Triaryl Oxonium Ions: Synthesis, Reactivity and Application as Precursors to Heterocyclic Arynes

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Doctor of Philosophy

of the

University of Oxford

For Nas

Nothing in my life is complete until I’ve shared it with you

Declaration

This dissertation describes work carried out in the Chemistry Research Laboratory at the University of Oxford between May 2022 and February 2025, as well as Vertex Pharmaceuticals (Oxford Research Site) between February 2025 and May 2025. The dissertation is the product of my own work and includes no results obtained through collaboration, except where specifically indicated in the text.

Edvinas Ališauskas

Acknowledgements

It is hard to believe it has been almost four years since I started my DPhil. Time really does fly. I still clearly remember walking through Oxford to the Manor Road Building for our taught modules and sharing a seminar room there with an amazing group of people: Aleksy, Anna, Carla, Katherine and Martin. Thank you for the wonderful memories and the laughs we shared, it was such a great way to start the course.

Afterwards, I moved on to my first lab rotation with the Dixon group. It was lovely to return to a place where I had previously learnt so much as a Part II student the year before. It was great seeing so many familiar faces and I am particularly grateful for the support I received from both Andrew and Darren.

I then started my second rotation in the Smith lab, when the group consisted only of a handful of people. Yet, they made me feel so welcome that within the first couple of weeks, I knew that this was where I wanted to be. Maddie, thank you for showing me the ways of the oxonium ions, it was genuinely a sad day when you left the lab. Pearse, thank you for being so incredibly helpful, your presence always brightened up the lab. Elliot, thank you for filling F5 with the sounds of country music and for trusting me with the reins of the glove box. Zac, thank you for all of your thoughtful suggestions, you were, and still are, the unofficial PI of the group. Morgan, thank you for the pleasant conversations we had over tea breaks. Mengxue, thank you for consistently wishing me a Merry Christmas, I am grateful for those cheerful emails.

As time passed, more and more people joined the Smith group and I am very grateful I shared my DPhil journey with them. Xiaofei, thanks for always being sincere and never having boring hair. Chai, thank you for always genuinely asking me how I am, it truly makes a difference to one's day. Callan, thank you for bringing the warm Australian Spirit

to our group. Sam, thanks for being such a good desk and lab buddy I can have a laugh with; perhaps I will win a Yahtzee game against you one day. Elvira, thank you for all of the gossip and drama – never a dull day in the CRL with you. Hafdis, thanks for the many great laughs in F4 and for putting up with my endless questions whether or not my crystals are 'good enough'. Thank you, Yang, for never failing to give me a smile when I walk past. Valentin, thanks for the lovely morning chats I have had with you, they were a perfect way to start the working day. Udey, thank you for always being so blunt and saying it how it actually is - we definitely need more people like you. Joe, thanks for being so friendly and kind, I hope my old fume hood will serve you as well as it did me. Rongyu, thank you for always being so well-dressed, it is nice to know I am not the only one with an obsession with shirts. William, thanks for your dedication and for always working hard. Anton, we were so eager to have you join us for so long, thank you for being such a helpful postdoc.

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follow the beat of your own drum. Evelyn, thanks for putting up with us at F4 banning Taylor Swift for your whole year. (Little) Sam, thank you for all the great times in the lab (or even at A&E). Yifei, thanks for being so keen and working incredibly hard.

Finally, but most importantly, I wanted to thank Professors Martin Smith and Jonathan Burton. I would not be where I am now without their professional guidance and the supportive environment they have created. I am truly grateful for their mentorship.

Glossary of Abbreviations and Symbols

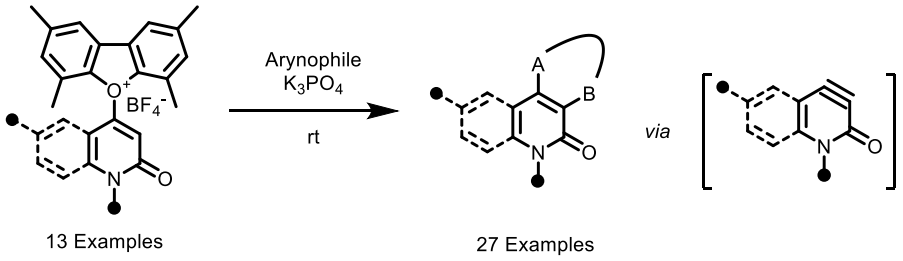
°C	degree(s) Celsius
Ac	acetyl
APCI	atmospheric pressure chemical ionisation
aq.	aqueous
Ar	argon
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bu	butyl
cm^{-1}	wavenumber(s), inverse centimetre(s)
Cy	cyclohexyl
d	doublet
DIPEA	diisopropylethylamine
DMAP	dimethylaminopyridine
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
dppf	1,1'-ferrocenediyl-bis(diphenylphosphine)
eq.	equivalent(s)
ESI	electrospray ionisaiton
Et	ethyl
et al.	*et alii* (Latin: and others)
g	gram(s)
h	hour(s)
hept	heptet
HMDS	hexamethyl disilylazide
HRMS	high resolution mass spectrometry
i-	*iso*-
IPA	isopropyl alcohol
IR	infrared spectroscopy
J	coupling constant
LG	leaving group
LRMS	low resolution mass spectrometry
m	multiplet
m-	*meta*-
*m*CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
mg	milligram(s)
mL	millilitre(s)
mol	mole(s)
mol%	mole per cent
MOM	methoxymethyl
MP	melting point
MS	mass spectrometry
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide

NMR	nuclear magnetic resonance spectroscopy
Nu	nucleophile
o-	*ortho*-
p-	*para*-
Ph	phenyl
Pin	pinacolato
ppm	parts per million
Pr	propyl
q	quartet
quant.	quantitative
rr	regioisomeric ratio
rt	room temperature
s	singlet
sat.	saturated
T	temperature
t	triplet
tert-	tertiary
Tf	trifluoromethanesulfonate
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TMS	trimethylsilyl
Ts	*para*-toluenesulfonyl
UPLC	ultra performance liquid chromatography
v/v	volume per volume
w/w	weight by weight
δ	NMR chemical shift

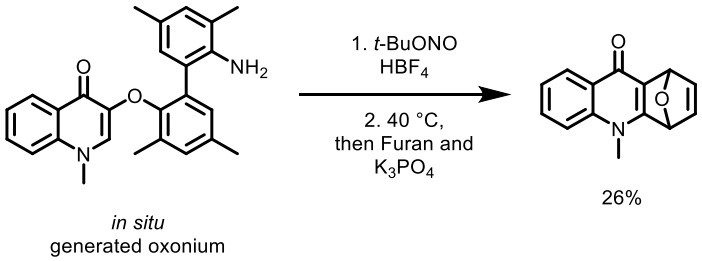
Abstract

The work described in this thesis explores the synthesis of heterocyclic triaryl oxonium ions and their application in hetaryne chemistry. It consists of four projects divided into concise chapters, each with a separate introduction, results and discussion, synthesis of starting materials, conclusion and future work sections.

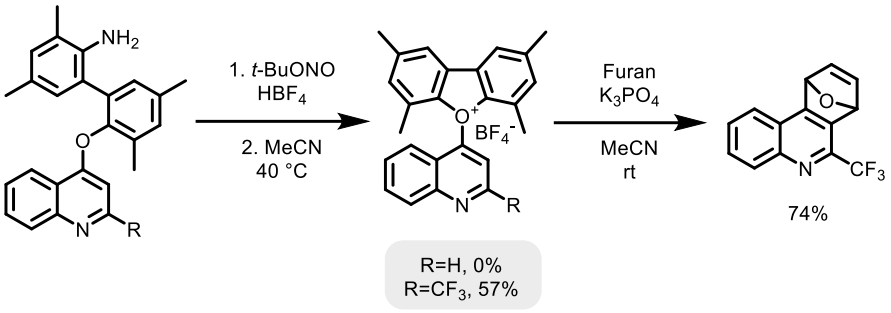
Chapter 1 summarises the work on 2-quinolone and 2-pyridone oxonium ions, including the development of their synthetic routes and application in hetaryne trapping reactions, as well as a discussion of the observed regioselectivity.



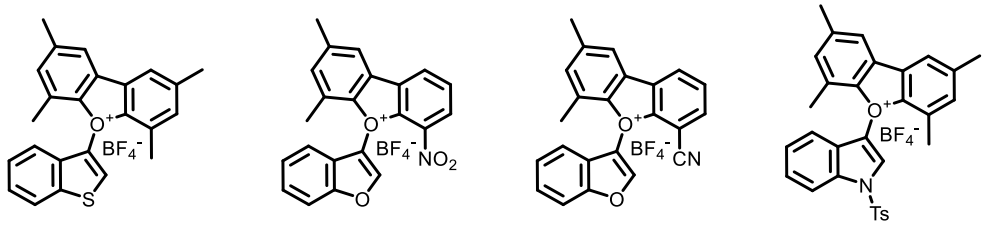
In Chapter 2, the *in situ* generation and furan trapping of a 4-quinolone oxonium ion is reported as well as the strategies explored to increase its kinetic stability. A chromone oxonium ion is also produced and its reactivity compared to its isoelectronic counterpart.



Chapter 3 illustrates the structural design and synthesis of quinoline oxonium ions, establishing the necessity of an electron withdrawing group in the 2- position. Furthermore, a route to isoquinoline oxonium ion precursors is also developed.



Finally, Chapter 4 discloses the synthesis of benzothiophene, benzofuran and indole-based oxonium ions and the efforts to access their corresponding hetarynes.



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General Overview

0.1 A Note on Nomenclature

There are a total of three isomers of didehydrobenzene: *ortho*-benzyne **1**, *meta*-benzyne **2** and *para*-benzyne **3** (**Figure 1**).[1] As *ortho*-benzyne and, as an extension, *ortho*-arynes are the focus of this thesis, they will be simply referred to as benzyne and arynes, respectively, unless otherwise specified.

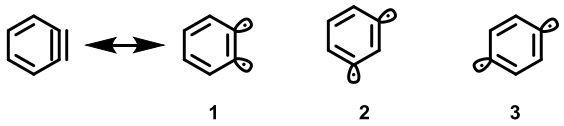


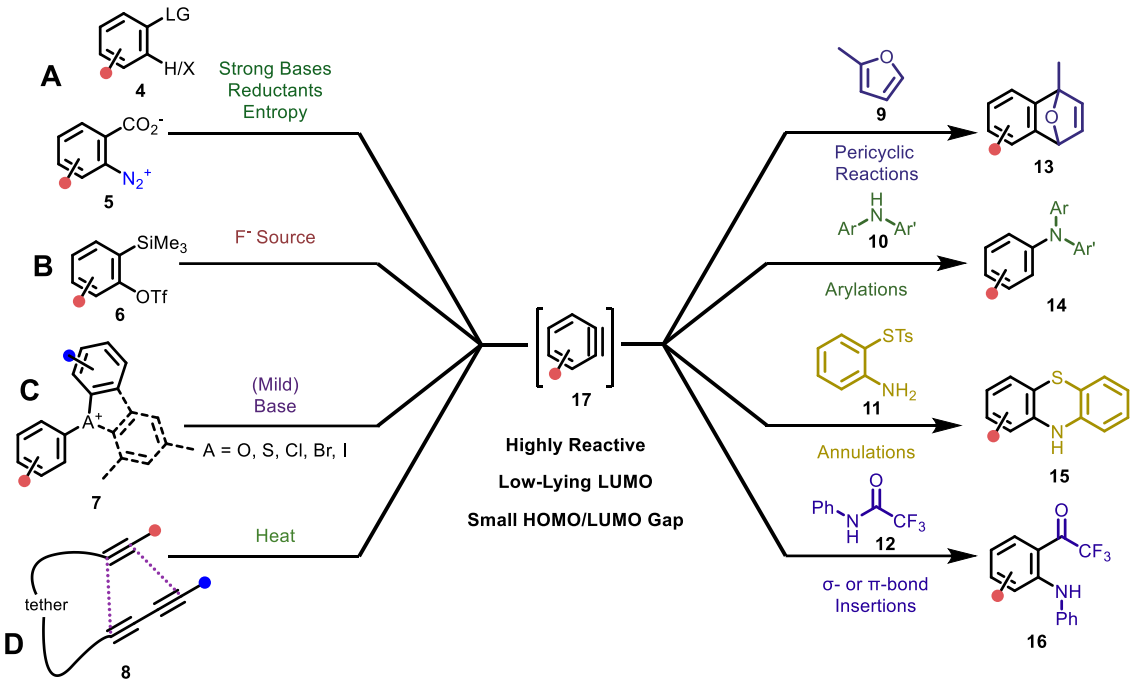
Figure 1. The three isomers of benzyne

0.2 Aryne Chemistry

Arynes are an important group of reactive intermediates in organic chemistry.[2] They owe their high reactivity to an angle-strained triple bond, which results in a small HOMO/LUMO gap and a low-lying LUMO.[3] Consequently, this highly electrophilic character of arynes allows them to react with a wide range of arynophiles and their chemistry is exploited in various pericyclic transformations,[3] arylations of nucleophiles,[4] intermolecular ring formations, and insertion reactions (**Scheme 1**).[5,6] There are many strategies for forming arynes in the literature,[7] however, the most widely employed protocols can be categorised into three large groups (**Scheme 1**, **A**–**D**).

Classically, arynes have been formed by deprotonative or dehalogenative mechanisms, relying on strong bases or reductants.[8] Additionally, the thermolysis or photolysis of the potentially explosive diazotised anthranilic acid derivatives **5** has also been utilised, entropically driven by the formation of nitrogen and carbon dioxide (**Scheme 1**–**A**).[9] Although these methods are still important, the harsh reaction conditions are incompatible

with many functional groups, leading chemists to develop contemporary ways of generating arynes *in situ*.



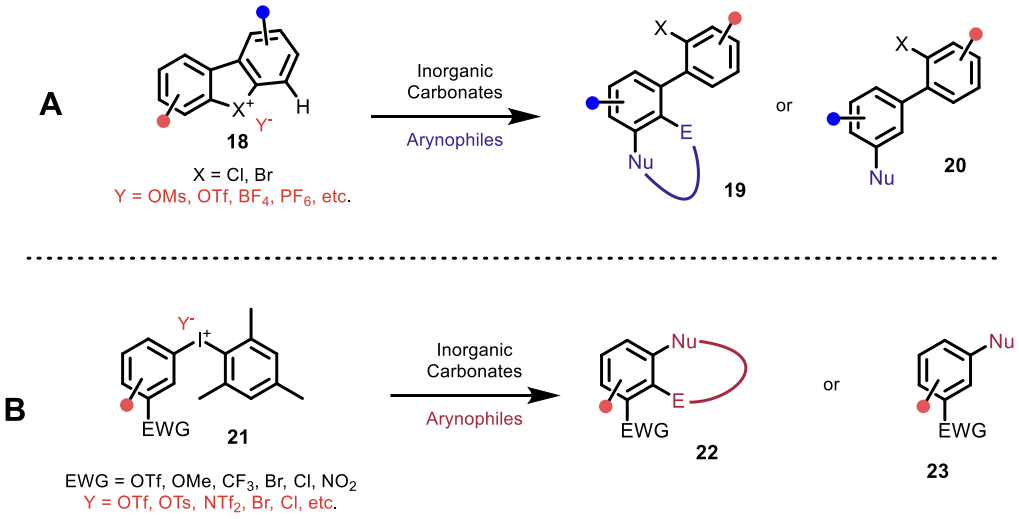
Scheme 1. General methods for forming arynes and their potential downstream reactivity

Perhaps the most widely used method today is the Kobayashi protocol, originally published in the early 1980s (**Scheme 1**–**B**),[10] where *ortho*-silylaryl triflate derivatives **6** are activated by a source of fluoride. Not only is this a milder way of forming arynes, the reaction conditions release the fleeting intermediate **17** in a continuous and low concentration, avoiding side reactivity such as dimerization.[11] Despite the fact that this mild approach is compatible with many functionalities, strong bases are generally used in the synthesis of these silylated aryne precursors,[12] limiting the diversity of the aromatic scaffold.

Another important group of reactive intermediates often employed in aryne generation is the chalcogen or halogen-based onium ions **7** (**Scheme 1**–**C**), with the chemistry of λ^3 -bromanes, -chloranes, and -iodanes being the most developed.[13] Owing to their excellent leaving group ability, these compounds generally only require a weak inorganic base to

liberate the free aryne *via* deprotonation and β-elimination. As a result, they exhibit a functional group compatibility that is complementary to the Kobayashi method.[14] In addition to this, the preparation of most onium ions requires simple synthetic transformations, increasing the variety of possible aryne precursors.[15]

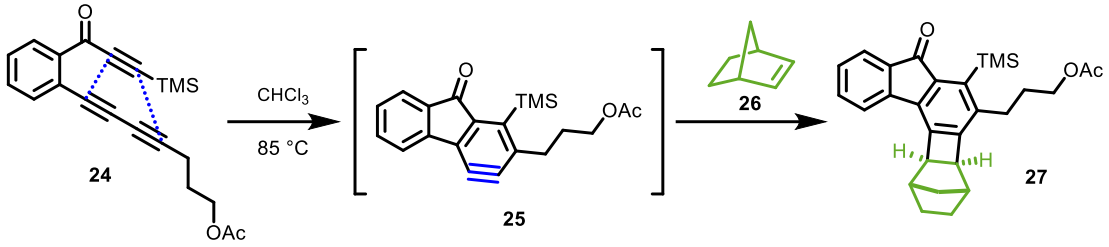
Although the use of hypervalent halogen reagents as aryne synthons is attractive, there are several drawbacks that need to be considered. Since most synthetically accessible λ³-bromanes and -chloranes possess a tricyclic framework, their utility as aryne precursors is largely limited to the synthesis of functionalised biaryl scaffolds **19** and **20** (**Scheme 2**–**A**).[16,17] Similarly, in the case of λ³-iodanes **21**, selective deprotonation with a weak base is only possible with the introduction of an electron-withdrawing group *meta*- to the iodine moiety (**Scheme 2**–**B**).[18,19]



Scheme 2. General aryne reactivity of λ³ -bromanes, -chloranes, and -iodanes with a mild inorganic base

Finally, another important class of aryne-generating reactions is the Hexadehydro Diels-Alder reaction (HDDA), initially reported by Ueda and Johnson in 1997,[20,21] and more recently developed by Hoye and co-workers in 2012 (**Scheme 1**–**D**).[22] In this 'reagentless' transformation, an intramolecular [4+2] cycloaddition occurs between an alkyne and a 1,3-diyne at elevated temperatures, generating a transient aryne intermediate, which is

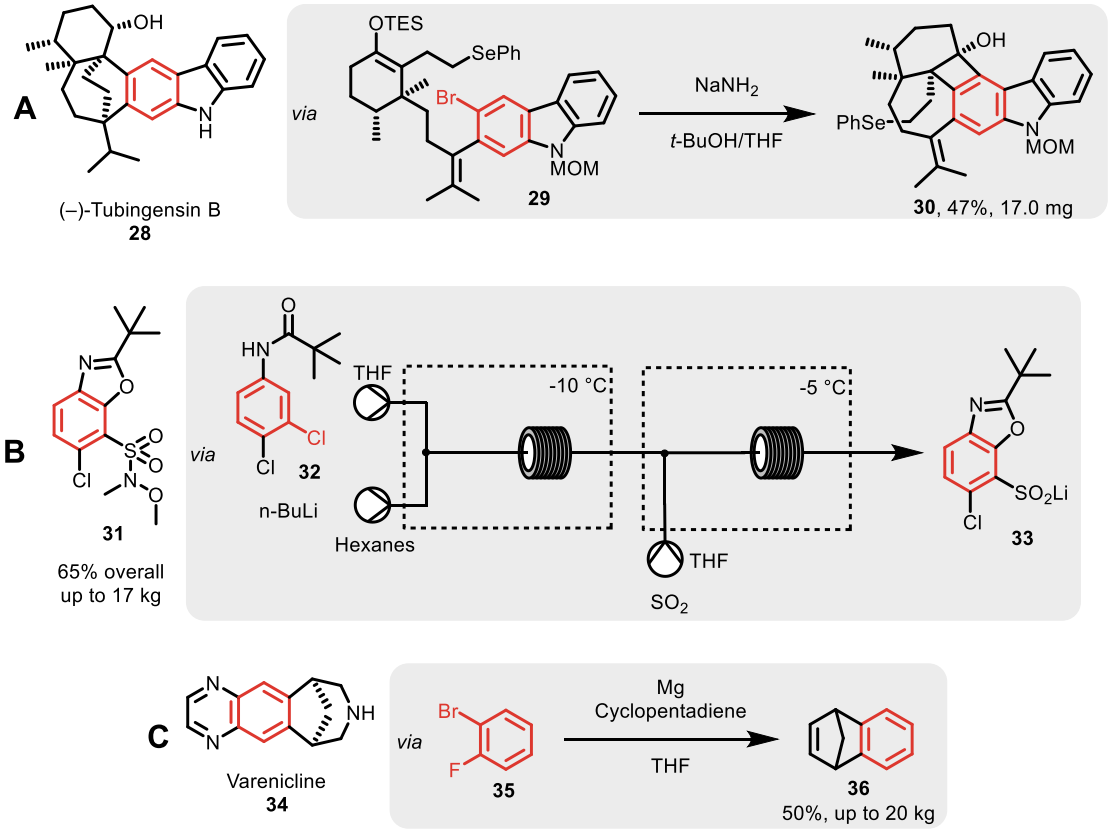
subsequently trapped by an arynophile. The main limitation of the HDDA reaction is the requirement of a three-atom tether for effective preorganisation.[23] Nevertheless, the protocol offers an efficient and atom-economical strategy to synthesise complex polycyclic structures, such as **27** (**Scheme 3**).[22]



Scheme 3. A selected example of a Hexadehydro Diels-Alder reaction forming an aryne intermediate that is trapped with norbornene

0.3 Application of Aryne Chemistry

Arynes have a broad application in synthetic chemistry for their high reactivity, short reaction times and the ability to forge two single bonds in a single synthetic step.[24] They appear in milligram-scale syntheses of natural products,[5] such as in the total synthesis of (-)-tubingensin B **28** by Garg *et al*. Here, an intramolecular aryne-based strategy was introduced to form a 4-membered ring with a neighbouring silyl enol ether in a 47% yield (**Scheme 4**–**A**).[25]



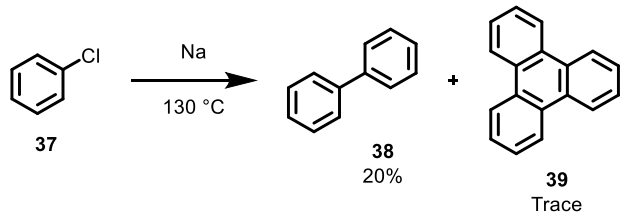
Scheme 4. Selected examples of aryne chemistry in the syntheses of (-)-Tubingensin B, a CXCR2 antagonist intermediate and Varenicline

Aryne formation can also be coupled to other synthetic techniques, such as continuous flow chemistry – an emerging method in the pharmaceutical industry.[26] A group of chemists in Novartis Pharma have developed a continuous process for the bulk-scale synthesis of a key benzoxazole core **33**, which was optimised to deliver the CXCR2 antagonist intermediate **31** in a 17 kg scale over a number of pilot-plant runs (**Scheme 4–B**).[27]

Although arynes exhibit high reactivity, and, in some cases, harsh reagents need to be used, their chemistry is still effectively applied on larger scales. Pfizer's Varenicline **34**, a smoking cessation drug, relied on a Diels-Alder reaction between benzyne **1** and cyclopentadiene in the original discovery route (**Scheme 4–C**).[28] This synthetic step was

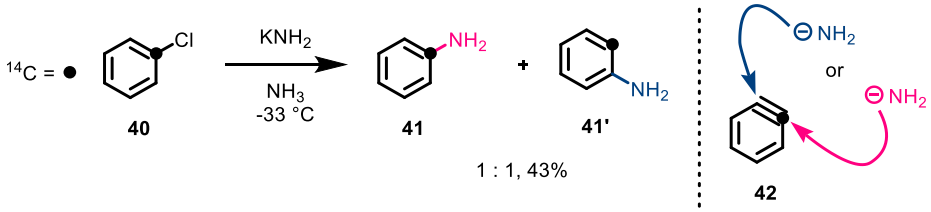
later scaled up to multiple multikilogram batches, supplying enough material for toxicology and early clinical studies.

0.4 Benzyne



Scheme 5. Biphenyl formation investigated by Bachman and Clarke

Benzyne **1** represents the prototypical example of an aryne. One of the first accounts involving a hypothesis of a benzyne intermediate was published in 1927 by Bachman and Clarke, who were investigating biphenyl **38** formation by refluxing metallic sodium in chlorobenzene **37** (**Scheme 5**).[29] One of the minor side products isolated was triphenylene **39**, believed to be a result of benzyne **1** trimerization.[30]



Scheme 6. Chlorobenzene amination reaction investigated by Roberts et al.

It was not until 1953 that the indirect evidence of the involvement of a symmetrical aryne intermediate **42** was determined by Roberts *et al.* (**Scheme 6**).[31] In their seminal work, potassium amide was added to ^{14}C-labelled chlorobenzene **40** in liquid ammonia at -33 °C, where an equimolar mixture of anilines **41** and **41'** was isolated after the full consumption of the starting material.

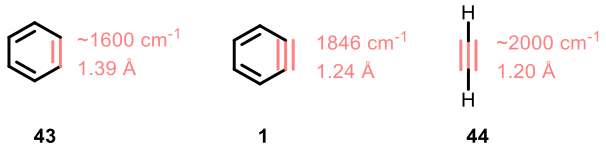
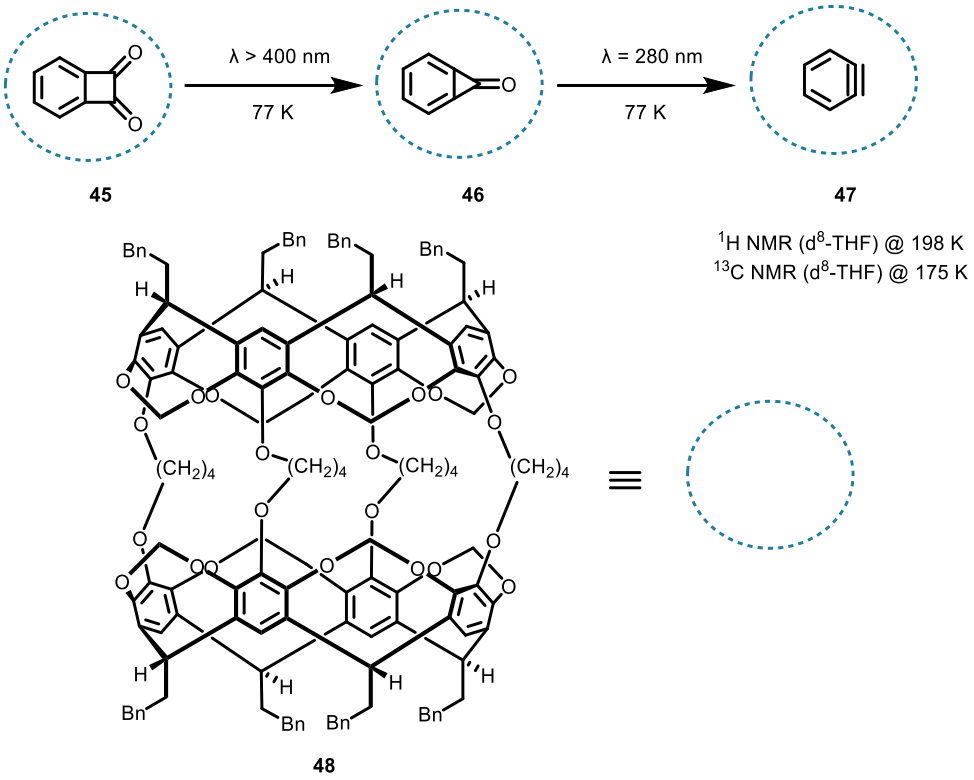


Figure 2. Comparison of bond lengths and stretching frequencies in benzene, benzyne and acetylene

Unsurprisingly, as a consequence of the short-lived nature of this reactive species, it is very difficult to observe and characterize benzyne **1** directly. Chapman *et al.* were the first to record an IR spectrum by the photochemical degradation of phthaloyl peroxide, isolated in an argon matrix at 8 K.[32] The stretching frequency of the C≡C bond was determined to be 1846 cm^{-1},[33] which is notably lower than that of an unstrained alkyne, but higher than the C=C stretch in benzene **43**.[34] A similar conclusion was drawn from the experimentally determined C≡C bond length of 1.24 Å (**Figure 2**).[35]

Interestingly, in 1997, a solution NMR spectrum of benzyne was recorded by generating it within the cavity of a hemicarcerand.[36] Warmuth and co-workers melted benzocyclobutenedione together with hemicarcerand **48** to form hemicarceplex **45**, which was subjected to two rounds of irradiation at cryogenic temperatures before recording ^{1}H and ^{13}C spectra of **47** in solution (**Scheme 7**). It is important to note that even at 198 K incarcerated benzyne fully reacted with the inside of the host molecule within 30 minutes, with a lifetime determined to be 205 s at this temperature. The chemical shifts of free benzyne **1** were estimated by comparison to benzene **43** shielded within carcerand **48** and compared well to computationally predicted NMR data (**Figure 3**).[37]



Scheme 7. Photochemical generation of incarcerated benzyne by Warmuth et al.

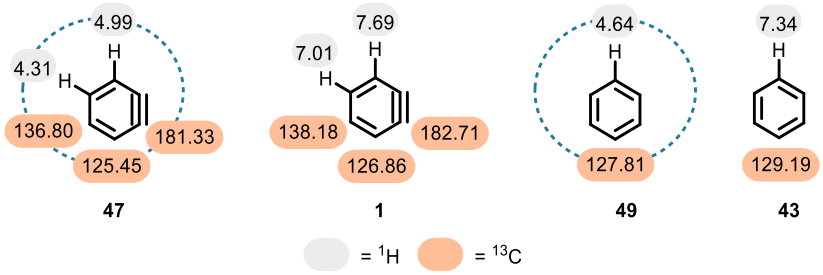


Figure 3. Chemical shifts of free benzyne as determined by comparison with benzene

0.5 Hetarynes

Heterocyclic motifs are present in many organic structures and can be found naturally,[38] or in synthetic compounds of pharmaceutical and agrochemical importance,[39,40] as well as in materials science.[41] As a consequence, researchers have been investigating heterocyclic aryne systems since the early 1900s.[42] As a matter of fact, the first aryne ever proposed in the literature was that of 2,3-benzofuranyne. However, the existence of such extremely strained species is still disputed and will be covered in more detail in **Chapter IV**.[43]

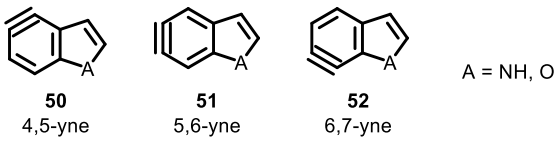
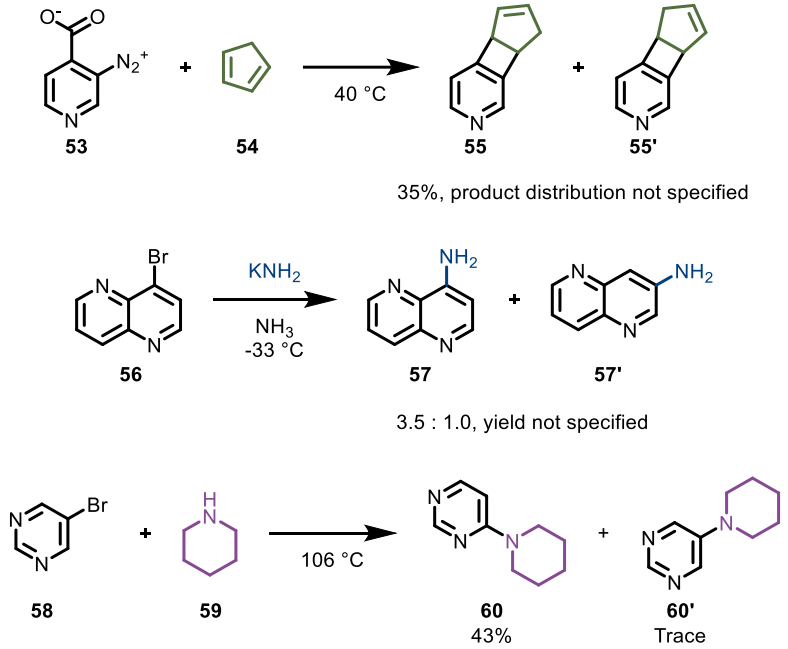
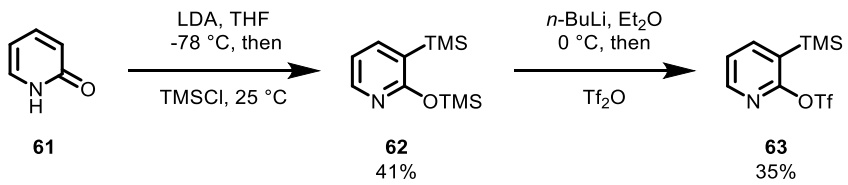


Figure 4. Selected isomers of benzofuranyne and indolyne

In many sources, certain isomers of indolyne and benzofuranyne are considered to be hetarynes, despite the fact that the triple bond is positioned within the carbocyclic ring (**Figure 4**). For the purposes of this thesis, we will only cover hetarynes with triple bonds located within a ring containing heteroatoms.



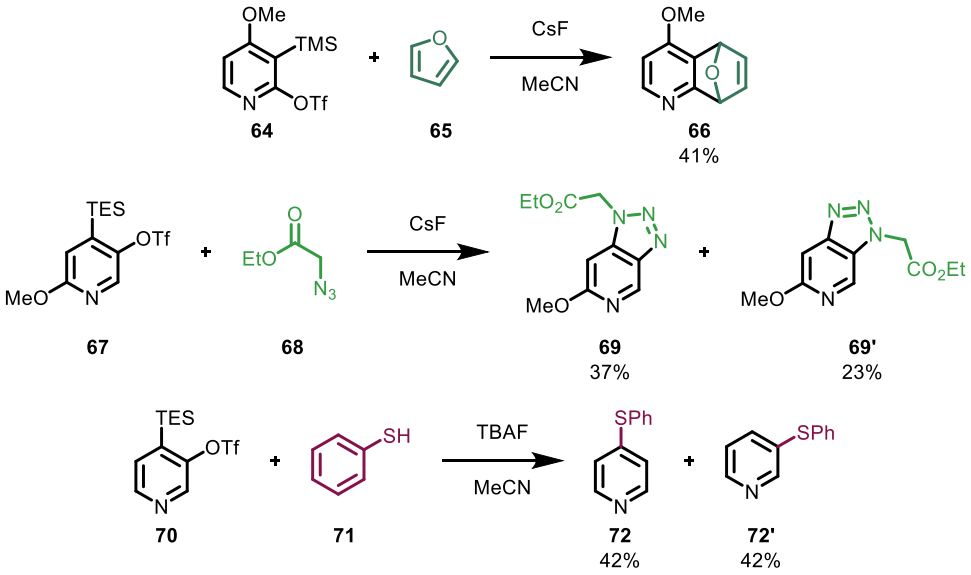
Scheme 8. Selected early examples of hetaryne chemistry, including work on pyridines, naphthyridines and pyrimidines



Scheme 9. The first published synthesis of a 2,3-pyridyne Kobayashi precursor by Effenberger and Daub

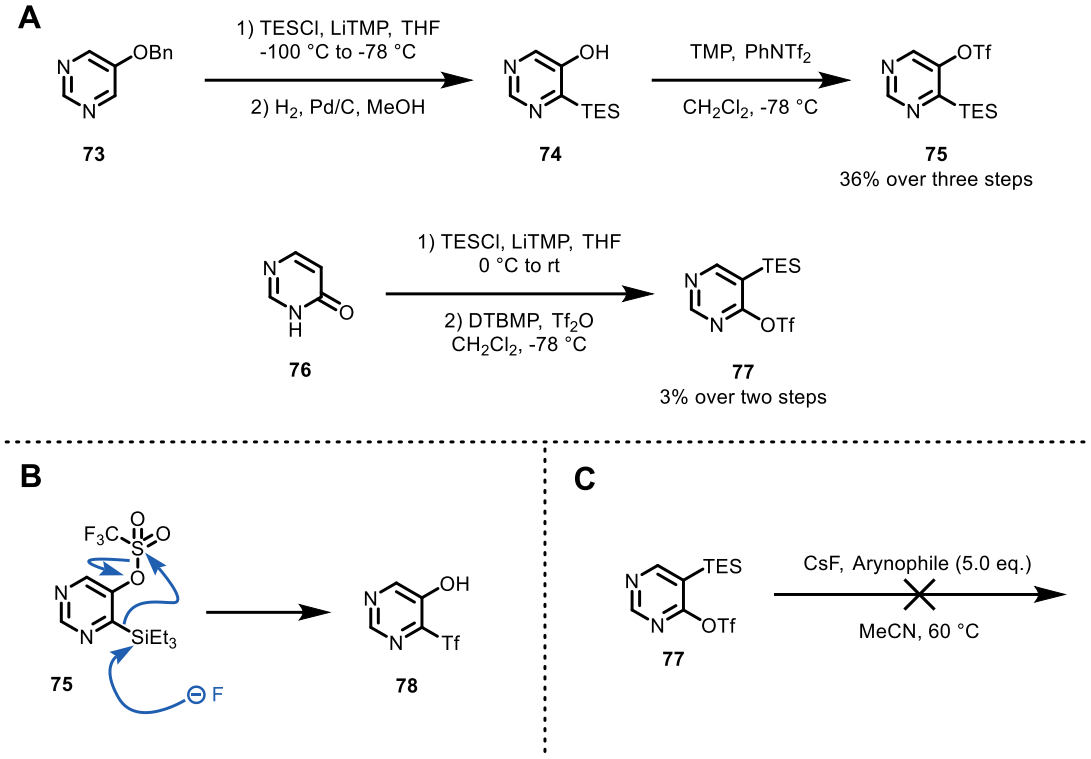
The early work on hetarynes mostly encompasses 6-membered heterocycles containing nitrogen, such as pyridine, 1,5-naphthyridine and pyrimidine (**Scheme 8**).[44] Because

harsh conditions are employed, many of these reactions suffer from low yields, and the trapping agents used are limited to the base itself or robust dienes. This limitation, along with the resurgence of the Kobayashi method, led to a growing interest in hetarynes, starting with the first published synthesis of a pyridine-based *ortho*-silylaryl triflate **63** in 1991 (**Scheme 9**).[45] Following this, additional substituted and unsubstituted 2,3- and 3,4-pyridyne precursors were synthesised by various groups and demonstrated to react with a wider range of arynophiles, such as dienes,[46] 1,3-dipoles,[47] and a variety of nucleophiles (**Scheme 10**).[48,49]



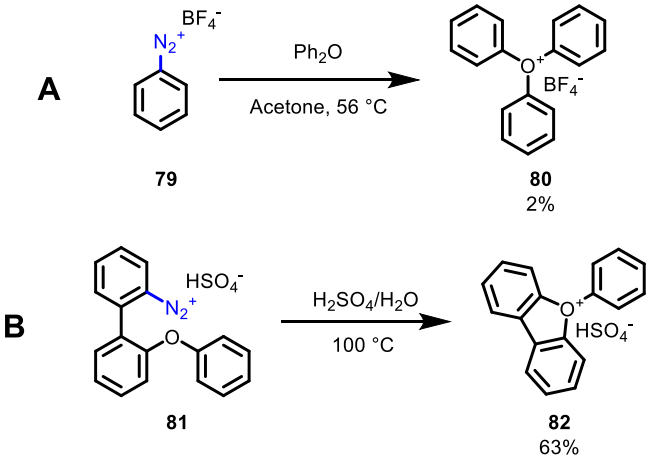
Scheme 10. Selected examples of the Kobayashi method-generated pyridyne chemistry

Not all Kobayashi precursors can lead to successful (het)aryne generation. Garg and co-workers developed a novel route to synthesise two variants of a 4,5-pyrimidyne precursor (**Scheme 11**).[50] Interestingly, **75** was observed to break down *via* a thia-Fries rearrangement when subjected to CsF in various aryne-trapping conditions, whereas constitutional isomer **77** decomposed into a complex mixture of products.



Scheme 11. The synthesis of two 4,5-pyrimidyne precursors and their unsuccesful trapping reactions by Garg et al.

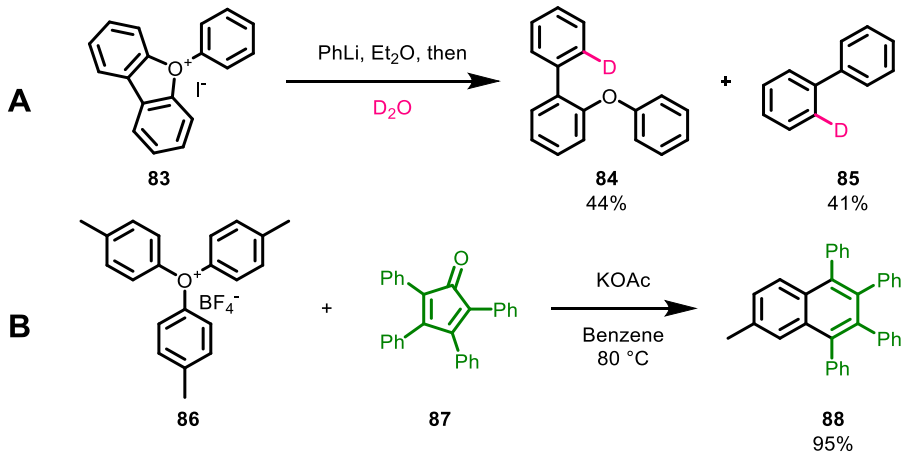
0.6 Triaryl Oxonium Ions as (Het)aryne Precursors



Scheme 12. Two early examples of the generation of triaryl oxonium ions

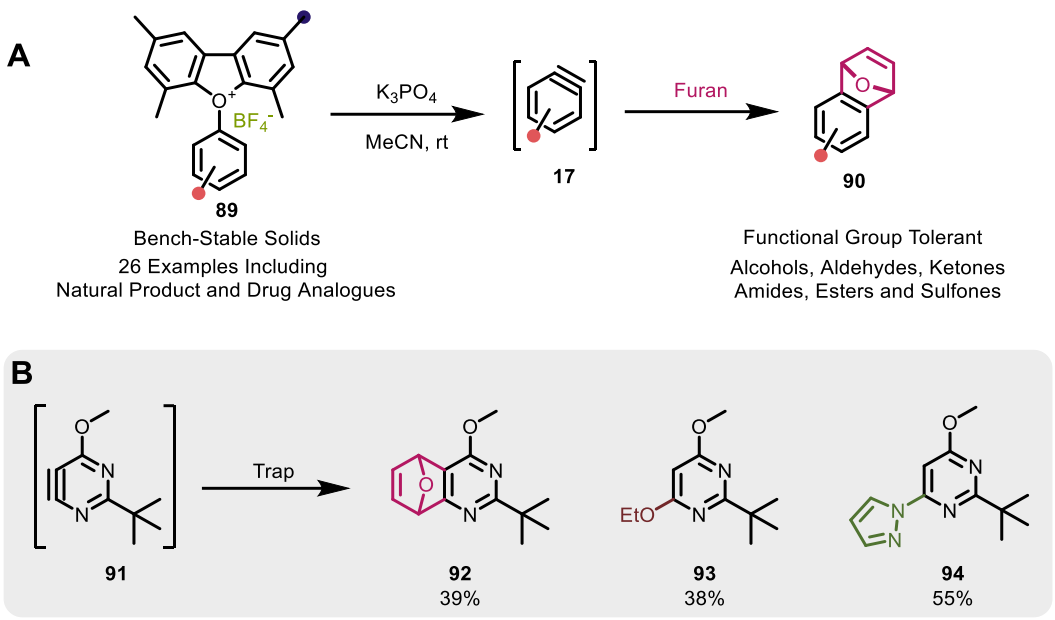
The first synthesis of a triaryl oxonium ion was reported in 1957 by Nesmeyanov *et al.*, where benzenediazonium tetrafluoroborate **79** was heated in acetone with an excess of diphenyl ether to generate **80** in a 2% yield (**Scheme 12**–**A**).[51] The yield was later improved by an intramolecular cyclisation strategy (**Scheme 12**–**B**).[52] It was not until

1972 that this oxonium ion was utilised in aryne formation when Hellwinkel and Seifert treated **83** with PhLi, observing two different products after quenching with D_2O (**Scheme 13**–**A**).[53] In a similar fashion, Tolstaya and co-workers exploited a symmetrical triaryl oxonium ion **86** along with a weak base, KOAc, to form and trap the corresponding aryne with tetracyclone **87** in an exceptional yield (**Scheme 13**–**B**).[54]



Scheme 13. Early examples of aryne formation from triaryl oxonium ions

Inspired by this fundamental work, the Smith and Burton groups generalised the synthesis of triaryl oxonium ions and developed an optimal methodology for generating arynes under mild conditions with an excellent functional group tolerance (**Scheme 14**–**A**).[15] Furthermore, the formed oxonium tetrafluoroborates are bench-stable and the aryne trapping step can be conducted under an ambient atmosphere.



Scheme 14. The Smith and Burton group protocol for generating arynes from triaryl oxonium ions and its application to 4,5-pyrimidynes

In contrast to the Kobayashi method,[50] the protocol was also successfully applied to a pyrimidyne system, where moderate yields were observed with arynophiles such as furan, ethanol, pyrazole and *N*-methylaniline (**Scheme 14**–**B**).

0.7 Project Aims

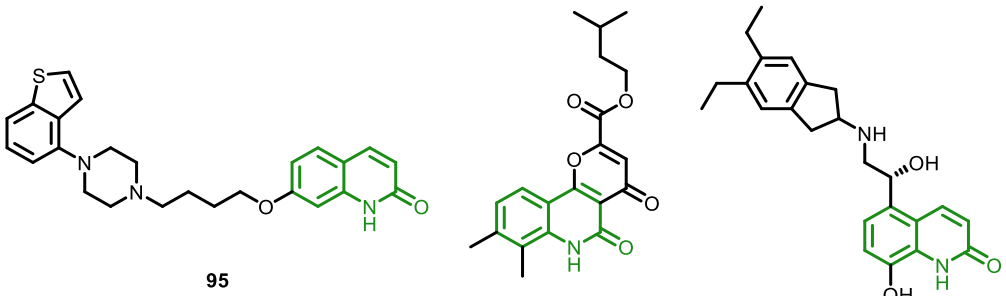
Consequently, the purpose of this DPhil project was to synthesise new families of oxonium ions containing heterocycles and utilise them for the formation of hetarynes. We wanted to specifically focus on scaffolds that lack known routes for the synthesis of their corresponding Kobayashi precursors, as well as medicinally relevant heterocycles.

1 2-Quinolone Oxonium Ions

1.1 Introduction

1.1.1 2-Quinolones in Medicinal and Synthetic Chemistry

2-Quinolones are a prevalent scaffold in medicinal chemistry.[55] This heterocycle can be found in drugs of a wide range of biological activities, such as antipsychotics, antihistamines and broncholytics (**Figure 5**).[56–58]



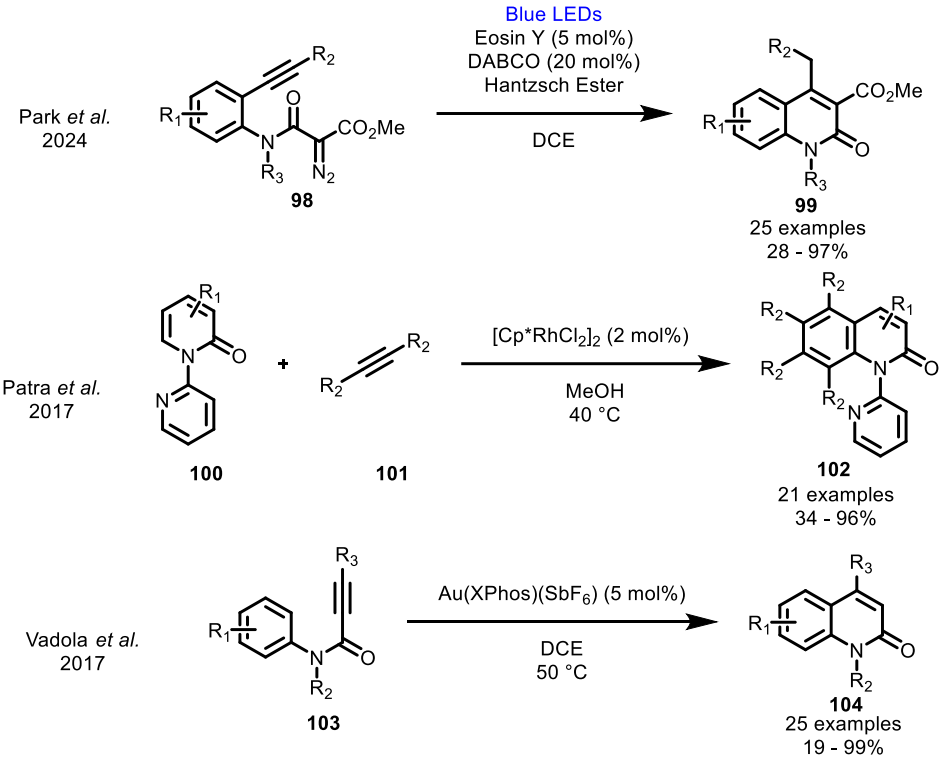
95
Brexpiprazole
Antipsychotic

96
Repirinast
Antihistamine

97
Indacaterol
Bronchodilator

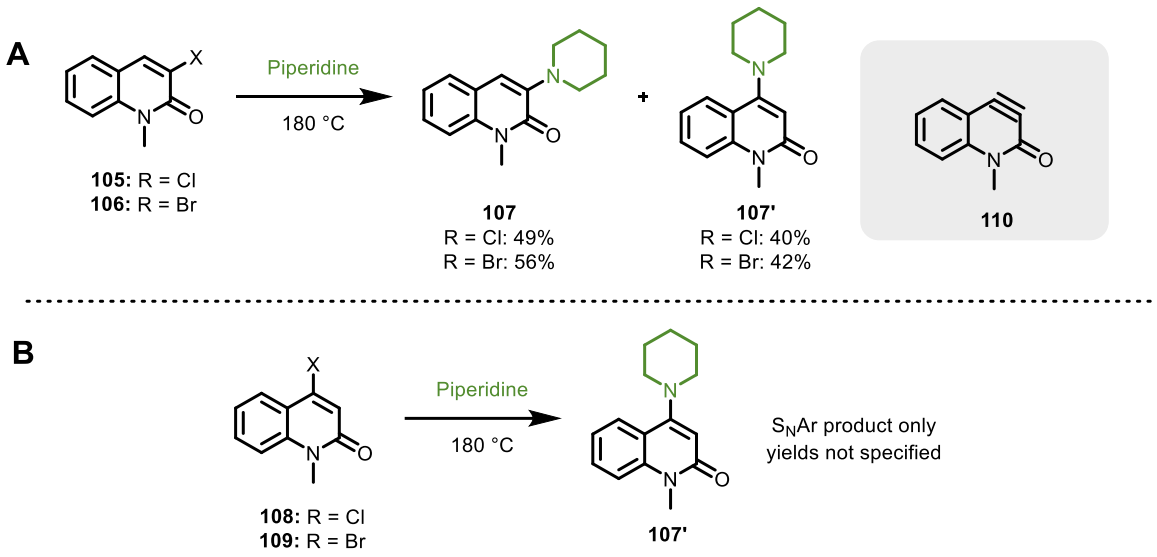
Figure 5. Selected examples of biologically active molecules containing the 2-quinolone scaffold

As a result of this high interest in 2-quinolones, synthetic chemists are in pursuit of novel and reliable synthetic methods for the construction of this motif and, in modern literature, you can find a range of photocatalytic and transition metal-catalysed protocols (**Scheme 15**).[59–62] Although many of them are mild and appear to have good reaction generality, they lack the unique divergence that hetarynes can offer because of their broad reactivity and the potential to directly functionalise a pre-assembled heterocycle.[63]



Scheme 15. Selected modern examples of the synthesis of 2-quinolones

To our knowledge, there is only one example of a 2-quinolone engaging in aryne-like reactivity. In a report by Kauffman *et al*., various 3-halogeno-2-quinolone derivatives were refluxed in piperidine **59** (**Scheme 16**–**A**).[64] In all cases, a mixture of regioisomers was isolated in virtually equal ratios, giving rise to the postulation of intermediate **110**. Contrastingly, if the 4-isomers of the halides were subjected to the same conditions, only 4-piperidino compound **107'** was observed – characteristic of an S_NAr-like mechanism (**Scheme 16**–**B**).[65]



Scheme 16. Seminal work on 2-quinolones by Kauffman et al.

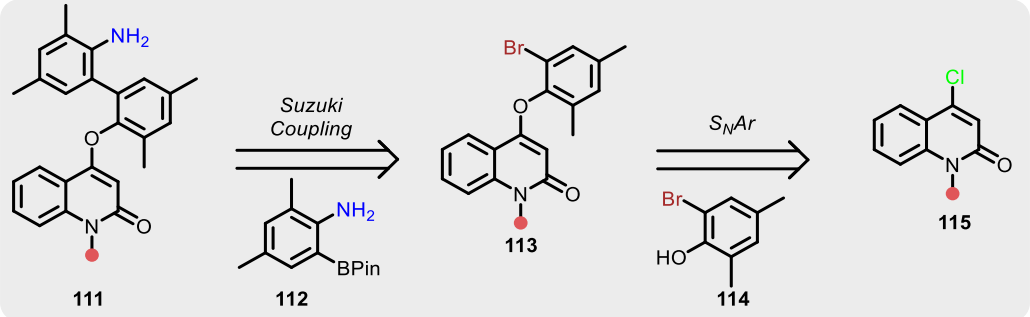
1.1.2 Project Aims

Inspired by Kauffman's foundational work on 2-quinolones from 1964, we decided to develop a synthetic route to synthesise the first 2-quinolone-based oxonium ion and exploit its potential reactivity.

1.2 Results and Discussion

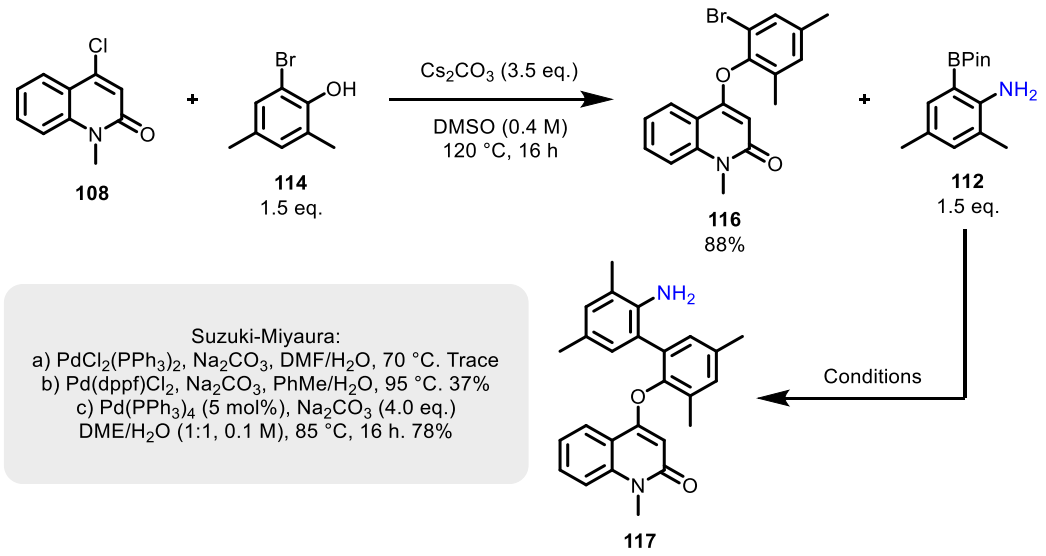
1.2.1 Developing a Synthetic Route to 2-Quinolone Oxonium Ions

In order to synthesise oxonium precursor **111**, we envisaged that we could apply a fragment-based approach by starting with a generic 4-chloro-2-quinolone derivative **115** and coupling it with bromophenol **114** *via* an S_NAr-like substitution,[66] followed by a Suzuki-Miyaura reaction with aniline **112** (**Scheme 17**).[67]



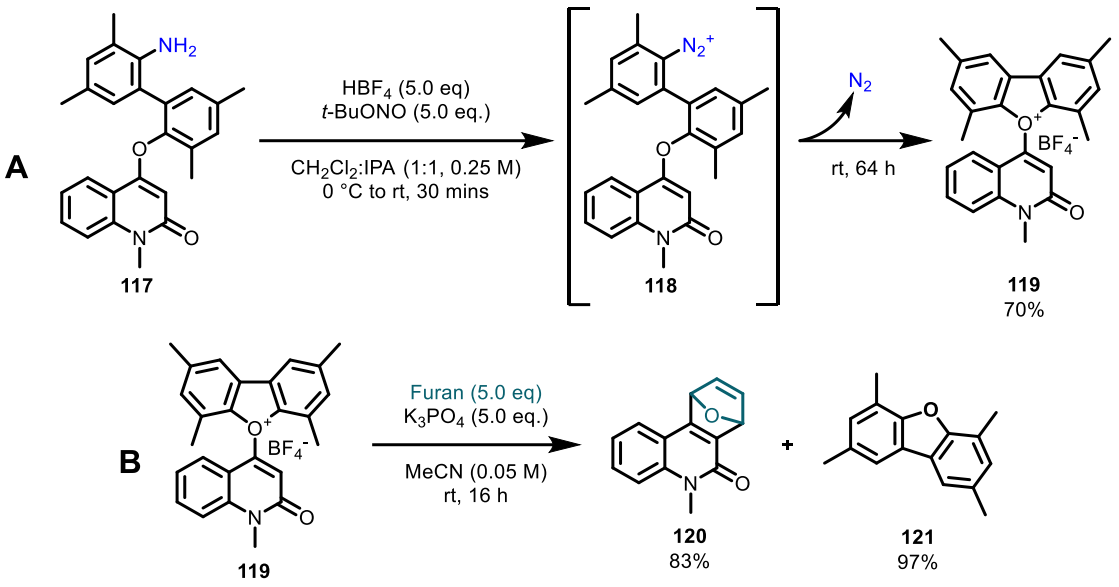
Scheme 17. Retrosynthetic analysis of 2-quinolone oxonium ion precursors from their parent heterocycle

An *N*-methylated quinolone **108** was selected as an initial model system. It was transformed into the ether intermediate **116** in an 88% yield by heating at 120 °C in DMSO under basic conditions with a slight excess of phenol **114** (**Scheme 18**). Then, bromoether **116** was subjected to three sets of conditions for coupling with boronic acid pinacol ester **112**, where $Pd(PPh_3)_4$ was identified as the optimal catalyst for the desired transformation.



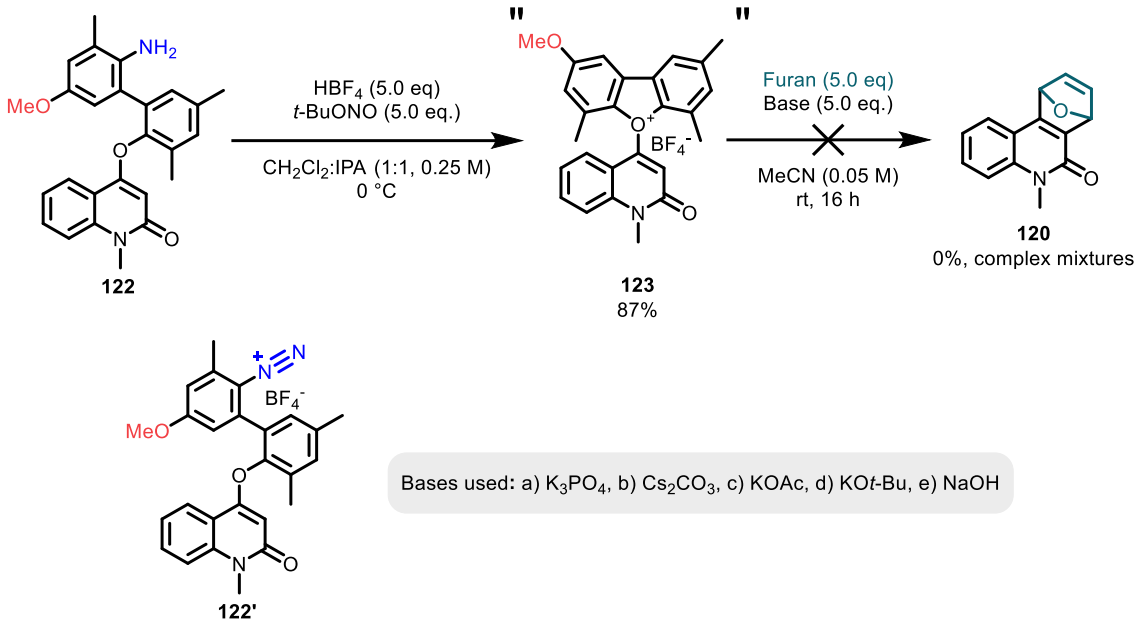
Scheme 18. The forward two-step synthesis of a 2-quinolone oxonium precursor

Having formed a sufficient amount of aniline **117** in our initial studies, we subjected it to diazotisation with *tert*-butyl nitrite and an aqueous solution of HBF_4 (**Scheme 19**).[68] After conversion to the respective diazonium salt, the solution was stirred at room temperature for 64 hours to fully convert **118** into oxonium **119**, which was isolated in a 70% yield following trituration (**Scheme 19**–**A**). Thereupon, the isolated salt was dissolved in acetonitrile along with furan **65**,[69] before adding solid K_3PO_4 and rapidly stirring overnight at room temperature. Pleasingly, furan adduct **120** was formed cleanly in an 83% yield, alongside the dibenzofuran leaving group **121** (**Scheme 19**–**B**).



Scheme 19. Formation of a 2-quinolone oxonium ion and its trapping with furan

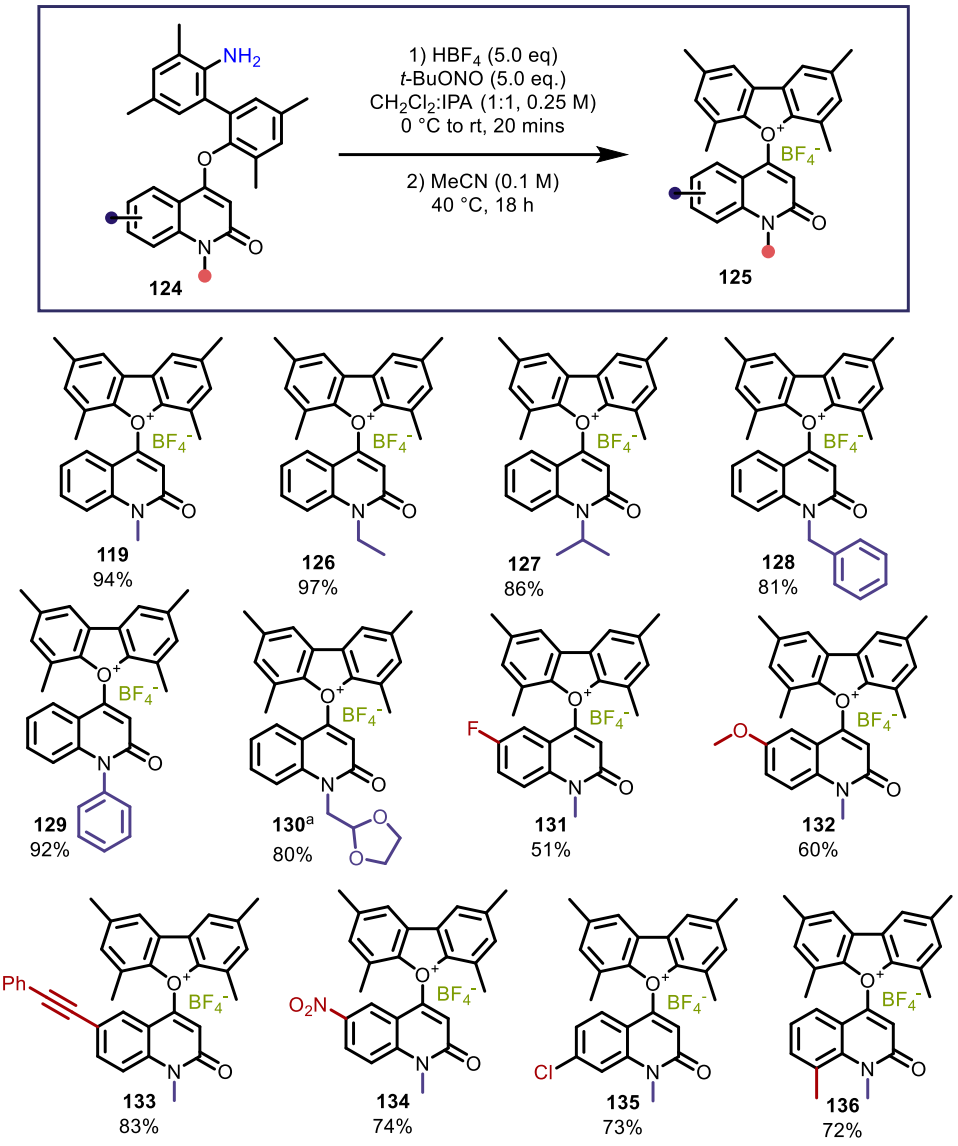
As a way to improve the suboptimal reaction time for the formation of oxonium **119**, we decided to modify the symmetric tetramethyl dibenzofuran scaffold by introducing an electron-donating methoxy group *para* to the aniline moiety as a way to stabilise the presumed aryl cation intermediate.[70] Interestingly, a precipitate was formed almost instantaneously upon a dropwise addition of *tert*-butyl nitrite to the cooled solution of aniline **122** (**Scheme 20**). The collected solid was dissolved in MeCN-d^3 and heated to 40 °C for 16 hours with no change in the overall ^{1}H NMR profile, therefore an assumption was made that the identity of the compound formed was oxonium **123**. Much to our surprise, when subjected to the same furan trapping conditions as used earlier, only non-specific decomposition was observed, even with a range of bases. The lack of desired reactivity possibly suggests that a stable diazonium **122'**, rather than an oxonium ion, was the species formed. This was later confirmed by infrared spectroscopy when the characteristic $N{\equiv}N^+$ absorption band was identified at ~2229 cm^{-1} (see the **Experimental** section for further details).



Scheme 20. The possible formation of a 2-quinolone oxonium ion with a modified scaffold and its unsuccessful trapping

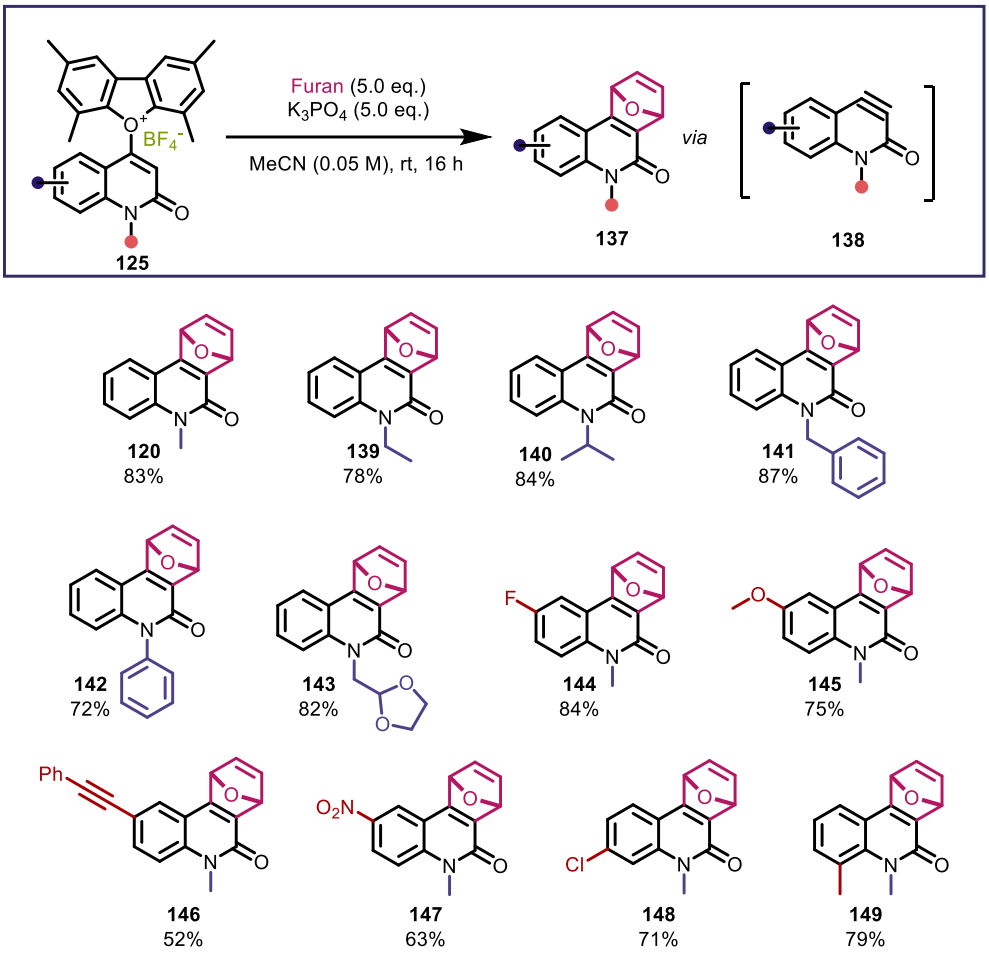
1.2.2 2-Quinolone Oxonium Ion Scope and Trapping with Furan

With a successful initial route to **119**, we were determined to synthesise a diverse scope of 2-quinolone oxonium tetrafluoroborates. We eventually improved the protocol by devising a telescoped two-step process, where aniline **124** was converted to the corresponding diazonium salt in CH_2Cl_2/IPA, followed by a solvent swap and overnight heating at 40 °C in acetonitrile (**Scheme 21**). A total of 12 different examples were produced, which include alkyl, benzyl and phenyl groups on the quinolone nitrogen (**Scheme 21**, **126–130**), as well as functionalities of varying electronic properties on the carbocyclic ring (**Scheme 21**, **131–136**). Pleasingly, all of these oxonium compounds can be synthesised in moderate to excellent yields (51-97%), even on scales of up to 1.16 grams (for compound **119**). Furthermore, these salts are bench stable and can be stored at room temperature.



Scheme 21. 2-Quinolone oxonium tetrafluoroborate scope. a: 1.0 eq. of HBF_4 used

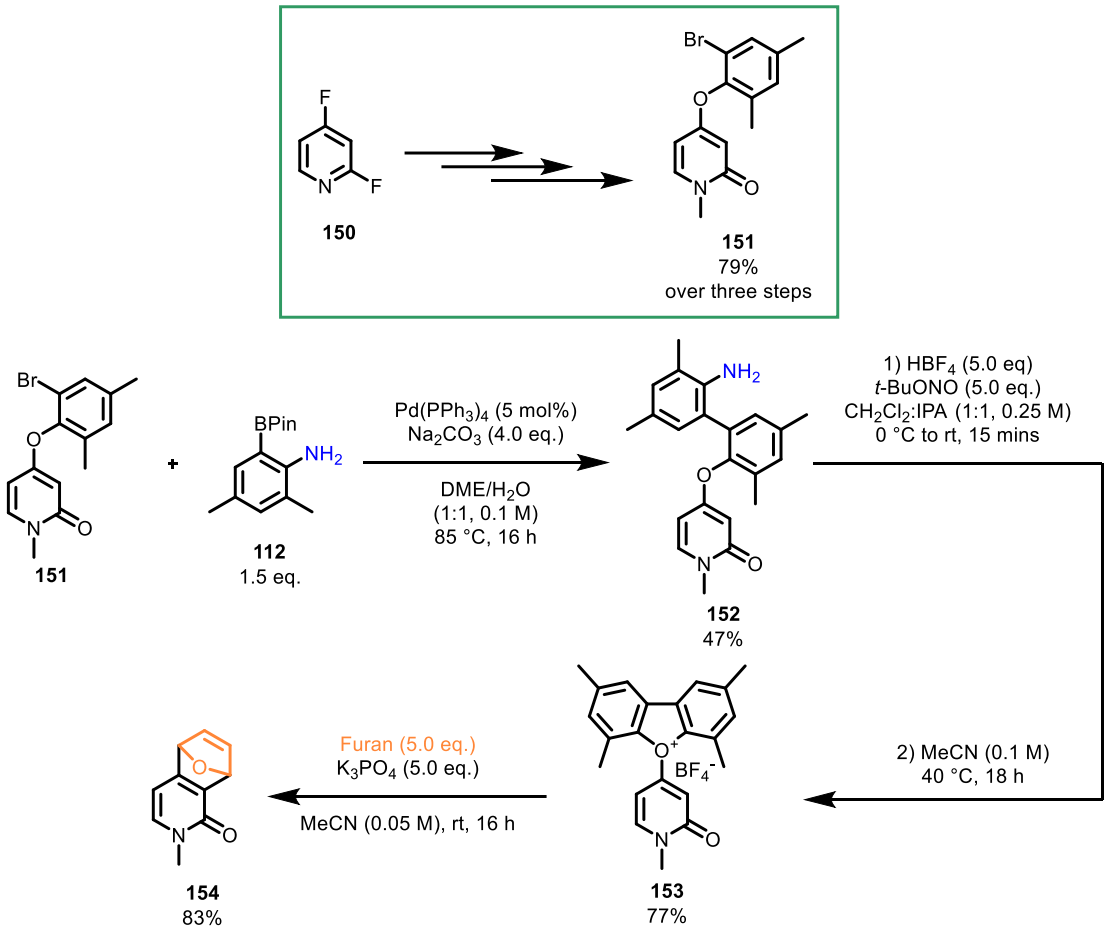
With these oxonium ions at our disposal, we then subjected them to mildly basic conditions for trapping with furan (**Scheme 22**). Unlike some protocols for aryne generation,[71] this method is very operationally simple, where a solution of an oxonium tetrafluoroborate in acetonitrile is rapidly stirred in a vial along with furan and solid K_3PO_4 under air. Pleasingly, on a 0.2 mmol scale, all scope examples trapped with furan in moderate to very good yields.



Scheme 22. 2-Quinolone furan adduct scope

1.2.3 A 2-Pyridone Oxonium Ion and Trapping with Furan

2-Pyridones are essential in pharmaceuticals and agrochemicals.[72] Because of their structural similarity to the 2-quinolone scaffold, we devised a route to synthesise the corresponding oxonium ion from 2,4-difluoropyridine **150** (**Scheme 23**). Regiospecific substitution was observed with bromophenol **114**, affording an ether intermediate, which was subsequently hydrolysed under acidic conditions and methylated. **151** was then coupled with aniline derivative **112** under previously optimised conditions to form precursor **152**, which was finally transformed into the desired oxonium tetrafluoroborate **153** in a 77% yield.



Scheme 23. The synthesis of a 2-pyridone oxonium ion and its reaction with furan

As structure **153** has two α-C–H bonds adjacent to the dibenzofuran nucleofuge, we envisaged the potential formation of two isomeric hetarynes, with the new strained bond forming in either the 3,4- or the 4,5- position (**Figure 6**). Interestingly, only one adduct **154** was isolated in a high yield, presumably, as a consequence of regiospecific deprotonation (**Scheme 23**).

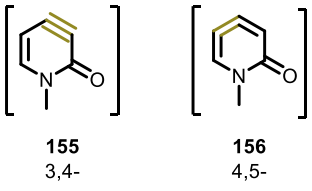


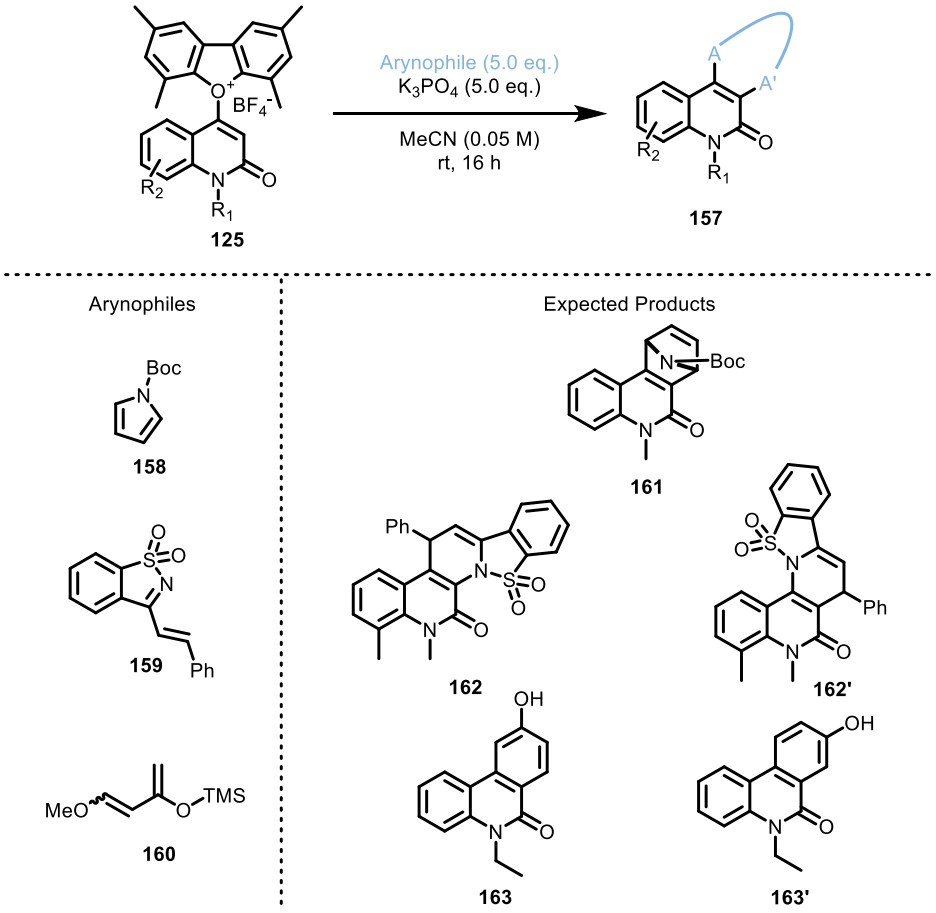
Figure 6. Two isomeric hetarynes that can potentially form by the deprotonation of the 2-pyridone oxonium ion

1.2.4 Exploring the Reactivity of 2-Quinolone Oxonium Ions

Having seen satisfactory yields in the reaction with furan (**Scheme 22**), we decided to further explore the aryne-like reactivity of 2-quinolone-based oxonium ions, starting with the frequently used pericyclic and pericyclic-like transformations.[73] All of the following test reactions were conducted on a 0.025 mmol scale, with the yields determined by quantitative ^{1}H NMR spectroscpoy, utilising the formation of dibenzofuran **121** as a pseudo-internal standard.

1.2.5 Exploring the Reactivity of 2-Quinolone Oxonium Ions. Cycloadditions

In many cases, cycloaddition reactions are convenient for assembling complex molecular structures.[74] Perhaps the most widely employed is the Diels-Alder reaction, where *in situ* generated arynes can be employed as highly reactive dienophiles.[75]



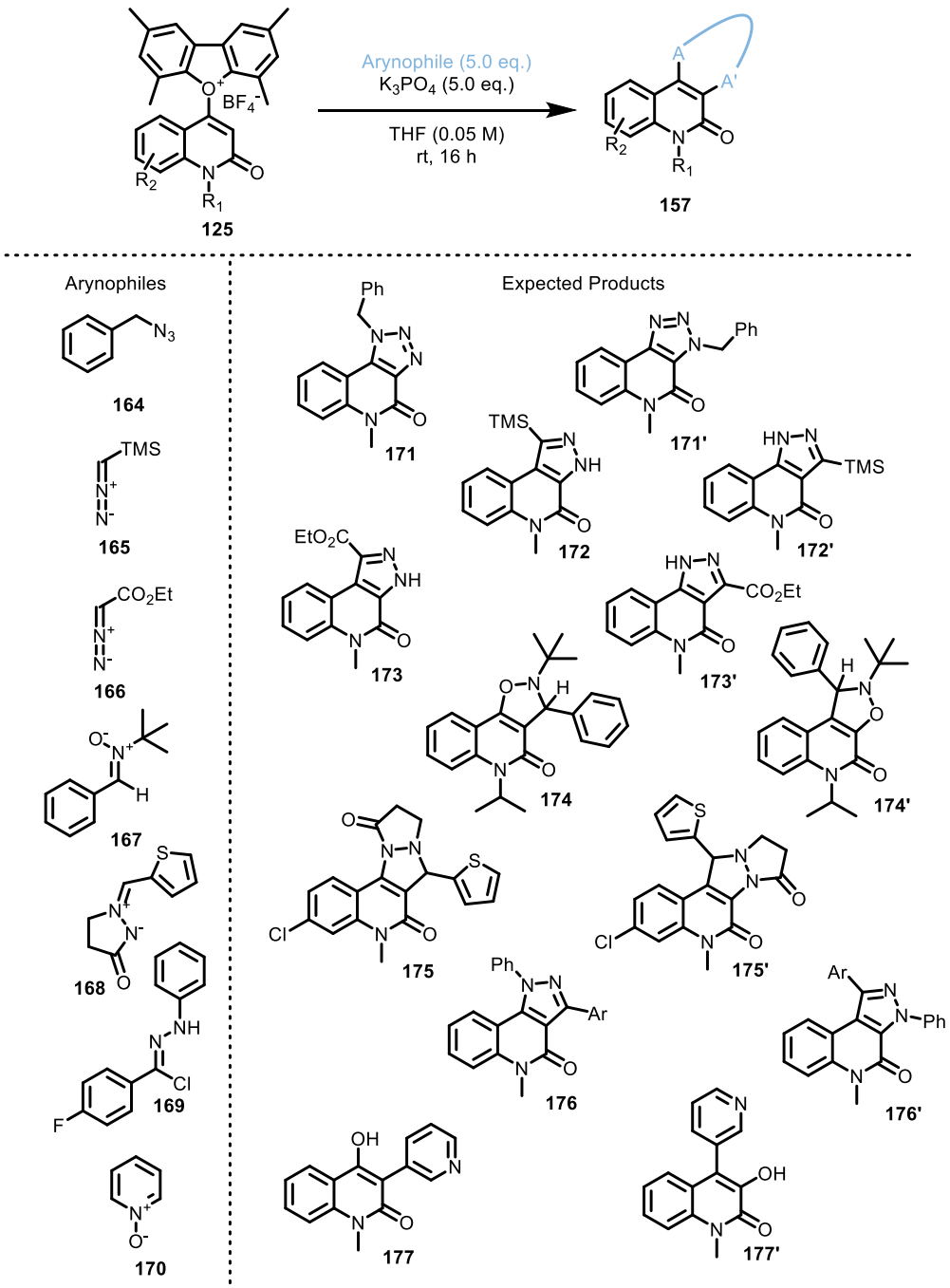
Scheme 24. 2-Quinolone oxonium [4+2] reactivity, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Type	Expected Product	Yield (NMR)[a]
1	Me	H	**158**	[4+2]	**161**	73%
2	Me	Me	**159**	[4+2]	**162** or **162'**	0%[b]
3[c]	Et	H	**160**	[4+2]	**163** or **163'**	22%[d,e]

*Table 1. 2-Quinolone oxonium [4+2] reactivity. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: THF used as solvent. d: one major regioisomer formed. e: the exact structure of the regioisomer(s) could not be determined*

Following the excellent reactivity with furan, we decided to attempt another set of [4+2] additions (**Scheme 24** and **Table 1**), observing adequate reactivity with *N*-Boc-pyrrole **158**,[76] but only non-specific decomposition with saccharin-derived heterodiene **159** (**Entries 1** and **2**).[77] Nevertheless, Danishefsky's diene **160**, which is widely employed in Diels-Alder transformations,[78] produced a reasonable amount of phenol derivative **163** (**Entry 3**).

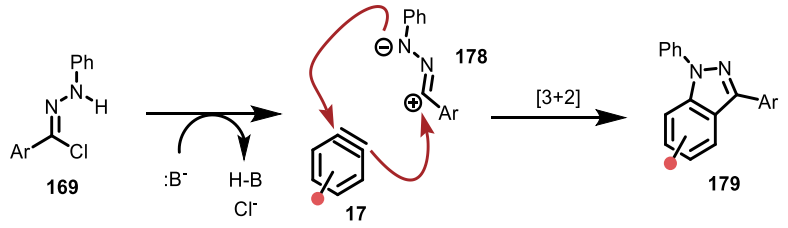
[3+2] Cycloadditions with 1,3-dipoles are an effective way of constructing five-membered ring heterocycles (**Scheme 25** and **Table 2**).[79] Triazole **171** was successfully synthesised using benzyl azide **164**, although with low regioselectivity (**Entry 1**).[80] The application of trimethysilyldiazomethane **165** and related reagent **166** as arynophiles led to complete decomposition (**Entries 2** and **3**),[81] but, pleasingly, nitrone **167** gave cycloadduct **174** in a 86% yield and high regioselectivity (**Entry 4**).[82] Azomethine imine **168** was also not compatible with the 2-quinolone system (**Entry 5**),[83] along with the base-generated nitrile imine **178** (**Entry 6** and **Scheme 26**).[84] The reaction of pyridine *N*-oxide **170** with arynes generated by the Kobayashi method is well established, even with tuneable regioselectivity (**Scheme 27**).[85,86] Unfortunately, analogous products were not observed in our system (**Table 2**, **Entry 7**).



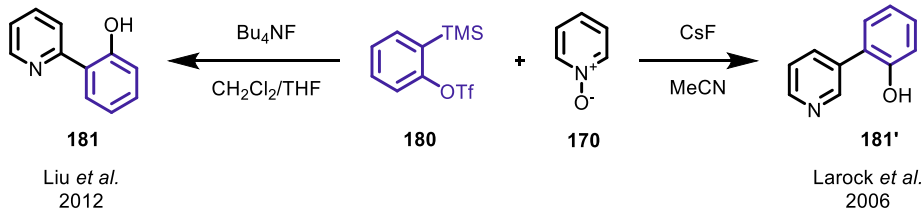
Scheme 25. 2-Quinolone oxonium [3+2] reactivity, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Type	Expected Product	Yield (NMR)[a]
1[c]	Me	H	**164**	[3+2]	**171** or **171'**	65%, 1.5 : 1.0 rr (**171** : **171'**)
2	Me	H	**165**	[3+2]	**172** or **172'**	0%[b]
3	Me	H	**166**	[3+2]	**173** or **173'**	0%[b]
4	*i*-Pr	H	**167**	[3+2]	**174** or **174'**	86%[d]
5	Me	Cl	**168**	[3+2]	**175** or **175'**	0%[b]
6	Me	H	**169**	[3+2]	**176** or **176'**	0%[b]
7	*i*-Pr	H	**170**	[3+2][e]	**177** or **177'**	0%[b]

*Table 2. 2-Quinolone oxonium [3+2] reactivity. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: MeCN used as solvent. d: one major regioisomer formed. e: corresponds to the posited first mechanistic step rather than overall transformation*



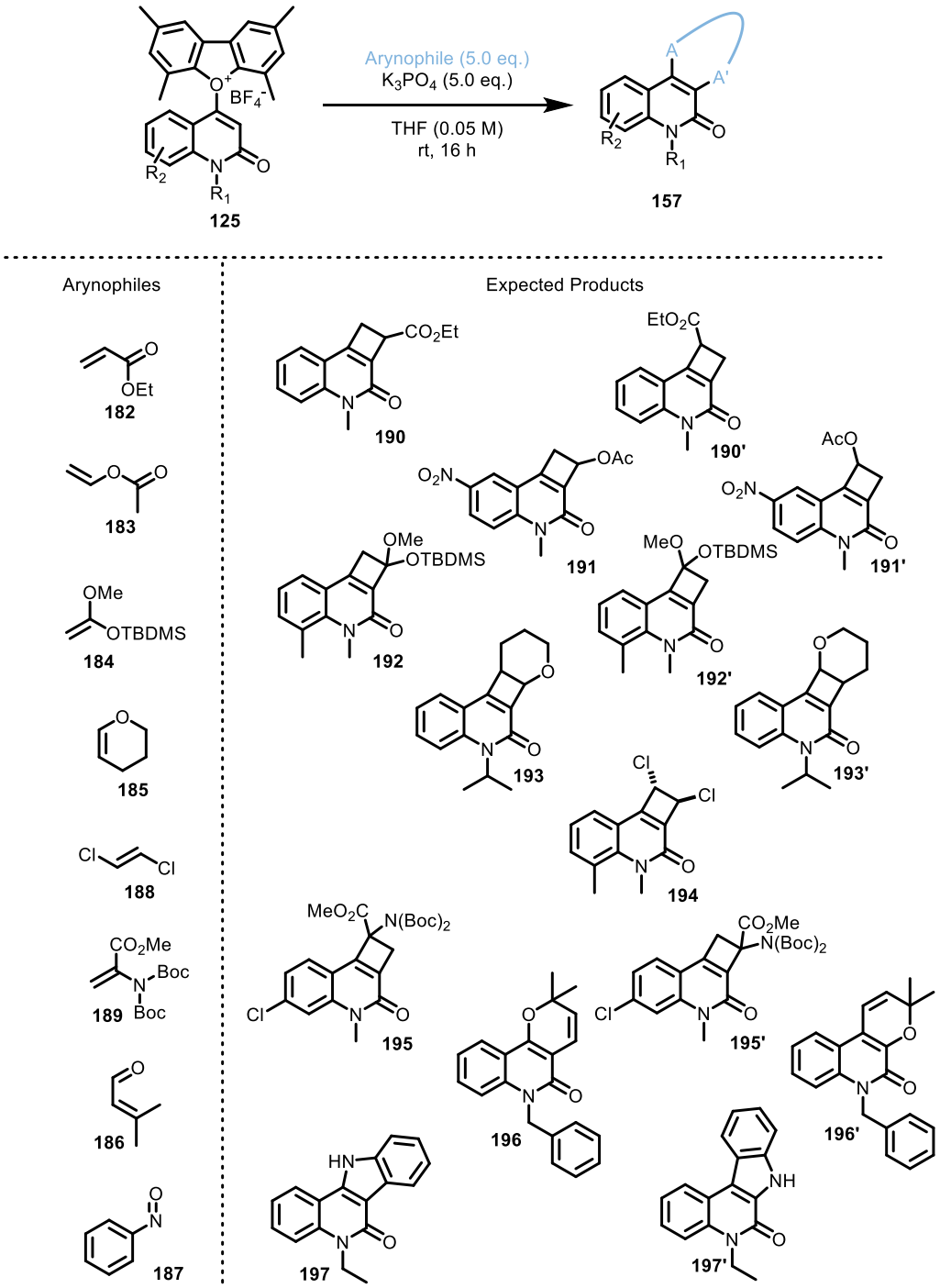
*Scheme 26. The base driven formation of nitrile imine **158** and its subsequent [3+2] reaction with arynes*



Scheme 27. Tuneable regioselectivity in the aryne trapping reaction with pyridine N-oxide reported by the Liu and Larock groups

Because of their characteristic ring strain, the synthesis of cyclobutene derivatives can be challenging, with [2+2] cycloadditions being the most general strategy (**Scheme 28** and **Table 3**).[87] Initial screening for reactivity started unsuccessfully with ethyl acrylate **182** (**Entry 1**),[88] but trace product was observed in the crude NMR spectrum with the more electron rich vinyl acetate **183** (**Entry 2**).[89] Even better yields were detected with more nucleophilic silyl enol ether **184** and 3,4-dihydropyran **185** (**Entries 3** and **4**).[90,91] Similarly to other electron-poor alkenes, trans-1,2-dichloroethene **188** failed to manifest the desired reactivity (**Entry 5**).[92] Dehydroalanine derivative **189** also resulted in complete decomposition (**Entry 6**).[93]

Although not producing a cyclobutane product, both α,β-unsaturated aldehyde **186** and nitrosobenzene **187** are proposed to involve a [2+2] cyclisation step in their reaction with arynes (**Schemes 29** and **30**).[94,95] Pleasingly, regiospecific formation of **196** was observed in high yield under our standard conditions (**Table 3**, **Entry 7**), but only trace carbazole derivative **197** could be detected (**Entry 8**).

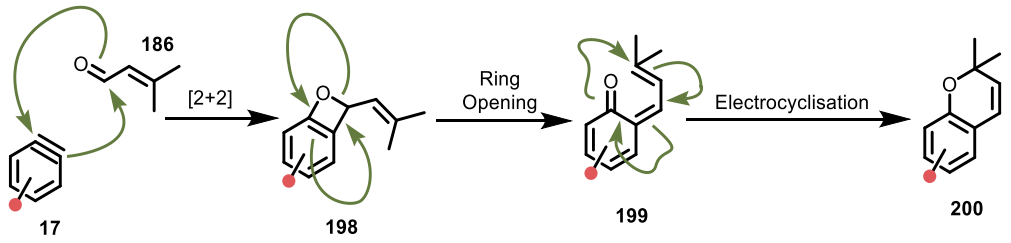


Scheme 28. 2-Quinolone oxonium [2+2] reactivity, arynophiles tested and their expected products

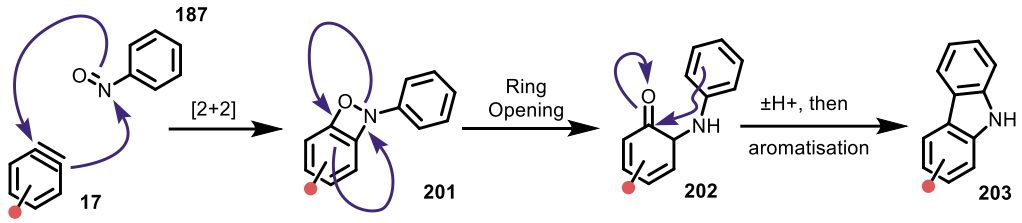
Entry	R_1	R_2	Arynophile	Type	Expected Product	Yield (NMR)[a]
1[c]	Me	H	**182**	[2+2]	**190** or **190'**	0%[b]
2[c]	Me	NO_2	**183**	[2+2]	**191** or **191'**	Trace[f]
3	Me	Me	**184**	[2+2]	**192** or **192'**	35%, 4.8 : 1.0 rr[g]
4	*i*-Pr	H	**185**	[2+2]	**193 or 193'**	81%, 1.6 : 1.0 rr[g]
5[c]	Me	Me	**188**	[2+2]	**194**	0%[b]

6	Me	Cl	**189**	[2+2]	**195** or **195'**	0%[b]
7	Bn	H	**186**	[2+2][e]	**196** or **196'**	81%[d,g]
8	Et	H	**187**	[2+2][e]	**197** or **197'**	Trace[f]

*Table 3. 2-Quinolone oxonium [2+2] reactivity. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: MeCN used as solvent. d: one major regioisomer formed. e: corresponds to the posited first mechanistic step rather than overall transformation. f: <5% with target m/z detected in LRMS. g: the exact structure of the regioisomer(s) could not be determined*



Scheme 29. The mechanism of the reaction between arynes and enals, as proposed by Wu et al.



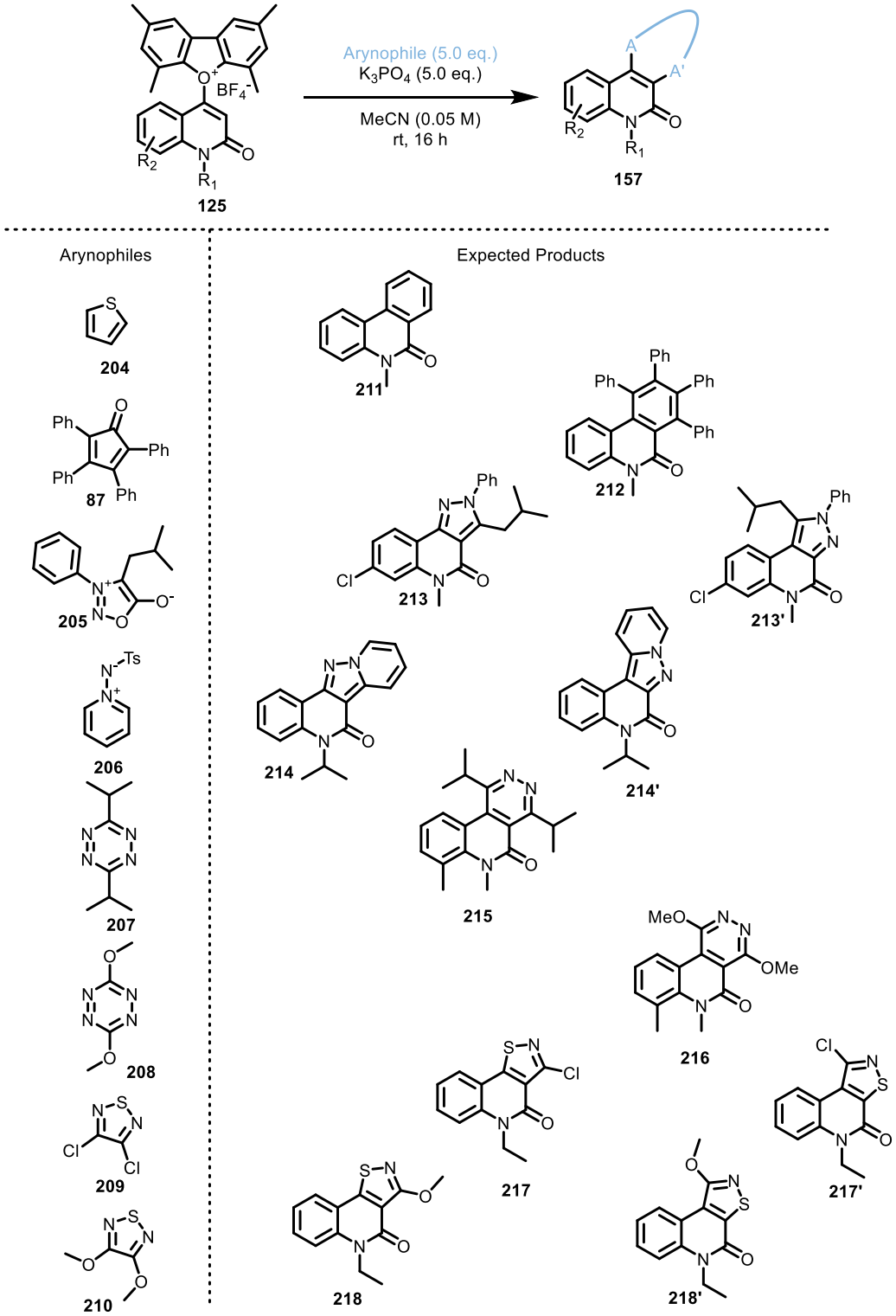
Scheme 30. The mechanism of the reaction between arynes and nitrosoarenes, as proposed by Studer et al.

1.2.6 Exploring the Reactivity of 2-Quinolone Oxonium Ions. Pericyclic Reactions Involving the Loss of a Small Molecule

Some pericyclic transformations include mechanistic steps where a gas or a charged molecule is released.[96] Usually these are entropically-favoured cheletropic or cycloreversion processes, resulting in rearomatisation.[97]

Owing to its lower degree of aromaticity when compared to benzene,[98] thiophene is known to form naphthalene by the extrusion of sulfur in the presence of benzyne **1** (**Scheme 31** and **Table 4**).[99] This known transformation, however, did not translate to the 2-quinolone system (**Entry 1**). Desired product formation was achieved with both tetracyclone **87** and sydnone **205**, where only a single regioisomer was observed (**Entries**

2 and **3**).[100,101] Ylide **206** produced indazole derivative **214** in excellent regioselectivity, where a tosylate leaving group is lost in order to facilitate aromatisation (**Entry 4**).[102]



Scheme 31. 2-Quinolone oxonium reactivity in reactions that release a small molecule, arynophiles tested and their expected products

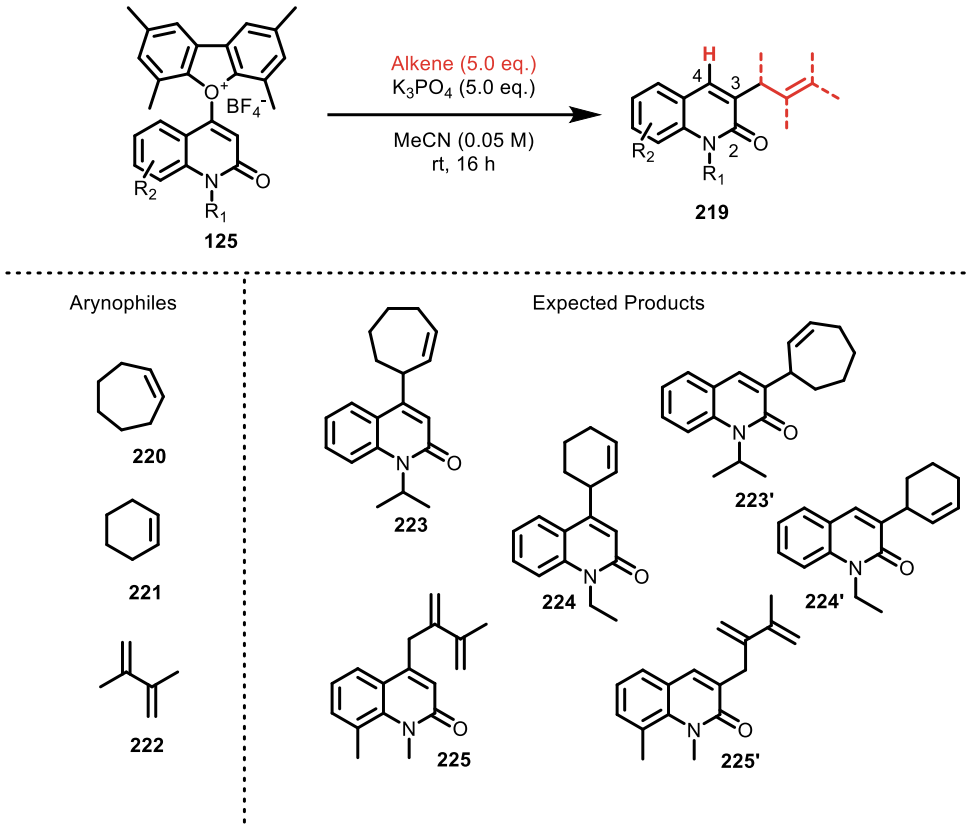
Entry	R_1	R_2	Arynophile	Leaving Group	Expected Product	Yield (NMR)[a]
1	Me	H	**204**	S	**211**	0%[b]
2	Me	H	**87**	CO	**212**	55%
3[c]	Me	Cl	**205**	CO_2	**213** or **213'**	90%[d,e]
4	*i*-Pr	H	**206**	Ts^-	**214** or **214'**	51%[d,e]
5[c]	Me	Me	**207**	N_2	**215**	0%[b]
6[c]	Me	Me	**208**	N_2	**216**	0%[b]
7	Et	H	**209**	ClC≡N	**217** or **217'**	35%, 1.6 : 1.0 rr[e]
8	Et	H	**210**	MeOC≡N	**218** or **218'**	96%, 1.6 : 1.0 rr[e]

*Table 4. 2-Quinolone oxonium reactivity in reactions that release a small molecule. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: THF used as solvent. d: one major regioisomer formed. e: the exact structure of the regioisomer(s) could not be determined*

As a consequence of their high reactivity and excellent yields in inverse-electron-demand Diels-Alder reactions, tetrazine derivatives are widely employed as reactive dienes.[103] Unfortunately, both tetrazine **207** and more electron rich dimethoxy-substituted **208** resulted in complex mixtures only (**Table 4**, **Entries 5** and **6**).[104] Contrastingly, thiadiazole **209** trapped the aryne sufficiently (**Entry 7**),[105] but a considerate boost in yield was observed when methoxy groups were incorporated in arynophile **210** (**Entry 8**).

1.2.7 Exploring the Reactivity of 2-Quinolone Oxonium Ions. Alder-Ene Reactions

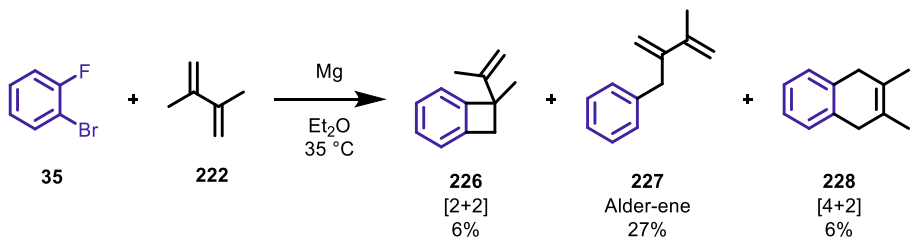
The ene-like reactivity of arynes has been known since the early 1960s,[106] providing an attractive way of forging carbon–carbon bonds with readily available alkenes (**Scheme 32** and **Table 5**).[107] Initially, we trialled two cyclic alkenes – cycloheptene **220** and cyclohexene **221** (**Entries 1** and **2**).[108] Excellent preference for the 3- position was noted in both cases, albeit in low yields. Pleasingly, an uplift in yield was observed with the use of dimethylbutadiene **222** (**Entry 3**). Interestingly, these conditions resulted in **225'** as the only aryne trapping product detected by ^{1}H NMR, despite the fact that other modes of reactivity have been reported with benzyne **1** in the literature (**Scheme 33**).[109,110]



Scheme 32. 2-Quinolone oxonium reactivity in Alder-ene reactions, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Expected Product	Yield (NMR)[a]
1[b]	*i*-Pr	H	220	223 or 223'	29%[c]
2	Et	H	221	224 or 224'	15%[c,d]
3	Me	Me	222	225 or 225'	46%[c]

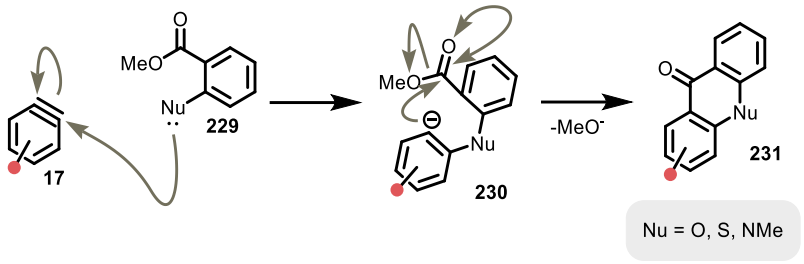
*Table 5. 2-Quinolone oxonium reactivity in Alder-ene reactions. a: yield determined assuming quantitative formation of **121**. b: THF used as solvent. c: one major regioisomer formed with C–C bond formation at the 3- position. d: isolated yield reported*



*Scheme 33. Benzyne trapping reaction with dimethylbutadiene **211** reported by Wittig and Durr*

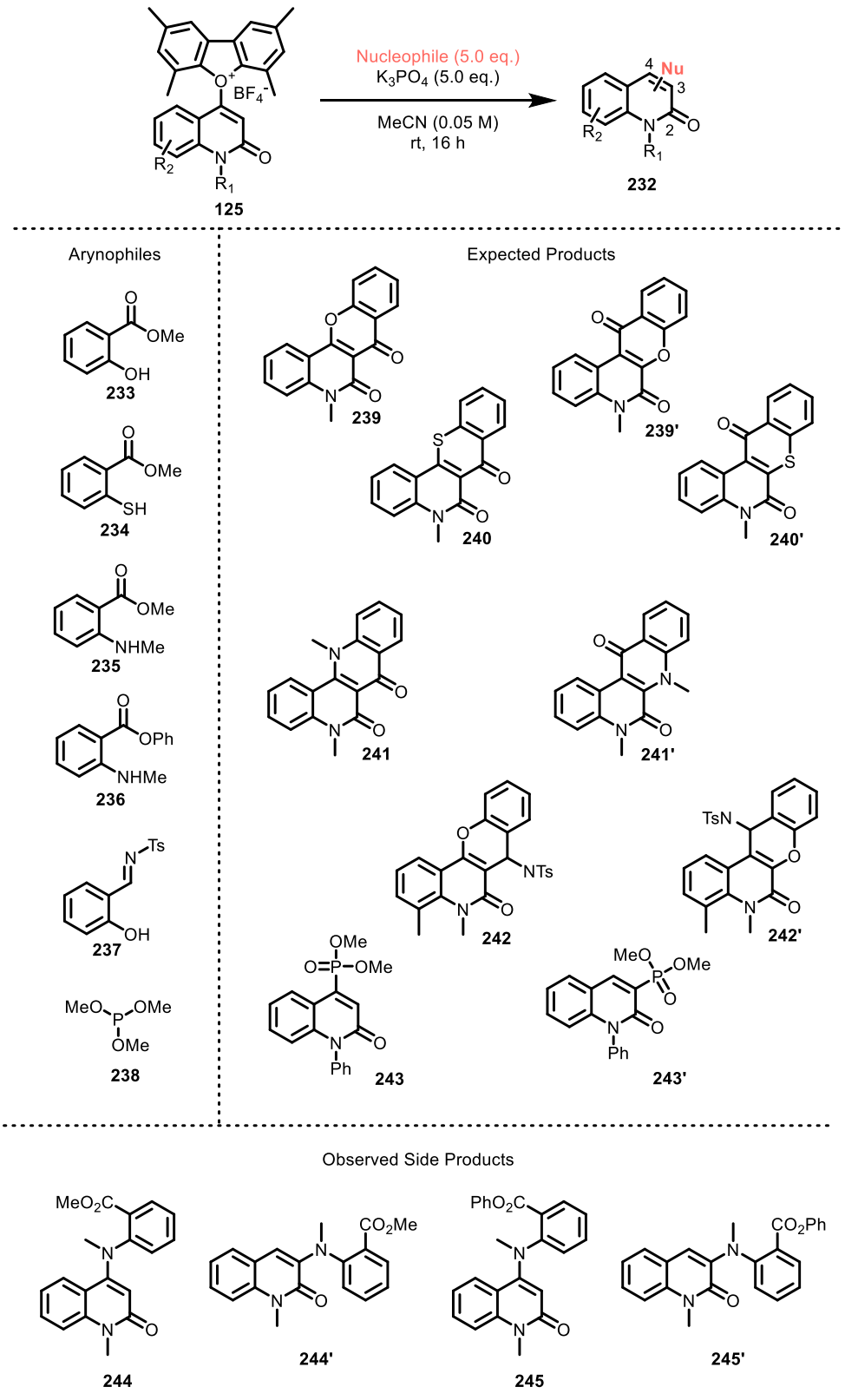
1.2.8 Exploring the Reactivity of 2-Quinolone Oxonium Ions. Nucleophiles

Arynes are indispensable when it comes to transition-metal-free arylation reactions, and can be used for both carbon-carbon and carbon-heteroatom bond formation.[111] Our initial studies focused on the reactivity of the 2-quinolone oxonium system with various heteroatom-centred nucleophiles. Typically, when a nucleophile attacks the triple bond of an aryne, a carbanion is generated on the vicinal carbon (**Scheme 34**, **230**). This is widely exploited in aryne multicomponent and annulation reactions.[112]



Scheme 34. Tandem aryne trapping reaction reported by Larock et al.

In 2006, Larock and co-workers published a tandem strategy for forming biologically-relevant xanthone, thioxanthone and acridone scaffolds (**Scheme 34**).[113] Inspired by their work, we decided to screen a number of *ortho*-substituted methyl benzoates, anticipating cyclised products (**Scheme 35** and **Table 6**). Disappointingly, phenol **233** and thiophenol **234** led to decomposition (**Entries 1** and **2**), while methylaniline derivative **235** provided two regioisomers **244** and **244'** without subsequent cyclisation (**Entry 3**). Moreover, ring formation could not be forced by switching to a phenolate leaving group and similar reactivity to the methyl ester was observed (**Entry 4**). Furthermore, attempted annulation with *N*-tosyl imine **237** was also unsuccessful (**Entry 5**).[114]

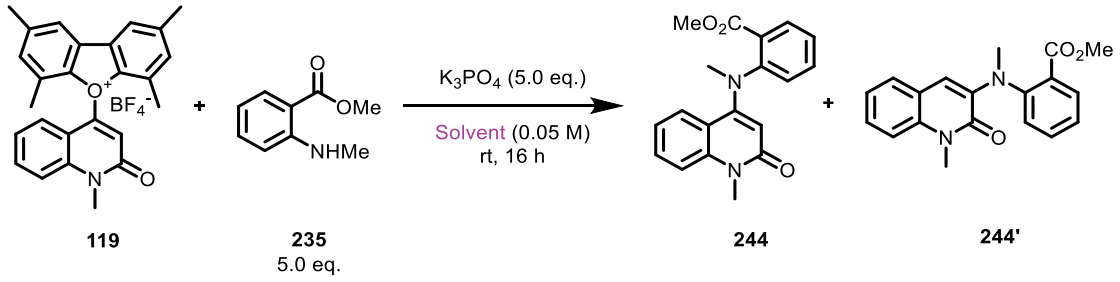


Scheme 35. 2-Quinolone oxonium reactivity with nucleophiles, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Expected Product	Yield (NMR)[a]
1	Me	H	233	239 or 239'	0%[b]
2	Me	H	234	240 or 240'	0%[b]
3	Me	H	234	241 or 241'	74%, 1.4 : 1.0 rr (244 : 244')
4[c]	Me	H	236	241 or 241'	72%, 9.3 : 1.0 rr (245' : 245)
5[c]	Me	Me	237	242 or 242'	0%[b]
6	Ph	H	238	243 or 243'	32%[d] (243')

*Table 6. 2-Quinolone oxonium reactivity with nucleophiles. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: THF used as solvent. d: one major regioisomer formed.*

As a way to modulate intermolecular proton transfer and encourage cyclisation, a solvent screen was conducted for the arylation reaction with dimethyl anthranilate (**Scheme 36** and **Table 7**). Unfortunately, no acridone formation was observed in any solvents that were tested. Interestingly, although the overall yield was practically unaffected by the change in solvent, the regioselectivity varied significantly. In fact, regioisomer **244** was the major product only in acetonitrile (**Entry 1**), and became the minor product in acetone, dimethoxyethane and THF (**Entries 3**, **4** and **5**).



