Borylative Cyclisation of Alkynes Using BCl$_3$

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Doctor of Philosophy

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School of Chemistry
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>6</td>
</tr>
<tr>
<td>Declaration/Copyright Status</td>
<td>7</td>
</tr>
<tr>
<td>List of Abbreviations</td>
<td>8</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>11</td>
</tr>
<tr>
<td><strong>Chapter 1: Introduction</strong></td>
<td>12</td>
</tr>
<tr>
<td>1.1.0 – Background</td>
<td>13</td>
</tr>
<tr>
<td>1.1.1 – Early Syntheses of Boronic Acids and Esters</td>
<td>14</td>
</tr>
<tr>
<td>1.1.2 – Recent Methodologies Towards Borylated Compounds</td>
<td>16</td>
</tr>
<tr>
<td>1.1.3 – Transition Metal Free Borylation</td>
<td>18</td>
</tr>
<tr>
<td>1.1.4 – Using Boron Trihalides for the Synthesis of Aryl/Vinyl Borylated Species</td>
<td>20</td>
</tr>
<tr>
<td>1.1.5 – Borocations and Their Applications Towards Aryl/Vinyl Borylated Species</td>
<td>22</td>
</tr>
<tr>
<td>1.1.6 – Alkyne Activation Towards Cyclisation Using Electrophiles</td>
<td>27</td>
</tr>
<tr>
<td>1.1.7 – Using Transition Metal Electrophiles as Catalysts</td>
<td>27</td>
</tr>
<tr>
<td>1.1.8 – Alkyne Activation Towards Cyclisation Using Main Group Reagents</td>
<td>29</td>
</tr>
<tr>
<td>1.1.9 – Summary and Scope</td>
<td>33</td>
</tr>
<tr>
<td>1.2.0 – References</td>
<td>36</td>
</tr>
<tr>
<td><strong>Chapter 2: Borylative Cyclisation of 1,4-Disubstituted But-1ynes</strong></td>
<td>42</td>
</tr>
<tr>
<td>2.1.0 – Introduction</td>
<td>43</td>
</tr>
<tr>
<td>2.1.1 – Main Group Electrophilic Cyclisation</td>
<td>43</td>
</tr>
<tr>
<td>2.1.2 – Aims</td>
<td>48</td>
</tr>
</tbody>
</table>
2.2.0 – Results and Discussion - Borylated Dihydronaphthalene from 1,4-Diarylated But-1-ynes 50
2.2.1 – Cyclisation of Alkynes Without Arylalkynyl Moieties 63
2.2.2 – Borylative Cyclisation Towards Heteroaromatic Scaffolds 67
2.2.3 – Attempts to Generate Five- and Seven-Membered Carbocycles 75
2.2.4 – Examining Further Reactivity – Couplings, Oxidations and Secondary Cyclisations 77
2.2.5 – Alkyne Activation with BCl₃ Towards 1,2-Trans-Carbaboration 83
2.2.6 – Conclusions and Future Work 85
2.3.0 – Experimental – General Considerations 87
2.3.1 – General Syntheses 88
2.3.2 – Alkynes 91
2.3.3 – Borylated Carbocycles 103
2.3.4 – Borylated Heterocycles 116
2.3.5 – Further Reactivity – Cross Coupling, Oxidation and Boracyle Formation 118
2.3.6 – Intermolecular 1,2-Trans-Carbaboration 122
2.3.7 – Crystal Data 123
2.4.0 – References 125

Chapter 3: Borylative Cyclisation of 2-Alkynylanisoles and 2-Alkynylthioanisoles 128
3.1.0 – Introduction 129
3.1.1 – Select Transition Metal Catalysed 1,2-Elementoboration of Alkynes 129
3.1.2 – 1,2-Elementoboration of Alkynes Using Boron Electrophiles 132
3.1.3 – Aims 138
3.2.0 – Results and Discussion – N-Directed Trans-Haloboration
3.2.1 – O-Alkynylanisoles: Borylative Cyclisation or Trans-Haloboration?
3.2.2 – Elucidating the Trans-Haloboration of O-Alkynylanisoles
3.2.3 – O-Alkynylanisoles: Further Reactivity and Investigation
3.2.4 – Functionality Screening
3.2.5 – Borylative Cyclisation of O-Alkynylthioanisoles
3.2.6 – Attempted Borylative Cyclisation to Produce Isocoumarins
3.2.7 – Conclusions and Future Work
3.3.0 – Experimental – General Considerations
3.3.1 – General Syntheses
3.3.2 – Alkynes
3.3.3 – Indole Formation Versus N-Directed Trans-Haloboration
3.3.4 – 3-Borylated Benzofurans
3.3.5 – O-Directed Trans-Haloboration Product
3.3.6 – Further Functionalisation
3.3.7 – Functionality Screening
3.3.8 – 3-Borylated Benzothiophenes
3.3.9 – Crystal Data
3.4.0 – References

Chapter 4: Borylative Cyclisation of 1,2-Bis(alkynyl)benzenes
4.1.0 – Introduction
4.1.1 – Transition Metal Catalysed Routes to Dibenzopentalenes From Bisalkynylarenes
4.1.2 – Dibenzopentalene Synthesis via Main Group Electrophiles
4.1.3 – Dibenzopentalene Synthesis via Boron Electrophiles

4.1.4 – Aims

4.2.0 – Results and Discussion

4.2.1 – Borylative Cyclisation of 1,2-bis(alkynyl)benzenes with Boron Electrophiles

4.2.2 – Conclusions and Future Work

4.3.0 – Experimental – General Considerations

4.3.1 – Synthesis of Diynes

4.3.2 – Cyclisation of Diynes

4.3.3 – Crystal Data

4.4.0 – References

Total Word Count: 57,645
Abstract

Boron trichloride, a cheap and commercially available Lewis acid, has been demonstrated to activate alkynes possessing appropriate nucleophiles, facilitating borylative cyclisation. This reaction furnishes polycyclic compounds possessing a new C(sp²)-B bond externally to the newly formed ring (through concomitant C-C and C-B bond formation). The RBCl₂ intermediates generated from cyclisation were esterified with pinacol to furnish air/moisture stable boronic esters. This methodology has been applied to the following classes of starting materials: 1,4-disubstituted but-1-ynes (including N- and O- linked analogues), 2-alkynylanisoles, 2-alkynylthioanisoles and 1,2-bis(alkynyl)benzenes. Thus, borylated scaffolds such as dihydronaphtthalenes, dihydroquinolines, 2H-chromenes, benzofurans, benzothiophenes, dibenzopentalenes and benzofulvenes have been synthesised.

A variety of functionalities (e.g. amines, esters, nitriles) were tolerated by the reaction, with a number of substrates cyclised on either a gram scale, or under ambient conditions, demonstrating the robust nature of this methodology. An oxidation reaction with [Ph₃C][BF₄] was carried out on some of the borylated dihydronaphtthalene compounds to obtain borylated naphthalenes. Suzuki-Miyaura cross-coupling reactions were carried out on certain borylated cycles to furnish new C-C bonds and generate analogues of established pharmaceuticals such as Nafoxidine or Raloxifene, demonstrating the synthetic value of these borylated cycles. Additionally, a one-pot borylative cyclisation/Suzuki-Miyaura cross-coupling reaction was also developed.

