-12 mL/mmol), passed through Celite® and eluted with MeCN (4 × 5 mL/mmol). The solvent was removed by a steady stream of N_2 or *in vacuo* at r.t. to give the desired oxonium ion.

General Procedure D for the trapping of arynes with furan:



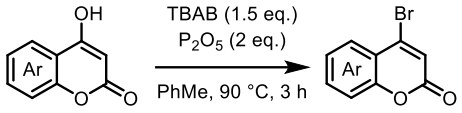
The appropriate oxonium ion (1 eq.) was dissolved in MeCN (2mL/mmol) in an oven-dried vial. Furan (5 eq.) and K_3PO_4 (5 eq.) were added sequentially, and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted with CH_2Cl_2 (4 × 2 mL/mmol), and concentrated *in vacuo*.

General procedure E for 4-hydroxycoumarin synthesis:



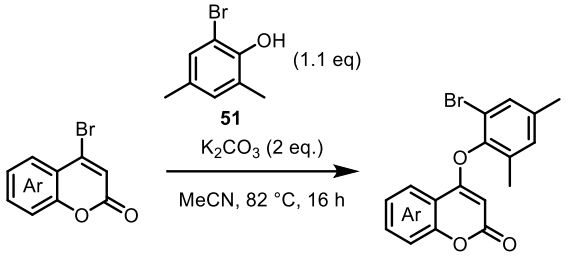
4-Hydroxycoumarins were synthesised according to a modified literature procedure.[152] A multi-neck RBF with a reflux condenser was flame dried and charged with NaH (60% in oil, 5 eq.) followed by evacuation and refill with N_2 x 3. Anhydrous PhMe (1.11 mL/mmol of phenol) was added, and the mixture was stirred at 0 °C for 15 minutes after which *the appropriate phenol* dissolved in anhydrous PhMe (1.67 mL/mmol) was added dropwise and the mixture was stirred at 0 °C for an additional 10 minutes. Diethylcarbonate (1.5 eq.) was then added dropwise, and the reaction was stirred for 30 minutes at 0 °C and then heated to 100 °C. After 3 h, the reaction mixture was cooled to r.t. and poured onto ice. HCl (1 M, 50 mL/mmol) was added and the resultant ppt was filtered, washed with HCl (1 M), and dried *in vacuo*.

General procedure F for 4-bromocoumarin synthesis:



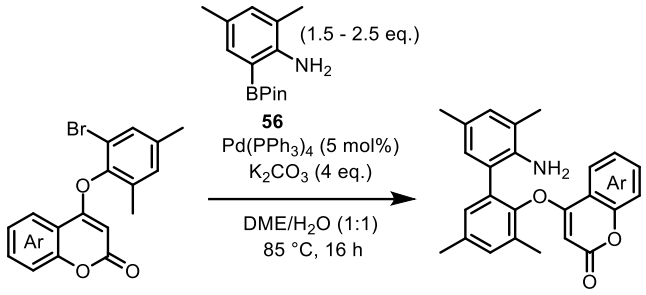
The 4-bromocoumarins were prepared according to a modified literature procedure.[152] *The appropriate 4-hydroxycoumarin* was added to a flame dried multi-neck RBF with a reflux condenser followed by evacuation and refill with N_2 x 3. Anhydrous PhMe (0.5 M) was added, and the mixture was heated to 90 °C. TBAB (1.5 eq.) and P_2O_5 (2 eq.) were added sequentially under and positive pressure of N_2. After 3 h, the hot reaction mixture was transferred to a separating funnel, H_2O (20 mL/mmol) was added, and the aqueous phase was extracted with hot PhMe (3 x 20 mL/mmol). The combined organic phases were washed sequentially with $NaHCO_3$ (sat., aq., 10 mL/mmol), H_2O (10 mL/mmol) and NaCl (sat., aq., 10 mL/mmol), dried ($MgSO_4$) and concentrated *in vacuo*.

General procedure G for S_NAr reaction with 4-bromocoumarins:



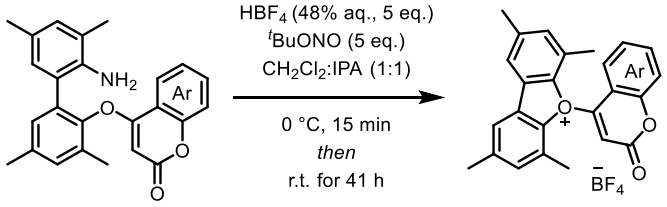
K_2CO_3 (2 eq.) was added to a solution of *the appropriate 4-bromocoumarin* (1 eq.) and 2-bromo-4,6-dimethylphenol **51** (1.1 eq.) in MeCN (0.3 M) and the reaction mixture heated to 82 °C. After 16 h, the reaction mixture was cooled to r.t. and concentrated *in vacuo* to remove MeCN. The mixture was dissolved in EtOAc (10 mL/mmol) and the organic phase was washed with H_2O (5 mL/mmol). The aqueous phase was extracted with EtOAc (3 x 10 mL/mmol) and the combined organic extracts were washed with NaCl (sat. aq., 10 mL/mmol), dried ($MgSO_4$) and concentrated *in vacuo*.

General procedure H for cross-coupling of aryl bromides:



The anilines were synthesised according to a modified literature procedure.[105] *The appropriate aryl bromide* (1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.5 – 2.5 eq.), $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 (4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 0.1 M) was added and the solution was sparged for 10 minutes and the reaction mixture was heated to 85 °C. After 16 h the reaction mixture was cooled to r.t., filtered over Celite® and eluted with EtOAc (3 x 10 mL/mmol). The mixture was then sequentially washed with NaOH (1 M, 20 mL/mmol) and NaCl (sat., aq., 20 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

General procedure I for coumarin-containing oxonium formation:

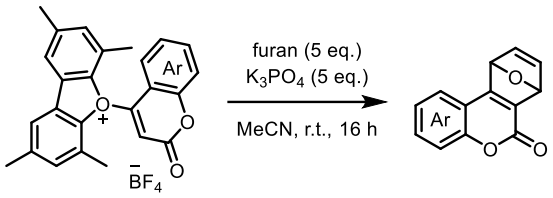


^{t}BuONO (5 eq.) was added to a solution of *the appropriate aniline* (1 eq.) and HBF_4 (48% aq., 5 eq.) in CH_2Cl_2:IPA (1:1, 4 mL/mmol) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (5 mL/mmol), washed with H_2O (2 mL/mmol) and warmed to r.t.. After 41 h, the solvent was removed by a steady stream of N_2 and Et_2O (5 mL/mmol) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the

solvent passed through Celite® (Et_2O, 4 x 1 mL/mmol). The solid was dissolved in MeCN (4-12 mL/mmol), passed through Celite® and eluted with MeCN (4 × 5 mL/mmol). The solvent was removed by a steady stream of N_2 or *in vacuo* at r.t. to give the desired oxonium ion.

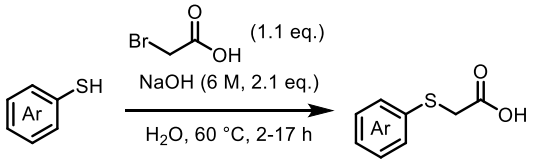
The oxonium was stored as a solid at 5 °C.

General procedure J for 3,4-coumaryne generation and trapping with furan:



The appropriate oxonium ion (0.20 mmol, 1 eq.) was dissolved in MeCN (4 mL) in an oven-dried vial. Furan (73 μL, 1.00 mmol, 5 eq.) and K_3PO_4 (212 mg, 1.00 mmol, 5 eq.) were added sequentially, and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted (CH_2Cl_2, 4 × 2 mL) and concentrated *in vacuo*.

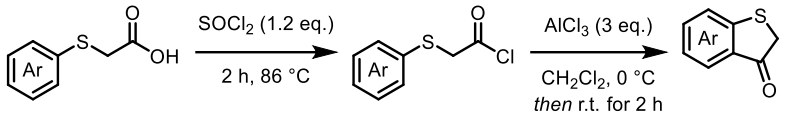
General procedure K for the S_N2 reaction of thiophenols:



The thioether acetic acids were synthesised using a literature procedure.[126] NaOH (2.1 eq., 6 M) was added to a stirred solution of *the appropriate thiophenol* (1 eq.), bromoacetic acid (1.1 eq.) and H_2O (0.5 M). The reaction mixture was heated at 60 °C. After 2-17 h the reaction was cooled to r.t., acidified with HCl (1 M), and the aqueous layer was and extracted with EtOAc (3 x 20 mL/mmol).

Longer reaction times were used for sparingly soluble thiophenols.

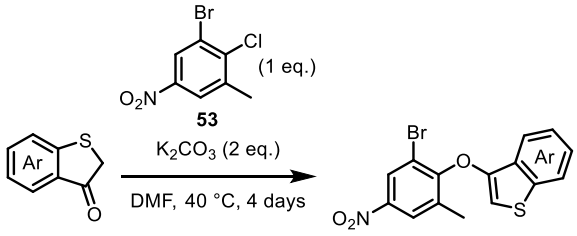
General procedure L for benzothiophenone synthesis:



The benzothiophenones were synthesised according to a modified literature procedure.[125] *The appropriate thioether acetic acid* (1 eq.) in $SOCl_2$ (1.2 eq.) was heated to 86 °C. After 2 h $SOCl_2$ was removed *in vacuo*. The crude residue was dissolved in anhydrous CH_2Cl_2 (10 mL/mmol) and was added dropwise to a flame dried multi-neck RBF containing powdered $AlCl_3$ (3 eq.) in anhydrous CH_2Cl_2 (10 mL/mmol) at 0 °C. After rigorous stirring for 2 h at r.t., the reaction mixture was poured onto ice. The aqueous layer was then extracted with CH_2Cl_2 (3 x 10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

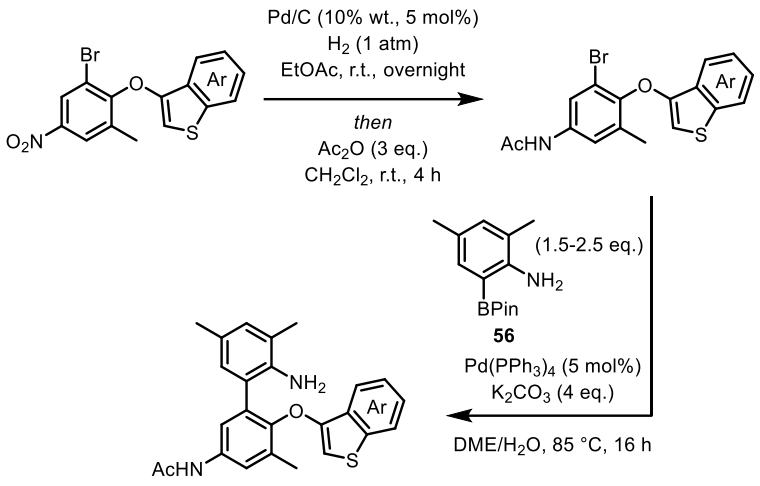
Significantly enhanced yields were observed when using powered, instead of granular, $AlCl_3$.

General procedure M for the S_NAr reaction with benzothiophenones:



K_2CO_3 (2 eq.) was added to a solution of *the appropriate benzothiophenone* (1 eq.) and 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1 eq.) in DMF (2 mL/mmol) and the reaction mixture was heated to 40 °C. After 4 days, the reaction mixture was cooled to r.t. and DMF was removed *in vacuo*. H_2O (5 mL/mmol) was added, and the reaction mixture was extracted Et_2O (3 × 10 mL/mmol). The combined organic layers were washed H_2O (10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

General procedure N for the reduction, acetylation, and cross-coupling reactions:

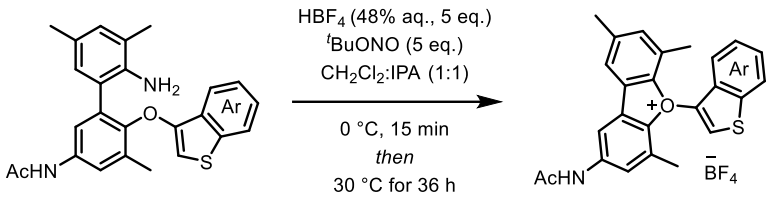


The *appropriate aryl ether* (1 eq.) and Pd/C (10% wt., 5 mol%) were added to an RBF. Following evacuation and backfilling of N_2 x 3, EtOAc (3 mL/mmol) was added. The mixture was purged with H_2 using a 3-skin balloon and an exit needle. After 5 minutes the balloon was replaced with a fresh H_2 balloon and the exit needle was removed. After stirring overnight, the reaction monitored by TLC. Then, the reaction was sparged with N_2 and the solution was filtered through Celite®, eluted EtOAc (4 x 1.5 mL/mmol) and concentrated *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (10 mL/mmol) and Ac_2O (3 eq.) was added. After 4 h, H_2O (10 mL/mmol) and $NaHCO_3$ (sat. aq., 10 mL/mmol) were added and the reaction mixture was extracted CH_2Cl_2 (3 x 20 mL/mmol). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was used in the subsequent step assuming 100% conversion.

The crude residue (1 eq.), 4- dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.5-2.5 eq.), $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 (4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 0.1 M) was added, the solution was sparged for a further 10 minutes and the reaction mixture was heated to 85 °C. After 16 h the reaction mixture was cooled to r.t, filtered over Celite®, and eluted with EtOAc (3 x 10 mL/mmol).

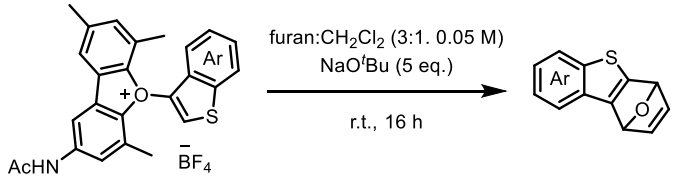
The mixture was then washed with NaOH (1 M, 10 mL/mmol) and NaCl (sat., aq., 10 mL/mmol), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

General procedure O for benzothiophene-containing oxonium formation:



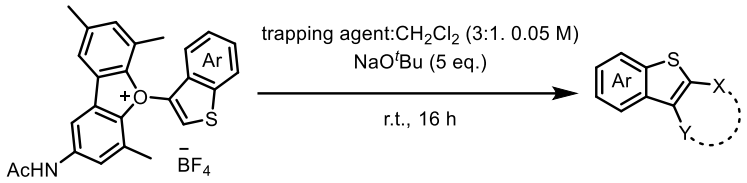
^{t}BuONO (5 eq.) was added to a solution of *the appropriate aniline* (1 eq.) and HBF_4 (48% aq., 5 eq.) in CH_2Cl_2:IPA (1:1, 4 mL/mmol) at 0 °C. After 1 h, the reaction mixture was diluted CH_2Cl_2 (5 mL/mmol), washed H_2O (2 mL/mmol) and warmed to 30 °C. After 36 h, the solvent was removed by a steady stream of N_2 and Et_2O (5 mL/mmol) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite® (1 mL/mmol). The solid precipitate was washed, and the solvent passed through Celite® Et_2O (4 x 1 mL/mmol). The solid was dissolved in MeCN (4-12 mL/mmol), passed through Celite® and eluted (MeCN, 4 × 5 mL/mmol). The solvent was removed by a steady stream of N_2 or *in vacuo* at r.t. to give the desired oxonium ion.

General procedure P for 2,3-thiophyne generation and trapping with furan:



The *appropriate oxonium* (0.30 mmol, 1 eq.) was added to a vial and dissolved in CH_2Cl_2 (1.5 mL) and furan (4.5 mL). NaO^{t}Bu (144 mg, 1.50 mmol, 5 eq.) was added and the reaction mixture was stirred (600 rpm) at r.t. for 16 h. The mixture was filtered through Celite® and eluted with CH_2Cl_2 (3 x 10 mL) and concentrated *in vacuo*.

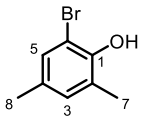
General procedure Q for 2,3-thiophyne generation with arynophiles:



The *appropriate oxonium ion* (0.30 mmol, 1 eq.) was dissolved in *the appropriate trapping agent* (4.5 *mL*) and CH_2Cl_2 (1.5 mL) in a vial. NaO^{t}Bu (144 mg, 1.50 mmol, 5 eq.) was added, and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite® and eluted CH_2Cl_2 (4 × 2 mL/mmol) and concentrated *in vacuo*.

4.3 Experimental Data

2-Bromo-4,6-dimethylphenol, 51:



A solution of bromine (4.41 mL, 13.8 g, 8.61 mmol, 1.05 eq.) in CH_2Cl_2 (20 mL) was added *via* a pressure equalising dropping funnel over 5 minutes to a stirred solution of 4,6-dimethylphenol (9.89 mL, 10.0 g, 8.20 mmol, 1 eq.) in CH_2Cl_2 (40 mL) at 0 °C. Once the addition was complete, the reaction was warmed to r.t.. After 1 h, Na_2SO_3 (sat. aq., 30 mL) was added and the aqueous layer was extracted (CH_2Cl_2, 30 mL). The combined organics were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the title compound as a pale-yellow oil (16.3 g, 99%).

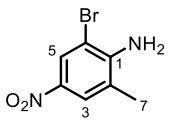
^{1}H (400 MHz, $CDCl_3$) δ_H = 7.16 – 7.10 (m, 1H, H_3), 6.93 – 6.86 (m, 1H, H_5), 5.46 (s, 1H, OH), 2.30 (s, 3H, H_7), 2.26 (s, 3H, H_8).

^{13}C (101 MHz, $CDCl_3$) δ_C = 148.2 (C_1), 131.2 (C_5), 130.7 (C_{Ar}), 129.5 (C_3), 125.5 (C_{Ar}), 109.8 (C_6), 20.2 (C_8), 16.7 (C_7).

IR (neat) ν_{max}/cm^{-1} = 3516, 2921, 1482, 1378, 1323, 1288, 1250, 1231, 1209, 1189, 1112, 989, 958, 849, 822, 763, 714.

HRMS (EI^+): m/z calculated for $C_8H_9BrO^+$, $[M]^+$ = 199.9831; m/z found = 199.9837. Δ = 3.40 ppm.

2-Bromo-6-methyl-4-nitroaniline, 53a:



A solution of bromine (3.41 mL, 6.65 mmol, 1 eq.) in MeOH (20 mL) was added *via* a pressure equalising dropping funnel over 5 minutes to a stirred solution of 2-methyl-4-nitroaniline (10.1 g, 6.65 mmol, 1 eq.) in MeOH (500 mL) at 0 °C. Once the addition was complete, the reaction was warmed to r.t.. After 1 h, the solid precipitate was collected by suction filtration, washed (MeOH, 2 × 15 mL) and dried to give the title compound as a bright yellow solid (11.2 g, 73 %).

m.p. = 176-177 °C.

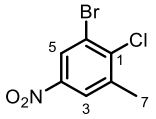
^{1}H (400 MHz, DMSO-d$_6$) δ_H = 8.12 (d, J = 2.6 Hz, 1H, H_5), 7.92 – 7.86 (m, 1H, H_3), 6.47 (s, 2H, NH), 2.22 (s, 3H, H_7).

^{13}C (101 MHz, DMSO-d$_6$) δ_C = 150.4 (C_4), 135.9 (C_1), 126.6 (C_5), 125.0 (C_3), 122.1 (C_2), 105.1 (C_6), 18.4 (C_7).

IR (neat) ν_{max}/cm^{-1} **=** 3487, 3385, 2922, 2359, 1617, 1480, 1298, 1279, 1203, 1103, 1037, 900, 821, 745, 701.

HRMS: Not found by ESI, APCI or EI.

1-Bromo-2-chloro-3-methyl-5-nitrobenzene, 53:



Two reactions of identical scale were carried out simultaneously for convenience: ^{t}BuONO (4.10 mL, 34.5 mmol, 1.6 eq.) was added to a stirred suspension of anhydrous $CuCl_2$ (3.86 g, 28.7 mmol, 1.33 eq.) in MeCN (250 mL). To this dark suspension, 2-bromo-6-methyl-4-nitroaniline **53a**, (5.00 g, 21.6 mmol, 1 eq.) was slowly added over 30 mins. After 2 h, H_2O (500 mL) was added to each reaction and the combined aqueous layers were extracted with Et_2O (3 × 400 mL). The combined organic layers were washed with H_2O (500 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

The crude residue was purified by flash column chromatography (CH_2Cl_2:pentane, 10:90, R_f = 0.4) to give the title compound as a pale yellow solid (9.01 g, 83%).

m.p. = 91-92 °C.

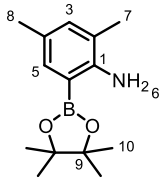
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.34 (d, *J* = 2.5 Hz, 1H, H_5), 8.10 – 8.03 (m, 1H, H_3), 2.55 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 146.0 (C_{Ar}), 141.8 (C_{Ar}), 139.9 (C_{Ar}), 126.3 (C_5), 124.2 (C_3), 123.7 (C_{Ar}), 22.1 (C_7).

IR (neat) ν_{max}/cm^{-1} **=** 3107, 2361, 1514, 1457, 1415, 1390, 1338, 1288, 1234, 1059, 941, 900, 871, 840, 760, 740, 695, 659.

HRMS (EI^+): *m/z* calculated for $C_7H_5O_2NBrCl^+$, $[M\text{-}e^-]^+$ = 248.9192; *m/z* found = 248.9187. Δ = - 2.85 ppm.

2,4-Dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline, 56:



Compound **56** was prepared according to a modified literature procedure.[34] 1,4-Dioxane (120 mL) was added to a mixture of 2-bromo-4,6-dimethylaniline **245** (3.00 g, 15.0 mmol, 1 eq.), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (366 mg, 0.45 mmol, 3 mol%), KOAc (4.41 g, 45.0 mmol, 3 eq.) and B_2Pin_2 (5.71 g, 22.50 mmol, 1.5 eq.) under N_2. Argon was bubbled through the mixture for 5 minutes and the reaction was heated to 95 °C. After 24 h, H_2O (100 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was suspended in pentane (100 mL), filtered through

Celite® (20 mL), eluted (pentane, 3 × 30 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 3:97, R_f = 0.2) to give the title compound as a bright yellow solid (3.37 g, 91%).

m.p. = 68-70 °C.

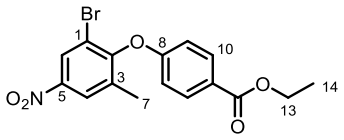
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.33 (s, 1H, H_5), 6.97 (s, 1H, H_3), 4.96 (s, 2H, H_6), 2.21 (s, 3H, H_8), 2.14 (s, 2H, H_7), 1.34 (s, 12H, H_{10}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 148.9 (C_1), 135.0 (C_3), 134.7 (C_5), 126.5 (C_4), 122.3 (C_2), 122.3 (C_6), 83.7 (C_9), 25.0 (C_{10}), 20.3 (C_8), 17.7 (C_7).

IR (film) ν_{max}/cm^{-1} = 3496, 3396, 2980, 1624, 1477, 1385, 1365, 1303, 1090, 966, 851, 668.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{23}O_2NBr^+$, $[M+H]^+$ = 248.1816; *m/z* found = 248.1815, Δ = -0.61 ppm.

Ethyl 4-(2-bromo-6-methyl-4-nitrophenoxy)benzoate, 73:



Compound **73** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), ethyl 4-hydroxybenzoate (664 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90, R_f = 0.2) to give the title compound as a bright yellow solid (1.05 g, 69%).

m.p. = 97-100 °C.

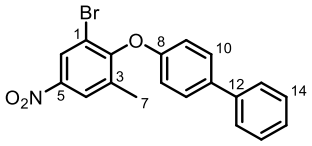
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.39 (d, 2.5 Hz, 1H, H_6), 8.14 (m, 1H, H_4), 8.05 – 7.98 (m, 2H, H_{10}), 6.84 – 6.77 (m, 2H, H_9), 4.35 (q, *J* = 7.1 Hz, 2H, H_{13}), 2.28 (s, 3H, H_7), 1.37 (t, *J* = 7.1 Hz, 3H, H_{14}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 165.9 (C_{12}), 159.6 (C_8), 154.8 (C_2), 145.3 (C_5), 135.2 (C_{11}), 132.1 (C_{10}), 127.2 (C_6), 125.9 (C_4), 125.5 (C_3), 118.3 (C_1), 114.8 (C_9), 61.1 (C_{13}), 17.4 (C_7), 14.5 (C_{14}).

IR (film) ν_{max}/cm^{-1} = 2981, 2885, 1713, 1605, 1577, 1527, 1503, 1461, 1434, 1417, 1393, 1367, 1344, 1307, 1278, 1258, 1218, 1163, 1109, 1095, 1015, 969, 945, 898, 867, 852, 801, 767, 743, 695, 637.

HRMS (ESI^+): *m/z* calculated for $C_{16}H_{15}O_5NBr^+$, $[M+H]^+$ = 380.0128; *m/z* found = 380.0130, Δ = 0.46 ppm.

4-(2-Bromo-6-methyl-4-nitrophenoxy)-1,1'-biphenyl, 74:



Compound **74** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), [1,1'-biphenyl]-4-ol (680 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 2:98, R_f = 0.4) to give the title compound as a white solid (1.12 g, 73%).

m.p. = 140-143 °C.

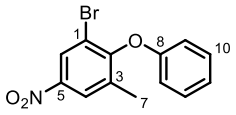
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.42 (dd, *J* = 2.7, 1.0 Hz, 1H, H_1), 8.15 (dd, *J* = 2.8, 0.9 Hz, 1H, H_4), 7.57 – 7.50 (m, 4H, H_{10}, H_{11}), 7.43 (dd, *J* = 8.5, 7.0 Hz, 2H, H_{14}), 7.37 – 7.30 (m, 1H, H_{15}), 6.89 – 6.82 (m, 2H, H_{13}), 2.33 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 155.8 (C_8), 155.5 (C_2), 145.1 (C_5), 140.3 (C_{11}), 136.2 (C_{12}), 135.4 (C_3), 129.0 (C_{14}), 128.8 ($C_{9/10}$), 127.3 ($C_{9/10}$), 127.1 (C_{15}), 127.0 (C_6), 125.9 (C_4), 118.6 (C_1), 115.4 (C_{13}), 17.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2922, 2360, 1607, 1525, 1484, 1459, 1344, 1258, 1216, 1168, 1090, 1006, 946, 897, 865, 841, 803, 763, 742, 724, 698, 623.

HRMS ($APCl^-$): *m/z* calculated for $C_{19}H_{13}O_3NBr^-$, $[M-H]^-$ = 382.0084; *m/z* found = 382.2215. Δ = -2.20 ppm.

1-Bromo-3-methyl-5-nitro-2-phenoxybenzene, 75:



Compound **75** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), phenol (376 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:100, R_f = 0.5) to give the title compound as a bright yellow solid (900 mg, 73%).

m.p. = 44-46 °C.

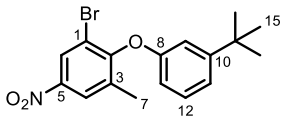
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.40 (d, *J* = 2.7 Hz, 1H, H_6), 8.13 (d, *J* = 2.7 Hz, 1H, H_4), 7.35 – 7.27 (m, 2H, H_{10}), 7.11 – 7.04 (m, 1H, H_{11}), 6.81 – 6.75 (m, 2H, H_9), 2.29 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 156.3 (C_8), 155.5 (C_2), 145.0 (C_5), 135.4 (C_3), 130.1 (C_{10}), 127.1 (C_6), 125.8 (C_4), 123.0 (C_{11}), 118.6 (C_1), 115.1 (C_9), 17.5 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3087, 2363, 1592, 1575, 1525, 1490, 1458, 1344, 1291, 1260, 1213, 1195, 1165, 1090, 946, 898, 861, 842, 799, 748, 689, 619.

HRMS ($APCl^-$): *m/z* calculated for $C_{13}H_9BrO_3N^-$, $[M-H]^-$ = 305.9771; *m/z* found = 305.9763. Δ = -2.64 ppm.

1-Bromo-2-(3-(*tert*-butyl)phenoxy)-3-methyl-5-nitrobenzene, 80:



Compound **80** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), 3-(*tert*-butyl)phenol (601 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:100, R_f = 0.8) to give the title compound as a bright yellow solid (1.28 g, 88%).

m.p. = 70-74 °C.

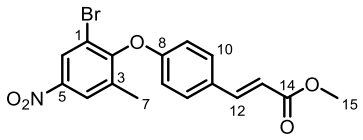
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.40 (d, *J* = 2.7 Hz, 1H, H_6), 8.13 (d, *J* = 2.7 Hz, 1H, H_4), 7.20 (t, *J* = 8.0 Hz, 1H, H_{12}), 7.11 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H, H_{11}), 6.94 (dd, *J* = 2.6, 1.8 Hz, 1H, H_9), 6.46 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H, H_{13}), 2.29 (t, *J* = 0.8 Hz, 3H, H_7), 1.30 (s, 9H, H_{15}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 156.2 (C_8), 155.7 (C_2), 154.0 (C_{10}), 144.9 (C_5), 135.3 (C_3), 129.4 (C_{12}), 127.0 (C_6), 125.8 (C_4), 120.1 (C_{11}), 118.6 (C_1), 112.9 (C_9), 111.4 (C_{13}), 34.9 (C_{14}), 31.4 (C_{15}), 17.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3090, 2964, 2867, 2363, 2156, 1605, 1573, 1527, 1485, 1460, 1431, 1343, 1260, 1213, 1189, 1113, 1089, 947, 921, 897, 872, 844, 802, 781, 759, 742, 716, 699, 667.

HRMS (EI^+): *m/z* calculated for $C_{17}H_{18}O_3NBr^+$, $[M\text{-}e^-]^+$ = 363.0470; *m/z* found = 363.0465. Δ = - 3.72 ppm.

Methyl (*E*)-3-(4-hydroxyphenyl)acrylate, 81:



Compound **81** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), 3-(*tert*-butyl)phenol (713 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (EtOAc:Pentane, 5:95, R_f = 0.3) to give the title compound as a yellow solid (1.02 g, 65%).

m.p. = 128-131 °C.

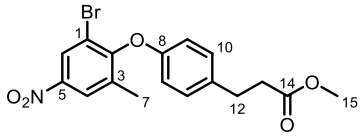
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.37 (dd, *J* = 2.7, 0.7 Hz, 1H, H_6), 8.13 (dd, *J* = 2.8, 0.8 Hz, 1H, H_4), 7.62 (d, *J* = 16.0 Hz, 1H, H_{12}), 7.51 – 7.44 (m, 2H, H_{10}), 6.81 – 6.76 (m, 2H, H_9), 6.33 (d, *J* = 16.0 Hz, 1H, H_{13}), 3.77 (s, 3H, H_{15}), 2.28 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 167.4 (C_{14}), 157.7 (C_8), 154.9 (C_2), 145.2 (C_5), 143.7 (C_{12}), 135.2 (C_3), 130.1 (C_{10}), 129.5 (C_{11}), 127.1 (C_6), 125.8 (C_4), 118.3 (C_1), 116.9 (C_{13}), 115.5 (C_9), 51.8 (C_{15}), 17.4 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2981, 2885, 1713, 1605, 1577, 1527, 1503, 1461, 1434, 1417, 1393, 1367, 1344, 1307, 1278, 1258, 1218, 1163, 1109, 1095, 1015, 969, 945, 898, 867, 852, 801, 767, 743, 695, 637.

HRMS (APCI⁻): *m/z* calculated for $C_{17}H_{13}BrO_5N^-$ $[M-H]^-$ = 389.9983; *m/z* found = 389.9970. Δ = -0.41 ppm.

Methyl 3-(4-(2-bromo-6-methyl-4-nitrophenoxy)phenyl)propanoate, 82:



Compound **82** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), methyl 3-(4-hydroxyphenyl)propanoate (721 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 6:94, R_f = 0.8) to give the title compound as a bright yellow solid (1.24 g, 79%).

m.p. = 45-47 °C.

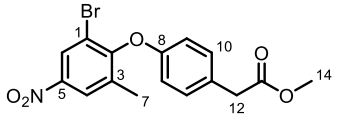
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.38 (d, *J* = 2.8 Hz, 1H, H_6), 8.12 (dd, *J* = 2.7, 0.9 Hz, 1H, H_4), 7.15 – 7.09 (m, 2H, H_{10}), 6.72 – 6.67 (m, 2H, H_9), 3.67 (s, 3H, H_{15}), 2.91 (t, *J* = 7.8 Hz, 2H, H_{12}), 2.61 (t, *J* = 7.8 Hz, 2H, H_{13}), 2.27 (d, *J* = 0.7 Hz, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 173.4 (C_{14}), 155.6 (C_2), 154.9 (C_8), 145.0 (C_5), 135.3 ($C_{3/11}$), 135.2 ($C_{3/11}$), 129.9 (C_{10}), 127.1 (C_6), 125.8 (C_4), 118.6 (C_1), 115.1 (C_9), 51.8 (C_{15}), 35.9 (C_{13}), 30.2 (C_{12}), 17.5 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3661, 2981, 1737, 1609, 1527, 1506, 1460, 1436, 1344, 1295, 1260, 1216, 1198, 1167, 1091, 1015, 946, 899, 865, 843, 743.

HRMS (APCl$^-$): *m/z* calculated for $C_{17}H_{15}O_5NBr^-$, $[M-H]^-$ = 392.0139, *m/z* found = 392.0137. Δ = -0.62 ppm.

Methyl 2-(4-(2-bromo-6-methyl-4-nitrophenoxy)phenyl)acetate, 83:



Compound **83** was prepared according to a modified **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), methyl 2-(4-hydroxyphenyl)acetate—methane (997 mg, 6.00 mmol, 1.5 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:Pentane, 10:90, R_f = 0.5) to give the title compound as a yellow solid (1.00 g, 66%).

m.p. = 146-148 °C.

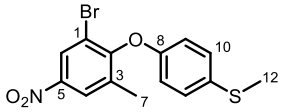
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.37 (dd, *J* = 2.5, 1.0 Hz, 1H, H_6), 8.12 (dd, *J* = 2.5, 1.0 Hz, 1H, H_4), 7.24 – 7.18 (m, 2H, H_{10}), 6.76 – 6.70 (m, 2H, H_9), 3.69 (s, 3H, H_{14}), 3.58 (s, 2H, H_{12}), 2.27 (d, *J* = 1.0 Hz, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 172.1 (C_{13}), 155.4 ($C_{2/8}$), 155.4 ($C_{2/8}$), 145.0 (C_5), 135.3 (C_3), 130.9 (C_{10}), 128.6 (C_{11}), 128.6 (C_{11}), 127.0 (C_6), 125.8 (C_4), 118.5 (C_1), 115.1 (C_9), 52.2 (C_{14}), 40.3 (C_{12}), 17.5 (C_7).

IR (film) ν_{max}/cm^{-1} = 2952, 1738, 1527, 1506, 1435, 1344, 1260, 1217, 1199, 1161, 1090, 1015, 946, 897, 866, 843, 743, 620.

HRMS (ESI$^-$): calculated for $C_{16}H_{13}O_5NBr^-$, $[M-H]^-$ = 379.9962; *m/z* found 337.9977, Δ = -1.56 ppm.

(4-(2-Bromo-6-methyl-4-nitrophenoxy)phenyl)(methyl)sulfane, 84:



Compound **84** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), 4-(methylthio)phenol (561 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:100, R_f = 0.5) to give the title compound as a bright yellow solid (1.11 g, 78%).

m.p. = 73-76 °C.

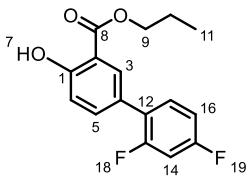
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.37 (d, *J* = 3.0 Hz, 1H, H_6), 8.12 (d, *J* = 3.0 Hz, 1H, H_4), 7.28 – 7.19 (m, 2H, H_{10}), 6.75 – 6.68 (m, 2H, H_9), 2.45 (s, 3H, H_{12}), 2.27 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 155.3 (C_2), 154.5 (C_8), 145.0 (C_5), 135.2 (C_3), 132.1 (C_{11}), 129.4 (C_{10}), 127.0 (C_6), 125.8 (C_4), 118.4 (C_1), 115.6 (C_9), 17.4 (C_7), 17.2 (C_{12}).

IR (film) ν_{max}/cm^{-1} **=** 3371, 3028, 2919, 1607, 1573, 1487, 1474, 1437, 1317, 1274, 1224, 1166, 1096, 1009, 969.

HRMS (ESI$^+$): calculated for $C_{14}H_{12}O_3NBrS^+$, $[M+H]^+$ = 352.9716; *m/z* found 352.9716, Δ = 0.10 ppm.

Propyl 2',4'-difluoro-4-hydroxy-[1,1'-biphenyl]-3-carboxylate, 85a:



Compound **85a** was prepared according to a literature procedure.[35] Carbonyl diimidizole (1.30 g, 8.00 mmol, 1 eq.) was added to a solution of diflunisal **86** (2.00 g, 8.00 mmol, 1 eq.) in DMF (40 mL). The reaction mixture was stirred at 50 °C. After 2 h *n*-PrOH (1.8 mL, 24.0 mmol, 3 eq.) was added dropwise and the resultant mixture was stirred at 50 °C. After 3 h the mixture was cooled to r.t., H_2O (50 mL) was added, and the aqueous layer was extracted with Et_2O (2 x 50 mL). The organic layer was washed with $NaHCO_3$ (sat. aq., 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 2:98, R_f = 0.7) to give the title compound as a white solid (968 mg, 42%).

m.p. = 40-42 °C.

^{1}H (500 MHz, $CDCl_3$) δ = 10.94 (s, 1H, H_7), 7.99 (dd, *J* = 2.5, 1.5 Hz, 1H, H_3), 7.58 (dt, *J* = 8.5, 2.0 Hz, 1H, H_5), 7.36 (td, *J* = 8.5, 6.5 Hz, 1H, H_{17}), 7.05 (d, *J* = 8.5 Hz, 1H, H_2), 6.94 (tdd, *J* = 8.0, 2.5, 1.0 Hz, 1H, H_{16}), 6.90 (ddd, *J* = 10.5, 8.5, 2.5 Hz, 1H, H_{14}), 4.34 (t, *J* = 6.5 Hz, 2H, H_9), 1.82 (m, 2H, H_{10}), 1.05 (t, *J* = 7.5 Hz, 3H, H_{11}).

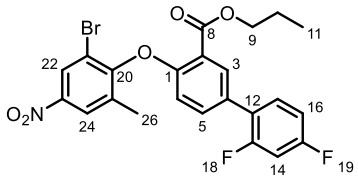
^{13}C (126 MHz, $CDCl_3$) δ = 170.1 (C_8), 163.1 (dd, *J* = 249.0, 12.0 Hz, C_{15}), 161.4 (C_1), 159.8 (dd, *J* = 250.0, 12.0 Hz, C_{13}), 136.1 (d, *J* = 3.0 Hz, C_5), 131.1 (dd, *J* = 9.5, 4.5 Hz, C_{17}), 130.2 (d, *J* = 3.0 Hz, C_3), 126.0 (C_4), 124.3 (dd, *J* = 13.5, 3.0 Hz, C_{12}), 117.9 (C_2), 112.8 (C_2), 111.7 (dd, *J* = 21.0, 4.0 Hz (C_{16}), 104.8 – 104.0 (m, C_{14}), 67.2 (C_9), 22.1 (C_{10}), 10.5 (C_{11}).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -111.24 – -111.59 (m), -113.66 – -113.85 (m).

IR (film) ν_{max}/cm^{-1} = 3657, 2982, 2971, 2883, 2360, 1676, 1617, 1591, 1513, 1484, 1398, 1334, 1291, 1267, 1252, 1225, 1205, 1141, 1091, 969, 939, 850, 815, 795, 730, 668, 633, 628, 613.

HRMS (ESI^+): calculated for $C_{16}H_{15}O_3F_2^+$, $[M+H]^+$ = 293.0985; m/z found 293.0985, Δ = 0.35 ppm.

Propyl 4-(2-bromo-6-methyl-4-nitrophenoxy)-2',4'-difluoro-[1,1'-biphenyl]-3-carboxylate, 85:



Compound **85** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (501 mg, 2.00 mmol, 1 eq.), propyl 2',4'-difluoro-4-hydroxy-[1,1'-biphenyl]-3-carboxylate **85a** (585 mg, 2.00 mmol, 1 eq.) and K_2CO_3 (553 mg g, 4.00 mmol, 2 eq.) in DMF (5 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f = 0.2) to give the title compound as a yellow oil (409 mg, 40%).

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.41 (d, *J* = 2.7 Hz, 1H, H_{22}), 8.16 (dd, *J* = 2.7, 0.9 Hz, 1H, H_{24}), 8.08 (dd, *J* = 2.4, 1.1 Hz, 1H, H_3), 7.50 – 7.46 (m, 1H, H_5), 7.40 (td, *J* = 8.7, 6.3 Hz, 1H, H_{17}), 6.99 – 6.94 (m, 1H, H_4), 6.91 (ddd, *J* = 11.0, 8.8, 2.6 Hz, 1H, H_{14}), 6.44 (m, 1H, H_{16}), 4.35 (t, *J* = 6.6 Hz, 2H, H_9), 2.36 (s, 3H, H_{26}), 1.81 (qn, *J* = 7.1 Hz, 2H, H_{10}), 1.03 (t, *J* = 7.4 Hz, 3H, H_{11}).

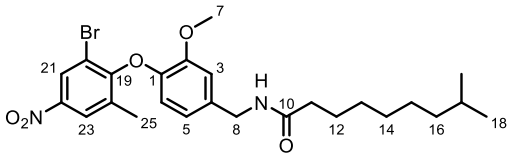
^{13}C (126 MHz, $CDCl_3$) δ_C = 165.5 (C_8), 162.6 (dd, *J* = 249.7, 11.9 Hz, C_{15}), 159.8 (dd, *J* = 250.7, 11.9 Hz, C_{13}), 155.1 (C_{20}), 154.8 (C_1), 145.3 (C_{23}), 135.2 (C_{25}), 133.8 (d, *J* = 3.5 Hz, C_5), 132.8 (d, *J* = 2.7 Hz, C_3), 131.3 (dd, *J* = 9.5, 4.7 Hz, C_{17}), 129.7 (C_4), 127.2 (C_{22}), 125.9 (C_{24}), 123.6 (dd, *J* = 13.4, 3.9 Hz, C_{12}), 121.0 (C_2), 118.3 (C_{21}), 114.1 (C_6), 112.0 (dd, *J* = 21.2, 3.7 Hz, C_{16}), 104.7 (t, *J* = 25.9 Hz, C_{14}), 67.2 (C_9), 22.3 (C_{10}), 17.4 (C_{26}), 10.7 (C_{11}).

^{19}F NMR (377 MHz, $CDCl_3$) δ = -111.1, -113.8.

IR (film) ν_{max}/cm^{-1} **=** 3089, 2971, 2360, 2343, 1728, 1610, 1583, 1528, 1485, 1462, 1434, 1404, 1344, 1317, 1294, 1261, 1221, 1178, 1142, 1103, 1090, 1081, 1040, 969, 946, 898, 880, 849, 813, 784, 758, 742, 664, 660, 653, 645, 638, 634, 628, 616, 610.

HRMS (ESI^+): *m/z* calculated for $C_{23}H_{19}O_5NBrF_2^+$, $[M+H]^+$ = 506.0409; *m/z* found = 506.0411. Δ = 0.37 ppm.

***N*-(4-(2-bromo-6-methyl-4-nitrophenoxy)-3-methoxybenzyl)-8-methylnonanamide, 87:**



Capsaicin **88** (900 mg, 2.94 mmol, 1 eq.) and Pd/C (10% wt., 78 mg, 2.5 mol%) were added to an RBF. Following evacuation and backfilling of N_2 x 3, EtOH (6 mL) was added. The mixture was purged with H_2 using a 3-skin balloon and an exit needle. After 5 minutes the balloon was replaced with a fresh H_2 balloon, and the exit needle was removed. After stirring overnight, the reaction monitored by TLC. Then the reaction was sparged with N_2 and the solution was filtered through Celite® and eluted (EtOH, 4 x 4 mL) and concentrated *in vacuo*. The crude residue was used without further purification assuming 100% conversion.

87 was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (501 mg, 2.00 mmol, 1 eq.), and the crude residue containing N-(4-hydroxy-3-methoxybenzyl)-8-methylnonanamide--methane (615 mg, 2.00 mmol, 1 eq.) and K_2CO_3 (553 mg, 4.00 mmol, 2 eq.) in DMF (5 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.2) to give the title compound as a yellow solid (875 g, 84%).

m.p. = 78-80 °C.

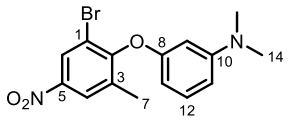
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.36 (m, 1H, H_{21}), 8.10 (qd, *J* = 1.8, 0.9 Hz, 1H, H_{23}), 6.95 (d, *J* = 2.0 Hz, 1H, H_3), 6.67 (m, 1H, H_5), 6.28 (dd, *J* = 8.2, 1.5 Hz, 1H, H_6), 5.81 (s, 1H, H_9), 4.39 (m, 2.4 Hz, 2H, H_8), 3.94 (d, *J* = 1.9 Hz, 3H, H_7), 2.27 (d, *J* = 1.7 Hz, 3H, H_{25}), 2.21 (t, *J* = 7.6 Hz, 2H, H_{11}), 1.64 (m, 2H, H_{12}), 1.53 – 1.44 (m, 1H, H_{17}), 1.36 – 1.19 (m, 6H, H_{13}, H_{14}, H_{15}), 1.16 – 1.09 (m, 2H, H_{16}), 0.84 (m, 6H, H_{18}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 173.2 (d, *J* = 2.1 Hz, C_{10}), 156.0 (C_{19}), 149.1 (d, *J* = 2.3 Hz, C_1), 144.9 (d, *J* = 2.1 Hz, C_2), 144.8 (d, *J* = 2.5 Hz, C_{22}), 135.0 (C_{24}), 134.2 (C_4), 127.1 (C_{21}), 125.8 (C_{23}), 120.0 (d, *J* = 1.9 Hz, C_5), 118.1 (C_{24}), 114.0 (C_6), 112.7 (d, *J* = 2.1 Hz, C_3), 56.4 (C_7), 43.3 (C_8), 39.1 (C_{16}), 36.9 (d, *J* = 2.6 Hz, C_{11}), 29.7 (C_{13}), 29.5 (C_{14}), 28.1 (C_{17}), 27.4 (C_{15}), 25.9 (C_{12}), 22.7 (C_{18}), 17.3 (C_{25}).

IR (film) ν_{max}/cm^{-1} **=** 3287, 3085, 2954, 2927, 2855, 2360, 2342, 1645, 1600, 1527, 1509, 1462, 1433, 1420, 1341, 1257, 1213, 1176, 1154, 1128, 1091, 1036, 946, 897, 852, 840, 793, 742, 685, 655, 643.

HRMS (ESI^+): *m/z* calculated for $C_{25}H_{34}O_5N_2Br^+$, $[M+H]^+$ = 521.1646; *m/z* found = 521.1642. Δ = -0.61 ppm.

3-(2-Bromo-6-methyl-4-nitrophenoxy)-*N*,*N*-dimethylaniline, 89:



Compound **89** was prepared according to **General Procedure A** using 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.00 g, 4.00 mmol, 1 eq.), 3-(dimethylamino)phenol (664 mg, 4.00 mmol, 1 eq.) and K_2CO_3 (1.11 g, 8.00 mmol, 2 eq.) in DMF (10 mL). The crude residue was

purified by flash column chromatography (Et_2O:pentane, 2:100, R_f = 0.7) to give the title compound as a bright yellow solid (446 mg, 32%).

m.p. = 107-109 °C.

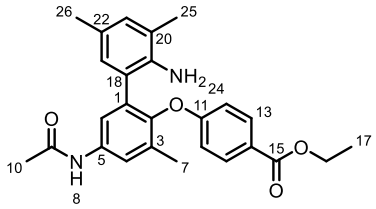
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.38 (d, *J* = 3.0 Hz, 1H, H_6), 8.11 (dd, *J* = 3.0, 1.0 Hz, 1H, H_4), 7.10 (t, *J* = 8.5 Hz, 1H, H_{12}), 6.45 (dd, *J* = 8.5, 2.5 Hz, 1H, H_{11}), 6.29 (s, 1H, H_9), 5.94 (dd, *J* = 8.5, 2.5 Hz, 1H, H_{13}), 2.94 (s, 6H, H_{14}), 2.30 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 157.5 (C_8), 155.8 (C_2), 152.2 (C_{10}), 144.8 (C_5), 135.5 (C_3), 130.2 (C_{12}), 126.9 (C_6), 125.7 (C_4), 118.7 (C_1), 107.4 (C_{11}), 102.1 (C_{13}), 99.7 (C_9), 40.6 (C_{14}), 17.5 (C_7).

IR (film) ν_{max}/cm^{-1} = 2917, 1616, 1568, 1524, 1503, 1437, 1343, 1261, 1213, 1176, 1139, 1090, 999, 946, 897, 843, 743, 684.

HRMS (ESI^+): *m/z* calculated for $C_{15}H_{16}O_3N_2Br^+$, $[M+H]^+$ = 353.0318; *m/z* found = 351.0316 Δ = -0.45 ppm.

Ethyl 4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)benzoate, 109:



Compound **109** was prepared according to **General Procedure B** using ethyl 4-(2-bromo-6-methyl-4-nitrophenoxy)benzoate **73** (760 mg, 2.00 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 50:50, R_f = 0.2) to give the title compound as a brown solid (507 mg, 59%).

m.p. = 157-159 °C.

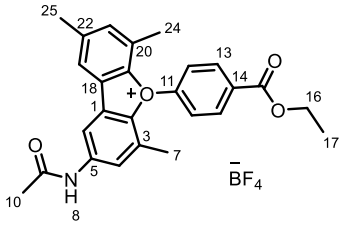
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.83 – 7.77 (m, 2H, H_{13}), 7.64 (d, *J* = 2.7 Hz, 1H, H_4), 7.43 (s, 1H, H_8), 7.16 (d, *J* = 2.5 Hz, 1H, H_6), 6.74 – 6.70 (m, 1H, H_{21}), 6.66 – 6.59 (m, 2H, H_{12}), 6.57 (d, *J* = 2.1 Hz, 1H, H_{23}), 4.30 (q, *J* = 7.1 Hz, 2H, H_{16}), 3.05 (s, 2H, H_{24}), 2.17 (s, 3H, H_7), 2.16 (s, 3H, H_{10}), 2.08 (s, 3H, H_{25}), 2.06 (s, 3H, H_{26}), 1.34 (t, *J* = 7.1 Hz, 3H, H_{17}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.5 (C_9), 166.4 (C_{15}), 161.9 (C_{11}), 146.6 (C_2), 139.5 (C_{19}), 135.6 (C_5), 134.0 (C_{22}), 133.0 (C_3), 131.4 (C_{13}), 130.8 (C_{21}), 128.8 (C_{23}), 126.9 (C_{20}), 123.7 (C_{14}), 122.8 (C_{18}), 122.6 (C_4), 121.2 (C_6), 114.9 (C_{12}), 60.8 (C_{16}), 24.6 (C_{10}), 20.3 (C_{26}), 17.9 (C_{25}), 17.0 (C_7), 14.5 (C_{17}). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} = 3311, 2978, 2927, 1711, 1605, 1551, 1504, 1469, 1419, 1368, 1276, 1231, 1197, 1161, 1101, 1015, 862, 768, 695, 645, 617.

HRMS (ESI$^+$) = *m*/*z* calculated for $C_{26}H_{29}N_2O_4^+$, $[M+H]^+$ = 433.2122; *m*/*z* found = 433.2126. Δ = 0.86 ppm.

2-Acetamido-5-(4-(ethoxycarbonyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 110:



Compound **110** was prepared according to **General Procedure C** using ethyl 4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)benzoate **109** (216 mg, 0.50 mmol, 1.00 eq.) to give the title compound as a red solid (166 mg, 66%).

m.p. = 186-188 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.82 (s, 1H, H_8), 8.43 (d, *J* = 2.4 Hz, 1H, H_6), 8.27 – 8.21 (m, 2H, H_{13}), 7.92 (d, *J* = 1.9 Hz, 1H, H_{23}), 7.90 – 7.83 (m, 2H, H_{12}), 7.47 – 7.43 (m, 1H, H_4), 7.30 (d, *J* = 2.0 Hz, 1H, H_{21}), 4.38 (q, *J* = 7.1 Hz, 2H, H_{16}), 2.49 (s, 3H, H_{25}), 2.13 (s, 3H, H_{10}), 2.11 (s, 6H, H_7, H_{24}), 1.36 (t, *J* = 7.1 Hz, 3H, H_{17}).

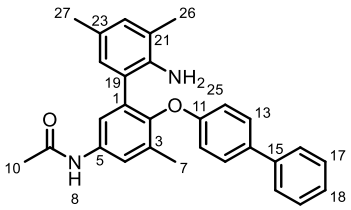
^{13}C (126 MHz, $CDCl_3$) δ_C = 170.4 (C_9), 165.0 (C_{15}), 162.8 (C_{11}), 161.4 (C_{19}), 157.9 (C_2), 143.2 (C_5), 142.6 (C_{22}), 135.7 (C_{14}), 135.3 (C_{21}), 133.9 (C_{13}), 126.0 (C_{Ar}), 125.1 (C_{Ar}), 124.8 (C_4), 124.3 (C_{Ar}), 124.3 (C_{Ar}), 122.7 (C_{23}), 122.4 (C_{12}), 111.6 (C_6), 63.0 (C_{16}), 24.5 (C_{10}), 21.1 (C_{25}), 17.1 ($C_{7/24}$), 16.8 ($C_{7/24}$), 14.4 (C_{17}).

^{19}F (377 MHz, CD_3CN) δ_F = -151.7.

IR (film) ν_{max}/cm^{-1} **=** 3649, 2999, 2981, 2885, 2230, 2197, 2159, 2086, 2023, 2004, 1460, 1394, 1381, 252, 1150, 1071.

HRMS (ESI^+): *m/z* calculated for $C_{26}H_{26}O_4N^+$, $[M]^+$ = 416.1856; *m/z* found = 416.1853. Δ = -0.72 ppm.

***N*-(6-([1,1'-biphenyl]-4-yloxy)-2'-amino-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide, 111:**



Compound **111** was prepared according to **General Procedure B** using 4-(2-bromo-6-methyl-4-nitrophenoxy)-1,1'-biphenyl **74** (768 mg, 2.00 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.10) to give the title compound as a white solid (332 mg, 38%).

m.p. = 154-156 °C.

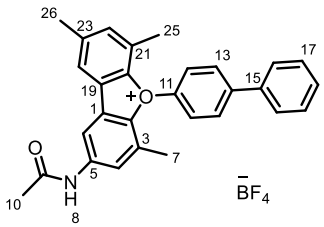
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.66 (d, *J* = 2.6 Hz, 1H, H_4), 7.49 – 7.43 (m, 2H, H_{16}), 7.38 (dd, *J* = 8.5, 7.0 Hz, 2H, H_{17}), 7.33 – 7.30 (m, 2H, H_{13}), 7.29 – 7.27 (m, 1H, H_{18}), 7.18 (s, 1H, H_8), 7.13 (d, *J* = 2.5 Hz, 1H, H_6), 6.74 (d, *J* = 2.1 Hz, 1H, H_{22}), 6.69 – 6.63 (m, 2H, H_{12}), 6.62 (d, *J* = 2.1 Hz, 1H, H_{24}), 2.24 (s, 3H, H_7), 2.18 (s, 3H, H_{10}), 2.10 (s, 3H, H_{26}), 2.06 (s, 3H, H_{27}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.3 (C_9), 158.0 (C_{11}), 147.6 (C_2), 140.9 (C_{13}), 139.6 (C_{20}), 135.1 (C_5), 134.5 (C_{15}), 134.2 (C_{19}), 133.3 (C_3), 130.7 (C_{22}), 129.0 (C_{24}), 128.8 (C_{17}), 127.9 (C_{13}), 126.9 (C_{23}), 126.8 (C_{13}), 123.3 (C_1), 122.6 (C_{18}), 122.6 (C_{16}, C_{23}), 121.2 (C_6), 115.8 (C_{12}), 24.7 (C_{10}), 20.4 (C_{27}), 17.9 (C_{26}), 17.2 (C_7). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} **=** 3661, 2981, 2885, 2361, 2341, 2015, 1609, 1462, 1382, 1252, 1148, 1073, 954, 751, 668, 619.

HRMS (ESI^+): *m/z* calculated for $C_{29}H_{29}O_2N_2^+$, $[M+H]^+$ = 437.2224; *m/z* found = 437.2222. Δ = -0.27 ppm.

5-([1,1'-Biphenyl]-4-yl)-2-acetamido-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 112:



Compound **112** was prepared according to **General Procedure C** using n-(6-([1,1'-biphenyl]-4-yloxy)-2'-amino-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide **111** (218 mg, 0.50 mmol, 1 eq.) to give the title compound as a red solid (187 mg, 74%).

m.p. = 191-194 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.79 (s, 1H, H_8), 8.45 (d, *J* = 2.3 Hz, 1H, H_6), 7.96 – 7.93 (m, 1H, H_{24}), 7.92 – 7.86 (m, 2H, $H_{12/13}$), 7.84 – 7.77 (m, 2H, $H_{12/13}$), 7.71 – 7.66 (m, 2H, H_{16}), 7.55 – 7.50 (m, 2H, H_{17}), 7.49 – 7.46 (m, 1H, H_{18}), 7.46 – 7.44 (m, 1H, H_4), 7.34 – 7.30 (m, 1H, H_{22}), 2.50 (s, 3H, H_{26}), 2.17 (s, 3H, H_7), 2.17 (s, 3H, H_{25}), 2.14 (s, 3H, H_{10}).

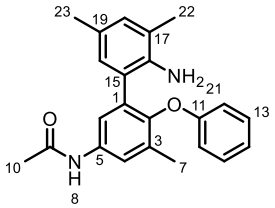
^{13}C (126 MHz, $CDCl_3$) δ_C = 170.4 (C_9), 161.2 (C_{20}), 160.3 (C_{11}), 157.8 (C_2), 146.0 (C_{15}), 143.0 (C_{23}), 142.4 (C_5), 138.9 (C_{14}), 135.6 (C_{22}), 131.0 ($C_{12/13}$), 130.2 (C_{17}), 129.9 (C_{18}), 128.4 (C_{16}), 126.0 (C_{Ar}), 125.1 (C_{Ar}), 124.8 (C_{Ar}), 124.4 (C_{Ar}), 124.3 (C_4), 122.6 (C_{24}), 122.1 ($C_{12/13}$), 111.6 (C_6), 24.4 (C_{10}), 21.1 (C_{26}), 17.2 ($C_{7/25}$), 16.9 ($C_{7/25}$).

^{19}F (377 MHz, CD_3CN) δ_F = -151.5.

IR (film) ν_{max}/cm^{-1} **=** 3788, 3662, 2981, 2886, 2356, 1583, 1550, 1462, 1382, 1252, 1152, 1073, 955, 749.

HRMS (ESI^+):*m*/*z* calculated for $C_{29}H_{29}O_2N^+$, $[M]^+$ = 420.1958; *m*/*z* found = 420.1945. Δ = -2.99 ppm.

***N*-(2'-Amino-3',5,5'-trimethyl-6-phenoxy-[1,1'-biphenyl]-3-yl)acetamide, 113:**



Compound **113** was prepared according to **General Procedure B** using 1-bromo-3-methyl-5-nitro-2-phenoxybenzene, **75** (616 mg, 2.00 mmol, 1 eq.). The crude residue was purified by flash

column chromatography (EtOAc:pentane, 40:60, R_f = 0.10) to give the title compound as a brown solid (559 mg, 63%).

m.p. = 133-135 °C.