Scheme 36. A solvent screen for the 2-quinolone oxonium reaction with dimethyl anthranilate

Entry	Solvent	Yield (NMR)	Regioisomeric Ratio (244 : 244')
1	MeCN	74%[a]	1.4 : 1.0
2	CH_2Cl_2	63%[b]	1.0 : 1.0
3	Acetone	62%[b]	1.0 : 1.3
4	DME	59%[b]	1.0 : 3.6
5	THF	60%[b]	1.0 : 4.2

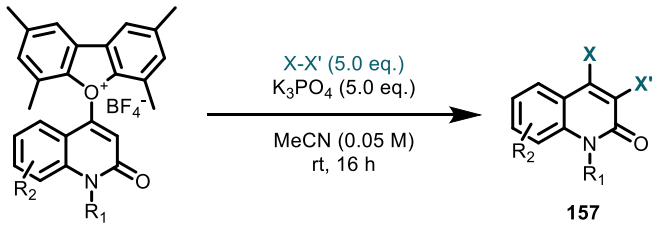
*Table 7. Solvent screen for the 2-quinolone oxonium reaction with dimethyl anthranilate. a: yield determined by using **121** as a pseudo-internal standard. b: yield determined by using 1,3,5-trimethoxybenzene as an internal standard*

In view of the fact that organophosphorus compounds are important in many areas of applied chemistry,[115] trimethyl phosphite **238** was also tested as a nucleophile for

arylation.[116] Pleasingly, Arbuzov-like product **243'** was detected in excellent regioselectivity towards the 3- position (**Table 6**, **Entry 6**).

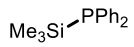
1.2.9 Exploring the Reactivity of 2-Quinolone Oxonium Ions. σ-Insertion Reactions

Arynes have been reported to formally 'insert' into a variety of single bonds, forming 1,2-disubstituted aromatic compounds that can be difficult to synthesise *via* conventional methods (**Scheme 37** and **Table 8**).[6] Our preliminary studies focused on the insertion reactions into dihetero bonds, where both Si–P and Sn–F bond-containing reagents failed to give their expected products (**Entries 1** and **2**).[117] In contrast, diiodination with iodine **249** and diselenylation with diphenyl diselenide **250** cleanly afforded their respective products in useful yields (**Entries 3** and **4**).[118,119] No formal σ-insertion reactivity was observed with *N*-chlorosuccinimide **251**, but the corresponding 4-chloro-2-quinolone side-product **262** was isolated in an 18% yield (**Entry 5**).



125 157

Arynophiles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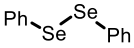
248


249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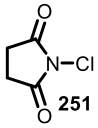
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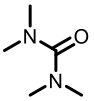
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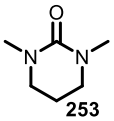
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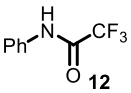
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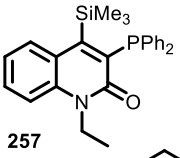
252


255


256

Expected Products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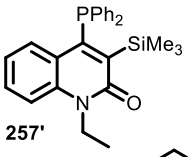
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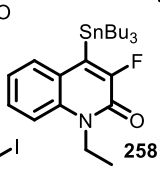
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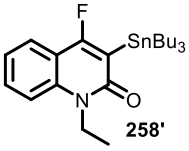
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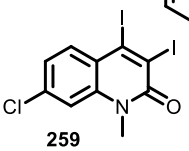
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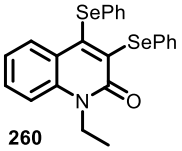
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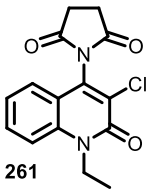
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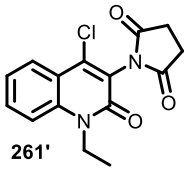
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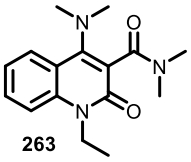
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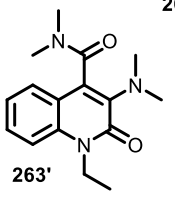
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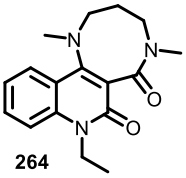
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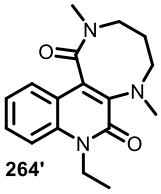
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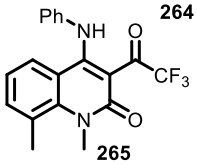
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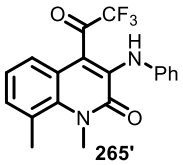
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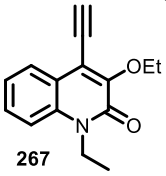
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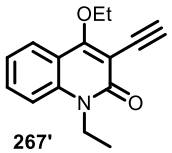
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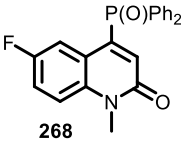
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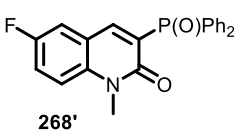
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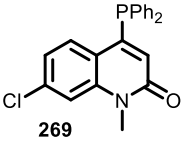
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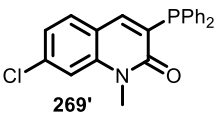
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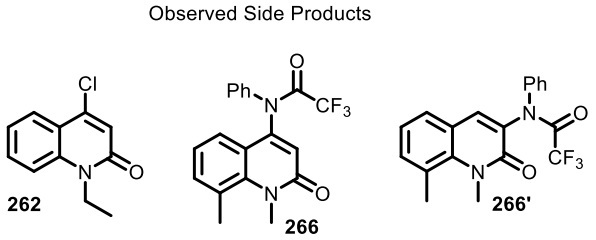


Scheme 37. 2-Quinolone oxonium reactivity in σ-insertion reactions with heteroatom-containing bonds, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Bond	Expected Product	Yield (NMR)[a]
1[c]	Et	H	**247**	Si–P	**257** or **257'**	0%[b]
2[c]	Et	H	**248**	Sn–F	**258** or **258'**	0%[b]
3	Me	Cl	**249**	I–I	**259**	38%
4[c]	Et	H	**250**	Se–Se	**260**	75%
5	Et	H	**251**	N–Cl	**261** or **261'**	18%[e] (**262**)
6	Et	H	**252**	C–N	**263** or **263'**	37%, 2.1 : 1.0 rr[f]
7	Et	H	**253**	C–N	**264** or **264'**	11%[d,f]
8[c]	Me	Me	**12**	C–N	**265** or **265'**	57%, 2.0 : 1.0 rr (**266** : **266'**)
9[c]	Et	H	**254**	C–O	**267** or **267'**	3%[e,f]
10[c]	Me	F	**255**	P–H	**268** or **268'**	0%[b]
11[c]	Me	Cl	**256**	P–H	**269** or **269'**	0%[b]

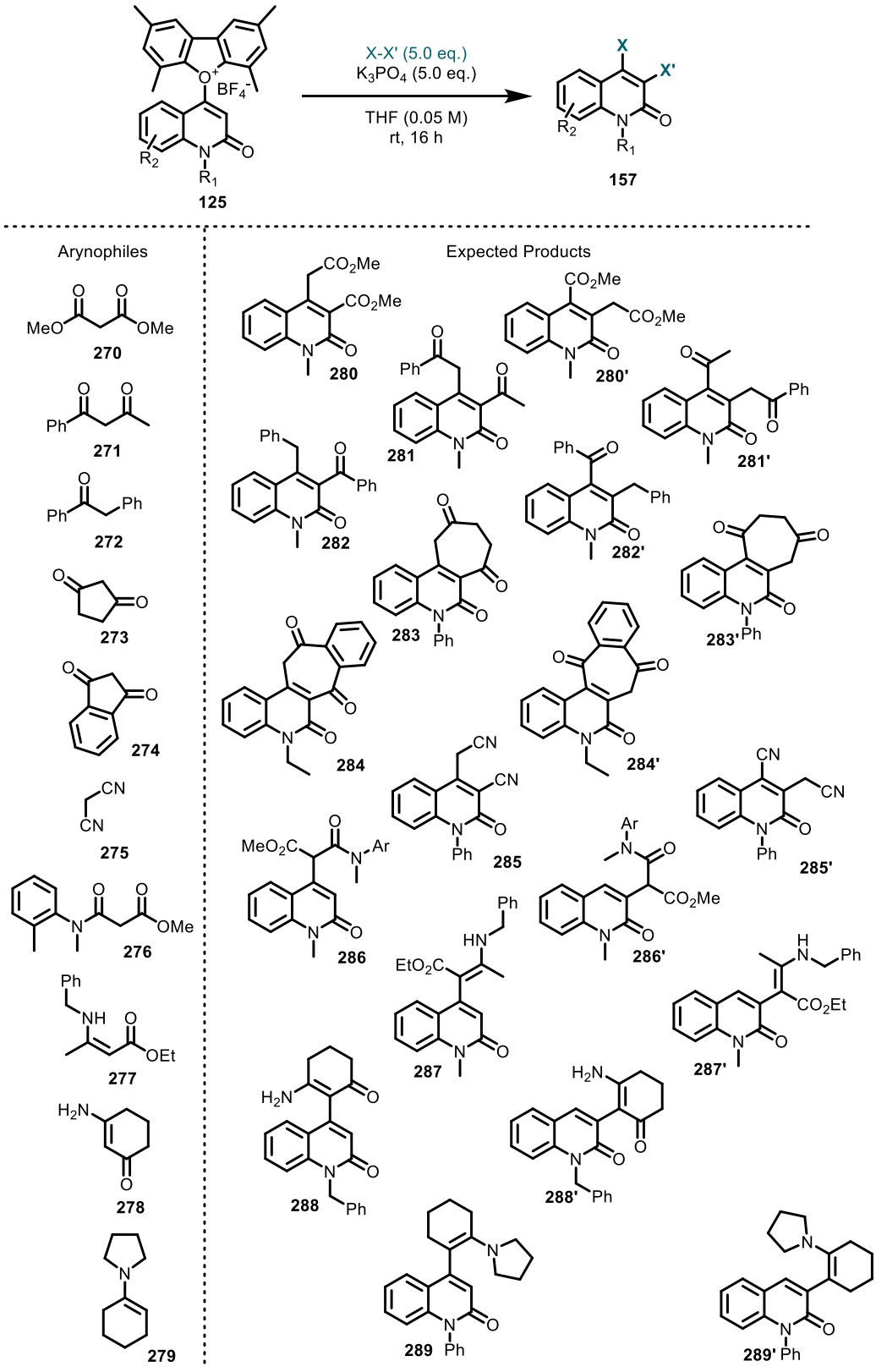
*Table 8. 2-Quinolone oxonium reactivity in σ-insertion reactions with heteroatom-containing bonds. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: THF used as solvent. d: one major regioisomer formed. e: isolated yield reported. f: the exact structure of the regioisomer(s) could not be determined*

Both urea **252** and cyclic urea **253** gave desired C–N insertion products, albeit in poor yields (**Entries 6** and **7**).[120] An analogous C–N insertion was not successful with amide **12** and direct N-arylation was observed as the major reaction pathway, favouring addition into the 4-position (**Entry 8**).[121] Additionally, C–O cleavage in ethoxyacetylene was detected in a low, but isolable, yield (**Entry 9**),[122] and, finally, P–H insertion failed with **255** and **256** (**Entries 10** and **11**).[123]

After some success with C–Heteroatom bonds, we decided to shift our focus to insertion reactions that formally cleave C–C or C–H bonds (**Scheme 38** and **Table 9**).[124] In the chemistry of Kobayashi aryne precursors, various β-dicarbonyl compounds are known to engage in facile reactivity towards 1,2- functionalisation.[125] We started our screening by

investigating the potential reactivity with dimethyl malonate **270**, which, in all cases, was pre-stirred with base prior to the addition of the oxonium, in order to pre-form some of the enolate. Unfortunately, only non-specific decomposition of the oxonium tetrafluoroborate was observed, even at different temperatures and in the presence of stronger base KO*t*-Bu (**Entry 1**). Comparably, no expected product was formed with the more acidic diketone **271** (**Entry 2**) and only trace product with 2-phenylacetophenone **272** (**Entry 3**). Interestingly, the reaction with 1,3-cyclopentanedione **273** gave two regioisomers in a combined 25% yield (**Entry 4**),[126] but upon subjecting the crude mixture to silica gel column chromatography, decomposition of these products was observed. Thereafter, a reduction in the yield was noted with 1,3-indandione **274**,[127] and full decomposition with malononitrile **275** (**Entries 5** and **6**).[128]

In contrast to β-diketone derivatives, malonamide esters normally react by α-arylation in the presence of arynes,[129] however, no expected product was observed with **276** under standard conditions, even with KO*t*-Bu as a strong base (**Table 9**, **Entry 7**). The desired reactivity was obtained with β-ketoester-derived enamine **277** (**Entry 8**). A similar yield and regioselectivity was observed with β-enamino ketone **278**,[130] but use of the more nucleophilic enamine **279** led to an indecipherable crude mixture (**Entries 9** and **10**).[131]



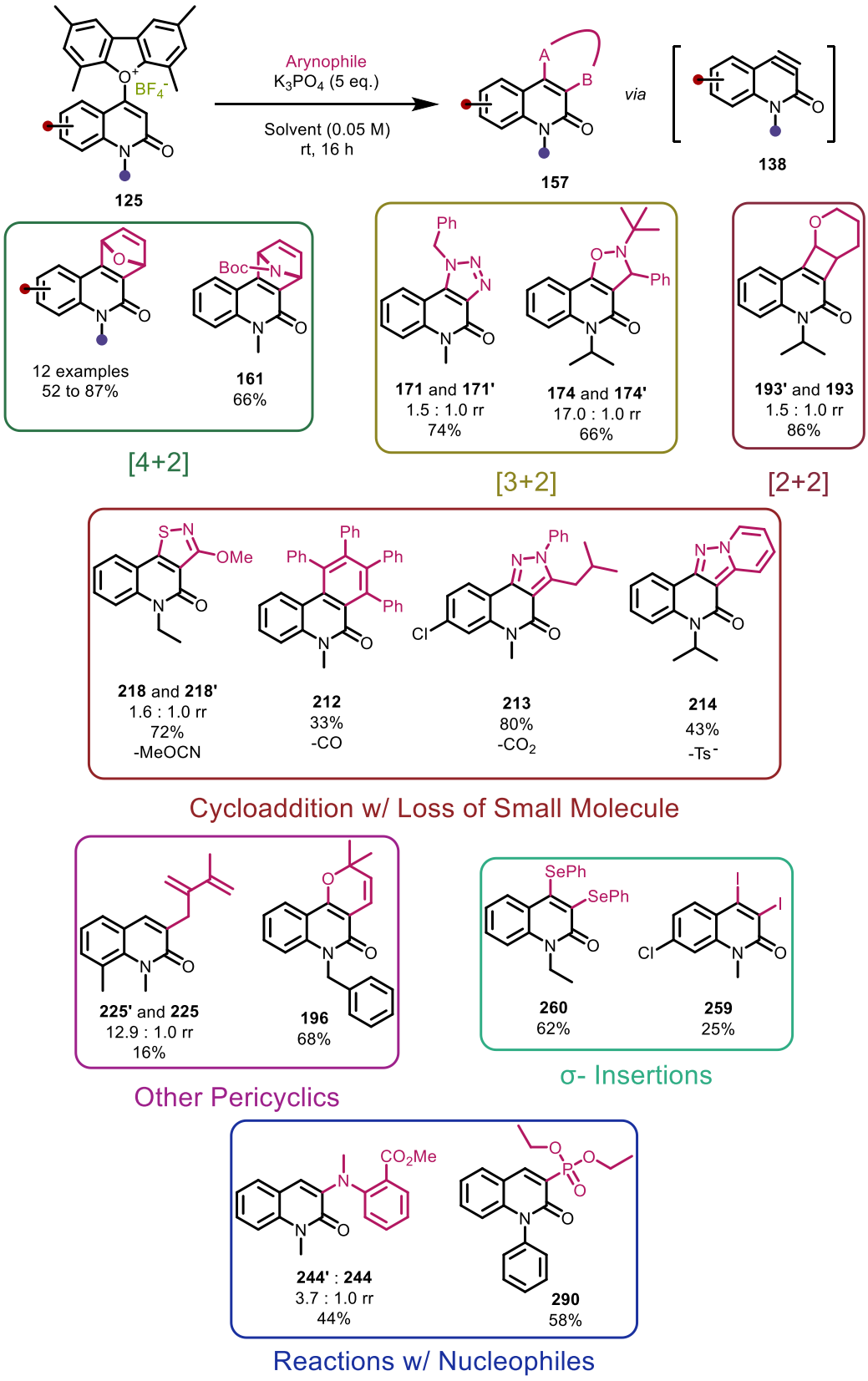
Scheme 38. 2-Quinolone oxonium reactivity in σ-insertion reactions with carbon-containing bonds, arynophiles tested and their expected products

Entry	R_1	R_2	Arynophile	Bond	Expected Product	Yield (NMR)[a]
1	Me	H	**270**	C-C	**280** or **280'**	0%[b,e,f]
2[c]	Me	H	**271**	C-C	**281** or **281'**	0%[b]
3	Me	H	**272**	C-C	**282** or **282'**	Trace[g]
4	Ph	H	**273**	C-C	**283** or **283'**	25%, 1.8 : 1.0 rr[h]
5[c]	Et	H	**274**	C-C	**284** or **284'**	12%[i]
6[c]	Ph	H	**275**	C-C	**285** or **285'**	0%[b]
7	Me	H	**276**	C-H	**286** or **286'**	0%[b,e]
8[d]	Me	H	**277**	C-H	**287** or **287'**	21%, 2.0 : 1.0 rr[h]
9	Bn	H	**278**	C-H	**288** or **288'**	19%, 2.2 : 1.0 rr[h]
10	Ph	H	**279**	C-H	**289** or **289'**	0%[b]

*Table 9. 2-Quinolone oxonium reactivity in σ-insertion reactions with carbon-containing bonds. a: yield determined assuming quantitative formation of **121**. b: complex mixture formed. c: MeCN used as solvent. d: DME used as solvent. e: both K_3PO_4 and KOt-Bu tested. f: tested at rt, 0 °C and 66 °C. g: <5% with target m/z detected in LRMS. h: the exact structure of the regioisomer(s) could not be determined. i: one major regioisomer formed*

1.2.10 Scaled-up 2-Quinolone Oxonium Ion Reaction Scope

With various results from the previous reactivity screen, we decided to scale-up 14 selected transformations to 0.2 mmol, in some cases applying modifications to the reaction conditions (**Scheme 39**). The Diels-Alder reaction with N-Boc pyrrole afforded product **161** in a 66% isolated yield. Isomeric triazoles **171** and **171'** were successfully synthesised in a combined 74% yield and separated by flash column chromatography. The [3+2] transformation producing product **174** was also successfully scaled-up, with the larger scale allowing a facile determination of the regioisomeric ratio. By virtue of its volatility, the formal [2+2] cycloaddition with 3,4-dihydropyran was performed neat, exhibiting not only a higher yield of products **193** and **193'**, but also a cleaner reaction profile, aiding purification.



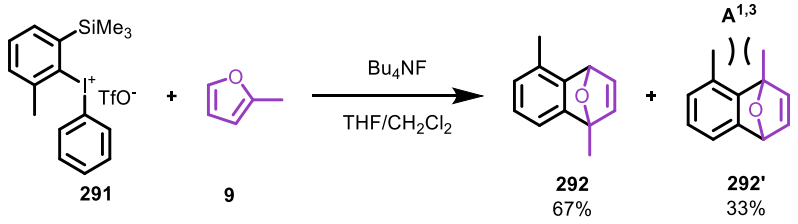
Scheme 39. The full scope of 2-quinolone oxonium ion reactions, scaled up to 0.2 mmol. In each case, the structure of the major regioisomer is depicted.

3,4-Dimethoxy-1,2,5-thiadiazole **210** gave a separable mixture of compounds **218** and **218'** in a 72% yield, however, their exact structures could not be determined unambiguously by ROESY and NOESY experiments. Owing to the poor solubility of tetracyclone **87**, a reduced yield of adduct **212** was isolated as a result of a challenging purification. On the other hand, the reaction with sydnone **205** resulted in a high yield after straightforward purification, where 80% of a single regioisomer **213** was isolated. Similarly, the synthesis of **214** also went in a regiospecific fashion, affording the heterocycle in a 43% yield.

Interestingly, upon scale-up, a depletion in yield was observed for the Alder-ene product **225'**, which meant that the minor regioisomer could not be isolated for full characterisation. Moreover, as anticipated, pyran derivative **196** formed regiospecifically, in a 68% yield.

The two highest-yielding σ-insertion reactions were also subjected to scale-up, providing products **260** and **259** in a 62% and 25% yield, respectively. THF was selected as the solvent for the arylation of dimethyl anthranilate, as it provided the highest regioisomeric ratio and preference for the 3- position in product **244'**, which corresponds to the overall yield, as the minor isomer could not be isolated in sufficient purity. Finally, the reaction with triethylphosphite afforded compound **290** in a 58% yield. Only one equivalent of the arynophile was used, as this prevented unwanted side-reactions.

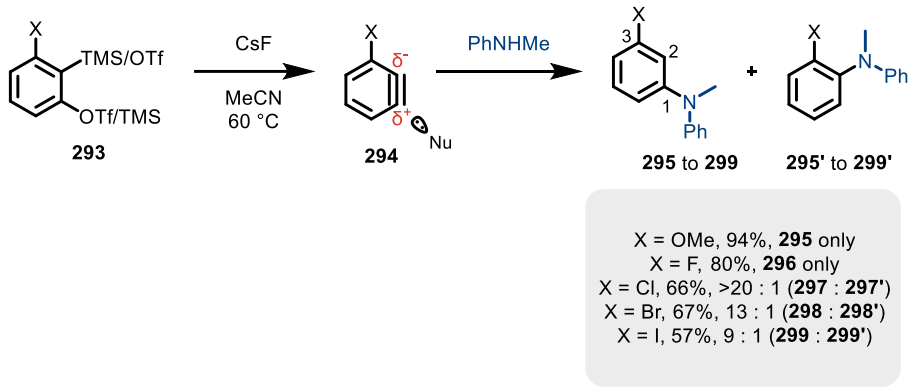
1.2.11 A Comment on Regioselectivity



Scheme 40. A reaction between an aryne and 2-methylfuran illustrating regioselectivity as proposed by the steric model

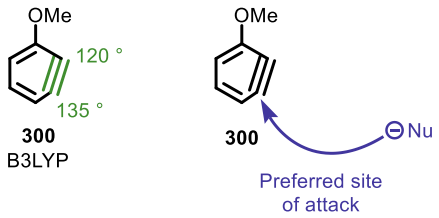
There are three widely-accepted models for determining the regioselectivity of reactions involving arynes: the steric, the charge-controlled and the aryne distortion models.[132]

In the simplest of these models, steric hinderance in the products, and, indirectly, the transition state, determines the selectivity. For instance, in the Diels-Alder reaction between hypervalent iodine aryne precursor **291** and 2-methylfuran **9**, a two-fold preference for adduct **292** is observed as a result of the lower 1,3-allylic strain (**Scheme 40**).[133,134]



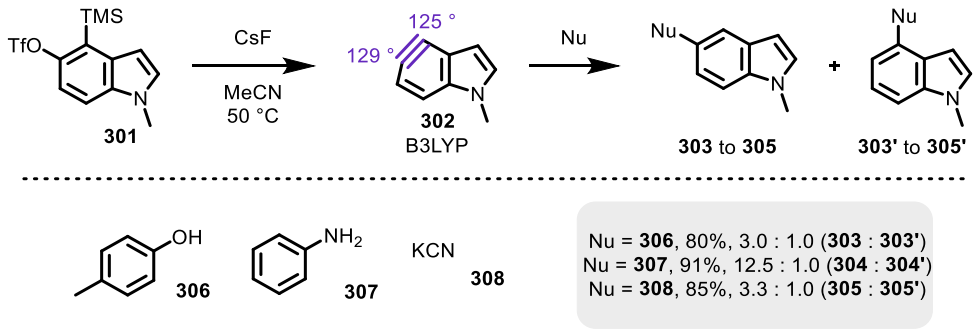
Scheme 41. An aryne reaction with N-methylaniline and its trend in regioselectivity with respect to the electronegativity of the heteroatom

In the charge-controlled model, an electronegative atom, usually halide, polarises the triple bond *via* the inductive effect, attracting nucleophiles towards the *meta* position (**Scheme 41**, **294**).[132] This selectivity is markedly reflected in a series of aryne trapping reactions with *N*-methylaniline. Sole nucleophilic addition to the 1- position was observed with arynes bearing the most inductively-withdrawing substituents, such as the methoxy group or fluoride. Mixtures of regioisomers were formed with the other halogens, with the selectivity decreasing in accordance with electronegativity.



Scheme 42. The computed internal angles of 3-methoxybenzyne and the preferred site of nucleophilic attack

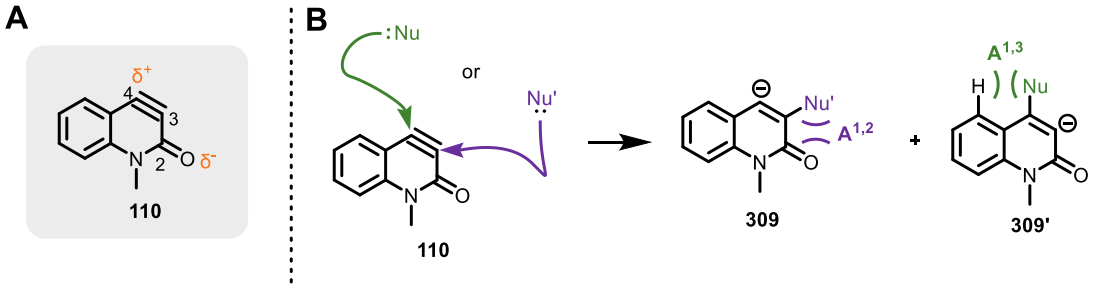
More recently, the distortion/interaction model was applied to aryne chemistry by Houk, Garg and co-workers.[135] In this computational model, distortions to the geometry of the aryne are considered, with nucleophilic addition favoured at the carbon that requires the minimum reorganisation to achieve the structure of the transition state, i.e. the carbon with the larger internal angle, as exemplified by 3-methoxybenzyne **300** (**Scheme 42**). These quantum-mechanical calculations have been successful in predicting the regioselectivities in systems where the other two models cannot be applied without ambiguity, such as 4,5-indolyne (**Scheme 43**).[136]



Scheme 43. 4,5-Indolyne reaction with various nucleophiles and its trend in regioselectivity as predicted by the distortion/interaction model

Analysis of a hypothetical 2-quinolone-derived aryne **110** by the qualitative charge-controlled model, we would expect nucleophilic attack to be favoured at the 4- position (**Scheme 44**–**A**). However, examining the structures of its nucleophilic trapping products, we see the contrary: triethylphosphite was incorporated into the 3- position and in many

solvents dimethyl anthranilate also preferred the same site (**Scheme 39**, Structures **290** and **244**; **Table 7**).

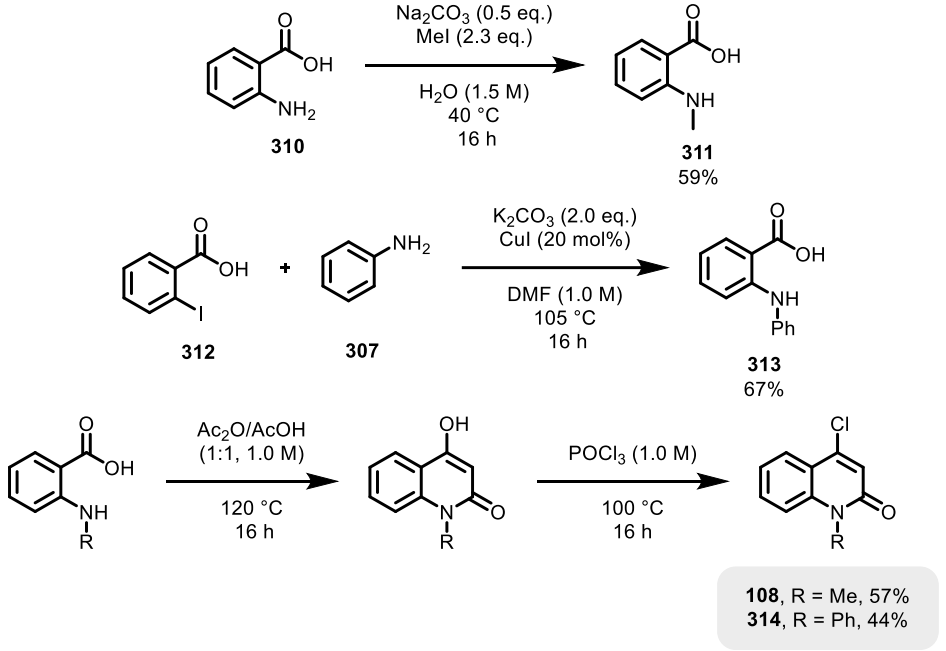


Scheme 44. The charge-controlled and steric models applied to a hypothetical 2-quinolone aryne

The application of the steric model is not as clear-cut. If the nucleophile approaches the 3- position, we can envisage 1,2-allylic strain developing between the carbonyl oxygen and the new substituent (**Scheme 44–B**, **309**).[137] In parallel, 1,3-allylic strain is of concern if the addition takes place at the 4- position (**Scheme 44–B**, **309'**) and appears to be the primary rationale for the high selectivities in products **174**, **213** and **214** (**Scheme 39**). Further investigation into the patterns of selectivity is needed for the 2-quinolone aryne system, with the quantitative distortion model yet to be applied.

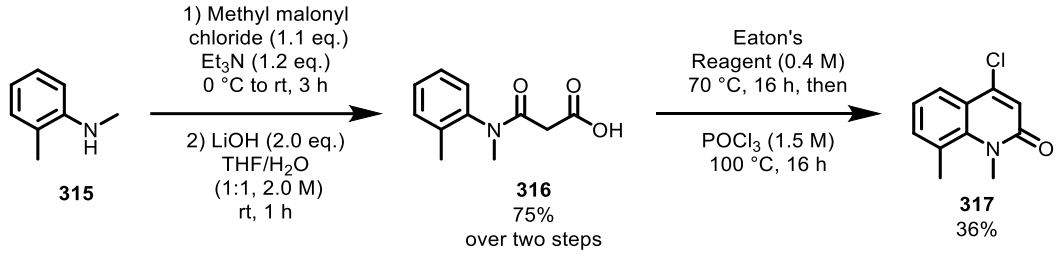
1.3 Synthesis

1.3.1 4-Chloro-2-Quinolone Derivatives



Scheme 45. The synthesis of N-substituted anthranilic acid derivatives and their use as intermediates in the production of 4-chloro-2-quinolones

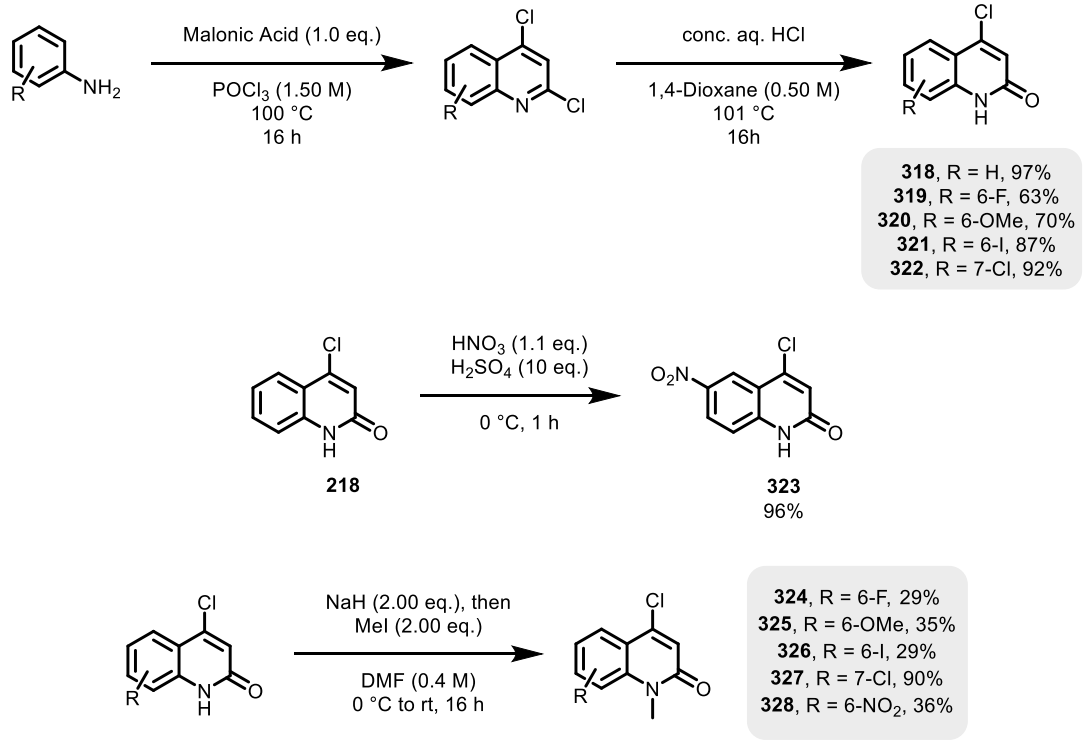
The 4-chloro-2-quinolone derivatives used for the synthesis of oxonium ions have been made in various ways. For instance, the examples containing methyl and phenyl groups on the quinolone nitrogen (**108** and **314**, respectively) were synthesised from their corresponding anthranilic acid derivatives (**Scheme 45**), whereas quinolone **317**, bearing a methyl group in the 8- position, was produced by an Eaton's Reagent-promoted Friedel-Crafts acylation (**Scheme 46**).



*Scheme 46. A three-step synthesis of 2-quinolone derivative **317** from its respective methylaniline*

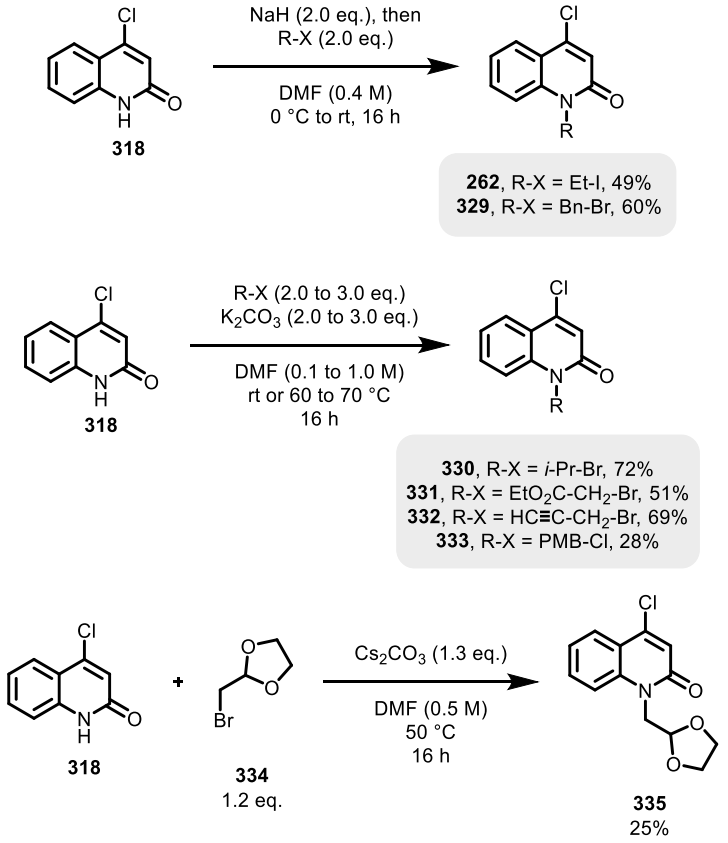
The majority of the compounds with substituents on the carbocyclic ring, however, were accessed directly from their respective anilines, first forming 2,4-dichloroquinoline

derivatives (**Scheme 47**). The 2- position was then selectively hydrolysed under acidic conditions, followed by methylation of the unsubstituted nitrogen. Due to the lower reactivity 4-nitroaniline, a nitro group was introduced via the acid-catalysed nitration of quinolone **218**.



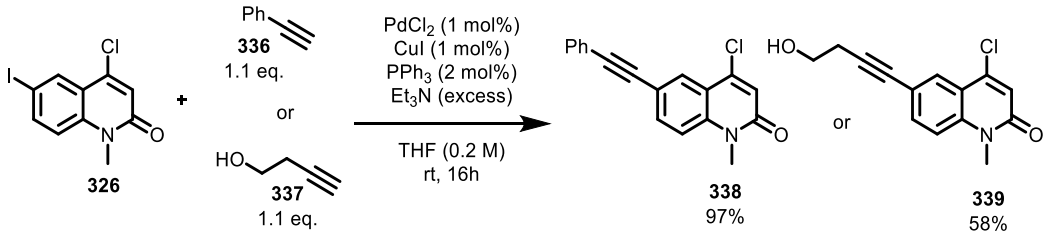
Scheme 47. Synthesis of N-methylated 4-chloro-2-quinolones with substituents on the carbocyclic ring

Non-methyl substituents were introduced in a similar fashion, by either employing NaH as a strong base, or relying on weaker carbonate bases and elevated temperatures (**Scheme 48**).



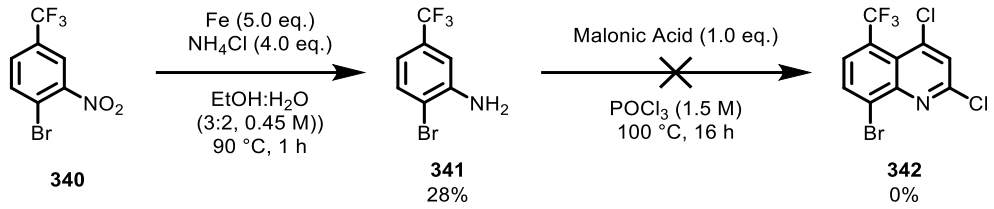
Scheme 48. The introduction of non-methyl substituents onto 4-chloro-2-quinolones

By using iodine as functional handle on 2-quinolone **326**, we were able to introduce two internal alkyne substituents onto compounds **338** and **339** *via* Sonogashira coupling (**Scheme 49**).



Scheme 49. Synthesis of substituted 4-chloro-2-quinolones via Sonogashira coupling

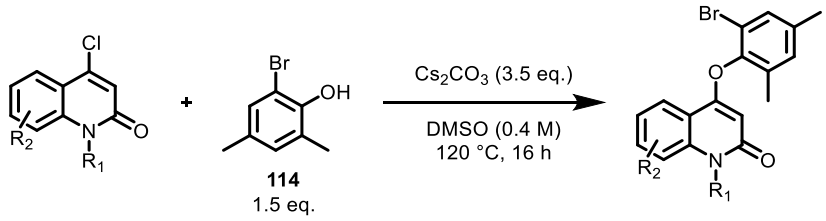
Unfortunately, introducing a substituent into the 5- position was not trivial, as reaction between aniline **341** and malonic acid in $POCl_3$ did not give the desired intermediate, but rather a complex mixture of products (**Scheme 50**).

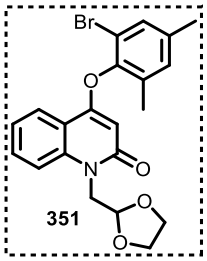


Scheme 50. An unsuccessful attempt to synthesise a 2,4-dichloroquinoline intermediate with a trifluoromethyl group in the 5- position

1.3.2 2-Quinolone and 2-Bromophenol Ether Derivatives

2-Quinolone and 2-bromophenol ether derivatives were mostly made by the base-mediated reaction of 4-chloro-2-quinolones and bromophenol **114** in DMSO, heating overnight at 120 °C (**Scheme 51**). However, not all examples were compatible with these conditions. We observed no reactivity with unsubstituted quinolone **318**. In other cases, full decomposition was noted, such as in the use of a pendant ester or a terminal alkyne group in **331** and **332**, as well as a free alcohol in quinolone **339**.



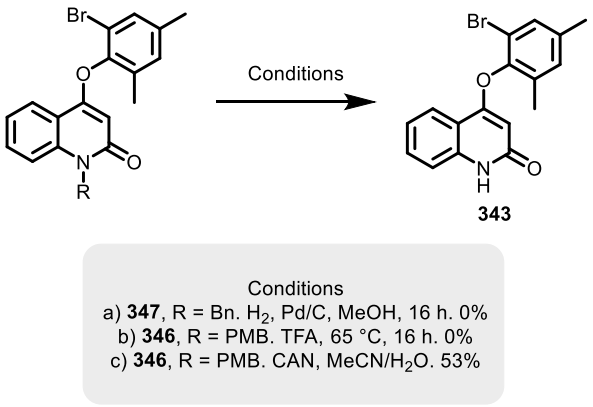


343, R_1 = H, R_2 = H, 0%
116, R_1 = Me, R_2 = H, 88%
344, R_1 = Et, R_2 = H, 85%
345, R_1 = i-Pr, R_2 = H, 62%
346, R_1 = PMB, R_2 = H, 40%
347, R_1 = Bn, R_2 = H, 80%
348, R_1 = Ph, R_2 = H, 96%
349, R_1 = CH_2CO_2Et, R_2 = H, 0%
350, R_1 = $CH_2C{\equiv}CH$, R_2 = H, 0%
351, 90%
352, R_1 = Me, R_2 = 6-F, 80%
353, R_1 = Me, R_2 = 6-OMe, 85%
354, R_1 = Me, R_2 = 6-C≡C-Ph, 57%
355, R_1 = Me, R_2 = 6-C≡C-C_2H_4OH, 0%
356, R_1 = Me, R_2 = 6-NO_2, 51%
357, R_1 = Me, R_2 = 7-Cl, 78%
358, R_1 = Me, R_2 = 8-Me, 81%

*Scheme 51. The synthesis of ether intermediates, formed by the reaction between 4-chloro-2-quinolones and bromophenol **114***

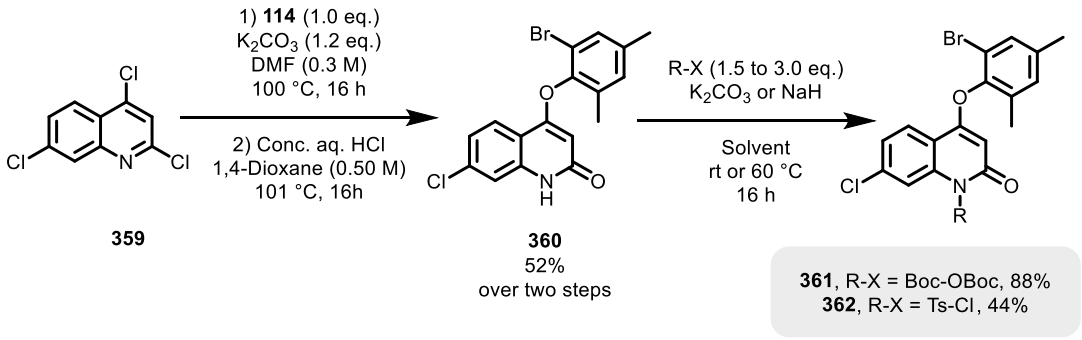
Due to the fact that an *N*-unsubstituted ether **343** could not be made directly, we decided to investigate some deprotective strategies (**Scheme 52**). A simple hydrogenation set-up

failed to remove a benzyl group from the 2-quinolone nitrogen, but a *para*-methoxy benzyl could be removed by oxidation with ceric ammonium nitrate.



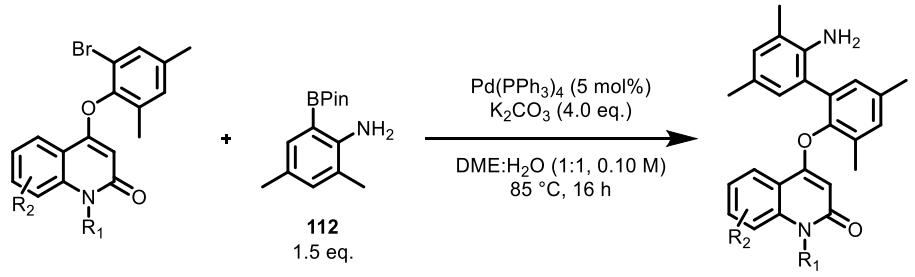
*Scheme 52. A protecting group removal strategy for the synthesis of intermediate **343***

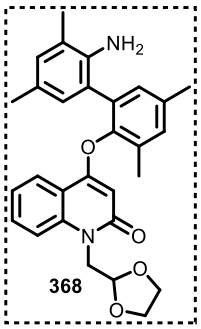
The related compound **360** was obtained by a regioselective S_NAr reaction with quinoline **359** and acidic hydrolysis (**Scheme 53**). Furthermore, a Boc group was also successfully introduced by circumventing the previous harsh conditions. Analogously, a tosyl group can also be introduced, however, **362** was found to not be bench-stable, thus the compound was not elaborated further.



*Scheme 53. Synthesis of intermediate **360** from a 2,4-dichloroquinoline derivative and the introduction of Boc and Ts groups*

1.3.3 2-Quinolone Oxonium Precursors

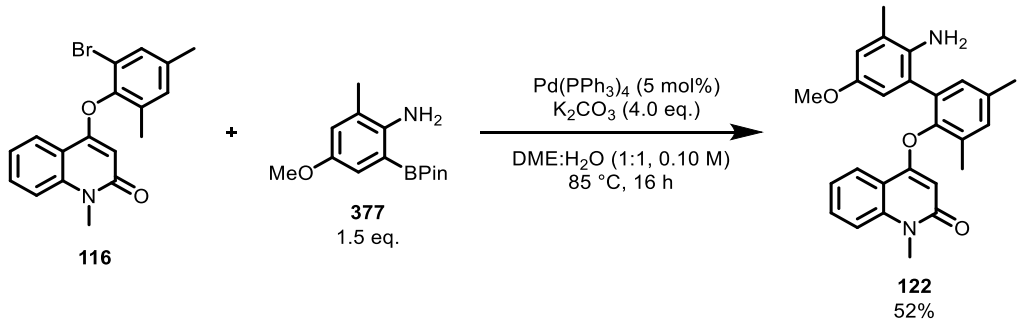




363, R_1 = H, R_2 = H, 0%
117, R_1 = Me, R_2 = H, 63%
364, R_1 = Et, R_2 = H, 87%
365, R_1 = i-Pr, R_2 = H, 95%
366, R_1 = Bn, R_2 = H, 77%
367, R_1 = Ph, R_2 = H, 62%
368, 71%
368, R_1 = Me, R_2 = 6-F, 42%
370, R_1 = Me, R_2 = 6-OMe, 80%
371, R_1 = Me, R_2 = 6-C≡C-Ph, 79%
372, R_1 = Me, R_2 = 6-NO_2, 72%[a]
373, R_1 = Me, R_2 = 7-Cl, 71%
374, R_1 = Me, R_2 = 8-Me, 78%
375, R_1 = H, R_2 = 7-Cl, 58%
376, R_1 = Boc, R_2 = 7-Cl, 0%

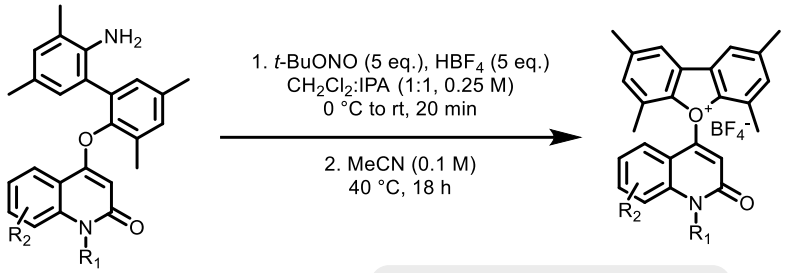
Scheme 54. Synthesis of 2-quinolone oxonium ion precursors via Suzuki-Miyaura coupling. a: Pd(dppf)Cl_2 catalyst used instead of Pd(PPh_3)$_4$

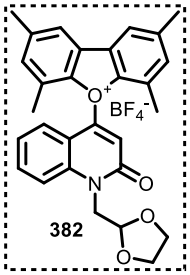
Many oxonium precursors were successfully synthesised by a Suzuki-Miyaura coupling with aniline **112** or aniline **377** (**Schemes 54** and **55**). However, decomposition was observed with unsubstituted quinolone **343**. Only trace product **372** was isolated under standard conditions, but, pleasingly, the yield increased to 72% when the catalyst was switched to Pd(ddpf)Cl_2. The Boc group was also lost under these conditions, giving precursor **375** in a 58% yield.



*Scheme 55. A Suzuki-Miyaura coupling reaction between ether **116** and boronic acid pinacol ester **377***

1.3.4 2-Quinolone Oxonium Tetrafluoroborates

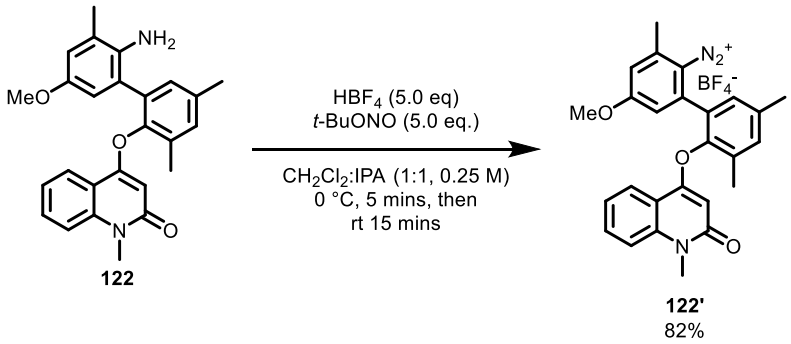




119, R_1 = Me, R_2 = H, 94%
378, R_1 = Et, R_2 = H, 97%
379, R_1 = i-Pr, R_2 = H, 86%
380, R_1 = Bn, R_2 = H, 81%
381, R_1 = Ph, R_2 = H, 92%
382[a], 84%
383, R_1 = Me, R_2 = 6-F, 51%
384, R_1 = Me, R_2 = 6-OMe, 60%
385, R_1 = Me, R_2 = 6-C≡C-Ph, 83%
386, R_1 = Me, R_2 = 6-NO_2, 74%
387, R_1 = Me, R_2 = 7-Cl, 73%
388, R_1 = Me, R_2 = 8-Me, 72%
389, R_1 = H, R_2 = 7-Cl, 0%

Scheme 56. The synthesis of 2-quinolone oxonium tetrafluoroborates. a: 1.0 eq. of HBF_4 used

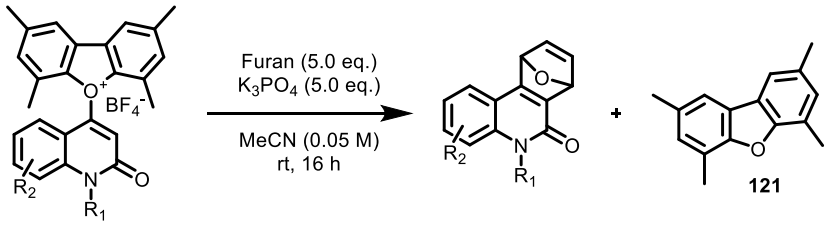
All 2-quinolone oxonium tetrafluoroborates were synthesised under standardised conditions with *tert*-butyl nitrite and aqueous HBF_4, followed by overnight heating in acetonitrile (**Scheme 56**). Interestingly, although traces of oxonium ion **389** were isolated on small scales, no desired product could be obtained upon scale up. The diazotisation of aniline **122** resulted in the formation of stable diazonium **122'**, however, the exact structure of the compound could only be identified by infrared spectroscopy (**Scheme 57**).

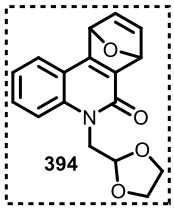


*Scheme 57. Diazotisation of aniline **122***

1.3.5 2-Quinolone Oxonium Furan Trapping

All previously synthesised oxonium ions were subjected to trapping with furan under the influence of solid K_3PO_4 (**Scheme 58**). Moderate to high yields were observed throughout.



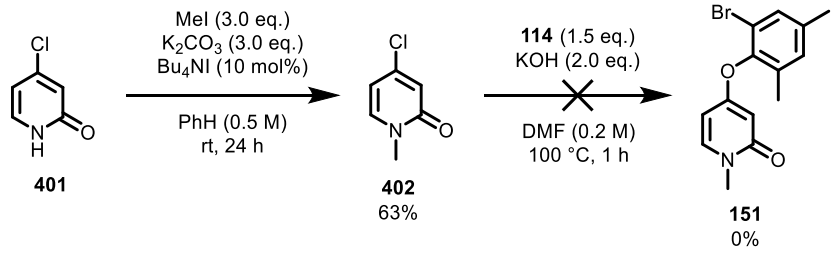


120, R_1 = Me, R_2 = H, 83%
390, R_1 = Et, R_2 = H, 78%
391, R_1 = i-Pr, R_2 = H, 84%
392, R_1 = Bn, R_2 = H, 87%
393, R_1 = Ph, R_2 = H, 72%
394, 82%
395, R_1 = Me, R_2 = 6-F, 84%
396, R_1 = Me, R_2 = 6-OMe, 75%
397, R_1 = Me, R_2 = 6-C≡C-Ph, 52%
398, R_1 = Me, R_2 = 6-NO_2, 63%
399, R_1 = Me, R_2 = 7-Cl, 71%
400, R_1 = Me, R_2 = 8-Me, 79%

Scheme 58. Synthesis of 2-quinolone-based furan adducts by the base-mediated hetaryne formation from oxonium ions

1.3.6 2-Pyridone Oxonium Ion and Trapping with Furan

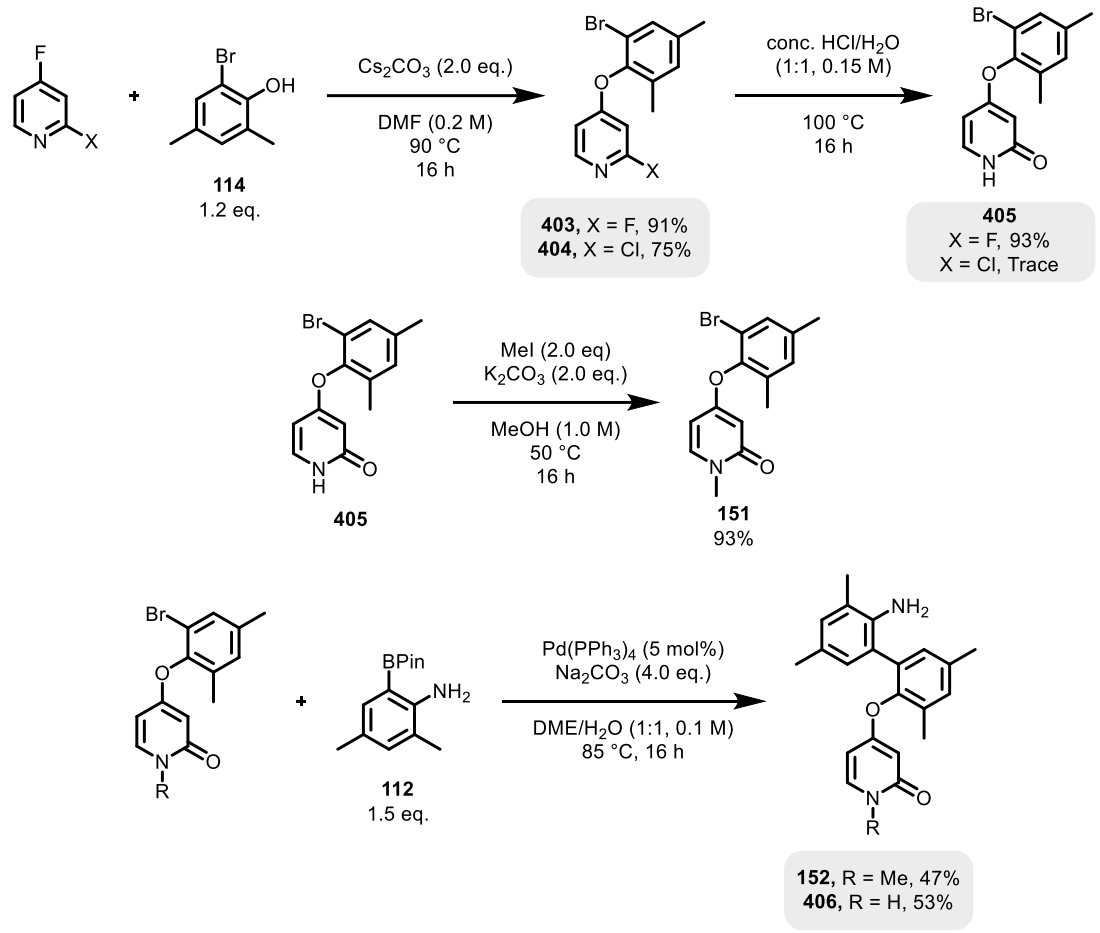
The initial attempts to synthesise 2-pyridone oxonium ion precursors and their intermediates started with the methylation of 2-pyridone **401**, but was followed by an unsuccessful S_NAr reaction with bromophenol **114** (**Scheme 59**).



*Scheme 59. The unsuccessful attempt to synthesise intermediate **151** from **401***

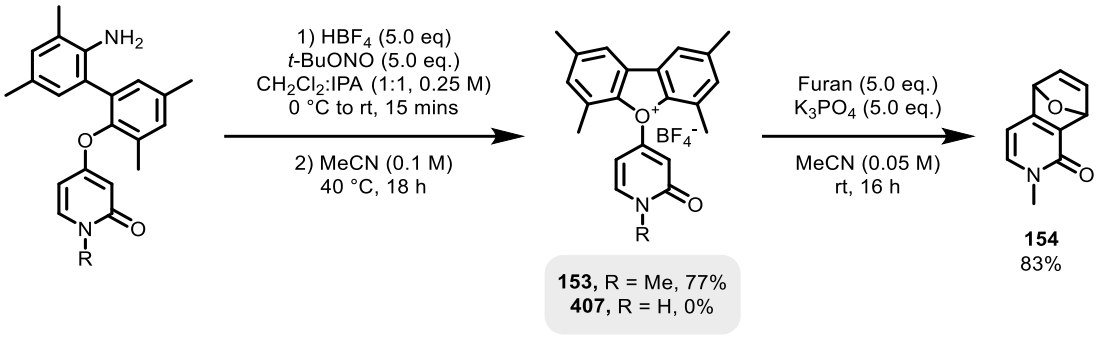
Our next strategy involved the use of dihalogenated pyridines and their regiospecific S_NAr reactions producing intermediates **403** and **404** (**Scheme 60**). The ethers were then subjected to acid-mediated hydrolysis, however, only the 2-fluoro species gave product

405 in substantial yields. **405** was then diversified by methylation on the pyridone nitrogen and both precursors **152** and **406** were successfully formed under our standard Suzuki-Miyaura coupling conditions.



*Scheme 60. The synthesis of oxonium precursors **152** and **406***

The two resulting anilines were then subjected to diazotisation and oxonium formation, with **153** being formed in a 77% isolated yield, but only non-specific decomposition was observed in the synthesis of **407** (**Scheme 61**). Oxonium salt **153** was then subjected to trapping with furan, obtaining sole trapping product **154** in an 83% yield.



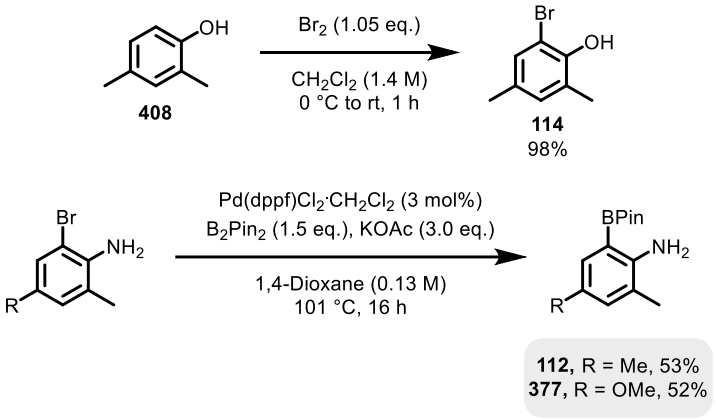
*Scheme 61. The formation of 2-pyridone-based oxonium tetrafluoroborate **153** and its trapping with furan*

1.3.7 2-Quinolone Oxonium Trapping with Other Arynophiles

2-Quinolone oxonium tetrafluoroborate trapping with non-furan trapping agents has been already discussed in full detail in Section 1.2.10.

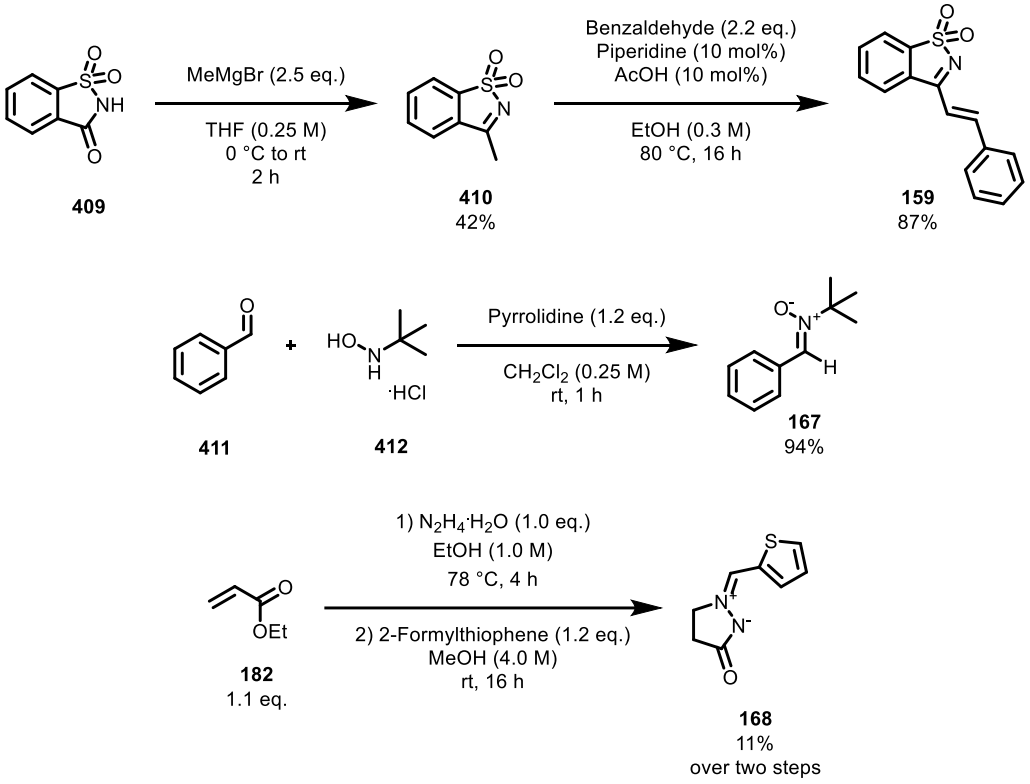
1.3.8 Fragments for the Oxonium Ion Scaffold Construction

Bromophenol **114** was directly obtained by the bromination of phenol **408** (**Scheme 62**). Boronic acid pinacol esters **112** and **377** were synthesised from their corresponding bromoanilines *via* a Miyaura borylation reaction, utilising $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ as a catalyst.



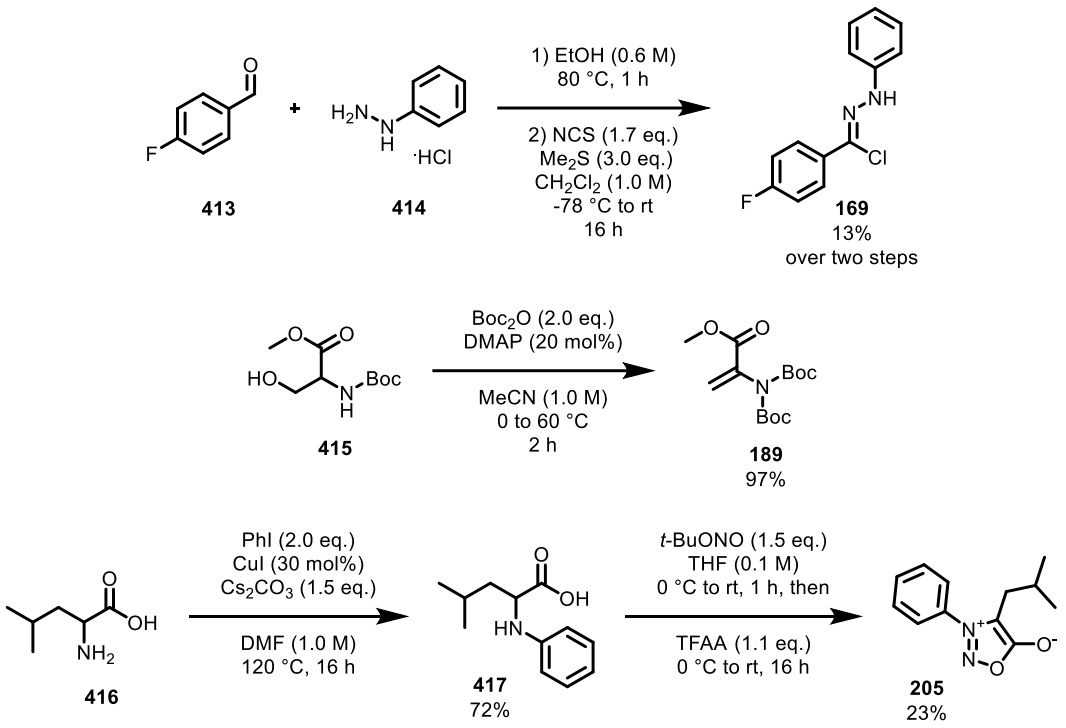
*Scheme 62. Synthesis of bromophenol **114** and anilines **112** and **377***

1.3.9 Arynophiles



*Scheme 63. Synthesis of arynophiles **159**, **167** and **168***

A number of trapping agents could not be obtained from commercial sources and thus needed to be synthesised. Diene **159** was produced in a two-step process by the methylation of saccharin **409** and a pseudo-aldol reaction of the obtained intermediate with benzaldehyde **411** (**Scheme 63**). Nitrone **167** was directly obtained by a base-mediated reaction with *N-tert*-butylhyroxyloamine **412**. 1,3-dipole **168** was made from ethyl acrylate **182** in an 11% yield over two synthetic steps.

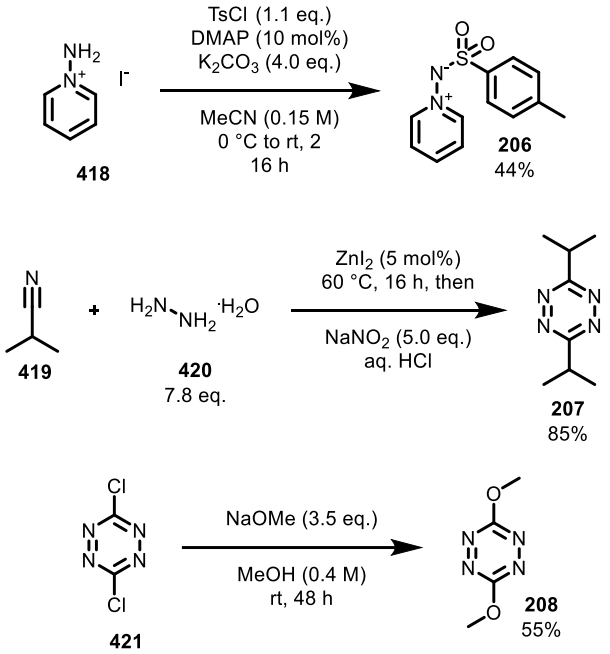


*Scheme 64. Synthesis of arynophiles **169**, **189** and **205***

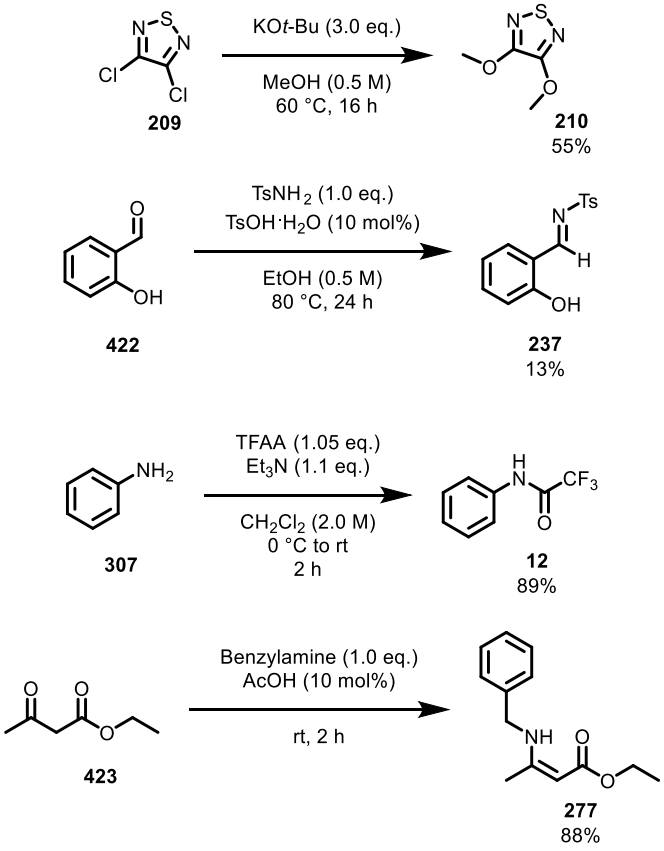
169 was synthesised in two steps by hydrazone formation from **413** and **414**, followed by chlorination with NCS and Me_2S (**Scheme 64**). Dehydroalanine derivative **189** was produced by the DMAP-catalysed Boc protection of serine derivative **415**. Furthermore, sydnone **205** was acquired from *N*-phenyl leucine **417**.

Tosylation of **418** achieved arynophile **206** in a 44 % yield (**Scheme 65**). Tetrazines **207** and **208** were made by cyclisation/oxidation or nucleophilic aromatic substitution, respectively.

Thiadiazole **210** was synthesised by refluxing **209** with an excess of KO*t*-Bu in MeOH overnight and tosylhydrazone **237** was produced by an acid-catalysed condensation reaction (**Scheme 66**). Amide **12** came as a result of treating aniline **307** with TFAA and, finally, **277** was made by the direct enamine formation between benzylamine and ethylacetoacetate **423**.



*Scheme 65. Synthesis of arynophiles **206**, **207** and **208***



*Scheme 66. Synthesis of arynophiles **210**, **237**, **12** and **277***

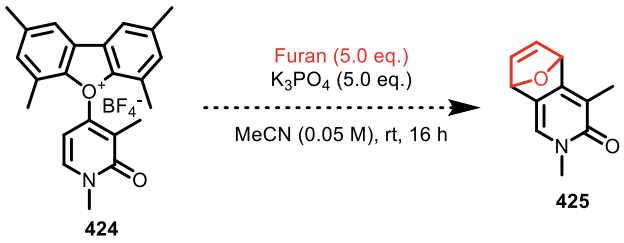
1.4 Conclusion

As part of this work, we developed generalised routes to synthesise two new families of oxonium ions: the 2-quinolones and 2-pyridones. We expanded the scope of 2-quinonolones and demonstrated good functional group tolerance in the oxonium forming step. Pleasingly, all of these oxonium ions could serve as hetaryne precursors by treating them with solid K_3PO_4, exhibiting reactivity with a wide range of arynophiles.

1.5 Future Work

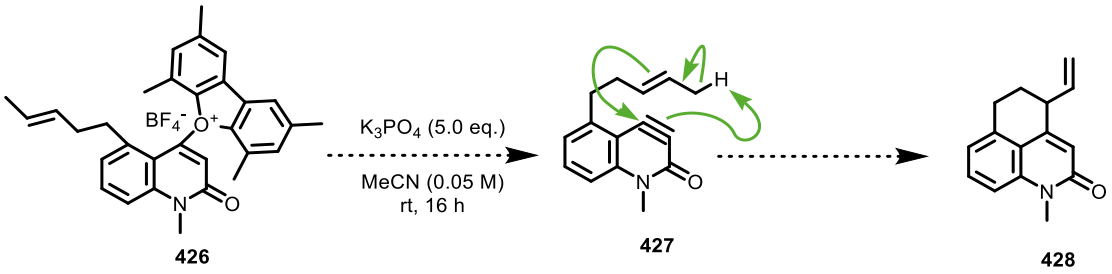
Although we observed diverse reactivity with the oxonium ions, several test reactions had low desired product yields and complex reaction profiles, therefore, further work on the optimisation of the hetaryne trapping step should be carried out.

It was interesting to note the regiospecificity for the 3,4- position in the 2-pyridone oxonium ion trapping reaction with furan (**Scheme 23**). A way to test if reactivity via the 4,5- position is viable would be to introduce a methyl group in the 3- position, enforcing deprotonation at the 5- position (**Scheme 67**).



*Scheme 67. A hypothetical furan trapping reaction of 2-pyridone oxonium **424***

Intramolecular trapping reactions have also not been investigated in our system and could be another useful strategy for cyclisation. An example of this could be a pendant chain containing an alkene in position for an Alder-ene pericyclic transformation, resulting in the construction of a tricyclic core in **428** (**Scheme 68**).



*Scheme 68. A hypothetical intramolecular Alder-ene reaction of aryne **427**, produced by the deprotonation of oxonium **426***

2 A 4-Quinolone Oxonium Ion

2.1 Introduction

2.1.1 4-Quinolones in Medicinal and Synthetic Chemistry

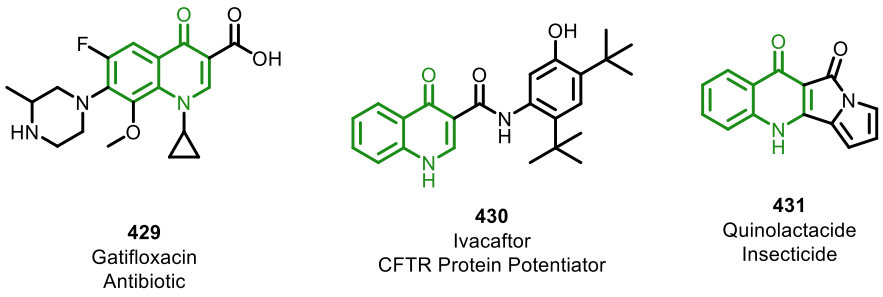
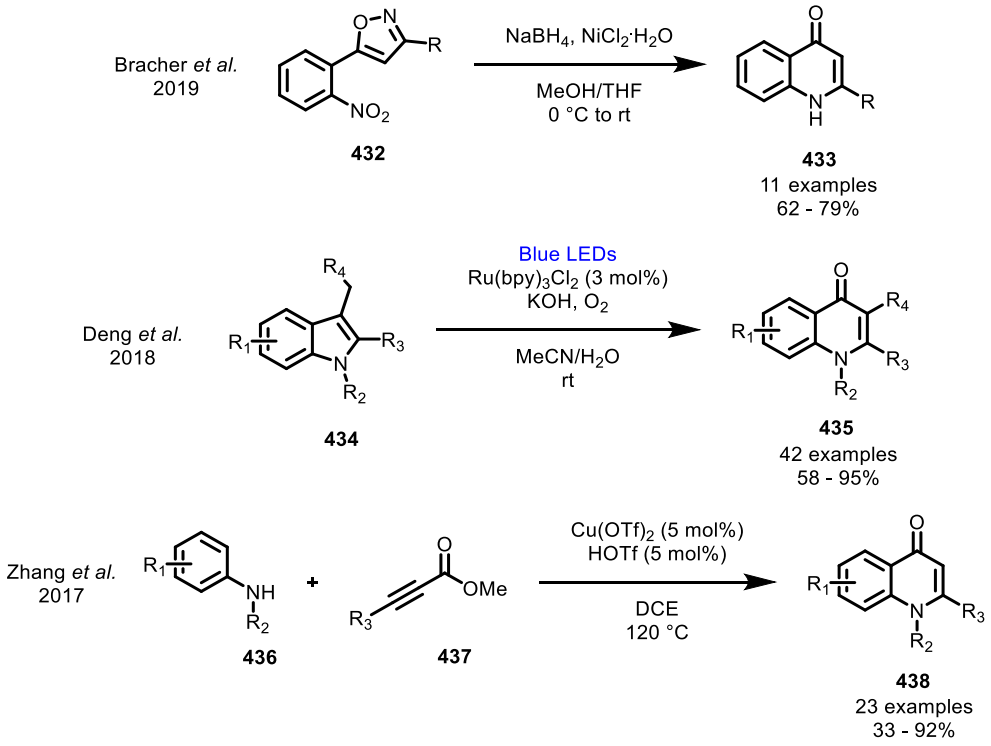


Figure 7. Selected examples of biologically important molecules containing the 4-quinolone scaffold

Similarly to 2-quinolones, the 4-quinolones are a privileged scaffold in medicinal chemistry.[138] They are important historically as a large group of broad-spectrum antibiotics discovered in the early 1960s, but also appear as a scaffold in contemporary drugs and agrochemicals (**Figure 7**).[139,140]



Scheme 69. Selected modern examples of the synthesis of 4-quinolones

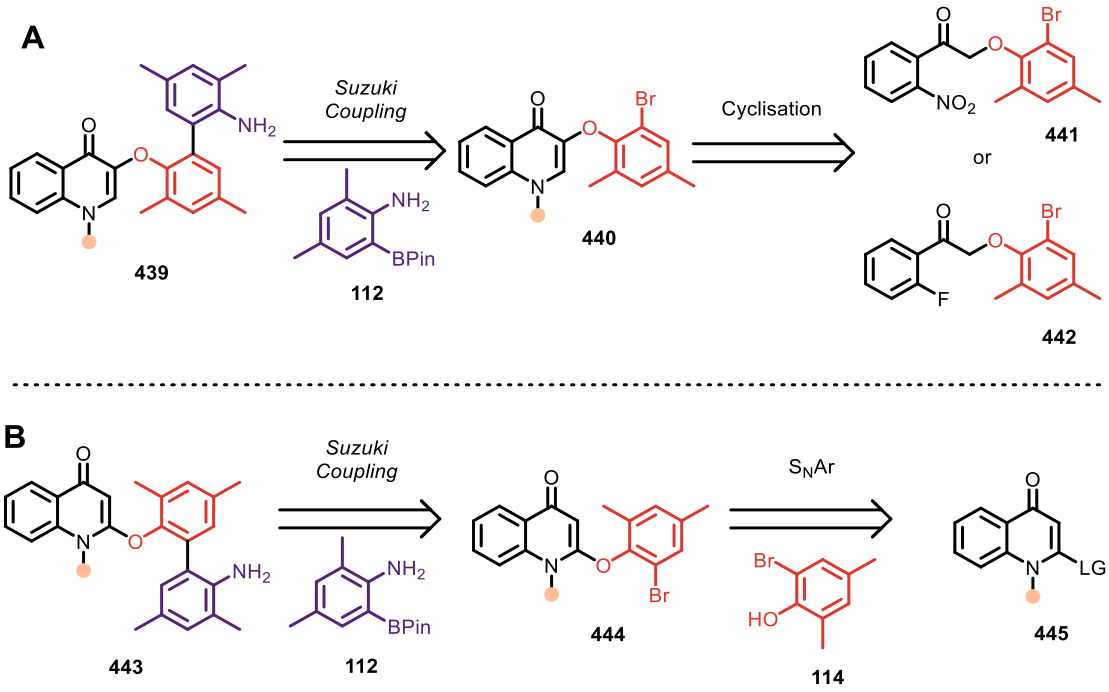
Due to the importance of this heterocycle, modern approaches for the synthesis of functionalised 4-quinolone derivatives have been created, involving mild and highly efficient transformations (**Scheme 69**).[141–145]

2.1.2 Project Aims

As far as we are aware, there are no examples of hetarynes possessing the 4-quinolone scaffold. Having seen success with 2-quinolones previously, we decided to further explore the application of the triaryl oxonium ion strategy to this important scaffold to access its potential aryne-like reactivity.

2.2 Results and Discussion

2.2.1 Retrosynthetic Analysis of a 4-Quinolone Oxonium Ion Precursor



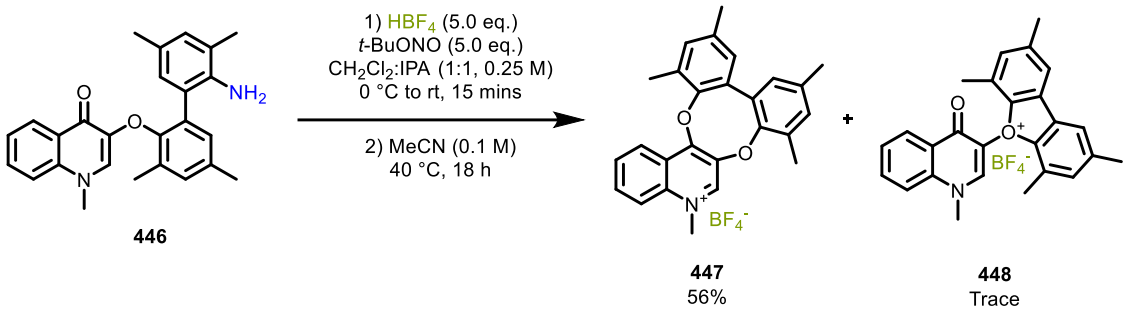
*Scheme 70. A retrosynthetic analysis of oxonium precursors **439** and **443***

Depending on the location of the dibenzofuran leaving group, we envisaged two potential routes for the synthesis of 4-quinolone oxonium ion precursors (**Scheme 70**). The first strategy would exploit hypothetical ethers **441** and **442**, arising from 2-bromoacetophenone derivatives, where the 4-quinolone motif is introduced *via*

condensation reactions before the final Suzuki-Miyaura coupling (**Scheme 70**–**A**). Equally, we could start with the parent heterocycle bearing a leaving group in the 2-position **445** and introduce the pivotal fragments in this fashion (**Scheme 70**–**B**). Pleasingly, both of these approaches were converted into successful synthetic routes.

2.2.2 An *In Situ* Generated 4-Quinolone Oxonium Ion

Having synthesised oxonium precursor **446**, we subjected it to diazotisation conditions that were originally optimised for the 2-quinolone system (**Scheme 71**). We observed a clean formation of diazonium salt **449**, however, after heating it to 40 °C overnight, the major product observed was not the expected oxonium ion **448**, but rather pyridinium ion **447**, resulting from cyclisation *via* the carbonyl oxygen.



*Scheme 71. The unsuccessful formation of oxonium **448** with unwanted side-product **447***

We decided to further investigate this reaction, monitoring it by a quantitative ^{1}H NMR experiment at 40 °C for 4.5 hours (**Figure 8** and **Table 10**). As expected, diazonium salt **449** was observed to decay in a first-order process, converting into both oxonium **448** and side product **447**. Eventually, the concentration of the oxonium ion reaches a plateau and **448** starts decomposing into a complex mixture, as illustrated by the overall mass balance for the reaction. Some precipitation was noted in the NMR tube and could explain the slight inconsistency between the isolated yield of pyridinium salt **447** previously and the NMR yields.

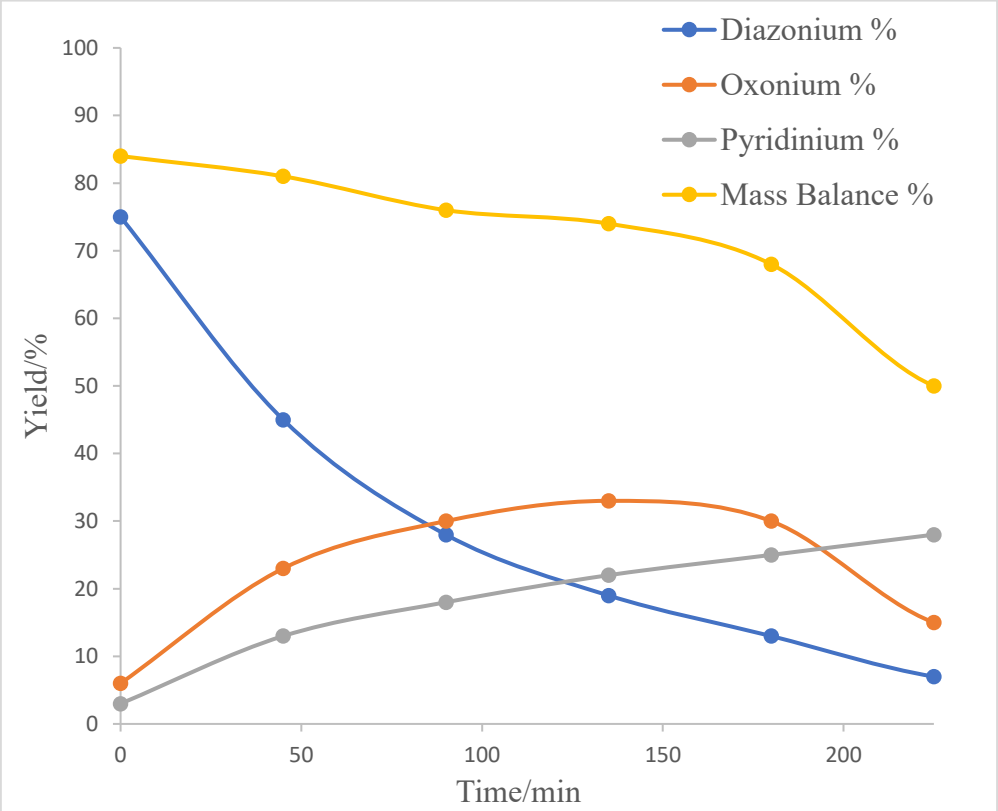
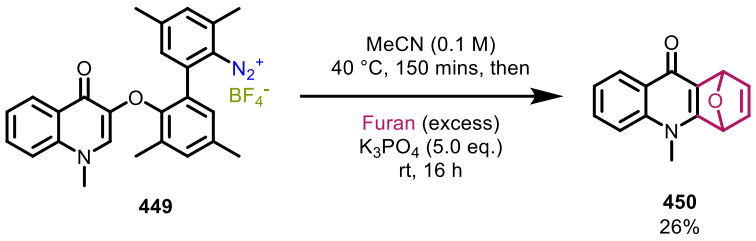


*Figure 8. A graph depicting the change in the NMR yields of diazonium **438** and the formation of its products*

Time/min	Diazonium 449	Oxonium 448	Pyridinium 447	Mass Balance[b]
0[a]	75%	6%	3%	84%
45	45%	23%	13%	81%
90	28%	30%	18%	76%
135	19%	33%	22%	74%
180	13%	30%	25%	68%
225	7%	15%	28%	50%
270	5%	12%	31%	48%

*Table 10. Monitoring the first order decay of diazonium **449**. All yields reported are NMR yields and were recorded by using 1,2,4,5-tetramethylbenzene as an internal standard. a: corresponds to the first quantitative NMR recorded after dissolution of diazonium **449** in CD_3CN. b: corresponds to the sum of the yields of all species of interest*

Although the oxonium ion could not be isolated, we wanted to test if the hetaryne could still be generated. An analogous reaction was intercepted at *ca.* 150 minutes of heating by cooling to room temperature and diluting with a large excess of furan, followed by the addition of solid K_3PO_4 with rapid overnight stirring (**Scheme 72**). Pleasingly, after silica gel column chromatography, furan adduct **450** was isolated in a 26% yield.



Scheme 72. The successful furan trapping of an in situ generated 4-quinolone oxonium ion

2.2.3 Efforts to Improve the Kinetic Stability of 4-Quinolone Oxonium Ions

Whilst the synthetic utility of a 4-quinolone oxonium ion was demonstrated by its trapping with furan (**Scheme 72**), we wanted to improve the kinetic stability of such species. As the major side reactivity arose from the nucleophilicity of the oxygen in the 4- position, we anticipated electron withdrawing groups on either the nitrogen or oxygen would inhibit the unwanted cyclisation (**Figure 9**–**A**). Accordingly, transposing the dibenzofuran scaffold from the 3- to the 2- position would also favour oxonium formation (**Figure 9**–**B**).

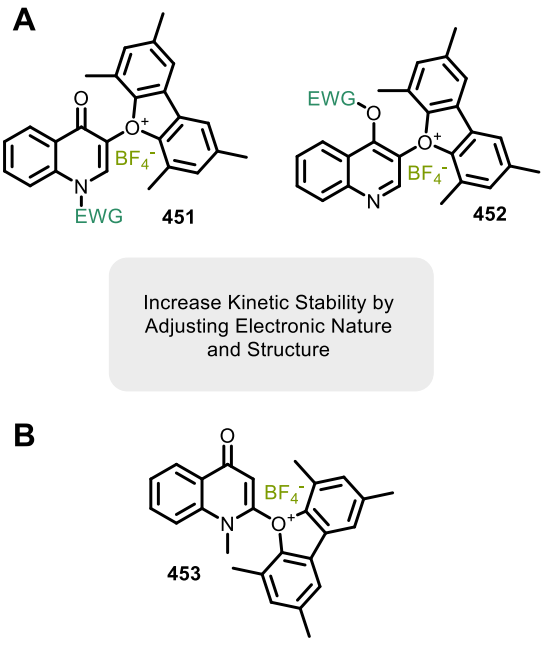
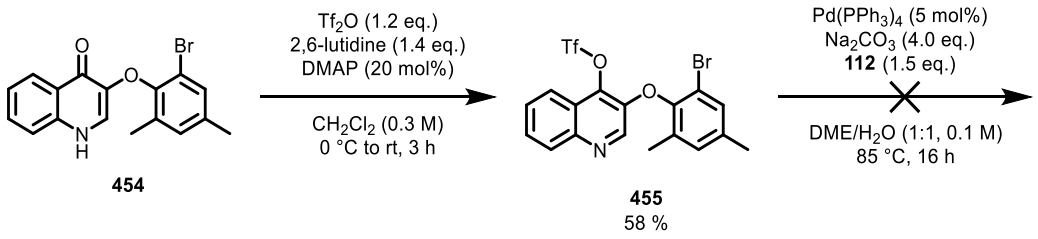


Figure 9. The potential strategies for the kinetic stabilisation of a 4-quinolone oxonium ion

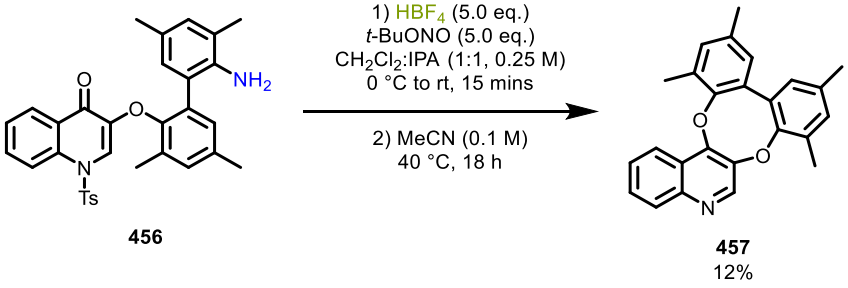
The initial attempts to introduce a triflate protecting group into the scaffold were not successful, as the final Suzuki-Miyaura coupling step resulted in the formation of a

complex mixture of products. Presumably due to no selectivity for either the triflate or the bromide (**Scheme 73**).



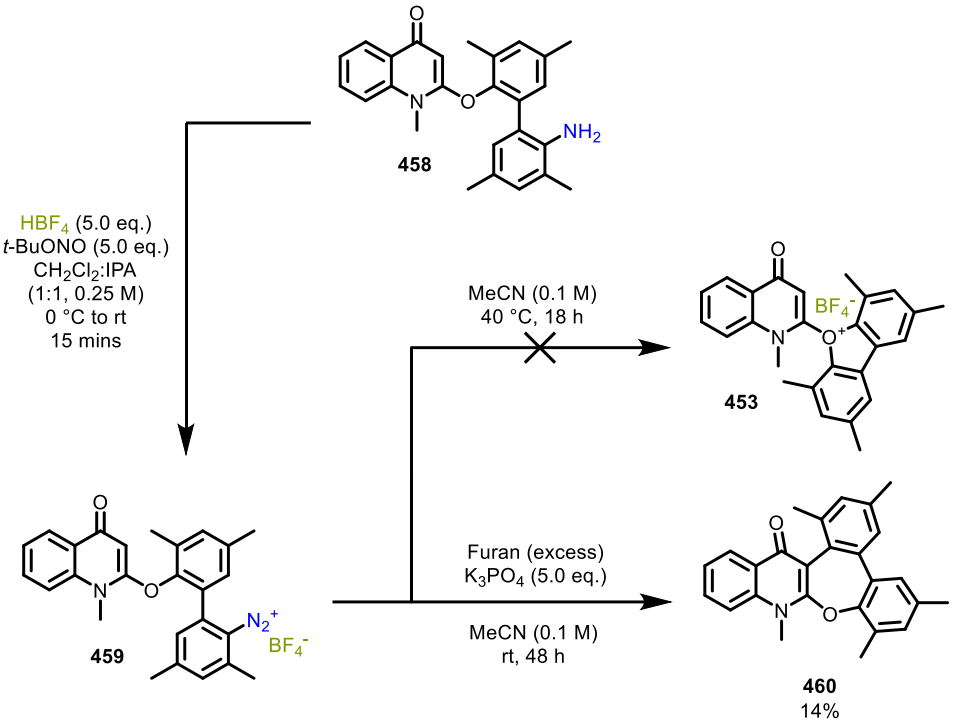
*Scheme 73. The unsuccessful Suzuki-Miyaura coupling of triflated 4-quinolone equivalent **455***

The introduction of a tosyl group onto the nitrogen was less problematic, but, in parallel to the previous oxonium formation, it resulted in another cyclic by-product **457** (**Scheme 74**).



*Scheme 74. The unsuccessful oxonium formation from tosylated precursor **456***

Aniline **458** was also synthesised as an isomer to the original 4-quinolone oxonium precursor **446**. Dissimilarly, only non-specific decomposition occurred in the oxonium forming step, alongside the formation of the dibenzofuran leaving group **121** (**Scheme 75**). Assuming the potentially transient formation of a low stability oxonium **453**, the diazonium **459** was directly treated with furan and K_3PO_4 for 48 hours. Unfortunately, another unwanted cyclisation was observed in this case, forming the 7-membered ring structure in **460**.

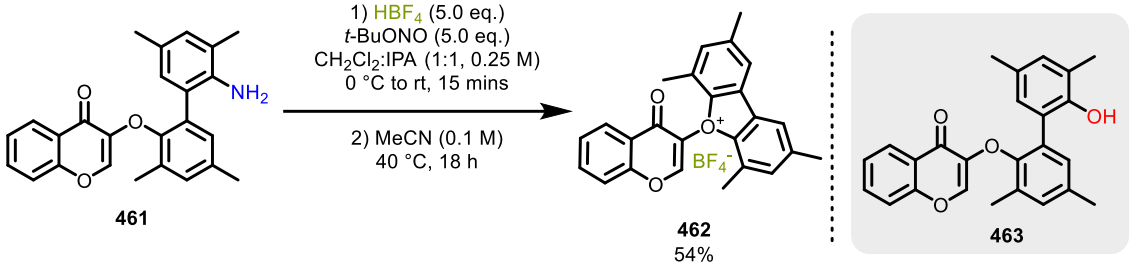


*Scheme 75. Formation of diazonium **459** from aniline **458** and unsuccessful attempts to generate an oxonium ion or its furan trapping product*

2.2.4 A Chromone Oxonium Ion

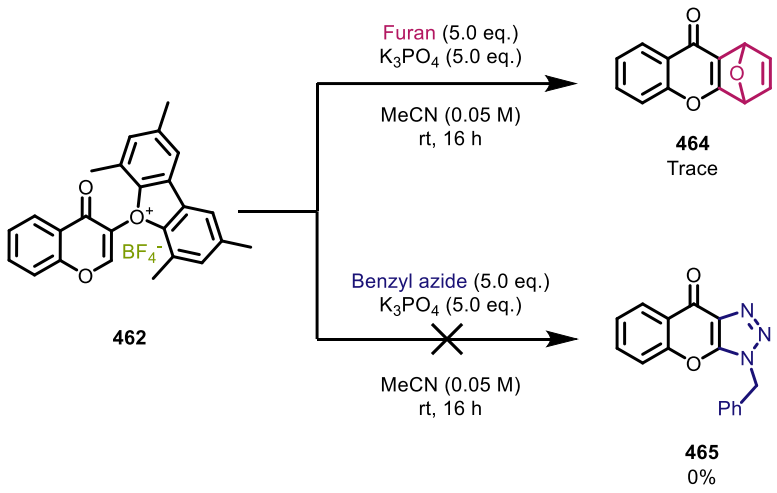
Having observed the *in situ* formation of 4-quinolone oxonium ion **448**, we were interested to see if the formation of an isoelectronic chromone-based oxonium ion was also possible. Being a bioisostere to 4-quinolones,[55] chromones are also wide-spread in medicinal chemistry, as well as natural products.[146]

Aniline **461** was synthesised in a similar fashion to the 4-quinolone oxonium precursor **458**. After subjecting it to diazotisation and overnight heating, a kinetically stable chromone oxonium tetrafluoroborate **462** was isolated in a 54% yield (**Scheme 76**). Interestingly, it did not possess the same stability in solution as the 2-quinolone oxonium ions (**Scheme 21**), and the major product of decomposition was identified as **463**, resulting from hydrolysis in acetonitrile. Correspondingly, solid **462** was stored below 5 °C, with no evident decomposition over the span of approximately three months.



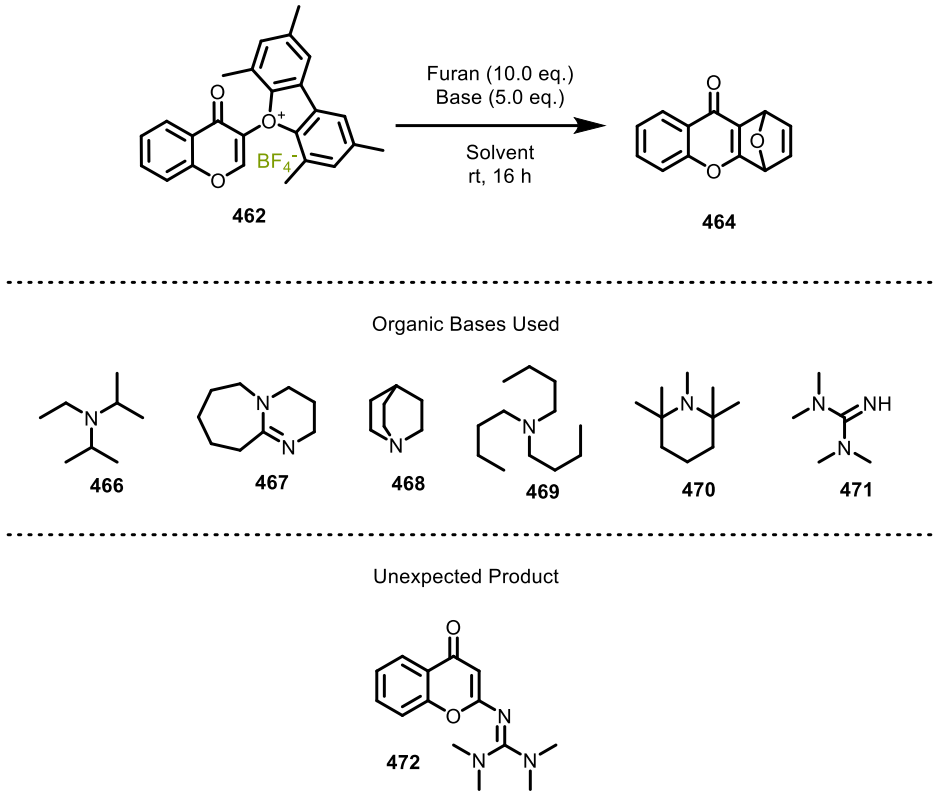
Scheme 76. The formation of a chromone oxonium ion and its hydrolysis product

Thereupon, chromone-based oxonium salt **462** was subjected to our standard aryne-forming conditions (**Scheme 77**). Dissimilarly to the quinolone systems and their aryne-like reactivity, only trace furan adduct **464** was observed and the use of benzyl azide led to complete decomposition.



Scheme 77. Unsuccessful attempts to generate and trap a hetaryne from a chromone-based oxonium ion

2.2.5 Optimising the Furan Trapping Reaction



Scheme 78. An optimisation of the chromone oxonium ion furan trapping reaction, organic bases used depicted

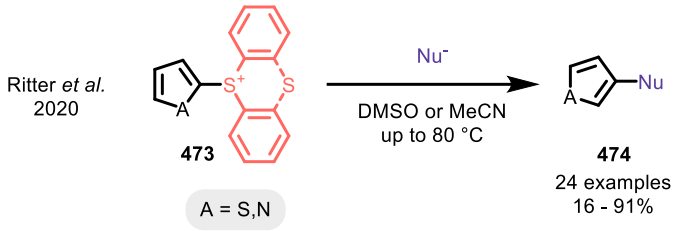
Entry	Base	Solvent	Yield (NMR)[a,b]
1	K_3PO_4	MeCN (0.05 M)	3%
2	K_3PO_4	CH_2Cl_2 (0.05 M)	3%
3	KO*t*-Bu	CH_2Cl_2 (0.05 M)	1%
4	KO*t*-Bu	CH_2Cl_2:Furan (1:1, 0.05 M)	0%
5	K_3PO_4	MeCN (0.025 M)	0%
6	K_2CO_3	MeCN (0.05 M)	0%
7	KOAc	MeCN (0.05 M)	0%
8	K_2HPO_4	MeCN (0.05 M)	0%
9	**466**	MeCN (0.05 M)	7%
10	**467**	MeCN (0.05 M)	0%
11	**468**	MeCN (0.05 M)	6%
12	**469**	MeCN (0.05 M)	1%
13	**470**	MeCN (0.05 M)	4%
14	**471**	MeCN (0.05 M)	0% (**464**), 73%[c] (**472**)

*Table 11. An optimisation of the chromone oxonium ion furan trapping reaction. All test reactions were conducted on a 0.025 mmol scale. a: yield determined by using 1,2,4,5-tetramethylbenzene as an internal standard. b: in all cases leaving group **121** was formed in >65% NMR yield. c: isolated in a 54% yield.*

As some desired product was observed in the furan trapping reaction, we decided to further optimise the conditions for this step, mainly focusing on the identity of the base

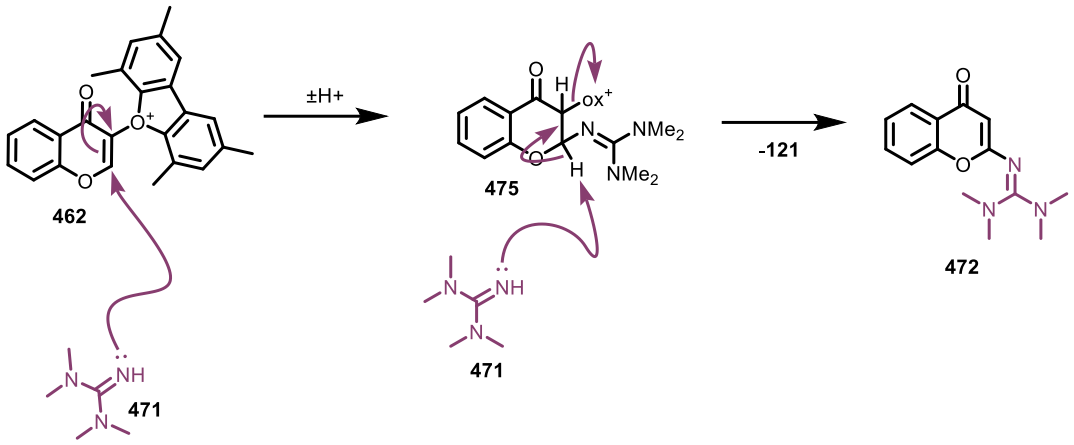
(**Scheme 78** and **Table 11**). K_3PO_4 gave a 3% ^1H NMR yield in both MeCN and CH_2Cl_2 (**Entries 1** and **2**), but strong base KO*t*-Bu did not improve the yield, even with furan as a co-solvent (**Entries 3** and **4**). Furthermore, a two-fold dilution with K_3PO_4 in MeCN also diminished the yield (**Entry 5**) and the use of other weak inorganic bases was not successful either (**Entries 6** to **8**).

We then shifted our focus to homogenous organic bases and noted an uplift in yield with DIPEA **466**, quinuclidine **468** and pempidine **470**, however, the reaction profile for these reactions was even more complex, indicating additional side reactions (**Table 11**, **Entries 9**, **11** and **13**). A new mode of reactivity was discovered serendipitously, when 1,1,3,3-tetramethylguanidine **471** was used as a potential base (**Entry 14**). No furan adduct was observed in this case, but the guanidine was selectively incorporated into the 2- position, with compound **472** being isolated in a 54% yield.



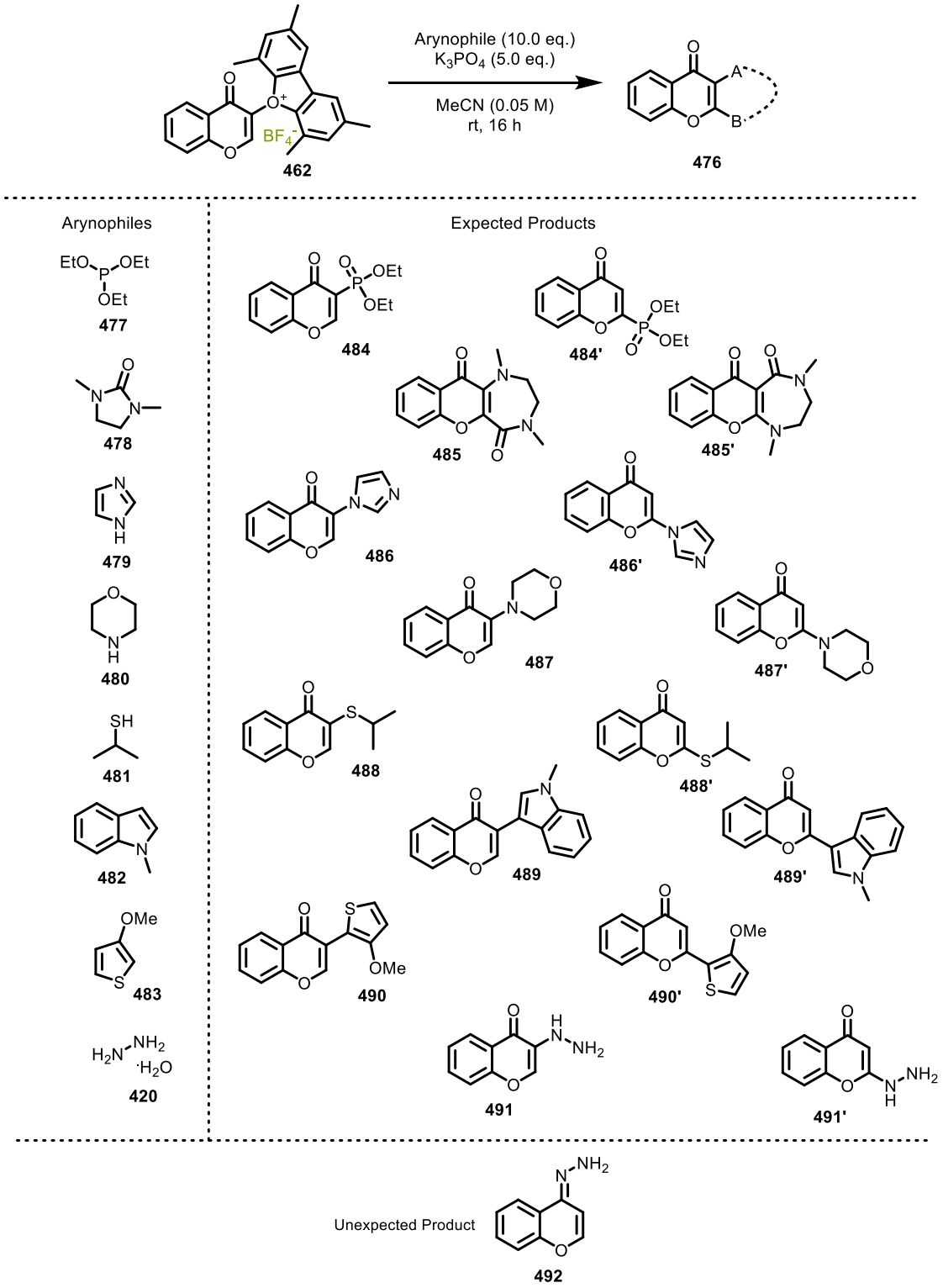
Scheme 79. Cine-substitution reactions with hetarylsulfonium salts as published by Ritter et al.

A comparable transformation was disclosed in 2020 by Ritter *et al.*, where *cine*-substitution reactions were reported with electron rich five-membered hetarylsulfonium salts and a number of nucleophilic species (**Scheme 79**).[147] They speculate that the sulfonium motif both encourages the pseudo-Michael addition of nucleophiles and acts as an excellent leaving group. Analogously, a hypothetical mechanism could be proposed for our system, involving initial 1,4-addition of the guanidine, followed by an elimination step, which would explain the regiospecificity of this reaction and the lack of the aryne-like reactivity with previously tested arynophiles (**Scheme 80**).



Scheme 80. A hypothetical mechanism between a chromone oxonium ion and 1,1,3,3-tetramethyl guanidine that does not involve a hetaryne intermediate

2.2.6 Chromone Oxonium Reactivity with Other Nucleophiles



Scheme 81. The reactivity of the chromone oxonium ion with various nucleophiles, nucleophiles tested and their expected products depicted

Entry	Arynophile	Expected Product	Yield (NMR/Isolated)[a,b]
1	477	484 or 484'	7%[c] (484)
2	478	485 or 485'	0%
3	479	486 or 486'	0%
4[d]	480	487 or 487'	45%/41% (487) and 11%[c] (487')
5	481	488 or 488'	26%/22% (488)
6	482	489 or 489'	0%
7	483	490 or 490'	0%
8[d]	420	491 or 491'	41%[e] (492)

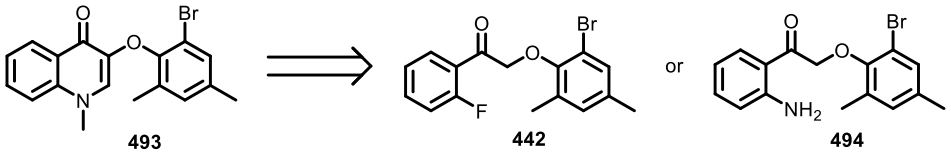
*Table 12. The reactivity of the chromone oxonium ion with various nucleophiles. All test reactions were conducted on a 0.025 mmol scale. a: NMR yield determined by using 1,2,4,5-tetramethylbenzene as an internal standard. b: in all cases leaving group **121** was formed in >49% NMR yield. c: NMR yield reported, could not be isolated in sufficient purity. d: no K_3PO_4 used. e: NMR yield only, compound not isolated*

After witnessing reactivity with 1,1,3,3-tetramethylguanidine **471**, we wanted to screen other nucleophilic species (**Scheme 81** and **Table 12**). The use of triethyl phosphite **477** gave the expected product **484** in a 7% ^{1}H NMR yield, but, contrary to our previous observation, the C–P bond was formed at the 3- position (**Entry 1**). Both DMI **478** and imidazole **479** gave complex mixtures (**Entries 2** and **3**), but morpholine **480** resulted in two regioisomers with a combined NMR yield of 56% and a ratio of 4.1 : 1.0, favouring the 3- position (**Entry 4**). Full regioselectivity for this position was also observed with isopropyl thiol **481** (**Entry 5**). Nucleophilic heterocycles **482** and **483** were not successful (**Entries 6** and **7**) and the only product observed with hydrazine hydrate was hydrazone **492** (**Entry 8**). In view of the fact that in some cases we saw complete selectivity for the 2- or the 3- position and mixtures of isomers, the mechanism we posited earlier is not necessarily universal and the formation of a hetaryne intermediate is still plausible.

2.3 Synthesis

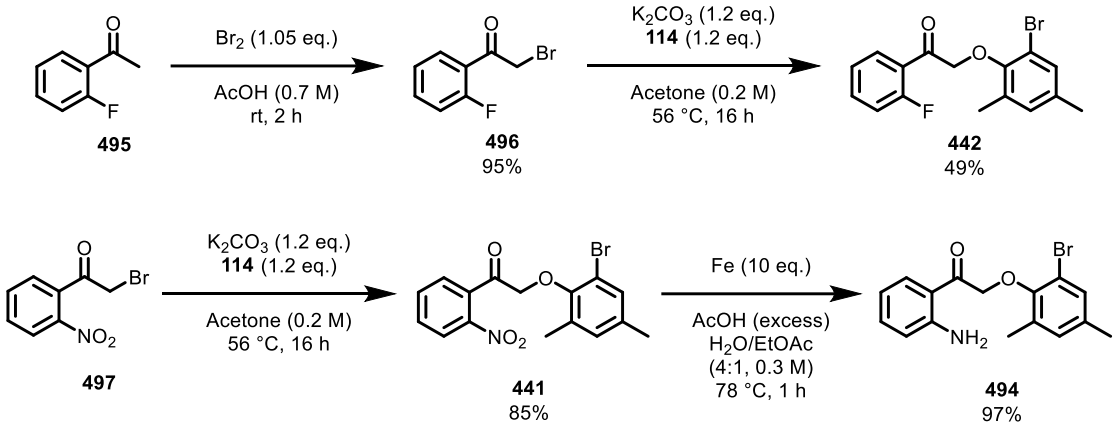
2.3.1 *De Novo* Construction of the 4-Quinolone Motif

As introduced in section 3.2.1, we initially envisaged synthesising a 4-quinolone oxonium ion precursor by assembling the quinolone scaffold in the middle of the synthetic route. We had two strategies in mind for the synthesis of intermediate **492**, involving either aryl fluoride **442** or aniline **494** (**Scheme 82**).



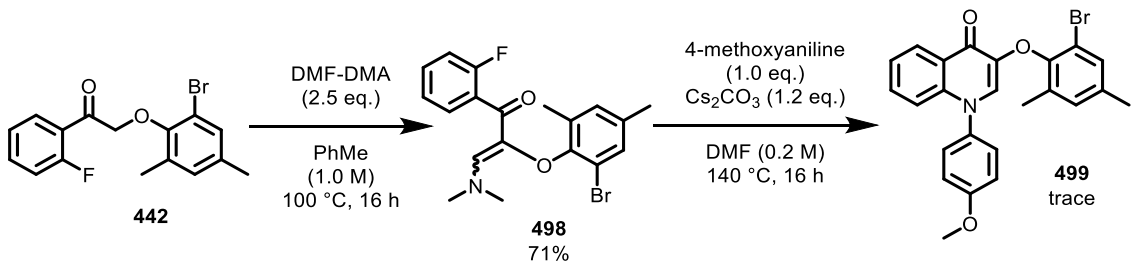
*Scheme 82. Retrosynthetic analysis of intermediate **493** from ethers **442** and **494***

The two ethers in question were synthesised from their corresponding 2-bromoacetophenone derivatives (**Scheme 83**). 2'-Fluoroacetophenone **495** was first monobrominated under acidic conditions to form **496**, which was subsequently subjected to an S_N2 reaction with phenol **114** under basic conditions. The same set up was also successfully applied to commercially available acetophenone **497** to generate compound **441** in an 85% yield. The nitro group was then reduced with an excess of iron under acidic conditions.