Throughout this investigation, alternative reactivity has been observed when using BCl₃ to activate certain alkynes, including intermolecular 1,2-trans-carboboration and a rare example of N- and O-directed 1,2-trans-haloboration. Additionally, multiple borylative cyclisations have been carried out on an appropriate alkyne to obtain a B-doped polyaromatic hydrocarbon (PAH), which has potential material-based applications.
Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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# List of Abbreviations

## General

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>APCI</td>
<td>Atmospheric Pressure Chemical Ionisation</td>
</tr>
<tr>
<td>EDG</td>
<td>Electron Donating Group</td>
</tr>
<tr>
<td>ESI</td>
<td>Electrospray Ionisation</td>
</tr>
<tr>
<td>EWG</td>
<td>Electron Withdrawing Group</td>
</tr>
<tr>
<td>FLP</td>
<td>Frustrated Lewis Pair</td>
</tr>
<tr>
<td>GC-MS</td>
<td>Gas Chromatography-Mass Spectrometry</td>
</tr>
<tr>
<td>HOMO</td>
<td>Highest Occupied Molecular Orbital</td>
</tr>
<tr>
<td>LUMO</td>
<td>Lowest Unoccupied Molecular Orbital</td>
</tr>
<tr>
<td>NBO</td>
<td>Natural Bond Order</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear Magnetic Resonance</td>
</tr>
<tr>
<td>PAH</td>
<td>Polyaromatic Hydrocarbon</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>COSY</td>
<td>Correlation Spectroscopy</td>
</tr>
<tr>
<td>NOESY</td>
<td>Nuclear Overhauser Effect</td>
</tr>
<tr>
<td>SEAr</td>
<td>Electrophilic Aromatic Substitution</td>
</tr>
<tr>
<td>SNAr</td>
<td>Nucleophilic Aromatic Substitution</td>
</tr>
<tr>
<td>XRD</td>
<td>X-Ray Diffraction</td>
</tr>
</tbody>
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## Chemicals

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Full Form</th>
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</thead>
<tbody>
<tr>
<td>2-DMAP</td>
<td>2-Dimethylaminopyridine</td>
</tr>
<tr>
<td>2,6-lut</td>
<td>2,6-Lutidine (2,6-dimethylpyridine)</td>
</tr>
<tr>
<td>2,6-Cl2Py</td>
<td>2,6-Dichloropyridine</td>
</tr>
<tr>
<td>9-BBN</td>
<td>9-Borabicyclo[3.3.1]nonane</td>
</tr>
<tr>
<td>Aliquat-336</td>
<td>Methyltrioctylammonium Chloride</td>
</tr>
<tr>
<td>BCF</td>
<td>Tris(pentafluorophenyl)borane</td>
</tr>
<tr>
<td>Bn</td>
<td>Benzyl</td>
</tr>
<tr>
<td>Cat</td>
<td>Catecholato</td>
</tr>
<tr>
<td>Symbol</td>
<td>Name</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>CatBCl</td>
<td>Catecholborane</td>
</tr>
<tr>
<td>[CbBr₆]⁻</td>
<td>[closo-1-H-CB₁₁H₅Br₆]⁻</td>
</tr>
<tr>
<td>COD</td>
<td>Cyclooctadiene</td>
</tr>
<tr>
<td>Dan</td>
<td>1,8-Diaminonaphthalene</td>
</tr>
<tr>
<td>DCE</td>
<td>1,2-Dichloroethane</td>
</tr>
<tr>
<td>DCM</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethylsulfoxide</td>
</tr>
<tr>
<td>DMT</td>
<td>N,N-Dimethyl-p-toluidine</td>
</tr>
<tr>
<td>DTBMP</td>
<td>2,4-di-tert-butyl-4-methylpyridine</td>
</tr>
<tr>
<td>DTBPY</td>
<td>4,4'-di-tert-butyl-2,2'-bipyridine</td>
</tr>
<tr>
<td>Hex</td>
<td>Hexyl</td>
</tr>
<tr>
<td>IPr</td>
<td>N,N-Diisopropylphenyl NHC</td>
</tr>
<tr>
<td>LDA</td>
<td>Lithiumdiisopropylamide</td>
</tr>
<tr>
<td>LiHMDS</td>
<td>Lithium Bis(trimethylsilyl)amide</td>
</tr>
<tr>
<td>Mes</td>
<td>Mesityl (2,4,6-trimethylphenyl-)</td>
</tr>
<tr>
<td>MIDA</td>
<td>N-Methyliminodiacetic acid</td>
</tr>
<tr>
<td>NaTFA</td>
<td>Sodium Trifluoroacetate</td>
</tr>
<tr>
<td>nBuLi</td>
<td>n-Butyllithium</td>
</tr>
<tr>
<td>NBS</td>
<td>N-Bromosuccinimide</td>
</tr>
<tr>
<td>NET₃</td>
<td>Triethylamine</td>
</tr>
<tr>
<td>NHC</td>
<td>N-Heterocyclic Carbene</td>
</tr>
<tr>
<td>Ns</td>
<td>Nosyl (2-nitrophenylsulfonyl-)</td>
</tr>
<tr>
<td>NTf₂</td>
<td>Triflimide</td>
</tr>
<tr>
<td>o-DCB</td>
<td>o-Dichlorobenzene</td>
</tr>
<tr>
<td>Oct</td>
<td>Octyl</td>
</tr>
<tr>
<td>OTf</td>
<td>Triflate</td>
</tr>
<tr>
<td>PCE</td>
<td>Pentachloroethane</td>
</tr>
<tr>
<td>[Ph₃C][BF₄]</td>
<td>Trityl tetrafluoroborate</td>
</tr>
<tr>
<td>Pin</td>
<td>Pinacolato</td>
</tr>
<tr>
<td>Py</td>
<td>Pyridine</td>
</tr>
<tr>
<td>TBP</td>
<td>Tri-tert-butylpyridine</td>
</tr>
<tr>
<td>TCE</td>
<td>1,1',2,2'-Tetrachloroethane</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Name</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>TMP</td>
<td>2,2',6,6’-Tetramethylpiperidine</td>
</tr>
<tr>
<td>TMS</td>
<td>Trimethylsilyl</td>
</tr>
<tr>
<td>Ts</td>
<td>Tosyl (4-toluenesulfonyl-)</td>
</tr>
</tbody>
</table>
Acknowledgements

As my time at the University of Manchester draws to a close, I feel I must express my thanks to a number of people. Firstly, my thanks go to Dr. Michael Ingleson for allowing me to join the group back in 2013 and undertake this work. I’ve thoroughly enjoyed the project and we’ve had a lot of positive results. Mike’s been an excellent supervisor, and has always been there to offer guidance and advice during the more frustrating times we all encounter at one time or another in research. Next, I’d like to thank everyone in the Ingleson group for their advice with any issues that have arisen in the chemistry described in this thesis. In particular, I’d like to thank John McGough for going through the arduous journey that is a PhD with me and for being a good friend throughout it all, alongside Richard Proctor. You both made my time in the lab much more enjoyable, and as such you have my appreciation. Next up for thanks is Dr. Daniel Crossley. Humorously pedantic as he can be, he tends to be quite the fountain of knowledge, and has been a massive help to me throughout my PhD.