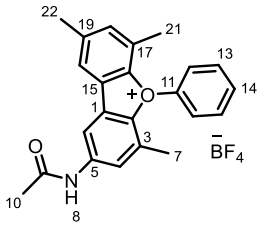
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.62 (d, *J* = 3.00 Hz, 1H, H_4), 7.32 (s, 1H, H_8), 7.11 (d, *J* = 3.00 Hz, 1H, H_6), 7.10 – 7.06 (m, 2H, H_{12}), 6.87 – 6.80 (m, 1H, H_{14}), 6.73 (d, *J* = 2.00 Hz, 1H, H_{18}), 6.62 – 6.57 (m, 3H, H_{13}, H_{20}), 3.44 (s, 2H, H_{21}), 2.19 (s, 3H, H_7), 2.15 (s, 3H, H_{10}), 2.09 (s, 3H, H_{22}), 2.06 (s, 3H, H_{23}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.4 (C_9), 158.3 (C_{11}), 147.4 (C_2), 139.6 (C_{16}), 135.0 (C_5), 134.2 (C_1), 133.3 (C_3), 130.6 (C_{18}), 129.2 (C_{13}), 129.0 (C_{20}), 126.8 (C_{19}), 123.4 (C_{15}), 122.6 (C_4), 122.5 (C_{17}), 121.4 (C_{14}), 121.2 (C_6), 115.4 (C_{12}), 24.6 (C_{10}), 20.4 (C_{23}), 17.9 (C_{22}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3301, 2920, 2850, 2370, 2337, 2136, 2066, 2042, 2016, 1966, 1667, 1601, 1552, 1489, 1471, 1370, 1218, 1164, 1035, 856, 751, 690, 666.

HRMS (MSS^+): *m/z* calculated for $C_{23}H_{25}O_2N_2^+$, $[M+H]^+$ = 361.1911; *m/z* found = 361.1905. Δ = -1.65 ppm.

2-Acetamido-4,6,8-trimethyl-5-phenyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 114:



Compound **114** was prepared according to **General Procedure C** using n-(2'-amino-3',5,5'-trimethyl-6-phenoxy-[1,1'-biphenyl]-3-yl)acetamide **113** (375 mg, 1.00 mmol, 1 eq.) to give the title compound as an orange solid (354 mg, 82%).

m.p. = 189-192 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.76 (s, 1H, H_8), 8.43 (d, *J* = 2.4 Hz, 1H, H_6), 7.95 – 7.90 (m, 1H, H_{20}), 7.78 – 7.65 (m, 5H, $H_{12\text{-}14}$), 7.43 (dd, *J* = 2.4, 1.0 Hz, 1H, H_4), 7.30 (dd, *J* = 2.0, 1.0 Hz, 1H, H_{18}), 2.49 (s, 3H, H_{22}), 2.13 (s, 3H, H_{10}), 2.09 (s, 3H, H_7), 2.09 (s, 3H, H_{21}).

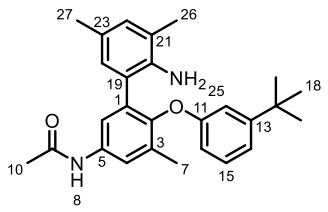
^{13}C (126 MHz, $CDCl_3$) δ_C = 170.3 (C_9), 161.1 (C_{11}), 161.0 (C_{16}), 157.7 (C_2), 142.9 (C_5), 142.4 (C_{19}), 135.6 (C_{18}), 133.5 (C_{14}), 132.9 (C_{12}), 125.9 (C_{Ar}), 125.1 (C_{Ar}), 124.8 (C_{Ar}), 124.4 (C_{Ar}), 124.3 (C_4), 122.6 (C_{20}), 121.8 (C_{13}), 111.5 (C_6), 24.4 (C_{10}), 21.0 (C_{22}), 17.1 ($C_{7/21}$), 16.8 ($C_{7/21}$).

^{19}F (377 MHz, CD_3CN) δ_F = -151.7.

IR (film) ν_{max}/cm^{-1} **=** 3661, 3356, 2981, 2888, 1691, 1553, 1462, 1383, 1259, 1150, 1072, 955, 859, 805, 736, 694, 635, 610.

HRMS (ESI^+):*m*/*z* calculated for $C_{23}H_{22}O_2N^+$, $[M]^+$ = 344.1645; *m*/*z* found = 344.1644. Δ = -0.22 ppm.

***N*-(2'-Amino-6-(3-(*tert*-butyl)phenoxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide, 123:**



Compound **124** was prepared according to **General Procedure B** using 1-bromo-2-(3-(*tert*-butyl)phenoxy)-3-methyl-5-nitrobenzene **80** (729 mg, 2.00 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.10) to give the title compound as a brown solid (449 mg, 54%).

m.p. = 64-66 °C.

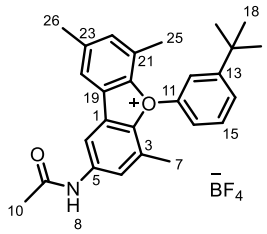
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.61 (d, *J* = 2.7 Hz, 1H, H_4), 7.39 (s, 1H, H_8), 7.10 (d, *J* = 2.7 Hz, 1H, H_6), 6.99 (t, *J* = 7.9 Hz, 1H, H_{12}), 6.84 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H, H_{14}), 6.69 (d, *J* = 2.0 Hz, 1H, H_{22}), 6.59 (t, *J* = 2.2 Hz, 1H, H_{15}), 6.55 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.38 (ddd, *J* = 8.1, 2.5, 0.9 Hz, 1H, H_{16}), 3.14 (s, 2H, H_{25}), 2.23 (s, 3H, H_7), 2.14 (s, 3H, H_{10}), 2.07 (s, 3H, H_{26}), 2.04 (s, 3H, H_{27}), 1.16 (s, 9H, H_{18}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.5 (C_9), 158.2 (C_{11}), 152.6 (C_{13}), 148.1 (C_2), 139.5 (C_{20}), 134.9 (C_5), 134.0 (C_{19}), 133.2 (C_3), 130.6 (C_{22}), 129.1 (C_{24}), 128.5 (C_{12}), 126.7 (C_{23}), 123.7 (C_1), 122.4 (C_{21}), 122.4 (C_4), 121.1 (C_6), 118.6 (C_{14}), 113.2 (C_{15}), 112.5 (C_{16}), 34.7 (C_{17}), 31.3 (C_{18}), 24.6 (C_{10}), 20.3 (C_{27}), 17.9 (C_{26}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3648, 2981, 2885, 2360, 2341, 1668, 1604, 1552, 1473, 1382, 1252, 1214, 1152, 1073, 954, 863.

HRMS (ESI^+): *m/z* calculated for $C_{27}H_{33}O_2N_2^+$, $[M+H]^+$ =417.2537; *m/z* found = 417.2549. Δ = 3.06 ppm.

2-Acetamido-5-(3-(*tert*-butyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 124:



Compound **124** was prepared according to **General Procedure C** using n-(2'-amino-6-(3-(*tert*-butyl)phenoxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide **123** (313 mg, 0.75 mmol, 1.00 eq.) to give the title compound as a red solid (202 mg, 55%).

m.p. = 138-141 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.78 (s, 1H, H_8), 8.42 (d, *J* = 2.4 Hz, 1H, H_6), 7.98 (dd, *J* = 2.90, 1.7 Hz, 1H, H_{12}), 7.91 (d, *J* = 2.0 Hz, 1H, H_{22}), 7.76 (ddd, *J* = 7.8, 1.6, 0.8 Hz, 1H, H_{14}), 7.56 (dd, *J* = 8.6, 7.9 Hz, 1H, H_{15}), 7.43 (dd, *J* = 2.4, 1.0 Hz, 1H, H_4), 7.35 (ddd, *J* = 8.7, 2.9, 0.8 Hz, 1H, H_{16}), 7.29 (d, *J* = 1.9 Hz, 1H, H_{24}), 2.49 (s, 3H, H_{26}), 2.13 (s, 3H, H_{10}), 2.07 (s, 6H, H_7, H_{25}), 1.33 (s, 9H, H_{18}).

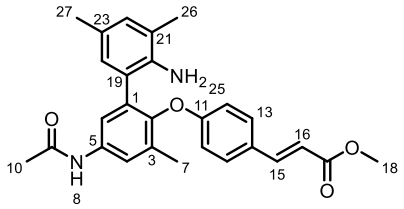
^{13}C (126 MHz, $CDCl_3$) δ_C = 170.4 (C_9), 161.3 (C_{20}), 160.6 (C_{11}), 157.4 (C_2), 157.2 (C_{13}), 142.8 (C_{23}), 142.2 (C_5), 135.6 (C_{24}), 132.6 (C_{15}), 130.1 (C_{14}), 125.8 (C_{Ar}), 125.1 (C_{Ar}), 124.7 (C_{Ar}), 124.4 (C_{Ar}), 124.3 (C_4), 122.5 (C_{22}), 119.6 (C_{12}), 118.2 (C_{16}), 111.5 (C_6), 36.4 (C_{17}), 31.0 (C_{18}), 24.5 (C_{10}), 21.0 (C_{26}), 17.1 ($C_{7/25}$), 16.8 ($C_{7/25}$).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.7.

IR (film) ν_{max}/cm^{-1} **=** 3662, 3360, 2980, 2884, 2361, 2342, 1703, 1563, 1462, 1383, 1260, 1073, 954, 873, 807, 764.

HRMS (ESI^+): m/z calculated for $C_{27}H_{30}O_2N^+$, $[M]^+$ =400.2271; m/z found = 400.2264. Δ = -1.66 ppm.

Methyl (*E*)-3-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)acrylate, 125:



Compound **125** was synthesised according to a modified literature procedure.[36] Methyl (*E*)-3-(4-hydroxyphenyl)acrylate **81** (484 mg, 2.00 mmol, 1 eq.) was dissolved in EtOH (7.00 mL). Fe (335 mg, 6.00 mmol, 3 eq.), NH_4Cl (53 mg, 1.00 mmol, 0.5 eq.) and H_2O (1.8 mL) were sequentially added to the solution. The reaction mixture was heated to 85 °C for 1 h. The reaction mixture was cooled to r.t., filtered through Celite®, eluted (EtOH:CH_2Cl_2, 1:1, 3 × 5 mL), and concentrated *in vacuo*. The crude residue was dissolved in EtOAc (20 mL) and the mixture was washed with H_2O (2 x 5 mL) and NaCl (sat. aq., 1 x 5 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

The crude residue was then dissolved in CH_2Cl_2 (2.5 mL) and Ac_2O (0.57 mL, 6.00 mmol, 3 eq.) was added. After 4 h, $NaHCO_3$ (sat. aq., 30 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were washed with $NaHCO_3$ (sat. aq., 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

The crude residue, 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (741 mg, 3.00 mmol, 1.50 eq.) as a solution in PhMe (12 mL), and H_2O (20 mL) were sequentially added to Pd(dppf)Cl_2·CH_2Cl_2 (82 mg, 0.10 mmol, 5 mol%) and Na_2CO_3 (848 mg, 8.00 mmol, 4 eq.) in PhMe (8 mL) under N_2 at r.t.. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.10) to give the title compound as a brown solid (448 mg, 50%).

m.p. = 167-169 °C.

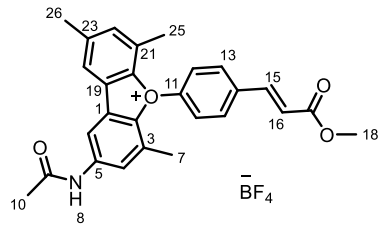
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.65 (s, 1H, H_4), 7.55 (d, *J* = 16.0 Hz, 1H, H_{15}), 7.28 (m, 2H, H_{12}), 7.15 (s, 1H, H_6), 6.73 (d, *J* = 1.9 Hz, 1H, H_{22}), 6.61 (d, *J* = 8.5 Hz, 2H, H_{13}), 6.57 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.23 (d, *J* = 16.0 Hz, 1H, H_{16}), 3.77 (s, 3H, H_{18}), 2.2 (s, 3H, H_7), 2.19 (s, 3H, H_{10}), 2.09 (s, 3H, H_{26}), 2.05 (s, 3H, H_{27}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.4 (C_9), 167.8 (C_{17}), 160.1 (C_{11}), 147.0 (C_2), 144.5 (C_{15}), 139.5 (C_{20}), 135.3 (C_5), 134.1 (C_{19}), 133.1 (C_3), 130.8 (C_{22}), 129.5 (C_{13}), 128.9 (C_{24}), 127.9 (C_{14}), 126.9 (C_{23}), 122.9 (C_1), 122.6 (C_{21}), 122.6 (C_4), 121.2 (C_6), 115.8 (C_{13}), 115.6 (C_{12}), 51.7 (C_{18}), 24.8 (C_{10}), 20.4 (C_{27}), 17.9 (C_{26}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3310, 2947, 1713, 1632, 1602, 1551, 1505, 1470, 1434, 1369, 1325, 1276, 1229, 1197, 1166, 1107, 1035, 982, 864, 831, 735, 702, 610.

HRMS (ESI^+): *m/z* calculated for $C_{27}H_{29}O_4N_2^+$, $[M+H]^+$ = 445.2122; *m/z* found = 445.2118. Δ = -0.95 ppm.

(*E*)-2-Acetamido-5-(4-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 126:



Compound **126** was prepared according to **General Procedure C** using methyl (*E*)-3-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)acrylate **125** (333 mg, 0.75 mmol, 1 eq.) to give the title compound as a red solid (283 mg, 73%).

m.p. = 180-183 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.76 (s, 1H, H_8), 8.44 (d, *J* = 2.4 Hz, 1H, H_6), 7.93 (d, *J* = 1.9 Hz, 1H, H_{24}), 7.90 – 7.83 (m, 2H, H_{13}), 7.81 – 7.74 (m, 2H, H_{12}), 7.71 (d, *J* = 16.1 Hz, 1H, H_{15}), 7.43 (dd, *J* = 2.5, 1.0 Hz, 1H, H_4), 7.30 (dt, *J* = 1.9, 0.8 Hz, 1H, H_{22}), 6.64 (d, *J* = 16.1 Hz, 1H, H_{16}), 3.77 (s, 3H, H_{18}), 2.49 (s, 3H, H_{26}), 2.14 (s, 3H, H_{10}), 2.13 (s, 3H, H_7), 2.12 (s, 3H, H_{25}).

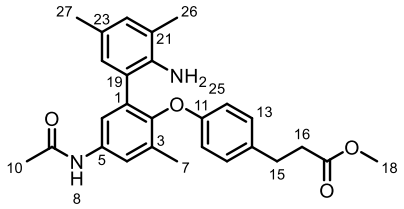
^{13}C (126 MHz, $CDCl_3$) δ_C = 170.4 (C_9), 167.2 (C_{17}), 161.3 (C_{20}), 161.0 (C_{11}), 157.8 (C_2), 143.1 (C_5), 142.5 (C_{23}), 141.9 (C_{15}), 139.6 (C_{14}), 135.6 (C_{22}), 132.2 (C_{13}), 125.9 (C_{Ar}), 125.1 (C_{Ar}), 124.8 (C_{Ar}), 124.4 (C_{Ar}), 124.2 (C_{Ar}), 123.3 (C_{16}), 122.7 (C_{24}), 122.4 (C_{12}), 111.6 (C_6), 52.6 (C_{18}), 24.4 (C_{10}), 21.0 (C_{26}), 17.1 ($C_{7/25}$), 16.8 ($C_{7/25}$).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.7.

IR (film) ν_{max}/cm^{-1} **=** 3662, 2981, 2888, 2361, 2340, 1462, 1382, 1252, 1145, 1074, 954, 763, 668.

HRMS (ESI^+): *m*/*z* calculated for $C_{27}H_{26}O_4N^+$, $[M]^+$ = 428.1856; *m*/*z* found = 428.1852. Δ = -1.13 ppm.

Methyl 3-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)propanoate, 127:



Compound **127** was prepared according to **General Procedure B** using methyl 2-(4-(2-bromo-6-methyl-4-nitrophenoxy)phenyl)acetate **82** (788 mg, 2.00 mmol, 1 eq.). The crude residue was

purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.10) to give the title compound as a brown solid (490 mg, 55%).

m.p. = 51-54 °C.

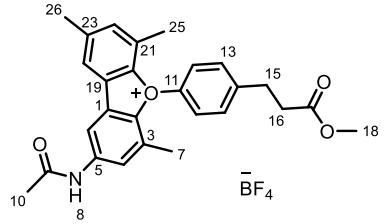
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.67 – 7.55 (m, 2H, H_4, H_8), 7.11 (d, *J* = 2.3 Hz, 1H, H_6), 6.89 (d, *J* = 8.4 Hz, 2H, H_{13}), 6.72 (d, *J* = 2.1 Hz, 1H, H_{22}), 6.56 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.52 – 6.46 (m, 2H, H_{12}), 3.63 (s, 3H, H_{18}), 3.44 – 3.23 (m, 2H, H_{25}), 2.79 (t, *J* = 7.8 Hz, 2H, H_{15}), 2.51 (t, *J* = 7.9 Hz, 2H, H_{16}), 2.16 (s, 3H, H_7), 2.12 (s, 3H, H_{10}), 2.08 (s, 3H, H_{26}), 2.05 (s, 3H, H_{27}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 173.5 (C_{17}), 168.6 (C_9), 156.8 (C_{11}), 147.5 (C_2), 139.5 (C_{20}), 135.1 (C_5), 134.1 (C_{19}), 133.3 (C_{14}), 133.1 (C_3), 130.5 (C_{22}), 129.0 (C_{24}), 128.9 (C_{13}), 126.7 (C_{23}), 123.5 (C_{21}), 122.6 (C_4), 122.4 (C_1), 121.2 (C_6), 115.4 (C_{12}), 51.7 (C_{18}), 36.0 (C_{16}), 30.1 (C_{15}), 24.5 (C_{10}), 20.3 (C_{27}), 17.9 (C_{26}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3658, 3376, 2981, 2020, 1712, 1610, 1549, 1506, 1469, 1369, 1288, 1255, 1222, 1168, 1103, 1072, 955, 873, 847, 768, 699, 640, 619, 610.

HRMS (ESI^+): *m/z* calculated for $C_{27}H_{31}O_4N_2^+$, $[M+H]^+$ = 447.2278; *m/z* found = 447.2272. Δ = -1.41 ppm.

2-Acetamido-5-(4-(3-methoxy-3-oxopropyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 128:



Compound **128** was prepared according to **General Procedure C** using methyl 3-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)propanoate **127** (223 mg, 0.50 mmol, 1 eq.) to give the title compound as a red solid (193 mg, 74%).

m.p. = 98-102 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.74 (s, 1H, H_8), 8.42 (d, *J* = 2.3 Hz, 1H, H_6), 7.94 – 7.90 (m, 1H, H_{24}), 7.67 – 7.62 (m, 2H, H_{12}), 7.52 – 7.48 (m, 2H, H_{13}), 7.42 (dd, *J* = 2.5, 0.9 Hz, 1H, H_4), 7.29 (dd, *J* = 2.0, 0.9 Hz, 1H, H_{22}), 3.59 (s, 3H, H_{18}), 3.01 (t, *J* = 7.6 Hz, 2H, H_{15}), 2.65 (t, *J* = 7.5 Hz, 2H, H_{16}), 2.49 (s, 3H, H_{26}), 2.13 (s, 3H, H_{10}), 2.09 (s, 3H, H_7), 2.08 (s, 3H, H_{25}).

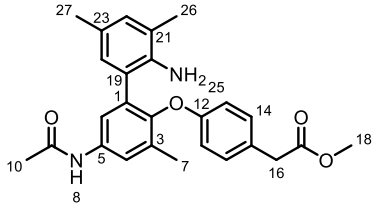
^{13}C (126 MHz, $CDCl_3$) δ_C = 173.5 (C_{17}), 170.3 (C_9), 161.0 (C_{20}), 159.4 (C_{11}), 157.6 (C_2), 147.3 (C_{14}), 142.9 (C_{23}), 142.3 (C_5), 135.6 (C_{22}), 132.6 (C_{13}), 125.9 (C_{Ar}), 125.0 (C_{Ar}), 124.7 (C_{Ar}), 124.3 (C_{Ar}), 124.2 (C_4), 122.5 (C_{24}), 121.6 (C_{12}), 111.5 (C_6), 52.1 (C_{18}), 35.6 (C_{16}), 30.9 (C_{15}), 24.4 (C_{10}), 21.0 (C_{10}), 17.1 ($C_{7/25}$), 16.8 ($C_{7/25}$).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.7.

IR (film) ν_{max}/cm^{-1} **=** 3649, 2981, 2884, 2362, 1734, 1559, 1490, 1459, 1384, 1253, 1150, 1071, 955, 855, 624.

HRMS (ESI^+): *m/z* calculated for $C_{27}H_{28}O_4N^+$, $[M]^+$ = 430.2013; *m/z* found = 430.2013. Δ = 0.07 ppm.

Methyl 2-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)acetate, 129:



Compound **129** was prepared according to **General Procedure B** using methyl 2-(4-(2-bromo-6-methyl-4-nitrophenoxy)phenyl)acetate **83** (258 mg, 0.68 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 50:50, R_f = 0.30) to give the title compound as a brown solid (289 mg, 98%).

m.p. = 104-106 °C.

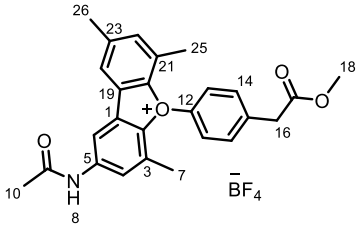
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.69 (s, 1H, H_8), 7.57 (d, *J* = 2.7 Hz, 1H, H_4), 7.12 (d, *J* = 2.7 Hz, 1H, H_6), 7.01 – 6.94 (m, 2H, H_{14}), 6.72 (d, *J* = 2.1 Hz, 1H, H_{22}), 6.57 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.56 – 6.50 (m, 2H, H_{13}), 3.64 (s, 3H, H_{18}), 3.46 (s, 2H, H_{16}), 3.45 – 3.23 (m, 2H, H_{25}), 2.15 (s, 3H, H_7), 2.09 (s, 3H, H_{10}), 2.07 (s, 3H, H_{26}), 2.05 (s, 3H, H_{27}).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 172.4 (C_{17}), 168.6 (C_9), 157.4 (C_{12}), 147.3 (C_2), 139.5 (C_{20}), 135.2 (C_5), 134.1 (C_{Ar}), 130.1 (C_{Ar}), 130.6 (C_{22}), 130.0 (C_{14}), 129.0 (C_{24}), 126.8 (C_{15}), 123.5 (C_{Ar}), 122.5 (C_4), 122.5 (C_{Ar}), 121.2 (C_6), 115.5 (C_{13}), 52.0 (C_{18}), 40.3 (C_{16}), 24.5 (C_{10}), 20.3 (C_{27}), 17.8 (C_{26}), 17.1 (C_7). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} **=** 3019, 1737, 1667, 1506, 1222, 860.

HRMS (MSS^+) = calculated for $C_{26}H_{29}O_4N_2^+$, $[M+H]^+$ = 433.2122; *m/z* found = 433.2113, Δ = -1.96 ppm.

2-Acetamido-5-(4-(2-methoxy-2-oxoethyl)phenyl)-4,6,8-trimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 130:



Compound **130** was prepared according to **General Procedure C** using methyl 2-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)phenyl)acetate **129** (133 mg, 0.31 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 50:50, R_f = 0.30) to give the title compound as a brown solid (121 mg, 78%).

m.p. = 142-144 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 8.80 (s, 1H, H_8), 8.42 (d, *J* = 2.4 Hz, 1H, H_6), 7.94 – 7.90 (m, 1H, H_{24}), 7.72 – 7.66 (m, 2H, H_{13}), 7.59 – 7.52 (m, 2H, H_{14}), 7.45 – 7.41 (m, 1H, H_4), 7.32 – 7.28 (m, 1H, H_{22}), 3.78 (s, 2H, H_{16}), 3.66 (s, 3H, H_{18}), 2.49 (s, 3H, H_{26}), 2.14 (s, 3H, H_{10}), 2.10 (s, 3H, $H_{7/25}$), 2.10 (s, 3H, $H_{7/25}$).

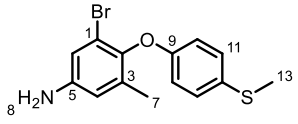
^{13}C (126 MHz, $CDCl_3$) δ_C = 171.8 (C_{17}), 170.6 (C_9), 161.1 (C_{20}), 159.8 (C_{12}), 157.7 (C_2), 142.9 (C_{Ar}), 142.3 (C_5), 140.8 (C_{15}), 135.6 (C_{22}), 133.8 (C_{14}), 125.9 (C_{Ar}), 125.0 (C_{Ar}), 124.7 (C_4), 124.4 (C_{Ar}), 124.3 (C_{Ar}), 122.6 (C_{24}), 121.6 (C_{13}), 111.6 (C_6), 52.8 (C_{18}), 40.3 (C_{16}), 24.4 (C_{10}), 21.0 (C_{26}), 17.1 (C_7), 16.8 (C_{25}).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -150.4.

IR (film) ν_{max}/cm^{-1} **=** 3655, 2358, 1462, 1382, 1252, 1152, 1072, 954, 816.

HRMS (ESI$^+$): calculated for $C_{26}H_{26}NO_4^+$, $[M]^+$ = 416.1856; *m/z* found = 416.1851, Δ = -1.13 ppm.

3-Bromo-5-methyl-4-(4-(methylthio)phenoxy)aniline, 131a:



(4-(2-Bromo-6-methyl-4-nitrophenoxy)phenyl)(methyl)sulfane **84** (708 mg, 2.00 mmol, 1 eq.) was dissolved in MeCN:MeOH:AcOH (1:1:1, 40 mL). Fe (168 mg, 3.00 mmol, 1.5 eq.) was added and the reaction mixture was stirred at 50 °C. After 4 h the mixture was cooled to r.t., the organic layer was washed with $NaHCO_3$ (sat. aq., 10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 20:80, R_f = 0.4) to give the title compound as a yellow solid (594 mg, 86%).

m.p. = 82-85 °C.

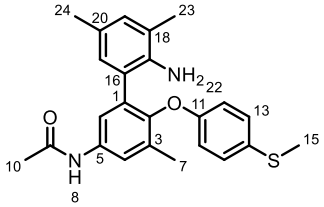
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.24 – 7.20 (m, 2H, H_{11}), 6.80 (d, *J* = 3.0 Hz, 1H, H_6), 6.76 – 6.71 (m, 2H, H_{10}), 6.53 – 6.49 (m, 1H, H_4), 3.65 (s, 2H, H_8), 2.44 (s, 3H, H_{13}), 2.07 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 156.4 (C_9), 144.5 (C_2), 142.0 (C_5), 134.2 (C_3), 130.1 (C_{12}), 129.8 (C_{11}), 118.0 (C_1), 117.2 (C_6), 117.0 (C_4), 115.5 (C_{10}), 17.7 (C_{13}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3371, 3028, 2919, 1607, 1573, 1487, 1474, 1437, 1317, 1274, 1224, 1166, 1096, 1009, 969, 860, 824, 783, 621.

HRMS (ESI$^+$): calculated for $C_{14}H_{15}BrNO_4S^+$, $[M]^+$ = 324.0052; *m/z* found = 324.0053, Δ = 0.36 ppm.

N-(2'-amino-3',5,5'-trimethyl-6-(4-(methylthio)phenoxy)-[1,1'-biphenyl]-3-yl)acetamide, 131:



3-Bromo-5-methyl-4-(4-(methylthio)phenoxy)aniline **131a** (391 mg, 1.20 mmol, 1 eq.) was dissolved in CH_2Cl_2 (6 mL) and Ac_2O (341 μL, 3.61 mmol, 3 eq.) was added. After 4 h, $NaHCO_3$ (sat. aq., 18 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 6 mL). The organic extracts were washed with $NaHCO_3$ (sat. aq., 12 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue, 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (446 mg, 1.80 mmol, 1.50 eq.) as a solution in PhMe (7 mL), and water (12 mL/mmol) were sequentially added to $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (49 mg, 0.60 mmol, 5 mol%) and Na_2CO_3 (510 mg, 4.81 mmol, 4 eq.) in PhMe (5 mL) under N_2 at r.t.. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 12 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.1) to give the title compound as a brown solid (268 mg, 66%).

m.p. = 135-137 °C.

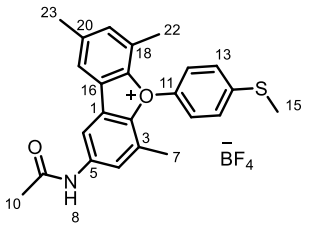
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.61 (d, *J* = 3.00 Hz, 1H, H_4), 7.30 (s, 1H, H_8), 7.11 (d, *J* = 3.00 Hz, 1H, H_6), 7.07 – 7.02 (m, 2H, H_{12}/H_{13}), 6.74 (d, *J* = 2.00 Hz, 1H, H_{19}), 6.57 (d, *J* = 2.00 Hz, 1H, H_{21}), 6.56 – 6.51 (m, 2H, H_{12}/H_{13}), 3.45 (s, 2H, H_{22}), 2.37 (s, 3H, H_{15}), 2.18 (s, 3H, H_7), 2.15 (s, 3H, H_{10}), 2.09 (s, 3H, H_{23}), 2.07 (s, 3H, H_{24}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.4 (C_9), 156.8 (C_{11}), 147.4 (C_2), 139.6 (C_{17}), 135.1 (C_5), 134.2 (C_{16}), 133.2 (C_3), 130.7 (C_{21}), 129.7 (C_{14}), 129.5 (C_{13}), 129.0 (C_{19}), 126.8 (C_{20}), 123.2 (C_1), 122.6 (C_4), 122.5 (C_{18}), 121.2 (C_6), 116.1 (C_{12}), 24.6 (C_{10}), 20.4 (C_{24}), 17.9 ($C_{7/23}$), 17.8 ($C_{7/23}$), 17.1 (C_{15}).

IR (film) ν_{max}/cm^{-1} = 3661, 2980, 2888, 1573, 1530, 1461, 1432, 1381, 1344, 1261, 1213, 1166, 1089, 948, 898, 843.

HRMS (ESI^+) = calculated for $C_{24}H_{27}O_2N_2S^+$, $[M+H]^+$ = 407.1788; *m/z* found = 407.1791, Δ = -1.66 ppm.

2-Acetamido-4,6,8-trimethyl-5-(4-(methylthio)phenyl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 132:



Compound **132** was prepared according to **General Procedure C** using *N*-(2'-amino-3',5,5'-trimethyl-6-(4-(methylthio)phenoxy)-[1,1'-biphenyl]-3-yl)acetamide **131** (203 mg, 0.50 mmol, 1 eq.), HBF_4 (48% aq., 0.33 mL, 1.50 mmol, 5 eq.), ^{t}BuONO (0.30 mL, 1.50 mmol, 1 eq.), CH_2Cl_2 (1 mL) and IPA (1 mL) to give the title compound as a red solid (201 mg, 84%)

m.p. = 173-177 °C.

^{1}H (500 MHz, CD_3CN) δ_H = 8.80 (s, 1H, H_8), 8.40 (d, *J* = 2.5 Hz, 1H, H_6), 7.91 – 7.87 (m, 1H, H_{21}), 7.67 – 7.59 (m, 2H, $H_{12/13}$), 7.47 – 7.40 (m, 3H, H_4, $H_{12/13}$), 7.32 – 7.27 (m, 1H, H_{19}), 2.53 (s, 3H, H_{15}), 2.48 (s, 3H, H_{23}), 2.13 (s, 3H, H_{10}), 2.13 (s, 6H, H_7, H_{22}).

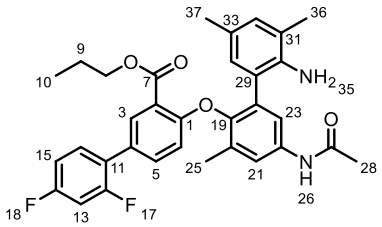
^{13}C (126 MHz, CD_3CN) δ_C = 170.4 (C_9), 160.9 (C_{17}), 157.7 (C_{11}), 157.5 (C_2), 146.3 (C_{14}), 142.7 (C_5), 142.1 (C_{20}), 135.4 (C_{19}), 128.3 ($C_{12/13}$), 125.7 (C_{Ar}), 124.8 (C_{Ar}), 124.5 (C_4), 124.2 (C_{Ar}), 124.1 (C_{Ar}), 122.4 (C_{21}), 121.8 ($C_{12/13}$), 111.4 (C_6), 24.2 (C_{10}), 20.9 (C_{23}), 17.0 ($C_{7/22}$), 16.7 ($C_{7/22}$), 15.2 (C_{15}).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -150.9.

IR (film) ν_{max}/cm^{-1} **=** 3791, 3662, 2981, 2887, 2357, 1565, 1550, 1462, 1382, 1252, 1153, 1072, 954, 816, 750.

HRMS (ESI^+) = calculated for $C_{24}H_{24}O_2NS^+$, $[M]^+$ = 390.1522; *m/z* found = 390.1523, Δ = 0.30 ppm.

Propyl 4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-2',4'-difluoro-[1,1'-biphenyl]-3-carboxylate, 133:



Compound **133** was prepared according to **General Procedure B** using propyl 4-(2-bromo-6-methyl-4-nitrophenoxy)-2',4'-difluoro-[1,1'-biphenyl]-3-carboxylate **85** (506 mg, 1.00 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 50:50, R_f = 0.1) to give the title compound as a yellow solid (253 mg, 45%).

m.p. = 80-82 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.27 (s, 1H, H_{26}), 7.84 – 7.81 (m, 1H, H_3), 7.59 (d, *J* = 2.8 Hz, 1H, H_{21}), 7.33 – 7.29 (m, 1H, H_5), 7.29 – 7.24 (m, 1H, H_5), 7.20 (s, 1H, H_{23}), 6.94 – 6.89 (m, 1H, H_{15}), 6.87 (ddd, *J* = 11.1, 8.8, 2.6 Hz, 1H, H_{13}), 6.72 (s, 1H, H_{32}), 6.61 (s, 1H, H_{34}), 6.50 (d, *J* = 8.7

Hz, 1H, H_6), 4.27 (t, *J* = 6.6 Hz, 2H, H_8), 3.79 (s, 2H, H_{35}), 2.21 (s, 3H, H_{25}), 2.12 (s, 3H, H_{28}), 2.08 (s, 3H, H_{37}), 2.07 – 2.04 (m, 3H, H_{36}), 1.79 (h, *J* = 7.1 Hz, 2H, H_9), 1.04 (t, *J* = 7.4 Hz, 3H, H_{10}).

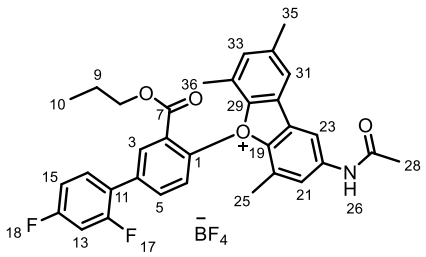
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 168.9 (C_{27}), 165.5 (C_7), 162.2 (dd, *J* = 249.1, 11.6 Hz, H_{14}), 159.7 (dd, *J* = 250.2, 11.9 Hz, H_{12}), 157.3 (C_1), 146.4 (C_{19}), 139.2 (C_{30}), 135.8 (C_{22}), 133.6 (C_{Ar}), 133.4 (C_5), 132.5 (C_{20}), 132.0 (d, *J* = 2.7 Hz, H_3), 131.1 (dd, *J* = 9.4, 4.7 Hz, H_{16}), 130.8 (C_{32}), 129.2 (C_{34}), 127.7 (C_{Ar}), 127.5 (d, *J* = 21.3 Hz, C_4), 123.9 (dd, *J* = 13.6, 3.8 Hz, C_{11}), 123.3 (C_{23}), 122.6 (C_{Ar}), 121.5 (C_{Ar}), 119.6 (C_2), 115.2 (C_6), 111.7 (dd, *J* = 21.1, 3.7 Hz, C_{15}), 104.4 (t, *J* = 25.9 Hz, C_{13}), 66.6 (C_8), 24.3 (C_{28}), 22.2 (C_9), 20.3 (C_{37}), 17.8 (C_{36}), 16.8 (C_{25}), 10.7 (C_{10}). One aromatic carbon peak was not observed.

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -111.1, -113.8.

IR (film) ν_{max}/cm^{-1} **=** 3651, 2982, 2971, 2883, 2359, 2343, 1685, 1617, 1558, 1473, 1382, 1251, 1151, 1079, 957, 815, 668, 653, 645, 638, 632, 628, 619.

HRMS (ESI^+) = *m*/*z* calculated for $C_{33}H_{33}O_4N_2F_2^+$, $[M+H]^+$ = 559.2403; *m*/*z* found = 559.2399. Δ = -0.65 ppm.

2-Acetamido-5-(2',4'-difluoro-3-(propoxycarbonyl)-[1,1'-biphenyl]-4-yl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 134:



Compound **134** was prepared according to **General Procedure C** using propyl 4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-2',4'-difluoro-[1,1'-biphenyl]-3-carboxylate **133** (152 mg, 0.27 mmol, 1 eq.) to give the title compound as a red solid (73 mg, 43%).

m.p. = 204-206 °C.

^{1}H (500 MHz, CD_3CN) δ_H = 8.82 (d, *J* = 4.5 Hz, 1H, H_{26}), 8.48 – 8.43 (m, 2H, H_3, H_{23}), 8.01 (ddd, *J* = 9.0, 2.5, 1.0 Hz, 1H, H_5), 7.95 (q, *J* = 2.5 Hz, 1H, H_{31}), 7.74 (d, *J* = 9.0 Hz, 1H, H_6), 7.67 (td, *J* = 9.0, 6.5 Hz, 1H, H_{16}), 7.49 (d, *J* = 2.5 Hz, 1H, H_{21}), 7.32 (s, 1H, H_{33}), 7.21 – 7.11 (m, 2H, H_{13}, H_{16}), 4.27 (t, *J* = 6.5 Hz, 2H, H_8), 2.51 – 2.48 (m, 3H, H_{35}), 2.14 (s, 3H, H_{28}), 2.02 (2 x s, 2 x 3H, H_{25}, H_{36}), 1.66 – 1.56 (m, 2H, H_9), 0.82 (t, *J* = 7.5 Hz, 3H, H_{10}).

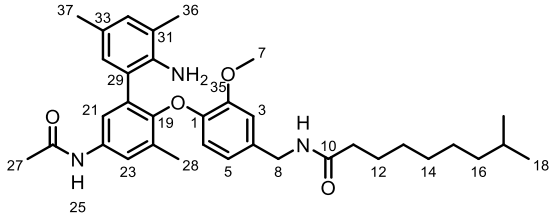
^{13}C (126 MHz, CD_3CN) δ_C = 170.4 (C_{27}), 164.5 (dd, *J* = 250.0, 12.0 Hz, $C_{12/14}$), 162.8 (C_7), 160.2 (C_1), 156.8 (C_{29}), 156.0 (C_{19}), 142.5 (C_{32}), 142.0 (C_{22}), 140.9 (C_4), 137.7 (d, *J* = 3.5 Hz, C_5), 136.1 (C_{33}), 134.6 (d, *J* = 4.0 Hz, C_3), 133.3 (dd, *J* = 10.0, 4.0 Hz, C_{16}), 125.9 (C_2), 124.8 (C_{Ar}), 124.7 (C_{Ar}), 124.4 (d, *J* = 2.0 Hz, C_{21}), 124.2 (C_{Ar}), 123.7 (C_{Ar}), 123.6 (C_6), 122.7 (C_{31}), 122.6 (dd, *J* = 13.0, 3.8 Hz, C_{11}), 113.4 (dd, *J* = 21.5, 3.5 Hz, C_{15}), 111.7 (C_{23}), 105.6 (t, *J* = 26.5 Hz, C_{13}), 69.6 (C_8), 24.4 (C_{28}), 22.3 (C_9), 20.9 (C_{35}), 16.8 ($C_{25/36}$), 16.5 ($C_{25/36}$), 10.4 (C_{10}).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -109.16 – -109.51 (m), -114.32 (m), -151.2.

IR (film) ν_{max}/cm^{-1} = 3648, 2982, 2971, 2883, 2360, 2343, 2261, 1726, 1701, 1653, 1617, 1559, 1511, 1473, 1386, 1319, 1259, 1226, 1146, 1068, 1037, 969, 857, 730, 697, 668, 638, 628, 613.

HRMS (ESI^+)**:** *m*/*z* calculated for $C_{33}H_{30}O_4NF_2^+$, $[M]^+$ = 542.2137; *m*/*z* found = 542.2132, Δ = -1.01 ppm.

***N*-(4-((5-Acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-3-methoxybenzyl)-8-methylnonanamide, 135:**



Compound **135** was prepared according to **General Procedure B** using propyl 4-(2-bromo-6-methyl-4-nitrophenoxy)-2',4'-difluoro-[1,1'-biphenyl]-3-carboxylate **85** (526 mg, 0.98 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 50:50, R_f = 0.2) to give the title compound as a brown solid (236 mg, 41%).

m.p. = 78-82 °C.

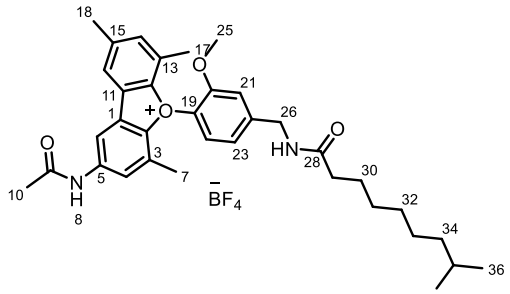
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.05 (s, 1H, H_{25}), 7.54 (d, *J* = 2.7 Hz, 1H, H_{23}), 7.13 (d, *J* = 2.7 Hz, 1H, H_{21}), 6.66 (d, *J* = 2.1 Hz, 1H, H_{32}), 6.57 (d, *J* = 2.0 Hz, 1H, H_3), 6.56 – 6.51 (m, 1H, H_{34}), 6.46 (dd, *J* = 8.2, 2.0 Hz, 1H, H_5), 6.27 (d, *J* = 8.2 Hz, 1H, H_6), 5.84 (t, *J* = 5.5 Hz, 1H, H_9), 4.19 (d, *J* = 4.9 Hz, 2H, H_8), 3.63 (s, 3H, H_7), 3.38 (s, 2H, H_{35}), 2.16 (s, 3H, H_{28}), 2.12 (t, *J* = 7.6 Hz, 2H, H_{11}), 2.06 (s, 3H, H_{27}), 2.02 (s, 3H, H_{36}), 2.01 (s, 3H, H_{37}), 1.59 (p, *J* = 7.6 Hz, 2H, H_{12}), 1.48 (hept, *J* = 6.7 Hz, 1H, H_{17}), 1.32 – 1.18 (m, 6H, H_{13}, H_{14}, H_{15}), 1.12 (q, *J* = 6.9 Hz, 2H, H_{16}), 0.83 (d, *J* = 6.9 Hz, 6H, H_{18}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 173.1 (C_{10}), 168.8 (C_{26}), 148.9 (C_2), 147.8 (C_{19}), 147.3 (C_1), 139.6 (C_{30}), 135.3 (C_{22}), 133.5 ($C_{20/29}$), 132.8 (C_{24}), 131.9 (C_4), 130.3 (C_{32}), 129.0 (C_{34}), 126.5 (C_{33}), 123.4 ($C_{20/29}$), 122.4 (C_{23}), 122.4 (C_{31}), 121.2 (C_{21}), 119.7 (C_5), 114.7 (C_6), 112.0 (C_3), 56.0 (C_7), 43.3 (C_8), 39.0 (C_{16}), 36.8 (C_{13}), 29.7 (C_{15}), 29.4 (C_{16}), 28.0 (C_{17}), 27.3 (C_{15}), 25.9 (C_{14}), 24.3 (C_{27}), 22.7 (C_{18}), 20.3 (C_{37}), 17.8 (C_{36}), 16.8 (C_{28}).

IR (film) ν_{max}/cm^{-1} **=** 3291, 2925, 2855, 2360, 2341, 1645, 1600, 1551, 1509, 1467, 1421, 1368, 1265, 1215, 1160, 1128, 1035, 909, 863, 813, 731, 647.

HRMS (ESI^+): *m/z* calculated for $C_{35}H_{48}O_4N_3^+$, $[M+H]^+$ = 574.3639; *m/z* found = 574.3635. Δ = -0.71 ppm.

2-Acetamido-5-(2-methoxy-4-((8-methylnonanamido)methyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate, 136:



Compound **136** was prepared according to **General Procedure C** using n-(4-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-3-methoxybenzyl)-8-methylnonanamide **135** (215 mg, 0.38 mmol, 1 eq.) to give the title compound as a red solid (211 mg, 86%).

m.p. = 140-145 °C.

^{1}H (500 MHz, CD_3CN) δ_H = 8.76 (s, 1H, H_8), 8.39 (d, *J* = 2.2 Hz, 1H, H_6), 7.89 (d, *J* = 1.9 Hz, 1H, H_{16}), 7.58 (d, *J* = 8.7 Hz, 1H, H_{24}), 7.44 (d, *J* = 2.3 Hz, 1H, H_4), 7.37 (s, 1H, H_{21}), 7.28 (s, 1H, H_{14}), 7.10 – 7.01 (m, 1H, H_{23}), 4.45 (d, *J* = 6.0 Hz, 2H, H_{26}), 3.83 (s, 3H, H_{25}), 2.48 (s, $3H_{18}$), 2.28 (t, *J* = 7.5 Hz, 1H, H_{29}), 2.13 (s, 3H, H_{10}), 2.06 (s, 3H, $H_{7/17}$), 2.06 (s, 2H, $H_{7/17}$), 1.59 (p, *J* = 7.2 Hz, 2H, H_{30}), 1.55 – 1.42 (m, 1H, H_{35}), 1.26 (m, 6H, H_{31}, H_{32}, H_{33}), 1.19 – 1.07 (m, 2H, H_{34}), 0.84 (d, *J* = 6.6 Hz, 6H, H_{36}).

^{13}C (126 MHz, CD_3CN) δ_C = 175.7 (C_{28}), 170.3 (C_9), 160.6 (C_{12}), 157.2 (C_2), 151.0 (C_{20}), 146.8 (C_{19}), 146.3 (C_{22}), 142.4 (C_{15}), 141.9 (C_5), 135.5 (C_{14}), 125.0 (C_{Ar}), 124.6 (C_{Ar}), 124.2 (C_{Ar}), 123.9

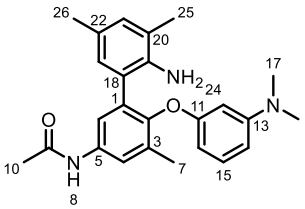
(C_{Ar}), 123.8 (C_4), 123.1 (C_{Ar}), 122.4 (C_{16}), 121.6 (C_{23}), 115.2 (C_{24}), 111.4 (C_6), 57.8 (C_{25}), 43.5 (C_{26}), 39.6 (C_{34}), 36.3 (C_{29}), 30.2 (C_{31}), 29.8 (C_{32}), 28.7 (C_{33}), 27.9 (C_{35}), 26.5 (C_{30}), 24.4 (C_{10}), 22.9 (C_{36}), 21.0 (C_{18}), 16.1 ($C_{7/17}$), 15.8 ($C_{7/17}$).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.5.

IR (film) ν_{max}/cm^{-1} **=** 3368, 2928, 2360, 2342, 1644, 1619, 1559, 1492, 1464, 1424, 1385, 1266, 1066, 1040, 870, 729, 701, 669, 642, 619.

HRMS (ESI^+): *m/z* calculated for $C_{35}H_{45}O_4N_2^+$, $[M]^+$ = 557.3374; *m/z* found, = 557.3367. Δ = -1.28 ppm.

***N*-(2'-Amino-6-(3-(dimethylamino)phenoxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide, 137:**



Compound **137** was prepared according to **General Procedure B** using 3-(2-bromo-6-methyl-4-nitrophenoxy)-N,N-dimethylaniline **89** (351 mg, 1.00 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:Pentane, 40:60, R*f*= 0.10) to give the title compound as a brown solid (250 mg, 62%).

m.p. = 160-163 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.60 (d, *J* = 2.50 Hz, 1H, H_4), 7.23 (s, 1H, H_8), 7.10 (d, *J* = 2.50 Hz, 1H, H_6), 6.93 (t, *J* = 8.00 Hz, 1H, H_{15}), 6.74 (d, *J* = 2.00 Hz, 1H, H_{21}), 6.64 (d, *J* = 2.00 Hz, 1H, H_{23}), 6.26 (dd, *J* = 8.00, 2.50 Hz, 1H, H_{16}), 6.06 (t, *J* = 2.50 Hz, 1H, H_{12}), 5.95 (dd, *J* = 8.00, 2.50

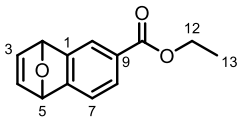
Hz, 1H, H_{14}), 2.81 (s, 6H, H_{17}), 2.21 (s, 3H, H_7), 2.15 (d, *J* = 2.00 Hz, 3H, H_{10}), 2.09 (s, 6H, H_{25}, H_{26}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.3 (C_9), 159.4 (C_{11}), 151.7 (C_{13}), 147.8 (C_2), 139.7 (C_{19}), 134.8 (C_5), 134.3 (C_{18}), 133.4 (C_3), 130.6 (C_{21}), 129.4 (C_{15}), 129.2 (C_{23}), 126.8 (C_{22}), 123.7 (C_1), 122.5 (C_4), 122.4 (C_{20}), 121.0 (C_6), 106.5 (C_{16}), 104.1 (C_{14}), 100.9 (C_{12}), 40.8 (C_{17}), 24.7 (C_{10}), 20.4 (C_{26}), 17.9 (C_{25}), 17.2 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3674, 3650, 2998, 2981, 2969, 2886, 1613, 1474, 1460, 1395, 1381, 1251, 1236, 1166, 1150, 1089, 1071, 999, 969, 954, 940, 830, 627.

HRMS (ESI^+) = *m*/*z* calculated for $C_{23}H_{30}O_2N_3^+$, $[M]^+$ = 404.2333; *m*/*z* found = 404.2334. Δ = 0.28 ppm.

Ethyl 1,4-dihydro-1,4-epoxynaphthalene-6-carboxylate, 139:



Compound **139** was prepared according to **General procedure D** using 2-acetamido-5-(4-(ethoxycarbonyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **110** (151 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 40:60, R_f = 0.5) to give the title compound as a yellow oil (61 mg, 94%).

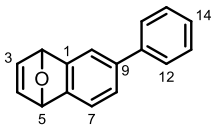
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.87 (dt, *J* = 7.2, 0.8 Hz, 1H, H_{10}), 7.76 (dd, *J* = 7.4, 1.4 Hz, 1H, H_8), 7.29 (dt, *J* = 7.4, 0.8 Hz, 1H, H_7), 7.04 (dd, *J* = 5.6, 1.9 Hz, 1H, H_3), 7.00 (dd, *J* = 5.6, 1.9 Hz, 1H, H_4), 5.75 (dt, *J* = 1.8, 0.8 Hz, 1H, H_5), 5.73 (dt, *J* = 1.8, 0.8 Hz, 1H, H_4), 4.34 (q, *J* = 7.1 Hz, 2H, H_{12}), 1.37 (t, *J* = 7.1 Hz, 3H, H_{13}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 166.5 (C_{10}), 154.4 (C_1), 149.6 (C_6), 143.4 (C_3), 142.5 (C_4), 128.1 (C_8), 127.7 (C_9), 120.7 (C_{10}), 120.0 (C_7), 82.2 ($C_{4/5}$), 82.2 ($C_{4/5}$), 61.0 (C_{12}), 14.4 (C_{13}).

IR (film) ν_{max}/cm^{-1} **=** 2981, 2928, 1710, 1617, 1595, 1464, 1420, 1390, 1367, 1349, 1287, 1254, 1193, 1168, 1141, 1102, 1072, 1020, 994, 912, 873, 846, 794, 768, 750, 742, 698, 664, 640.

HRMS (ESI^+): *m/z* calculated for $C_{13}H_{13}O_3^+$, $[M+H]^+$ = 217.0859; *m/z* found = 217.0860. Δ = 0.29 ppm.

6-Phenyl-1,4-dihydro-1,4-epoxynaphthalene, 148:



Compound **148** was prepared according to **General procedure D** using 5-([1,1'-biphenyl]-4-yl)-2-acetamido-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **112** (152 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f = 0.8) to give the title compound as a pale yellow oil (57 mg, 86%).

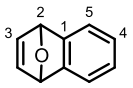
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.59 – 7.53 (m, 2H, H_{12}), 7.51 (d, *J* = 1.5 Hz, 1H, H_{10}), 7.44 (dd, *J* = 8.4, 6.9 Hz, 2H, H_{13}), 7.37 – 7.34 (m, 1H, H_{14}), 7.33 (d, *J* = 7.5 Hz, 1H, H_7), 7.22 (dd, *J* = 7.3, 1.6 Hz, 1H, H_8), 7.11 – 7.05 (m, 2H, H_3, H_4), 5.79 (d, *J* = 4.0 Hz, 2H, H_2, H_5).

^{13}C (126 MHz, $CDCl_3$) δ_C = 150.0 (C_1), 148.1 (C_6), 143.1 ($C_{3/4}$), 143.1 ($C_{3/4}$), 141.4 (C_{11}), 138.7 (C_9), 128.8 (C_{13}), 127.3 (C_{12}), 127.3 (C_{14}), 124.1 (C_8), 120.5 (C_7), 119.7 (C_{10}), 82.5 ($C_{2/5}$), 82.3 ($C_{2/5}$).

IR (film) ν_{max}/cm^{-1} **=** 3791, 3661, 2981, 2887, 2358, 1659, 1588, 1549, 1462, 1382, 1252, 1153, 1073, 954, 750.

HRMS (ESI$^+$): *m*/*z* calculated for $C_{16}H_{13}O^+$, $[M+H]^+$ = 221.0961; *m*/*z* found = 221.0963. Δ = 0.93 ppm.

1,4-Dihydro-1,4-epoxynaphthalene, 18:



Compound **18** was prepared according to **General Procedure D** using 2-acetamido-4,6,8-trimethyl-5-phenyl-5*H*-dibenzo[*b*,*d*]furan-5-ium tetrafluoroborate **114** (129 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f = 0.8) to give the title compound as a pale yellow solid (35 mg, 81%).

m.p. = 53-54 °C.

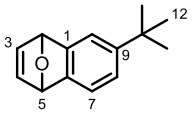
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.32 – 7.24 (m, 2H, H_5), 7.06 (t, *J* = 1.0 Hz, 2H, H_3), 7.00 (dd, *J* = 5.1, 3.0 Hz, 2H, H_4), 5.74 (t, *J* = 1.0 Hz, 2H, H_2).

^{13}C (126 MHz, $CDCl_3$) δ_C = 149.1 (C_1), 143.2 (C_3), 125.1 (C_4), 120.4 (C_5), 82.5 (C_2).

IR (film) ν_{max}/cm^{-1} **=** 3314, 3053, 2927, 2852, 1596, 1580, 1517, 1455, 1386, 1363, 1278, 1197, 1132, 1084, 1044, 1015, 991, 871, 846, 795, 773, 760, 741, 691, 636.

HRMS (ESI$^+$): *m*/*z* calculated for $C_{10}H_9O^+$, $[M+H]^+$ = 145.0648; *m*/*z* found = 145.0649. Δ = 0.47 ppm.

6-(*tert*-Butyl)-1,4-dihydro-1,4-epoxynaphthalene, 154:



Compound **154** was prepared according to **General procedure D** using 2-acetamido-5-(3-(*tert*-butyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **124** (146 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 15:85, R_f = 0.7) to give the title compound as a pale yellow oil (52 mg, 87%).

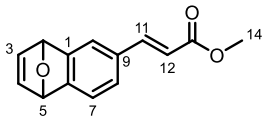
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.35 (d, *J* = 1.7 Hz, 1H, H_{10}), 7.18 (d, *J* = 7.5 Hz, 1H, H_7), 7.03 (d, *J* = 0.9 Hz, 2H, H_3, H_4), 6.99 (dd, *J* = 7.5, 1.7 Hz, 1H, H_8), 5.70 (t, *J* = 1.1 Hz, 2H, H_2, H_5), 1.31 (s, 9H, H_{12}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 149.0 (C_1), 148.4 (C_9), 146.0 (C_6), 143.1 ($C_{3/4}$), 143.0 ($C_{3/4}$), 121.3 (C_8), 119.7 (C_7), 118.3 (C_{10}), 82.6 ($C_{2/5}$), 82.3 ($C_{2/5}$), 34.8 (C_{11}), 31.6 (C_{12}).

IR (film) ν_{max}/cm^{-1} **=** 3012, 2960, 2360, 2342, 1723, 1477, 1409, 1364, 1262, 1099, 1018, 989, 870, 851, 838, 750, 730, 698, 668, 655, 633.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{17}O^+$, $[M+H]^+$ = 201.1274; *m/z* found = 201.1277. Δ = 1.31 ppm.

Methyl (*E*)-3-(1,4-dihydro-1,4-epoxynaphthalen-6-yl)acrylate, 155:



Compound **155** was prepared according to **General procedure D** using (*E*)-2-acetamido-5-(4-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **126** (155 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 30:70, R_f = 0.4) to give the title compound as a pale yellow oil (59 mg, 86%).

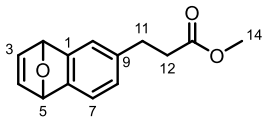
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.65 (d, *J* = 16.0 Hz, 1H, H_{11}), 7.44 (t, *J* = 1.0 Hz, 1H, H_{10}), 7.25 (d, *J* = 7.3 Hz, 1H, H_7), 7.12 (dd, *J* = 7.4, 1.5 Hz, 1H, H_8), 7.06 – 6.98 (m, 2H, H_3, H_4), 6.37 (d, *J* = 16.0 Hz, 1H, H_{12}), 5.72 (m, 2H, H_2, H_5), 3.79 (s, 3H, H_{14}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 167.6 (C_{13}), 151.6 (C_6), 150.1 (C_1), 144.9 (C_{11}), 143.1 ($C_{3/4}$), 142.7 ($C_{3/4}$), 131.8 (C_9), 127.1 (C_8), 120.6 (C_7), 118.7 (C_{10}), 117.3 (C_{12}), 82.2 (C_4, C_5), 51.8 (C_{14}).

IR (film) ν_{max}/cm^{-1} **=** 3775, 3660, 2981, 2888, 1711, 1639, 1549, 1462, 1382, 1263, 1169, 1073, 955, 836, 750, 700.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{13}O_3^+$, $[M+H]^+$ = 229.0859; *m/z* found = 229.0862. Δ = 1.27 ppm.

Methyl 3-(1,4-dihydro-1,4-epoxynaphthalen-6-yl)propanoate, 156:



Compound **156** was prepared according to **General procedure D** using 2-acetamido-5-(4-(3-methoxy-3-oxopropyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **128** (155 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 40:60, R_f = 0.6) to give the title compound as a pale yellow oil (37 mg, 54%).

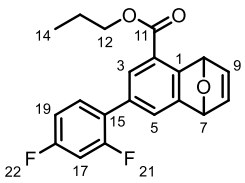
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.15 (d, *J* = 7.2 Hz, 1H, H_7), 7.11 (d, *J* = 1.5 Hz, 1H, H_{10}), 7.03 – 6.99 (m, 2H, H_3, H_4), 6.79 (dd, *J* = 7.2, 1.5 Hz, 1H, H_8), 5.71 – 5.66 (m, 2H, H_2, H_5), 3.66 (s, 3H, H_{14}), 2.89 (t, *J* = 7.9 Hz, 2H, H_{11}), 2.59 (t, *J* = 8.0 Hz, 2H, H_{12}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 173.4 (C_{13}), 149.7 (C_1), 147.1 (C_6), 143.2 ($C_{3/4}$), 142.9 ($C_{3/4}$), 137.7 (C_9), 124.7 (C_8), 120.9 (C_{10}), 120.3 (C_7), 82.4 ($C_{2/5}$), 82.3 ($C_{2/5}$), 51.7 (C_{14}), 35.9 (C_{12}), 30.9 (C_{11}).