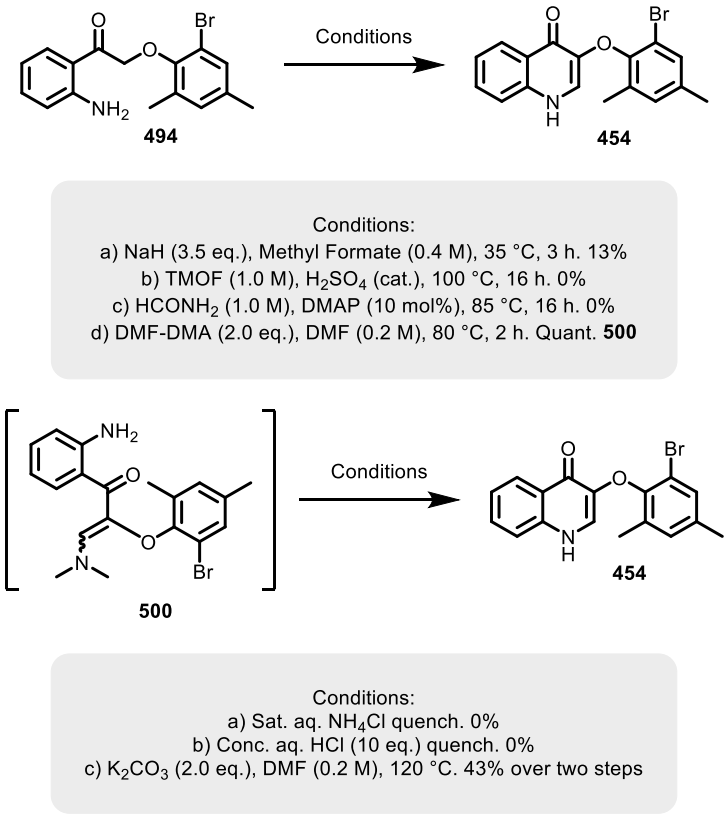
*Scheme 83. The synthesis of ethers **442** and **494** from their respective 2-bromoacetophenone derivatives*

Ketone **442** was then treated with *N*,*N*-dimethylformamide dimethyl acetal under reflux with toluene to form key intermediate **498** (**Scheme 84**). Finally, we employed the highly nucleophilic 4-methoxyaniline in order to engage in both S_NAr and 1,4-addition-elimination to form 4-quinolone **499**, however, only trace product was observed in the complex mixture.



*Scheme 84. Unsuccessful synthesis of 4-quinolone-based intermediate **499***

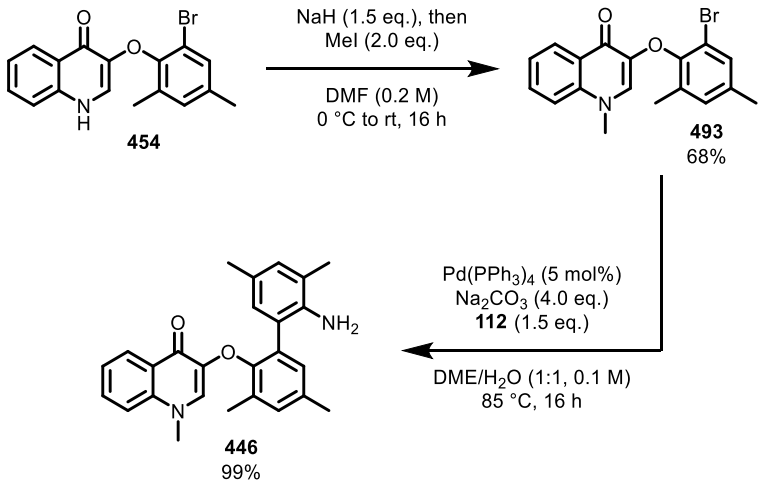
Various conditions were applied to ether **494** in order to construct **454** (**Scheme 85**). The use of NaH in methyl formate generated the expected product in a 13% yield. Trimethyl orthoformate lead to complete decomposition, whereas catalytic DMAP in formamide failed to show any reactivity. Finally, DMF-DMA cleanly produced intermediate **500** in a quantitative yield, but no cyclised product **454**.



*Scheme 85. Sets of conditions screened for the synthesis of compound **454***

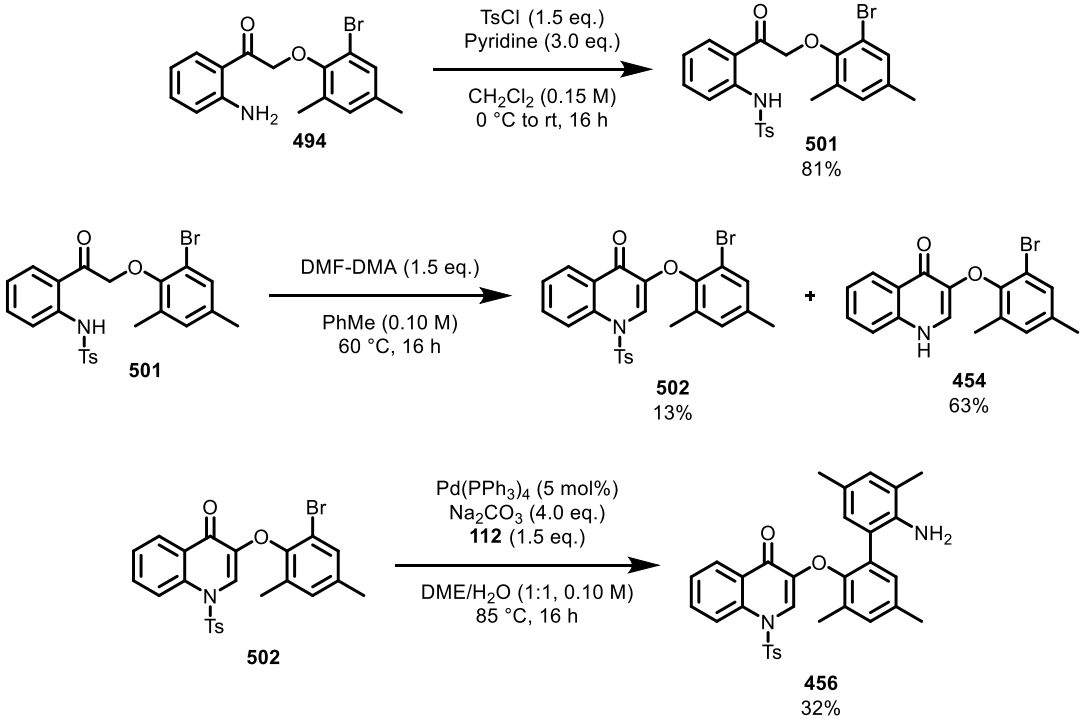
Initially, we tried to encourage the desired cyclisation by quenching with acids (**Scheme 85**). NH_4Cl showed no reactivity, but 10 equivalents of HCl lead to decomposition.

Subsequently, we switched to basic conditions and heated intermediate **500** in DMF with K_2CO_3 to obtain **454** in a moderate 43% yield.



*Scheme 86. The methylation of compound **454**, followed by a Suzuki-Miyaura coupling with **112***

Quinolone **454** was then methylated by full deprotonation with NaH, followed by the addition of MeI (**Scheme 86**). Intermediate **493** was the subjected to standard Suzuki-Miyaura conditions and aniline **446** was formed in an excellent yield.

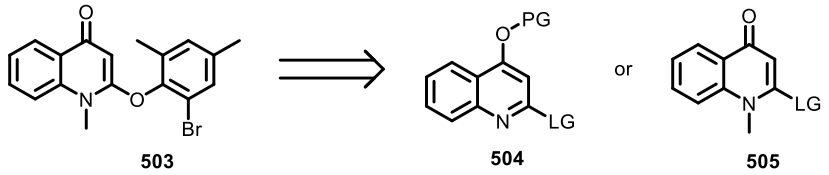


*Scheme 87. Synthesis of a tosyl-protected 4-quinolone oxonium precursor **456***

The tosyl-protected analogue of **446** was produced in a similar fashion (**Scheme 87**). First, aniline **494** was tosylated with TsCl and pyridine as base to obtain **501**. It was then subjected to DMF-DMA in toluene under 60 °C. Unfortunately, the major product of this reaction was 4-quinolone **454**, but desired product **502** was also isolated in a substantial amount for further synthetic steps, including the formation of its oxonium precursor **456**.

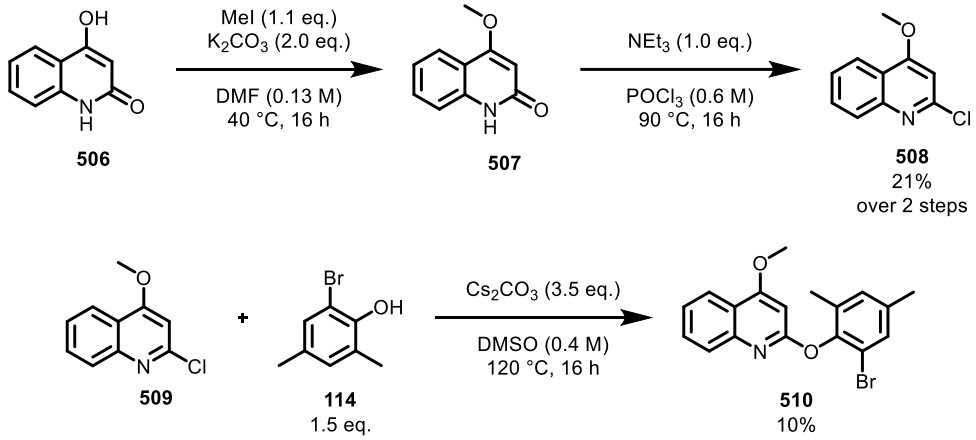
2.3.2 4-Quinolones and Their Analogues Bearing Leaving Groups

In order to construct the dibenzofuran leaving group scaffold in the 2- position, we anticipated a strategy based on the use of 4-quinolones or their protected analogues bearing leaving groups in place for nucleophilic aromatic substitution (**Scheme 88**).



*Scheme 88. Retrosynthetic analysis of intermediate **503** from compounds **504** and **505***

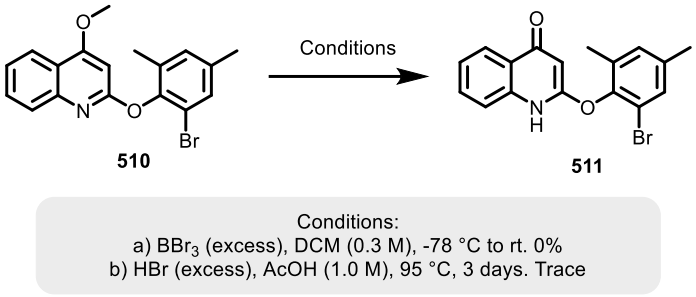
The first 4-quinolone analogue we synthesised was substituted quinoline **508**, acquired in a 21% yield in two synthetic steps (**Scheme 89**). It was then coupled with bromophenol **114**, however, only 10% of the desired product **510** was isolated under these conditions.



*Scheme 89. The synthesis of of 4-quinolone analogues **508** and **510***

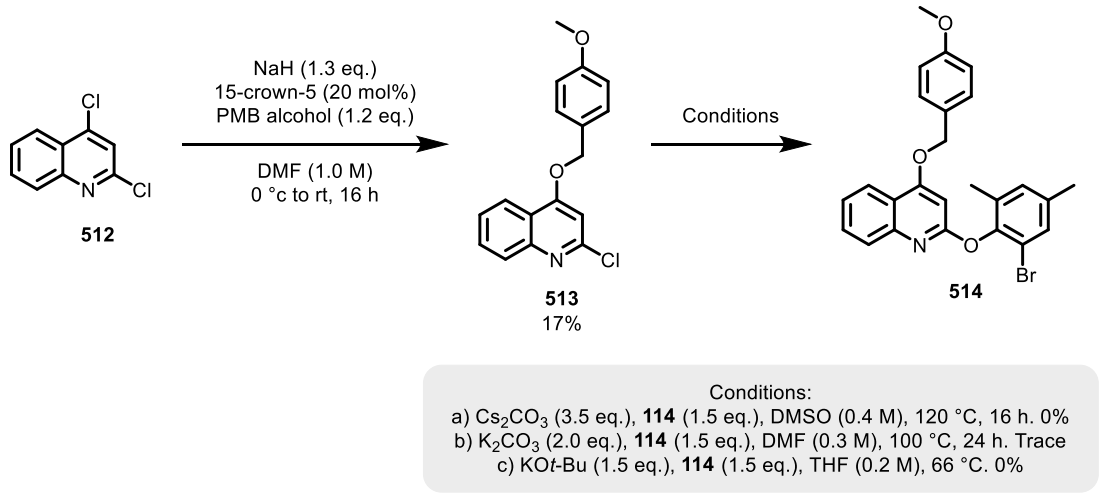
The protected 4-quinolone derivative **510** was then subjected to two sets of conditions for demethylation (**Scheme 90**). An excess of Lewis acid BBr_3 showed no reactivity, but

refluxing intermediate **510** in AcOH with HBr led to a sluggish reaction, mainly producing unwanted side products.



*Scheme 90. Unsuccessful attempts to demethylate compound **510***

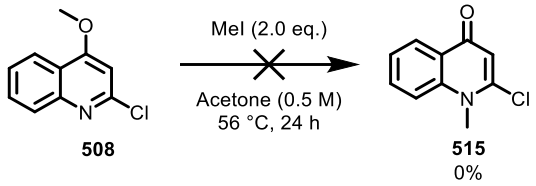
We then imagined replacing the methyl group in the 4- position with a *para*-methoxy benzyl protective group, as this could be deprotected under Lewis acidic, hydrogenative or oxidative conditions (**Scheme 91**). Unfortunately, crucial intermediate **513** could not be isolated in large amounts due to the poor selectivity of the S_NAr reaction with 4-methoxybenzyl alcohol and difficult purification. Furthermore, various conditions for coupling with bromophenol **114** were unsuccessful as a result of decomposition.



*Scheme 91. The synthesis of intermediate **513** and unsuccessful S_NAr attempts with bromophenol **114***

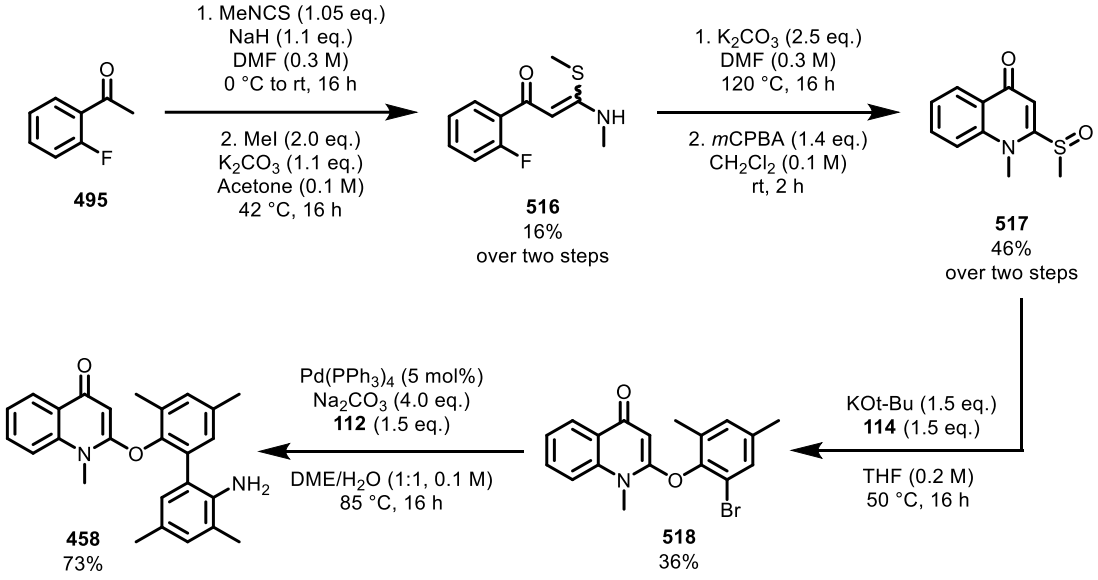
We then shifted our focus to 4-quinolones bearing leaving groups that were not protected. Initially, we envisaged of deprotecting previously synthesised intermediate **508** by

simultaneous methylation on the nitrogen, however, no reactivity was observed, even at reflux (**Scheme 92**).



*Scheme 92. An unsuccessful attempt to synthesise compound **515***

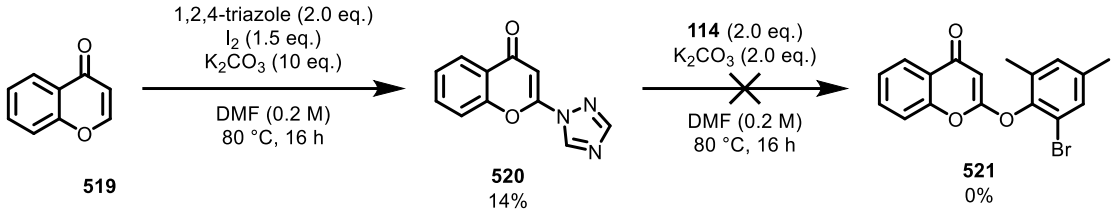
Ultimately, 4-quinolone **517** was synthesised by a set of modified literature procedures, then successfully coupled with bromophenol **114** under basic conditions and finally oxonium precursor **458** was formed in a 73% yield with respect to the final palladium-catalysed step (**Scheme 93**).



*Scheme 93. The complete synthetic route for the synthesis of 4-quinolone oxonium ion precursor **458** from 2'-fluoroacetophenone*

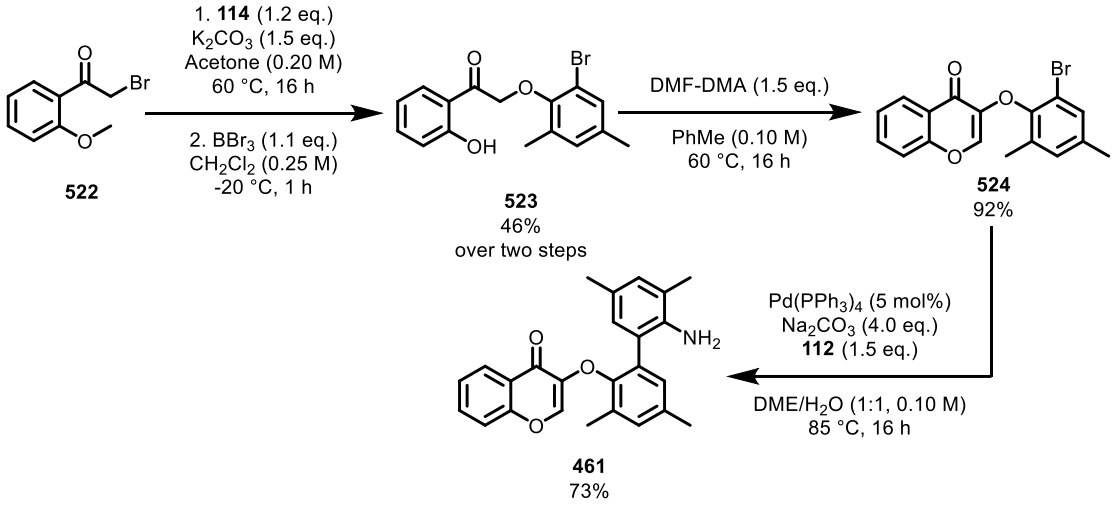
2.3.3 Synthesis of a Chromone Oxonium Ion Precursor

Our initial attempts to synthesise intermediate **521** started by forming chromone derivative **520**, bearing a triazole leaving group (**Scheme 94**). Unfortunately, the S_NAr reaction with bromophenol **114** was not successful.



*Scheme 94. Attempted synthesis of intermediate **521** from compound **520***

Eventually, the chromone oxonium ion precursor **461** was synthesised from 2-bromoacetophenone derivative **522** and its S_NAr reaction with bromophenol **114**, followed by demethylation and the construction of the chromone motif with DMF-DMA (**Scheme 95**). Finally, the aniline moiety in **461** was installed via a Suzuki-Miyaura coupling reaction.



*Scheme 95. Full route for the synthesis of oxonium precursor **461** from 2-bromoacetophenone derivative **522***

2.4 Conclusion

As part of this work, we developed a route to both a 4-quinolone and a chromone oxonium ion. Although the 4-quinolone oxonium ion could not be isolated as a kinetically stable solid, its reactivity with furan was exploited by an *in situ* approach (**Scheme 72**). Contrastingly, the chromone oxonium ion could be isolated as a solid, though its reactivity did not mimic that of 2-quinolones, but it was observed to engage in reactions with various nucleophiles (**Table 12**).

2.5 Future Work

While we demonstrated the feasibility of the 4-quinolone oxonium ion to act as a hetaryne precursor, follow-up work needs to be executed in order to form an isolable oxonium ion. Following from our preliminary work, this would most likely be finding the suitable 4-quinolone equivalent that lacks nucleophilicity on the oxygen.

Regarding the work on the chromone oxonium ions, further investigation into its unusual reactivity is required, screening a wider variety of nucleophiles and other arynophiles.

Furthermore, the viability of 4-pyridone (**525** or **526**) and pyrone (**527** and **528**) oxonium ions should also be looked into, as these heterocycles could be valuable building blocks in aryne-like reactions (**Figure 10**).

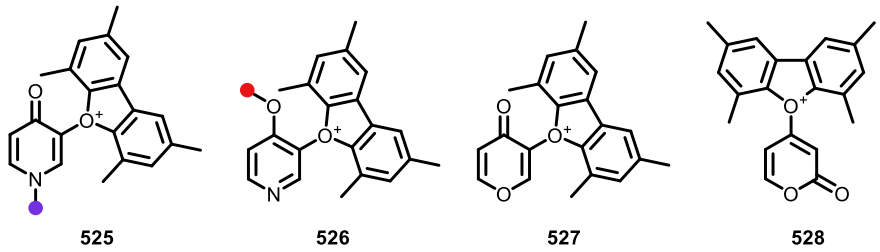


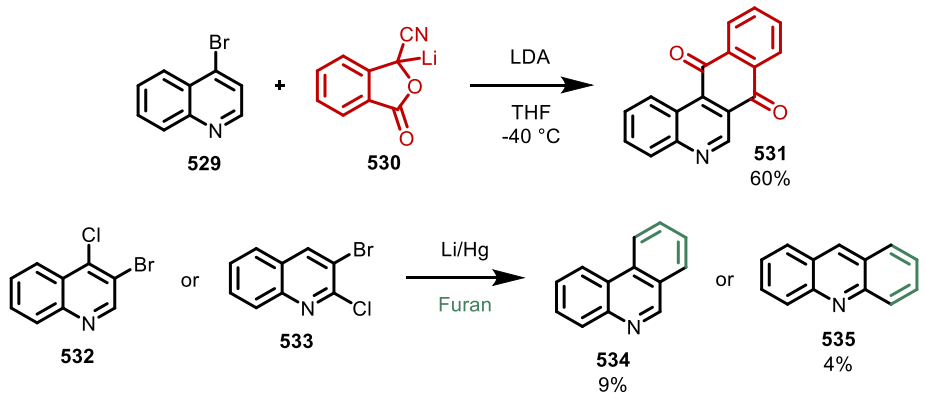
Figure 10. Hypothetical 4-pyridone and pyrone-based oxonium ions

3 Quinoline Oxonium Ions and the Work Towards an Isoquinoline Oxonium Ion

3.1 Introduction

3.1.1 The Hetaryne Chemistry of Quinolines and Isoquinolines

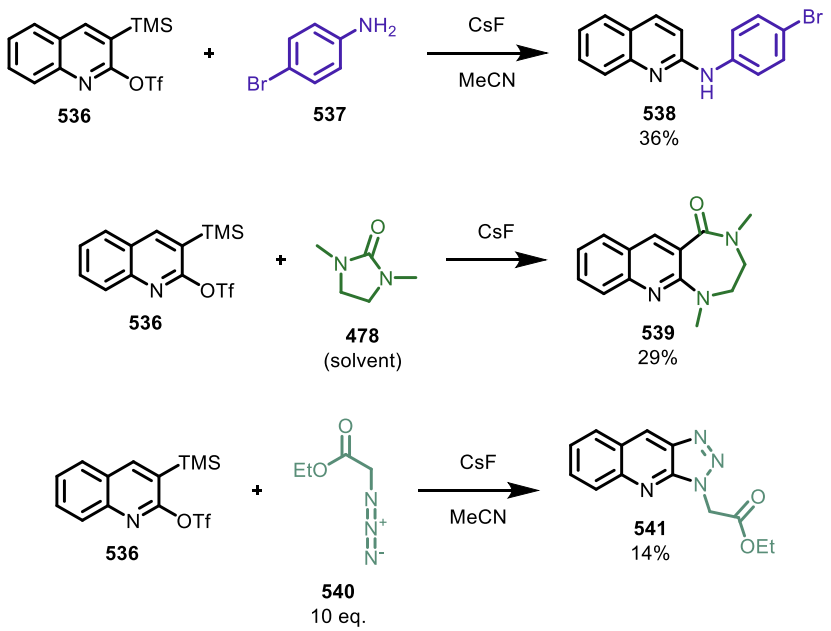
Quinolines and isoquinolines are both fundamental heterocycles, extensively found in a diverse range of natural products and pharmaceuticals.[148,149] Due to the relative simplicity of these scaffolds, their respective hetaryne chemistry has been known as early as the 1960s.[150]



Scheme 96. Selected early examples of 2,3- and 4,5-quinolyne chemistry

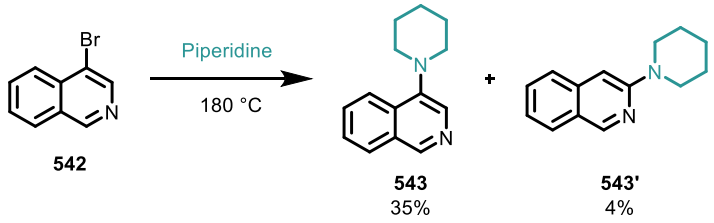
The triple bond in a quinoline-based hetaryne can be manifested in either the 2,3- or the 3,4- position. Some examples of this would include the use of halogenated quinoline derivatives with strong bases like LDA or the highly reducing lithium amalgam (**Scheme 96**).[44,151]

To the best of our knowledge, there is only one Kobayashi-type precursor for the generation of quinolyne. Originally synthesised by the Larock group in 2012,[48] but also utilised by others,[47,152] it forms the strained bond in the 2,3-position and shows complete regioselectivity in its reactions (**Scheme 97**).



*Scheme 97. Selected examples of 2,3-quinolyne chemistry, employing Kobayashi precursor **536***

The chemistry of isoquinolynes is even less developed and, as far as we are aware, only one example can be found in the literature, where two regioisomeric products are formed when 4-bromoisoquinoline **542** is refluxed in anhydrous piperidine (**Scheme 98**).[44]



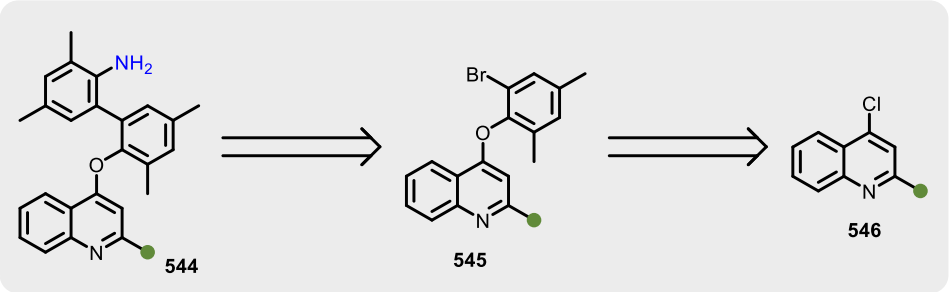
*Scheme 98. The products of the reaction of 4-bromoisoquinoline **542** with piperidine under reflux*

3.1.2 Project Aims

Due to the lack of modern aryne-forming protocols with both quinolines and isoquinolines, we wanted to develop triaryl oxonium ions containing these heterocycles to determine if the generation of these hetarynes is viable *via* this method. By reason of the existence of *ortho*-silylaryl triflate **536** that forms the reactive triple bond in the 2,3-position, we wanted to focus on generating 3,4-quinolynes, where only methods calling for harsh reaction conditions are currently available.

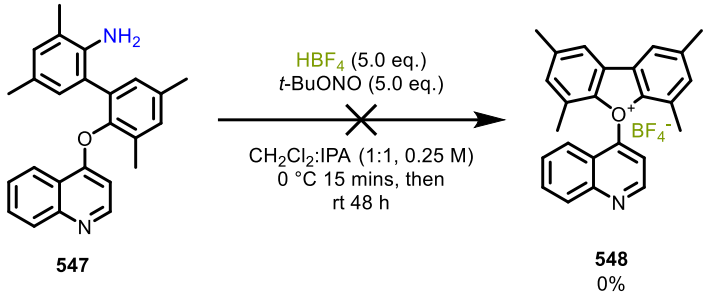
3.2 Results and Discussion

3.2.1 Quinoline Oxonium Ions. Preliminary Work



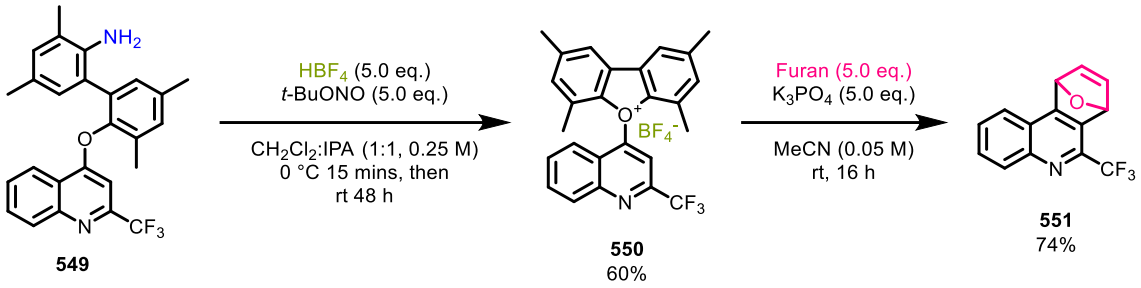
*Scheme 99. Retrosynthetic analysis of oxonium precursor **544**, incorporating fragments **545** and **546***

As a consequence of the similarity between 2-quinolones and quinolines, oxonium precursor **544** was constructed in a similar approach, installing fragments **112** and **114** in a step-wise fashion (**Scheme 99**). When **547** was subjected to diazotisation and stirred at room temperature for 48 hours, only non-specific decomposition was detected (**Scheme 100**).



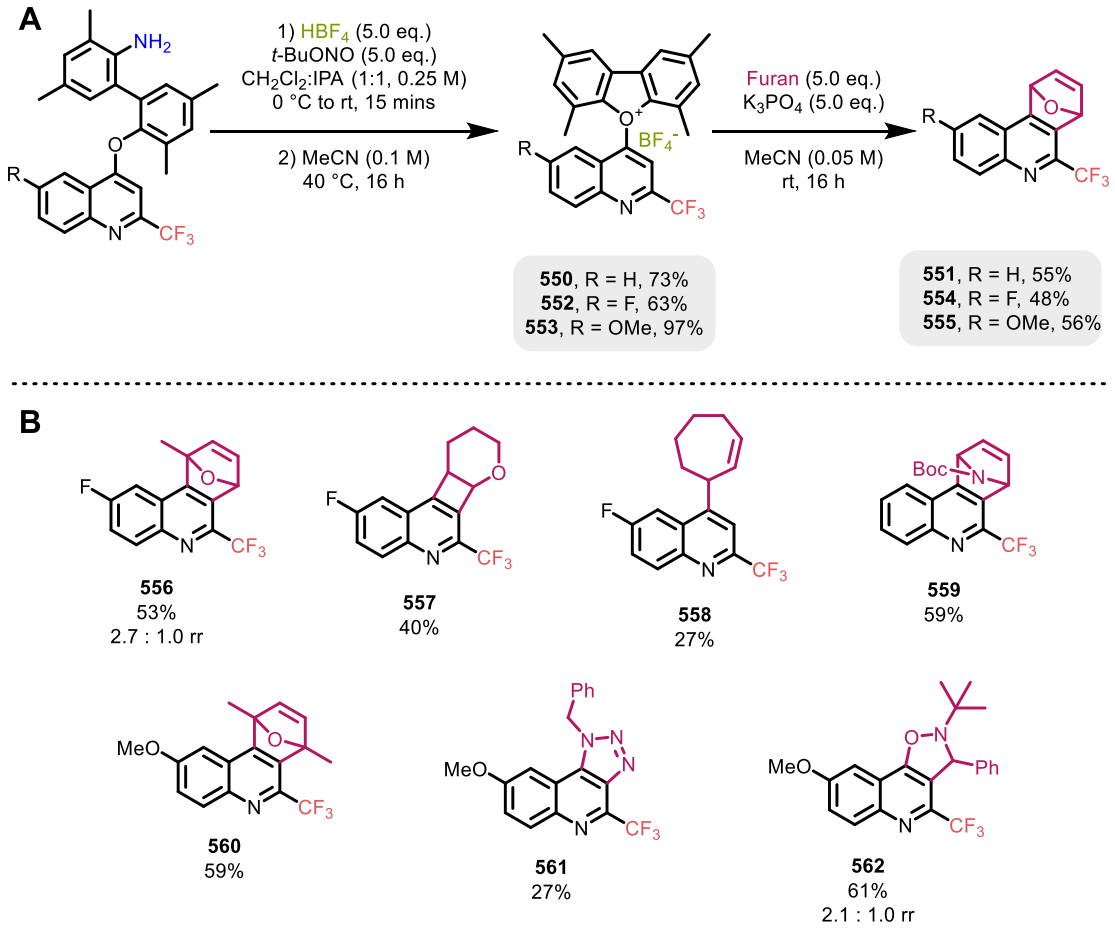
*Scheme 100. The unsuccessful formation of oxonium ion **548** from precursor **547***

We hypothesised that the oxonium formation was not successful due to the nucleophilicity of the quinoline nitrogen.[153] As a way to modulate this unwanted reactivity, we installed an electron-withdrawing trifluoromethyl group in the 2-position (**Scheme 101**). Pleasingly, although now taking 48 hours at room temperature, oxonium **550** formed cleanly in a 60% isolated yield. Furthermore, its aryne-like reactivity was demonstrated in a K_3PO_4-mediated trapping reaction with furan.



*Scheme 101. The formation of oxonium **550** and successful trapping with furan*

3.2.2 Quinoline Oxonium Ions. Scale-Up and Scope

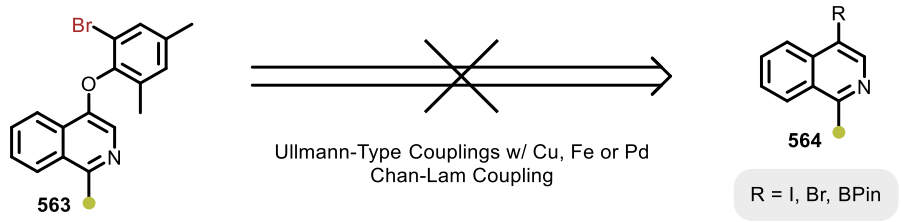


Scheme 102. A scope of quinoline-based oxonium tetrafluoroborates and their aryne-like reactivity in various pericyclic reactions. All compounds in this scheme have been synthesised by Part II student Jacob Kessler in the 2023/2024 academic year. Where regioisomers are formed, the structure of the major product is depicted

After identifying the necessity of an electron withdrawing group in the 2-position, a total of three quinoline oxonium ions were synthesised by Part II student Jacob Kessler (**Scheme 102**–**A**). We demonstrated the feasibility of both electron donating and

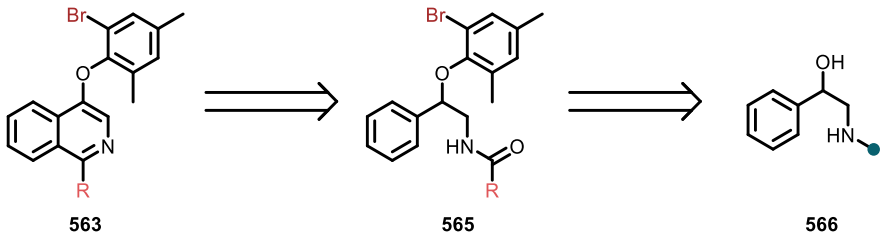
withdrawing groups on the carbocyclic ring, successfully trapping the relevant oxonium ions with furan, as well as in other pericyclic transformations (**Scheme 102**–**B**).

3.2.3 Developing a Route to an Isoquinoline Oxonium Ion Precursor. Initial Strategies



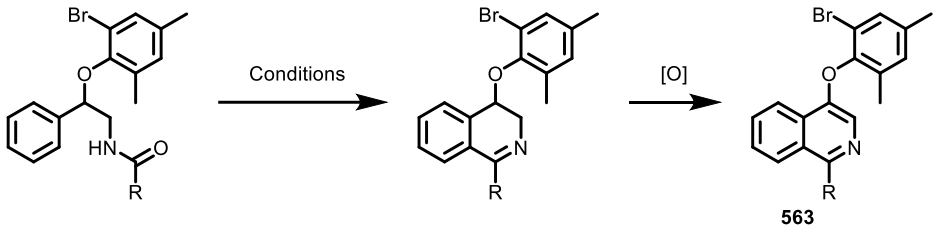
*Scheme 103. Unsuccessful transition metal-catalysed cross coupling strategies to form intermediate **552***

Without an obvious way to involve an isoquinoline as an electrophilic partner in S_NAr, we initially trialled various transition metal-catalysed transformations in order to form a C–O bond between isoquinoline **564** and bromophenol **114** (**Scheme 103**). Unfortunately, all conditions tested resulted in either no reactivity or complete decomposition of the starting materials.



*Scheme 104. A de novo approach for the synthesis of intermediate **563***

We then changed our approach for the synthesis of **563** by attempting the construction of the isoquinoline motif from amino alcohol-derived ethers **565** (**Scheme 104**). Various conditions were tested for the crucial cyclisation step, but, unfortunately, none of them proved to be viable (**Scheme 105**).

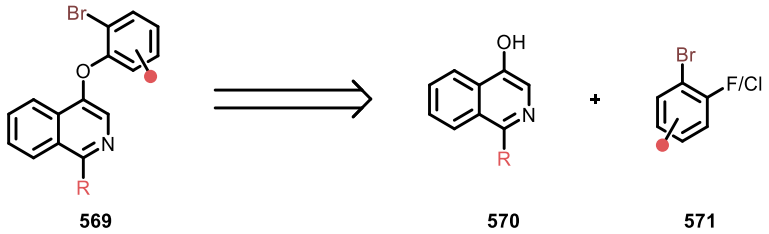


Conditions
a) **567**, R = Me, $POCl_3$ (5.0 eq.), MeCN (0.3 M), 80° C, 16 h. 0% (complex mixture)
b) **568**, R = CF_3, $POCl_3$ (10.0 eq.), CH_2Cl_2 (0.1 M), 40 °C, 24 h. 0% (no reaction)
c) **568**, R = CF_3, Tf_2O (1.2 eq.), 2-chloropyridine (1.2 eq.), CH_2Cl_2 (0.2 M), -78 °C to rt, 16 h. 0% (complex mixture)

*Scheme 105. Unsuccessful attempts to synthesise a precursor to intermediate **563***

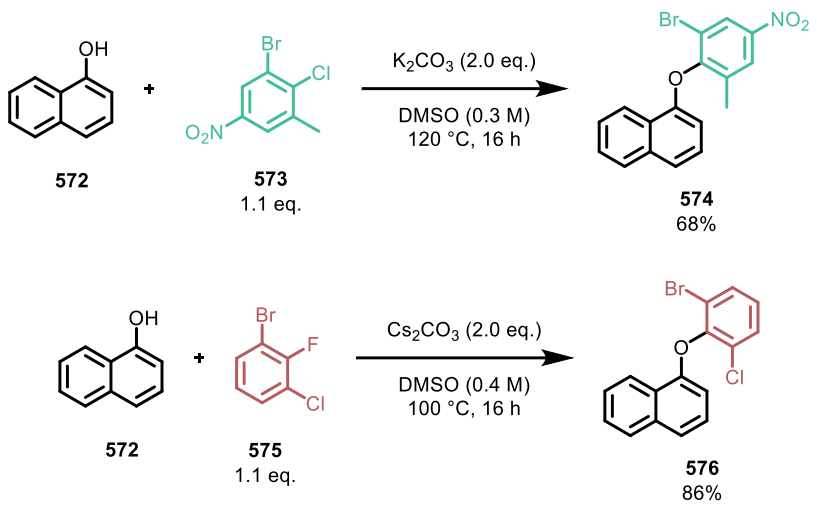
3.2.4 Developing a Route to an Isoquinoline Oxonium Ion Precursor. Isoquinolines as Nucleophiles in S_NAr reactions

Although not very well developed in the literature, another potential strategy that we wanted to investigate was the use of phenolic isoquinoline derivatives **570** in S_NAr reactions with various electrophilic partners (**Scheme 106**).

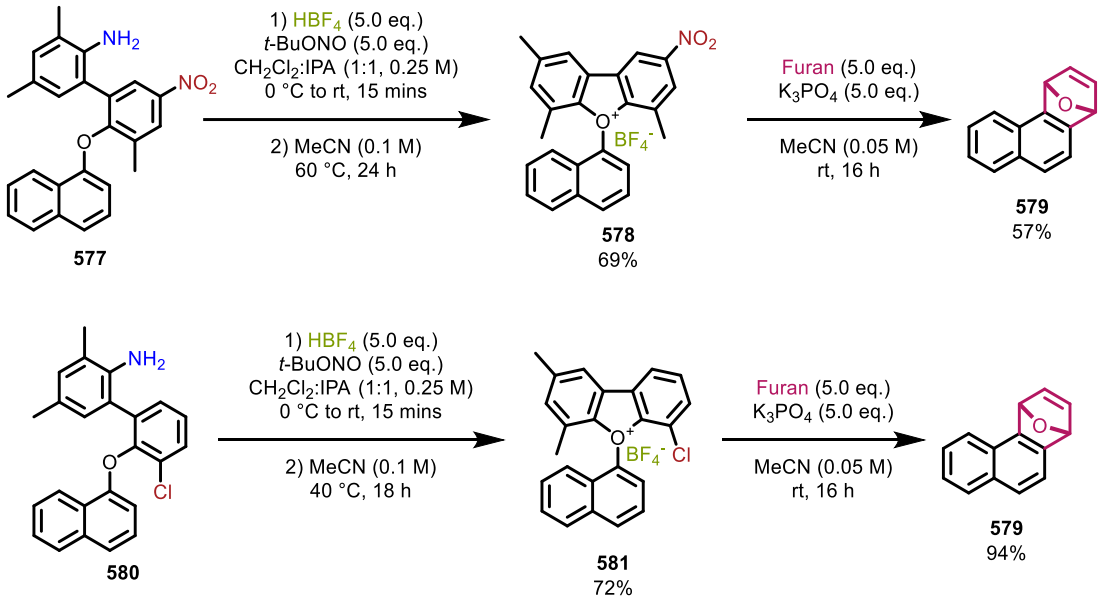


*Scheme 106. An S_NAr approach to synthesise intermediate **569** from phenolic isqouinoline derivative **570***

Our initial studies focused on the nucleophilic aromatic substitution reactions involving 1-naphthol **572** as our model system (**Scheme 107**). As we were simultaneously developing unprecedented oxonium ion scaffolds, we did not want any nucleophilic or basic heteroatoms to inflict false negative results in the final oxonium formation step. Pleasingly, we found that both aryl chloride **573** and aryl fluoride **575** gave their corresponding ether intermediates in good yields, which were further subjected to a Suzuki-Miyaura coupling with **112**, furnishing oxonium ion precursors **577** and **580** (**Scheme 108**).



*Scheme 107. S_NAr reactions between 1-naphthol and arenes **573** and **575***

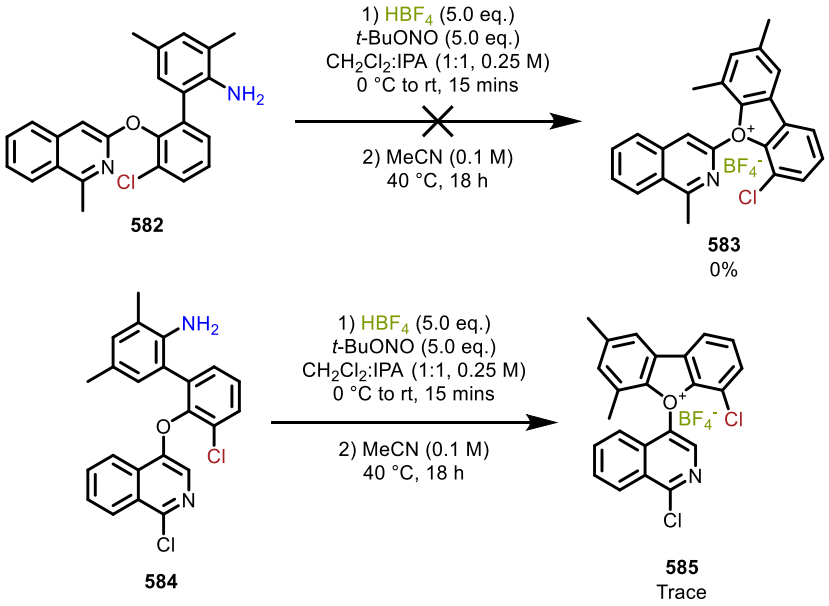


*Scheme 108. The successful synthesis of oxonium ions **578** and **581** and their trapping reactions with furan*

The aforementioned anilines were then subjected to diazotisation, followed by heating in acetonitrile in order to determine if the formation of their oxonium ions was viable (**Scheme 108**). Both **578** and **581** were isolated in good yields following trituration and, satisfyingly, both served as aryne precursors in the final furan trapping step. However, lower stability for oxonium tetrafluoroborate **578** was noted as the solid was found to partially decompose at room temperature. No bench stability issues were observed with

oxonium **581**, therefore we decided to employ this dibenzofuran scaffold into our isoquinoline system.

Following the findings of 1-naphthol-derived oxonium ions, we synthesised compounds **582** and **584** before subjecting them to our standard oxonium forming conditions (**Scheme 109**). Although diazonium ions were formed in both cases, aniline **582** ultimately decomposed into a complex mixture of products. Regarding oxonium ion **585**, only traces of it were detected following trituration amongst at least three other charged or highly polar compounds.

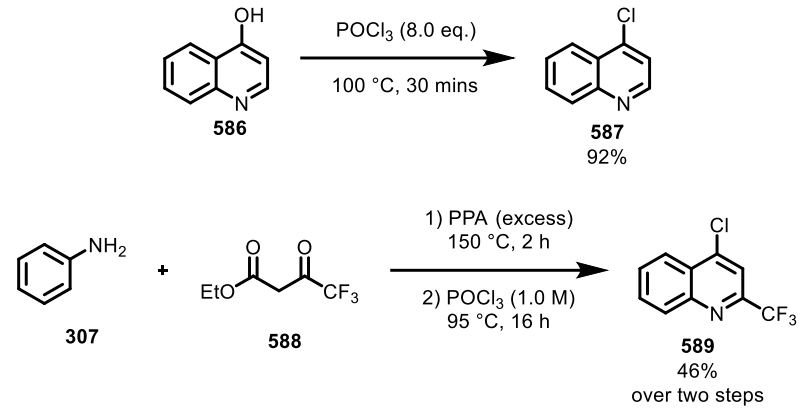


*Scheme 109. The unsuccessful attempts to synthesise isoquinoline-based oxonium ions **583** and **585***

3.3 Synthesis

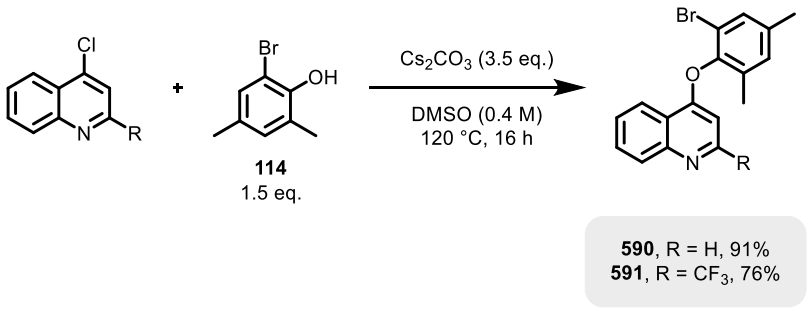
3.3.1 Synthesis of Quinoline Oxonium Ion Precursors

4-Chloroquinoline derivatives used to synthesis quinoline oxonium ion precursors were obtained by the chlorination of their corresponding 4-hydroxyquinolines (**Scheme 110**). Quinoline **586** was commercially available and produced **587** in a 92% isolated yield, whereas **589** was synthesised in a two-step process from aniline **307** and **588**.



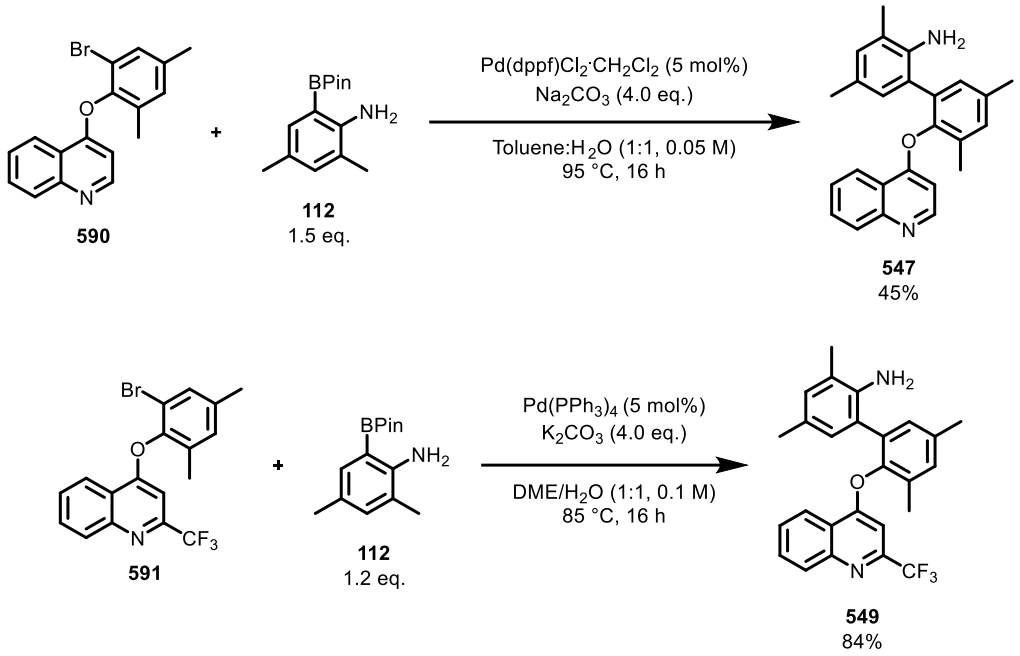
*Scheme 110. Synthesis of 4-chloroquinoline derivatives **587** and **589***

Subsequently, heterocycles **5787** and **589** were coupled with bromophenol **114** to obtain ether intermediates **590** and **591** in very good yields (**Scheme 111**).



*Scheme 111. Synthesis of compounds **590** and **591** via an S_NAr reaction with **114***

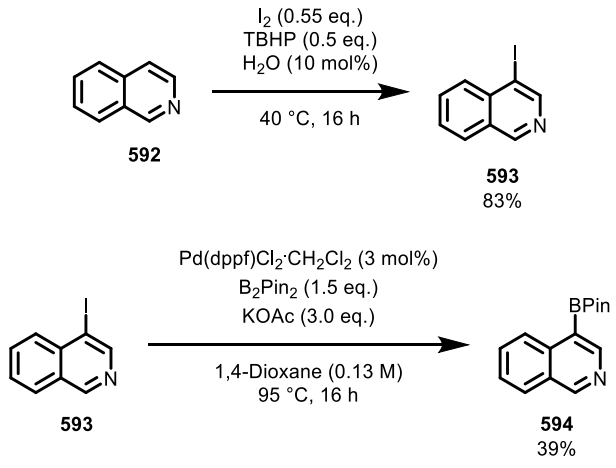
Finally, the preceding compounds were subjected to Suzuki-Miyaura coupling with boronic acid pinacol ester **112** to obtain their respective isoquinoline oxonium ion precursors (**Scheme 112**).



*Scheme 112. Synthesis of anilines **547** and **549** via Suzuki-Miyaura coupling*

3.3.2 Synthesis of Isoquinoline Oxonium Ion Precursors. Cross Coupling Strategies

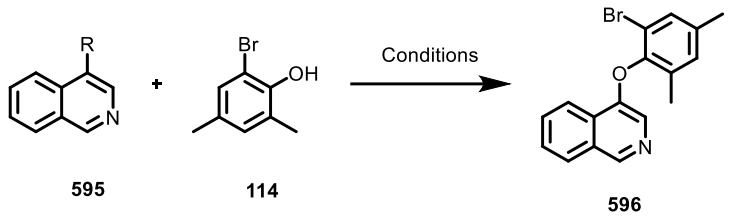
4-Bromoisoquinoline **542** used in an Ullmann-type coupling with bromophenol **114** was obtained commercially, whereas both 4-iodoisoquinoline **593** and boronic acid pinacol ester **594** were produced by synthesis (**Scheme 113**).



*Scheme 113. The synthesis of 4-substituted isoquinolines **593** and **594***

A number of transition metal-catalysed coupling conditions were tested (**Scheme 114** and **Table 13**). These include Ullman-type protocols with Cu (**Entries 1** to **3** and **6**) and Fe

(**Entry 4**), as well as a Buchwald-Hartwig-type transformation (**Entry 5**). A Chan-Lam coupling with **594** also only led to decomposition (**Entry 7**).



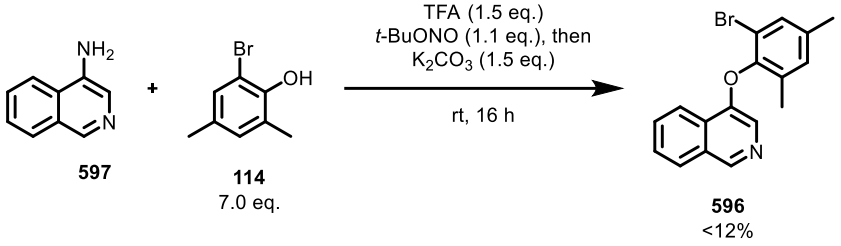
*Scheme 114. A general scheme for the synthesis of ether **596** from various isoquinoline derivatives and bromophenol **114***

Entry	R	Conditions	Yield
1	I	CuI (10 mol%), Picolinic acid (20 mol%), K_3PO_4, DMSO (1.0 M), 110 °C, 24 h	0% (decomposition)
2	I	CuI (30 mol%), 18-crown-6 (10 mol%), K_2CO_3, DMSO (0.5 M), 100 °C, 24 h	0% (decomposition)
3	I	CuI (20 mol%), *N*,*N*-dimethylglycine (60 mol%), Cs_2CO_3, 1,4-dioxane (0.3 M), 100 °C, 48 h	0% (no reaction)
4	I	$FeCl_3$ (10 mol%), dipivaloylmethane (80 mol%), Cs_2CO_3, DMF (0.5 M), 135 °C, 24 h	0% (decomposition)
5	I	$Pd(dba)_2$ (10 mol%), $(t\text{-}Bu)_3PHBF_4$ (20 mol%), t-BuONa, PhMe (0.1 M), 100 °C, 24 h	0% (no reaction)
6	Br	CuI (10 mol%), Picolinic acid (20 mol%), K_3PO_4, DMSO (1.0 M), 90 °C, 24 h	0% (no reaction)
7	BPin	$Cu(OAc)_2$ (30 mol%), $B(OH)_3$, 4 Å MS, air, MeCN (0.3 M), 80 °C, 16 h	0% (decomposition)

*Table 13. Conditions tested for the cross-coupling strategy to form isoquinoline-based intermediate **585***

3.3.3 Synthesis of Isoquinoline Oxonium Ion Precursors. Diazonium Ion Strategy

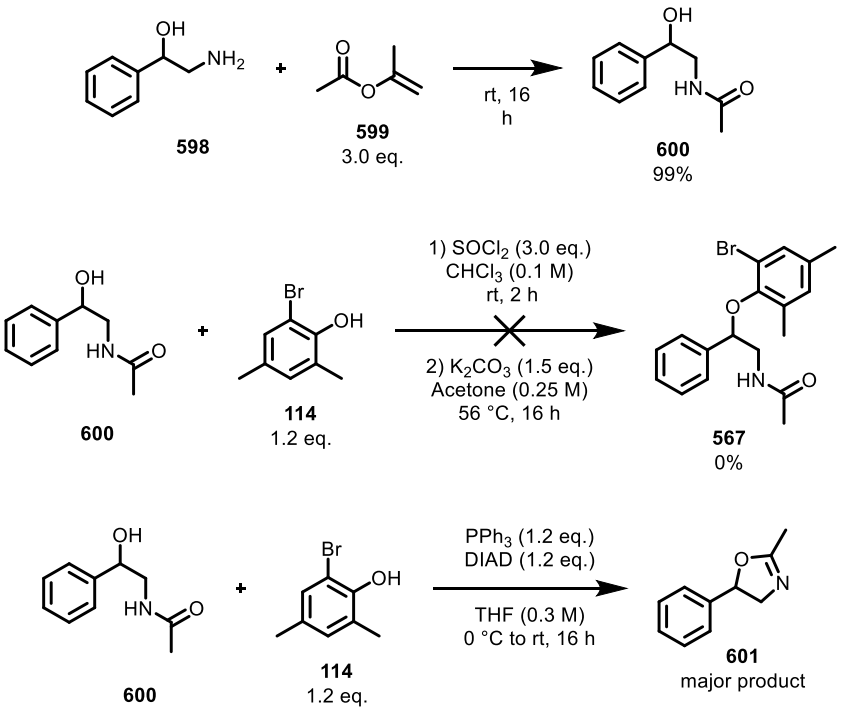
The only strategy that showed any potential was the Sandmeyer-like reaction between 4-aminoisoquinoline **597** and **114** as a reaction solvent (**Scheme 115**). About 12% of compound **596** was isolated, however, it could not be purified fully and thus was not subjected to any further synthetic transformations.



*Scheme 115. Synthesis of compound **596** via the diazotisation of 4-aminoisoquinoline **597***

3.3.4 Synthesis of Isoquinoline Oxonium Ion Precursors. Amino Alcohol Derivatives

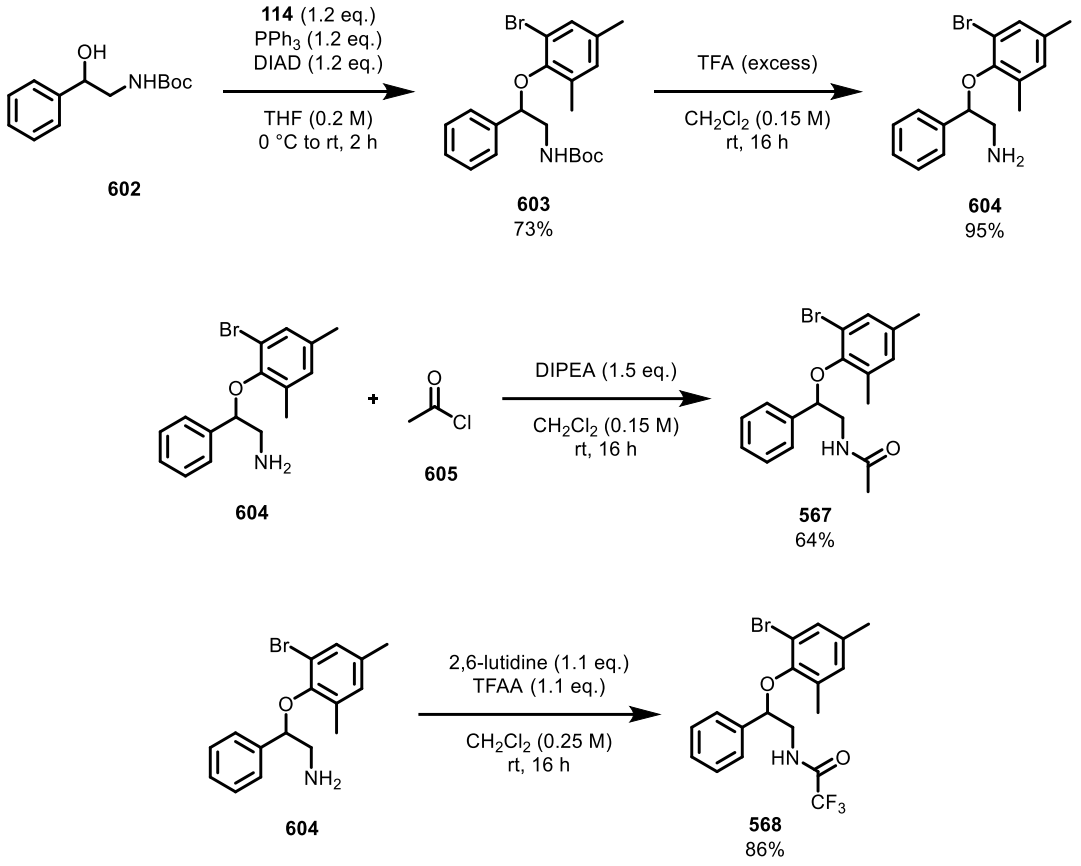
Our initial efforts to synthesise amino alcohol-derived ether **567** included the initial step of acetylation of **598** with isopropenyl acetate **599** (**Scheme 116**). **600** was then subjected to chlorination with thionyl chloride, but the subsequent base-mediated S_N2 step with bromophenol **114** showed no reactivity. Alternatively, we envisaged forging the C–O bond *via* a Mitsunobu reaction, however, the major product of this transformation was identified as oxazolidine **601**.



*Scheme 116. The synthesis of amino alcohol derivative **600** and unsuccessful attempts to produce **567***

In order to prevent the unwanted cyclisation in the aforesaid Mitsunobu reaction, we relied on the Boc protection in compound **602**, which successfully furnished ether

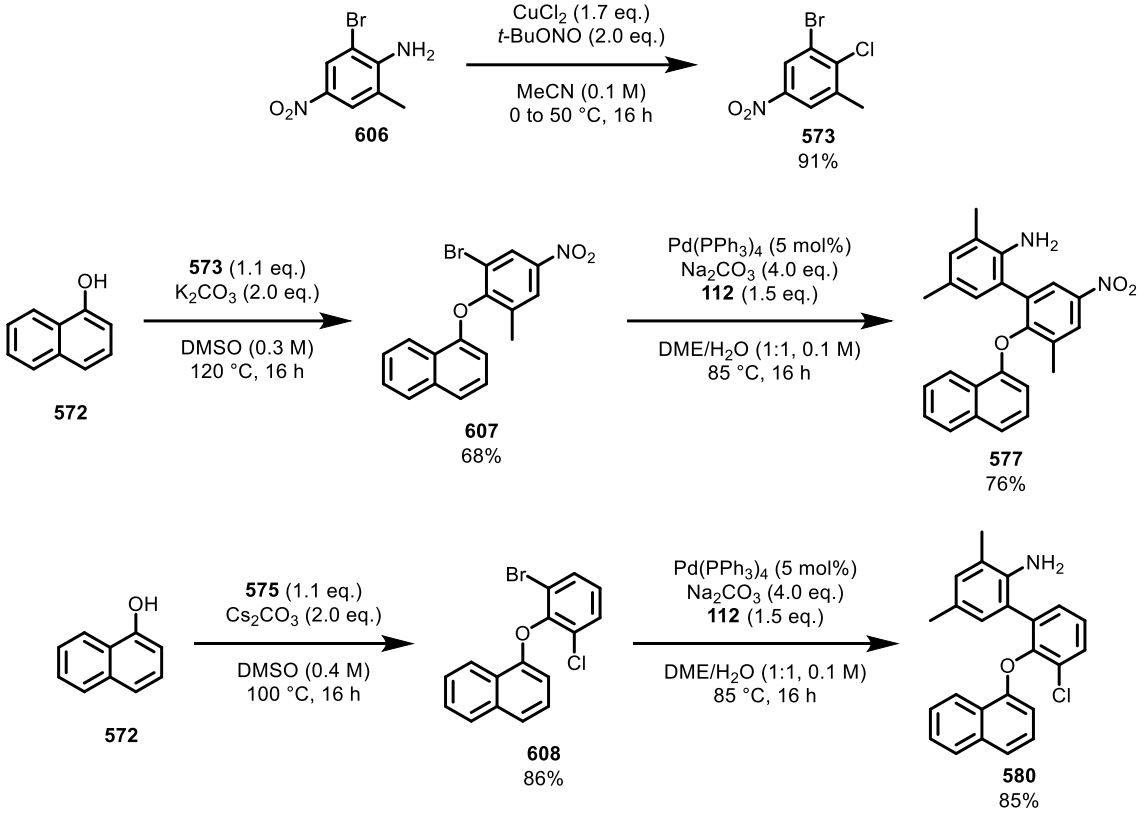
intermediate **603**, followed by subsequent deprotection by excess TFA in CH_2Cl_2 (**Scheme 117**). With **604** in hand, it was further subjected to two sets of amide formation, installing an acetyl group in **567** and a trifluoroacetyl group in **568**.



*Scheme 117. The synthesis of amino alcohol-derived ether **604** and its products of acetylation and trifluoroacetylation*

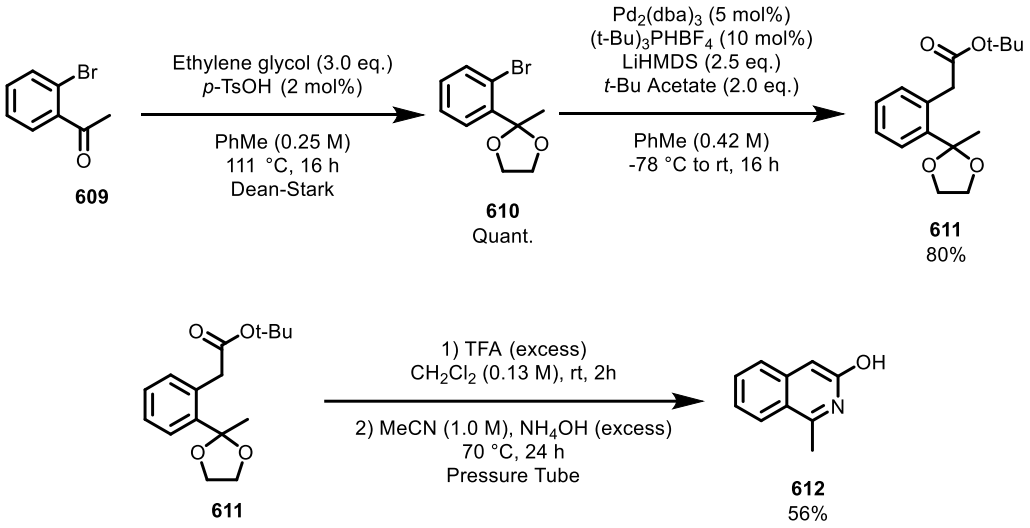
3.3.5 Synthesis of 1-Naphtol Oxonium Ion Precursors

Aryl chloride **573**, required for its reaction with 1-naphthol **572** was synthesised by a Sandmeyer reaction with aniline **606** and $CuCl_2$ as a source of chloride (**Scheme 118**). Aryl fluoride **575** was obtained from commercial sources. Ether intermediates **607** and **608** were produced by base-mediated S_NAr reactions at elevated temperatures, followed by the Suzuki-Miyaura coupling with aniline **112** to produce oxonium ion precursors **577** and **580** in good yields.



*Scheme 118. The synthesis of aryl chloride **573**, as well as 1-naphthol-containing ethers **607** and **608** and their Suzuki-Miyaura products **577** and **580***

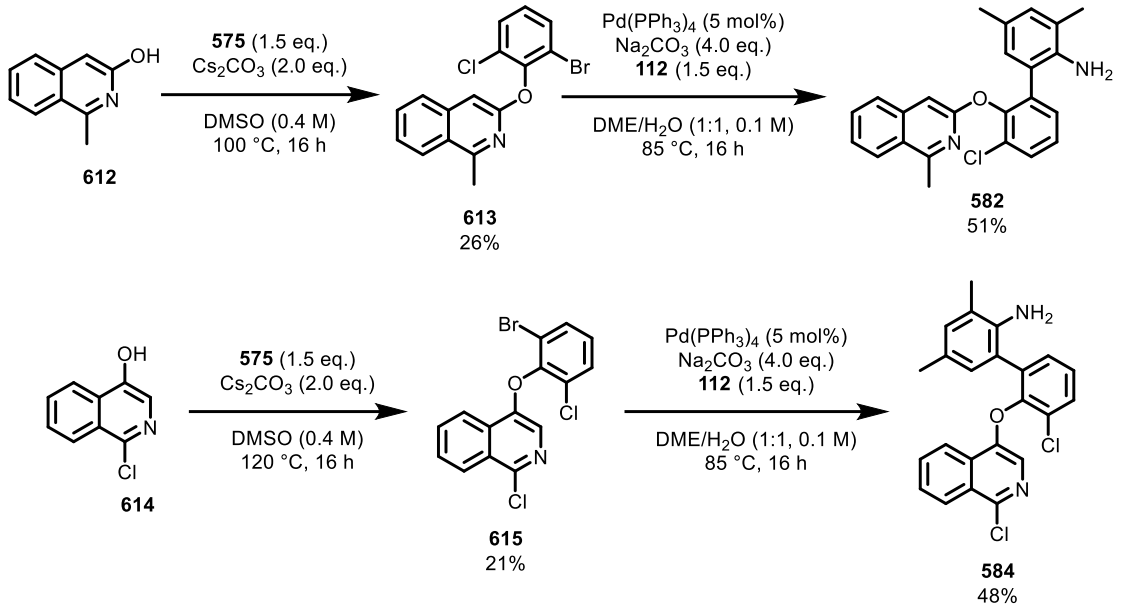
3.3.6 Synthesis of Isoquinoline Oxonium Ion Precursors. SNAr Approach



*Scheme 119. The synthesis of isoquinoline derivative **612** from 2'-bromoacetophenone*

Phenolic isoquinoline derivative **612** was synthesised in 4 steps, starting with the ketal protection of 2'-bromoacetophenone **609**, followed by a palladium-catalysed cross coupling with *tert*-butyl acetate (**Scheme 119**). **612** was ultimately produced by treating

611 with an excess of TFA, followed by heating with concentrated aqueous ammonia in a pressure tube.



*Scheme 120. A two-step synthesis of isoquinoline oxonium ion precursors **582** and **584***

Isoquinoline derivatives **612** and **614** were subjected to an S_NAr reaction with aryl fluoride **575**, supplying intermediates **613** and **615** in a 26% and 21% yield, respectively (**Scheme 120**). Finally, anilines **582** and **584** were obtained via a Suzuki-Miyaura coupling.

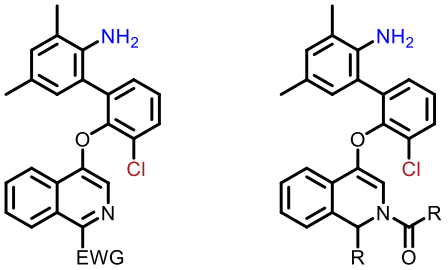
3.4 Conclusion

Within the context of this chapter, we developed a route to both quinoline and isoquinoline oxonium ion precursors. With regard to the quinolines, we demonstrated the importance of an electron withdrawing trifluoromethyl group in the 2- position for the stability of the corresponding oxonium ion. Eventually, a small reaction scope of three different quinoline oxonium ions was developed. So far, an isoquinoline oxonium ion could not be synthesised, but a viable route to its precursors was obtained.

3.5 Future Work

Although we demonstrated the synthetic utility of quinoline-based oxonium ions in various pericyclic reactions, other modes of reactivity should be explored as well as the functional group compatibility explored.

Furthermore, since an isoquinoline oxonium ion has not been synthesised as of yet, further synthetic work is required to optimise the scaffold electronically. Seeing decomposition in the oxonium ion formation of an unsubstituted quinoline (**Scheme 100**), electron-withdrawing group-bearing isoquinoline analogues such as **616** or **617** should be investigated (**Figure 11**).



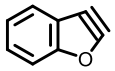
616 **617**

Figure 11. Hypothetical isoquinoline oxonium ion precursors, bearing electron-withdrawing groups

4 Five-Membered Ring Hetarynes

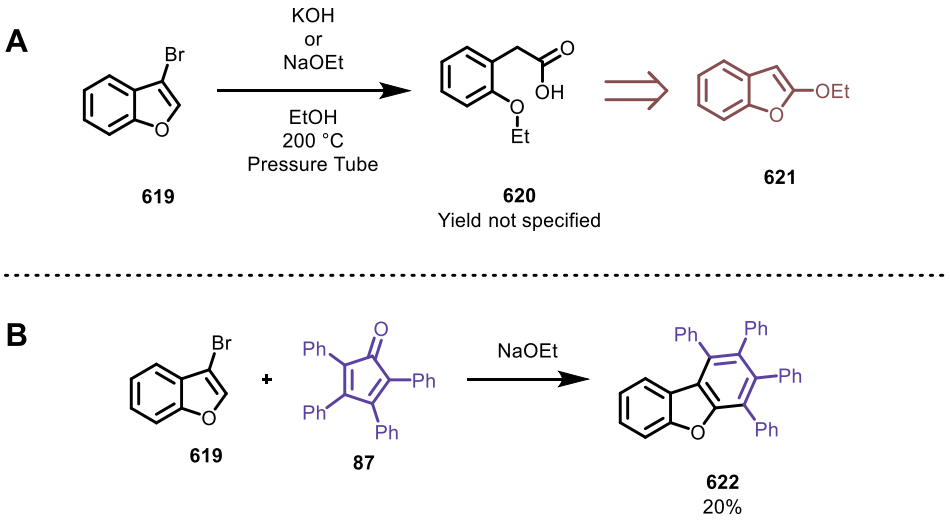
4.1 Introduction

4.1.1 Benzofuranyne as the First Proposed Hetaryne



618
2,3-benzofuranyne

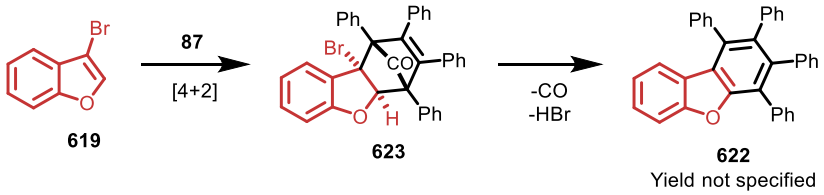
Figure 12. The structure of 2,3-benzofuranyne



*Scheme 121. Selected early examples of the hetaryne-like chemistry of 3-bromobenzofuran **608***

Although benzyne **1** is arguably the most recognisable aryne, it was 2,3-benzofuranyne **618** that was the first example of such reactive intermediate posited in the literature (**Figure 12**). Originally reported in 1902, Stoermer and Kahlert subjected 3-bromobenzofuran **619** to an ethanolic solution of sodium ethoxide or potassium hydroxide under high temperature and pressure, obtaining carboxylic acid **620** as one to the major products (**Scheme 121**–**A**).[42] The authors proposed that compound **620** came as a result of the hydrolysis of intermediate **621** during work up which, in turn, was formed by the nucleophilic addition of ethoxide into hetaryne **618**. The involvement of **618** was also consistent with the findings of Wittig et al., where cycloadduct **622** was

isolated in a 20% yield alongside trace formation of the two ethoxybenzofuran isomers (**Scheme 121**–**B**).[154]

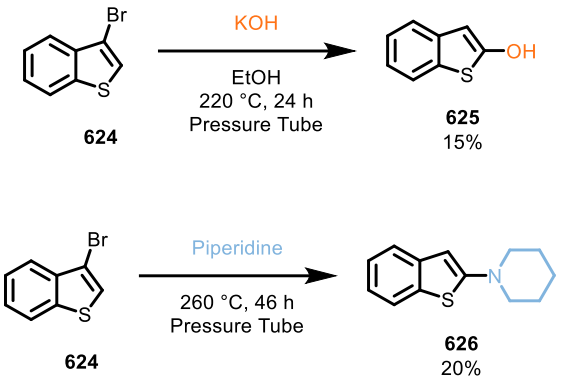


*Scheme 122. The base-free reaction of 3-bromobenzofuran **619** and tetracyclone **87***

The existence of didehydrobenzofuran **618** had been called into question as early as the 1980s, when Reinecke argued that the experimental data mentioned earlier were too ambiguous.[43] The original report lacked clarity on the exact purity and structure of the bromobenzofuran used and, in addition, the pivotal 2-ethoxybenzofuran intermediate **621** was never isolated. Furthermore, it was found that 3-bromobenzofuran **619** can react with tetracyclone **87** with no added base, suggesting an alternative Diels-Alder addition-elimination mechanism (**Scheme 122**).

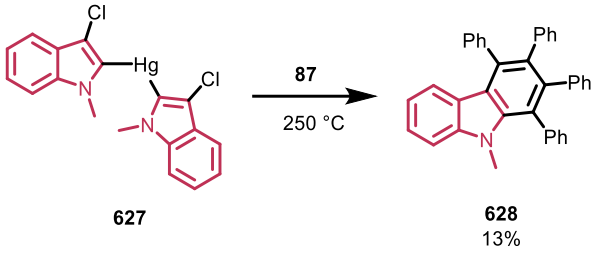
4.1.2 Other Examples of Five-Membered Ring Hetarynes

Owing to their high ring strain and issues arising from the inclusion of heteroatoms, the examples of 5-membered hetarynes remain scarce, especially in modern literature. The majority of the reactions that do appear to involve aryne-like reactivity were published in the mid-20th century, so, distinctly, they rely on harsh conditions.[44,155] For example, the reaction of 3-bromobenzothiophene **624** with either potassium hydroxide or piperidine was only observed at temperatures exceeding 200 °C (**Scheme 123**). In a similar manner to the seminal 1902 publication for 2,3-benzofuranyne **618**, complete selectivity for the 2-position was reported.



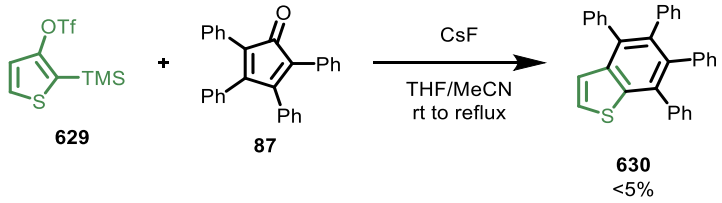
*Scheme 123. Selected early examples of the hetaryne-like chemistry of 3-bromobenzothiophene **624***

The possibility of a 2,3-indolyne species has also been postulated when organomercury compound **627** was heated in the presence of tetracyclone **87**, obtaining the apparent aryne trapping product **628** along with mercury(II) chloride (**Scheme 124**).[154]



*Scheme 124. The reaction between organomercury compound **627** and tetracyclone **87** under high temperatures*

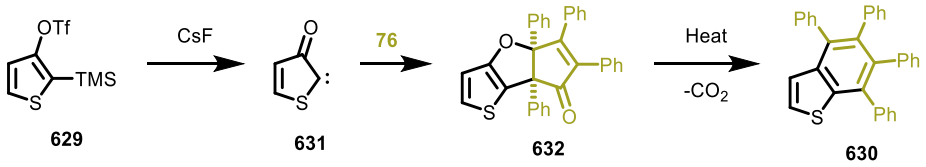
4.1.3 Five-Membered Ring Hetarynes in Modern Literature



*Scheme 125. The apparent hetaryne-like reactivity of Kobayashi precursor **629** and tetracyclone **87***

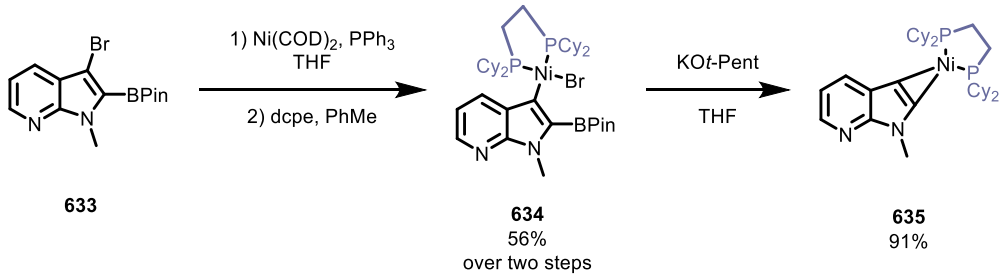
As discussed in the General Overview, the Kobayashi method for generating (het)arynes is arguably the most commonly applied protocol today, however, the synthesis of novel *ortho*-silylaryl triflates can pose a significant challenge.[156] To the best of our understanding, there is only one example of a Kobayashi-like precursor incorporating a 5-membered ring. Perez and co-workers designed an 8-step route to synthesise crucial

intermediate **629**.[157] Although many widely-used arynophiles such as furan or anthracene did not seem to trap the hetaryne expected to form upon treatment with fluoride, tetracyclone **87** furnished heterocycle **630** in an approximately 5% yield (**Scheme 125**).



*Scheme 126. A mechanism explaining the reactivity of Kobayashi precursor **629** by the involvment of a ketocarbene intermediate*

Uncertain about the feasibility of 2,3-thiophyne, the group conducted significant mechanistic studies and computational calculations, deducing a mechanism with the involvement of ketocarbene **631**, which forms intermediate **632** that can rearrange to the ultimate product at high temperatures with the loss of carbon dioxide (**Scheme 126**).



Scheme 127. The three-step synthesis of an azaindolyne complex with Ni

In 2024, Roberts *et al*. utilised an organometallic strategy to stabilise a 7-aza-2,3-indolyne system.[158] The group employed an azaindole-based *ortho*-borylaryl bromide **633**, introducing nickel *via* oxidative addition and subsequent ligand exchange, followed by a deborylative elimination step (**Scheme 127**).

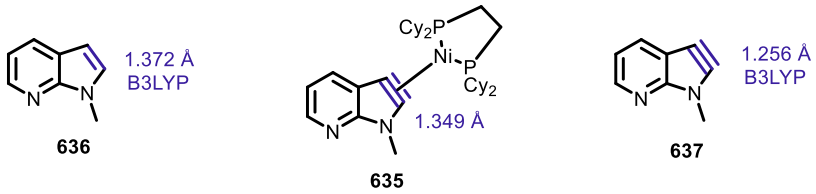
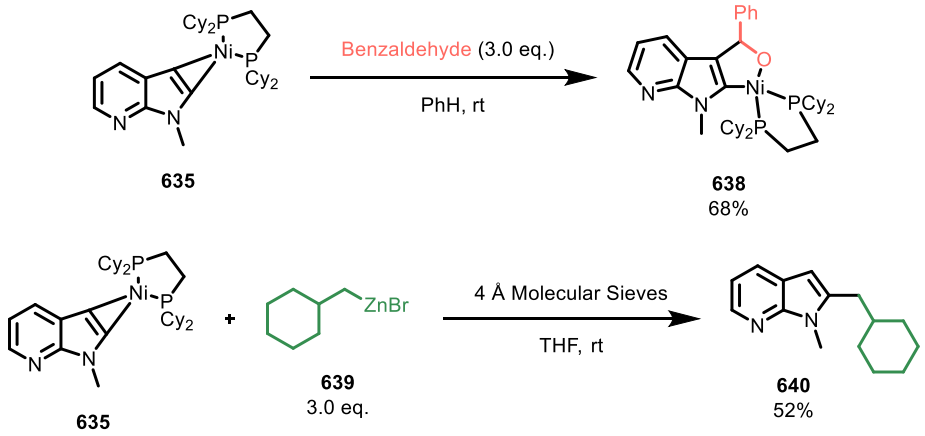


Figure 13. The calculated and experimental bond lengths of 7-azaindole derivatives

Following the synthesis of **635**, it was characterised by x-ray crystallography. The measured C_2–C_3 bond length was considerably affected by the back-donation from the electron-rich Ni centre, as compared to the bond length in 7-aza-2,3-indolyne **637** determined by quantum mechanical calculations (**Figure 13**). The metal complex was then demonstrated to exhibit ambiphilic character, showing reactivity with some electrophiles and nucleophilic organometallic agents (**Scheme 128**).



*Scheme 128. Selected examples of the reactivity of Ni-based organometallic complex **635***

4.1.4 The Feasibility of Five-Membered Hetarynes

In 2012, Garg, Houk, Paton and co-workers published a computational model for predicting the synthetic feasibility of various heterocyclic arynes based on the energies of their dehydrogenation, which were determined by B3LYP (**Figure 14**).[159] Three different groups were put forward by the authors of a) accessible (het)arynes, b) potentially accessible hetarynes and c) hetarynes that are unlikely to be generated. The various computed (het)arynes were then sorted into these groups based on their energies and the availability of their aryne-like reactivity in quality literature. In essence, all 6-membered hetarynes, such as the pyridynes, were found to be accessible and the majority of 5-membered hetarynes were predicted to not be energetically feasible. Interestingly,

benzothiophyne **645** and the two isomers of thiophyne **643** and **644** were considered to be attainable, though, owing to its high ring strain, difficult to synthesise.

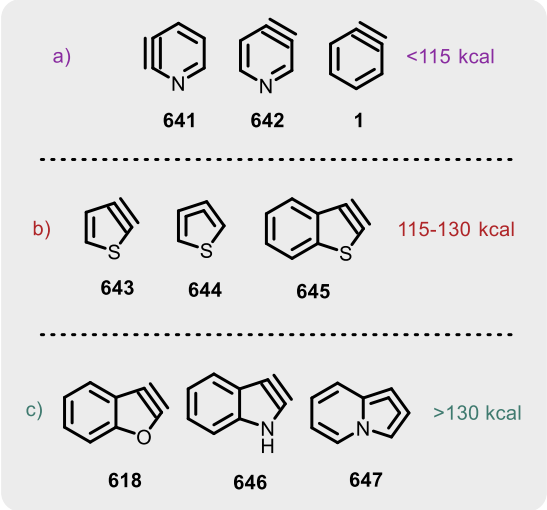


Figure 14. A computational model predicting the feasibility of various (het)arynes based on the energies of their dehydrogenation. a) Accessible (het)arynes, b) potentially accessible hetarynes and c) hetarynes that are unlikely to be generated

4.1.5 Project Aims

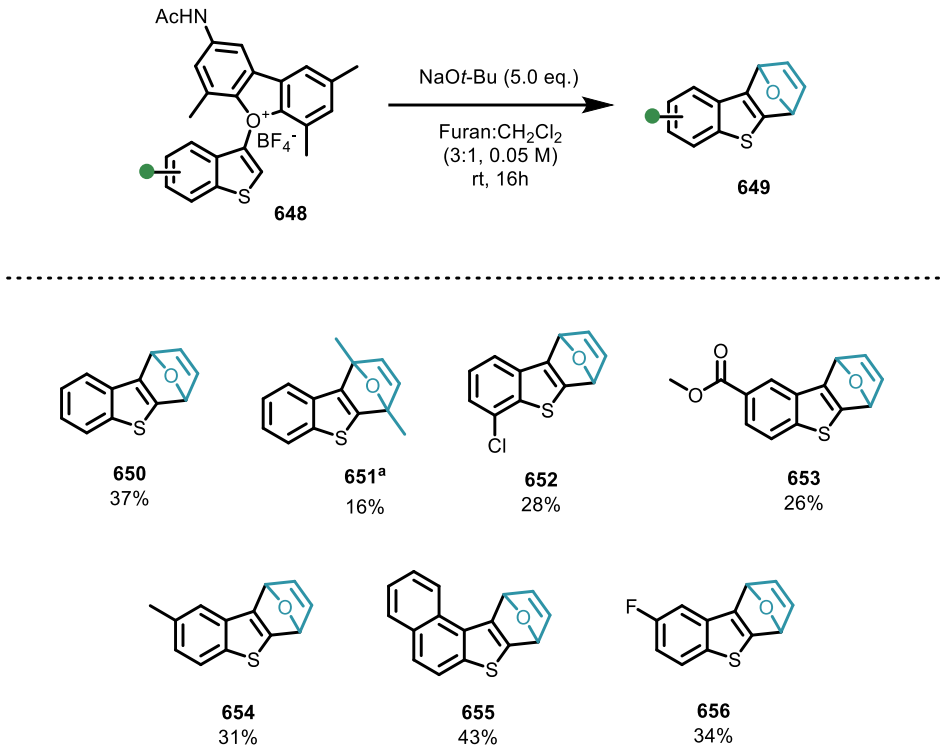
Due to extremely high ring strain, the chemistry of 5-membered arynes is limited, even in modern literature. Having seen the success of triaryl oxonium ions as precursors to 6-membered arynes, we decided to further explore if we can direct the formation of their 5-membered counterparts by the use of this positively-charged leaving group.

4.2 Results and Discussion

4.2.1 Benzothiophene Oxonium Ions. Previous Work

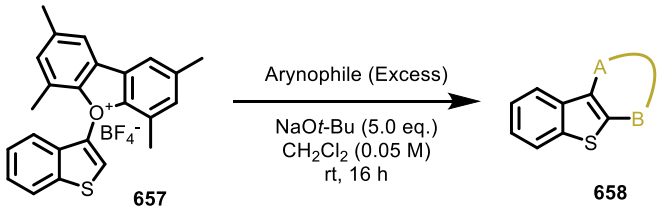
Owing to the fact that 2,3-benzothiophyne **645** was predicted to be a likely accessible hetaryne by Garg's computational model, this heterocycle served as the starting point in our work on five-membered hetarynes. Dr Madeleine Hindson (Martin Smith Group) and Dmitrii Petropavlovskikh (Jonathan Burton Group) developed a route to form six different examples of benzothiophene oxonium ions (**Scheme 129**). Pleasingly, all of them formed their respective furan adducts under basic conditions. It is important to note at this point that the yields of these trapping reactions are significantly lower than the

ones we observed with six-membered systems, likely a consequence of the various side reactions resulting from the high strain imposed on the five-membered ring. During optimisation, NaO*t*-Bu was selected as the best base for this reaction and furan was used as a co-solvent with CH_2Cl_2.



Scheme 129. The furan trapping reaction of benzothiophene oxonium ions under basic conditions. All compounds in this scheme have been synthesised by Dr Madeleine Hindson and Dmitrii Petropavlovskikh. a: 2,5-dimethylfuran used instead of furan

4.2.2 Benzothiophene Oxonium Ions. Other Arynophiles



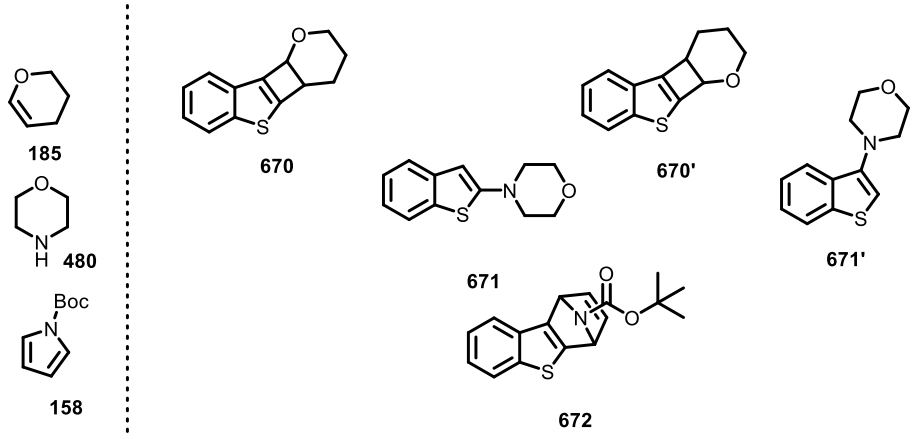
657 658

Arynophiles

659 660 205 167 210 206 207 238 164

Expected Products

661 662 662' 663 663' 664 664' 665 665' 666 667 667' 668 668' 669 669'



Scheme 130. Benzothiophene-based oxonium reactivity, arynophiles tested and their expected products

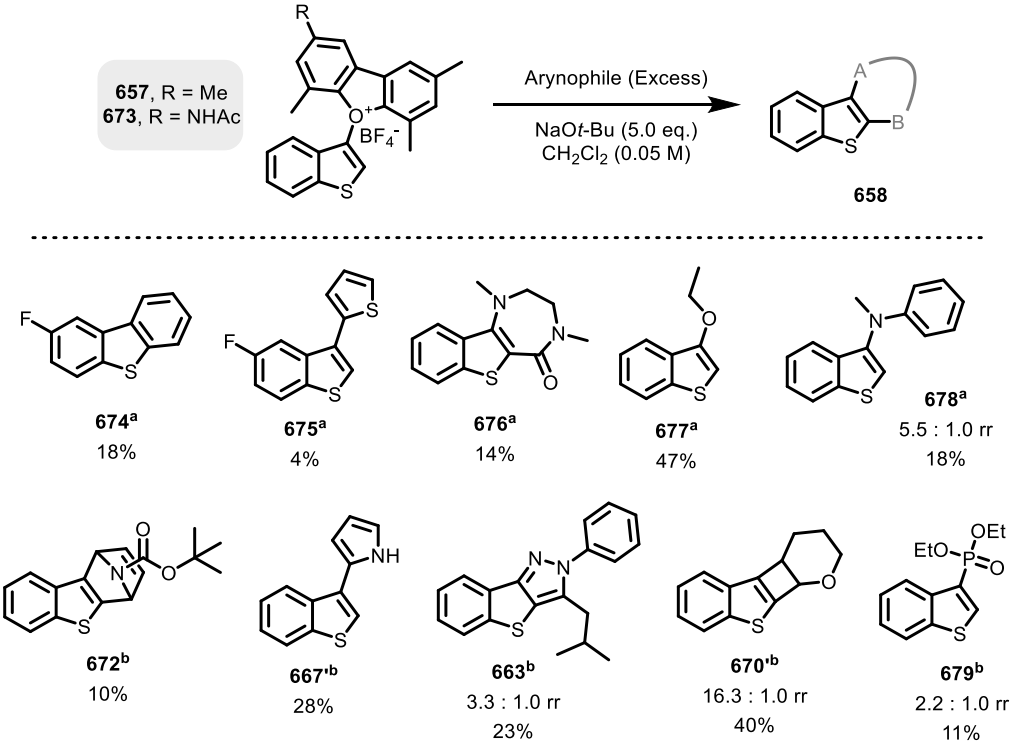
Entry	Arynophile	Expected Product	Yield
1	**659** (10 eq.)	**661**	0%[a]
2	(**660**:CH_2Cl_2, 1:3)	**662** or **662'**	18%, 5.4 : 1.0 rr[b,d]
3	**205** (10 eq.)	**663** or **663'**	9% (**663**), 8% (**663'**)
4	**167** (20 eq.)	**664** or **664'**	0%[a]
5	**210** (15 eq.)	**665** or **665'**	0%[a]
6	**206** (10 eq.)	**666**	10%[c,d]
7	**207** (25 eq.)	**667** or **667'**	27%[c,d]
8	**238** (20 eq.)	**668** or **668'**	22%, 6.7 : 1.0 rr[b] (**668'**:**668**)
9	**164** (20 eq.)	**669** or **669'**	5%, 4.0 : 1.0 rr[b,d]
10	(**185**:CH_2Cl_2, 1:1)	**670** or **670'**	35%[c,d]
11	**480** (25 eq.)	**671** or **671'**	9%, 10.7 : 1.0 rr[b]
12	**158** (25 eq.)	**672**	13%

Table 14. Benzothiophene-based oxonium reactivity. All reactions were conducted on a 0.05 mmol scale, the regioisomeric ratios were determined by qNMR of the isolated product mixtures. a: complex mixture formed. b: the two regioisomers could not be separated by silica gel column chromatography. c: one major regioisomer formed. d: the exact structure of the regioisomer(s) was not determined

After seeing a promising start with furan trapping reactions, we decided to screen further arynophiles in order to assess what modes of reactivity can be compatible with our system (**Scheme 130** and **Table 14**). The use of anthracene led to decomposition (**Entry 1**), but, differently to the 2-quinolone oxonium ions, diethyl malonate **660** furnished two isomeric C–C bond insertion products **662** and **662'** in a combined yield of 18% (**Entry 2**). Trapping with sydnone **205** produced two regioisomers in nearly equal amounts (**Entry 3**), but the anticipated 1,3-dipolar cycloaddition with **167** only gave non-specific decomposition (**Entry 4**), much like thiadiazole **210** (**Entry 5**). *N*-tosylpyridinium imide

206 produced compound **666** in a 10% isolated yield and pyrrole **207** formed **667** in high selectivity (**Entries 6** and **7**). Inseparable mixture of isomers were formed with triethyl phosphite **238**, benzyl azide **164** and morpholine **480** (**Entries 8**, **9** and **11**), but only one major regioisomer was detected with dihydropyran **185** on the test scale (**Entry 10**). Finally, a Diels-Alder adduct **672** was obtained at a 13% yield with *N*-Boc pyrrole **158** (**Entry 12**).

4.2.3 Benzothiophene Oxonium Ions. Scale Up of the Trapping Reactions

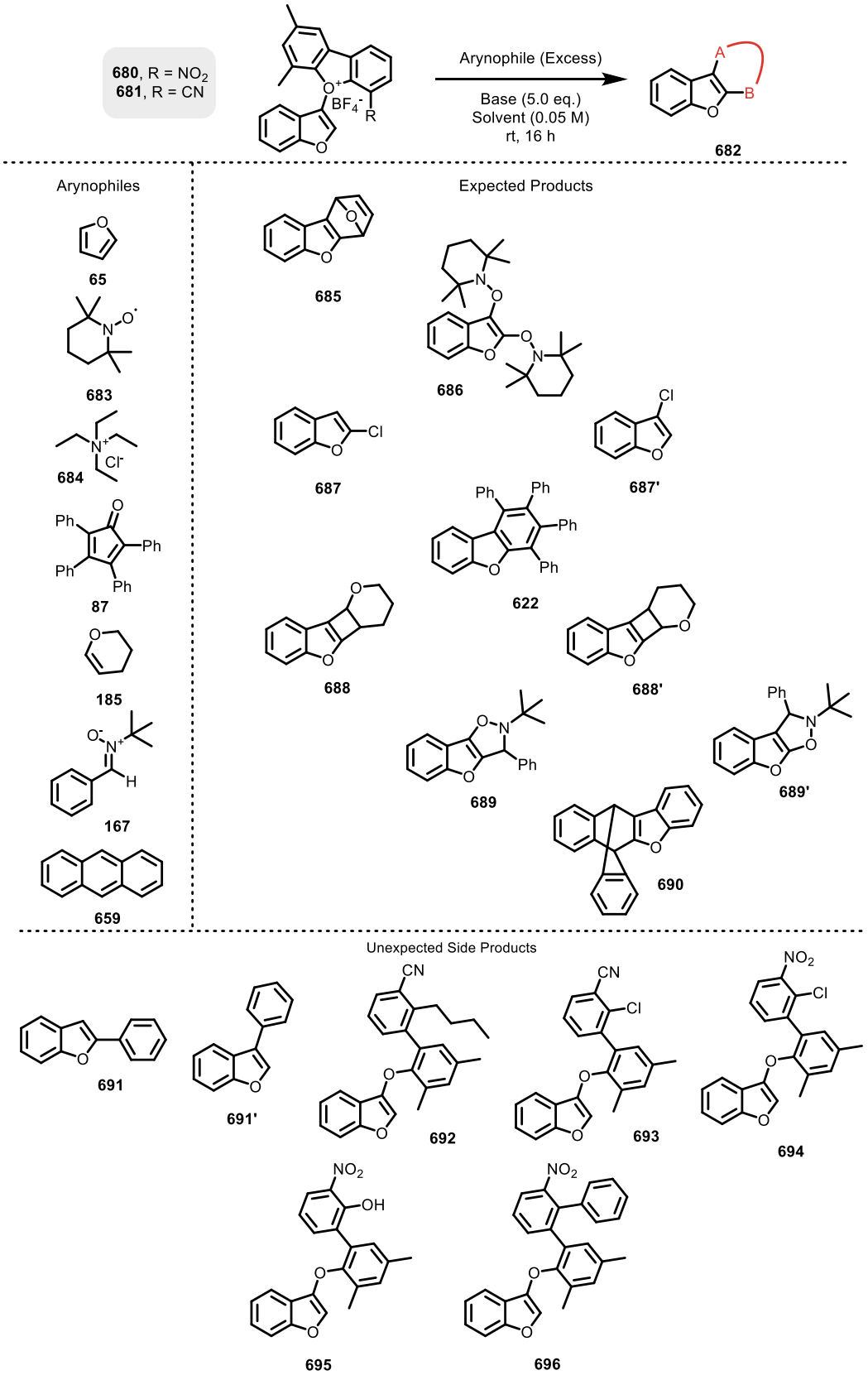


*Scheme 131. Benzothiophene-based oxonium ion reactions with arynophiles on a 0.3 mmol scale. The structure of the major isomer is depicted where regioisomeric ratios are specified. a: synthesised by Dr Madeleine Hindson using oxonium **673**. b: synthesised using oxonium **657***

Following the varied results from the previous reactivity screen, we decided to scale up selected transformations to 0.3 mmol (**Scheme 131**). The trapping with thiophene **204** yielded two different compounds **674** and **675** in a combined yield of 22%, whereas complete regioselectivity was observed with cyclic urea for compound **676**. Similarly, the trapping with ethanol occurred in a regiospecific fashion to obtain **677**. *N*-

methylaniline furnished an inseparable mixture of isomers **678** and **678'**, whereas **663** and **663'** resulting from reaction with sydnone **205** could be easily separated by silica gel column chromatography. Whilst Boc-protected pyrrole **158** gave a [4+2] product **672** in a 10% yield, pyrrole **207** selectively arylated the benzothiophene in the 3-position, obtaining **667'**. Finally, oxonium tetrafluoroborate **657** was trapped with dihydropyran **185** to form regioisomers **670** and **670'**, as well as triethylphosphite to attain **679** and **679'**.

4.2.4 Benzofuran Oxonium Ions. Unsuccessful Trapping Reactions



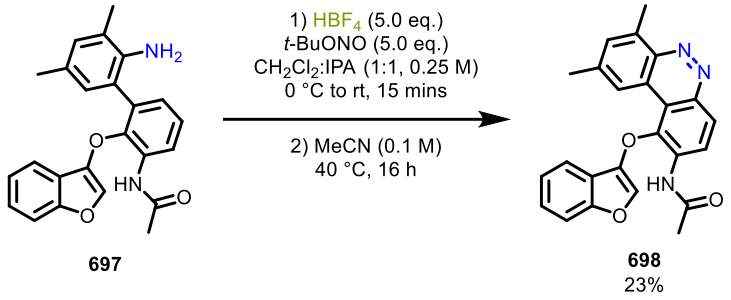
Scheme 132. Benzofuran-based oxonium ion reactivity, arynophiles tested and their expected products

Entry	Arynophile	Base	Solvent	Expected Product	Yield
1[a]	**65**	K_3PO_4	**65**:CH_2Cl_2, 3:1	**685**	0%[c]
2[b]	**65**	K_3PO_4	**65**:CH_2Cl_2, 3:1	**685**	0%[c]
3[a]	**65**	NaO*t*-Bu	**65**:CH_2Cl_2, 3:1	**685**	0%[c]
4[b]	**65**	NaO*t*-Bu	**65**:CH_2Cl_2, 3:1	**685**	0%[c]
5[a]	**65**	KHMDS[d]	**65**:CH_2Cl_2, 3:1	**685**	0%[c]
6[a]	**65**	n-BuLi[d]	**65**:CH_2Cl_2, 3:1	**685**	4% (**692**)
7[a]	**683** (10 eq.)	NaO*t*-Bu	CH_2Cl_2	**686**	0%[c]
8[b]	**683** (10 eq.)	K_3PO_4	MeCN	**686**	55% (**695**)
9[b]	**683** (10 eq.)	PhLi[d]	THF	**686**	0%[c]
10[a]	**684** (10 eq.)	NaO*t*-Bu	CH_2Cl_2	**687** or **687'**	61% (**693**)
11[b]	**684** (10 eq.)	K_3PO_4	MeCN	**687** or **687'**	80% (**694**)
12[b]	**684** (10 eq.)	None	MeCN	**687** or **687'**	46% (**694**)
13[a]	**87** (5 eq.)	NaO*t*-Bu	CH_2Cl_2	**622**	0%[c]
14[b]	**185**	K_3PO_4	**185**	**688** or **688'**	0%[c]
15[b]	**167** (10 eq.)	K_3PO_4	MeCN	**689** or **689'**	21% (**695**)
16[b]	**659** (10 eq.)	K_3PO_4	THF	**690**	43% (**695**)
17[b]	**659** (10 eq.)	KO*t*-Bu	THF	**690**	0%[c]
18[b]	**659** (10 eq.)	LDA[d]	THF	**690**	0%[c]
19[b]	**659** (10 eq.)	PhLi[d]	THF	**690**	0%[c]
20[b]	PhLi[d]		THF[e]	**691** or **691'**	31% (**696**)

*Table 15. Benzofuran-based oxonium ion reactivity. All reactions were conducted on a 0.05 mmol scale. Anhydrous conditions where possible were employed, this includes the use of a Schlenk line, oven-dried vials and stir bars, anhydrous solvents and dried K_3PO_4 (250 °C under high vacuum, 5 hours). a: oxonium **681** used for the reaction. b: oxonium **680** used for the reaction. c: a complex mixture is formed. d: reaction was conducted at -78 °C for 1 h. e: 0.025M*

Having demonstrated the feasibility of 2,3-benzothiophyne **645** using triaryl oxonium ion chemistry, we shifted our focus to an even more challenging system – 2,3-benzofuranyne **618**. We developed a route for the synthesis of oxonium ions **680** and **681**, which were subjected to various aryne-generating conditions (**Scheme 132** and **Table 15**). Unfortunately, no arynophiles that were tested formed the expected products and, furthermore, neither of the two dibenzofuran leaving groups were observed in any of test reactions. All experiments with furan **65** resulted in non-specific decomposition (**Entries 1** to **6**). Interestingly, with n-BuLi as base, a butyl group was incorporated into the dibenzofuran scaffold *via* an S_NAr reaction, giving **692** and revealing a structural flaw in the design of these oxonium ions. Similarly, trapping with TEMPO **683** furnished no desired products, and, in the case with K_3PO_4, the substrate was found to be sensitive

towards hydrolysis, attaining **695** (**Entries 7** to **9**). Tetraethylammonium chloride **684** took part in an analogous side reaction to obtain **693** or **694**, even without a base present (**Entries 10** to **12**). Complex mixtures were also noted with trapping agents **87**, **185** and **167** (**Entries 13** to **15**). Polycyclic aromatic hydrocarbon anthracene **659** also furnished no desired products with a variety of bases used (**Entries 16** to **19**), and, finally, PhLi selected as a base and a nucleophilic arynophile, displaced the oxonium leaving group from the undesired aromatic ring to form compound **696** (**Entry 20**).



697 **698** 23%

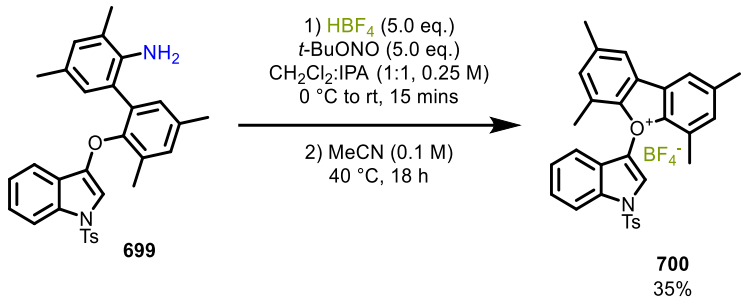
*Scheme 133. An unsuccessful attempt to generate an oxonium ion from aniline **697***

It was made evident by the unwanted S_NAr side reactions that the dibenzofuran scaffolds within the oxonium ions were far from ideal. The electron withdrawing groups in the *ortho* position were an artefact of the synthetic route utilising a nucleophilic benzofuran derivative. As a way to prevent unwanted side reactivity, we envisaged replacing the electron poor -NO_2 group with an electron donating -NHAc by simple synthetic transformations. Unfortunately, this substituent could not be tolerated in the oxonium forming step as it activated the *para* position towards intramolecular cyclisation with the transient diazonium species to form **698** (**Scheme 133**).

4.2.5 An Indole Oxonium Ion

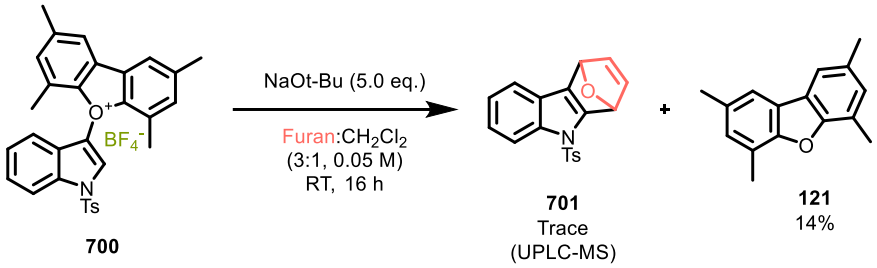
Alongside the benzofuran oxonium ions we also developed a route for an indole-based oxonium ion **700** (**Scheme 134**). Unfortunately, many of the steps in the route to

synthesise oxonium precursor **699** were poor-yielding, however, enough material was isolated for full characterisation and a single test reaction.



*Scheme 134. The generation of indole-based oxonium tetrafluoroborate **700***

After purification by trituration, oxonium tetrafluoroborate salt **700** was subjected to furan trapping conditions that were optimised for the 2,3-benzothiophyne **645** system (**Scheme 135**). Unfortunately, a very complex mixture of products was formed with only trace furan adduct **701** detected in UPLC-MS, which could not be isolated. Differently to the benzofuran oxonium ions, however, a substantial amount of leaving group **121** was observed.

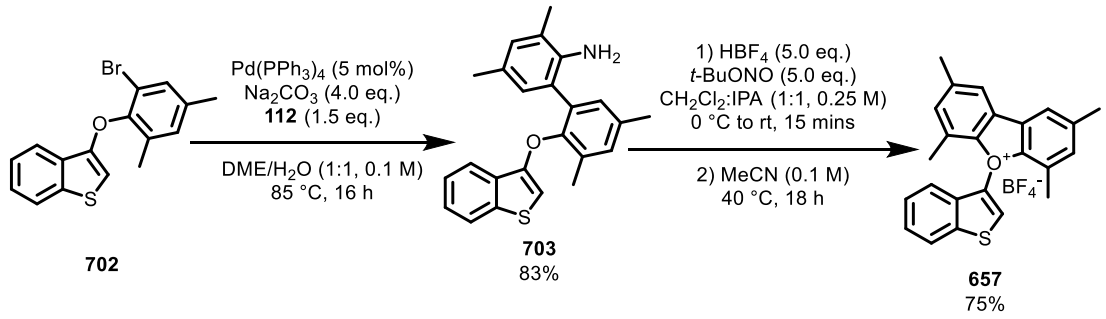


*Scheme 135. The furan-trapping reaction of oxonium **700***

4.3 Synthesis

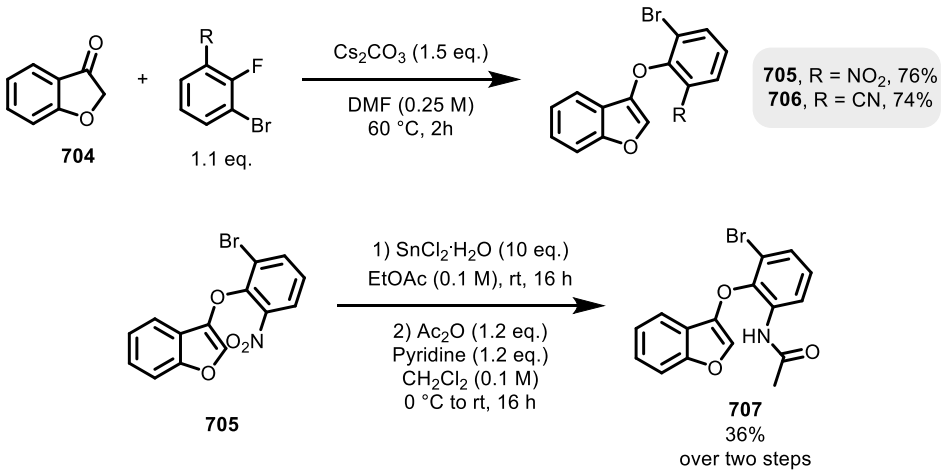
4.3.1 A Benzothiophene Oxonium Ion

The synthesis of oxonium ion **657** started with intermediate **702**, which was available in our group (**Scheme 136**). It was coupled with aniline **112** *via* Suzuki-Miyaura coupling to obtain precursor **703** in an 83% yield. The compound was then subjected to our standard oxonium-forming conditions to yield oxonium tetrafluoroborate **657**.



*Scheme 136. The synthesis of oxonium **657** from compound **702**. Compound **702**, as well as the route to oxonium **657** was provided by Dr Madeleine Hindson*

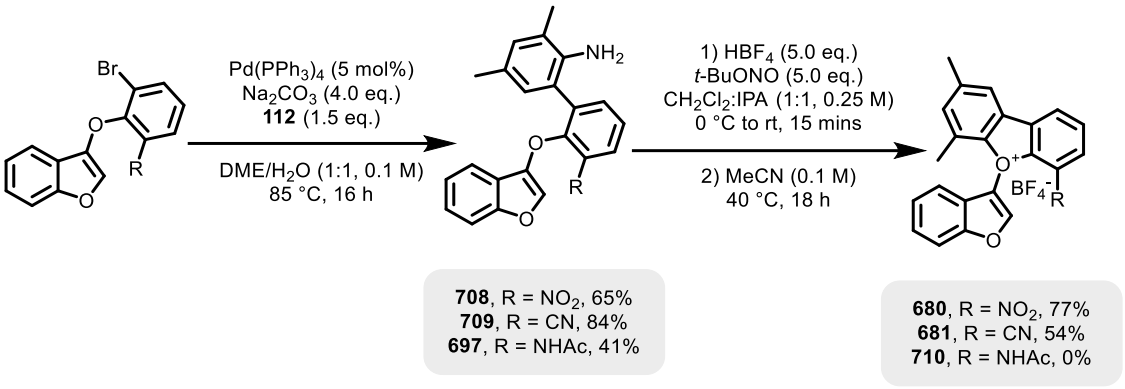
4.3.2 Benzofuran Oxonium Ions



*Scheme 137. The synthesis of intermediates **705**, **706** and **707***

The benzofuran oxonium ions were synthesised from nucleophilic compound **704**, coupling it with various electron withdrawing group-bearing aryl fluorides via an S_NAr reaction to obtain **705** and **706** (**Scheme 137**). The -NHAc group in **707** was introduced by a tin-mediated reduction of **705**, followed by acetylation.