Next, my thanks go to the people outside of these four walls. My family and friends have all provided me with the utmost support throughout my PhD, particularly during the writing of this thesis, which has seen me spending many long nights in the office, facilitating the observation of more sunrises than I care to admit. I truly thank each and every one of you, and my sincerest apologies to those who’ve missed my presence during my time writing.

Overall, Manchester has treated me well, and without my PhD position here, I wouldn’t have met some of the people I call my best friends now. It has given me the opportunity to pursue two of my greatest passions, chemistry and music, in the space of one city. Now it’s on to the next chapter of my life, where finally I pop the student label in the tin and join the real world. Have a good one everybody!
Chapter 1:

Introduction
1.1.0 – Background

Boronic acids and their derivatives are ubiquitous in synthesis as valuable functional groups that can undergo a variety of conversions to other functional groups including (but not limited to) alcohols,[1] amines,[2-4] azides,[5] carbonyls,[6] halides[7] and nitriles[8] (Figure 1).

![Figure 1](image)

Figure 1 – Some of the possible functional groups obtainable through the use of boronic acids and esters.[1-8]

One of the most common uses of boronic acids and esters is in the Suzuki-Miyaura cross-coupling reaction to furnish new C-C bonds[9] from an aryl/vinyl halide (or pseudohalide) and an organoboron reagent, generally in the presence of a palladium catalyst and a suitable base. With the variety of transformations utilising compounds possessing C-B bonds, it is clear they are incredibly useful building blocks that can be utilised for the synthesis of complex molecules including pharmaceuticals and agrochemicals.[10] Therefore, the synthesis of these species remains important, including the development of new and efficient methods utilising simple reagents. This introduction will first describe early methods of synthesising C(sp^2)-organoboronic acids and esters, then focus on the transition metal catalysed borylation of aromatics (and vinyls), followed by transition metal free examples. Subsequently, the use of boron Lewis acids will be discussed for the synthesis of C(sp^2)-B bonds, including arene C-H borylation, alkyne haloboration and carboboration. Next, the activation of alkynes by electrophiles for nucleophilic attack will be discussed,
highlighting the uses of transition metals and main group reagents as the activating electrophilic component of the reaction. These discussions will place in context the overarching theme of this project: the activation of alkynes by BCl$_3$ for nucleophilic attack, enabling the generation of new polycyclic compounds possessing C(sp$^2$)-B moieties.

1.1.1 – Early Syntheses of Boronic Acids and Esters

C(sp$^2$)-B bonds have been known in the literature dating back as far as 1880, where Michaelis et al. synthesised phenylboronic acid via the transmetallation between BCl$_3$/BBr$_3$ and diphenylmercury,$^{[11]}$ with a variety of diarylmercury reagents also found to be applicable in later reports$^{[12-14]}$(Scheme 1).

**Scheme 1** – Early synthesis of arylboronic acids by reacting diarylmercury reagents with boron trihalides.$^{[11-14]}$

Additionally, alternative reagents applicable to a transmetallation methodology for forming arylboronic acids are arylstannanes (and arylsilanes). When arylstannanes are reacted with BX$_3$ (X = Cl or Br) and followed by an aqueous workup, arylboronic acids are obtained (Scheme 2)$^{[15]}$.

**Scheme 2** – Synthesis of arylboronic acids via transmetallation of ary!stannanes with boron tribromide with a subsequent hydrolysis step.$^{[15]}$

A related, but much more widely employed synthesis of boronic acids involves the use of organolithium or Grignard reagents and borate esters followed by a hydrolysis step. An example includes phenylboronic acid, which has been synthesised using trimethyl borate and phenylmagnesium bromide (Scheme 3)$^{[10]}$. However, this method suffers from an incompatibility with many
functional groups, which add extra steps (protection/deprotection) to the sequence, as well as the necessity for cryogenic temperatures.

![Scheme 3](image)

Scheme 3 – Synthesis of phenylboronic acid from phenylmagnesium bromide and trimethyl borate with a subsequent hydrolysis step.\[10\]

Besides transmetallation, the other most established route builds on pioneering work dating back to 1956 when hydroboration of unsaturated hydrocarbons was demonstrated by Brown et al.\[16\] as a powerful route to generate vinyl boronic acids from alkynes. For example, HBBBr\(_2\).SMe\(_2\) can be reacted with terminal alkynes to generate vinyl-BBr\(_2\) species that undergo hydrolysis to the corresponding boronic acids or alcoholysis to generate boronic esters (Scheme 4).\[17\]

![Scheme 4](image)

Scheme 4 – Using HBBBr\(_2\).SMe\(_2\) to hydroborate alkynes with a subsequent hydrolysis (or alcoholysis) step to furnish boronic acids/esters.\[17\]

In 2004, Hoshi and co-workers further developed the use of hydroboration to obtain C(sp\(^2\))-B moieties, where they reported the combined use of neat pinacolborane and dicyclohexylborane (a bulky borane catalyst) to generate a variety of trans-vinyl-Bpin compounds from terminal alkynes in the absence of solvent.\[18\]

Transition metal catalysed hydroboration was also developed after an initial observation (by Kono and Ito) of the oxidative addition of catecholborane to Wilkinson’s catalyst ([ClRh(PPh\(_3\))\(_3\)]\(^-\))\[19\] with the first metal catalysed hydroboration (using a cobalt catalyst) reported by Sneddon in 1980.\[20\] A notable early example of transition metal catalysed hydroboration was reported by Nöth in 1985.\[21\] [ClRh(PPh\(_3\))\(_3\)] was employed to activate unsaturated C-C bonds to hydroboration using catecholborane, where an example utilising hex-1-yne was shown to yield the corresponding vinyl-BCat in a moderate yield of
ca. 52%. Notably, the presence of the catalyst was necessary for hydroboration of the unsaturated C-C bond to occur (Scheme 5). Additionally, the catalysed reaction was chemoselective towards alkenes, even in the presence of aldehydes (which underwent hydroboration selectively in the absence of catalyst).

![Scheme 5 – Rhodium catalysed hydroboration of hex-1-yne.][21]

Many other catalysts have been developed for hydroboration, including examples that afford both Markovnikov[22] and anti-Markovnikov[23] selectivity, as well as examples showing chemoselectivity[21] and enantioselectivity[24] (when alkenes are employed in hydroboration). However, full coverage of these developments to the hydroboration reaction is beyond the scope of this introduction, thus the reader is directed to reviews by Crudden[25] and Guiry[26] on transition metal catalysed hydroboration.