IR (film) ν_{max}/cm^{-1} **=** 3011, 2952, 2241, 2186, 2160, 2007, 1734, 1436, 1366, 1281, 1198, 1168, 1088, 989, 870, 850, 749, 697, 643, 611.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{15}O_3^+$, $[M+H]^+$ = 231.1016; *m/z* found = 231.1018. Δ = 0.89 ppm.

Propyl 7-(2,4-difluorophenyl)-1,4-dihydro-1,4-epoxynaphthalene-5-carboxylate, 157:



Compound **157** was prepared according to **General procedure D** using 2-acetamido-5-(2',4'-difluoro-3-(propoxycarbonyl)-[1,1'-biphenyl]-4-yl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **134** (63 mg, 0.10 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f = 0.4) to give the title compound as a pale yellow oil (30 mg, 88%).

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.68 (t, *J* = 1.2 Hz, 1H, H_3), 7.53 (d, *J* = 1.7 Hz, 1H, H_5), 7.39 (td, *J* = 8.7, 6.4 Hz, 1H, H_{20}), 7.10 (m, 2H, H_8, H_9), 6.95 (tdd, *J* = 8.0, 2.3, 1.0 Hz, 1H, H_{19}), 6.91 (ddd, *J* = 10.5, 8.8, 2.6 Hz, 1H, H_{17}), 6.40 (dt, *J* = 1.8, 0.8 Hz, 1H, H_{10}), 5.79 (t, *J* = 1.3 Hz, 1H, H_7), 4.33 (t, *J* = 6.6 Hz, 2H, H_{12}), 1.88 – 1.76 (m, 2H, H_{13}), 1.06 (t, *J* = 7.4 Hz, 3H, H_{14}).

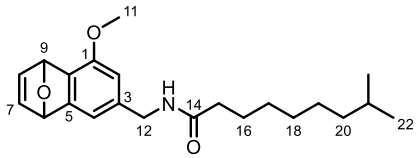
^{13}C (126 MHz, $CDCl_3$) δ_C = 165.9 (C_{11}), 162.6 (dd, *J* = 249.6, 11.9 Hz, C_{18}), 159.9 (dd, *J* = 250.7, 11.9 Hz, C_{16}), 151.8 (C_1), 150.8 (C_6), 143.9 (C_9), 142.5 (C_8), 132.5 (C_4), 131.6 (dd, *J* = 9.6, 4.7 Hz, C_{20}), 126.1 (d, *J* = 2.3 Hz, C_3), 124.6 (t, *J* = 3.3 Hz, C_5), 124.5 (d, *J* = 3.8 Hz, C_{15}), 124.3 (C_2), 111.8 (dd, *J* = 21.0, 3.8 Hz, C_{19}), 104.6 (t, *J* = 26.0 Hz, C_{17}), 82.9 (C_7), 82.0 (C_{10}), 67.0 (C_{12}), 22.3 (C_{13}), 10.8 (C_{14}).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -110.7 (d, *J* = 7.5 Hz), -113.2 (d, *J* = 7.5 Hz).

IR (film) ν_{max}/cm^{-1} **=** 3080, 2917, 2849, 2360, 2341, 1716, 1619, 1591, 1509, 1453, 1428, 1353, 1280, 1266, 1217, 1180, 1141, 1118, 1097, 1058, 1042, 1018, 969, 947, 910, 873, 846, 815, 786, 729, 694, 649, 623, 607.

HRMS (ESI^+) = *m*/*z* calculated for $C_{20}H_{17}F_2O_3^+$, $[M+H]^+$ = 343.1140; *m*/*z* found = 343.1137. Δ = -0.9 ppm.

***N*-((8-Methoxy-1,4-dihydro-1,4-epoxynaphthalen-6-yl)methyl)-8-methylnonanamide, 158:**



Compound **158** was prepared according to **General procedure D** using, 2-acetamido-5-(2-methoxy-4-((8-methylnonanamido)methyl)phenyl)-4,6,8-trimethyl-5*H*-dibenzo[*b,d*]furan-5-ium tetrafluoroborate **136** (61 mg, 0.10 mmol, 1 eq.). The crude residue was purified by semi-preparative HPLC (YMC AAmylose-SA (10 x 250 mm), 15% EtOH/Hexane, 5 mL/min) to give the title compound as a colourless oil (11 mg, 31%).

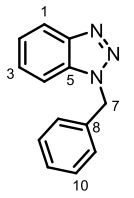
^{1}H (500 MHz, $CDCl_3$) δ = 7.05 (dd, *J* = 5.5, 1.8 Hz, 1H, H_8), 7.00 (dd, *J* = 5.6, 1.8 Hz, 1H, H_7), 6.86 (s, 1H, H_4), 6.50 (s, 1H, H_2), 5.94 – 5.90 (m, 1H, H_9), 5.65 (m, 2H, H_4, H_{15}), 4.36 (dd, *J* = 5.7, 1.6 Hz, 2H, H_{12}), 3.81 (s, 3H, H_{11}), 2.19 (t, *J* = 7.6 Hz, 2H, H_{15}), 1.64 (m, 2H, H_{16}), 1.51 (m, 1H, H_{21}), 1.37 – 1.21 (m, 6H, H_{17}, H_{18}, H_{19}), 1.14 (m, 2H, H_{20}), 0.86 (d, *J* = 6.6 Hz, 6H, H_{22}).

^{13}C (126 MHz, $CDCl_3$) δ = 173.0 (C_{14}), 153.0 (C_5), 152.6 (C_1), 143.2 (C_8), 142.9 (C_7), 138.1 (C_3), 134.6 (C_{10}), 113.7 (C_4), 110.4 (C_2), 82.6 (C_6), 80.2 (C_9), 56.0 (C_{11}), 43.7 (C_{12}), 39.1 (C_{20}), 37.0 (C_{15}), 29.8 (C_{17}), 29.5 (C_{18}), 28.1 (C_{21}), 27.4 (C_{16}), 25.9 (C_{16}), 22.8 (C_{22}).

IR (film) ν_{max}/cm^{-1} **=** 3855, 3725, 3650, 3297, 2981, 2929, 2889, 2361, 2342, 1647, 1605, 1541, 1463, 1383, 1293, 1252, 1146, 1071, 1000, 955, 850, 818, 745, 711, 685, 669, 656, 643, 617.

HRMS (ESI^+): *m/z* calculated for $C_{22}H_{32}NO_3^+$, $[M+H]^+$ = 358.2377; *m/z* found = 358.2373. Δ = -1.03 ppm.

1-Benzyl-1*H*-benzo[d][1,2,3]triazole, 114:



2-Acetamido-4,6,8-trimethyl-5-phenyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **114** (194 mg, 0.30 mmol, 1 eq.) was dissolved in MeCN (6 mL) in an oven-dried vial. Benzyl azide (188 μL, 1.50 mmol, 5 eq.) and K_3PO_4 (318 mg, 1.50 mmol, 5 eq.) were added sequentially and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted (CH_2Cl_2, 4 × 5 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90, R_f = 0.3) to give the title compound as a pale yellow solid (53 mg, 84%).

m.p. = 82-92 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H 8.08 (d, *J* = 8.2 Hz, 1H, H_1), 7.41 (dd, *J* = 2.5, 0.5 Hz, 1H, H_3), 7.37 (dd, *J* = 8.1, 1.6 Hz, 2H, H_2, H_4), 7.36 – 7.31 (m, 3H, H_{10}, H_{11}), 7.28 (dq, *J* = 7.8, 1.7 Hz, 2H, H_9), 5.86 (s, 2H, H_7).

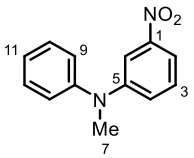
^{13}C (126 MHz, $CDCl_3$) δ_C = 146.2 (C_1), 134.8 (C_8), 133.0 (C_5), 129.2 (C_{10}), 128.7 (C_{11}), 127.8 (C_9), 127.7 (C_3), 124.3 (C_4), 120.2 (C_1), 109.9 (C_2), 52.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3821, 3735, 3628, 3032, 2980, 2918, 2850, 2360, 2341, 1717, 1615, 1523, 1496, 1456, 1386, 1263, 1226, 1159, 1094, 1071, 1028, 1001, 949, 914, 773, 747, 723, 696, 669, 623.

HRMS (ESI^+): *m/z* calculated for $C_{13}H_{12}N_3^+$, $[M+H]^+$ = 210.1026; *m/z* found = 210.1027. Δ = 0.78 ppm.

Data in accordance with the literature.[153]

***N*-Methyl-2-nitro-*N*-phenylaniline, 168:**



K_3PO_4 (318 mg, 1.50 mmol, 5.00 eq.) was added to a solution of 2,4,6,8-tetramethyl-5-(2-nitrophenyl)-5*H*-dibenzo[*b*,*d*]furan-5-ium tetrafluoroborate **104** (129 mg, 0.30 mmol, 1.00 eq.) and N-methyl aniline (162 μL, 161 mg, 1.50 mmol, 5.00 eq.) in MeCN (6 mL). After 16 h, the reaction was filtered through Celite® (1.5 mL), eluted (CH_2Cl_2, 4 × 5 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 2:98, R_f = 0.4) to give the title compound as a bright orange oil (54 mg, 74%).

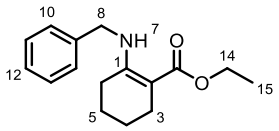
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.65 (t, *J* = 2.4 Hz, 1H, H_6), 7.62 (ddd, *J* = 8.1, 2.2, 0.9 Hz, 1H, H_2), 7.45 – 7.36 (m, 2H, H_{10}), 7.29 (t, *J* = 8.2 Hz, 1H, H_3), 7.23 – 7.16 (m, 3H, H_9, H_{11}), 7.09 (ddd, *J* = 8.4, 2.5, 0.9 Hz, 1H, H_4), 3.37 (s, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 149.9 (C_6), 149.3 (C_1), 147.5 (C_8), 130.0 (C_{10}), 129.4 (C_3), 125.2 (C_{11}), 125.0 (C_9), 121.5 (C_4), 113.1 (C_2), 109.6 (C_5), 40.4 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2360, 1619, 1595, 1571, 1529, 1496, 1351, 1254, 1135, 1090, 991, 913, 840, 736, 701, 669.

HRMS (ESI$^+$): *m/z* calculated for $C_{13}H_{12}N_2O_2^+$, $[M+H]^+$ = 229.0972; *m/z* found = 229.0970, Δ = -0.76 ppm.

Ethyl 2-(benzylamino)cyclohex-1-ene-1-carboxylate, 169:



Compound **169** was prepared according to a literature procedure.[45] Benzyl amine (164 μL, 1.5 mmol, 1.50 eq.) and Na_2SO_4 (862 mg, 4.00 mmol, 4.00 eq.) were added to a stirred solution of ethyl 2-oxocyclohexane-1-carboxylate (141 μL, 1.00 mmol, 1.00 eq.) in C_6H_6 (1.4 mL) at 80 °C. After 12 h, the solution was cooled to r.t. and filtered through a plug of Na_2SO_4, eluted (C_6H_6, 3 x 5 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:*n*-hexane, 1:20, R_f = 0.1) to give the title compound as a colourless oil (156 mg, 60%).

^{1}H (500 MHz, $CDCl_3$) δ_H = 9.36 (d, *J* = 6.5 Hz, 1H, H_7), 7.38 – 7.32 (m, 2H, H_{11}), 7.31 – 7.25 (m, 3H, H_{10}, H_{12}), 4.42 (d, *J* = 6.5 Hz, 2H, H_8), 4.16 (q, *J* = 7.0 Hz, 2H, H_{14}), 2.31 (t, *J* = 6.5 Hz, 3H, H_3, H_6), 1.68 – 1.52 (m, 4H, H_4, H_5), 1.30 (t, *J* = 7.0 Hz, 3H, H_{15}).

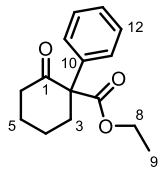
^{13}C (126 MHz, $CDCl_3$) δ_C = 171.0 (C_{13}), 159.5 (C_1), 139.7 (C_9), 128.8 (C_{11}), 127.2 (C_{12}), 126.9 (C_{10}), 90.7 (C_2), 58.9 (C_{14}), 46.2 (C_8), 26.4 ($C_{3/6}$), 24.0 ($C_{3/6}$), 22.8 ($C_{4/5}$), 22.4 ($C_{4/5}$), 14.8 (C_{15}).

IR (film) ν_{max}/cm^{-1} **=** 2980, 2931, 2858, 1746, 1719, 1647, 1597, 1496, 1452, 1384, 1363, 1258, 1223, 1178, 1155, 1093, 1062, 1028, 967, 831, 776, 733, 697.

HRMS (ESI$^+$): m/z calculated for $C_{16}H_{22}O_2N^+$, $[M+H]^+$ = 260.1645; m/z found = 260.1645. Δ = -0.18 ppm.

Data in accordance with literature.[45]

Ethyl (*R*)-2-oxo-1-phenylcyclohexane-1-carboxylate, 170:



Compound **114** (194 mg, 0.45 mmol, 1.5 eq.) was dissolved in MeCN (6 mL) in an oven-dried vial. Ethyl 2-(benzylamino)cyclohex-1-ene-1-carboxylate **169** (82 mg, 0.30 mmol, 1.00 eq.) in MeCN (1 mL) and K_3PO_4 (318 mg, 1.50 mmol, 5 eq.) were added sequentially and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite® (2 mL), eluted (CH_2Cl_2, 4 × 5 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 50:50, R_f = 0.3) to give the title compound as a colourless oil (156 mg, 71%).

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.39 – 7.34 (m, 2H, H_{12}), 7.32 – 7.28 (m, 1H, H_{13}), 7.25 – 7.21 (m, 2H, H_{11}), 4.22 (qd, *J* = 7.0, 4.5 Hz, 2H, H_8), 2.82 – 2.71 (m, 1H, H_3), 2.64 – 2.49 (m, 2H, H_6), 2.36 (dddd, *J* = 14.0, 9.0, 3.5, 1.5 Hz, 1H, H_3), 2.05 – 1.92 (m, 1H, H_5), 1.90 – 1.70 (m, 3H, H_5, H_4), 1.24 (t, *J* = 7.0 Hz, 3H, H_9).

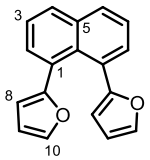
^{13}C (126 MHz, $CDCl_3$) δ_C = 206.8 (C_1), 171.4 (C_7), 136.9 (C_{10}), 128.5 (C_{12}), 127.9 (C_{11}), 127.7 (C_{13}), 66.6 (C_2), 61.8 (C_8), 41.0 (C_6), 35.4 (C_3), 29.8 (C_9), 27.8 (C_4), 22.3 (C_5), 14.1 (C_9).

IR (film) ν_{max}/cm^{-1} **=** 3674, 3649, 2999, 2981, 2886, 1715, 1460, 1394, 1381, 1252, 1237, 1151, 1072, 969, 954, 940, 624.

HRMS (ESI^+): m/z calculated for $C_{15}H_{18}O_3Na^+$, $[M+Na]^+$ = 269.1148; m/z found = 269.1148. Δ = 0.08 ppm.

Data in accordance with literature.[86]

1,8-Di(furan-2-yl)naphthalene, 172:



Compound **172** was synthesised according to a modified literature procedure.[47] Under an inert atmosphere *n*-BuLi in hexane (1.23 mL, 1.6 M, 30.6 mmol, 10.2 eq.) was added dropwise to a stirred solution furan in anhydrous THF (3.69 mL, 0.6 M, 30.6 mmol, 10.2 eq.) at 0 °C. After 30 minute the mixture was slowly added over a stirred mixture of $InCl_3$ (2.26 g 10.2 mmol, 3.4 eq.) in THF (11 mL) at -78 °C under an inert atmosphere. After 30 minutes the solution was slowly warmed to r.t. and was slowly added to a refluxing solution of 1,8-dibromonapthalene (856 mg, 3 mmol, 1 eq.) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (123 mg, 0.15 mmol, 5 mol%) in THF (100 mL) and refluxed. After 18 h the mixture was cooled to r.t., MeOH (1 mL) was added, and the mixture was concentrated *in vacuo*. The mixture was dissolved in Et_2O (20 mL) and washed with HCl (10 %, 20 mL) and $NaHCO_3$ (sat. aq., 20 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (pentane, R_f = 0.5) to give the title compound as a yellow solid (374 mg, 72%).

m.p. = 77-80 °C.

^{1}H (400 MHz, $CDCl_3$) δ_H = 7.92 (dd, *J* = 8.0, 1.5 Hz, 2H, H_4), 7.67 (dt, *J* = 7.0, 1.5 Hz, 2H, H_2), 7.54 (dd, *J* = 8.0, 7.0 Hz, 2H, H_3), 7.17 (dt, *J* = 2.0, 1.0 Hz, 2H, H_8), 6.22 (ddd, *J* = 3.5, 2.0, 1.0 Hz, 2H, H_9), 6.13 (dt, *J* = 3.5, 1.0 Hz, 2H, H_{10}).

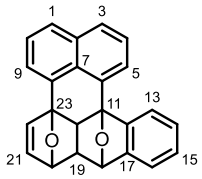
^{13}C (126 MHz, $CDCl_3$) δ_C = 154.5 (C_7), 141.6 (C_8), 135.1 (C_{Ar}), 130.3 (C_8), 129.4 (C_4), 128.9 (C_{Ar}), 128.8 (C_{Ar}), 125.2 (C_3), 111.0 (C_2), 107.3 (C_{10}).

IR (film) ν_{max}/cm^{-1} = 3649, 3054, 2981, 2362, 1717, 1560, 1508, 1496, 1457, 1363, 1264, 1223, 1184, 1157, 1112, 1076, 1014, 984, 940, 898, 885, 829, 801, 770, 726, 706, 686.

HRMS (ESI^+) = calculated for $C_{18}H_{13}O_2^+$, $[M+H]^+$ = 261.0910; m/z found = 261.0912, Δ = 0.81 ppm.

Data in accordance with the literature.[47]

3b1,6a-Dihydro-6H,7H-3b,6:7,11b-diepoxybenzo[a]perylene, 173:



2-Acetamido-4,6,8-trimethyl-5-phenyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **114** (194 mg, 0.45 mmol, 1.50 eq.) was dissolved in MeCN (6 mL) in an oven-dried vial. 1,8-di(furan-2-yl)naphthalene (78 mg, 0.30 mmol, 1.00 eq.) and K_3PO_4 (318 mg, 1.50 mmol, 5.00 eq.) were added sequentially and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite® (2 mL), eluted (CH_2Cl_2, 4 × 5 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:PhMe, 30:70, R_f = 0.2) to give the title compound as a brown solid (67 mg, 66%).

m.p. = 177-179 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.94 (td, *J* = 8.3, 1.3 Hz, 2H, H_4, H_{10}), 7.87 (dd, *J* = 7.1, 1.3 Hz, 1H, $H_{5/9}$), 7.75 (dd, *J* = 7.0, 1.3 Hz, 1H, $H_{5/90}$), 7.54 (ddd, *J* = 10.7, 8.2, 7.0 Hz, 2H, H_1, H_3), 7.30 – 7.28 (m, 1H, H_{16}), 7.20 – 7.17 (m, 1H, H_{13}), 7.17 – 7.12 (m, 2H, H_{14}, H_{15}), 6.70 (d, *J* = 5.6 Hz, 1H, H_{22}), 6.65 (dd, *J* = 5.6, 1.8 Hz, 1H, H_{21}), 5.38 (s, 1H, H_{18}), 5.16 (d, *J* = 1.7 Hz, 1H, H_{20}), 2.39 – 2.32 (m, 2H, H_{19}, H_{24}).

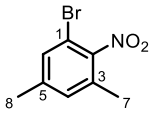
^{13}C (126 MHz, $CDCl_3$) δ_C = 148.6 (C_{12}), 147.8 (C_{17}), 140.4 (C_{21}), 140.0 (C_{22}), 134.2 (C_2), 130.7 (C_{Ar}), 130.3 ($C_{4/10}$), 130.3 ($C_{4/10}$), 129.8 (C_{Ar}), 128.8 ($C_{5/9}$), 128.4 ($C_{5/9}$), 128.1 (C_{Ar}), 126.8 ($C_{14/15}$), 126.8 ($C_{14/15}$), 126.0 ($C_{1/3}$), 125.9 ($C_{1/3}$), 120.0 (C_{13}), 119.8 (C_{16}), 86.0 (C_{23}), 86.0 (C_{11}), 82.2 (C_{20}), 80.8 (C_{18}), 53.6 (C_{19}), 51.1 (C_{24}).

IR (film) ν_{max}/cm^{-1} **=** 3664, 3301, 2981, 2360, 2339, 2040, 1660, 1564, 1484, 1379, 1326, 1264, 1183, 1126, 1029, 966, 859, 828, 754, 625.

HRMS (ESI^+): m/z calculated for $C_{24}H_{17}O_2^+$, $[M+H]^+$ = 337.1223; m/z found = 337.1223. Δ = 0.11 ppm.

Data in accordance with the literature.[154]

1-Bromo-3,5-dimethyl-2-nitrobenzene, 120:



Compound **120** was synthesised according to a modified literature procedure.[155] *m*-CPBA (4.31 g, 25.0 mmol, 5 eq.) was added slowly to a stirred solution of 2-bromo-4,6-dimethylaniline (1.00 g, 5.00 mmol, 1 eq.) dissolved in PhMe (21 mL). The reaction mixture was refluxed for 3 h and then cooled to r.t.. H_2O (50 mL) was added and the reaction mixture was extracted (EtOAc, 3 x 50 mL). The combined organic layers were washed NaOH (1 M, 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:Pentane, 1:99) to give the title compound as a bright yellow solid (711 g, 62%).

m.p. = low melting point solid**.**

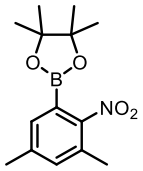
^{1}H (500 MHz, $CDCl_3$) δ = 7.32 – 7.29 (m, 1H), 7.03 (dt, *J* = 1.6, 0.8 Hz, 1H), 2.34 (d, *J* = 0.9 Hz, 3H), 2.30 (s, 3H).

^{13}C (126 MHz, $CDCl_3$) δ = 150 (C_2), 142 (C_5), 132 (C_6), 131 (C_3), 131 (C_4), 113 (C_1), 21 (C_8), 18 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2962, 2925, 1603, 1574, 1531, 1445, 1366, 1287, 1266, 1229, 1174, 1089, 1038, 997, 910, 850, 813, 733, 649.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{16}BrFN_4O_3^+$, $[M+H]^+$ = 386.0387; *m/z* found = 386.0384. Δ = 0.76 ppm.

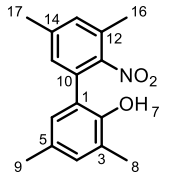
2-(3,5-Dimethyl-2-nitrophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, 247:



Compound **247** was prepared according to a modified literature procedure.[34] 1,4-Dioxane (45 mL) was added to a mixture of 1-bromo-3,5-dimethyl-2-nitrobenzene **246** (1.15g, 5.00 mmol, 1 eq.), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (123 mg, 0.15 mmol, 3 mol%), KOAc (884 g, 15.0 mmol, 3 eq.) and B_2Pin_2 (1.91 g, 7.50 mmol, 1.5 eq.) under N_2. Argon was bubbled through the mixture for 5 minutes and the reaction was heated to 95 °C. After 24 h, H_2O (50 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was suspended in pentane (50 mL), filtered through Celite®, eluted with pentane (3 × 30 mL) and concentrated *in vacuo*.

247 was stored in solid form and used without further purification assuming 100% conversion.

3,3',5,5'-Tetramethyl-2'-nitro-[1,1'-biphenyl]-2-ol, 125:



2-Bromo-4,6-dimethylphenol **51** (670 mg, 3.33 mmol, 1 eq.) and 2-(3,5-dimethyl-2-nitrophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **247** (1.39 g, 5.00 mmol, 1.5 eq.) as a solution in PhMe (33 mL) and water (33 mL) were sequentially added to $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (139 mg, 0.17 mmol, 5 mol%) and Na_2CO_3 (1.41 g, 13.3 mmol, 4 eq.) under N_2 at r.t.. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 5:95) to give the title compound as a bright yellow solid (408 mg, 45%).

m.p. = low melting point solid.

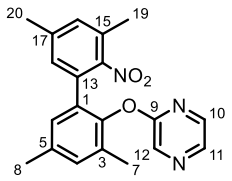
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.14 (td, *J* = 1.5, 1.0 Hz, 1H, H_{13}), 7.05 – 7.03 (m, 1H, H_{15}), 6.98 – 6.94 (m, 1H, H_4), 6.74 (d, *J* = 2.0 Hz, 1H, H_6), 4.68 (s, 1H, H_7), 2.39 (s, 3H, H_{17}), 2.37 (s, 3H, H_{16}), 2.24 (s, 3H, H_8), 2.23 (s, 3H, H_9).

^{13}C (126 MHz, $CDCl_3$) δ_C = 149.7 (C_{11}), 148.9 (C_2), 141.0 (C_{14}), 132.4 (C_4), 131.8 (C_{13}), 130.6 (C_{Ar}), 130.5 (C_{Ar}), 130.1 (C_{15}), 129.7 (C_{Ar}), 127.9 (C_6), 124.7 (C_1), 123.2 (C_{10}), 21.3 (C_{17}), 20.5 (C_9), 17.9 (C_{16}), 16.1 (C_8).

IR (film) ν_{max}/cm^{-1} **=** 3556, 2980, 2921, 1598, 1525, 1484, 1366, 1318, 1227, 1194, 1172, 1142, 1035, 935, 861, 839, 789, 751, 727.

HRMS (ESI^+): *m/z* calculated for $C_{16}H_{17}NO_3Na^+$, $[M+Na]^+$ = 294.1101; *m/z* found = 294.1101. Δ = 0.25 ppm.

2-((3,3',5,5'-Tetramethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)pyrazine, 249:



Compound **248** (50 mg, 0.18 mmol, 1 eq.) and 2-chloropyrazine (33 μL, 42 mg, 0.37 mmol, 2 eq.) were added to a flame dried RBF. Following evacuation and refill with N_2 x 3, anhydrous DMF (0.5 mL) and K_2CO_3 (51 mg, 0.37 mmol, 2 eq.) were sequentially added and the reaction mixture was heated to 90 °C. After 18 h the reaction mixture was cooled to r.t., H_2O (5 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90) to give the title compound as a yellow solid (52 mg, 83%).

m.p. = 135-142 °C.

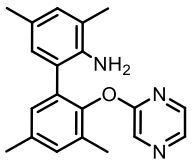
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.21 (s, 1H, H_{12}), 8.15 – 8.09 (m, 1H, H_{11}), 7.99 (s, 1H, H_{10}), 7.13 (d, J = 2.0 Hz, 1H, H_4), 7.00 (d, J = 2.0 Hz, 1H, H_6), 6.98 – 6.94 (m, 1H, H_{16}), 6.86 (d, J = 2.0 Hz, 1H, H_{18}), 2.36 (s, 3H, H_8), 2.30 (s, 3H, H_{19}), 2.21 (s, 3H, H_{20}), 2.12 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 159.8 (C_9), 148.6 (C_{14}), 146.2 (C_2), 141.3 (C_{10}), 140.3 (C_{17}), 137.4 (C_{11}), 136.0 (C_5), 134.8 (C_{12}), 132.6 (C_4), 131.6 (C_{16}), 131.4 (C_3), 131.1 (C_{15}), 130.5 (C_{13}), 130.0 (C_{18}), 129.0 (C_6), 21.1 (C_8/C_{20}), 21.1 (C_8/C_{20}), 18.3 (C_{19}), 16.8 (C_7). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} = 3811, 3662, 3638, 2980, 2922, 2361, 1726, 1691, 1659, 1597, 1526, 1465, 1400, 1363, 1280, 1202, 1176, 1151, 1136, 1059, 1008, 956, 860, 839, 750.

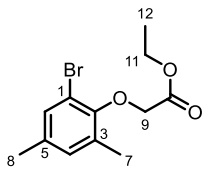
HRMS (ESI^+): m/z calculated for $C_{20}H_{20}N_3O_3^+$, $[M+H]^+$ = 350.1501; m/z found = 350.1499. Δ = 0.39 ppm.

3,3',5,5'-Tetramethyl-2'-(pyrazin-2-yloxy)-[1,1'-biphenyl]-2-amine, 250:



2-((3,3',5,5'-Tetramethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)pyrazine **249** (20 mg, 0.06 mmol, 1 eq.) and Pd/C (10 % wt, 3 mg, 0.003 mmol, 5 mol%) were added to an RBF. Following evacuation and backfilling of N_2 x 3, EtOAc (0.2 mL) was added. The mixture was purged with H_2 using a 3-skin balloon and an exit needle. After 5 minutes the balloon was replaced with a fresh H_2 balloon and the exit needle was removed. NEt_3 (19 μL, 0.13 mmol, 2.2 eq.) was added and the reaction was stirred overnight. After 18 h the reaction was sparged with N_2 and the solution was filtered through Celite®, eluted with EtOAc (4 x 1.5 mL), and concentrated *in vacuo* to afford a brown solid. The product was used without further purification assuming 100% conversion to the desired product.

Ethyl 2-(2-bromo-4,6-dimethylphenoxy)acetate, 260:



2-Bromo-4,6-dimethylphenol **51** (20.1 g, 100 mmol, 1 eq.) was dissolved in acetone (300 mL). Ethyl 2-bromoacetate (13.3 mL, 120 mmol, 1.2 eq.) and K_2CO_3 (27.6 g, 200 mmol, 2 eq.) were added sequentially and the mixture was stirred at 56 °C. After 16 h the mixture was cooled to r.t. and EtOAc (100 mL was added). The organic layer was washed sequentially with H_2O (50 mL)

and NaCl (sat aq., 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford the title compound as an orange oil (28.0 g, 98%).

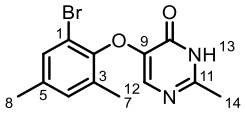
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.20 – 7.17 (m, 1H, H_6), 6.92 (td, J = 1.5, 1.0 Hz, 1H, H_4), 4.51 (s, 2H, H_9), 4.30 (d, J = 7.0 Hz, 2H, H_{11}), 2.31 (s, 3H, H_7), 2.25 (s, 3H, H_8), 1.33 (t, J = 7.0 Hz, 3H, H_{12}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 168.8 (C_{10}), 151.5 (C_2), 135.7 (C_5), 132.9 (C_3), 131.5 (C_6), 131.3 (C_4), 116.5 (C_1), 69.5 (C_9), 61.4 (C_{11}), 20.6 (C_8), 16.7 (C_7), 14.4 (C_{12}).

IR (film) ν_{max}/cm^{-1} **=** 3650, 2981, 2361, 2339, 1764, 1740, 1603, 1559, 1474, 1436, 1380, 1278, 1201, 1127, 1069, 852, 828, 790, 689, 626.

HRMS (ESI^+): m/z calculated for $C_{12}H_{16}BrO_3^+$, $[M+H]^+$ = 287.0277; m/z found = 287.0278. Δ = 0.13 ppm.

5-(2-Bromo-4,6-dimethylphenoxy)-2-methylpyrimidin-4-ol, 261:



Compound **261** was prepared according to a modified literature procedure.[95] A solution of NaH (60% in oil, 548 mg, 13.7 mmol, 1.1 eq.) in anhydrous Et_2O (7 mL) was cooled to 0 °C. Ethyl formate (1 mL, 12.5 mmol, 1 eq.) and ethyl 2-(2-bromo-4,6-dimethylphenoxy)acetate **260** (3.58 g, 12.5 mmol, 1 eq.) were sequentially added and the mixture was stirred at r.t.. After 18 h the solution was washed with pentane (100 mL) and recrystalised with anhydrous Et_2O. The pale orange precipitate was used without further purification assuming 100% conversion to the desired product.

The crude precipitate was added to a mixture of acetamidinium chloride (1.77 g, 18.7 mmol, 1.5 eq.), K_2CO_3 (2.58 g, 18.7 mmol, 1.5 eq.) and MeCN (37 mL) and the resultant mixture was stirred at 82 °C. After 16 h the reaction was cooled to r.t. and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (MeOH:CH_2Cl_2, 10:90, R_f = 0.1) to give the title compound as a yellow solid (1.69 g, 44%).

m.p. = 180-186 °C.

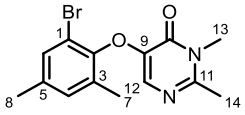
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.29 – 7.27 (m, 1H, H_6), 7.06 (s, 1H, H_{12}), 7.03 – 6.99 (m, 1H, H_4), 2.51 (s, 3H, H_{14}), 2.31 (s, 3H, H_8), 2.22 (s, 3H, H_7).

^{13}C (151 MHz, $CDCl_3$) δ_C = 159.5 (C_{10}), 152.4 (C_{11}), 146.9 (C_2), 142.7 (C_9), 137.2 (C_5), 134.2 (C_{12}), 132.5 (C_3), 132.0 (C_6), 131.6 (C_4), 116.1 (C_1), 21.4 (C_{14}), 20.7 (C_8), 16.7 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3840, 3746, 3734, 3649, 2981, 2361, 2338, 2032, 1672, 1607, 1472, 1383, 1279, 1208, 1121, 957, 849, 809, 750, 646, 627, 617.

HRMS (ESI^+): *m/z* calculated for $C_{13}H_{14}BrO_2N_2^+$, $[M+H]^+$ = 309.0233; *m/z* found = 309.0236. Δ = 0.79 ppm.

5-(2-Bromo-4,6-dimethylphenoxy)-2,3-dimethylpyrimidin-4(3H)-one, 262:



5-(2-Bromo-4,6-dimethylphenoxy)-2-methylpyrimidin-4-ol **261** (457 mg, 1.30 mmol, 1 eq.) was added to a flame dried RBF and dissolved in anhydrous DMF (3.5 mL). K_2CO_3 (359 g, 2.60 mmol, 2 eq.) and MeI (122 μL, 277 mg, 1.95 mmol, 1.5 eq.) were added sequentially and the mixture was stirred at r.t. for 16 h. H_2O (5 mL) was added, and the aqueous layer was washed with EtOAc (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f = 0.9) to give the title compound as a yellow solid (375 mg, 89%).

m.p. = 118-122 °C

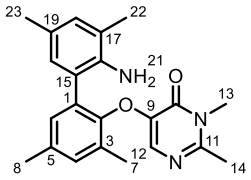
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.26 – 7.23 (m, 1H, H_6), 7.00 – 6.97 (m, 1H, H_4), 6.90 (s, 1H, H_{12}), 3.61 (s, 3H, H_{13}), 2.48 (s, 3H, H_{14}), 2.29 (s, 3H, H_8), 2.18 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 157.7 (C_{10}), 152.6 (C_{11}), 147.0 (C_2), 142.5 (C_9), 136.9 (C_5), 132.5 (C_3), 131.9 (C_6), 131.5 (C_4), 130.8 (C_{12}), 116.1 (C_1), 31.7 (C_{13}), 31.7 (C_{14}), 20.7 (C_8), 16.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2920, 2850, 2359, 1675, 1596, 1555, 1471, 1429, 1397, 1379, 1349, 1280, 1212, 1193, 1151, 1124, 1073, 1037, 991, 905, 853, 830, 791, 775, 733, 688, 642, 608.

HRMS (ESI^+): *m/z* calculated for $C_{14}H_{16}BrO_2N_2^+$, $[M+H]^+$ = 323.0390; *m/z* found = 323.0391 Δ = 0.48 ppm.

5-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2,3-dimethylpyrimidin-4(3*H*)-one, 263:



PhMe (6 mL) and H_2O (6 mL) were added to 5-(2-bromo-4,6-dimethylphenoxy)-2,3-dimethylpyrimidin-4(3H)-one, **262**, (203 mg, 0.63 mmol, 1 eq.) 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (234 mg, 0.95 mmol, 1.5 eq.), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (25 mg, 0.03, 5 mol%) and Na_2CO_3 (267 mg, 2.52 mmol, 4 eq.) in under N_2. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL/mmol), dried ($MgSO_4$), filtered, and

concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 60:40, R*f*= 0.1) to give the title compound as a yellow solid (96 mg, 42%).

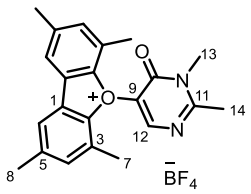
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.06 (s, 1H, H_{Ar}), 6.94 (s, 1H, H_{Ar}), 6.93 (s, 1H, H_{12}), 6.77 – 6.73 (m, 1H, H_{Ar}), 6.68 (s, 1H, H_{Ar}), 3.41 (s, 3H, H_{13}), 2.34 (s, 3H, H_{14}), 2.33 (s, 3H, $H_{8/23}$), 2.26 (s, 3H, $H_{8/23}$), 2.14 (s, 3H, $H_{7/22}$), 2.11 (s, 3H, $H_{7/22}$).

^{13}C (126 MHz, $CDCl_3$) δ_C = 157.7 (C_{10}), 151.9 (C_{11}), 148.7 (C_{Ar}), 143.3 (C_{Ar}), 139.8 (C_{Ar}), 135.1 (C_{Ar}), 132.6 (C_{Ar}), 131.6 (C_{Ar}), 131.5 (C_{Ar}), 130.7 (C_{Ar}), 130.4 (C_{Ar}), 130.3 (C_{Ar}), 129.0 (C_{Ar}), 126.8 (C_{Ar}), 123.7 (C_{Ar}), 122.7 (C_{Ar}), 31.8 (C_{13}), 23.1 (C_{14}), 20.9 ($C_{8/23}$), 20.4 ($C_{8/23}$), 18.1 ($C_{7/22}$), 16.6 ($C_{7/22}$).

IR (film) ν_{max}/cm^{-1} = 2981, 1717, 1382, 1211, 1512, 955.

HRMS (ESI^+): *m/z* calculated for $C_{22}H_{26}O_2N_3^+$, $[M+H]^+$ = 364.2020; *m/z* found = 364.2020. Δ = 0.20 ppm.

5-(1,2-Dimethyl-6-oxo-1,6-dihydropyrimidin-5-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 264:



^{t}BuONO (0.15 mL, 1.31 mmol, 5 eq.) was added to a solution of 5-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2,3-dimethylpyrimidin-4(3H)-one **263** (95 mg, 0.26 mmol, 1 eq.) and HBF_4 (48% aq., 0.17mL, 1.31 mmol, 5 eq.) in CH_2Cl_2:IPA (1:1, 1 mL) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (5 mL), washed with H_2O (2 mL), and warmed to r.t.. After 36 h, the solvent was removed by a steady stream of N_2 and Et_2O (5 mL) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed,

and the solvent passed through Celite® with Et_2O (4 x 1 mL). The solid was dissolved in MeCN (5 mL), passed through Celite® and eluted with MeCN (4 × 5 mL). The solvent was removed by a steady stream of N_2 or *in vacuo* at r.t. to give the title compound as a red solid (92 mg, 81%).

m.p. = 137-145 °C.

^{1}H (600 MHz, CD_3CN) δ_H = 9.09 (s, 1H, H_{12}), 7.85 (d, *J* = 2.1 Hz, 2H, H_6), 7.31 (s, 2H, H_4), 3.39 (s, 3H, H_1), 2.64 (s, 3H, H_{14}), 2.49 (s, 6H, H_8), 2.37 (s, 6H, H_7).

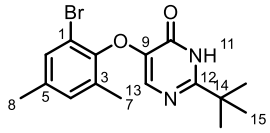
^{13}C (151 MHz, CD_3CN) δ_C = 167.4 (C_{Ar}), 159.8 (C_2), 153.4 (C_{Ar}), 148.9 (C_{12}), 143.8 (C_{Ar}), 142.8 (C_{Ar}), 135.1 (C_4), 124.7 (C_1), 123.9 (C_3), 122.3 (C_6), 33.2 (C_{13}), 24.0 (C_{14}), 21.0 (C_8), 16.5 (C_7).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -150.4.

IR (film) ν_{max}/cm^{-1} **=** 3662, 2981, 2885, 2285, 2185, 2130, 1382, 1260, 1152, 1072, 953, 749, 627.

HRMS (ESI^+): *m/z* calculated for $C_{22}H_{23}O_2N_2^+$, $[M]^+$ = 347.1756; *m/z* found = 347.1754. Δ = 0.47 ppm.

5-(2-Bromo-4,6-dimethylphenoxy)-2-(*tert*-butyl)pyrimidin-4(3*H*)-one, 266:



Compound **266** was prepared according to a modified literature procedure.[95] A solution of NaH (60% in oil, 440 mg, 11.0 mmol, 1.1 eq.) in anhydrous Et_2O (6 mL) was cooled to 0 °C. Ethyl formate (0.8 mL, 10.0 mmol, 1 eq.) and ethyl 2-(2-bromo-4,6-dimethylphenoxy)acetate **260** (2.87 g, 10.0 mmol, 1 eq.) were sequentially added and the mixture was stirred at r.t.. After 18 h the solution was washed with pentane (100 mL) and recrystalised with anhydrous Et_2O. The crude precipitate was added to a mixture of pivalimidamide hydrochloride (1.50 g, 11.0 mmol, 1.1 eq.),

K_2CO_3 (1.52 g, 11.0 mmol, 1.1 eq.) and CH_3CN (30 mL). The mixture was stirred at 82 °C for 16 h and then concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f= 0.1) to give the title compound as a pale yellow solid (1.69 g, 48%).

m.p. = 202-203 °C.

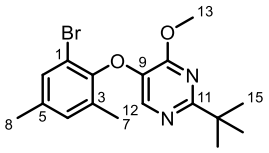
^{1}H (500 MHz, $CDCl_3$) δ_H = 11.32 (s, 1H, H_{11}), 7.25 (d, J = 2.0 Hz, 1H, H_6), 7.14 (s, 1H, H_{13}), 6.99 – 6.97 (m, 1H, H_4), 2.29 (s, 3H, H_8), 2.22 (s, 3H, H_7), 1.34 (s, 9H, H_{15}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 161.2 (C_{12}), 158.5 (C_{10}), 147.3 (C_3), 142.6 (C_9), 136.8 (C_5), 134.3 (C_{13}), 132.5 (C_2), 131.8 (C_6), 131.4 (C_4), 116.1 (C_1), 37.2 (C_{14}), 28.5 (C_{15}), 20.7 (C_8), 16.8 (C_7).

IR (film) ν_{max}/cm^{-1} = 3853, 3839, 3802, 3735, 3676, 3650, 2981, 2361, 2341, 1734, 1671, 1594, 1559, 1541, 1507, 1473, 1395, 1279, 1237, 1211, 1139, 1067, 979, 844, 804, 752, 669, 627, 618.

HRMS (ESI^+) = calculated for $C_{16}H_{20}BrO_2N_2$ $[M+H]^+$ = 351.0703; m/z found = 351.0705, Δ = 0.65 ppm.

5-(2-Bromo-4,6-dimethylphenoxy)-2-(*tert*-butyl)-4-methoxypyrimidine, 268:



5-(2-Bromo-4,6-dimethylphenoxy)-2-(*tert*-butyl)pyrimidin-4(3*H*)-one **267** (1.97 g, 5.61 mmol, 1 eq.) was added to a flame dried RBF and dissolved in anhydrous DMF (14 mL). K_2CO_3 (1.55 g, 11.2 mmol, 2 eq.) and MeI (0.53 mL, 8.42 mmol, 1.5 eq.) were added sequentially and the mixture was stirred at r.t. for 16 h. H_2O (20 mL) was added, and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated

in vacuo. The crude residue was purified by flash column chromatography (Et_2O:pentane, 10:90, R_f = 0.9) to give the title compound as a yellow solid (1.58 g, 77%).

m.p. = 80-83 °C.

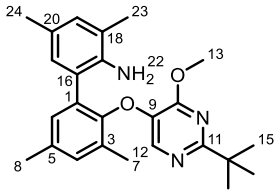
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.26 (s, 1H, C_{12}), 7.04 (d, *J* = 2.0 Hz, 1H, C_6), 6.78 – 6.74 (m, 1H, C_4), 3.90 (s, 3H, C_{13}), 2.07 (s, 3H, C_8), 1.94 (s, 3H, C_7), 1.13 (s, 9H, C_{15}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 169.6 (C_{11}), 158.6 (C_{10}), 147.0 (C_2), 138.9 (C_{12}), 137.7 (C_9), 136.9 (C_5), 132.5 (C_3), 131.7 (C_6), 131.3 (C_4), 116.3 (C_1), 53.8 (C_{13}), 38.9 (C_{14}), 29.6 (C_{15}), 20.6 (C_8), 16.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2958, 2361, 2340, 1569, 1479, 1416, 1394, 1370, 1328, 1278, 1234, 1209, 1178, 1154, 1121, 1017, 937, 853, 825, 810, 781.

HRMS (ESI^+) = calculated for $C_{17}H_{22}O_2N_2Br^+$, $[M+H]^+$ = 365.0859; *m/z* found = 365.0860, Δ = 0.22 ppm.

2'-((2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)oxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine, 269:



PhMe (5.5 mL) and H_2O (5.5 mL) were added to 5-(2-bromo-4,6-dimethylphenoxy)-2-(*tert*-butyl)-4-methoxypyrimidine **268** (2.00 g, 5.48 mmol, 1 eq.). 2,4-Dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (234 mg, 0.95 mmol, 1.5 eq.), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (228 mg, 0.27, 5 mol%) and Na_2CO_3 (2.32 g, 21.9 mmol, 4 eq.) in under N_2. Argon was bubbled through the solution for 5 minutes and the reaction mixture was heated to 95 °C. After 24 h, the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL/mmol), dried ($MgSO_4$), filtered, and

concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 14:86, R_f = 0.20) to give the title compound as a pale yellow solid (1.04 g, 47%).

m.p. = 94-99 °C.

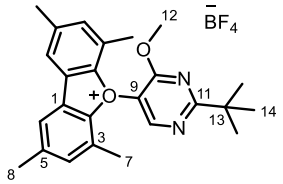
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.53 (s, 1H, H_{12}), 7.06 (dt, *J* = 2.3, 0.8 Hz, 1H, H_4), 6.94 (d, *J* = 2.3 Hz, 1H, H_6), 6.70 (m, 1H, H_{21}), 6.54 (d, *J* = 2.1 Hz, 1H, H_{19}), 3.83 (s, 3H, H_{13}), 3.40 (s, 2H, H_{22}), 2.32 (s, 3H, H_8), 2.29 (s, 3H, H_7), 2.08 (s, 3H, H_{24}), 2.06 (s, 3H, H_{23}), 1.26 (s, 9H, H_{15}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 169.1 (C_{11}), 158.8 (C_{10}), 149.7 (C_2), 141.2 (C_{12}), 139.6 (C_{17}), 139.1 (C_9), 135.2 (C_5), 131.7 (C_{16}), 131.4 (C_4), 131.2 (C_3), 130.4 (C_6), 130.3 (C_{21}), 128.8 (C_{19}), 126.6 (C_{20}), 123.1 (C_1), 122.2 (C_{18}), 53.5 (C_{23}), 38.8 (C_{14}), 29.6 (C_{15}), 20.9 (C_8), 20.3 (C_{24}), 17.8 (C_{23}), 16.5 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3649, 3382, 2980, 2360, 2342, 1623, 1567, 1479, 1416, 1392, 1379, 1326, 1238, 1204, 1178, 1148, 1018, 940, 860, 795, 748, 722, 670, 657, 648, 633, 618.

HRMS (ESI^+) = calculated for $C_{25}H_{32}O_2N_3^+$, $[M+H]^+$ = 406.2489; *m/z* found = 406.2485, Δ = -1.06 ppm.

5-(2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 269:



^{t}BuONO (713 μL, 6.00 mmol, 5 eq.) was added to a solution of 2'-((2-(*tert*-butyl)-4-methoxypyrimidin-5-yl)oxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine **268** (487 mg, 1.20 mmol, 1 eq.) and HBF_4 (48% aq., 782 μL, 6.00 mmol, 5 eq.) in CH_2Cl_2:IPA (1:1, 5 mL) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (5 mL), washed with H_2O (2 mL), and warmed to

r.t.. After 36 h, the solvent was removed by a steady stream of N_2 and Et_2O (5 mL) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® with Et_2O (4 x 1 mL). The solid was dissolved in MeCN (5 mL), passed through Celite® and eluted with MeCN (4 × 5 mL). The solvent was removed by a steady stream of N_2 or *in vacuo* at r.t. to give the title compound as an orange solid (271 mg, 50%).

m.p. = 184-186 °C.

^{1}H (500 MHz, CD_3CN) δ_H = 9.05 (s, 1H, H_{10}), 7.97 – 7.77 (m, 2H, H_6), 7.42 – 7.14 (m, 2H, H_4), 3.93 (s, 3H, H_{12}), 2.50 (s, 6H, H_8), 2.17 (s, 6H, H_7), 1.40 (s, 9H, H_{14}).

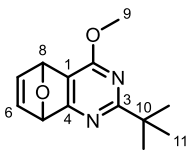
^{13}C (126 MHz, CD_3CN) δ_C = 181.7 (C_{11}), 161.1 (C_2), 158.9 (C_{10}), 151.9 (C_{12}), 142.9 (C_9), 141.5 (C_5), 135.3 (C_4), 124.0 (C_3), 123.8 (C_1), 122.5 (C_6), 56.4 (C_{12}), 41.0 (C_{13}), 29.5 (C_{14}), 21.1 (C_8), 16.2 (C_7).

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.8.

IR (film) ν_{max}/cm^{-1} **=** 3853, 3734, 3650, 3211, 2981, 2359, 2338, 1587, 1484, 1459, 1412, 1395, 1324, 1234, 1168, 1060, 993, 958, 856, 816, 749, 715, 669, 657, 626.

HRMS (ESI^+) = calculated for $C_{25}H_{29}O_2N_2^+$, $[M]^+$ = 389.2224; *m/z* found = 389.2224, Δ = 0.15 ppm.

2-(*tert*-Butyl)-4-methoxy-5,8-dihydro-5,8-epoxyquinazoline, 271:



5-(2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **269** (95 mg, 0.20 mmol, 1 eq.) was dissolved in MeCN:furan (1:2, 6 mL) in an oven-dried vial. K_3PO_4 (212 mg, 1.00 mmol, 5 eq.) was then added and the reaction mixture was stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted with CH_2Cl_2 (4 × 2 mL), and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f = 0.2) to give the title compound as a pale yellow oil (18 mg, 39%).

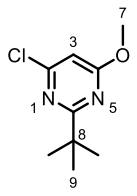
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.11 (dd, *J* = 5.5, 1.8 Hz, 1H, H_6), 7.09 (dd, *J* = 5.5, 1.9 Hz, 1H, H_7), 5.91 – 5.87 (m, 1H, H_5), 5.59 (dd, *J* = 2.0, 0.9 Hz, 1H, H_8), 3.96 (s, 3H, H_9), 1.36 (s, 9H, H_{11}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 184.8 (C_2), 174.7 (C_3), 160.0 (C_2), 144.4 (C_6), 141.8 (C_7), 120.8 (C_1), 83.0 (C_8), 79.4 (C_5), 53.3 (C_9), 39.5 (C_{10}), 29.8 (C_{11}).

IR (film) ν_{max}/cm^{-1} **=** 2958, 2360, 1612, 1579, 1483, 1460, 1400, 1369, 1280, 1253, 1235, 1120, 1092, 1069, 998, 912.

HRMS (ESI^+) = calculated for $C_{13}H_{17}N_2O_2^+$, $[M+H]^+$ = 233.1285; *m/z* found = 233.1282, Δ = -1.22 ppm.

2-(*tert*-Butyl)-4-chloro-6-methoxypyrimidine, 273:



Compound **273** was prepared according to a modified literature procedure.[96] 2-(*tert*-Butyl)-4,6-dichloropyrimidine **272** (205 mg, 1.00 mmol, 1 eq.) and anhydrous MeOH (1.5 mL) were added to

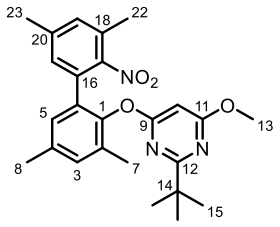
a flame dried RBF under N_2. NaOMe (30% in MeOH, 186 μL, 1.00 mol, 1 eq.) was added and the resultant white suspension was refluxed for 30 minutes. The reaction mixture was cooled to r.t., concentrated *in vacuo*. Et_2O (20 mL) was added, and the mixture was filtered over a pad of Celite®. The filtrate was concentrated *in vacuo* to give the title compound as a colourless liquid (201 mg, quant.).

^{1}H (500 MHz, $CDCl_3$) δ_H = 6.54 (s, 1H, H_3), 3.97 (s, 3H, H_7), 1.36 (s, 9H, H_9).

^{13}C (126 MHz, $CDCl_3$) δ_C = 178.3 (C_6), 170.3 (C_4), 160.5 (C_2), 104.0 (C_3), 54.1 (C_7), 39.8 (C_8), 29.4 (C_9).

IR (film) ν_{max}/cm^{-1} = 2960, 2360, 1553, 1483, 1462, 1386, 1359, 1331, 1223, 1177, 1103, 1043, 1024, 984, 935, 856, 839, 793, 647.

2-(*tert*-Butyl)-4-methoxy-6-((3,3',5,5'-tetramethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)pyrimidine, 274:



3,3',5,5'-Tetramethyl-2'-nitro-[1,1'-biphenyl]-2-ol **248** (240 mg, 0.88 mmol, 1 eq.) and 2-(*tert*-butyl)-4-chloro-6-methoxypyrimidine **273** (177 mg, 0.88 mmol, 1 eq.) were added to a flame dried RBF. Following evacuating and backfilling with N_2 x 3, anhydrous DMF (0.9 mL) and NaO^{t}Bu were added sequentially, and the reaction mixture was heated to 100 °C. After 16 h the reaction mixture was cooled to r.t., H_2O (5 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL), dried ($MgSO_4$), filtered,

and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90) to give the title compound as a pale yellow solid (21 mg, 5%).

m.p. = 100-102 °C.

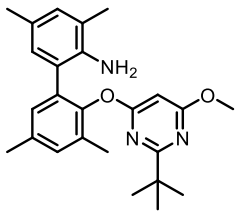
^{1}H (500 MHz, $CDCl_3$) δ = 7.06 – 7.04 (m, 1H, H_{Ar}), 6.96 – 6.95 (m, 1H, H_{Ar}), 6.95 – 6.94 (m, 1H, H_{Ar}), 6.91 (dt, *J* = 2.5, 1.0 Hz, 1H, H_{Ar}), 5.77 (s, 1H, H_{10}), 3.87 (s, 3H, H_{13}), 2.33 (s, 3H, $H_{8/23}$), 2.30 (s, 3H, $H_{7/22}$), 2.21 (s, 3H, $H_{7/22}$), 2.07 (s, 3H, $H_{8/23}$), 1.19 (s, 9H, H_{15}).

^{13}C (126 MHz, $CDCl_3$) δ = 176.9 (C_{12}), 171.7 (C_{11}), 170.4 (C_9), 148.7 ($C_{1/17}$), 146.5 ($C_{1/17}$), 140.0 (C_{20}), 135.3 (C_4), 132.1 ($C_{3/19}$), 131.6 ($C_{2/18}$), 131.2 ($C_{5/20}$), 131.2 ($C_{6/16}$), 130.4 ($C_{2/18}$), 130.3 ($C_{3/19}$), 130.1 ($C_{6/16}$), 128.3 ($C_{5/20}$), 86.7 (C_{10}), 53.9 (C_{13}), 39.2 (C_{14}), 29.2 (C_{15}), 21.1 ($C_{7/22}$), 21.0 ($C_{8/23}$), 18.3 ($C_{7/22}$), 16.7 ($C_{8/23}$).

IR (film) ν_{max}/cm^{-1} **=** 3660, 2980, 2925, 2360, 2336, 1580, 1528, 1463, 1399, 1377, 1253, 1228, 1203, 1181, 1155, 1052, 993, 979, 941, 860, 838, 751, 624.

HRMS (ESI^+) = calculated for $C_{25}H_{30}O_4N_3^+$, $[M+H]^+$ = 436.2231; *m/z* found = 436.2226, Δ = -1.05 ppm.

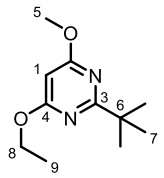
2'-((2-(*tert*-Butyl)-6-methoxypyrimidin-4-yl)oxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine, 275:



2-(*tert*-Butyl)-4-methoxy-6-((3,3',5,5'-tetramethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)pyrimidine **274** (10 mg, 0.02 mmol, 1 eq.) and Pd/C (10 % wt, 2 mg, 0.001 mmol, 5 mol%) were added to an RBF.

Following evacuation and backfilling of N_2 x 3, EtOH (0.25 mL) was added. The mixture was purged with H_2 using a 3-skin balloon and an exit needle. After 5 minutes the balloon was replaced with a fresh H_2 balloon, and the exit needle was removed. NEt_3 (4 μL, 0.03 mmol, 1.5 eq.) was added and the reaction was stirred overnight. After 18 h the reaction was sparged with N_2 and the solution was filtered through Celite®, eluted EtOAc (4 x 1.5 mL), and concentrated *in vacuo*. The solid was dissolved in EtOAc (5 mL) and washed with $NaHCO_3$ (sat. aq., 5 mL), dried ($MgSO_4$) and concentrated *in vacuo* to afford a brown solid. The product was used without further purification assuming 100% conversion.

2-(*tert*-Butyl)-4-ethoxy-6-methoxypyrimidine, 278:



5-(2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **269** (95 mg, 0.20 mmol, 1 eq.) was dissolved in MeCN:EtOH (1:2, 6 mL) in an oven-dried vial. K_3PO_4 (212, 1.00 mmol, 5 eq.) was then added and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted (CH_2Cl_2, 4 × 2 mL/mmol) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (pentane, R_f = 0.2) to give the title compound as a colourless oil (16 mg, 38%).

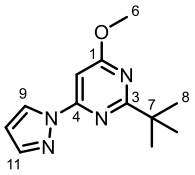
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 5.80 (s, 1H, H_1), 4.36 (q, J = 7.0 Hz, 2H, H_8), 3.92 (s, 3H, H_5), 1.38 (t, J = 7.1 Hz, 3H, H_9), 1.34 (s, 9H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 176.9 (C_3), 171.3 (C_2), 171.0 (C_4), 86.3 (C_3), 62.4 (C_8), 53.8 (C_5), 39.5 (C_6), 29.4 (C_7), 14.7 (C_9).

IR (film) ν_{max}/cm^{-1} **=** 2961, 2360, 2341, 1589, 1465, 1424, 1390, 1347, 1259, 1230, 1186, 1167, 1060, 1026, 991, 942, 833, 735, 639.

HRMS (ESI^+) = calculated for $C_{11}H_{19}N_2O_2^+$, $[M+H]^+$ = 211.1441; *m/z* found = 211.1140 , Δ = -0.29 ppm.

2-(*tert*-Butyl)-4-methoxy-6-(1*H*-pyrazol-1-yl)pyrimidine, 279:



5-(2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)-2,4,6,8-tetramethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **269** (95 mg, 0.20 mmol, 1 eq.) and pyrazole (68 mg, 0.10 mmol, 5 eq.) were dissolved in MeCN (4 mL) in an oven-dried vial. K_3PO_4 (212 mg, 1.00 mmol, 5 eq.) was then added and the reaction mixture was stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted (CH_2Cl_2, 4 × 2 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:9, R_f = 0.2) to give the title compound a white solid (24 mg, 55%).

m.p. = 65-66 °C.