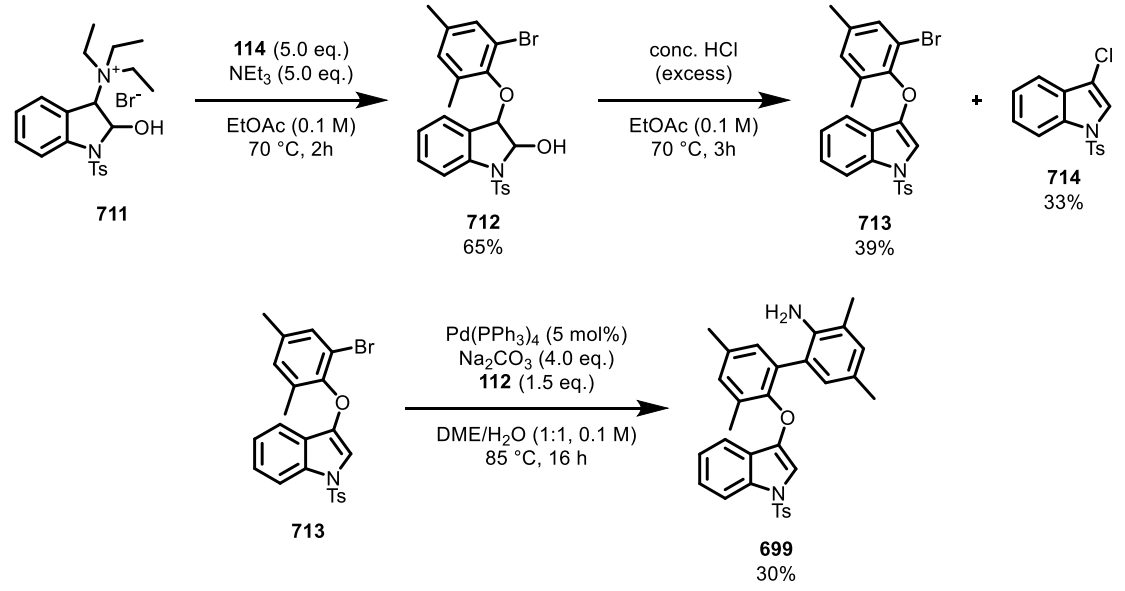
All three ethers were subjected to Suzuki-Miyaura coupling to obtain their corresponding oxonium ion precursors (**Scheme 138**). These anilines were then subjected to standard oxonium-forming conditions with *t*-BuONO and aqueous HBF_4, followed by heating in MeCN to acquire **680** and **681**. As discussed previously, oxonium precursor **697** did not furnish the desired oxonium ion, but rather an unwanted cyclised product **698**.



*Scheme 138. The synthesis of oxonium ions **680** and **681**, and the unsuccessful attempt to synthesise oxonium **710***

4.3.3 An Indole Oxonium Ion Precursor

The indole-based oxonium ion precursor was synthesised by employing salt **711** as a surrogate for an indole 2,3-epoxide (**Scheme 139**). It was coupled with an excess of bromophenol **114** under basic conditions to furnish hemiaminal **712**. An excess of aqueous HCl was then used in order to eliminate H_2O from the molecule and form the aromatic indole ring. Only moderate yields were achieved, as the bromophenol motif was substituted by chloride to obtain side product **714**. Having synthesised **713**, we subjected it to Suzuki-Miyaura coupling to furnish the corresponding oxonium ion precursor **699** in a 30% yield.



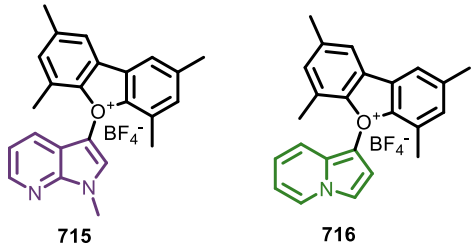
*Scheme 139. The synthesis of oxonium precursor **699** from the indole 2,3-epoxide equivalent **711***

4.4 Conclusion

As part of the work on five-membered hetarynes, we developed synthetic routes for the generation of benzothiophene-, benzofuran- and indole-based oxonium ions. Furthermore, we demonstrated the aryne-like reactivity of benzothiophene oxonium tetrafluoroborates under basic conditions in the presence of arynophiles.

4.5 Future Work

While our work demonstrated that benzothiophene-based oxonium ions can act as hetaryne precursors, further work needs to be done on the other five-membered ring systems. Firstly, an appropriate scaffold needs to be found for benzofuran oxonium ions that would not encourage unwanted S_NAr reactivity with nucleophiles. Secondly, although the dibenzofuran leaving group **121** was detected in the indole oxonium ion reaction with furan and could indirectly suggest hetaryne formation, further experiments need to be set up to rule out any other means of reactivity. Transition metal catalysis could also be introduced into the system in order to stabilise the transient intermediate, as many electron-rich metals are known to form complexes with arynes.[160]



715 **716**

*Figure 15. Hypothetical oxonium ions **715** and **716** as precursors to 7-aza-2,3-indolyne and 1,2-indolizyne*

Finally, based on the aforementioned computational model,[159] some other 5-membered heterocyclic arynes are predicted to be lower energy than benzofuranyne **618** and indolyne **646**, such as 7-aza-2,3-indolyne and 1,2-indolizyne. Synthetic routes should be

developed for their oxonium ions in order to test the synthetic feasibility of these hetarynes (**Figure 15**).

5 Experimental

5.1 General Information

5.1.1 Naming and Numbering

Compound names were generated using ChemDraw 20.1.1 in accordance with the guidelines stipulated by the International Union of Pure and Applied Chemistry (IUPAC). The atomic numbering within each compound does not correspond to the IUPAC numbering system, but has been arbitrarily chosen for the purpose of consistent assignment of NMR spectra.

5.1.2 Materials

All reagents were obtained from major chemical suppliers and were used as supplied or purified using standard laboratory techniques. Anhydrous reaction solvents (CH_2Cl_2, 1,4-dioxane, DMF, THF, PhMe, Et_3N, *i*-Pr_2NH) were obtained from an MBraun SPS5 solvent purification system having been dried over activated alumina columns. Unless specified, all other solvents were used without prior drying.

5.1.3 Reaction Conditions

Reactions were carried out under ambient conditions unless specified otherwise in the procedure. The glassware for reactions conducted using an inert atmosphere was oven-dried or flame-dried under vacuum and then placed under N_2. Solvents were degassed by sparging with N_2 for 30 minutes. Reactions were heated using a DrySyn® heating block or an oil bath and a contact thermometer. Room temperature (rt) is defined as 20-25 °C. Temperatures of 0 °C were obtained using an ice water bath, −20 °C using an ice/sodium chloride bath and −78 °C using a dry ice/acetone bath. Reactions were monitored by thin layer chromatography (TLC) using silica gel on pre-coated 0.25 mm aluminium sheets (Merck Kieselgel 60 F_{254}) and visualized with UV irradiation (λ = 254 nm) followed by

staining with a basic $KMnO_4$ solution or ethanolic acidic vanillin. An UltrawaveU1250D Ultrasonic water bath (50-60 Hz) was used for sonication.

5.1.4 Column Chromatography

Flash column chromatography was carried out on Silica Gel 60 (0.043-0.063 nm, VWR) under pressure (0.2-0.4 bar) from the house N_2 supply.

5.1.5 NMR Spectroscopy

NMR spectra were recorded on Bruker AVIII/AVIIIHD (700, 600, 500 and 400 MHz (^{1}H)) and Bruker NEO (600 MHz (^{1}H)) spectrometers in the deuterated solvent specified. NMR data are reported as chemical shifts (δ) and quoted in parts per million (ppm). ^{1}H NMR are referenced to the non-deuterated residual solvent peak, ^{13}C NMR are referenced to the residual solvent peak and ^{19}F NMR are 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), pentet (p), sextet (sext), and multiplet (m) or combinations of the above. Coupling constants, *J*, are measured to the nearest 0.1 Hz and are presented as observed. NMR Spectra were processed using MestReNova 14.0 and where spectra are assigned, this was carried out with the aid of COSY, HSQC and HMBC experiments and, where appropriate, NOESY and ROESY experiments. Peak assignments were also done by comparison with published spectra of similar compounds. Where an assignment could not be made unambiguously, possible assignments are listed.

5.1.6 Infrared Spectroscopy

Fourier Transform infrared spectra were recorded on a Bruker Tensor 27 FTIR spectrometer equipped with a diamond ATR module. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}) for the range 3500 – 600 cm^{-1}.

5.1.7 Mass Spectrometry

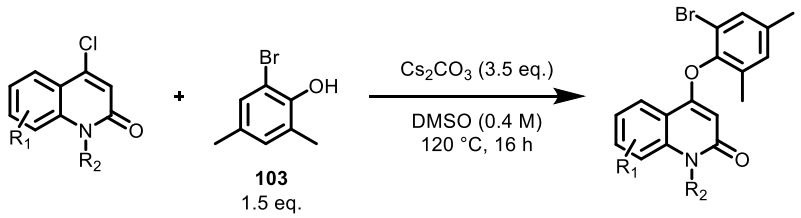
Low-resolution mass spectra (LRMS) were recorded on a Micro Mass LCT Premier spectrometer under conditions of electrospray ionisation (ESI). High resolution mass spectra (HRMS) using electrospray ionization (ESI) were recorded on a Thermo Exactive orbitrap spectrometer equipped with a Waters Acquity LC system. High resolution mass spectra using atmospheric pressure chemical ionization (APCI) or electron ionization (EI) were recorded on an Agilent 7200 Accurate Mass Q-TOF GC-MS spectrometer connected to a 7890 GC system DIP solid/liquid state thermal probe and a CTC Analytics HTS PAL Sample Manager. All reported found values are within a tolerance of 5 ppm unless otherwise stated.

5.1.8 Melting Points

Melting points (MP) were determined using a Reichert melting point apparatus and are uncorrected. Unless otherwise stated, the solid material analysed was obtained from *in vacuo* removal of the solvent system used for flash column chromatography or the deuterated solvent used for NMR characterisation.

5.2 General Procedures

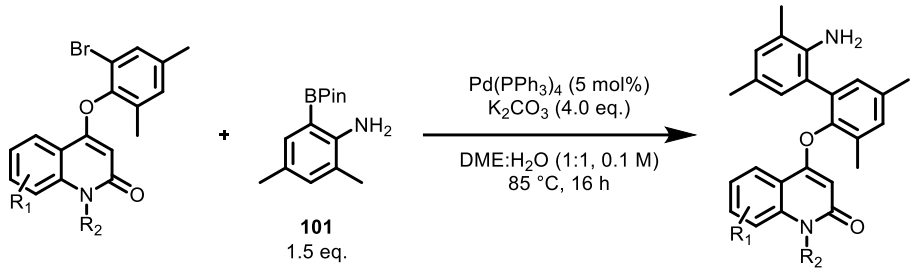
5.2.1 General Procedure A for the Addition-Elimination Reactions of 4-Chloro-2-Quinolones



An oven-dried round bottom flask was charged with the appropriate quinolone (1.0 eq.) before adding anhydrous DMSO (0.4 M), followed by 2-bromo-4,6-dimethylphenol (1.5 eq.). Cs_2CO_3 (3.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 120 °C for 16 hours under nitrogen. After the reaction time, the

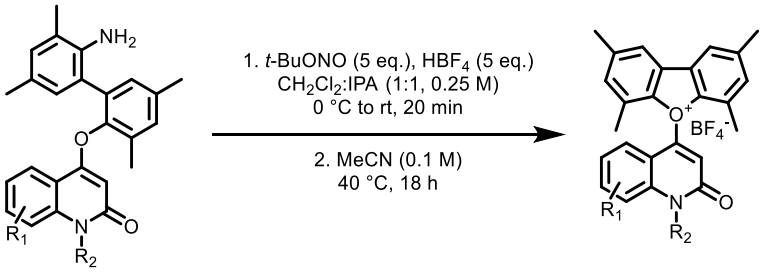
mixture was cooled to room temperature and poured into deionised water (~10 mL per 1 mL of DMSO), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil or solid. The crude was purified by flash column chromatography to obtain the pure compound.

5.2.2 General Procedure B for the Suzuki-Miyaura Reaction of 2-Quinolone or 2-Pyridone-Based Aryl Bromide Derivatives



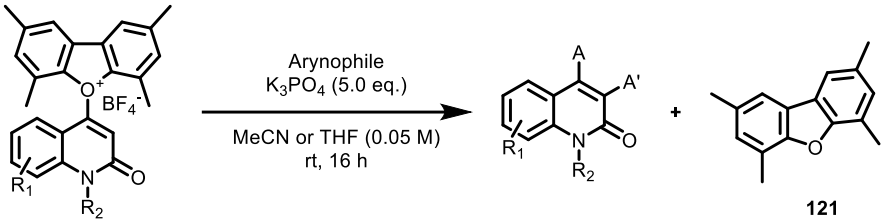
A 2- or 3-neck round bottom flask was charged with the appropriate aryl bromide (1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.5 eq.), $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 (4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 0.1 M). The suspension was sparged with argon for 15 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil or solid. The crude was purified by flash column chromatography to obtain the pure compound.

5.2.3 General Procedure C for the Formation of 2-Quinolone or 2-Pyridone Oxonium Tetrafluoroborates



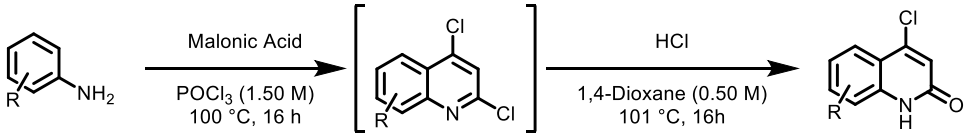
A round bottom flask was charged with the appropriate oxonium precursor (1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was transferred to a separatory funnel and diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then filtered and concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was redissolved in anhydrous MeCN (0.1 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under rotary evaporation (water bath set to 35 °C) or, alternatively, a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through a pad of Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under rotary evaporation (water bath set to 35 °C) or a steady stream of nitrogen to obtain the pure compound.

5.2.4 General Procedure D for the Trapping of 2-Quinolone or 2-Pyridone Oxonium Tetrafluoroborates



A glass screw cap vial was charged with the appropriate oxonium tetrafluoroborate (0.2 mmol, 1.0 eq.) before dissolving in anhydrous MeCN or THF (4 mL, 0.05 M) and adding the arynophile. K_3PO_4 (212.3 mg, 5.0 eq.) was then added in one portion before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil or solid. The crude was purified by flash column chromatography to obtain the pure compound.

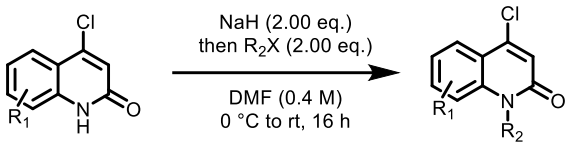
5.2.5 General Procedure E for the synthesis of 4-Chloro-2-Quinolone Derivatives



A round bottom flask was charged with $POCl_3$ (1.50 M) and cooled to 0 °C before adding malonic acid (1.0 eq.) with stirring. To the suspension, the appropriate aniline (1.0 eq.) was added slowly at 0 °C and stirred until fuming fully subsided. After full addition, the mixture was refluxed at 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (at least 10 mL per 1 mL of $POCl_3$) with vigorous stirring and left to stand until it reached room temperature. The formed suspension was then filtered, washing the solid with ice-cold water and drying under the air flow. At the same time, the filtrate was transferred to a separatory funnel and extracted with EtOAc (x3), then dried with brine and $MgSO_4$ before concentrating under vacuum to obtain a crude solid, which was recombined with the solid

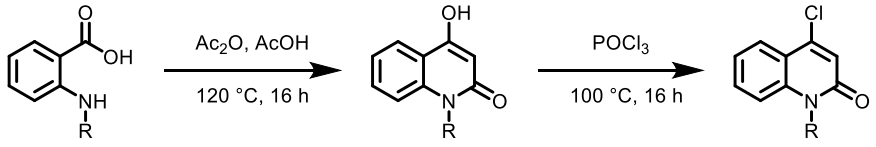
isolated via filtration. The combined crude solid was redissolved in 1,4-dioxane (0.50 M) and concentrated aqueous HCl (1.52 mL per mmol of aniline) was added with stirring. The solution was refluxed at 101 °C for 16 hours under nitrogen, before cooling to room temperature and partially concentrating under vacuum. The solution was ten poured over crushed ice with vigorous shaking to crash out the solid product, which was then filtered, washed with ice-cold water and dried under vacuum to obtain a solid which was used without further purification.

5.2.6 General Procedure F for the Alkylation of 4-Chloro-2-Quinolone Derivatives



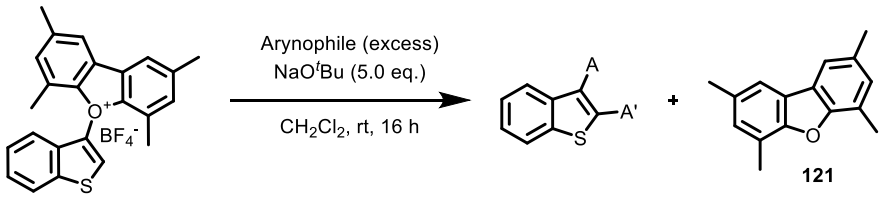
An oven-dried round bottom flask was charged with the appropriate 4-chloro-2-quinolone (1.0 eq.), before adding anhydrous DMF (0.4 M) and cooling to 0 °C. With stirring, NaH (60% dispersion in mineral oil, 2.0 eq.) was added in small portions. After full addition and gas evolution, the reaction mixture was stirred at 0 °C for 15 minutes. The appropriate alkyl halide (2.0 eq.) was then added dropwise at 0 °C and the reaction was stirred for 16 hours under nitrogen at room temperature. After the reaction time, the mixture was poured into deionised water (~10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil or solid. The crude was purified by flash column chromatography to obtain the pure compound.

5.2.7 General Procedure G for the synthesis of Alkylated 4-Chloro-2-Quinolone Derivatives



An oven-dried round bottom flask was charged with the appropriate carboxylic acid (1.0 eq.) before adding acetic acid (0.5 mL per mmol) and acetic anhydride (0.5 mL per mmol). The reaction mixture was refluxed at 120 °C for 16 hours under nitrogen. After the reaction time, the suspension was cooled to room temperature and poured into ice water (at least 15 mL per mmol) and stirred until the ice fully melted. The suspension was then extracted with EtOAc (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The solid was dissolved in a minimum amount of hot aqueous 3 M NaOH, then the formed solution was cooled to room temperature, followed by a slow addition of concentrated aqueous HCl to neutralise the solution and crash out the intermediate product. The suspension was then cooled to 0 °C and filtered, washing the solid with ice-cold water and dried under vacuum to obtain a solid. The solid was then slowly transferred to an oven-dried round bottom flask containing $POCl_3$ (1.0 M) and refluxed at 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (at least 10 mL per 1 mL of $POCl_3$) with vigorous shaking and left to stand until it reached room temperature. The formed suspension was neutralised by adding solid Na_2CO_3 with shaking, then transferred to a separatory funnel and extracted with EtOAc (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography to obtain the pure compound.

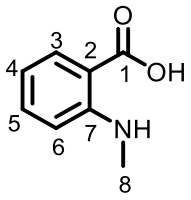
5.2.8 General Procedure H for the Trapping of Thiophene Oxonium Tetrafluoroborates



A glass screw cap vial was charged with the appropriate oxonium tetrafluoroborate (0.05-0.3 mmol, 1.0 eq.) before suspending in anhydrous CH_2Cl_2 and adding the arynophile. NaO*t*-Bu (24.0-144.0 mg, 5.0 eq.) was then added in one portion before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil or solid. The crude was purified by flash column chromatography to obtain the pure compound.

5.3 Experimental Data

2-(Methylamino)benzoic acid, 311:



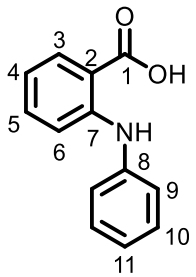
A 50 mL round bottom flask was charged with Na_2CO_3 (2.00 g, 19.0 mmol, 0.5 eq.) before adding deionised water (25 mL). With stirring, anthranilic acid (5.0 g, 36.5 mmol, 1.00 eq.) was added portion-wise, followed by MeI (5.3 mL, 12.0 g, 84.7 mmol, 2.3 eq.). The reaction mixture was refluxed at 40 °C for 16 hours. After the reaction time, the suspension was cooled to 0 °C and then filtered, washing with ice-cold water (50 mL) and dried under vacuum to obtain the title compound as a solid (3.24 g, 21.43 mmol, 59%), which was used without further purification. The NMR spectra are consistent with those available in the literature.[161]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 1.7 Hz, 1H, H-3), 7.43 (ddd, *J* = 8.7, 7.0, 1.7 Hz, 1H, H-5), 6.69 (dd, *J* = 8.7, 1.1 Hz, 1H, H-6), 6.63 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, H-4), 2.94 (s, 3H, H-8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1 (C-1), 152.8 (C-7), 135.8 (C-5), 132.7 (C-3), 114.7 (C-4), 111.0 (C-6), 108.7 (C-2), 29.7 (C-8).

HRMS (ESI) exact mass calculated for $C_8H_{10}NO_2^+$ $[M+H]^+$ requires *m/z* 152.0706, found *m/z* 152.0706.

2-(Phenylamino)benzoic acid, 313:



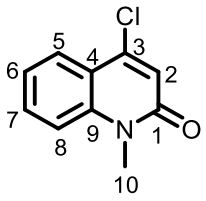
A 50 mL 2-neck round bottom flask was charged with 2-Iodobenzoic acid (4.96 g, 20.0 mmol, 1.0 eq.), K_2CO_3 (5.53 g, 40.0 mmol, 2.0 eq.) and CuI (761.8 mg, 20 mol%) before degassing with vacuum and nitrogen cycles (x3). Degassed anhydrous DMF (20 mL, 1.0 M) was then added, followed by aniline (1.85 mL, 1.86 g, 20.0 mmol, 1.0 eq,). The suspension was sparged with argon for 10 minutes, then heated to 105 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (80 mL) before slowly acidifying with concentrated aqueous HCl (7 mL). The formed suspension was then filtered, washing the solid with ice-cold water and drying under the air flow. The resulting solid was redissolved in EtOAc and further filtered with the filtrate concentrated under vacuum to obtain the title compound as a solid (2.87 g, 13.46 mmol, 67%), which was used without further purification. The NMR spectra are consistent with those available in the literature.[162]

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H, NH), 8.07 (dd, *J* = 8.1, 1.7 Hz, 1H, H-3), 7.43 – 7.33 (m, 3H, H-5,10), 7.31 – 7.27 (m, 2H, H-9), 7.24 (dd, *J* = 8.5, 1.1 Hz, 1H, H-6), 7.19 – 7.10 (m, 1H, H-11), 6.77 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H, H-4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9 (C-1), 149.0 (C-7), 140.4 (C-8), 135.3 (C-5), 132.7 (C-3), 129.5 (C-10), 124.1 (C-11), 123.2 (C-9), 117.2 (C-4), 114.1 (C-6), 110.5 (C-2).

HRMS (ESI) exact mass calculated for $C_{13}H_{10}NO_2^-$ $[M-H]^-$ requires *m/z* 212.0717, found *m/z* 212.0712.

4-Chloro-1-methylquinolin-2(1H)-one, 108:



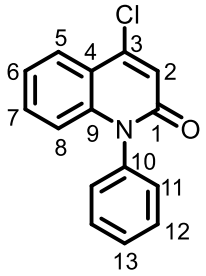
108 was prepared according to **General Procedure G** on a 15.40 mmol scale using 2-(methylamino)benzoic acid (2.33 g, 15.40 mmol, 1.0 eq.). The crude was purified by flash column chromatography (50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.70 g, 8.78 mmol, 57%). The NMR spectra are consistent with those available in the literature.[163]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 1H, H-5), 7.63 (t, *J* = 8.0 Hz, 1H, H-7), 7.38 (d, *J* = 8.5 Hz, 1H, H-8), 7.31 (t, *J* = 7.6 Hz, 1H, H-6), 6.88 (s, 1H, H-2), 3.70 (s, 3H, H-10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0 (C-1), 144.4 (C-3), 139.8 (C-9), 132.0 (C-7), 126.3 (C-5), 122.7 (C-6), 121.1 (C-2), 119.3 (C-4), 114.5 (C-8), 29.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_9ClNO^+$ $[M+H]^+$ requires *m/z* 194.0367, found *m/z* 194.0368.

4-Chloro-1-phenylquinolin-2(1H)-one, 314:



314 was prepared according to **General Procedure G** on a 12.24 mmol scale using 2-(phenylamino)benzoic acid (2.61 g, 12.24 mmol, 1.0 eq.). The crude was purified by flash column chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.37 g, 5.36 mmol, 44%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.64 – 7.58 (m, 2H, H-11), 7.57 – 7.51 (m, 1H, H-13), 7.40 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H, H-7), 7.32 – 7.26 (m, 3H, H-12,6), 6.98 (s, 1H, H-2), 6.70 (dd, *J* = 8.6, 1.0 Hz, 1H, H-7).

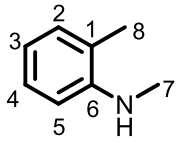
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.0 (C-1), 145.3 (C-3), 140.9 (C-10), 137.2 (C-9), 131.5 (C-7), 130.4 (C-11), 129.3 (C-13), 128.9 (C-12), 125.9 (C-5), 122.9 (C-6), 121.5 (C-2), 119.0 (C-4), 116.4 (C-8).

HRMS (ESI) exact mass calculated for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ requires *m/z* 256.0524, found *m/z* 256.0521.

IR (thin film) ν_{max}/cm^{-1} 3455, 3077, 1651, 1589, 1492, 1448, 1356, 966, 852.

MP 146-148 °C.

***N*,2-Dimethylaniline, 315:**



An oven-dried round bottom flask was charged with *o*-toluidine (10.0 g, 93.3 mmol, 1.0 eq.) before adding anhydrous DMF (0.4 M), followed by K_2CO_3 (16.8 g, 121.3 mmol, 1.3

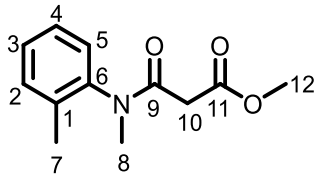
eq.). MeI (7.0 mL, 15.88 g, 111.9 mmol, 1.2 eq.) was then added dropwise with stirring before heating the reaction mixture to 42 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and filtered through celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 Et_2O:pentane, v:v) to obtain the title compound as a solid (2.76 g, 22.78 mmol, 24%). The NMR spectra are consistent with those available in the literature.[164]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 1H, H-4), 7.12 (ddd, *J* = 7.3, 1.8, 0.9 Hz, 1H, H-2), 6.74 (td, *J* = 7.3, 1.2 Hz, 1H, H-3), 6.67 (dd, *J* = 8.0, 1.2 Hz, 1H, H-5), 3.60 (s, 1H, H-NH), 2.95 (s, 3H, H-7), 2.19 (s, 3H, H-8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3 (C-6), 130.0 (C-2), 127.3 (C-4), 122.0 (C-1), 116.9 (C-3), 109.2 (C-5), 30.9 (C-7), 17.5 (C-8).

HRMS (ESI) exact mass calculated for $C_8H_{12}N^+$ $[M+H]^+$ requires *m/z* 122.0964, found *m/z* 122.0965.

Methyl 3-(methyl(o-tolyl)amino)-3-oxopropanoate, 276:



An oven-dried round bottom flask was charged with methyl malonyl chloride (2.7 mL, 3.52 g, 25.0 mmol, 1.1 eq.) before dissolving in anhydrous CH_2Cl_2 (113 mL, 0.2 M) and cooling to 0 °C. *N*,2-dimethylaniline (2.75 g, 22.7 mmol, 1.0 eq.) was added dropwise, followed by Et_3N (3.8 mL, 2.75 g, 27.2 mmol, 1.2 eq.) and the reaction was left to stir under nitrogen at room temperature for 3 hours. After the reaction time, the reaction mixture was concentrated under vacuum and redissolved in EtOAc (250 mL), then

washed with deionised water (x3), followed by saturated aqueous $NaHCO_3$ (x3). Dried with brine, $MgSO_4$ and concentrated under vacuum to obtain an oil (4.23 g, 19.12 mmol, 84%), which was used without any further purification.

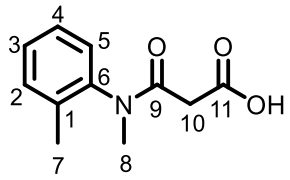
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H, H-3,4), 7.23 – 7.19 (m, 1H, H-5), 7.11 (dd, *J* = 7.6, 1.4 Hz, 1H, H-2), 3.62 (s, 3H, H-12), 3.18 (s, 3H, H-8), 3.06 (d, *J* = 15.5 Hz, 1H, H-10), 3.05 (d, *J* = 15.5 Hz, 1H, H-10'), 2.22 (s, 3H, H-7).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0 (C-11), 166.1 (C-9), 141.9 (C-6), 135.5 (C-1), 131.7 (C-4), 128.9 (C-3), 128.1 (C-2), 127.6 (C-5), 52.2 (C-12), 41.0 (C-10), 36.1 (C-8), 17.3 (C-7).

HRMS (ESI) exact mass calculated for $C_{12}H_{16}NO_3^+$ $[M+H]^+$ requires *m/z* 222.1125, found *m/z* 222.1119.

IR (thin film) ν_{max}/cm^{-1} 3506, 2954, 1747, 1665, 1602, 1580, 1437, 1384, 1251, 1159, 1104, 1019, 775, 731.

3-(Methyl(o-tolyl)amino)-3-oxopropanoic acid, 316:



A round bottom flask was charged with methyl 3-(methyl(o-tolyl)amino)-3-oxopropanoate (3.70 g, 16.72 mmol, 1.0 eq.) before adding THF, followed by H_2O (1:1, 8.4 mL, 2.0 M). Lithium hydroxide monohydrate (1.40 g, 33.44 mmol, 2.0 eq.) was then added in small portions, then stirred at room temperature for 1 hour. After the reaction time, the reaction mixture was quenched by a slow addition of 1 M HCl (150 mL), then extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and

concentrated under vacuum to obtain a solid (3.07 g, 14.81 mmol, 89%), which was used without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 3H, H-3,4,5), 7.10 (dd, *J* = 7.5, 1.1 Hz, 1H, H-2), 3.27 (s, 3H, H-8), 3.09 (d, *J* = 19.4 Hz, 1H, H-10), 2.89 (d, *J* = 19.4 Hz, 1H, H-10'), 2.22 (s, 3H, H-7).

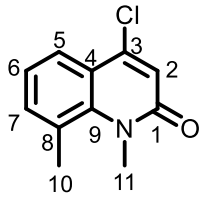
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.2 (C-11), 167.7 (C-9), 140.1 (C-6), 134.9 (C-1), 132.2 (C-4), 129.8 (C-3), 128.3 (C-5), 127.4 (C-2), 36.47 (C-8 or 10), 36.45 (C-8 or 10), 17.2 (C-7).

HRMS (ESI) exact mass calculated for $C_{11}H_{12}NO_3^-$ $[M-H]^-$ requires *m/z* 206.0823, found *m/z* 206.0816.

IR (thin film) ν_{max}/cm^{-1} 2931, 1738, 1621, 1600, 1580, 1494, 1394, 1308, 1241, 1137, 1106, 1040, 952, 907, 774, 730.

MP 91-96 °C.

4-Chloro-1,8-dimethylquinolin-2(1H)-one, 317:



An oven-dried round bottom flask was charged with 3-(methyl(o-tolyl)amino)-3-oxopropanoic acid (3.01 g, 14.52 mmol, 1.0 eq.) before adding Eaton's Reagent (36.0 mL, 0.4 M). The reaction mixture was refluxed at 70 °C for 16 hours under nitrogen. After the reaction time, it was cooled to room temperature, poured into ice water (400 mL) and stirred until the ice fully melted. The suspension was then filtered, washing the solid with additional water, then Et_2O and pentane, and dried under vacuum to obtain a solid (2.31 g). The solid was then slowly transferred to an oven-dried round bottom flask

containing $POCl_3$ (10.0 mL, 1.5 M) and refluxed at 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (150 mL) with vigorous shaking and left to stand until it reached room temperature. The formed suspension was neutralised by adding solid Na_2CO_3 with shaking, then transferred to a separatory funnel and extracted with EtOAc (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.08 g, 5.20 mmol, 36%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.41 (ddd, *J* = 7.4, 1.5, 0.8 Hz, 1H, H-7), 7.20 (t, *J* = 7.7 Hz, 1H, H-6), 6.86 (s, 1H, H-2), 3.78 (s, 3H, H-11), 2.70 (s, 3H, H-10).

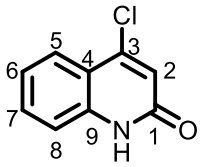
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2 (C-1), 145.1 (C-3), 141.4 (C-9), 136.5 (C-7), 125.5 (C-8), 124.5 (C-5), 123.0 (C-6), 121.0 (C-4), 120.8 (C-2), 37.3 (C-11), 24.0 (C-10).

HRMS (ESI) exact mass calculated for $C_{11}H_{11}ClNO^+$ $[M+H]^+$ requires *m/z* 208.0524, found *m/z* 208.0519.

IR (thin film) ν_{max}/cm^{-1} 2929, 1646, 1584, 1455, 1402, 1377, 1355, 1297, 1174, 1027, 937, 861, 745.

MP 82-84 °C.

4-Chloroquinolin-2(1H)-one, 318:



318 was prepared according to **General Procedure E** on a 90 mmol scale using aniline (8.2 mL, 8.57 g, 90 mmol, 1.0 eq.) and malonic acid (9.37 g, 90 mmol, 1.0 eq.) to obtain

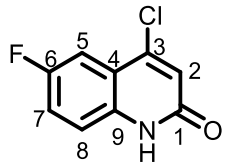
the title compound as a solid (15.8 g, 87.97 mmol, 97%). The NMR spectra are consistent with those available in the literature.[165]

^{1}H NMR (400 MHz, DMSO) δ 12.04 (s, 1H, N-H), 7.84 (dd, *J* = 8.2, 1.4 Hz, 1H, H-5), 7.62 (ddd, *J* = 8.4, 7.2, 1.4 Hz, 1H, H-7), 7.38 (dd, *J* = 8.4, 1.1 Hz, 1H, H-8), 7.29 (ddd, *J* = 8.2, 7.2, 1.1 Hz, 1H, H-6), 6.81 (s, 1H, H-2).

^{13}C NMR (101 MHz, DMSO) δ 160.4 (C-1), 144.0 (C-3), 138.6 (C-9), 131.9 (C-7), 124.6 (C-5), 122.6 (C-6), 121.3 (C-2), 117.2 (C-4), 115.8 (C-8).

HRMS (ESI) exact mass calculated for $C_9H_7ClNO^+$ $[M+H]^+$ requires *m/z* 180.0211, found *m/z* 180.0211.

4-Chloro-6-fluoroquinolin-2(1H)-one, 319:



319 was prepared according to **General Procedure E** on a 45 mmol scale using 4-fluoroaniline (4.3 mL, 5.0 g, 45 mmol, 1.0 eq.) and malonic acid (4.68 g, 45 mmol, 1.0 eq.). The crude was further purified by trituration with CH_2Cl_2 and Et_2O to obtain the title compound as a solid (5.58 g, 28.24 mmol, 63%).

^{1}H NMR (600 MHz, DMSO) δ 12.12 (s, 1H, H-NH), 7.60 (dd, *J* = 9.4, 2.9 Hz, 1H, H-5), 7.54 (td, *J* = 9.0, 2.9 Hz, 1H, H-7), 7.42 (dd, *J* = 9.0, 4.8 Hz, 1H, H-8), 6.89 (s, 1H, H-2).

^{13}C NMR (151 MHz, DMSO) δ 160.6 (C-1), 157.8 (d, *J* = 239.7 Hz, C-6), 143.5 (d, *J* = 3.3 Hz, C-3), 135.8 (d, *J* = 1.1 Hz, C-9), 122.9 (C-2), 120.7 (d, *J* = 24.5 Hz, C-7), 118.6 (d, *J* = 8.9 Hz, C-4), 118.4 (d, *J* = 8.4 Hz, C-8), 110.3 (d, *J* = 25.1 Hz, C-5).

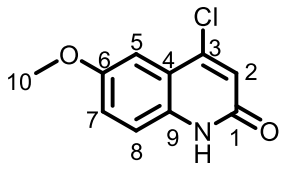
^{19}F NMR (471 MHz, DMSO) δ -119.4.

HRMS (ESI) exact mass calculated for $C_9H_6ClFNO^+$ $[M+H]^+$ requires *m/z* 198.0117, found *m/z* 198.0116.

IR (thin film) ν_{max}/cm^{-1} 3071, 1663, 1538, 1508, 1222, 1156, 1098, 837.

MP >250°C.

4-Chloro-6-methoxyquinolin-2(1H)-one, 320:



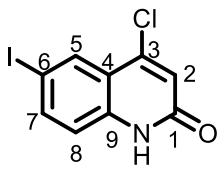
320 was prepared according to **General Procedure E** on a 45 mmol scale using p-anisidine (5.54 g, 45 mmol, 1.0 eq.) and malonic acid (4.68 g, 45 mmol, 1.0 eq.). The crude was further purified by trituration with CH_2Cl_2 and Et_2O to obtain the title compound as a solid (6.57 g, 31.34 mmol, 70%). The NMR spectra are consistent with those available in the literature.[166]

^{1}H NMR (400 MHz, DMSO) δ 11.97 (s, 1H, H-NH), 7.34 (d, *J* = 8.9 Hz, 1H, H-8), 7.30 (d, *J* = 2.7 Hz, 1H, H-5), 7.24 (d, *J* = 2.7 Hz, 1H, H-7), 6.82 (s, 1H, H-2), 3.83 (s, 3H, H-10).

^{13}C NMR (101 MHz, DMSO) δ 160.0 (C-1), 154.7 (C-6), 143.4 (C-3), 133.1 (C-9), 121.7 (C-5), 121.3 (C-5), 117.8 (C-4), 117.4 (C-8), 105.9 (C-7), 55.6 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_9ClNO_2^+$ $[M+H]^+$ requires *m/z* 210.0316, found *m/z* 210.0316.

4-Chloro-6-iodoquinolin-2(1H)-one, 321:



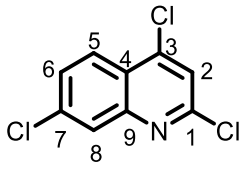
321 was prepared according to **General Procedure E** on a 45 mmol scale using 4-iodoaniline (9.86 g, 45 mmol, 1.0 eq.) and malonic acid (4.68 g, 45 mmol, 1.0 eq.) to obtain the title compound as a solid (11.97 g, 39.18 mmol, 87%). The NMR spectra are consistent with those available in the literature.[167]

^{1}H NMR (400 MHz, DMSO) δ 12.14 (s, 1H, H-NH), 8.08 (d, *J* = 1.9 Hz, 1H, H-5), 7.90 (dd, *J* = 8.6, 1.9 Hz, 1H, H-7), 7.18 (d, *J* = 8.6 Hz, 1H, H-8), 6.84 (s, 1H, H-2).

^{13}C NMR (101 MHz, DMSO) δ 160.2 (C-1), 142.6 (C-3), 140.1 (C-7), 138.1 (C-9), 132.4 (C-5), 122.2 (C-2), 119.2 (C-4), 118.0 (C-8), 86.0 (C-6).

HRMS (ESI) exact mass calculated for $C_9H_6ClINO^+$ $[M+H]^+$ requires *m/z* 305.9177, found *m/z* 305.9174.

2,4,7-Trichloroquinoline, 717:



An oven-dried round bottom flask was charged with 4,7-dichloroquinoline (10.0 g, 50.49 mmol, 1.0 eq.) before adding CH_2Cl_2 (200 mL, 0.25 M) and forming a solution. With stirring, *m*CPBA (77%, 15.8 g, 70.69 mmol, 1.4 eq.) was added in small portions, then the reaction mixture was refluxed at 40 °C for 2 hours. After the reaction time, it was cooled to room temperature, diluted with further CH_2Cl_2 (200 mL) and washed with saturated aqueous $Na_2S_2O_3$ (x3), then saturated aqueous $NaHCO_3$ (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The solid was then slowly transferred to an oven-dried round bottom flask containing $POCl_3$ (38 mL) and refluxed at 100 °C for 2 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (500 mL) with vigorous shaking and

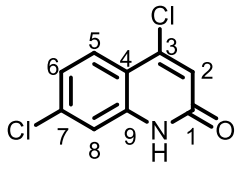
left to stand until it reached room temperature. The formed suspension was then filtered, washed with water and dried under vacuum to obtain a solid which was used without further purification (9.91 g, 42.63 mmol, 84%). The NMR spectra are consistent with those available in the literature.[168]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.9 Hz, 1H, H-5), 8.02 (d, *J* = 2.1 Hz, 1H, H-8), 7.60 (dd, *J* = 8.9, 2.1 Hz, 1H, H-6), 7.50 (s, 1H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3 (C-1), 148.6 (C-9), 144.5 (C-3), 138.0 (C-7), 129.1 (C-6), 128.1 (C-8), 125.7 (C-5), 123.9 (C-4), 122.3 (C-2).

HRMS (ESI) exact mass calculated for $C_9H_5Cl_3N^+$ $[M+H]^+$ requires *m/z* 231.9482, found *m/z* 231.9480.

4,7-Dichloroquinolin-2(1H)-one, 322:



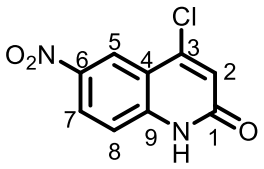
2,4,7-Trichloroquinoline (6.50 g, 27.96 mmol, 1.0 eq.) was dissolved in 1,4-dioxane (160 mL, 0.17 M) and 15% aqueous H_2SO_4 (325 mL) was added with stirring. The solution was refluxed at 110 °C for 16 hours under nitrogen, before cooling to room temperature, followed by cooling at 0 °C. The suspension was then filtered, washed with ice-cold water and dried under vacuum to obtain a solid (5.52 g, 25.79 mmol, 92%) which was used without further purification. The NMR spectra are consistent with those available in the literature.[169]

^{1}H NMR (400 MHz, DMSO) δ 12.09 (s, 1H, H-NH), 7.84 (d, *J* = 8.7 Hz, 1H, H-5), 7.38 (d, *J* = 2.1 Hz, 1H, H-8), 7.33 (dd, *J* = 8.7, 2.1 Hz, 1H, H-6), 6.84 (s, 1H, H-2).

^{13}C NMR (101 MHz, DMSO) δ 160.3 (C-1), 143.5 (C-3), 139.4 (C-9), 136.3 (C-7), 126.6 (C-5), 122.7 (C-6), 121.6 (C-2), 116.1 (C-4), 114.9 (C-8).

HRMS (ESI) exact mass calculated for $C_9H_6Cl_2NO^+$ $[M+H]^+$ requires *m/z* 213.9821, found *m/z* 213.9820.

4-Chloro-6-nitroquinolin-2(1H)-one, 323:



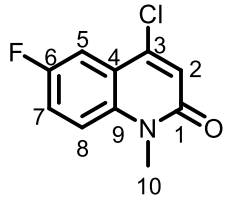
4-Chloroquinolin-2(1H)-one (6.32 g, 35.19 mmol, 1.0 eq.) was suspended in concentrated H_2SO_4 (18.5 mL, 1.9 M) and cooled to 0 °C. Concentrated HNO_3 (3.5 mL) was then added dropwise with stirring and left to stir at 0 °C for 1 hour. After this time, the reaction mixture was poured over crushed ice, then allowed to reach room temperature. The suspension was then filtered, washed with ice-cold water and dried under vacuum to obtain a solid (7.60 g, 33.84 mmol, 96%) which was used without further purification. The NMR spectra are consistent with those available in the literature.[170]

^{1}H NMR (400 MHz, DMSO) δ 12.57 (s, 1H, H-NH), 8.56 (d, *J* = 2.5 Hz, 1H, H-5), 8.41 (dd, *J* = 9.1, 2.5 Hz, 1H, H-7), 7.49 (d, *J* = 9.1 Hz, 1H, H-8), 7.02 (s, 1H, H-2).

^{13}C NMR (101 MHz, DMSO) δ 160.6 (C-1), 143.6 (C-6), 142.9 (C-9), 142.0 (C-3), 126.6 (C-7), 123.4 (C-2), 121.0 (C-5), 117.2 (C-8), 117.0 (C-4).

HRMS (ESI) exact mass calculated for $C_9H_6ClN_2O_3^+$ $[M+H]^+$ requires *m/z* 225.0062, found *m/z* 225.0061.

4-Chloro-6-fluoro-1-methylquinolin-2(1H)-one, 324:



324 was prepared according to **General Procedure F** on a 15.18 mmol scale using 4-chloro-6-fluoroquinolin-2(1H)-one (3.00 g, 15.18 mmol, 1.0 eq.), methyl iodide (1.9 mL, 4.31 g, 30.36 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 1.21 g, 30.36 mmol, 2.0 eq.). The crude was purified by flash column chromatography (35:65 to 45:55 EtOAc:pentane, v:v) to obtain the title compound as a solid (944.6 mg, 4.36 mmol, 29%). The NMR spectra are consistent with those available in the literature.[171]

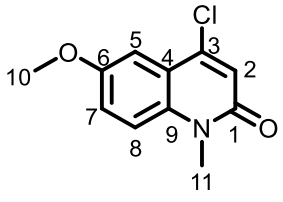
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (ddd, *J* = 9.0, 2.2, 1.2 Hz, 1H, H-5), 7.39 – 7.34 (m, 2H, H-7,8), 6.92 (d, *J* = 0.7 Hz, 1H, H-2), 3.70 (s, 3H, H-10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5 (C-1), 158.1 (d, *J* = 243.4 Hz, C-6), 143.1 (d, *J* = 3.2 Hz, C-3), 136.3 (C-9), 122.2 (C-2), 120.3 (d, *J* = 8.5 Hz, C-4), 119.7 (d, *J* = 23.9 Hz, C-7), 116.2 (d, *J* = 8.0 Hz, C-8), 111.7 (d, *J* = 24.9 Hz, C-5), 29.9 (C-10).

^{19}F NMR (377 MHz, $CDCl_3$) δ -119.4.

HRMS (ESI) exact mass calculated for $C_{10}H_8ClFNO^+$ $[M+H]^+$ requires *m/z* 212.0273, found *m/z* 212.0272.

4-Chloro-6-methoxy-1-methylquinolin-2(1H)-one, 325:



325 was prepared according to **General Procedure F** on a 16.70 mmol scale using 4-chloro-6-methoxyquinolin-2(1H)-one (3.50 g, 16.70 mmol, 1.0 eq.), methyl iodide (2.1 mL, 4.74 g, 33.40 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil,

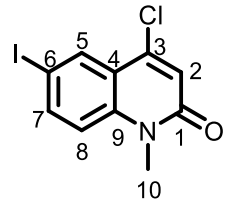
1.34 g, 33.40 mmol, 2.0 eq.). The crude was purified by flash column chromatography (40:60 to 50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.32 g, 5.90 mmol, 35%). The NMR spectra are consistent with those available in the literature.[172]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 2.9 Hz, 1H, H-5), 7.32 (d, *J* = 9.2 Hz, 1H, H-8), 7.24 (dd, *J* = 9.2, 2.9 Hz, 1H, H-7), 6.89 (s, 1H, H-2), 3.90 (s, 3H, H-10), 3.69 (s, 3H, H-11).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6 (C-1), 155.2 (C-6), 143.6 (C-3), 134.4 (C-9), 121.6 (C-2), 120.8 (C-7), 120.1 (C-4), 116.0 (C-8), 107.9 (C-5), 55.9 (C-10), 29.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{11}H_{11}ClNO_2^+$ $[M+H]^+$ requires *m/z* 224.0473, found *m/z* 224.0471.

4-Chloro-6-iodo-1-methylquinolin-2(1H)-one, 326:



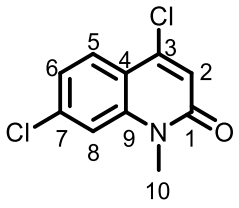
326 was prepared according to **General Procedure F** on a 38.04 mmol scale using 4-chloro-6-iodoquinolin-2(1H)-one (11.62 g, 38.04 mmol, 1.0 eq.), methyl iodide (4.8 mL, 10.80 g, 76.08 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 3.04 g, 76.08 mmol, 2.0 eq.). The crude was purified by flash column chromatography (40:60 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.32 g, 4.13 mmol, 35%). The NMR spectra are consistent with those available in the literature.[167]

^{1}H NMR (400 MHz, DMSO) δ 8.16 (d, *J* = 2.1 Hz, 1H, H-5), 8.01 (dd, *J* = 8.9, 2.1 Hz, 1H, H-7), 7.44 (d, *J* = 8.9 Hz, 1H, H-8), 6.98 (s, 1H, H-2), 3.58 (s, 3H, H-10).

^{13}C NMR (101 MHz, DMSO) δ 159.9, 142.0, 140.7, 139.6, 133.4, 122.0, 120.5, 118.3, 87.0, 29.9.

HRMS (ESI) exact mass calculated for $C_{10}H_8ClINO^+$ $[M+H]^+$ requires *m/z* 319.9334, found *m/z* 319.9332.

4,7-Dichloro-1-methylquinolin-2(1H)-one, 327:



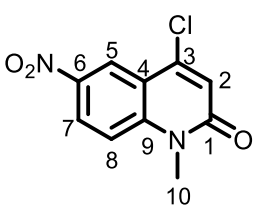
327 was prepared according to a modified **General Procedure F** on a 25.74 mmol scale using 4,7-dichloroquinolin-2(1H)-one (5.51 g, 25.74 mmol, 1.0 eq.), methyl iodide (3.2 mL, 7.31 g, 51.48 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 2.06 g, 51.48 mmol, 2.0 eq.) in anhydrous DMF (85.0 mL, 0.3 M). After the reaction time the mixture was poured into ice water (500 mL) to crash out the product and the suspension was filtered, washing the solid with additional water and pentane, then drying under vacuum to obtain a solid (5.30 g, 23.24 mmol, 90%) which was used without further purification. The NMR spectra are consistent with those available in the literature.[173]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 1H, H-5), 7.38 (d, *J* = 1.9 Hz, 1H, H-8), 7.27 (dd, *J* = 8.6, 1.9 Hz, 1H, H-6), 6.86 (s, 1H, H-2), 3.67 (s, 3H, H-10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (C-1), 143.9 (C-3), 140.6 (C-9), 138.4 (C-7), 127.6 (C-5), 123.1 (C-6), 121.1 (C-2), 117.9 (C-4), 114.6 (C-8), 29.8 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_8Cl_2NO^+$ $[M+H]^+$ requires *m/z* 227.9978, found *m/z* 227.9976.

4-Chloro-1-methyl-6-nitroquinolin-2(1H)-one, 328:



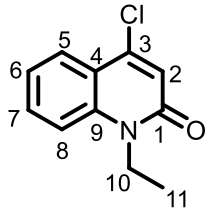
328 was prepared according to **General Procedure F** on a 33.84 mmol scale using 4-chloro-6-nitroquinolin-2(1H)-one (7.60 g, 33.84 mmol, 1.0 eq.), methyl iodide (4.2 mL, 9.61 g, 67.68 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 2.71 g, 67.68 mmol, 2.0 eq.). The crude was purified by flash column chromatography (40:60 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.87 g, 12.03 mmol, 36%). The NMR spectra are consistent with those available in the literature.[170]

^{1}H NMR (400 MHz, DMSO) δ 8.61 (d, *J* = 2.7 Hz, 1H, H-5), 8.47 (dd, *J* = 9.4, 2.7 Hz, 1H, H-7), 7.80 (d, *J* = 9.4 Hz, 1H, H-8), 7.16 (s, 1H, H-2), 3.65 (s, 3H, H-10).

^{13}C NMR (101 MHz, DMSO) δ 159.8 (C-1), 143.6 (C-6), 142.5 (C-3), 141.8 (C-9), 126.4 (C-7), 122.6 (C-2), 121.0 (C-5), 117.9 (C-4), 117.0 (C-8), 30.1 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_8ClN_2O_3^+$ $[M+H]^+$ requires *m/z* 239.0218, found *m/z* 239.0214.

4-Chloro-1-ethylquinolin-2(1H)-one, 262:



262 was prepared according to **General Procedure F** on a 6.70 mmol scale using 4-chloroquinolin-2(1H)-one (1.20 g, 6.70 mmol, 1.0 eq.), ethyl iodide (1.1 mL, 2.09 g, 13.40 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 536.0 mg, 13.40 mmol, 2.0 eq.). The crude was purified by flash column chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as solid (686.2 mg, 3.30 mmol, 49%). The NMR spectra are consistent with those available in the literature.[171]

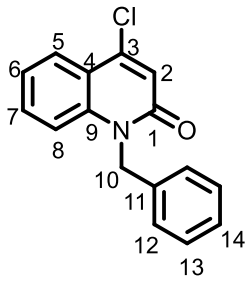
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.2, 1.5 Hz, 1H, H-5), 7.63 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H, H-7), 7.41 (dd, *J* = 8.6, 1.0 Hz, 1H, H-8), 7.30 (ddd, *J* = 8.2, 7.2, 1.0 Hz,

1H, H-6), 6.87 (s, 1H, H-2), 4.34 (q, *J* = 7.2 Hz, 2H, H-10), 1.35 (t, *J* = 7.2 Hz, 3H, H-11).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6 (C-1), 144.3 (C-3), 138.9 (C-9), 131.9 (C-7), 126.5 (C-5), 122.5 (C-6), 121.2 (C-2), 119.6 (C-4), 114.4 (C-8), 37.6 (C-10), 12.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{11}H_{11}ClNO^+$ $[M+H]^+$ requires *m/z* 208.0524, found *m/z* 208.0521.

1-Benzyl-4-chloroquinolin-2(1H)-one, 329:



329 was prepared according to **General Procedure F** on a 4.50 mmol scale using 4-chloroquinolin-2(1H)-one (808.2 mg, 4.50 mmol, 1.0 eq.), benzyl bromide (1.1 mL, 1.54 g, 9.00 mmol, 2.0 eq.) and sodium hydride (60 % dispersion in mineral oil, 360.0 mg, 9.00 mmol, 2.0 eq.). The crude was purified by flash column chromatography (25:75 Et_2O:pentane, v:v) to obtain the title compound as a solid (732.6 mg, 2.72 mmol, 60%).

^{1}H NMR (600 MHz, DMSO) δ 7.97 (dd, *J* = 8.0, 1.5 Hz, 1H, H-5), 7.62 (ddd, *J* = 8.7, 7.1, 1.5 Hz, 1H, H-7), 7.47 (d, *J* = 8.7 Hz, 1H, H-8), 7.38 – 7.32 (m, 1H, H-6), 7.32 – 7.19 (m, 5H, Ar Hs), 7.07 (s, 1H, H-2), 5.53 (s, 2H, H-10).

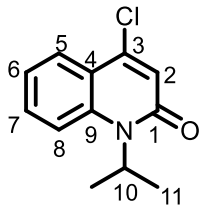
^{13}C NMR (151 MHz, DMSO) δ 160.0 (C-1), 143.6 (C-3), 138.8 (C-9), 136.3 (C-11), 132.3 (C-7), 128.7 (C-13), 127.1 (C-14), 126.5 (C-12), 125.6 (C-5), 122.9 (C-6), 120.6 (C-2), 118.4 (C-4), 115.7 (C-8), 44.8 (C-10).

HRMS (ESI) exact mass calculated for $C_{16}H_{13}ClNO^+$ $[M+H]^+$ requires *m/z* 270.0680, found *m/z* 270.0677.

IR (thin film) ν_{max}/cm^{-1} 2918, 1651, 1589, 1492, 1454, 1360, 1311, 942.

MP 108 °C.

4-Chloro-1-isopropylquinolin-2(1H)-one, 330:



An oven-dried 25 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (808.2 mg, 4.50 mmol, 1.0 eq.) before adding anhydrous DMF (5 mL, 0.9 M) and isopropyl bromide (1.3 mL, 1.66 g, 13.50 mmol, 3.0 eq.). With stirring, K_2CO_3 (1.87 g, 13.50 mmol, 3.0 eq.) was added, then heated at 60 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (2:98 EtOAc:pentane, v:v) to obtain the title compound as an oil (716.5 mg, 3.23 mmol, 72%).

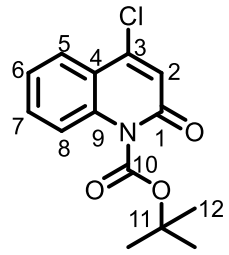
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (ddd, *J* = 8.2, 1.5, 0.6 Hz, 1H, H-5), 7.82 (ddd, *J* = 8.4, 1.2, 0.6 Hz, 1H, H-8), 7.65 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.44 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, H-6), 6.98 (s, 1H, H-2), 5.56 (hept, *J* = 6.2 Hz, 1H, H-10), 1.41 (d, *J* = 6.2 Hz, 6H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3 (C-1), 147.3 (C-3), 143.7 (C-9), 130.5 (C-7), 127.7 (C-8), 124.6 (C-6), 124.1 (C-5), 123.3 (C-4), 113.7 (C-2), 68.7 (C-10), 22.1 (C-11).

HRMS (ESI) exact mass calculated for $C_{12}H_{13}ClNO^+$ $[M+H]^+$ requires *m/z* 222.0680, found *m/z* 222.0679.

IR (thin film) ν_{max}/cm^{-1} 2980, 1598, 1564, 1501, 1410, 1395, 1312, 1303, 1111, 966.

***tert*-Butyl 4-chloro-2-oxoquinoline-1(2H)-carboxylate, 718:**



An oven-dried 25 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (500.0 mg, 2.78 mmol, 1.0 eq.) before adding anhydrous dichloromethane (11.0 mL, 0.25 M) and triethylamine (0.390 mL, 281.3 mg, 2.78 mmol, 1.0 eq.). With stirring, Boc_2O (910.2 mg, 4.17 mmol, 1.5 eq.) was added, followed by DMAP (34.2 mg, 10 mol%) then left to stir at room temperature for 16 hours under nitrogen. After the reaction time, the mixture was concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 to 20:80 Et_2O:pentane, v:v) to obtain the title compound as a solid (233.8 mg, 0.84 mmol, 30%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dd, J = 8.5, 1.5 Hz, 1H, H-8), 8.02 (d, J = 8.5 Hz, 1H, H-5), 7.76 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.62 (ddt, J = 8.4, 6.9, 1.5 Hz, 1H, H-6), 7.38 (s, 1H, H-2), 1.58 (s, 9H, H-12).

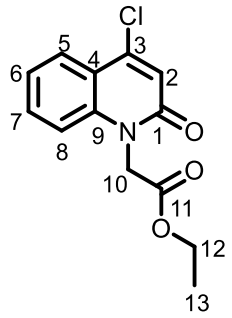
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.6 (C-1), 150.7 (C-10), 146.8 (C-3), 145.2 (C-9), 131.3 (C-7), 129.2 (C-5), 127.5 (C-6), 125.4 (C-4), 124.2 (C-8), 115.4 (C-2), 84.7 (C-11), 27.8 (C-12).

HRMS (ESI) exact mass calculated for $C_{14}H_{15}ClNO_3^+$ $[M+H]^+$ requires *m/z* 280.0735, found *m/z* 280.0735.

IR (thin film) ν_{max}/cm^{-1} 2986, 2931, 1762, 1592, 1567, 1500, 1371, 1268, 1246, 1228, 1144, 1123, 850.

MP 76 °C.

Ethyl 2-(4-chloro-2-oxoquinolin-1(2H)-yl)acetate, 331:



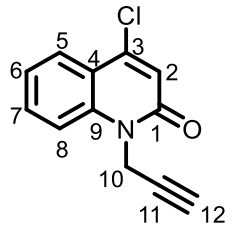
An oven-dried 100 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (808.2 mg, 4.50 mmol, 1.0 eq.) before adding anhydrous DMF (35 mL, 0.13 M) and ethyl chloroacetate (0.970 mL, 1.10 g, 9.00 mmol, 2.0 eq.). With stirring, K_2CO_3 (1.24 g, 9.0 mmol, 2.00 eq.) was added, then left to stir at room temperature for 16 hours under nitrogen. After the reaction time, the mixture was poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 to 100:0 Et_2O:pentane, v:v) to obtain the title compound as a solid (604.1 mg, 2.27 mmol, 51%). The NMR spectra are consistent with those available in the literature.[174]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.60 (ddd, *J* = 8.7, 7.3, 1.5 Hz, 1H, H-7), 7.33 (ddd, *J* = 8.1, 7.3, 1.0 Hz, 1H, H-6), 7.18 – 7.10 (m, 1H, H-8), 6.92 (s, 1H, H-2), 5.08 (s, 2H, H-10), 4.23 (q, *J* = 7.1 Hz, 2H, H-12), 1.26 (t, *J* = 7.1 Hz, 3H, H-13).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9 (C-11), 160.7 (C-1), 145.5 (C-9), 139.2 (C-9), 132.2 (C-7), 126.7 (C-5), 123.1 (C-6), 120.7 (C-2), 119.5 (C-4), 114.0 (C-8), 62.0 (C-12), 43.9 (C-10), 14.3 (C-13).

HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO_3^+$ $[M+H]^+$ requires *m/z* 266.0579, found *m/z* 266.0576.

4-Chloro-1-(prop-2-yn-1-yl)quinolin-2(1H)-one, 332:



An oven-dried 25 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (808.2 mg, 4.50 mmol, 1.0 eq.) before adding anhydrous DMF (4.5 mL, 1.0 M) and propargyl bromide (80% wt. in toluene, 1.5 mL, 13.50 mmol, 3.0 eq.). With stirring, K_2CO_3 (1.87 g, 13.50 mmol, 3.0 eq.) was added, then heated at 70 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (40:60 to 60:40 Et_2O:pentane, v:v) to obtain the title compound as a solid (677.3 mg, 3.11 mmol, 69%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.2, 1.5 Hz, 1H, H-5), 7.68 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H, H-7), 7.56 (dt, *J* = 8.6, 0.7 Hz, 1H, H-8), 7.35 (ddd, *J* = 8.2, 7.2, 0.7 Hz, 1H, H-6), 6.89 (s, 1H, H-2), 5.09 (d, *J* = 2.5 Hz, 2H, H-10), 2.25 (t, *J* = 2.5 Hz, 1H, H-12).

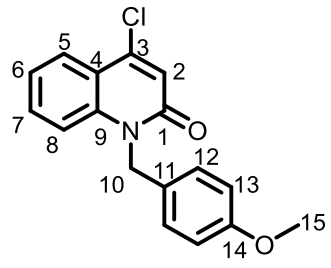
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1 (C-1), 145.3 (C-3), 138.5 (C-9), 132.2 (C-7), 126.5 (C-5), 123.1 (C-6), 120.8 (C-2), 119.6 (C-4), 115.0 (C-8), 77.7 (C-11), 72.9 (C-12), 31.9 (C-10).

HRMS (ESI) exact mass calculated for $C_{12}H_9ClNO^+$ $[M+H]^+$ requires *m/z* 218.0367, found *m/z* 218.0367.

IR (thin film) ν_{max}/cm^{-1} 3215, 2926, 2854, 2113, 1644, 1587, 1452, 1360, 1305, 1087, 951, 932, 861.

MP 155 °C.

4-Chloro-1-(4-methoxybenzyl)quinolin-2(1H)-one, 333:



An oven-dried 250 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (7.53 g, 41.93 mmol, 1.0 eq.) before adding anhydrous DMF (140 mL, 0.3 M) and 4-methoxybenzyl chloride (13.1 g, 83.85 mmol, 2.0 eq.). With stirring, K_2CO_3 (17.4 g, 125.8 mmol, 3.0 eq.) was added, then heated at 60 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (30:70 to 100:0 CH_2Cl_2:pentane, v:v) to obtain the title compound as a solid (3.57 g, 11.91 mmol, 28%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.50 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H, H-7), 7.37 – 7.32 (m, 1H, H-8), 7.29 – 7.26 (m, 1H, H-6), 7.18 – 7.13 (m, 2H, H-12), 6.98 (s, 1H, H-2), 6.86 – 6.80 (m, 2H, H-13), 5.60 – 5.36 (m, 2H, H-10), 3.76 (s, 3H, H-15).

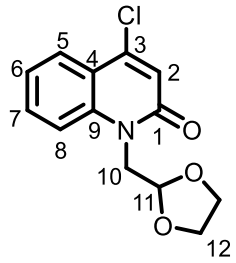
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3 (C-1), 159.1 (C-14), 144.9 (C-3), 139.4 (C-9), 132.0 (C-7), 128.11 (C-11), 128.08 (C-12), 126.4 (C-5), 122.8 (C-6), 121.1 (C-2), 119.6 (C-4), 115.4 (C-8), 114.4 (C-13), 55.4 (C-15), 45.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}ClNO_2^+$ $[M+H]^+$ requires *m/z* 300.0786, found *m/z* 300.0778.

IR (thin film) ν_{max}/cm^{-1} 2923, 1651, 1615, 1513, 1490, 1360, 1307, 1249, 1178, 1033, 941, 851, 755, 648, 630.

MP 106-109 °C.

1-((1,3-Dioxolan-2-yl)methyl)-4-chloroquinolin-2(1H)-one, 335:



An oven-dried 25 mL round bottom flask was charged with 4-chloroquinolin-2(1H)-one (1.20 g, 6.70 mmol, 1.0 eq.) before adding anhydrous DMF (13.4 mL, 0.5 M) and 2-bromomethyl-1,3-dioxolane (0.850 mL, 1.34 g, 8.04 mmol, 1.2 eq.). With stirring, Cs_2CO_3 (2.84 g, 8.71 mmol, 1.3 eq.) was added, then heated at 50 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (35:65 EtOAc:pentane, v:v) to obtain the title compound as a solid (441.2 mg, 1.66 mmol, 25%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 – 7.98 (m, 1H, H-5), 7.65 – 7.58 (m, 2H, H-7,8), 7.30 (m, 1H, H-6), 6.90 (s, 1H, H-2), 5.24 (t, *J* = 4.4 Hz, 1H, H-11), 4.53 (d, *J* = 4.4 Hz, 2H, H-10), 4.07 – 3.99 (m, 2H, H-12), 3.91 – 3.83 (m, 2H, H-12').

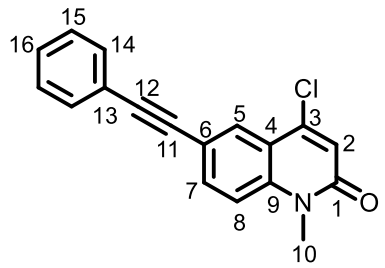
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.2 (C-1), 145.0 (C-3), 139.8 (C-9), 131.8 (C-7), 126.3 (C-5), 122.8 (C-6), 121.0 (C-2), 119.4 (C-4), 115.5 (C-8), 101.8 (C-11), 65.2 (C-12), 45.0 (C-10).

HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO_3^+$ $[M+H]^+$ requires *m/z* 266.0579, found *m/z* 266.0573.

IR (thin film) ν_{max}/cm^{-1} 3547, 2892, 1655, 1590, 1454, 1360, 1142, 951, 930, 860,

MP 110-112 °C.

4-Chloro-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one, 338:



A 3-neck round bottom flask was charged with 4-chloro-6-iodo-1-methylquinolin-2(1H)-one (1.74 g, 5.45 mmol, 1.0 eq.), $PdCl_2$ (9.8 mg, 1 mol%), CuI (10.5 mg, 1 mol%) and PPh_3 (28.6 mg, 2 mol%) before degassing with vacuum and nitrogen cycles (x3). Degassed THF (27.0 mL, 0.2 M) was then added, followed by degassed NEt_3 (2.3 mL, 0.42 mL/mmol) and phenylacetylene (0.660 mL, 612.8 mg, 6.00 mmol, 1.1 eq.). The reaction mixture was left to stir at room temperature for 16 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude oil, then purified by flash column chromatography (0:100 to 5:95 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (1.55 g, 5.28 g, 97%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, *J* = 1.9 Hz, 1H, H-5), 7.76 (dd, *J* = 8.7, 1.9 Hz, 1H, H-7), 7.61 – 7.53 (m, 2H, H-14), 7.37 (m, 4H, H-8,15,16), 6.92 (s, 1H, H-2), 3.71 (s, 3H, H-10).

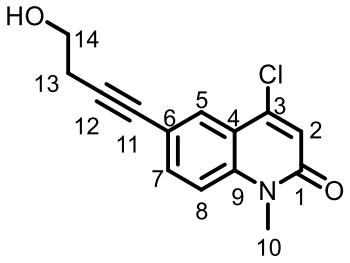
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9 (C-1), 143.9 (C-3), 139.4 (C-9), 134.9 (C-7), 131.8 (C-14), 129.4 (C-5), 128.7 (C-16), 128.6 (C-15), 122.9 (C-4), 121.8 (C-2), 119.4 (C-13), 118.0 (C-6), 114.8 (C-8), 90.3 (C-12), 88.1 (C-11), 29.8 (C-10).

HRMS (ESI) exact mass calculated for $C_{18}H_{13}ClNO^+$ $[M+H]^+$ requires *m/z* 294.0680, found *m/z* 294.0674.

IR (thin film) ν_{max}/cm^{-1} 3446, 2975, 2767, 2681, 2479, 2358, 1660, 1558, 1422, 1312, 1036, 759

MP 144-145 °C.

4-Chloro-6-(4-hydroxybut-1-yn-1-yl)-1-methylquinolin-2(1H)-one, 339:



A 3-neck round bottom flask was charged with 4-chloro-6-iodo-1-methylquinolin-2(1H)-one (1.50 g, 4.69 mmol, 1.0 eq.), $PdCl_2$ (8.9 mg, 1 mol%), CuI (9.5 mg, 1 mol%) and PPh_3 (23.6 mg, 2 mol%) before degassing with vacuum and nitrogen cycles (x3). Degassed THF (23.5 mL, 0.2 M) was then added, followed by degassed NEt_3 (2.0 mL, 0.42 mL/mmol) and 3-butyn-1-ol (0.390 mL, 361.7 mg, 5.16 mmol, 1.1 eq.). The reaction mixture was left to stir at room temperature for 16 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude oil, then purified by flash column chromatography (0:100 to 3:97 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (777.1 mg, 2.97 mmol, 58%).

^{1}H NMR (600 MHz, MeOD) δ 8.00 (d, *J* = 1.9 Hz, 1H, H-5), 7.70 (dd, *J* = 8.8, 1.9 Hz, 1H, H-7), 7.56 (d, *J* = 8.8 Hz, 1H, H-8), 6.88 (s, 1H, H-2), 4.59 (s, 1H, H-OH), 3.76 (t, *J* = 6.7 Hz, 2H, H-14), 3.70 (s, 3H, H-10), 2.66 (t, *J* = 6.7 Hz, 2H, H-13).

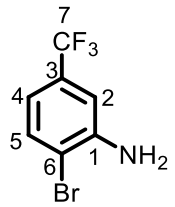
^{13}C NMR (151 MHz, MeOD) δ 162.6 (C-1), 145.4 (C-3), 140.1 (C-9), 136.3 (C-7), 129.6 (C-5), 121.8 (C-2), 120.3 (C-4), 120.2 (C-6), 116.7 (C-8), 89.3 (C-12), 80.8 (C-11), 61.6 (C-14), 30.3 (C-10), 24.2 (C-13).

HRMS (ESI) exact mass calculated for $C_{14}H_{13}ClNO_2^+$ $[M+H]^+$ requires *m/z* 262.0629, found *m/z* 262.0624.

IR (thin film) ν_{max}/cm^{-1} 3356, 2942, 1726, 1637, 1558, 1496, 1459, 1362, 1270, 1173, 1063, 966, 899, 821, 736, 668.

MP 157-158 °C.

2-Bromo-5-(trifluoromethyl)aniline, 341:



An oven-dried 500 mL round bottom flask was charged with 1-bromo-2-nitro-4-(trifluoromethyl)benzene (10.0 g, 37.0 mmol, 1.0 eq.) and iron powder (10.34 g, 185.2 mmol, 5.0 eq.) before adding EtOH:H_2O (1.5:1, 82.3 mL, 0.45 M), followed by solid NH_4Cl (7.92 g, 148.14 mmol, 4.0 eq.).The suspension was heated at 90 °C for 2 hours. After the reaction time, the suspension was cooled to room temperature before diluting with EtOAc to twice its volume, then neutralised with solid Na_2CO_3 and passed through a short plug of Celite, eluting with further EtOAc. Combined organics were washed with deionised water (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid, then purified by flash column chromatography (5:95 to 10:90 Et_2O:pentane,

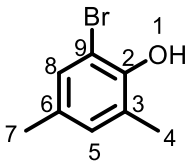
v:v) to obtain the title compound as a solid (2.45 g, 10.21 mmol, 28%). The NMR spectra are consistent with those available in the literature.[175]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 1H, H-5), 6.97 (d, *J* = 2.1 Hz, 1H, H-2), 6.85 (dd, *J* = 8.2, 2.1 Hz, 1H, H-4), 4.28 (s, 2H, H-NH_2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6 (C-1), 133.2 (C-5), 131.0 (q, *J* = 32.6 Hz, C-3), 124.0 (q, *J* = 272.2 Hz, C-7), 115.7 (q, *J* = 3.9 Hz, C-4), 112.5 (C-6), 112.0 (q, *J* = 3.9 Hz, H-2).

^{19}F NMR (377 MHz, $CDCl_3$) δ -63.0.

2-Bromo-4,6-dimethylphenol, 114:



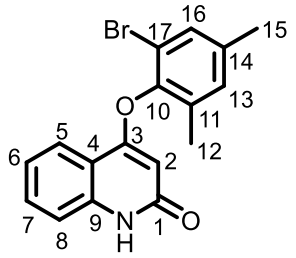
A flame-dried round bottom flask was charged with 2,4-dimethylphenol (10.00 g, 81.9 mmol, 1.0 eq.) before dissolving in CH_2Cl_2 (40 mL) and cooling to 0 °C. Br_2 (4.41 mL, 13.74 g, 86.0 mmol, 1.05 eq.) dissolved in CH_2Cl_2 (20 mL) was added dropwise over 10 minutes via a dropping funnel, then the solution was stirred at room temperature for 1 hour. After the reaction time, the solution was quenched with saturated aqueous $Na_2S_2O_3$ (30 mL) and transferred to a separatory funnel. The aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain an oil (16.15 g, 80.32 mmol, 98%), which was used without further purification. The NMR spectra are consistent with those available in the literature.[176]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 2.0 Hz, 1H), 6.89 – 6.87 (m, 1H), 5.41 (s, 1H), 2.27 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 131.3, 130.8, 129.5, 125.5, 109.8, 20.3, 16.7.

HRMS (ESI) exact mass calculated for $C_8H_8BrO^-$ $[M-H]^-$ requires *m/z* 198.9764, found *m/z* 198.9757.

4-(2-Bromo-4,6-dimethylphenoxy)quinolin-2(1H)-one, 343:



A 250 mL round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)-1-(4-methoxybenzyl)quinolin-2(1H)-one (1.88 g, 4.05 mmol, 1.0 eq.) before dissolving in MeCN (81 mL, 0.05 M) and adding deionised water (24 mL) to form a fine suspension. The suspension was cooled to 0 °C, then solid CAN (4.44 g, 8.10 mmol. 2.0 eq.) was added portion wise, then stirred at room temperature for 3 hours. After the reaction time, the solution was poured into 100 mL of H_2O and extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid oil, which was purified by flash column chromatography (0:100 to 5:94 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (672.4 mg, 1.95 mmol, 48%).

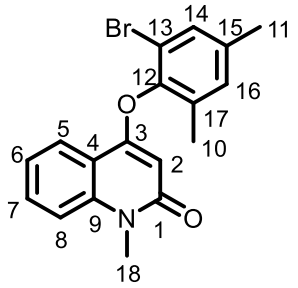
^{1}H NMR (600 MHz, $CDCl_3$) δ 11.72 (s, 1H, H-NH), 8.17 (dd, *J* = 8.2, 1.4 Hz, 1H, H-5), 7.56 (ddd, *J* = 8.4, 7.2, 1.5 Hz, 1H, H-7), 7.39 – 7.35 (m, 1H, H-8), 7.32 (d, *J* = 2.1 Hz, 1H, H-16), 7.29 (ddd, *J* = 8.4, 7.2, 1.1 Hz, 1H, H-6), 7.05 (dd, *J* = 2.1, 1.0 Hz, 1H, H-13), 5.57 (s, 1H, H-2), 2.35 (s, 3H, H-15), 2.19 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7 (C-1), 162.7 (C-3), 146.3 (C-10), 138.9 (C-9), 137.7 (C-14), 132.6 (C-11), 132.0 (C-16), 131.7 (C-7), 131.6 (C-13), 123.1 (C-5), 122.6 (C-6), 116.3 (C-4), 116.1 (C-8), 115.0 (C-17), 98.9 (C-2), 20.8 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}BrNO_2^+$ $[M+H]^+$ requires *m/z* 344.0281, found *m/z* 344.0276.

MP 222 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-methylquinolin-2(1H)-one, 116:



116 was prepared according to **General Procedure A** on an 8.78 mmol scale using 4-chloro-1-methylquinolin-2(1H)-one (1.70 g, 8.78 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (2.65 g, 13.17 mmol, 1.5 eq.). Purified by flash column chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.77 g, 7.73 mmol, 88%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.65 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-7), 7.39 (d, *J* = 8.7 Hz, 1H, H-8), 7.32 (ddd, *J* = 8.0, 7.2, 1.0 Hz, 1H, H-6), 7.31 – 7.29 (m, 1H, H-14), 7.03 (dd, *J* = 2.2, 1.0 Hz, 1H, H-16), 5.60 (s, 1H, H-2), 3.67 (s, 3H, H-18), 2.33 (s, 3H, H-11), 2.16 (s, 3H, H-10).

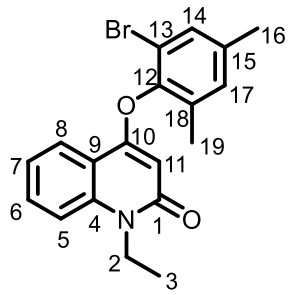
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-1), 160.4 (C-3), 146.1 (C-12), 140.3 (C-9), 137.6 (C-15), 132.6 (C-17), 131.9 (C-14), 131.7 (C-7), 131.5 (C-16), 123.6 (C-5), 122.1 (C-6), 116.3 (C-4), 115.8 (C-13), 114.3 (C-8), 99.3 (C-2), 29.3 (C-18), 20.7 (C-11), 16.5 (C-10).

HRMS (ESI) exact mass calculated for $C_{18}H_{17}BrNO_2^+$ $[M+H]^+$ requires *m/z* 358.0437, found *m/z* 358.0434.

IR (thin film) ν_{max}/cm^{-1} 3009, 2360, 1655, 1641, 1592, 1389, 1210, 842.

MP 165-167 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-ethylquinolin-2(1H)-one, 344:



344 was prepared according to **General Procedure A** on a 3.23 mmol scale using 4-chloro-1-ethylquinolin-2(1H)-one (671.3 mg, 3.23 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (975.1 mg, 4.85 mmol, 1.5 eq.). Purified by flash column chromatography (25:75 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.02 g, 2.74 mmol, 85%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 8.0, 1.6 Hz, 1H, H-8), 7.64 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H, H-6), 7.42 (d, *J* = 8.6 Hz, 1H, H-5), 7.33 – 7.29 (m, 2H, H-7,14), 7.04 – 7.01 (m, 1H, H-17), 5.59 (s, 1H, H-11), 4.32 (ddt, *J* = 18.2, 14.2, 7.1 Hz, 2H, H-2), 2.33 (s, 3H, H-16), 2.17 (s, 3H, H-19), 1.35 (t, *J* = 7.1 Hz, 3H, H-3).

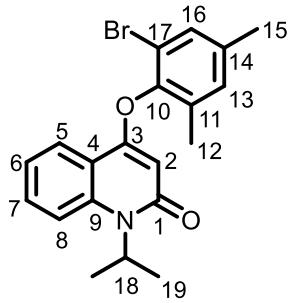
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2 (C-1), 160.3 (C-10), 146.2 (C-12), 139.3 (C-4), 137.5 (C-15), 132.6 (C-18), 131.9 (C-14), 131.6 (C-6), 131.5 (C-17), 123.9 (C-8), 121.8 (C-7), 116.4 (C-9), 116.0 (C-13), 114.2 (C-5), 99.4 (C-11), 37.2 (C-2), 20.7 (C-16), 16.6 (C-19), 13.0 (C-3).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}BrNO_2^+$ $[M+H]^+$ requires *m/z* 372.0594, found *m/z* 372.0587.

IR (thin film) ν_{max}/cm^{-1} 2976, 1644, 1592, 1454, 1390, 1323, 1279, 1209, 1126, 843.

MP 166 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-isopropylquinolin-2(1H)-one, 345:



345 was prepared according to **General Procedure A** on a 3.16 mmol scale using 4-chloro-1-isopropylquinolin-2(1H)-one (700.0 mg, 3.16 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (953.0 mg, 4.74 mmol, 1.5 eq.). Purified by flash column chromatography (2:98 Et_2O:pentane, v:v) to obtain the title compound as a solid (761.0 mg, 1.97 mmol, 62%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.2, 1.5 Hz, 1H, H-5), 7.83 – 7.80 (m, 1H, H-8), 7.66 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.42 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, H-6), 7.35 – 7.31 (m, 1H, H-16), 7.07 – 7.03 (m, 1H, H-13), 5.74 (s, 1H, H-2), 5.54 (hept, *J* = 6.2 Hz, 1H, H-18), 2.35 (s, 3H, H-15), 2.17 (s, 3H, H-12), 1.36 (d, *J* = 6.2 Hz, 6H, H-19).

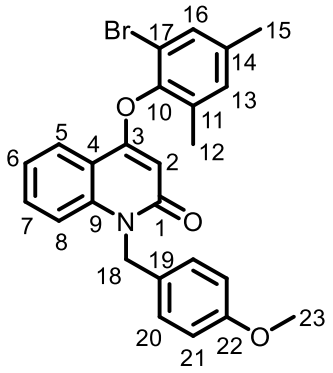
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.9 (C-1), 161.6 (C-3), 147.9 (C-10), 146.9 (C-9), 137.2 (C-14), 132.9 (C-11), 131.9 (C-16), 131.6 (C-13), 130.2 (C-7), 127.1 (C-8), 123.5 (C-6), 122.0 (C-5), 118.5 (C-4), 116.7 (C-17), 93.9 (C-2), 68.2 (C-18), 22.2 (C-19), 20.7 (C-15), 16.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{20}H_{20}BrNO_2^+$ $[M+H]^+$ requires *m/z* 386.0750, found *m/z* 386.0746.

IR (thin film) ν_{max}/cm^{-1} 2978, 1625, 1603, 1574, 1421, 1404, 1362, 1210, 1172, 1110, 899.

MP 86-88 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-(4-methoxybenzyl)quinolin-2(1H)-one, 346:



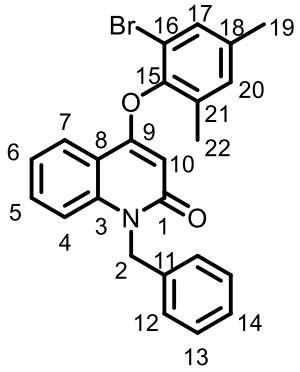
346 was prepared according to **General Procedure A** on an 10.74 mmol scale using 4-chloro-1-(4-methoxybenzyl)quinolin-2(1H)-one (3.22 g, 10.71 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (3.24 g, 16.11 mmol, 1.5 eq.). Purified by flash column chromatography (30:70 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.01 g, 4.33 mmol, 40%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 8.4, 1.6 Hz, 1H, H-5), 7.52 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H-7), 7.35 – 7.31 (m, 2H, H-8,16), 7.28 (ddd, *J* = 8.4, 7.3, 1.1 Hz, 1H, H-6), 7.21 – 7.16 (m, 2H, H-20), 7.06 – 7.04 (m, 1H, H-13), 6.86 – 6.82 (m, 2H, H-21), 5.68 (s, 1H, H-2), 5.62 – 5.24 (m, 2H, H-18), 3.76 (s, 3H, H-23), 2.35 (s, 3H, H-15), 2.21 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-1), 160.7 (C-3), 158.9 (C-22), 146.2 (C-10), 139.8 (C-9), 137.6 (C-14), 132.6 (C-11), 132.0 (C-16), 131.7 (C-7), 131.6 (C-13), 128.7 (C-19), 128.1 (C-20), 123.7 (C-5), 122.1 (C-6), 116.4 (C-4), 116.1 (C-17), 115.2 (C-5), 114.3 (C-21), 99.2 (C-2), 55.4 (C-23), 45.3 (C-18), 20.5 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{25}H_{23}BrNO_3^+$ $[M+H]^+$ requires *m/z* 464.0856, found *m/z* 464.0850.

1-Benzyl-4-(2-bromo-4,6-dimethylphenoxy)quinolin-2(1H)-one, 347:



347 was prepared according to **General Procedure A** on a 2.68 mmol scale using 1-benzyl-4-chloroquinolin-2(1H)-one (723.5 mg, 2.68 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (808.3 mg, 4.02 mmol, 1.5 eq.). Purified by flash column chromatography (20:80 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (929.8 mg, 2.14 mmol, 80%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.0, 1.6 Hz, 1H, H-7), 7.50 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H, H-5), 7.33 (d, *J* = 2.0 Hz, 1H, H-17), 7.32 – 7.21 (m, 7H, H-4,6,12,13,14), 7.06 (d, *J* = 2.0 Hz, 1H, H-20), 5.70 (s, 1H, H-10), 5.60 – 5.46 (m, 2H, H-2), 2.35 (s, 3H, H-19), 2.22 (s, 3H, H-22).

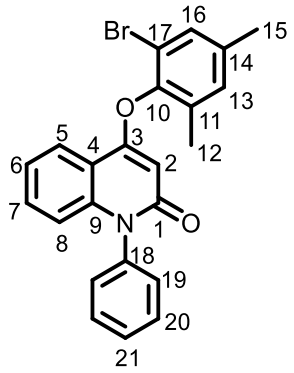
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-1), 160.8 (C-9), 146.2 (C-15), 139.8 (C-3), 137.6 (C-11), 136.7 (C-18), 132.6 (C-21), 132.0 (C-17), 131.7 (C-5), 131.6 (C-20), 128.9 (C-13), 127.3 (C-14), 126.7 (C-12), 123.7 (C-7), 122.2 (C-6), 116.3 (C-8), 116.1 (C-16), 99.2 (C-10), 45.9 (C-2), 20.7 (C-19), 16.6 (C-22).

HRMS (ESI) exact mass calculated for $C_{24}H_{21}BrNO_2^+$ $[M+H]^+$ requires *m/z* 434.0750, found *m/z* 434.0741.

IR (thin film) ν_{max}/cm^{-1} 3008, 1645, 1571, 1497, 1472, 1455, 1391, 1205, 1079.

MP 169-174 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-phenylquinolin-2(1H)-one, 348:



348 was prepared according to **General Procedure A** on a 5.24 mmol scale using 4-chloro-1-phenylquinolin-2(1H)-one (1.34 g, 5.24 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (1.58 g, 18.34 mmol, 1.5 eq.). Purified by flash column chromatography (25:75 to 30:70 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.12 g, 5.04 mmol, 96%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.1, 1.6 Hz, 1H, H-5), 7.60 (tt, *J* = 6.8, 1.7 Hz, 2H, H-19), 7.56 – 7.48 (m, 1H, H-21), 7.42 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H, H-7), 7.35 – 7.33 (m, 1H, H-16), 7.33 – 7.28 (m, 3H, H-6,20), 7.06 (d, *J* = 2.0 Hz, 1H, H-13), 6.70 (dd, *J* = 8.6, 1.0 Hz, 1H, H-8), 5.69 (s, 1H, H-2), 2.35 (s, 3H, H-15), 2.25 (s, 3H, H-12).

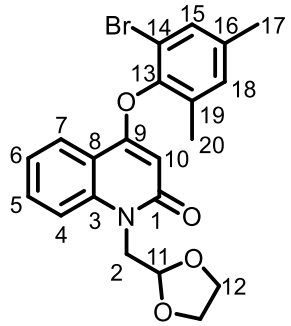
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.7 (C-1), 161.1 (C-3), 146.1 (C-10), 141.4 (C-9), 137.7 (C-18), 132.6 (C-14), 132.0 (C-16), 131.6 (C-13), 131.2 (C-7), 130.3 (C-19), 129.3 (C-11), 129.1 (C-20), 129.0 (C-21), 123.3 (C-5), 122.3 (C-6), 116.3 (C-4), 116.1 (C-8), 115.5 (C-17), 99.5 (C-2), 20.7 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{23}H_{19}BrNO_2^+$ $[M+H]^+$ requires *m/z* 420.0594, found *m/z* 420.0587.

IR (thin film) ν_{max}/cm^{-1} 3053, 2922, 1726, 1658, 1569, 1497, 1387, 1323, 1208, 1125, 1052, 813.

MP 131-136 °C.

1-((1,3-Dioxolan-2-yl)methyl)-4-(2-bromo-4,6-dimethylphenoxy)quinolin-2(1H)-one, 351:



351 was prepared according to **General Procedure A** on a 1.62 mmol scale using 1-((1,3-dioxolan-2-yl)methyl)-4-chloroquinolin-2(1H)-one (430.5 mg, 1.62 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (488.6 mg, 2.43 mmol, 1.5 eq.). Purified by flash column chromatography (40:60 EtOAc:pentane, v:v) to obtain the title compound as a solid (628.2 mg, 1.46 mmol, 90%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (dt, *J* = 8.0, 1.1 Hz, 1H, H-7), 7.66 – 7.61 (m, 2H, H-5,4), 7.35 – 7.31 (m, 1H, H-6), 7.31 – 7.29 (m, 1H, H-15), 7.04 – 7.00 (m, 1H, H-18), 5.59 (s, 1H, H-10), 5.24 (t, *J* = 4.4 Hz, 1H, H-11), 4.54 (dd, *J* = 14.7, 4.4 Hz, 1H, H-2), 4.47 (dd, *J* = 14.7, 4.4 Hz, 1H, H-2'), 4.09 – 4.00 (m, 2H, H-12), 3.92 – 3.83 (m, 2H, H-12'), 2.33 (s, 3H, H-17), 2.16 (s, 3H, H-20).

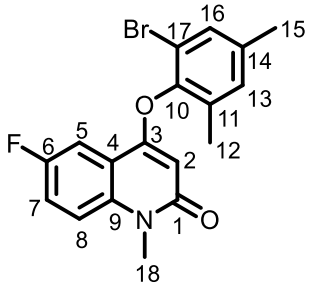
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-1), 160.7 (C-9), 146.1 (C-13), 140.2 (C-3), 137.6 (C-16), 132.6 (C-19), 131.9 (C-15), 131.5 (C-18 and 5 overlap), 123.6 (C-7), 122.2 (C-6), 116.3 (C-8), 115.9 (C-14), 115.2 (C-4), 102.2 (C-11), 99.1 (C-10), 65.2 (C-12), 44.9 (C-2), 20.7 (C-17), 16.6 (C-20).

HRMS (ESI) exact mass calculated for $C_{21}H_{21}BrNO_4^+$ $[M+H]^+$ requires *m/z* 430.0649, found *m/z* 430.0642.

IR (thin film) ν_{max}/cm^{-1} 2893, 1648, 1594, 1571, 1473, 1456, 1390, 1321, 1205, 1131, 945, 842.

MP 152-156 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-6-fluoro-1-methylquinolin-2(1H)-one, 352:



352 was prepared according to **General Procedure A** on a 4.70 mmol scale using 4-chloro-6-fluoro-1-methylquinolin-2(1H)-one (928.6 mg, 4.70 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (1.42 g, 7.05 mmol, 1.5 eq.). Purified by flash column chromatography (35:65 to 40:60 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.42 g, 3.77 mmol, 80%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (td, *J* = 7.2, 1.8 Hz, 1H, H-8), 7.32 (tdd, *J* = 7.4, 5.2, 1.8 Hz, 1H, H-5), 7.11 (d, *J* = 1.5 Hz, 1H, H-16), 7.03 (ddd, *J* = 9.4, 8.1, 1.0 Hz, 1H, H-7), 6.93 – 6.88 (m, 1H, H-13), 6.47 – 6.37 (m, 1H, H-2), 3.19 (s, 3H, H-18), 2.42 (s, 3H, H-15), 2.22 (s, 3H, H-12).

^{13}C NMR (126 MHz, $CDCl_3$) δ 182.2 (C-1), 159.1 (d, *J* = 248.8 Hz, C-6), 150.1 (C-3), 144.6 (C-2), 133.5 (C-10), 132.7 (C-9), 132.0 (C-14), 131.5 (C-16), 130.9 (C-13), 130.7 (d, *J* = 8.0 Hz, C-5), 130.5 (d, *J* = 3.5 Hz, C-8), 128.5 (C-11), 128.4 (C-4), 115.8 (d, *J* = 22.0 Hz, C-7), 112.4 (C-17), 43.4 (C-18), 20.3 (C-12), 17.9 (C-15).

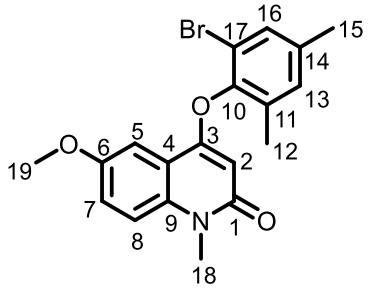
^{19}F NMR (470 MHz, $CDCl_3$) δ -113.7.

HRMS (ESI) exact mass calculated for $C_{18}H_{16}BrFNO_2^+$ $[M+H]^+$ requires *m/z* 376.0343, found *m/z* 376.0336.

IR (thin film) ν_{max}/cm^{-1} 2921, 1649, 1609, 1578, 1508, 1446, 1416, 1374, 1317, 1269, 1208, 1179, 1123, 1093, 948.

MP 174-176 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-6-methoxy-1-methylquinolin-2(1H)-one, 353:



353 was prepared according to **General Procedure A** on a 5.77 mmol scale using 4-chloro-6-methoxy-1-methylquinolin-2(1H)-one (1.29 g, 5.77 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (1.74 g, 8.65 mmol, 1.5 eq.). Purified by flash column chromatography (40:60 to 45:55 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.90 g, 4.89 mmol, 85%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 2.9 Hz, 1H, H-5), 7.33 (d, *J* = 9.2 Hz, 1H, H-8), 7.30 (d, *J* = 2.1 Hz, 1H, H-16), 7.28 – 7.25 (m, 1H, H-7), 7.05 – 7.01 (m, 1H, H-13), 5.61 (s, 1H, H-2), 3.92 (s, 3H, H-19), 3.66 (s, 3H, H-18), 2.33 (s, 3H, H-15), 2.17 (s, 3H, H-12).

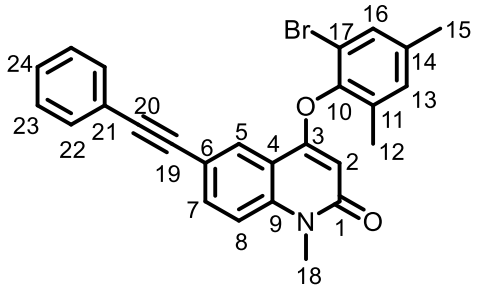
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2 (C-1), 159.8 (C-3), 154.9 (C-6), 146.1 (C-10), 137.6 (C-9), 134.9 (C-14), 132.6 (C-11), 131.9 (C-16), 131.5 (C-13), 120.6 (C-7), 116.4 (C-4), 116.3 (C-17), 115.8 (C-8), 105.3 (C-5), 99.8 (C-2), 55.9 (C-19), 29.4 (C-18), 20.7 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}BrNO_3^+$ $[M+H]^+$ requires *m/z* 388.0543, found *m/z* 388.0536.

IR (thin film) ν_{max}/cm^{-1} 2921, 1650, 1627, 1577, 1507, 1466, 1381, 1320, 1279, 1236, 1210, 1097, 1036, 979.

MP 154-156 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one, 354:



354 was prepared according to **General Procedure A** on a 5.21 mmol scale using 4-chloro-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one (1.53 g, 5.21 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (1.57 g, 7.81 mmol, 1.5 eq.). Purified by flash column chromatography (0:100 to 100:0 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (1.37 g, 2.99 mmol, 57%).

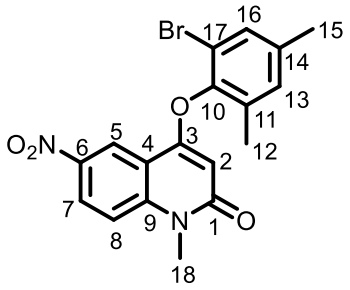
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.0 Hz, 1H, H-5), 7.79 (dd, *J* = 8.7, 2.0 Hz, 1H, H-7), 7.60 – 7.54 (m, 2H, H-22), 7.37 (m, 4H, H-8,23,24), 7.32 (d, *J* = 2.0 Hz, 1H, H-16), 7.05 – 7.04 (m, 1H, H-13), 5.61 (s, 1H, H-2), 3.68 (s, 3H, H-18), 2.34 (s, 3H, H-15), 2.18 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.5 (C-1), 159.9 (C-3), 146.0 (C-10), 139.9 (C-9), 137.7 (C-14), 134.7 (C-7), 132.6 (C-11), 132.0 (C-16), 131.8 (C-22,24), 131.6 (C-13), 128.6 (C-23), 127.0 (C-5), 123.2 (C-21), 117.2 (C-4), 116.3 (C-6), 115.9 (C-17), 114.6 (C-8), 99.8 (C-2), 89.8 (C-20), 88.6 (C-19), 29.5 (C-18), 20.8 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{26}H_{21}BrNO_2^+$ $[M+H]^+$ requires *m/z* 458.0750, found *m/z* 458.0739.

IR (thin film) ν_{max}/cm^{-1} 3054, 2921, 1646, 1603, 1569, 1471, 1431, 1210, 1097, 844, 757, 692.

4-(2-Bromo-4,6-dimethylphenoxy)-1-methyl-6-nitroquinolin-2(1H)-one, 356:



356 was prepared according to **General Procedure A** on a 12.07 mmol scale using 4-chloro-1-methyl-6-nitroquinolin-2(1H)-one (2.88 g, 12.07 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (3.64 g, 18.10 mmol, 1.5 eq.). Purified by flash column chromatography (35:65 to 50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.49 g, 6.18 mmol, 51%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.7 Hz, 1H, H-5), 8.48 (dd, *J* = 9.3, 2.7 Hz, 1H, H-7), 7.49 (d, *J* = 9.3 Hz, 1H, H-8), 7.33 – 7.30 (m, 1H, H-16), 7.07 – 7.04 (m, 1H, H-13), 5.67 (s, 1H, H-2), 3.71 (s, 3H, H-18), 2.34 (s, 3H, H-15), 2.18 (s, 3H, H-12).

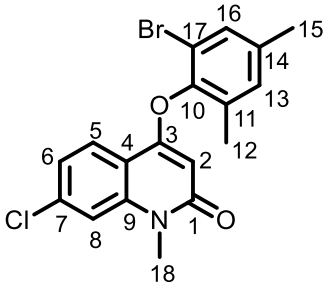
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.3 (C-1), 159.8 (C-3), 145.6 (C-10), 144.0 (C-6), 142.3 (C-9), 138.1 (C-11), 132.3 (C-14), 132.1 (C-16), 131.7 (C-13), 126.4 (C-7), 120.2 (C-5), 116.0 (C-4), 115.6 (C-17), 115.1 (C-8), 100.7 (C-2), 29.9 (C-18), 20.7 (C-15), 16.5 (C-12).

HRMS (ESI) exact mass calculated for $C_{18}H_{16}BrN_2O_4^+$ $[M+H]^+$ requires *m/z* 403.0288, found *m/z* 403.0282.

IR (thin film) ν_{max}/cm^{-1} 3094, 1660, 1606, 1498, 1443, 1341, 1298, 1132, 1055, 931, 849, 739.

MP 213 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-7-chloro-1-methylquinolin-2(1H)-one, 357:



357 was prepared according to **General Procedure A** on a 10.0 mmol scale using 4,7-dichloro-1-methylquinolin-2(1H)-one (2.88 g, 10.0 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (3.02 g, 15.0 mmol, 1.5 eq.). Purified by flash column chromatography (20:80 to 40:60 EtOAc:pentane, v:v) to obtain the title compound as a solid (3.04 g, 7.74 mmol, 78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 1H, H-5), 7.40 (d, *J* = 1.8 Hz, 1H, H-8), 7.32 – 7.28 (m, 2H, H-6,16), 7.05 – 7.01 (m, 1H, H-13), 5.57 (s, 1H, H-2), 3.64 (s, 3H, H-18), 2.33 (s, 3H, H-15), 2.16 (s, 3H, H-12).

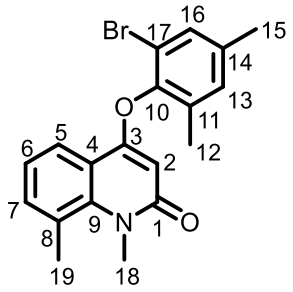
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5 (C-1), 160.0 (C-3), 146.0 (C-10), 141.1 (C-9), 138.0 (C-7), 137.8 (C-14), 132.5 (C-11), 132.0 (C-16), 131.6 (C-13), 125.0 (C-2), 122.5 (C-6), 116.2 (C-4), 114.4 (C-8), 114.3 (C-17), 99.3 (C-2), 29.4 (C-18), 20.7 (C-15), 16.5 (C-12).

HRMS (ESI) exact mass calculated for $C_{18}H_{16}BrClNO_2^+$ $[M+H]^+$ requires *m/z* 392.0047, found *m/z* 392.0035.

IR (thin film) ν_{max}/cm^{-1} 2952, 1736, 1649, 1590, 1561, 1500, 1471, 1408, 1059, 842, 819, 737.

MP 158-160 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1,8-dimethylquinolin-2(1H)-one, 358:



358 was prepared according to **General Procedure A** on a 5.10 mmol scale 4-chloro-1,8-dimethylquinolin-2(1H)-one (1.06 g, 5.10 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (1.54 g, 7.66 mmol, 1.5 eq.). Purified by flash column chromatography (45:55 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.10 g, 4.13 mmol, 81%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.43 (ddd, *J* = 7.4, 1.6, 0.8 Hz, 1H, H-7), 7.30 (d, *J* = 2.0 Hz, 1H, H-16), 7.21 (t, *J* = 7.7 Hz, 1H, H-6), 7.04 – 7.00 (m, 1H, H-13), 5.57 (s, 1H, H-2), 3.78 (s, 3H, H-18), 2.73 (s, 3H, H-19), 2.33 (s, 3H, H-15), 2.16 (s, 3H, H-12).

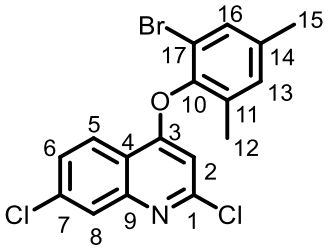
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7 (C-1), 160.8 (C-3), 146.3 (C-10), 141.7 (C-9), 137.5 (C-14), 136.2 (C-7), 132.6 (C-11), 131.9 (C-16), 131.5 (C-13), 125.3 (C-8), 122.5 (C-6), 121.7 (C-5), 117.5 (C-4), 116.4 (C-17), 98.9 (C-2), 36.7 (C-18), 24.2 (C-19), 20.7 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}BrNO_2^+$ $[M+H]^+$ requires *m/z* 372.0594, found *m/z* 372.0583.

IR (thin film) ν_{max}/cm^{-1} 2929, 1652, 1586, 1575, 1469, 1390, 1323, 1309, 1280, 1211, 1142, 1123, 1110, 942, 899, 794, 736.

MP 100-106 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-2,7-dichloroquinoline, 719:



An oven-dried 100 mL round bottom flask was charged with 2,4,7-trichloroquinoline (3.00 g, 12.90 mmol, 1.0 eq.) before adding anhydrous DMF (42 mL, 0.3 M), followed by 2-bromo-4,6-dimethylphenol (2.59 g, 12.90 mmol, 1.0 eq.). K_2CO_3 (2.14 g, 15.48, 1.2 eq.) was then added in one portion with stirring before heating the reaction mixture to 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and filtered through Celite, eluting with EtOAc. Combined organics were concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (1:99 to 10:90 Et_2O:pentane, v:v) to obtain the title compound as an oil (2.79 g, 7.03 mmol, 54%).

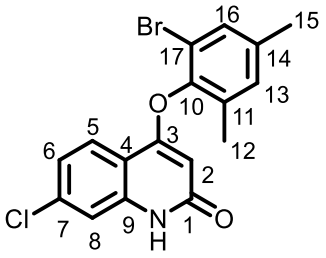
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.8 Hz, 1H, H-5), 8.00 (d, *J* = 2.0 Hz, 1H, H-8), 7.56 (dd, *J* = 8.8, 2.0 Hz, 1H, H-6), 7.39 – 7.31 (m, 1H, H-16), 7.09 (dt, *J* = 2.4, 0.9 Hz, 1H, H-13), 6.26 (s, 1H, H-2), 2.37 (s, 3H, H-15), 2.16 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.5 (C-3), 152.7 (C-1), 149.3 (C-10), 146.1 (C-9), 138.1 (C-7), 137.5 (C-14), 132.5 (C-11), 132.2 (C-16), 131.8 (C-13), 127.6 (C-6), 127.5 (C-8), 123.6 (C-5), 118.3 (C-4), 116.1 (C-17), 103.8 (C-2), 20.8 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{17}H_{13}BrCl_2NO^+$ $[M+H]^+$ requires *m/z* 395.9552, found *m/z* 395.9543.

IR (thin film) ν_{max}/cm^{-1} 2981, 1612, 1563, 1491, 1412, 1302, 1277, 1208, 1127, 1074, 920, 879, 823, 793, 740.

4-(2-Bromo-4,6-dimethylphenoxy)-7-chloroquinolin-2(1H)-one, 360:



4-(2-Bromo-4,6-dimethylphenoxy)-2,7-dichloroquinoline (2.71 g, 6.82 mmol, 1.0 eq.) was dissolved in 1,4-dioxane (14 mL, 0.50 M) and concentrated aqueous HCl (10.5 mL) was added with stirring. The solution was refluxed at 101 °C for 16 hours under nitrogen, before cooling to room temperature and partially concentrating under vacuum. The solution was ten poured over crushed ice with vigorous shaking to crash out the solid product, which was then filtered, washed with ice-cold water and dried under vacuum to obtain a solid (2.47 g, 6.52 mmol, 96%) which was used without further purification.

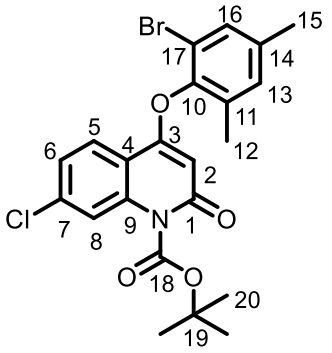
^{1}H NMR (600 MHz, $CDCl_3$) δ 12.58 (s, 1H, H-NH), 8.09 (d, *J* = 8.5 Hz, 1H, H-5), 7.43 (d, *J* = 1.9 Hz, 1H, H-8), 7.32 (d, *J* = 1.9 Hz, 1H, H-16), 7.26 – 7.24 (m, 1H, H-6), 7.05 (dt, *J* = 1.9, 0.9 Hz, 1H, H-13), 5.57 (s, 1H, H-2), 2.35 (s, 3H, H-15), 2.18 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3 (C-1), 162.5 (C-3), 146.1 (C-10), 139.8 (C-9), 138.1 (C-7), 137.9 (C-14), 132.5 (C-11), 132.1 (C-16), 131.6 (C-13), 124.4 (C-5), 123.4 (C-6), 116.2 (C-17), 115.9 (C-8), 113.5 (C-4), 98.8 (C-2), 20.8 (C-15), 16.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{17}H_{13}BrClNO_2^+$ $[M+H]^+$ requires *m/z* 377.9891, found *m/z* 377.9882.

IR (thin film) ν_{max}/cm^{-1} 2981, 1654, 1608, 1559, 1472, 1406, 1376, 1207, 1148, 1126, 1091, 844, 749, 656, 630.

***tert*-Butyl 4-(2-bromo-4,6-dimethylphenoxy)-7-chloro-2-oxoquinoline-1(2H)-carboxylate, 361:**



A flame-dried round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)-7-chloroquinolin-2(1H)-one (1.10 g, 2.91 mmol, 1.0 eq.), before adding anhydrous DMF (29 mL, 0.1 M) and cooling to 0 °C. With stirring, NaH (60% suspension in mineral oil, 232.4 mg, 5.81 mmol, 2.0 eq.) was added in small portions. After full addition and gas evolution, the reaction mixture was stirred at 0 °C for 15 minutes. Di-*tert*-butyl dicarbonate (1.91 g, 8.73 mmol, 2.0 eq.) was added portion wise at 0 °C and the reaction mixture was brought to room temperature, then refluxed under nitrogen at 40 °C for 16 hours. After the reaction time, the mixture was poured into deionised water (10 mL per 1 mL of DMF) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 Et_2O:pentane, v:v) to obtain the title compound as a solid (1.23 g, 2.57 mmol, 88%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, J = 8.9 Hz, 1H, H-5), 8.15 – 7.89 (m, 1H, H-8), 7.54 (dd, J = 8.9, 2.0 Hz, 1H, H-6), 7.35 (dt, J = 2.3, 0.8 Hz, 1H, H-16), 7.08 (dt, J = 2.3, 0.8 Hz, 1H, H-13), 6.04 (s, 1H, H-2), 2.36 (s, 3H, H-15), 2.16 (s, 3H, H-12), 1.52 (s, 9H, H-20).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.8 (C-1), 158.4 (C-3), 150.1 (C-18), 148.1 (C-10), 146.3 (C-7), 137.9 (C-9), 137.1 (C-14), 132.7 (C-11), 132.1 (C-16), 131.7 (C-13), 127.7

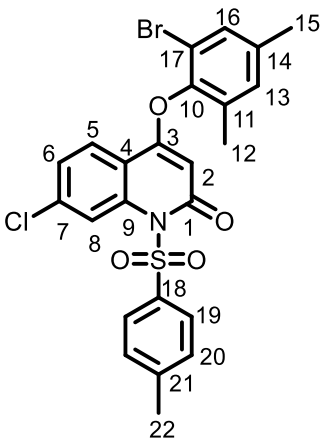
(C-8), 127.0 (C-6), 123.5 (C-5), 118.3 (C-4), 116.3 (C-17), 96.5 (C-2), 84.4 (C-19), 27.8 (C-20), 20.8 (C-15), 16.6 (C-12).

HRMS (ESI) exact mass calculated for $C_{22}H_{21}BrClNO_4^+$ $[M+H]^+$ requires *m/z* 478.0415, found *m/z* 478.0401.

IR (thin film) ν_{max}/cm^{-1} 1762, 1619, 1576, 1498, 1472, 1419, 1371, 1353, 1246, 1207, 1153, 1124, 1084, 923, 823, 735, 686.

MP 118-122 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-7-chloro-1-tosylquinolin-2(1H)-one, 362:

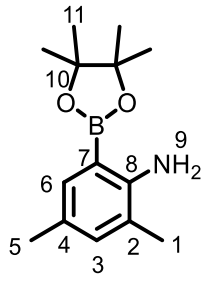


An oven-dried round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)-7-chloroquinolin-2(1H)-one (1.15 g, 3.04 mmol, 1.0 eq.) before suspending it in acetone (15.2 mL, 0.20 M). TsCl (869.4 mg, 4.56 mmol, 1.5 eq.) was then added in one portion, followed by K_2CO_3 (840.3 mg, 6.08 mmol, 2.0 eq.) with stirring before heating the reaction mixture to 60 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with acetone. The solution was then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain a solid (708.1 mg, 1.33 mmol, 44%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.8 Hz, 1H, H-8), 8.02 – 7.95 (m, 2H, H-19), 7.84 (d, *J* = 2.0 Hz, 1H, H-6), 7.52 (dd, *J* = 8.9, 2.0 Hz, 1H, H-6), 7.38 – 7.33 (m, 3H, H-16,20), 7.11 – 7.06 (m, 1H, H-13), 5.98 (s, 1H, H-2), 2.45 (s, 3H, H-22), 2.37 (s, 3H, H-15), 2.12 (s, 3H, H-12).

Due to the poor stability of the title compound, no further characterisation was performed.

2,4-Dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline, 112:



A flame-dried 3-neck round bottom flask was charged with 2-bromo-4,6-dimethylaniline (7.50 g, 37.5 mmol, 1.0 eq.), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (918.7 mg, 3 mol%), B_2Pin_2 (14.30 g, 56.3 mmol, 1.50 eq.) and KOAc (11.00 g, 112.5 mmol, 3.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Anhydrous 1,4-dioxane (300 mL, 0.13 M) was added to form a suspension, which was then sparged with argon for 20 minutes. After sparging, the reaction mixture was heated to 101 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc (~300 mL). The solution was washed with deionised water, dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 5:95 Et_2O:pentane, v:v) to obtain a solid (4.91 g, 19.87 mmol, 53%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 2.3 Hz, 1H, H-6), 6.97 (d, *J* = 2.3 Hz, 1H, H-3), 4.63 (s, 2H, H-9), 2.21 (s, 3H, H-5), 2.12 (s, 3H, H-1), 1.35 (s, 12H, H-11).

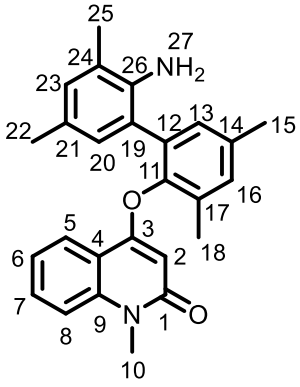
^{13}C NMR (151 MHz, $CDCl_3$) δ 149.6 (C-8), 134.9 (C-3), 134.7 (C-6), 125.9 (C-4), 121.8 (C-2), 83.6 (C-10), 25.0 (C-11), 20.3 (C-5), 17.7 (C-1).

HRMS (ESI) exact mass calculated for $C_{14}H_{23}BNO_2^+$ $[M+H]^+$ requires *m/z* 248.1815, found *m/z* 248.1816.

IR (thin film) ν_{max}/cm^{-1} 3496, 3395, 2980, 2922, 1622, 1301, 1138, 850.

MP 116-118 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-2(1H)-one, 117:



117 was prepared according to **General Procedure B** on a 5.48 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-methylquinolin-2(1H)-one (1.96 g, 5.48 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (2.03 g, 8.22 mmol, 1.5 eq.). Purified by flash column chromatography (45:55 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.38 g, 3.46 mmol, 63%).