1.1.2 – Recent Methodologies Towards Borylated Compounds

In recent years, multiple new routes to form C(sp²)-B bonds have been developed to obtain wider varieties of boronic acids, the most widely used of which are discussed below. Miyaura reported the palladium catalysed borylation of aromatic C-X groups in 1995.[27] Mechanistically, it is similar to the Suzuki-Miyaura cross coupling reaction mentioned above, but employs a diboron reagent such as B₂pin₂ instead of the boronic acid, leading to the formation of C(sp²)-B bonds (Scheme 6). Notably, the choice of base used in the reaction is important to prevent the newly formed boronic ester from participating in the reaction. Thus, bases such as KOAc and KOPh[28] are used in the reaction instead of NaOH (commonly employed in Suzuki-Miyaura cross-coupling reactions). Further developments have greatly increased the scope of reactivity, such as facilitating the use of pinacolborane towards borylation instead of the diboron reagent.[29]
Alternatively, the use of an aryl halide can be avoided as demonstrated in the catalytic C-H borylation of benzene described by Smith and Iverson, initially using [Ir(Cp*)(H)(Bpin)] as the catalyst.\textsuperscript{30} The use of B\textsubscript{2}pin\textsubscript{2} and an alternative catalyst, [Ir(OMe)(cod)]\textsubscript{2}, were found to successfully borylate benzene at 25\textdegree{}C in the presence of a bulky ligand, 4,4'-di-tert-butyl-2,2'-bipyridine (DTBPY).\textsuperscript{31-32} Due to the hindered nature of the active species involved in arene borylation, the regiochemistry was observed to be dictated by the steric bulk of the substituents on the aromatic ring, with borylation ortho- to substituents or ring junctions highly disfavoured (Scheme 7).\textsuperscript{33} This regioselectivity is further demonstrated in a report by Smith III, where borylation of 1,3-disubstituted aryls showed complete meta-selectivity, solely generating 1,3,5-trisubstituted arenes.\textsuperscript{34} Interestingly, when heteroaromatics were utilised, borylation was observed predominantly at positions possessing the most acidic C-H bonds, suggesting the influence on heteroaromatic regioselectivity was a combination of both electronic and steric factors (where bulky R groups bound to N resulted in borylation at the C-3 position preferentially).
Many other transition metal catalysed borylation methodologies have been reported (for example, iron, cobalt and nickel) and a full coverage is beyond the scope of this introduction. The reader is therefore directed to the multiple reviews and monographs on this topic.

1.1.3 – Transition Metal Free Borylation

In addition to the original work using organolithium/Grignard reagents, there is a growing number of transition metal free routes to access C(sp²)-boronic acids. Recently, examples of metal free borylation of aryl halides via radical mechanisms have been reported. A notable publication by Li et al. described an important improvement on the work by Miyaura: the photolytic borylation of aryl halides in the absence of transition metal catalysts using diboron reagents (Scheme 8). This reaction was found to be tolerant to many functional groups and could be carried out in flow reactors. A wide variety of arylboronic esters were synthesised in excellent yield using B₂pin₂. Additionally, aryl potassium trifluoroborates were obtained by employing B₂(OH)₄ and KHF₂.

An example of a non-radical, transition metal free borylation was reported by Ito and co-workers in 2012, where aryl/vinyl halides were reacted with
silylboranes in the presence of alkoxy bases (Scheme 9).\textsuperscript{[46]} A major benefit to this reaction was the tolerance towards certain functionalities (e.g. esters, amides, amines), where a control reaction involving an aryl bromide possessing an allyloxy moiety was shown to undergo borylation via the silylborane methodology. The corresponding borylation using palladium led to decomposition of the starting material via de-allylation by the palladium catalyst.

\[
\begin{align*}
\text{R} & \quad \text{Br} \quad + \quad \text{Me-Si-B-O-Me} \\
\text{Ph} & \quad \text{(1.5 eq.)} \\
\text{KOMe (1.2 eq.)} & \quad \text{DME, 30°C, 1h} \\
\end{align*}
\]

Scheme 9 – Metal free borylation using silylborane reagents and alkoxy bases.\textsuperscript{[46]}

The mechanism of these transformations was unclear; however control reactions involving the addition of transition metals or radical scavengers (e.g. 9,10-dihydroanthracene) led to no change in the rate of reaction or yields of the products, indicating the process was not transition metal or radical mediated.

Based on reports using 1,1-bisborylalkanes (RCH(Bpin)\textsubscript{2}) as suitable cross coupling reagents,\textsuperscript{[47-48]} Cho and co-workers recently described a transition metal free method to form new C-B bonds and obtain aryl/vinyl-Bpin products (Scheme 10, bottom)\textsuperscript{[49]}. This reactivity significantly differed to an earlier report by Morken and co-workers, where benzyl- and allyl-Bpin species were obtained (Scheme 10, top)\textsuperscript{[50]} via the Pd catalysed reaction of aryl/vinyl iodides with 1,1-bisborylalkane in the presence of NaOtBu.

\[
\begin{align*}
\text{R}^1 & \quad \text{X} \quad + \quad \text{pinB-Bpin} \\
\text{X = Br, I, OTf} & \quad \text{R}^2 = \text{H, alkyl} \\
\text{cat. [Pd]/L} & \quad \text{base} \\
\text{Chemoselective C-C} & \quad \text{bond formation} \\
\text{R}^1 & \quad \text{X} \quad + \quad \text{pinB-Bpin} \\
\text{X = Br, I} & \quad \text{R}^2 = \text{H, Me} \\
\text{NaOtBu} & \quad \text{Excellent C-B selectivity} \\
\end{align*}
\]

Scheme 10 – The transition metal catalysed reactivity (top) and metal-free reactivity\textsuperscript{[49]} (bottom) of aryl/vinyl halides and 1,1-bisborylalkanes.\textsuperscript{[50]}
Through computational study, the mechanism was proposed to proceed via a reaction of the bisborylalkane and NaOtBu to furnish tBuO-Bpin and pinBCH₂Na as intermediates. The latter of the two then reacts with the aryl/vinyl iodide to generate an aryl/vinyl anion intermediate and pinBCH₂I. The anion then reacts with the tBuO-Bpin species to furnish the aryl/vinyl-Bpin product and regenerate the NaOtBu. Electron deficient aromatics were shown to undergo borylation much more rapidly than electron rich aromatics, supporting the proposal of an aryl anion. Additionally, the possibilities of transition metal and radical mediated pathways were eliminated, based on control reactions involving the deliberate addition of transition metals or radical scavengers.

These metal-free borylations (for further examples of transition metal free borylation of aryl halides, see the review article by Ito[42]) offer synthetic routes that are potentially viable in the synthesis of pharmaceuticals, given that routes to these compounds cannot utilise methods that involve expensive transition metal catalysts due to high process costs and the presence of highly toxic heavy-metal impurities in the final products.[51] However, it is notable that the majority of metal free methods described utilise aryl/vinyl halides, resulting in lower atom efficiencies of multistep reactions (with additional steps usually required to obtain the desired aryl/vinyl halide), thus transition metal free C-H borylation methodologies would be of more significance. These are more limited in the literature,[52] with one exception being the development of a boron analogue of the Friedel-Crafts reaction, which is discussed in more details below.

1.1.4 – Using Boron Trihalides for the Synthesis of Aryl/Vinyl Borylated Species

The fundamental chemistry of boron trihalides is well known, in which the boron atom possesses a formally empty p₂ orbital, leading to its observed Lewis acidic behaviour, in which it readily accepts a pair of electrons from a Lewis base. Boron trihalides are strong Lewis acids (due to the inductive withdrawing effect of the halides and weak π-donation) commonly employed in synthesis (for example, ether cleavage[53] with BBr₃ or carbonyl activation[54] with BF₃), and their Lewis acidity generally follows the trend of BI₃ > BBr₃ > BCl₃ > BF₃.[55]
Based on electronegativity, it would be expected that BF$_3$ should show the most Lewis acidic character, however this trend of Lewis acidity is actually observed due to the efficiency of the orbital overlap between the halides and the boron’s empty p$_z$ orbital. Thus, the lower Lewis acidity in BF$_3$ is due to the significant loss in $\pi$-bonding upon pyramidalisation, plus the repulsion between the electron density of the fluorine ligands close in space in the tetrahedral complexes.$^{[56]}$ Notably, the larger halides (BI$_3$) conjugate less strongly, resulting in increased Lewis acidity and a lower pyramidalisation energy.