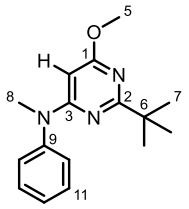
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.61 (dd, *J* = 2.5, 1.0 Hz, 1H, H_{11}), 7.74 (dd, *J* = 1.5, 1.0 Hz, 1H, H_9), 7.05 (s, 1H, H_5), 6.45 (dd, *J* = 2.5, 1.5 Hz, 1H, H_{10}), 4.01 (s, 3H, H_6), 1.40 (s, 9H, H_8).

^{13}C (126 MHz, $CDCl_3$) δ_C = 177.4 (C_3), 171.5 (C_1), 158.2 (C_4), 143.0 (C_9), 128.0 (C_{11}), 108.0 (C_{10}), 90.2 (C_5), 54.1 (C_4), 39.6 (C_7), 29.9 (C_8).

IR (film) ν_{max}/cm^{-1} **=** 2960, 2361, 1593, 1573, 1524, 1474, 1459, 1439, 1408, 1396, 1367, 1300, 1257, 1214, 1107, 1060, 1039, 990, 950, 915, 847, 839, 785, 760, 648.

HRMS (ESI$^+$): calculated for $C_{12}H_{17}N_4O^+$, $[M+H]^+$ = 233.1397; *m/z* found = 233.1400, Δ = 1.34 ppm.

2-(*tert*-Butyl)-6-methoxy-*N*-methyl-*N*-phenylpyrimidin-4-amine, 280:



5-(2-(*tert*-Butyl)-4-methoxypyrimidin-5-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **269** (95 mg, 0.20 mmol, 1 eq.) and *N*-methyl aniline (108 μL, 107 mg, 1.00 mmol, 5 eq.) were dissolved in MeCN (4 mL) in an oven-dried vial. K_3PO_4 (212 mg, 1.00 mmol, 5 eq.) was then added and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite®, eluted (CH_2Cl_2, 4 × 2 mL) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:9, R_f = 0.2) to give the title compound a yellow oil (13 mg, 24%).

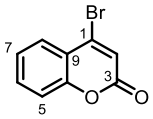
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.46 – 7.39 (m, 2H, H_{11}), 7.31 – 7.21 (m, 3H, H_{10}, H_{12}), 5.48 (s, 1H, H_4), 3.83 (s, 3H, H_5), 3.52 (s, 3H, H_8), 1.38 (s, 9H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_H = 176.5 (C_2), 170.4 (C_1), 164.5 (C_3), 145.6 (C_9), 130.0 (C_{11}), 127.2 (C_{10}), 126.6 (C_{12}), 83.5 (C_4), 53.4 (C_5), 39.7 (C_6), 38.0 (C_8), 29.7 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3648, 2982, 2971, 2883, 2360, 2343, 2261, 1726, 1701, 1653, 1617, 1559, 1511, 1473, 1386, 1319, 1259, 1226, 1146, 1068, 1037, 969, 857, 730, 697, 668, 638, 628, 613.

HRMS (ESI$^+$): calculated for $C_{16}H_{22}N_3O^+$, $[M+H]^+$ = 272.1757; *m/z* found = 272.1755, Δ = -0.74 ppm.

4-Bromo-2*H*-chromen-2-one, 284:



Compound **284** was prepared according to **General procedure F** using 4-hydroxy-2*H*-chromen-2-one **283** (9.73 g, 60.0 mmol, 1 eq.), TBAB (29.0 g, 90.0 mmol, 1.5 eq.), and P_2O_5 (17.0 g, 120 mmol, 2 eq.) in PhMe (120 mL). The crude residue was used without further purification to give the title compound as an orange solid (12.4 g, 92%).

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.85 (dd, *J* = 7.9, 1.5 Hz, 1H, H_8), 7.61 (ddd, *J* = 8.3, 7.4, 1.5 Hz, 1H, H_6), 7.42 – 7.31 (m, 2H, H_5, H_7), 6.87 (s, 1H, H_2).

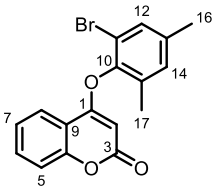
^{13}C (126 MHz, $CDCl_3$) δ_C = 158.7 (C_3), 152.6 (C_4), 141.5 (C_1), 133.3 (C_2), 128.1 (C_8), 125.0 (C_6), 119.7 (C_2), 119.0 (C_9), 117.1 (C_7).

IR (film) ν_{max}/cm^{-1} = 3980, 1723, 1305, 1559, 1340, 1176, 766.

HRMS (ESI^+): calculated for $C_9H_6BrO_2^+$, $[M+H]^+$ = 224.9546; *m*/*z* found = 224.9549, Δ = 1.45 ppm.

Data in accordance with literature.[156]

4-(2-Bromo-4,6-dimethylphenoxy)-2*H*-chromen-2-one, 258:



Compound **258** was prepared according to **General Procedure G** 4-bromo-2*H*-chromen-2-one **284** (4.50 g, 20.0 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (4.42 g, 22.0 mmol, 1.1 eq.) and K_2CO_3 (5.53 g, 40.0 mmol, 2 eq.) in MeCN (67 mL). The crude residue was used without further purification to give the title compound as a yellow solid (6.61 g, 61%).

m.p. = 122-124 °C.

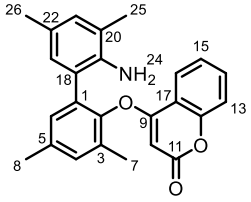
^{1}H (500 MHz, $CDCl_3$) δ_H = 8.08 (dd, *J* = 7.9, 1.6 Hz, 1H, H_8), 7.63 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H_6), 7.40 – 7.36 (m, 2H, H_5, H_7), 7.33 (dt, *J* = 2.2, 0.7 Hz, 1H, H_{12}), 7.09 – 7.04 (m, 1H, H_{14}), 5.26 (s, 1H, H_2), 2.35 (s, 3H, H_{16}), 2.19 (s, 3H, H_{17}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 164.2 (C_3), 162.7 (C_1), 153.9 (C_4), 145.6 (C_{10}), 138.3 (C_{13}), 133.0 (C_6), 132.2 (C_{15}), 132.1 (C_{12}), 131.7 (C_{14}), 124.4 (C_7), 123.3 (C_8), 117.1 (C_5), 115.8 (C_{11}), 115.1 (C_9), 93.1 (C_2), 20.8 (C_{16}), 16.5 (C_{17}).

IR (film) ν_{max}/cm^{-1} **=** 3044, 2924, 2360, 2342, 2251, 1727, 1684, 1627, 1609, 1569, 1541, 1492, 1472, 1453, 1387, 1327, 1275, 1218, 1206, 1179, 1152, 1137, 1122, 1085, 1032, 992, 931, 913, 874, 854, 835, 797, 765, 733, 673, 648, 616.

HRMS (ESI^+): calculated for $C_{17}H_{14}BrO_3^+$, $[M+H]^+$ = 345.0121; *m/z* found = 345.0111, Δ = -2.75 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one, 286:



Compound **286** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-2*H*-chromen-2-one, **537** (5.178 g, 15.0 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (4.42 g, 22.5 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (867 mg, 0.75 mmol, 5 mol%) and K_2CO_3 (8.29 g, 60.0 mmol, 4 eq.) in DME (75 mL) and H_2O (75 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 1:9, R_f = 0.2) to give the title compound a brown solid (2.47 g, 43%).

m.p. = 172-176 °C.

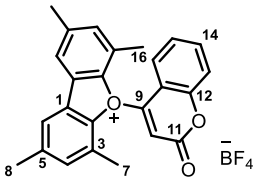
^{1}H NMR (600 MHz, DMSO-d$_6$, 363 K) δ_H = 7.90 (dd, *J* = 7.9, 1.7 Hz, 1H, H_{16}), 7.63 – 7.57 (m, 1H, H_{14}), 7.32 (td, *J* = 7.6, 1.1 Hz, 1H, H_{15}), 7.28 (dd, *J* = 8.4, 1.1 Hz, 1H, H_{13}), 7.23 – 7.20 (m, 1H, H_{Ar}), 7.07 (d, *J* = 2.3 Hz, 1H, H_{Ar}), 6.60 (s, 1H, H_{Ar}), 6.57 – 6.53 (m, 1H, H_{Ar}), 5.12 (s, 1H, H_{10}), 4.01 (s, 2H, H_{24}), 2.38 (s, 3H, $H_{8/26}$), 2.22 (s, 3H, $H_{8/26}$), 1.97 (s, 3H, $H_{7/25}$), 1.96 (s, 3H, $H_{7/25}$).

^{13}C NMR (151 MHz, DMSO-d$_6$, 363 K) δ_c = 163.6 (C_{Ar}), 160.3 (C_{Ar}), 152.3 (C_{Ar}), 145.6 (C_{Ar}), 139.7 (C_{Ar}), 135.6 (C_{Ar}), 132.1 (C_{14}), 131.7 (C_{Ar}), 130.6 (C_{Ar}), 129.6 (C_{Ar}), 129.6 (C_{Ar}), 129.5 (C_{Ar}), 127.7 (C_{Ar}), 123.8 (C_{Ar}), 123.2 (C_{15}), 122.3 (C_{16}), 121.3 (C_{Ar}), 120.5 (C_{Ar}), 115.5 (C_{13}), 114.1 (C_{Ar}), 91.7 (C_{10}), 19.7 ($C_{8/26}$), 19.0 ($C_{8/26}$), 16.8 ($C_{7/25}$), 14.9 ($C_{7/25}$).

IR (film) ν_{max}/cm^{-1} = 2980, 2341, 1725, 1626, 1608, 1568, 1487, 1452, 1388, 1327, 1275, 1222, 1199, 1179, 1146, 1087, 1032, 933, 875, 832, 812, 767, 750, 641, 641.

HRMS (ESI^+): calculated for $C_{25}H_{24}NO_3^+$, $[M+H]^+$ = 386.1751; *m/z* found = 386.1751, Δ = -0.85 ppm.

2,4,6,8-Tetramethyl-5-(2-oxo-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 287:



Compound **287** was prepared according to **General Procedure I** using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one **286** (1.15 g, 2.99 mmol, 1 eq.), HBF_4 (48% wt., 2.0 mL, 15.0 mmol, 5 eq.), ^{t}BuONO (2.0 mL, 15.0 mmol, 5 eq.) in CH_2Cl_2 (6 mL) and IPA (6 mL) to give the title product as an orange solid (658 mg, 48%).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.27 (d, *J* = 8.0 Hz, 1H, H_{16}), 7.85 (t, *J* = 7.9 Hz, 1H, H_{14}), 7.76 (s, 2H, H_6), 7.59 (t, *J* = 7.7 Hz, 1H, H_{15}), 7.56 (d, *J* = 8.4 Hz, 1H, H_{13}), 7.18 (s, 2H, H_4), 6.72 (s, 1H, H_{10}), 2.46 (s, 6H, H_8), 2.26 (s, 6H, H_7).

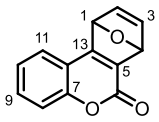
NMR (126 MHz, $CDCl_3$) δ_C =166.8 (C_9), 162.5 (C_2), 157.6 (C_{11}), 153.1 (C_{12}), 142.5 (C_5), 136.5 (C_{14}), 135.1 (C_4), 127.3 (C_{15}), 123.8 (C_{16}), 123.7 (C_3), 123.0 (C_1), 122.1 (C_6), 118.2 (C_{13}), 111.5 (C_{17}), 110.3 (C_{10}), 21.2 (C_8), 17.3 (C_7).

^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -153.8.

IR (film) ν_{max}/cm^{-1} = 2257, 1757, 1607, 1388, 1062, 913, 735.

HRMS (ESI^+): calculated for $C_{25}H_{21}O_3^+$, $[M]^+$ = 369.1485; *m/z* found = 369.1480, Δ = -1.31 ppm.

7,10-Dihydro-6*H*-7,10-epoxybenzo[c]chromen-6-one, 288:



Compound **288** was prepared according to **General Procedure I** using 2,4,6,8-tetramethyl-5-(2-oxo-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **287** (91 mg, 0.20 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:Pentane, 30:70, R_f = 0.2) to give the title compound as a yellow solid (31 mg, 73%).

m.p. = 140-144 °C.

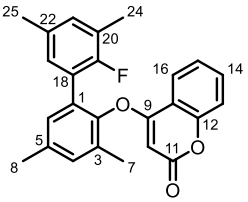
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.56 (ddd, *J* = 7.5, 6.2, 1.7 Hz, 2H, H_9, H_{11}), 7.40 (dd, *J* = 8.8, 1.3 Hz, 1H, H_8), 7.35 – 7.27 (m, 2H, H_{10}, H_2), 7.13 (dd, *J* = 5.4, 2.1 Hz, 1H, H_3), 6.09 – 6.06 (m, 1H, H_4), 5.99 – 5.96 (m, 1H, H_1).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 169.4 (C_{13}), 157.9 (C_6), 154.4 (C_7), 145.6 (C_2), 141.0 (C_3), 136.9 (C_5), 132.5 (C_9), 124.6 (C_{10}), 123.7 (C_{11}), 117.4 (C_8), 116.6 (C_{12}), 81.8 (C_4), 81.5 (C_1).

IR (film) ν_{max}/cm^{-1} = 1720, 1619, 1041, 868, 756, 740.

HRMS (ESI^+): calculated for $C_{13}H_9O_3^+$, $[M+H]^+$ = 213.0546; *m*/*z* found = 213.0542, Δ = -1.93 ppm.

4-((2'-Fluoro-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one, 289:



^{t}BuONO (2.0 mL, 15.0 mmol, 5 eq.) was added to a solution of 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2H-chromen-2-one **286** (1.15 g, 2.99 mmol, 1 eq.) and HBF_4 (48% wt., 2.0 mL, 15.0 mmol, 5 eq.) in CH_2Cl_2 (6 mL) and IPA (6 mL) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (15 mL), washed with H_2O (6 mL) and warmed to r.t.. After 41 h, the solvent was removed by a steady stream of N_2 and Et_2O (15 mL) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® (Et_2O, 4 x 3 mL). The filtrate was collected and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 5:95, R_f = 0.2) to give the title compound as a brown solid (77 mg, 5%).

m.p. = 176-178 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.96 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{16}), 7.53 (ddd, *J* = 8.3, 7.3, 1.6 Hz, 1H, H_{14}), 7.31 – 7.27 (m, 1H, H_{15}), 7.26 – 7.24 (m, 1H, H_{13}), 7.17 – 7.12 (m, 1H, H_4), 7.08 (d, *J* = 2.1 Hz, 1H, H_6), 6.87 (dd, *J* = 6.6, 2.3 Hz, 1H, H_{23}), 6.82 – 6.74 (m, 1H, H_{21}), 5.18 (s, 1H, H_{10}), 2.39 (s, 3H, H_8), 2.21 (s, 3H, H_7), 2.15 (d, *J* = 1.1 Hz, 3H, H_{25}), 2.12 (d, *J* = 2.2 Hz, 3H, H_{24}).

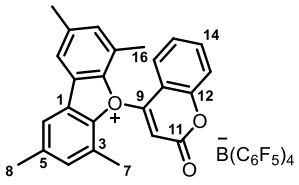
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 164.9 (C_9), 162.9 (C_{11}), 156.3 (d, *J* = 244.5 Hz, C_{19}), 153.6 (C_{12}), 146.1 (C_2), 136.6 (C_5), 132.8 (d, *J* = 4.1 Hz, C_{18}), 132.6 (C_{14}), 132.2 (C_4), 131.9 (d, *J* = 4.8 Hz, C_{21}), 130.3 (C_6), 129.5 (C_{22}), 129.3 (d, *J* = 2.8 Hz, C_{23}), 124.6 (d, *J* = 18.3 Hz, C_{20}), 124.0 (C_{15}), 123.7 (d, *J* = 16.9 Hz, C_1), 123.1 (C_{16}), 116.8 (C_{13}), 115.3 (C_{17}), 92.8 (C_{10}), 21.0 (C_8), 20.6 (C_{25}), 16.2 (C_7), 14.7 (d, *J* = 4.2 Hz, C_{24}). One aromatic carbon peak was not observed.

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -123.5.

IR (film) ν_{max}/cm^{-1} = 2962, 1732, 1628, 1388, 1179, 812.

HRMS (ESI^+): calculated for $C_{25}H_{22}FO_3^+$, $[M+H]^+$ = 389.1548; *m/z* found = 389.1543, Δ = -0.49 ppm.

2,4,6,8-Tetramethyl-5-(2-oxo-2H-chromen-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrakis(perfluorophenyl)borate, 294:

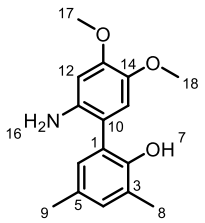


^{t}BuONO (19 μL, 0.15 mmol, 5 eq.) was added to a solution of 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2H-chromen-2-one **286** (12 mg, 0.03 mmol, 1 eq.) and HBF_4 (48% wt., 20 μL, 0.15 mmol, 5 eq.) in CH_2Cl_2 (60 μL) and IPA (60 μL) at 0 °C. After 15 minutes, the reaction mixture was diluted with CH_2Cl_2 (0.5 mL) and washed with H_2O (0.5 mL). $KB(C_6F_5)_4$ (35 mg, 0.049 mmol, 1.62 eq.) was added at r.t. and the reaction mixture was washed H_2O (3 x 0.5 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. $CDCl_3$ (0.5 mL) was added and the mixture was left for 16 h in an NMR tube. After 16 h, the solvent was removed by a steady stream of N_2 and pentane (2 mL) was added resulting in a solid precipitate. The pentane layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® (pentane, 4 x 3 mL). The solid was dissolved in Et_2O (5 mL), passed through Celite® and eluted with Et_2O (4 × 3 mL). The solvent was removed by a steady stream of N_2 to give the title compound as an orange solid (25 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.91 (dd, *J* = 8.2, 1.5 Hz, 1H, H_{16}), 7.85 (td, *J* = 7.9, 1.5 Hz, 1H, H_{14}), 7.64 – 7.59 (m, 2H, $H_{4/6}$), 7.58 – 7.49 (m, 2H, H_{13}, H_{15}), 7.14 – 7.09 (m, 2H, $H_{4/6}$), 6.24 (s, 1H, H_{10}), 2.39 (s, 6H, H_8), 2.05 (s, 6H, H_7).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -132.8 (dd, *J* = 23.5, 10.1 Hz), -162.49 – -162.80 (m), -166.69 (t, *J* = 22.2 Hz).

2'-Amino-4',5'-dimethoxy-3,5-dimethyl-[1,1'-biphenyl]-2-ol, 296:



Compound **296** was synthesised according to a literature procedure.[113] To a stirred solution of 2,4-dimethylphenol (100 μL, 0.90 mmol, 1.5 eq.), 3,4-dimethoxyaniline **295** (92 mg, 0.60 mmol, 1.0 eq.) and Mn[TPP]Cl (42 mg, 0.006 mmol, 1 mol %) in HFIP (1.2 mL), UHP (84 mg, 0.90 mmol, 1.5 eq.) was added in one portion at r.t. and the reaction was stirred at r.t.. After 16 h the volatiles were removed under reduced pressure and the crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound a brown solid (80 mg, 33%).

m.p. = 156-160 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 6.99 (d, *J* = 2.3 Hz, 1H, H_4), 6.92 (d, *J* = 2.3 Hz, 1H, H_6), 6.76 (s, 1H, $H_{12/15}$), 6.44 (s, 1H, $H_{12/15}$), 3.88 (s, 3H, $H_{17/18}$), 3.83 (s, 3H, $H_{17/18}$), 2.30 (s, 3H, H_9), 2.30 (s, 3H, H_8).

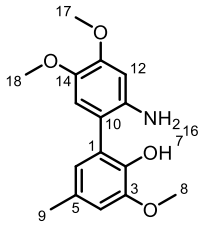
^{13}C NMR (151 MHz, CDCl3) δ_C = 149.7 ($C_{13/14}$), 149.7 (C_2), 143.7 ($C_{13/14}$), 135.5 (C_{Ar}), 131.2 (C_4), 129.7 (C_{Ar}), 128.9 (C_6), 126.8 (C_3), 125.4 (C_{Ar}), 118.0 (C_1), 115.2 ($C_{12/15}$), 102.1 ($C_{12/15}$), 56.6 ($C_{17/18}$), 56.1 ($C_{17/18}$), 20.6 (C_9), 16.6 (C_8).

IR (film) ν_{max}/cm^{-1} = 2981, 1515, 1256, 1216, 858, 731.

HRMS (ESI^+): calculated for $C_{16}H_{20}O_3N^+$, $[M+H]^+$ = 274.1438; m/z found = 274.1437, Δ = -0.23 ppm.

Data in accordance with literature.[113]

2'-Amino-3,4',5'-trimethoxy-5-methyl-[1,1'-biphenyl]-2-ol, 297:



Compound **295** was synthesised according to a literature procedure.[113] To a stirred solution of 2-methoxy-4-methylphenol (0.28 mL, 2.25 mmol, 1.5 eq.), 3,4-dimethoxyaniline (230 mg, 1.50 mmol, 1.0 eq.) and Mn[TPP]Cl (11 mg, 0.015 mmol, 1 mol %) in HFIP (3 mL), UHP (212 mg, 2.25 mmol, 1.5 eq.) was added in one portion and the reaction was stirred at r.t.. After 16 h the volatiles were removed under reduced pressure and the crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.1) to give the title compound a brown solid (278 mg, 64%).

m.p. = 100-104 °C.

^{1}H (600 MHz, $CDCl_3$) δ_H = 6.75 (s, 1H, $H_{12/15}$), 6.71 (d, J = 2.0 Hz, 1H, H_4), 6.70 – 6.68 (m, 1H, H_6), 6.42 (s, 1H, $H_{12/13}$), 3.91 (q, J = 1.0 Hz, 3H, $H_{17/18}$), 3.87 (q, J = 1.5 Hz, 3H, $H_{17/18}$), 3.82 (s, 3H, H_8), 2.33 (s, 3H, H_9).

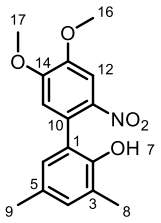
^{13}C (151 MHz, $CDCl_3$) δ_C = 149.6 ($C_{13/14}$), 147.9 ($C_{13/14}$), 143.0 (C_3), 140.7 (C_2), 136.6 (C_{Ar}), 129.9 (C_5), 125.8 (C_{Ar}), 123.5 (C_6), 117.2 (C_1), 115.0 ($C_{12/15}$), 111.4 (C_4), 101.9 ($C_{12/15}$), 56.6 (C_8), 56.2 ($C_{17/18}$), 56.0 ($C_{17/18}$), 21.3 (C_9).

IR (film) ν_{max}/cm^{-1} **=** 3791, 3705, 3663, 3016, 2935, 2857, 2361, 2340, 1691, 1600, 1548, 1515, 1466, 1407, 1259, 1216, 1104, 1027, 839, 797, 766, 669, 635.

HRMS (ESI^+): m/z calculated for $C_{16}H_{20}NO_4^+$, $[M+H]^+$ = 290.1387; m/z found = 290.1385, Δ = -0.7 ppm.

Data in accordance with literature.[113]

4',5'-Dimethoxy-3,5-dimethyl-2'-nitro-[1,1'-biphenyl]-2-ol, 298:



m-CPBA (77%, 658 mg, 2.94 mmol, 3.86 eq.) was added portion wise to a solution of 2'-amino-4',5'-dimethoxy-3,5-dimethyl-[1,1'-biphenyl]-2-ol **296** (209 mg, 0.76 mmol, 1 eq.) in CH_2Cl_2 (5.3 mL) and stirred at r.t.. for 18 h. H_2O (50 mL) was added at 0 °C and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with NaOH (1 M, 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:Pentane, 30:70, R_f = 0.6) to give the title compound as an orange solid (70 mg, 30%).

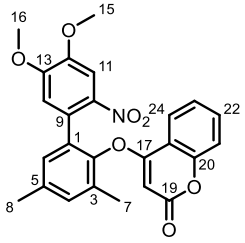
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.61 (s, 1H, H_{12}), 7.00 – 6.97 (m, 1H, H_4), 6.80 (d, J = 2.0 Hz, 1H, H_6), 6.78 (s, 1H, H_{15}), 4.56 (s, 1H, H_7), 3.99 (s, 3H, H_{16}), 3.95 (s, 3H, H_{17}), 2.28 (s, 3H, H_9), 2.26 (s, 3H, H_8).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 152.8 (C_{14}), 148.7 (C_2), 148.4 (C_{13}), 142.1 (C_{Ar}), 131.8 (C_{10}), 130.1 (C_{Ar}), 127.8 (C_6), 127.2 (C_{Ar}), 125.3 (C_{Ar}), 123.9 (C_3), 114.3 (C_{15}), 107.9 (C_{12}), 56.7 (C_{17}), 56.6 (C_{16}), 20.6 (C_9), 16.0 (C_8).

IR (film) ν_{max}/cm^{-1} **=** 3494, 2918, 2849, 2360, 2341, 1728, 1612, 1578, 1521, 1484, 1464, 1441, 1344, 1270, 1217, 1182, 1119, 1057, 1031, 970, 913, 865, 804, 787, 771, 748, 703, 669, 640.

HRMS (ESI$^+$): *m/z* calculated for $C_{16}H_{18}NO_5^+$, $[M+H]^+$ = 304.1179; *m/z* found = 304.1179, Δ = -0.20 ppm.

4-((4',5'-Dimethoxy-3,5-dimethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)-2H-chromen-2-one, 299:



A mixture of 4',5'-dimethoxy-3,5-dimethyl-2'-nitro-[1,1'-biphenyl]-2-ol **298** (88 mg, 0.29 mmol, 1 eq.), 4-bromo-2H-chromen-2-one **284** (99 mg, 0.44 mmol, 1.5 eq.), K_2CO_3 (95 mg, 0.68 mmol, 1.2 eq.) and acetone (1.6 mL) was refluxed for 48 h. The mixture was concentrated *in vacuo* and the crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.1) to give the title compound as a pale brown solid (121 mg, 93%).

m.p. = 50-52 °C.

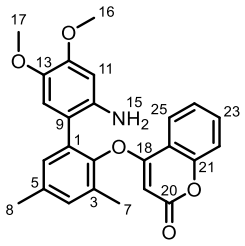
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.83 – 7.78 (m, 1H, H_{24}), 7.57 – 7.51 (m, 1H, H_{22}), 7.43 (s, 1H, H_{11}), 7.30 (t, *J* = 7.5 Hz, 1H, H_{23}), 7.27 (m, 1H, H_{21}), 7.18 – 7.15 (m, 1H, H_4), 7.08 (s, 1H, H_6), 6.69 (s, 1H, H_{14}), 5.15 (s, 1H, H_{18}), 3.89 (s, 3H, H_{16}), 3.84 (s, 3H, H_{15}), 2.44 (s, 3H, H_8), 2.14 (s, 3H, H_7).

^{13}C (151 MHz, $CDCl_3$) δ_C = 164.8 (C_{17}), 162.5 (C_{19}), 153.5 (C_{20}), 152.6 (C_{13}), 148.3 (C_{12}), 145.0 (C_2), 141.1 (C_{10}), 137.3 (C_5), 132.8 (C_{22}), 132.5 (C_4), 131.6 (C_{Ar}), 130.3 (C_3), 128.4 (C_6), 125.8 (C_{Ar}), 124.3 (C_{23}), 123.1 (C_{24}), 116.7 (C_{21}), 114.6 (C_{Ar}), 113.6 (C_{14}), 107.6 (C_{11}), 92.7 (C_{18}), 56.6 (C_{16}), 56.3 (C_{15}), 21.0 (C_8), 15.9 (C_7).

IR (film) ν_{max}/cm^{-1} = 2929, 2360, 2342, 1726, 1626, 1608, 1570, 1521, 1465, 1386, 1346, 1269, 1220, 1201, 1179, 1136, 1123, 1087, 1061, 1031, 931, 873, 832, 799, 771, 751, 735, 668, 646.

HRMS (ESI^+): *m/z* calculated for $C_{25}H_{22}NO_7^+$, $[M+H]^+$ = 448.1391; *m/z* found = 448.1389, Δ = -0.50 ppm.

4-((2'-Amino-4',5'-dimethoxy-3,5-dimethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one, 300:



A mixture of 4-((4',5'-dimethoxy-3,5-dimethyl-2'-nitro-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one **299** (121 mg, 0.27 mmol, 1 eq.), Zn (106 mg, 1.62 mmol, 6 eq.), and AcOH (0.27 mL) in THF (1.4 mL) were stirred for 4 h. The mixture was filtered over Celite® and concentrated *in vacuo* to give the title compound as a brown solid (112 mg, 99%) which was used without further purification.

m.p. = 144-146 °C.

^{1}H NMR (600 MHz, DMSO-d$_6$, 373 K) δ_H = 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H, H_{25}), 7.63 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H, H_{23}), 7.34 (td, *J* = 7.7, 1.1 Hz, 1H, H_{24}), 7.33 – 7.28 (m, 1H, H_{22}), 7.20 (d, *J* = 2.2 Hz, 1H, H_4), 7.11 (d, *J* = 2.2 Hz, 1H, H_6), 6.58 (s, 1H, $H_{11/14}$), 6.34 (s, 1H, $H_{11/14}$), 5.17 (s, 1H, H_{19}), 3.60 (s, 3H, $H_{16/17}$), 3.49 (s, 3H, $H_{16/17}$), 2.38 (s, 3H, H_8), 2.21 (s, 3H, H_7).

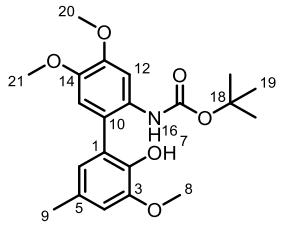
^{13}C (126 MHz, DMSO-d$_6$, 373 K) δ_C = 163.7 (C_{18}), 160.4 (C_{20}), 152.5 (C_{21}), 149.5 (C_{12}), 145.7 (C_2), 140.6 (C_{13}), 138.5 (C_{Ar}), 135.6 (C_5), 132.3 (C_{23}), 131.1 (C_{Ar}), 130.6 (C_4), 129.8 (C_6), 129.7 (C_{Ar}), 123.5

(C_{24}), 122.4 (C_{25}), 116.3 ($C_{11/14}$), 115.7 (C_{22}), 114.2 (C_{26}), 101.4 ($C_{11/14}$), 91.7 (C_{19}), 56.5 ($C_{16/17}$), 55.2 ($C_{16/17}$), 19.8 (C_8), 15.0 (C_7). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} = 2970, 1728, 1608, 1493, 1388, 1223, 1179, 931, 769.

HRMS (ESI$^+$): *m*/*z* calculated for $C_{25}H_{24}NO_5$ $[M+H]^+$ = 418.1667; *m*/*z* found = 418.1667, Δ = 4.29 ppm.

***tert*-Butyl (2'-hydroxy-3',4,5-trimethoxy-5'-methyl-[1,1'-biphenyl]-2-yl)carbamate, 301:**



Compound **301** was prepared according to a literature procedure.[115] Boc_2O (1.51 g, 6.91 mmol, 2 eq.) was added to a solution of 2'-amino-3,4',5'-trimethoxy-5-methyl-[1,1'-biphenyl]-2-ol **297** (1.00 g, 3.46 mmol, 1 eq.) in THF (1.7 mL) and the mixture was stirred at r.t.. After 12 h the reaction mixture was concentrated *in vacuo* and the crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.3) to give the title compound as a pale brown solid (949 mg, 70%).

m.p. = 103-105 °C.

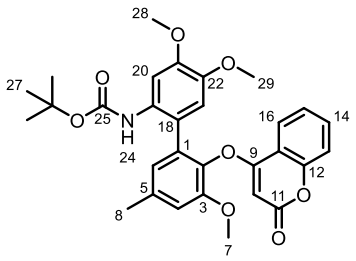
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.63 (s, 1H, H_{16}), 6.74 – 6.73 (m, 1H, H_6), 6.72 (s, 1H, $H_{12/15}$), 6.67 (s, 1H, $H_{12/15}$), 6.66 – 6.63 (m, 1H, H_4), 5.76 (s, 1H, H_7), 3.94 (s, 3H, H_{21}), 3.94 (s, 3H, H_8), 3.84 (s, 3H, H_{20}), 2.34 (s, 3H, H_9), 1.45 (s, 9H, H_{19}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 153.7 (C_{17}), 148.9 (C_{14}), 146.6 (C_3), 145.1 (C_{13}), 140.4 (C_2), 130.0 (C_{Ar}), 129.7 (C_5), 124.3 (C_{Ar}), 123.9 (C_6), 120.2 (C_1), 113.7 (C_{Ar}), 111.3 (C_4), 105.7 (C_{10}), 80.1 (C_{18}), 56.3 ($C_{8/20/21}$), 56.3 ($C_{8/20/21}$), 56.1 ($C_{8/20/21}$), 28.5 (C_{19}), 21.3 (C_9).

IR (film) ν_{max}/cm^{-1} **=** 2980, 1712, 1601, 1522, 1493, 1207, 1160, 1110, 911, 732.

HRMS: not found by ESI.

***tert*-Butyl (3',4,5-trimethoxy-5'-methyl-2'-((2-oxo-2*H*-chromen-4-yl)oxy)-[1,1'-biphenyl]-2-yl)carbamate, 302:**



KO^{t}Bu (320 mg, 2.85 mmol, 1.5 eq.) was added to a stirred solution of *tert*-Butyl (2'-hydroxy-3',4,5-trimethoxy-5'-methyl-[1,1'-biphenyl]-2-yl)carbamate **301** (741 mg, 1.90 mmol, 1 eq.) and 4-bromo-2*H*-chromen-2-one, **534**, (856 mg, 3.81 mmol, 2 eq.) in THF (1 mL) and the reaction mixture was refluxed for 4 days. The reaction was cooled to r.t., concentrated *in vacuo*, and the crude residue was purified by flash column chromatography (EtOAc:Pentane, 30:70, R_f = 0.1) to give the title compound as a yellow solid (349 mg, 55%).

m.p. = 128-130 °C.

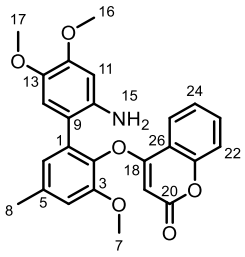
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.78 (dd, J = 7.9, 1.6 Hz, 1H, H_{16}), 7.58 (s, 1H, H_{20}), 7.52 (ddd, J = 8.6, 7.3, 1.6 Hz, 1H, H_{14}), 7.27 (d, J = 8.5 Hz, 1H, H_{13}), 7.22 (td, J = 7.6, 1.1 Hz, 1H, H_{15}), 6.90 (d, J = 1.9 Hz, 1H, H_4), 6.80 – 6.76 (m, 1H, H_6), 6.60 (s, 1H, H_{23}), 6.30 (s, 1H, H_{24}), 5.30 (s, 1H, H_{10}), 3.84 (s, 3H, H_7), 3.83 (s, 3H, $H_{28/29}$), 3.70 (s, 3H, $H_{28/29}$), 2.45 (s, 3H, H_8), 1.51 (s, 9H, H_{27}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 165.2 (C_9), 162.9 (C_{11}), 153.6 (C_{12}), 153.1 (C_{25}), 151.6 (C_3), 149.1 ($C_{21/22}$), 144.6 ($C_{21/22}$), 138.3 (C_5), 136.4 (C_2), 132.7 (C_{14}), 132.2 (C_1), 129.4 (C_{19}), 124.1 (C_6, C_{15}), 123.1 (C_{16}), 117.7 (C_{18}), 116.8 (C_{13}), 115.2 (C_{17}), 113.4 (C_4), 113.0 (C_{23}), 104.7 (C_{20}), 92.8 (C_{10}), 80.6 (C_{26}), 56.2 ($C_{7/28/29}$), 56.2 ($C_{7/28/29}$), 56.0 ($C_{7/28/29}$), 28.5 (C_{27}), 21.7 (C_8).

IR (film) ν_{max}/cm^{-1} = 2979, 1723, 1627, 1523, 1389, 1156, 733.

HRMS (ESI^+): *m/z* calculated for $C_{30}H_{32}NO_8^+$, $[M+H]^+$ = 534.2122; *m/z* found = 534.2112, Δ = -1.9 ppm.

4-((2'-Amino-3,4',5'-trimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one, 303:



Compound **303** was prepared according to a literature procedure.[116] ***tert*-**Butyl (3',4,5-trimethoxy-5'-methyl-2'-((2-oxo-2*H*-chromen-4-yl)oxy)-[1,1'-biphenyl]-2-yl)carbamate **302** (559 mg, 1.05 mmol, 1 eq.) and TFA (0.24 mL, 3.15 mmol, 3 eq.) in CH_2Cl_2 (5 mL) were stirred for 2 h at r.t.. The volatiles were then removed *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (20 mL) and washed with $NaHCO_3$ (sat. aq., 20 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were washed with NaCl (sat. aq., 20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the title compound as an off white solid (326 mg, 72%) which was used without further purification.

m.p. = 72-76 °C.

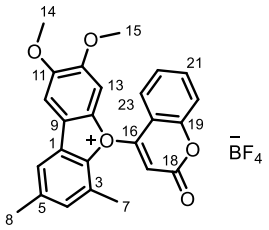
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.89 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{25}), 7.52 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H_{23}), 7.27 (d, *J* = 8.5 Hz, 1H, H_{22}), 7.24 (td, *J* = 7.6, 1.0 Hz, 1H, H_{24}), 6.86 (d, *J* = 2.0 Hz, 1H, H_6), 6.85 (d, *J* = 2.0 Hz, 1H, H_4), 6.60 (s, 1H, $H_{11/14}$), 6.23 (d, *J* = 1.9 Hz, 1H, $H_{11/14}$), 5.33 (s, 1H, H_{19}), 3.82 (s, 3H, H_7), 3.75 (br, s, 2H, H_{15}), 3.65 (s, 3H, $H_{16/17}$), 3.07 (s, 3H, $H_{15/17}$), 2.43 (s, 3H, H_8).

^{13}C (151 MHz, $CDCl_3$) δ_C = 165.5 (C_{18}), 163.2 (C_{20}), 153.6 (C_{Ar}), 151.7 (C_3), 149.8 (C_{Ar}), 141.9 (C_{Ar}), 138.0 (C_{Ar}), 137.8 (C_{Ar}), 136.5 (C_{Ar}), 133.2 (C_{Ar}), 132.5 (C_{23}), 124.1 (C_6), 123.2 (C_{25}), 116.8 (C_{22}), 115.4 (C_{26}), 114.3 (C_{Ar}), 113.1 (C_{Ar}), 112.8 (C_4), 100.8 (C_{Ar}), 92.7 (C_{19}), 56.6 ($C_{16/17}$), 56.1 (C_7), 55.8 ($C_{16/17}$), 21.7 (C_8).

IR (film) ν_{max}/cm^{-1} **=** 2981, 2360, 2341, 1723, 1626, 1609, 1567, 1549, 1515, 1493, 1464, 1452, 1390, 1327, 1261, 1223, 1207, 1180, 1146, 1122, 1089, 1032, 998, 913, 876, 832, 767, 737, 669, 647.

HRMS (ESI^+): *m/z* calculated for $C_{25}H_{24}NO_6^+$, $[M+H]^+$ = 434.1598; *m/z* found = 434.1590, Δ = -2.0 ppm.

2,3-Dimethoxy-6,8-dimethyl-5-(2-oxo-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 304:



^{t}BuONO (24 μL, 0.20 mmol, 1 eq.) was added to a solution of 4-((2'-Amino-4',5'-dimethoxy-3,5-dimethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one **300** (17 mg, 0.04 mmol, 1 eq) and HBF_4 (48% aq., 26 μL, 0.20 mmol, 5 eq.) in CH_2Cl_2:IPA (1:1, 0.5 mL:0.5 mL) at 0 °C. After 15 mins, the reaction mixture was diluted with CH_2Cl_2 (1 mL), washed with H_2O (0.5 mL), dried ($MgSO_4$),

filtered and the solvent was removed by a steady stream of N_2. The reaction was diluted in $CDCl_3$ (1 mL) and left for 1 h at r.t.. The solvent was then removed by a steady stream of N_2 to give the title compound as a dark red solid (16 mg, 89%).

m.p. = 130-134 °C.

^{1}H (600 MHz, CD_3CN) δ_H = 8.03 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{23}), 7.74 (s, 1H, $H_{10/13}$), 7.67 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H, H_{21}), 7.51 – 7.47 (m, 1H, H_4), 7.45 – 7.38 (m, 2H, $H_{10/13}$, H_{22}), 7.36 (d, *J* = 2.1 Hz, 1H, H_6), 7.32 (dd, *J* = 8.4, 1.1 Hz, 1H, H_{20}), 5.15 (s, 1H, H_{17}), 4.02 (s, 3H, $H_{14/15}$), 3.85 (s, 3H, $H_{14/15}$), 2.46 (s, 3H, H_8), 2.25 (s, 3H, H_7).

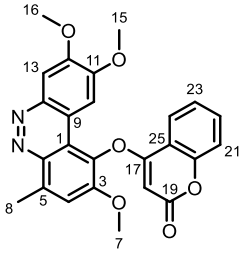
^{13}C (126 MHz, $CDCl_3$) δ_C = 165.0 (C_{16}), 162.2 (C_{14}), 154.6 (C_{19}), 151.0 ($C_{11/12}$), 145.9 (C_2), 140.8 ($C_{11/12}$), 139.5 (C_{Ar}), 136.8 (C_4), 134.3 (C_{Ar}), 133.3 (C_{21}), 130.9 (C_6), 126.6 (C_{Ar}), 125.5 (C_{22}), 123.7 (C_{23}), 117.6 (C_{Ar}), 116.8 (C_{20}), 115.4 ($C_{10/14}$), 113.0 ($C_{10/14}$), 101.1 (C_{Ar}), 94.5 (C_{17}), 59.0 ($C_{14/15}$), 57.6 ($C_{14/15}$), 20.9 (C_8), 16.5 (C_7). Two aromatic carbon peaks were not observed.

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -150.6.

IR (film) ν_{max}/cm^{-1} = 2981, 2361, 2341, 1719, 1683, 1624, 1607, 1568, 1507, 1474, 1389, 1271, 1220, 1183, 1145, 1076, 1002, 934, 874, 769, 692, 631.

HRMS (ESI^+): *m*/*z* calculated for $C_{25}H_{21}O_5^+$, $[M]^+$ = 401.1384; *m*/*z* found 401.1378, Δ = -1.27 ppm.

4-((2,8,9-Trimethoxy-4-methylbenzo[c]cinnolin-1-yl)oxy)-2*H*-chromen-2-one, 307:



^{t}BuONO (59 μL, 0.50 mmol, 5 eq.) was added to a solution of 4-((2'-amino-3,4',5'-trimethoxy-5-methyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one **307** (43 mg, 0.10 mmol, 5 eq.) and HBF_4 (48% aq., 65 μL, 0.50 mmol, 5 eq.) in CH_2Cl_2:IPA (1:1, 1 mL:1 mL) at 0 °C. After 15 mins, the reaction mixture was diluted with CH_2Cl_2 (2.5 mL), washed with H_2O (1 mL), dried ($MgSO_4$), filtered and the solvent was removed by a steady stream of N_2. The reaction was diluted in $CDCl_3$ (1 mL) and left for 1 h. The solvent was then removed by a steady stream of N_2 to give the title compound as an orange solid (44 mg, 98%).

m.p. = dec.>200 °C.

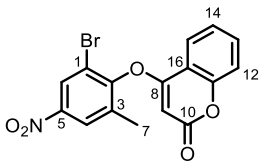
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.32 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{24}), 8.15 (s, 1H, $H_{10/13}$), 8.11 (d, *J* = 2.1 Hz, 1H, $H_{10/13}$), 7.86 (s, 1H, H_4), 7.75 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H, H_{22}), 7.51 (td, *J* = 7.7, 1.1 Hz, 1H, H_{23}), 7.47 (d, *J* = 8.4 Hz, 1H, H_{21}), 5.25 (d, *J* = 1.6 Hz, 1H, H_{18}), 4.19 (s, 3H, $H_{15/16}$), 4.15 (s, 3H, $H_{15/16}$), 3.49 (s, 3H, H_8), 3.02 (s, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 163.4 (C_2), 161.5 (C_{19}), 158.1 (C_{Ar}), 155.9 (C_{Ar}), 155.5 (C_{Ar}), 154.0 (C_{20}), 145.8 (C_{Ar}), 137.9 (C_{Ar}), 134.9 (C_{Ar}), 134.0 (C_{22}), 131.6 (C_{Ar}), 124.8 (C_{23}), 122.8 (C_{24}), 121.1 (C_{Ar}), 120.7 (C_{Ar}), 118.6 (C_4), 117.8 (C_{21}), 114.5 (C_{25}), 103.8 ($C_{10/13}$), 101.4 ($C_{10/13}$), 93.6 (C_{18}), 57.9 ($C_{15/16}$), 57.9 ($C_{15/16}$), 56.5 (C_7), 19.0 (C_8).

IR (film) ν_{max}/cm^{-1} **=** 3076, 2918, 2850, 1726, 1683, 1628, 1608, 1568, 1514, 1493, 1467, 1439, 1417, 1391, 1353, 1306, 1267, 1231, 1181, 1138, 1080, 1061, 1031, 989, 956, 934, 879, 831, 770, 735, 655, 631.

HRMS (ESI^+): *m/z* calculated for $C_{25}H_{21}N_2O_6^+$, $[M+H]^+$ = 445.1394; *m/z* found = 445.1392, Δ = -0.49 ppm.

4-(2-Bromo-6-methyl-4-nitrophenoxy)-2*H*-chromen-2-one, 309:



K_2CO_3 (1.24 g, 9.00 mmol, 1.5 eq.) was added to a solution of 4-hydroxy-2*H*-chromen-2-one **283** (1.60 g, 9.00 mmol, 1.5 eq.) and 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (1.50 g, 6.00 mmol, 1 eq.) in DMF (12 mL) and the reaction mixture heated to 110 °C. After 3 days, the reaction mixture was cooled, H_2O (100 mL) was added and the reaction mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90, R_f = 0.2) to give the title compound as a yellow solid (291 mg, 13%).

m.p. = 118-120 °C.

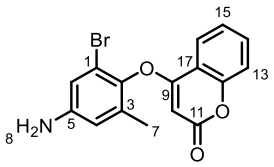
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.44 (d, *J* = 2.7 Hz, 1H, H_6), 8.20 (dd, *J* = 2.6, 1.0 Hz, 1H, H_4), 8.07 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{15}), 7.68 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H_{13}), 7.42 (td, *J* = 8.1, 1.3 Hz, 2H, H_{12}, H_{14}), 5.21 (s, 1H, H_9), 2.38 (s, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 162.9 (C_8), 161.6 (C_{10}), 153.8 (C_{11}), 152.6 (C_2), 146.1 (C_5), 134.5 (C_3), 133.4 (C_{13}), 127.2 (C_6), 125.9 (C_4), 125.9 (C_4), 124.5 (C_{14}), 123.0 (C_{15}), 117.4 (C_1), 117.2 (C_{12}), 114.3 (C_{16}), 93.4 (C_9), 16.9 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3090, 2360, 2341, 1729, 1630, 1608, 1570, 1532, 1492, 1454, 1386, 1343, 1252, 1222, 1175, 1151, 1135, 1095, 1032, 935, 912, 875, 847, 768, 746, 710.

HRMS (ESI$^+$): *m/z* calculated for $C_{16}H_{11}BrNO_5^+$, $[M+H]^+$ = 375.9812; *m/z* found = 375.9815, Δ = -0.84 ppm.

4-(4-Amino-2-bromo-6-methylphenoxy)-2*H*-chromen-2-one, 310:



H_2 was sparged through a solution of 4-(2-bromo-6-methyl-4-nitrophenoxy)-2*H*-chromen-2-one **283** (285 mg, 0.76 mmol, 1 eq.) and Pd/C (10% wt., 40 mg, 0.038 mmol, 5 mol%) and EtOAc (5 mL) under N_2 for 5 minutes and kept under a H_2 pressure (1 atm). After 16 h, N_2 was sparged through the solution for 10 mins, the reaction was filtered over Celite® and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 20:80, R_f = 0.1) to give the title compound as a yellow solid (163 mg, 62%).

m.p. = 180-184 °C.

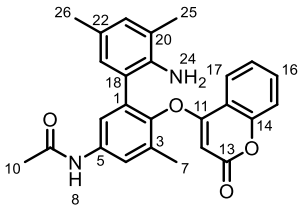
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.07 (dd, *J* = 7.9, 1.6 Hz, 1H, H_{16}), 7.62 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H_{14}), 7.39 – 7.32 (m, 2H, H_{13}, H_{15}), 6.81 (d, *J* = 2.7 Hz, 1H, H_6), 6.53 (d, *J* = 2.7 Hz, 1H, H_4), 5.34 (s, 1H, H_{10}), 3.73 (s, 2H, H_8), 2.12 (s, 3H, H_7).

^{13}C (126 MHz, $CDCl_3$) δ_C = 164.8 (C_9), 162.8 (C_{11}), 153.8 (C_{12}), 145.8 (C_2), 139.6 (C_5), 132.9 (C_3), 132.8 (C_{14}), 124.2 (C_{15}),123.2 (C_{16}), 117.1 (C_6), 116.9 (C_{13}), 116.6 (C_4), 116.4 (C_1), 115.1 (C_{17}), 92.9 (C_{10}), 16.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3368, 2360, 2341, 1720, 1626, 1610, 1568, 1477, 1389, 1275, 1221, 1182, 1138, 1087, 1031, 937, 876, 837, 767, 737, 670.

HRMS (ESI$^+$): *m/z* calculated for $C_{16}H_{13}BrNO_3^+$, $[M+H]^+$ = 346.0073; *m/z* found = 346.0067, Δ = -1.88 ppm.

***N*-(2'-Amino-3',5,5'-trimethyl-6-((2-oxo-2*H*-chromen-4-yl)oxy)-[1,1'-biphenyl]-3-yl)acetamide, 312:**



4-(4-Amino-2-bromo-6-methylphenoxy)-2*H*-chromen-2-one **310** (118mg, 0.34 mmol, 1 eq.) was dissolved in CH_2Cl_2 (1.7 mL) and Ac_2O (97 μL, 1.03 mmol, 3 eq.) was added. After 4 h, $NaHCO_3$ (sat. aq., 5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 5 mL). The organic extracts were washed with $NaHCO_3$ (sat. aq., 10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue, 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (101 mg, 0.41 mmol, 1.2 eq.), $Pd(PPh_3)_4$ (2 mg, 0.0017 mmol, 5 mol%) and K_2CO_3 (190 mg, 1.37 mmol, 4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 1.7 mL/1.7 mL, 0.1 M) was added and the solution was sparged for 10 minutes. The reaction mixture was then heated to 85 °C. After 16 h the reaction mixture was cooled to r.t, filtered over Celite® and eluted with EtOAc (10 mL x 3). The mixture was then washed with NaOH (1 M, 5 mL) and NaCl (sat., aq., 10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 55:45, R_f = 0.2) to give the title compound as an orange solid (40 mg, 27%).

m.p. = 124-126 °C.

*Note: **312** is atropisomeric therefore peak broadening was observed at r.t.. For full assignment the NMR should be conducted at an elevated temperature.*

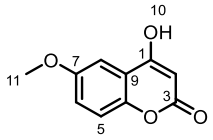
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.98 – 7.80 (m, 1H, H_{Ar}), 7.74 – 7.56 (m, 2H, H_{Ar}), 7.57 – 7.30 (m, 2H, H_{Ar}), 7.22 (m, 1H, H_{Ar}), 6.88 – 6.50 (m, 2H, H_{Ar}), 5.36 – 5.05 (m, 1H, H_{Ar}), 3.45 (s, 2H, H_{24}), 2.23 (s, 3H, H_{26}), 2.17 (s, 3H, H_{10}), 2.04 (s, 6H, H_7, H_{25}).

^{13}C (151 MHz, $CDCl_3$) δ_C = 168.6 (C_{11}), 165.2 (C_{Ar}), 162.9 (C_{Ar}), 153.5 (C_{Ar}), 144.5 (C_{Ar}), 137.1 (C_{Ar}), 132.8 (C_{Ar}), 132.6 (C_{Ar}), 132.2 (C_{Ar}), 132.2 (C_{Ar}), 132.2 (C_{Ar}), 131.2 (C_{Ar}), 128.9 (C_{Ar}), 128.7 (C_{Ar}), 128.7 (C_{Ar}), 123.9 (C_{Ar}), 123.1 (C_{Ar}), 122.4 (C_{Ar}), 121.2 (C_{Ar}), 116.7 (C_{Ar}), 115.2 (C_{Ar}), 93.0 (C_{12}), 24.7 (C_{10}), 20.3 (C_{26}), 17.9 ($C_{7/25}$), 16.5 ($C_{7/25}$).

IR (film) ν_{max}/cm^{-1} = 3309, 2981, 1717, 1683, 1624, 1388, 1182, 735.

HRMS (ESI^+): *m/z* calculated for $C_{26}H_{25}N_2O_4^+$, $[M+H]^+$ = 429.1809; *m/z* found = 429.1801, Δ = -1.94 ppm.

4-Hydroxy-6-methoxy-2*H*-chromen-2-one, 314:



Compound **314** was prepared according to **General Procedure E** using 1-(2-hydroxy-5-methoxyphenyl)ethan-1-one (2.00 g, 12.0 mmol, 1.00 eq.), NaH (60% in oil, 24.1 g, 60.2 mmol, 5 eq.) and diethylcarbonate (2.2 mL, 18.1 mmol, 1.5 eq.) to afford a white solid (1.54 g, 67%).

m.p. = 240-242 °C.

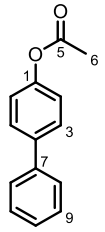
^{1}H NMR (600 MHz, DMSO-d_6) δ_H = 7.32 (dd, J = 8.2, 1.2 Hz, 1H, H_{Ar}), 7.25 – 7.21 (m, 2H, H_8, H_{Ar}), 5.60 (s, 1H, H_2), 3.81 (s, 3H, H_{11}).

^{13}C NMR (151 MHz, DMSO-d_6) δ_C = 165.4 (C_1), 162.1 (C_3), 155.3 (C_7), 147.9 (C_{Ar}), 120.4 (C_{Ar}), 117.7 (C_{Ar}), 116.2 (C_{Ar}), 105.0 (C_{Ar}), 91.2 (C_2), 55.7 (C_{11}).

IR (film) ν_{max}/cm^{-1} = 2924, 2854, 1677, 1612, 1465, 1275.

HRMS (ESI^+): calculated for $C_{10}H_9O_4^+$, $[M+H]^+$ = 193.0496; *m/z* found = 193.0495, Δ = 0.29 ppm.

[1,1'-Biphenyl]-4-yl acetate, 315a:



Compound **315a** was synthesised according to a literature procedure.[157] Acetyl chloride (2.6 mL, 36.0 mmol, 1.2 eq.) was added dropwise to a solution of [1,1'-biphenyl]-4-ol (5.12 g, 30.0 mmol, 1 eq.) and pyridine (2.7 mL, 36.0 mmol, 1.2 eq.) in CH_2Cl_2 (45 mL). After stirring for 3 h at r.t., the reaction mixture was washed sequentially with H_2O (30 mL), HCl (30 mL, 1 M), H_2O (30 mL) and $NaHCO_3$ (sat. aq., 30 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The title compound was obtained as a white solid (5.67 g, 89%) and was used without further purification.

m.p. = 69-71 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.62 – 7.58 (m, 2H, H_3), 7.58 – 7.55 (m, 2H, H_8), 7.44 (t, *J* = 8.0 Hz, 2H, H_9), 7.36 (td, *J* = 7.5, 1.0 Hz, 1H, H_{10}), 7.20 – 7.14 (m, 2H, H_2), 2.33 (s, 3H, H_6).

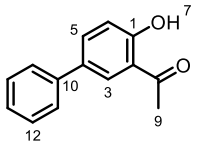
^{13}C (126 MHz, $CDCl_3$) δ_C = 169.7 (C_5), 150.2 (C_1), 140.5 (C_7), 139.2 (C_4), 128.9 (C_9), 128.3 (C_3), 127.5 (C_{10}), 127.3 (C_8), 122.0 (C_2), 21.3 (C_6).

IR (film) ν_{max}/cm^{-1} **=** 3791, 3697, 2361, 1751, 1599, 1549, 1515, 1485, 1431, 1374, 1218, 1195, 1166, 1019, 1009, 943, 907, 851, 766, 735, 700, 651.

HRMS (ESI$^+$): m/z calculated for $C_{14}H_{13}O_2^+$, $[M+H]^+$ = 213.0910; m/z found = 213.0910, Δ = 0.20 ppm.

Data in accordance with literature.[158]

1-(4-Hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one, 315b:



Compound **315b** was synthesised according to a modified literature procedure.[157] $AlCl_3$ (2.80 g, 21.0 mmol, 1.05 eq.) was added to a flame dried flask and evacuated and refilled with N_2 x 3. 1,2-Dichlorobenzene (10 mL) was added followed by [1,1'-biphenyl]-4-yl acetate **315a** (4.24 g, 20.0 mmol, 1 eq.) dissolved in 1,2-dichlorobenzene (10 mL) and then heated to 100 °C for 24 h. The reaction mixture was cooled to r.t., CH_2Cl_2 (50 mL) was added, and the resultant mixture was poured onto HCl (50 mL, 1 M) cooled to 0 °C. The organic phase was separated and washed sequentially with HCl (1 M, 2 x 10 mL) and H_2O (20 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* at 100 °C. The title compound was obtained as a yellow solid (1.91 g, 45%) and used without further purification.

m.p. = 54-56 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 12.26 (s, 1H, H_7), 7.92 (d, J = 2.3 Hz, 1H, H_3), 7.72 (dd, J = 8.6, 2.3 Hz, 1H, H_5), 7.56 – 7.51 (m, 2H, H_{11}), 7.45 (dd, J = 8.5, 7.0 Hz, 2H, H_{12}), 7.39 – 7.33 (m, 1H, H_{13}), 7.07 (d, J = 8.6 Hz, 1H, H_6), 2.70 (s, 3H, H_9).

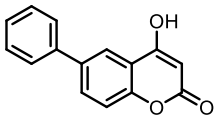
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 204.7 (C_8), 162.0 (C_1), 140.1 ($C_{4/10}$), 135.5 (C_5), 132.6 ($C_{4/10}$), 129.2 (C_3), 129.1 (C_{12}), 127.4 (C_{13}), 126.9 (C_{11}), 119.9 (C_2), 119.0 (C_6), 26.9 (C_9).

IR (film) ν_{max}/cm^{-1} = 2981, 1645, 1602, 1479, 1369, 1215, 770.

HRMS (ESI^+): calculated for $C_{14}H_{13}O_2^+$, $[M+H]^+$ = 213.0910; *m/z* found = 213.0909, Δ = -0.46 ppm.

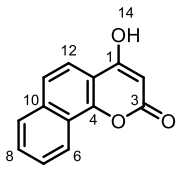
Data in accordance with literature.[159]

4-Hydroxy-6-phenyl-2*H*-chromen-2-one, 315:



Compound **315** was prepared according to **General Procedure E** using 1-(4-Hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one **315b** (1.50 g, 9.00 mmol, 1.00 eq.), NaH (60% in oil, 1.80 g, 45.0 mmol, 5 eq.) and diethylcarbonate (1.6 mL, 13.5 mmol, 1.5 eq.) to afford an impure white solid which was used in the subsequent step without further purification assuming 100% conversion.

4-Hydroxy-2*H*-benzo[h]chromen-2-one, 316:



Compound **316** was prepared according to **General Procedure E** using 1-(1-hydroxynaphthalen-2-yl)ethan-1-one (2.79 g, 15.0 mmol, 1 eq.), NaH (60% in oil, 3.00 g, 75.0 mmol, 5 eq.) and diethylcarbonate (2.7 mL, 22.5 mmol, 1.5 eq.) to afford a white solid (2.06 g, 65%).

m.p. = 264-266 °C.