^{1}H NMR (500 MHz, DMSO, 100 °C) δ 8.00 (dd, *J* = 7.9, 1.6 Hz, 1H, H-5), 7.58 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H, H-7), 7.39 (d, *J* = 8.5 Hz, 1H, H-8), 7.25 – 7.18 (m, 2H, H-6,16), 7.05 (d, *J* = 2.2 Hz, 1H, H-13), 6.61 (d, *J* = 2.2 Hz, 1H, H-20), 6.55 (d, *J* = 2.2 Hz, 1H, H-23), 5.33 (s, 1H, H-2), 3.47 (s, 3H, H-10), 2.37 (s, 3H, H-15), 2.18 (s, 3H, H-22), 1.98 (s, 3H, H-25), 1.97 (s, 3H, H-18).

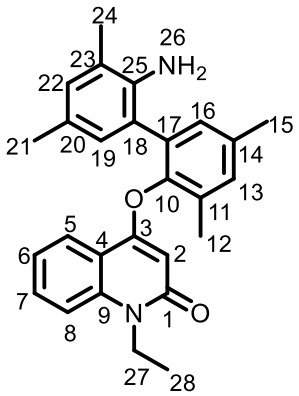
^{13}C NMR (126 MHz, DMSO) δ 161.4 (C-1), 160.0 (C-3), 146.2 (C-11), 139.6 (C-26), 139.2 (C-9), 135.1 (C-14), 132.2 (C-17), 130.8 (C-7), 130.6 (C-16), 130.0 (C-21), 129.57 (C-23), 129.56 (C-13), 127.9 (C-20), 124.0 (C-12), 122.3 (C-5), 121.5 (C-19), 121.4 (C-24), 120.7 (C-6), 114.6 (C-4), 113.7 (C-8), 98.0 (C-2), 28.0 (C-10), 19.8 (C-15), 19.1 (C-18), 16.9 (C-25), 15.1 (C-22).

HRMS (ESI) exact mass calculated for $C_{26}H_{27}N_2O_2^+$ $[M+H]^+$ requires *m/z* 399.2067, found *m/z* 399.2060.

IR (thin film) ν_{max}/cm^{-1} 3350, 2922, 2361, 2341, 1637, 1591, 1391, 1330, 1210, 1043, 862.

MP decomposes 127 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-ethylquinolin-2(1H)-one, 364:



364 was prepared according to **General Procedure B** on a 2.65 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-ethylquinolin-2(1H)-one (987.0 mg, 2.65 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (983.7 mg, 3.98 mmol, 1.5 eq.). Purified by flash column chromatography (60:40 EtOAc:pentane, v:v) to obtain the title compound as a solid (950.3 mg, 2.30 mmol, 87%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.01 (dd, *J* = 7.9, 1.7 Hz, 1H, H-5), 7.58 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H, H-7), 7.42 (d, *J* = 8.7 Hz, 1H, H-8), 7.22 – 7.17 (m, 2H, H-6,13),

7.05 (d, *J* = 2.2 Hz, 1H, H-19), 6.59 (s, 1H, H-16), 6.53 (d, *J* = 2.2 Hz, 1H, H-22), 5.32 (s, 1H, H-2), 4.15 (q, *J* = 7.1 Hz, 2H, H-27), 3.99 (s, 2H, H-26), 2.37 (s, 3H, H-15), 2.18 (s, 3H, H-21), 1.97 (s, 3H, H-24), 1.95 (s, 3H, H-24), 1.15 (t, *J* = 7.1 Hz, 3H, H-28).

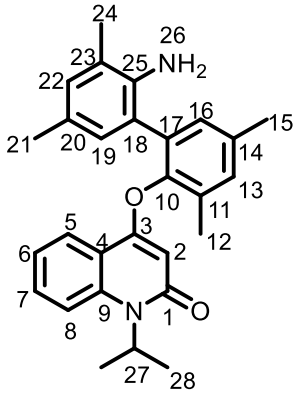
^{13}C NMR (126 MHz, DMSO) δ 162.0 (C-1), 161.0 (C-3), 147.3 (C-10), 140.8 (C-25), 139.1 (C-9), 136.1 (C-14), 133.2 (C-11), 131.9 (C-7), 131.6 (C-13), 131.0 (C-20), 130.6 (C-22 or 19), 130.5 (C-22 or 19), 128.9 (C-16), 124.8 (C-18), 123.6 (C-5), 122.3 (C-23), 121.5 (C-6), 115.8 (C-4), 114.5 (C-8), 99.2 (C-2), 36.5 (C-27), 20.8 (C-15), 20.1 (C-12), 17.9 (C-24), 16.1 (C-21), 13.1 (C-28).

HRMS (ESI) exact mass calculated for $C_{27}H_{29}N_2O_2^+$ $[M+H]^+$ requires *m/z* 413.2224, found *m/z* 413.2217.

IR (thin film) ν_{max}/cm^{-1} 3466, 2978, 1642, 1590, 1454, 1391, 1322, 1208, 1159, 1108, 862, 842.

MP 157-161 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-isopropylquinolin-2(1H)-one, 365:



365 was prepared according to **General Procedure B** on a 1.82 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-isopropylquinolin-2(1H)-one (704.1 mg, 1.82 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (674.7 mg,

2.73 mmol, 1.5 eq.). Purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (735.2 mg, 1.72 mmol, 95%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.07 (dd, *J* = 8.3, 1.4 Hz, 1H, H-5), 7.61 – 7.52 (m, 2H, H-7,8), 7.31 (ddd, *J* = 8.3, 6.5, 1.7 Hz, 1H, H-6), 7.20 (d, *J* = 2.2 Hz, 1H, H-13), 7.04 (d, *J* = 2.2 Hz, 1H, H-16), 6.54 (s, 1H, H-19), 6.49 (d, *J* = 2.1 Hz, 1H, H-22), 5.64 (s, 1H, H-2), 5.36 (hept, *J* = 6.2 Hz, 1H, H-27), 3.97 (s, 2H, H-26), 2.37 (s, 3H, H-15), 2.15 (s, 3H, H-21), 1.93 (s, 3H, H-24), 1.90 (s, 3H, H-12), 1.26 (d, *J* = 6.2 Hz, 6H, H-28).

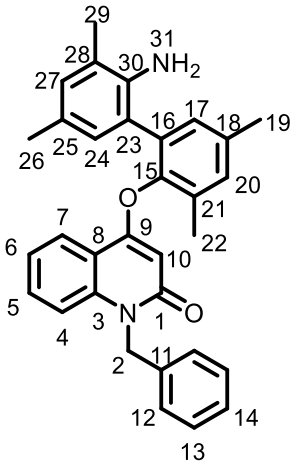
^{13}C NMR (126 MHz, DMSO, 90 °C) δ 161.9 (C-1), 161.6 (C-3), 146.8 (C-10), 146.5 (C-25), 139.9 (C-9), 135.2 (C-14), 132.4 (C-11), 130.8 (C-13), 130.3 (C-20), 129.8 (C-16), 129.6 (C-22), 129.5 (C-7), 128.0 (C-19), 126.0 (C-8), 123.9 (C-17), 122.6 (C-6), 121.5 (C-18), 121.4 (C-23), 121.2 (C-5), 117.7 (C-4), 93.3 (C-2), 67.2 (C-27), 21.4 (C-28), 20.0 (C-15), 19.2 (C-12), 17.0 (C-24), 15.3 (C-21).

HRMS (ESI) exact mass calculated for $C_{28}H_{31}N_2O_2^+$ $[M+H]^+$ requires *m/z* 427.2380, found *m/z* 427.2374.

IR (thin film) ν_{max}/cm^{-1} 3388, 2978, 2923, 1624, 1603, 1574, 1468, 1421, 1403, 1318, 1204, 1171, 1111, 1012, 862.

MP 106-110 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-benzylquinolin-2(1H)-one, 366:



366 was prepared according to **General Procedure B** on a 1.93 mmol scale using 1-benzyl-4-(2-bromo-4,6-dimethylphenoxy)quinolin-2(1H)-one (837.7 mg, 1.93 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (714.3 mg, 2.89 mmol, 1.5 eq.). Purified by flash column chromatography (30:70 EtOAc:pentane, v:v) to obtain the title compound as an oil (700.8 mg, 1.47 mmol, 77%).

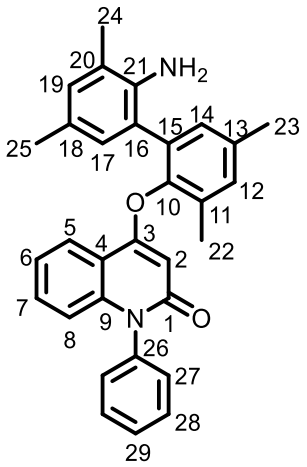
^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.01 (dd, *J* = 8.1, 1.6 Hz, 1H, H-7), 7.45 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-5), 7.30 – 7.19 (m, 5H, H-4,13,14,27), 7.17 (t, *J* = 7.6 Hz, 1H, H-6), 7.11 – 7.05 (m, 3H, H-20,12), 6.61 (s, 1H, H-24), 6.55 (d, *J* = 2.2 Hz, 1H, H-17), 5.42 (s, 1H, H-10), 5.38 (s, 2H, H-2), 4.00 (s, 2H, H-31), 2.39 (s, 3H, H-19), 2.23 (s, 3H, H-26), 1.96 (s, 4H, H-29), 1.95 (s, 3H, H-22).

^{13}C NMR (126 MHz, DMSO) δ 161.7 (C-1), 160.5 (C-9), 146.4 (C-15), 139.9 (C-30), 138.5 (C-18), 136.7 (C-11), 135.2 (C-21), 132.2 (C-25), 130.8 (C-5), 130.7 (C-4), 130.1 (C-16), 129.61 (C-17), 129.56 (C-20), 128.0 (C-13), 127.9 (C-24), 126.4 (C-14), 125.9 (C-12), 123.8 (C-23), 122.6 (C-7), 121.4 (C-8), 120.9 (C-6), 115.0 (C-3), 114.3 (C-27), 98.0 (C-10), 43.8 (C-2), 19.9 (C-19), 19.2 (C-22), 17.0 (C-29), 15.2 (C-26).

HRMS (ESI) exact mass calculated for $C_{32}H_{31}N_2O_2^+$ $[M+H]^+$ requires *m/z* 475.2380, found *m/z* 475.2372.

IR (thin film) ν_{max}/cm^{-1} 3377, 2922, 2361, 2341, 1641, 1592, 1455, 1392, 1216, 1199, 923, 841, 755, 695.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-phenylquinolin-2(1H)-one, 367:



367 was prepared according to **General Procedure B** on a 2.50 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-phenylquinolin-2(1H)-one (1.05 g, 2.50 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (926.8 mg, 3.75 mmol, 1.5 eq.). Purified by flash column chromatography (45:55 to 55:45 EtOAc:pentane, v:v) to obtain the title compound as a solid (716.7 mg, 1.56 mmol, 62%).

^{1}H NMR (600 MHz, DMSO, 100 °C) δ 8.02 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.56 (td, *J* = 7.5, 7.1, 1.0 Hz, 2H, H-27), 7.52 – 7.46 (m, 1H, H-29), 7.36 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H, H-7), 7.27 – 7.21 (m, 1H, H-12), 7.21 – 7.13 (m, 3H, H-6,28), 7.10 – 7.06 (m, 1H, H-17), 6.64 (s, 1H, H-14), 6.59 (d, *J* = 2.2 Hz, 1H, H-19), 6.48 (dd, *J* = 8.6, 1.1 Hz, 1H, H-8), 5.39 (s, 1H, H-2), 4.00 (s, 2H, NH_2), 2.39 (s, 3H, H-23), 2.26 (s, 3H, H-25), 2.00 (s, 3H, H-22 or 24), 1.99 (s, 3H, H-22 or 24).

^{13}C NMR (151 MHz, DMSO) δ 161.3 (C-1), 160.9 (C-3), 146.5 (C-10), 140.1 (C-21), 139.9 (C-9), 137.2 (C-26), 135.2 (C-13), 132.1 (C-11), 130.6 (C-12), 130.4 (C-7), 130.0 (C-18), 129.59 (C-17 or 19), 129.56 (C-17 or 19), 129.2 (C-27), 128.6 (C-28), 127.92 (C-

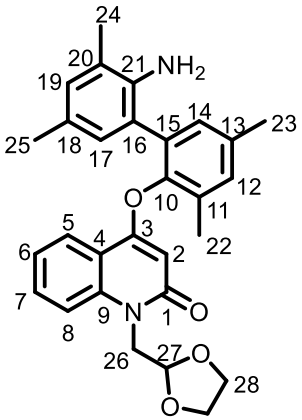
14), 127.85 (C-29), 123.9 (C-16), 122.3 (C-5), 121.4 (C-20), 121.3 (C-5), 120.9 (C-6), 114.5 (C-8), 98.6 (C-2), 19.8 (C-23), 19.2 (C-24), 16.9 (C-22), 15.2 (C-25).

HRMS (ESI) exact mass calculated for $C_{31}H_{29}N_2O_2^+$ $[M+H]^+$ requires *m/z* 461.2224, found *m/z* 461.2211.

IR (thin film) ν_{max}/cm^{-1} 3378, 3047, 1650, 1598, 1486, 1451, 1210, 1159, 1052, 1028, 840, 735.

MP 169-174 °C.

1-((1,3-Dioxolan-2-yl)methyl)-4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)quinolin-2(1H)-one, 368:



368 was prepared according to **General Procedure B** on a 1.40 mmol scale using 1-((1,3-dioxolan-2-yl)methyl)-4-(2-bromo-4,6-dimethylphenoxy)quinolin-2(1H)-one (601.0 mg, 1.40 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (519.0 mg, 2.10 mmol, 1.5 eq.). Purified by flash column chromatography (65:35 EtOAc:pentane, v:v) to obtain the title compound as a solid (469.2 mg, 1.00 mmol, 71%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.03 – 7.98 (m, 1H, H-5), 7.59 – 7.50 (m, 2H, H-7,8), 7.25 – 7.17 (m, 2H, H-6,12), 7.08 – 7.04 (m, 1H, H-17), 6.61 (s, 1H, H-14), 6.55 (d, *J* = 2.1 Hz, 1H, H-19), 5.33 (s, 1H, H-2), 5.05 (t, *J* = 4.5 Hz, 1H, H-27), 4.30 (d, *J* = 4.5

Hz, 2H, H-26), 4.00 (s, 2H, NH_2), 3.97 – 3.88 (m, 2H, H-28), 3.82 – 3.73 (m, 2H, H-28'), 2.37 (s, 3H, H-23), 2.18 (s, 3H, H-25), 1.98 (s, 3H, H-24), 1.97 (s, 3H, H-22).

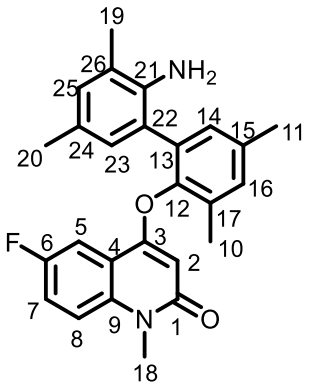
^{13}C NMR (126 MHz, DMSO) δ 162.6 (C-1), 161.4 (C-3), 147.2 (C-10), 140.8 (C-21), 140.1 (C-9), 132.0 (C-13), 131.9 (C-11), 131.6 (C-8 or 12), 131.5 (C-8 or 12), 130.6 (C-17 or 19), 130.5 (C-17 or 19), 129.1 (C-18), 129.0 (C-15), 128.9 (C-14), 124.8 (C-16), 123.3 (C-5), 122.3 (C-20), 121.8 (C-6), 115.7 (C-4), 115.6 (C-7), 101.9 (C-27), 98.7 (C-2), 64.9 (C-28), 44.6 (C-26), 20.8 (C-23), 20.2 (C-22), 17.9 (C-24), 16.1 (C-25).

HRMS (ESI) exact mass calculated for $C_{29}H_{31}N_2O_4^+$ $[M+H]^+$ requires *m/z* 471.2278, found *m/z* 471.2269.

IR (thin film) ν_{max}/cm^{-1} 3350, 3078, 2925, 1651, 1590, 1492, 1448, 1357, 1318, 1289, 966.

MP 150 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-fluoro-1-methylquinolin-2(1H)-one, 369:



369 was prepared according to **General Procedure B** on a 3.27 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-6-fluoro-1-methylquinolin-2(1H)-one (1.23 g, 3.27 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.21 g, 4.90 mmol, 1.5 eq.). Purified by flash column chromatography (40:60 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (571.2 mg, 1.37 mmol, 42%).

^{1}H NMR (500 MHz, DMSO, 100 °C) δ 7.44 – 7.41 (m, 2H, H-5,8), 7.26 (m, 1H, H-7), 7.21 (d, *J* = 2.2 Hz, 1H, H-16), 7.06 – 7.02 (m, 1H, H-23), 6.57 (s, 1H, H-14), 6.54 (d, *J* = 2.1 Hz, 1H. H-25), 5.37 (s, 1H, H-2), 3.97 (s, 2H, H-NH_2), 3.47 (s, 3H, H-18), 2.38 (s, 3H, H-11), 2.20 (s, 3H, H-20), 1.97 (s, 3H, H-19), 1.96 (s, 3H, H-10).

^{13}C NMR (126 MHz, DMSO, 100 °C) δ 161.1 (C-1), 159.2 (d, *J* = 3.2 Hz, C-3), 156.5 (d, *J* = 239.1 Hz, C-6), 146.4 (C-12), 139.8 (C-21), 135.9 (d, *J* = 1.3 Hz, C-9), 135.2 (C-15), 132.1 (C-17), 130.6 (C-16), 130.0 (C-23), 129.5 (C-24,14), 127.9 (C-25), 127.1 (C-7), 123.9 (C-13), 121.4 (C-26), 118.3 (d, *J* = 23.8 Hz, C-5), 115.9 (d, *J* = 8.1 Hz, C-8), 115.7 (d, *J* = 8.7 Hz, C-4), 99.3 (C-2), 28.3 (C-18), 19.8 (C-11), 19.1 (C-10), 16.8 (C-19), 15.0 (C-20).

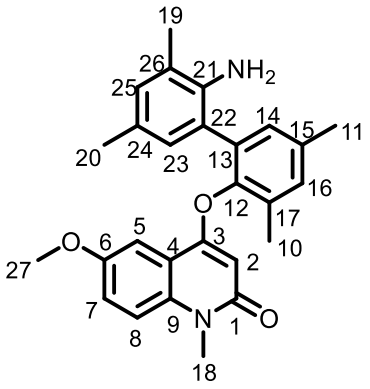
^{19}F NMR (470 MHz, DMSO, 95 °C) δ -121.9.

HRMS (ESI) exact mass calculated for $C_{26}H_{26}FN_2O_2^+$ $[M+H]^+$ requires *m/z* 417.1973, found *m/z* 417.1967.

IR (thin film) ν_{max}/cm^{-1} 3364, 2921, 1646, 1603, 1577, 1485, 1445, 1319, 1267, 1204, 1183, 1095, 1054, 948, 815.

MP 198-204 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-methoxy-1-methylquinolin-2(1H)-one, 370:



370 was prepared according to **General Procedure B** on a 3.17 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-6-methoxy-1-methylquinolin-2(1H)-one (1.23 g, 3.17 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.17 g, 4.75 mmol, 1.5 eq.). Purified by flash column chromatography (50:50 to 70:30 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.09 g, 2.54 mmol, 80%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 7.47 (d, *J* = 2.9 Hz, 1H, H-5), 7.34 (d, *J* = 9.1 Hz, 1H, H-8), 7.26 – 7.17 (m, 2H, H-7,16), 7.04 (s, 1H, H-23), 6.61 (s, 1H, H-14), 6.57 (d, *J* = 2.1 Hz, 1H, H-25), 5.31 (s, 1H, H-2), 4.00 (s, 2H, H-NH_2), 3.84 (s, 3H, H-27), 3.45 (s, 3H, H-18), 2.37 (s, 3H, H-11), 2.18 (s, 3H, H-20), 1.98 (s, 3H, H-19), 1.97 (s, 3H, H-10).

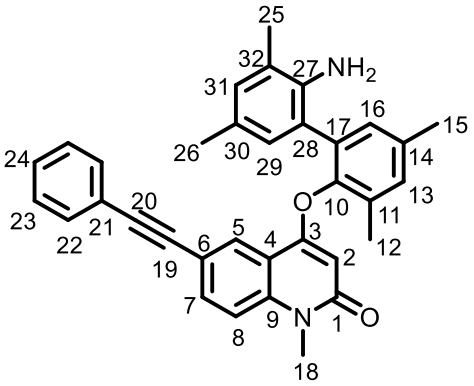
^{13}C NMR (126 MHz, DMSO) δ 161.1 (C-1), 159.5 (C-3), 153.7 (C-6), 146.3 (C-12), 139.9 (C-21), 135.2 (C-15), 133.9 (C-9), 132.3 (C-17), 130.7 (C-16), 130.1 (C-24), 129.6 (C-23,25), 128.0 (C-14), 123.8 (C-22), 121.3 (C-26), 119.3 (C-7), 115.4 (C-4), 115.3 (C-8), 105.1 (C-5), 98.5 (C-2), 55.3 (C-27), 28.2 (C-18), 19.9 (C-11), 19.2 (C-10), 17.0 (C-19), 15.2 (C-20).

HRMS (ESI) exact mass calculated for $C_{27}H_{29}N_2O_3^+$ $[M+H]^+$ requires *m/z* 429.2173, found *m/z* 429.2164.

IR (thin film) ν_{max}/cm^{-1} 3374, 2922, 1646, 1624, 1577, 1463, 1433, 1381, 1324, 1236, 1206, 1119, 1067, 1036, 931, 862, 841.

MP 182-184 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one, 371:



371 was prepared according to **General Procedure B** on a 2.95 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one (1.35 g, 2.95 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.09 g, 4.42 mmol, 1.5 eq.). Purified by flash column chromatography (0:100 to 2:98 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (1.16 g, 2.33 mmol, 79%).

^{1}H NMR (600 MHz, DMSO, 80 °C) δ 8.11 (s, 1H, H-13), 7.71 (dd, *J* = 8.7, 2.1 Hz, 1H, H-5), 7.64 – 7.35 (m, 7H, H-7,8,22,23,24), 7.22 (d, *J* = 2.2 Hz, 1H, H-29), 7.06 (s, 1H, H-16), 6.55 (d, *J* = 2.2 Hz, 1H, H-31), 5.36 (s, 1H, H-2), 4.03 (s, 2H, NH_2), 3.48 (s, 3H, H-18), 2.38 (s, 3H, H-15), 2.21 (s, 3H, H-26), 1.99 (s, 3H, H-12), 1.98 (s, 3H, H-25).

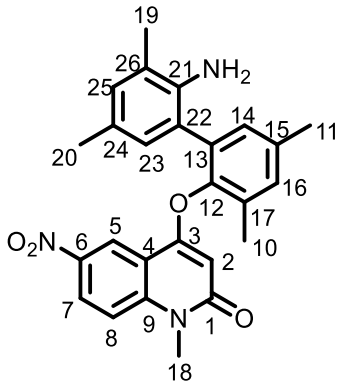
^{13}C NMR (151 MHz, DMSO, 80 °C) δ 161.4 (C-1), 159.6 (C-3), 146.5 (C-10), 140.0 (C-27), 139.0 (C-9), 135.4 (C-7), 133.6 (C-5), 132.2 (C-14), 130.9 (C-22), 130.7 (C-29), 130.2 (C-11), 129.7 (C-16 or 31), 129.6 (C-16 or 31), 128.3 (C-30), 128.2 (C-23), 128.0 (C-24), 125.6 (C-13), 123.9 (C-28), 122.1 (C-32), 121.5 (C-21), 115.0 (C-4), 114.9 (C-6), 114.6 (C-8), 99.0 (C-2), 88.6 (C-20), 88.4 (C-19), 28.4 (C-18), 20.0 (C-15), 19.3 (C-12), 17.1 (C-25), 15.3 (C-26).

HRMS (ESI) exact mass calculated for $C_{34}H_{31}N_2O_2^+$ $[M+H]^+$ requires *m/z* 499.2380, found *m/z* 499.2369.

IR (thin film) ν_{max}/cm^{-1} 3390, 2918, 1644, 1598, 1569, 1503, 1486, 1429, 1380, 1210, 1153, 1099, 1028, 1009, 844, 819, 757, 737.

MP 148-152 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methyl-6-nitroquinolin-2(1H)-one, 372:



372 was prepared according to a modified **General Procedure B** on a 3.89 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-methyl-6-nitroquinolin-2(1H)-one (1.57 g, 3.89 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.44 g, 5.84 mmol, 1.5 eq.), [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (142.3 mg, 5 mol%), Na_2CO_3 (1.65 g, 15.56 mmol, 4.0 eq.) and PhMe:H_2O (1:1, 78 mL, 0.05 M). Purified by flash column chromatography (50:50 to 55:45 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.24 g, 2.80 mmol, 72%).

^{1}H NMR (600 MHz, DMSO, 90 °C) δ 8.72 (s, 1H, H-5), 8.33 (dd, *J* = 9.3, 2.7 Hz, 1H, H-7), 7.58 (d, *J* = 9.3 Hz, 1H, H-8), 7.23 (d, *J* = 2.2 Hz, 1H, H-16), 7.06 – 7.03 (m, 1H, H-14), 6.54 (d, *J* = 7.9 Hz, 1H, H-23), 6.50 – 6.45 (m, 1H, H-25), 5.49 (s, 1H, H-2), 3.98 (s, 2H, H-NH_2), 3.52 (s, 3H, H-18), 2.38 (s, 3H, H-11), 2.24 (s, 3H, H-20), 1.91 (s, 3H, H-19), 1.90 (s, 3H, H-10).

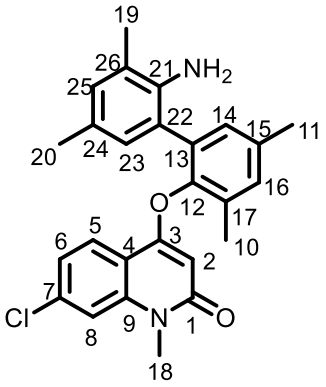
^{13}C NMR (151 MHz, DMSO, 90 °C) δ 161.4 (C-1), 159.6 (C-3), 146.7 (C-12), 143.0 (C-21), 140.9 (C-6), 139.9 (C-9), 135.5 (C-15), 131.9 (C-17), 130.7 (C-16), 130.1 (C-24), 129.6 (C-14 or 25), 129.5 (C-14 or 25), 127.9 (C-23), 125.2 (C-7), 123.9 (C-13), 121.4 (C-22), 120.9 (C-26), 118.4 (C-5), 115.2 (C-8), 114.6 (C-4), 100.2 (C-2), 28.8 (C-18), 19.9 (C-11), 19.0 (C-19), 16.7 (C-10), 15.1 (C-20).

HRMS (ESI) exact mass calculated for $C_{26}H_{26}N_3O_4^+$ $[M+H]^+$ requires *m/z* 444.1918, found *m/z* 444.1914.

IR (thin film) ν_{max}/cm^{-1} 3481, 3381, 2921, 2858, 1659, 1605, 1497, 1421, 1342, 1266, 1215, 1200, 1145, 1095, 1014, 931, 829, 740, 702.

MP 218 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-chloro-1-methylquinolin-2(1H)-one, 373:



373 was prepared according to **General Procedure B** on a 3.00 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-7-chloro-1-methylquinolin-2(1H)-one (1.18 g, 3.0 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.11 g, 4.5 mmol, 1.5 eq.). Purified by flash column chromatography (60:40 EtOAc:pentane, v:v) to obtain the title compound as a solid (925.8 mg, 2.14 mmol, 71%).

^{1}H NMR (600 MHz, DMSO, 80 °C) δ 7.98 (d, *J* = 8.5 Hz, 1H, H-5), 7.47 (d, *J* = 1.9 Hz, 1H, H-8), 7.25 (dd, *J* = 8.5, 1.9 Hz, 1H, H-6), 7.21 (d, *J* = 2.2 Hz, 1H, H-16), 7.04 (s, 1H, H-14), 6.58 (s, 1H, H-23), 6.55 (d, *J* = 2.0 Hz, 1H, H-25), 5.32 (s, 1H, H-2), 4.01 (s, 2H, H-NH_2), 3.46 (s, 3H, H-18), 2.37 (s, 3H, H-11), 2.17 (s, 3H, H-20), 1.97 (s, 6H, H-10,19).

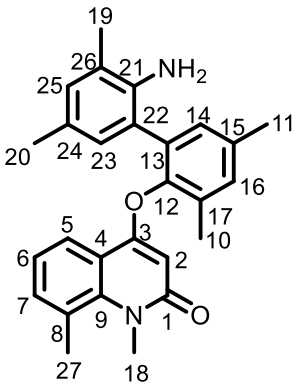
^{13}C NMR (151 MHz, DMSO, 80 °C) δ 161.5 (C-1), 159.7 (C-3), 146.2 (C-12), 140.2 (C-21), 140.0 (C-9), 136.0 (C-7), 135.4 (C-15), 132.2 (C-17), 130.7 (C-16), 130.1 (C-14 or 23), 129.7 (C-14 or 23), 128.0 (C-25), 124.2 (C-5), 123.9 (C-22), 121.5 (C-26), 121.0 (C-6), 113.8 (C-8), 113.5 (C-4), 98.3 (C-2), 28.4 (C-18), 20.0 (C-11), 19.3 (C-19), 17.1 (C-10), 15.2 (C-20).

HRMS (ESI) exact mass calculated for $C_{26}H_{26}ClN_2O_2^+$ $[M+H]^+$ requires *m/z* 433.1677, found *m/z* 433.1665.

IR (thin film) ν_{max}/cm^{-1} 3462, 3371, 2921, 2858, 1645, 1588, 1485, 1382, 1265, 1157, 1104, 1059, 1031, 955, 863, 737, 703.

MP 203-207 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1,8-dimethylquinolin-2(1H)-one, 374:



374 was prepared according to **General Procedure B** on a 3.25 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1,8-dimethylquinolin-2(1H)-one (1.21 g, 3.25 mmol, 1.0

eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.21 g, 4.88 mmol, 1.5 eq.). Purified by flash column chromatography (60:40 to 75:25 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.05 g, 2.55 mmol, 78%).

^{1}H NMR (600 MHz, DMSO, 90 °C) δ 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.42 – 7.34 (m, 1H, H-7), 7.20 (d, *J* = 2.2 Hz, 1H, H-16), 7.10 (t, *J* = 7.7 Hz, 1H, H-6), 7.04 (d, *J* = 2.3 Hz, 1H, H-23), 6.60 (s, 1H, H-14), 6.56 (d, *J* = 2.3 Hz, 1H, H-25), 5.29 (s, 1H, H-2), 3.99 (s, 2H, H-NH_2), 3.59 (s, 3H, H-18), 2.63 (s, 3H, H-27), 2.37 (s, 3H, H-11), 2.16 (s, 3H, H-20), 1.98 (s, 3H, H-19), 1.97 (s, 3H, H-10).

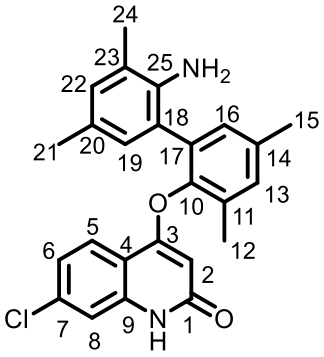
^{13}C NMR (151 MHz, DMSO, 90 °C) δ 163.4 (C-1), 160.4 (C-3), 146.3 (C-12), 140.3 (C-21), 139.9 (C-4), 135.3 (C-7), 132.3 (C-15), 131.4 (C-8), 131.0 (C-16), 130.7 (C-25), 130.1 (C-17), 129.6 (C-24), 128.2 (C-13), 127.9 (C-23), 124.3 (C-14), 123.8 (C-6), 121.4 (C-22), 121.2 (C-26), 120.6 (C-5), 116.4 (C-4), 97.7 (C-2), 34.8 (C-18), 22.8 (C-20), 19.9 (C-11), 19.2 (C-27), 17.0 (C-19), 15.1 (C-10).

HRMS (ESI) exact mass calculated for $C_{27}H_{29}N_2O_2^+$ $[M+H]^+$ requires *m/z* 413.2224, found *m/z* 413.2213.

IR (thin film) ν_{max}/cm^{-1} 3470, 3380, 2981, 2923, 2859, 1650, 1576, 1486, 1390, 1265, 1201, 1157, 1070, 1014, 898, 841, 736.

MP 118 °C.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-chloroquinolin-2(1H)-one, 375:



375 was prepared according to **General Procedure B** on a 2.30 mmol scale using *tert*-butyl 4-(2-bromo-4,6-dimethylphenoxy)-7-chloro-2-oxoquinoline-1(2H)-carboxylate (1.10 g, 2.30 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (852.7 mg, 3.45 mmol, 1.5 eq.). Purified by flash column chromatography (60:40 to 70:30 EtOAc:pentane, v:v) to obtain the title compound as a solid (562.8 mg, 1.34 mmol, 58%).

^{1}H NMR (500 MHz, DMSO, 95 °C) δ 10.94 (s, 1H, H-NH), 7.86 (d, *J* = 8.6 Hz, 1H, H-5), 7.27 (d, *J* = 2.1 Hz, 1H, H-8), 7.20 (d, *J* = 2.3 Hz, 1H, H-19), 7.12 (dd, *J* = 8.6, 2.1 Hz, 1H, H-6), 7.04 (s, 1H, H-16), 6.57 (d, *J* = 4.6 Hz, 2H, H-13,22), 5.19 (s, 1H, H-2), 3.97 (s, 2H, H-NH_2), 2.37 (s, 3H, H-15), 2.18 (s, 3H, H-21), 1.98 (s, 6H, H-12,24).

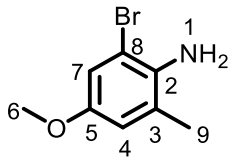
^{13}C NMR (126 MHz, DMSO, 95 °C) δ 162.1 (C-1), 160.9 (C-3), 146.3 (C-10), 139.8 (C-25), 139.3 (C-9), 135.2 (C-7), 135.1 (C-14), 132.1 (C-13), 130.6 (C-22), 130.0 (C-11), 129.6 (C-20), 129.6 (C-17), 127.9 (C-19), 123.9 (C-5), 123.8 (C-16), 121.4 (C-18,23), 120.7 (C-6), 113.8 (C-8), 112.6 (C-4), 98.7 (C-2), 19.8 (C-21), 19.2 (C-15), 16.9 (C-24), 15.1 (C-12).

HRMS (ESI) exact mass calculated for $C_{25}H_{24}ClN_2O_2^+$ $[M+H]^+$ requires *m/z* 419.1521, found *m/z* 419.1508.

IR (thin film) ν_{max}/cm^{-1} 3650, 2981, 2889, 1653, 1606, 1559, 1473, 1400, 1244, 1205, 1156, 1090, 1005, 956, 862, 819, 757.

MP 68-72 °C.

2-Bromo-4-methoxy-6-methylaniline, 720:



A flame-dried round bottom flask was charged with 4-methoxy-2-methylaniline (1.88 g, 13.70 mmol, 1.0 eq.) before dissolving in $CHCl_3$ (47 mL) and cooling to 0 °C. Br_2 (0.700 mL, 2.19 g, 13.70 mmol, 1.0 eq.) dissolved in $CHCl_3$ (11 mL) was added dropwise over 30 minutes via a dropping funnel, then the solution was stirred at 0 °C for 10 minutes. After the reaction time, the solution was diluted with $CHCl_3$ (100 mL), then washed with 2 M aqueous NaOH (x3), followed by saturated aqueous $Na_2S_2O_3$ (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil, which was purified by flash column chromatography (10:90 to 20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.09 g, 5.04 mmol, 37%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.90 (d, *J* = 2.8 Hz, 1H, H-7), 6.65 (dd, *J* = 2.8, 1.0 Hz, 1H, H-4), 3.75 (s, 2H, H-1), 3.72 (s, 3H, H-6), 2.20 (s, 3H, H-9).

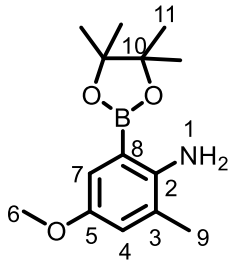
^{13}C NMR (151 MHz, $CDCl_3$) δ 152.2 (C-5), 136.4 (C-2), 124.9 (C-3), 116.7 (C-7), 115.1 (C-4), 109.7 (C-8), 56.0 (C-6), 18.8 (C-9).

HRMS (ESI) exact mass calculated for $C_8H_{11}BrNO^+$ $[M+H]^+$ requires *m/z* 216.0019, found *m/z* 216.0017.

IR (thin film) ν_{max}/cm^{-1} 3458, 3372, 2999, 2938, 2834, 2361, 2341, 1599, 1569, 1486, 1418, 1242, 1149, 1055.

MP 50 °C.

4-Methoxy-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline, 377:



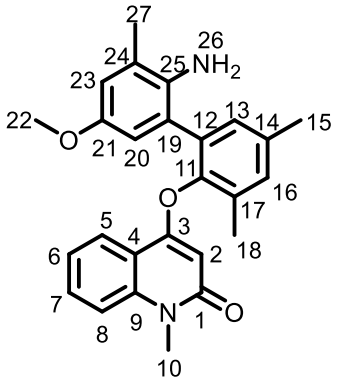
A flame-dried 100 mL 3-neck round bottom flask was charged with 2-bromo-4-methoxy-6-methylaniline (1.05 g, 4.65 mmol, 1.0 eq.), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (114.3 mg, 3 mol%), B_2Pin_2 (1.54 g, 6.05 mmol, 1.3 eq.) and KOAc (1.37 g, 13.95 mmol, 3.00 eq.) before degassing with vacuum and nitrogen cycles (x3). Anhydrous 1,4-dioxane (37.2 mL, 0.13 M) was added to form a suspension, which was then sparged with argon for 20 minutes. After sparging, the reaction mixture was heated to 101 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of celite, eluting with EtOAc (~100 mL). The solution was washed with deionised water, dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (5:95 to 15:85 EtOAc:pentane, v:v) to obtain a solid (628.8 mg, 2.39 mmol, 52%). The NMR spectra are consistent with those available in the literature.[177]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 3.1 Hz, 1H, H-7), 6.78 (d, *J* = 3.1, 1H, H-4), 4.48 (s, 2H, H-1), 3.75 (s, 3H, H-6), 2.12 (s, 3H, H-9), 1.33 (s, 12H, H-11).

^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2 (C-5), 146.3 (C-2), 123.8 (C-3), 121.9 (C-7), 117.1 (C-4), 83.7 (C-10), 56.0 (C-6), 25.0 (C-11), 18.0 (C-9).

HRMS (ESI) exact mass calculated for $C_{14}H_{23}BNO_3^+$ $[M+H]^+$ requires *m/z* 264.1766, found *m/z* 264.1763.

4-((2'-Amino-5'-methoxy-3,3',5-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-2(1H)-one, 122:



An oven-dried three-neck round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)-1-methylquinolin-2(1H)-one (283.0 mg, 0.79 mmol, 1.0 eq.), 4-methoxy-2-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (250.0 mg, 0.95 mmol, 1.20 eq.), $Pd(PPh_3)_4$ (46.2 mg, 5 mol%) and K_2CO_3 (436.7 mg, 3.16 mmol, 4.00 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 7.9 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (50:50 to 70:30 EtOAc:pentane, v:v) to obtain the title compound as a solid (171.0 mg, 0.41 mmol, 52%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.65 (m, 1H, H-7), 7.59 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-8), 7.54 (ddd, *J* = 8.4, 6.7, 3.1 Hz, 1H, H-6), 7.40 (d, *J* = 8.5 Hz, 1H, H-20), 7.25 – 7.18 (m, 2H, H-23,16), 7.07 (d, *J* = 2.2 Hz, 1H, H-13), 5.35 (s, 1H, H-2), 3.89 (s, 2H, H-26), 3.48 (s, 3H, H-22), 3.47 (s, 3H, H-10), 2.38 (s, 3H, H-15), 2.18 (s, 3H, H-27), 2.01 (s, 3H, H-18).

^{13}C NMR (126 MHz, DMSO, 90 °C) δ 161.5 (C-1), 160.1 (C-3), 150.0 (C-21), 146.2 (C-11), 139.3 (C-25), 136.4 (C-9), 135.3 (C-14), 132.1 (C-17), 131.04 (C-8/7), 130.96 (C-

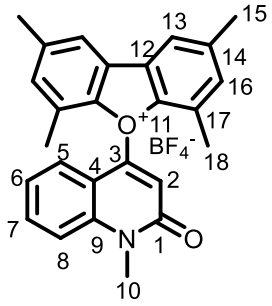
8/7), 130.87 (C-23), 130.2 (C-12), 129.6 (C-13), 128.2 (C-24), 128.1 (C-6), 123.1 (C-19), 122.4 (C-5), 120.8 (C-16), 114.6 (C-4), 113.8 (C-20), 98.0 (C-2), 55.0 (C-22), 28.1 (C-10), 19.9 (C-15), 17.3 (C-18), 15.1 (C-27).

HRMS (ESI) exact mass calculated for $C_{26}H_{27}N_2O_3^+$ $[M+H]^+$ requires *m/z* 415.2016, found *m/z* 415.2010.

IR (thin film) ν_{max}/cm^{-1} 3363, 3012, 2925, 2852, 1639, 1592, 1484, 1390, 1211, 1060.

MP 186°C.

2,4,6,8-Tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 119:



119 was prepared according to **General Procedure C** on a 2.63 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-2(1H)-one (1.05 g, 2.63 mmol, 1.00 eq.) to obtain the title compound as a solid (1.16 g, 2.47 mmol, 94%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.30 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.95 (ddd, *J* = 9.0, 7.4, 1.5 Hz, 1H, H-7), 7.93 (d, *J* = 2.1 Hz, 2H, H-13), 7.79 (d, *J* = 8.7 Hz, 1H, H-8), 7.56 (ddd, *J* = 8.1, 7.4, 0.9 Hz, 1H, H-6), 7.32 (d, *J* = 2.1, 2H, H-16), 6.83 (s, 1H, H-2), 3.71 (s, 3H, H-10), 2.51 (s, 6H, H-18), 2.06 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 164.5 (C-1), 162.2 (C-11), 160.8 (C-3), 143.0 (C-12), 141.6 (C-14), 135.7 (C-16), 135.6 (C-7), 124.9 (C-6), 124.4 (C-17), 124.3 (C-9), 123.5

(C-5), 122.7 (C-13), 117.6 (C-8), 114.5 (C-2), 113.6 (C-4), 31.2 (C-10), 21.1 (C-18), 17.2 (C-15).

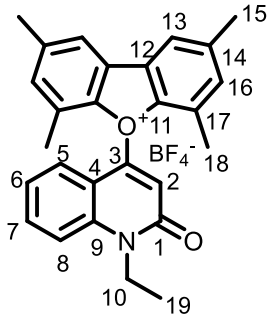
^{19}F NMR (565 MHz, CD_3CN) δ -151.9.

HRMS (ESI) exact mass calculated for $C_{26}H_{24}NO_2^+$ $[M]^+$ requires *m/z* 382.1802, found *m/z* 382.1790.

IR (thin film) ν_{max}/cm^{-1} 3058, 2349, 1669, 1597, 1566, 1459, 1372, 1312, 1062.

MP 158-159 °C.

5-(1-Ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 378:



378 was prepared according to **General Procedure C** on a 2.18 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-ethylquinolin-2(1H)-one (900.3 mg, 2.18 mmol, 1.0 eq.) to obtain the title compound as a solid (1.02 g, 2.11 mmol, 97%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.33 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.98 – 7.94 (m, 1H, H-7), 7.94 – 7.93 (m, 2H, H-13), 7.83 (d, *J* = 8.8 Hz, 1H, H-8), 7.56 (ddd, *J* = 8.1, 7.2, 0.9 Hz, 1H, H-6), 7.31 (dt, *J* = 1.8, 0.9 Hz, 2H, H-16), 6.82 (s, 1H, H-2), 4.35 (q, *J* = 7.2 Hz, 2H, H-10), 2.51 (s, 6H, H-18), 2.05 (s, 6H, H-15), 1.33 (t, *J* = 7.2 Hz, 3H, H-19).

^{13}C NMR (151 MHz, CD_3CN) δ 164.6 (C-1), 162.3 (C-3), 160.4 (C-9), 143.0 (C-14), 140.6 (C-11), 135.7 (C-16), 135.7 (C-7), 124.9 (C-6), 124.5 (C-12), 124.3 (C-17), 123.8

(C-5), 122.8 (C-13), 117.4 (C-8), 114.6 (C-2), 113.8 (C-4), 39.7 (C-10), 21.1 (C-18), 17.2 (C-15), 12.9 (C-19).

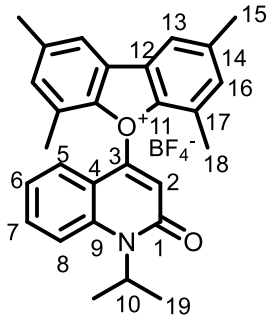
^{19}F NMR (471 MHz, CD_3CN) δ -151.6.

HRMS (ESI) exact mass calculated for $C_{27}H_{26}NO_2^+$ $[M]^+$ requires *m/z* 396.1958, found *m/z* 396.1951.

IR (thin film) ν_{max}/cm^{-1} 2990, 1668, 1641, 1599, 1567, 1456, 1392, 1323, 1202, 1064, 922, 864.

MP 142 °C.

5-(1-Isopropyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 379:



379 was prepared according to **General Procedure C** on a 1.61 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-isopropylquinolin-2(1H)-one (685.6 mg, 1.61 mmol, 1.0 eq.) to obtain the title compound as a solid (689.4 mg, 1.39 mmol, 86%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.39 (dd, *J* = 8.3, 1.2 Hz, 1H, H-5), 8.08 (dt, *J* = 8.6, 0.8 Hz, 1H, H-8), 8.03 – 7.99 (m, 1H, H-7), 7.99 – 7.98 (m, 2H, H-13), 7.78 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H, H-6), 7.32 (m, 2H, H-16), 7.07 (s, 1H, H-2), 5.56 (hept, *J* = 6.2 Hz, 1H, H-10), 2.54 (s, 6H, H-18), 1.90 (s, 6H, H-15), 1.39 (d, *J* = 6.2 Hz, 6H, H-19).

^{13}C NMR (126 MHz, CD_3CN) δ 164.2 (C-1), 162.7 (C-3), 162.4 (C-9), 149.2 (C-14), 143.1 (C-11), 135.7 (C-16), 134.1 (C-7), 129.2 (C-8), 128.2 (C-6), 124.5 (C-12), 124.3 (C-17), 122.8 (C-13), 121.4 (C-5), 117.1 (C-4), 106.9 (C-2), 71.9 (C-10), 21.9 (C-19), 21.1 (C-18), 16.9 (C-15).

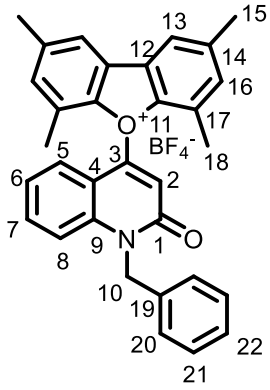
^{19}F NMR (470 MHz, CD_3CN) δ -151.5.

HRMS (ESI) exact mass calculated for $C_{28}H_{28}NO_2^+$ $[M]^+$ requires *m/z* 410.2115, found *m/z* 410.2106.

IR (thin film) ν_{max}/cm^{-1} 2983, 1641, 1608, 1557, 1476, 1418, 1309, 1270, 1063, 1004, 951, 860.

MP decomposes 158 °C.

5-(1-Benzyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 380:



380 was prepared according to **General Procedure C** on a 1.39 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-benzylquinolin-2(1H)-one (661.1 mg, 1.39 mmol, 1.0 eq.) to obtain the title compound as a solid (616.3 mg, 1.13 mmol, 81%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.35 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.97 – 7.93 (m, 2H, H-13), 7.82 (ddd, *J* = 8.8, 7.2, 1.5 Hz, 1H, H-7), 7.65 (d, *J* = 8.8 Hz, 1H, H-8), 7.53 (ddd, *J* = 8.2, 7.2, 0.9 Hz, 1H, H-6), 7.38 – 7.32 (m, 4H, H-16,21), 7.32 – 7.26 (m, 1H, H-22),

7.24 (dd, *J* = 7.1, 1.5 Hz, 2H, H-20), 6.97 (s, 1H, H-2), 5.56 (s, 2H, H-10), 2.52 (s, 6H, H-18), 2.08 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 164.6 (C-1), 162.3 (C-11), 161.1 (C-3), 143.1 (C-12), 140.7 (C-14), 136.6 (C-19), 135.8 (C-21), 135.6 (C-7), 130.0 (C-16), 128.7 (C-22), 127.5 (C-20), 125.3 (C-6), 124.5 (C-17), 124.3 (C-9), 123.9 (C-5), 122.8 (C-13), 118.1 (C-8), 114.9 (C-2), 114.0 (C-4), 47.4 (C-10), 21.1 (C-18), 17.4 (C-15).

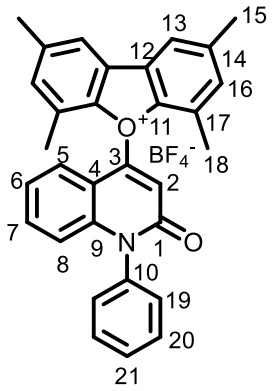
^{19}F NMR (471 MHz, CD_3CN) δ -151.9.

HRMS (ESI) exact mass calculated for $C_{32}H_{28}NO_2^+$ $[M]^+$ requires *m/z* 458.2107, found *m/z* 458.2115.

IR (thin film) ν_{max}/cm^{-1} 3628, 2360, 2341, 1647, 1063, 669.

MP 143 °C.

2,4,6,8-Tetramethyl-5-(2-oxo-1-phenyl-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 381:



381 was prepared according to **General Procedure C** on a 1.32 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-phenylquinolin-2(1H)-one (607.9 mg, 1.32 mmol, 1.0 eq.) to obtain the title compound as a solid (644.0 mg, 1.21 mmol, 92%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.39 (dd, *J* = 8.2, 1.4 Hz, 1H, H-5), 7.95 (d, *J* = 2.1 Hz, 2H, H-13), 7.71 (ddd, *J* = 8.8, 7.3, 1.4 Hz, 1H, H-7), 7.67 (dd, *J* = 8.3, 6.8 Hz, 2H, H-19), 7.66 – 7.59 (m, 1H, H-21), 7.54 (ddd, *J* = 8.2, 7.3, 1.0 Hz, 1H, H-6), 7.42 – 7.38 (m, 2H, H-20), 7.36 (dt, *J* = 2.1, 1.0 Hz, 2H, H-16), 6.91 (d, *J* = 8.8 Hz, 1H, H-8), 6.90 (s, 1H, H-2), 2.53 (s, 6H, H-18), 2.19 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 165.3 (C-1), 162.6 (C-3), 160.8 (C-9), 143.1 (C-14), 142.3 (C-10), 137.7 (C-11), 135.7 (C-16), 135.3 (C-7), 131.4 (C-19), 130.7 (C-21), 129.6 (C-20), 125.3 (C-6), 124.6 (C-12), 124.4 (C-17), 123.5 (C-5), 122.8 (C-13), 118.6 (C-8), 115.2 (C-2), 113.5 (C-4), 21.1 (C-18), 17.5 (C-15).

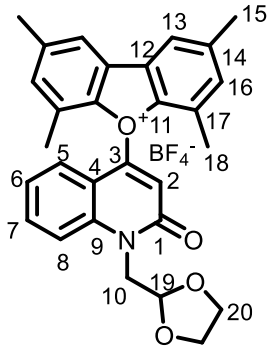
^{19}F NMR (565 MHz, CD_3CN) δ -151.6.

HRMS (ESI) exact mass calculated for $C_{31}H_{26}NO_2^+$ $[M]^+$ requires *m/z* 444.1958, found *m/z* 444.1948.

IR (thin film) ν_{max}/cm^{-1} 3478, 3363, 3066, 1670, 1644, 1586, 1565, 1491, 1452, 1210, 1059, 972, 860.

MP decomposes 146 °C.

5-(1-((1,3-Dioxolan-2-yl)methyl)-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 382:



382 was prepared according to a modified **General Procedure C** on a 0.92 mmol scale using 1-((1,3-dioxolan-2-yl)methyl)-4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-

yl)oxy)quinolin-2(1H)-one (433.6 mg, 0.92 mmol, 1.00 eq.) and HBF_4 (48 wt.% in H_2O, 132 μL, 1.1 eq.) to obtain the title compound as a solid (416.2 mg, 0.77 mmol, 84%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.31 (dd, *J* = 8.1, 1.4 Hz, 1H, H-5), 7.98 (d, *J* = 8.8 Hz, 1H, H-8), 7.94 – 7.93 (m, 2H, H-7), 7.93 – 7.91 (m, 1H, H-7), 7.56 (ddd, *J* = 8.1, 7.1, 1.0 Hz, 1H, H-6), 7.31 (dt, *J* = 1.8, 0.9 Hz, 2H, H-16), 6.87 (s, 1H, H-2), 5.21 (t, *J* = 4.2 Hz, 1H, H-19), 4.52 (d, *J* = 4.2 Hz, 2H, H-10), 3.99 – 3.90 (m, 2H, H-20), 3.88 – 3.79 (m, 2H, H-20'), 2.51 (s, 6H, H-18), 2.05 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 164.7 (C-1), 162.3 (C-3), 161.0 (C-9), 143.1 (C-14), 141.5 (C-11), 135.8 (C-16), 135.3 (C-13), 125.1 (C-6), 124.4 (C-12), 124.3 (C-17), 123.4 (C-5), 122.8 (C-7), 118.7 (C-8), 114.5 (C-2), 113.7 (C-5), 102.2 (C-19), 66.0 (C-20), 46.6 (C-10), 21.1 (C-18), 17.2 (C-15).

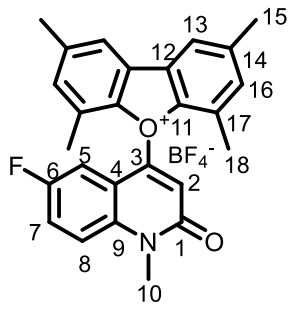
^{19}F NMR (470 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{29}H_{28}NO_4^+$ $[M]^+$ requires *m/z* 454.2013, found *m/z* 454.2005.

IR (thin film) ν_{max}/cm^{-1} 2925, 2360, 2342, 1711, 1667, 1601, 1530, 1456, 1349, 1209, 1059, 857.

MP 145 °C.

5-(6-Fluoro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 383:



383 was prepared according to **General Procedure C** on a 1.30 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-fluoro-1-methylquinolin-2(1H)-one (541.7 mg, 1.3 mmol, 1.0 eq.) to obtain the title compound as a solid (322.8 mg, 0.66 mmol, 51%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.17 (dd, *J* = 8.3, 2.9 Hz, 1H, H-5), 7.97 – 7.91 (m, 2H, H-13), 7.83 (dd, *J* = 9.5, 4.3 Hz, 1H, H-8), 7.76 (ddd, *J* = 9.5, 8.1, 2.9 Hz, 1H, H-7), 7.33 (dt, *J* = 1.9, 0.9 Hz, 2H, H-16), 6.89 (s, 1H, H-2), 3.70 (s, 3H, H-10), 2.51 (s, 6H, H-18), 2.07 (s, 6H, H-15).

^{13}C NMR (126 MHz, CD_3CN) δ 163.3 (d, *J* = 3.3 Hz, C-3), 162.6 (C-1), 160.4 (C-9), 159.3 (d, *J* = 244.6 Hz, C-6), 143.1 (C-14), 138.4 (C-11), 135.7 (C-16), 124.3 (d, *J* = 23.7 Hz, C-7), 123.8 (C-17), 123.7 (C-12), 122.8 (C-13), 120.4 (d, *J* = 8.5 Hz, C-8), 116.0 (C-2), 114.5 (d, *J* = 9.5 Hz, C-4), 109.0 (d, *J* = 26.7 Hz, C-5), 31.4 (C-10), 21.1 (C-18), 17.3 (C-15).

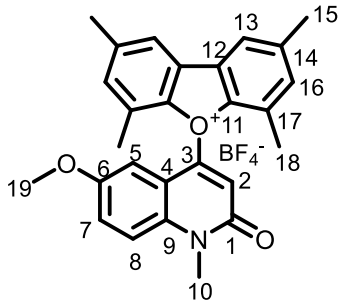
^{19}F NMR (471 MHz, CD_3CN) δ -118.2, -151.8 (BF_4).

HRMS (ESI) exact mass calculated for $C_{26}H_{23}FNO_2^+$ $[M]^+$ requires *m/z* 400.1707, found *m/z* 400.1701.

IR (thin film) ν_{max}/cm^{-1} 3627, 2366, 2342, 1670, 1445, 1097, 669.

MP 126 °C.

5-(6-Methoxy-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 384:



384 was prepared according to **General Procedure C** on a 2.47 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-6-methoxy-1-methylquinolin-2(1H)-one (1.06 g, 2.47 mmol, 1.0 eq.) to obtain the title compound as a solid (739.5 mg, 1.48 mmol, 60%).

^{1}H NMR (600 MHz, CD_3CN) δ 7.93 (dt, *J* = 1.8, 0.7 Hz, 2H, H-13), 7.76 (d, *J* = 2.8 Hz, 1H, H-8), 7.74 (d, *J* = 9.5 Hz, 1H, H-5), 7.57 (dd, *J* = 9.5, 2.8 Hz, 1H, H-7), 7.33 (dt, *J* = 1.8, 0.7 Hz, 2H, H-16), 6.78 (s, 1H, H-2), 3.89 (s, 3H, H-19), 3.70 (s, 3H, H-10), 2.51 (d, *J* = 0.7 Hz, 6H, H-18), 2.09 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 163.9 (C-1), 162.3 (C-6), 160.4 (C-3), 157.0 (C-9), 143.0 (C-14), 136.5 (C-4), 135.7 (C-16), 125.3 (C-7), 124.5 (C-11), 124.3 (C-12), 122.7 (C-13), 119.5 (C-5), 114.5 (C-2), 114.4 (C-17), 104.3 (C-8), 57.2 (C-19), 31.3 (C-10), 21.1 (C-18), 17.2 (C-15).

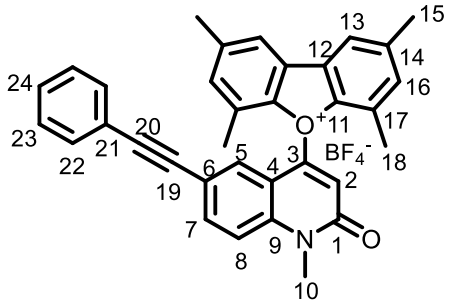
^{19}F NMR (565 MHz, CD_3CN) δ -151.9.

HRMS (ESI) exact mass calculated for $C_{27}H_{26}NO_3^+$ $[M]^+$ requires *m/z* 412.1907, found *m/z* 412.1903.

IR (thin film) ν_{max}/cm^{-1} 2360, 2341, 1667, 1636, 1568, 1503, 1460, 1379, 1316, 1275, 1242, 1061, 897.

MP decomposes 163 °C.

2,4,6,8-Tetramethyl-5-(1-methyl-2-oxo-6-(phenylethynyl)-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 385:



385 was prepared according to **General Procedure C** on a 2.21 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methyl-6-(phenylethynyl)quinolin-2(1H)-one (1.10 g, 2.21 mmol, 1.0 eq.) to obtain the title compound as a solid (1.05 g, 1.84 mmol, 83%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.57 (d, *J* = 1.9 Hz, 1H, H-5), 8.04 (dd, *J* = 9.0, 1.9 Hz, 1H, H-7), 7.92 (d, *J* = 2.1 Hz, 2H, H-13), 7.80 (d, *J* = 9.0 Hz, 1H, H-8), 7.56 – 7.52 (m, 2H, H-22), 7.41 (m, 3H, H-23,24), 7.31 (d, *J* = 2.1 Hz, 2H, H-16), 6.86 (s, 1H, H-2), 3.71 (s, 3H, H-10), 2.51 (s, 6H, H-18), 2.07 (s, 6H, H-15).

^{13}C NMR (126 MHz, CD_3CN) δ 163.6 (C-1), 162.5 (C-3), 160.6 (C-9), 143.1 (C-14), 141.1 (C-11), 137.9 (C-7), 135.8 (C-16), 132.5 (C-22), 130.2 (C-24), 129.8 (C-23), 126.0 (C-5), 124.4 (C-12), 124.2 (C-17), 123.2 (C-21), 122.8 (C-13), 119.7 (C-4), 118.3 (C-8), 115.4 (C-2), 114.0 (C-6), 91.9 (C-20), 87.9 (C-19), 31.3 (C-10), 21.1 (C-18), 17.4 (C-15).

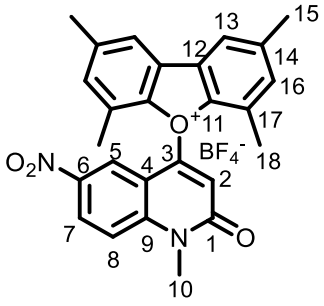
^{19}F NMR (470 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{34}H_{28}NO_2^+$ $[M]^+$ requires *m/z* 482.2115, found *m/z* 482.2103.

IR (thin film) ν_{max}/cm^{-1} 2357, 1673, 1639, 1440, 1183, 1063, 911, 380, 665.

MP decomposes 191 °C.

2,4,6,8-Tetramethyl-5-(1-methyl-6-nitro-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 386:



386 was prepared according to **General Procedure C** on a 2.66 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methyl-6-nitroquinolin-2(1H)-one (1.18 g, 2.66 mmol, 1.0 eq.) to obtain the title compound as a solid (1.01 g, 1.96 mmol, 74%).

^{1}H NMR (500 MHz, CD_3CN) δ 9.34 (d, *J* = 2.5 Hz, 1H, H-5), 8.67 (dd, *J* = 9.5, 2.5 Hz, 1H, H-7), 7.98 – 7.87 (m, 3H, H-8,13), 7.35 – 7.31 (m, 2H, H-16), 6.98 (s, 1H, H-2), 3.73 (s, 3H, H-10), 2.51 (s, 6H, H-18), 2.08 (s, 6H, H-15).

^{13}C NMR (126 MHz, CD_3CN) δ 163.5 (C-1), 163.2 (C-3), 160.8 (C-9), 144.8 (C-6), 144.4 (C-11), 143.3 (C-14), 135.7 (C-16), 129.4 (C-7), 124.5 (C-12), 124.3 (C-17), 122.8 (C-13), 120.0 (C-5), 119.1 (C-8), 117.1 (C-2), 113.4 (C-4), 31.8 (C-10), 21.1 (C-18), 17.6 (C-15).

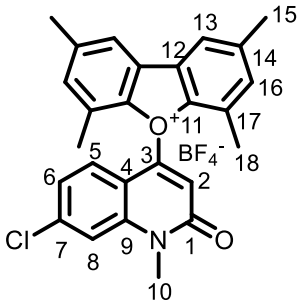
^{19}F NMR (471 MHz, CD_3CN) δ -151.7.

HRMS (ESI) exact mass calculated for $C_{26}H_{23}N_2O_4^+$ $[M]^+$ requires *m/z* 427.1652, found *m/z* 427.1641.

IR (thin film) ν_{max}/cm^{-1} 3072, 1677, 1613, 1575, 1494, 1349, 1269, 1213, 1059, 904, 810, 735.

MP decomposes 149 °C.

5-(7-Chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 387:



387 was prepared according to **General Procedure C** on a 1.98 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-chloro-1-methylquinolin-2(1H)-one (858.6 mg, 1.98 mmol, 1.0 eq.) to obtain the title compound as a solid (724.1 mg, 1.44 mmol, 73%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.32 (d, *J* = 8.7 Hz, 1H, H-5), 7.94 – 7.92 (m, 2H, H-13), 7.85 (d, *J* = 1.8 Hz, 1H, H-8), 7.57 (dd, *J* = 8.7, 1.8 Hz, 1H, H-6), 7.34 – 7.30 (m, 2H, H-16), 6.83 (s, 1H, H-2), 3.67 (s, 3H, H-10), 2.51 (s, 6H, H-18), 2.07 (s, 6H, H-15).

^{13}C NMR (126 MHz, CD_3CN) δ 164.0 (C-1), 162.5 (C-3), 160.7 (C-9), 143.1 (C-14), 142.4 (C-7), 141.4 (C-11), 135.7 (C-16), 125.4 (C-6), 125.2 (C-5), 124.4 (C-12), 124.3 (C-17), 122.8 (C-13), 117.6 (C-8), 114.7 (C-2), 112.3 (C-4), 31.4 (C-10), 21.1 (C-18), 17.3 (C-15).

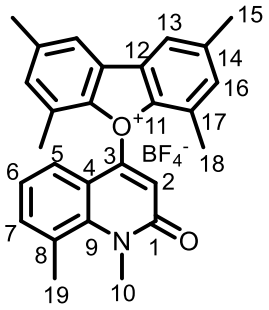
^{19}F NMR (471 MHz, CD_3CN) δ -151.7.

HRMS (ESI) exact mass calculated for $C_{26}H_{23}ClNO_2^+$ $[M]^+$ requires *m/z* 416.1412, found *m/z* 416.1400.

IR (thin film) ν_{max}/cm^{-1} 3055, 1664, 1643, 1596, 1552, 1460, 1410, 1383, 1284, 1209, 1062, 930, 861, 773.

MP 145-147 °C.

5-(1,8-Dimethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 388:



388 was prepared according to **General Procedure C** on a 2.38 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1,8-dimethylquinolin-2(1H)-one (982.4 mg, 2.38 mmol, 1.0 eq.) to obtain the title compound as a solid (831.4 mg, 1.72 mmol, 72%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.23 – 8.13 (m, 1H, H-5), 7.97 – 7.88 (m, 2H, H-13), 7.81 – 7.71 (m, 1H, H-7), 7.45 (t, *J* = 7.8 Hz, 1H, H-6), 7.31 (dt, *J* = 1.9, 0.9 Hz, 2H, H-16), 6.78 (s, 1H, H-2), 3.82 (s, 3H, H-10), 2.83 (s, 3H, H-19), 2.51 (s, 6H, H-18), 2.05 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 165.3 (C-1), 162.4 (C-3), 162.2 (C-14), 143.0 (C-9), 142.7 (C-11), 139.9 (C-7), 135.7 (C-16), 129.0 (C-12), 125.2 (C-6), 124.4 (C-8), 124.3 (C-17), 122.7 (C-13), 121.8 (C-5), 115.3 (C-4), 113.7 (C-2), 38.0 (C-10), 24.4 (C-19), 21.1 (C-18), 17.2 (C-15).

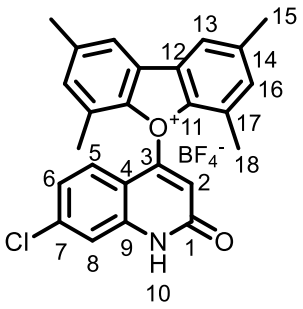
^{19}F NMR (471 MHz, CD_3CN) δ -151.7.

HRMS (ESI) exact mass calculated for $C_{27}H_{26}NO_2^+$ $[M]^+$ requires *m/z* 396.1958, found *m/z* 396.1948.

IR (thin film) ν_{max}/cm^{-1} 2999, 1666, 1638, 1589, 1571, 1457, 1374, 1301, 1203, 1056, 981, 905, 861, 733.

MP 130-134 °C.

5-(7-Chloro-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 389:



389 was prepared according to **General Procedure C** on a 0.06 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-7-chloroquinolin-2(1H)-one (26.6 mg, 0.06 mmol, 1.0 eq.) to obtain the title compound as a solid (9.5 mg, 0.02 mmol, 32%).

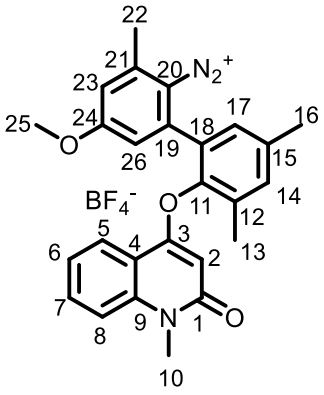
^{1}H NMR (600 MHz, CD_3CN) δ 10.41 (s, 1H, H-10), 8.20 (d, *J* = 8.7 Hz, 1H, H-5), 7.91 (dt, *J* = 2.3, 0.8 Hz, 2H, H-16), 7.58 (d, *J* = 1.9 Hz, 1H, H-8), 7.50 (dd, *J* = 8.7, 1.9 Hz, 1H, H-6), 7.32 (dt, *J* = 1.8, 0.9 Hz, 2H, H-13), 6.75 (s, 1H, H-2), 2.51 (d, *J* = 0.7 Hz, 6H, H-18), 2.09 (d, *J* = 0.7 Hz, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 165.0 (C-1), 162.4 (C-3), 160.5 (C-9), 143.1 (C-14), 141.0 (C-7), 140.8 (C-11), 135.7 (C-16), 125.7 (C-6), 124.8 (C-5), 124.5 (C-12), 124.3 (C-17), 122.8 (C-13), 117.3 (C-8), 116.0 (C-2), 111.6 (C-4), 21.1 (C-18), 17.3 (C-15).

^{19}F NMR (565 MHz, CD_3CN) δ -151.8.

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

5-Methoxy-3,3',5'-trimethyl-2'-((1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)oxy)-[1,1'-biphenyl]-2-diazonium tetrafluoroborate, 122':



A glass screw-cap vial was charged with 4-((2'-amino-5'-methoxy-3,3',5-trimethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-2(1H)-one (105.3 mg, 0.25 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (1.0 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 163 µL, 0.14 mmol, 1.1 eq.). The solution was cooled to 0 °C and *t*-BuONO (149 µL, 61.9 mg, 0.60 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude solid. The resulting crude was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (105.3 mg, 0.21 mmol, 82%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.11 (dd, *J* = 8.0, 1.6 Hz, 1H, H-5), 7.66 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-7), 7.47 (d, *J* = 2.2 Hz, 1H, H-8), 7.43 (d, *J* = 8.7 Hz, 1H, H-17), 7.34 (d, *J* = 2.6 Hz, 1H, H-6), 7.32 (d, *J* = 7.7 Hz, 1H, H-26), 7.28 – 7.17 (m, 1H, H-14), 7.08

(d, J = 2.6 Hz, 1H, H-23), 5.35 (s, 1H, H-2), 3.94 (s, 3H, H-25), 3.48 (s, 3H, H-10), 2.60 (s, 3H, H-16), 2.44 (s, 3H, H-22), 2.21 (s, 3H, H-13).

^{13}C NMR (151 MHz, CD_3CN) δ 170.5, 163.2, 161.5, 150.3, 146.6, 146.0, 141.3, 139.0, 136.8, 133.5, 133.1, 130.5, 127.0, 123.6, 123.1, 119.1, 118.8, 115.8, 115.7, 102.5, 100.6, 58.7, 29.5, 20.9, 19.5, 16.1.

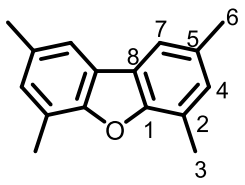
^{19}F NMR (565 MHz, CD_3CN) δ -151.5.

HRMS (ESI) exact mass calculated for $C_{26}H_{24}NO_3^+$ $[M\text{-}N_2]^+$ requires *m/z* 398.1751, found *m/z* 398.1747.

IR (thin film) ν_{max}/cm^{-1} 3089, 2349, 2229 ($N{\equiv}N^+$ stretch), 1638, 1587, 1390, 1350, 1279, 1241, 1097, 1057, 935.

MP decomposes 98 °C.

2,4,6,8-Tetramethyldibenzo[b,d]furan, 121:



Isolated as a leaving group in hetaryne-generating reactions.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (s, 2H, H-7), 7.05 (s, 2H, H-4), 2.56 (s, 6H, H-3), 2.47 (s, 6H, H-6).

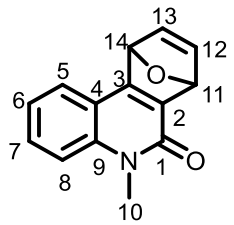
^{13}C NMR (151 MHz, $CDCl_3$) δ 153.8 (C-1), 131.8 (C-5), 129.1 (C-4), 124.2 (C-8), 121.4 (C-2), 118.1 (C-7), 21.4 (C-6), 15.3 (C-3).

HRMS (ESI) exact mass calculated for $C_{16}H_{17}O^+$ $[M+H]^+$ requires *m/z* 225.1274, found *m/z* 225.1273.

IR (thin film) ν_{max}/cm^{-1} 2921, 1619, 1490, 1460, 1183, 1126, 847, 822.

MP 148-151 °C.

5-Methyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 120:



120 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (93.9 mg, 0.20 mmol, 1.0 eq.), furan (73 μL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (65:35 EtOAc:pentane, v:v) to obtain the title compound as a solid (40.3 mg, 0.18 mmol, 83%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H, H-5), 7.59 (ddd, *J* = 8.7, 7.2, 1.5 Hz, 1H, H-7), 7.40 (d, *J* = 8.7 Hz, 1H, H-8), 7.32 – 7.27 (m, 2H, H-6,12), 7.14 (dd, *J* = 5.4, 1.5 Hz, 1H, H-13), 6.13 (dd, *J* = 2.0, 1.1 Hz, 1H, H-14), 6.08 (dd, *J* = 2.0, 1.1 Hz, 1H, H-11), 3.73 (s, 3H, H-10).

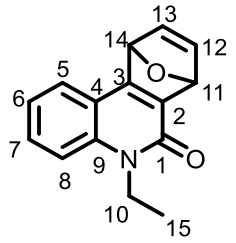
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.8 (C-1), 158.8 (C-3), 145.6 (C-12), 141.8 (C-13), 141.0 (C-9), 139.8 (C-2), 131.0 (C-7), 124.2 (C-5), 122.3 (C-6), 117.3 (C-4), 115.2 (C-8), 82.0 (C-11), 81.9 (C-14), 29.6 (C-10).

HRMS (ESI) exact mass calculated for $C_{14}H_{12}NO_2^+$ $[M+H]^+$ requires *m/z* 226.0863, found *m/z* 226.0861.

IR (thin film) ν_{max}/cm^{-1} 3011, 2360, 2341, 1646, 1585, 1561, 1452, 1217.

MP 147-154 °C.

5-Ethyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 390:



390 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (96.7 mg, 0.20 mmol, 1.0 eq.), furan (73 μL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (55:45 EtOAc:pentane, v:v) to obtain the title compound as a solid (37.5 mg, 0.16 mmol, 78%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.9, 1.6 Hz, 1H, H-5), 7.57 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H, H-7), 7.41 (d, *J* = 8.7 Hz, 1H, H-8), 7.30 (dd, *J* = 5.4, 1.9 Hz, 1H, H-12), 7.28 – 7.23 (m, 1H, H-6), 7.13 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 6.11 (dd, *J* = 2.0, 1.0 Hz, 1H, H-14), 6.07 (dd, *J* = 1.9, 1.0 Hz, 1H, H-11), 4.52 – 4.22 (m, *J* = 7.2 Hz, 2H, H-10), 1.32 (t, *J* = 7.2 Hz, 3H, H-15).

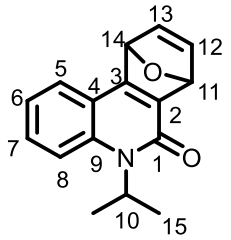
^{13}C NMR (151 MHz, CDCl3) δ 162.6 (C-1), 158.2 (C-3), 145.6 (C-12), 141.6 (C-13), 140.8 (C-2), 138.7 (C-9), 131.0 (C-7), 124.4 (C-5), 122.1 (C-6), 117.5 (C-4), 115.0 (C-8), 81.84 (C-11 or 14), 81.81 (C-11 or 14), 37.4 (C-10), 13.1 (C-15).

HRMS (ESI) exact mass calculated for $C_{15}H_{14}NO_2^+$ $[M+H]^+$ requires *m/z* 240.1019, found *m/z* 240.1015.

IR (thin film) ν_{max}/cm^{-1} 2981, 1645, 1584, 1560, 1450, 1307, 1273, 1104, 1089, 1049, 1012, 869, 822.

MP 88-94 °C.

5-Isopropyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 391:



391 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-isopropyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (99.5 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (5:95 EtOAc:pentane, v:v) to obtain the title compound as an oil (42.5 mg, 0.17 mmol, 84%).

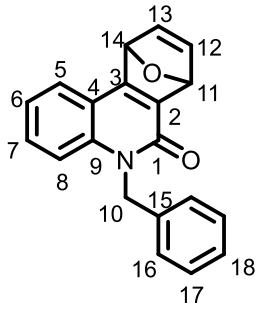
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.5 Hz, 1H, H-5), 7.72 (d, *J* = 8.1 Hz, 1H, H-8), 7.60 – 7.53 (m, 1H, H-7), 7.36 (t, *J* = 7.5 Hz, 1H, H-6), 7.27 (dd, *J* = 5.5, 2.0 Hz, 1H, H-12), 7.18 (dd, *J* = 5.5, 2.0 Hz, 1H, H-13), 6.20 (d, *J* = 2.0 Hz, 1H, H-14), 6.07 (d, *J* = 2.0 Hz, 1H, H-11), 5.60 (hept, *J* = 6.2 Hz, 1H, H-10), 1.44 (d, *J* = 6.2 Hz, 3H, H-15), 1.41 (d, *J* = 6.2 Hz, 3H, H-15').

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9 (C-1), 156.3 (C-3), 146.4 (C-2), 145.3 (C-12), 142.7 (C-13), 134.1 (C-9), 129.3 (C-7), 128.0 (C-5), 123.9 (C-6), 122.8 (C-8), 120.9 (C-4), 81.5 (C-14), 81.1 (C-11), 68.2 (C-10), 22.34 (C-15), 22.29 (C-15').

HRMS (ESI) exact mass calculated for $C_{16}H_{16}NO_2^+$ $[M+H]^+$ requires *m/z* 254.1176, found *m/z* 254.1174.

IR (thin film) ν_{max}/cm^{-1} 2979, 2933, 2363, 1623, 1592, 1514, 1457, 1431, 1373, 1319, 1211, 1178, 958, 869.

5-Benzyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 392:



392 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-benzyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (109.1 mg, 0.20 mmol, 1.0 eq.), furan (73 μL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (35:65 EtOAc:pentane, v:v) to obtain the title compound as a solid (52.5 mg, 0.17 mmol, 87%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.9, 1.5 Hz, 1H, H-5), 7.43 (ddd, *J* = 8.7, 7.1, 1.5 Hz, 1H, H-7), 7.35 (dd, *J* = 5.4, 1.9 Hz, 1H, H-12), 7.32 – 7.26 (m, 3H, H-8,16), 7.24 – 7.20 (m, 2H, H-6,18), 7.18 (m, 3H, H-13,17), 6.16 (m, 1H, H-14), 6.14 – 6.13 (m, 1H, H-11), 5.68 (d, *J* = 16.0 Hz, 1H, H-10'), 5.46 (d, *J* = 16.0 Hz, 1H, H-10'').

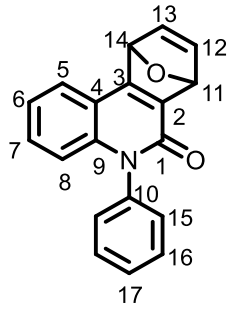
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4 (C-1), 158.8 (C-3), 145.7 (C-13), 141.7 (C-12), 140.8 (C-2), 139.3 (C-9), 136.5 (C-15), 131.0 (C-7), 128.9 (C-16), 127.4 (C-18), 126.6 (C-17), 124.2 (C-5), 122.4 (C-6), 117.6 (C-4), 116.0 (C-8), 82.0 (C-14/11), 81.9 (C-14/11), 46.0 (C-10).

HRMS (ESI) exact mass calculated for $C_{20}H_{16}NO_2^+$ $[M+H]^+$ requires *m/z* 302.1176, found *m/z* 302.1170.

IR (thin film) ν_{max}/cm^{-1} 3031, 2950, 1654, 1589, 1560, 1498, 1451, 823, 804.

MP 175-178 °C.

5-Phenyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 393:



393 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(2-oxo-1-phenyl-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (106.3 mg, 0.20 mmol, 1.0 eq.), furan (73 μL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (41.1 mg, 0.14 mmol, 72%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.9, 1.5 Hz, 1H, H-5), 7.59 (dtd, *J* = 11.6, 7.6, 1.7 Hz, 2H, H-15), 7.52 (tt, *J* = 7.5, 1.3 Hz, 1H, H-17), 7.36 (dd, *J* = 5.5, 2.0 Hz, 1H, H-12), 7.34 – 7.32 (m, 1H, H-7), 7.28 – 7.22 (m, 3H, H-6 and 16), 7.20 (dd, *J* = 5.5, 2.0 Hz, 1H, H-13), 6.68 (dd, *J* = 8.7, 1.1 Hz, 1H, H-8), 6.19 (dd, *J* = 2.0, 1.1 Hz, 1H, H-11), 6.10 (dd, *J* = 2.0, 1.1 Hz, 1H, H-14).

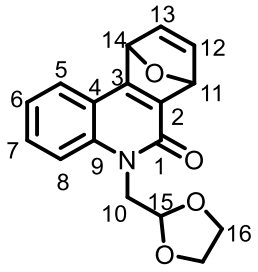
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-1), 158.7 (C-3), 145.8 (C-12), 141.6 (C-13), 141.3 (C-10), 141.1 (C-9), 137.9 (C-2), 130.6 (C-7), 130.4 (C-15), 130.2 (C-15'), 129.2 (C-17), 129.01 (C-16), 128.95 (C-16'), 123.7 (C-5), 122.5 (C-6), 117.02 (C-4), 116.97 (C-8), 81.95 (C-11 or 14), 81.88 (C-11 or 14).

HRMS (ESI) exact mass calculated for $C_{19}H_{13}NO_2^+$ $[M+H]^+$ requires *m/z* 288.1019, found *m/z* 288.1013.

IR (thin film) ν_{max}/cm^{-1} 3057, 2921, 1656, 1589, 1556, 1493, 1448, 1311, 1272, 1077, 869, 849.

MP 188 °C.

5-((1,3-Dioxolan-2-yl)methyl)-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 394:



394 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-((1,3-dioxolan-2-yl)methyl)-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (108.3 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (70:30 EtOAc:pentane, v:v) to obtain the title compound as a solid (48.5 mg, 0.16 mmol, 82%).

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 2H, H-5,8), 7.55 (ddd, *J* = 8.7, 7.4, 1.4 Hz, 1H, H-7), 7.28 (dd, *J* = 5.5, 2.0 Hz, 1H, H-12), 7.25 (t, *J* = 7.4 Hz, 1H, H-6), 7.12 (dd, *J* = 5.5, 2.0 Hz, 1H, H-13), 6.10 (d, *J* = 2.0 Hz, 1H, H-14), 6.05 (d, *J* = 2.0 Hz, 1H, H-11), 5.22 (t, *J* = 4.5 Hz, 1H, H-15), 4.59 (dd, *J* = 14.7, 4.5 Hz, 1H, H-10), 4.50 (dd, *J* = 14.7, 4.5 Hz, 1H, H-10'), 4.08 – 3.96 (m, 2H, H-16), 3.90 – 3.81 (m, 2H, H-16').

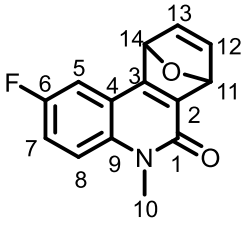
^{13}C NMR (176 MHz, $CDCl_3$) δ 163.3 (C-1), 158.8 (C-3), 145.6 (C-12), 141.6 (C-13), 140.6 (C-2), 139.7 (C-9), 130.8 (C-7), 124.1 (C-5), 122.4 (C-6), 117.5 (C-4), 116.0 (C-8), 102.0 (C-15), 81.8 (C-11,14), 65.1 (C-16), 44.9 (C-10).

HRMS (ESI) exact mass calculated for $C_{17}H_{16}NO_4^+$ $[M+H]^+$ requires *m/z* 298.1074, found *m/z* 298.1069.

IR (thin film) ν_{max}/cm^{-1} 3017, 2924, 1655, 1588, 1561, 1450, 1306, 1273, 1143, 1041, 944, 868, 839.

MP 108-112 °C.

2-Fluoro-5-methyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 395:



395 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(6-fluoro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (97.5 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (40.9 mg, 0.17 mmol, 84%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 4H, H-5,7,8,12), 7.15 – 7.12 (m, 1H, H-13), 6.05 (s, 1H, H-11 or 14), 6.04 (s, 1H, H-11 or 14), 3.70 (s, 3H, H-10).

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.0 (d, J = 3.9 Hz, C-1), 158.3 (C-3), 157.9 (d, J = 244.5 Hz, C-6), 145.5 (C-12), 142.7 (C-2), 141.8 (C-13), 136.4 (d, J = 1.7 Hz, C-9), 118.8 (d, J = 24.0 Hz, C-7), 117.8 (d, J = 8.7 Hz, C-4), 116.8 (d, J = 8.2 Hz, C-8), 109.2 (d, J = 22.7 Hz, C-5), 82.0 (C-11 or 14), 81.8 (C-11 or 14), 29.8 (C-10).

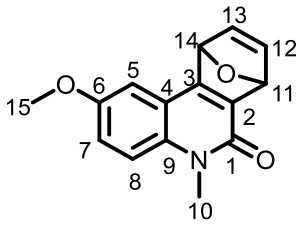
^{19}F NMR (471 MHz, $CDCl_3$) δ -120.5.

HRMS (ESI) exact mass calculated for $C_{14}H_{11}FNO_2^+$ $[M+H]^+$ requires *m/z* 244.0768, found *m/z* 244.0769.

IR (thin film) ν_{max}/cm^{-1} 3077, 2925, 2360, 1649, 1593, 1569, 1439, 1299, 1272, 1223, 1143, 1080, 1041, 1013, 870.

MP 168-170 °C.

2-Methoxy-5-methyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 396:



396 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(6-methoxy-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (99.9 mg, 0.20 mmol, 1.00 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (65:35 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (38.1 mg, 0.15 mmol, 75%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (d, *J* = 9.3 Hz, 1H, H-8), 7.28 (dd, *J* = 5.4, 2.0 Hz, 1H, H-12), 7.19 (dd, *J* = 9.3, 2.9 Hz, 1H, H-7), 7.14 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 7.00 (d, *J* = 2.9 Hz, 1H, H-5), 6.08 (dd, *J* = 2.0, 1.0 Hz, 1H, H-14), 6.05 (dd, *J* = 2.0, 1.0 Hz, 1H, H-11), 3.89 (s, 3H, H-15), 3.69 (s, 3H, H-10).

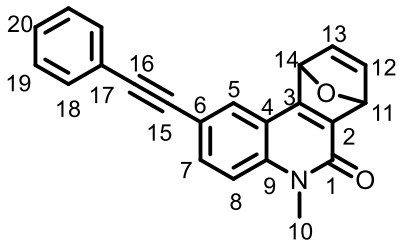
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0 (C-1), 158.2 (C-6), 154.9 (C-3), 145.6 (C-12), 141.7 (C-13), 141.5 (C-2), 134.5 (C-9), 119.9 (C-7), 117.8 (C-4), 116.5 (C-8), 105.6 (C-5), 82.0 (C-11 or 14), 81.8 (C- 11 or 14), 55.9 (C-15), 29.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{15}H_{14}NO_3^+$ $[M+H]^+$ requires *m/z* 256.0968, found *m/z* 256.0966.

IR (thin film) ν_{max}/cm^{-1} 2941, 1645, 1621, 1566, 1456, 1428, 1390, 1273, 1224, 1181, 1044, 980, 867.

MP 156-158 °C.

5-Methyl-2-(phenylethynyl)-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 397:



397 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-6-(phenylethynyl)-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (113.9 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (45:55 to 100:0 EtOAc:pentane, v:v) to obtain the title compound as a solid (33.7 mg, 0.10 mmol, 52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 2.0 Hz, 1H, H-5), 7.70 (dd, *J* = 8.8, 2.0 Hz, 1H, H-7), 7.60 – 7.51 (m, 2H, H-18), 7.41 – 7.33 (m, 4H, H-8,19,20), 7.30 (dd, *J* = 5.4, 1.9 Hz, 1H, H-12), 7.15 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 6.13 (dd, *J* = 2.0, 1.1 Hz, 1H, H-14), 6.07 (dd, *J* = 1.9, 1.1 Hz, 1H, H-11), 3.72 (s, 3H, H-10).

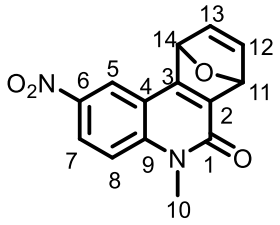
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (C-1), 158.5 (C-3), 145.6 (C-12), 141.9 (C-9), 141.8 (C-13), 139.2 (C-2), 133.8 (C-7), 131.7 (C-18), 128.7 (C-20), 128.6 (C-19), 127.2 (C-5), 123.0 (C-17), 117.4 (C-4), 117.2 (C-6), 115.3 (C-8), 90.1 (C-16), 88.2 (C-15), 81.9 (C-11 or 14), 81.8 (C-11 or 14), 29.7 (C-10).

HRMS (ESI) exact mass calculated for $[M+H]^+$ requires *m/z* 326.1176, found *m/z* 326.1169.

IR (thin film) ν_{max}/cm^{-1} 3057, 2360, 1652, 1586, 1554, 1458, 1427, 1300, 1076, 1040, 867, 817, 662.

MP 165 °C.

5-Methyl-2-nitro-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 398:



398 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-6-nitro-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (102.9 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 to 55:45 EtOAc:pentane, v:v) to obtain the title compound as a solid (34.2 mg, 0.13 mmol, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 2.6 Hz, 1H, H-5), 8.40 (dd, *J* = 9.4, 2.6 Hz, 1H, H-7), 7.49 (d, *J* = 9.4 Hz, 1H, H-8), 7.32 (dd, *J* = 5.4, 2.0 Hz, 1H, H-12), 7.20 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 6.20 (dd, *J* = 2.0, 1.0 Hz, 1H, H-14), 6.08 (dd, *J* = 2.0, 1.0 Hz, 1H, H-11), 3.77 (s, 3H, H-10).

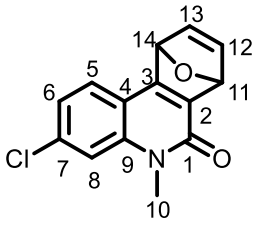
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1 (C-1), 158.4 (C-3), 145.5 (C-12), 144.1 (C-6), 143.3 (C-9), 142.2 (C-2), 142.0 (C-13), 125.2 (C-7), 120.2 (C-5), 116.7 (C-4), 115.8 (C-8), 82.04 (C-11 or 14), 81.99 (C-11 or 14), 30.2 (C-10).

HRMS (ESI) exact mass calculated for $C_{14}H_{11}N_2O_4^+$ $[M+H]^+$ requires *m/z* 271.0713, found *m/z* 271.0710.

IR (thin film) ν_{max}/cm^{-1} 3089, 1657, 1600, 1518, 1421, 1283, 1192, 1096, 1040, 1008, 971, 904, 846, 805, 734, 720.

MP decomposes 240 °C.

3-Chloro-5-methyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 399:



399 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(7-chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (100.7 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 EtOAc:pentane, v:v) to obtain the title compound as a solid (37.0 mg, 0.14 mmol, 71%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 1H, H-5), 7.38 (d, *J* = 1.9 Hz, 1H, H-8), 7.28 (dd, *J* = 5.4, 2.0 Hz, 1H, H-12), 7.23 (dd, *J* = 8.4, 1.9 Hz, 1H, H-6), 7.12 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 6.07 (dd, *J* = 2.0, 1.1 Hz, 1H, H-14), 6.04 (dd, *J* = 2.0, 1.1 Hz, 1H, H-11), 3.67 (s, 3H, H-10).

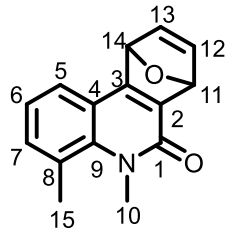
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3 (C-1), 158.5 (C-3), 145.6 (C-12), 141.6 (C-13), 141.2 (C-9), 140.5 (C-2), 137.2 (C-7), 125.2 (C-5), 122.8 (C-6), 115.7 (C-4), 115.2 (C-8), 81.9 (C-11 or 14), 81.8 (C-11 or 14), 29.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{14}H_{11}ClNO_2^+$ $[M+H]^+$ requires *m/z* 260.0473, found *m/z* 260.0467.

IR (thin film) ν_{max}/cm^{-1} 3084, 1654, 1586, 1547, 1426, 1339, 1273, 1142, 1077, 989, 949, 825, 769, 732, 712.

MP 198-202 °C.

4,5-Dimethyl-7,10-dihydro-7,10-epoxyphenanthridin-6(5H)-one, 400:



400 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1,8-dimethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (96.7 mg, 0.20 mmol, 1.0 eq.), furan (73 µL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 to 70:30 EtOAc:pentane, v:v) to obtain the title compound as a solid (37.9 mg, 0.16 mmol, 79%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.6, 1.6 Hz, 1H, H-5), 7.34 (ddd, *J* = 7.6, 1.6, 0.8 Hz, 1H, H-7), 7.27 (dd, *J* = 5.4, 1.9 Hz, 1H, H-12), 7.15 (t, *J* = 7.6 Hz, 1H, H-6), 7.11 (dd, *J* = 5.4, 2.0 Hz, 1H, H-13), 6.07 (dd, *J* = 2.0, 1.1 Hz, 1H, H-14), 6.04 (dd, *J* = 1.9, 1.1 Hz, 1H, H-11), 3.80 (s, 3H, H-10), 2.69 (s, 3H, H-15).

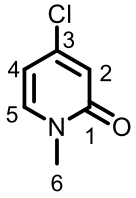
^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4 (C-1), 160.6 (C-3), 145.5 (C-12), 141.6 (C-13), 141.3 (C-9), 140.2 (C-2), 135.5 (C-7), 125.9 (C-8), 122.7 (C-6), 122.3 (C-5), 118.9 (C-4), 82.0 (C-47), 81.8 (C-11), 36.7 (C-10), 24.3 (C-15).

HRMS (ESI) exact mass calculated for $C_{15}H_{14}NO_2^+$ $[M+H]^+$ requires *m/z* 240.1019, found *m/z* 240.1017.

IR (thin film) ν_{max}/cm^{-1} 3053, 1651, 1586, 1565, 1457, 1375, 1309, 1227, 1078, 1036, 943, 787, 739.

MP 106-108 °C.

4-Chloro-1-methylpyridin-2(1H)-one, 402:



An oven-dried 50 mL round bottom flask was charged with 2-hydroxy-4-chloropyridine (2.0 g, 15.44 mmol, 1.0 eq.) before adding anhydrous benzene (31 mL, 0.5 M) and MeI (2.9 mL, 6.57 g, 46.32 mmol, 3.0 eq.). With stirring, K_2CO_3 (6.40 g, 46.32 mmol, 3.0 eq.) was added, followed by TBAI (568.8 mg, 10 mol%) then stirred at room temperature for 24 hours under nitrogen. After the reaction time, the reaction mixture was filtered through a pad of Celite, eluting with EtOAc, then partially concentrated under vacuum to obtain a crude oil. The crude oil was poured into deionised water (300 mL), then extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain an oil (1.40 g, 9.75 mmol, 63%), which was used without any further purification. The NMR spectra are consistent with those available in the literature.[169]

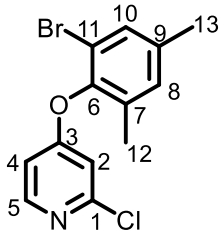
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (d, *J* = 7.2 Hz, 1H, H-5), 6.58 (d, *J* = 2.3 Hz, 1H, H-2), 6.17 (dd, *J* = 7.2, 2.3 Hz, 1H, H-4), 3.49 (s, 3H, H-6).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1 (C-1), 146.7 (C-3), 138.4 (C-5), 119.3 (C-2), 107.8 (C-4), 37.4 (C-6).

HRMS (ESI) exact mass calculated for $C_6H_7ClNO^+$ $[M+H]^+$ requires *m/z* 144.0211, found *m/z* 144.0209.

IR (thin film) ν_{max}/cm^{-1} 1654, 1591, 1532, 1461, 1414, 1340, 1144, 1059, 1041, 931, 843, 765, 723.

4-(2-Bromo-4,6-dimethylphenoxy)-2-chloropyridine, 404:



An oven-dried round bottom flask was charged with 2-bromo-4,6-dimethylphenol (3.36 g, 16.7 mmol, 1.1 eq.) before dissolving in anhydrous NMP (38 mL, 0.4 M) under nitrogen. The solution was cooled to 0 °C before adding KO*t*-Bu (2.04 g, 18.2 mmol, 1.2 eq.) in small portions, then stirred for 30 minutes. 2-Chloro-4-fluoropyridine (1.4 mL, 15.2 mmol, 1.0 eq.) was then added dropwise at 0 °C, then brought to room temperature and-heated to to 70 °C under nitrogen for 16 hours. After the reaction time, the reaction mixture was filtered through a pad of celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude oil was poured into deionised water (400 mL), then extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude oil, which was purified by flash column chromatography (5:95 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (3.56 g, 11.39 mmol, 75%).

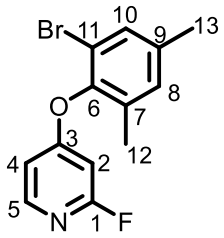
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 5.7 Hz, 1H, H-5), 7.29 (d, *J* = 2.1 Hz, 1H, H-10), 7.10 – 6.96 (m, 1H, H-8), 6.70 – 6.66 (m, 2H, H-2,4), 2.32 (s, 3H, H-13), 2.11 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2 (C-3), 153.0 (C-1), 150.9 (C-5), 146.0 (C-6), 137.7 (C-9), 132.6 (C-10), 132.0 (C-7), 131.7 (C-8), 116.4 (C-11), 110.7 (C-2), 110.2 (C-4), 20.7 (C-13), 16.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{13}H_{12}BrClNO^+$ $[M+H]^+$ requires *m/z* 311.9785, found *m/z* 311.9777.

IR (thin film) ν_{max}/cm^{-1} 2981, 1605, 1581, 1563, 1462, 1384, 1295, 1250, 1234, 1204, 1122, 1067, 989, 960, 852, 828, 791, 734.

4-(2-Bromo-4,6-dimethylphenoxy)-2-fluoropyridine, 403:



An oven-dried round bottom flask was charged with 2,4-difluoropyridine (2.0 g, 17.4 mmol, 1.0 eq.) before dissolving in anhydrous DMF (80 mL, 0.2 M) and adding 2-bromo-4,6-dimethylphenol (3.50 g, 17.4 mmol, 1.0 eq.), followed by Cs_2CO_3 (11.3 g, 34.8 mmol, 2.0 eq.). The suspension was heated to to 90 °C under nitrogen for 16 hours. After the reaction time, the reaction mixture was filtered through a pad of celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude oil was poured into deionised water (200 mL), then extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain an oil (4.70 g, 15.87 mmol, 91%), which was used without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (d, *J* = 5.9 Hz, 1H, H-5), 7.31 (d, *J* = 2.1 Hz, 1H, H-8), 7.04 (d, *J* = 2.1 Hz, 1H, H-10), 6.67 (dd, *J* = 5.9, 2.1 Hz, 1H, H-4), 6.24 (d, *J* = 2.1 Hz, 1H, H-2), 2.33 (s, 3H, H-12), 2.13 (s, 3H, H-13).

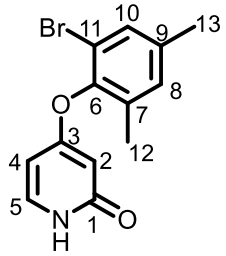
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4 (d, *J* = 11.5 Hz, C-3), 165.5 (d, *J* = 236.0 Hz, C-1), 148.8 (d, *J* = 18.3 Hz, C-6), 146.2 (C-5), 137.8 (C-9), 132.7 (C-10), 132.1 (C-7), 131.7 (C-8), 116.4 (C-11), 109.5 (d, *J* = 4.1 Hz, C-4), 95.8 (d, *J* = 42.1 Hz, C-2), 20.7 (C-13), 16.7 (C-12).

^{19}F NMR (471 MHz, $CDCl_3$) δ -66.1.

HRMS (ESI) exact mass calculated for $C_{13}H_{12}BrFNO^+$ $[M+H]^+$ requires *m/z* 296.0081, found *m/z* 296.0075.

IR (thin film) ν_{max}/cm^{-1} 2924, 1611, 1598, 1584, 1471, 1415, 1320, 1278, 1209, 1148, 1121, 1040, 977, 845, 778.

4-(2-Bromo-4,6-dimethylphenoxy)pyridin-2(1H)-one, 405:



A round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)-2-fluoropyridine (4.51 g, 15.2 mmol, 1.0 eq.) before suspending it in a mixture of H_2O and concentrated HCl (1:1, 102 mL, 0.15 M). The suspension was refluxed at 100 °C for 16 hours under nitrogen, before cooling to room temperature. The reaction mixture was ten poured over crushed ice (500 mL) with vigorous shaking and neutralised by adding solid Na_2CO_3, then transferred to a separatory funnel and extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a solid (4.17 g, 14.18 mmol, 93%), which was used without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 12.93 (s, 1H, H-NH), 7.30 – 7.26 (m, 2H, H-5,10), 6.99 (d, *J* = 2.0 Hz, 1H, H-8), 6.14 (dd, *J* = 7.2, 2.5 Hz, 1H, H-4), 5.56 (d, *J* = 2.5 Hz, 1H, H-2), 2.30 (s, 3H, H-13), 2.14 (s, 3H, H-12).

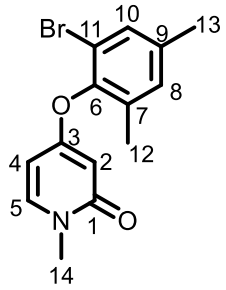
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.6 (C-1), 167.3 (C-3), 146.1 (C-6), 137.5 (C-5), 135.8 (C-9), 132.7 (C-10), 131.9 (C-7), 131.5 (C-8), 116.4 (C-11), 100.4 (C-4), 100.0 (C-2), 20.7 (C-13), 16.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{13}H_{13}BrNO_2^+$ $[M+H]^+$ requires *m/z* 294.0124, found *m/z* 294.0118.

IR (thin film) ν_{max}/cm^{-1} 3129, 2981, 2854, 1651, 1546, 1469, 1280, 1142, 1209, 1176, 1001, 805, 771, 735.

MP 194 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-1-methylpyridin-2(1H)-one, 151:



An oven-dried microwave vial was charged with 4-(2-bromo-4,6-dimethylphenoxy)pyridin-2(1H)-one (294.2 mg, 1.0 mmol, 1.0 eq.) before adding anhydrous MeOH (3.0 mL, 0.33 M) and methyl iodide (0.130 mL, 283.9 mg, 2.0 mmol, 2.0 eq.). With stirring, K_2CO_3 (276.4 mg, 2.0 mmol, 2.0 eq.) was added, then the vial was capped and heated at 60 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~50 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain an oil (305.0 mg, 0.99 mmol, 99%), which was used without any further purification.

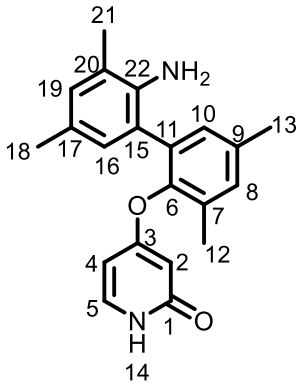
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (m, 1H, H-10), 7.24 (d, *J* = 7.5 Hz, 1H, H-5), 6.98 (d, *J* = 2.1 Hz, 1H, H-8), 6.09 (dd, *J* = 7.5, 2.7 Hz, 1H, H-4), 5.54 (d, *J* = 2.7 Hz, 1H, H-2), 3.48 (s, 3H, H-14), 2.30 (s, 3H, H-13), 2.13 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9 (C-1), 164.4 (C-3), 146.1 (C-6), 139.1 (C-5), 137.4 (C-9), 132.6 (C-10), 131.8 (C-7), 131.5 (C-8), 116.4 (C-11), 100.0 (C-4), 99.7 (C-2), 37.1 (C-14), 20.7 (C-13), 16.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{14}H_{15}BrNO_2^+$ $[M+H]^+$ requires *m/z* 308.0281, found *m/z* 308.0276.

IR (thin film) ν_{max}/cm^{-1} 2920, 1658, 1607, 1592, 1551, 1470, 1415, 1346, 1280, 1213, 1189, 1137, 1043, 978, 834, 704.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)pyridin-2(1H)-one, 406:



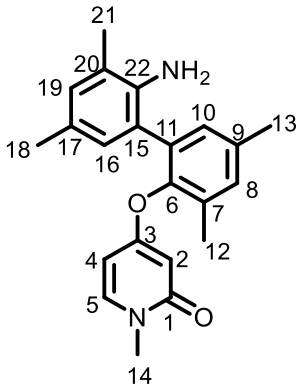
406 was prepared according to **General Procedure B** on a 0.10 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)pyridin-2(1H)-one (29.4 mg, 0.10 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (37.1 mg, 0.15 mmol, 1.5 eq.). Purified by flash column chromatography (0:100 to 5:95 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (17.6 mg, 0.05 mmol, 53%).

^{1}H NMR (200 MHz, $CDCl_3$) δ 12.78 (s, 1H, H-14), 6.78 (d, *J* = 2.1 Hz, 1H, H-5), 6.67 (d, *J* = 2.1 Hz, 1H, H-16), 6.11 (ddd, *J* = 8.4, 7.2, 2.5 Hz, 1H, H-10), 5.87 (dd, *J* = 7.3, 2.5 Hz, 1H, H-8), 5.57 (dd, *J* = 11.9, 2.4 Hz, 1H, H-19), 5.51 (d, *J* = 2.4 Hz, 1H, H-4), 3.57 (s, 2H, H-NH_2), 2.33 (s, 3H, H-13), 2.16 (s, 3H, H-18), 2.12 (s, 6H, H-12,21).

LRMS (ESI) exact mass calculated for $C_{21}H_{23}N_2O_2^+$ $[M+H]^+$ requires *m/z* 335.2, found *m/z* 335.2.

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

4-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylpyridin-2(1H)-one, 152:



152 was prepared according to **General Procedure B** on a 0.95 mmol scale using 4-(2-bromo-4,6-dimethylphenoxy)-1-methylpyridin-2(1H)-one (293.0 mg, 0.95 mmol, 1.0 eq.) and 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (353.4 mg, 1.43 mmol, 1.5 eq.). Purified by flash column chromatography (pure EtOAc) to obtain the title compound as a solid (154.7 mg, 0.44 mmol, 47%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 (d, *J* = 2.2 Hz, 1H, H-16), 7.03 – 7.00 (m, 2H, H-5,19), 6.78 (d, *J* = 2.1 Hz, 1H, H-10), 6.69 (d, *J* = 2.1 Hz, 1H, H-8), 5.80 (dd, *J* = 7.6, 2.7 Hz, 1H, H-4), 5.53 (d, *J* = 2.7 Hz, 1H, H-2), 3.56 – 3.42 (m, 2H, H-NH_2), 3.38 (s, 3H, H-14), 2.33 (s, 3H, H-13), 2.15 (s, 3H, H-18), 2.14 (s, 3H, H-21), 2.12 (s, 3H, H-12).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.9 (C-1), 164.3 (C-3), 146.9 (C-6), 139.6 (C-22), 138.5 (C-5), 136.2 (C-9), 132.8 (C-8), 131.7 (C-19), 131.3 (C-7), 130.6 (C-17), 130.5 (C-16),

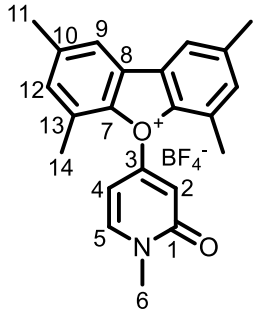
129.0 (C-11), 126.7 (C-10), 123.1 (C-15), 122.4 (C-20), 100.0 (C-2), 99.9 (C-4), 36.9 (C-14), 20.9 (C-18), 20.4 (C-13), 17.9 (C-21), 16.4 (C-12).

HRMS (ESI) exact mass calculated for $C_{22}H_{25}N_2O_2^+$ $[M+H]^+$ requires *m/z* 349.1911, found *m/z* 349.1903.

IR (thin film) ν_{max}/cm^{-1} 3463, 3351, 2919, 2859, 1657, 1598, 1549, 1484, 1345, 1208, 1133, 1040, 979, 862, 836, 736.

MP 195-198 °C.

2,4,6,8-Tetramethyl-5-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 153:



153 was prepared according to **General Procedure C** on a 0.35 mmol scale using 4-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylpyridin-2(1H)-one (123.0 mg, 0.35 mmol, 1.0 eq.) to obtain the title compound as a solid (113.1 mg, 0.27 mmol, 77%).

^{1}H NMR (600 MHz, CD_3CN) δ 7.86 (d, *J* = 2.1 Hz, 2H, H-12), 7.77 (d, *J* = 7.9 Hz, 1H, H-5), 7.34 (d, *J* = 2.1 Hz, 2H, H-9), 6.99 (d, *J* = 3.1 Hz, 1H, H-2), 6.28 (dd, *J* = 7.9, 3.1 Hz, 1H, H-4), 3.48 (s, 3H, H-6), 2.50 (s, 6H, H-14), 2.39 (s, 6H, H-11).

^{13}C NMR (151 MHz, CD_3CN) δ 167.7 (C-1), 162.0 (C-3), 160.4 (C-5), 145.5 (C-10), 143.4 (C-7), 135.4 (C-8), 125.2 (C-13), 124.7 (C-12), 122.6 (C-9), 111.9 (C-2), 97.0 (C-4), 38.4 (C-6), 21.2 (C-14), 16.8 (C-11).

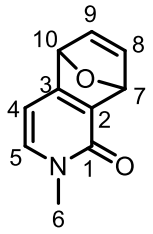
^{19}F NMR (565 MHz, CD_3CN) δ -151.7.

HRMS (ESI) exact mass calculated for $C_{22}H_{22}NO_2^+$ $[M]^+$ requires *m/z* 332.1645, found *m/z* 332.1640.

IR (thin film) ν_{max}/cm^{-1} 3069, 1670, 1560, 1525, 1459, 1345, 1270, 1222, 1059, 923, 735.

MP 156-158 °C.

2-Methyl-5,8-dihydro-5,8-epoxyisoquinolin-1(2H)-one, 154:



154 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (83.8 mg, 0.20 mmol, 1.0 eq.), furan (73 μL, 68.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 2:98 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (28.9 mg, 0.16 mmol, 83%).

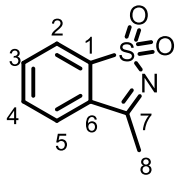
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 5.5, 1.8 Hz, 1H, H-9), 7.16 (d, *J* = 6.4 Hz, 1H, H-5), 7.00 (dd, *J* = 5.5, 1.9 Hz, 1H, H-), 6.37 (d, *J* = 6.4 Hz, 1H), 5.95 – 5.87 (m, 1H), 5.62 (dd, *J* = 1.9, 1.0 Hz, 1H), 3.53 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6 (C-1), 158.5 (C-3), 144.9 (C-9), 141.8 (C-5), 138.6 (C-9), 137.9 (C-2), 101.7 (C-4), 83.1 (C-7), 80.8 (C-10), 37.7 (C-6).

HRMS (ESI) exact mass calculated for $C_{10}H_{10}NO_2^+$ $[M+H]^+$ requires *m/z* 176.0706, found *m/z* 176.0703.

IR (thin film) ν_{max}/cm^{-1} 2925, 2852, 1654, 1572, 1544, 1439, 1408, 1364, 1302, 1277, 1208, 1028, 949, 837, 733.

3-Methylbenzo[d]isothiazole 1,1-dioxide, 410:



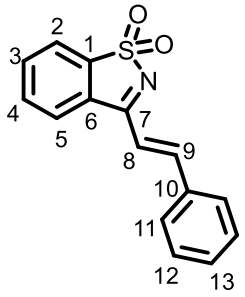
An oven-dried round bottom flask was charged with saccharin (1.50 g, 8.19 mmol, 1.0 eq.), before adding anhydrous THF (33 mL, 0.25 M) and cooling to 0 °C. With stirring, MeMgBr (3.0 M in Et_2O, 6.8 mL, 2.5 eq.) was added dropwise at 0 °C and the reaction was stirred for 2 hours under nitrogen at room temperature. After the reaction time, 1 M aqueous HCl (20 mL) was added dropwise to quench the reaction, then poured into deionised water (100 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crud solid. The crude was purified by flash column chromatography (50:50 to 75:25 EtOAc:pentane, v:v) to obtain the title compound as a solid (630.0 mg, 3.48 mmol, 42%). The NMR spectra are consistent with those available in the literature.[178]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.89 (m, 1H, H-2), 7.78 – 7.73 (m, 2H, H-3,5), 7.71 – 7.67 (m, 1H, H-4), 2.67 (s, 3H, H-8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4 (C-7), 139.7 (C-1), 134.1 (C-3 or 5), 133.7 (C-3 or 5), 131.7 (C-6), 124.3 (C-4), 122.5 (C-2), 17.7 (C-8).

HRMS (ESI) exact mass calculated for $C_8H_8NO_2S^+$ $[M+H]^+$ requires *m/z* 182.0270, found *m/z* 182.0270.

(E)-3-styrylbenzo[d]isothiazole 1,1-dioxide, 159:



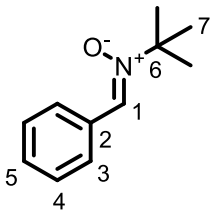
An oven-dried round bottom flask was charged with 3-methylbenzo[d]isothiazole 1,1-dioxide (605.8 mg, 3.34 mmol, 1.0 eq.), before adding EtOH (12 mL, 0.3 M) and heating to 80 °C. With stirring at 80 °C, benzaldehyde (0.750 mL, 2.2 eq.) was added dropwise, followed by piperidine (33 μL, 10 mol%) and the reaction was stirred for 15 minutes under nitrogen. After this time, glacial acetic acid (19 μL, 10 mol%) was added dropwise at 80 °C and the reaction was left to stir for 18 hours. After the reaction time, the mixture was cooled to 0 °C and then filtered, washing the obtained solid with ice-cold EtOH, and dried under vacuum to obtain a solid (779.7 mg, 2.90 mmol, 87%) which was used without further purification. The NMR spectra are consistent with those available in the literature.[179]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 15.7 Hz, 1H, H-8), 8.03 – 7.85 (m, 2H, H-2,3), 7.80 – 7.67 (m, 4H, H-4,5,11), 7.49 (dd, *J* = 5.2, 2.0 Hz, 3H, H-12,13), 7.30 (d, *J* = 15.7 Hz, 1H, H-9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (C-7), 148.0 (C-9), 133.7 (C-4), 133.7 (C-3), 132.0 (C-13), 129.4 (C-12), 129.2 (C-11), 123.9 (C-5), 123.0 (C-2), 113.7 (C-8).