In 1959, Muetteties and Lappert each independently reported the intermolecular borylation of aromatics using the boron trihalides, BCl$_3$, BBr$_3$ and BI$_3$, in the presence of aluminium (Scheme 11)$^{[57-59]}$ BF$_3$ was found to be unreactive under the same conditions. The reaction was proposed to proceed in a fashion similar to an AlCl$_3$ mediated S$_E$Ar mechanism, with an [ArH.BCl$_2$][AlCl$_4$] species proposed.

Scheme 11 – Intermolecular borylation of aromatics using BCl$_3$ in the presence of aluminium. $^{[57-59]}

Since these early reports, the electrophilic borylation of arenes was rare (a notable exception by Paetzold describes the use of HBX$_2$ in direct arene borylation$^{[60]}$) up until the use of borocations (discussed in section 1.1.5), with many existing borylations requiring higher temperatures and strong Lewis/Brønsted acidic species, leading to isomeric mixtures of borylated products in certain cases.$^{[59]}$ Notably, this excludes the larger number of intramolecular borylations that proceed via S$_E$Ar with directing groups (for an overview of functional group directed C-H borylation, see the review by Fernández and Lassaletta$^{[61]}$), which are not discussed herein as the intermediates are not well characterised.
Shortly after the borylation of arenes with BCl$_3$/Al was disclosed, the generation of a variety of vinyl-BCl$_2$ species was reported by Lappert, via the haloboration of terminal alkynes using boron trihalides.$^{[62]}$ This reaction was proposed to proceed in a concerted fashion, furnishing the Markovnikov product. The reaction was unsuccessful when diphenylacetylene was employed, indicating its lack of reactivity towards internal alkynes, although BBr$_3$ was successfully able to bromoborate this alkyne, albeit reversibly (Scheme 12). This chemistry was later developed to facilitate the generation of halogenated vinyl-(9-BBN) species from B-halo-9-BBN reagents and alkynes.$^{[63]}$

![Scheme 12 – Haloboration of terminal alkynes using BCl$_3$, with an internal alkyne haloborated by BBr$_3$.][62]

However, the scope and use of alkyne haloboration with BX$_3$ has been limited since then, with only sporadic reports of the application of this methodology in organic synthetic endeavours.

1.1.5 – Borocations and Their Applications Towards Aryl/Vinyl Borylated Species

The lack of reactivity observed during the haloboration of internal alkynes is most likely due to a lack of electrophilicity for BCl$_3$, resulting in haloboration being endergonic (this was supported by recent calculations$^{[64]}$). Cationic three-coordinate boron species are generally higher in Lewis acidity than boron trihalides, due to the unit positive charge. Borocations can be generated via a number of routes, including the electrophilic attack$^{[65]}$ of a boron-nitrogen bond in an aminoborane, and nucleophilic displacement of an anionic ligand by a neutral ligand$^{[66]}$ but the most widely known and utilised methodology is abstraction to effect heterolysis of a boron-halogen bond using a halophilic Lewis acid such as AlCl$_3$.$^{[67]}$ This allows borocations to be readily generated.

22
using cheap starting materials, making them desirable electrophilic reagents (Scheme 13).

\[
\text{BCl}_3 \xrightarrow{\text{Lewis Base}} \text{Adduct} \overset{\text{Formation}}{\longrightarrow} \text{LB} \xrightarrow{\text{BCl}_3} \text{Halide} \overset{\text{Abstraction}}{\longrightarrow} \left[ \text{LB} \xrightarrow{\oplus} \text{BCl}_2 \right] \left[ \text{AlCl}_4 \right]
\]

Scheme 13 – A general synthesis of borocations from boron trihalides and a Lewis base in the presence of AlCl₃. In these borenium cations the positive charge is shown on boron based on NBO calculations⁶⁸ but in reality it will be delocalised throughout the molecule.

Based on the coordination number of the boron atom, borocations are termed boriniums (2-coordinate), boreniums (3-coordinate) and boroniums (4-coordinate).⁶⁷ Given that the work discussed herein does not involve borinium salts, they shall not be discussed further. Typically, borenium cations are more electrophilic than boroniums (hence boroniums are much more well-studied) due to one fewer ligand donating to the boron atom (thus, a less stable species). This led to the much earlier characterisation of a boronium, \([H_2B(NH_3)_2][BH_4]\), in 1958,⁶⁹ with the first borenium, \([\text{Cl}_2B(4\text{-picoline})][\text{AlCl}_4]\), reported in 1970 (Figure 2).⁷⁰

![Figure 2 - Structures of the first observable borenium (left)⁷⁰ and boronium (right)⁶⁹ cations.](image)

Over the last decade, chemists have been investigating the employment of borocations to generate new C(sp²)-B bonds in an efficient manner via electrophilic borylation, both intra- and intermolecularly. In 2009, Vedejs reported an intramolecular aromatic borylation employing \(N,N\)-dimethylbenzylamine to form an adduct with BH₃.⁷¹ This was followed by
hydride abstraction with \([\text{Ph}_3\text{C}]\)[B(C_6F_5)_4]\) to generate a hydride bridged borenium equivalent, that was sufficiently electrophilic to be attacked by the nucleophilic aromatic ring. This led to the liberation of \(\text{H}_2\) and the generation a cyclic borenium species, which was successfully hydrolysed to yield an aryl boronic acid (Scheme 14).

Scheme 14 – The generation of arylboronic acids via a cyclic borenium intermediate.\textsuperscript{[71]}

Subsequently, catalytic intermolecular aromatic borylation was reported by Ingleson in 2010\textsuperscript{[72]} using borocations based on [CatB]\textsuperscript{+} moieties with the weakly coordinating anion \([\text{CbBr}_6]\) (where \([\text{CbBr}_6]\) is an anionic carborane: \([\text{closo-1-H-CB}_{11}\text{H}_3\text{Br}_6]\)). Later in 2011, the same group\textsuperscript{[73]} used the borenium salts, [CatB(NEt\textsubscript{3})][AlCl\textsubscript{4}] and [Cl\textsubscript{4}-CatB(NEt\textsubscript{3})][AlCl\textsubscript{4}] to induce intermolecular borylation, where the latter was more electrophilic due to the reduced electron donating ability of the Cl\textsubscript{4}-catecholato moiety. After the electrophilic borylation, a facile esterification step with pinacol was carried out to produce aryl boronic esters in excellent yields (Scheme 15), with reasonable functional group tolerance observed. A notable benefit to this methodology is that the regioselectivity of these borylation reactions are a consequence of both electronic and steric effects, which gives complementary selectivity in borylation to the iridium catalysed borylations which rely on stercics.\textsuperscript{[33]}
Scheme 15 – Intermolecular aromatic borylation using boreniums to generate aryl boronic esters.\[73\]

Around the same time, Vedejs reported the synthesis of a hindered cyclic boronium cation, an adduct generated simply from mixing 1,8-bis(N,N-dimethylamino)naphthalene and 9-BBN triflimide, that was sufficiently electrophilic to borylate a number of indoles and pyrroles in excellent yield (Scheme 16).\[74\]

Scheme 16 – The formation of the strained cyclic boronium cation A and subsequent borylation to furnish borylated N-heterocycles (top), and borylation using 9-BBN bis-triflimide and DTBMP (bottom).\[74\]

The unusual nature of adduct compound A lies in its highly strained boracycle (due to the bulky and rigid nature of the Lewis acid and base). In the presence of 2,4-di-tert-butyl-4-methylpyridine (DTBMP), 9-BBN triflimide was also able to borylate N-methylindole in seconds at room temperature.