^{1}H NMR (600 MHz, DMSO-d$_6$) δ_H= 12.66 (s, 1H, H_{14}), 8.38 – 8.31 (m, 1H, H_6), 8.05 – 8.00 (m, 1H, H_9), 7.81 (s, 2H, H_7, H_8), 7.76 – 7.67 (m, 2H, H_{11}, H_{12}), 5.72 (s, 1H, H_2).

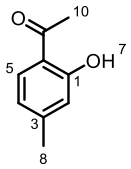
^{13}C NMR (151 MHz, DMSO-d$_6$) δ_C = 166.6 (C_1), 161.8 (C_3), 150.7 (C_4), 134.8 (C_{10}), 128.7 ($C_{7/8}$), 128.1 (C_9), 127.3 ($C_{7/8}$), 123.5 (C_{11}), 122.2 (C_5), 121.7 (C_6), 118.9 (C_{12}), 111.1 (C_{13}), 90.6 (C_2).

IR (film) ν_{max}/cm^{-1} = 2927, 1688, 1638, 1605, 1499, 1308, 1259, 1090, 970, 816, 745.

HRMS (ESI^+): calculated for $C_{13}H_9O_3^+$, $[M+H]^+$ = 213.0546; *m/z* found = 213.0544, Δ = -0.23 ppm.

Data in accordance with literature.[160]

1-(2-Hydroxy-4-methylphenyl)ethan-1-one, 317a:



Compound **317a** was synthesised according to a modified literature procedure.[157] $AlCl_3$ (6.67 g, 50.0 mmol, 2 eq.) was added to a flame dried flask and evacuated and refilled with N_2 x 3. 1,2-Dichlorobenzene (25 mL) was added followed by *m*-tolyl acetate (3.75 g, 25.0 mmol, 1 eq.) dissolved in 1,2-dichlorobenzene (25 mL) and the reaction mixture was then heated to 100 °C for 24 h. The reaction mixture was cooled to r.t. and CH_2Cl_2 (50 mL) was added and the resultant mixture was poured onto HCl (50 mL, 1 M) cooled to 0 °C. The organic phase was separated and washed sequentially with HCl (2 x 10 mL, 1 M) and H_2O (20 mL), dried ($MgSO_4$) and concentrated *in vacuo* at 100 °C. The crude residue was purified by flash column chromatography (Et_2O:pentane, 2:98, R_f = 0.7) to give the title compound as an orange oil (1.34 g, 36%).

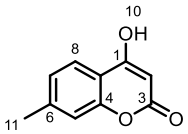
^{1}H NMR (600 MHz, CDCl$_3$) δ_H = 12.28 (s, 1H, H_7), 7.60 (d, *J* = 8.1 Hz, 1H, H_5), 6.79 – 6.76 (m, 1H, H_2), 6.70 (dd, *J* = 8.1, 1.6 Hz, 1H, H_4), 2.59 (s, 3H, H_{10}), 2.34 (s, 3H, H_8).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 203.9 (C_9), 162.5 (C_1), 148.1 (C_3), 130.6 (C_5), 120.2 (C_4), 118.4 (C_2), 117.6 (C_6), 26.5 (C_{10}), 21.9 (C_8).

IR (film) ν_{max}/cm^{-1} = 3000, 1638, 1577, 1368, 1248, 1166, 997, 794.

HRMS (ESI^+): calculated for $C_9H_1O_2^+$, $[M+H]^+$ = 151.0754; *m/z* found = 151.0751, Δ = -1.80 ppm.

4-Hydroxy-7-methyl-2*H*-chromen-2-one, 317:



Compound **317** was prepared according to **General Procedure E** using 1-(2-hydroxy-4-methylphenyl)ethan-1-one **317a** (1.05 g, 7.00 mmol, 1 eq.), NaH (60% in oil, 1.40 g, 35.0 mmol, 5 eq.) and diethylcarbonate (1.3 mL, 10.5 mmol, 1.5 eq.) to afford a white solid (997 mg, 81%).

m.p. = 200-202 °C.

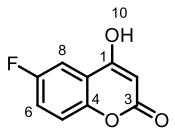
^{1}H NMR (600 MHz, DMSO-d_6) δ_H = 12.42 (s, 1H, H_{10}), 7.69 (d, *J* = 8.0 Hz, 1H, H_8), 7.20 – 7.17 (m, 1H, H_5), 7.16 (ddd, *J* = 8.0, 1.6, 0.7 Hz, 1H, H_7), 5.54 (s, 1H, H_2), 2.40 (s, 3H, H_{11}).

IR (film) ν_{max}/cm^{-1} = 2926, 2586, 1697, 1604, 1560, 1317, 1814.

HRMS (ESI^+): calculated for $C_{10}H_9O_3^+$, $[M+H]^+$ = 177.0546; *m/z* found = 177.0546, Δ = -0.42 ppm.

Data in accordance with literature.[161]

6-Fluoro-4-hydroxy-2*H*-chromen-2-one, 318:



Compound **318** was prepared according to **General Procedure E** using 1-(5-fluoro-2-hydroxyphenyl)ethan-1-one (2.06 g, 13.3 mmol, 1 eq.), NaH (60% in oil, 2.67 g, 66.7 mmol, 5 eq.) and diethylcarbonate (2.4 mL, 20.0 mmol, 1.5 eq.) to afford an off-white solid (2.24 g, 93%).

m.p. = 245-247 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$) δ_H = 12.75 (s, 1H, H_{10}), 7.56 – 7.49 (m, 2H, H_6, H_8), 7.46 – 7.39 (m, 1H, H_5), 5.65 (s, 1H, H_2).

^{13}C NMR (101 MHz, DMSO-d$_6$) δ_C = 164.8 (d, J = 2.5 Hz, C_1), 161.7 (C_3), 157.9 (d, J = 240.9 Hz, C_7), 149.8 (d, J = 1.7 Hz, C_4), 120.0 (d, J = 24.4 Hz, C_6), 118.5 (d, J = 8.4 Hz, C_5), 117.0 (d, J = 8.8 Hz, C_9), 108.7 (d, J = 25.1 Hz, C_8), 91.6 (C_2).

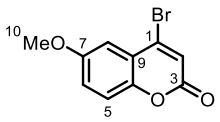
^{19}F NMR (376 MHz, DMSO-d$_6$) δ_F = -118.0.

IR (film) ν_{max}/cm^{-1} = 3088, 1700, 1573, 1308, 1226, 819.

HRMS (ESI^+): m/z calculated for $C_9H_6O_3F^+$, $[M+H]^+$ = 181.0295; m/z found 181.0299, Δ = 1.68 ppm.

Data in accordance with literature.[162]

4-Bromo-6-methoxy-2*H*-chromen-2-one, 319a:



Compound **319a** was prepared according to **General procedure F** using 4-hydroxy-6-methoxy-2*H*-chromen-2-one **314** (1.50 g, 7.81 mmol, 1 eq.), TBAB (3.77 g, 11.7 mmol, 1.5 eq.), and P_2O_5 (2.21 g, 15.6 mmol, 2 eq.) in PhMe (16 mL). The crude residue was used without further purification to give the title compound as a brown solid (1.00 g, 50%).

m.p. = 150-152 °C.

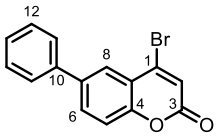
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.25 – 7.23 (m, 2H, H_5, H_8), 7.14 (dd, *J* = 9.0, 2.9 Hz, 1H, H_6), 6.85 (s, 1H, H_2), 3.87 (s, 3H, H_{10}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 159.0 (C_3), 156.6 (C_7), 147.1 (C_4), 141.3 (C_1), 121.1 (C_6), 120.0 (C_2), 119.6 (C_9), 118.4 (C_5), 110.3 (C_8), 56.1 (C_{10}).

IR (film) ν_{max}/cm^{-1} **=** 3083, 1746, 1725, 1540, 1265, 913, 739.

HRMS (ESI^+): calculated for $C_{10}H_8BrO_3^+$, $[M+H]^+$ = 254.9651; *m/z* found = 254.9645, Δ = -2.34 ppm.

4-Bromo-6-phenyl-2*H*-chromen-2-one, 320a:



Compound **320a** was prepared according to **General procedure F** using 4-hydroxy-6-methoxy-2*H*-chromen-2-one **315** (1.79 g, 7.50 mmol, 1 eq.), TBAB (3.63 g, 11.3 mmol, 1.5 eq.), and P_2O_5 (2.13 g, 15.0 mmol, 2 eq.) in PhMe (15 mL). The crude residue was used without further purification to give the title compound as an orange solid (1.65 g, 73%).

***315** was carried through as an impure mixture therefore the yield is reported over 2 steps.*

m.p. = 108-110 °C.

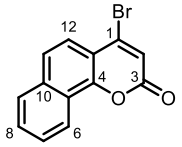
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.00 (d, *J* = 2.2 Hz, 1H, H_8), 7.80 (dd, *J* = 8.5, 2.2 Hz, 1H, H_6), 7.64 – 7.56 (m, 2H, H_{11}), 7.53 – 7.45 (m, 2H, H_{12}), 7.43 – 7.38 (m, 2H, H_5, H_{13}), 6.89 (s, 1H, H_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 158.7 (C_3), 151.9 (C_4), 141.6 (C_1), 139.2 (C_{Ar}), 138.5 (C_{Ar}), 132.2 (C_6), 129.2 (C_{11}), 128.2 (C_{13}), 127.3 (C_{12}), 126.3 (C_8), 120.0 (C_2), 119.2 (C_9), 117.6 (C_5).

IR (film) ν_{max}/cm^{-1} = 2956, 1737, 1478, 1185, 1133, 949.

HRMS (ESI^+): calculated for $C_{15}H_{10}BrO_2^+$, $[M+H]^+$ = 300.9859; *m/z* found = 300.9855, Δ = -1.32 ppm.

4-Bromo-2*H*-benzo[h]chromen-2-one, 321a:



Compound **321a** was prepared according to **General procedure F** using 4-hydroxy-6-methoxy-2*H*-chromen-2-one **316** (1.70 g, 8.00 mmol, 1 eq.), TBAB (3.87 g, 12.0 mmol, 1.5 eq.), and P_2O_5 (2.27 g, 16.0 mmol, 2 eq.) in PhMe (16 mL). The crude residue was used without further purification to give the title compound as a green solid (1.59 g, 72%).

m.p. = 138-140 °C.

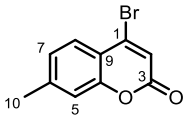
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.48 – 8.39 (m, 1H, H_{12}), 7.84 – 7.75 (m, 1H, H_6), 7.71 (dd, *J* = 9.1, 2.3 Hz, 1H, H_9), 7.66 – 7.54 (m, 3H, H_7, H_8, H_{11}), 6.83 (s, 1H, H_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 158.9 (C_3), 150.2 (C_4), 142.6 (C_1), 135.4 (C_{10}), 129.6 (C_{11}), 127.9 (C_6), 127.7 ($C_{7/9}$), 125.0 ($C_{7/9}$), 123.1 (C_8), 122.9 (C_{12}), 122.7 (C_5), 118.7 (C_2), 114.5 (C_{13}).

IR (film) ν_{max}/cm^{-1} **=** 2925, 1732, 1465, 918, 740.

HRMS (ESI^+): calculated for $C_{13}H_8BrO_2^+$, $[M+H]^+$ = 274.9702; *m/z* found = 274.9702, Δ = -0.08 ppm.

4-Bromo-7-methyl-2*H*-chromen-2-one, 322a:



Compound **322a** was prepared according to **General procedure F** using 4-hydroxy-7-methyl-2*H*-chromen-2-one **317** (881 mg, 5.00 mmol, 1 eq.), TBAB (2.42 g, 7.50 mmol, 1.5 eq.), and P_2O_5 (1.42 g, 10.0 mmol, 2 eq.) in PhMe (10 mL). The crude residue was used without further purification to give the title compound as a green solid (915 mg, 77%).

m.p. = 124-126 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.67 (d, *J* = 8.1 Hz, 1H, H_8), 7.14 (d, *J* = 8.2, 1H, H_7), 7.10 (s, 1H, H_5), 6.75 (s, 1H, H_2), 2.46 (s, 3H, H_{10}).

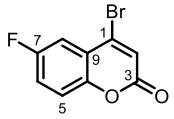
^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 159.0 (C_3), 152.6 (C_4), 144.8 (C_6), 141.6 (C_1), 127.7 (C_8), 126.2 (C_7), 118.4 (C_2), 117.1 (C_5), 116.7 (C_9), 21.7 (C_{10}).

IR (film) ν_{max}/cm^{-1} **=** 1740, 1723, 1599, 1344, 923, 740.

HRMS (ESI^+): calculated for $C_{10}H_8BrO_2^+$, $[M+H]^+$ = 238.9702; *m/z* found = 238.9700, Δ = -0.93 ppm.

Data in accordance with literature.[163]

4-Bromo-6-fluoro-2*H*-chromen-2-one, 323a:



Compound **323a** was prepared according to **General procedure F** using 6-fluoro-4-hydroxy-2*H*-chromen-2-one, **318** (1.20 g, 6.66 mmol, 1 eq.), TBAB (3.22 g, 9.99 mmol, 1.5 eq.), and P_2O_5 (1.89 g, 13.3 mmol, 2 eq.) in PhMe (13 mL). The crude residue was used without further purification to give the title compound as a brown solid (963 mg, 59%).

m.p. = 110-112 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.55 (dd, *J* = 8.5, 2.7 Hz, 1H, H_8), 7.36 – 7.28 (m, 2H, H_5, H_6), 6.91 (s, 1H, H_2).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 159.4 (d, *J* = 199.0 Hz, C_7), 157.9 (C_3), 148.8 (d, *J* = 2.1 Hz, C_4), 140.3 (d, *J* = 2.9 Hz, C_1), 120.8 (d, *J* = 24.6 Hz, C_6), 120.7 (C_2), 120.2 (d, *J* = 9.1 Hz, C_9), 118.9 (d, *J* = 8.3 Hz, C_5), 113.9 (d, *J* = 26.3 Hz, C_8).

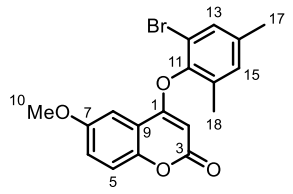
^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -115.7.

IR (film) ν_{max}/cm^{-1} **=** 3083, 2958, 2875, 2181, 1716, 1609, 1565, 1490, 1466, 1424, 1389, 1356, 1318, 1274, 1258, 1237, 1198, 1180, 1144, 1029, 927, 913, 873, 844, 823, 804, 736, 655, 647, 640, 616.

HRMS (ESI^+): calculated for $C_9H_5BrFO_2^+$, $[M+H]^+$ = 242.9451; *m/z* found = 242.9444, Δ = -3.29 ppm.

Data in accordance with literature.[164]

4-(2-Bromo-4,6-dimethylphenoxy)-6-methoxy-2*H*-chromen-2-one, 319b:



Compound **319b** was prepared according to **General Procedure G** using 4-bromo-6-methoxy-2*H*-chromen-2-one **319a** (893 mg, 3.50 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (774 mg, 3.85 mmol, 1.1 eq.) and K_2CO_3 (967 mg, 7.00 mmol, 2 eq.) in MeCN (12 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.3) to give the title compound as an orange solid (1.19 g, 91%).

m.p. = 170-172 °C.

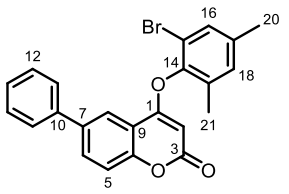
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.49 (d, *J* = 3.0 Hz, 1H, H_8), 7.35 – 7.30 (m, 2H, H_5, H_{13}), 7.20 (dd, *J* = 9.1, 3.0 Hz, 1H, H_6), 7.06 (dt, *J* = 2.4, 0.8 Hz, 1H, H_{15}), 5.26 (s, 1H, H_2), 3.91 (s, 3H, H_{10}), 2.35 (s, 3H, H_{17}), 2.19 (s, 3H, H_{18}).

^{13}C (126 MHz, $CDCl_3$) δ_C = 164.0 ($C_{1/3}$), 162.9 ($C_{1/3}$), 156.3 (C_7), 148.4 (C_4), 145.6 (C_{11}), 138.3 (C_{16}), 132.2 (C_{14}), 132.1 (C_{13}), 131.7 (C_{15}), 121.1 (C_6), 118.2 (C_5), 115.8 (C_{12}), 115.4 (C_9), 105.1 (C_8), 93.3 (C_2), 56.1 (C_{10}), 20.8 (C_{17}), 16.5 (C_{18}).

IR (film) ν_{max}/cm^{-1} **=** 3003, 2951, 2838, 2361, 2341, 2252, 1719, 1634, 1612, 1578, 1540, 1496, 1453, 1428, 1374, 1335, 1272, 1248, 1210, 1172, 1123, 1076, 1035, 930, 913, 854, 831, 793, 736, 669, 649, 608.

HRMS (ESI^+): calculated for $C_{18}H_{16}BrO_4^+$, $[M+H]^+$ = 375.0227; m/z found = 375.2015, Δ = -3.19 ppm.

4-(2-Bromo-4,6-dimethylphenoxy)-6-phenyl-2*H*-chromen-2-one, 320b:



Compound **320b** was prepared according to **General Procedure G** using 4-bromo-6-phenyl-2*H*-chromen-2-one **320a** (1.51 g, 5.00 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (1.12 g, 5.50 mmol, 1.1 eq.) and K_2CO_3 (1.38 g, 10.0 mmol, 2 eq.) in MeCN (17 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 15:85, R_f = 0.3) to give the title compound as a yellow solid (1.47 g, 70%).

m.p. = 166-168 °C.

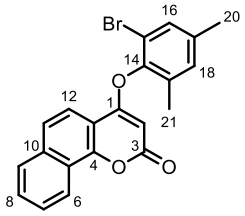
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.28 (d, *J* = 2.3 Hz, 1H, H_8), 7.86 (dd, *J* = 8.6, 2.2 Hz, 1H, H_6), 7.70 – 7.64 (m, 2H, H_{11}), 7.52 – 7.45 (m, 3H, H_5, H_{12}), 7.43 – 7.37 (m, 1H, H_{13}), 7.34 (d, *J* = 2.0 Hz, 1H, H_{16}), 7.09 – 7.06 (m, 1H, H_{18}), 5.31 (s, 1H, H_2), 2.36 (s, 3H, H_{20}), 2.22 (s, 3H, H_{21}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 164.2 (C_1), 162.6 (C_3), 153.3 (C_4), 145.5 (C_{14}), 139.6 (C_{Ar}), 138.3 (C_{17}), 137.8 (C_{Ar}), 132.2 (C_{Ar}), 132.1 (C_{16}), 131.8 (C_6), 131.7 (C_{18}), 129.2 (C_{12}), 128.0 (C_{13}), 127.3 (C_{11}), 121.4 (C_8), 117.5 (C_5), 115.8 (C_{15}), 115.3 (C_{Ar}), 93.3 (C_2), 20.8 (C_{20}), 16.5 (C_{21}).

IR (film) ν_{max}/cm^{-1} = 1720, 632, 1577, 1371, 909, 832, 732.

HRMS (ESI^+): calculated for $C_{23}H_{18}BrO_3^+$, $[M+H]^+$ = 421.0434; *m/z* found = 421.0430, Δ = -0.85 ppm.

4-(2-Bromo-4,6-dimethylphenoxy)-2*H*-benzo[h]chromen-2-one, 321b:



Compound **321b** was prepared according to **General Procedure G** using 4-bromo-2*H*-benzo[h]chromen-2-one **321a** (1.38 g, 5.00 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (1.12 g, 5.50 mmol, 1.1 eq.) and K_2CO_3 (1.38 g, 10.0 mmol, 2 eq.) in MeCN (17 mL). The crude residue was purified by flash column chromatography (EtOAc:Pentane, 15:85, R_f = 0.3) to give the title compound as an orange solid (1.53 g, 77%).

m.p. = 168-172 °C.

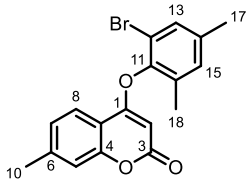
^{1}H NMR (600 MHz, $CDCl_3$) δ_C = 8.61 – 8.57 (m, 1H, H_6), 8.07 (d, *J* = 8.7 Hz, 1H, H_{12}), 7.94 – 7.91 (m, 1H, H_{11}), 7.80 – 7.77 (m, 1H, H_9), 7.70 – 7.64 (m, 2H, H_7, H_8, 7.35 (dt, *J* = 2.2, 0.7 Hz, 1H, H_{16}), 7.10 – 7.06 (m, 1H, H_{18}), 5.36 (s, 1H, H_2), 2.36 (s, 3H, H_{20}), 2.22 (s, 3H, H_{21}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 165.2 (C_1), 162.7 (C_3), 151.5 (C_4), 145.6 (C_{14}), 138.1 (C_{17}), 135.5 (C_{Ar}), 132.1 (C_{Ar}), 132.0 (C_{16}), 131.6 (C_{18}), 129.0 ($C_{7/8}$), 127.9 (C_9), 127.2 ($C_{7/8}$), 124.2 (C_{11}), 123.0 (C_{Ar}), 122.8 (C_6), 118.5 (C_{12}), 115.7 (C_{15}), 110.3 (C_{13}), 92.4 (C_2), 20.7 (C_{20}), 16.4 (C_{21}).

IR (film) ν_{max}/cm^{-1} = 1725, 1614, 1470, 1386, 1209, 780.

HRMS (ESI^+): calculated for $C_{21}H_{16}BrO_3^+$, $[M+H]^+$ = 395.0277; *m/z* found = 395.0274, Δ = -0.84 ppm.

4-(2-Bromo-4,6-dimethylphenoxy)-7-methyl-2*H*-chromen-2-one, 322b:



Compound **322b** was prepared according to **General Procedure G** using 4-bromo-7-methyl-2*H*-chromen-2-one **322a** (837 mg, 3.50 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (774 mg, 3.85 mmol, 1.1 eq.) and K_2CO_3 (967 mg, 7.00 mmol, 2 eq.) in MeCN (12 mL). The crude residue was purified by flash column chromatography (EtOAc:Pentane, 15:85, R_f = 0.3) to give the title compound as an orange solid (1.05 g, 84%).

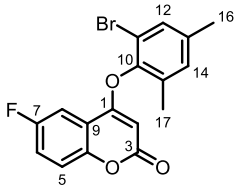
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.95 (d, *J* = 7.9 Hz, 1H, H_8), 7.32 (d, *J* = 2.1 Hz, 1H, H_{13}), 7.19 (d, *J* = 7.8 Hz, 2H, H_5, H_7), 7.08 – 7.03 (m, 1H, H_{15}), 5.20 (s, 1H, H_2), 2.49 (s, 3H, H_{10}), 2.34 (s, 3H, H_{17}), 2.18 (s, 3H, H_{18}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 164.3 (C_1), 162.9 (C_3), 153.9 (C_4), 145.5 (C_{11}), 144.2 (C_6), 138.0 (C_{14}), 132.1 (C_{16}), 132.0 (C_{13}), 131.5 (C_{15}), 125.4 (C_7), 122.9 (C_8), 117.0 (C_5), 115.7 (C_{12}), 112.4 (C_9), 92.0 (C_2), 21.8 (C_{10}), 20.6 (C_{17}), 16.4 (C_{18}).

IR (film) ν_{max}/cm^{-1} = 2980, 2250, 1726, 1626, 1390, 1219, 733.

HRMS (ESI^+): calculated for $C_{18}H_{16}BrO_3^+$, $[M+H]^+$ = 359.0277; m/z found = 359.0272, Δ = -1.52 ppm.

4-(2-Bromo-4,6-dimethylphenoxy)-6-fluoro-2*H*-chromen-2-one, 323b:



Compound **323b** was prepared according to **General Procedure G** using 4-bromo-6-fluoro-2*H*-chromen-2-one **323a** (851 mg, 3.50 mmol, 1 eq.), 2-bromo-4,6-dimethylphenol **51** (774 mg, 3.85 mmol, 1.1 eq.) and K_2CO_3 (967 mg, 7.00 mmol, 2 eq.) in MeCN (12 mL). The crude residue was used without further purification to give the title compound as an orange solid (1.27 g, quant.).

m.p. = 130-134 °C.

^{1}H (500 MHz, $CDCl_3$) δ_H = 7.74 (dd, *J* = 8.2, 2.9 Hz, 1H, $H_{6/8}$), 7.39 – 7.31 (m, 3H, H_5, $H_{6/8}$, H_{12}), 7.09 – 7.05 (m, 1H, H_{14}), 5.30 (s, 1H, H_2), 2.35 (s, 3H, H_{16}), 2.19 (s, 3H, H_{17}).

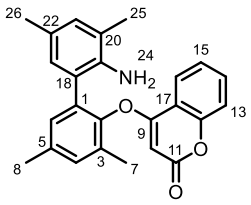
^{13}C (126 MHz, $CDCl_3$) δ_C = 163.4 (d, *J* = 2.7 Hz, C_1), 162.2 (C_3), 158.9 (d, *J* = 244.6 Hz, C_7), 150.0 (d, *J* = 2.1 Hz, C_4), 145.3 (C_{10}), 138.5 (C_{13}), 132.2 (C_{12}), 132.1 (C_{15}), 131.7 (C_{14}), 120.5 (d, *J* = 24.5 Hz, $C_{6/8}$), 118.7 (d, *J* = 8.2 Hz, C_5), 116.0 (d, *J* = 9.0 Hz, C_9), 115.7 (C_{11}), 109.2 (d, *J* = 25.1, $C_{6/8}$), 93.8 (C_2), 20.8 (C_{16}), 16.5 (C_{17}).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -116.7.

IR (film) ν_{max}/cm^{-1} = 3083, 2982, 2954, 2360, 2342, 1728, 1633, 1577, 1495, 1473, 1442, 1370, 1323, 1281, 1254, 1208, 1194, 1166, 1122, 1065, 933, 913, 874, 830, 794, 735, 648, 608.

HRMS (ESI^+): calculated for $C_{17}H_{13}BrFO_3^+$, $[M+H]^+$ = 363.0027; *m/z* found = 363.0015, Δ = -3.22 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2*H*-chromen-2-one, 319c:



Compound **319c** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-2*H*-chromen-2-one **319b** (5.18 g, 15.0 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (4.42 g, 22.5 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (867 mg, 0.75 mmol, 5 mol%) and K_2CO_3 (8.29 g, 60.0 mmol, 4 eq.) in DME (75 mL) and H_2O (75 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 1:9, R_f = 0.2) to give the title compound a brown solid (2.47 g, 43%).

m.p. = 172-176 °C.

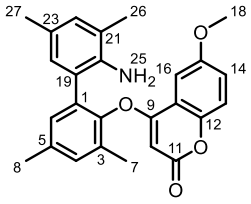
^{1}H NMR (600 MHz, DMSO-d$_6$, 363 K) δ_H = 7.90 (dd, *J* = 7.9, 1.7 Hz, 1H, H_{16}), 7.63 – 7.57 (m, 1H, H_{14}), 7.32 (td, *J* = 7.6, 1.1 Hz, 1H, H_{15}), 7.28 (dd, *J* = 8.4, 1.1 Hz, 1H_{13}), 7.23 – 7.20 (m, 1H, H_{Ar}), 7.07 (d, *J* = 2.3 Hz, 1H, H_{Ar}), 6.60 (s, 1H, H_{Ar}), 6.57 – 6.53 (m, 1H, H_{Ar}), 5.12 (s, 1H, H_{10}), 4.01 (s, 2H, H_{24}), 2.38 (s, 3H, H_{Alk}), 2.22 (s, 3H, H_{Alk}), 1.97 (s, 3H, H_{Alk}), 1.96 (s, H_{Alk}).

^{13}C NMR (151 MHz, DMSO-d$_6$, 363 K) δ_c = 163.6 (C_{Ar}), 160.3 (C_{Ar}), 152.3 (C_{Ar}), 145.6 (C_{Ar}), 139.7 (C_{Ar}), 135.6 (C_{Ar}), 132.1 (C_{14}), 131.7 (C_{Ar}), 130.6 (C_{Ar}), 129.6 (C_{Ar}), 129.6 (C_{Ar}), 129.5 (C_{Ar}), 127.7 (C_{Ar}), 123.8 (C_{Ar}), 123.2 (C_{15}), 122.3 (C_{16}), 121.3 (C_{Ar}), 120.5 (C_{Ar}), 115.5 (C_{13}), 114.1 (C_{Ar}), 91.7 (C_{10}), 19.7 (C_{Alk}), 19.0 (C_{Alk}), 16.8 (C_{Alk}), 14.9 (C_{Alk}).

IR (film) ν_{max}/cm^{-1} = 2980, 2341, 1725, 1626, 1608, 1568, 1487, 1452, 1388, 1327, 1275, 1222, 1199, 1179, 1146, 1087, 1032, 933, 875, 832, 812, 767, 750, 641, 641.

HRMS (ESI$^+$): calculated for $C_{25}H_{24}NO_3^+$, $[M+H]^+$ = 386.1751; *m/z* found = 386.1751, Δ = -0.85 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-methoxy-2*H*-chromen-2-one, 319c:



Compound **319c** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-6-methoxy-2*H*-chromen-2-one **319b** (520 mg, 1.39 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (856 mg, 3.46 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (80 mg, 0.069 mmol, 5 mol%) and K_2CO_3 (766 mg, 5.54 mmol, 4 eq.) in DME (7 mL) and H_2O (7 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 15:85, R_f = 0.2) to give the title compound a yellow solid (442 mg, 73%).

m.p. = 176-180 °C.

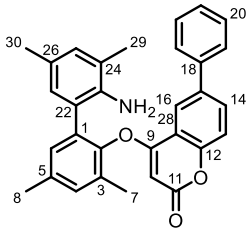
^{1}H NMR (500 MHz, DMSO-d$_6$, 363 K) δ_H = 7.34 (d, *J* = 2.8 Hz, 1H, H_{16}), 7.25 – 7.17 (m, 3H, H_4, H_{13}, H_{14}), 7.09 – 7.05 (m, 1H, H_6), 6.60 (s, 1H, $H_{22/24}$), 6.59 (s, 1H, $H_{22/24}$), 5.11 (s, 1H, H_{10}), 3.84 (s, 3H, H_{18}), 2.38 (s, 3H, H_8), 2.23 (s, 3H, H_7), 1.98 (s, 3H, H_{27}), 1.98 (s, 3H, H_{26}).

^{13}C NMR (126 MHz, DMSO-d$_6$, 363 K) δ_c = 163.5 (C_9), 160.5 (C_{11}), 155.2 (C_{15}), 146.9 (C_{12}), 145.8 (C_2), 139.8 (C_{20}), 135.7 (C_5), 131.8 (C_{Ar}), 130.7 (C_4), 129.7 (C_{Ar}), 129.7 (C_6), 129.6 (C_{Ar}), 127.8 (C_{Ar}), 123.9 (C_{Ar}), 121.4 (C_{Ar}), 119.8 (C_{14}), 116.7 (C_{13}), 114.7 (C_{17}), 105.3 (C_{16}), 92.1 (C_{10}), 55.5 (C_{18}), 19.8 (C_8), 19.1 (C_{27}), 16.8 (C_{26}), 15.0 (C_7). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} = 2980, 1715, 1576, 1212, 737.

HRMS (ESI$^+$): calculated for $C_{26}H_{26}NO_4^+$, $[M+H]^+$ = 416.1856; *m/z* found = 416.1845, Δ = -2.72 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-phenyl-2H-chromen-2-one, 320c:



Compound **320c** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-6-phenyl-2*H*-chromen-2-one **320b** (280 mg, 0.66 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (411 mg, 1.66 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (38 mg, 0.033 mmol, 5 mol%) and K_2CO_3 (367 mg, 2.66 mmol, 4 eq.) in DME (3.3 mL) and H_2O (3.3 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 15:85, R_f = 0.2) to give the title compound a yellow solid (262 mg, 86%).

m.p. = 176-178 °C.

^{1}H NMR (600 MHz, DMSO-d$_6$, 363 K) δ_H = 8.07 (d, *J* = 2.4 Hz, 1H, H_{16}), 7.87 (dd, *J* = 8.6, 2.3 Hz, 1H, H_{14}), 7.69 – 7.64 (m, 2H, H_{19}), 7.50 (dd, *J* = 8.5, 7.0 Hz, 2H, H_{20}), 7.43 – 7.38 (m, 1H, H_{21}), 7.36 (d, *J* = 8.6 Hz, 1H, H_{13}), 7.24 (d, J = 2.3 Hz, 1H, H_4), 7.07 (d, J = 2.2 Hz, 1H, H_6), 6.61 (s, 1H, $H_{25/27}$), 6.54 (m, 1H, $H_{25/27}$), 5.17 (s, 1H, H_{10}), 3.98 (s, 2H, H_{28}), 2.39 (s, 3H, H_8), 2.26 (s, 3H, H_7), 1.92 (s, 3H, H_{30}), 1.90 (s, 3H, H_{29}).

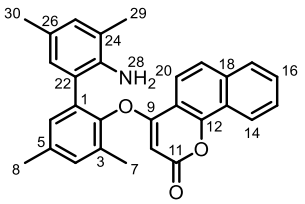
^{13}C NMR (151 MHz, DMSO-d$_6$, 363 K) δ_c = 163.8 (C_9), 160.4 (C_{11}), 151.9 (C_{12}), 146.0 (C_2), 139.8 (C_{23}), 138.4 (C_{18}), 135.8 (C_{15}), 135.8 (C_5), 131.8 (C_{Ar}), 130.7 ($C_{25/27}$), 130.6 (C_{14}), 129.8 (C_{Ar}), 129.7

(C_6), 129.6 (C_{Ar}), 128.5 (C_{20}), 127.8 ($C_{25/27}$), 127.2 (C_{21}), 126.2 (C_{19}), 124.0 (C_{Ar}), 121.5 (C_{Ar}), 120.8 (C_{Ar}), 120.0 (C_{16}), 116.2 (C_{13}), 114.6 (C_{17}), 92.3 (C_{10}), 19.9 (C_8), 19.1 (C_{30}), 16.7 (C_{29}), 15.1 (C_7).

IR (film) ν_{max}/cm^{-1} = 2980, 1668, 1472, 1366, 1204, 728.

HRMS (ESI^+) = calculated for $C_{31}H_{28}NO_3^+$, $[M+H]^+$ = 462.2057; *m/z* found = 462.2064, Δ = -1.35 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-2H-benzo[h]chromen-2-one, 321c:



Compound **321c** was prepared according to **General Procedure H** using 4-(2-Bromo-4,6-dimethylphenoxy)-2*H*-benzo[h]chromen-2-one **321b** (791 mg, 2.00 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.24 g, 5.00 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (116 mg, 0.10 mmol, 5 mol%) and K_2CO_3 (1.12 g, 8.01 mmol, 4 eq.) in DME (10 mL) and H_2O (10 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 15:85, R_f = 0.2) to give the title compound a yellow solid (789 mg, 91%).

m.p. = 98-100 °C.

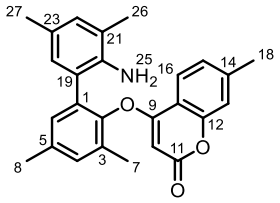
^{1}H NMR (600 MHz, DMSO-d_6, 373K) δ_H = 8.34 – 8.29 (m, 1H, $H_{14/17}$), 8.03 (dd, *J* = 7.5, 1.6 Hz, 1H, $H_{14/17}$), 7.91 (d, *J* = 8.7 Hz, 1H, $H_{19/20}$), 7.81 (d, *J* = 8.7 Hz, 1H, $H_{19/20}$), 7.71 (dddd, *J* = 16.8, 8.3, 6.9, 1.4 Hz, 2H, H_{15}, H_{16}), 7.26 (d, *J* = 2.2 Hz, 1H, $H_{4/25}$), 7.10 (d, *J* = 2.2 Hz, 1H, $H_{6/27}$), 6.64 (s, 1H, $H_{6/27}$), 6.53 – 6.50 (m, 1H, $H_{4/25}$), 5.23 (s, 1H, H_{10}), 4.04 (s, 2H, H_{28}), 2.41 (s, 3H, $H_{8/30}$), 2.26 (s, 3H, $H_{7/29}$), 1.96 (s, 6H, $H_{7/29}$, $H_{8/30}$).

^{13}C NMR (151 MHz, DMSO-d_6, 373 K) δ_C = 165.7 (C_9), 161.3 (C_{11}), 150.7 (C_{12}), 146.9 ($C_{2/23}$), 140.9 ($C_{2/23}$), 136.8 (C_{Ar}), 135.4 (C_{Ar}), 132.8 (C_{Ar}), 131.7 ($C_{4/25}$), 130.8 (C_{Ar}), 130.7 ($C_{4/25}$), 130.6 ($C_{6/27}$), 129.3 ($C_{15/16}$), 128.8 ($C_{6/27}$), 128.5 ($C_{14/17}$), 127.8 ($C_{15/16}$), 124.9 (C_{Ar}), 124.0 ($C_{19/20}$), 122.6 (C_{Ar}), 122.5 (C_{Ar}), 122.1 ($C_{14/17}$), 119.0 ($C_{19/20}$), 110.7 (C_{Ar}), 92.3 (C_{10}), 79.6 (C_{Ar}), 20.8 ($C_{8/30}$), 20.1 ($C_{8/30}$), 17.8 ($C_{7/29}$), 16.0 ($C_{7/29}$).

IR (film) ν_{max}/cm^{-1} = 2980, 1720, 1612, 1565, 1476, 1385, 1211, 962, 737.

HRMS (ESI^+): calculated for $C_{29}H_{26}NO_3^+$, $[M+H]^+$ = 436.1907; *m/z* found = 436.1900, Δ = -0.72 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-methyl-2H-chromen-2-one, 322c:



Compound **322c** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-7-methyl-2H-chromen-2-one **322b** (718 mg, 2.00 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.24 g, 5.00 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (116 mg, 0.10 mmol, 5 mol%) and K_2CO_3 (1.12 g, 8.01 mmol, 4 eq.) in DME (10 mL) and H_2O (10 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 15:85, R_f = 0.2) to give the title compound a yellow solid (660 mg, 83%).

m.p. = 168-170 °C.

^{1}H NMR (500 MHz, DMSO-d_6, 373K) δ_H = 7.77 (d, *J* = 8.0 Hz, 1H, H_{16}), 7.21 (d, *J* = 2.2 Hz, 1H, H_4), 7.13 (d, *J* = 8.1 Hz, 1H, H_{15}), 7.10 (s, 1H, H_{13}), 7.07 (s, 1H, H_6), 6.61 (s, 1H, $H_{22/24}$), 6.58

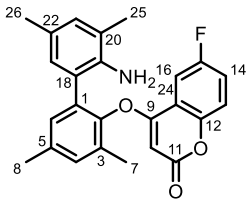
(s, 1H, $H_{22/24}$), 5.06 (s, 1H, H_{10}), 4.00 (s, 2H, H_{25}), 2.39 (s, 3H, H_{18}), 2.37 (s, 3H, H_8), 2.21 (s, 3H, H_7), 2.00 – 1.96 (m, 6H, H_{26}, H_{27}).

^{13}C NMR (126 MHz, DMSO-d$_6$, 373 K) δ_C = 163.9 (C_9), 160.5 (C_{11}), 152.6 (C_{12}), 145.7 (C_2), 143.1 (C_{14}), 139.8 (C_{20}), 135.7 (C_{Ar}), 131.9 (C_{Ar}), 130.7 (C_4), 129.7 (C_6), 129.7 ($C_{22/24}$), 129.6 (C_{Ar}), 127.8 ($C_{22/24}$), 124.4 (C_{15}), 123.9 (C_{Ar}), 122.1 (C_{16}), 121.5 (C_{Ar}), 120.7 (C_{Ar}), 115.6 (C_{13}), 111.7 (C_{17}), 90.8 (C_{10}), 20.5 (C_{18}), 19.8 (C_8), 19.1 (C_{27}), 16.8 (C_{26}), 14.9 (C_7).

IR (film) ν_{max}/cm^{-1} = 2981, 1720, 1624, 1390, 1188, 737.

HRMS (ESI^+): calculated for $C_{26}H_{26}NO_3^+$, $[M+H]^+$ = 400.1907; *m/z* found = 400.1900, Δ = -1.80 ppm.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-fluoro-2*H*-chromen-2-one, 323c:



Compound **323c** was prepared according to **General Procedure H** using 4-(2-bromo-4,6-dimethylphenoxy)-6-fluoro-2*H*-chromen-2-one **323b** (350 mg, 0.96 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (595 mg, 2.41 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (56 mg, 0.048 mmol, 5 mol%) and K_2CO_3 (533 mg, 3.85 mmol, 4 eq.) in DME (4.8 mL) and H_2O (4.8 mL). The crude residue was purified by flash column chromatography (EtOAc:pentane, 20:80, R_f = 0.2) to give the title compound a yellow solid (155 mg, 40%).

m.p. = 150-152 °C.

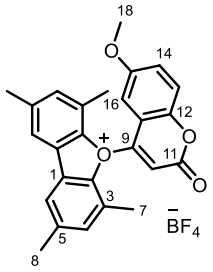
^{1}H NMR (500 MHz, DMSO-d_6, 373K) δ_H = 7.60 (dd, *J* = 8.7, 3.1 Hz, 1H, H_{16}), 7.43 (td, *J* = 8.7, 3.1 Hz, 1H, H_{14}), 7.33 (dd, *J* = 9.1, 4.4 Hz, 1H, H_{13}), 7.25 – 7.21 (m, 1H, H_4), 7.07 (d, *J* = 2.2 Hz, 1H, H_6), 6.58 (s, 1H, $H_{21/23}$), 6.56 (d, *J* = 2.0 Hz, 1H, $H_{21/23}$), 5.18 (s, 1H, H_{10}), 2.38 (s, 3H, H_8), 2.24 (s, 3H, H_7), 1.98 (s, 3H, H_{26}), 1.97 (s, 3H, H_{25}).

^{13}C NMR (126 MHz, DMSO-d_6, 373 K) δ_C = 162.9 (C_9), 160.1 (C_{11}), 157.5 (d, J = 241.3 Hz, C_{15}), 148.7 (C_{12}), 145.9 (C_2), 139.8 (C_{19}), 135.8 (C_5), 131.7 (C_{Ar}), 130.7 (C_4), 129.7 (C_6), 129.5 ($C_{21/23}$), 129.5 (C_{Ar}), 127.8 ($C_{21/23}$), 124.0 (C_{Ar}), 121.5 (C_{Ar}), 120.9 (C_{Ar}) 119.4 (d, J = 24.7 Hz, C_{14}), 117.6 (d, J = 8.4 Hz, C_{13}), 115.3 (d, J = 9.4 Hz, C_{17}), 108.0 (d, J = 25.9 Hz, C_{16}), 92.8 (C_{10}), 19.8 (C_8), 19.0 (c_{26}), 16.7 (C_{25}), 14.9 (C_7).

IR (film) ν_{max}/cm^{-1} = 2980, 1724, 1576, 1443, 1203, 737.

HRMS (ESI^+): calculated for $C_{25}H_{23}FNO_3^+$, $[M+H]^+$ = 404.1657; *m/z* found = 404.1651, Δ = -1.37 ppm.

5-(6-Methoxy-2-oxo-2H-chromen-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 319d:



Compound **319d** was prepared according to **General Procedure I** using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-methoxy-2*H*-chromen-2-one **319c** (348 mg, 0.84 mmol, 1 eq.), HBF_4 (48% wt., 0.55 mL, 4.19 mmol, 5 eq.), ^{t}BuONO (0.50 mL, 4.19 mmol, 5 eq.) in CH_2Cl_2 (1.7 mL) and IPA (1.7 mL) to give the title product as an orange solid (198 mg, 49%).

^{1}H NMR (400 MHz, CD_3CN) δ_H = 7.95 – 7.90 (m, 2H, H_6), 7.77 (d, *J* = 2.9 Hz, 1H, H_{16}), 7.60 (d, *J* = 9.2 Hz, 1H, H_{13}), 7.52 (dd, *J* = 9.2, 2.9 Hz, 1H, H_{14}), 7.36 (d, *J* = 2.0 Hz, 2H, H_4), 6.69 (s, 1H, H_{10}), 3.90 (s, 3H, H_{18}), 2.52 (s, 6H, H_8), 2.20 (s, 6H, H_7).

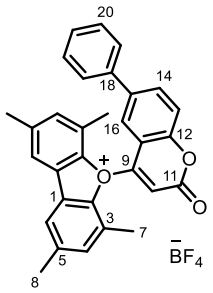
^{13}C NMR (101 MHz, CD_3CN) δ_C = 167.1 (C_9), 163.1 (C_2, C_{11}), 158.3 (C_{15}), 148.8 (C_{12}), 143.4 (C_5), 135.7 (C_4), 125.7 (C_1), 124.7 (C_{14}), 124.3 (C_3), 122.8 (C_6), 120.7 (C_{13}), 113.6 (C_{17}), 111.6 (C_{10}), 105.1 (C_{16}), 57.3 (C_{18}), 21.0 (C_8), 17.4 (C_7).

^{19}F NMR (376 MHz, CD_3CN) δ_F = -151.9.

IR (film) ν_{max}/cm^{-1} = 1729, 1574, 1062, 736.

HRMS (ESI^+): calculated for $C_{26}H_{23}O_4^+$, $[M]^+$ = 399.1591; *m/z* found = 399.1581, Δ = -0.98 ppm.

2,4,6,8-Tetramethyl-5-(2-oxo-6-phenyl-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 320d:



Compound **320d** was prepared according to **General Procedure I** using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-phenyl-2*H*-chromen-2-one **320c** (191 mg, 0.46 mmol, 1 eq.), HBF_4 (48% wt., 0.30 mL, 2.29 mmol, 5 eq.), ^{t}BuONO (0.27 mL, 2.29 mmol, 5 eq.) in CH_2Cl_2 (0.92 mL) and IPA (0.92 mL) to give the title product as an orange solid (107 mg, 44%).

^{1}H NMR (600 MHz, CD_3CN) δ_H = 8.62 (d, *J* = 2.2 Hz, 1H, H_{16}), 8.23 (dd, *J* = 8.8, 2.2 Hz, 1H, H_{14}), 7.95 – 7.90 (m, 2H, H_6), 7.77 – 7.72 (m, 3H, H_{13}, H_{19}), 7.55 – 7.49 (m, 2H, H_{20}), 7.48 – 7.44 (m, 1H, H_{21}), 7.37 – 7.34 (m, 2H, H_4), 6.74 (s, 1H, H_{10}), 2.52 (s, 6H, H_8), 2.22 (s, 6H, H_7).

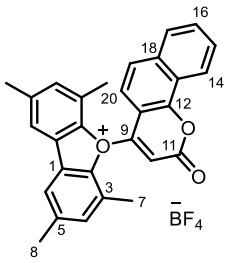
^{13}C NMR (151 MHz, CD_3CN) δ_C = 167.4 (C_9), 163.4 (C_2), 158.9 (C_{11}), 153.5 (C_{12}), 143.5 (C_{Ar}), 140.2 (C_{Ar}), 138.9 (C_{Ar}), 135.8 (C_{Ar}), 135.7 (C_{Ar}), 130.2 (C_{Ar}), 129.7 (C_{Ar}), 128.4 (C_{Ar}), 128.3 (C_{Ar}), 124.8 (C_{Ar}), 124.4 (C_{Ar}), 122.9 (C_{Ar}), 121.5 (C_{Ar}), 119.8 (C_{Ar}), 113.7 (C_{Ar}), 112.1 (C_{Ar}), 112.0 (C_{Ar}), 21.1 (C_8), 17.7 (C_7).

^{19}F NMR (376 MHz, CD_3CN) δ_F = -146.6.

IR (film) ν_{max}/cm^{-1} = 1762, 5172, 1455, 1060, 771, 670.

HRMS (ESI^+): calculated for $C_{31}H_{25}O_3^+$, $[M]^+$ = 445.1798; *m/z* found = 445.1790, Δ = -1.89 ppm.

2,4,6,8-Tetramethyl-5-(2-oxo-2*H*-benzo[h]chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 321d:



Compound **321d** was prepared according to **General Procedure I** using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-phenyl-2*H*-chromen-2-one **321c** (698 mg, 1.60 mmol, 1 eq.), HBF_4 (48% wt., 1.0 mL, 8.01 mmol, 5 eq.), ^{t}BuONO (0.95 mL, 8.01 mmol, 5 eq.) in CH_2Cl_2 (3.2 mL) and IPA (3.2 mL) to give the title product as an orange solid (235 mg, 29%).

^{1}H NMR (400 MHz, CD_3CN) δ_H = 8.56 (dd, *J* = 8.4, 1.4 Hz, 1H, H_{14}), 8.23 (d, *J* = 8.8 Hz, 1H, H_{20}), 8.15 (dd, *J* = 7.7, 1.4 Hz, 1H, H_{17}), 8.10 (d, *J* = 8.8 Hz, 1H, H_{19}), 7.94 (d, *J* = 2.0 Hz, 2H, H_6),

7.91 – 7.82 (m, 2H, H_{15}, H_{16}), 7.37 – 7.32 (m, 2H, H_4), 6.76 (s, 1H, H_{10}), 2.52 (s, 6H, H_8), 2.19 (s, 6H, H_7).

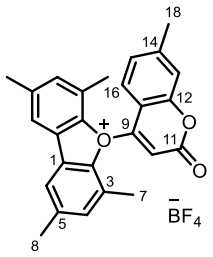
^{13}C NMR (101 MHz, CD_3CN) δ_C = 168.2 (C_9), 163.1 (C_2), 159.0 (C_{11}), 153.0 (C_{12}), 143.4 (C_5), 137.2 (C_{Ar}), 135.6 (C_4), 132.2 ($C_{15/16}$), 129.9 ($C_{15/16}$), 129.6 (C_{17}), 127.5 (C_{19}), 124.7 (C_{Ar}), 124.3 (C_3), 123.7 (C_{Ar}), 123.6 (C_{14}), 122.8 (C_6), 117.8 (C_{20}), 110.0 (C_{10}), 108.8 (C_{21}), 21.0 (C_8), 17.3 (C_7).

^{19}F NMR (376 MHz, CD_3CN) δ_F = -151.8.

IR (film) ν_{max}/cm^{-1} = 2974, 1722, 1386, 1129, 1061, 953, 670.

HRMS (ESI^+): calculated for $C_{29}H_{23}O_3^+$, $[M]^+$ = 419.1642; *m/z* found = 419.1631, Δ = -2.67 ppm.

2,4,6,8-Tetramethyl-5-(7-methyl-2-oxo-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 322d:



Compound **322d** was prepared according to **General Procedure I** using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-methyl-2*H*-chromen-2-one **322c** (427 mg, 1.07 mmol, 1 eq.), HBF_4 (48% wt., 0.70 mL, 5.34 mmol, 5 eq.), ^{t}BuONO (0.64 mL, 5.34 mmol, 5 eq.) in CH_2Cl_2 (2.1 mL) and IPA (2.1 mL) to give the title product as an orange solid (220 mg, 44%).

^{1}H NMR (400 MHz, CD_3CN) δ_H = 8.15 (d, *J* = 8.1 Hz, 1H, H_{16}), 7.95 – 7.90 (m, 2H, H_6), 7.52 – 7.44 (m, 2H, H_{13}, H_{15}), 7.34 (m, 2H, H_4), 6.64 (s, 1H, H_{10}), 2.57 (s, 3H, H_{18}), 2.51 (s, 6H, H_8), 2.19 (s, 6H, H_7).

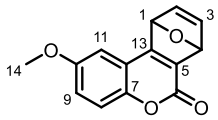
^{13}C NMR (101 MHz, CD_3CN) δ_C = 167.6 (C_9), 162.9 (C_2), 159.1 (C_{11}), 154.3 (C_{12}), 149.6 (C_{14}), 143.4 (C_5), 135.6 (C_4), 128.4 (C_{15}), 124.7 (C_{16}), 124.3 (C_{Ar}), 123.5 (C_{Ar}), 122.8 (C_6), 119.2 (C_{13}), 110.6 (C_{17}), 110.2 (C_{10}), 22.1 (C_{18}), 21.0 (C_8), 17.3 (C_7).

^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -151.9.

IR (film) ν_{max}/cm^{-1} = 2975, 1751, 1649, 1135, 1064, 952, 670.

HRMS (ESI^+): calculated for $C_{26}H_{23}O_3^+$, $[M]^+$ = 383.1642; *m/z* found = 383.1631, Δ = -2.76 ppm.

2-Methoxy-7,10-dihydro-6H-7,10-epoxybenzo[c]chromen-6-one, 325:



Compound **325** was prepared according to **General Procedure J** using 5-(6-methoxy-2-oxo-2*H*-chromen-4-yl)-2,4,6,8-tetramethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **319d** (97 mg, 0.20 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound as a yellow solid (28 mg, 58%).

m.p. = 156-158 °C.

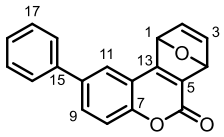
^{1}H NMR (700 MHz, $CDCl_3$) δ_H = 7.33 (d, *J* = 9.1 Hz, 1H, H_8), 7.31 (dd, *J* = 5.4, 1.9 Hz, 1H, H_2), 7.16 – 7.11 (m, 2H, H_3, H_9), 6.95 (d, *J* = 2.9 Hz, 1H, H_{11}), 6.05 (dd, *J* = 2.1, 1.1 Hz, 1H, H_4), 5.97 (dd, *J* = 1.9, 1.0 Hz, 1H, H_1), 3.88 (s, 3H, H_{14}).

^{13}C NMR (176 MHz, $CDCl_3$) δ_C = 169.0 (C_{13}), 158.0 (C_6), 156.2 (C_{10}), 148.8 (C_7), 145.5 (C_2), 140.9 (C_3), 137.1 (C_5), 120.2 (C_9), 118.3 (C_8), 116.7 (C_{12}), 105.7 (C_{11}), 81.7 (C_4), 81.5 (C_1), 55.9 (C_{14}).

IR (film) ν_{max}/cm^{-1} = 3092, 2970, 1715, 1568, 1276, 1046, 867, 835, 742.

HRMS (ESI$^+$): calculated for $C_{14}H_{11}O_4^+$, $[M+H]^+$ = 243.0652; *m/z* found = 243.0647, Δ = -2.03 ppm.

2-Phenyl-7,10-dihydro-6*H*-7,10-epoxybenzo[c]chromen-6-one, 326:



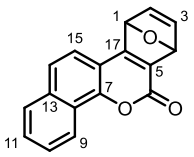
Compound **326** was prepared according to **General Procedure J** using 2,4,6,8-tetramethyl-5-(2-oxo-6-phenyl-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **320d** (106 mg, 0.20 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound as an orange oil (32 mg, 70%).

^{1}H NMR (700 MHz, $CDCl_3$) δ_H = 7.78 (dd, *J* = 8.6, 2.2 Hz, 1H, H_9), 7.72 (d, *J* = 2.2 Hz, 1H, H_{11}), 7.64 – 7.57 (m, 2H, H_{16}), 7.53 – 7.46 (m, 3H, H_8, H_{17}), 7.45 – 7.38 (m, 1H, H_{18}), 7.33 (dd, *J* = 5.3, 1.9 Hz, 1H, H_2), 7.16 (dd, *J* = 5.3, 2.1 Hz, 1H, H_3), 6.14 (dd, *J* = 2.1, 1.0 Hz, 1H, H_4), 6.00 (dd, *J* = 1.9, 1.0 Hz, 1H, H_1).

^{13}C NMR (176 MHz, $CDCl_3$) δ_C = 169.5 (C_{13}), 157.9 (C_6), 153.7 (C_7), 145.6 (C_2), 141.1 (C_3), 139.5 (C_{10}), 138.1 (C_{15}), 137.3 (C_5), 131.5 (C_9), 129.2 (C_{17}), 128.1 (C_{18}), 127.3 (C_{16}), 121.9 (C_{11}), 117.7 (C_8), 116.8 (C_{12}), 81.8 (C_4), 81.6 (C_1).

IR (film) ν_{max}/cm^{-1} = 1722, 1624, 1567, 1050, 912, 764.

7,10-Dihydro-6*H*-7,10-epoxydibenzo[c,h]chromen-6-one, 327:



Compound **327** was prepared according to **General Procedure J** using 2,4,6,8-tetramethyl-5-(2-oxo-2*H*-benzo[h]chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, **321d** (101 mg, 0.20 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound as a yellow solid (40 mg, 76%).

m.p. = 186-188 °C.

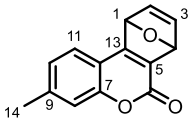
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.61 – 8.56 (m, 1H, H_9), 7.92 – 7.85 (m, 1H, H_{12}), 7.73 (d, *J* = 8.6 Hz, 1H, H_{14}), 7.69 – 7.61 (m, 2H, H_{10}, H_{11}), 7.55 (d, *J* = 8.6 Hz, 1H, H_{15}), 7.35 (dd, *J* = 5.4, 1.9 Hz, 1H, H_2), 7.17 (dd, *J* = 5.4, 2.1 Hz, 1H, H_3), 6.16 (dd, *J* = 2.1, 1.0 Hz, 1H, H_4), 6.05 (dd, *J* = 2.0, 1.0 Hz, 1H, H_1).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 170.2 (C_{17}), 158.0 (C_6), 151.9 (C_7), 145.7 (C_2), 141.1 (C_3), 135.5 (C_5), 135.2 (C_{Ar}), 129.2 ($C_{10/11}$), 128.1 (C_{12}), 127.7 ($C_{10/11}$), 124.9 (C_{14}), 123.4 (C_{Ar}), 123.3 (C_9), 119.6 (C_{15}), 112.1 (C_{16}), 82.0 (C_4), 81.5 (C_1).

IR (film) ν_{max}/cm^{-1} = 2981, 1704, 1651, 1630, 753.

HRMS (ESI^+): calculated for $C_{17}H_{11}O_3^+$, $[M+H]^+$ = 263.0703; *m*/*z* found = 263.0698, Δ = -1.83 ppm.

2-Methyl-7,10-dihydro-6*H*-7,10-epoxybenzo[c]chromen-6-one, 328:



Compound **328** was prepared according to **General Procedure J** using 2,4,6,8-tetramethyl-5-(7-methyl-2-oxo-2*H*-chromen-4-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **322d** (94 mg, 0.20 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound as a yellow solid (33 mg, 73%).

m.p. = 136-138 °C.

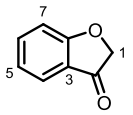
^{1}H NMR (700 MHz, $CDCl_3$) δ_H = 7.44 (d, *J* = 8.0 Hz, 1H, H_{11}), 7.30 (dd, *J* = 5.4, 1.9 Hz, 1H, H_2), 7.23 – 7.20 (m, 1H, H_8), 7.16 – 7.13 (m, 1H, H_{10}), 7.11 (dd, *J* = 5.4, 2.0 Hz, 1H, H_3), 6.04 (dd, *J* = 2.1, 1.1 Hz, 1H, H_4), 5.97 (dd, *J* = 2.0, 1.0 Hz, 1H, H_1), 2.46 (s, 3H, H_{14}).

^{13}C NMR (176 MHz, $CDCl_3$) δ_C = 169.4 (C_{13}), 158.2 (C_6), 154.6 (C_7), 145.6 (C_2), 144.0 (C_9), 140.9 (C_3), 135.2 (C_5), 125.8 (C_{10}), 123.4 (C_{11}), 117.6 (C_8), 114.3 (C_{12}), 81.8 (C_4), 81.5 (C_1), 22.1 (C_{14}).

IR (film) ν_{max}/cm^{-1} = 1723, 1621, 869, 717.

HRMS (ESI^+): calculated for $C_{14}H_{11}O_3^+$, $[M+H]^+$ = 227.0703; *m/z* found = 227.0699, Δ = -1.85 ppm.