HRMS (ESI) exact mass calculated for $C_{15}H_{12}NO_2S^+$ $[M+H]^+$ requires *m/z* 270.0583, found *m/z* 270.0579.

(Z)-*N*-tert-butyl-1-phenylmethanimine oxide, 167:



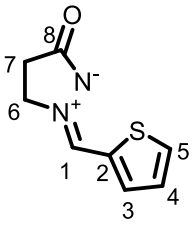
An oven-dried round bottom flask was charged with *N*-tert-butylhydroxylamine hydrochloride (1.00 g, 7.96 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (32 mL, 0.25 M) and adding benzaldehyde (0.810 mL, 844.7 mg, 7.96 mmol, 1.0 eq.). Pyrrolidine (0.790 mL, 679.2 mg, 9.55 mmol, 1.2 eq.) was added dropwise, then the reaction mixture was left to stir at room temperature for 1 h. After the reaction time, the solution was concentrated under vacuum and purified by flash column chromatography (50:50 EtOAc:pentane, v:v) to obtain a solid (1.33 g, 7.50 mmol, 94%). The NMR spectra are consistent with those available in the literature.[180]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 7.6, 2.3 Hz, 2H, H-3), 7.54 (s, 1H, H-1), 7.45 – 7.36 (m, 3H, H-4,5), 1.61 (s, 9H, H-7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 131.1 (C-5), 130.2 (C-1), 130.0 (C-2), 128.9 (C-3), 128.5 (C-4), 70.9 (C-6), 28.4 (C-7).

HRMS (ESI) exact mass calculated for $C_{11}H_{16}NO^+$ $[M+H]^+$ requires *m/z* 178.1226, found *m/z* 178.1225.

(Z)-5-oxo-2-(thiophen-2-ylmethylene)pyrazolidin-2-ium-1-ide, 168:



An oven-dried round bottom flask was charged with ethyl acrylate (2.4 mL, 2.20 g, 22.0 mmol, 1.1 eq.), before dissolving in EtOH (20 mL, 1.0 M) and adding hydrazine

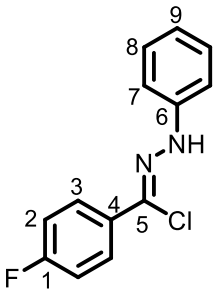
monohydrate (0.970 mL, 1.00 g, 20.0 mmol, 1.0 eq.) dropwise. The reaction mixture was then refluxed at 78 °C for 3 hours. After the reaction time, the mixture was cooled to room temperature and concentrated under vacuum to obtain a crude reside that was redissolved in MeOH (5 mL, 4.0 M). With stirring, 2-thiophenecarboxaldehyde (2.2 mL, 2.69 g, 24.0 mmol, 1.2 eq.) was added dropwise at room temperature and the reaction was left to stir for 18 hours. After the reaction time, the mixture was concentrated under vacuum to obtain a crude solid that was purified by trituration with CH_2Cl_2 and Et_2O to obtain the title compound (395.1 mg, 2.19 mmol, 11%). The NMR spectra are consistent with those available in the literature.[181]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 5.0 Hz, 1H, H-5), 7.56 (d, *J* = 3.9 Hz, 1H, H-3), 7.47 (s, 1H, H-1), 7.19 (dd, *J* = 5.0, 3.9 Hz, 1H, H-4), 4.59 – 4.32 (m, 2H, H-6), 3.09 – 2.73 (m, 2H, H-7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3 (C-8), 135.7 (C-5), 133.3 (C-3), 132.4 (C-2), 127.7 (C-4), 126.6 (C-1), 55.6 (C-6), 30.6 (C-7).

HRMS (ESI) exact mass calculated for $C_8H_9N_2OS^+$ $[M+H]^+$ requires *m/z* 181.0430, found *m/z* 181.0426.

(Z)-4-fluoro-*N*-phenylbenzohydrazonoyl chloride, 169:



An oven-dried round bottom flask was charged with phenylhydrazine hydrochloride (1.35 g, 9.32 mmol, 1.0 eq.), before suspending in EtOH (15.5 mL, 0.6 M) and adding 4-

fluorobenzaldehyde (1.0 mL, 1.16 g, 9.32 mmol, 1.0 eq.) dropwise. The reaction mixture was then refluxed at 80 °C for 1 hour. After the reaction time, the mixture was cooled to room temperature and concentrated under vacuum to obtain a crude residue of (E)-1-(4-fluorobenzylidene)-2-phenylhydrazine. In a separate flame-dried three-neck round bottom flask a suspension was prepared of NCS (2.12 g, 15.84 mmol, 1.7 eq.) in CH_2Cl_2 (10 mL, 1.0 M) under nitrogen, which was cooled to 0 °C. Me_2S (2.05 mL, 1.74 g, 27.96 mmol, 3.0 eq.) was added dropwise, then the reaction mixture was stirred for a further 30 minutes at 0 °C, then cooled to -78 °C. A suspension of the crude residue of (E)-1-(4-fluorobenzylidene)-2-phenylhydrazine in CH_2Cl_2 (10 mL) was then added dropwise, followed by stirring for 16 hours, allowing the reaction mixture to slowly reach room temperature overnight. After the reaction time, the mixture was transferred to a separatory funnel and diluted with CH_2Cl_2 (200 mL) before washing with deionised water (x3) and drying with $MgSO_4$. The solution was then concentrated under vacuum and purified by flash column chromatography (5:95 to 10:90 EtOAc:pentane, v:v) to obtain a solid (289.8 mg, 1.16 mmol, 13%). The NMR spectra are consistent with those available in the literature.[182]

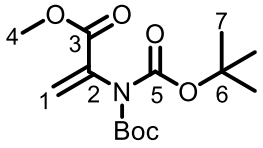
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H, H-NH), 7.93 – 7.82 (m, 2H, H-7), 7.10 – 7.03 (m, 6H, H-2,3,8), 7.01 – 6.95 (m, 1H, H-9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5 (d, J = 249.6 Hz, C-1), 141.9 (C-6), 130.9 (d, J = 7.9 Hz, C-5), 130.4 (C-8), 128.3 (d, J = 8.6 Hz, C-3), 123.8 (C-9), 115.6 (d, J = 22.0 Hz, C-4), 115.2 (d, J = 21.4 Hz, C-2), 113.6 (C-7).

^{19}F NMR (377 MHz, $CDCl_3$) δ -111.8.

HRMS (ESI) exact mass could not be detected.

Methyl 2-(bis(*tert*-butoxycarbonyl)amino)acrylate, 189:



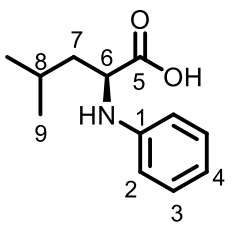
An oven-dried round bottom flask was charged with Boc-L-serine methyl ester (500.0 mg, 2.28 mmol, 1.0 eq.), before dissolving in anhydrous MeCN (2.3 mL, 1.0 M) and adding DMAP (56.2 mg, 20 mol%). The reaction mixture was then cooled to 0 °C and di-*tert*-butyl dicarbonate (995.2 mg, 4.56 mmol, 2.0 eq.) was added in small portions, then refluxed at 60 °C for 2 hours. After the reaction time, the mixture was cooled to room temperature and concentrated under vacuum to obtain a crude reside that was redissolved in EtOAc (100 mL). The obtained solution was then washed with 1 M aqueous $KHSO_4$ (x3), followed by saturated aqueous $NaHCO_3$ (x3), then dried with brine and $MgSO_4$. Following drying, it was concentrated under vacuum to obtain a crude solid (685.0 mg, 2.27 mmol, quantitative) that was used without further purification. The NMR spectra are consistent with those available in the literature.[183]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32 (s, 1H, H-1), 5.63 (s, 1H, H-1'), 3.78 (s, 3H, H-4), 1.45 (s, 18H, H-7).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1 (C-3), 150.8 (C-5), 136.2 (C-2), 124.8 (C-1), 83.3 (C-6), 52.5 (C-4), 28.0 (C-7).

HRMS (ESI) exact mass calculated for $C_{14}H_{24}NO_6^+$ $[M+H]^+$ requires *m/z* 302.1598, found *m/z* 302.1592.

Phenyl-L-leucine, 417:



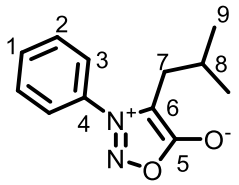
An oven-dried three-neck round bottom flask was charged with leucine (2.0 g, 15.24 mmol, 1.0 eq.), CuI (870.7 mg, 30 mol%) and Cs_2CO_3 (7.45 g, 22.86 mmol, 1.5 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DMF (15.2 mL, 1.0 M) was then added, followed by iodobenzene (2.1 mL, 3.73 g, 18.29 mmol, 1.2 eq.). The suspension was sparged with argon for 15 minutes, then heated to 120 °C for 16 hours. After the reaction time, the mixture was slowly transferred to a separatory funnel containing 1 M aqueous HCl (200 mL), then extracted with EtOAc (x3). Combined organics were washed with deionised water (x3), then dried with brine and $MgSO_4$. The solution was then concentrated under vacuum to obtain a crude solid, which was purified by passing it through a plug of silica, first eluting with CH_2Cl_2 to remove impurities, then flushed with EtOAc to remove the title compound from the column and obtain a solid (2.26 g, 10.90 mmol, 72%). The NMR spectra are consistent with those available in the literature.[184]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.7 Hz, 2H, H-3), 6.79 (t, *J* = 7.4 Hz, 1H, H-4), 6.64 (d, *J* = 7.8 Hz, 2H, H-2), 4.04 (s, 1H, H-6), 1.85 (h, *J* = 6.6 Hz, 1H, H-8), 1.70 (ddt, *J* = 28.5, 13.9, 7.4 Hz, 2H), 1.00 (d, *J* = 6.3 Hz, 3H, H-9), 0.95 (d, *J* = 6.3 Hz, 3H, H-9').

HRMS (ESI) exact mass calculated for $C_{12}H_{16}NO_2^-$ $[M-H]^-$ requires *m/z* 206.1187, found *m/z* 206.1180.

Due to the poor solubility of the title compound in $CDCl_3$, a quality ^{13}C spectrum could not be obtained.

4-Isobutyl-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate, 205:



An oven-dried round bottom flask was charged with phenyl-L-leucine (2.25 g, 10.86 mmol, 1.0 eq.) before dissolving in anhydrous THF (109 mL, 0.10 M) and cooling to 0 °C. *tert*-Butyl nitrite (1.9 mL, 1.68 g, 16.28 mmol, 1.5 eq.) was added dropwise, then the reaction mixture was brought to room temperature and left to stir for 1 h, until the full consumption of the starting material. The solution was cooled to 0 °C again before adding TFAA (1.6 mL, 2.51 g, 11.95 mmol, 1.1 eq.) dropwise. The reaction mixture was left to stir for 16 h, allowing it to slowly reach room temperature overnight. After the reaction time, the solution was partially concentrated under vacuum and poured into deionised water (200 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by passing through a plug of silica (eluting with 50:50 Et_2O:pentane, v:v) to obtain a crude, which was further purified by recrystallisation from EtOH to obtain a solid (548.5 mg, 2.51 mmol, 23%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.57 (m, 3H), 7.49 (d, J = 7.6 Hz, 2H), 2.37 (d, J = 7.3 Hz, 2H), 1.93 (hept, J = 6.7 Hz, 1H), 0.82 (d, J = 6.5 Hz, 6H).

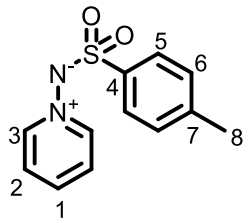
^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 134.1, 132.2, 130.2, 125.1, 109.0, 31.3, 27.4, 22.2.

HRMS (ESI) exact mass calculated for $C_{12}H_{15}N_2O_2^+$ $[M+H]^+$ requires *m/z* 219.1128, found *m/z* 219.1124.

IR (thin film) ν_{max}/cm^{-1} 3058, 2962, 2931, 2873, 1731, 1651, 1499, 1478, 1390, 1340, 1285, 1255, 1088, 939, 895, 861, 754, 737.

MP 108-110 °C.

Pyridin-1-ium-1-yl(tosyl)amide, 206:



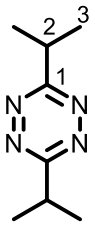
An oven-dried round bottom flask was charged with 1-aminopyridinium iodide (1.50 g, 6.76 mmol, 1.0 eq.) before suspending in anhydrous MeCN (45 mL, 0.15 M) and cooling to 0 °C. TsCl (1.42 g, 7.44 mmol, 1.1 eq.) was added, followed by DMAP (83.1 mg, 10 mol%) and K_2CO_3 (3.74 g, 27.0 mmol, 4.0 eq.). The reaction mixture was left to stir for 16 h, allowing it to slowly reach room temperature overnight. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was concentrated under vacuum and purified by flash column chromatography (0:100 to 5:95 MeOH:CH_2Cl_2, v:v) to obtain a solid (734.8 mg, 2.96 mmol, 44%). The NMR spectra are consistent with those available in the literature.[185]

^{1}H NMR (400 MHz, DMSO) δ 8.50 – 8.37 (m, 2H), 8.20 (tt, *J* = 7.7, 1.3 Hz, 1H), 7.86 – 7.75 (m, 2H), 7.45 – 7.37 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.31 (s, 3H).

^{13}C NMR (101 MHz, DMSO) δ 145.2, 140.8, 140.1, 139.2, 129.2, 127.4, 126.5, 20.8.

HRMS (ESI) exact mass calculated for $C_{12}H_{13}N_2O_2S^+$ $[M+H]^+$ requires *m/z* 249.0692, found *m/z* 249.0688.

3,6-Diisopropyl-1,2,4,5-tetrazine, 207:



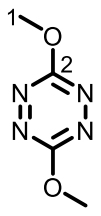
An oven-dried 50 mL round bottom flask was charged with hydrazine hydrate (7.5 mL, 7.81 g, 156.0 mmol, 7.8 eq.) before adding isobutyronitrile (1.8 mL, 1.38 g, 20.0 mmol, 1.0 eq.) dropwise, followed by ZnI_2 (320.0 mg, 5 mol%) in small portions. The reaction mixture was stirred at room temperature for 10 minutes, then refluxed at 60 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and transferred to a 250 mL conical flask containing a stir bar and cooled to 0 °C. With rapid stirring, a 0 °C solution of $NaNO_2$ (6.9 g, 100.0 mmol, 5.0 eq.) in deionised water (100 mL) was added dropwise to the suspension. After full addition, the reaction mixture was stirred for a further 10 minutes. Thereupon, 3 M aqueous HCl (approximately 70 mL) was added at 0 °C until cessation of gas formation and a pH of ~2. The reaction mixture was then poured into a separatory funnel and extracted with Et_2O (x3). Combined organics were washed with deionised water (x3), then dried with brine and $MgSO_4$. The solution was then concentrated under vacuum (water bath set at 45 °C, >500 mbar) to obtain a volatile oil (1.42 g, 8.54 mmol, 85%) that was used without further purification. The NMR spectra are consistent with those available in the literature.[186]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (hept, *J* = 6.9 Hz, 1H, H-2), 1.50 (d, *J* = 6.9 Hz, 6H, H-3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9 (C-1), 34.3 (C-2), 21.4 (C-3).

HRMS (ESI) exact mass calculated for $C_8H_{15}N_4^+$ $[M+H]^+$ requires *m/z* 167.1291, found *m/z* 167.1291.

3,6-Dimethoxy-1,2,4,5-tetrazine, 208:



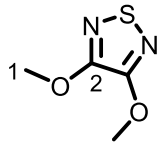
An oven-dried 50 mL round bottom flask was charged with 3,6-dichloro-1,2,4,5-tetrazine (1.0 g, 6.62 mmol, 1.0 eq.) before adding anhydrous MeOH (17 mL, 0.4 M), followed by NaOMe (1.25 g, 23.17 mmol, 3.5 eq.) in small portions. The reaction mixture was then stirred at room temperature for 48 hours. After the reaction time, the mixture was poured into EtOAc (200 mL) and washed with deionised water (x3), then dried with brine and $MgSO_4$. The solution was then concentrated under vacuum to obtain a solid (520.5 mg, 3.66 mmol, 55%) that was used without further purification. The NMR spectra are consistent with those available in the literature.[187]

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (s, 6H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (C-2), 56.8 (C-1).

HRMS (ESI) exact mass calculated for $C_4H_6N_4O_2^+$ $[M+H]^+$ requires *m/z* 143.0564, found *m/z* 143.0563.

3,4-Dimethoxy-1,2,5-thiadiazole, 210:



A flame-dried 2-neck round bottom flask was charged with anhydrous MeOH (21.0 mL, 0.5 M), then cooled to 0 °C. KO*t*-Bu (3.58 g, 31.9 mmol, 3.0 eq.) was added portion-wise with stirring. After full addition, 3,4-dichloro-1,2,5-thiadiazole (1.0 mL, 1.64 g, 10.6 mmol, 1.0 eq.) was added dropwise, then the reaction mixture was brought to room temperature and heated at 60 °C under nitrogen for 16 hours. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (200 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash

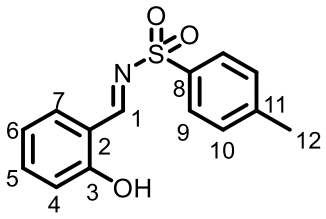
column chromatography (10:90 Et_2O:pentane, v:v) to obtain a solid (397.7 mg, 2.72 mmol, 26%). The NMR spectra are consistent with those available in the literature.[188]

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 57.7.

HRMS (APCI) exact mass calculated for $C_4H_7N_2O_2S^+$ $[M+H]^+$ requires *m/z* 147.0223, found *m/z* 147.0224.

(E)-*N*-(2-hydroxybenzylidene)-4-methylbenzenesulfonamide, 237:



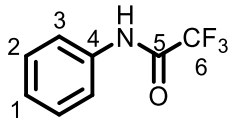
An oven-dried round bottom flask was charged with salicaldehyde (0.870 mL, 1.00 g, 8.19 mmol, 1.0 eq.) and 4-toluene sulfonamide (1.40 g, 8.19 mmol, 1.0 eq.) before adding EtOH (16 mL, 0.5 M), followed by p-toluenesulfonic acid monohydrate (156.0 mg, 10 mol%) in small portions. The reaction mixture was then refluxed at 80 °C for 24 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature, then poured into a separatory funnel containing ice water (200 mL) and extracted with EtOAc (x3). Combined organics were washed with deionised water (x3), then dried with brine and $MgSO_4$. The solution was then concentrated under vacuum to obtain a crude solid which was purified by flash column chromatography (25:75 to 35:65 Et_2O:pentane, v:v) to obtain a solid that was further purified by recrystallisation from EtOH (291.6 mg, 1.06 mmol, 13%). The NMR spectra are consistent with those available in the literature.[189]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (s, 1H, H-OH), 9.09 (s, 1H, H-1), 7.91 – 7.79 (m, 2H, H-9), 7.57 – 7.44 (m, 2H, H-5,7), 7.35 (d, *J* = 8.0 Hz, 2H, H-10), 7.07 – 6.95 (m, 2H, H-4,6), 2.44 (s, 3H, H-12).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6 (C-1), 162.3 (C-3), 145.2 (C-11), 137.5 (C-5), 135.5 (C-7), 135.2 (C-8), 130.2 (C-10), 128.1 (C-9), 120.4 (C-6), 118.1 (C-4), 116.8 (C-2), 21.8 (C-12).

HRMS (ESI) exact mass calculated for $C_{14}H_{14}NO_3S^+$ $[M+H]^+$ requires *m/z* 276.0689, found *m/z* 276.0683.

2,2,2-Trifluoro-*N*-phenylacetamide, 12:



A flame-dried round bottom flask was charged with aniline (1.0 mL, 1.02 g, 11.0 mmol, 1.0 eq.) and triethylamine (1.70 mL, 1.22 g, 12.1 mmol, 1.1 eq.) before dissolving in anhydrous CH_2Cl_2 (5.5 mL, 2.0 M) and cooling to 0 °C. TFAA (1.6 mL, 2.42 g, 11.52 mmol, 1.05 eq.) was added dropwise, then the reaction mixture was brought to room temperature and left to stir for 2 h, until the full consumption of the starting material. After the reaction time, the solution was partially concentrated under vacuum and poured into deionised water (100 mL), then extracted with EtOAc (x3). Combined organics were washed with 1 M aqueous HCl (x3), followed by saturated $NaHCO_3$ (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid, which was used without any further purification (1.86 g, 9.83 mmol, 89%). The NMR spectra are consistent with those available in the literature.[190]

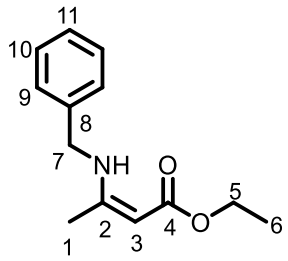
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H, H-NH), 7.60 – 7.53 (m, 2H, H-3), 7.40 (dd, *J* = 8.7, 7.2 Hz, 2H, H-2), 7.29 – 7.19 (m, 1H, H-1).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0 (q, *J* = 37.3 Hz, C-5), 135.2 (C-4), 129.5 (C-2), 126.6 (C-1), 120.7 (C-3), 115.9 (q, *J* = 288.7 Hz, C-6).

^{19}F NMR (377 MHz, $CDCl_3$) δ -75.7.

HRMS (ESI) exact mass not detected.

Ethyl (Z)-3-(benzylamino)but-2-enoate, 277:



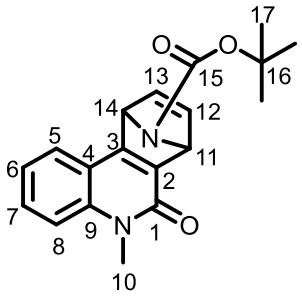
An oven-dried round bottom flask was charged with ethyl acetoacetate (0.970 mL, 999.5 mg, 7.68 mmol, 1.0 eq.) and benzylamine (0.840 mL, 822.9 mg, 7.68 mmol, 1.0 eq.) before adding glacial acetic acid (45 µL, 10 mol%) very slowly. The reaction mixture was then stirred at room temperature for two hours. After the reaction time, the mixture was poured into a separatory funnel containing CH_2Cl_2 (100 mL), then dried with brine and $MgSO_4$. The solution was then concentrated under vacuum to obtain a crude oil which was purified by flash column chromatography (5:95 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (1.49 g, 6.79 mmol, 88%). The NMR spectra are consistent with those available in the literature.[191]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H, H-NH), 7.41 – 7.19 (m, 5H, Ar Hs), 4.52 (s, 1H, H-3), 4.41 (d, *J* = 6.4 Hz, 2H, H-7), 4.09 (q, *J* = 7.1 Hz, 2H, H-5), 1.90 (s, 3H, H-1), 1.24 (t, *J* = 7.1 Hz, 3H, H-6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7 (C-4), 161.9 (C-2), 138.8 (C-8), 128.9 (C-10), 127.4 (C-9), 126.8 (C-11), 83.3 (C-3), 58.5 (C-5), 46.9 (C-7), 19.5 (C-1), 14.7 (C-6).

HRMS (ESI) exact mass calculated for $C_{13}H_{18}NO_2^+$ $[M+H]^+$ requires *m/z* 220.1332, found *m/z* 220.1328.

***tert*-Butyl 5-methyl-6-oxo-5,6,7,10-tetrahydro-7,10-epiminophenanthridine-11-carboxylate, 161:**



161 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (93.9 mg, 0.20 mmol, 1.0 eq.), *N*-Boc-pyrrole (0.170 mL, 167.2 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (40:60 to 45:55 EtOAc:pentane, v:v) to obtain the title compound as a solid (43.0 mg, 0.13 mmol, 66%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.9, 1.5 Hz, 1H, H-5), 7.57 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H, H-7), 7.40 – 7.35 (m, 1H, H-8), 7.31 – 7.24 (m, 1H, H-6), 7.23 – 7.18 (m, 1H, H-12), 7.10 (s, 1H, H-13), 5.93 (s, 1H, H-14), 5.87 (s, 1H, H-11), 3.71 (s, 3H, H-10), 1.39 (s, 9H, H-17).

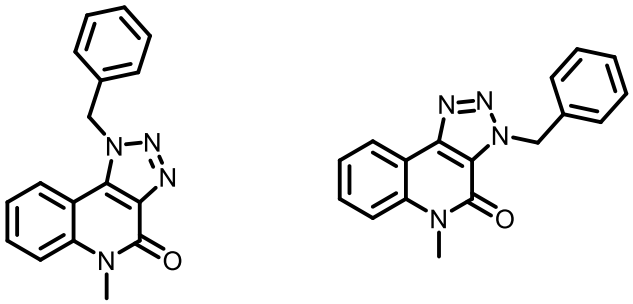
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.4 (C-1), 158.5 (C-15), 154.6 (C-9), 145.0 (C-12), 142.4 (C-13), 140.0 (C-3), 139.6 (C-2), 131.0 (C-7), 124.4 (C-5), 122.3 (C-6), 117.5 (C-4), 115.1 (C-8), 81.3 (C-16), 65.8 (C-11 or 14), 65.5 (C-11 or 14), 29.6 (C-10), 28.3 (C-17).

HRMS (ESI) exact mass calculated for $C_{19}H_{21}N_2O_3^+$ $[M+H]^+$ requires *m/z* 325.1547, found *m/z* 325.1538.

IR (thin film) ν_{max}/cm^{-1} 2979, 1711, 1650, 1587, 1561, 1453, 1393, 1369, 1256, 1165, 1082, 841, 759, 736.

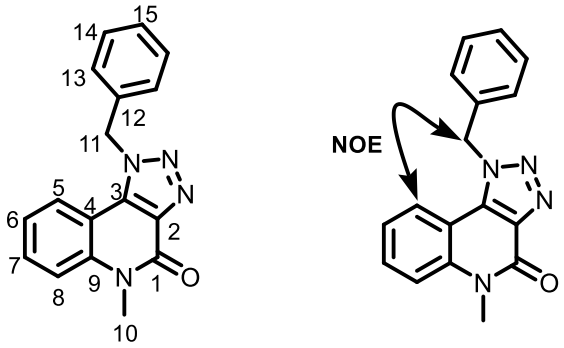
MP 177-179 °C.

1-Benzyl-5-methyl-1,5-dihydro-4H-[1,2,3]triazolo[4,5-c]quinolin-4-one, 171, and 3-benzyl-5-methyl-3,5-dihydro-4H-[1,2,3]triazolo[4,5-c]quinolin-4-one, 171':



171 and **171'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (93.9 mg, 0.20 mmol, 1.0 eq.), benzyl azide (125 μL, 133.2 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (50:50 to 95:5 EtOAc:pentane, v:v) to obtain major regioisomer **171** as a solid (34.8 mg, 0.12 mmol, 60%) and minor regioisomer **171'** as a solid (8.0 mg, 0.03 mmol, 14%). The overall yield refers to the combined masses of the two products. The regioisomeric ratio (1.5 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

1-Benzyl-5-methyl-1,5-dihydro-4H-[1,2,3]triazolo[4,5-c]quinolin-4-one, 171:



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.2, 1.5 Hz, 1H, H-5), 7.59 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H, H-7), 7.49 (dd, *J* = 8.6, 1.0 Hz, 1H, H-8), 7.37 – 7.29 (m, 3H, H-13,15), 7.22 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H, H-6), 7.16 (ddd, *J* = 8.0, 1.7, 0.9 Hz, 2H, H-14), 6.13 (s, 2H, H-11), 3.81 (s, 3H, H-10).

^{13}C NMR (151 MHz, $CDCl_3$) δ 156.6 (C-1), 139.5 (C-9), 137.3 (C-12), 134.4 (C-2), 134.1 (C-3), 131.1 (C-7), 129.5 (C-13), 128.7 (C-15), 126.5 (C-14), 123.8 (C-5), 122.8 (C-6), 116.2 (C-8), 110.3 (C-4), 54.0 (C-11), 29.9 (C-10).

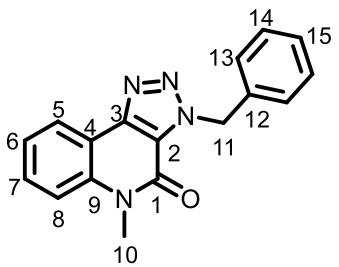
The NMR spectra are consistent with those available in the literature.

HRMS (ESI) exact mass calculated for $C_{17}H_{15}N_4O^+$ $[M+H]^+$ requires *m/z* 291.1240, found *m/z* 291.1235.

IR (thin film) ν_{max}/cm^{-1} 2927, 2854, 1679, 1624, 1578, 1561, 1520, 1497, 1456, 1438, 1419, 1326, 1244, 1119, 1050, 979, 903, 748.

MP 225-227 °C.

3-Benzyl-5-methyl-3,5-dihydro-4H-[1,2,3]triazolo[4,5-c]quinolin-4-one, 171':



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 7.9, 1.6 Hz, 1H, H-5), 7.58 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-7), 7.54 – 7.49 (m, 2H, H-13), 7.44 (d, *J* = 8.6 Hz, 1H, H-8), 7.42 – 7.38 (m, 1H, H-6), 7.36 – 7.27 (m, 3H, H-14,15), 6.12 (s, 2H, H-11), 3.78 (s, 3H, H-10).

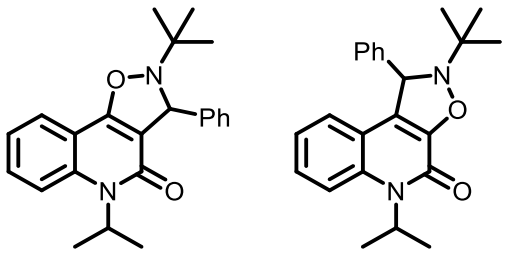
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.4 (C-1), 146.4 (C-3), 138.1 (C-9), 135.4 (C-12), 129.9 (C-7), 129.0 (C-14), 128.7 (C-13), 128.6 (C-15), 123.6 (C-6), 123.5 (C-5), 123.1 (C-2), 115.4 (C-8), 114.9 (C-4), 53.5 (C-11), 29.6 (C-10).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}N_4O^+$ $[M+H]^+$ requires *m/z* 291.1240, found *m/z* 291.1233.

IR (thin film) ν_{max}/cm^{-1} 2926, 2854, 1677, 1562, 1496, 1457, 1417, 1324, 1245, 1196, 1119, 1042, 984, 905, 796, 749.

MP 170-174 °C.

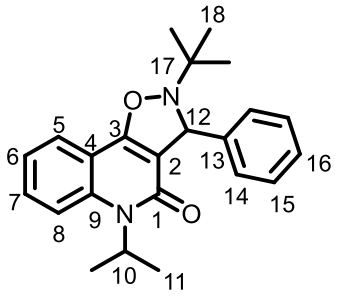
2-(*tert*-Butyl)-5-isopropyl-3-phenyl-3,5-dihydroisoxazolo[4,5-c]quinolin-4(2H)-one, 174, and 2-(*tert*-butyl)-5-isopropyl-1-phenyl-1,2-dihydroisoxazolo[5,4-c]quinolin-4(5H)-one, 174':



174 and **174'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-isopropyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (99.4 mg, 0.20 mmol, 1.0 eq.), (Z)-N-*tert*-butyl-1-phenylmethanimine oxide (177.3 mg, 1.0 mmol, 5.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 2:98 EtOAc:pentane, v:v) to obtain major regioisomer **174** as a solid (45.0 mg, 0.12 mmol, 62%) and minor

regioisomer **174'** as an oil (2.9 mg, 0.01 mmol, 4%). The overall yield refers to the combined masses of the two products. The regioisomeric ratio (17.0 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

2-(*tert*-Butyl)-5-isopropyl-3-phenyl-3,5-dihydroisoxazolo[4,5-c]quinolin-4(2H)-one, 174:



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (ddd, *J* = 8.2, 1.6, 0.7 Hz, 1H, H-5), 7.77 (dt, *J* = 8.5, 0.9 Hz, 1H, H-8), 7.58 (ddd, *J* = 8.5, 6.9, 1.6 Hz, 1H, H-7), 7.49 – 7.44 (m, 2H, H-14), 7.34 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H, H-6), 7.32 – 7.28 (m, 2H, H-15), 7.25 – 7.22 (m, 1H, H-16), 5.73 (s, 1H, H-12), 5.43 (hept, *J* = 6.2 Hz, 1H, H-10), 1.36 (d, *J* = 6.2 Hz, 3H, H-11), 1.26 (s, 9H, H-18), 1.01 (d, *J* = 6.2 Hz, 3H, H-11').

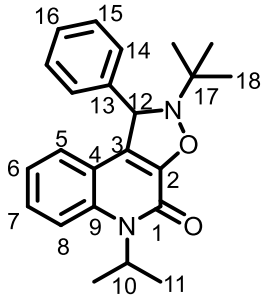
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9 (C-1), 158.5 (C-3), 148.2 (C-9), 142.7 (C-13), 129.9 (C-7), 128.2 (C-15), 127.9 (C-14), 127.4 (C-15), 127.2 (C-8), 123.3 (C-6), 121.9 (C-5), 113.3 (C-4), 108.3 (C-2), 68.3 (C-10), 65.7 (C-12), 62.0 (C-17), 25.4 (C-18), 22.3 (C-11), 21.8 (C-11').

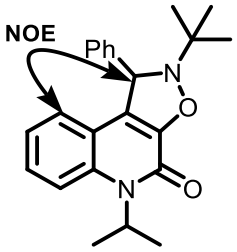
HRMS (ESI) exact mass calculated for $C_{23}H_{27}N_2O_2^+$ $[M+H]^+$ requires *m/z* 363.2067, found *m/z* 363.2057.

IR (thin film) ν_{max}/cm^{-1} 3063, 3033, 2977, 2932, 2360, 1685, 1649, 1606, 1515, 1494, 1435, 1402, 1325, 1234, 1209, 1173, 1110, 1028, 941, 852, 724.

MP 59-62 °C.

2-(*tert*-Butyl)-5-isopropyl-1-phenyl-1,2-dihydroisoxazolo[5,4-c]quinolin-4(5H)-one, 174':





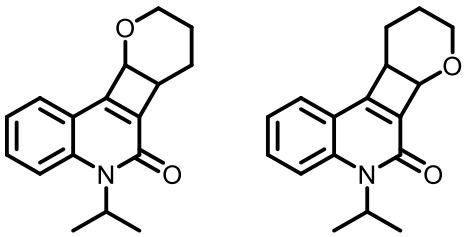
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.4, 1.2 Hz, 1H, H-8), 7.44 – 7.40 (m, 2H, H-15), 7.37 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H, H-6), 7.32 (t, *J* = 7.6 Hz, 2H, H-14), 7.27 – 7.24 (m, 2H, H-5,16), 7.17 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H, H-7), 5.92 (s, 1H, H-12), 5.66 (hept, *J* = 6.2 Hz, 1H, H-10), 1.49 (d, *J* = 6.2 Hz, 3H, H-11), 1.48 (d, *J* = 6.2 Hz, 3H, H-11'), 1.23 (s, 9H, H-18).

^{13}C NMR (151 MHz, $CDCl_3$) δ 149.1 (C-1), 143.1 (C-2), 142.4 (C-9), 141.3 (C-13), 128.9 (C-14), 128.8 (C-4), 128.3 (C-15), 128.0 (C-16), 127.5 (C-8), 126.2 (C-6), 124.5 (C-7), 122.3 (C-3), 122.0 (C-5), 69.2 (C-10), 67.8 (C-12), 61.8 (C-17), 25.4 (C-18), 22.2 (C-11), 22.1 (C-11').

HRMS (ESI) exact mass calculated for $C_{23}H_{27}N_2O_2^+$ $[M+H]^+$ requires *m/z* 363.2067, found *m/z* 363.2059.

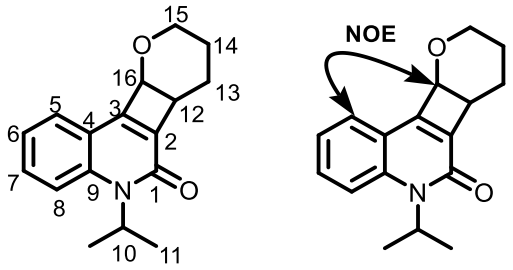
IR (thin film) ν_{max}/cm^{-1} 3055, 2960, 2927, 2853, 2342, 1804, 1728, 1623, 1577, 1474, 1405, 1323, 1242, 1206, 1150, 1110, 1028, 972, 844, 752.

5-Isopropyl-6b,8,9,10a-tetrahydro-5H-pyrano[2',3':3,4]cyclobuta[1,2-c]quinolin-6(7H)-one, 193', and 5-isopropyl-5,6b,8,9,10,10a-hexahydro-6H-pyrano[3',2':3,4]cyclobuta[1,2-c]quinolin-6-one, 193:



193 and **193'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-isopropyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (99.5 mg, 0.20 mmol, 1.0 eq.) and 3,4-dihydro-2H-pyran (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 3:97 EtOAc:pentane, v:v) to obtain major regioisomer **193'** as an oil (29.3 mg, 0.11 mmol, 54%) and minor regioisomer **193** as an oil (17.0 mg, 0.06 mmol, 32%). The overall yield refers to the combined masses of the two products. The regioisomeric ratio (1.5 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

5-Isopropyl-6b,8,9,10a-tetrahydro-5H-pyrano[2',3':3,4]cyclobuta[1,2-c]quinolin-6(7H)-one, 193':



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 8.5, 0.9 Hz, 1H, H-8), 7.77 (dd, *J* = 8.0, 1.5 Hz, 1H, H-5), 7.57 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H, H-7), 7.37 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H, H-6), 5.57 (hept, *J* = 6.2 Hz, 1H, H-10), 5.34 (d, *J* = 4.3 Hz, 1H, H-16), 3.86 (dt, *J* = 6.3, 4.5 Hz, 1H, H-12), 3.84 – 3.79 (m, 1H, H-15), 3.74 (ddd, *J* = 11.3, 7.8, 5.7 Hz, 1H, H-15'), 2.24 (dddd, *J* = 13.8, 10.0, 6.3, 5.2 Hz, 1H, H-13), 2.07 (ddt, *J* = 13.8, 6.5, 5.0

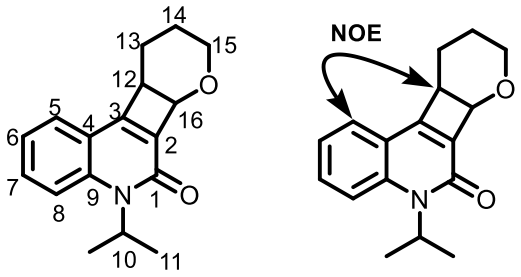
Hz, 1H, H-13'), 1.73 – 1.56 (m, 1H, H-14), 1.46 – 1.42 (m, 1H, H-14'), 1.41 (d, *J* = 6.2 Hz, 3H, H-11), 1.40 (d, *J* = 6.2 Hz, 3H, H-11').

^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3 (C-1), 155.8 (C-3), 147.2 (C-9), 130.9 (C-2), 128.8 (C-7), 128.5 (C-8), 124.4 (C-6), 122.9 (C-5), 122.3 (C-4), 73.1 (C-16), 68.2 (C-10), 62.6 (C-15), 42.5 (C-12), 22.7 (C-13), 22.3 (C-11), 19.9 (C-14).

HRMS (ESI) exact mass calculated for $C_{17}H_{20}NO_2^+$ $[M+H]^+$ requires *m/z* 270.1489, found *m/z* 270.1483.

IR (thin film) ν_{max}/cm^{-1} 3064, 2978, 2942, 2871, 1629, 1602, 1561, 1459, 1386, 1275, 1228, 1166, 1109, 1015, 983, 890, 842, 763.

5-Isopropyl-5,6b,8,9,10,10a-hexahydro-6H-pyrano[3',2':3,4]cyclobuta[1,2-c]quinolin-6-one, 193:



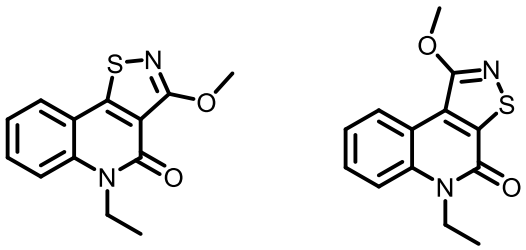
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (dt, *J* = 8.4, 0.9 Hz, 1H, H-8), 7.64 (ddd, *J* = 8.0, 1.5, 0.7 Hz, 1H, H-5), 7.60 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H, H-7), 7.35 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H, H-6), 5.49 (hept, *J* = 6.2 Hz, 1H, H-10), 5.26 (d, *J* = 4.3 Hz, 1H, H-16), 3.91 (dt, *J* = 6.3, 4.7 Hz, 1H, H-12), 3.83 (t, *J* = 7.2 Hz, 2H, H-15), 2.33 (dddd, *J* = 13.7, 9.7, 6.4, 5.2 Hz, 1H, H-13), 2.12 (ddt, *J* = 13.7, 6.8, 5.2 Hz, 1H, H-13'), 1.64 (ddd, *J* = 13.7, 6.9, 5.3 Hz, 1H, H-14), 1.43 (m, 7H, H-11,14').

^{13}C NMR (151 MHz, $CDCl_3$) δ 158.3 (C-1), 157.2 (C-3), 148.4 (C-9), 129.7 (C-7), 128.8 (C-8), 128.6 (C-2), 124.1 (C-6), 122.9 (C-5), 122.0 (C-4), 72.9 (C-16), 69.0 (C-10), 62.0 (C-15), 42.9 (C-12), 22.9 (C-13), 22.5 (C-11), 22.4 (C-11'), 19.8 (C-14).

HRMS (ESI) exact mass calculated for $C_{17}H_{20}NO_2^+$ $[M+H]^+$ requires *m/z* 270.1489, found *m/z* 270.1482.

IR (thin film) ν_{max}/cm^{-1} 3059, 2978, 2943, 2871, 1774, 1733, 1627, 1561, 1459, 1388, 1321, 1290, 1232, 1169, 1145, 1074, 1019, 959, 840, 764.

5-Ethyl-3-methoxyisothiazolo[4,5-c]quinolin-4(5H)-one, 218, and 5-ethyl-1-methoxyisothiazolo[5,4-c]quinolin-4(5H)-one, 218':



218 and **218'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-Ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (96.7 mg, 0.20 mmol, 1.0 eq.), 3,4-dimethoxy-1,2,5-thiadiazole (146.2 mg, 1.0 mmol, 5.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (10:90 to 50:50 EtOAc:pentane, v:v) to obtain the major regioisomer as a solid (22.6 mg, 0.09 mmol, 43%) and the minor regioisomer as a solid (15.2 mg, 0.06 mmol, 29%). The overall yield refers to the combined masses of the two products. The regioisomeric ratio (1.6 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture. The regiochemistry of each product could not be determined unambiguously by 2D NMR techniques, therefore the following spectra have been left unassigned.

Major Regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.57 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H), 7.47 (dd, *J* = 8.7, 1.1 Hz, 1H), 7.33 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 4.28 (s, 3H), 1.42 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 156.2, 148.8, 137.5, 129.3, 124.9, 124.4, 122.8, 117.4, 114.9, 56.8, 37.7, 12.9.

HRMS (ESI) exact mass calculated for $C_{13}H_{13}N_2O_2S^+$ $[M+H]^+$ requires *m/z* 261.0692, found *m/z* 261.0689.

IR (thin film) ν_{max}/cm^{-1} 2926, 1734, 1644, 1581, 1511, 1447, 1405, 1350, 1313, 1182, 1102, 1046, 969, 822, 746.

MP 126 °C.

Minor Regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.63 (ddd, *J* = 8.7, 7.3, 1.5 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.31 – 7.24 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.21 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H).

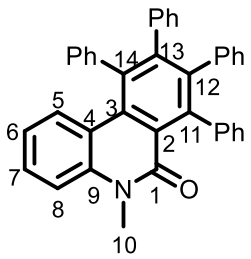
^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 164.6, 157.1, 137.6, 132.1, 125.4, 122.5, 115.7, 115.5, 113.5, 56.8, 37.4, 12.9.

HRMS (ESI) exact mass calculated for $C_{13}H_{13}N_2O_2S^+$ $[M+H]^+$ requires *m/z* 261.0692, found *m/z* 261.0688.

IR (thin film) ν_{max}/cm^{-1} 2982, 1664, 1613, 1575, 1505, 1439, 1396, 1309, 1277, 1176, 1097, 1029, 995, 753.

MP 146-148 °C.

5-Methyl-7,8,9,10-tetraphenylphenanthridin-6(5H)-one, 212:



212 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (93.9 mg, 0.20 mmol, 1.0 eq.), 2,3,4,5-tetraphenylcyclopenta-2,4-dien-1-one (192.2 mg, 0.5 mmol, 2.5 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (10:90 to 50:50 Et_2O:pentane, v:v) to obtain the title compound as a solid (33.5 mg, 0.07 mmol, 33%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.29 (m, 2H, Ar Hs), 7.21 (dt, J = 8.4, 1.0 Hz, 1H, H-8), 7.17 – 7.02 (m, 10H, Ar Hs), 6.88 – 6.80 (m, 6H, Ar Hs), 6.75 – 6.62 (m, 5H, Ar Hs), 3.63 (s, 3H, H-10).

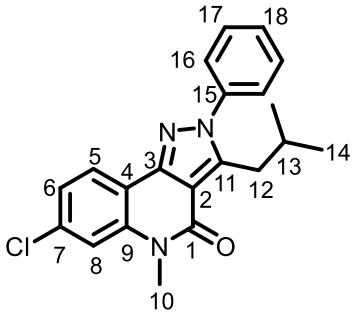
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.3 (C-1), 145.9, 143.0, 142.8, 142.6, 141.7, 139.8, 139.6, 138.8, 137.5, 133.7, 131.5, 131.3, 131.0, 129.9, 129.3, 128.6, 128.4, 127.1, 126.8, 126.6, 125.7, 125.7, 125.5, 125.1, 120.8, 120.3, 114.4, 30.8 (C-10). *Note that the unassigned peaks correspond to aromatic carbons.*

HRMS (ESI) exact mass calculated for $C_{38}H_{28}NO^+$ $[M+H]^+$ requires *m/z* 514.2165, found *m/z* 514.2150.

IR (thin film) ν_{max}/cm^{-1} 3056, 2928, 2854, 1677, 1655, 1571, 1522, 1457, 1417, 1340, 1262, 1223, 1159, 1089, 1027, 1013, 983, 905, 795, 750, 720.

MP 292-232 °C.

7-Chloro-3-isobutyl-5-methyl-2-phenyl-2,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one, 213:



213 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(7-chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (100.7 mg, 0.20 mmol, 1.0 eq.), 4-isobutyl-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (218.3 mg, 1.0 mmol, 5.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 25:75 EtOAc:pentane, v:v) to obtain the title compound as a solid (58.4 mg, 0.16 mmol, 80%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 8.4, 1.0 Hz, 1H, H-5), 7.56 – 7.47 (m, 5H, H-16,17,18), 7.33 (t, *J* = 1.5 Hz, 1H, H-8), 7.20 (ddd, *J* = 8.4, 1.8, 0.9 Hz, 1H, H-6), 3.66 (s, 3H, H-10), 3.07 (d, *J* = 7.5 Hz, 2H, H-12), 2.08 – 2.00 (m, 1H, H-13), 0.79 (d, *J* = 6.7 Hz, 6H, H-14).

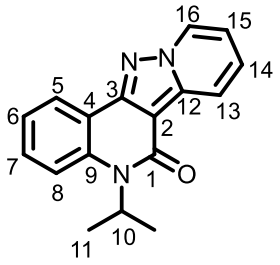
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1 (C-1), 147.4 (C-11), 146.7 (C-3), 140.5 (C-9), 139.4 (C-15), 135.3 (C-7), 129.5 (C-17), 129.4 (C-18), 126.7 (C-16), 124.3 (C-5), 122.5 (C-6), 115.3 (C-8), 114.5 (C-4), 110.2 (C-2), 33.9 (C-12), 29.0 (C-13), 28.9 (C-10), 22.4 (C-14).

HRMS (ESI) exact mass calculated for $C_{21}H_{21}ClN_3O^+$ $[M+H]^+$ requires *m/z* 366.1368, found *m/z* 366.1359.

IR (thin film) ν_{max}/cm^{-1} 2959, 2870, 1725, 1662, 1616, 1500, 1459, 1393, 1313, 1254, 1229, 1163, 1101, 1027, 1008, 912, 820, 739.

MP 170-174 °C.

5-Isopropylindolizino[1,2-c]quinolin-6(5H)-one, 214:



214 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-isopropyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (99.4 mg, 0.20 mmol, 1.0 eq.), pyridin-1-ium-1-yl(tosyl)amide (74.5 mg, 0.3 mmol, 1.5 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (23.7 mg, 0.09 mmol, 43%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (dt, *J* = 6.9, 1.1 Hz, 1H, H-16), 8.50 (dd, *J* = 7.8, 1.6 Hz, 1H, H-5), 8.26 (dt, *J* = 8.7, 1.2 Hz, 1H, H-13), 7.90 (dd, *J* = 8.4, 1.2 Hz, 1H, H-8), 7.65 (ddd, *J* = 8.4, 7.0, 1.6 Hz, 1H, H-7), 7.48 (m, 2H), 7.15 (td, *J* = 6.9, 1.5 Hz, 1H, H-15), 5.85 (hept, *J* = 6.2 Hz, 1H, H-10), 1.55 (d, *J* = 6.2 Hz, 6H, H-11).

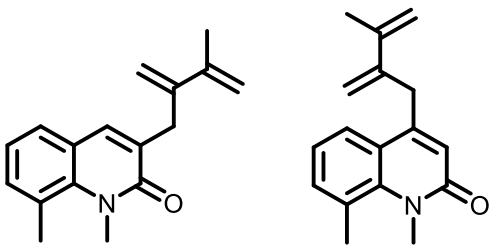
^{13}C NMR (151 MHz, $CDCl_3$) δ 157.7 (C-1), 152.7 (C-3), 146.1 (C-9), 136.4 (C-2), 129.4 (C-12), 128.9 (C-16), 127.6 (C-8), 125.5 (C-6), 123.8 (C-14), 122.7 (C-5), 119.7 (C-13), 117.7 (C-4), 115.3 (C-15), 100.4 (C-2), 68.3 (C-10), 22.5 (C-11).

HRMS (ESI) exact mass calculated for $C_{17}H_{16}N_3O^+$ $[M+H]^+$ requires *m/z* 278.1288, found *m/z* 278.1275.

IR (thin film) ν_{max}/cm^{-1} 2979, 2930, 1685, 1644, 1620, 1592, 1530, 1461, 1442, 1383, 1354, 1308, 1205, 1143, 1052, 923, 838, 751.

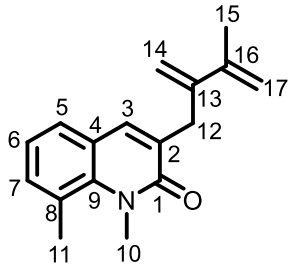
MP 115-118 °C.

1,8-Dimethyl-3-(3-methyl-2-methylenebut-3-en-1-yl)quinolin-2(1H)-one, 225', and 1,8-dimethyl-4-(3-methyl-2-methylenebut-3-en-1-yl)quinolin-2(1H)-one, 225:



225 and **225'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1,8-dimethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (96.7 mg, 0.20 mmol, 1.0 eq.), 2,3-dimethyl-1,3-butadiene (114 µL, 82.1 mg, 1.0 mmol, 5.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 30:70 EtOAc:pentane, v:v) to obtain major regioisomer **225'** as an oil (8.0 mg, 0.03 mmol, 16%). Minor regioisomer **225** could not be isolated, therefore the overall yield refers to the mass of major regioisomer **225'**. The regioisomeric ratio (12.9 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

1,8-Dimethyl-3-(3-methyl-2-methylenebut-3-en-1-yl)quinolin-2(1H)-one, 225':



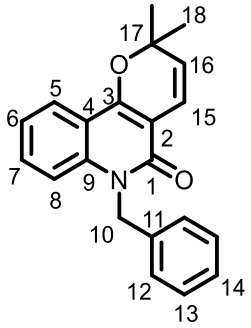
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 1.5 Hz, 1H, H-3), 7.31 (dd, *J* = 7.5, 1.7 Hz, 1H, H-5), 7.27 (d, *J* = 7.5 Hz, 1H, H-7), 7.08 (t, *J* = 7.5 Hz, 1H, H-6), 5.35 (d, *J* = 1.4 Hz, 1H, H-17), 5.08 (s, 1H, H-17'), 5.07 (s, 1H, H-14), 4.97 (d, *J* = 1.3 Hz, 1H, H-14'), 3.87 (s, 3H, H-10), 3.64 (d, *J* = 1.3 Hz, 2H, H-12), 2.72 (s, 3H, H-11), 1.97 (d, *J* = 1.4 Hz, 3H, H-15).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6 (C-1), 145.2 (C-13), 141.9 (C-16), 140.3 (C-9), 136.4 (C-3), 134.2 (C-7), 131.5 (C-2), 126.9 (C-8), 124.7 (C-5), 122.5 (C-6), 122.4 (C-4), 115.6 (C-14), 114.3 (C-17), 37.0 (C-12), 34.6 (C-10), 24.1 (C-15), 21.1 (C-11).

HRMS (ESI) exact mass calculated for $C_{17}H_{20}NO^+$ $[M+H]^+$ requires *m/z* 254.1539, found *m/z* 254.1536.

IR (thin film) ν_{max}/cm^{-1} 2929, 1650, 1624, 1591, 1575, 1459, 1388, 1293, 1234, 1150, 1125, 1077, 1040, 969, 901, 763, 737.

6-Benzyl-2,2-dimethyl-2,6-dihydro-5H-pyrano[3,2-c]quinolin-5-one, 196:



196 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-benzyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (109.1 mg, 0.20 mmol, 1.0 eq.), 3-methylbut-2-enal (96 μL, 84.1 mg, 1.0 mmol, 5.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 15:85 EtOAc:pentane, v:v) to obtain the title compound as a solid (42.9 mg, 0.14 mmol, 68%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.9, 1.6 Hz, 1H, H-5), 7.39 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H, H-7), 7.31 – 7.26 (m, 2H, H-12), 7.22 (m, 4H, H-8,13,14), 7.17 (ddd, *J* = 7.9, 7.1, 1.0 Hz, 1H, H-6), 6.82 (d, *J* = 9.9 Hz, 1H, H-15), 5.57 (d, *J* = 9.9 Hz, 1H, H-16), 5.54 (s, 2H, H-10), 1.55 (s, 6H, H-18).

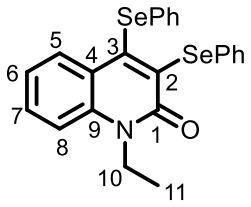
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.3 (C-1), 155.7 (C-3), 138.9 (C-9), 136.9 (C-11), 131.0 (C-7), 128.8 (C-12), 127.2 (C-8), 126.7 (C-13), 126.5 (C-16), 123.3 (C-5), 121.9 (C-6), 118.1 (C-15), 116.4 (C-14), 115.0 (C-4), 105.7 (C-2), 79.1 (C-17), 45.9 (C-10), 28.5 (C-18).

HRMS (ESI) exact mass calculated for $C_{21}H_{20}NO_2^+$ $[M+H]^+$ requires *m/z* 318.1489, found *m/z* 318.1481.

IR (thin film) ν_{max}/cm^{-1} 2979, 1649, 1568, 1498, 1456, 1417, 1361, 1323, 1229, 1144, 1118, 1078, 1028, 972, 889, 841, 733.

MP 80-81 °C.

1-Ethyl-3,4-bis(phenylselanyl)quinolin-2(1H)-one, 260:



260 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (96.7 mg, 0.20 mmol, 1.0 eq.), diphenyl diselenide (124.9 mg, 0.4 mmol, 2.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (20:80 to 25:75 EtOAC:pentane, v:v) to obtain the title compound as a solid (60.3 mg, 0.12 mmol, 62%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 8.2, 1.5 Hz, 1H, H-5), 7.51 (ddd, *J* = 8.6, 7.1, 1.5 Hz, 1H, H-7), 7.47 – 7.43 (m, 2H, H-Ar Hs), 7.36 (dd, *J* = 8.6, 1.0 Hz, 1H, H-8), 7.33 – 7.29 (m, 2H, H-Ar Hs), 7.23 – 7.19 (m, 3H, H-Ar Hs), 7.18 (qd, *J* = 3.9, 1.8 Hz, 3H, H-Ar Hs), 7.10 (ddd, *J* = 8.2, 7.1, 1.0 Hz, 1H, H-6), 4.35 (q, *J* = 7.1 Hz, 2H, H-10), 1.35 (t, *J* = 7.1 Hz, 3H, H-11).

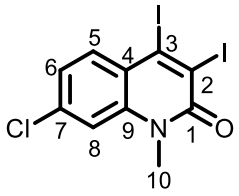
^{13}C NMR (151 MHz, $CDCl_3$) δ 158.7 (C-1), 148.6 (C-3), 138.6 (C-2), 137.0 (C-9), 132.7 (C-Ar C), 132.3 (C-Ar C), 132.1 (C-Ar C), 131.9 (C-5), 131.3 (C-Ar C), 131.0 (C-7), 129.6 (C-Ar C), 129.2 (C-Ar C), 127.2 (C-Ar C), 127.1 (C-Ar C), 122.4 (C-4), 122.3 (C-6), 114.3 (C-8), 39.0 (C-10), 12.7 (C-11).

HRMS (ESI) exact mass calculated for $C_{23}H_{20}NOSe_2^+$ $[M+H]^+$ requires *m/z* 485.9870, found *m/z* 485.9861.

IR (thin film) ν_{max}/cm^{-1} 3056, 2981, 1683, 1646, 1601, 1577, 1495, 1459, 1417, 1328, 1263, 1158, 1090, 1022, 941, 807, 737.

MP 72-74 °C.

7-Chloro-3,4-diiodo-1-methylquinolin-2(1H)-one, 259:



259 was prepared according to **General Procedure D** on a 0.20 mmol scale using 5-(7-chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (100.7 mg, 0.20 mmol, 1.0 eq.), iodine (101.5 mg, 0.4 mmol, 2.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (10:90 to 20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (22.5 mg, 0.05 mmol, 25%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.8 Hz, 1H, H-5), 7.30 (d, *J* = 1.9 Hz, 1H, H-8), 7.16 (dd, *J* = 8.8, 1.9 Hz, 1H, H-6), 3.76 (s, 3H, H-10).

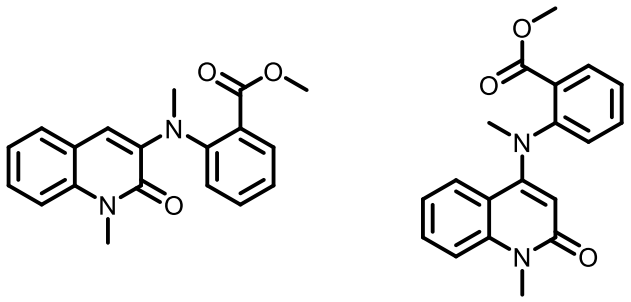
^{13}C NMR (151 MHz, $CDCl_3$) δ 158.0 (C-1), 138.9 (C-4), 138.7 (C-5), 138.3 (C-7), 127.8 (C-3), 124.3 (C-6), 122.5 (C-4), 114.6 (C-8), 32.3 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_7ClI_2NO^+$ $[M+H]^+$ requires *m/z* 445.8300, found *m/z* 445.8291.

IR (thin film) ν_{max}/cm^{-1} 2930, 2870, 1734, 1647, 1568, 1459, 1388, 1321, 1290, 1273, 1257, 1170, 1148, 1110, 1039, 907, 839, 765, 702.

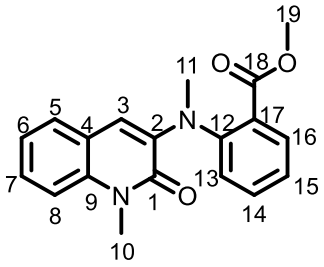
MP 205-206 °C.

Methyl 2-(methyl(1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)amino)benzoate, 244', and methyl 2-(methyl(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)amino)benzoate, 244:



244 and **244'** were prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (93.9 mg, 0.20 mmol, 1.0 eq.), methyl 2-(methylamino)benzoate (66.1 mg, 0.4 mmol, 2.0 eq.) and THF (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 60:40 EtOAc:pentane, v:v) to obtain major regioisomer **244'** as an oil (28.1 mg, 0.09 mmol, 44%). Minor regioisomer **244** could not be isolated in a sufficient purity, therefore the overall yield refers to the mass of major regioisomer **244'**. The regioisomeric ratio (3.7 : 1.0) was determined by quantitative ^1H NMR analysis of the crude reaction mixture.

Methyl 2-(methyl(1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)amino)benzoate, 244':



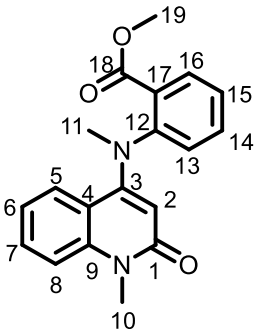
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.6, 1.7 Hz, 1H, H-5), 7.48 – 7.43 (m, 2H, H-7,16), 7.39 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H, H-14), 7.28 (d, *J* = 8.4 Hz, 1H, H-8), 7.17 (m, 3H, H-6,13,15), 7.05 (s, 1H, H-3), 3.68 (s, 3H, H-19), 3.61 (s, 3H, H-10), 3.34 (s, 3H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8 (C-18), 159.1 (C-1), 149.5 (C-12), 139.9 (C-9), 136.4 (C-2), 132.6 (C-7), 131.2 (C-5), 127.3 (C-14), 127.2 (C-16), 126.2 (C-4), 124.4 (C-15), 123.8 (C-13), 122.4 (C-6), 121.5 (C-17), 119.6 (C-3), 113.8 (C-8), 52.0 (C-10), 41.7 (C-11), 30.1 (C-19).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}N_2O_3^+$ $[M+H]^+$ requires *m/z* 323.1390, found *m/z* 323.1384.

IR (thin film) ν_{max}/cm^{-1} 2949, 1725, 1648, 1598, 1489, 1470, 1346, 1308, 1245, 1118, 1081, 1043, 994, 737, 638.

Methyl 2-(methyl(1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)amino)benzoate, 244:



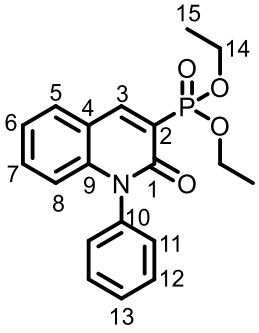
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (dt, *J* = 7.8, 1.2 Hz, 1H, H-5), 7.40 (m, 2H, H-14,16), 7.36 – 7.29 (m, 2H, H-7,13), 7.20 (t, *J* = 7.8 Hz, 1H, H-6), 6.93 (d, *J* = 8.0 Hz, 1H, H-8), 6.89 (t, *J* = 7.7 Hz, 1H, H-15), 6.35 (s, 1H, H-2), 3.83 (s, 3H, H-19), 3.70 (s, 3H, H-10), 3.28 (s, 3H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.3 (C-18), 163.3 (C-1), 154.7 (C-3), 149.6 (C-12), 140.8 (C-9), 133.1 (C-7), 131.9 (C-5), 130.2 (C-14), 127.1 (C-17), 127.0 (C-16), 126.3

(C-8), 125.3 (C-6), 121.2 (C-15), 117.5 (C-4), 114.6 (C-13), 107.0 (C-2), 52.5 (C-19), 43.8 (C-11), 29.4 (C-10).

Due to the low purity of the title compound, no further characterisation was performed.

Diethyl (2-oxo-1-phenyl-1,2-dihydroquinolin-3-yl)phosphonate, 290:



290 was prepared according to **General Procedure D** on a 0.20 mmol scale using 2,4,6,8-tetramethyl-5-(2-oxo-1-phenyl-1,2-dihydroquinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (106.3 mg, 0.20 mmol, 1.0 eq.), triethyl phosphite (35 µL, 33.2 mg, 0.20 mmol, 1.0 eq.) and MeCN (4.0 mL, 0.05 M). Purified by flash column chromatography (0:100 to 2:98 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (41.2 mg, 0.12 mmol, 58%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 17.6 Hz, 1H), 7.69 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.42 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H), 7.28 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 8.5 Hz, 1H), 4.35 – 4.25 (m, 4H), 1.36 (t, *J* = 7.0 Hz, 6H).

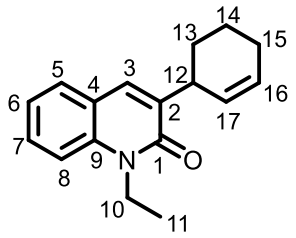
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.3 (d, J = 12.3 Hz, C-1), 149.6 (d, J = 6.2 Hz, C-3), 142.9 (d, J = 2.1 Hz, C-9), 137.2 (C-10), 132.6 (C-12), 130.4 (C-5), 130.0 (C-13), 129.2 (C-11), 129.0 (C-7), 122.9 (C-6), 122.5 (d, J = 196.5 Hz, C-2), 119.2 (d, J = 16.4 Hz, C-4), 116.2 (C-8), 63.4 (d, J = 6.2 Hz, C-14), 16.6 (d, J = 6.3 Hz, C-15).

^{31}P NMR (243 MHz, $CDCl_3$) δ 13.1.

HRMS (ESI) exact mass calculated for $C_{19}H_{21}NO_4P^+$ $[M+H]^+$ requires *m/z* 358.1203, found *m/z* 358.1193.

IR (thin film) ν_{max}/cm^{-1} 2985, 2928, 1661, 1617, 1595, 1562, 1494, 1450, 1390, 1322, 1294, 1247, 1129, 1026, 971, 759.

3-(Cyclohex-2-en-1-yl)-1-ethylquinolin-2(1H)-one, 224':

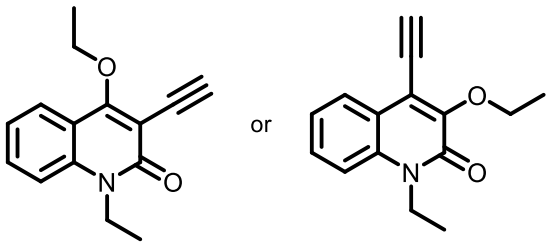


224' was prepared according to **General Procedure D** on a 0.025 mmol scale using 5-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (12.1 mg, 0.025 mmol, 1.0 eq.), cyclohexane (13 µL, 10.5 mg, 0.125 mmol, 5.0 eq.) and MeCN (0.5 mL, 0.05 M). Purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (0.9 mg, 0.004 mmol, 15%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H, H-5), 7.50 (m, 2H, H-3,7), 7.36 (d, *J* = 8.5 Hz, 1H, H-8), 7.20 (t, *J* = 7.5 Hz, 1H, H-6), 6.05 – 5.95 (m, 1H, H-17), 5.68 (d, *J* = 10.2 Hz, 1H, H-16), 4.52 – 4.30 (m, 2H, H-10), 3.88 (m, 1H, H-12), 2.08 (m, 3H, H-13,14 or 15), 1.62 (m, 3H, H-13,14 or 15), 1.37 (t, *J* = 7.1 Hz, 3H, H-11).

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

4-Ethoxy-1-ethyl-3-ethynylquinolin-2(1H)-one, 267, or 3-ethoxy-1-ethyl-4-ethynylquinolin-2(1H)-one, 267':

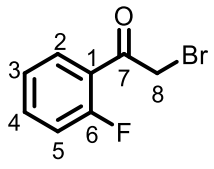


267 or **267'** was prepared according to **General Procedure D** on a 0.025 mmol scale using 5-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (12.1 mg, 0.025 mmol, 1.0 eq.), ethoxyacetylene (ca. 50% w/w in hexanes, 25 μL, 0.125 mmol, 5.0 eq.) and MeCN (0.5 mL, 0.05 M). Purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (0.2 mg, 0.0008 mmol, 3%). The regiochemistry of the product could not be determined unambiguously, therefore the following spectrum has been left unassigned.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 4.45 (q, *J* = 7.0 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 1H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.37 (t, *J* = 7.2 Hz, 3H).

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

2-Bromo-1-(2-fluorophenyl)ethan-1-one, 496:



A flame-dried round bottom flask was charged with 1-(2-fluorophenyl)ethan-1-one (1.72 g, 12.45 mmol, 1.0 eq.) before dissolving in AcOH (18 mL, 0.7 M) and partially cooling the solution in an ice bath close to its freezing point. Br_2 (0.670 mL, 2.09 g, 13.07 mmol,

1.05 eq.) was added dropwise with stirring, then the solution was stirred at room temperature for 3 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude oil, which was redissolved in EtOAc (300 mL) and washed with deionised water (x3), saturated aqueous $NaHCO_3$ (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain an oil that was used without any further purification (2.57 g, 11.84 mmol, 95%). The NMR spectra are consistent with those available in the literature.[192]

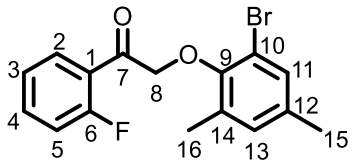
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (td, *J* = 7.6, 1.9 Hz, 1H, H-2), 7.58 (dddd, *J* = 8.4, 7.2, 5.1, 1.9 Hz, 1H, H-4), 7.30 – 7.24 (m, 1H, H-3), 7.16 (ddd, *J* = 11.3, 8.4, 1.1 Hz, 1H, H-5), 4.52 (d, *J* = 2.4 Hz, 2H, H-8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.2 (d, *J* = 4.2 Hz, C-7), 161.8 (d, *J* = 254.7 Hz, C-6), 135.8 (d, *J* = 9.3 Hz, C-4), 131.6 (d, *J* = 2.3 Hz, C-2), 125.0 (d, *J* = 3.4 Hz, C-3), 122.8 (d, *J* = 12.9 Hz, C-1), 116.8 (d, *J* = 23.8 Hz, C-5), 36.1 (d, *J* = 10.2 Hz, H-8).

^{19}F NMR (377 MHz, $CDCl_3$) δ -108.4.

HRMS (ESI) exact mass not detected.

2-(2-Bromo-4,6-dimethylphenoxy)-1-(2-fluorophenyl)ethan-1-one, 442:



An oven-dried 100 mL round bottom flask was charged with 2-bromo-1-(2-fluorophenyl)ethan-1-one (2.50 g, 11.52 mmol, 1.0 eq.) before adding acetone (58 mL, 0.20 M), followed by 2-bromo-4,6-dimethylphenol (2.78 g, 13.82 mmol, 1.2 eq.). K_2CO_3 (2.39 g, 17.28 mmol, 1.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 56 °C for 16 hours under nitrogen. After the reaction time, the

mixture was cooled to room temperature and filtered through Celite, eluting with EtOAc. Combined organics were concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.92 g, 5.69 mmol, 49%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (td, *J* = 7.5, 1.9 Hz, 1H, H-2), 7.57 (dddd, *J* = 8.3, 7.2, 5.2, 1.9 Hz, 1H, H-4), 7.30 (td, *J* = 7.5, 1.0 Hz, 1H, H-3), 7.20 (d, *J* = 2.4 Hz, 1H, H-11), 7.14 (ddd, *J* = 11.2, 8.3, 1.0 Hz, 1H, H-5), 6.95 – 6.93 (m, 1H, H-13), 5.13 (d, *J* = 3.2 Hz, 2H, H-8), 2.31 (s, 3H, H-15), 2.26 (s, 3H, H-16).

^{13}C NMR (151 MHz, $CDCl_3$) δ 191.8 (d, *J* = 4.9 Hz, C-7), 162.3 (d, *J* = 254.0 Hz, C-6), 151.7 (C-9), 135.6 (C-12), 135.5 (d, *J* = 9.4 Hz, C-4), 132.9 (C-14), 131.5 (C-11), 131.3 (C-13), 131.0 (d, *J* = 3.1 Hz, C-2), 125.0 (d, *J* = 3.2 Hz, C-3), 123.0 (d, *J* = 14.7 Hz, C-1), 116.7 (d, *J* = 11.5 Hz, C-5), 116.6 (C-10), 77.6 (d, *J* = 12.6 Hz, C-8), 20.6 (C-16), 16.7 (C-15).

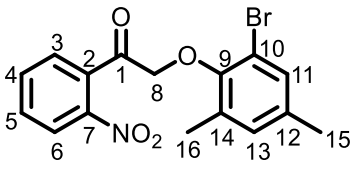
^{19}F NMR (471 MHz, $CDCl_3$) δ -107.8.

HRMS (ESI) exact mass calculated for $C_{16}H_{15}BrFO_2^+$ $[M+H]^+$ requires *m/z* 337.0234, found *m/z* 337.0228.

IR (thin film) ν_{max}/cm^{-1} 2920, 1697, 1611, 1478, 1454, 1374, 1278, 1224, 1209, 1127, 1105, 1068, 1037, 977, 865, 827, 808, 758, 738.

MP 88-90 °C.

2-(2-Bromo-4,6-dimethylphenoxy)-1-(2-nitrophenyl)ethan-1-one, 441:



An oven-dried 100 mL round bottom flask was charged with 2-bromo-2′-nitroacetophenone (2.0 g, 8.20 mmol, 1.0 eq.) before adding acetone (41 mL, 0.20 M),

followed by 2-bromo-4,6-dimethylphenol (1.98 g, 9.84 mmol, 1.2 eq.). K_2CO_3 (1.70 g, 12.30, 1.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 56 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and filtered through Celite, eluting with EtOAc. Combined organics were concentrated under vacuum to obtain a crude solid. The crude was purified by trituration with CH_2Cl_2/pentane to obtain the title compound as a solid (2.54 g, 6.97 mmol, 85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 8.2, 1.1 Hz, 1H, H-6), 7.78 (td, *J* = 7.5, 1.1 Hz, 1H, H-5), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H, H-4), 7.55 (dd, *J* = 7.5, 1.4 Hz, 1H, H-3), 7.11 (d, *J* = 2.1 Hz, 1H, H-11), 6.87 (d, *J* = 2.1 Hz, 1H, H-13), 4.75 (s, 2H, H-8), 2.21 (s, 3H, H-15), 2.15 (s, 3H, H-16).

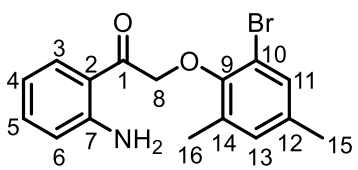
^{13}C NMR (126 MHz, $CDCl_3$) δ 200.0 (C-1), 150.6 (C-9), 147.0 (C-7), 135.9 (C-12), 135.4 (C-2), 134.5 (C-5), 132.8 (C-14), 131.4 (C-11 or 13), 131.3 (C-11 or 13), 131.1 (C-4), 128.5 (C-3), 123.8 (C-6), 116.3 (C-10), 75.5 (C-8), 20.5 (C-15), 16.4 (C-16).

HRMS (ESI) exact mass calculated for $C_{16}H_{15}BrNO_4^+$ $[M+H]^+$ requires *m/z* 364.0179, found *m/z* 364.0177.

IR (thin film) ν_{max}/cm^{-1} 2923, 1715, 1572, 1530, 1349, 1278, 1245, 1211, 1127, 1045, 1029, 983.

MP 104 °C.

1-(2-Aminophenyl)-2-(2-bromo-4,6-dimethylphenoxy)ethan-1-one, 494:



An oven-dried 100 mL round bottom flask was charged with 2-(2-bromo-4,6-dimethylphenoxy)-1-(2-nitrophenyl)ethan-1-one (2.44 g, 6.70 mmol, 1.00 eq.) and iron powder (3.74 g, 67.00 mmol, 10.00 eq.) before adding EtOAc:H_2O (4:1, 22.5 mL, 0.30 M), followed by glacial acetic acid (13.4 mL, 2 mL per mmol).The suspension was heated at 78 °C for 2 hours. After the reaction time, the suspension was cooled to room temperature before diluting with EtOAc to twice its volume, then neutralised with solid Na_2CO_3 and passed through a short plug of Celite, eluting with further EtOAc. Combined organics were washed with saturated aqueous Na_2CO_3 (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid (2.18 g, 6.52 mmol, 97%), which was used without further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.2, 1.5 Hz, 1H, H-3), 7.28 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1H, H-5), 7.21 (d, *J* = 2.1 Hz, 1H, H-11), 6.94 (d, *J* = 2.1 Hz, 1H, H-13), 6.69 (dd, *J* = 8.4, 1.1 Hz, 1H, H-6), 6.62 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H, H-4), 6.35 (s, 2H, H-NH_2), 5.13 (s, 2H, H-8), 2.30 (s, 3H, H-15), 2.26 (s, 3H, H-16).

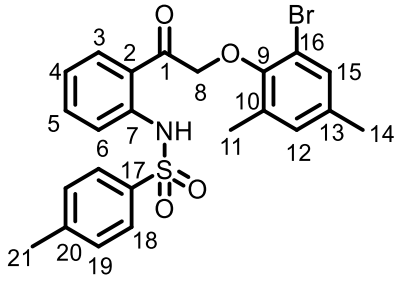
^{13}C NMR (151 MHz, $CDCl_3$) δ 195.0 (C-1), 151.9 (C-9), 150.8 (C-7), 135.6 (C-12), 134.9 (C-5), 132.9 (C-14), 131.5 (C-11), 131.3 (C-13), 129.9 (C-3), 117.6 (C-6), 116.8 (C-2), 116.0 (C-4), 115.6 (C-10), 74.5 (C-8), 20.6 (C-16), 16.8 (C-15).

HRMS (ESI) exact mass calculated for $C_{16}H_{17}BrNO_2^+$ $[M+H]^+$ requires *m/z* 334.0437, found *m/z* 334.0430.

IR (thin film) ν_{max}/cm^{-1} 3460, 3349, 3046, 2922, 1663, 1618, 1587, 1552, 1454, 1279, 1213, 1061, 968, 853.

MP 95-100 °C.

***N*-(2-(2-(2-Bromo-4,6-dimethylphenoxy)acetyl)phenyl)-4-methylbenzenesulfonamide, 501**:



An oven-dried round bottom flask was charged with 1-(2-aminophenyl)-2-(2-bromo-4,6-dimethylphenoxy)ethan-1-one (900.6 mg, 2.69 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (18.0 mL, 0.15 M). TsCl (768.3 mg, 4.03 mmol, 1.5 eq.) was added in portions and the solution was cooled to 0 °C before adding anhydrous pyridine (0.650 mL, 8.07 mmol, 3.0 eq.) dropwise. After full addition, the reaction mixture was slowly brought to room temperature and left to stir under nitrogen for 16 hours. After the reaction time, the mixture was poured into deionised water (~200 mL) and extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid, which was purified by flash column chromatography (20:80 EtOAc:Pentane, v:v) to give the title compound as a solid (1.07 g, 2.19 mmol, 81%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 11.21 (s, 1H, H-NH), 7.78 (dd, *J* = 8.7, 1.1 Hz, 1H, H-3), 7.77 – 7.74 (m, 3H, H-6,18), 7.50 (ddd, *J* = 8.7, 7.3, 1.5 Hz, 1H, H-4), 7.23 (d, *J* = 8.0 Hz, 2H, H-19), 7.20 (d, *J* = 2.0 Hz, 1H, H-15), 7.06 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H, H-5), 6.94 (dd, *J* = 2.1, 1.0 Hz, 1H, H-12), 5.05 (s, 2H, H-8), 2.36 (s, 3H, H-21), 2.26 (s, 3H, H-14), 2.25 (s, 3H, H-11).

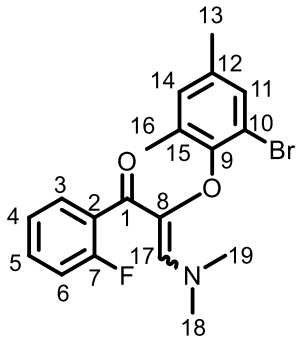
^{13}C NMR (151 MHz, $CDCl_3$) δ 197.2 (C-1), 151.5 (C-9), 144.1 (C-20), 140.6 (C-7), 136.7 (C-17), 136.0 (C-13), 135.5 (C-5), 132.8 (C-15), 131.6 (C-3), 131.4 (C-10), 130.4 (C-12), 129.8 (C-19), 127.4 (C-18), 122.9 (C-2), 120.2 (C-4), 119.7 (C-6), 116.5 (C-16), 74.7 (C-8), 21.7 (C-21), 20.6 (C-14), 16.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{23}H_{23}BrNO_4S^+$ $[M+H]^+$ requires *m/z* 488.0526, found *m/z* 488.0517.

IR (thin film) ν_{max}/cm^{-1} 3184, 1673, 1640, 1604, 1497, 1453, 1342, 1266, 1162, 1092, 1070, 976, 814.

MP 158-163 °C.

2-(2-Bromo-4,6-dimethylphenoxy)-3-(dimethylamino)-1-(2-fluorophenyl)prop-2-en-1-one, 498:



An oven-dried microwave vial was charged with 2-(2-bromo-4,6-dimethylphenoxy)-1-(2-fluorophenyl)ethan-1-one (168.6 mg, 0.5 mmol, 1.0 eq.) before dissolving in anhydrous toluene (0.5 mL, 1.0 M). *N*,*N*-Dimethylformamide dimethyl acetal (90 µL, 89.4 mg, 0.75 mmol, 1.5 eq.) was added and the solution was refluxed at 100 °C for 16 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude oil, which was purified by flash column chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as an oil (138.9 mg, 0.35 mmol, 71%).

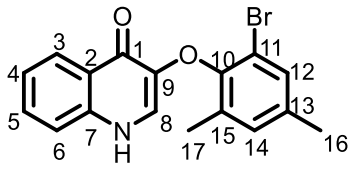
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.7, 2.7 Hz, 1H, H-3), 7.46 – 7.33 (m, 3H, H-4,5,6), 7.30 (d, *J* = 2.0 Hz, 1H, H-11), 7.05 – 7.01 (m, 1H, H-14), 5.63 (s, 1H, H-17), 3.67 (s, 6H, H-18,19), 2.33 (s, 3H, H-13), 2.16 (s, 3H, H-16).

^{13}C NMR (126 MHz, $CDCl_3$) δ 161.5 (C-1), 157.7 (d, *J* = 3.1 Hz, C-9), 156.3 (d, *J* = 242.3 Hz, C-7), 144.2 (C-17), 136.0 (C-12), 135.1 (d, *J* = 1.7 Hz, C-8), 130.7 (C-5), 130.2

(C-11), 129.8 (C-3), 117.7 (d, *J* = 24.0 Hz, C-15), 115.0 (d, *J* = 8.6 Hz, C-14), 114.4 (C-4), 114.3 (d, *J* = 8.0 Hz, C-2), 107.5 (d, *J* = 24.3 Hz, C-6), 98.5 (C-10), 27.8 (C-18,19), 19.0 (C-13), 14.8 (C-16).

^{19}F NMR (470 MHz, $CDCl_3$) δ -120.5.

3-(2-Bromo-4,6-dimethylphenoxy)quinolin-4(1H)-one, 454:



An oven-dried round bottom flask was charged with *N*-(2-(2-(2-Bromo-4,6-dimethylphenoxy)acetyl)phenyl)-4-methylbenzenesulfonamide (932.0 mg, 1.91 mmol, 1.0 eq.) before dissolving in anhydrous toluene (19.0 mL, 0.10 M). *N*,*N*-Dimethylformamide dimethyl acetal (0.380 mL, 340.8 mg, 2.86 mmol, 1.5 eq.) was added and the solution was refluxed at 60 °C under nitrogen for 16 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude solid, which was passed through a plug of silica, eluting it with 30:70 EtOAc:pentane, v:v to remove impurities, then flushed with MeOH to obtain the title compound as a solid (416.3 mg, 1.06 mmol, 63%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 13.36 (s, 1H, H-NH), 8.47 (m, 1H, H-3), 7.93 (s, 1H, H-8), 7.55 (d, *J* = 7.8 Hz, 1H, H-5), 7.32 (t, *J* = 7.8 Hz, 1H, H-4), 7.16 – 7.11 (m, 1H, H-6), 7.02 (s, 1H, H-12), 6.75 (s, 1H, H-14), 2.29 (s, 3H, H-16), 1.78 (s, 3H, H-17).

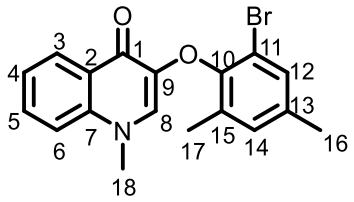
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.5 (C-1), 147.4 (C-10), 140.7 (C-7), 139.1 (C-9), 136.2 (C-13), 132.6 (C-15), 131.8 (C-12), 131.5 (C-14), 131.3 (C-5), 125.2 (C-3), 125.1 (C-3), 124.2 (C-6), 123.2 (C-4), 119.6 (C-8), 116.6 (C-11), 20.8 (C-16), 16.4 (C-17).

HRMS (ESI) exact mass calculated for $C_{19}H_{20}BrFNO_2^+$ $[M+H]^+$ requires *m/z* 344.0281, found *m/z* 344.0274.

IR (thin film) ν_{max}/cm^{-1} 2925, 2360, 1694, 1562, 1511, 1474, 1371, 1280, 1217, 1125, 981, 853.

MP 244-245 °C.

3-(2-Bromo-4,6-dimethylphenoxy)-1-methylquinolin-4(1H)-one, 493:



An oven-dried round bottom flask was charged with 3-(2-bromo-4,6-dimethylphenoxy)quinolin-4(1H)-one (416.3 mg, 1.21 mmol, 1.0 eq.), before adding anhydrous DMF (6.1 mL, 0.2 M) and cooling to 0 °C. With stirring, NaH (60% suspension in mineral oil, 72.4 mg, 1.81 mmol, 1.5 eq.) was added in small portions. After full addition and gas evolution, the reaction mixture was stirred at 0 °C for 10 minutes. Methyl iodide (0.150 mL, 343.5 mg, 2.42 mmol, 2.0 eq.) was added dropwise at 0 °C and the reaction was stirred for 16 hours under nitrogen at room temperature. After the reaction time, the mixture was poured into deionised water (~100 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a solid (410.8 mg, 1.15 mmol, 95%) which was used without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 – 8.53 (m, 1H, H-3), 7.66 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H, H-5), 7.41 – 7.35 (m, 2H, H-4,6), 7.27 (d, *J* = 2.1 Hz, 1H, H-12), 7.03 – 6.99 (m, 1H, H-14), 6.91 (s, 1H, H-8), 3.72 (s, 3H, H-18), 2.32 (s, 3H, H-16), 2.24 (s, 3H, H-17).

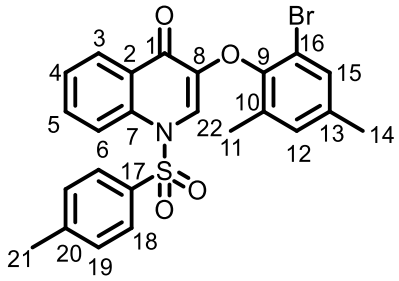
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.8 (C-1), 148.4 (C-10), 140.8 (C-9), 139.2 (C-7), 136.3 (C-13), 133.0 (C-15), 131.9 (C-5), 131.8 (C-12), 131.6 (C-14), 128.5 (C-8), 127.5 (C-3), 126.7 (C-2), 122.9 (C-4), 116.6 (C-11), 115.1 (C-6), 40.9 (C-18), 20.7 (C-16), 17.0 (C-17).

HRMS (ESI) exact mass calculated for $C_{18}H_{17}BrNO_2^+$ $[M+H]^+$ requires *m/z* 358.0437, found *m/z* 358.0430.

IR (thin film) ν_{max}/cm^{-1} 2925, 1627, 1592, 1551, 1505, 1472, 1305, 1282, 1215, 1163, 1129, 1043, 979.

MP 218 °C.

3-(2-Bromo-4,6-dimethylphenoxy)-1-tosylquinolin-4(1H)-one, 502:



An oven-dried round bottom flask was charged with N-(2-(2-(2-Bromo-4,6-dimethylphenoxy)acetyl)phenyl)-4-methylbenzenesulfonamide (932.0 mg, 1.91 mmol, 1.0 eq.) before dissolving in anhydrous toluene (19.0 mL, 0.10 M). *N*,*N*-Dimethylformamide dimethyl acetal (0.380 mL, 340.8 mg, 2.86 mmol, 1.5 eq.) was added and the solution was refluxed at 60 °C under nitrogen for 16 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude solid, which was purified by flash column chromatography (30:70 EtOAc:pentane, v:v) to obtain the title compound as a solid (120.9 mg, 0.24 mmol, 13%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 8.1, 1.7 Hz, 1H, H-3), 8.32 (d, *J* = 8.8 Hz, 1H, H-6), 7.79 (s, 1H, H-22), 7.65 – 7.62 (m, 2H, H-18), 7.60 (ddd, *J* = 8.8, 7.1, 1.7 Hz, 1H, H-5), 7.39 (ddd, *J* = 8.1, 7.1, 0.9 Hz, 1H, H-4), 7.33 (d, *J* = 1.9 Hz, 1H, H-15), 7.25 (d, *J* = 8.1 Hz, 2H, H-19), 7.07 (dd, *J* = 2.3, 1.1 Hz, 1H, H-12), 2.37 (s, 3H, H-21), 2.35 (s, 3H, H-14), 2.25 (s, 3H, H-11).

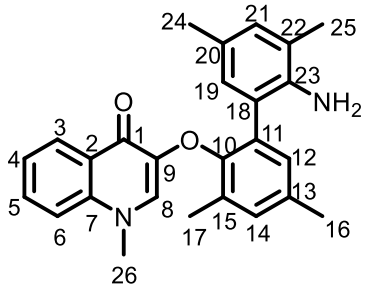
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4 (C-1), 147.1 (C-9), 146.5 (C-20), 141.4 (C-8), 137.2 (C-13), 136.2 (C-17), 133.6 (C-7), 132.8 (C-5), 132.7 (C-15), 132.2 (C-10), 131.9 (C-12), 130.4 (C-19), 127.6 (C-2), 127.6 (C-6), 126.3 (C-18), 125.3 (C-3), 121.1 (C-4), 118.5 (C-22), 116.0 (C-16), 21.8 (C-20), 20.8 (C-14), 16.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{24}H_{21}BrNO_4S^+$ $[M+H]^+$ requires *m/z* 498.0369, found *m/z* 498.0356.

IR (thin film) ν_{max}/cm^{-1} 3650, 2981, 2888, 1473, 1382, 1251, 1151, 1073, 955, 817.

MP 86 °C.

3-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-4(1H)-one, 446:



A three-neck round bottom flask was charged with 3-(2-bromo-4,6-dimethylphenoxy)-1-methylquinolin-4(1H)-one (400.0 mg, 1.12 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (405.4 mg, 1.67 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (64.7 mg, 5 mol%) and K_2CO_3 (619.2 mg, 4.48 mmol, 4.0 eq.) before degassing with

vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 11.2 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (50:50 to 65:35 EtOAc:pentane, v:v) to obtain the title compound as a solid (316.4 mg, 0.79 mmol, 71%).

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 8.1, 1.6 Hz, 1H, H-3), 7.69 – 7.63 (m, 1H, H-5), 7.54 (m, 1H, H-4), 7.45 (ddd, *J* = 8.9, 5.4, 2.4 Hz, 1H, H-6), 7.07 (d, *J* = 2.7 Hz, 1H, H-14), 6.82 (s, 1H, H-8), 6.81 (d, *J* = 2.7 Hz, 1H, H-12), 6.66 (d, *J* = 2.2 Hz, 1H, H-19), 6.63 (d, *J* = 2.2 Hz, 1H, H-21), 3.45 (s, 3H, H-26), 3.39 – 3.29 (s, 2H, H-NH_2), 2.44 (s, 3H, H-16), 2.29 (s, 3H, H-24), 2.05 (s, 3H, H-25), 1.78 (s, 3H, H-17).

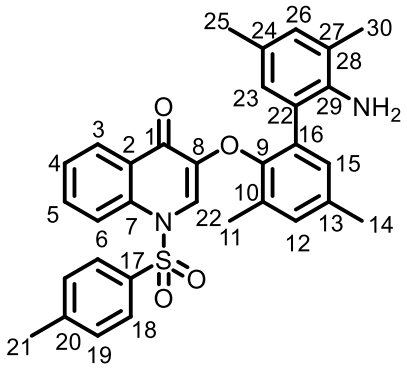
^{13}C NMR (176 MHz, $CDCl_3$) δ 171.0 (C-1), 150.7 (C-10), 140.4 (C-9), 140.3 (C-23), 138.6 (C-7), 133.7 (C-13), 133.6 (C-8), 132.2 (C-20), 132.1 (C-15), 132.05 (C-11), 132.03 (C-2), 131.6 (C-14), 131.35 (C-4), 131.30 (C-18), 130.1 (C-22), 129.7 (C-12), 129.6 (C-21), 128.9 (C-19), 128.6 (C-6), 127.0 (C-3), 126.8 (C-5), 40.1 (C-26), 20.8 (C-24), 20.2 (C-25), 17.4 (C-17), 17.1 (C-16).

HRMS (ESI) exact mass calculated for $C_{26}H_{27}N_2O_2^+$ $[M+H]^+$ requires *m/z* 399.2067, found *m/z* 399.2057.

IR (thin film) ν_{max}/cm^{-1} 3064, 1640, 1600, 1579, 1530, 1479, 1394, 1357, 1291, 1194, 1136, 1064, 860.

MP >250 °C.

3-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-tosylquinolin-4(1H)-one, 456:



A microwave vial was charged with 3-(2-bromo-4,6-dimethylphenoxy)-1-tosylquinolin-4(1H)-one (129.5 mg, 0.26 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (96.4 mg, 0.39 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (15.0 mg, 5 mol%) and K_2CO_3 (143.7 mg, 1.04 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 2.6 mL, 0.1 M). The vial was then capped and sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (20:80 to 40:60 EtOAc:pentane, v:v) to obtain the title compound as a solid (45.2 mg, 0.08 mmol, 32%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (s, 1H, H-22), 7.91 (m, 3H, H-3,18), 7.67 (d, J = 8.3 Hz, 1H, H-6), 7.52 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H, H-4), 7.41 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H, H-5), 7.35 (d, J = 8.0 Hz, 2H, H-19), 7.11 (d, J = 2.3 Hz, 1H, H-23), 6.97 (d, J = 2.3 Hz, 1H, H-26), 6.43 (d, J = 2.1 Hz, 1H, H-15), 6.35 (s, 1H, H-12), 3.31 (s, 2H, H-NH_2),

2.47 (s, 3H, H-21), 2.35 (s, 3H, H-14), 2.26 (s, 3H, H-25), 1.90 (s, 3H, H-30), 1.82 (s, 3H, H-11).

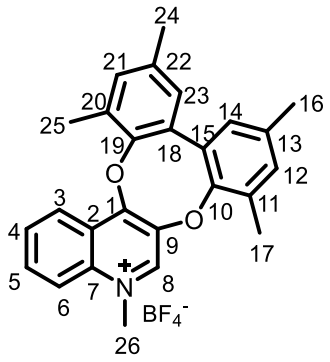
^{13}C NMR (151 MHz, $CDCl_3$) δ 148.7, 145.7, 145.3, 143.3, 142.5, 139.7, 138.7, 135.9, 134.0, 132.4, 131.6, 131.4, 130.6, 130.5, 129.9, 129.0, 128.7, 128.6, 127.8, 127.6, 126.9, 124.0, 122.8, 122.7, 121.6, 21.9, 21.0, 20.0, 17.6, 16.5.

HRMS (ESI) exact mass calculated for $C_{32}H_{31}N_2O_5S^+$ $[M+H]^+$ requires *m/z* 539.1999, found *m/z* 539.1986.

IR (thin film) ν_{max}/cm^{-1} 3243, 2921, 2697, 1590, 1526, 1479, 1432, 1294, 1195, 1122, 1033, 1010, 857, 815, 764, 683, 660.

MP 144-146 °C.

2,4,7,13,15-Pentamethyldibenzo[5,6:7,8][1,4]dioxocino[2,3-c]quinolin-7-ium tetrafluoroborate, 447:



A glass screw-cap vial was charged with 3-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-4(1H)-one (48.2 mg, 0.12 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.480 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 19 μL, 0.14 mmol, 1.1 eq.). The solution was cooled to 0 °C and *t*-BuONO (72 μL, 61.9 mg, 0.60 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 45 minutes at room temperature. After the reaction

time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN-d_3 (0.600 mL, 0.20 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (31.4 mg, 0.07 mmol, 56%).

^{1}H NMR (600 MHz, CD_3CN) δ 9.30 (s, 1H, H-8), 8.81 – 8.73 (m, 1H, H-6), 8.28 (dt, *J* = 9.0, 0.8 Hz, 1H,H-3), 8.19 (ddd, *J* = 9.0, 6.9, 1.4 Hz, 1H, H-4), 8.00 (ddd, *J* = 8.1, 6.9, 0.8 Hz, 1H, H-5), 7.25 (d, *J* = 2.4 Hz, 1H, H-14), 7.20 (dt, *J* = 2.4, 0.8 Hz, 1H, H-23), 7.17 (d, *J* = 2.4 Hz, 1H, H-12), 7.17 – 7.16 (m, 1H, H-21), 4.49 (s, 3H, H-26), 2.38 (s, 3H, H-24 or 16), 2.37 (s, 3H, H-24 or 16), 2.33 (s, 3H, H-25 or 17), 2.13 (s, 3H, H-25 or 17).

^{13}C NMR (151 MHz, CD_3CN) δ 159.4 (C-10), 149.2 (C-19), 148.7 (C-1), 148.1 (C-8), 140.8 (C-7), 139.2 (C-9), 138.8 (C-13), 138.4 (C-22), 135.8 (C-4), 134.0 (C-21), 133.8 (C-23), 132.5 (C-11), 132.0 (C-20), 131.7 (C-15), 131.1 (C-5), 129.4 (C-12), 128.2 (C-14), 125.2 (C-18), 125.1 (C-6), 119.8 (C-3), 118.3 (C-2), 45.7 (C-26), 20.9 (C-24 or 16), 20.8 (C-24 or 16), 17.3 (C-25 or 17), 16.7 (C-25 or 17).

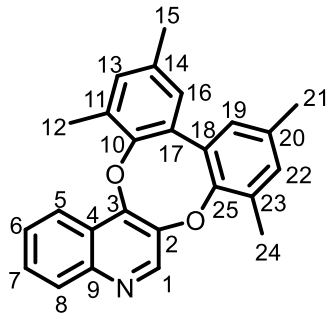
^{19}F NMR (565 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{26}H_{24}NO_2^+$ $[M]^+$ requires *m/z* 382.1802, found *m/z* 382.1793.

IR (thin film) ν_{max}/cm^{-1} 3064, 1640, 1600, 1579, 1530, 1479, 1394, 1357, 1291, 1194, 1136, 1064, 860.

MP >250 °C.

2,4,13,15-Tetramethyldibenzo[5,6:7,8][1,4]dioxocino[2,3-c]quinoline, 457:



A glass screw-cap vial was charged with 3-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-tosylquinolin-4(1H)-one (30.3 mg, 0.06 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.240 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 39 µL, 0.30 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (36 µL, 30.9 mg, 0.30 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 45 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (0.600 mL, 0.1 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was purified by column chromatography (0:100 to 1:99 MeOH:$CHCl_3$, v/v) to obtain the title compound as a solid (2.7 mg, 0.01 mmol, 12%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H, H-1), 8.07 (d, *J* = 8.5 Hz, 1H, H-5), 7.98 – 7.88 (m, 1H, H-8), 7.63 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 1H, H-6), 7.53 (ddd, *J* = 8.2, 6.8, 1.3

Hz, 1H, H-7), 7.12 – 7.08 (m, 3H, H-16,19,22), 7.02 (d, J = 2.1 Hz, 1H, H-13), 2.38 (s, 3H, H-15 or 21), 2.36 (s, 3H, H-15 or 21), 2.33 (s, 3H, H-12 or 24), 2.28 (s, 3H, H-12 or 24).

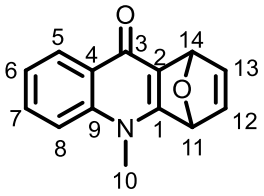
^{13}C NMR (151 MHz, $CDCl_3$) δ 148.2 (C-9), 147.8 (C-25), 145.5 (C-10), 139.8 (C-3), 137.4 (C-2), 137.0 (C-22), 137.0 (C-20), 135.2 (C-13), 134.9 (C-14), 134.5 (C-7), 133.8 (C-1), 132.8 (C-8), 131.8 (C-11), 131.1 (C-23), 130.3 (C-6), 128.3 (C-18), 128.2 (C-16 or 19), 126.7 (C-16 or 19), 126.2 (C-17), 121.2 (C-5), 118.8 (C-4), 21.1 (C-15 or 21), 21.0 (C-15 or 21), 18.9 (C-12 or 24), 17.0 (C-12 or 24).

HRMS (ESI) exact mass could not be detected.

IR (thin film) ν_{max}/cm^{-1} 2920, 2850, 1591, 1569, 1514, 1477, 1389, 1303, 1272, 1214, 1194, 1151, 1124, 1037, 980, 884, 856, 758, 735, 660, 619.

MP >250 °C.

10-Methyl-1,10-dihydro-1,4-epoxyacridin-9(4H)-one, 450:



A vial was charged with 3-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-4(1H)-one (79.7 mg, 0.20 mmol, 1.0 eq.), before dissolving in a mixture of CH_2Cl_2 and IPA (1:1, 0.200 mL, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 0.130 mL, 1.0 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (0.120 mL, 103. 1 mg, 1.0 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 10 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then filtered through a plug of cotton and

concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was then redissolved in anhydrous MeCN (2.0 mL, 0.1 M) and transferred to a 10 mL microwave vial containing a stir bar. The vial was then capped and a vent needle with an empty balloon was attached through the septum. The vial was then placed in a preheated oil bath and heated at 40 °C for 150 minutes. After heating, the solution was brought to room temperature and the cap was removed, then furan (2.0 mL, 10 mL/mmol) was added, followed by K_3PO_4 (212.3 mg, 1.0 mmol, 5.0 eq.) in one portion. The microwave vial was re-capped and the suspension was rapidly stirred for 16 hours. After the reaction time, the suspension was filtered through a pad of Celite, eluting with EtOAc, and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 3:97 MeOH:CH_2Cl_2, v:v) to obtain the title compound as a solid (11.6 mg, 0.05 mmol, 26%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 8.1, 1.6 Hz, 1H, H-5), 7.63 (ddd, *J* = 8.5, 7.0, 1.6 Hz, 1H, H-7), 7.45 (d, *J* = 8.5 Hz, 1H, H-8), 7.43 – 7.39 (m, 2H, H-6,13), 7.03 (dd, *J* = 5.4, 2.0 Hz, 1H, H-12), 6.16 (t, *J* = 1.5 Hz, 1H, H-14), 5.86 (dd, *J* = 2.0, 1.1 Hz, 1H, H-11), 3.88 (s, 3H, H-10).

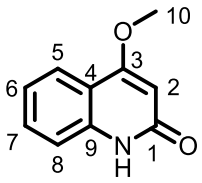
^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1 (C-3), 169.0 (C-1), 148.4 (C-9), 139.5 (C-13), 138.7 (C-12), 131.5 (C-7), 128.8 (C-6), 127.1 (C-2), 126.2 (C-5), 124.7 (C-4), 115.4 (C-8), 81.8 (C-11), 81.3 (C-14), 36.5 (C-20).

HRMS (ESI) exact mass calculated for $C_{14}H_{12}NO_2^+$ $[M+H]^+$ requires *m/z* 226.0863, found *m/z* 226.0860.

IR (thin film) ν_{max}/cm^{-1} 2971, 1679, 1618, 1591, 1539, 1504, 1459, 1371, 1269, 1155, 1094, 954, 876, 820, 720, 682.

MP 100-104 °C.

4-Methoxyquinolin-2(1H)-one, 507:

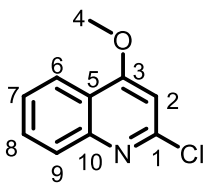


An oven-dried 500 mL round bottom flask was charged with 2,4-dihydroxyquinoline (4.00 g, 25.75 mmol, 1.0 eq.) before adding anhydrous DMF (191 mL, 0.13 M), followed by iodomethane (1.70 mL, 28.33 mmol, 1.1 eq.). K_2CO_3 (6.86 g, 51.5 mmol, 2.0 eq.) was then added in one portion with stirring before heating the reaction mixture to 45 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into ice water (800 mL) with vigorous shaking to form a suspension. The suspension was then transferred to a separatory funnel and extracted with EtOAc (x3). Combined organics were washed with deionised water (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain an impure crude solid (3.08 g) which was used in the next step without any further purification. The ^{1}H NMR spectrum is consistent with those available in the literature.[193]

^{1}H NMR (400 MHz, DMSO) δ 11.35 (s, 1H, H-NH), 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H, H-5), 7.50 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, H-7), 7.28 (dd, *J* = 8.3, 1.1 Hz, 1H, H-8), 7.15 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, H-6), 5.88 (s, 1H, H-2), 3.92 (s, 3H, H-10).

Due to the impurities isolated with the title compound, a quality ^{13}C spectrum could not be obtained.

2-Chloro-4-methoxyquinoline, 508:

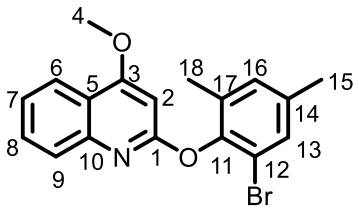


A round bottom flask was charged with $POCl_3$ (29 mL, 0.6 M) and cooled to 0 °C before adding the impure 4-methoxyquinolin-2(1H)-one synthesised in the previous step (3.08 g) with stirring. After full addition, triethylamine (2.5 mL, 1.0 eq.) was added dropwise and the mixture was refluxed at 90 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (at least 10 mL per 1 mL of $POCl_3$) with vigorous stirring and left to stand until it reached room temperature. The formed suspension was neutralised by adding solid Na_2CO_3 with shaking, then transferred to a separatory funnel and extracted with EtOAc (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 30:70 EtOAc:pentane, v/v) to obtain the title compound as a solid (1.02 g, 5.27 mmol, 21% over two synthetic steps). The NMR spectra are consistent with those available in the literature.[193]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (ddd, *J* = 8.3, 1.6, 0.6 Hz, 1H, H-6), 7.91 (ddd, *J* = 8.5, 1.2, 0.6 Hz, 1H, H-9), 7.68 (ddd, *J* = 8.5, 6.9, 1.6 Hz, 1H, H-7), 7.47 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H, H-8), 6.70 (s, 1H, H-2), 4.02 (s, 3H, H-4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8 (C-3), 151.6 (C-1), 148.2 (C-10), 130.9 (C-7), 128.2 (C-9), 126.1 (C-8), 122.1 (C-6), 120.4 (C-5), 101.2 (C-2), 56.3 (C-4).

2-(2-Bromo-4,6-dimethylphenoxy)-4-methoxyquinoline, 510:



An oven-dried round bottom flask was charged with 2-chloro-4-methoxyquinoline (876.8 mg, 4.53 mmol, 1.0 eq.) before adding anhydrous DMSO (11.3 mL, 0.4 M), followed by 2-bromo-4,6-dimethylphenol (1.37 g, 6.79 mmol, 1.5 eq.). Cs_2CO_3 (5.17 g, 15.86 mmol,

3.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 120 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~200 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (5:95 to 10:90 Et_2O: pentane, v/v) to obtain the title compound as an oil (162.5 mg, 0.45 mmol, 10%).

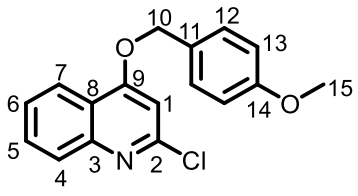
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.2, 1.6 Hz, 1H, H-6), 7.67 – 7.65 (m, 1H, H-9), 7.55 (ddd, *J* = 8.2, 6.9, 1.5 Hz, 1H, H-7), 7.35 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, H-8), 7.32 (d, *J* = 2.2 Hz, 1H, H-13), 7.04 (dd, *J* = 2.2, 1.0 Hz, 1H, H-16), 6.48 (s, 1H, H-2), 4.06 (s, 3H, H-4), 2.35 (s, 3H, H-15), 2.19 (s, 3H, H-18).

^{13}C NMR (176 MHz, $CDCl_3$) δ 165.0 (C-1), 161.9 (C-3), 147.1 (C-11), 147.0 (C-10), 136.2 (C-14), 133.5 (C-17), 131.2 (C-13), 130.9 (C-16), 130.1 (C-7), 127.7 (C-9), 123.9 (C-8), 121.8 (C-6), 119.6 (C-5), 117.2 (C-12), 90.0 (C-2), 55.8 (C-4), 20.8 (C-15), 17.4 (C-17).

HRMS (ESI) exact mass calculated for $C_{18}H_{17}BrNO_2^+$ $[M+H]^+$ requires *m/z* 358.0437, found *m/z* 358.0426.

IR (thin film) ν_{max}/cm^{-1} 2923, 1622, 1599, 1582, 1475, 1448, 1420, 1356, 1278, 1209, 1162, 1005, 983.

2-Chloro-4-((4-methoxybenzyl)oxy)quinoline, 513:



A flame-dried round bottom flask was charged with anhydrous DMF (10.1 mL, 1.0 M) before adding NaH (60% suspension in mineral oil, 525.2 mg, 13.13 mmol, 1.3 eq.) in small portions and cooling to 0 °C. With stirring under nitrogen, 4-methoxybenzyl alcohol (1.67 g, 12.12 mmol, 1.2 eq.) was added dropwise and left to stir for 15 minutes after full addition. Subsequently, 15-crown-5 (0.400 mL, 20 mol%) was added dropwise and stirred at 0 °C for 10 minutes. After this time, 2,4-dichloroquinoline (2.0 g, 10.10 mmol, 1.0 eq.) was added in small portions and the reaction mixture was stirred at room temperature for 16 hours, followed by reflux at 60 °C for another 3 hours. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~200 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 15:85 EtOAc:pentane, v/v) to obtain the title compound as a solid (506.4 mg, 1.69 mmol, 17%). The NMR spectra are consistent with those available in the literature.[194]

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.5, 1.5 Hz, 1H, H-7), 7.93 (dd, *J* = 8.5, 1.1 Hz, 1H, H-4), 7.69 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H, H-6), 7.47 (ddd, *J* = 8.5, 6.9, 1.1 Hz, 1H, H-5), 7.44 – 7.39 (m, 2H, H-12), 6.99 – 6.94 (m, 2H, H-13), 6.81 (s, 1H, H-1), 5.18 (s, 2H, H-10), 3.84 (s, 3H, H-15).

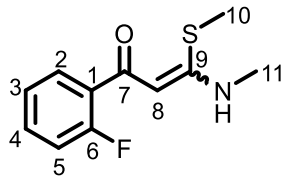
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.9 (C-9), 160.1 (C-14), 151.6 (C-2), 148.3 (C-3), 131.0 (C-6), 129.6 (C-12), 128.2 (C-4), 127.2 (C-11), 126.1 (C-5), 122.3 (C-7), 120.6 (C-8), 114.4 (C-13), 102.2 (C-1), 70.9 (C-10), 55.5 (C-15).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}ClNO_2^+$ $[M+H]^+$ requires *m/z* 300.0786, found *m/z* 300.0785.

IR (thin film) ν_{max}/cm^{-1} 2934, 1615, 1579, 1517, 1427, 1385, 1333, 1318, 1235, 1097, 1033, 932, 915.

MP 98-100 °C

1-(2-Fluorophenyl)-3-(methylamino)-3-(methylthio)prop-2-en-1-one, 516:



A flame-dried round bottom flask was charged with anhydrous DMF (48 mL, 0.3 M) before adding NaH (60% suspension in mineral oil, 637.2 mg, 15.93 mmol, 1.1 eq.) in small portions and cooling to 0 °C. With stirring, and under nitrogen, 1-(2-fluorophenyl)ethan-1-one (1.8 mL, 2.0 g, 14.48 mmol, 1.0 eq.) was added dropwise and left to stir for 30 minutes after full addition. Subsequently, methyl isothiocyanate (1.1 mL, 1.11 g, 15.20 mmol, 1.05 eq.) dissolved in 1.5 mL of anhydrous DMF was added dropwise at 0 °C, then the reaction mixture was stirred at room temperature for 16 hours. After the reaction time, the mixture was poured into deionised water (~250 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil containing 3-(2-fluorophenyl)-*N*-methyl-3-oxopropanethioamide (1.60 g). Assuming a quantitative conversion, the crude oil was redissolved in acetone (145 mL, 0.10 M), before adding K_2CO_3 (2.20 g, 15.93 mmol, 1.1 eq.) in one portion, followed by MeI (1.8 mL, 4.11 g, 28.96 mmol, 2.0 eq.) dropwise. The reaction mixture was then refluxed at 40 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 to 15:85

EtOAc:pentane, v/v) to obtain the title compound as an oil (526.4 mg, 2.34 mmol, 16% over two synthetic steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.71 (s, 1H), 7.81 (td, *J* = 7.7, 1.9 Hz, 1H, H-2), 7.35 (dddd, *J* = 8.2, 7.1, 5.0, 1.9 Hz, 1H, H-4), 7.18 (td, *J* = 7.7, 1.2 Hz, 1H, H-3), 7.05 (ddd, *J* = 11.2, 8.2, 1.2 Hz, 1H, H-5), 5.64 (d, *J* = 1.2 Hz, 1H, H-8), 3.06 (d, *J* = 5.2 Hz, 3H, H-11), 2.43 (s, 3H, H-10).

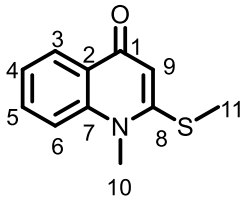
^{13}C NMR (151 MHz, $CDCl_3$) δ 181.3 (d, *J* = 3.3 Hz, C-7), 171.3 (C-9), 160.2 (d, *J* = 250.4 Hz, C-6), 131.5 (d, *J* = 8.7 Hz, C-4), 130.5 (d, *J* = 3.2 Hz, C-2), 129.1 (d, *J* = 13.2 Hz, C-1), 124.2 (d, *J* = 3.6 Hz, C-3), 116.2 (d, *J* = 24.3 Hz, C-5), 90.8 (d, *J* = 10.4 Hz, C-8), 30.4 (C-11), 14.3 (C-10).

^{19}F NMR (471 MHz, $CDCl_3$) δ -112.7.

HRMS (ESI) exact mass calculated for $C_{11}H_{13}FNOS^+$ $[M+H]^+$ requires *m/z* 226.0696, found *m/z* 226.0694.