With the more electrophilic borocations essential to effect wider scope (hetero)arene borylations, and given the notable lack of reaction towards
internal alkynes with BCl₃, Ingleson et al. applied both borenium and boronium cations in 2013 to haloboration of alkynes,[75] specifically using the borocations [Cl₂B(2-DMAP)][AlCl₄], [Br₂B(2-DMAP)][BBr₄] and [Cl₂B(2,6-lutidine)][AlCl₄]. [Cl₂B(2-DMAP)][AlCl₄] was observed to only haloborate terminal alkynes whereas [Br₂B(2-DMAP)][BBr₄] was able to haloborate both terminal and dialkyl alkynes, likely due to increased electrophilicity. Notably, the less nucleophilic diaryl- and alkyaryl alkynes were not haloborated with [Br₂B(2-DMAP)][BBr₄], and the more electrophilic borenium, [Cl₂B(2,6-lutidine)][AlCl₄], was employed, leading to successful haloboration of these internal alkynes (Scheme 17). All borylated species were esterified with pinacol and isolated in excellent yields.

Scheme 17 – Haloboration of terminal and internal alkynes using borocations.[75]

It is worth noting that alongside these discussed examples, a variety of other borocation based C-B bond formations have been developed, including (but not limited to) carboxaboration (both 1,2-carboxaboration[76] and 1,1-carboxaboration[77]), aliphatic C-H borylation[71][78] and cis-hydroboration.[79-80]

Scheme 18 – Catalytic trans-hydroboration towards cis-vinyl-9BBN.NHC species.[81]

A recent example of C-B formation using borenium species was reported by Ingleson,[81] demonstrating that trans-hydroboration can be carried out using a bulky NHC.9-BBN(H) adduct and catalytic quantities of BCF to obtain cis-vinyl-
9BBN.NHC species in high yields that can undergo Suzuki coupling reactions after facile deprotection with BF$_3$ (Scheme 18).

The overall outcome of the last decade of research towards aryl and vinyl boronic acids and esters using borocations is the facile nature in which a wide scope of these air and moisture stable products can be obtained, both stereo- and regioselectively. Additionally, these reactions can be scaled up efficiently, proceed under mild conditions, and do not necessitate expensive, toxic transition metal catalysts. The full scope of applications for borocations in synthesis is beyond the scope of this introduction, therefore the reader is directed to reviews and monographs on the topic.$^{[82-83]}

1.1.6 – Alkyne Activation Towards Cyclisation Using Electrophiles

With BCl$_3$ and borocations able to activate alkynes for a range of elemento-borations it was surprising that they had not been used in alkyne activation / cyclisation reactions. As introduced below, a range of other electrophiles have been applied successfully for this application. Notably, excluding the recent work using BCF (which is discussed at the start of the relevant later chapters), the use of boron electrophiles for this purpose was significantly underdeveloped.

1.1.7 Using Transition Metal Electrophiles as Catalysts

A powerful method of forming new cyclic products is to activate alkynes towards nucleophilic attack from intramolecular nucleophiles (π-nucleophiles, heteroatoms etc.). A wide variety of work to generate new carbocycles has been reported utilising transition metals, including (but not limited to) platinum,$^{[84]}$ palladium,$^{[85]}$ rhodium,$^{[86]}$ and gold.$^{[87]}$ Some general examples that implement this methodology for generating new cyclic compounds will be discussed herein, with a focus on examples where the metal is acting as a π-acid only, avoiding examples involving more complex mechanisms (e.g. metallacycles$^{[88]}$/carbenes$^{[89]}$ etc.).

An example of cycloisomerisation using AuCl$_3$ was reported by Hashmi in 2000,$^{[90]}$ furnishing a variety of arenes from furans with pendant terminal alkynes. The reaction was tolerant of a range of functionalities including ethers,
amines and esters. The mechanism is unclear, but is proposed to proceed via initial activation of the alkyne by the Lewis acidic Au$^{\text{III}}$ species to an intramolecular Diels-Alder reaction with the furan moiety. This furnishes an O-bridged intermediate, where the oxygen atom coordinates to the Lewis acidic Au$^{\text{III}}$ species, inducing ring-opening to generate a cationic species. It is next proposed that external water acts as a nucleophile, leading to a diol species which undergoes dehydration to furnish the final product as one isomer (Scheme 19).

Scheme 19 – Proposed mechanism of AuCl$_3$ mediated cycloisomerisation.$^{[90]}$

Larock and co-workers also employed AuCl$_3$ as the Lewis acidic activator of 2-(1-alkynyl)-2-alken-1-ones to furnish a wide variety of polycycles possessing a furan scaffold.$^{[91]}$ The reaction pathway is a sequential nucleophilic domino attack onto the metal complexed alkyne, initiated by an external nucleophile. The result is the simultaneous formation of a C-O bond and a remote carbon-nucleophile bond (Scheme 20).

Scheme 20 – Furan synthesis via AuCl$_3$ mediated cycloisomerisation.$^{[91]}$
The first intramolecular hydroamination catalysed by silver was reported in 2013 by Hii and co-workers.\textsuperscript{[92]} [Ag(py)\textsubscript{2}][OTf] was employed as the Lewis acidic activator of the alkyne moiety in a number of propargylic trichloroacetimidates, furnishing a variety of methylene substituted heterocycles (Scheme 21).

Scheme 21 – Silver mediated intramolecular hydroamination.\textsuperscript{[92]}

The pyridine ligand was necessary for the reaction to proceed, as it served as a Brønsted base to abstract the imine proton and sequester the triflic acid generated as a by-product of the reaction. Notably, the use of a chelating ligand such as phenanthroline inhibited the reaction.

Transition metal catalysed cyclisations of alkynes offer a facile method of obtaining a wide variety of cyclic scaffolds, but notably demetallate before completion, leading to less downstream functionalisation. Additionally, as discussed in section 1.1.3, metal-catalysed routes tend to be less viable in the production of pharmaceuticals due to toxic impurities. As the work undertaken in this thesis does not employ transition metals for alkyne activation, they will not be discussed further. The reader is therefore directed to multiple reviews on this topic.\textsuperscript{[93-94]}

1.1.8 – Alkyne Activation Towards Cyclisation Using Main Group Reagents

New developments are continuously being reported to supplement the existing methodology of alkyne activation, particularly through the use of main group electrophiles. Examples of alkyne activation with main group reagents will be discussed herein. However, examples that generate scaffolds directly related to
the work undertaken in this project will only be discussed in their respective chapters. Additionally, most examples using boron reagents will be discussed in chapters 2, 3 and 4.