Benzofuran-3(2*H*)-one, 332:



Compound **332** was synthesised according to a modified literature procedure.[125] Anhydrous CH_2Cl_2 (30 mL) was added to a multi-neck flame dried RBF containing anhydrous $AlCl_3$ (8.00 g, 60.0 mmol, 2 eq.) under N_2 and the resultant mixture was stirred vigorously at 0 °C. This suspension, 2-phenoxyacetyl chloride **331** (5.12 g, 30.0 mmol, 1 eq.) dissolved in anhydrous CH_2Cl_2 (30 mL) was added slowly and the mixture was stirred at 0 °C. After 15 minutes, the mixture was warmed to r.t., stirred for a further 30 minutes, and then poured onto ice. The organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (50 mL x 3). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 5:95, R_f = 0.2) to give the title compound as a bright yellow solid (997 mg, 25%).

m.p. = 66-68 °C.

^{1}H (400 MHz, $CDCl_3$) δ_H = 7.68 (ddd, *J* = 7.7, 1.5, 0.7 Hz, 1H, H_4), 7.61 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, H_6), 7.14 (dd, *J* = 8.4, 0.8 Hz, 1H, H_7), 7.12 – 7.07 (m, 1H, H_5), 4.63 (s, 2H, H_1).

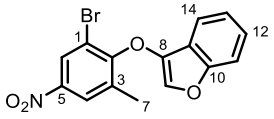
^{13}C (101 MHz, $CDCl_3$) δ_C = 200.0 (C_2), 174.2 (C_8), 138.0 (C_6), 124.2 (C_4), 122.1 (C_5), 121.3 (C_3), 113.8 (C_7), 74.8 (C_1).

IR (film) ν_{max}/cm^{-1} **=** 2973, 1728, 1705, 1613, 1464, 1215, 756.

HRMS (ESI^+): calculated for $C_8H_7O_2^+$, $[M+H]^+$ = 135.0441; *m/z* found = 135.0437, Δ = -2.55 ppm.

Data in accordance with literature.[165]

3-(2-Bromo-6-methyl-4-nitrophenoxy)benzofuran, 337:



K_2CO_3 (415 mg, 3.00 mmol, 1.5 eq.) was added to a solution of benzofuran-3(2H)-one **332** (268 mg, 2.00 mmol, 1 eq.) and 1-bromo-2-fluoro-3-methyl-5-nitrobenzene **53** (468 mg, 2.00 mmol, 1 eq.) in DMF (4 mL) and the reaction mixture was heated to 100 °C. After 16 h, the reaction mixture was cooled to r.t., H_2O (10 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with H_2O (30 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f = 0.5) to give the title compound as an orange solid (97 mg, 14%).

m.p. = 52-54 °C.

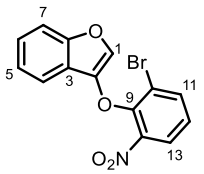
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.40 (d, *J* = 2.7 Hz, 1H, H_6), 8.14 (dd, *J* = 2.7, 0.9 Hz, 1H, H_4), 7.60 (dt, *J* = 7.8, 1.1 Hz, 1H, H_{14}), 7.48 – 7.41 (m, 1H, H_{11}), 7.37 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H, H_{12}), 7.29 (td, *J* = 7.5, 1.0 Hz, 1H, H_{13}), 6.98 (s, 1H, H_9), 2.41 (s, 3H, H_7).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 156.8 (C_2), 153.9 (C_{10}), 145.3 (C_5), 141.7 (C_8), 134.5 (C_3), 127.9 (C_9), 127.2 (C_6), 126.0 (C_4), 125.7 (C_{12}), 123.0 (C_{13}), 120.8 (C_{15}), 118.7 (C_{14}), 117.5 (C_1), 112.3 (C_{11}), 17.2 (C_7).

IR (film) ν_{max}/cm^{-1} = 2926, 1827, 1531, 1349, 1190, 1092, 743.

HRMS (ESI^+): calculated for $C_{15}H_{11}BrNO_4^+$, $[M+H]^+$ = 347.9866; *m/z* found = 347.9856, Δ = -2.89 ppm.

3-(2-Bromo-6-nitrophenoxy)benzofuran, 339:



K_2CO_3 (552 mg, 4.00 mmol, 2 eq.) was added to a solution of benzofuran-3(2*H*)-one **332** (268 mg, 2.00 mmol, 1 eq.) and 1-bromo-2-fluoro-3-nitrobenzene **338** (440 mg, 2.00 mmol, 1 eq.) in DMF (4 mL) and the reaction mixture was heated to 110 °C. After 16 h, the reaction mixture was cooled to r.t., H_2O (10 mL) was added, and the reaction mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with H_2O (30 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 5:95, R_f = 0.2) to give the title compound as a yellow oil (467 mg, 70%).

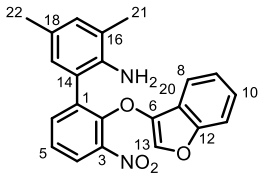
^{1}H (500 MHz, $CDCl_3$) δ_H = 7.94 – 7.92 (m, 1H, H_{13}), 7.92 – 7.90 (m, 1H, H_{11}), 7.58 (ddd, *J* = 7.8, 1.4, 0.7 Hz, 1H, H_4), 7.43 (dt, *J* = 8.4, 0.8 Hz, 1H, H_7), 7.34 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H, H_6), 7.31 (td, *J* = 8.2, 0.6 Hz, 1H, H_{12}), 7.29 – 7.24 (m, 1H, H_5), 7.11 (s, 1H, H_1).

^{13}C (126 MHz, $CDCl_3$) δ_C = 153.7 (C_8), 147.0 (C_9), 144.5 (C_{14}), 142.5 (C_2), 138.6 (C_{11}), 128.9 (C_1), 126.9 (C_{12}), 125.5 (C_6), 124.9 (C_{13}), 123.0 (C_5), 121.1 (C_3), 119.4 (C_{10}), 118.9 (C_4), 112.2 (C_7).

IR (film) ν_{max}/cm^{-1} = 3083, 2951, 2361, 2342, 1700, 1618, 1581, 1533, 1488, 1452, 1369, 1353, 1284, 1241, 1188, 1122, 1094, 1081, 1008, 913, 877, 854, 791, 743, 714, 648, 639.

HRMS (ESI^+): calculated for $C_{14}H_9BrNO_2^+$, $[M+H]^+$ = 333.9710; *m/z* found = 333.9700, Δ = -2.75 ppm.

2'-(Benzofuran-3-yloxy)-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-amine, 341:



3-(2-Bromo-6-nitrophenoxy)benzofuran **339** (167 mg, 0.50 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (161 mg, 0.65 mmol, 1.3 eq.), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol, 5 mol%) and K_2CO_3 (276 mg, 2.00 mmol, 4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 2.5 mL/2.5mL, 0.1 M) was added and the solution was sparged for a further 10 minutes. The reaction mixture was then heated to 85 °C. After 16 h the reaction mixture was cooled to r.t, filtered over Celite®, and eluted with EtOAc (10 mL x 3). The mixture was then washed with NaOH (1 M, 5 mL) and NaCl (sat., aq., 10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90, R_f = 0.2) to give the title compound as a bright orange solid (94 mg, 50%).

m.p. = 120-122 °C.

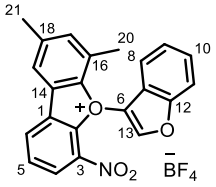
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.91 (dd, *J* = 8.1, 1.7 Hz, 1H, H_4), 7.59 (dd, *J* = 7.7, 1.7 Hz, 1H, H_6), 7.41 (dd, *J* = 8.1, 7.7 Hz, 1H, H_5), 7.27 – 7.24 (m, 1H, H_{11}), 7.19 (td, *J* = 8.0, 1.1 Hz, 2H, H_8, H_9), 7.07 (ddd, *J* = 8.1, 7.0, 1.0 Hz, 1H, H_{10}), 7.01 (s, 1H, H_{13}), 6.68 – 6.64 (m, 1H, H_{17}), 6.59 – 6.55 (m, 1H, H_{19}), 3.28 (s, 2H, H_{20}), 2.04 (s, 3H, H_{22}), 1.99 (s, 3H, H_{21}).

^{13}C (151 MHz, $CDCl_3$) δ_C = 153.3 ($C_{6/12}$), 147.8 (C_2), 144.3 (C_3), 142.6 ($C_{6/12}$), 139.5 (C_{15}), 137.1 (C_6), 135.8 ($C_{14/16}$), 131.5 (C_{17}), 130.3 (C_{13}), 128.8 (C_{19}), 127.3 (C_{18}), 125.7 (C_5), 124.9 (C_9), 124.5 (C_4), 122.9 ($C_{14/16}$), 122.4 (C_{10}), 121.4 (C_7), 120.6 (C_1), 118.5 (C_8), 111.6 (C_{11}), 20.2 (C_{22}), 17.7 (C_{21}).

IR (film) ν_{max}/cm^{-1} = 2949, 2855, 2361, 2342, 2258, 1772, 1699, 1622, 1605, 1574, 1534, 1507, 1487, 1452, 1362, 1284, 1232, 1189, 1149, 1121, 1087, 1012, 912, 855, 795, 740, 686, 667, 649, 625.

HRMS (ESI^+): calculated for $C_{22}H_{19}N_2O_4^+$, $[M+H]^+$ = 375.1339; *m/z* found = 375.1332, Δ = -2.03 ppm.

5-(Benzofuran-3-yl)-2,4-dimethyl-6-nitro-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 342:



^{t}BuONO (98 μL, 0.83 mmol, 5 eq.) was added to a solution of 2'-(benzofuran-3-yloxy)-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-amine **341** (62 mg, 0.83 mmol, 1 eq.) and HBF_4 (48% aq., 108 μL, 0.83 mmol, 5 eq.) in CH_2Cl_2 (2.0 mL) and IPA (2.0 mL) at 0 °C. After 1 h, the reaction mixture was warmed to r.t., diluted with CH_2Cl_2 (5 mL), and washed with H_2O (2 mL), dried ($MgSO_4$), filtered, and dissolved in $CDCl_3$ (2 mL). After 16 h, the solvent was removed by a steady stream

of N_2 and Et_2O (5 mL) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® (Et_2O, 4 x 1 mL). The solid was dissolved in MeCN (4 mL), passed through Celite® and eluted (MeCN, 4 × 5 mL). The solvent was removed by a steady stream of N_2 to give the title compound at a brown solid (70 g, 95%).

m.p. = dec.>98 °C.

^{1}H (600 MHz, CD_3CN) δ_H = 8.79 (s, 1H, H_{13}), 8.67 (dd, *J* = 7.8, 1.4 Hz, 1H, H_6), 8.36 (dd, *J* = 8.2, 1.3 Hz, 1H, H_4), 8.13 – 8.09 (m, 2H, H_5, H_{19}), 7.68 (dt, *J* = 8.6, 0.8 Hz, 1H, H_{11}), 7.49 (ddd, *J* = 8.6, 7.3, 1.2 Hz, 1H, H_{10}), 7.45 – 7.40 (m, 1H, H_{17}), 7.27 (ddd, *J* = 8.1, 7.3, 0.8 Hz, 1H, H_9), 6.95 (ddd, *J* = 8.1, 1.3, 0.7 Hz, 1H, H_8), 2.54 (s, 3H, H_{21}), 2.32 (s, 3H, H_{20}).

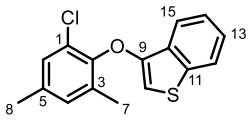
^{13}C (151 MHz, CD_3CN) δ_C = 165.5 (C_{15}), 153.7 (C_2), 153.4 (C_{12}), 144.3 (C_{18}), 142.3 (C_{13}), 137.1 (C_{17}), 136.7 (C_{Ar}), 134.4 (C_5), 131.3 (C_6), 128.7 (C_{10}), 128.3 (C_4), 127.7 (C_{Ar}), 126.7 (C_9), 125.1 (C_{16}), 123.8 (C_{19}), 121.2 (C_{Ar}), 118.3 (C_{11}), 116.6 (C_7), 114.4 (C_8), 21.1 (C_{21}), 16.1 (C_{20}). One aromatic carbon peak was not observed.

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -150.5.

IR (film) ν_{max}/cm^{-1} = 2979, 1553, 1351, 1063, 735.

HRMS (ESI^+): calculated for $C_{22}H_{16}NO_4^+$, $[M]^+$ = 358.1074; *m/z* found = 358.1070, Δ = -1.02 ppm.

3-(2-Chloro-4,6-dimethylphenoxy)benzo[b]thiophene, 352:



Compound **352** was synthesised according to a modified literature procedure.[121] $Cu(acac)_2$ (7 mg, 0.025 mmol, 5 mol%), $Fe(acac)_3$ (9 mg, 0.025 mmol, 5 mol%), triphenylphosphine oxide (56 mg, 0.2 mmol, 0.4 eq.), K_2CO_3 (138 g, 1.00 mmol, 2 eq.) and PhMe (0.8 mL) were added to a microwave vial and stirred for 10 min at r.t.. 2-Chloro-4,6-dimethylphenol **351** (118 mg, 0.75 mmol, 1.5 eq.) and 3-bromobenzo[b]thiophene **345** (107 mg, 0.50 mmol, 1 eq.) were added and the mixture was stirred at 145 °C. After 24 h the reaction mixture was cooled to r.t., passed through silica gel, eluted with Et_2O (3 x 5 mL), and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (pentane, R_f (**352**) = 0.3, R_f (**353**) = 0.2) to give the title compound **352** as a colourless oil (13 mg, 9%) and **353** as a colourless oil (24 mg, 19%).

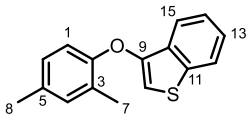
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.83 – 7.78 (m, 2H, H_{Ar}), 7.42 – 7.38 (m, 2H, H_{Ar}), 7.13 (s, 1H, H_4), 7.02 (s, 1H, H_6), 6.42 (s, 1H, H_{10}), 2.34 (s, 3H, H_8), 2.26 (s, 3H, H_7).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 153.6 (C_2), 148.5 (C_9), 138.2 (C_{Ar}), 133.4 (C_4), 127.7 (C_{Ar}), 125.5 (C_{Ar}), 125.4 (C_{Ar}), 124.3 (C_{Ar}), 123.2 (C_{Ar}), 123.2 (C_{Ar}), 123.2 (C_{Ar}), 121.1 (C_{Ar}), 119.4 (C_6), 104.6 (C_{10}), 19.4 (C_8), 15.6 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 3111, 1569, 1524, 1487, 1431, 1366, 1265, 1186, 1156, 1097, 1053, 1016, 985, 887, 856, 823, 756, 729, 634.

HRMS (ESI^+): calculated for $C_{16}H_{14}ClOS^+$, $[M+H]^+$ = 289.0448; *m/z* found = 289.0448, Δ = -0.05 ppm.

3-(2,4-Dimethylphenoxy)benzo[b]thiophene, 353:



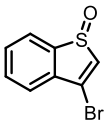
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.92 – 7.86 (m, 1H, H_{Ar}), 7.86 – 7.79 (m, 1H, H_{Ar}), 7.46 – 7.39 (m, 2H, H_{Ar}), 7.12 (s, 1H, H_6), 7.03 – 6.99 (m, 1H, H_6), 6.98 (dd, J = 8.2, 1.5 Hz, 1H, H_1), 6.32 (s, 1H, H_{10}), 2.37 (s, 3H, H_8), 2.31 (s, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 152.9 (C_2), 149.4 (C_{Ar}), 138.1 (C_{Ar}), 133.9 (C_5), 132.2 (C_4), 132.1 (C_{Ar}), 129.1 (C_3), 127.6 (C_6), 125.2 (C_{Ar}), 124.0 (C_{Ar}), 123.0 (C_{Ar}), 121.1 (C_{Ar}), 119.1 (C_1), 102.9 (C_{10}), 20.8 (C_8), 15.9 (C_7).

IR (film) ν_{max}/cm^{-1} = 3476, 3110, 3061, 2920, 1570, 1526, 1497, 1464, 1431, 1367, 1248, 1210, 1153, 1134, 1124, 1094, 1052, 1016, 985, 913, 866, 824, 798, 756, 729, 710, 632.

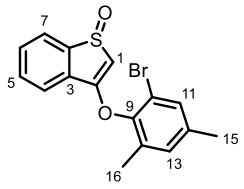
HRMS (ESI^+): calculated for $C_{16}H_{15}OS^+$, $[M+H]^+$ = 255.0838; m/z found = 255.0828, Δ = -3.99 ppm.

3-Bromobenzo[b]thiophene 1-oxide, 346:



Compound **346** was synthesised according to literature procedure.[123] Trifluoroacetic acid (4 mL) was added to a stirred solution of 3-bromobenzo[b]thiophene (426 mg, 2.00 mmol, 1 eq.) in CH_2Cl_2 (4 mL). After 5 min of stirring at r.t., H_2O_2 (35% aq., 162 μL, 2.00 mmol, 1 eq.) was added and the resulting mixture was stirred at r.t.. After 3 h the reaction mixture was then neutralized at 0°C with Na_2CO_3 (sat. aq.) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were sequentially washed with $NaHCO_3$ (50 mL) and H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give a pale yellow solid (412 mg, 90%) which was used without further purification in the subsequent step.

3-(2-Bromo-4,6-dimethylphenoxy)benzo[b]thiophene 1-oxide, 354:



K_2CO_3 (4.98 g, 36.0 mmol, 1.5 eq.) was added to a solution of 3-bromobenzo[b]thiophene 1-oxide **346** (4.12 g, 18.0 mmol, 1 eq.) and 2-bromo-4,6-dimethylphenol **51** (5.43 g, 36.0 mmol, 1.5 eq.) in DMF (36 mL) and the reaction mixture was heated to 100 °C. After 16 h, the reaction mixture was cooled to r.t., H_2O (100 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 200 mL). The combined organic layers were washed with H_2O (200 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title compound as a pale purple solid (5.77 g, 92%).

m.p. = 154-156 °C.

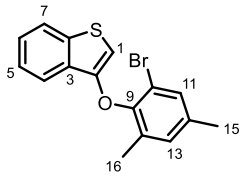
^{1}H (600 MHz, $CDCl_3$) δ_H = 7.92 (dt, *J* = 7.4, 1.0 Hz, 1H, H_7), 7.81 (dt, *J* = 7.6, 0.9 Hz, 1H, H_4), 7.64 (td, *J* = 7.5, 1.1 Hz, 1H, H_5), 7.59 (td, *J* = 7.6, 1.2 Hz, 1H, H_6), 7.31 (s, 1H, H_{11}), 7.04 (s, 1H, H_{13}), 5.62 (s, 1H, H_8), 2.34 (s, 3H, H_{15}), 2.26 (s, 3H, H_{16}).

^{13}C (151 MHz, $CDCl_3$) δ_C = 159.1 (C_2), 147.4 (C_9), 145.9 (C_8), 138.0 (C_{12}), 132.7 (C_{14}), 132.0 (C_5), 132.0 (C_{11}), 131.6 (C_{13}), 130.3 (C_6), 126.3 (C_7), 122.1 (C_4), 115.5 (C_{10}), 107.9 (C_1), 20.8 (C_{15}), 16.6 (C_{16}). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} **=** 2981, 1605, 1556, 1474, 1362, 1305, 1279, 1208, 1153, 1132, 1096, 1056, 1037, 856, 833, 769, 735, 638.

HRMS (ESI$^+$): calculated for $C_{16}H_{14}BrO_2S^+$, $[M+H]^+$ = 348.9892; *m/z* found = 348.9884, Δ = -2.32 ppm.

3-(2-Bromo-4,6-dimethylphenoxy)benzo[b]thiophene, 355:



Compound **355** was synthesised according to a modified literature procedure.[123] 3-(2-Bromo-4,6-dimethylphenoxy)benzo[b]thiophene 1-oxide **354** (300 mg, 0.86 mmol, 1 eq.) was added to a flame-dried RBF followed by evacuation and refill N_2 x 3. Anhydrous PhMe (3 mL) was added, and the mixture was cooled to 0 °C. DIBAL-*H* (1 M in THF, 1.1 mL, 1.08 mmol, 1.25 eq.) was added dropwise and the mixture was heated to 65 °C. After 5 h, the reaction was cooled to 0 °C and NaOH (1 M, 10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with H_2O until the pH was neutral, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 20:80, R_f = 0.6) to give the title compound as a yellow oil (152 mg, 53%).

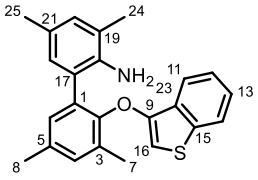
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.05 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.79 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.48 – 7.44 (m, 1H, H_{Ar}), 7.44 – 7.39 (m, 1H, H_{Ar}), 7.33 (s, 1H, H_{11}), 7.04 (s, 1H, H_{13}), 5.96 (s, 1H, H_1), 2.34 (s, 3H, H_{15}), 2.22 (s, 3H, H_{16}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 149.2 (C_9), 148.6 (C_{Ar}), 138.2 (C_{Ar}), 136.7 (C_{12}), 132.8 (C_{Ar}), 131.8 (C_{11}), 131.6 (C_{Ar}), 131.5 (C_{13}), 125.4 (C_{Ar}), 124.2 (C_{Ar}), 123.1 (C_{Ar}), 121.2 (C_{Ar}), 116.6 (C_{10}), 99.9 (C_1), 20.7 (C_{15}), 16.7 (C_{16}).

IR (film) ν_{max}/cm^{-1} = 1571, 1528, 1474, 1432, 1368, 1279, 1214, 1152, 1134, 1092, 1052, 1016, 864, 834, 791, 758, 727, 710, 626.

HRMS (APCI$^+$): calculated for $C_{16}H_{14}BrOS^+$, $[M+H]^+$ = 332.9943; *m/z* found = 332.9940, Δ = -1.07 ppm.

2'-(Benzo[b]thiophen-3-yloxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine, 356:



3-(2-Bromo-4,6-dimethylphenoxy)benzo[b]thiophene **355** (666 mg, 2.00 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (643 mg, 3.00 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (116 mg, 0.10 mmol, 5 mol%) and K_2CO_3 (1.11 g, 8.00 mmol, 4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 10 mL/10 mL, 0.1 M) was added and the solution was sparged for a further 10 minutes. The reaction mixture was then heated to 85 °C. After 16 h the reaction mixture was cooled to r.t, filtered over Celite® and eluted with EtOAc (50 mL x 3). The organic layer was sequentially washed with NaOH (1 M, 50 mL) and NaCl (sat., aq., 50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 4:96, R_f = 0.6) to give the title compound as a yellow solid (460 mg, 61%).

m.p. = 38-40 °C.

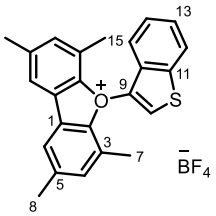
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.72 (ddd, *J* = 6.4, 3.1, 2.0 Hz, 1H, H_{Ar}), 7.68 – 7.60 (m, 1H, H_{Ar}), 7.32 – 7.29 (m, 2H, H_{Ar}), 7.12 (s, 1H, $H_{4/20}$), 7.06 (s, 1H, $H_{6/22}$), 6.68 (s, 1H, $H_{6/22}$), 6.61 (s, 1H, $H_{4/20}$), 5.99 (s, 1H, H_{16}), 3.51 (s, 2H, H_{23}), 2.39 (s, 3H, $H_{8/25}$), 2.29 (s, 3H, $H_{7/24}$), 2.04 (s, 3H, $H_{8/25}$), 2.04 (s, 3H, $H_{7/24}$).

^{13}C (151 MHz, $CDCl_3$) δ_C = 150.4 (C_{Ar}), 150.0 (C_{Ar}), 139.5 (C_{Ar}), 137.7 (C_{Ar}), 135.2 (C_{Ar}), 132.9 (C_{Ar}), 131.9 (C_{Ar}), 131.6 ($C_{4/20}$), 131.4 ($C_{6/22}$), 130.5 ($C_{4/20}$), 130.4 ($C_{6/22}$), 129.0 (C_{Ar}), 126.7 (C_{Ar}), 124.9 (C_{Ar}), 123.7 (C_{Ar}), 123.6 (C_{Ar}), 122.7 (C_{Ar}), 122.5 (C_{Ar}), 120.9 (C_{Ar}), 100.6 (C_{16}), 21.0 ($C_{8/25}$), 20.3 ($C_{8/25}$), 17.9 ($C_{7/24}$), 16.5 ($C_{7/24}$).

IR (film) ν_{max}/cm^{-1} = 3385, 2913, 2361, 1622, 1571, 1528, 1484, 1431, 1366, 1279, 1208, 1159, 1111, 1015, 866, 809, 758, 728, 627.

HRMS (ESI^+): calculated for $C_{24}H_{24}NOS^+$, $[M+H]^+$ = 374.1573; *m/z* found = 374.1564, Δ = -2.52 ppm.

5-(Benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 357:



^{t}BuONO (0.73 mL, 6.16 mmol, 5 eq.) was added to a solution of 2'-(benzo[b]thiophen-3-yloxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine **356** (460 mg, 1.23 mmol, 1 eq.) and HBF_4 (48% aq., 0.80 mL, 6.16 mmol, 5 eq.) in CH_2Cl_2 (5 mL) IPA (5 mL) at 0 °C. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with H_2O (4 mL) and warmed to 30 °C. After 16 h, the solvent was removed by a steady stream of N_2 and Et_2O (10 mL) was added resulting in a solid precipitate. The Et_2O layer was passed through Celite®. The solid precipitate was washed, and the solvent passed through Celite® (Et_2O, 4 x 3 mL). The solid was dissolved in MeCN (6 mL), passed through Celite® and eluted (MeCN, 4 × 10 mL). The solvent was removed by a steady stream of N_2 to give the title compound at a brown solid (490 mg, 90%).

m.p. = 200-212 °C.

^{1}H NMR (600 MHz, CD_3CN) δ_H = 8.47 (s, 1H, H_{10}), 8.14 (dt, *J* = 8.4, 0.9 Hz, 1H, $H_{12/15}$), 7.95 (s, 2H, H_6), 7.63 – 7.57 (m, 1H, $H_{13/14}$), 7.50 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H, $H_{13/14}$), 7.43 (dt, *J* = 8.2, 1.0 Hz, 1H, $H_{12/15}$), 7.29 (s, 2H, H_4), 2.51 (s, 6H, H_8), 2.02 (s, 6H, H_7).

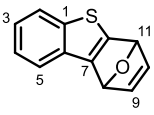
^{13}C NMR (151 MHz, CD_3CN) δ_C = 160.9 (C_2), 144.0 (C_9), 142.8 (C_{Ar}), 137.8 (C_{Ar}), 135.6 (C_4), 128.3 ($C_{13/14}$), 128.0 ($C_{13/14}$), 125.6 ($C_{12/15}$), 124.9 (C_{Ar}), 124.5 (C_{Ar}), 123.6 (C_{10}), 122.7 (C_6), 120.1 ($C_{12/15}$), 21.0 (C_8), 16.4 (C_7). One aromatic carbon peak was not observed.

^{19}F NMR (377 MHz, CD_3CN) δ_F = -151.9.

IR (film) ν_{max}/cm^{-1} = 3604, 2981, 2360, 1630, 1525, 1450, 1367, 1206, 1062, 864, 761, 734, 702, 668.

HRMS (ESI^+): calculated for $C_{24}H_{21}OS^+$, $[M]^+$ = 357.1308; *m/z* found = 357.1300, Δ = -2.22 ppm.

1,4-Dihydro-1,4-epoxydibenzo[b,d]thiophene, 358:



Compound **358** was prepared according to **General procedure O** using 2-acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f (**358**) = 0.2, R_f (**358b**) = 0.8) to give the **358** as an orange oil (22 mg, 37%) and **358b** as a yellow oil (6 mg, 10%).

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.77 (dt, *J* = 8.2, 0.8 Hz, 1H, $H_{1/5}$), 7.67 (dt, *J* = 8.0, 0.9 Hz, 1H, $H_{1/5}$), 7.35 (ddd, *J* = 8.0, 7.1, 1.1 Hz, 1H, $H_{3/4}$), 7.24 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, $H_{3/4}$), 7.21

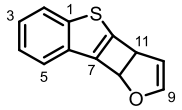
(qd, J = 5.4, 1.8 Hz, 2H, H_9, H_{10}), 6.04 (dd, J = 1.8, 0.7 Hz, 1H, $H_{8/11}$), 5.91 (dd, J = 1.8, 0.7 Hz, 1H, $H_{8/11}$).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 156.0 (C_{Ar}), 152.9 (C_{Ar}), 145.2 (C_{Ar}), 144.4 ($C_{9/10}$), 144.2 ($C_{9/10}$), 132.9 (C_{Ar}), 124.9 ($C_{3/4}$), 124.0 ($C_{1/5}$), 123.7 ($C_{3/4}$), 121.2 ($C_{1/5}$), 82.9 ($C_{8/11}$), 81.8 ($C_{8/11}$).

IR (film) ν_{max}/cm^{-1} = 2981, 1766, 1269, 1027, 860, 732.

HRMS (ESI^+): calculated for $C_{12}H_9OS^+$, $[M+H]^+$ = 201.0369; *m/z* found = 201.0367, Δ = -0.62 ppm.

3a,8c-Dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]furan, 358b:



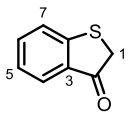
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.89 (dd, J = 8.0, 1.0 Hz, 1H, H_2), 7.78 (dt, J = 7.9, 1.0 Hz, 1H, H_5), 7.41 – 7.37 (m, 1H, H_4), 7.33 – 7.30 (m, 1H, H_3), 6.40 (d, J = 3.0 Hz, 1H, H_9), 6.00 (d, J = 3.6 Hz, 1H, H_8), 5.38 (t, J = 2.7 Hz, 1H, H_{10}), 4.74 – 4.71 (m, 1H, H_{11}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 153.6 (C_{12}), 149.8 (C_9), 144.8 (C_1), 143.2 (C_7), 133.8 (C_6), 125.0 (C_4), 124.1 (C_3), 123.7 (C_2), 121.4 (C_5), 103.8 (C_{10}), 80.2 (C_{11}), 53.6 (C_{10}).

IR (film) ν_{max}/cm^{-1} **=** 2931, 1600, 1460, 1149, 772.

HRMS (ESI^+): calculated for $C_{12}H_9OS^+$, $[M+H]^+$ = 201.0369; *m/z* found = 201.0370, Δ = 0.75 ppm.

Benzo[b]thiophen-3(2H)-one, 347:



Compound **347** was synthesised according to a modified literature procedure.[125] 2-(Phenylthio)acetyl chloride **362** (1.48 mL, 10.0 mmol, 1 eq.) in anhydrous CH_2Cl_2 (15 mL) was added dropwise to a flame dried multi-neck RBF containing powdered $AlCl_3$ (4.00 g, 30.0 mmol, 3 eq.) in anhydrous CH_2Cl_2 (15 mL) at 0 °C. After rigorous stirring for 2 h at r.t., the reaction mixture was poured onto ice, and the aqueous solution was extracted with CH_2Cl_2 (3 x 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the title compound at an orange solid (1.49 g, 99%).

m.p. = 62-64 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.78 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H, H_4), 7.55 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H, H_6), 7.43 (dt, *J* = 8.0, 0.8 Hz, 1H, H_7), 7.22 (ddd, *J* = 7.9, 7.2, 0.9 Hz, 1H, H_5), 3.80 (s, 2H, H_1).

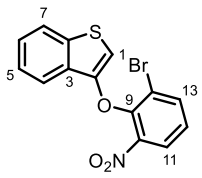
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 200.2 (C_2), 154.4 (C_8), 135.8 (C_6), 131.1 (C_3), 126.8 (C_4), 124.9 (C_5), 124.8 (C_7), 39.4 (C_1).

IR (film) ν_{max}/cm^{-1} **=** 2980, 2890, 1722, 1607, 1372, 1215, 761.

HRMS (ESI^+): calculated for $C_8H_7OS^+$, $[M+H]^+$ = 151.0212; m/z found = 151.0211, Δ = -0.86 ppm.

Data in accordance with the literature.[166]

3-(2-Bromo-6-nitrophenoxy)benzo[b]thiophene, 363:



K_2CO_3 (622 mg, 4.50 mmol, 1.5 eq.) was added to a solution of benzo[b]thiophen-3(2H)-one **347** (451 g, 3.00 mmol, 1 eq.) and 1-bromo-2-fluoro-3-nitrobenzene **338** (990 mg, 4.50 mmol, 1.5 eq.) in DMF (6 mL) and the reaction mixture heated to 110 °C. After 16 h, the reaction mixture was cooled, H_2O (100 mL) was added, and the aqueous phase was extracted with EtOAc (3 × 200 mL). The combined organic layers were sequentially washed with H_2O (200 mL) and NaCl (sat. aq., 100 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 3:97, R_f = 0.2) to give the title compound as an orange solid (767 mg, 73%).

m.p. = 82-84 °C.

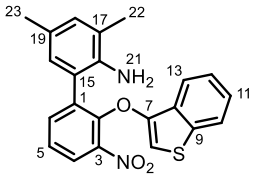
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.02 – 7.98 (m, 1H, $H_{4/7}$), 7.96 (dd, *J* = 8.2, 1.6 Hz, 1H, H_{11}), 7.93 (dd, *J* = 8.1, 1.6 Hz, 1H, H_{13}), 7.79 (dt, *J* = 7.8, 0.9 Hz, 1H, $H_{4/7}$), 7.47 (ddd, *J* = 7.9, 7.1, 1.2 Hz, 1H, $H_{5/6}$), 7.43 (td, *J* = 7.6, 1.4 Hz, 1H, $H_{5/6}$), 7.31 (td, *J* = 8.2, 0.6 Hz, 1H, H_{12}), 6.12 (s, 1H, H_1).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 147.7 (C_{Ar}), 146.6 (C_9), 144.6 (C_{10}), 138.5 (C_{13}), 137.8 (C_{Ar}), 131.1 (C_{Ar}), 126.7 (C_{12}), 125.7 (C_5), 124.8 (C_{11}), 124.4 (C_6), 122.9 (C_4), 121.1 (C_7), 119.8 (C_{14}), 101.7 (C_1).

IR (film) ν_{max}/cm^{-1} **=** 2970, 1720, 1567, 949, 867, 740.

HRMS (ESI$^+$): calculated for $C_{14}H_9BrNO_3S^+$, $[M+H]^+$ = 349.9481; *m/z* found = 349.9477, Δ = -0.41 ppm.

2'-(Benzo[b]thiophen-3-yloxy)-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-amine, 364:



3-(2-Bromo-6-nitrophenoxy)benzo[b]thiophene **363** (350 mg, 1.00 mmol, 1 eq.), 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (371 mg, 1.50 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol, 5 mol%) and K_2CO_3 (553 g, 4.00 mmol, 4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 5 mL/5 mL, 0.1 M) was added and the solution was sparged for 10 minutes. The reaction mixture was then heated to 85 °C. After 16 h the reaction mixture was cooled to r.t, filtered over Celite® and eluted with EtOAc (50 mL x 3). The organic layer was then sequentially washed with NaOH (1 M, 50 mL) and NaCl (sat., aq., 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 20:80, R_f = 0.1) to give the title compound as a yellow solid (252 mg, 65%).

m.p. = 144-146 °C.

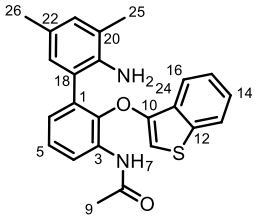
^{1}H NMR (400 MHz, DMSO-d$_6$) δ_H = 8.09 (dd, *J* = 8.1, 1.7 Hz, 1H, H_4), 7.78 (dt, *J* = 7.1, 3.5 Hz, 1H, H_{10}), 7.70 (dd, *J* = 7.7, 1.7 Hz, 1H, H_6), 7.68 (s, 1H, H_{13}), 7.57 (t, *J* = 7.9 Hz, 1H, H_5), 7.34 (dt, *J* = 6.0, 3.5 Hz, 2H, H_{11}, H_{12}), 6.70 (s, 1H, H_8), 6.57 (d, *J* = 2.2 Hz, 1H, H_{20}), 6.49 (d, *J* = 2.1 Hz, 1H, H_{18}), 4.31 (s, 2H, H_{21}), 1.94 (s, 3H, H_{22}), 1.91 (s, 3H, H_{23}).

^{13}C NMR (101 MHz, DMSO-d_6) δ_C = 148.3 (C_7), 146.1 (C_2), 143.7 (C_3), 140.7 (C_{16}), 137.5 (C_6), 136.5 (C_9), 135.8 (C_1), 130.9 (C_{15}), 130.6 (C_{18}), 128.1 (C_{20}), 126.2 (C_5), 125.2 ($C_{11/12}$), 124.5 (C_4), 123.8 ($C_{11/12}$, H_{19}), 122.8 (C_{10}), 121.9 (C_{17}), 120.3 (C_{13}), 119.1 (C_{14}), 103.0 (C_8), 19.7 (C_{23}), 17.8 (C_{22}).

IR (film) ν_{max}/cm^{-1} = 2981, 1531, 1366, 1234, 1096, 865, 731.

HRMS (ESI^+): calculated for $C_{22}H_{19}N_2O_3S^+$, $[M+H]^+$ = 391.1111; *m/z* found = 391.1106, Δ = -0.50 ppm.

***N*-(2'-Amino-2-(benzo[b]thiophen-3-yloxy)-3',5'-dimethyl-[1,1'-biphenyl]-3-yl)acetamide, 367:**



3-(2-Bromo-6-nitrophenoxy)benzo[b]thiophene **363** (264 mg, 0.75 mmol, 1 eq.) and Pd/C (10% wt., 40 mg, 0.038 mmol, 5 mol%) were added to an RBF. Following evacuation and backfilling of N_2 x 3, EtOAc (2.3 mL) was added. The mixture was purged with H_2 using a 3-skin balloon and an exit needle. After 5 minutes the balloon was replaced with a fresh H_2 balloon and the exit needle was removed. After stirring overnight, the reaction monitored by TLC. Then the reaction was sparged with N_2 and the solution was filtered through Celite® and eluted with EtOAc (4 x 5 mL) and concentrated *in vacuo*. The crude residue was dissolved in CH_2Cl_2 (7.5 mL) and Ac_2O (212 μL, 2.25 mmol, 3.00 eq.) was added. After 3 h, H_2O (8 mL) and $NaHCO_3$ (sat. aq., 10 mL) were added and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*.

The crude residue along with 4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (278 mg, 1.13 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (43 mg, 0.038 mmol, 5 mol%) and K_2CO_3 (415 mg, 3.00 mmol, 4 eq.) were added to a flask which was subsequently sealed and sparged with Ar for 10 minutes. DME/H_2O (1:1 v/v, 3.8 mL/3.8 mL, 0.1 M) was added and the solution was sparged for 10 minutes. The reaction mixture was then heated to 85 °C. After 16 h the reaction mixture was cooled to r.t., filtered over Celite®, and eluted with EtOAc (50 mL x 3). The filtrate was then sequentially washed with NaOH (1 M, 50 mL) and NaCl (sat., aq., 50 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 40:60, R_f = 0.2) to give the title compound as a yellow solid (180 mg, 60%).

m.p. = 150-152 °C.

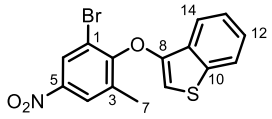
^{1}H NMR (500 MHz, DMSO-d_6, 373 K) δ_H = 9.25 (s, 1H, H_7), 8.00 – 7.96 (m, 1H, $H_{4/6}$), 7.76 – 7.71 (m, 1H, H_{13}), 7.69 – 7.63 (m, 1H, H_{16}), 7.33 – 7.30 (m, 1H, H_5), 7.30 – 7.27 (m, 2H, H_{14}, H_{15}), 7.08 (dd, J = 7.6, 1.6 Hz, 1H, $H_{4/6}$), 6.52 – 6.48 (m, 2H, H_{21}, H_{23}), 6.30 (s, 1H, H_{11}), 1.98 (s, 3H, H_{25}), 1.93 (s, 3H, H_9), 1.90 (s, 3H, H_{26}).

^{13}C NMR (126 MHz, DMSO-d_6, 373 K) δ_C = 168.4 (C_8), 148.4 (C_{10}), 145.2 (C_{Ar}), 138.3 (C_{19}), 136.4 (C_{12}), 132.4 (C_{18}), 131.7 (C_{Ar}), 131.2 (C_{Ar}), 129.7 (C_{21}), 128.1 (C_{23}), 127.0 (C_{Ar}), 125.2 (C_{22}), 125.0 (C_{Ar}), 124.6 (C_{Ar}), 124.5 (C_{Ar}), 123.3 (C_{20}), 123.0 (C_{Ar}), 122.5 (C_{Ar}), 122.2 (C_{Ar}), 120.4 (C_{Ar}), 102.2 (C_{11}), 24.6 (C_9), 19.4 (C_{26}), 17.2 (C_{25}).

IR (film) ν_{max}/cm^{-1} = 3429, 2980, 1694, 1608, 1570, 1473, 1416, 1363, 1194, 1096, 864, 731.

HRMS (ESI^+): calculated for $C_{24}H_{23}N_2O_2S^+$, $[M+H]^+$ = 403.1475; m/z found = 403.1472, Δ = -0.80 ppm.

3-(2-Bromo-6-methyl-4-nitrophenoxy)benzo[b]thiophene, 370:



Compound **370** was prepared using **General procedure M** using benzo[b]thiophen-3(2*H*)-one **347** (540 mg, 3.60 mmol, 1 eq.), 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (901 mg, 3.60 mmol, 1 eq.), K_2CO_3 (995 mg, 7.20, 2 eq.), and DMF (7.2 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, $R_f = 0.4$) to give the title compound as a yellow solid (538 mg, 41%).

m.p. = 100-102 °C.

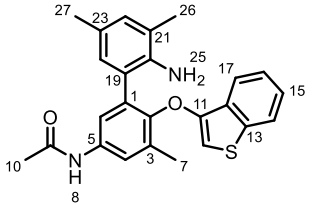
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.42 (dd, *J* = 2.8, 0.7 Hz, 1H, H_6), 8.21 – 8.14 (m, 1H, H_4), 8.06 – 7.96 (m, 1H, H_{Ar}), 7.87 – 7.77 (m, 1H, H_{Ar}), 7.52 – 7.41 (m, 2H, H_{Ar}), 5.99 (s, 1H, H_9), 2.37 (t, *J* = 0.7 Hz, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 156.5 (C_2), 147.0 (C_{Ar}), 145.1 (C_5), 138.0 (C_{Ar}), 134.8 (C_3), 131.0 (C_{Ar}), 127.1 (C_6), 125.8 (C_4), 125.8 (C_{Ar}), 124.4 (C_{Ar}), 123.1 (C_{Ar}), 120.9 (C_{Ar}), 117.9 (C_1), 100.8 (C_9), 17.08 (C_7).

IR (film) ν_{max}/cm^{-1} = 2981, 1726, 1528, 1367, 1344, 1257, 1099, 749.

HRMS (ESI^+): calculated for $C_{15}H_{11}BrNO_3S^+$, $[M+H]^+$ = 363.9638; *m/z* found = 363.9638, Δ = 0.12 ppm.

***N*-(2'-amino-6-(benzo[b]thiophen-3-yloxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide, 372:**



Compound **372** was synthesised accordanceing to **General procedure N** using 3-(2-bromo-6-methyl-4-nitrophenoxy)benzo[b]thiophene **370** (439 mg, 1.21 mmol, 1 eq.) and Pd/C (10% wt., 64 mg, 0.95 mmol, 5 mol%). The crude residue was used in the subsequent step along with Ac_2O (0.34 mL, 3.62 mmol, 3 eq.). The crude residue was then used in the following step along with 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (449 mg, 1.82 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (70 mg, 0.06 mmol, 5 mol%), and K_2CO_3 (666 mg, 4.82 mmol, 4 eq.). The crude residue was purified by dry column vacuum chromatography (EtOAc:pentane, 0:100 to 100:0) to give the title product as a yellow solid (226 mg, 45%).

m.p. = 60-64 °C.

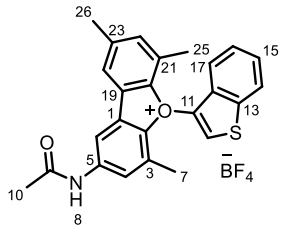
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.74 – 7.59 (m, 3H, H_4, $2H_{Ar}$), 7.32 – 7.26 (m, 2H, H_{Ar}), 7.14 (d, *J* = 2.7 Hz, 1H, H_6), 7.12 (s, 1H, H_8), 6.65 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.58 (s, $1H_{22}$), 5.97 (s, 1H, H_{12}), 2.30 (s, 3H, H_7), 2.19 (s, 3H, H_{10}), 2.01 (s, 3H, H_{26}), 2.00 (s, 3H, H_{27}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 168.4 (C_9), 149.8 (C_{11}), 149.0 (C_2), 139.5 (C_{20}), 137.7 (C_{Ar}), 135.1 (C_{Ar}), 133.7 (C_{Ar}), 132.7 (C_{Ar}), 132.2 (C_{Ar}), 131.8 (C_{Ar}), 130.6 (C_{22}), 128.9 (C_{24}), 128.6 (C_{Ar}), 126.8 (C_{Ar}), 125.0 (C_{Ar}), 123.6 (C_{Ar}), 122.7 (C_{Ar}), 122.5 (C_{Ar}), 121.1 (C_6), 120.9 (C_4), 100.7 (C_{12}), 24.7 (C_{10}), 20.3 (C_{27}), 17.8 (C_{26}), 16.8 (C_7).

IR (film) ν_{max}/cm^{-1} = 1734, 1685, 1558, 1524, 1474, 1367, 1205, 1120, 870, 729.

HRMS (ESI$^+$): calculated for $C_{25}H_{25}N_2O_2S^+$, $[M+H]^+$ = 417.1631; *m/z* found = 417.1626, Δ = -1.20 ppm.

2-Acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 373:



Compound **373** was prepared according to **General Procedure O** using *N*-(2'-amino-6-(benzo[b]thiophen-3-yloxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide **372** (486 mg, 1.17 mmol, 1 eq.), HBF_4 (0.76 mL, 5.83 mmol, 5 eq.), and ^{t}BuONO (0.69 mL, 5.83 mmol, 5 eq.) to give the title compound as an orange solid (456 mg, 80%).

m.p. = dec. > 140 °C.

^{1}H NMR (600 MHz, CD_3CN) δ_H = 8.77 (s, 1H, H_8), 8.52 (d, *J* = 2.4 Hz, 1H, H_6), 8.47 (s, 1H, H_{12}), 8.13 (dt, *J* = 8.3, 0.9 Hz, 1H, $H_{14/17}$), 8.01 – 7.98 (m, 1H, H_{24}), 7.60 (ddt, *J* = 8.0, 6.9, 1.2 Hz, 1H, $H_{15/16}$), 7.51 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H, $H_{15/16}$), 7.45 (dt, *J* = 8.1, 1.0 Hz, 1H, $H_{14/17}$), 7.43 – 7.41 (m, 1H, H_4), 7.32 – 7.28 (m, 1H, H_{22}), 2.51 (s, 3H, H_{26}), 2.14 (s, 3H, H_{10}), 2.02 (s, 3H, H_7), 2.02 (s, 3H, H_{25}).

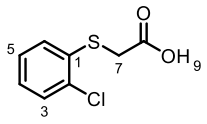
^{13}C NMR (151 MHz, CD_3CN) δ_C = 170.3 (C_9), 161.2 (C_{20}), 157.8 (C_2), 144.1 (C_{Ar}), 142.9 (C_{23}), 142.3 (C_{Ar}), 137.8 (C_{Ar}), 135.8 (C_{22}), 128.3 ($C_{15/16}$), 128.1 ($C_{15/16}$), 127.9 (C_{Ar}), 125.6 (C_{Ar}), 125.6 (C_{Ar}), 124.9 ($C_{13/17}$), 124.5 (C_4), 124.3 (C_{Ar}), 123.6 ($C_{13/17}$), 122.9 (C_{24}), 120.2 (C_{Ar}), 111.8 (C_6), 24.4 (C_{10}), 21.0 (C_{26}), 16.7 (C_7), 16.4 (C_{25}). One aromatic carbon peak was not observed.

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -149.5.

IR (film) ν_{max}/cm^{-1} = 3107, 1736, 1698, 1560, 1489, 1071, 873, 700.

HRMS (ESI^+): calculated for $C_{25}H_{22}NO_2S^+$, $[M]^+$ = 400.1366; *m/z* found = 400.1361, Δ = -1.26 ppm.

2-((2-Chlorophenyl)thio)acetic acid, 375:



Compound **375** was prepared according to **General procedure K** using 2-chlorobenzenethiol (1.74 mL, 15.0 mmol, 1 eq.), bromoacetic acid (2.28 g, 16.5 mmol, 1.1 eq.) and NaOH (6 M, 1.20 g, 31.5 mmol, 2.1 eq.). The reaction was heated at 60 °C for 2 h to give the title product as a white solid (2.60 g, 86%) which was used without further purification.

m.p. = 90-92 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$) δ_H = 12.92 (s, 1H, H_9), 7.46 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.38 – 7.28 (m, 2H, H_{Ar}), 7.25 – 7.14 (m, 1H, H_{Ar}), 3.91 (s, 2H, H_7).

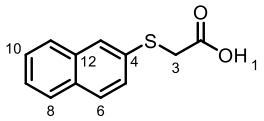
^{13}C NMR (101 MHz, DMSO-d$_6$) δ_H = 170.6 (C_8), 135.7 (C_1), 131.0 (C_2), 129.9 (C_{Ar}), 128.2 (C_{Ar}), 127.5 (C_{Ar}), 127.0 (C_{Ar}), 34.1 (C_7).

IR (film) ν_{max}/cm^{-1} **=** 2981, 1698, 1432, 1202, 912, 751.

HRMS (ESI^-): calculated for $C_8H_6ClO_2S^-$, $[M-H]^-$ = 200.9783; *m/z* found = 277.9777, Δ = -2.77 ppm.

Data in accordance with literature.[167]

2-(Naphthalen-2-ylthio)acetic acid, 378:



Compound **378** was prepared according to **General procedure K** using 2-thionapthalene (4.81 g, 30.0 mmol, 1 eq.), bromoacetic acid (4.55 g, 33.0 mmol, 1.1 eq.) and NaOH (6 M, 2.52 g, 63.0 mmol, 2.1 eq.). The reaction mixture was heated at 60 °C for 2 h. The crude residue was purified by flash column chromatography (MeOH:CH_2Cl_2, 10:90, R_f = 0.4) to give the title product as a white solid (2.57 g, 39%).

m.p. = 80-82 °C.

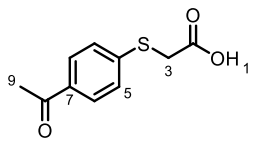
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.87 (d, *J* = 1.9 Hz, 1H, H_{13}), 7.83 – 7.73 (m, 3H, H_{Ar}), 7.47 (dqd, *J* = 8.4, 6.8, 1.6 Hz, 3H, H_{Ar}), 3.76 (s, 2H, H_3).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 175.4 (C_2), 133.7 (C_{Ar}), 132.3 (C_{Ar}), 131.8 (C_4), 128.9 (C_{Ar}), 128.5 (C_{13}), 127.7 (C_{Ar}), 127.5 (C_{Ar}), 127.4 (C_{Ar}), 126.7 (C_{Ar}), 126.3 (C_{Ar}), 36.5 (C_3).

IR (film) ν_{max}/cm^{-1} = 3085, 1702, 910, 807, 737.

HRMS (ESI^+): calculated for $C_{12}H_{11}O_2S^+$, $[M+H]^+$ = 219.0474; *m/z* found = 219.0480, Δ = 2.61 ppm.

2-((4-Acetylphenyl)thio)acetic acid, 379:



Compound **379** was prepared according to **General procedure K** using 1-(4-mercaptophenyl)ethan-1-one (296 mg, 1.94 mmol, 1 eq.), bromoacetic acid (295 mg, 2.14 mmol, 1.1 eq.) and NaOH (6 M, 163 mg, 4.05 mmol, 2.1 eq.). The reaction mixture was heated at 60 °C for 17 h to give the title product as a white solid (314 mg, 77%) and which was used without further purification.

m.p. = 134-136 °C.

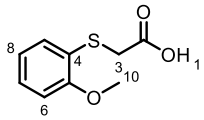
^{1}H NMR (600 MHz, DMSO-d$_6$) δ_H = 12.89 (s, 1H, H_1), 7.90 – 7.84 (m, 2H, H_6), 7.44 – 7.38 (m, 2H, H_5), 3.95 (s, 2H, H_3), 2.54 (s, 3H, H_9).

^{13}C NMR (151 MHz, DMSO-d$_6$) δ_C = 196.9 (C_8), 170.2 (C_2), 143.0 (C_4), 133.7 (C_7), 128.7 (C_6), 125.9 (C_5), 33.6 (C_3), 26.5 (C_9).

HRMS (ESI$^-$): calculated for $C_{10}H_9O_3S^-$, $[M-H]^-$ = 209.0278; *m/z* found = 209.0272, Δ = -3.04 ppm.

Data in accordance with literature.[168]

1a,7a-Dihydro-7*H*-oxireno[2,3-b]chromen-7-one, 380:



Compound **380** was prepared according to **General procedure K** using 2-methoxybenzenethiol (1.8 mL, 15.0 mmol, 1 eq.), bromoacetic acid (2.28 g, 16.5 mmol, 1.1 eq.) and NaOH (6 M, 1.20 g, 31.5 mmol, 2.1 eq.). The reaction was heated at 60 °C for 16 h to give the title product as a white solid (2.33 g, 78%) and which was used without further purification.

m.p. = 82-92 °C

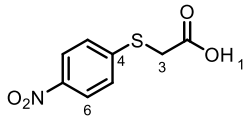
^{1}H NMR (400 MHz, DMSO-d_6) δ_H = 12.71 (s, 1H, H_1), 7.23 – 7.16 (m, 2H, H_7, H_9), 6.98 (dd, *J* = 8.1, 1.2 Hz, 1H, H_6), 6.93 (td, *J* = 7.6, 1.2 Hz, 1H, H_8), 3.82 (s, 3H, H_{10}), 3.70 (s, 2H, H_3).

^{13}C NMR (101 MHz, DMSO-d_6) δ_C = 171.2 (C_2), 156.6 (C_5), 127.9 ($C_{7/9}$), 127.3 ($C_{7/9}$), 124.3 (C_4), 121.5 (C_8), 111.3 (C_6), 56.2 (C_{10}), 33.8 (C_3).

IR (film) ν_{max}/cm^{-1} = 3005, 1737, 1699, 1345, 1246, 1246, 1201, 1022, 910, 756.

HRMS (ESI^+): calculated for $C_9H_{11}O_3S^+$, $[M+H]^+$ = 199.0423; *m/z* found = 199.0422, Δ = -0.86 ppm.

2-((4-Nitrophenyl)thio)acetic acid, 724:



Compound **390** was prepared according to **General procedure K** using 4-nitrobenzenethiol (4.66 g, 30.0 mmol, 1 eq.), bromoacetic acid (4.59 g, 33.0 mmol, 1.1 eq.) and NaOH (6 M, 2.40 g, 62.0 mmol, 2.1 eq.). The reaction was heated at 60 °C for 4 h to give the title product as a bright yellow solid (5.82 g, 91%) and which was used without further purification.

m.p. = 140-142 °C

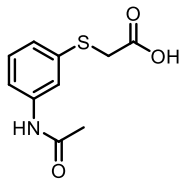
^{1}H NMR (400 MHz, DMSO-d_6) δ_H = 13.02 (s, 1H, H_1), 8.14 (d, *J* = 8.5 Hz, 2H, $H_{5/6}$), 7.50 (d, *J* = 8.5 Hz, 2H, $H_{5/6}$), 4.04 (s, 2H, H_3).

^{13}C NMR (101 MHz, DMSO-d_6) δ_C = 169.9 (C_2), 146.7 (C_4), 144.6 (C_7), 126.2 ($C_{5/6}$), 123.9 ($C_{5/6}$), 33.6 (C_3).

IR (film) ν_{max}/cm^{-1} = 2970, 1739, 1398, 1504, 1329, 1203, 741.

HRMS (ESI$^-$): calculated for $C_8H_6NO_4S^-$, $[M-H]^-$ = 212.0023; *m/z* found = 212.0018, Δ = -2.32 ppm.

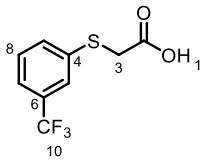
2-((3-Acetamidophenyl)thio)acetic acid, 391:



Compound **391** was prepared according to a modified literature procedure.[169] A_2O (3.4 mL, 35.9 mmol, 1.1 eq.) was added to a stirred solution of 3-aminobenzenethiol (4.08 g, 32.6 mmol, 1 eq.) in AcOH (20 mL). After 10 mins, the reaction was poured onto H_2O (50 mL) and EtOAc (100 mL) was added. The organic layer was removed, and the aqueous layer was extracted with EtOAc (50 mL x 3). The combined organic extracts were washed with NaCl (sat. aq., 100 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give a crude residue.

H_2O (65 mL) and bromoacetic acid (4.95 g, 35.9 mmol, 1.1 eq.) were sequentially added to the crude residue followed by NaOH (6M, 2.74 g, 68.5 mmol, 2.1 eq.) and the reaction mixture was heated at 60 °C. After 16 h the reaction was cooled to r.t. and acidified with HCl (1 M) to form a ppt. The ppt was filtered, washed with HCl (1 M), and dried *in vacuo* to give the title compound as a white solid (5.00 g, 68%) and was used without further purification.

2-((3-(Trifluoromethyl)phenyl)thio)acetic acid, 792:



Compound **392** was prepared accordanceing to **General procedure K** using 3-(trifluoromethyl)benzenethiol (4.45 g, 25.0 mmol, 1 eq.), bromoacetic acid (3.79 g, 27.5 mmol, 1.1

eq.) and NaOH (6 M, 2.10 g, 52.5 mmol, 2.1 eq.). The reaction was heated at 60 °C for 2 h to give the title product as a yellow solid (5.39 g, 91%) and which was used without further purification.

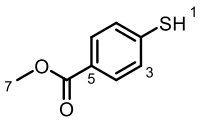
m.p. = 36-38 °C.

^{1}H NMR (400 MHz, DMSO-d$_6$) δ_H = 12.87 (s, 1H, H_1), 7.67 – 7.61 (m, 2H, H_{Ar}), 7.55 – 7.51 (m, 2H, H_{Ar}), 3.94 (s, 2H, H_3).

^{13}C NMR (101 MHz, DMSO-d$_6$) δ_C = 170.4 (C_2), 137.9 (C_4), 131.2 (C_{Ar}), 129.9 (q, J = 32.1 Hz, C_6), 129.9 (C_{Ar}), 125.3 (q, J = 272.2, C_{10}), 123.5 (q, J = 3.9 Hz, C_{Ar}), 122.4 – 122.2 (m, C_{Ar}), 34.4 (C_3).

HRMS (ESI$^-$): calculated for $C_9H_6F_3O_2S^-$, $[M-H]^-$ = 235.0046; m/z found = 235.0043, Δ = -1.49 ppm.

Methyl 4-mercaptobenzoate, 394a:



Compound **394a** was prepared according to a modified literature procedure.[170] Conc. H_2SO_4 (3 drops) was added to a stirred solution of 4-mercaptobenzoic acid (3.99 g, 25.9 mmol, 1 eq.) and MeOH (20 mL) and the resultant mixture was heated to 90 °C. After 20 h the reaction was cooled to r.t. and the MeOH was removed *in vacuo*. The crude residue was diluted with EtOAc (50 mL) and the organic layer was sequentially washed with H_2O (2 x 30 mL) and $NaHCO_3$ (sat. aq., 30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the title compound as a yellow solid (3.61 g, 83%).

m.p. = 38-42°C.