IR (thin film) ν_{max}/cm^{-1} 2928, 1571, 1490, 1477, 1423, 1293, 1245, 1153, 1106, 1085, 1033, 1020, 976, 881, 820, 758, 717.

1-Methyl-2-(methylthio)quinolin-4(1H)-one, 721:



An oven-dried round bottom flask was charged with 1-(2-fluorophenyl)-3-(methylamino)-3-(methylthio)prop-2-en-1-one (448.3 mg, 1.99 mmol, 1.0 eq.), followed by anhydrous DMF (6.6 mL, 0.3 M). K_2CO_3 (686.9 mg, 4.97 mmol, 2.5 eq.) was added in one portion, then the suspension was refluxed at 120 °C for 16 hours. After the reaction

time, the mixture was poured into deionised water (~100 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude solid was purified by trituration with Et_2O to obtain the pure title compound (247.8 mg, 1.21 mmol, 61%).

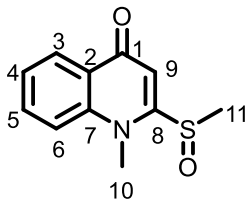
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (dd, *J* = 8.0, 1.7 Hz, 1H, H-3), 7.61 (ddd, *J* = 8.7, 7.0, 1.7 Hz, 1H, H-5), 7.40 (d, *J* = 8.7Hz, 1H, H-6), 7.33 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H, H-4), 6.14 (s, 1H, H-9), 3.79 (s, 3H, H-10), 2.52 (s, 3H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8 (C-1), 156.5 (C-8), 142.2 (C-7), 132.2 (C-5), 126.8 (C-3), 125.9 (C-2), 123.5 (C-4), 115.0 (C-6), 106.3 (C-9), 35.0 (C-10), 16.2 (C-11).

HRMS (ESI) exact mass calculated for $C_{11}H_{12}NOS^+$ $[M+H]^+$ requires *m/z* 206.0634, found *m/z* 206.0632.

IR (thin film) ν_{max}/cm^{-1} 2926, 1672, 1616, 1593, 1522, 1488, 1436, 1397, 1304, 1267, 1148, 1123, 1078, 1046, 987, 851, 823, 760, 705.

1-Methyl-2-(methylsulfinyl)quinolin-4(1H)-one, 517:



An oven-dried round bottom flask was charged with 1-methyl-2-(methylthio)quinolin-4(1H)-one (225.5 mg, 1.10 mmol, 1.0 eq.), followed by anhydrous CH_2Cl_2 (11 mL, 0.1 M). 3-Chloroperoxybenzoic acid (77% purity, 345.1 mg, 1.54 mmol, 1.4 eq.) was added in small portions, then the reaction mixture was stirred at room temperature for 2 hours. After the reaction time, it was diluted with further CH_2Cl_2 (100 mL) and washed with saturated aqueous $Na_2S_2O_3$ (x3), then saturated aqueous $NaHCO_3$ (x3), dried with brine,

$MgSO_4$ and concentrated under vacuum to obtain a crude oil (185.1 mg, 0.84 mmol, 76%), which was used without any further purification.

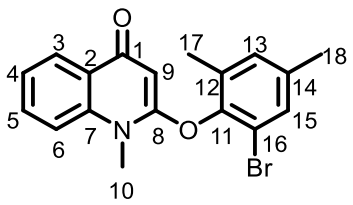
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (dt, *J* = 8.0, 1.7 Hz, 1H, H-3), 7.71 (ddt, *J* = 8.6, 7.0, 1.7 Hz, 1H, H-5), 7.48 (d, *J* = 8.6 Hz, 1H, H-6), 7.42 – 7.37 (m, 1H, H-4), 6.89 (d, *J* = 1.5 Hz, 1H, H-9), 3.76 (d, *J* = 1.2 Hz, 3H, H-10), 2.87 (d, *J* = 0.9 Hz, 3H, H-11).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5 (C-1), 159.1 (C-8), 141.9 (C-7), 133.3 (C-5), 127.2 (C-2), 127.1 (C-3), 124.7 (C-4), 115.2 (C-6), 106.4 (C-9), 41.8 (C-11), 34.3 (C-10).

HRMS (ESI) exact mass calculated for $C_{11}H_{12}NO_2S^+$ $[M+H]^+$ requires *m/z* 222.0583, found *m/z* 222.0581.

IR (thin film) ν_{max}/cm^{-1} 2922, 1618, 1599, 1497, 1470, 1405, 1306, 1191, 1077, 960, 759, 645.

2-(2-Bromo-4,6-dimethylphenoxy)-1-methylquinolin-4(1H)-one, 518:



A flame-dried round bottom flask was charged with 1-methyl-2-(methylsulfinyl)quinolin-4(1H)-one (139.5 mg, 0.63 mmol, 1.0 eq.), before adding anhydrous MeOH (3.2 mL, 0.2 M), followed by 2-bromo-4,6-dimethylphenol (191.0 mg, 0.95 mmol, 1.5 eq.). KO*t*-Bu (106.6 mg, 0.95 mmol, 1.5 eq.) was added portion-wise with stirring, then the reaction mixture was heated at 50 °C under nitrogen for 16 hours. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (50 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was

purified by flash column chromatography (0:100 to 1:96 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (81.0 mg, 0.23 mmol, 36%).

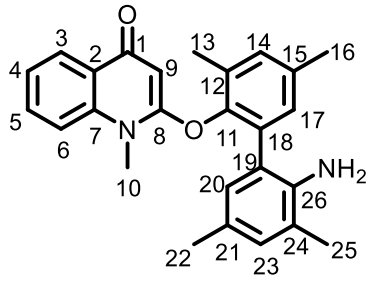
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 8.0, 1.7 Hz, 1H, H-3), 7.69 (ddd, *J* = 8.7, 7.1, 1.7 Hz, 1H, H-5), 7.55 (dd, *J* = 8.7, 1.0 Hz, 1H, H-6), 7.37 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H, H-4), 7.30 (dt, *J* = 2.2, 0.8 Hz, 1H, H-15), 7.04 (dt, *J* = 2.2, 0.8 Hz, 1H, H-13), 5.38 (s, 1H, H-9), 3.95 (s, 3H, H-10), 2.33 (s, 3H, H-18), 2.21 (s, 3H, H-17).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.7 (C-1), 158.6 (C-8), 145.3 (C-11), 140.0 (C-7), 138.2 (C-14), 132.6 (C-12), 132.4 (C-5), 132.1 (C-15), 131.7 (C-13), 126.9 (C-3), 125.7 (C-2), 123.5 (C-4), 116.1 (C-16), 115.1 (C-6), 92.0 (C-9), 31.2 (C-10), 20.7 (C-18), 16.7 (C-17).

HRMS (ESI) exact mass calculated for $C_{18}H_{17}BrNO_2^+$ $[M+H]^+$ requires *m/z* 358.0437, found *m/z* 358.0430.

IR (thin film) ν_{max}/cm^{-1} 2923, 1623, 1601, 1543, 1507, 1472, 1417, 1280, 1210, 820, 760, 651, 645, 636.

2-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-4(1H)-one, 458:



An oven-dried 10 mL microwave vial was charged with 2-(2-bromo-4,6-dimethylphenoxy)-1-methylquinolin-4(1H)-one (81.0 mg, 0.23 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (84.0 mg, 0.34 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (13.3 mg, 5 mol%) and K_2CO_3 (127.2 mg, 0.92 mmol, 4.0 eq.) before

degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 2.4 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 2:98 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (66.9 mg, 0.17 mmol, 73%).

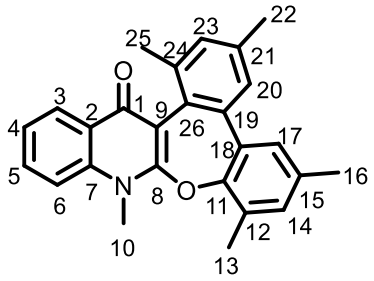
^{1}H NMR (600 MHz, DMSO, 80 °C) δ 8.06 (dd, *J* = 7.9, 1.6 Hz, 1H, H-3), 7.65 (ddd, *J* = 8.7, 6.9, 1.6 Hz, 1H, H-5), 7.58 (d, *J* = 8.7 Hz, 1H, H-6), 7.33 – 7.27 (m, 1H, H-4), 7.26 – 7.22 (m, 1H, H-14), 7.04 (s, 1H, H-17), 6.68 – 6.64 (m, 1H, H-20), 6.51 (s, 1H, H-23), 5.03 (s, 1H, H-9), 4.09 – 3.92 (m, 2H, H-NH_2), 3.55 (s, 3H, H-10), 2.38 (s, 3H, H-16), 2.25 (s, 3H, H-22), 2.05 (s, 3H, H-25), 1.89 (s, 3H, H-13).

^{13}C NMR (151 MHz, DMSO, 80 °C) δ 175.8 (C-1), 158.8 (C-8), 146.0 (C-11), 140.1 (C-26), 139.1 (C-7), 135.8 (C-15), 132.1 (C-12), 131.5 (C-5), 130.9 (C-14), 130.2 (C-20), 129.9 (C-21), 129.8 (C-17), 127.7 (C-23), 124.9 (C-3), 124.6 (C-2), 123.9 (C-19), 122.3 (C-4), 121.5 (C-24), 115.4 (C-6), 90.8 (C-9), 29.9 (C-10), 20.0 (C-16), 19.2 (C-13), 17.1 (C-25), 15.2 (C-22).

HRMS (ESI) exact mass calculated for $C_{26}H_{27}N_2O_2^+$ $[M+H]^+$ requires *m/z* 399.2067, found *m/z* 399.2052.

IR (thin film) ν_{max}/cm^{-1} 3438, 2922, 1617, 1603, 1581, 1542, 1505, 1448, 1409, 1265, 1198, 1160, 1118, 1072, 1026, 863, 799, 762, 649.

1,3,6,8,10-Pentamethyldibenzo[4,5:6,7]oxepino[2,3-b]quinolin-15(10H)-one, 460:



A vial was charged with 2-((2'-amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-1-methylquinolin-4(1H)-one (48.3 mg, 0.12 mmol, 1.0 eq.), before dissolving in a mixture of CH_2Cl_2 and IPA (1:1, 0.480 mL, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 80 µL, 0.61 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (73 µL, 62.8 mg, 0.61 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 10 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then filtered through a plug of cotton and concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was then redissolved in anhydrous MeCN (2.4 mL, 0.05 M) and transferred to a 10 mL microwave vial containing a stir bar. Subsequently, furan (44 µL, 0.61 mmol, 5.0 eq) was added, followed by K_3PO_4 (129.5 mg, 0.61 mmol, 5.0 eq.) in one portion. The vial was then capped and a vent needle with an empty balloon was attached through the septum. The vial was then rapidly stirred at room temperature for 48 hours. After the reaction time, the suspension was filtered through a pad of Celite, eluting with EtOAc, and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 5:95 MeOH:CH_2Cl_2, v:v) to obtain the title compound as an oil (6.5 mg, 0.02 mmol, 14%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 8.0, 1.6 Hz, 1H, H-3), 7.68 (ddd, *J* = 8.6, 7.0, 1.6 Hz, 1H, H-5), 7.50 (d, *J* = 8.6 Hz, 1H, H-6), 7.37 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H,

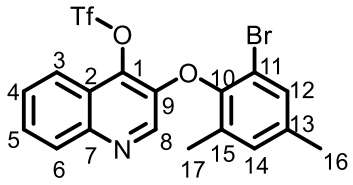
H-4), 7.29 (d, *J* = 2.3 Hz, 1H, H-20), 7.14 (dd, *J* = 1.9, 1.0 Hz, 1H, H-14), 7.12 (d, *J* = 1.9 Hz, 1H, H-17), 6.94 (dt, *J* = 2.3, 1.0 Hz, 1H, H-23), 4.07 (s, 3H, H-10), 2.51 (s, 3H, H-25), 2.39 (s, 3H, H-16), 2.32 (s, 3H, H-22), 2.26 (s, 3H, H-13).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.2 (C-1), 161.4 (C-8), 156.8 (C-11), 139.1 (C-7), 138.5 (C-21), 136.7 (C-26), 136.3 (C-24), 135.8 (C-19), 133.7 (C-15), 132.4 (C-5), 131.3 (C-23), 131.1 (C-14), 128.8 (C-12), 128.5 (C-20), 127.62 (C-2), 127.60 (C-3), 127.5 (C-17), 125.6 (C-18), 123.6 (C-4), 115.2 (C-6), 110.5 (C-9), 33.4 (C-10), 21.3 (C-16), 21.2 (C-13), 20.8 (C-22), 18.9 (C-25).

HRMS (ESI) exact mass calculated for $C_{26}H_{24}NO_2^+$ $[M+H]^+$ requires *m/z* 382.1802, found *m/z* 382.1788.

IR (thin film) ν_{max}/cm^{-1} 2921, 1620, 1599, 1543, 1493, 1475, 1434, 1393, 1320, 1278, 1222, 1174, 1145, 1119, 1035, 949, 855, 832, 692, 654.

3-(2-Bromo-4,6-dimethylphenoxy)quinolin-4-yl trifluoromethanesulfonate, 455:



A flame-dried round bottom flask was charged with 3-(2-bromo-4,6-dimethylphenoxy)quinolin-4(1H)-one (35.2 mg, 0.10 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (1.0 mL, 0.1 M) and cooling to 0 °C. 2,6-Lutidine (17 µL, 12.9 mg, 0.12 mmol, 1.2 eq.) was then added, followed by DMAP (2.5 mg, 20 mol%). Subsequently, Tf_2O (20 µL, 39.5 mg, 0.14 mmol, 1.4 eq.) was added dropwise, then the reaction mixture was brought to room temperature and left to stir for 3 hours, until the full consumption of the starting material. After the reaction time, the solution was poured into deionised water (100 mL), then extracted with EtOAc (x3). Combined organics were

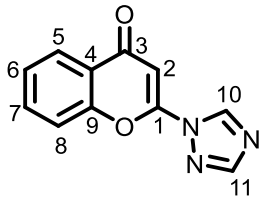
washed with saturated $NaHCO_3$ (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (25:75 to 40:60 EtOAc:pentane, v/v) to obtain the title compound as a solid (28.3 mg, 0.06 mmol, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H, H-8), 8.14 – 8.05 (m, 2H, H-3,5), 7.82 – 7.60 (m, 2H, H-4,6), 7.35 (d, *J* = 2.1 Hz, 1H, H-12), 7.09 (dt, *J* = 2.0, 0.9 Hz, 1H, H-14), 2.36 (s, 3H, H-16), 2.24 (s, 3H, H-17).

^{19}F NMR (377 MHz, $CDCl_3$) δ -72.3.

All of the isolated material was subjected to further synthetic transformations and hence no other characterisation was performed.

2-(1H-1,2,4-Triazol-1-yl)-4H-chromen-4-one, 520:



An oven-dried round bottom flask was charged with chromone (2.00 g, 13.69 mmol, 1.0 eq.) and 1,2,4-triazole (1.89 g, 27.38 mmol, 2.0 eq.) before dissolving in anhydrous DMF (68 mL, 0.2 M). Iodine (5.21 g, 20.53 mmol, 1.5 eq.) was then added, followed by K_2CO_3 (18.9 g, 136.9 mmol, 10.0 eq.), and the suspension was refluxed at 80 °C for 16 hours. After the reaction time, the reaction mixture was cooled to room temperature and quenched with saturated aqueous $Na_2S_2O_3$ (~100 mL), then poured into a separatory funnel containing deionised water (600 mL). The aqueous layer was then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (30:70 to 100:0 EtOAc:pentane, v/v) to obtain the title compound as a

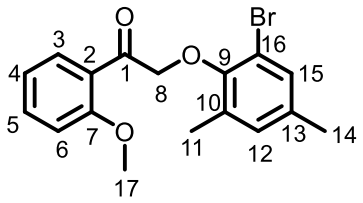
solid (414.1 mg, 1.94 mmol, 14%). The NMR spectra are consistent with those available in the literature.[195]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H, H-10), 8.23 (dd, *J* = 7.9, 1.7 Hz, 1H, H-5), 8.17 (s, 1H, H-11), 7.75 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H, H-7), 7.56 (dd, *J* = 8.7, 1.1 Hz, 1H, H-8), 7.49 (ddd, *J* = 7.9, 7.1, 1.1 Hz, 1H, H-6), 6.88 (s, 1H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7 (C-3), 154.2 (C-1), 154.1 (C-9), 153.0 (C-11), 142.1 (C-10), 134.6 (C-7), 126.5 (C-5), 126.4 (C-6), 123.8 (C-4), 117.7 (C-8), 98.3 (C-2).

HRMS (ESI) exact mass calculated for $C_{11}H_8N_3O_2^+$ $[M+H]^+$ requires *m/z* 214.0611, found *m/z* 214.0607.

2-(2-Bromo-4,6-dimethylphenoxy)-1-(2-methoxyphenyl)ethan-1-one, 722:



An oven-dried round bottom flask was charged with 2-bromo-1-(2-methoxyphenyl)ethan-1-one (1.50 g, 6.55 mmol, 1.0 eq.) before adding acetone (33 mL, 0.20 M), followed by 2-bromo-4,6-dimethylphenol (1.58 g, 7.86 mmol, 1.2 eq.). K_2CO_3 (1.36 g, 9.83 mmol, 1.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 60 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and filtered through Celite, eluting with EtOAc. Combined organics were concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v/v) to obtain the title compound as a solid (1.28 g, 3.67 mmol, 56%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.8, 1.8 Hz, 1H, H-3), 7.51 (ddd, *J* = 8.6, 7.3, 1.8 Hz, 1H, H-5), 7.21 (d, *J* = 2.0 Hz, 1H, H-15), 7.07 (t, *J* = 7.5 Hz, 1H, H-4), 6.97

(d, *J* = 8.4 Hz, 1H, H-6), 6.94 (d, *J* = 2.0 Hz, 1H, H-12), 5.12 (s, 2H, H-8), 3.88 (s, 3H, H-17), 2.31 (s, 3H, H-14), 2.26 (s, 3H, H-11).

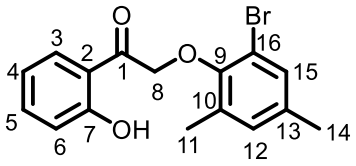
^{13}C NMR (151 MHz, $CDCl_3$) δ 194.5 (C-1), 159.3 (C-7), 152.0 (C-9), 135.3 (C-13), 134.7 (C-5), 133.1 (C-15), 131.4 (C-10), 131.2 (C-12), 131.2 (C-3), 125.0 (C-2), 121.1 (C-4), 116.9 (C-16), 111.6 (C-6), 78.3 (C-8), 55.7 (C-17), 20.6 (C-14), 16.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{17}H_{18}BrO_3^+$ $[M+H]^+$ requires *m/z* 349.0434, found *m/z* 349.0429.

IR (thin film) ν_{max}/cm^{-1} 2918, 1684, 1599, 1470, 1442, 1377, 1291, 1279, 1206, 1164, 1126, 1050, 1020, 973, 867, 819, 758.

MP 101-103 °C.

2-(2-Bromo-4,6-dimethylphenoxy)-1-(2-hydroxyphenyl)ethan-1-one, 523:



A flame-dried round bottom flask was charged with 2-(2-bromo-4,6-dimethylphenoxy)-1-(2-methoxyphenyl)ethan-1-one (1.25 g, 3.58 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (14.0 mL, 0.25 M) and cooling to -20 °C. BBr_3 (1.0 M in CH_2Cl_2, 3.9 mL, 3.94 mmol, 1.1 eq.) was added dropwise, then the reaction mixture was left to stir for 1 h. After the reaction time, the solution was quenched with saturated aqueous $NaHCO_3$ (10 mL) and brought to room temperature, then transferred to a separatory funnel containing more $NaHCO_3$ (~150 mL). The aqueous layer was then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column

chromatography (0:100 to 5:95 EtOAc:pentane, v/v) to obtain the title compound as a solid (978.1 mg, 2.92 mmol, 82%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 11.92 (s, 1H, H-OH), 7.71 (dd, *J* = 8.2, 1.6 Hz, 1H, H-3), 7.51 (ddd, *J* = 8.64, 7.1, 1.6 Hz, 1H, H-5), 7.22 (d, *J* = 2.1 Hz, 1H, H-15), 7.04 (dd, *J* = 8.4, 1.2 Hz, 1H, H-6), 6.99 – 6.94 (m, 1H, H-12), 6.91 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H, H-4), 5.19 (s, 2H, H-8), 2.30 (s, 3H, H-14), 2.27 (s, 3H, H-11).

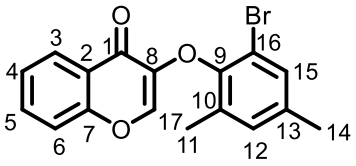
^{13}C NMR (151 MHz, $CDCl_3$) δ 199.1 (C-1), 162.7 (C-7), 151.6 (C-9), 137.0 (C-5), 136.0 (C-13), 132.9 (C-15), 131.6 (C-3), 131.4 (C-10), 129.0 (C-12), 119.3 (C-4), 118.9 (C-2), 117.6 (C-6), 116.6 (C-16), 73.8 (C-8), 20.6 (C-14), 16.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{16}H_{14}BrO_3^-$ $[M-H]^-$ requires *m/z* 333.0132, found *m/z* 333.0134.

IR (thin film) ν_{max}/cm^{-1} 3055, 2925, 1694, 1657, 1619, 1582, 1477, 1450, 1354, 1310, 1208, 1160, 1124, 1070, 1036, 978, 853, 832, 810, 753, 731.

MP 68-70 °C.

3-(2-Bromo-4,6-dimethylphenoxy)-4H-chromen-4-one, 524:



An oven-dried round bottom flask was charged with 2-(2-bromo-4,6-dimethylphenoxy)-1-(2-hydroxyphenyl)ethan-1-one (967.1 mg, 2.89 mmol, 1.0 eq.) before dissolving in anhydrous toluene (29 mL, 0.10 M). *N*,*N*-Dimethylformamide dimethyl acetal (0.580 mL, 516.0 mg, 4.33 mmol, 1.5 eq.) was added dropwise and the solution was refluxed at 80 °C under nitrogen for 4 hours. After the reaction time, the solution was concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography

(10:90 EtOAc:pentane, v/v) to obtain the title compound as a solid (920.6 mg, 2.67 mmol, 92%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 8.1, 1.7 Hz, 1H, H-3), 7.66 (ddd, *J* = 8.6, 7.1, 1.7 Hz, 1H, H-5), 7.43 (dd, *J* = 8.6, 1.0 Hz, 1H, H-6), 7.41 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H, H-4), 7.32 (s, 1H, H-17), 7.27 (d, *J* = 2.0 Hz, 1H, H-15), 7.03 – 6.99 (m, 1H, H-12), 2.31 (s, 3H, H-14), 2.25 (s, 3H, H-11).

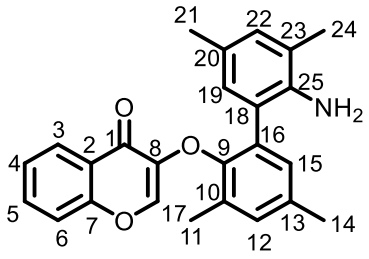
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.0 (C-1), 155.9 (C-7), 147.4 (C-9), 142.7 (C-17), 140.6 (C-8), 137.0 (C-13), 133.6 (C-5), 132.5 (C-15), 132.0 (C-12), 131.6 (C-10), 126.4 (C-3), 124.8 (C-2), 124.2 (C-4), 118.3 (C-6), 116.0 (C-16), 20.7 (C-14), 16.7 (C-11).

HRMS (ESI) exact mass calculated for $C_{17}H_{14}BrO_3^+$ $[M+H]^+$ requires *m/z* 345.0121, found *m/z* 345.0115.

IR (thin film) ν_{max}/cm^{-1} 3081, 1707, 1655, 1613, 1569, 1519, 1469, 1389, 1348, 1316, 1281, 1209, 1187, 1166, 1148, 1107, 1038, 970, 856, 763, 735.

MP 96-98 °C.

3-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-4H-chromen-4-one, 461:



An oven-dried three-neck round bottom flask was charged with 3-(2-Bromo-4,6-dimethylphenoxy)-4H-chromen-4-one (847.6 mg, 2.46 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (729.1 mg, 2.95 mmol, 1.2 eq.), $Pd(PPh_3)_4$ (142.1 mg, 5 mol%) and K_2CO_3 (1.36 g, 9.84 mmol, 4.0 eq.) before degassing

with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 24.6 mL, 0.1 M). The suspension was sparged with argon for 15 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (15:85 to 20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (694.3 mg, 1.80 mmol, 73%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 8.4, 1.7 Hz, 1H, H-3), 7.57 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H, H-5), 7.33 – 7.28 (m, 3H, H-4,6,17), 7.08 (d, *J* = 2.3 Hz, 1H, H-19), 6.90 (d, *J* = 2.3 Hz, 1H, H-22), 6.66 (d, *J* = 2.1 Hz, 1H, H-15), 6.65 – 6.60 (m, 1H, H-12), 3.56 – 3.36 (m, 2H, H-NH_2), 2.37 (s, 3H, H-14), 2.32 (s, 3H, H-21), 2.03 (s, 3H, H-24), 1.93 (s, 3H, H-11).

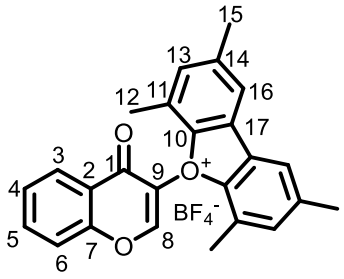
^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1 (C-1), 155.4 (C-7), 149.4 (C-9), 143.4 (C-17), 143.0 (C-25), 139.9 (C-8), 134.7 (C-5), 133.1 (C-13), 131.7 (C-12), 130.9 (C-22), 130.8 (C-20), 130.5 (C-10), 130.1 (C-19), 129.0 (C-3), 127.0 (C-16), 125.9 (C-2), 124.4 (C-15), 124.3 (C-4), 123.6 (C-18), 122.6 (C-23), 117.9 (C-6), 20.9 (C-21), 20.2 (C-14), 17.6 (C-24), 16.8 (C-11).

HRMS (ESI) exact mass calculated for $C_{25}H_{24}NO_3^+$ $[M+H]^+$ requires *m/z* 386.1751, found *m/z* 386.1743.

IR (thin film) ν_{max}/cm^{-1} 3373, 2922, 2858, 1651, 1613, 1485, 1468, 1344, 1310, 1273, 1203, 1167, 1108, 1015, 973, 863, 759, 738.

MP 152 °C.

2,4,6,8-Tetramethyl-5-(4-oxo-4H-chromen-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 462:



A round bottom flask was charged with 3-((2'-Amino-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-4H-chromen-4-one (664.4 mg, 1.72 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (7.0 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 1.1 mL, 8.62 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (1.0 mL, 888.9 mg, 8.62 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (17.0 mL, 0.20 M) and transferred to a flame-dried round bottom flask, then heated to 40 °C for 18 hours under nitrogen. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with anhydrous CH_2Cl_2 and anhydrous Et_2O, passing the suspension through Celite and washing the solid with additional anhydrous Et_2O. Subsequently, an appropriate volume of anhydrous MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (422.3 mg, 0.93 mmol, 54%), which was stored below 5 °C.

^{1}H NMR (500 MHz, CD_3CN) δ 9.60 (s, 1H, H-8), 8.08 (dd, *J* = 8.1, 1.7 Hz, 1H, H-3), 7.97 (ddd, *J* = 8.5, 7.2, 1.7 Hz, 1H, H-5), 7.91 – 7.87 (m, 2H, H-13), 7.82 (dd, *J* = 8.5, 1.0 Hz, 1H, H-6), 7.61 (ddd, *J* = 8.1, 7.2, 1.0 Hz, 1H, H-4), 7.30 (dq, *J* = 1.9, 0.8 Hz, 2H, H-16), 2.50 (s, 6H, H-12), 2.41 (s, 6H, H-15).

^{13}C NMR (126 MHz, CD_3CN) δ 168.1 (C-1), 160.6 (C-7), 157.7 (C-8), 157.1 (C-14), 145.1 (C-10), 142.9 (C-5), 137.5 (C-9), 135.4 (C-17), 128.6 (C-13), 126.8 (C-11), 125.6 (C-2), 124.4 (C-4), 123.9 (C-3), 122.5 (C-16), 120.3 (C-6), 21.1 (C-12), 16.8 (C-15).

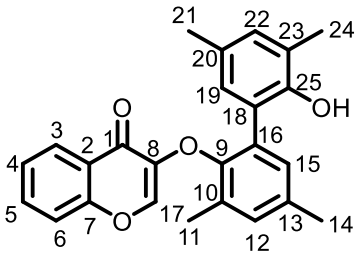
^{19}F NMR (471 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{25}H_{21}O_3^+$ $[M]^+$ requires *m/z* 369.1485, found *m/z* 369.1475.

IR (thin film) ν_{max}/cm^{-1} 2926, 2856, 1670, 1633, 1609, 1464, 1391, 1347, 1307, 1269, 1230, 1178, 1142, 1065, 951, 930, 853, 781, 736.

MP 170-174 °C.

3-((2'-Hydroxy-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-yl)oxy)-4H-chromen-4-one, 463:

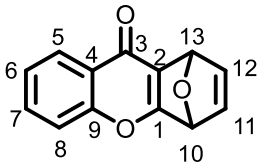


^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 8.4, 1.8 Hz, 1H, H-3), 7.59 (td, *J* = 7.7, 7.0, 1.6 Hz, 1H, H-5), 7.40 (s, 1H, H-17), 7.36 – 7.29 (m, 2H, H-4,6), 7.08 (d, *J* = 2.2 Hz, 1H, H-12), 6.94 (d, *J* = 2.3 Hz, 1H, H-22), 6.74 (s, 2H, H-15,19), 2.34 (s, 3H, H-21), 2.31 (s, 3H, H-14), 2.11 (s, 3H, H-11), 2.06 (s, 3H, H-24).

LRMS (ESI) exact mass calculated for $C_{25}H_{23}O_4^+$ $[M+H]^+$ requires *m/z* 387.1, found *m/z* 387.0.

The title compound appears as a minor impurity during the synthesis of 2,4,6,8-tetramethyl-5-(4-oxo-4H-chromen-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, hence no other characterisation was performed.

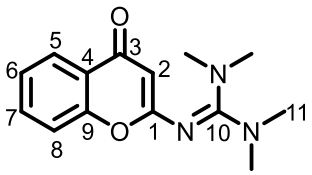
1,4-Dihydro-9H-1,4-epoxyxanthen-9-one, 464:



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 7.9, 1.7 Hz, 1H, H-5), 7.70 – 7.61 (m, 1H, H-7), 7.55 – 7.49 (m, 1H, H-8), 7.45 (t, *J* = 7.6 Hz, 1H, H-6), 7.41 (dd, *J* = 5.4, 1.9 Hz, 1H, H-11 or 12), 7.18 (dd, *J* = 5.5, 2.0 Hz, 1H, H-11 or 12), 6.06 (s, 1H, H-10 or 13), 5.61 – 5.52 (m, 1H, H-10 or 13).

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

1,1,3,3-Tetramethyl-2-(4-oxo-4H-chromen-2-yl)guanidine, 472:



A glass screw cap vial was charged with 2,4,6,8-tetramethyl-5-(4-oxo-4H-chromen-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (11.4 mg, 0.025 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (0.5 mL, 0.05 M). 1,1,3,3-Tetramethylguanidine (15.6 μL, 14.4 mg, 0.125 mmol, 5.0 eq.) was then added before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through

a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 5:95 MeOH:$CHCl_3$, v/v) to obtain the title compound as an oil (3.5 mg, 0.01 mmol, 54%).

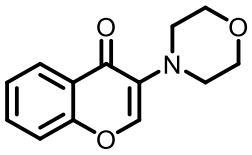
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 7.8, 1.7 Hz, 1H, H-5), 7.52 (ddd, *J* = 8.5, 7.1, 1.7 Hz, 1H, H-7), 7.32 (dd, *J* = 8.5, 1.1 Hz, 1H, H-8), 7.30 (ddd, *J* = 7.8, 7.1, 1.1 Hz, 1H, H-6), 5.28 (s, 1H, H-2), 2.93 (s, 12H, H-11).

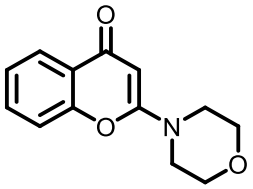
^{13}C NMR (151 MHz, $CDCl_3$) δ 178.5 (C-3), 166.0 (C-1), 163.2 (C-9), 155.1 (C-10), 132.1 (C-7), 125.5 (C-5), 124.2 (C-6), 123.5 (C-4), 117.2 (C-8), 94.1 (C-2), 40.1 (C-11).

HRMS (ESI) exact mass calculated for $C_{14}H_{18}N_3O_2^+$ $[M+H]^+$ requires *m/z* 260.1394, found *m/z* 260.1383.

IR (thin film) ν_{max}/cm^{-1} 1612, 1513, 1461, 1422, 1398, 1356, 1273, 1244, 1160, 1132, 1033, 963, 879, 827, 774, 707.

3-Morpholino-4H-chromen-4-one, 487, and 2-morpholino-4H-chromen-4-one, 487':

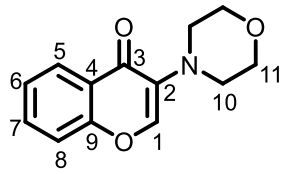




A glass screw cap vial was charged with 2,4,6,8-tetramethyl-5-(4-oxo-4H-chromen-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (11.4 mg, 0.025 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (0.5 mL, 0.05 M). Morpholine (22 μL, 21.8 mg, 0.25 mmol, 10.0 eq.) was then added before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 1:99 MeOH:$CHCl_3$, v/v) to obtain the

major regioisomer **487** as an oil (2.4 mg, 0.01 mmol, 41%). The minor regioisomer could not be isolated in sufficient purity, therefore, only its NMR yield is reported (11%).

3-Morpholino-4H-chromen-4-one, 487:



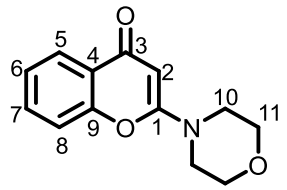
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (s, 1H, H-1), 7.66 (ddd, *J* = 7.6, 1.5, 0.7 Hz, 1H, H-5), 7.54 (dt, *J* = 8.2, 0.9 Hz, 1H, H-8), 7.37 (ddd, *J* = 8.3, 7.2, 1.5 Hz, 1H, H-7), 7.33 (td, *J* = 7.6, 1.1 Hz, 1H, H-6), 3.74 (s, 8H, H-10,11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-3), 154.9 (C-9), 145.8 (C-1), 125.5 (C-7), 125.3 (C-2), 124.0 (C-5), 121.0 (C-6), 116.8 (C-4), 112.0 (C-8), 67.2 (C-10,11).

HRMS (ESI) exact mass calculated for $C_{13}H_{14}NO_3^+$ $[M+H]^+$ requires *m/z* 232.0968, found *m/z* 232.0958.

IR (thin film) ν_{max}/cm^{-1} 2855, 1629, 1562, 1479, 1451, 1431, 1363, 1288, 1269, 1239, 1172, 1113, 1065, 1002, 933, 859, 835, 751.

2-Morpholino-4H-chromen-4-one, 487':



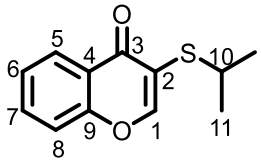
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (s, 1H, H-1), 7.66 (ddd, *J* = 7.6, 1.5, 0.7 Hz, 1H, H-5), 7.54 (dt, *J* = 8.2, 0.9 Hz, 1H, H-8), 7.37 (ddd, *J* = 8.3, 7.2, 1.5 Hz, 1H, H-7), 7.33 (td, *J* = 7.6, 1.1 Hz, 1H, H-6), 3.74 (s, 8H, H-10,11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8 (C-3), 154.9 (C-9), 145.8 (C-1), 125.5 (C-7), 125.3 (C-2), 124.0 (C-5), 121.0 (C-6), 116.8 (C-4), 112.0 (C-8), 67.2 (C-10,11).

HRMS (ESI) exact mass calculated for $C_{13}H_{14}NO_3^+$ $[M+H]^+$ requires *m/z* 232.0968, found *m/z* 232.0961.

Due to the low purity of the title compound, no further characterisation was performed.

3-(Isopropylthio)-4H-chromen-4-one, 488:



A glass screw cap vial was charged with 2,4,6,8-tetramethyl-5-(4-oxo-4H-chromen-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (11.4 mg, 0.025 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (0.5 mL, 0.05 M). 2-Propanethiol (24 µL, 19.0 mg, 0.25 mmol, 10.0 eq.) was then added, followed by K_3PO_4 (26.5 mg, 0.125 mmol, 5.0 eq.) in one portion, before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 5:95 EtOAc:hexane, v/v) to obtain the title compound as an oil (1.7 mg, 0.01 mmol, 22%).

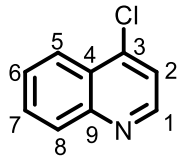
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (s, 1H, H-1), 7.58 (dd, *J* = 7.6, 1.3 Hz, 1H, H-5), 7.29 (td, *J* = 7.8, 1.3 Hz, 1H, H-7), 7.18 (td, *J* = 7.6, 1.0 Hz, 1H, H-6), 7.10 (dt, *J* = 7.8, 1.3 Hz, 1H, H-8), 3.49 (hept, *J* = 6.8 Hz, 1H, H-10), 1.51 (d, *J* = 6.8 Hz, 6H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.8 (C-3), 153.1 (C-9), 144.2 (C-1), 129.1 (C-7), 124.0 (C-4), 123.7 (C-6), 123.5 (C-5), 117.0 (C-2), 110.5 (C-8), 40.8 (C-10), 23.9 (C-11).

HRMS (ESI) exact mass calculated for $C_{12}H_{13}O_2S^+$ $[M+H]^+$ requires *m/z* 221.0631, found *m/z* 221.0623.

IR (thin film) ν_{max}/cm^{-1} 2920, 1775, 1602, 1581, 1459, 1357, 1307, 1271, 1235, 1205, 1149, 1126, 1078, 1057, 1017, 958, 853, 769, 747, 718.

4-Chloroquinoline, 587:



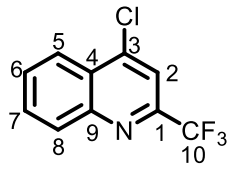
A round bottom flask was charged with $POCl_3$ (25 mL, 1.4 M) and cooled to 0 °C before adding 4-hydroxyquinoline (5.0 g, 34.40 mmol, 1.0 eq.) with stirring. After full addition, the mixture was refluxed at 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (at least 10 mL per 1 mL of $POCl_3$) with vigorous stirring and left to stand until it reached room temperature. The formed suspension was neutralised by adding solid Na_2CO_3 with shaking, then transferred to a separatory funnel and extracted with $CHCl_3$ (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid (5.3 g, 32.40 mmol, 94%). The crude was used without further purification. The NMR spectra are consistent with those available in the literature.[196]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.7 Hz, 1H, H-1), 8.21 (dd, *J* = 8.5, 1.4 Hz, 1H, H-5), 8.11 (dt, *J* = 8.5, 0.8 Hz, 1H, H-8), 7.75 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H, H-7), 7.62 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H, H-6), 7.47 (d, *J* = 4.7 Hz, 1H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0 (C-1), 149.2 (C-9), 142.7 (C-3), 130.5 (C-7), 129.9 (C-8), 127.7 (C-6), 126.6 (C-4), 124.2 (C-5), 121.3 (C-2).

HRMS (ESI) exact mass calculated for $C_9H_7ClN^+$ $[M+H]^+$ requires *m/z* 164.0262, found *m/z* 164.0258.

4-Chloro-2-(trifluoromethyl)quinoline, 589:



A round bottom flask was charged with aniline (1.50 mL, 1.52 g, 16.30 mmol, 1.0 eq.) and ethyl 4,4,4-trifluoroacetoacetate (2.40 mL, 3.00 g, 16.30 mmol, 1.0 eq.) before adding polyphosphoric acid (13.1 g) and refluxing at 150 °C for 2 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (~100 mL) with vigorous stirring, followed by sonication. The formed suspension was then filtered, washing the solid with ice-cold water and drying under air flow, followed by vacuum to obtain a crude solid. The solid was then slowly transferred to an oven-dried round bottom flask containing $POCl_3$ (10 mL) and refluxed at 95 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly poured over ice water (at least 10 mL per 1 mL of $POCl_3$) with vigorous stirring and left to stand until it reached room temperature. The formed suspension was neutralised by adding solid Na_2CO_3 with shaking, then transferred to a separatory funnel and extracted with EtOAc (x3), dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (5:95 Et_2O:pentane, v/v) to obtain the title compound as a solid (1.65 g, 7.12 mmol, 46%). The NMR spectra are consistent with those available in the literature.[197]

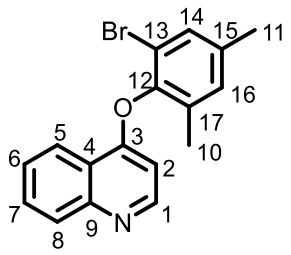
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 8.5, 1.5 Hz, 1H, H-8), 8.24 (dt, J = 8.5, 0.9 Hz, 1H, H-5), 7.88 (ddd, J = 8.5, 6.9, 1.5 Hz, 1H, H-7), 7.82 (s, 1H, H-2), 7.77 (ddd, J = 8.5, 6.9, 1.2 Hz, 1H, H-6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1 (C-9), 147.8 (q, *J* = 35.3 Hz, C-1), 144.8 (C-3), 131.8 (C-7), 130.7 (C-8), 127.2 (C-4), 124.3 (C-5), 121.1 (q, *J* = 275.5 Hz, C-10), 117.4 (q, *J* = 2.3 Hz, C-2).

^{19}F NMR (377 MHz, $CDCl_3$) δ -67.6.

HRMS (ESI) exact mass calculated for $C_{10}H_6ClF_3N^+$ $[M+H]^+$ requires *m/z* 232.0135, found *m/z* 232.0132.

4-(2-Bromo-4,6-dimethylphenoxy)quinoline, 590:



An oven-dried round bottom flask was charged with 4-chloroquinoline (500.0 mg, 3.06 mmol, 1.0 eq.) before adding anhydrous DMSO (7.7 mL, 0.40 M), followed by 2-bromo-4,6-dimethylphenol (924.9 mg, 4.60 mmol, 1.5 eq.). Cs_2CO_3 (3.49 g, 10.71 mmol, 3.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 120 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~150 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (918.0 mg, 2.80 mmol, 91%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (d, *J* = 5.1 Hz, 1H, H-1), 8.47 (dd, *J* = 8.4, 1.4 Hz, 1H, H-5), 8.11 (dd, *J* = 8.4, 1.1 Hz, 1H, H-8), 7.77 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H, H-7), 7.61 (ddd, *J* = 8.4, 6.8, 1.1 Hz, 1H, H-6), 7.37 – 7.34 (m, 1H, H-14), 7.09 – 7.06 (m, 1H, H-16), 6.29 (d, *J* = 5.1 Hz, 1H, H-2), 2.36 (s, 3H, H-11), 2.15 (s, 3H, H-10).

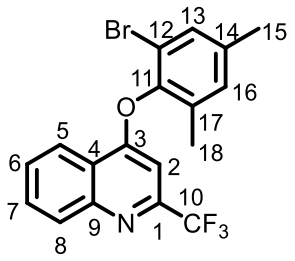
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1 (C-3), 151.3 (C-1), 149.9 (C-12), 146.8 (C-9), 137.4 (C-15), 132.9 (C-17), 132.0 (C-14), 131.6 (C-16), 130.2 (C-7), 129.2 (C-8), 126.2 (C-6), 122.0 (C-5), 120.9 (C-4), 116.7 (C-13), 102.6 (C-2), 20.8 (C-11), 16.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}BrNO^+$ $[M+H]^+$ requires *m/z* 328.0332, found *m/z* 328.0326.

IR (thin film) ν_{max}/cm^{-1} 3431, 3063, 2949, 1595, 1568, 1503, 1210, 765.

MP 56-60 °C.

4-(2-Bromo-4,6-dimethylphenoxy)-2-(trifluoromethyl)quinoline, 591:



An oven-dried microwave vial was charged with 4-chloro-2-(trifluoromethyl)quinoline (185.3 mg, 0.80 mmol, 1.0 eq.) before adding anhydrous DMSO (2.0 mL, 0.40 M), followed by 2-bromo-4,6-dimethylphenol (241.3 mg, 1.20 mmol, 1.5 eq.). Cs_2CO_3 (912.3 mg, 2.8 mmol, 3.5 eq.) was then added in one portion with stirring before capping and heating the reaction mixture to 120 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~100 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by

flash column chromatography (5:95 Et_2O:pentane, v:v) to obtain the title compound as a solid (239.7 mg, 0.60 mmol, 76%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 – 8.50 (m, 1H, H-5), 8.23 (d, *J* = 8.6 Hz, 1H, H-8), 7.87 (ddd, *J* = 8.6, 7.0, 1.5 Hz, 1H, H-7), 7.73 (t, *J* = 7.7 Hz, 1H, H-6), 7.38 (d, *J* = 2.6 Hz, 1H, H-13), 7.11 (d, *J* = 2.6 Hz, 1H, H-16), 6.58 (s, 1H, H-2), 2.39 (s, 3H, H-15), 2.16 (s, 3H, H-18).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.7 (C-3), 149.0 (q, *J* = 34.4 Hz, C-1), 148.9 (C-11), 146.2 (C-9), 138.0 (C-14), 132.6 (C-17), 132.3 (C-13), 131.9 (C-16), 131.5 (C-7), 130.0 (C-8), 128.2 (C-6), 122.1 (C-5), 121.5 (q, *J* = 275.0 Hz, C-10), 121.3 (C-4), 116.3 (C-12), 98.5 (q, *J* = 2.4 Hz, C-2), 20.8 (C-15), 16.7 (C-18).

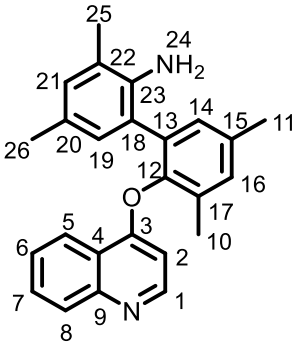
^{19}F NMR (470 MHz, $CDCl_3$) δ -67.6.

HRMS (ESI) exact mass calculated for $C_{18}H_{14}BrF_3NO^+$ $[M+H]^+$ requires *m/z* 396.0205, found *m/z* 396.0197.

IR (thin film) ν_{max}/cm^{-1} 2926, 1598, 1574, 1509, 1470, 1428, 1377, 1252, 1141, 929.

MP 118-120 °C.

3,3',5,5'-Tetramethyl-2'-(quinolin-4-yloxy)-[1,1'-biphenyl]-2-amine, 547:



A 100 mL 3-neck round bottom flask was charged with 4-(2-bromo-4,6-dimethylphenoxy)quinoline (850.0 mg, 2.59 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-

tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (961.4 mg, 3.89 mmol, 1.5 eq.), Pd(dppf)Cl_2 · CH_2Cl_2 (106.2 mg, 5 mol%) and Na_2CO_3 (1.10 g, 10.36 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed PhMe was then added, followed by degassed H_2O (1:1, 52 mL, 0.05 M). The suspension was sparged with argon for 15 minutes, then heated to 95 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (35:65 EtOAc:pentane, v:v) to obtain the title compound as a solid (431.6 mg, 1.17 mmol, 45%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (d, *J* = 5.2 Hz, 1H, H-1), 8.24 (dd, *J* = 8.4, 1.5 Hz, 1H, H-5), 7.95 (d, *J* = 8.4 Hz, 1H, H-8), 7.64 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.46 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H, H-6), 7.15 (d, *J* = 2.2 Hz, 1H, H-16), 7.11 (s, 1H, H-19), 6.54 (br s, 2H, H-14,21), 6.29 (d, *J* = 5.2 Hz, 1H, H-2), 3.54 (s, 2H, H-NH_2), 2.40 (s, 3H, H-11), 2.19 (s, 3H, H-26), 1.98 (s, 3H, H-25), 1.97 (s, 3H, H-10).

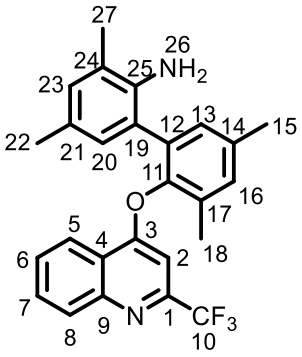
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.1 (C-6), 150.9 (C-1), 149.6 (C-9), 147.6 (C-12), 139.4 (C-23), 136.2 (C-21), 133.2 (C-15), 131.7 (C-16), 130.6 (C-14,21), 129.8 (C-7), 128.9 (C-20), 128.8 (C-8), 126.7 (C-17), 125.5 (C-6), 122.5 (C-18), 121.9 (C-5), 121.1 (C-4), 103.1 (C-2), 21.0 (C-11), 20.2 (C-10), 17.8 (C-25), 16.4 (C-26).

HRMS (ESI) exact mass calculated for $C_{25}H_{25}N_2O^+$ $[M+H]^+$ requires *m/z* 369.1961, found *m/z* 369.1954.

IR (thin film) ν_{max}/cm^{-1} 3026, 2920, 2857, 1622, 1571, 1504, 1393, 1305, 1202, 766.

MP decomposes 160 °C.

3,3',5,5'-Tetramethyl-2'-((2-(trifluoromethyl)quinolin-4-yl)oxy)-[1,1'-biphenyl]-2-amine, 549:



An oven-dried 10 mL microwave vial was charged with 4-(2-bromo-4,6-dimethylphenoxy)-2-(trifluoromethyl)quinoline (201.0 mg, 0.51 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (150.8 mg, 0.61 mmol, 1.2 eq.), $Pd(PPh_3)_4$ (34.7 mg, 5 mol%) and K_2CO_3 (281.9 mg, 1.04 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 5.1 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (187.9 mg, 0.43 mmol, 84%).

^{1}H NMR (500 MHz, DMSO, 85 °C) δ 8.34 (dd, *J* = 8.4, 1.5 Hz, 1H, H-5), 7.99 (d, *J* = 8.4 Hz, 1H, H-8), 7.83 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H, H-7), 7.69 (ddd, *J* = 8.4, 6.9, 1.2 Hz, 1H, H-6), 7.26 (d, *J* = 2.1 Hz, 1H, H-16), 7.08 (d, *J* = 2.1 Hz, 1H, H-20), 6.63 (s, 1H, H-2), 6.48 (s, 1H, H-13), 6.38 (d, *J* = 2.1 Hz, 1H, H-23), 4.02 (s, 2H, H-26), 2.39 (s, 3H, H-15), 2.22 (s, 3H, H-22), 1.84 (s, 3H, H-27), 1.83 (s, 3H, H-18).

^{13}C NMR (126 MHz, DMSO) δ 161.6 (C-3), 147.4 (C-9), 146.9 (q, *J* = 34.1 Hz, C-1), 146.6 (C-11), 139.8 (C-25), 135.6 (C-14), 132.0 (C-16,7), 131.0 (C-20), 130.9 (C-23), 130.2 (C-21), 129.8 (C-17), 129.6 (C-8), 128.5 (C-13), 127.9 (C-6), 127.3 (C-12), 123.8 (C-19), 121.4 (C-5), 121.3 (C-24), 120.9 (q, *J* = 275.5 Hz, C-10), 120.4 (C-4), 98.5 (C-2), 20.0 (C-15), 19.0 (C-18), 16.8 (C-22), 15.2 (C-27).

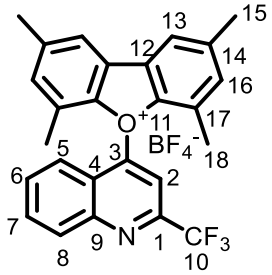
^{19}F NMR (471 MHz, DMSO, 90 °C) δ -66.7.

HRMS (ESI) exact mass calculated for $C_{26}H_{24}F_3N_2O^+$ $[M+H]^+$ requires *m/z* 437.1835, found *m/z* 437.1823.

IR (thin film) ν_{max}/cm^{-1} 3734, 3314, 2923, 2360, 2341, 1592, 1573, 1533, 1459, 1287, 1184, 1134, 1026, 931.

MP 174-178 °C.

2,4,6,8-Tetramethyl-5-(2-(trifluoromethyl)quinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 550:



A glass screw-cap vial was charged with 3,3',5,5'-tetramethyl-2'-((2-(trifluoromethyl)quinolin-4-yl)oxy)-[1,1'-biphenyl]-2-amine (99.5 mg, 0.23 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.920 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 0.150 mL, 1.15 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (0.140 mL, 118.6 mg, 1.15 mmol, 5.00 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature.

After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (2.3 mL, 0.10 M) and heated to 40 °C for 24 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (66.7 mg, 0.13 mmol, 57%).

^{1}H NMR (600 MHz, CD_3CN) δ 8.75 (dd, *J* = 8.5, 1.4 Hz, 1H, H-5), 8.51 (d, *J* = 8.6 Hz, 1H, H-8), 8.27 (ddd, *J* = 8.6, 7.0, 1.4 Hz, 1H, H-7), 8.21 (ddd, *J* = 8.5, 7.0, 1.4 Hz, 1H, H-6), 8.03 – 8.01 (m, 2H, H-13), 8.01 (s, 1H, H-2), 7.32 – 7.28 (m, 2H, H-16), 2.53 (s, 6H, H-18), 1.80 (s, 6H, H-15).

^{13}C NMR (151 MHz, CD_3CN) δ 163.30 (s, C-9), 163.29 (C-11), 150.8 (C-3), 149.8 (q, *J* = 37.2 Hz, C-1), 143.5 (C-12), 135.8 (C-16), 135.5 (C-7), 134.4 (C-6), 132.1 (C-8), 124.7 (C-14), 124.5 (C-17), 123.1 (C-13), 121.7 (C-5), 121.34 (C-4), 121.32 (q, *J* = 275.3 Hz, C-10), 110.9 (q, *J* = 2.3 Hz, C-2), 21.1 (C-18), 17.0 (C-15).

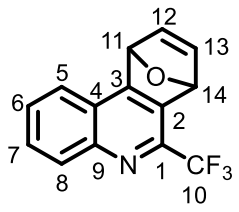
^{19}F NMR (471 MHz, CD_3CN) δ -67.7 (CF_3), -151.48 (BF_4^-), -151.54 (BF_4^-).

HRMS (ESI) exact mass calculated for $C_{26}H_{21}F_3NO^+$ $[M]^+$ requires *m/z* 420.1570, found *m/z* 420.1568.

IR (thin film) ν_{max}/cm^{-1} 3076, 2349, 1610, 1473, 1348, 1270, 1205, 1148, 1061, 996, 903, 862.

MP 168 °C.

6-(Trifluoromethyl)-7,10-dihydro-7,10-epoxyphenanthridine, 551:



A glass screw cap vial was charged with 2,4,6,8-tetramethyl-5-(2-(trifluoromethyl)quinolin-4-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (58.8 mg, 0.12 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (2.4 mL, 0.05 M). Furan (44 μL, 40.8 mg, 0.60 mmol, 5.0 eq.) was then added, followed by K_3PO_4 (127.4 mg, 0.60 mmol, 5.0 eq.) in one portion, before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v/v) to obtain the title compound as a solid (22.9 mg, 0.09 mmol, 74%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (dt, *J* = 8.7, 1.0 Hz, 1H, H-5), 7.88 (ddd, *J* = 8.4, 1.4, 1.0 Hz, 1H, H-8), 7.75 (ddd, *J* = 8.7, 6.8, 1.4 Hz, 1H, H-7), 7.63 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H, H-6), 7.26 (dd, *J* = 5.5, 1.9 Hz, 1H, H-13), 7.20 (dd, *J* = 5.5, 1.9 Hz, 1H, H-12), 6.31 (dd, *J* = 2.0, 1.0 Hz, 1H, H-11), 6.27 (td, *J* = 1.7, 1.0 Hz, 1H, H-14).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4 (C-3), 146.5 (C-9), 145.1 (C-12), 142.9 (C-13), 140.8 (C-2), 140.3 (q, *J* = 36.0 Hz, C-1), 130.9 (C-7), 130.7 (C-5), 128.7 (C-6), 123.9 (C-4), 123.1 (C-8), 121.9 (q, *J* = 274.8 Hz, C-10), 82.3 (q, *J* = 2.5 Hz, C-14), 80.9 (C-11).

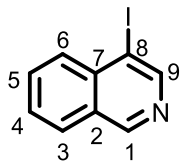
^{19}F NMR (565 MHz, $CDCl_3$) δ -65.4.

HRMS (APCI) exact mass calculated for $C_{14}H_9F_3NO^+$ $[M+H]^+$ requires *m/z* 264.0631, found *m/z* 264.0628.

IR (thin film) ν_{max}/cm^{-1} 3050, 2920, 2851, 1457, 1279, 1193, 1138, 1059, 1016.

MP 108 °C.

4-Iodoisoquinoline, 593:



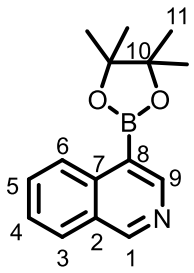
A round bottom flask was charged with isoquinoline (1.4 mL, 1.50 g, 11.60 mmol, 1.0 eq.), iodine (1.62 g, 6.38 mmol, 0.55 eq.), H_2O (21 μL, 10 mol%) and TBHP (6.0 M in decane, 281.9 mg, 1.0 mL, 0.5 eq.) before heating the reaction mixture to 40 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and diluted with EtOAc (10 mL), then poured into a separatory funnel containing saturated aqueous $Na_2S_2O_3$ (100 mL). The aqueous layer was then extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (15:85 to 20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.99 g, 11.72 mmol, 83%). The NMR spectra are consistent with those available in the literature.[198]

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 0.8 Hz, 1H, H-1), 8.93 (s, 1H, H-9), 7.97 (dq, *J* = 8.5, 0.9 Hz, 1H, H-6), 7.88 (dt, *J* = 8.1, 0.9 Hz, 1H, H-3), 7.77 (ddd, *J* = 8.5, 6.9, 1.1 Hz, 1H, H-4), 7.65 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7 (C-1), 151.1 (C-9), 137.2 (C-7), 132.1 (C-5), 130.8 (C-6), 129.8 (C-2), 128.4 (C-4), 128.3 (C-3), 96.9 (C-8).

HRMS (ESI) exact mass calculated for $C_9H_7IN^+$ $[M+H]^+$ requires *m/z* 255.9618, found *m/z* 255.9616.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)isoquinoline, 594:

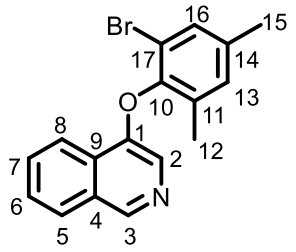


A flame-dried 3-neck round bottom flask was charged with 4-iodoisoquinoline (255.1 mg, 1.0 mmol, 1.0 eq.), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (24.5 mg, 3 mol%), B_2Pin_2 (380.9 mg, 1.5 mmol, 1.5 eq.) and KOAc (294.4 mg, 3.0 mmol, 3.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Anhydrous 1,4-dioxane (8.0 mL, 0.13 M) was added to form a suspension, which was then sparged with argon for 10 minutes. After sparging, the reaction mixture was heated to 95 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with deionised water, dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid (99.1 mg, 0.39 mmol, 39%), which was used without any further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (d, *J* = 5.7 Hz, 1H, H-1), 7.96 (dt, *J* = 8.2, 1.0 Hz, 1H, H-6), 7.81 (dd, *J* = 8.3, 1.1 Hz, 1H, H-3), 7.69 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, H-4), 7.64 (d, *J* = 5.7 Hz, 1H, H-9), 7.60 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H, H-5), 1.25 (s, 12H, H-11).

^{13}C NMR (151 MHz, $CDCl_3$) δ 152.6 (C-9), 143.0 (C-1), 135.9 (C-7), 130.5 (C-2), 127.8 (C-5), 127.4 (C-3), 126.6 (C-4), 120.6 (C-6), 82.0 (C-10), 24.2 (C-11).

4-(2-Bromo-4,6-dimethylphenoxy)isoquinoline, 596:



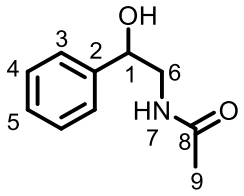
A glass screw cap vial was charged with 4-aminoisoquionline (61.5 mg, 0.43 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (601.2 mg, 2.99 mmol, 7.0 eq.), before adding TFA (50 µL, 0.65 mmol, 1.5 eq.) dropwise and cooling to 0 °C. *t*-BuONO (56 µL, 48.5 mg, 0.47 mmol, 1.1 eq.) was then added dropwise and the reaction mixture was stirred at room temperature for 15 minutes. Subsequently, K_2CO_3 (89.8 mg, 0.65 mmol, 1.5 eq.) was added in small portions and the reaction was left to stir for 1 hour. After the reaction time, the mixture was diluted with EtOAc (10 mL), then poured into a separatory funnel containing 1 M aqueous NaOH (50 mL). The aqueous layer was then extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (25:75 EtOAc:pentane, v:v) to obtain the title compound as an impure oil (16.4 mg, <0.05 mmol, <12%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.32 (s, 1H, H-3), 8.88 (s, 1H, H-2), 8.51 (dd, *J* = 8.5, 1.0 Hz, 1H, H-8), 8.09 (dt, *J* = 8.2, 1.0 Hz, 1H, H-5), 7.87 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H, H-6), 7.75 – 7.71 (m, 1H, H-7), 7.71 (d, *J* = 2.6 Hz, 1H, H-16), 7.15 – 7.12 (m, 1H, H-13), 2.39 (s, 3H, H-15), 2.33 (s, 3H, H-12).

HRMS (ESI) exact mass calculated for $C_{17}H_{15}BrNO^+$ $[M+H]^+$ requires *m/z* 328.0332, found *m/z* 328.0331.

Due to the impurities isolated with the title compound, a quality ^{13}C spectrum could not be obtained and no further characterisation was performed.

***N*-(2-hydroxy-2-phenylethyl)acetamide, 600:**



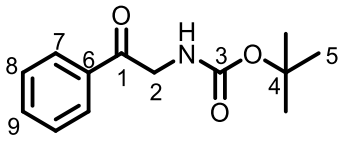
An oven-dried round bottom flask was charged with phenylethanolamine (3.9 g, 28.40 mmol, 1.0 eq.) and isopropyl acetate (9.4 mL, 8.71 g, 85.3 mmol, 3.0 eq.) before the sonication of the reaction mixture for 5 minutes. After this time, the mixture was stirred at room temperature for 16 hours. Subsequently, the reaction was concentrated under vacuum to obtain a crude solid (5.07 g, 28.29 mmol, 99%), which was used without any further purification. The NMR spectra are consistent with those available in the literature.[199]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H, Ar Hs), 6.21 (s, 1H, H-7), 4.79 (dd, *J* = 8.1, 3.4 Hz, 1H, H-1), 3.64 (ddd, *J* = 14.1, 6.9, 3.4 Hz, 1H, H-6), 3.28 (ddd, *J* = 14.1, 8.1, 4.9 Hz, 1H, H-6'), 1.95 (s, 3H, H-9).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8 (C-8), 141.9 (C-2), 128.6 (C-4), 128.0 (C-5), 125.9 (C-3), 73.6 (C-1), 47.6 (C-6), 23.2 (C-9).

HRMS (ESI) exact mass calculated for $C_{10}H_{14}NO_2^+$ $[M+H]^+$ requires *m/z* 180.1019, found *m/z* 180.1017.

***tert*-Butyl (2-oxo-2-phenylethyl)carbamate, 602:**



A 500 mL round bottom flask was charged with 2-aminoacetophenone hydrochloride (5.0 g, 29.13 mmol, 1.0 eq.), before adding deionised water (99 mL) and MeOH (100 mL, 0.3

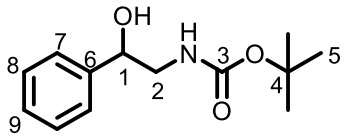
M). Boc_2O (9.54 g, 43.70 mmol, 1.5 eq.) was then added in one portion, followed by solid $NaHCO_3$ (6.12 g, 72.83 mmol, 2.5 eq.). The reaction mixture was then stirred at room temperature for 16 hours. After the reaction time, the mixture was poured into ice water (~350 mL) and the formed suspension was filtered, then further dried under vacuum to obtain a crude solid (4.16 g, 17.68 mmol, 61%), which was used without any further purification. The NMR spectra are consistent with those available in the literature.[200]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.91 (m, 2H, H-7), 7.62 – 7.56 (m, 1H, H-9), 7.50 – 7.44 (m, 2H, H-8), 5.58 (t, *J* = 4.6 Hz, 1H, NH), 4.66 (d, *J* = 4.6 Hz, 2H, H-2), 1.47 (s, 9H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6 (C-1), 155.9 (C-3), 134.6 (C-6), 134.0 (C-9), 129.0 (C-8), 127.9 (C-7), 79.9 (C-4), 47.6 (C-2), 28.5 (C-5).

HRMS (ESI) exact mass calculated for $C_{13}H_{18}NO_3^+$ $[M+H]^+$ requires *m/z* 236.1281, found *m/z* 236.1280.

***tert*-Butyl (2-hydroxy-2-phenylethyl)carbamate, 603:**



An oven-dried round bottom flash was charged with tert-butyl (2-oxo-2-phenylethyl)carbamate (4.00 g, 17.0 mmol, 1.0 eq.), before adding MeOH (57 mL, 0.3 M) cooling to 0 °C. With vigorous stirring, $NaBH_4$ (3.22 g, 85.0 mmol, 5.0 eq.) was added slowly in small portions, then the reaction mixture was brought to room temperature and stirred for 30 minutes. After the reaction time, the mixture was quenched with deionised water (~2 mL), then partially concentrated under vacuum before redissolving in EtOAc (200 mL). The solutions was then washed with deionised water (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid (1.86 g, 7.84 mmol,

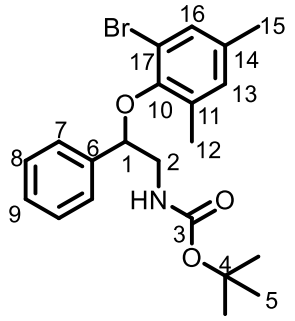
46%), which was used without any further purification. The NMR spectra are consistent with those available in the literature.[201]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 5H, Ar Hs), 5.00 (s, 1H, NH), 4.81 (dt, *J* = 7.7, 3.3 Hz, 1H, H-1), 3.47 (dt, *J* = 14.3, 4.7 Hz, 1H, H-2), 3.34 – 3.15 (m, 2H, H-2', OH), 1.44 (s, 9H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1 (C-3), 141.9 (C-6), 128.6 (C-8), 127.9 (C-9), 126.0 (C-7), 80.0 (C-4), 74.1 (C-1), 48.5 (C-2), 28.5 (C-5).

HRMS (ESI) exact mass calculated for $C_{13}H_{20}NO_3^+$ $[M+H]^+$ requires *m/z* 238.1438, found *m/z* 238.1436.

***tert*-Butyl (2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethyl)carbamate, 603:**



An oven-dried round bottom flash was charged with *tert*-butyl (2-hydroxy-2-phenylethyl)carbamate (1.50 g, 6.32 mmol, 1.0 eq.) and PPh_3 (1.99 g, 7.58 mmol, 1.2 eq.), before adding anhydrous THF (32 mL, 0.2 M) and 2-bromo-4,6-dimethylphenol (1.52 g, 7.58 mmol, 1.2 eq.). The solution was cooled to 0 °C and, under nitrogen, DIAD (1.5 mL, 1.53 g, 7.58 mmol, 1.2 eq.) was added dropwise. After full addition, the reaction mixture was brought to room temperature and stirred for 2 hours. After the reaction time, the mixture was poured into a separatory funnel containing deionised water (~300 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash

column chromatography (5:95 to 15:85 Et_2O:pentane, v:v) to obtain the title compound as an oil (1.93 g, 4.59 mmol, 73%).

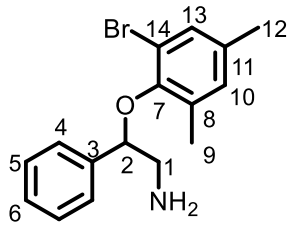
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H, H-7,8,9), 7.18 (d, *J* = 2.2 Hz, 1H, H-16), 6.79 (d, *J* = 2.2 Hz, 1H, H-13), 5.22 (t, *J* = 6.1 Hz, 1H, H-1), 4.94 (t, *J* = 6.2 Hz, 1H, H-NH), 3.85 – 3.79 (m, 1H, H-2), 3.67 – 3.61 (m, 1H, H-2'), 2.21 (s, 3H, H-15), 1.94 (s, 3H, H-12), 1.38 (s, 9H, H-5).

^{13}C NMR (151 MHz, $CDCl_3$) δ 156.0 (C-3), 150.7 (C-10), 138.2 (C-6), 134.7 (C-14), 133.1 (C-11), 131.7 (C-16), 131.5 (C-13), 128.6 (C-8), 128.4 (C-9), 127.9 (C-7), 116.8 (C-17), 83.0 (C-1), 79.4 (C-4), 45.4 (C-2), 28.5 (C-5), 20.4 (C-15), 17.7 (C-12).

HRMS (ESI) exact mass calculated for $C_{21}H_{27}BrNO_3^+$ $[M+H]^+$ requires *m/z* 420.1169, found *m/z* 420.1164.

IR (thin film) ν_{max}/cm^{-1} 3445, 2979, 1766, 1712, 1505, 1473, 1456, 1392, 1366, 1274, 1250, 1220, 1171, 1125, 1067, 1031, 966, 898, 816, 759, 700.

2-(2-Bromo-4,6-dimethylphenoxy)-2-phenylethan-1-amine, 604:



An oven-dried round bottom flash was charged with *tert*-butyl (2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethyl)carbamate (1.88 g, 4.47 mmol, 1.0 eq.), before adding anhydrous CH_2Cl_2 (30 mL, 0.15 M). With stirring, TFA (3.6 mL) was added dropwise, then the reaction mixture was stirred at room temperature for 16 hours. After the reaction time, the mixture was partially concentrated under vacuum before redissolving in EtOAc (250 mL). The solution was then washed with saturated aqueous $NaHCO_3$ (x3) and

deionised water (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil (1.36 g, 4.25 mmol, 95%), which was used without any further purification.

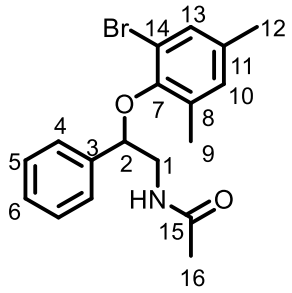
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 5H, Ar Hs), 7.19 (d, *J* = 2.2 Hz, 1H, H-13), 6.80 (dd, *J* = 2.2, 1.2 Hz, 1H, H-10), 5.06 (t, *J* = 5.7 Hz, 1H, H-2), 3.33 (dd, *J* = 13.5, 5.5 Hz, 1H, H-1), 3.24 (dd, *J* = 13.5, 6.0 Hz, 1H, H-1'), 2.21 (s, 3H, H-12), 1.95 (s, 3H, H-9).

^{13}C NMR (151 MHz, $CDCl_3$) δ 151.1 (C-7), 138.8 (C-3), 134.6 (C-11), 133.2 (C-8), 131.7 (C-13), 131.4 (C-10), 128.5 (C-5), 128.4 (C-6), 127.9 (C-4), 116.9 (C-14), 86.2 (C-2), 46.8 (C-1), 20.4 (C-12), 17.7 (C-9).

HRMS (ESI) exact mass calculated for $C_{16}H_{19}BrNO^+$ $[M+H]^+$ requires *m/z* 320.0645, found *m/z* 320.0638.

IR (thin film) ν_{max}/cm^{-1} 3032, 2921, 1764, 1602, 1473, 1376, 1275, 1221, 1201, 1125, 1077, 1037, 972, 914, 853, 765, 738, 700.

***N*-(2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethyl)acetamide, 567:**



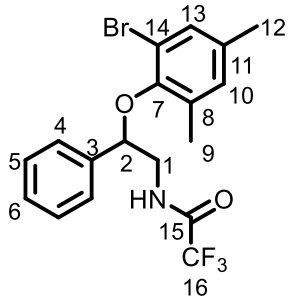
An oven-dried microwave vial was charged with 2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethan-1-amine (45.0 mg, 0.14 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (0.6 mL, 0.25 M), capping and cooling to 0 °C. DIPEA (37 µL, 27.1 mg, 0.21 mmol, 1.5 eq.) was then added, followed by acetyl chloride (12 µL, 13.3 mg, 0.17 mmol,

1.2 eq.) dropwise. The reaction mixture was then brought to room temperature and left to stir for 16 hours. After the reaction time, the solution was poured into deionised water (50 mL), then extracted with EtOAc (x3). Combined organics were washed with saturated $NaHCO_3$ (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (40:60 EtOAc:pentane, v/v) to obtain the title compound as a solid (32.7 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H, H-4,5,6), 7.16 (d, *J* = 2.2 Hz, 1H, H-13), 6.78 – 6.73 (m, 1H, H-10), 6.21 (d, *J* = 5.9 Hz, 1H, H-NH), 5.23 (dd, *J* = 7.5, 4.9 Hz, 1H, H-2), 3.85 (qdd, *J* = 13.9, 7.0, 5.0 Hz, 2H, H-1), 2.19 (s, 3H, H-12), 1.89 (s, 3H, H-16), 1.86 (s, 3H, H-9).

All of the isolated material was subjected to further synthetic transformations and hence no other characterisation was performed.

***N*-(2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethyl)-2,2,2-trifluoroacetamide, 568:**



A flame-dried round bottom flask was charged with 2-(2-bromo-4,6-dimethylphenoxy)-2-phenylethan-1-amine (1.30 g, 4.06 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (16.0 mL, 0.25 M) and cooling to 0 °C. 2,6-Lutidine (0.520 mL, 479.0 mg, 4.47 mmol, 1.1 eq.) was then added, followed by TFAA (0.620 mL, 938.8 mg, 4.47 mmol, 1.1 eq.) dropwise. The reaction mixture was then brought to room temperature and left to stir for 16 hours. After the reaction time, the solution was diluted with CH_2Cl_2 (~200 mL),

then washed with 1 M aqueous HCl (x3), followed by saturated $NaHCO_3$ (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v/v) to obtain the title compound as an oil (1.45 g, 3.48 mmol, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H, H-Ar Hs), 7.20 (d, *J* = 2.2 Hz, 1H, H-13), 7.19 (s, 1H, H-NH), 6.80 – 6.76 (m, 1H, H-10), 5.29 (dd, *J* = 7.9, 4.1 Hz, 1H, H-2), 4.03 (ddd, *J* = 13.3, 7.9, 5.0 Hz, 1H, H-1), 3.94 (ddd, *J* = 14.0, 6.5, 4.1 Hz, 1H, H-1'), 2.22 (s, 3H, H-12), 1.82 (s, 3H, H-9).

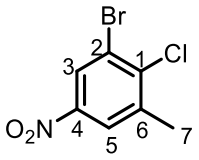
^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3 (q, *J* = 37.2 Hz, C-15), 149.9 (C-7), 136.7 (C-3), 135.4 (C-11), 133.3 (C-8), 131.8 (C-10 or 13), 131.7 (C-10 or 13), 129.3 (C-6), 128.6 (C-5), 127.7 (C-4), 116.4 (C-14), 115.9 (q, *J* = 288.0 Hz, C-16), 81.7 (C-2), 44.4 (C-1), 20.4 (C-12), 17.5 (C-9).

^{19}F NMR (471 MHz, $CDCl_3$) δ -75.9.

HRMS (ESI) exact mass not detected.

IR (thin film) ν_{max}/cm^{-1} 3319, 3036, 2925, 2362, 1716, 1545, 1473, 1348, 1275, 1214, 1179, 1125, 1018, 913, 853, 811, 767, 728.

1-Bromo-2-chloro-3-methyl-5-nitrobenzene, 573:



A round bottom flask was charged with 2-bromo-6-methyl-4-nitroaniline (4.00 g, 17.31 mmol, 1.0 eq.) before adding anhydrous MeCN (170 mL, 0.1 M), followed by anhydrous $CuCl_2$ (3.95 g, 29.4 mmol, 1.7 eq.). The suspension was then cooled to 0 °C and *tert*-butyl nitrite (4.1 mL, 3.56 g, 34.5 mmol, 2.0 eq.) was added dropwise. After full addition, the

reaction mixture was brought to room temperature and then heated to 50 °C for 16 hours. After the reaction time, deionised water (500 mL) was added and the aqueous layer was extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude residue was purified by flash column chromatography (5:95, Et_2O:pentane, v/v) to give the title compound as a solid (3.94 g, 15.73 mmol, 91%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, *J* = 2.6 Hz, 1H, H-3), 8.07 (dq, *J* = 2.6, 0.8 Hz, 1H, H-5), 2.55 (s, 3H, H-7).

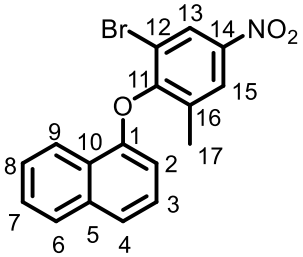
^{13}C NMR (151 MHz, $CDCl_3$) δ 146.0 (C-4), 141.8 (C-1), 139.9 (C-6), 126.3 (C-3), 124.2 (C-5), 123.7 (C-2), 22.1 (C-7).

HRMS (ESI) exact mass calculated for $C_7H_6BrClNO_2^+$ $[M+H]^+$ requires *m/z* 248.9192, found *m/z* 248.9187.

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

MP 91-92 °C.

1-(2-Bromo-6-methyl-4-nitrophenoxy)naphthalene, 607:



An oven-dried round bottom flask was charged with 1-naphthol (144.2 mg, 1.0 mmol, 1.0 eq.) before adding anhydrous DMSO (3.3 mL, 0.3 M), followed by 1-bromo-2-chloro-3-methyl-5-nitrobenzene (275.5 mg, 1.1 mmol, 1.1 eq.). K_2CO_3 (276.4 mg, 2.0 mmol, 2.0 eq.) was then added in one portion with stirring before heating the reaction mixture to

120 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~100 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (5:95 Et_2O:pentane, v:v) to obtain the title compound as a solid (233.4 mg, 0.65 mmol, 68%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 – 8.47 (m, 1H, H-9), 8.46 (d, *J* = 2.7 Hz, 1H, H-13), 8.20 (d, *J* = 2.7 Hz, 1H, H-15), 7.96 – 7.88 (m, 1H, H-7), 7.63 (m, 2H, H-6,8), 7.59 (d, *J* = 8.1 Hz, 1H, H-4), 7.28 (t, *J* = 7.9 Hz, 1H, H-3), 6.33 (d, *J* = 7.6 Hz, 1H, H-2), 2.32 (s, 3H, H-17).

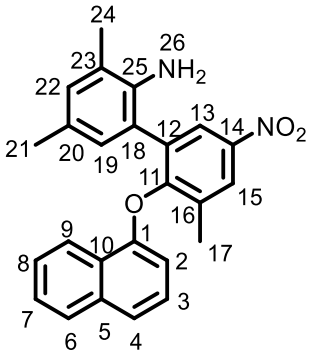
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9 (C-11), 152.0 (C-1), 145.1 (C-14), 135.4 (C-5), 135.1 (C-16), 127.9 (C-7), 127.2 (C-13), 127.1 (C-8), 126.2 (C-6), 125.8 (C-15), 125.5 (C-3), 124.9 (C-10), 122.9 (C-4), 121.9 (C-9), 118.6 (C-12), 106.8 (C-2), 17.3 (C-17).

HRMS (APCI) exact mass calculated for $C_{17}H_{13}BrNO_3^+$ $[M+H]^+$ requires *m/z* 358.0073, found *m/z* 358.0076.

IR (thin film) ν_{max}/cm^{-1} 3088, 2921, 2851, 1599, 1574, 1530, 1461, 1393, 1346, 1260, 1094.

MP 101-106 °C.

3,3',5-Trimethyl-2'-(naphthalen-1-yloxy)-5'-nitro-[1,1'-biphenyl]-2-amine, 577:



An oven-dried 10 mL microwave vial was charged with 1-(2-bromo-6-methyl-4-nitrophenoxy)naphthalene (172.4 mg, 0.50 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (148.3 mg, 0.60 mmol, 1.2 eq.), $Pd(PPh_3)_4$ (28.8 mg, 5 mol%) and K_2CO_3 (276.4 mg, 2.00 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 5.0 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (151.3 mg, 0.38 mmol, 76%).

^{1}H NMR (500 MHz, DMSO, 90 °C) δ 8.27 (d, *J* = 2.9 Hz, 1H, H-13), 8.25 – 8.19 (m, 1H, H-9), 8.04 (d, *J* = 2.9 Hz, 1H, H-15), 7.82 – 7.75 (m, 1H, H-7), 7.48 (m, 2H, H-8,6), 7.42 (d, *J* = 8.2 Hz, 1H, H-4), 7.19 (t, *J* = 7.6 Hz, 1H, H-3), 6.58 (s, 1H, H-19), 6.51 (d, *J* = 7.6 Hz, 1H, H-2), 6.46 (d, *J* = 2.2 Hz, 1H, H-22), 4.12 (s, 2H, H-26), 2.31 (s, 3H, H-17), 1.93 (s, 3H, H-21), 1.87 (s, 3H, H-24).

^{13}C NMR (126 MHz, DMSO, 90 °C) δ 156.1 (C-11), 152.2 (C-1), 144.2 (C-25), 140.0 (C-14), 134.3 (C-5), 133.7 (C-20), 133.3 (C-16), 130.1 (C-22), 127.7 (C-19), 126.7 (C-

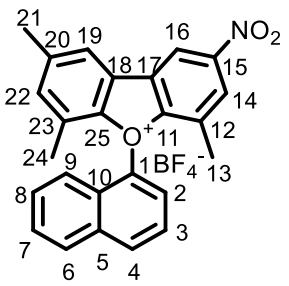
7), 125.9 (C-6), 124.85 (C-8), 124.80 (C-3), 124.77 (C-13), 124.69 (C-15), 124.1 (C-12), 123.8 (C-18), 121.6 (C-10), 121.2 (C-4), 120.9 (C-9), 119.6 (C-23), 107.5 (C-2), 19.1 (C-24), 16.9 (C-21), 15.7 (C-17).

HRMS (ESI) exact mass calculated for $C_{25}H_{23}N_2O_3^+$ $[M+H]^+$ requires *m/z* 399.1703, found *m/z* 399.1701.

IR (thin film) ν_{max}/cm^{-1} 3390, 2918, 1625, 1598, 1575, 1524, 1392, 1350, 1229, 1206, 1155, 1095, 1015, 950.

MP 134-136 °C.

2,4,6-Trimethyl-5-(naphthalen-1-yl)-8-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 578:



A glass screw-cap vial was charged with 3,3',5-trimethyl-2'-(naphthalen-1-yloxy)-5'-nitro-[1,1'-biphenyl]-2-amine (86.3 mg, 0.22 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.9 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 140 µL, 1.10 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (130 µL, 113.4 mg, 1.10 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was redissolved in anhydrous MeCN (2.2 mL, 0.1 M) and heated to 60 °C for 16 hours. After the reaction time, the solution was

concentrated under a steady stream of nitrogen to obtain a crude solid. The resulting crude was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (72.2 mg, 0.15 mmol, 69%).

^{1}H NMR (600 MHz, CD_3CN) δ 9.00 (dd, *J* = 2.6, 0.7 Hz, 1H, H-2), 8.41 – 8.36 (m, 1H, H-9), 8.31 (dd, *J* = 2.6, 1.0 Hz, 1H, H-16), 8.29 – 8.25 (m, 2H, H-3,14), 8.18 – 8.15 (m, 1H, H-19), 7.89 (m, 2H, H-4,8), 7.78 (dt, *J* = 8.2, 0.8 Hz, 1H, H-6), 7.67 (t, *J* = 8.1 Hz, 1H, H-7), 7.37 (dt, *J* = 1.9, 0.9 Hz, 1H, H-22), 2.54 (s, 3H, H-13), 1.84 (s, 3H, H-24), 1.71 (s, 3H, H-21).

^{13}C NMR (151 MHz, CD_3CN) δ 162.9 (C-15), 162.5 (C-18), 156.3 (C-11), 149.7 (C-20), 143.1 (C-17), 137.3 (C-22), 136.2 (C-5), 134.7 (C-9), 131.6 (C-4), 130.4 (C-3), 130.2 (C-8), 129.8 (C-16), 127.3 (C-25), 127.0 (C-7), 126.4 (C-1), 125.6 (C-23), 124.4 (C-12), 123.5 (C-19), 122.6 (C-10), 120.22 (C-6 or 14), 120.21 (C-6 or 14), 118.2 (C-2), 21.1 (C-13), 17.2 (C-24), 16.7 (C-21).

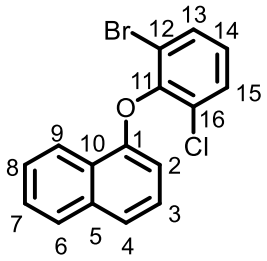
^{19}F NMR (565 MHz, CD3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{25}H_{20}NO_3^+$ $[M]^+$ requires *m/z* 382.1438, found *m/z* 382.1426.

IR (thin film) ν_{max}/cm^{-1} 3369, 3076, 2918, 2361, 2342, 1666, 1526, 1351, 1261, 1241, 1214, 1100.

MP decomposes 144 °C.

1-(2-Bromo-6-chlorophenoxy)naphthalene, 608:



An oven-dried round bottom flask was charged with 1-naphthol (500.0 mg, 3.47 mmol, 1.0 eq.) before adding anhydrous DMSO (8.7 mL, 0.4 M), followed by 1-bromo-3-chloro-2-fluorobenzene (1.09 g, 5.21 mmol, 1.5 eq.). Cs_2CO_3 (2.26 g, 6.94 mmol, 2.0 eq.) was then added in one portion with stirring before heating the reaction mixture to 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~150 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (2:98 to 5:95 Et_2O:pentane, v:v) to obtain the title compound as a solid (1.00 g, 3.00 mmol, 86%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (ddd, *J* = 8.5, 1.6, 0.8 Hz, 1H, H-9), 7.91 – 7.86 (m, 1H, H-6), 7.63 – 7.55 (m, 4H, H-4,7,8,13), 7.49 (dd, *J* = 8.1, 1.5 Hz, 1H, H-15), 7.28 (t, *J* = 8.0 Hz, 1H, H-3), 7.13 (t, *J* = 8.1 Hz, 1H, H-14), 6.40 (dd, *J* = 8.0, 1.0 Hz, 1H, H-2).

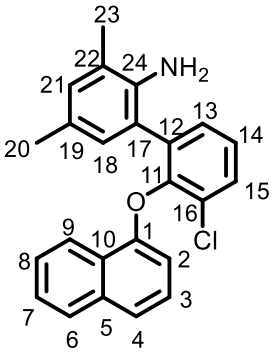
^{13}C NMR (151 MHz, $CDCl_3$) δ 152.5 (C-1), 148.8 (C-11), 135.0 (C-5), 132.4 (C-13), 130.1 (C-15), 130.0 (C-16), 127.7 (C-6), 127.1 (C-14), 126.9 (C-7), 125.9 (C-8), 125.5 (C-3), 125.1 (C-10), 122.5 (C-4), 122.3 (C-9), 119.2 (C-12), 106.9 (C-2).

HRMS (ESI) exact mass not detected.

IR (thin film) ν_{max}/cm^{-1} 1599, 1566, 1508, 1439, 1391, 1247, 1155, 1081, 1043, 1016, 891, 829, 791, 767, 701, 384, 632.

MP 42 °C.

3'-Chloro-3,5-dimethyl-2'-(naphthalen-1-yloxy)-[1,1'-biphenyl]-2-amine, 580:



An oven-dried three-neck round bottom flask was charged with 1-(2-bromo-6-chlorophenoxy)naphthalene (1.00 g, 3.02 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.11 g, 4.52 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (173.3 mg, 5 mol%) and K_2CO_3 (1.67 g, 12.08 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 30 mL, 0.1 M). The suspension was sparged with argon for 15 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (5:95 to 15:85 EtOAc:pentane, v:v) to obtain the title compound as an oil (963.7 mg, 2.58 mmol, 85%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 – 8.22 (m, 1H, H-9), 7.75 – 7.69 (m, 1H, H-6), 7.54 (dd, *J* = 7.8, 1.7 Hz, 1H, H-15), 7.46 – 7.40 (m, 2H, H-7,13), 7.38 – 7.34 (m, 2H, H-4,8), 7.29 (t, *J* = 7.8 Hz, 1H, H-14), 7.16 (t, *J* = 7.9 Hz, 1H, H-3), 6.63 (s, 1H, H-18), 6.54 (d, *J* = 2.2 Hz, 1H, H-21), 6.42 (dd, *J* = 7.9, 0.9 Hz, 1H, H-2), 3.48 (s, 2H, H-NH_2), 1.97 (s, 6H, H-20,23).

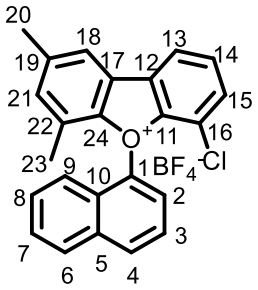
^{13}C NMR (151 MHz, $CDCl_3$) δ 153.8 (C-1), 149.5 (C-11), 139.5 (C-24), 136.1 (C-5), 134.6 (C-12), 131.0 (C-8), 130.8 (C-21), 130.1 (C-15), 129.2 (C-19), 129.0 (C-18), 127.3

(C-6), 126.7 (C-13), 126.4 (C-14), 125.3 (C-17), 125.2 (C-3), 125.1 (C-7), 122.6 (C-10), 122.4 (C-22), 122.1 (C-9), 121.8 (C-4), 107.9 (C-2), 20.2 (C-23), 17.7 (C-20).

HRMS (ESI) exact mass calculated for $C_{24}H_{21}ClNO^+$ $[M+H]^+$ requires *m/z* 374.1306, found *m/z* 374.1297.

IR (thin film) ν_{max}/cm^{-1} 2980, 2898, 1623, 1578, 1507, 1460, 1391, 1236, 1083, 1043, 1016, 964, 891, 861, 791, 713, 668.

6-Chloro-2,4-dimethyl-5-(naphthalen-1-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 581:



A glass screw-cap vial was charged with 3'-chloro-3,5-dimethyl-2'-(naphthalen-1-yloxy)-[1,1'-biphenyl]-2-amine (737.0 mg, 1.97 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (8.0 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 1.3 mL, 9.86 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (1.2 mL, 1.02 g, 9.86 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was redissolved in anhydrous MeCN (20 mL, 0.1 M) and heated to 40 °C for 16 hours. After the reaction time, the solution was concentrated under a steady stream of nitrogen to obtain a crude solid. The resulting crude was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with

additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (632.0 mg, 1.42 mmol, 72%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.42 – 8.37 (m, 1H, H-9), 8.34 (dt, *J* = 8.0, 1.2 Hz, 1H, H-13), 8.28 (dd, *J* = 7.8, 1.3 Hz, 1H, H-2), 8.24 (dd, *J* = 8.1, 1.1 Hz, 1H, H-6), 8.09 – 8.05 (m, 1H, H-18), 7.91 (ddd, *J* = 8.4, 7.0, 1.2 Hz, 1H, H-8), 7.87 – 7.80 (m, 2H, H-3,7), 7.68 – 7.64 (m, 2H, H-4,15), 7.61 (t, *J* = 8.0 Hz, 1H, H-14), 7.33 (dt, *J* = 2.1, 1.0 Hz, 1H, H-21), 2.53 (s, 3H, H-23), 1.70 (s, 3H, H-20).

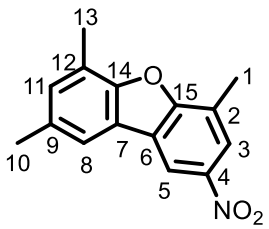
^{13}C NMR (126 MHz, CD_3CN) δ 162.7 (C-17), 157.6 (C-19), 157.0 (C-5), 143.1 (C-12), 136.6 (C-21), 136.0 (C-1), 134.3 (C-13), 133.5 (C-15), 133.1 (C-3), 131.0 (C-8), 130.0 (C-6), 129.9 (C-7), 127.1 (C-11), 126.8 (C-14), 126.3 (C-24), 124.4 (C-22), 123.5 (C-2), 123.2 (C-10), 123.1 (C-18), 121.0 (C-9), 119.6 (C-16), 119.2 (C-4), 21.0 (C-23), 16.8 (C-20).

^{19}F NMR (471 MHz, CD_3CN) δ -151.7.

HRMS (ESI) exact mass calculated for $C_{24}H_{18}ClO^+$ $[M]^+$ requires *m/z* 357.1041, found *m/z* 357.1032.

IR (thin film) ν_{max}/cm^{-1} 2981, 2888, 1457, 1382, 1262, 1151, 1057, 952, 866, 823, 797, 765, 732.

2,4,6-Trimethyl-8-nitrodibenzo[b,d]furan, 723:



A glass screw cap vial was charged with 2,4,6-trimethyl-5-(naphthalen-1-yl)-8-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (58.7 mg, 0.13 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (2.6 mL, 0.05 M). Furan (46 μL, 42.9 mg, 0.63 mmol, 5.0 eq.) was then added, followed by K_3PO_4 (133.7 mg, 0.63 mmol, 5.0 eq.) in one portion, before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v/v) to obtain the title compound as a solid (20.3 mg, 0.08 mmol, 61%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 2.3 Hz, 1H, H-5), 8.15 (dd, *J* = 2.3, 1.0 Hz, 1H. H-3), 7.57 – 7.56 (m, 1H, H-8), 7.16 – 7.15 (m, 1H-11), 2.65 (s, 3H, H-1), 2.57 (s, 3H, H-13), 2.49 (s, 3H, H-10).

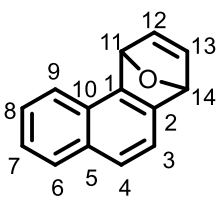
^{13}C NMR (151 MHz, $CDCl_3$) δ 158.4 (C-15), 154.7 (C-14), 143.6 (C-4), 133.5 (C-9), 131.0 (C-11), 124.7 (C-7), 123.2 (C-3), 123.1 (C-6), 122.9 (C-12), 122.1 (C-2), 118.6 (C-8), 114.7 (C-5), 21.4 (C-10), 15.4 (C-1), 15.2 (C-13).

HRMS (ESI) exact mass calculated for $C_{15}H_{14}NO_3^+$ $[M+H]^+$ requires *m/z* 256.0968, found *m/z* 256.0962.

IR (thin film) ν_{max}/cm^{-1} 2925, 2854, 2359, 2342, 1772, 1578, 1524, 1462, 1392, 1349, 1261, 1213, 1184, 1134, 1099, 1043, 888, 789, 773, 748.

MP 174-178 °C.

1,4-Dihydro-1,4-epoxyphenanthrene, 579:



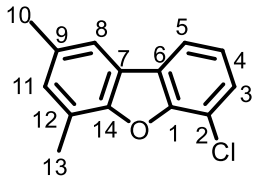
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.78 (m, 2H, H-6,9), 7.58 (d, *J* = 8.0 Hz, 1H, H-4), 7.54 (d, *J* = 8.0 Hz, 1H, H-3), 7.46 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, H-7), 7.38 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, H-8), 7.21 (m, 2H, H-12,13), 6.27 (t, *J* = 1.0 Hz, 1H, H-11), 5.93 (q, *J* = 1.0 Hz, 1H, H-14).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5 (C-2), 148.0 (C-1), 145.0 (C-13), 143.5 (C-12), 131.9 (C-5), 128.9 (C-6), 127.8 (C-10), 126.3 (C-7), 125.5 (C-4), 125.2 (C-8), 122.8 (C-9), 119.4 (C-3), 83.5 (C-14), 81.4 (C-11).

HRMS (ESI) exact mass calculated for $C_{14}H_{11}O^+$ $[M+H]^+$ requires *m/z* 195.0804, found *m/z* 195.0799.

The NMR spectra are consistent with those available in the literature.[202]

6-Chloro-2,4-dimethyldibenzo[b,d]furan, 724:



A glass screw cap vial was charged with 6-chloro-2,4-dimethyl-5-(naphthalen-1-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (16.0 mg, 0.04 mmol, 1.0 eq.) before dissolving in anhydrous MeCN (0.7 mL, 0.05 M). Furan (13 μL, 12.3 mg, 0.18 mmol, 5.0 eq.) was then added, followed by K_3PO_4 (38.2 mg, 0.18 mmol, 5.0 eq.) in one portion, before capping and rapidly stirring at room temperature for 16 hours. After the reaction time, the mixture was passed through a pad of Celite, eluting with EtOAc, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 5:95 EtOAc:pentane, v/v) to obtain the title compound as an oil (5.6 mg, 0.02 mmol, 67%).

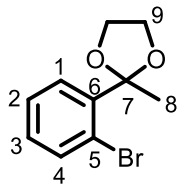
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.8, 1.1 Hz, 1H, H-5), 7.55 (dt, *J* = 1.8, 0.9 Hz, 1H, H-8), 7.42 (dd, *J* = 7.8, 1.1 Hz, 1H, H-3), 7.24 (t, *J* = 7.8 Hz, 1H, H-4), 7.12 (dt, *J* = 1.8, 0.9 Hz, 1H, H-11), 2.60 (s, 3H, H-13), 2.48 (s, 3H, H-10).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.7 (C-14), 152.2 (C-1), 132.9 (C-9), 130.2 (C-11), 126.9 (C-3), 126.6 (C-6), 123.7 (C-7), 123.4 (C-4), 121.9 (C-12), 119.1 (C-5), 118.4 (C-8), 117.2 (C-2), 21.4 (C-10), 15.3 (C-13).

HRMS (ESI) exact mass not detected.

IR (thin film) ν_{max}/cm^{-1} 2919, 1583, 1483, 1458, 1417, 1379, 1345, 1313, 1255, 1234, 1187, 1162, 1145, 1116, 1054, 928, 850, 810, 783, 746, 729, 657.

2-(2-Bromophenyl)-2-methyl-1,3-dioxolane, 610:



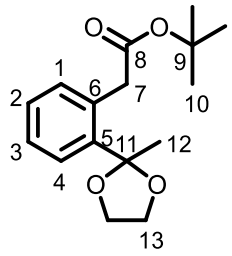
An oven-dried round bottom flask fitted with a Dean-Stark apparatus was charged with 2'-bromoacetophenone (2.0 g, 10.1 mmol, 1.0 eq.), ethylene glycol (1.7 mL, 1.87 g, 30.1 mmol, 3.0 eq.) and p-toluenesulfonic acid monohydrate (38.2 mg, 2 mol%) before adding anhydrous toluene (40 mL, 0.25 M). The reaction mixture was then heated to 135 °C for 16 hours. After the reaction time, the mixture was concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (10:90 Et_2O:pentane, v:v) to obtain the title compound as an oil (2.54 g, 10.0 mmol, quantitative). The NMR spectra are consistent with those available in the literature.[203]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.9, 1.8 Hz, 1H, H-4), 7.59 (dd, *J* = 7.9, 1.3 Hz, 1H, H-1), 7.27 (td, *J* = 7.5, 1.3 Hz, 1H, H-3), 7.12 (ddd, *J* = 7.9, 7.3, 1.8 Hz, 1H, H-2), 4.07 – 4.02 (m, 2H, H-9), 3.77 – 3.72 (m, 2H, H-9'), 1.80 (s, 3H, H-8).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2 (C-6), 135.1 (C-1), 129.6 (C-2), 128.0 (C-4), 127.2 (C-3), 120.6 (C-5), 108.8 (C-7), 64.3 (C-9), 25.4 (C-8).

HRMS (APCI) exact mass calculated for $C_{10}H_{11}BrO_2^+$ $[M+H]^+$ requires *m/z* 234.0015, found *m/z* 243.0015.

***tert*-Butyl 2-(2-(2-methyl-1,3-dioxolan-2-yl)phenyl)acetate, 611:**



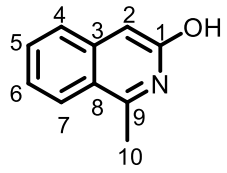
A flame-dried three-neck round bottom flask was charged with tri-*tert*-butylphosphonium tetrafluoroborate (298.8 mg, 10 mol%) and $Pd_2(dba)_3$ (471.6 mg, 5 mol%) before degassing with vacuum and nitrogen cycles (x3). A degassed solution of 2-(2-bromophenyl)-2-methyl-1,3-dioxolane (2.50 g, 10.3 mmol, 1.0 eq.) in anhydrous toluene (25 mL) was then added, followed by *tert*-butyl acetate (2.8 mL, 2.39 g, 20.6 mmol, 2.0 eq.) The suspension was sparged with argon for 15 minutes, then cooled to -78 °C. LiHMDS (1.0 M in toluene, 25.8 mL, 25.8 mmol, 2.5 eq.) was then added dropwise *via* a syringe pump over 1 hour. After full addition, the reaction mixture was sparged again for another 15 minutes. Subsequently, the solution was left to stir for 16 hours, allowing the reaction to slowly reach room temperature overnight. After the reaction time, the mixture was quenched with saturated aqueous $NaHCO_3$ (~100 mL), then transferred to a separatory funnel. The aqueous layer was then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (5:95 EtOAc:pentane, v:v) to obtain the title compound as a solid (2.28 g, 8.19 mmol, 80%). The NMR spectra are consistent with those available in the literature.[204]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.56 (m, 1H, H-2), 7.30 – 7.17 (m, 4H, H-1,3,4), 3.99 – 3.94 (m, 2H, H-13), 3.79 (s, 2H, H-7), 3.73 – 3.68 (m, 2H, H-13'), 1.68 (s, 3H, H-12), 1.47 (s, 9H, H-10).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6 (C-8), 141.2 (C-5), 132.6 (C-1), 132.3 (C-6), 128.2 (C-2), 127.1 (C-3), 126.4 (C-4), 109.2 (C-11), 80.4 (C-9), 64.3 (C-13), 40.4 (C-7), 28.2 (C-10), 27.6 (C-12).

HRMS (HRMS) exact mass calculated for $C_{16}H_{23}O_4^+$ $[M+H]^+$ requires *m/z* 279.1591, found *m/z* 279.1583.

1-Methylisoquinolin-3-ol, 612:



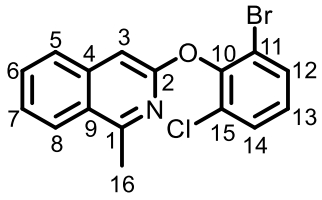
An oven-dried round bottom flask was charged with *tert*-butyl 2-(2-(2-methyl-1,3-dioxolan-2-yl)phenyl)acetate (2.20 g, 7.90 mmol, 1.0 eq.), then anhydrous CH_2Cl_2 (61 mL, 0.13 M) was added, followed by TFA (20 mL). The solution was left to stir for 2 hours, then concentrated under vacuum to obtain a crude oil. The crude was redissolved in MeCN (7.9 mL, 1.0 M) and transferred to a pressure tube containing aqueous ammonia (35% w/w, 15.8 mL). The pressure tube was capped and heated in an oil bath at 70 °C for 24 hours. After the reaction time, the pressure tube was completely cooled to room temperature, then placed in a freezer (< -18 °C) for one week. The precipitate was then filtered, washing the solid with a minimal amount of ice-cold MeCN to obtain the title compound as a solid (733.5 mg, 4.61 mmol, 56%). The NMR spectra are consistent with those available in the literature.[205]

^{1}H NMR (600 MHz, DMSO) δ 7.98 (dt, *J* = 8.5, 1.0 Hz, 1H, H-7), 7.62 (d, *J* = 8.5 Hz, 1H, H-4), 7.51 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1H, H-5), 7.26 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1H, H-6), 6.69 (s, 1H, H-2), 2.77 (s, 3H, H-10).

^{13}C NMR (151 MHz, DMSO) δ 159.4 (C-1), 156.7 (C-9), 140.1 (C-3), 130.3 (C-5), 126.0 (C-7), 125.7 (C-4), 123.1 (C-6), 121.6 (C-8), 99.0 (C-2), 20.8 (C-10).

HRMS (ESI) exact mass calculated for $C_{10}H_{10}NO^+$ $[M+H]^+$ requires *m/z* 160.0757, found *m/z* 160.0756.

3-(2-Bromo-6-chlorophenoxy)-1-methylisoquinoline, 613:



An oven-dried round bottom flask was charged with 1-methylisoquinolin-3-ol (398.0 mg, 2.50 mmol, 1.0 eq.) before adding anhydrous DMSO (6.3 mL, 0.4 M), followed by 1-bromo-3-chloro-2-fluorobenzene (796.0 mg, 3.80 mmol, 1.5 eq.). Cs_2CO_3 (1.63 g, 5.00 mmol, 2.0 eq.) was then added in one portion with stirring before heating the reaction mixture to 100 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~150 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 5:95 EtOAc:pentane, v:v) to obtain the title compound as a solid (222.6 mg, 0.64 mmol, 26%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (dq, *J* = 8.5, 1.0 Hz, 1H, H-8), 7.71 – 7.63 (m, 1H, H-5), 7.62 – 7.55 (m, 2H, H-6,12), 7.46 (dd, *J* = 8.2, 1.5 Hz, 1H, H-14), 7.43 (ddd, *J* =

8.2, 6.7, 1.2 Hz, 1H, H-13), 7.11 (t, *J* = 8.1 Hz, 1H, H-7), 6.76 (s, 1H, H-3), 2.88 (s, 3H, H-16).

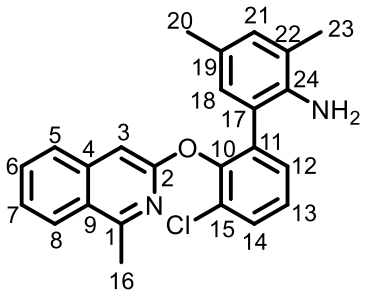
^{13}C NMR (151 MHz, $CDCl_3$) δ 159.0 (C-2), 157.8 (C-9), 147.9 (C-10), 139.4 (C-4), 132.1 (C-12), 130.4 (C-14), 130.1 (C-6), 129.8 (C-15), 127.0 (C-7), 126.8 (C-5), 126.0 (C-9), 125.1 (C-13), 125.1 (C-8), 119.3 (C-11), 99.7 (C-3), 22.3 (C-16).

HRMS (ESI) exact mass calculated for $C_{16}H_{12}BrClNO^+$ $[M+H]^+$ requires *m/z* 347.9785, found *m/z* 347.9778.

IR (thin film) ν_{max}/cm^{-1} 2981, 2889, 1684, 1653, 1627, 1594, 1561, 1541, 1521, 1433, 1328, 1279, 1169, 1131, 1004, 867, 757, 683.

MP 126-128 °C.

3'-Chloro-3,5-dimethyl-2'-((1-methylisoquinolin-3-yl)oxy)-[1,1'-biphenyl]-2-amine, 582:



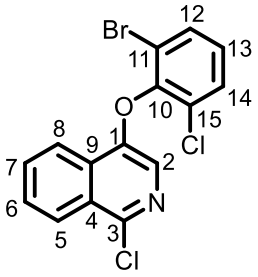
An oven-dried 10 mL microwave vial was charged with 3-(2-bromo-6-chlorophenoxy)-1-methylisoquinoline (34.9 mg, 0.10 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (37.1 mg, 0.15 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (5.8 mg, 5 mol%) and K_2CO_3 (55.3 mg, 0.40 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 1.0 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room

temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (19.7 mg, 0.05 mmol, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.7, 1.1 Hz, 1H, H-8), 7.58 (dt, *J* = 8.3, 1.0 Hz, 1H, H-5), 7.56 – 7.46 (m, 2H, H-6,14), 7.44 – 7.27 (m, 3H, H-7,12,13), 6.71 (dd, *J* = 10.2, 3.0 Hz, 3H, H-3,18,21), 3.63 (s, 2H, H-NH_2), 2.77 (s, 3H, H-16), 2.06 (s, 3H, H-20), 2.02 (s, 3H, H-23).

All of the isolated material was subjected to further synthetic transformations and hence no other characterisation was performed.

4-(2-Bromo-6-chlorophenoxy)-1-chloroisoquinoline, 615:



An oven-dried round bottom flask was charged with 1-chloroisoquinolin-4-ol (200.0 mg, 1.11 mmol, 1.0 eq.) before adding anhydrous DMSO (2.8 mL, 0.4 M), followed by 1-bromo-3-chloro-2-fluorobenzene (349.8 mg, 1.67 mmol, 1.5 eq.). Cs_2CO_3 (723.3 mg, 5.00 mmol, 2.0 eq.) was then added in one portion with stirring before heating the reaction mixture to 120 °C for 16 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~100 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column

chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (87.1 mg, 0.24 mmol, 21%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (dt, *J* = 8.3, 0.9 Hz, 1H, H-8), 8.34 (d, *J* = 8.5 Hz, 1H, H-5), 7.88 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H, H-7), 7.79 (ddd, *J* = 8.5, 7.0, 1.3 Hz, 1H, H-6), 7.62 (dd, *J* = 8.1, 1.5 Hz, 1H, H-12), 7.50 (dd, *J* = 8.1, 1.5 Hz, 1H, H-14), 7.35 (s, 1H, H-2), 7.17 (t, *J* = 8.1 Hz, 1H, H-13).

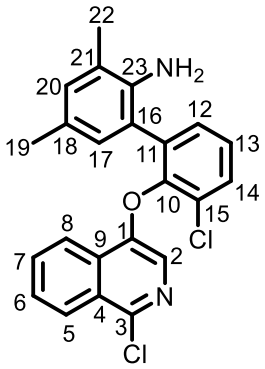
^{13}C NMR (151 MHz, $CDCl_3$) δ 148.0 (C-10), 147.9 (C-3), 144.9 (C-1), 132.6 (C-12), 131.1 (C-14), 130.3 (C-7), 129.8 (C-2), 129.4 (C-9), 129.3 (C-6), 127.8 (C-15), 127.6 (C-4), 126.5 (C-5), 124.4 (C-13), 122.1 (C-8), 118.5 (C-18).

HRMS (ESI) exact mass calculated for $C_{15}H_9BrCl_2NO^+$ $[M+H]^+$ requires *m/z* 367.9239, found *m/z* 367.9235.

IR (thin film) ν_{max}/cm^{-1} 2981, 1581, 1567, 1500, 1441, 1410, 1383, 1309, 1263, 1152, 1079, 1026, 967, 871, 840, 762, 699, 655, 638.

MP 118-121 °C.

3'-Chloro-2'-((1-chloroisoquinolin-4-yl)oxy)-3,5-dimethyl-[1,1'-biphenyl]-2-amine, 584:



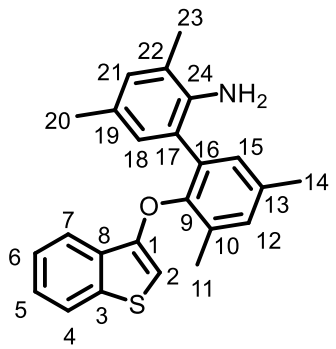
An oven-dried 10 mL microwave vial was charged with 4-(2-bromo-6-chlorophenoxy)-1-chloroisoquinoline (70.3 mg, 0.19 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-

1,3,2-dioxaborolan-2-yl)aniline (69.2 mg, 0.28 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (10.9 mg, 5 mol%) and K_2CO_3 (105.0 mg, 0.76 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 2.0 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0: 100 to 30:70 EtOAc:pentane, v:v) to obtain the title compound as a solid (37.7 mg, 0.09 mmol, 48%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.4 Hz, 1H, H-8), 8.01 (d, *J* = 8.5 Hz, 1H, H-5), 7.81 (ddd, *J* = 8.5, 6.9, 1.1 Hz, 1H, H-6), 7.68 (s, 1H, H-2), 7.66 – 7.58 (m, 2H, H-7,14), 7.51 (dd, *J* = 8.1, 1.4 Hz, 1H, H-12), 7.16 (t, *J* = 8.1 Hz, 1H, H-13), 6.99 (d, *J* = 2.1 Hz, 1H, H-17), 6.97 (d, *J* = 2.1 Hz, 1H, H-20), 3.93 (s, 2H, H-NH_2), 2.28 (s, 3H, H-19), 2.23 (s, 3H, H-22).

All of the isolated material was subjected to further synthetic transformations and hence no other characterisation was performed.

2'-(Benzo[b]thiophen-3-yloxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine, 703:



A three-neck round bottom flask was charged with 3-(2-bromo-4,6-dimethylphenoxy)benzo[b]thiophene (1.76 g, 5.28 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.94 g, 7.84 mmol, 1.50 eq.), $Pd(PPh_3)_4$ (304.6 mg, 5 mol%) and K_2CO_3 (2.92 g, 21.1 mmol, 4.0 eq.) followed by evacuation and refill with N_2 x 3. Degassed DME (26 mL) was then added, followed by degassed H_2O (26 mL). The suspension was sparged with argon for 15 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc (300 mL). The solution was washed with 1 M aqueous NaOH (3 x 100 mL), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 20:80 EtOAc:heptane, v/v) to give the title compound as a solid (1.64 g, 4.39 mmol, 83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.70 (m, 1H, H-7), 7.67 – 7.60 (m, 1H, H-4), 7.30 – 7.26 (m, 2H, H-5,6), 7.11 (dt, *J* = 2.3, 0.8 Hz, 1H, H-18), 7.04 (dt, *J* = 2.2, 0.7 Hz, 1H, H-21), 6.71 – 6.66 (m, 1H, H-15), 6.61 (dt, *J* = 2.3, 0.9 Hz, 1H, H-12), 5.96 (s, 1H, H-2), 4.11 (s, 2H, H-NH_2), 2.37 (s, 3H, H-14), 2.27 (s, 3H, H-20), 2.07 (s, 3H, H-23), 2.03 (s, 3H, H-11).

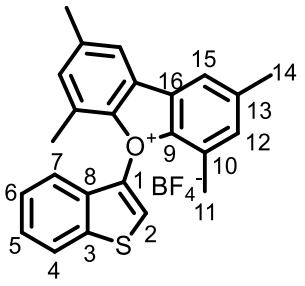
^{13}C NMR (126 MHz, $CDCl_3$) δ 150.3 (C-1), 149.9 (C-9), 138.2 (C-24), 137.7 (C-3), 135.4 (C-13), 132.6 (C-21), 131.8 (C-12), 131.7 (C-22), 131.5 (C-10), 130.6 (C-18), 130.5 (C-16), 129.1 (C-8), 127.7 (C-5), 125.0 (C-15), 124.4 (C-6), 123.6 (C-17), 123.3 (C-22), 122.6 (C-7), 121.0 (C-4), 100.6 (C-2), 21.0 (C-20), 20.4 (C-14), 18.0 (C-23), 16.5 (C-11).

HRMS (ESI) exact mass calculated for $C_{24}H_{24}NOS^+$ $[M+H]^+$ requires *m/z* 374.1573, found *m/z* 374.1564.