A classic example of the activation of unsaturated hydrocarbons with main group reagents is through the use of halogens, leading to halonium intermediates, which are susceptible to nucleophilic attack.\textsuperscript{95} When this methodology is employed with internal nucleophiles, new cyclic structures can be generated, where a benefit over the previously discussed transition metal examples is that the resulting product is halogenated (the metal catalysed examples protodemetallate during the cycloisomerisation reactions, resulting in unfunctionalised materials). The high synthetic value of iodinated cycles has led to a number of reports focused on their synthesis. Yamamoto reported an iodine mediated cyclisation of alkynes possessing internal azide groups to generate iodinated isoquinolines in excellent yield.\textsuperscript{96} This was proposed to proceed via an iodonium intermediate, with subsequent nucleophilic attack by the azide group. Finally, deprotonation by a base and loss of N\textsubscript{2} furnished the isoquinoline (Scheme 22). Interestingly, only the 6-endo-dig product was observed, with no trace of 5-exo-dig cyclisation leading to an isoindole product. This and many other cyclisations using G17 Lewis acids generate new organic electrophiles. In contrast, the synthesis of organic electrophiles by using Lewis acids that are less electronegative than carbon to induce cyclisation is much less developed.

\begin{center}
\includegraphics[width=\textwidth]{Scheme22.png}
\end{center}

\textbf{Scheme 22} - Iodine mediated cyclisation to generate iodinated isoquinolines.\textsuperscript{96}

One example of electrophilic cyclisation utilising a group 13 reagent is via the use of GaCl\textsubscript{3}, where 2,5-disubstituted furans have been generated from alkynes possessing epoxides in the presence of external nucleophiles.\textsuperscript{97} The reaction was proposed to proceed via activation of both the alkyne and epoxide by GaCl\textsubscript{3}, with subsequent intermolecular nucleophilic attack leading to opening of
the epoxide to furnish an alcohol group which attacks the alkyne. Deprotonation and the loss of an acetate group rearomatises the system, followed by protodemetallation to furnish the 2,5-disubstituted furan (Scheme 23). This reaction was also tested with InCl₃ for comparison, which led to lower yields of the desired product.

Scheme 23 – GaCl₃ mediated electrophilic cyclisation to generate 2,5-disubstituted furans.\[^{97}\]

Very recently, an example of a group 14 electrophile activating alkyne towards cyclisation was reported by Unsworth,\[^{98}\] where a variety of spirocyclic dienones were synthesised via the electrophilic cyclisation of appropriate ynones using the tin reagent, SnCl₂.2H₂O (Scheme 24). Interestingly, the reaction dearomatises the aromatic nucleophile.

Scheme 24 – Tin mediated synthesis of spirocyclic dienones via electrophilic cyclisation.\[^{98}\]

Notably, higher yields and faster reactions were observed when the aromatic group directly bound to the alkyne was electron rich (R = anisole or N,N-dimethylaniline), with no reaction observed for unsubstituted and alkylated alkynes. This was presumed simply to be due to electron rich alkynes more readily interacting with the Lewis acidic additive, promoting spirocyclisation.

In a similar fashion to the transition metal catalysed examples described herein, the heavier group 13 and 14 Lewis acids also undergo protodemetallation and do not furnish functionalised products that are useful for
further transformations. This is presumably due to the weak, polar E-C bond, which in the presence of strong acids undergoes rapid protodemetalation. This is in contrast to reactions mediated by boron electrophiles, which induce cyclisation and retain the B-C bond in the final product. An early cyclisation of alkynes utilising a boron electrophile was reported by Wrackmeyer in 1989.\textsuperscript{[99]} This involved the 1,1-carboboration of bis-alkynylsilanes with triethylborane, furnishing siloles possessing a BEt\textsubscript{2} moiety at the C-3 position (Scheme 25).

During the course of this project, a number of alkyne cyclisations solely mediated by boron electrophiles have been reported\textsuperscript{[100-101]} (including the publication of the work described in chapter 2\textsuperscript{[102]} and 3\textsuperscript{[103]}). However, prior to the completion of this thesis, the boron reagent most commonly utilised towards alkyne cyclisation was the highly electrophilic Lewis acid, BCF, leading to a variety of cyclic systems possessing C-B bonds.

An example of BCF-mediated cyclisation was the generation of borylated 1,3-dioxoliums from propargyl esters.\textsuperscript{[104]} The reaction was proposed to take place via initial activation of the alkyne with BCF, leading to nucleophilic attack by the carbonyl oxygen atom to generate a five-membered zwitterionic intermediate which subsequently ring opens, generating an intermediate possessing a terminal alkene moiety. Next, a ring closure occurs followed by a 1,3-boron allyl shift (which have been observed previously\textsuperscript{[105]}) to situate the boron on the least substituted carbon atom and furnish the 1,3-dioxolium, possessing a B(C\textsubscript{6}F\textsubscript{5})\textsubscript{3} moiety externally to the newly formed ring (Scheme 26).
This chemistry was later adapted to enynoate precursors to generate pyrylium borate species (Scheme 27). The overall mechanism was proposed to be similar to the formation of the 1,3-dioxolium species, but shows complete preference to the 6-endo-dig cyclisation pathway, presumably due to the formation of a stable 6-membered, planar, delocalised $6\pi$ Hückel aromatic system over the less stable furanium alternative.

The majority of examples employing BCF for the activation of alkynes are discussed later (for an overview of cyclisations using BCF, see the review article by Melen). It should be noted that a drawback of using BCF is that the C(sp$^2$)-B(C$_6$F$_5$)$_3$ products are not widely utilisable in subsequent functional group transformations.

1.1.9 – Summary and Scope

This introduction has highlighted the significance of C(sp$^2$)-B bonds in synthesis, particularly the uses of aryl/vinyl boronic acids in the Suzuki-Miyaura coupling reaction, as well as their conventional synthesis employing
organometallic reagents and transition metal catalysts. The use of boron Lewis acids to form C-B bonds from $\pi$-nucleophiles was introduced and this area has enjoyed a recent renaissance.

This thesis discusses several new methods for the formation of C(sp$^2$)-B bonds using boron Lewis acids for the activation of alkynes towards intramolecular reaction with both $\pi$ and heteroatomic nucleophiles. More specifically the aims of the project are set out as follows:

Chapter 2 is inspired by the pioneering work of Barluenga (using G17 electrophiles),$^{[109]}$ and examines the propensity of 1,4-disubstituted but-1-ynes to undergo borylative cyclisation with simple boron Lewis acids, thus furnishing new C-C and C-B bonds concomitantly. This methodology affords 3-borylated dihydronaphthalenes (Scheme 28, middle) that are useful for further reactivity including Suzuki-Miyaura cross-coupling to furnish 3,4-diarylated dihydronaphthalenes (Scheme 28, right bottom) or oxidation (Scheme 28, right top) to the 3-borylated naphthalenes.

Scheme 28 – General overview of the chemistry described in Chapter 2.