^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.89 (dq, *J* = 8.3, 2.1 Hz, 2H, H_4), 7.28 (dq, *J* = 7.7, 2.1 Hz, 2H, H_3), 3.90 (q, *J* = 1.9 Hz, 3H, H_7), 3.63 (s, 1H, H_1).

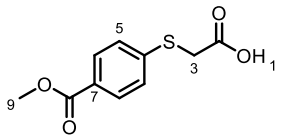
^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 166.7 (C_6), 138.5 (C_2), 130.3 (C_4), 128.2 (C_3), 127.2 (C_5), 52.2 (C_7).

IR (film) ν_{max}/cm^{-1} = 2960, 2554, 1718, 1596, 1434, 1279, 1112, 759.

HRMS (ESI^+): calculated for $C_8H_9O_2S^+$, $[M+H]^+$ = 169.0319; *m/z* found = 169.0317, Δ = -0.26 ppm.

Data in accordance with literature.[171]

2-((4-(Methoxycarbonyl)phenyl)thio)acetic acid, 394:



K_2CO_3 (5.75g, 41.4 mmol, 2 eq.) was added to a stirred solution of methyl 4-mercaptobenzoate **394a** (3.50 g, 20.8 mmol, 1 eq.), bromoacetic acid (4.38 g, 31.2 mmol, 1.5 eq.) and MeCN (42 mL). The resultant mixture was heated to 82 °C. After 6 h the reaction mixture was cooled to r.t. and MeCN was removed *in vacuo*. The crude residue was acidified until pH = 1 using HCl (1 M). The suspension was filtered, the ppt was washed with HCl (1 M, 3 x 30 mL), and the filtrate was removed. The ppt was dissolved in CH_2Cl_2 and eluted with CH_2Cl_2 (3 x 30 mL). The filtrate was concentrated *in vacuo* to give the title compound as a white solid (3.79 g, 81%).

m.p. = 104-106 °C.

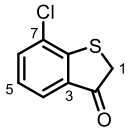
^{1}H NMR (500 MHz, DMSO-d_6) δ_H = 12.91 (s, 1H, H_1), 7.90 – 7.82 (m, 2H, H_6), 7.44 – 7.37 (m, 2H, H_5), 3.95 (s, 2H, H_3), 3.83 (s, 3H, H_9).

^{13}C NMR (126 MHz, DMSO-d_6) δ_C = 170.6 (C_2), 166.3 (C_8), 143.7 (C_4), 130.0 (C_6), 126.7 (C_7), 126.5 (C_5), 52.5 (C_9), 34.1 (C_3).

IR (film) ν_{max}/cm^{-1} = 3727, 2956, 1721, 1700, 1324, 1287, 1115, 740.

HRMS (ESI^-): calculated for $C_{10}H_9O_4S^-$, $[M-H]^-$ = 225.0227; *m/z* found = 225.0222, Δ = -2.06 ppm.

7-Chlorobenzo[b]thiophen-3(2*H*)-one, 395:



Compound **395** was synthesised accordanceing to **General procedure L** using 2-((2-chlorophenyl)thio)acetic acid **375** (2.50 g, 12.3 mmol, 1 eq.) and $SOCl_2$ (1.1 mL, 14.8 mmol, 1.2 eq.) The crude residue was then used along with $AlCl_3$ (4.94 g, 37.0 mmol, 3 eq.) to give the title compound as a pink solid (2.00 g, 88%) and which was used without further purification.

m.p. = 90-92 °C.

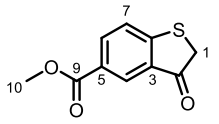
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.70 (dd, *J* = 7.7, 1.1 Hz, 1H, H_6), 7.57 (dd, *J* = 7.7, 1.1 Hz, 1H, H_4), 7.20 (t, *J* = 7.7 Hz, 1H, H_5), 3.84 (s, 2H, H_1).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 199.4 (C_2), 153.2 (C_8), 135.2 (C_6), 133.1 (C_3), 130.2 (C_7), 126.2 (C_5), 124.9 (C_4), 40.0 (C_1).

IR (film) ν_{max}/cm^{-1} **=** 3076, 2982, 1720, 1700, 1584, 1454, 1262, 783, 733.

HRMS (ESI$^-$): calculated for $C_8H_4ClOS^-$, $[M-H]^-$ = 182.9677; *m/z* found = 182.9670, Δ = -3.75 ppm.

Methyl 3-oxo-2,3-dihydrobenzo[b]thiophene-5-carboxylate, 396:



Compound **396** was synthesised accordanceing to **General procedure L** using 2-((4-(Methoxycarbonyl)phenyl)thio)acetic acid **394** (3.53 g, 15.6 mmol, 1 eq.) and $SOCl_2$ (1.2 mL, 17.2 mmol, 1.2 eq.) The crude residue was then used along with $AlCl_3$ (6.25 g, 46.8 mmol, 3 eq.) to give the title compound as a pink solid (3.03 g, 93%) and was used without further purification.

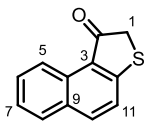
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.42 (dd, *J* = 1.7, 0.6 Hz, 1H, H_4), 8.21 (dd, *J* = 8.3, 1.8 Hz, 1H, H_6), 7.49 (dd, *J* = 8.3, 0.7 Hz, 1H, H_7), 3.93 (s, 3H, H_{10}), 3.86 (s, 2H, H_1).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 199.0 (C_2), 166.0 (C_9), 159.5 (C_8), 136.3 (C_6), 131.2 (C_3), 128.2 (C_4), 127.4 (C_5), 124.7 (C_7), 52.5 (C_{10}), 40.0 (C_1).

IR (film) ν_{max}/cm^{-1} = 2981, 1719, 1689, 1603, 1435, 1245, 1083, 758.

HRMS (ESI$^+$): calculated for $C_{10}H_9O_3S^+$, $[M+H]^+$ = 209.0267; *m/z* found = 209.0266, Δ = -0.48 ppm.

Naphtho[2,1-b]thiophen-1(2*H*)-one, 399:



Compound **399** was synthesised according to a literature procedure.[126] To a flame-dried RBF, (2-naphthylthio)acetic acid **378** (2.18 g, 10.0 mmol, 1 eq.) was added followed by evacuation and refill

with N_2 x 3. Anhydrous CH_2Cl_2 (15 mL) was added followed by dropwise addition of triflic acid (4.4 mL, 50.0 mmol, 5 eq.). The resultant mixture was stirred at 40 °C for 5 h and then cooled to r.t. before being slowly poured onto ice. The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL) and the combined organic extracts were washed with $NaHCO_3$ (sat. aq., 30 mL) and NaCl (sat. aq., 30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (EtOAc:pentane, 10:90, R_f = 0.2) to give the title product as a brown solid (1.40 g, 70%).

m.p. = 102-104 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 9.20 (dq, *J* = 8.5, 0.9 Hz, 1H, H_5), 7.97 (d, *J* = 8.6 Hz, 1H, H_{11}), 7.87 – 7.81 (m, 1H, H_8), 7.67 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H, H_6), 7.52 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, H_7), 7.46 (d, *J* = 8.7 Hz, 1H, H_{10}), 3.91 (s, 2H, H_1).

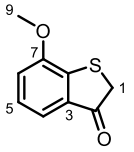
^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 200.4 (C_2), 159.7 (C_{12}), 136.7 (C_{11}), 131.2 (C_{Ar}), 131.1 (C_{Ar}), 129.7 (C_6), 128.4 (C_8), 126.3 (C_7), 123.6 (C_3), 122.6 (C_5), 122.4 (C_{10}), 40.0 (C_1).

IR (film) ν_{max}/cm^{-1} = 2981, 1678, 1580, 1385, 1134, 738.

HRMS (ESI$^-$): calculated for $C_{12}H_7O\,S^-$, $[M\text{-}H]^-$ = 199.0223; *m/z* found = 199.0217, Δ = -3.19 ppm.

Data in accordance with literature.[172]

7-Methoxybenzo[b]thiophen-3(2*H*)-one, 401:



Compound **401** was synthesised accordanceing to **General procedure L** using 1a,7a-dihydro-7H-oxireno[2,3-b]chromen-7-one **380** (1.47 g, 7.43 mmol, 1 eq.) and $SOCl_2$ (0.65 mL, 8.91 mmol, 1.2 eq.) The crude residue was then used along with $AlCl_3$ (2.97 g, 22.3 mmol, 3 eq.) to give a crude residue that was purified by flash column chromatography (EtOAc:pentane, 4:96, R_f = 0.3) to give the title product as a pink solid (465 mg, 35%).

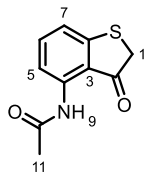
m.p. = 100-102 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.42 – 7.36 (m, 1H, H_4), 7.19 (t, *J* = 7.8 Hz, 1H, H_5), 7.01 (d, *J* = 7.8 Hz, 1H, H_6), 3.94 (s, 3H, H_9), 3.78 (s, 2H, H_1).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 200.5 (C2), 155.3 (C7), 143.6 (C8), 132.6 (C3), 126.2 (C5), 118.4 (C4), 115.3 (C6), 56.1 (C9), 39.6 (C1).

Data in accordance with literature.[173]

***N*-(3-oxo-2,3-dihydrobenzo[b]thiophen-4-yl)acetamide, 403:**



Compound **403** was synthesised accordanceing to **General procedure L** using 2-((3-acetamidophenyl)thio)acetic acid **391** (326 mg, 1.34 mmol, 1 eq.) and $SOCl_2$ (0.12 mL, 1.61 mmol, 1.2 eq.) The crude residue was then used along with $AlCl_3$ (536 mg, 4.02 mmol, 3 eq.) to give a crude residue that was purified by flash column chromatography (EtOAc:pentane, 30:70, R_f = 0.2) to give the title product as a brown solid (68 mg, 24%).

m.p. = 80-82 °C.

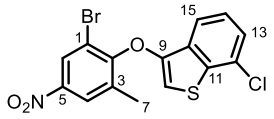
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 10.73 (s, 1H, H_9), 8.30 (dd, *J* = 8.2, 0.9 Hz, 1H, H_7), 7.48 (t, *J* = 8.1 Hz, 1H, H_6), 7.04 (dd, *J* = 7.9, 0.8 Hz, 1H, H_5), 3.83 (s, 2H, H_1), 2.24 (s, 3H, H_{11}).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 202.5 (C_2), 169.6 (C_{10}), 155.4 (C_8), 141.4 (C_4), 138.0 (C_6), 118.6 (C_5), 116.7 (C_3), 114.5 (C_7), 39.6 (C_1), 25.3 (C_{11}).

IR (film) ν_{max}/cm^{-1} = 2981, 1711, 1576, 1527, 1283, 1259, 728.

HRMS (ESI^+): calculated for $C_{10}H_{10}NO_2S^+$, $[M+H]^+$ = 208.0427; *m/z* found = 208.0427, Δ = -0.01 ppm.

3-(2-Bromo-6-methyl-4-nitrophenoxy)-7-chlorobenzo[b]thiophene, 405:



Compound **405** was prepared accordanceing to **General procedure M** using 7-chlorobenzo[b]thiophen-3(2H)-one **395** (186 mg, 1.00 mmol, 1 eq.), 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (250 mg, 1.00 mmol, 1 eq.), and K_2CO_3 (276 mg, 2.00 mmol, 2 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 0.5:95.5, R_f = 0.4) to give the title product as a yellow solid (198 mg, 50%).

m.p. = 142-143 °C.

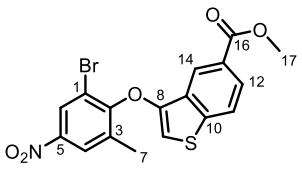
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.42 (d, *J* = 2.7 Hz, 1H, H_6), 8.17 (dd, *J* = 2.7, 0.9 Hz, 1H, H_4), 7.94 (dd, *J* = 7.3, 1.7 Hz, 1H, H_{15}), 7.50 – 7.40 (m, 2H, H_{13}, H_{14}), 6.07 (s, 1H, H_{10}), 2.37 (s, 3H, H_7).

^{13}C NMR (151 MHz, $CDCl_3$) δ_c = 156.2 (C_2), 147.2 (C_9), 145.2 (C_5), 137.1 ($C_{11/16}$), 134.7 (C_3), 132.5 ($C_{11/16}$), 128.4 (C_{12}), 127.1 (C_6), 125.8 (C_4), 125.8 ($C_{13/14}$), 125.4 ($C_{13/14}$), 119.4 (C_{15}), 117.8 (C_1), 102.1 (C_{10}), 17.1 (C_7).

IR (film) ν_{max}/cm^{-1} = 3107, 2982, 1179, 1525, 1365, 1349, 911, 742.

HRMS (ESI^-): calculated for $C_{15}H_8NO_3BrClS^-$, $[M-H]^-$ = 395.9096; *m/z* found = 395.9102, Δ = -1.59 ppm.

Methyl 3-(2-bromo-6-methyl-4-nitrophenoxy)benzo[b]thiophene-5-carboxylate, 406:



Compound **406** was prepared accordanceing to **General procedure M** using methyl 3-oxo-2,3-dihydrobenzo[b]thiophene-5-carboxylate **396** (2.71 g, 13.0 mmol, 1 eq.), 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (3.26 g, 13.0 mmol, 1 eq.), and K_2CO_3 (3.59 mg, 26.0 mmol, 2 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 4:96, R_f = 0.2) to give the title product as a yellow solid (968 mg, 19%).

m.p. = 170-172 °C.

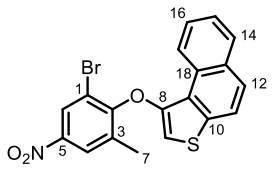
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.73 (dd, *J* = 1.7, 0.7 Hz, 1H, H_{14}), 8.43 (d, *J* = 2.6 Hz, 1H, H_6), 8.18 (dd, *J* = 2.7, 0.9 Hz, 1H, H_4), 8.11 (dd, *J* = 8.5, 1.7 Hz, 1H, H_{12}), 7.86 (dd, *J* = 8.5, 0.7 Hz, 1H, H_{11}), 6.05 (s, 1H, H_9), 3.99 (s, 3H, H_{17}), 2.38 (s, 3H, H_7).

^{13}C NMR (126 MHz, $CDCl_3$) δ_H = 167.2 (C_{16}), 156.3 (C_2), 147.5 (C_8), 145.4 (C_5), 142.5 (C_{10}), 134.9 (C_3), 130.9 (C_{15}), 127.3 (C_6), 126.9 (C_{13}), 126.3 (C_{12}), 126.0 (C_4), 123.2 (C_{11}), 123.1 (C_{14}), 117.9 (C_1), 101.9 (C_9), 52.5 (C_{17}), 17.2 (C_7).

IR (film) ν_{max}/cm^{-1} = 2981, 1720, 1530, 1347, 1258, 945, 740.

HRMS (ESI^-): calculated for $C_{17}H_{11}BrO_5NS^-$ $[M-H]^-$ = 419.9547; *m/z* found = 419.9541, Δ = -1.31 ppm.

1-(2-Bromo-6-methyl-4-nitrophenoxy)naphtho[2,1-b]thiophene, 409:



Compound **409** was prepared accordanceing to **General procedure M** using methyl naphtho[2,1-b]thiophen-1(2*H*)-one, **822**, (200 mg, 1.00 mmol, 1 eq.), 1-bromo-2-chloro-3-methyl-5-nitrobenzene **53** (250 mg, 1.00 mmol, 1 eq.), and K_2CO_3 (276 mg, 2.00 mmol, 2 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 0.5:95.5, R_f = 0.4) to give the title product as an orange solid (120 mg, 29%).

m.p. = 166-168 °°C.

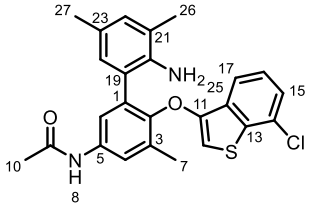
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 9.14 (dd, *J* = 8.4, 1.2 Hz, 1H, H_{17}), 8.47 (d, *J* = 2.7 Hz, 1H, H_6), 8.21 (d, *J* = 2.7, 1H, H_4), 8.00 (dd, *J* = 8.2, 1.4 Hz, 1H, H_{14}), 7.85 – 7.76 (m, 2H, H_{11}, H_{12}), 7.67 (ddd, *J* = 8.5, 7.0, 1.4 Hz, 1H, H_{16}), 7.61 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H, H_{15}), 6.14 (s, 1H, H_9), 2.41 (s, 3H, H_7).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 156.8 (C_2), 150.5 (C_{Ar}), 145.3 (C_5), 137.0 (C_{Ar}), 135.0 (C_3), 131.7 (C_{Ar}), 129.4 (C_{Ar}), 128.6 (C_{14}), 127.3 (C_6), 126.9 (C_{16}), 126.8 ($C_{11/12}$), 126.0 (C_4), 125.8 (C_{15}), 125.0 (C_{Ar}), 124.4 (C_{17}), 121.2 (C_{12}), 118.2 (C_1), 101.1 (C_9), 17.4 (C_7).

IR (film) ν_{max}/cm^{-1} = 3106, 1526, 1349, 1258, 909, 733.

HRMS (ESI^+): calculated for $C_{19}H_{13}BrNO_3S^+$, $[M+H]^+$ = 413.9794; *m/z* found = 413.9792, Δ = -0.50 ppm.

N-(2'-amino-6-((7-chlorobenzo[b]thiophen-3-yl)oxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide, 413a:



Compound **413a** was synthesised accordanceing to **General procedure N** using 3-(2-bromo-6-methyl-4-nitrophenoxy)-7-chlorobenzo[b]thiophene, **405**, (1.63 g, 4.07 mmol, 1 eq.) and Pd/C (10% wt., 217 mg, 0.20 mmol, 5 mol%). The crude residue was used in the subsequent step along with Ac_2O (1.2 mL, 12.2 mmol, 3 eq.). Assuming full conversion to the acylated product, the crude residue (1.15 g, 2.80 mmol, 1 eq.), 2,4- dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.73 g, 6.99 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (162 mg, 0.14 mmol, 5 mol%), and K_2CO_3 (1.55 g, 11.2 mmol, 4 eq.). The crude residue was purified by dry column vacuum chromatography (EtOAc:pentane, 0:100 to 100:0) to give the title product as an orange solid (972 mg, 77%).

m.p. = 164-166 °C.

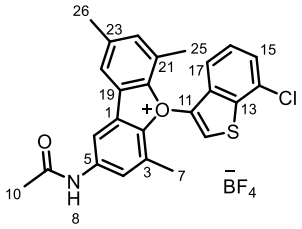
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.64 (d, *J* = 3.0 Hz, 1H, H_4), 7.60 (dd, *J* = 7.8, 1.1 Hz, 1H, H_{17}), 7.35 (s, 1H, H_8), 7.29 (dd, *J* = 7.7, 1.1 Hz, 1H, H_{15}), 7.22 (t, *J* = 7.7 Hz, 1H, H_{16}), 7.15 (d, *J* = 2.7 Hz, 1H, H_6), 6.61 (d, *J* = 2.1 Hz, 1H, H_{24}), 6.57 (d, *J* = 2.1 Hz, 1H, H_{22}), 6.05 (d, *J* = 1.1 Hz, 1H, H_{12}), 3.46 (s, 2H, H_{25}), 2.29 (s, 3H, H_7), 2.17 (m, 3H, H_{10}), 2.00 (s, 3H, H_{26}), 2.00 (s, 3H, H_{27}).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 168.5 (C_9), 150.1 (C_{11}), 148.9 (C_2), 139.4 (C_{20}), 136.6 (C_{Ar}), 135.3 (C_{Ar}), 133.6 (C_{Ar}), 133.4 (C_{Ar}), 132.6 (C_{Ar}), 130.7 (C_{22}), 128.9 (C_{24}), 127.9 (C_{Ar}), 126.8 (C_{Ar}), 124.9 (C_{16}), 124.7 (C_{15}), 122.6 (C_{Ar}), 122.6 (C_{Ar}), 122.5 (C_4), 121.2 (C_6), 119.4 (C_{17}), 102.1 (C_{12}), 24.7 (C_{10}), 20.3 (C_{27}), 17.8 (C_{26}), 16.8 (C_7).

IR (film) ν_{max}/cm^{-1} = 3294, 1667, 1364, 1203, 909, 734.

HRMS (ESI^+): calculated for $C_{25}H_{24}ClN_2O_2S^+$, $[M+H]^+$ = 451.1242; *m/z* found = 451.1231, Δ = -2.33 ppm.

2-Acetamido-5-(7-chlorobenzo[b]thiophen-3-yl)-4,6,8-trimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 413b:



Compound **413b** was prepared accordanceing to **General procedure O** using *N*-(2'-amino-6-((7-chlorobenzo[b]thiophen-3-yl)oxy)-3',5,5'-trimethyl-[1,1'-biphenyl]-3-yl)acetamide **413a** (499 mg, 1.11 mmol, 1 eq.), HBF_4 (48% aq., 0.72 mL, 5.53 mmol, 5 eq.), and ^{t}BuONO (0.66 mL, 5.53 mmol, 5 eq.) to give the title compound as an orange solid (400 mg, 69%).

m.p. = 176-178 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 9.24 (s, 1H, H_{12}), 8.78 (s, 1H, H_8), 8.07 (d, *J* = 2.4 Hz, 1H, H_6), 7.71 – 7.67 (m, 1H, H_4), 7.55 – 7.51 (m, 1H, H_{24}), 7.43 (d, *J* = 7.7 Hz, 1H, $H_{15/17}$), 7.16 (t, *J* = 8.0 Hz, 1H, H_{16}), 7.09 – 7.06 (m, 1H, H_{22}), 6.44 (d, *J* = 8.2 Hz, 1H, $H_{15/17}$), 2.46 (s, 3H, H_{26}), 2.23 (s, 3H, H_{25}), 2.09 (s, 3H, H_7), 2.02 (s, 3H, H_{10}).

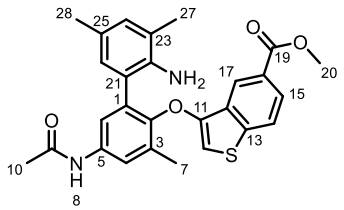
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 169.9 (C_9), 159.1 (C_2), 155.7 (C_{20}), 142.4 (C_{Ar}), 142.2 (C_{Ar}), 141.6 (C_{Ar}), 136.1 (C_{Ar}), 134.9 (C_{22}), 130.0 (C_{Ar}), 128.5 (C_{16}), 127.2 (C_{Ar}), 126.9 (C_{Ar}), 126.5 (C_{12}), 124.6 (C_{Ar}), 124.0 (C_{Ar}), 123.5 (C_4), 122.6 (C_{Ar}), 122.4 (C_{Ar}), 121.8 (C_{24}), 117.2 (C_{Ar}), 110.5 (C_6), 24.3 (C_{10}), 21.3 (C_{26}), 16.5 ($C_{7/25}$), 16.4 ($C_{7/25}$).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -149.3.

IR (film) ν_{max}/cm^{-1} = 3373, 2929, 1698, 1561, 1498, 1077, 912, 773, 737.

HRMS (ESI^+): calculated for $C_{25}H_{21}ClNO_2S^+$, $[M]^+$ = 434.0976; *m/z* found = 434.0971, Δ = -1.16 ppm.

Methyl 3-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)benzo[b]thiophene-5-carboxylate, 414a:



Compound **414a** was synthesised accordanceing to **General procedure N** using methyl 3-(2-bromo-6-methyl-4-nitrophenoxy)benzo[b]thiophene-5-carboxylate **406** (739 mg, 1.89 mmol, 1 eq.) and Pd/C (10% wt., 100 mg, 0.95 mmol, 5 mol%). The crude residue was used in the subsequent step along with Ac_2O (0.54 mL, 5.67 mmol, 3 eq.). The crude residue was then used in the following step along with 2,4- dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (1.17 g, 4.73 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (109 mg, 0.95 mmol, 5 mol%), and K_2CO_3 (1.05 g, 7.56 mmol, 4 eq.). The crude residue was purified by dry column vacuum chromatography (EtOAc:pentane, 0:100 to 100:0) to give the title product as an orange solid (572 mg, 64%).

m.p. = 82-84 °C.

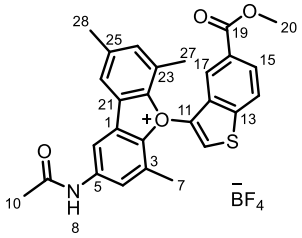
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.37 (d, *J* = 1.6 Hz, 1H, H_{17}), 7.95 – 7.90 (m, 1H, H_{15}), 7.69 – 7.63 (m, 2H, H_4, H_{14}), 7.14 (s, 1H, H_6), 6.59 (s, 1H, H_{26}), 6.52 – 6.47 (m, 1H, H_{24}), 6.08 – 6.04 (m, 1H, H_{12}), 3.95 (s, 3H, H_{20}), 2.32 (s, 3H, H_7), 2.18 (s, 3H, H_{10}), 1.97 (s, 3H, H_{28}), 1.96 (s, 3H, H_{27}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 168.4 (C_9), 167.5 (C_{19}), 150.5 (C_{11}), 149.2 (C_2), 141.9 (C_{13}), 139.4 (C_{22}), 135.3 (C_{Ar}), 135.3 (C_{Ar}), 133.6 (C_{Ar}), 132.6 (C_{Ar}), 131.7 (C_{18}), 130.5 (C_{24}), 128.8 (C_{26}), 126.7 (C_{Ar}), 125.9 (C_{16}), 125.4 (C_{15}), 123.0 (C_{17}), 122.6 (C_{Ar}), 122.5 (C_4, C_{14}), 121.2 (C_6), 102.3 (C_{12}), 52.2 (C_{20}), 24.7 (C_{10}), 20.2 (C_{28}), 17.7 (C_{27}), 16.8 (C_7).

IR (film) ν_{max}/cm^{-1} = 2980, 2882, 1721, 1671, 1277, 1242, 1204, 952.

HRMS (ESI^+): calculated for $C_{27}H_{27}N_2O_4S^+$, $[M+H]^+$ = 475.1686; *m/z* found = 475.1698, Δ = 2.50 ppm.

2-Acetamido-5-(5-(methoxycarbonyl)benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate, 414b:



Compound **414b** was prepared accordanceing to **General procedure O** using methyl 3-((5-acetamido-2'-amino-3,3',5'-trimethyl-[1,1'-biphenyl]-2-yl)oxy)benzo[b]thiophene-5-carboxylate **414a** (172 mg, 0.36 mmol, 1 eq.), HBF_4 (48% aq., 0.24 mL, 1.81 mmol, 5 eq.), and ^{t}BuONO (0.22 mL, 1.81 mmol, 5 eq.) to give the title compound as an orange solid (147 mg, 74%).

m.p. = 196-198 °C.

^{1}H NMR (500 MHz, $CDCl_3$) = 9.22 (s, 1H, H_{12}), 8.80 (s, 1H, H_8, 8.25 (d, *J* = 2.4 Hz, 1H, H_6), 8.09 (dd, *J* = 8.7, 1.5 Hz, 1H, H_{15}), 7.99 (d, *J* = 8.6 Hz, 1H, H_{14}), 7.65 (d, *J* = 2.0 Hz, 1H, H_{26}), 7.60 (d, *J* = 2.3 Hz, 1H, H_4), 7.27 – 7.26 (m, 1H, H_{17}), 7.12 – 7.08 (m, 1H, H_{24}), 3.80 (s, 3H, H_{20}), 2.49 (s, 3H, H_{28}), 2.19 (s, 3H, H_{27}), 2.05 (s, 3H, H, H_7), 2.02 (s, 3H, H_{10}).

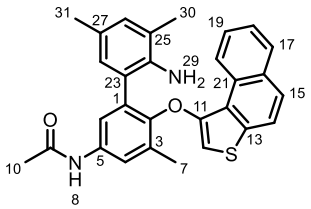
^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 170.0 (C_9), 165.3 (C_{19}), 159.2 (C_{22}), 155.8 (C_2), 142.8 (C_{Ar}), 142.2 (C_{Ar}), 141.7 (C_{Ar}), 140.6 (C_{Ar}), 135.0 (C_{24}), 129.5 (C_{16}), 127.7 (C_{15}), 126.9 (C_{12}), 125.9 (C_{Ar}), 124.6 (C_{14}), 124.4 (C_{Ar}), 123.8 (C_{Ar}), 123.8 (C_4), 122.7 (C_{Ar}), 122.4 (C_{Ar}), 121.9 (C_{26}), 120.3 (C_{17}), 110.6 (C_6), 52.9 (C_{20}), 24.3 (C_{10}), 21.3 (C_{28}), 16.4 (C_7, C_{27}).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -149.5.

IR (film) ν_{max}/cm^{-1} = 3371, 2105, 1724, 1650, 1275, 1249, 1064, 914, 732.

HRMS (ESI^+): calculated for $C_{27}H_{24}NO_4S^+$, $[M]^+$ = 458.1421; m/z found = 458.1414, Δ = -1.54 ppm.

N-(2'-amino-3',5,5'-trimethyl-6-(naphtho[2,1-b]thiophen-1-yloxy)-[1,1'-biphenyl]-3-yl)acetamide, 417a:



Compound **417a** was synthesised accordanceing to **General procedure N** using 1-(2-bromo-6-methyl-4-nitrophenoxy)naphtho[2,1-b]thiophene **409** (437 mg, 1.05 mmol, 1 eq.) and Pd/C (10% wt., 56 mg, 0.053 mmol, 5 mol%). The crude residue was used in the subsequent step along with Ac_2O (0.30 mL, 3.15 mmol, 3 eq.). The crude residue was then used in the following step along with 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline **56** (649 g, 2.63 mmol, 2.5 eq.), $Pd(PPh_3)_4$ (61 mg, 0.053 mmol, 5 mol%), and K_2CO_3 (580 g, 4.20 mmol, 4 eq.). The crude residue was purified by dry column vacuum chromatography (EtOAc:pentane, 0:100 to 100:0) to give the title product as a white solid (248 mg, 51%).

m.p. = 222-224 °C.

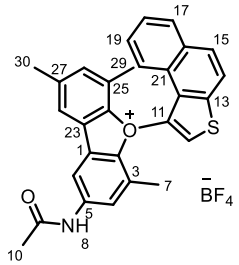
^{1}H NMR (500 MHz, DMSO-d_6, 373 K) δ_H = 9.69 (s, 1H, H_8), 9.04 (d, *J* = 8.4 Hz, 1H, H_{20}), 7.98 – 7.92 (m, 1H, H_{17}), 7.80 – 7.71 (m, 2H, H_{14}, H_{15}), 7.64 – 7.58 (m, 2H, H_4, H_{19}), 7.53 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H, H_{18}), 7.47 (d, *J* = 2.7 Hz, 1H, H_6), 6.64 (s, 1H, H_{28}), 6.41 – 6.37 (m, 2H, H_{12}, H_{26}), 2.25 (s, 3H, H_7), 2.08 (s, 3H, H_{10}), 1.88 (s, 3H, H_{30}), 1.78 (s, 3H, H_{31}).

^{13}C NMR (126 MHz, DMSO-d_6, 373 K) δ_C = 167.6 (C_9), 152.3 (C_{Ar}), 147.1 (C_{Ar}), 139.6 (C_{Ar}), 136.2 (C_{Ar}), 135.2 (C_{Ar}), 132.6 (C_{Ar}), 130.5 (C_{Ar}), 129.3 (C_{26}), 128.3 (C_{Ar}), 127.7 (C_{Ar}), 127.4 (C_{Ar}), 125.5 (C_{19}), 125.0 (C_{14}), 124.6 (C_{18}), 124.3 (C_{Ar}), 123.7 (C_{Ar}), 123.5 (C_{20}), 121.1 (C_{Ar}), 120.9 (C_6), 120.5 (C_{Ar}), 119.9 (C_{Ar}), 100.6 (C_{12}), 23.3 (C_{10}), 19.0 (C_{31}), 16.8 (C_{30}), 15.7 (C_7). Two aromatic carbon peaks were not observed.

IR (film) ν_{max}/cm^{-1} = 3317, 3056, 2919, 1670, 1560, 1471, 1203, 746.

HRMS (ESI^+): calculated for $C_{29}H_{27}N_2O_2S^+$, $[M+H]^+$ = 467.1788; *m*/*z* found = 467.1781, Δ = -1.39 ppm.

2-Acetamido-4,6,8-trimethyl-5-(naphtho[2,1-b]thiophen-1-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 417b:



Compound **417b** was prepared accordanceing to **General procedure O** using *N*-(2'-amino-3',5,5'-trimethyl-6-(naphtho[2,1-b]thiophen-1-yloxy)-[1,1'-biphenyl]-3-yl)acetamide **417a** (197 mg, 0.42 mmol, 1 eq.), HBF_4 (48% wt., 0.28 mL, 2.11 mmol, 5 eq.), and ^{t}BuONO (0.25 mL, 2.11 mmol, 5 eq.) to give the title compound as an orange solid (200 mg, 88%).

m.p. = 196-198 °°C

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 9.39 (s, 1H, H, H_8), 8.53 (s, 1H, H_6), 8.48 – 8.43 (m, 1H, $H_{17/20}$), 8.24 – 8.16 (m, 1H, $H_{17/20}$), 8.10 (d, *J* = 8.9 Hz, 1H, $H_{14/15}$), 8.06 (s, 1H, H_4), 7.99 (d, *J* = 8.9 Hz, 1H, $H_{14/15}$), 7.97 – 7.94 (m, 1H, H_{28}), 7.83 – 7.76 (m, 2H, H_{18}, H_{19}), 7.67 (s, 1H, H_{12}), 7.14 (s, 1H, H_{26}), 2.53 (s, 3H, H_{30}), 2.28 (s, 3H, H_{10}), 1.82 (s, 3H, $H_{7/29}$), 1.81 (s, 3H, $H_{7/29}$).

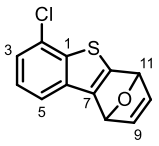
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 170.9 (C_9), 162.2 (C_{24}), 159.5 (C_2), 147.5 (C_{11}), 142.7 (C_{Ar}), 142.5 (C_{Ar}), 136.2 (C_{Ar}), 134.7 (C_{26}), 132.6 (C_{Ar}), 130.5 ($C_{17/20}$), 129.8 ($C_{14/15}$), 129.4 ($C_{18/19}$), 128.2 ($C_{18/19}$), 126.4 (C_{Ar}), 125.1 (C_4), 123.7 (C_{Ar}), 123.3 (C_{Ar}), 123.3 (C_{Ar}), 122.9 (C_{28}), 122.5 (C_{Ar}), 122.4 (C_{Ar}), 122.3 ($C_{17/20}$), 121.1 ($C_{14/15}$), 118.7 (C_{12}), 112.5 (C_6), 24.7 (C_{10}), 21.3 (C_{30}), 15.9 (C_7), 15.8 (C_{29}).

^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -149.6.

IR (film) ν_{max}/cm^{-1} = 1739, 1559, 1375, 1037, 987, 737.

HRMS (ESI^+): calculated for $C_{29}H_{24}NO_2S^+$, $[M]^+$ = 450.1522; *m/z* found = 450.1534, Δ = 1.17 ppm.

6-Chloro-1,4-dihydro-1,4-epoxydibenzo[b,d]thiophene, 418a:



Compound **418a** was prepared according to **General procedure P** using 2-acetamido-5-(7-chlorobenzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **413b** (157 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 5:95, R_f (**418a**) = 0.2, R_f (**418b**) = 0.6) to give the **418a** as a yellow solid (20 mg, 28%) and **418b** as a yellow solid (4 mg, 6%).

m.p. = 84-86 °C.

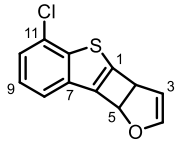
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.60 (dd, *J* = 7.9, 1.0 Hz, 1H, H_5), 7.34 (t, *J* = 7.8 Hz, 1H, H_4), 7.30 – 7.21 (m, 3H, H_3, H_9, H_{10}), 6.05 (d, *J* = 1.7 Hz, 1H, $H_{8/11}$), 5.96 (d, *J* = 1.6 Hz, 1H, $H_{8/11}$).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 157.0 (C_{12}), 153.8 (C_7), 144.4 ($C_{9/10}$), 144.3 ($C_{9/10}$), 143.8 (C_1), 134.2 (C_6), 128.4 (C_2), 126.0 (C_4), 123.3 (C_3), 119.6 (C_5), 82.9 ($C_{8/11}$), 81.9 ($C_{8/11}$).

IR (film) ν_{max}/cm^{-1} = 1363, 1152, 961, 860, 844.

HRMS (ESI^+): calculated for $C_{12}H_8ClOS^+$, $[M+H]^+$ = 234.9979; *m/z* found = 234.9975, Δ = -1.76 ppm.

5-Chloro-3a,8c-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]furan, 418b:



m.p. = 70-78 °C.

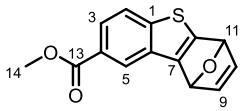
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.67 (dd, *J* = 7.3, 1.6 Hz, 1H, H_{Ar}), 7.37 – 7.27 (m, 2H, H_{Ar}), 6.37 (d, *J* = 3.0 Hz, 1H, H_4), 5.99 (d, *J* = 3.7 Hz, 1H, H_5), 5.37 (t, *J* = 2.7 Hz, 1H, H_3), 4.74 – 4.70 (m, 1H, H_2).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 154.5 (C_1), 149.8 (C_4), 143.7 (C_6), 135.5 (C_{Ar}), 129.0 (C_{Ar}), 126.1 (C_{Ar}), 124.0 (C_{Ar}), 119.7 (C_{Ar}), 103.7 (C_3), 80.6 (C_5), 53.9 (C_2). One aromatic carbon peak was not observed.

IR (film) ν_{max}/cm^{-1} = 2975, 2920, 1459, 1035, 860, 721.

HRMS (ESI$^+$): calculated for $C_{12}H_7ClOS^+$, $[M+H]^+$ = 234.9979, *m/z* found = 223.9977, Δ = -0.83 ppm.

Methyl 1,4-dihydro-1,4-epoxydibenzo[b,d]thiophene-8-carboxylate, 419a:



Compound **419a** was prepared accordanceing to **General procedure P** using 2-acetamido-5-(5-(methoxycarbonyl)benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **414b** (164 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (EtOAc:pentane, 2:98, R_f (**419a**) = 0.2, R_f (**419b**) = 0.7) to give the **419a** as a yellow solid (20 mg, 26%) and **419b** as a yellow solid (4 mg, 5%).

m.p. = 92-94 °C.

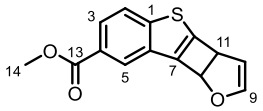
^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 8.38 (dd, *J* = 1.7, 0.7 Hz, 1H, H_5), 7.90 (dd, *J* = 8.6, 1.7 Hz, 1H, H_3), 7.80 (dd, *J* = 8.5, 0.8 Hz, 1H, H_2), 7.25 – 7.19 (m, 2H, H_9, H_{10}), 6.08 (d, *J* = 1.7 Hz, 1H, $H_{8/11}$), 5.93 (d, *J* = 1.6 Hz, 1H, $H_{8/11}$), 3.96 (s, 3H, H_{14}).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 167.4 (C_{13}), 157.8 (C_{12}), 153.6 (C_7), 149.3 (C_1), 144.4 (C_9, C_{10}), 132.5 (C_6), 127.1 (C_4), 124.1 (C_3), 123.8 (C_2), 123.0 (C_5), 82.9 ($C_{10/11}$), 81.9 ($C_{10/11}$), 52.4 (C_{14}).

IR (film) ν_{max}/cm^{-1} = 2952, 1720, 1453, 1278, 1247, 1167, 848, 761.

HRMS (ESI$^+$): calculated for $C_{14}H_{11}O_3S^+$, $[M+H]^+$ = 259.0423; *m/z* found = 259.0422, Δ = -0.66 ppm.

Methyl 3a,8c-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]furan-7-carboxylate, 419b:



m.p. = 48-50 °C.

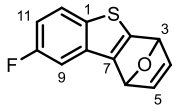
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 8.47 (dd, *J* = 1.6, 0.7 Hz, 1H, H_5), 7.97 (dd, *J* = 8.5, 1.7 Hz, 1H, H_3), 7.91 (dd, *J* = 8.5, 0.7 Hz, 1H, H_2), 6.38 (dd, *J* = 3.0, 0.8 Hz, 1H, H_9), 5.99 (dd, *J* = 3.7, 0.7 Hz, 1H, H_8), 5.36 (t, *J* = 2.7 Hz, 1H, H_{10}), 4.73 (dd, *J* = 3.6, 2.5 Hz, 1H, H_{11}), 3.95 (s, 3H, H_{14}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 167.4 (C_{13}), 154.9 (C_{12}), 150.0 (C_9), 149.1 (C_1), 143.5 (C_7), 133.7 (C_6), 127.2 (C_4), 124.7 (C_3), 123.5 (C_2), 123.1 (C_5), 103.5 (C_{10}), 80.1 (C_8), 54.0 (C_{11}), 52.4 (C_{14}).

IR (film) ν_{max}/cm^{-1} = 2929, 2856, 1723, 1220, 770.

HRMS (ESI^+): calculated for $C_{14}H_{11}O_3S^+$, $[M+H]^+$ = 259.0423; *m/z* found = 259.0424, Δ = 0.16 ppm.

8-Fluoro-1,4-dihydro-1,4-epoxydibenzo[b,d]thiophene, 420a:



Compound **420a** was prepared accordanceing to **General procedure P** using 2-acetamido-5-(5-fluorobenzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **415b** (152 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f (**420a**) = 0.2, R_f (**420b**) = 0.5) to give the **420a** as a pale yellow solid (22 mg, 34%) and **420b** as a colourless oil (1 mg, 2%).

m.p. = 88-90 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ_H = 7.68 (dd, *J* = 8.9, 4.8 Hz, 1H, H_{12}), 7.32 (dd, *J* = 9.4, 2.5 Hz, 1H, H_9), 7.21 (m, 2H, H_4, H_5), 7.00 (td, *J* = 8.9, 2.5 Hz, 1H, H_{11}), 6.00 (d, *J* = 1.6 Hz, 1H, $H_{3/6}$), 5.90 (d, *J* = 1.6 Hz, 1H, $H_{3/6}$).

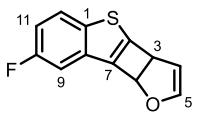
^{13}C NMR (126 MHz, $CDCl_3$) δ_C = 161.2 (d, *J* = 242.2 Hz, C_{10}), 158.8 (C_2), 152.5 (d, *J* = 4.6 Hz, C_7), 144.3 ($C_{4/5}$), 144.2 ($C_{4/5}$), 140.4 (d, *J* = 1.7 Hz, C_1), 133.6 (d, *J* = 10.0 Hz, C_8), 125.0 (d, *J* = 9.6 Hz, C_{12}), 112.4 (d, *J* = 25.4 Hz, C_{11}), 106.9 (d, *J* = 23.6 Hz, C_9), 82.9 ($C_{3/6}$), 81.7 ($C_{3/6}$).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -117.8.

IR (film) ν_{max}/cm^{-1} = 3083, 1738, 1601, 1083, 848, 731.

HRMS (ESI^+): calculated for $C_{12}H_8FOS^+$, $[M+H]^+$ = 219.0274; *m/z* found = 219.0272, Δ = -1.23 ppm.

7-Fluoro-3a,8c-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]furan, 420b:



^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.77 (dd, *J* = 8.8, 4.8 Hz, 1H, H_{12}), 7.42 (dd, *J* = 9.2, 2.5 Hz, 1H, H_9), 7.05 (td, *J* = 8.8, 2.6 Hz, 1H, H_{11}), 6.38 (d, *J* = 3.0 Hz, 1H, H_5), 5.95 (d, *J* = 3.6 Hz, 1H, H_6), 5.35 (t, *J* = 2.8 Hz, 1H, H_4), 4.71 (t, *J* = 3.1 Hz, 1H, H_3).

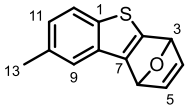
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 161.3 (d, *J* = 242.6 Hz, C_{10}), 156.2 (C_2), 149.9 (C_5), 143.0 (d, *J* = 4.3 Hz, C_7), 139.9 (d, *J* = 1.4 Hz, C_1), 135.0 (d, *J* = 10.1 Hz, C_8), 124.5 (d, *J* = 9.3 Hz, C_{12}), 112.6 (d, *J* = 25.1 Hz, C_{11}), 107.5 (d, *J* = 23.9 Hz, C_9), 103.6 (C_4), 80.1 (C_6), 53.9 (C_3).

^{19}F NMR (377 MHz, $CDCl_3$) δ_F = -117.7.

IR (film) ν_{max}/cm^{-1} = 2925, 1739, 1366, 1149, 911, 738.

HRMS (ESI^-): calculated for $C_{12}H_6FOS^-$, $[M-H]^-$ = 217.0129; *m/z* found = 217.0123, Δ = -2.85 ppm.

8-Methyl-1,4-dihydro-1,4-epoxydibenzo[b,d]thiophene, 421a:



Compound **421a** was prepared accordanceing to **General procedure P** using 2-acetamido-4,6,8-trimethyl-5-(5-methylbenzo[b]thiophen-3-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **416b** (150 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f (**421a**) = 0.3, R_f (**421b**) = 0.7) to give the **421a** as a yellow oil (20 mg, 31%) and **421b** as a white oil (1 mg, 5%).

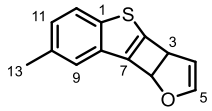
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.64 (d, *J* = 8.3 Hz, 1H, H_{12}), 7.48 (d, *J* = 1.7, 1H, H_9), 7.20 (dd, *J* = 5.4, 1.8 Hz, 1H, H_5), 7.18 (dd, *J* = 5.4, 1.8 Hz, 1H, H_4), 7.08 (dd, *J* = 8.3, 1.7 Hz, 1H, H, H_{11}), 6.01 (dd, *J* = 1.8, 0.7 Hz, 1H, H_3), 5.88 (dd, *J* = 1.8, 0.7 Hz, 1H, H_6), 2.46 (s, 3H, H_{13}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 156.0 (C_2), 152.4 (C_7), 144.3 ($C_{4/5}$), 144.1 ($C_{4/5}$), 142.5 (C_8), 134.7 (C_{10}), 133.2 (C_1), 125.5 (C_{11}), 123.5 (C_{12}), 121.3 (C_9), 82.9 (C_6), 81.8 (C_3), 21.6 (C_{13}).

IR (film) ν_{max}/cm^{-1} = 2916, 1738, 1024, 861, 847, 736.

HRMS (ESI^+): calculated for $C_{13}H_{11}OS^+$, $[M+H]^+$ = 215.0525; *m/z* found = 215.0524, Δ = -0.34 ppm.

7-Methyl-3a,8c-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]furan, 421b:



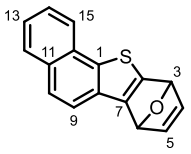
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.73 (d, *J* = 8.3 Hz, 1H, H_{12}), 7.57 (d, *J* = 1.7 Hz, 1H, H_9), 7.12 (dd, *J* = 8.3, 1.7 Hz, 1H, H_{11}), 6.36 (d, *J* = 3.0 Hz, 1H, H_5), 5.95 (dd, *J* = 3.7, 0.7 Hz, 1H, H_6), 5.35 (t, *J* = 2.7 Hz, 1H, H_4), 4.68 (dd, *J* = 3.6, 2.5 Hz, 1H, H_3), 2.45 (s, 3H, H_{13}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 153.7 (C_2), 149.7 (C_5), 142.9 (C_1), 141.9 (C_8), 134.9 (C_{10}), 134.1 (C_7), 125.7 (C_{11}), 123.2 (C_{12}), 121.6 (C_9), 103.8 (C_4), 80.2 (C_6), 53.6 (C_3), 21.5 (C_{13}).

IR (film) ν_{max}/cm^{-1} = 2970, 1738, 1288, 926, 737.

HRMS (ESI^+): calculated for $C_{13}H_{11}OS^+$, $[M+H]^+$ = 215.0525; *m/z* found = 215.0524, Δ = -0.48 ppm.

7,10-Dihydro-7,10-epoxybenzo[b]naphtho[2,1-d]thiophene, 422a:



Compound **422a** was prepared accordanceing to **General procedure P** using 2-acetamido-4,6,8-trimethyl-5-(naphtho[1,2-b]thiophen-3-yl)-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **417b** (161 mg, 0.30 mmol, 1 eq.). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f = 0.3) to give the **422a** as a yellow oil (32 mg, 43%).

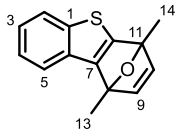
^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.28 – 8.21 (m, 1H, $H_{12/15}$), 7.95 – 7.88 (m, 1H, $H_{12/15}$), 7.75 (d, *J* = 8.8 Hz, 1H, $H_{9/10}$), 7.65 – 7.57 (m, 2H, $H_{9/10}$, $H_{13/14}$), 7.52 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H, $H_{13/14}$), 7.29 – 7.22 (m, 2H, H_4, H_5), 6.48 (d, *J* = 1.3 Hz, 1H, $H_{3/6}$), 5.96 (d, *J* = 1.2 Hz, 1H, $H_{3/6}$).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 155.1 ($C_{2/7}$), 153.4 ($C_{2/7}$), 144.8 ($C_{4/5}$), 144.5 ($C_{4/5}$), 141.7 (C_{Ar}), 131.7 (C_{Ar}), 130.1 (C_{Ar}), 128.8 (C_{Ar}), 128.7 ($C_{12/15}$), 126.5 ($C_{13/14}$), 125.7 ($C_{13/14}$), 124.3 ($C_{9/10}$), 124.1 ($C_{12/15}$), 122.0 ($C_{9/10}$), 83.6 ($C_{3/6}$), 82.5 ($C_{3/6}$).

IR (film) ν_{max}/cm^{-1} = 2981, 1269, 1026, 863, 841, 802, 739, 711.

HRMS (ESI^+): calculated for $C_{16}H_{11}OS^+$, $[M+H]^+$ = 251.0525; *m/z* found = 251.0514, Δ = -1.12 ppm.

1,4-Dimethyl-1,4-dihydro-1,4-epoxydibenzo[b,d]thiophene, 423:



Compound **423** was prepared accordanceing to **General procedure Q** using 2-acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.) and 2,5-dimethylfuran (4.5 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 3:97, R_f = 0.3) to give the **X** as a yellow oil (11 mg, 16%).

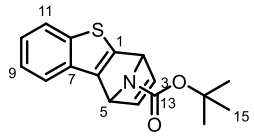
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.77 (dq, *J* = 8.3, 0.8 Hz, 1H, H_5), 7.67 (ddt, *J* = 8.0, 1.3, 0.7 Hz, 1H, H_2), 7.35 (ddt, *J* = 8.0, 7.1, 0.8 Hz, 1H, H_4), 7.24 – 7.20 (m, 1H, H_3), 7.03 – 6.97 (m, 2H, H_9, H_{10}), 2.13 (s, 3H, H_{14}), 1.95 (s, 3H, H_{13}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 159.5 (C_{Ar}), 155.0 (C_{Ar}), 148.6 ($C_{9/10}$), 148.4 ($C_{9/10}$), 144.9 (C_{Ar}), 133.4 (C_6), 124.8 (C_4), 124.2 (C_5), 123.2 (C_3), 120.8 (C_2), 91.2 ($C_{11/12}$), 91.1 ($C_{11/12}$), 16.9 ($C_{13/14}$), 16.8 ($C_{13/14}$).

IR (film) ν_{max}/cm^{-1} = 3392, 2977, 2930, 1462, 1144, 857, 729.

HRMS (ESI$^+$): calculated for $C_{14}H_{13}OS^+$, $[M+H]^+$ = 229.0682; *m/z* found = 229.0681, Δ = -0.16 ppm.

***tert*-Butyl 1,4-dihydro-1,4-epiminodibenzo[b,d]thiophene-10-carboxylate, 424a:**



Compound **424a** was prepared accordanceing to **General procedure Q** using 2-acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.) and *tert*-Butyl 1*H*-pyrrole-1-carboxylate (4.5 mL). *tert*-Butyl 1*H*-pyrrole-1-carboxylate was removed at 2 mbar and 80 °C. The crude residue was purified by flash column chromatography (Et_2O:pentane, 5:95, R_f (**424a**) = 0.4 and R_f (**424b**) = 0.5, R_f (**424c**) = 0.55) to give **424a** as an orange solid (14 mg, 16%) **424c** as a pink solid (3 mg, 5%), and **424b** as an orange oil (1 mg, 2%).

m.p. = 60-62 °C.

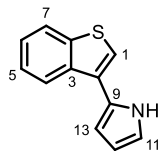
^{1}H NMR (600 MHz, $CDCl_3$) δ_C = 7.75 (d, *J* = 8.2 Hz, 1H, $H_{8/11}$), 7.70 (d, *J* = 7.9 Hz, 1H, $H_{8/11}$), 7.35 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H, $H_{9/10}$), 7.23 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, $H_{9/10}$), 7.19 – 7.06 (m, 2H, H_3, H_4), 5.80 (d, *J* = 39.0 Hz, 1H, $H_{5/4}$), 5.67 (d, *J* = 36.2 Hz, 1H, $H_{4/5}$), 1.39 (s, 9H, H_{15}).

^{13}C NMR: Insufficient amount of material was isolated for full characterisation by ^{13}C NMR. This compound will be remade for publication.

IR (film) ν_{max}/cm^{-1} = 2974, 1740, 1369, 1336, 1170, 736.

HRMS (ESI$^+$): calculated for $C_{17}H_{18}NO_2S^+$, $[M+H]^+$ = 300.1053; *m/z* found = 300.1052, Δ = -0.29 ppm.

2-(Benzo[b]thiophen-3-yl)-1*H*-pyrrole, 424c:



m.p. = 76-78 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_C = 8.46 (s, 1H, H_{10}), 8.08 (ddd, *J* = 8.0, 1.4, 0.7 Hz, 1H, $H_{4/7}$), 7.89 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H, $H_{4/7}$), 7.43 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H, $H_{5/6}$), 7.41 – 7.38 (m, 1H, $H_{5/6}$), 7.34 (s, 1H, H_1), 6.93 (td, *J* = 2.7, 1.4 Hz, 1H, $H_{11/13}$), 6.56 (ddd, *J* = 3.7, 2.6, 1.5 Hz, 1H, $H_{11/13}$), 6.38 (dt, *J* = 3.5, 2.7 Hz, 1H, H_{12}).

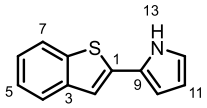
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 140.7 ($C_{3/8}$), 137.5 ($C_{3/8}$), 130.0 ($C_{2/9}$), 127.0 ($C_{2/9}$), 124.8 ($C_{5/6}$), 124.7 ($C_{5/6}$), 123.2 ($C_{4/7}$), 123.1 ($C_{4/7}$), 121.0 (C_1), 118.4 ($C_{11/13}$), 109.8 (C_{12}), 107.8 ($C_{11/13}$).

IR (film) ν_{max}/cm^{-1} = 3734, 1737, 1717, 1369, 1346, 1231, 911, 761, 736.

HRMS (ESI^+): calculated for $C_{12}H_{10}NS^+$, $[M+H]^+$ = 200.0529; *m/z* found = 200.0527, Δ = -0.97 ppm.

Data in accordance with literature.[174]

2-(Benzo[b]thiophen-2-yl)-1*H*-pyrrole, 424b:



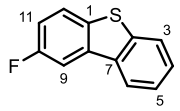
^{1}H NMR (600 MHz, $CDCl_3$) δ_C = 11.20 (s, 1H, H_{13}), 8.33 (dt, *J* = 8.2, 1.0 Hz, 1H, H_7), 7.80 (dt, *J* = 8.0, 0.9 Hz, 1H, H_4), 7.50 – 7.45 (m, 2H, H_2, H_5), 7.42 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H, H_6), 7.03 (m, 1H, $H_{10/12}$), 6.84 (m, 1H, H, $H_{10/12}$), 6.41 (m, 1H, H_{11}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 140.6 (C_8), 138.9 (C_3), 134.3 (C_1), 129.4 (C_9), 127.3 (C_5), 126.5 (C_7), 124.8 (C_6), 122.3 (C_4), 119.3 ($C_{10/12}$), 118.9 (C_4), 111.8 ($C_{10/12}$), 109.3 (C_{11}).

IR (film) ν_{max}/cm^{-1} = 1737, 1686, 1370, 1246, 912, 761.

HRMS (ESI^+): calculated for $C_{12}H_{10}NS^+$, $[M+H]^+$ = 200.0529; *m/z* found = 200.0529, Δ = 0.03 ppm.

2-Fluorodibenzo[b,d]thiophene, 425a:



Compound **425a** was prepared accordanceing to **General procedure Q** using 2-acetamido-5-(5-fluorobenzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **416b** (146 mg, 0.30 mmol, 1 eq.) and thiophene (4.5 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 1:99, R_f (**425a**) = 0.5 and R_f (**425b**) = 0.3) to give **425a** as a white solid (11 mg, 18%) and **425b** as a yellow oil (3 mg, 4%).

m.p. = 89-91 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ_C = 8.13 – 8.06 (m, 1H, H_6), 7.87 – 7.84 (m, 1H, H_3), 7.82 (dd, *J* = 9.2, 2.6 Hz, 1H, H_9), 7.78 (dd, *J* = 8.7, 4.8 Hz, 1H, H_{12}), 7.51 – 7.44 (m, 2H, H_4, H_5), 7.21 (td, *J* = 8.7, 2.5 Hz, 1H, H_{11}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_H = 161.1 (d, *J* = 242.5 Hz, C_{10}), 140.9 (C_2), 137.1 (d, *J* = 8.9 Hz, C_8), 135.2 (d, *J* = 4.0 Hz, C_7), 134.6 (d, *J* = 2.1 Hz, C_1), 127.4 ($C_{4/5}$), 124.6 ($C_{4/5}$), 124.0 (d, *J* = 8.8 Hz, C_{12}), 123.1 (C_3), 122.0 (C_6), 115.0 (d, *J* = 25.0 Hz, C_{11}), 108.0 (d, *J* = 23.4 Hz, C_9).

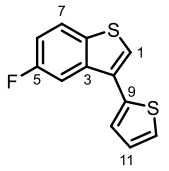
^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -118.3.

IR (film) ν_{max}/cm^{-1} = 2961, 2852, 1473, 1378, 1183, 664.

HRMS: Not found by ESI, APCI or EI.

Data in accordance with literature.[175]

5-Fluoro-3-(thiophen-2-yl)benzo[b]thiophene, 424b:



^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.81 (ddd, *J* = 8.8, 4.6, 0.5 Hz, 1H, H_7), 7.72 (s, 1H, H_1), 7.60 – 7.54 (m, 1H, H_4), 7.18 (tdd, *J* = 8.7, 2.5, 0.5 Hz, 1H, H_6), 6.59 (dd, *J* = 9.8, 0.8 Hz, 1H, H_{10}), 5.61 (dd, *J* = 9.8, 2.4 Hz, 1H, H_{11}), 3.50 (dd, *J* = 2.4, 0.8 Hz, 1H, H_{12}).

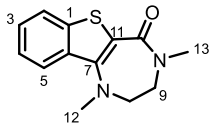
^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 161.5 (d, *J* = 243.2 Hz, C_5), 141.0 (C_{10}), 140.6 (d, *J* = 9.6 Hz, H_3), 135.2 (d, *J* = 1.6 Hz, H_8), 132.7 (C_1), 124.4 (d, *J* = 9.2 Hz, H_7), 123.9 (d, *J* = 5.0 Hz, H_2), 114.3 (d, *J* = 25.5 Hz, H_6), 108.7 (d, *J* = 24.2 Hz, H_4), 105.6 (C_{11}), 86.3 (C_{12}), 79.4 (C_9).

^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -117.0.

IR (film) ν_{max}/cm^{-1} = 3307, 2958, 2850, 1603, 1430, 1246, 1193, 884, 794, 649.

HRMS (ESI^+): calculated for $C_{12}H_8FS_2^+$, $[M+H]^+$ = 235.0046; *m/z* found = 235.0035, Δ = -4.69 ppm.