IR (thin film) ν_{max}/cm^{-1} 3385, 2913, 2361, 1622, 1571, 1528, 1484, 1431, 1366, 1279, 1208, 1159, 1111, 1015, 866, 809, 758, 728, 627.

MP 38-40 °C.

5-(Benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 657:



t-BuONO (2.5 mL, 2.17 g, 21.0 mmol, 5.0 eq.) was added dropwise to a solution of 2'-(benzo[b]thiophen-3-yloxy)-3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2-amine (1.57 g, 4.2 mmol, 1.0 eq.) and HBF_4 (48 wt% aq., 2.7 mL, 21.0 mmol, 5.0 eq.) in CH_2Cl_2:IPA (17 mL, 1:1, 0.25 M) at 0 °C. After stirring at room temperature for 15 mins, the mixture was transferred to a separatory funnel and diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then filtered and concentrated under a steady stream of nitrogen to obtain a crude solid. The crude was redissolved in anhydrous MeCN (42 mL, 0.1 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under rotary evaporation (water bath set to 30 °C). The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through a pad of Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified oxonium salt. Finally, the solution was concentrated under rotary evaporation (water bath set to 30 °C) to obtain the pure title compound as a solid (1.40 g, 3.15 mmol, 75%).

^{1}H NMR (400 MHz, CD_3CN) δ 8.48 (d, *J* = 0.5 Hz, 1H, H-2), 8.14 (dt, *J* = 8.3, 0.9 Hz, 1H, H-4), 7.96 (dt, *J* = 2.1, 0.7 Hz, 2H, H-12), 7.60 (dddd, *J* = 8.4, 7.1, 1.3, 0.5 Hz, 1H, H-5), 7.50 (ddd, *J* = 8.2, 7.1, 1.0 Hz, 1H, H-6), 7.42 (dt, *J* = 8.1, 1.1 Hz, 1H, H-7), 7.29 (dp, *J* = 2.4, 0.8 Hz, 2H, H-15), 2.51 (t, *J* = 0.7 Hz, 6H, H-11), 2.02 (d, *J* = 0.7 Hz, 6H, H-14).

^{13}C NMR (101 MHz, CD_3CN) δ 160.9 (C-3), 144.0 (C-13), 142.9 (C-9), 137.9 (C-1), 135.7 (C-16), 128.4 (C-12), 128.1 (C-10), 128.0 (C-5), 125.7 (C-7), 125.0 (C-6), 124.5 (C-8), 123.6 (C-2), 122.7 (C-15), 120.2 (C-4), 21.1 (C-11), 16.5 (C-14).

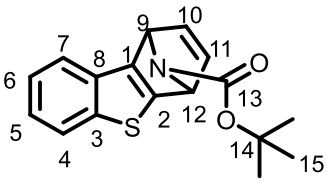
^{19}F NMR (376 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{24}H_{21}OS^+$ $[M]^+$ requires *m/z* 357.1308, found *m/z* 357.1300.

IR (thin film) ν_{max}/cm^{-1} 3604, 2981, 2360, 1630, 1525, 1450, 1367, 1206, 1062, 864, 761, 734, 702, 668.

MP 210-212 °C.

***tert*-Butyl 1,4-dihydro-1,4-epiminodibenzo[b,d]thiophene-10-carboxylate, 672:**



672 was prepared according to **General Procedure H** using 5-(Benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (133.0 mg, 0.30 mmol, 1.0 eq.), *tert*-butyl 1H-pyrrole-1-carboxylate (1.25 mL, 1.25 g, 7.48 mmol, 25 eq.) and CH_2Cl_2 (6.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 10:90 EtOAc:heptane, v/v) to give the title compound as a solid (9.1 mg, 0.03 mmol, 10%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 1H, H-7), 7.70 (d, *J* = 8.1 Hz, 1H, H-4), 7.35 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, H-5), 7.23 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H, H-6), 7.13 (m, 2H, H-10,11), 5.80 (d, *J* = 22.3 Hz, 1H, H-12), 5.68 (d, *J* = 20.2 Hz, 1H, H-9), 1.40 (s, 9H, H-15).

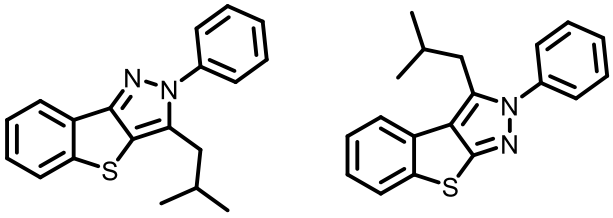
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8 (C-13), 144.1 (C-1), 143.6 (C-3), 133.5 (C-2), 124.8 (C-8), 123.8 (C-5), 123.7 (C-6), 121.4 (C-7), 121.0 (C-4), 81.1 (C-14), 67.1 (C-12), 65.2 (C-9), 28.3 (C-15).

HRMS (ESI) exact mass calculated for $C_{17}H_{18}NO_2S^+$ $[M+H]^+$ requires *m/z* 300.1053, found *m/z* 300.1052.

IR (thin film) ν_{max}/cm^{-1} 2974, 1740, 1369, 1336, 1170, 736.

MP 60-62 °C.

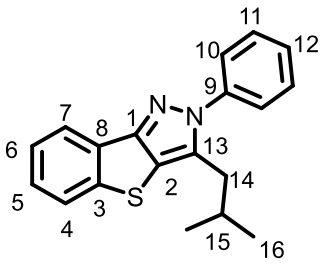
3-Isobutyl-2-phenyl-2H-benzo[4,5]thieno[3,2-c]pyrazole, 663, and 3-isobutyl-2-phenyl-2H-benzo[4,5]thieno[2,3-c]pyrazole, 663':



663 and **663'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (135.3 mg, 0.30 mmol, 1.0 eq.), 4-isobutyl-3-phenyl-1,2,3-oxadiazol-3-ium-5-olate (936.9 mg, 4.3 mmol, 14.0 eq.) and CH_2Cl_2 (6.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 10:90 EtOAc:heptane, v/v) to give major regioisomer **663** as an oil (15.4 mg, 0.05 mmol, 16%) and minor regioisomer **663'** as an oil (6.3 mg, 0.02 mmol, 7%). The overall yield refers to the

combined masses of the two products. The regioisomeric ratio (3.3 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

3-Isobutyl-2-phenyl-2H-benzo[4,5]thieno[3,2-c]pyrazole, 663:



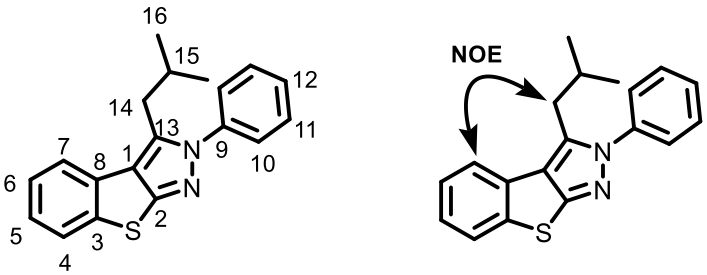
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 – 8.12 (m, 1H, H-7), 7.77 – 7.70 (m, 1H, H-4), 7.56 – 7.50 (m, 4H, H-10,11), 7.49 – 7.44 (m, 1H, H-12), 7.42 – 7.38 (m, 2H, H-5,6), 2.73 (d, *J* = 7.4 Hz, 2H, H-14), 2.17 – 2.07 (m, 1H, H-14), 0.94 (d, *J* = 6.6 Hz, 6H, H-16).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1 (C-13), 145.3 (C-1), 140.3 (C-3), 135.6 (C-9), 129.4 (C-11), 128.7 (C-5), 128.0 (C-8), 127.0 (C-12), 126.5 (C-6), 124.9 (C-10), 124.0 (C-2), 122.2 (C-4), 117.9 (C-7), 35.4 (C-14), 28.4 (C-15), 22.8 (C-16).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}N_2S^+$ $[M+H]^+$ requires *m/z* 307.1263, found *m/z* 307.1256.

IR (thin film) ν_{max}/cm^{-1} 2957, 1597, 1573, 1500, 1463, 1439, 1379, 1183, 1126, 1057, 1023, 983, 852, 757, 732, 695.

3-Isobutyl-2-phenyl-2H-benzo[4,5]thieno[2,3-c]pyrazole, 663':



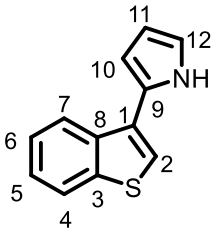
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 1H, H-7), 7.73 (dt, *J* = 7.9, 0.9 Hz, 1H, H-4), 7.54 – 7.46 (m, 5H, H-10,11,12), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H, H-6), 7.30 (td, *J* = 7.6, 1.3 Hz, 1H, H-5), 2.97 (d, *J* = 7.4 Hz, 2H, H-14), 1.99 (dq, *J* = 13.8, 6.9 Hz, 1H, H-15), 0.86 (d, *J* = 6.6 Hz, 6H, H-16).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8 (C-2), 142.5 (C-13), 140.2 (C-9), 137.2 (C-3), 130.2 (C-8), 129.3 (C-11), 128.7 (C-5), 126.6 (C-12), 124.9 (C-6), 124.8 (C-10), 124.1 (C-4), 123.1 (C-7), 121.5 (C-1), 34.9 (C-14), 29.3 (C-15), 22.6 (C-16).

HRMS (ESI) exact mass calculated for $C_{19}H_{19}N_2S^+$ $[M+H]^+$ requires *m/z* 307.1263, found *m/z* 307.1253.

IR (thin film) ν_{max}/cm^{-1} 2957, 1598, 1504, 1485, 1462, 1435, 1371, 1265, 1173, 1111, 1057, 1019, 971, 763, 735, 696.

2-(Benzo[b]thiophen-3-yl)-1H-pyrrole, 667':



667' was prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (133.0 mg, 0.30 mmol, 1 eq.), pyrrole (0.530 mL, 510.0 mg, 7.6 mmol, 25 eq.) and CH_2Cl_2 (6.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 15:85 EtOAc:heptane, v/v) to give the title product as an oil (16.9 mg, 0.08 mmol, 28%).

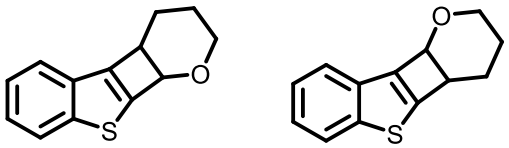
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H, H-NH), 8.14 – 8.05 (m, 1H, H-7), 7.93 – 7.87 (m, 1H, H-4), 7.48 – 7.37 (m, 2H, H-5,6), 7.32 (s, 1H, H-2), 6.92 (td, *J* = 2.7, 1.4 Hz, 1H, H-12), 6.58 (ddd, *J* = 3.8, 2.6, 1.4 Hz, 1H, H-10), 6.40 (dt, *J* = 3.5, 2.7 Hz, 1H, H-11).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7 (C-3), 137.5 (C-8), 129.9 (C-9), 127.0 (C-2), 124.8 (C-6), 124.6 (C-1), 123.2 (C-5), 123.1 (C-7), 121.0 (C-4), 118.4 (C-12), 109.8 (C-11), 107.7 (C-10).

HRMS (ESI) exact mass calculated for $C_{12}H_{10}NS^+$ $[M+H]^+$ requires *m/z* 200.0528, found *m/z* 200.0524.

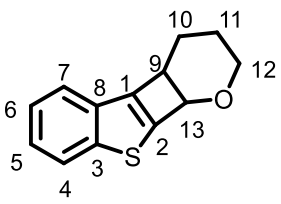
IR (thin film) ν_{max}/cm^{-1} 3429, 1684, 1507, 1421, 1344, 1262, 1096, 1062, 1037, 984, 897, 880, 759, 731.

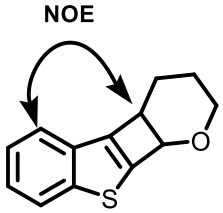
3,4,4a,9b-Tetrahydro-2H-benzo[4',5']thieno[3',2':3,4]cyclobuta[1,2-b]pyran, 670', and 3,4,4a,9c-tetrahydro-2H-benzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-b]pyran, 670:



670 and **670'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (133.0 mg, 0.30 mmol, 1 eq.), 3,4-dihydropyran (3.0 mL) and CH_2Cl_2 (3.0 mL). The crude residue was purified by flash column chromatography (0:100 to 5:95 EtOAc:heptane, v/v) to give the major regioisomer **670'** and as an oil (25.6 mg, 0.12 mmol, 40%). The minor regioisomer **670** could not be isolated in sufficient purity, therefore the overall yield refers to the mass of major regioisomer **670'**. The regioisomeric ratio (16.3 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

3,4,4a,9b-Tetrahydro-2H-benzo[4',5']thieno[3',2':3,4]cyclobuta[1,2-b]pyran, 670':





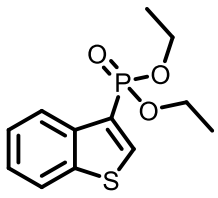
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 1H, H-7), 7.71 – 7.68 (m, 1H, H-4), 7.39 – 7.32 (m, 2H, H-5,6), 5.34 (d, *J* = 4.0 Hz, 1H, H-13), 3.90 – 3.79 (m, 3H, H-9,12), 2.26 – 2.10 (m, 2H, H-10), 1.69 – 1.59 (m, 1H, H-11), 1.45 – 1.35 (m, 1H, H-11').

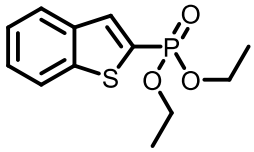
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.4 (C-3), 147.2 (C-2), 143.7 (C-8), 134.1 (C-1), 124.6 (C-5), 124.5 (C-6), 124.0 (C-7), 121.7 (C-4), 74.0 (C-13), 61.7 (C-12), 42.1 (C-9), 23.1 (C-10), 19.4 (C-11).

HRMS (ESI) exact mass calculated for $C_{13}H_{13}OS^+$ $[M+H]^+$ requires *m/z* 217.0682, found *m/z* 217.0678.

IR (thin film) ν_{max}/cm^{-1} 2940, 2870, 1717, 1653, 1559, 1541, 1524, 1458, 1427, 1341, 1261, 1341, 1261, 1184, 1094, 1052, 935, 857, 757.

Diethyl benzo[b]thiophen-3-ylphosphonate, 679, and diethyl benzo[b]thiophen-2-ylphosphonate, 679':

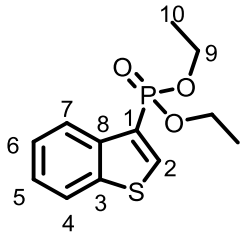




679 and **679'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (133.0 mg, 0.30 mmol, 1.0 eq.), triethyl phosphite (1.0 mL, 963.7 mg, 5.8 mmol, 20 eq.) and CH_2Cl_2 (6.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 100:0 [3:1 EtOAc:EtOH]:heptane, v/v) to give the

major regioisomer **679** as an oil (8.5 mg, 0.03 mmol, 11%). The minor regioisomer **679'** could not be isolated in sufficient purity, therefore the overall yield refers to the mass of major regioisomer **679**. The regioisomeric ratio (2.2 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

Diethyl benzo[b]thiophen-3-ylphosphonate, 679:



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.6 Hz, 1H, H-2), 8.20 – 8.11 (m, 1H, H-7), 7.94 – 7.89 (m, 1H, H-4), 7.46 (ddd, *J* = 8.1, 7.2, 1.3 Hz, 1H, H-6), 7.42 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H, H-5), 4.23 – 4.06 (m, 4H, H-9), 1.32 (t, *J* = 7.1 Hz, 6H, H-10).

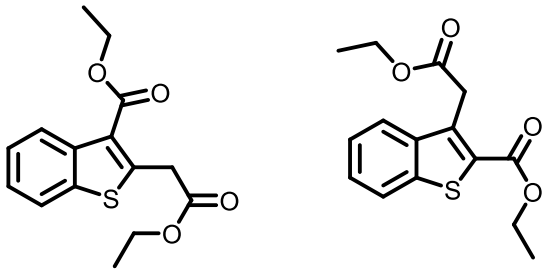
^{13}C NMR (126 MHz, $CDCl_3$) δ 141.0 (d, *J* = 17.3 Hz, C-3), 139.5 (d, *J* = 17.4 Hz, C-8), 138.3 (d, *J* = 16.1 Hz, C-2), 125.3 (C-6), 125.3 (d, *J* = 5.2 Hz, C-5), 124.3 (C-4,7), 122.7 (C-1), 62.4 (d, *J* = 5.2 Hz, C-9), 16.5 (d, *J* = 6.6 Hz, C-10).

^{31}P NMR (202 MHz, $CDCl_3$) δ 12.2.

HRMS (ESI) exact mass calculated for $C_{12}H_{16}O_3PS^+$ $[M+H]^+$ requires *m/z* 271.0552, found *m/z* 271.0543.

IR (thin film) ν_{max}/cm^{-1} 2982, 1488, 1456, 1423, 1392, 1243, 1163, 1049, 1019, 994, 968, 793, 760, 733.

Ethyl 2-(2-ethoxy-2-oxoethyl)benzo[b]thiophene-3-carboxylate, 662, and ethyl 3-(2-ethoxy-2-oxoethyl)benzo[b]thiophene-2-carboxylate, 662':



662 and **662'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (22.2 mg, 0.05 mmol, 1.0 eq.), diethyl malonate (0.250 mL) and CH_2Cl_2 (0.750 mL). The crude residue was purified by flash column chromatography (0:100 to 30:70 EtOAc:heptane, v/v) to give an inseparable mixture of the two regioisomers as an oil (2.7 mg, 0.01 mmol, 18%). The regioisomeric ratio (5.4 : 1.0) was determined by quantitative ^{1}H NMR analysis of the purified reaction mixture. The exact regiochemistry of the products could not be determined unambiguously, therefore the following spectra have been left unassigned.

LRMS (ESI) exact mass calculated for $C_{15}H_{17}O_4S^+$ $[M+H]^+$ requires *m/z* 293.1, found *m/z* 293.3.

Major Regioisomer:

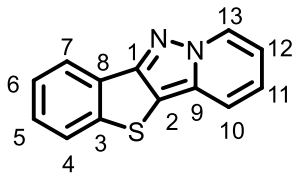
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (ddd, *J* = 7.8, 1.4, 0.7 Hz, 1H), 7.53 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.42 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.20 (ddd, *J* = 7.9, 7.1, 0.9 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 4H), 3.78 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 6H).

Minor Regioisomer:

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.04 (m, 1H), 7.86 – 7.83 (m, 1H), 7.52 – 7.48 (m, 2H), 5.30 (s, 2H), 4.28 – 4.24 (m, 4H), 1.57 – 1.51 (m, 6H).

Due to the limited quantity of the mixture of the title compounds isolated, no further characterisation was performed.

Benzo[4',5']thieno[3',2':3,4]pyrazolo[1,5-a]pyridine, 666:



666 was prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (22.2 mg, 0.05 mmol, 1.0 eq.), pyridin-1-ium-1-yl(tosyl)amide (124.0 mg, 0.5 mmol, 10 eq.) and CH_2Cl_2 (1.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 40:60 EtOAc:heptane, v/v) to give the title compound as an oil (1.1 mg, 0.005 mmol, 10%).

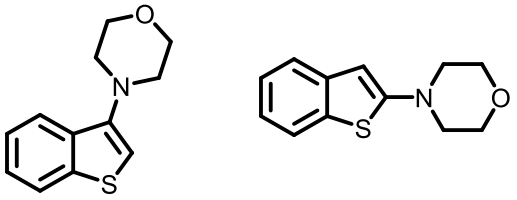
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (dt, *J* = 7.1, 1.1 Hz, 1H, H-7), 8.29 – 8.22 (m, 1H, H-13), 7.89 – 7.83 (m, 1H, H-10), 7.71 (dt, *J* = 8.9, 1.2 Hz, 1H, H-4), 7.53 – 7.45 (m, 2H, H-11,12), 7.26 – 7.22 (m, 1H, H-5), 6.91 (td, *J* = 6.9, 1.4 Hz, 1H, H-6).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.8 (C-1), 145.3 (C-3), 134.0 (C-2), 129.8 (C-8), 127.4 (C-5), 127.3 (C-13), 125.0 (C-9), 124.3 (C-6), 123.3 (C-11), 122.6 (C-4), 117.4 (C-7), 112.9 (C-10), 109.1 (C-12).

HRMS (ESI) exact mass calculated for $C_{13}H_9N_2S^+$ $[M+H]^+$ requires *m/z* 225.0481, found *m/z* 225.0477.

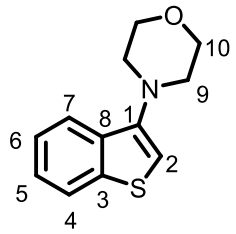
IR (thin film) ν_{max}/cm^{-1} 2923, 2853, 1636, 1526, 1453, 1362, 1313, 1151, 1060, 1019, 738.

4-(Benzo[b]thiophen-3-yl)morpholine, 671', and 4-(benzo[b]thiophen-2-yl)morpholine, 671:



671 and **671'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (22.2 mg, 0.05 mmol, 1.0 eq.), morpholine (110 µL, 108.9 mg, 1.25 mmol, 25 eq.) and CH_2Cl_2 (1.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 20:80 EtOAc:heptane, v/v) to give the major regioisomer **671'** as an oil (1.0 mg, 0.005 mmol, 9%). The minor regioisomer **671** could not be isolated in sufficient purity, therefore the overall yield refers to the mass of major regioisomer **671'**. The regioisomeric ratio (10.7 : 1.0) was determined by quantitative ^{1}H NMR analysis of the crude reaction mixture.

4-(Benzo[b]thiophen-3-yl)morpholine, 671':

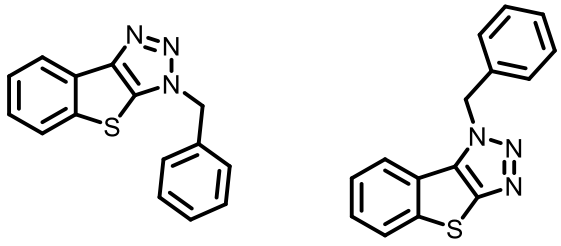


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 2H, H-4,7), 7.42 – 7.33 (m, 2H, H-5,6), 6.78 (s, 1H, H-2), 4.03 – 3.94 (m, 4H, H-10), 3.24 – 3.16 (m, 4H, H-9).

LRMS (ESI) exact mass calculated for $C_{12}H_{14}NOS^+$ $[M+H]^+$ requires *m/z* 220.1, found *m/z* 220.2.

Due to the limited quantity of the title compound isolated, no further characterisation was performed.

3-Benzyl-3H-benzo[4,5]thieno[2,3-d][1,2,3]triazole, 669, and 1-benzyl-1H-benzo[4,5]thieno[2,3-d][1,2,3]triazole, 669':



669 and **669'** were prepared according to **General Procedure H** using 5-(benzo[b]thiophen-3-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate (22.2 mg, 0.05 mmol, 1.0 eq.), benzyl azide (125 μL, 133.2 mg, 1.0 mmol, 20 eq.) and CH_2Cl_2 (1.0 mL, 0.05 M). The crude residue was purified by flash column chromatography (0:100 to 40:60 EtOAc:heptane, v/v) to give an inseparable mixture of the two regioisomers as an oil (0.8 mg, 0.003 mmol, 6%). The regioisomeric ratio (4.0 : 1.0) was determined by quantitative ^{1}H NMR analysis of the purified reaction mixture. The exact regiochemistry of the products could not be determined unambiguously, therefore the following spectra have been left unassigned.

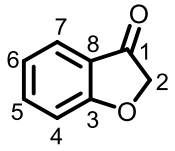
LRMS (ESI) exact mass calculated for $C_{15}H_{12}N_3S^+$ $[M+H]^+$ requires *m/z* 266.1, found *m/z* 266.3.

Major Regioisomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.55 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.46 – 7.28 (m, 7H), 5.96 (s, 2H).

Due to the limited quantity of the mixture of the title compounds isolated, no further characterisation was performed. The ^{1}H NMR of the minor regioisomer could not be easily distinguished due to the overlap with the major regioisomer peaks.

Benzofuran-3(2H)-one, 704:



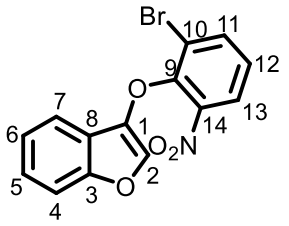
An oven-dried two-neck round bottom flask was charged with anhydrous $CuBr_2$ (32.8 g, 146.9 mmol, 2.0 eq.) before suspending in anhydrous EtOAc (122 mL) and heating to 77 °C. With stirring, a solution of 2'-hydroxyacetophenone (1.0 g, 73.4 mmol, 1.0 eq.) in anhydrous chloroform (61 mL) was added dropwise *via* an addition funnel, then the reaction mixture was left to reflux under nitrogen for 16 hours. After the reaction time, the mixture was cooled to room temperature and filtered through Celite, eluting with EtOAc, then washed with deionised water (x3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude mixture of 2-bromo-1-(2-hydroxyphenyl)ethan-1-one (15.4 g). The crude residue was then redissolved in anhydrous MeCN (145 mL, 0.5 M) and cooled to 0 °C before adding Et_3N (20.5 mL, 14.86 g, 146.9 mmol, 2.0 eq.) dropwise. The reaction mixture was stirred at 0 °C for 1 hour, then quenched with deionised water (~300 mL). The aqueous layer was then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (20:80 to 25:75 Et_2O:pentane, v:v) to obtain the title compound as a solid (5.08 g, 37.87 mmol, 52%). The NMR spectra are consistent with those available in the literature.[206]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.6, 1.5 Hz, 1H, H-7), 7.61 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, H-5), 7.14 (d, *J* = 8.5 Hz, 1H, H-4), 7.12 – 7.06 (m, 1H, H-6), 4.62 (s, 2H, H-2).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0 (C-1), 174.1 (C-3), 138.0 (C-5), 124.2 (C-7), 122.1 (C-6), 121.3 (C-8), 113.8 (C-4), 74.8 (C-2).

HRMS (ESI) exact mass calculated for $C_8H_7O_2^+$ $[M+H]^+$ requires *m/z* 135.0441, found *m/z* 135.0440.

3-(2-Bromo-6-nitrophenoxy)benzofuran, 705:



An oven-dried round bottom flask was charged with benzofuran-3(2H)-one (1.50 g, 11.18 mmol, 1.0 eq.) before adding anhydrous DMF (45 mL, 0.25 M), followed by 1-bromo-2-fluoro-3-nitrobenzene (2.71 g, 12.30 mmol, 1.1 eq.). Cs_2CO_3 (5.46 g, 16.77 mmol, 1.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 60 °C for 2 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~500 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (1.91 g, 5.72 mmol, 51%).

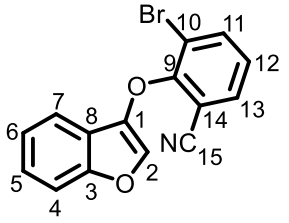
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 – 7.87 (m, 2H, H-11,13), 7.58 (dt, *J* = 7.7, 1.0 Hz, 1H, H-7), 7.43 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.34 (ddd, *J* = 8.4, 7.2, 1.0 Hz, 1H, H-5), 7.30 (t, *J* = 8.2 Hz, 1H, H-12), 7.29 – 7.25 (m, 1H, H-6), 7.12 (s, 1H, H-2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.7 (C-3), 147.0 (C-9), 144.5 (C-14), 142.5 (C-1), 138.6 (C-11), 128.8 (C-2), 126.9 (C-13), 125.5 (C-5), 124.9 (C-12), 123.0 (C-6), 121.0 (C-8), 119.4 (C-7), 118.9 (C-10), 112.1 (C-4).

HRMS (ESI) exact mass calculated for $C_{14}H_9BrNO_4^+$ $[M+H]^+$ requires *m/z* 333.9709, found *m/z* 333.9705.

IR (thin film) ν_{max}/cm^{-1} 1580, 1531, 1451, 1351, 1283, 1240, 1187, 1122, 1094, 1081, 1007, 877, 790.

2-(Benzofuran-3-yloxy)-3-bromobenzonitrile, 706:



An oven-dried round bottom flask was charged with benzofuran-3(2H)-one (1.00 g, 7.46 mmol, 1.0 eq.) before adding anhydrous DMF (30 mL, 0.25 M), followed by 3-bromo-2-fluorobenzonitrile (1.64 g, 8.21 mmol, 1.1 eq.). Cs_2CO_3 (2.91 g, 8.95 mmol, 1.5 eq.) was then added in one portion with stirring before heating the reaction mixture to 60 °C for 3 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and poured into deionised water (~300 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as a solid (1.72 g, 5.48 mmol, 74%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.1, 1.5 Hz, 1H, H-11), 7.66 (dd, *J* = 7.7, 1.5 Hz, 1H, H-13), 7.57 (dt, *J* = 7.7, 0.9 Hz, 1H, H-7), 7.45 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.35 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H, H-5), 7.28 – 7.23 (m, 2H, H-6,12), 7.16 (s, 1H, H-2).

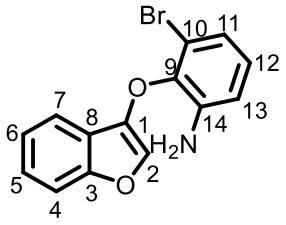
^{13}C NMR (151 MHz, $CDCl_3$) δ 155.3 (C-3), 153.8 (C-9), 142.4 (C-1), 138.9 (C-11), 133.3 (C-13), 129.4 (C-2), 127.1 (C-5), 125.6 (C-12), 123.0 (C-6), 121.0 (C-7), 118.9 (C-8), 117.6 (C-10), 114.4 (C-15), 112.2 (C-4), 108.9 (C-14).

HRMS (ESI) exact mass calculated for $C_{15}H_9BrNO_2^+$ $[M+H]^+$ requires *m/z* 313.9811, found *m/z* 313.9811.

IR (thin film) ν_{max}/cm^{-1} 1701, 1617, 1582, 1483, 1442, 1369, 1285, 1245, 1231, 1187, 1157, 1122, 1096, 1077, 1043, 851, 785, 746, 697.

MP >250 °C.

2-(Benzofuran-3-yloxy)-3-bromoaniline, 725:



A round bottom flask was charged with 3-(2-bromo-6-nitrophenoxy)benzofuran (182.7 mg, 0.55 mmol, 1.0 eq.) before adding EtOAc (5.5 mL, 0.1 M), followed by tin(II) chloride dihydrate (1.23 g, 5.50 mmol, 10 eq.). The reaction mixture was left to stir at room temperature for 16 hours. After the reaction time, the mixture was diluted with CH_2Cl_2 (10 mL), then the formed suspension was filtered to partially remove excess tin salts. The filtrate was then washed with saturated aqueous $NaHCO_3$ (x3) and deionised water (x3), then dried with brine and $MgSO_4$ and concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 10:90 EtOAc:pentane, v:v) to obtain the title compound as an oil (93.5 mg, 0.31 mmol, 56%).

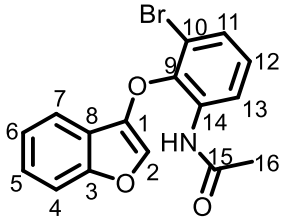
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dt, *J* = 7.8, 1.1 Hz, 1H, H-7), 7.42 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.33 (ddd, *J* = 8.4, 7.1, 1.1 Hz, 1H, H-5), 7.29 – 7.24 (m, 1H, H-6), 7.11 (s, 1H, H-2), 6.98 (dd, *J* = 8.0, 1.5 Hz, 1H, H-11), 6.92 (t, *J* = 8.0 Hz, 1H, H-12), 6.74 (dd, *J* = 8.0, 1.5 Hz, 1H, H-13), 3.92 (s, 2H, H-NH_2).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.9 (C-3), 141.9 (C-9), 140.8 (C-14), 140.5 (C-1), 128.3 (C-2), 127.4 (C-5), 125.2 (C-11), 122.7 (C-12), 122.7 (C-6), 121.3 (C-7), 118.9 (C-8), 117.0 (C-13), 115.7 (C-10), 112.1 (C-4).

HRMS (ESI) exact mass calculated for $C_{14}H_{11}BrNO_2^+$ $[M+H]^+$ requires *m/z* 303.9968, found *m/z* 303.9964.

IR (thin film) ν_{max}/cm^{-1} 3388, 1616, 1584, 1476, 1453, 1369, 1315, 1283, 1217, 1187, 1122, 1089, 887, 853, 829, 767, 741.

***N*-(2-(benzofuran-3-yloxy)-3-bromophenyl)acetamide, 707:**



An oven-dried round bottom flask was charged with 2-(benzofuran-3-yloxy)-3-bromoaniline (93.5 mg, 0.31 mmol, 1.0 eq.) before dissolving in anhydrous CH_2Cl_2 (3.1 mL, 0.1 M). Anhydrous pyridine (37 µL, 36.4 mg, 0.46 mmol, 1.2 eq.) was added dropwise and the solution was cooled to 0 °C before adding acetic anhydride (35 µL, 37.8 mg, 0.37 mmol, 1.5 eq.) dropwise. After full addition, the reaction mixture was brought to room temperature and left to stir under nitrogen for 16 hours. After the reaction time, the mixture was poured into deionised water (~100 mL) and extracted with EtOAc (x3). Combined organics were dried with brine, $MgSO_4$ and concentrated under vacuum to obtain a crude oil, which was purified by flash column chromatography (20:80 EtOAc:Pentane, v:v) to give the title compound as a solid (59.5 mg, 0.17 mmol, 55%).

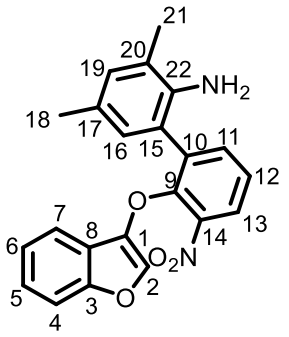
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.2 Hz, 1H, H-13), 7.67 (s, 1H, H-NH), 7.64 – 7.58 (m, 1H, H-7), 7.45 (d, *J* = 8.4 Hz, 1H, H-4), 7.39 – 7.33 (m, 2H, H-5,11), 7.28 (td,

J = 7.5, 1.0 Hz, 1H, H-6), 7.14 (t, *J* = 8.2 Hz, 1H, H-12), 7.07 (s, 1H, H-2), 2.07 (s, 3H, H-16).

^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6 (C-15), 153.9 (C-3), 142.5 (C-9), 142.0 (C-1), 132.8 (C-14), 128.7 (C-2), 128.4 (C-11), 127.4 (C-12), 125.6 (C-5), 123.0 (C-6), 120.9 (C-13), 120.6 (C-7), 118.6 (C-8), 115.9 (C-10), 112.3 (C-4), 24.9 (C-16).

HRMS (ESI) exact mass calculated for $C_{16}H_{13}BrNO_3^+$ $[M+H]^+$ requires *m/z* 346.0073, found *m/z* 346.0068.

2'-(Benzofuran-3-yloxy)-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-amine, 708:



A three-neck round bottom flask was charged with 3-(2-bromo-6-nitrophenoxy)benzofuran (1.00 g, 2.99 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.11 g, 4.49 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (173.3 mg, 5 mol%) and K_2CO_3 (1.65 g, 11.96 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 30.0 mL, 0.1 M). The suspension was sparged with argon for 15 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column

chromatography (20:80 EtOAc:pentane, v:v) to obtain the title compound as an oil (722.0 mg, 1.93 mmol, 65%).

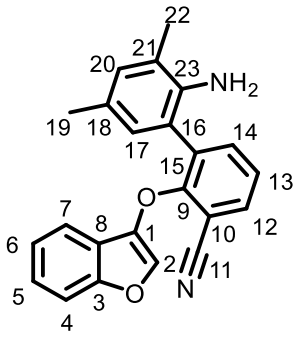
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.2, 1.7 Hz, 1H, H-13), 7.65 (dd, *J* = 7.7, 1.7 Hz, 1H, H-11), 7.48 (t, *J* = 7.9 Hz, 1H, H-12), 7.34 – 7.32 (m, 1H, H-7), 7.28 – 7.24 (m, 2H, H-4,5), 7.14 (td, *J* = 7.4, 1.0 Hz, 1H, H-6), 7.09 (s, 1H, H-2), 6.77 – 6.70 (m, 1H, H-16), 6.68 – 6.61 (m, 1H, H-19), 3.37 (s, 2H, H-NH_2), 2.11 (s, 3H, H-18), 2.06 (s, 3H, H-21).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.2 (C-3), 147.7 (C-9), 144.3 (C-22), 142.6 (C-14), 139.4 (C-1), 137.1 (C-11), 135.8 (C-2), 131.5 (C-19), 130.2 (C-10), 128.7 (C-16), 127.2 (C-17), 125.6 (C-15), 124.9 (C-13), 124.4 (C-5), 122.8 (C-20), 122.3 (C-12), 121.3 (C-6), 120.5 (C-8), 118.5 (C-7), 111.5 (C-4), 20.2 (C-18), 17.7 (C-21).

HRMS (ESI) exact mass calculated for $C_{22}H_{19}N_2O_4^+$ $[M+H]^+$ requires *m/z* 375.1339, found *m/z* 375.1326.

IR (thin film) ν_{max}/cm^{-1} 1620, 1583, 1531, 1485, 1452, 1364, 1283, 1231, 1188, 1157, 1122, 1093, 1009, 854, 815, 794, 744.

2'-Amino-2-(benzofuran-3-yloxy)-3',5'-dimethyl-[1,1'-biphenyl]-3-carbonitrile, 709:



A three-neck round bottom flask was charged with 2-(benzofuran-3-yloxy)-3-bromobenzonitrile (685.0 mg, 2.18 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-

1,3,2-dioxaborolan-2-yl)aniline (900.0 mg, 3.64 mmol, 1.7 eq.), $Pd(PPh_3)_4$ (125.0 mg, 5 mol%) and K_2CO_3 (1.24 g, 8.97 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 18.0 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 80:20 EtOAc:heptane, v:v) to obtain the title compound as an oil (1.24 g, 3.50 mmol, 84%).

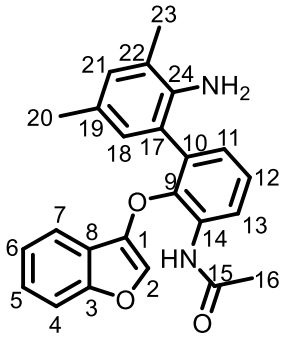
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.59 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.42 – 7.33 (m, 1H), 7.28 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.25 – 7.18 (m, 2H), 7.10 (ddd, *J* = 7.9, 7.2, 0.9 Hz, 1H), 7.02 (s, 1H), 6.71 (d, *J* = 2.1 Hz, 1H), 6.58 – 6.54 (m, 1H), 2.05 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5, 153.3, 142.3, 137.5, 133.2, 130.8, 128.8, 126.1, 125.0, 122.5, 121.3, 118.6, 115.7, 111.7, 105.2, 20.4, 18.6.

HRMS (ESI) exact mass calculated for $C_{23}H_{19}N_2O_2^+$ $[M+H]^+$ requires *m/z* 355.1441, found *m/z* 355.1429.

IR (thin film) ν_{max}/cm^{-1} 2918, 2234, 1619, 1486, 1452, 1367, 1267, 1226, 1188, 1122, 1096, 850, 794, 739.

***N*-(2'-amino-2-(benzofuran-3-yloxy)-3',5'-dimethyl-[1,1'-biphenyl]-3-yl)acetamide, 699:**



A 10 mL microwave vial was charged with *N*-(2-(benzofuran-3-yloxy)-3-bromophenyl)acetamide (59.5 mg, 0.17 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (64.3 mg, 0.26 mmol, 1.5 eq.), $Pd(PPh_3)_4$ (9.8 mg, 5 mol%) and K_2CO_3 (94.0 mg, 0.68 mmol, 4.0 eq.) before capping and degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 1.7 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 40:60 EtOAc:pentane, v:v) to obtain the title compound as an oil (29.6 mg, 0.08 mmol, 45%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 8.3, 1.6 Hz, 1H, H-13), 7.86 (s, 1H, H-NH), 7.32 – 7.27 (m, 2H, H-7,12), 7.21 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H, H-6), 7.15 (ddd, *J* = 7.8, 1.4, 0.7 Hz, 1H, H-4), 7.09 (ddd, *J* = 7.8, 7.1, 0.9 Hz, 1H, H-5), 7.04 (dd, *J* = 7.7, 1.6 Hz, 1H, H-11), 6.94 (s, 1H, H-2), 6.64 (d, *J* = 2.1 Hz, 1H, H-18), 6.51 (d, *J* = 2.1 Hz, 1H, H-21), 3.29 (s, 2H, H-NH_2), 2.15 (s, 3H, H-20), 2.00 (s, 6H, H-16,23).

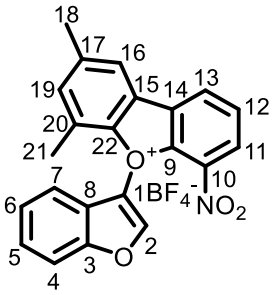
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7 (C-15), 153.4 (C-3), 143.6 (C-24), 142.2 (C-9), 139.4 (C-1), 131.6 (C-2), 130.8 (C-14), 130.2 (C-21), 128.7 (C-19), 128.7 (C-18), 128.6

(C-10), 126.9 (C-17), 126.2 (C-5), 124.9 (C-12), 122.5 (C-22), 122.4 (C-6), 122.1 (C-13), 121.4 (C-11), 120.4 (C-7), 118.2 (C-8), 111.7 (C-4), 25.1 (C-16), 20.2 (C-20), 17.7 (C-23).

HRMS (ESI) exact mass calculated for $C_{24}H_{23}N_2O_3^+$ $[M+H]^+$ requires *m/z* 387.1703, found *m/z* 387.1684.

IR (thin film) ν_{max}/cm^{-1} 3367, 1683, 1608, 1525, 1473, 1452, 1418, 1366, 1334, 1299, 1244, 1195, 1121, 1083, 1013, 852, 791.

5-(Benzofuran-3-yl)-2,4-dimethyl-6-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 680:



A glass screw-cap vial was charged with 2'-(benzofuran-3-yloxy)-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-amine (658.7 mg, 1.76 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (7.0 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 1.2 mL, 8.80 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (1.1 mL, 907.5 mg, 8.80 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 45 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (17.6 mL, 0.10 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room

temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (600.3 mg, 1.35 mmol, 77%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.79 (s, 1H, H-2), 8.67 (dt, *J* = 7.7, 1.1 Hz, 1H, H-11), 8.37 (dd, *J* = 8.1, 1.4 Hz, 1H, H-13), 8.13 – 8.08 (m, 2H, H-12,16), 7.68 (d, *J* = 8.6 Hz, 1H, H-7), 7.49 (ddd, *J* = 8.7, 7.4, 1.3 Hz, 1H, H-6), 7.45 – 7.42 (m, 1H, H-19), 7.27 (t, *J* = 7.7 Hz, 1H, H-5), 6.99 – 6.92 (m, 1H, H-4), 2.54 (s, 3H, H-21), 2.32 (s, 3H, H-18).

^{13}C NMR (151 MHz, CD_3CN) δ 165.6 (C-3), 153.8 (C-10), 153.5 (C-2), 144.4 (C-17), 144.1 (C-22), 142.4 (C-15), 137.2 (C-14), 136.7 (C-9), 134.4 (C-19), 131.3 (C-20), 128.8 (C-13), 128.3 (C-5), 127.8 (C-11), 126.7 (C-12), 125.1 (C-8), 123.9 (C-16), 121.3 (C-6), 118.3 (C-7), 116.7 (C-1), 114.4 (C-4), 21.2 (C-21), 16.1 (C-18).

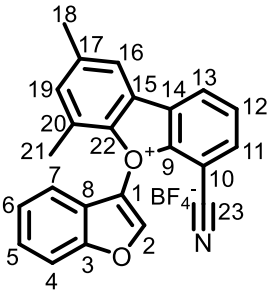
^{19}F NMR (470 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{22}H_{16}NO_4^+$ $[M]^+$ requires *m/z* 358.1074, found *m/z* 358.1067.

IR (thin film) ν_{max}/cm^{-1} 1549, 1482, 1449, 1351, 1179, 1061, 847, 815, 733.

MP decomposes 104 °C.

5-(Benzofuran-3-yl)-6-cyano-2,4-dimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 681:



A glass screw-cap vial was charged with 2'-amino-2-(benzofuran-3-yloxy)-3',5'-dimethyl-[1,1'-biphenyl]-3-carbonitrile (640.0 mg, 1.81 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (7.2 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 1.2 mL, 8.4 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (1.0 mL, 866.2 mg, 8.4 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (28 mL, 0.10 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (485.7 mg, 1.14 mmol, 63%).

^{1}H NMR (500 MHz, CD_3CN) δ 9.00 (s, 1H, H-2), 8.61 (dt, *J* = 7.8, 1.2 Hz, 1H, H-7), 8.12 (dq, *J* = 2.0, 0.7 Hz, 1H, H-16), 8.07 (dd, *J* = 7.7, 1.4 Hz, 1H, H-4), 8.01 (td, *J* = 7.7, 0.9 Hz, 1H, H-6), 7.82 (dt, *J* = 8.7, 0.8 Hz, 1H, H-13), 7.60 (ddd, *J* = 8.5, 7.3, 1.2 Hz, 1H,

H-12), 7.48 – 7.45 (m, 1H, H-19), 7.38 (td, *J* = 7.6, 0.9 Hz, 1H, H-5), 7.15 (dt, *J* = 8.0, 0.9 Hz, 1H, H-11), 2.55 (d, *J* = 0.9 Hz, 3H, H-21), 2.24 (s, 3H, H-18).

^{13}C NMR (126 MHz, CD_3CN) δ 162.4 (C-3), 158.5 (C-9), 153.9 (C-2), 143.8 (C-11), 141.5 (C-22), 137.2 (C-14), 136.9 (C-19), 132.9 (C-20), 130.3 (C-12), 129.3 (C-15), 127.0 (C-5), 125.3 (C-8), 124.3 (C-16), 123.7 (C-13), 121.2 (C-6), 117.7 (C-7), 114.6 (C-23), 111.5 (C-4), 99.6 (C-10), 21.1 (C-21), 15.9 (C-18).

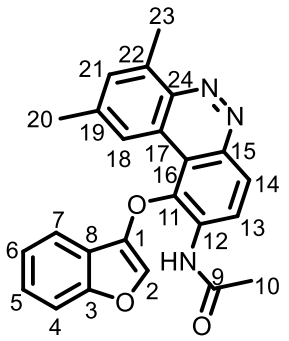
^{19}F NMR (471 MHz, CD_3CN) δ -151.8.

HRMS (ESI) exact mass calculated for $C_{23}H_{16}NO_2^+$ $[M]^+$ requires *m/z* 338.1176, found *m/z* 338.1161.

IR (thin film) ν_{max}/cm^{-1} 2922, 1598, 1569, 1471, 1448, 1365, 1270, 1211, 1174, 1110, 1095, 976, 855, 812, 740, 717.

MP decomposes 181 °C.

***N*-(1-(benzofuran-3-yloxy)-7,9-dimethylbenzo[c]cinnolin-2-yl)acetamide, 698:**



A glass screw-cap vial was charged with N-(2'-amino-2-(benzofuran-3-yloxy)-3',5'-dimethyl-[1,1'-biphenyl]-3-yl)acetamide (29.6 mg, 0.08 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.3 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 50 μL, 0.38 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (46 μL, 39.2 mg, 0.38 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture

was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (0.75 mL, 0.10 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then purified by flash column chromatography (0:100 to 20:80 EtOAc:hexane, v/v) to obtain the title compound as an oil (6.9 mg, 0.02 mmol, 23%).

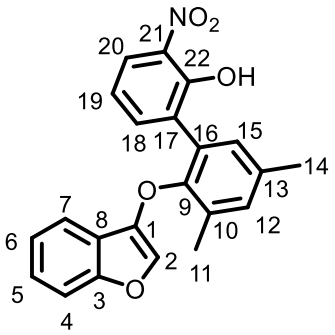
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.32 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.28 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.24 (d, *J* = 1.0 Hz, 1H), 7.21 – 7.19 (m, 2H), 7.17 – 7.15 (m, 2H), 7.10 (td, *J* = 7.5, 1.2 Hz, 1H), 6.80 (s, 1H), 2.54 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 164.0 (C-9), 153.6 (C-3), 150.2 (C-15), 148.9 (C-24), 143.3 (C-1), 141.3 (C-11,19), 135.2 (C-22), 132.5 (C-21), 131.2 (C-12), 129.9 (C-2), 128.8 (C-17), 127.9 (C-5), 125.8 (C-13), 124.8 (C-18), 124.1 (C-12), 122.3 (C-6), 121.4 (C-7), 118.6 (C-8), 118.6 (C-16), 111.7 (C-4), 21.1 (C-10), 16.5 (C-20), 14.5 (C-23).

HRMS (ESI) exact mass not detected.

IR (thin film) ν_{max}/cm^{-1} 3067, 2920, 2850, 1734, 1686, 1615, 1577, 1466, 1420, 1288, 1211, 1173, 1157, 1086, 926, 800, 747.

2'-(Benzofuran-3-yloxy)-3',5'-dimethyl-3-nitro-[1,1'-biphenyl]-2-ol, 695:

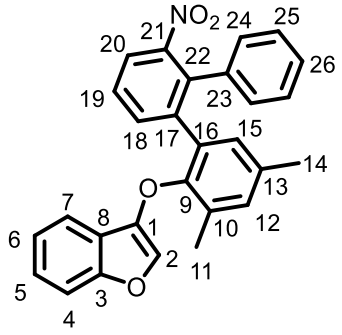


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.2, 1.7 Hz, 1H, H-20), 7.26 – 7.14 (m, 3H, H-4,7,18), 7.07 (td, *J* = 7.3, 1.5 Hz, 1H, H-5), 7.01 (d, *J* = 7.3 Hz, 1H, H-15), 6.97 (m, 1H, H-6), 6.79 (d, *J* = 9.2 Hz, 1H, H-12), 6.70 (t, *J* = 7.9 Hz, 1H, H-20), 6.63 (s, 1H, H-2), 2.22 (s, 3H, H-14), 2.20 (s, 3H, H-11).

LRMS (ESI) exact mass calculated for $C_{22}H_{16}NO_5^-$ $[M-H]^-$ requires *m/z* 374.1, found *m/z* 374.4.

The title compound appears as a side product under hetaryne generating conditions when K_3PO_4 is used as base along with 5-(benzofuran-3-yl)-2,4-dimethyl-6-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate. Due to the limited quantities isolated, no other characterisation was performed.

3-((3,5-Dimethyl-3'-nitro-[1,1':2',1''-terphenyl]-2-yl)oxy)benzofuran, 696:



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.2, 1.7 Hz, 1H, H-20), 7.63 (dd, *J* = 7.7, 1.7 Hz, 1H, H-18), 7.38 (dt, *J* = 7.7, 1.1 Hz, 1H, H-7), 7.32 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.26 – 7.23 (m, 1H, H-5), 7.18 (m, 1H, H-19), 7.17 – 7.08 (m, 3H, H-6,24), 6.99 (t, *J* = 0.8 Hz, 2H, H-12,15), 6.95 – 6.90 (m, 1H, H-26), 6.61 – 6.57 (m, 2H, H-25), 6.56 (s, 1H, H-2), 2.26 (s, 3H, H-14), 2.17 (s, 3H, H-11).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.4 (C-3), 153.5 (C-9), 149.8 (C-1), 145.8 (C-23), 143.1 (C-17), 136.6 (C-22), 134.6 (C-18), 134.4 (C-13), 132.5 (C-2), 130.6 (C-16), 129.9 (C-24), 129.2 (C-12), 128.2 (C-25), 128.0 (C-10), 124.9 (C-19), 124.7 (C-15), 124.4 (C-26),

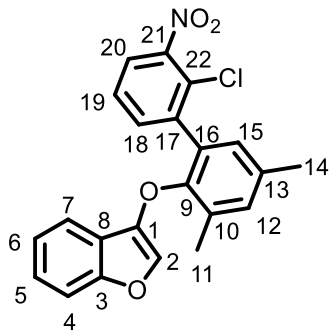
122.5 (C-5), 122.3 (C-20), 121.1 (C-6), 118.6 (C-7), 115.9 (C-8), 111.7 (C-4), 20.7 (C-14), 16.1 (C-11).

HRMS (ESI) exact mass calculated for $C_{28}H_{22}NO_4^+$ $[M+H]^+$ requires *m/z* 436.1543, found *m/z* 436.1535.

IR (thin film) ν_{max}/cm^{-1} 2924, 2854, 1731, 1697, 1581, 1534, 1489, 1453, 1361, 1285, 1241, 1209, 1191, 1128, 1088, 864, 795, 744.

The title compound appears as a side product under hetaryne generating conditions when PhLi is used as base along with 5-(benzofuran-3-yl)-2,4-dimethyl-6-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate.

3-((2'-Chloro-3,5-dimethyl-3'-nitro-[1,1'-biphenyl]-2-yl)oxy)benzofuran, 694:



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.1, 1.6 Hz, 1H, H-20), 7.38 (dd, *J* = 7.7, 1.6 Hz, 1H, H-18), 7.33 (dt, *J* = 7.7, 1.0 Hz, 1H, H-7), 7.28 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.22 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H, H-5), 7.20 – 7.18 (m, 1H, H-15), 7.16 (t, *J* = 7.9 Hz, 1H, H-19), 7.12 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H, H-6), 6.97 – 6.94 (m, 1H, H-12), 6.86 (s, 1H, H-2), 2.39 (s, 3H, H-14), 2.32 (s, 3H, H-11).

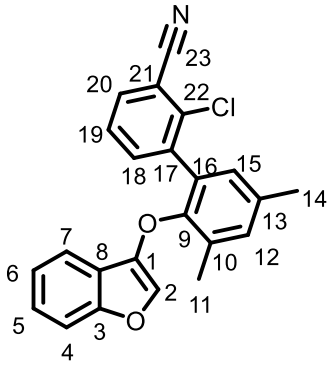
^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6 (C-3), 150.2 (C-9), 149.2 (C-21), 143.4 (C-1), 139.8 (C-17), 135.1 (C-18), 134.6 (C-13), 133.1 (C-2), 131.1 (C-12), 130.6 (C-10), 129.6 (C-19), 128.1 (C-16), 126.5 (C-15), 125.9 (C-22), 125.0 (C-5), 124.1 (C-20), 122.4 (C-6), 121.2 (C-7), 118.7 (C-8), 111.8 (C-4), 21.0 (C-14), 16.3 (C-11).

HRMS (ESI) exact mass calculated for $C_{22}H_{17}ClNO_4^+$ $[M+H]^+$ requires *m/z* 394.0841, found *m/z* 394.0834.

IR (thin film) ν_{max}/cm^{-1} 2924, 2854, 1686, 1581, 1536, 1453, 1363, 1285, 1209, 1190, 1157, 1132, 1089, 1054, 863, 839, 740.

The title compound appears as a side product under hetaryne generating conditions when tetraethylammonium chloride is used along with 5-(benzofuran-3-yl)-2,4-dimethyl-6-nitro-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate.

2'-(Benzofuran-3-yloxy)-2-chloro-3',5'-dimethyl-[1,1'-biphenyl]-3-carbonitrile, 693:

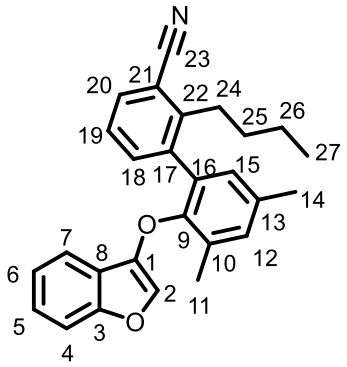


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 2H, H-18,20), 7.33 (dt, *J* = 7.7, 1.1 Hz, 1H, H-7), 7.28 (dt, *J* = 8.4, 0.9 Hz, 1H, H-4), 7.23 (ddd, *J* = 8.4, 7.1, 1.4 Hz, 1H, H-6), 7.18 (dt, *J* = 2.3, 0.8 Hz, 1H, H-15), 7.17 – 7.11 (m, 2H, H-5,19), 6.97 – 6.92 (m, 1H, H-12), 6.84 (s, 1H, H-2), 2.39 (d, *J* = 0.8 Hz, 3H, H-14), 2.31 (s, 3H, H-11).

LRMS (ESI) exact mass calculated for $C_{23}H_{17}ClNO_2^+$ $[M+H]^+$ requires *m/z* 374.1, found *m/z* 374.4.

The title compound appears as a side product under hetaryne generating conditions when tetraethylammonium chloride is used along with 5-(benzofuran-3-yl)-6-cyano-2,4-dimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate. Due to the limited quantities isolated, no other characterisation was performed.

2'-(Benzofuran-3-yloxy)-2-butyl-3',5'-dimethyl-[1,1'-biphenyl]-3-carbonitrile, 692:

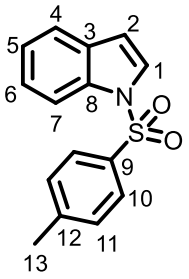


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.7, 1.4 Hz, 1H, H-7), 7.39 (dd, *J* = 7.8, 1.4 Hz, 1H, H-4), 7.26 (m, 5H, H-5,15,18,19,20), 7.12 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, H-6), 6.96 (d, *J* = 2.2 Hz, 1H, H-12), 6.77 (s, 1H, H-2), 2.40 (d, *J* = 3.9 Hz, 3H, H-14), 2.32 (s, 3H, H-11), 2.25 – 2.20 (m, 2H, H-24), 2.05 – 1.97 (m, 2H, H-25), 1.63 (q, *J* = 7.3 Hz, 2H, H-26), 0.92 – 0.82 (m, 3H, H-27).

LRMS (ESI) exact mass calculated for $C_{27}H_{26}NO_2^+$ $[M+H]^+$ requires *m/z* 396.2, found *m/z* 396.6.

The title compound appears as a side product under hetaryne generating conditions when BuLi is used as base along with 5-(benzofuran-3-yl)-6-cyano-2,4-dimethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate. Due to the limited quantities isolated, no other characterisation was performed.

1-Tosyl-1H-indole, 726:



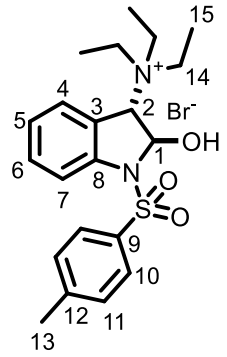
A flame-dried round bottom flask was charged with indole (4.0 g, 34.14 mmol, 1.0 eq.), before dissolving in anhydrous MeCN (171 mL, 0.2 M) and cooling to 0 °C. NaH (60% suspension in mineral oil, 1.91 g, 47.80 mmol, 1.4 eq.) was then added in small portions. After stirring for 15 minutes, tosyl chloride (7.16 g, 37.55 mmol, 1.1 eq.) was added in small portions, then the reaction mixture was brought to room temperature and left to stir for 16 hours under nitrogen. After the reaction time, the mixture was slowly poured into saturated aqueous NH_4Cl (~200 mL) and the aqueous layer was extracted with EtOAc (x3), combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (5:95 EtOAc:pentane, v/v) to obtain the title compound as a solid (8.75 g, 32.25 mmol, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dq, *J* = 8.4, 0.9 Hz, 1H, H-7), 7.81 – 7.74 (m, 2H, H-10), 7.58 (d, *J* = 3.7 Hz, 1H, H-1), 7.53 (dt, *J* = 7.7, 1.0 Hz, 1H, H-4), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, H-6), 7.25 – 7.18 (m, 3H, H-5,11), 6.66 (dd, *J* = 3.7, 1.0 Hz, 1H, H-2), 2.32 (s, 3H, H-13).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0 (C-12), 135.4 (C-9), 134.9 (C-8), 130.9 (C-3), 130.0 (C-11), 126.9(C-10), 126.4 (C-1), 124.6 (C-6), 123.4 (C-5), 121.5 (C-4), 113.6 (C-7), 109.1 (C-2), 21.6 (C-13).

HRMS (ESI) exact mass calculated for $C_{15}H_{14}NO_2S^+$ $[M+H]^+$ requires *m/z* 272.0740, found *m/z* 272.0735.

***N,N,N*-triethyl-2-hydroxy-1-tosylindolin-3-aminium bromide, 711:**

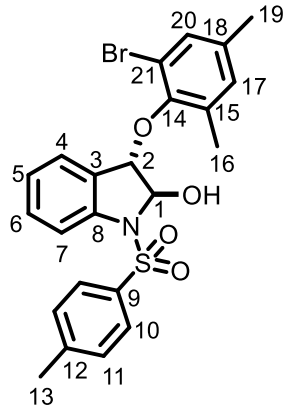


1-Tosyl-1H-indole (3.00 g, 11.0 mmol, 1.0 eq.) was dissolved in acetone (110 mL, 0.1 M) and deionised H_2O (2.0 mL, 110 mmol, 10 eq.) was added with stirring. Subsequently, NBS (2.17 g, 12.0 mmol, 1.1 eq) was added portion-wise, followed by Et_3N (1.7 mL, 12.0 mmol, 1.1 eq.) dropwise. After full addition, the reaction mixture was left to stir at room temperature for 1 hour. After the reaction time, the suspension formed was filtered, washed with ice-cold acetone and dried under vacuum to obtain a solid (3.10 g, 6.60 mmol, 60%), which was used without further purification. The ^{1}H NMR spectrum is consistent with those available in the literature.[207]

^{1}H NMR (400 MHz, DMSO) δ 8.10 – 8.02 (m, 2H, H-10), 7.88 (d, *J* = 6.0 Hz, 1H, H-2), 7.64 – 7.57 (m, 1H, H-7), 7.51 (td, *J* = 7.8, 1.2 Hz, 1H, H-5), 7.45 – 7.41 (m, 2H, H-11), 7.40 (dd, *J* = 8.3, 1.0 Hz, 1H, H-4), 7.17 (td, *J* = 7.6, 1.1 Hz, 1H, H-6), 6.39 (d, *J* = 5.7 Hz, 1H, H-1), 4.89 (s, 1H, H-OH), 3.43 (dp, *J* = 27.2, 7.2 Hz, 6H, H-14), 2.36 (s, 3H, H-13), 1.05 (t, *J* = 7.1 Hz, 9H, H-15).

HRMS (ESI) exact mass calculated for $C_{21}H_{29}N_2O_3S^+$ $[M]^+$ requires *m/z* 389.1893, found *m/z* 389.1888.

3-(2-Bromo-4,6-dimethylphenoxy)-1-tosylindolin-2-ol, 712:



N,N,N-triethyl-2-hydroxy-1-tosylindolin-3-aminium bromide (1.25 g, 2.66 mmol, 1.0 eq.) and 2-bromo-4,6-dimethylphenol (2.70 g, 13.43 mmol, 5.0 eq.) were dissolved in EtOAc (25 mL, 0.1 M), before adding Et_3N (1.8 mL, 13.43 mmol, 5.0 eq.) dropwise. After full addition, the reaction mixture was heated to 70 °C for 2 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and concentrated under vacuum to obtain a crude oil. The crude was purified by flash column chromatography (0:100 to 50:50 EtOAc:heptane, v/v) to obtain the title compound as a solid (850.0 mg, 1.74 mmol, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H, H-10), 7.62 – 7.57 (m, 1H, H-4), 7.36 – 7.31 (m, 1H, H-5), 7.26 – 7.24 (m, 2H, H-11), 7.16 (dt, *J* = 2.1, 0.7 Hz, 1H, H-20), 6.86 (td, *J* = 7.5, 1.0 Hz, 1H, H-6), 6.73 (dt, *J* = 2.2, 0.8 Hz, 1H, H-17), 6.67 – 6.61 (m, 1H, H-7), 5.99 (d, *J* = 0.9 Hz, 1H, H-1), 5.54 (d, *J* = 0.9 Hz, 1H, H-2) 2.36 (s, 3H, H-13), 2.22 (s, 3H, H-19), 1.31 (s, 3H, H-16).

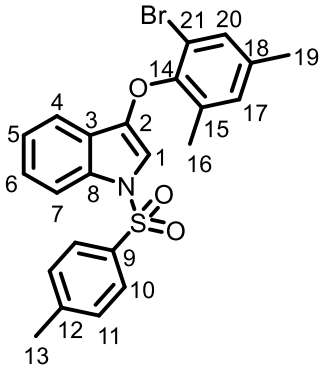
^{13}C NMR (126 MHz, $CDCl_3$) δ 148.5 (C-14), 144.7 (C-12), 141.8 (C-8), 135.7 (C-9), 135.6 (C-18), 133.9 (C-20), 131.7 (C-15), 131.1 (C-17), 131.0 (C-11), 130.0 (C-6), 127.4 (C-3), 127.2 (C-10), 126.7 (C-4), 123.5 (C-5), 117.1 (C-7), 114.2 (C-21), 91.2 (C-1), 83.9 (C-2), 21.6 (C-13), 20.6 (C-19), 16.3 (C-16).

HRMS (ESI) exact mass not detected.

IR (thin film) ν_{max}/cm^{-1} 3484, 2923, 1602, 1467, 1354, 1274, 1213, 1167, 1110, 1094, 999, 969, 854, 813, 753, 705.

MP 100-103 °C.

3-(2-Bromo-4,6-dimethylphenoxy)-1-tosyl-1H-indole, 713:



3-(2-Bromo-4,6-dimethylphenoxy)-1-tosylindolin-2-ol (720 mg, 1.47 mmol, 1.0 eq.) was dissolved in EtOAc (15 mL, 0.1 M), before adding concentrated aqueous HCl (3.7 mL) dropwise. After full addition, the reaction mixture was heated to 70 °C for 3 hours under nitrogen. After the reaction time, the mixture was cooled to room temperature and slowly added to a separatory funnel containing saturated aqueous $NaHCO_3$ (100 mL), then extracted with EtOAc (x3). Combined organics were dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 20:80 EtOAc:pentane, v:v) to obtain the title compound as a solid (267.6 mg, 0.57 mmol, 39%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (dt, *J* = 8.3, 0.9 Hz, 1H, H-7), 7.67 (dt, *J* = 7.8, 1.2 Hz, 1H, H-4), 7.63 – 7.59 (m, 2H, H-10), 7.36 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H, H-6), 7.30 (dt, *J* = 2.2, 0.7 Hz, 1H, H-5), 7.30 – 7.26 (m, 1H, H-20), 7.17 – 7.14 (m, 2H, H-11), 7.03 (dt, *J* = 2.1, 0.8 Hz, 1H, H-17), 6.53 (s, 1H, H-1), 2.36 (s, 3H, H-13), 2.32 (s, 3H, H-19), 2.16 (s, 3H, H-16).

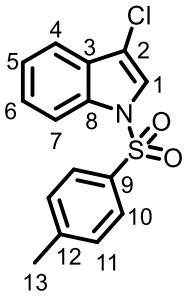
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1 (C-14), 144.8 (C-12), 144.1 (C-2), 137.0 (C-18), 134.5 (C-8), 132.5 (C-9), 132.0 (C-20), 131.7 (C-15), 129.7 (C-17), 126.9 (C-11), 125.9 (C-6), 124.3 (C-10), 123.7 (C-5), 118.7 (C-1), 116.0 (C-3), 114.6 (C-4), 107.5 (C-7), 21.7 (C-13), 20.8 (C-19), 16.6 (C-16).

HRMS (ESI) exact mass calculated for $C_{23}H_{21}BrNO_3S^+$ $[M+H]^+$ requires *m/z* 470.0420, found *m/z* 470.0403.

IR (thin film) ν_{max}/cm^{-1} 2921, 1598, 1569, 1471, 1447, 1366, 1268, 1211, 1174, 1111, 1018, 976, 854, 835, 739, 717.

MP 136-138 °C.

3-Chloro-1-tosyl-1H-indole, 714:



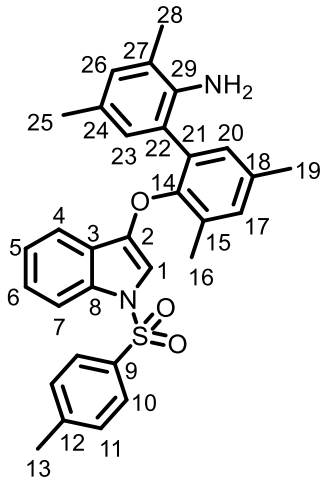
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dt, *J* = 8.4, 0.9 Hz, 1H, H-7), 7.80 – 7.73 (m, 2H, H-10), 7.55 (s, 1H, H-1), 7.55 – 7.53 (m, 1H, H-4), 7.38 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H, H-6), 7.31 (ddd, *J* = 8.1, 7.3, 1.0 Hz, 1H, H-5), 7.25 – 7.21 (m, 2H, H-11), 2.34 (s, 3H, H-13).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5 (C-12), 135.0 (C-9), 134.2 (C-8), 130.1 (C-11), 128.6 (C-3), 127.0 (C-10), 125.9 (C-1), 123.9 (C-6), 122.5 (C-5), 119.2 (C-4), 114.0 (C-2), 113.9 (C-7), 21.7 (C-13).

HRMS (ESI) exact mass calculated for $C_{15}H_{13}ClNO_2S^+$ $[M+H]^+$ requires *m/z* 306.0350, found *m/z* 306.0341.

The title compound appears as a minor impurity during the synthesis of 3-(2-bromo-4,6-dimethylphenoxy)-1-tosyl-1H-indole. The NMR spectra are consistent with those available in the literature.[208]

3,3',5,5'-Tetramethyl-2'-((1-tosyl-1H-indol-3-yl)oxy)-[1,1'-biphenyl]-2-amine, 699:



A three-neck round bottom flask was charged with 3-(2-bromo-4,6-dimethylphenoxy)-1-tosyl-1H-indole (220.0 mg, 0.47 mmol, 1.0 eq.), 2,4-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (186.5 mg, 0.75 mmol, 1.6 eq.), $Pd(PPh_3)_4$ (27.2 mg, 5 mol%) and K_2CO_3 (262.7 mg, 1.90 mmol, 4.0 eq.) before degassing with vacuum and nitrogen cycles (x3). Degassed DME was then added, followed by degassed H_2O (1:1, 4.8 mL, 0.1 M). The suspension was sparged with argon for 10 minutes, then heated to 85 °C for 16 hours. After the reaction time, the mixture was cooled to room temperature and passed through a pad of Celite, eluting with EtOAc. The solution was washed with 1 M aqueous NaOH (x 3), dried with brine and $MgSO_4$, then concentrated under vacuum to obtain a crude solid. The crude was purified by flash column chromatography (0:100 to 40:60 EtOAc:heptane, v:v) to obtain the title compound as a solid (72.1 mg, 0.14 mmol, 30%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dt, *J* = 8.4, 0.9 Hz, 1H, H-7), 7.53 – 7.49 (m, 2H, H-10), 7.44 (dt, *J* = 7.9, 1.0 Hz, 1H, H-4), 7.24 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, H-6), 7.16 – 7.11 (m, 3H, H-5,11), 7.10 (dt, *J* = 2.4, 0.8 Hz, 1H, H-23), 7.04 – 7.01 (m, 1H, H-26), 6.71 (d, *J* = 2.2 Hz, 1H, H-20), 6.70 (d, *J* = 2.1 Hz, 1H, H-17), 6.57 (s, 1H, H-1), 2.38 (s, 3H, H-13), 2.31 (s, 3H, H-19), 2.18 (s, 3H, H-25), 2.11 (s, 3H, H-28), 2.02 (s, 3H, H-16).

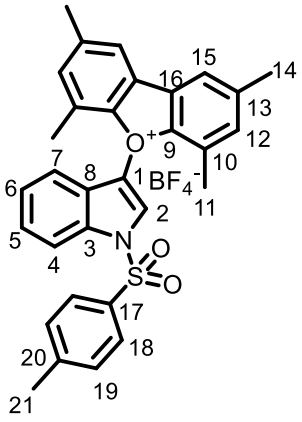
^{13}C NMR (126 MHz, $CDCl_3$) δ 150.1 (C-14), 144.7 (C-29), 144.6 (C-12), 135.8 (C-2), 134.9 (C-8), 133.8 (C-9), 132.1 (C-18), 132.0 (C-26), 131.1 (C-17), 130.7 (C-11), 130.5 (C-24), 129.7 (C-23), 129.0 (C-6), 126.8 (C-10), 125.4 (C-20), 124.4 (C-5), 123.1 (C-1), 118.7 (C-4), 113.9 (C-3), 108.0 (C-7), 21.7 (C-13), 21.0 (C-25), 20.4 (C-19), 18.0 (C-28), 16.4 (C-16).

HRMS (ESI) exact mass calculated for $C_{31}H_{31}N_2O_3S^+$ $[M+H]^+$ requires *m/z* 511.2050, found *m/z* 511.2028.

IR (thin film) ν_{max}/cm^{-1} 2922, 1602, 1569, 1447, 1364, 1270, 1210, 1174, 1093, 1017, 979, 861, 812, 739, 103, 670.

MP 186-190 °C.

2,4,6,8-Tetramethyl-5-(1-tosyl-1H-indol-3-yl)-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 700:



A glass screw-cap vial was charged with 3,3',5,5'-tetramethyl-2'-((1-tosyl-1H-indol-3-yl)oxy)-[1,1'-biphenyl]-2-amine (25.4 mg, 0.05 mmol, 1.0 eq.) before dissolving in a mixture of CH_2Cl_2 and IPA (0.250 mL, 1:1, 0.25 M) and slowly adding HBF_4 (48 wt.% in H_2O, 32 µL, 0.25 mmol, 5.0 eq.). The solution was cooled to 0 °C and *t*-BuONO (32 µL, 25.8 mg, 0.25 mmol, 5.0 eq.) was added dropwise, then stirred at 0 °C for 5 minutes, followed by another 15 minutes at room temperature. After the reaction time, the mixture was diluted with CH_2Cl_2 to twice its volume before washing with deionised water (x2) and drying with $MgSO_4$. The solution was then concentrated under a steady stream of nitrogen to obtain a crude oil. The crude was redissolved in anhydrous MeCN (0.750 mL, 0.10 M) and heated to 40 °C for 18 hours. After heating, the solution was cooled to room temperature and concentrated under a steady stream of nitrogen. The resulting crude solid was then triturated with CH_2Cl_2 and Et_2O, passing the suspension through Celite and washing the solid with additional Et_2O and pentane. Subsequently, an appropriate volume of MeCN was passed through the Celite and collected to obtain a solution of the purified salt. Finally, the solution was concentrated under a steady stream of nitrogen to obtain the pure compound (10.1 mg, 0.02 mmol, 35%).

^{1}H NMR (500 MHz, CD_3CN) δ 8.68 (s, 1H, H-2), 8.18 (dt, *J* = 8.5, 0.8 Hz, 1H, H-7), 7.93 – 7.89 (m, 4H, H-12,18), 7.53 (ddd, *J* = 8.6, 7.3, 1.1 Hz, 1H, H-6), 7.43 – 7.37 (m, 2H, H-19), 7.29 (ddd, *J* = 8.2, 7.3, 0.9 Hz, 1H, H-5), 7.24 (dt, *J* = 2.0, 0.8 Hz, 2H, H-15), 6.97 (dt, *J* = 8.1, 1.0 Hz, 1H, H-4), 2.49 (d, *J* = 0.8 Hz, 6H, H-11), 2.40 (s, 3H, H-21), 1.96 (d, *J* = 0.9 Hz, 6H, H-14).

^{13}C NMR (126 MHz, CD_3CN) δ 161.7 (C-20), 148.6 (C-3), 143.2 (C-13), 140.7 (C-9), 135.6 (C-1), 134.5 (C-17), 133.1 (C-16), 131.6 (C-12), 128.8 (C-19), 128.3 (C-10), 126.9

(C-2), 124.5 (C-5), 123.4 (C-18), 122.9 (C-8), 122.8 (C-7), 119.8 (C-6), 117.8 (C-15), 115.8 (C-4), 21.7 (C-11), 21.1 (C-21), 16.2 (C-14).

^{19}F NMR (471 MHz, CD_3CN) δ -151.9.

HRMS (ESI) exact mass calculated for $C_{31}H_{28}NO_3S^+$ $[M]^+$ requires *m/z* 494.1784, found *m/z* 494.1763.

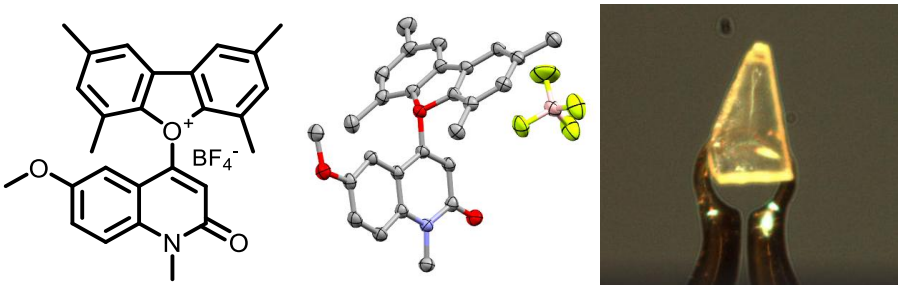
IR (thin film) ν_{max}/cm^{-1} 1541, 1457, 1389, 1273, 1223, 1177, 1056, 740, 668.

MP decomposes 236 °C.

5.4 X-Ray Crystallography

Single crystal X-ray diffraction was carried out by Hafdis Haraldsdottir using a (Rigaku) Oxford Diffraction/Agilent Supernovae A diffractometer (Cu-Kα radiation, λ = 1.54180 Å) within the Department of Chemistry, University of Oxford. Samples were mounted in perfluoropoly-ethyl ether oil and cooled to 150 K during the data collection by an N_2 Crysostream open-flow cooling device.[209] The raw frame data was integrated and reduced using CrysalisPro. SuperFlip embedded within CRYSTALS was used to obtain an *ab initio* solution using CRYSTALS and for structure refinement.[210–212] Molecular graphics of the structure solutions were created using Mercury and are shown with displacement ellipsoid plots of the best fit model drawn at 50% probability.[213]

5-(6-Methoxy-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 132:

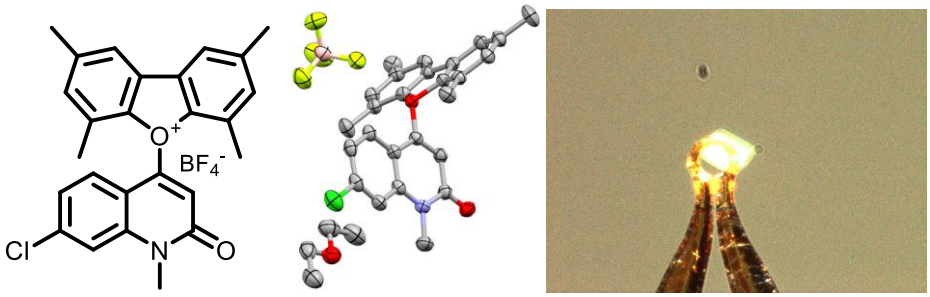


Crystals of x-ray quality were grown by vapour diffusion of Et_2O into a solution of **121** (3 mg) in CH_2Cl_2 (0.3 mL).

Identification Code	009hh24
Empirical Formula	$C_{27}H_{26}BF_4NO_3$
***M*$_r$**	499.31
Temperature	150 K
Wavelength	λ = 1.54180 Å (Cu Kα)
Crystal System	Triclinic
Space Group	P -1
Unit Cell Dimensions	a = 7.6595(3) Å α = 72.042(3)° b = 11.1469(4) Å β = 80.452(3)° c = 15.1065(5) Å γ = 71.984(3)°
Volume	1163.25(7) Å^3
Z	2
Density (Calculated)	1.425 Mg m^{-3}
Absorption Coefficient	0.956 mm^{-1}
Crystal Size	0.09 x 0.23 x 0.40 mm^3
Theta range for data collection	3.085 to 76.253°
Index Ranges	-9<=h<=9 , -14<=k<=13 , -18<=l<=18
Reflections Collected	22130
Independent Reflections	4819 [R(int) = 0.024]
Completeness to theta = 73.965°	99.6%
Absorption Correction	multi-scan
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	0.9641

Final R indices [I>2σ(I)]	$R_1 = 0.0427$, $wR_2 = 0.1207$
R indices (all data)	$R_1 = 0.0470$, $wR_2 = 0.1268$

5-(7-Chloro-1-methyl-2-oxo-1,2-dihydroquinolin-4-yl)-2,4,6,8-tetramethyl-5H-dibenzo[b,d]furan-5-ium tetrafluoroborate, 135:



Crystals of x-ray quality were grown by vapour diffusion of Et_2O into a solution of **124** (2 mg) in CH_2Cl_2 (0.3 mL).

Identification Code	045hh25
Empirical Formula	$C_{26}H_{23}BClF_4NO_2$
***M*$_r$**	577.85
Temperature	150 K
Wavelength	λ = 1.54180 Å (Cu Kα)
Crystal System	Monoclinic
Space Group	$P2_1/c$
Unit Cell Dimensions	a = 11.8446(4) Å α = 90° b = 14.4414(3) Å β = 93.444(2)° c = 16.6594(4) Å γ = 90°
Volume	2844.49(12) Å^3
Z	4
Density (Calculated)	1.349 Mg m^{-3}
Absorption Coefficient	1.698 mm^{-1}

Crystal Size	0.06 x 0.08 x 0.09 mm^3
Theta range for data collection	3.738 to 76.110°
Index Ranges	-14<=h<=14 , -18<=k<=12 , -20<=l<=20
Reflections Collected	23419
Independent Reflections	5897 [R(int) = 0.049]
Completeness to theta = 74.588°	99.8%
Absorption Correction	multi-scan
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1.0202
Final R indices [I>2σ(I)]	R_1 = 0.0567, wR_2 = 0.1420
R indices (all data)	R_1 = 0.0768, wR_2 = 0.1680

6 Bibliography

1 E. Kraka and D. Cremer, *Chem. Phys. Lett.*, 1993, **216**, 333–340.

2 P. M. Tadross and B. M. Stoltz, *Chem. Rev.*, 2012, **112**, 3550–3577.

3 S. S. Bhojgude, A. Bhunia and A. T. Biju, *Acc. Chem. Res.*, 2016, **49**, 1658–1670.

4 K. Kamikawa, *Nat. Rev. Chem.*, 2023, **7**, 496–510.

5 P. M. Tadross and B. M. Stoltz, *Chem. Rev.*, 2012, **112**, 3550–3577.

6 M. Asamdi and K. H. Chikhalia, *Asian J. Org. Chem.*, 2017, **6**, 1331–1348.

7 N. Kim, M. Choi, S.-E. Suh and D. M. Chenoweth, *Chem. Rev.*, 2024, **124**, 11435–11522.

8 T. Kitamura, *Aust. J. Chem.*, 2010, **63**, 987–1001.

9 Martin. Stiles, R. G. Miller and Urs. Burckhardt, *J. Am. Chem. Soc.*, 1963, **85**, 1792–1797.

10 Y. Himeshima, T. Sonoda and H. Kobayashi, *Chem. Lett.*, 1983, **12**, 1211–1214.

11 F. Hirsch, E. Reusch, P. Constantinidis, I. Fischer, S. Bakels, A. M. Rijs and P. Hemberger, *J. Phys. Chem. A*, 2018, **122**, 9563–9571.

12 M. Mesgar and O. Daugulis, *Org. Lett.*, 2016, **18**, 3910–3913.

13 M. Lanzi and J. Wencel-Delord, *Chem. Sci.*, 2024, **15**, 1557–1569.

14 R. A. Roberts, B. E. Metze, N. Javaly, T. M. McCormick and D. R. Stuart, *Chem. Sci.*, 2025, **16**, 5547–5558.

15 O. Smith, M. J. Hindson, A. Sreenithya, V. Tataru, R. S. Paton, J. W. Burton and M. D. Smith, *Nat. Synth.*, 2024, **3**, 58–66.

16 M. Lanzi, T. Rogge, T. S. Truong, K. N. Houk and J. Wencel-Delord, *J. Am. Chem. Soc.*, 2023, **145**, 345–358.

17 M. Lanzi, R. A. Ali Abdine, M. De Abreu and J. Wencel-Delord, *Org. Lett.*, 2021, **23**, 9047–9052.

18 X. Li, H. Chen, X. Liu, L. Wang and J. Han, *ChemistrySelect*, 2023, **8**, e202301890.

19 A. Nilova, B. Metze and D. R. Stuart, *Org. Lett.*, 2021, **23**, 4813–4817.

20 A. Z. Bradley and R. P. Johnson, *J. Am. Chem. Soc.*, 1997, **119**, 9917–9918.

21 K. Miyawaki, R. Suzuki, T. Kawano and I. Ueda, *Tetrahedron Lett.*, 1997, **38**, 3943–3946.

22 T. R. Hoye, B. Baire, D. Niu, P. H. Willoughby and B. P. Woods, *Nature*, 2012, **490**, 208–212.

23 L. L. Fluegel and T. R. Hoye, *Chem. Rev.*, 2021, **121**, 2413–2444.

24 H. Takikawa, A. Nishii, T. Sakai and K. Suzuki, *Chem. Soc. Rev.*, 2018, **47**, 8030–8056.

25 M. A. Corsello, J. Kim and N. K. Garg, *Nat. Chem.*, 2017, **9**, 944–949.

26 M. Baumann, T. S. Moody, M. Smyth and S. Wharry, *Org. Process Res. Dev.*, 2020, **24**, 1802–1813.

27 F. Susanne, B. Martin, M. Aubry, J. Sedelmeier, F. Lima, S. Sevinc, L. Piccioni, J. Haber, B. Schenkel and F. Venturoni, *Org. Process Res. Dev.*, 2017, **21**, 1779–1793.

28 J.-A. Funel and S. Abele, *Angew. Chem. Int. Ed.*, 2013, **52**, 3822–3863.

29 W. E. Bachmann and H. T. Clarke, *J. Am. Chem. Soc.*, 1927, **49**, 2089–2098.

30 F. Hirsch, E. Reusch, P. Constantinidis, I. Fischer, S. Bakels, A. M. Rijs and P. Hemberger, *J. Phys. Chem. A*, 2018, **122**, 9563–9571.

31 J. D. Roberts, H. E. Jr. Simmons, L. A. Carlsmith and C. W. Vaughan, *J. Am. Chem. Soc.*, 1953, **75**, 3290–3291.

32 O. L. Chapman, K. Mattes, C. L. McIntosh, J. Pacansky, G. V. Calder and G. Orr, *J. Am. Chem. Soc.*, 1973, **95**, 6134–6135.

33 J. G. Radziszewski, B. A. Hess and R. Zahradnik, *J. Am. Chem. Soc.*, 1992, **114**, 52–57.

34 J. M. Thompson, *Infrared Spectroscopy*, Jenny Stanford Publishing, New York, 2018.

35 A. M. Orendt, J. C. Facelli, J. G. Radziszewski, W. J. Horton, D. M. Grant and J. Michl, *J. Am. Chem. Soc.*, 1996, **118**, 846–852.

36 R. Warmuth, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1347–1350.

37 H. Jiao, P. von R. Schleyer, R. Warmuth, K. N. Houk and B. R. Beno, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2761–2764.

38 S. K. Misra and K. Pathak, *Phys. Sci. Rev.*, 2023, **8**, 1713–1740.

39 J. Jampilek, *Molecules*, 2019, **24**, 3839.

40 C. Lamberth and J. Dinges, in *Bioactive Heterocyclic Compound Classes*, John Wiley & Sons, Ltd, 2012, pp. 1–20.

41 C. A. Smith, M. R. Narouz, P. A. Lummis, I. Singh, A. Nazemi, C.-H. Li and C. M. Crudden, *Chem. Rev.*, 2019, **119**, 4986–5056.

42 R. Stoermer and B. Kahlert, *Berichte Dtsch. Chem. Ges.*, 1902, **35**, 1633–1640.

43 M. G. Reinecke, *Tetrahedron*, 1982, **38**, 427–498.

44 Th. Kauffmann, *Angew. Chem. Int. Ed. Engl.*, 1965, **4**, 543–557.

45 F. Effenberger and W. Daub, *Chem. Ber.*, 1991, **124**, 2119–2125.

46 M. A. Walters and J. J. Shay, *Tetrahedron Lett.*, 1995, **36**, 7575–7578.

47 Y. Sato, N. Saito and K. Nakamura, *HETEROCYCLES*, 2014, **88**, 929.

48 Y. Fang and R. C. Larock, *Tetrahedron*, 2012, **68**, 2819–2826.

49 M. Tsukazaki and V. Snieckus.

50 J. M. Medina, M. K. Jackl, R. B. Susick and N. K. Garg, *Tetrahedron*, 2016, **72**, 3629–3634.

51 A. N. Nesmeyanov, T. P. Tolstaya, “Triphenyloxonium salts”, Dokl. Akad. Nauk SSSR, 117:4 (1957), 626–628.

52 A. N. Nesmeyanov and T. P. Tolstaya, *Bull. Acad. Sci. USSR Div. Chem. Sci.*, 1959, **8**, 620–623.

53 D. Hellwinkel and H. Seifert, *Justus Liebigs Ann. Chem.*, 1972, **762**, 29–54.

54 T. P. Tolstaya, D. A. Tsariev and Y. N. Luzikov, *Tetrahedron Lett.*, 1997, **38**, 4457–4458.

55 P. Dhiman, N. Arora, P. V. Thanikachalam and V. Monga, *Bioorganic Chem.*, 2019, **92**, 103291.

56 S. L. Greig, *Drugs*, 2015, **75**, 1687–1697.

57 F. Suzuki, T. Kuroda, Y. Nakasato, H. Manabe, K. Ohmori, S. Kitamura, S. Ichikawa and T. Ohno, *J. Med. Chem.*, 1992, **35**, 4045–4053.

58 M. D. Moen, *Drugs*, 2010, **70**, 2269–2280.

59 J. Hou, A. Ee, W. Feng, J.-H. Xu, Y. Zhao and J. Wu, *J. Am. Chem. Soc.*, 2018, **140**, 5257–5263.

60 J. Bae, J. Chae and C.-M. Park, *Adv. Synth. Catal.*, 2024, **366**, 1827–1832.

61 A. Biswas, D. Giri, D. Das, A. De, S. K. Patra and R. Samanta, *J. Org. Chem.*, 2017, **82**, 10989–10996.

62 T. Vacala, L. P. Bejcek, C. G. Williams, A. C. Williamson and P. A. Vadola, *J. Org. Chem.*, 2017, **82**, 2558–2569.

63 D. B. Werz and A. T. Biju, *Angew. Chem. Int. Ed.*, 2020, **59**, 3385–3398.

64 Th. Kauffman, A. Risberg, J. Schulz and R. Weber, *Tetrahedron Lett.*, 1964, **5**, 3563–3568.

65 A. J. J. Lennox, *Angew. Chem. - Int. Ed.*, 2018, **57**, 14686–14688.

66 P. Roschger, W. Fiala and W. Stadlbauer, *J. Heterocycl. Chem.*, 1992, **29**, 225–231.

67 I. P. Beletskaya, F. Alonso and V. Tyurin, *Coord. Chem. Rev.*, 2019, **385**, 137–173.

68 A. Dahiya, A. K. Sahoo, T. Alam and B. K. Patel, *Chem. – Asian J.*, 2019, **14**, 4454–4492.

69 K. R. Buszek, D. Luo, M. Kondrashov, N. Brown and D. VanderVelde, *Org. Lett.*, 2007, **9**, 4135–4137.

70 G. D'Aprano, M. Leclerc and G. Zotti, *J. Electroanal. Chem.*, 1993, **351**, 145–158.

71 F. I. M. Idiris and C. R. Jones, *Org. Biomol. Chem.*, 2017, **15**, 9044–9056.

72 M. M. K. Amer, M. A. Aziz, W. S. Shehab, M. H. Abdellattif and S. M. Mouneir, *J. Saudi Chem. Soc.*, 2021, **25**, 101259.

73 R. Sanz, *Org. Prep. Proced. Int.*, 2008, **40**, 215–291.

74 M. Lautens, W. Klute and W. Tam, *Chem. Rev.*, 1996, **96**, 49–92.

75 S. S. Bhojgude, A. Bhunia and A. T. Biju, *Acc. Chem. Res.*, 2016, **49**, 1658–1670.

76 F. I. Carroll, T. P. Robinson, L. E. Brieaddy, R. N. Atkinson, S. W. Mascarella, M. I. Damaj, B. R. Martin and H. A. Navarro, *J. Med. Chem.*, 2007, **50**, 6383–6391.

77 I. N. C. Kiran, R. S. Reddy, C. Lagishetti, H. Xu, Z. Wang and Y. He, *J. Org. Chem.*, 2017, **82**, 1823–1832.

78 S. Danishefsky and T. Kitahara, *J. Am. Chem. Soc.*, 1974, **96**, 7807–7808.

79 M. Breugst and H.-U. Reissig, *Angew. Chem. Int. Ed.*, 2020, **59**, 12293–12307.

80 L. Campbell-Verduyn, P. H. Elsinga, L. Mirfeizi, R. A. Dierckx and B. L. Feringa, *Org. Biomol. Chem.*, 2008, **6**, 3461.

81 T. Jin and Y. Yamamoto, *Angew. Chem. Int. Ed.*, 2007, **46**, 3323–3325.

82 C. Lu, A. V. Dubrovskiy and R. C. Larock, *J. Org. Chem.*, 2012, **77**, 2279–2284.

83 F. Shi, R. Mancuso and R. C. Larock, *Tetrahedron Lett.*, 2009, **50**, 4067–4070.

84 C. Spiteri, S. Keeling and J. E. Moses, *Org. Lett.*, 2010, **12**, 3368–3371.

85 C. Raminelli, Z. Liu and R. C. Larock, *J. Org. Chem.*, 2006, **71**, 4689–4691.

86 B. S. Shaibu, R. K. Kawade and R.-S. Liu, *Org. Biomol. Chem.*, 2012, **10**, 6834–6839.

87 Y. Xu, M. L. Conner and M. K. Brown, *Angew. Chem. Int. Ed.*, 2015, **54**, 11918–11928.

88 Z. Chen, X. Han, J.-H. Liang, J. Yin, G.-A. Yu and S.-H. Liu, *Chin. Chem. Lett.*, 2014, **25**, 1535–1539.

89 V. R. Yedulla, P. Pradhan, L. Yang and M. K. Lakshman, *Eur. J. Org. Chem.*, 2015, **2015**, 750–764.

90 T. Tanaka, S. Tabata, K. Nakamura, Y. Hazama, Y. Sakata, T. Hosoya and S. Yoshida, *Bull. Chem. Soc. Jpn.*, 2025, **98**, uoaf001.

91 V. R. Yedulla, P. Pradhan, L. Yang and M. K. Lakshman, *Eur. J. Org. Chem.*, 2015, **2015**, 750–764.

92 M. Jr. Jones and R. H. Levin, *J. Am. Chem. Soc.*, 1969, **91**, 6411–6415.

93 A. Picard, S. Ciblat and Y. K. Ramtohul, *Synlett*, 2020, **31**, 507–511.

94 T. Zhang, X. Huang and A. Luling Wu, *Eur. J. Org. Chem.*, 2012, **2012**, 3507–3519.

95 S. Chakrabarty, I. Chatterjee, L. Tebben and A. Studer, *Angew. Chem. Int. Ed.*, 2013, **52**, 2968–2971.

96 K. N. Houk, Y. Li and J. D. Evanseck, *Angew. Chem. Int. Ed. Engl.*, 1992, **31**, 682–708.

97 P. Xu and A. Studer, *Acc. Chem. Res.*, 2025, **58**, 647–658.

98 K. Najmidin, A. Kerim, P. Abdirishit, H. Kalam and T. Tawar, *J. Mol. Model.*, 2013, **19**, 3529–3535.

99 M. G. Reinecke, J. G. Newsom and L.-J. Chen, *J. Am. Chem. Soc.*, 1981, **103**, 2760–2769.

100 G. Dauvergne, J.-V. Naubron, M. Giorgi, X. Bugaut, J. Rodriguez, Y. Carissan and Y. Coquerel, *Chem. – Eur. J.*, 2022, **28**, e202202473.

101 C. Wu, Y. Fang, R. C. Larock and F. Shi, *Org. Lett.*, 2010, **12**, 2234–2237.

102 J. Zhao, P. Li, C. Wu, H. Chen, W. Ai, R. Sun, H. Ren, R. C. Larock and F. Shi, *Org. Biomol. Chem.*, 2012, **10**, 1922–1930.

103 M. Arslan, A. Degirmenci, R. Sanyal and A. Sanyal, *Polym. Chem.*, 2024, **15**, 4173–4195.

104 S.-E. Suh, S. A. Barros and D. M. Chenoweth, *Chem. Sci.*, 2015, **6**, 5128–5132.

105 Y. Chen and M. C. Willis, *Org. Lett.*, 2015, **17**, 4786–4789.

106 Y. Yang and C. R. Jones, *Synthesis*, 2022, **54**, 5042–5054.

107 K. Mikami and M. Shimizu, *Chem. Rev.*, 1992, **92**, 1021–1050.

108 Z. Chen, J. Liang, J. Yin, G.-A. Yu and S. H. Liu, *Tetrahedron Lett.*, 2013, **54**, 5785–5787.

109 R. P. Thummel, W. E. Cravey and D. B. Cantu, *J. Org. Chem.*, 1980, **45**, 1633–1637.

110 G. Wittig and H. Dürr, *Justus Liebigs Ann. Chem.*, 1964, **672**, 55–62.

111 C.-L. Sun and Z.-J. Shi, *Chem. Rev.*, 2014, **114**, 9219–9280.

112 S. Ghorai and D. Lee, *Synlett*, 2020, **31**, 750–771.

113 J. Zhao and R. C. Larock, *J. Org. Chem.*, 2007, **72**, 583–588.

114 S.-S. Lu and C.-D. Lu, *Synlett*, 2013, **24**, 640–644.

115 J. B. Rodriguez and C. Gallo-Rodriguez, *ChemMedChem*, 2019, **14**, 190–216.

116 R. A. Dhokale and S. B. Mhaske, *Org. Lett.*, 2013, **15**, 2218–2221.

117 H. Yoshida, R. Yoshida and K. Takaki, *Angew. Chem. Int. Ed.*, 2013, **52**, 8629–8632.

118 D. Rodríguez-Lojo, A. Cobas, D. Peña, D. Pérez and E. Guitián, *Org. Lett.*, 2012, **14**, 1363–1365.

119 F. T. Toledo, H. Marques, J. V. Comasseto and C. Raminelli, *Tetrahedron Lett.*, 2007, **48**, 8125–8127.

120 H. Yoshida, E. Shirakawa, Y. Honda and T. Hiyama, *Angew. Chem. Int. Ed.*, 2002, **41**, 3247–3249.

121 Z. Liu and R. C. Larock, *J. Am. Chem. Soc.*, 2005, **127**, 13112–13113.

122 K. Z. Łączkowski, D. García, D. Peña, A. Cobas, D. Pérez and E. Guitián, *Org. Lett.*, 2011, **13**, 960–963.

123 G. Yang, C. Shen, M. Quan and W. Zhang, *Tetrahedron*, 2016, **72**, 333–337.

124 H. Yoshida and K. Takaki, *Synlett*, 2012, **23**, 1725–1732.

125 H. Yoshida, M. Watanabe, J. Ohshita and A. Kunai, *Chem. Commun.*, 2005, 3292.

126 I. Urruzuno, O. Mugica, M. Oiarbide and C. Palomo, *Angew. Chem. Int. Ed.*, 2017, **56**, 2059–2063.

127 R. Samineni, P. Srihari and G. Mehta, *Org. Lett.*, 2016, **18**, 2832–2835.

128 H. Yoshida, M. Watanabe, T. Morishita, J. Ohshita and A. Kunai, *Chem. Commun.*, 2007, 1505–1507.

129 R. A. Dhokale, P. R. Thakare and S. B. Mhaske, *Org. Lett.*, 2012, **14**, 3994–3997.

130 Y. K. Ramtohul and A. Chartrand, *Org. Lett.*, 2007, **9**, 1029–1032.

131 M. E. Kuehne, *J. Am. Chem. Soc.*, 1962, **84**, 837–847.

132 J. M. Medina, J. L. Mackey, N. K. Garg and K. N. Houk, *J. Am. Chem. Soc.*, 2014, **136**, 15798–15805.

133 T. Kitamura, M. Yamane, K. Inoue, M. Todaka, N. Fukatsu, Z. Meng and Y. Fujiwara, *J. Am. Chem. Soc.*, 1999, **121**, 11674–11679.

134 R. W. Hoffmann, *Chem. Rev.*, 1989, **89**, 1841–1860.

135 S. M. Bronner, J. L. Mackey, K. N. Houk and N. K. Garg, *J. Am. Chem. Soc.*, 2012, **134**, 13966–13969.

136 P. H.-Y. Cheong, R. S. Paton, S. M. Bronner, G.-Y. J. Im, N. K. Garg and K. N. Houk, *J. Am. Chem. Soc.*, 2010, **132**, 1267–1269.

137 H. Zhao, J. Brånalt, M. Perry and C. Tyrchan, *J. Med. Chem.*, 2023, **66**, 7730–7755.

138 I. Dine, E. Mulugeta, Y. Melaku and M. Belete, *RSC Adv.*, 2023, **13**, 8657–8682.

139 P. B. Davis, U. Yasothan and P. Kirkpatrick, *Nat. Rev. Drug Discov.*, 2012, **11**, 349–350.

140 M. ABE, T. IMAI, N. ISHII, M. USUI, T. OKUDA and T. OKI, *Biosci. Biotechnol. Biochem.*, 2005, **69**, 1202–1205.

141 B. Lohrer and F. Bracher, *Tetrahedron Lett.*, 2019, **60**, 151327.

142 X. Ji, D. Li, Z. Wang, M. Tan, H. Huang and G.-J. Deng, *Asian J. Org. Chem.*, 2018, **7**, 711–714.

143 *Org. Lett.*, 2017, **19**, 4984–4987.

144 G. Singh, V. Devi and V. Monga, *ChemistrySelect*, 2020, **5**, 14100–14129.

145 B. Lohrer and F. Bracher, *Tetrahedron Lett.*, 2019, **60**, 151327.

146 R. S. Keri, S. Budagumpi, R. K. Pai and R. G. Balakrishna, *Eur. J. Med. Chem.*, 2014, **78**, 340–374.

147 F. Berger, E. M. Alvarez, N. Frank, K. Bohdan, M. Kondratiuk, L. Torkowski, P. S. Engl, J. Barletta and T. Ritter, *Org. Lett.*, 2020, **22**, 5671–5674.

148 B. S. Matada, R. Pattanashettar and N. G. Yernale, *Bioorg. Med. Chem.*, 2021, **32**, 115973.

149 X.-F. Shang, C.-J. Yang, S. L. Morris-Natschke, J.-C. Li, X.-D. Yin, Y.-Q. Liu, X. Guo, J.-W. Peng, M. Goto, J.-Y. Zhang and K.-H. Lee, *Med. Res. Rev.*, 2020, **40**, 2212–2289.

150 T. Kauffmann, F.-P. Boettcher and J. Hansen, *Justus Liebigs Ann. Chem.*, 1962, **659**, 102–109.

151 S. P. KHANAPURE and E. R. BIEHL, *Conv. Synth. Azaanthraquinones Polar Addit. Hetaryne Intermed. Use Carbanions Deriv. 3-Cyano-13H-Isobenzofuranones*, 1988, **27**, 2643–2650.

152 N. Saito, K. Nakamura, S. Shibano, S. Ide, M. Minami and Y. Sato, *Org. Lett.*, 2013, **15**, 386–389.

153 M. Escolano, D. Gaviña, G. Alzuet-Piña, S. Díaz-Oltra, M. Sánchez-Roselló and C. del Pozo, *Chem. Rev.*, 2024, **124**, 1122–1246.

154 G. Wittig, *Pure Appl. Chem.*, 1963, **7**, 173–192.

155 K. R. BROWER and E. D. AMSTUTZ, *J. Org. Chem.*, 1954, **19**, 411–414.

156 S. Yoshida, K. Shimomori, T. Nonaka and T. Hosoya, *Chem. Lett.*, 2015, **44**, 1324–1326.

157 I. Pozo, A. Cobas, D. Peña, E. Guitián and D. Pérez, *Org. Lett.*, 2021, **23**, 7376–7380.

158 J. N. Humke, R. G. Belli, E. E. Plasek, S. S. Kargbo, A. Q. Ansel and C. C. Roberts, *Science*, 2024, **384**, 408–414.

159 A. E. Goetz, S. M. Bronner, J. D. Cisneros, J. M. Melamed, R. S. Paton, K. N. Houk and N. K. Garg, *Angew. Chem. Int. Ed.*, 2012, **51**, 2758–2762.

160 M. A. Bennett and H. P. Schwemlein, *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 1296–1320.

161 S. Wang, X. Li, J. Zang, M. Liu, S. Zhang, G. Jiang and F. Ji, *J. Org. Chem.*, 2020, **85**, 2672–2679.

162 L. Winfrey, L. Yun, G. Passeri, K. Suntharalingam and A. P. Pulis, *Chem. – Eur. J.*, 2024, **30**, e202303130.

163 W. H. Meyer, M. Deetlefs, M. Pohlmann, R. Scholz, M. W. Esterhuysen, G. R. Julius and H. G. Raubenheimer, *Dalton Trans.*, 2004, 413–420.

164 R. A. Green and J. F. Hartwig, *Angew. Chem. Int. Ed.*, 2015, **54**, 3768–3772.

165 X. Yu, S. Yang, N. Yan, Y. Fu, Y. Li, W. Wang and M. Bao, *Green Chem.*, 2024, **26**, 10818–10823.

166 G. C. Enoua, G. Lahm, G. Uray and W. Stadlbauer, *J. Heterocycl. Chem.*, 2014, **51**, E263–E275.

167 C. D. Haffner, J. D. Becherer, E. E. Boros, R. Cadilla, T. Carpenter, D. Cowan, D. N. Deaton, Y. Guo, W. Harrington, B. R. Henke, M. R. Jeune, I. Kaldor, N. Milliken, K. G. Petrov, F. Preugschat, C. Schulte, B. G. Shearer, T. Shearer, T. L. Jr. Smalley, E. L. Stewart, J. D. Stuart and J. C. Ulrich, *J. Med. Chem.*, 2015, **58**, 3548–3571.

168 WO2023168367A1, 2023.

169 S. Mandal, S. Bhuyan, S. Jana, J. Hossain, K. Chhetri and B. G. Roy, *Green Chem.*, 2021, **23**, 5049–5055.

170 M. G. Lloyd, R. Huckvale, K.-M. J. Cheung, M. J. Rodrigues, G. W. Collie, O. A. Pierrat, M. Gatti Iou, M. Carter, O. A. Davis, P. C. McAndrew, E. Gunnell, Y.-V. Le Bihan, R. Talbot, A. T. Henley, L. D. Johnson, A. Hayes, M. D. Bright, F. I. Raynaud, M. Meniconi, R. Burke, R. L. M. van Montfort, O. W. Rossanese, B. R. Bellenie and S. Hoelder, *J. Med. Chem.*, 2021, **64**, 17079–17097.

171 M. Naik, V. Humnabadkar, S. J. Tantry, M. Panda, A. Narayan, S. Guptha, V. Panduga, P. Manjrekar, L. kumar Jena, K. Koushik, G. Shanbhag, S. Jatheendranath, M. R. Manjunatha, G. Gorai, C. Bathula, S. Rudrapatna, V. Achar, S. Sharma, A. Ambady, N. Hegde, J. Mahadevaswamy, P. Kaur, V. K. Sambandamurthy, D. Awasthy, C. Narayan, S. Ravishankar, P. Madhavapeddi, J. Reddy, K. Prabhakar, R. Saralaya, M. Chatterji, J. Whiteaker, B. McLaughlin, L. R. Chiarelli, G. Riccardi, M. R. Pasca, C. Binda, J. Neres, N. Dhar, F. Signorino-Gelo, J. D. McKinney, V. Ramachandran, R. Shandil, R. Tommasi, P. S. Iyer, S. Narayanan, V. Hosagrahara, S. Kavanagh, N. Dinesh and S. R. Ghorpade, *J. Med. Chem.*, 2014, **57**, 5419–5434.

172 US2009054477A1, 2009.

173 S. Banu, K. Singh, S. Tyagi, A. Yadav and P. P. Yadav, *Org. Biomol. Chem.*, 2021, **19**, 9433–9438.

174 D. K. Kumar and S. P. Rajendran, *Tetrahedron Lett.*, 2012, **53**, 3230–3232.

175 C. Kong and T. G. Driver, *Org. Lett.*, 2015, **17**, 802–805.

176 I. Yadav, V. Prakash, M. R. Maurya and M. Sankar, *Inorg. Chem.*, 2023, **62**, 5292–5301.

177 M. R. I. Smith, R. Bisht, C. Haldar, G. Pandey, J. E. Dannatt, B. Ghaffari, R. E. Jr. Maleczka and B. Chattopadhyay, *ACS Catal.*, 2018, **8**, 6216–6223.

178 M. Kocúrik, J. Bartáček, P. Drabina, J. Váňa, J. Svoboda, L. Husáková, V. Finger, M. Hympánová and M. Sedlák, *J. Org. Chem.*, 2023, **88**, 15189–15197.

179 H. Xie, L. Chen, Z. Han, Z. Yang, J. Sun and H. Huang, *Org. Lett.*, 2023, **25**, 5011–5016.

180 R. Hammami, P. Maldivi, C. Philouze, S. Carret, B. Darses, S. Touil and J.-F. Poisson, *Adv. Synth. Catal.*, 2023, **365**, 1385–1390.

181 J. Li, L. Carli, S. H. Kyne and P. W. H. Chan, *Adv. Synth. Catal.*, 2023, **365**, 2422–2427.

182 K. Livingstone, S. Bertrand, A. R. Kennedy and C. Jamieson, *Chem. – Eur. J.*, 2020, **26**, 10591–10597.

183 R. Petracca, K. A. Bowen, L. McSweeney, S. O'Flaherty, V. Genna, B. Twamley, M. Devocelle and E. M. Scanlan, *Org. Lett.*, 2019, **21**, 3281–3285.

184 K. K. Sharma, S. Sharma, A. Kudwal and R. Jain, *Org. Biomol. Chem.*, 2015, **13**, 4637–4641.

185 E. Boudry, F. Bourdreux, J. Marrot, X. Moreau and C. Ghiazza, *J. Am. Chem. Soc.*, 2024, **146**, 2845–2854.

186 A. K. Steiger, Y. Yang, M. Royzen and M. D. Pluth, *Chem. Commun.*, 2017, **53**, 1378–1380.

187 G. D. D. L. Garza, A. P. Kaur, I. A. Shkrob, L. A. Robertson, S. A. Odom and A. J. McNeil, *J. Mater. Chem. A*, 2022, **10**, 18745–18752.

188 A. P. Komin, R. W. Street and M. Carmack, *J. Org. Chem.*, 1975, **40**, 2749–2752.

189 Y.-W. Guo, Y.-L. Shi, H.-B. Li and M. Shi, *Tetrahedron*, 2006, **62**, 5875–5882.

190 M. Tordeux, C. Francese and C. Walkselman, *J. Fluor. Chem.*, 1989, **43**, 27–34.

191 A. Stanisavljević, J. Aleksić, M. Stojanović and M. Baranac-Stojanović, *Org. Biomol. Chem.*, 2024, **22**, 7218–7230.

192 Y.-M. Chai, Q. Zou, Z.-X. Guo, Y.-J. Qin and P. Zhang, *Tetrahedron Lett.*, 2023, **122**, 154517.

193 Y.-L. Chen, H.-M. Hung, C.-M. Lu, K.-C. Li and C.-C. Tzeng, *Bioorg. Med. Chem.*, 2004, **12**, 6539–6546.

194 US6320051B1, 2001.

195 R. Samanta, R. Narayan, J. O. Bauer, C. Strohmann, S. Sievers and A. P. Antonchick, *Chem. Commun.*, 2014, **51**, 925–928.

196 R. A. Kehoe, M. E. Light, D. J. Jones and G. P. McGlacken, *Green Chem.*, 2023, **25**, 5654–5660.

197 A. Isobe, J. Takagi, T. Katagiri and K. Uneyama, *Org. Lett.*, 2008, **10**, 2657–2659.

198 J. Tang, X. Chen, C. Zhao, W. Li, S. Li, X. Zheng, M. Yuan, H. Fu, R. Li and H. Chen, *J. Org. Chem.*, 2021, **86**, 716–730.

199 L. Legnani and B. Morandi, *Angew. Chem. Int. Ed.*, 2016, **55**, 2248–2251.

200 C. Yin, R. Zhang, Y. Pan, S. Gao, X. Ding, S.-T. Bai, Q. Lang and X. Zhang, *J. Org. Chem.*, 2024, **89**, 527–533.

201 E. Sato, M. Fujii, H. Tanaka, K. Mitsudo, M. Kondo, S. Takizawa, H. Sasai, T. Washio, K. Ishikawa and S. Suga, *J. Org. Chem.*, 2021, **86**, 16035–16044.

202 M. Murai, T. Ogita and K. Takai, *Chem. Commun.*, 2019, **55**, 2332–2335.

203 B. A. Suslick and T. D. Tilley, *J. Am. Chem. Soc.*, 2020, **142**, 11203–11218.

204 A. N. Kim, A. Ngamnithiporn, E. R. Welin, M. T. Daiger, C. U. Grünanger, M. D. Bartberger, S. C. Virgil and B. M. Stoltz, *ACS Catal.*, 2020, **10**, 3241–3248.

205 K. M. Allan, B. D. Hong and B. M. Stoltz, *Org. Biomol. Chem.*, 2009, **7**, 4960–4964.

206 C. Shu, R. Liu, S. Liu, J.-Q. Li, Y.-F. Yu, Q. He, X. Lu and L.-W. Ye, *Chem. – Asian J.*, 2015, **10**, 91–95.

207 T. Abe, T. Suzuki, M. Anada, S. Matsunaga and K. Yamada, *Org. Lett.*, 2017, **19**, 4275–4278.

208 R. A. Rodriguez, C.-M. Pan, Y. Yabe, Y. Kawamata, M. D. Eastgate and P. S. Baran, *J. Am. Chem. Soc.*, 2014, **136**, 6908–6911.

209 J. Cosier and A. M. Glazer, *J. Appl. Crystallogr.*, 1986, **19**, 105–107.

210 (IUCr) SUPERFLIP – a computer program for the solution of crystal structures by charge flipping in arbitrary dimensions.

211 R. I. Cooper, A. L. Thompson and D. J. Watkin, *J. Appl. Crystallogr.*, 2010, **43**, 1100–1107.

212 P. Parois, R. I. Cooper and A. L. Thompson, *Chem. Cent. J.*, 2015, **9**, 30.

213 C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler and J. van de Streek, *J. Appl. Crystallogr.*, 2006, **39**, 453–457.