1,4-Dimethyl-1,2,3,4-tetrahydro-5*H*-benzo[4,5]thieno[3,2-e][1,4]diazepin-5-one, 430:



Compound **430** was prepared accordanceing to **General procedure Q** using 2-acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.) and 1,3-dimethyl-2-imidazolidinone (4.5 mL). 1,3-dimethyl-2-imidazolidinone was removed at 2 mbar and 100 °C. The crude residue was purified by flash column chromatography (EtOAc:pentane, 45:55, R_f = 0.2) to give the title compound as a brown oil (10 mg, 14%).

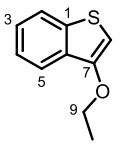
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.85 – 7.81 (m, 1H, H_5), 7.74 (dt, *J* = 8.0, 1.0 Hz, 1H, H_2), 7.38 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H, H_4), 7.32 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H, H_3), 3.64 – 3.59 (m, 2H, H_9), 3.48 – 3.42 (m, 2H, H_8), 3.22 (s, 3H, H_{13}), 3.15 (s, 3H, H_{12}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 163.8 (C_{10}), 144.2 (C_7), 140.2 (C_6), 135.7 (C_1), 126.5 (C_4), 124.3 (C_5), 123.6 (C_3), 123.2 (C_2), 121.1 (C_{11}), 55.3 (C_8), 47.2 (C_9), 43.3 (C_{12}), 37.9 (C_{13}).

IR (film) ν_{max}/cm^{-1} = 2928, 1597, 1486, 770, 747, 646.

HRMS (ESI^+): calculated for $C_{13}H_{15}N_2OS^+$, $[M+H]^+$ = 247.0900; *m/z* found = 247.0898, Δ = -0.55 ppm.

3-Ethoxybenzo[b]thiophene, 431:



Compound **431** was prepared accordanceing to **General procedure Q** using 2-acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.) and EtOH (4.5 mL). The crude residue was purified by flash column chromatography (Et_2O:pentane, 2:98, R_f = 0.2) to give the title compound as a yellow oil (25 mg, 47%).

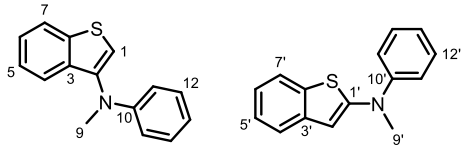
^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.86 – 7.79 (m, 1H, H_5), 7.78 – 7.72 (m, 1H, H_2), 7.40 – 7.32 (m, 2H, H_2, H_4), 6.27 (s, 1H, H_8), 4.19 (q, *J* = 7.0 Hz, 2H, H_9), 1.51 (t, *J* = 7.0 Hz, 3H, H_{10}).

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 151.2 (C_7), 137.8 (C_{Ar}), 132.5 (C_{Ar}), 125.3 ($C_{3/4}$), 123.8 ($C_{3/4}$), 122.9 (C_2), 121.1 (C_5), 95.9 (C_8), 65.7 (C_9), 14.9 (C_{10}).

IR (film) ν_{max}/cm^{-1} = 2981, 2927, 1366, 702.

HRMS (ESI^+): calculated for $C_{10}H_{11}OS^+$, $[M+H]^+$ = 179.0525; *m/z* found = 179.0522, Δ = -1.52 ppm.

***N*-methyl-*N*-phenylbenzo[b]thiophen-3-amine 432a and *N*-methyl-*N*-phenylbenzo[b]thiophen-2-amine 432b:**



2-Acetamido-5-(benzo[b]thiophen-3-yl)-4,6,8-trimethyl-5*H*-dibenzo[b,d]furan-5-ium tetrafluoroborate **373** (146 mg, 0.30 mmol, 1 eq.) was dissolved in MeCN (6 mL) in a vial. *N*-methyl aniline (162 μL, 6.00 mmol, 20 eq.) and NaO^{t}Bu (144 mg, 1.50 mmol, 5 eq.) were sequentially added, and the reaction mixture stirred (600 rpm) at r.t. for 16 h. Once complete, the reaction mixture was filtered through Celite® and eluted with CH_2Cl_2 (4 × 2 mL/mmol) and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (pentane, 2:98, R_f = 0.2) to give an inseparable mixture of the title compounds as a yellow oil (13 mg, 18%).

*The regioisomers **432a** and **432b** were isolated as an inseparable mixture (**432a:432b**; 5.5:1). NMR integrals are normalised to $H_{2'}$ is equal to 1 proton.*

^{1}H NMR (600 MHz, $CDCl_3$) δ_H = 7.84 (dt, *J* = 8.1, 0.9 Hz, 6H, $H_{4/7}$), 7.60 (dp, *J* = 8.0, 0.7 Hz, 1H, $H_{4'/7'}$), 7.52 (dt, *J* = 8.0, 1.0 Hz, 1H, $H_{4'/7'}$), 7.42 (dt, *J* = 8.1, 0.9 Hz, 6H, $H_{4/7}$), 7.38 – 7.30 (m, 8H, $H_{5/6}$, $H_{12'}$), 7.28 – 7.24 (m, 10H, $H_{5/6}$), 7.23 (dt, *J* = 7.8, 1.1 Hz, 2H, $H_{11'}$), 7.22 – 7.18 (m, 12H, H_{11}), 7.17 – 7.14 (m, 1H, $H_{5'/6'}$), 7.14 (s, 5H, H_1), 7.08 (tt, *J* = 7.3, 1.2 Hz, 1H, $H_{5'/6'}$), 6.83 (tt, *J* = 7.3, 1.1 Hz, 6H, H_{13}), 6.80 (m, 12H, H_{12}), 6.54 (s, 1H, $H_{2'}$), 3.43 (s, 3H, $H_{9'}$), 3.41 (s, 18H, H_9). Unable to assign $H_{13'}$.

^{13}C NMR (151 MHz, $CDCl_3$) δ_C = 154.3 ($C_{Ar'}$), 149.4 (C_{Ar}), 148.5 ($C_{Ar'}$), 142.1 (C_{Ar}), 140.0 ($C_{Ar'}$), 139.2 (C_{Ar}), 135.5 (C_{Ar}), 134.4 ($C_{Ar'}$), 129.4 ($C_{12'}$), 129.1 (C_{12}), 124.8 ($C_{5/6}$), 124.6 ($C_{13'}$), 124.1 ($C_{5/6}$), 123.4 ($C_{4/7}$), 123.2 ($C_{5'/6'}$), 122.6 ($C_{4/7}$), 122.4 ($C_{5'/6'}$), 121.9 ($C_{4'/7'}$), 121.6 ($C_{4'/7'}$), 120.9 ($C_{11'}$), 119.0 (C_{13}), 117.9 (C_1), 115.7 (C_{11}), 107.0 ($C_{2'}$), 42.2 ($C_{9'}$), 40.9 (C_9).

IR (film) ν_{max}/cm^{-1} = 2954, 1738, 1597, 1500, 1361, 763.

HRMS (ESI^+): calculated for $C_{15}H_{14}NS^+$, $[M+H]^+$ = 240.0842; *m/z* found = 240.0841, Δ = -0.06 ppm.

NMR data in accordance with literature for **432a**.[176]

4.4 Inversion Barrier Measurements

4.4.1 Equilibration of 11,13-Dimethyl-4,5-dihydrobenzo[*b*]benzo[6,7]oxepino[3,2,1-*hi*]benzofuran-10-ium, [*P*, (*R*)$_O$]-bis-(*R*)-BINOL borate, 462:

The barrier to diastereomerisation of **462** is quoted as an average of three experiments:

Experiment 1:

Oxonium salt **462** (8.8 mg, 0.01 mmol) at 94:6 d.r. was dissolved in CD_2Cl_2 (0.45 mL) in an NMR tube fitted with a J. Young valve. CH_2Br_2 (0.005 mmol) in CD_2Cl_2 (0.05 mL) was added as an internal standard and the diastereomeric ratio was monitored by ^{1}H NMR using a Bruker AVII 500 MHz spectrometer. The sample was maintained at 298 K for the duration of the experiment (using a Cambridge Reactor Design Polar Bear Plus). ^{1}H NMR spectra with extended relaxation times were recorded at 24 h intervals.

Experiment 2:

Oxonium salt **462** (8.8 mg, 0.01 mmol) at 97:3 d.r. was dissolved in CD_2Cl_2 (0.5 mL) in an NMR tube fitted with a J. Young valve under Argon. 1,2,4,5-Tetramethylbenzene (0.005 mmol) in CD_2Cl_2 (0.01 mL) was added as an internal standard and the diastereomeric ratio was monitored by ^{1}H NMR using a Bruker AVII 400 MHz spectrometer. The sample was maintained at 298 K for the duration of the experiment (using a Cambridge Reactor Design Polar Bear Plus).

Experiment 3:

Oxonium salt **462** (8.8 mg, 0.01 mmol) at 93:7 d.r. was dissolved in CD_2Cl_2 (0.5 mL) in an NMR tube fitted with a J. Young valve under Argon. 1,2,4,5-Tetramethylbenzene (0.005 mmol) in CD_2Cl_2 (0.01 mL) was added as an internal standard and the diastereomeric ratio was monitored

by ^{1}H NMR using a Bruker AVII 500 MHz spectrometer. The sample was maintained at 298 K for the duration of the experiment (using a Cambridge Reactor Design Polar Bear Plus).

To prepare the internal standard stock solution **Experiment 1**:

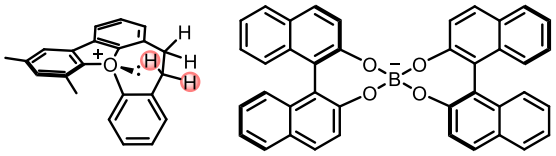
(1) CH_2Br_2 (10.5 µl, 26.1 mg, 0.15 mmol) was dissolved in CD_2Cl_2 (0.3 mL).

(2) 0.1 mL of (1) (0.05 mmol CH_2Br_2) was diluted with CD_2Cl_2 (0.4 mL).

To prepare the internal standard stock solution **Experiment 2 and 3**:

1,2,4,5-tetramethylbenzene (67.1 mg, 0.5 mmol) was dissolved in CD_2Cl_2 (1 mL).

Integration of the signals at 3.70 and 3.44 ppm relative to the internal standard were used to calculate the ratio. The signals correspond to one the H residues labelled in **Scheme 121** in the major and minor diastereoisomeric salt pair respectively,



462

Scheme 121: 11,13-Dimethyl-4,5-dihydrobenzo[*b*]benzo[6,7]oxepino[3,2,1-*hi*]benzofuran-10-ium, [*P*, $(R)_O$]-bis-(*R*)-BINOL borate **462**.

Experiment 1

time (s)	major (3.70 ppm)	minor (3.44 ppm)	sum	dr	de	$\ln(de_0/de_t)$
0	2.06	0.13	2.19	94.06	88.13	0
86400	2.04	0.15	2.19	93.15	86.30	0.020943174
172800	2.02	0.17	2.19	92.24	84.47	0.042334364
259200	2	0.19	2.19	91.32	82.65	0.064193158
354600	1.96	0.22	2.18	89.91	79.82	0.099058223
432000	1.94	0.24	2.18	88.99	77.98	0.122315085
518400	1.9	0.27	2.17	87.56	75.12	0.159765612
604800	1.87	0.29	2.16	86.57	73.15	0.186301834
				k_{rac}	3.12697E-07	s^{-1}

Experiment 2

time (s)	major (3.70 ppm)	minor (3.44 ppm)	sum	dr	de	$\ln(de_o/de_t)$
0	1.12	0.03	1.15	97.39	94.78	0
87480	1.17	0.06	1.23	95.12	90.24	0.049069908
168720	1.12	0.06	1.18	94.92	89.83	0.053661284
264720	1.02	0.08	1.1	92.73	85.45	0.103601337
331980	1.01	0.08	1.09	92.66	85.32	0.105164143
419280	1	0.1	1.1	90.91	81.82	0.147086449
530220	0.99	0.12	1.11	89.19	78.38	0.190037837
				k_{rac}	3.39823E-07	s^{-1}

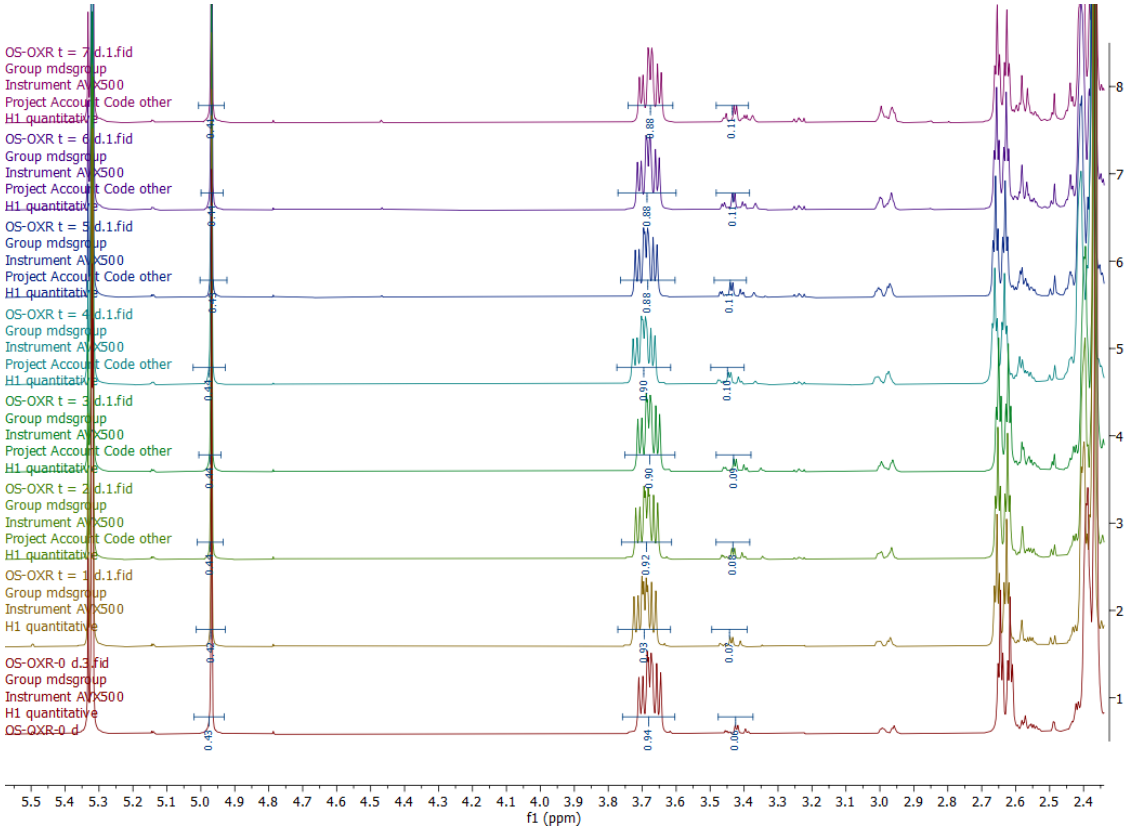
Experiment 3

time (s)	major (3.70 ppm)	minor (3.44 ppm)	sum	dr	de	$\ln(de_0/de_t)$
0	0.83	0.06	0.89	93.26	86.52	0
121560	0.86	0.07	0.93	92.47	84.95	0.018320693
192540	0.83	0.08	0.91	91.21	82.42	0.048540445
261540	0.84	0.09	0.93	90.32	80.65	0.070280432
347820	0.74	0.09	0.83	89.16	78.31	0.09962239
434220	0.77	0.1	0.87	88.51	77.01	0.116384551
520440	0.74	0.11	0.85	87.06	74.12	0.154685582
				k_{rac}	3.01899E-07	s^{-1}

Scheme 122: Integration of the peaks at δ = 3.70 ppm and δ = 3.44 ppm in the ^{1}H NMR spectrum of **462** over time for experiments 1, 2 and 3, and calculated dr, de and $\ln(de_0/de_t)$.

	Experiment 1	Experiment 2	Experiment 3	Unit
K_{eq}	1.02	1.02	1.02	
$k_{a\text{-}eq}$	3.13E-07	3.40E-07	3.02E-07	s^{-1}
$k_{a\text{-}b}$	1.58E-07	1.72E-07	1.52E-07	s^{-1}
Free energy	111786.8697	111584.6757	111877.8762	*J*
	26.71770309	26.66937755	26.73945415	*Kcal mol*$^{-1}$
Average free energy		26.70884493		*Kcal mol*$^{-1}$
Half-life	2213160.402	2039728.443	2295960.858	S
	614.7667784	566.5912342	637.7669051	H
	25.61528243	23.60796809	26.57362105	D
K_{eq}	1.02	1.02	1.02	s^{-1}
$k_{a\text{-}eq}$	3.13E-07	3.40E-07	3.02E-07	s^{-1}
$k_{b\text{-}a}$	1.55E-07	1.68E-07	1.49E-07	s^{-1}
Free energy	111835.9351	111633.7411	111926.9415	*J*
	26.72943	26.68110446	26.75118106	*Kcal mol*$^{-1}$
Average free energy		26.72057184		*Kcal mol*$^{-1}$
Half-life	2213160.402	2039728.443	2295960.858	s
	614.7667784	566.5912342	637.7669051	h
	25.61528243	23.60796809	26.57362105	d

Scheme 123: Free energy and half-life calculated from the rate constants, $k_{A\text{-}to\text{-}B}$ and $k_{B\text{-}to\text{-}A}$, and the equilibrium constant, K_{eq} for **462**.



Scheme 124: ^{1}H NMR spectra to show the thermal equilibration at 298K of enriched diastereomer **462** over 7 days (starting dr 94:6).

4.4.2 Enantiomeric ratio erosion study of 11,13-dimethyl-4,5-dihydrobenzo[b]benzo[6,7]oxepino[3,2,1-hi]benzofuran-10-ium hexafluorophosphate, enantioenriched-[*M*, (*S*)$_O$]-464:**

Three samples were prepared from the same enantioenriched material **464** at 97:3 e.r. and were dissolved in CH_2Cl_2 in a screw cap vial. The samples were maintained at 298 K for the duration of

** The absolute configuration of the major enantiomer in this 97:3 ratio was correlated with the known absolute configuration of **462** separated in the resolution process. This was achieved by comparing the HPLC retention times (under the above conditions: MeOH/H_2O, 10:1, 100mM $NaPF_6$) of the major/minor enantiomers of **460** with that of a sample of highly diastereoenriched **462** under these conditions. We assume that complete counterion metathesis to generate enantioenriched **464** and **465** occurs under these conditions.

the experiment (using a Cambridge Reactor Design Polar Bear Plus). Aliquots were taken from each sample over 5 days and dissolved in MeOH. The e.r. was monitored by HPLC.

		e.e.			
	Time (h)	**S1**	**S2**	**S3**	**Average**
S=0	0	92.09	93.11	93.03	92.74
S=1	12.25	91.43	91.65	90.7	91.26
S=2	39.45	86.72	87.52	87.31	87.18
S=3	61.25	82.67	85.46	85.27	84.47
S=4	85.4	78.7	82.8	82.58	81.36
S=5	113.5	73.45	80.14	78.38	77.32

Scheme 125: Measured erosion of e.r. of enantioenriched **464** over time (3 samples).

	Average ln(ee(0)/ee(t))	**Standard deviation**	**Standard error (SE)**
S=0	0	0.567215	0.327481976
S=1	0.016123246	0.497293	0.287112057
S=2	0.06182264	0.414769	0.239467001
S=3	0.093478842	1.558856	0.900006173
S=4	0.130952069	2.306252	1.331515427
S=5	0.181840057	3.467915	2.002201566
k_{rac}	4.4259E-07	s^{-1}	
k_{ent}	2.21295E-07	s^{-1}	
Free energy	111.0	$kJ\ mol^{-1}$	
	26.5	$Kcal\ mol^{-1}$	
Half life	1566115.667	s	
	435.0321296	h	
	18.12633873	d	

Scheme 126: Calculated $\ln(de_0/d_t)$ k_{rac}, k_{ent}, standard errors, free energy and half life from the measured e.r. of **462**.

5 Bibliography

1. Sam Chan, H. S., Nguyen, Q. N. N., Paton, R. S. & Burton, J. W. Synthesis, Characterization, and Reactivity of Complex Tricyclic Oxonium Ions, Proposed Intermediates in Natural Product Biosynthesis. *J. Am. Chem. Soc.* **141**, 15951–15962 (2019).
2. Meerwein, V. H., Battenberg, E., Gold, H. & Pfei, E. Über tertiäre oxoniumsalze, II. *J. Prakt. Chem.* **257**, 57–156 (1939).
3. Meerwein, H., Hinz, G., Hofmann, P., Kroningl, E. & Pfeil, E. Über Tertiäre Oxoniumsalze, I. *J. Prakt. Chem.* **147**, 257–285 (1937).
4. Meerwein, H. Triethyloxonium Fluoborate. *Org. Synth.* **46**, 113 (1966).
5. Nesmeyanov, A. N. & Thick, T. P. Triphenyloxonium salts. *Dokl. Akad. Nauk SSSR* **117**, 626–628 (1957).
6. Nesmeyanov, A. N., Makarova, L. , G. & Tolstaya, T. P. HETEROLYTlCDECOMPOSlTlONOFONIUMCOMPOUNDS (DIPHENYL HALOGENONIUM AND TRIPHENYLOXONIUM SALTS). *Tetrahedron* **1**, 145–157 (1957).
7. Nesmeyanov, A. N. & Tolstaya, T. P. SALTS OF o,o'-DIPHENYLENEPHENYLOXONIUM ION. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **133**, 620–623 (1959).
8. Hellwinkel, D. & Seifert, H. Ringschluβreaktionen yon 2'-heterosubstituierten Biphenyl-2-diazonium-Salzen zu (spiro)cyclischen Tetraarylammonium-Salzen und Tribenz[b.d.f]azepinen. *Chem. Ber.* **105**, 880–906 (1972).
9. Stoermer, R. & Kahlert, B. Ueber das 1- und 2-Brom-cumaron. *Ber. Dtsch. Chem. Ges.* **35**, 1633–1640 (1902).
10. Roberts, J. D., Simmons, H. E., Carlsmith, L. A. & Wheaton Vaughan, C. REARRANGEMENT IN THE REACTION OF CHLORO- BENZENE-l-C14 WITH POTASSIUM AMIDE. *J. Am. Chem. Soc.* **75**, 3290–3291 (1953).
11. Reinecke, M. G. Hetarynes. *Tetrahedron* **38**, 427–498 (1982).
12. Kauffmann, T. The Hetarynes. *Angew. Chem. Int. Ed.* **4**, 543–557 (1965).
13. Kauffmann, T. & Wirthweint, R. Progress in the Hetaryne Field. *Angew. Chem. Int. Ed.* **10**, 20–33 (1971).
14. Stiles, M. & Miller, R. G. Decomposition of benzenediazonium-2-carboxylate. *J. Am. Chem. Soc.* **82**, 3802 (1960).
15. Campbell, C. D. & Rees, C. W. Reactive Intermediates. Part 1. Synthesis and Oxidation of I- and 2-Aminobenzotriazole. *J. Am. Chem. Soc.* **5**, 742–747 (1969).
16. Himeshima, Y., Sonoda, T. & Kobayashi, H. Fluoride-induced 1,2-elimination of o-trimethylsilylphenyl triflate to benzyne under mild conditions. *Chem. Lett.* **121**, 1211–1214 (1983).
17. Peña, D., Cobas, A., Pérez, D. & Guitián, E. An efficient procedure for the synthesis of ortho-trialkylsilylaryl triflates: Easy access to precursors of functionalized arynes. *Synthesis* **10**, 1454–1458 (2002).

18. Hoye, T. R., Baire, B., Niu, D., Willoughby, P. H. & Woods, B. P. The hexadehydro-Diels-Alder reaction. *Nature* **490**, 208–211 (2012).

19. Bradley, A. Z. & Johnson, R. P. Thermolysis of 1 , 3 , 8-Nonatriyne : Evidence for Intramolecular [2 + 4] Cycloaromatization to a Benzyne Intermediate. *J. Org. Chem.* **119**, 9917–9918 (1997).

20. Miyawaki, K., Suzuki, R., Kawano, T. & Ueda, I. Cycloaromatization of a Non-Conjugated Polyenyne System: Synthesis of 5H-Benzo[d]fluoreno[3,2-b]pyrans via Diradicals Denerated from 1-[2-{4-(2-Alkoxymethylphenyl)butan-1,3-dinyl}]phenylpentan-2,4-diyn -1-ols and Trapping Evidence for the 1,2-Didehydroben. *Tetrahedron Lett.* **38**, 3943–3946 (1997).

21. Cant, A. A., Roberts, L. & Greaney, M. F. Generation of benzyne from benzoic acid using C–H activation. *Chem. Comm.* **46**, 8671 (2010).

22. Lanzi, M., Dherbassy, Q. & Wencel-Delord, J. Cyclic Diaryl λ^3-Bromanes as Original Aryne Precursors. *Angew. Chem. Int. Ed.* **60**, 14852–14857 (2021).

23. Lanzi, M., Ali Abdine, R. A., De Abreu, M. & Wencel-Delord, J. Cyclic Diaryl λ^3-Bromanes: A Rapid Access to Molecular Complexity via Cycloaddition Reactions. *Org. Lett.* **23**, 9047–9052 (2021).

24. Lanzi, M., Rogge, T., Truong, T. S., Houk, K. N. & Wencel-Delord, J. Cyclic Diaryl λ^3-Chloranes: Reagents and Their C-C and C-O Couplings with Phenols via Aryne Intermediates. *J. Am. Chem. Soc.* **145**, 345–358 (2023).

25. Rocq, C., Denis, M. & Canesi, S. Iodanes as multi-tools for the total synthesis of complex natural products. *Chem. Comm.* **59**, 6495–6508 (2023).

26. Yuan, H., Yin, W., Hu, J. & Li, Y. 3-Sulfonyloxyaryl(Mesityl)Iodonium Triflates As 1,2-Benzdiyne Precursors With Activation Via Ortho-Deprotonative Elimination Strategy. *Nat. Commun.* **14**, (2023).

27. Li, X., Chen, H., Liu, X., Wang, L. & Han, J. Meta-OTf-Substituted Diaryliodonium Salts Enabled Diels-Alder Cycloadditions of Furans via Aryne Intermediates. *ChemistrySelect* **8**, 10–14 (2023).

28. Nilova, A., Metze, B. & Stuart, D. R. Aryl(TMP)iodonium Tosylate Reagents as a Strategic Entry Point to Diverse Aryl Intermediates: Selective Access to Arynes. *Org. Lett.* **23**, 4813–4817 (2021).

29. Sundalam, S. K., Nilova, A., Seidl, T. L. & Stuart, D. R. A Selective C−H Deprotonation Strategy to Access Functionalized Arynes by Using Hypervalent Iodine. *Angew. Chem.* **128**, 8571–8574 (2016).

30. Metze, B., Roberts, R. A., Nilova, A. & Stuart, D. R. An efficient and chemoselective method to generate arynes. *Chem. Sci.* **47**, 13885–13892 (2023).

31. Hellwinkel, D. & Seifert, H. Zur Frage des pentakoordinierten Stickstoffs: Reaktionen yon (spiro)cyclischen Tetraarylammonium-Salzen mit Nucleophilen. *Ber. Dtsch. Chem. Ges.* **762**, 29–54 (1972).

32. Tolstaya, T. P., Tsariev, D. A. & Luzikov, Y. N. Reaction of Triaryloxonium Salts with Bases via Dehydroarenes. *Tetrahedron Lett.* **38**, 4457-4457 (1997).

33. Smith, O. *et al.* Harnessing triaryloxonium ions for aryne generation. *Nat. Synth.* **3**, 58–66 (2024).

34. Ishiyama, T., Murata, M. & Miyaura, N. Palladium(0)-Catalyzed Cross-Coupling Reaction of Alkoxydiboron with Haloarenes: A Direct Procedure for Arylboronic Esters. *J. Org. Chem.* **60**, 7508–7510 (1995).

35. Cesar Castro Palomino Laria, J., Marti Clauzel, L., Zorzano Olarte, A., Garcia Vicente, S. & Mian, A. Thiocarbonates as Anti-Inflammatory and Antioxidant Compounds Useful For Treating Metabolic Disorders. AU2010224866B2, (2012).

36. Lu, X. *et al.* A new class of 1,3,5-triazine-based selective estrogen receptor degraders (SERDs): Lead optimization, molecular docking and dynamic simulation. *Bioorg. Chem.* **97**, 103666 (2020).

37. Hoyos, L. J. *et al.* Sulfur poisoning and regeneration of palladium based catalysts. *J. Chem. Soc.* **88**, 3367–3373 (1992).

38. Hall, C., Henderson, J. L., Ernouf, G. & Greaney, M. F. Tandem thia-Fries rearrangement – cyclisation of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate benzyne precursors. *Chem. Comm.* **49**, 7602–7604 (2013).

39. Nakayama, J. & Akimoto, K. Reactions of Benzyne With Sulfur Compounds. *Sulfur reports* **16**, 61–111 (1994).

40. Bhojgude, S. S., Kaicharla, T., Bhunia, A. & Biju, A. T. A Practical and General Diels-Alder Reaction of Pentafulvenes with Arynes. *Org. Lett.* **14**, 4098–4101 (2012).

41. Lu, C., Dubrovskiy, A. V. & Larock, R. C. Synthesis of benzisoxazolines by the coupling of arynes with nitrones. *J. Org. Chem.* **77**, 2279–2284 (2012).

42. Yedulla, V. R., Pradhan, P., Yang, L. & Lakshman, M. K. Cycloaddition of Arynes and Cyclic Enol Ethers as a Platform for Access to Stereochemically Defined 1,2-Disubstituted Benzocyclobutenes. *Eur, J. Org. Chem.* **2015**, 750–764 (2015).

43. Reynolds, G. A. The Reaction of Organic Azides with Benzyne. *J. Org. Chem.* **29**, 3733–3734 (1964).

44. Li, P. F., Han, Y. & Chen, C. F. Synthesis and structures of triptycene-derived Tröger's base molecular clips. *Chin. Chem. Lett.* **26**, 839–842 (2015).

45. Picazo, E. *et al.* Arynes and Cyclic Alkynes as Synthetic Building Blocks for Stereodefined Quaternary Centers. *J. Am. Chem. Soc.* **140**, 7605–7610 (2018).

46. Karmakar, R., Mamidipalli, P., Young Yun, S. & Lee, D. Alder-Ene Reactions of Arynes. *Org. Lett.* **15**, 1938–1941 (2013).

47. Criado, A. *et al.* Stereoselective tandem cascade furan cycloadditions. *J. Org. Chem.* **78**, 12637–12649 (2013).

48. Yoshida, H., Shirakawa, E., Honda, Y. & Hiyama, T. Addition of ureas to arynes: Straightforward synthesis of benzodiazepine and benzodiazepine derivatives. *Angew. Chem. Int. Ed.* **41**, 3247–3249 (2002).

49. Goetz, A. E. *et al.* An efficient computational model to predict the synthetic utility of heterocyclic arynes. *Angew. Chem. Int. Ed.* **51**, 2758–2762 (2012).

50. Huisgen, R. & Sauer, J. Nucleophile aromatische Substitutionen über Arine. *Angew. Chem.* **72**, 91–108 (1960).

51. Sauer, J. & Huisgen, R. Nucleophile aromatische Substitutionen mit additivem Chemismus. *Angew. Chem.* **72**, 294–315 (1960).

52. Bordwell, F. G., Lampert, B. B. & McKellin, W. H. Thianaphthene Chemistry. III. The Reaction of 2,3-Dibromo-2,3-dihydro- and 2-Bromo-thianaphthene-1 -dioxides with Secondary Amines. *J. Am. Chem. Soc.* **71**, 1702–1705 (1949).

53. Nam, H. H. & Leroi, G. E. First Direct Observation of Pyridyne: Matrix Infrared Study of the Photolysis Products of 3,4-Pyridine Dicarboxylic Anhydride. *J. Am. Chem. Soc.* **110**, 4096–4097 (1988).

54. Chapman, O. L., Chang, C. C., Kolc, J., Rosenquist, N. R. & Tomioko, H. Photochemical method for the introduction of strained multiple bonds. Benzyne C≡C stretch. *J. Am. Chem. Soc.* **97**, 6586–6588 (1975).

55. Ye, X. S., Li, W. K., & Wong, H. N. C. 3, 4-Didehydrothiophene: Generation, Trapping, Reactions, and *Ab Initio* Study. *J. Am. Chem. Soc.* **118**, 2511–2512 (1996).

56. Liu, J. *et al.* Generation and Trapping Reactions of 1-tert-Butoxycarbonyl-3,4-didehydro-1H-pyrrole. *J. Org. Chem.* **64**, 1630–1634 (1999).

57. Wu, Y.-M., Yang, X.-P., Xue, F., Mak, T. C. W. & Wong, H. N. C. The Attempted Generation of 3,4-Didehydrofuran. *J. Chin. Chem. Soc.* **46**, 463–468 (1999).

58. Cordell, F. R. & Boggs, J. E. STRUCTURE AND DEGREE OF AROMATIC CHARACTER IN FURAN, PYRROLE, AND THIOPHENE. *J. Mol. Struct.* **85**, 163–178 (1981).

59. Wittig, Vgl. G. & Ebel, H. F. Uber das intermeditire Auftreten ber neue Cyano-Komplexe von 2.3-Dehydrothiophen. *Angew. Chem.* **72**, 492 (1961).

60. Wittig, G. & Rings, M. Zum Problem des intermediären Auftretens von Dehydrothiophen. *Justus Liebigs Ann. Chem.* **719**, 127–144 (1968).

61. Reinecke, M. G. & Newson, J. G. 2,3-Thiophyne. *J. Am. Chem. Soc.* **98**, 3021–3022 (1976).

62. Reinecke, M. G., Newson, J. G. & Chen, L.-J. Thermolysis of Thiophenedicarboxylic Acid Anhydrides as a Route to Five-Membered Hetarynes. *J. Am. Chem. Soc.* **103**, 2760–2769 (1981).

63. Pozo, I., Cobas, A., Peña, D., Guitián, E. & Pérez, D. Toward 2-Thiophyne: Ketocarbene versus Hetaryne Intermediates from 2-(Trimethylsilyl)thiophen-3-yl Triflate. *Org. Lett.* **23**, 7376–7380 (2021).

64. Van Der Plas, H. C., Smit, P. & Koudijs, A. HETABYNES XVI (1,2) Evidence for the occurrence of 4-t-butyl-5,6-pyrimidyne in the amination of both 6-bromo- and 5-bromo-4-t-butylpyrimidine. *Tetrahedron Lett.* **9**, 9–13 (1968).

65. Tiblemans, M. *et al.* REACTIVITY OF 2-t-BUTYL-4,5DIDEHYDROPYRIMIDINE AND ELECTRONIC STRUCTURE OF THEPARENTHETARYNE. *Tetrahedron* **48**, 10575–10586 (1992).

66. Medina, J. M., Jackl, M. K., Susick, R. B. & Garg, N. K. Synthetic studies pertaining to the 2,3-pyridyne and 4,5-pyrimidyne. *Tetrahedron* **72**, 3629–3634 (2016).

67. Kauffmann, T. & Boettcher, F.-P. 3.4-Dehydropyridin aus Pyridin-diazonium-(3)-carboxylat-(4)bzw. 4-Chlor-3-brom-pyridin. *Chem. Ber.* **95**, 821–1067 (1962).

68. Zoltewicz, J. A. & Smith, C. L. Mechanism of pyridyne formation from halopyridines. *Tetrahedron* **25**, 4331–4337 (1969).

69. Fleet, G. W. J. & Flemming, I. Preparation of some N-Aminotriazolo-pyridines and -quinolines, their Oxidation with Lead Tetra-acetate, and the Trapping of the Resulting

Pyridynes and Quinolynes with Tetraphenylcyclopentadienone (Tetracyclone). *J. Am. Chem. Soc.* 1758–1763 (1969).

70. Furukawa, N., Shibutani, T. & Fujihara, H. A NEW SOURCE FOR GENERATION OF BENZYNE AND PYRIDYNE: REACTIONS OF O-HALOPHENYL (OR 3-BROMO-4-PYRIDYL) PHENYL SULFOXIDES WITH GRIGNARD REAGENTS. *Tetrahedron Lett.* **28**, 2727–2730 (1987).

71. TSUKAZAKI, M. & SNIECKUS, V. Synthetic connection to the directed ortho metalation reaction. 3,4-Pyridynes from 4-trialkylsilyl-3-pyridyl triflates. *Heterocycles* **33**, 533–536 (1992).

72. Martens, R. J. & den Hertog, H. J. Indications for the occurrence of 2,3-pyridyne as an intermediate. *Tetrahedron Lett.* **3**, 643–645 (1962).

73. Walters, M. A. & Shay, J. J. 2,3-Pyridyne formation by fluoride induced desilylation-elimination. *Synth. Commun.* **27**, 3573–3579 (1997).

74. Several silyltriflate hetaryne precursors are available from Aldrich Chemical Co., Inc. The precursors and their product numbers are: 3,4-pyridyne precursor 34: L511633; bromopyridine precursor 38: L511641; 2,3-pyridyne precursor 45: L511668; 60 (R = H).

75. Julia, M., Huang, Y. & Igolen, J. Synthesis of 4-or 5-aminoindoles by arsenic substitution. *C.R. Acad. Sci, Ser. C* **265**, 110–112 (1967).

76. Buszek, K. R., Luo, D., Kondrashov, M., Brown, N. & VanderVelde, D. Indole-derived arynes and their Diels-Alder reactivity with furans. *Org. Lett.* **9**, 4135–4137 (2007).

77. Julia, M., Le Goffic, F., Igolen, J. & Baillarge, M. UNE NOUVELLE SYNTHESE DE L'ACIDE LYSERGIQUE. *Tetrahedron Lett.* **10**, 1569–1571 (1969).

78. Buszek, K. R., Brown, N. & Luo, D. Concise Total Synthesis of (±)- cis -Trikentrin A and (±)-Herbindole A via Intermolecular Indole Aryne Cycloaddition. *Org. Lett.* **11**, 201–204 (2009).

79. Brown, N., Luo, D., Decapo, J. A. & Buszek, K. R. New synthesis of (±)-cis-trikentrin A via tandem indole aryne cycloaddition/Negishi reaction. Applications to library development. *Tetrahedron Lett.* **50**, 7113–7115 (2009).

80. Huters, A. D., Quasdorf, K. W., Styduhar, E. D. & Garg, N. K. Total synthesis of (-)- N -methylwelwitindolinone C isothiocyanate. *J. Am. Chem. Soc.* **133**, 15797–15799 (2011).

81. Quasdorf, K. W., Huters, A. D., Lodewyk, M. W., Tantillo, D. J. & Garg, N. K. Total synthesis of oxidized welwitindolinones and (-)- N -methylwelwitindolinone C isonitrile. *J. Am. Chem. Soc.* **134**, 1396–1399 (2012).

82. Styduhar, E. D., Huters, A. D., Weires, N. A. & Garg, N. K. Enantiospecific total synthesis of N-methylwelwitindolinone D isonitrile. *Angew. Chem. Int. Ed.* **52**, 12422–12425 (2013).

83. Goetz, A. E., Silberstein, A. L., Corsello, M. A. & Garg, N. K. Concise enantiospecific total synthesis of tubingensin A. *J. Am. Chem. Soc.* **136**, 3036–3039 (2014).

84. Corsello, M. A., Kim, J. & Garg, N. K. Total synthesis of (-)-tubingensin B enabled by the strategic use of an aryne cyclization. *Nat. Chem.* **9**, 944–949 (2017).

85. Shah, T. K., Medina, J. M. & Garg, N. K. Expanding the Strained Alkyne Toolbox: Generation and Utility of Oxygen-Containing Strained Alkynes. *J. Am. Chem. Soc.* **138**, 4948–4954 (2016).

86. Picazo, E. *et al.* Arynes and Cyclic Alkynes as Synthetic Building Blocks for Stereodefined Quaternary Centers. *J. Am. Chem. Soc.* **140**, 7605–7610 (2018).

87. Kabir, E. & Uzzaman, M. A review on biological and medicinal impact of heterocyclic compounds. *Results Chem.* **4**, 100606 (2022).

88. Mortzfeld, F. B., Hashem, C., Vranková, K., Winkler, M. & Rudroff, F. Pyrazines: Synthesis and Industrial Application of these Valuable Flavor and Fragrance Compounds. *Biotechnol. J.* **15**, 1–7 (2020).

89. Walsh, K., Sneddon, H. F. & Moody, C. J. An efficient method for the synthesis of heteroaryl C-O bonds in the absence of added transition metal catalysts. *RSC Adv.* **4**, 28072–28077 (2014).

90. La Regina, G. *et al.* Discovery of 1,1'-Biphenyl-4-sulfonamides as a New Class of Potent and Selective Carbonic Anhydrase XIV Inhibitors. *J. Med. Chem.* **58**, 8564–8572 (2015).

91. Sirakanyan, S. N. *et al.* Synthesis and antimicrobial activity of new amino derivatives of pyrano[4",3":4',5']pyrido[3',2':4,5]thieno[3,2-d]pyrimidine. *An. Acad. Bras. Cienc.* **90**, 1043–1057 (2018).

92. Mahapatra, A., Prasad, T. & Sharma, T. Pyrimidine: A Review on Anticancer Activity with Key Emphasis on SAR. *Future J. Pharm. Sci.* **7**, 123 (2021).

93. Romeo, R. *et al.* Pyrimidine 2,4-Diones in the design of new HIV RT inhibitors. *Molecules* **24**, 1–14 (2019).

94. Awad, S. M., Zohny, Y. M., Ali, S. A., Mahgoub, S. & Said, A. M. Design, synthesis, molecular modeling, and biological evaluation of novel thiouracil derivatives as potential antithyroid agents. *Molecules* **23**, (2018).

95. Parsy, C. C., Alexandre, F.-R., Convard, T. & Surleraux, D. Macrocyclic Serine Protease Inhibitors, Pharmaceutical Compositions Thereof, and Their Use for Treating HCV Infections. WO2012109398 (2016).

96. Zhou, B., Taylor, B. & Kornau, K. Synthesis of unsymmetrical 4,6-diarylpyrimidines. *Tetrahedron Lett.* **46**, 3977–3979 (2005).

97. Vianna, D. R. *et al.* Selective cytotoxicity and apoptosis induction in glioma cell lines by 5-oxygenated-6,7-methylenedioxycoumarins from Pterocaulon species. *Eur. J. Med. Chem.* **57**, 268–274 (2012).

98. Kostova, I., Raleva, S., Genova, P. & Argirova, R. Structure-activity relationships of synthetic coumarins as HIV-1 inhibitors. *Bioinorg. Chem. Appl.* **2006**, 1–9 (2006).

99. Kresge, N., Simoni, R. D. & Hill, R. L. Hemorrhagic Sweet Clover Disease, Dicumarol, and Warfarin: the Work of Karl Paul Link. *J. Bio. Chem.* **280**, e6–e7 (2005).

100. Musicki, B. *et al.* Improved antibacterial activities of coumarin antibiotics bearing 5',5'-dialkylnoviose: Biological activity of RU79115. *Bioorg. Med. Chem. Lett.* **10**, 1695–1699 (2000).

101. Tosun, A., Akkol, E. K. & Yeşilada, E. Anti-inflammatory and antinociceptive activity of coumarins from Seseli gummiferum subsp. corymbosum (Apiaceae). *Z. Naturforsch C J. Biosci.* **64**, 56–62 (2009).

102. Nolan, M. T., Pardo, L. M., Prendergast, A. M. & McGlacken, G. P. Intramolecular Direct Arylation of 3-Halo-2-pyrones and 2-Coumarins. *J. Org. Chem.* **80**, 10904–10913 (2015).

103. Balalas, T., Abdul-Sada, A., Hadjipavlou-Litina, D. J. & Litinas, K. E. Pd-Catalyzed Efficient Synthesis of Azacoumestans Via Intramolecular Cross Coupling of 4-(Arylamino)coumarins in the Presence of Copper Acetate under Microwaves1. *Synthesis* **49**, 2575–2583 (2017).

104. Gašpar, J., Némethová, Z., Janeková, H., Gáplovský, A. & Stankovičová, H. Amino acid-sensitive reagents with coumarin moiety for latent prints examination. *Monatsh. Chem.* **149**, 1787–1794 (2018).

105. Kim, A. *et al.* Organocatalytic Atroposelective Synthesis of Isoquinolines via Dynamic Kinetic Resolution. *Org. Lett.* **24**, 1077–1082 (2022).

106. Atkins, P. & de Paula, J. The rates of chemical reactions. in *Atkins' Physical chemistry* 791–826 (W.H. Freeman, 2006).

107. Balz, G. & Schiemann, G. Über aromatische Fluorverbindungen, I.: Ein neues Verfahren zu ihrer Darstellung. *Chem. Ber.* **60**, 1186–1190 (1927).

108. Furuya, T., Klein, J. E. M. N. & Ritter, T. Carbon-fluorine bond formation for the synthesis of aryl fluorides. *Synthesis* **11**, 1804–1821 (2010).

109. Smith, O. *et al.* Harnessing triaryloxonium ions for aryne generation. *Nat. Synth.* **3**, 58–66 (2024).

110. Riddlestone, I. M., Kraft, A., Schaefer, J. & Krossing, I. Taming the Cationic Beast: Novel Developments in the Synthesis and Application of Weakly Coordinating Anions. *Angew. Chem. Int. Ed.* **57**, 13982–14024 (2018).

111. Golden, J. H., Mutolo, P. F., Lobkovsky, E. B. & DiSalvo, F. J. Lithium-Mediated Organofluorine Hydrogen Bonding: Structure of Lithium Tetrakis(3,5-bis(trifluoromethyl)phenyl)borate Tetrahydrate. *Inorg. Chem.* **33**, 5374–5375 (1994).

112. Massey, A. G. & Park, A. J. Perfluorophenyl derivatives of the elements I. Tris(pentafluorophenyl)boron. *J. Organomet. Chem.* **2**, 245–250 (1964).

113. Vershinin, V. & Pappo, D. M[TPP]Cl (M = Fe or Mn)-Catalyzed Oxidative Amination of Phenols by Primary and Secondary Anilines. *Org. Lett.* **22**, 1941–1946 (2020).

114. Sawai, Y. *et al.* Process for the preparation of an amorphous, peptide-like diabetes drug: Approach to a chromatography-free process. *Org. Process. Res. Dev.* **14**, 1110–1117 (2010).

115. González, P. B. *et al.* Experimental and computational investigation of the 1,3-dipolar cycloaddition of the ynamide *tert*-butyl N-Ethynyl-N-phenylcarbamate with c-carboxymethyl-N-phenylnitrilimine. *European J. Org. Chem.* 8108–8114 (2013).

116. Yadav, L., Tiwari, M. K., Shyamlal, B. R. K. & Chaudhary, S. Organocatalyst in Direct C(sp2)-H Arylation of Unactivated Arenes: [1-(2-Hydroxyethyl)-piperazine]-Catalyzed Inter-/Intra-molecular C-H Bond Activation. *J. Org. Chem.* **85**, 8121–8141 (2020).

117. Prof Th Kauffmann, B. D. The Hetarynes. *Angew. Chem. Int. Ed.* **4**, 543–618 (1965).

118. Smith, O. *et al. Harnessing Triaryloxonium Ions for Aryne Generation*. *Nat. Synth.* **3**, 58–66 (2024).

119. Lixiang, W. *et al.* Condensed ring compound containing boron nitrogen and dendritic structure, preparation method and application thereof, and organic electroluminescent device. (2022).

120. Liu, Y., Park, S. K., Xiao, Y. & Chae, J. Copper(ii)-catalyzed C-O coupling of aryl bromides with aliphatic diols: Synthesis of ethers, phenols, and benzo-fused cyclic ethers. *Org. Biomol. Chem.* **12**, 4747–4753 (2014).

121. Mitsudo, K. *et al.* Cu/Fe/O=PPh3-catalyzed etherification for the synthesis of aryl 3-benzo[b]thienyl ethers. *Chem. Lett.* **47**, 1044–1047 (2018).

122. Salvi, L., Davis, N. R., Ali, S. Z. & Buchwald, S. L. A new biarylphosphine ligand for the Pd-catalyzed synthesis of diaryl ethers under mild conditions. *Org. Lett.* **14**, 170–173 (2012).

123. David, E., Perrin, J., Pellet-Rostaing, S., Fournier Dit Chabert, J. & Lemaire, M. Efficient access to 2-aryl-3-substituted benzo[b]thiophenes. *J. Org. Chem.* **70**, 3569–3573 (2005).

124. Lixiang, W. *et al.* Fused ring compound containing boron atoms, chalcogen atoms and five-membered heteroaromatic ring and organic electroluminescent device. EP2555272A1, (2020).

125. Górski, K., Mech-Piskorz, J., Leśniewska, B., Pietraszkiewicz, O. & Pietraszkiewicz, M. Toward Soluble 5,10-Diheterotruxenes: Synthesis and Reactivity of 5,10-Dioxatruxenes, 5,10-Dithiatruxenes, and 5,10-Diazatruxenes. *J. Org. Chem.* **85**, 4672–4681 (2020).

126. Krell-Jørgensen, M. *et al.* Redshifted and thermally bistable one-way quantitative hemithioindigo-derived photoswitches enabled by isomer-specific excited state intramolecular proton transfer. *Chem. Comm.* **59**, 563–566 (2022).

127. Hoffmann, R. & Woodward, R. B. Selection Rules for Concerted Cycloaddition Reactions. *J. Am. Chem. Soc.* **87**, 2046–2048 (1965).

128. Rauk, A., Allen, L. C. & Mislow, K. Pyramidal Inversion. *Angew. Chem. Int. Ed.* **9**, 400–414 (1970).

129. Baechler, R. D. & Mislow, K. The Effect of Structure on the Rate of Pyramidal Inversion of Acyclic Phosphines. *J. Am. Chem. Soc.* **92**, 3090–3093 (1970).

130. Darwish, D. & Scott, C. E. The Racemization of Sulfonium Salts. 111. The Racemization of Arylsulfonium Salts. *Can. J. Chem.* **51**, 3647–3648 (1973).

131. Darwish, D. & Tomilson, R. L. The Preparation and Racemization of an Optically Active Sulfonium Ylide. (—)-Ethylmethylsulfonium Phenacylide Sir: *J. Org. Chem.* **1**, 5938–5939 (1968).

132. Brownstein, S. Inversion at Pyramidal Oxygen. *J. Am. Chem. Soc.* **98**, 2663–2664 (1975).

133. Andersen, K., Cinquini, M. & Papanikolaou, N. E. The Synthesis and Stereochemistry of Triarylsulfonium Salts. *J. Org. Chem.* **35**, 706–710 (1970).

134. Xiao, Y., Sun, Z., Guo, H. & Kwon, O. Chiral phosphines in nucleophilic organocatalysis. *Beilstein J. Org. Chem.* **10**, 2089–2121 (2014).

135. Skarżewski, J., Zielińska-Błajet, M. & Boratyński, P. J. Cinchona alkaloids-derivatives and Applications. *Alkaloids Chem. Biol.* 29–145 (2019).

136. Lambert, J. B. & Johnson, D. H. The Stereochemistry and Inversion of Trivalent Oxygen. *J. Am. Chem. Soc.* **90**, 1349–1350 (1968).

137. Krossing, I. The facile preparation of weakly coordinating anions: Structure and characterisation of silverpolyfluoroalkoxyaluminates $AgAl(ORF)_4$, calculation of the alkoxide ion affinity. *Chem. Eur. J.* **7**, 490–502 (2001).

138. Mascal, M., Hafezi, N., Meher, N. K. & Fettinger, J. C. Oxatriquinane and oxatriquinacene: Extraordinary oxonium ions. *J. Am. Chem. Soc.* **130**, 13532–13533 (2008).

139. Mascal, M., Hafezi, N. & Toney, M. D. 1,4,7-Trimethyloxatriquinane: SN2 Reaction at Tertiary Carbon. *J. Am. Chem. Soc.* **132**, 10662–10664 (2010).

140. Stoyanov, E. S. *et al.* The R 3 O + ⋯ H + Hydrogen Bond: Toward a Tetracoordinate Oxadionium (2 +) Ion. *J. Am. Chem. Soc.* **134**, 707–714 (2012).

141. Ōki, M. Recent Advances in Atropisomerism. *Topics in Stereochemistry* 1–81 (1983).

142. Lu, M. *et al.* Peraryl-X-onium ions of nitrogen and oxygen. *Org. Chem. Front.* **6**, 2640–2646 (2019).

143. Watkins, M. I., Ip, W. M., Olah, George, A. & Bau, R. Structure of Oxonium Ions: An X-ray Crystallographic Study of Triethyloxonium Hexafluorophosphate and Triphenyloxonium Tetraphenylborate. *J. Am. Chem. Soc.* **104**, 2365–2372 (1982).

144. Heeb, J. P., Clayden, J., Smith, M. D. & Armstrong, R. J. Interrogating the configurational stability of atropisomers. *Nat. Protoc.* **18**, 2745–2771 (2023).

145. Trapp, O. Fast and Precise Access to Enantiomerization Rate Constants in Dynamic Chromatography. *Chirality* **18**, 489–497 (2006).

146. Trapp, O. Unified equation for access to rate constants of first-order reactions in dynamic and on-column reaction chromatography. *Anal. Chem.* **78**, 189–198 (2006).

147. Trapp, O. The unified equation for the evaluation of degenerated first-order reactions in dynamic electrophoresis. *Electrophoresis* **27**, 2999–3006 (2006).

148. Trapp, O., Schoetz, G. & Schurig, V. Determination of enantiomerization barriers by dynamic and stopped-flow chromatographic methods. *Chirality* **13**, 403–414 (2001).

149. Claridge, T. D. W. *High-Resolution NMR Techniques in Organic Chemistry*. (Elsevier, 2016).

150. Smith, O. *et al.* Control of stereogenic oxygen in a helically chiral oxonium ion. *Nature* **615**, 430–435 (2023).

151. Reist, M., Testa, B., Carrupt, P.-A., Jung, M. & Schurig, V. Racemization, Enantiomerization, Diastereomerization, and Epimerization: Their Meaning and Pharmacological Significance. *Chirality* **7**, 396–400 (1995).

152. Balalas, T., Abdul-Sada, A., Hadjipavlou-Litina, D. J. & Litinas, K. E. Pd-Catalyzed Efficient Synthesis of Azacoumestans Via Intramolecular Cross Coupling of 4-(Arylamino)coumarins in the Presence of Copper Acetate under Microwaves1. *Synthesis* **49**, 2575–2583 (2017).

153. Luo, F. *et al.* Direct insertion into the C–C bond of unactivated ketones with NaH-mediated aryne chemistry. *Chemistry* **9**, 2620–2636 (2023).

154. Criado, A. *et al.* Stereoselective tandem cascade furan cycloadditions. *J. Org. Chem.* **78**, 12637–12649 (2013).

155. La Regina, G. *et al.* Discovery of 1,1'-Biphenyl-4-sulfonamides as a New Class of Potent and Selective Carbonic Anhydrase XIV Inhibitors. *J. Med. Chem.* **58**, 8564–8572 (2015).

156. Xu, Z. Y. *et al.* Photocatalytic Chemodivergent Synthesis of α-gem-Dihalovinyl Ketones and Chromen-2-Ones from Monoalkynes. *Adv. Synth. Catal* **364**, 2666–2672 (2022).

157. Pallavicini, M. *et al.* WB4101-related compounds: New, subtype-selective α1-adrenoreceptor antagonists (or inverse agonists?). *J. Med. Chem.* **49**, 7140–7149 (2006).

158. Chen, G. & Xu, B. Gold-Catalyzed C-O Cross-Coupling Reactions of Aryl Iodides with Silver Carboxylates. *Org. Lett.* **25**, 6334–6339 (2023).

159. Khan, D. & Parveen, I. Chroman-4-one-Based Amino Bidentate Ligand: An Efficient Ligand for Suzuki-Miyaura and Mizoroki-Heck Coupling Reactions in Aqueous Medium. *Eur. J. Org. Chem.* **2021**, 4946–4957 (2021).

160. Soman, S. S., Soni, J. N. & Patel, T. B. Synthesis of new naphthoisoxazole amide derivatives and study of their biological evaluations. *Med. Chem. Res.* **23**, 3803–3809 (2014).

161. Ji, Q. *et al.* Synthesis and biological evaluation of novel phosphoramidate derivatives of coumarin as chitin synthase inhibitors and antifungal agents. *Eur. J. Med. Chem.* **108**, 166–176 (2016).

162. Liu, J. *et al.* Novel Coumarin Derivatives Inhibit the Quorum Sensing System and Iron Homeostasis as Antibacterial Synergists against Pseudomonas aeruginosa. *J. Med. Chem.* **66**, 14735–14754 (2023).

163. Rao, M. L. N., Venkatesh, V. & Jadhav, D. N. Palladium-catalyzed synthesis of 4-arylcoumarins using triarylbismuth compounds as atom-Efficient multicoupling organometallic nucleophiles. *Eur. J. Org. Chem.* 3945–3955 (2010).

164. Sharma, A., Hazarika, H., Sarmah, M., Das, B. & Gogoi, P. Indane-Fused Spiropentadiene Chromanones: A Pd-Catalyzed Spiroannulation Followed by Cyclization via C-H Activation Strategy. *J. Org. Chem.* **85**, 11382–11395 (2020).

165. Liu, Y., Park, S. K., Xiao, Y. & Chae, J. Copper(ii)-catalyzed C-O coupling of aryl bromides with aliphatic diols: Synthesis of ethers, phenols, and benzo-fused cyclic ethers. *Org. Biomol. Chem.* **12**, 4747–4753 (2014).

166. Josef, V., Hampel, F. & Dube, H. Heterocyclic Hemithioindigos: Highly Advantageous Properties as Molecular Photoswitches. *Angew. Chem. Int. Ed.* **61**, (2022).

167. Wang, N. F., Saraf, S. & Pusztay, S. V. Arylsulfanyl compounds and compositions for delivering active agents. WO2008014430A1, (2008).

168. Gardinier, K. M. *et al.* Retinoid x receptor modulators. (2004).

169. Zhang, X., Ma, H. & He, S. Heteroaryl compounds as inhibitors of programmed necrosis pathway, composition and method using the same. WO2018017435A1, (2021).

170. Mori, S. *et al.* Development of retinoic acid receptor antagonists bearing trans-SF4-alkynyl structure as a linear linker. *Tetrahedron* **123**, 132967 (2022).

171. Curran, D. *et al.* Synthesis and cytotoxicity studies of novel NHC-gold(I) complexes derived from lepidiline A. *Molecules* **23**, 1–17 (2018).

172. Gernet, A., El Rhaz, A. & Jean, L. Easily Accessible Substituted Heterocyclic Hemithioindigos as Bistable Molecular Photoswitches. *Chem. Eur. J.* **29**, 1–6 (2023).

173. Mukherjee, C., Kamila, S. & De, A. Application of directed metalation in synthesis. Part 4: Expedient synthesis of substituted benzo[b]thiophene and naphthothiophene. *Tetrahedron* **59**, 4767–4774 (2003).

174. Schmidt, E. Y. *et al.* Synthesis and optical properties of 2-(Benzo[b]thiophene-3-yl)pyrroles and a new bodipy fluorophore (BODIPY = 4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene). *Chem. Eur. J.* **15**, 5823–5830 (2009).

175. Aganda, K. C. C., Na, S. & Lee, A. Catalyst-free, direct synthesis of dibenzothiophenes. *Tetrahedron Lett.* **104**, 154009 (2022).

176. Yonekura, K., Yoshimura, Y., Akehi, M. & Tsuchimoto, T. A Heteroarylamine Library: Indium-Catalyzed Nucleophilic Aromatic Substitution of Alkoxyheteroarenes with Amines. *Adv. Synth. Catal.* **360**, 1159–1181 (2018).