Chapter 3 describes our further development of the borylative cyclisation methodology (inspired by the work of Larock with G17 electrophiles),$^{[110-111]}$ employing 2-alkynylanisoles and 2-alkynylthioanisoles to provide a heteroatomic nucleophile capable of attacking the boron-activated alkyne for the synthesis of 3-borylated benzofurans and benzothiophenes (Scheme 29, top), thus generating C-O/C-S bonds and C-B bonds concomitantly. An additional goal is to develop a one-pot cyclisation/cross-coupling. (Scheme 29, bottom).
Chapter 4 focuses on the application of this methodology to 1,2-bis(alkynyl)benzenes, inspired by the work reported by Erker using BCF to induce cyclisation.\textsuperscript{[112]} The goal was to form borylated dibenzopentalenes that are useful for materials applications, however, mixtures of two borylated scaffolds, dibenzopentalenes and benzofulvenes, were observed based on the starting alkyne substituents. The work in this chapter describes investigations into understanding what key factors control the overall regioselectivity of the reaction (Scheme 30).

Scheme 30 – General overview of the chemistry described in Chapter 4.
1.2.0 – References

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Chapter 2:

Borylative Cyclisation of

1,4-Disubstituted But-1-ynes
2.1.0 – Introduction

Polycyclic scaffolds are ubiquitous across a range of applications, particularly in the pharmaceutical and organic material sectors. Of these frameworks, a number of naphthalenes, quinolines (including their dihydro-derivatives) and 2H-chromenes have been found to be key structures in biologically active compounds (Figure 1), with applications including anti-cancer drugs,[1] contraceptives[2] and cholesterol regulators.[3]

![Figure 1 – Structures of Nafoxidine, Centchroman and Pitavastatin](image)

Due to their prevalence in pharmaceuticals, a large number of syntheses have been developed to generate these scaffolds, and for a comprehensive coverage of these approaches see the multiple review articles published on these topics.[4-10] With the development of borylation methodologies that concomitantly activate alkynes for subsequent cyclisation being the major goal of this project, this introduction will focus predominantly on chemistry involving alkyne activation by main group electrophiles, leading to attack by $\pi$-nucleophiles. Transition metal catalysed borylative cyclisations are not included herein, however, for a review on this topic see the recent review from Cárdenas.[11]

2.1.1 – Main Group Electrophilic Cyclisation

An early report by Barluenga et al. described the employment of a combination of an iodonium salt, [Py$_2$I][BF$_4$], with a strong Brønsted acid in order to generate a variety of iodinated cyclic products via alkyne activation by an electrophilic I$^+$ species followed by attack by an intramolecular $\pi$-nucleophile in a 6-endo-dig
fashion. Amongst the many products described was a dihydronaphthalene derivative, generated from 1,4-diphenylbut-1-yne (Scheme 1). \[12\]

![Scheme 1](image)

Scheme 1 – The formation of an iodinated dihydronaphthalene via iodonium initiated electrophilic cyclisation. \[12\]

Based on this early chemistry, subsequent reports described the use of alternative electrophiles, including other halogens and pseudohalogenes (ICl, I\(_2\), Br\(_2\), and NBS) and chalcogens (ClSePh). \[13\] Further developments involved the use of aromatic electrophiles \[14\] (generated from alternative iodonium salts and a copper(I) catalyst) and calcium electrophiles. \[15\] These methods furnished halogenated, seleniated, arylated and alkylated dihydronaphthalenes respectively.

In a report by Murai et al., the use of gallium trichloride as a catalyst facilitated the generation of a variety of dihydronaphthalene and phenanthrene derivatives from alkynes possessing appropriately disposed internal \(\pi\)-nucleophiles through cycloisomerisation. \[16\] In these cases, the proposed mechanism proceeds via activation of the alkyne by the gallium electrophile, leading to the generation of a vinyl cation intermediate.

![Scheme 2](image)

Scheme 2 – The proposed mechanism of cycloisomerisation of alkynes catalysed by GaCl\(_3\). \[16\]
Subsequently, the vinyl cation is quenched by the pendant aromatic in a 6-exo-dig fashion to generate a bicyclic intermediate with the vinyl-GaCl₃ anionic moiety exo- to the newly formed ring. Next, a 1,3-hydride shift followed by the loss of GaCl₃ leads to a tetralin species, which tautomerises to generate the dihydronaphthalene. (Scheme 2). Notably, the majority of cycloisomerisations were significantly improved by the use of GaCl₃ as a catalyst, compared to Murai’s earlier work using Ru(II) and Pt(II) catalysts. The choice of GaCl₃ over other Lewis acids such as AlCl₃ and BF₃.Et₂O was due to their lack of reactivity, surmised to be due to coordination to the ester moieties on the substrate. The softer GaCl₃ was found to be highly successful in activating the alkyne in the presence of these ester groups, likely due to a weaker Ga-O bond than the corresponding Al/B-O bonds.

A similar reaction reported by Fürstner et al. was used to generate phenanthrenes (via 6-endo-dig cyclisation) and fluorenes (via 5-exo-dig cyclisation) from alkylnyl substituted biaryls, utilising a number of metal catalysts. Most relevant to this work was their use of InCl₃ and GaCl₃. The use of InCl₃ still resulted in cyclisation and subsequent protodemetallation, however it led to a 1 : 1 mixture of the two cyclisation pathways, whereas the use of GaCl₃ was much more selective towards the 6-endo-dig pathway. Thus, it can be concluded that heavier group 13 electrophiles can be highly proficient in the activation of alkyynes towards cyclisation by C-C bond formation.

Alkyne activation and subsequent π-nucleophilic attack has since been reported utilising boron reagents in a number of syntheses to generate new C-C bonds and a variety of novel compounds. One report by Erker et al. highlighted the reactivity between a variety of diyne substrates and Frustrated Lewis Pairs (FLPs) consisting of tris(pentafluorophenyl) borane (BCF) and bulky phosphines. One example is the reaction between BCF/P(o-tolyl)₃ and 1,7-octadiyne, which furnishes a new C-C bond and leads to the generation of a cyclohexane species (Scheme 3), indicating that boron electrophiles can also be utilised for electrophilic cyclisation.
Scheme 3 – The reaction of the FLP, BCF/P(o-tolyl)$_3$, with 1,7-octadiyne.$^{[19]}$

In the following years, Stephan et al. reported a method of cyclopropanation and subsequent 1,4-carboboration via the reaction of various 1,6-enynes with BCF (Scheme 4).$^{[20]}$ This reaction generates both cyclopentane and cyclohexane species that involve C$_6$F$_5$ and B(C$_6$F$_5$)$_2$ disposed in a 1,4-fashion. The final ring size is dependent on the substitution of the alkene moiety, where unsubstituted alkenes lead to mixtures of the cyclopentane and cyclohexane derivatives, and mono/disubstituted alkenes provide enough stabilisation for the cyclopropane intermediate to preclude ring opening and facilitate isolation.

Scheme 4 – BCF initiated 1,1-carboboration/cyclopropanation followed by subsequent ring opening to give formal 1,4-carboboration.$^{[20]}$

The reaction proceeds via activation of the alkyne by the BCF, which facilitates nucleophilic attack by the alkene moiety to generate a cyclopentane zwitterionic intermediate possessing an R-B(C$_6$F$_5$)$_3$ anion and secondary alkyl carbocation. The alkene then quenches the carbocation, furnishing the zwitterionic cyclopropane species with a subsequent transfer of a C$_6$F$_5$, which generates a neutral 1,1 carboborated product. Finally, providing there is no stabilisation of the cyclopropane, the 3-membered ring opens to give the cyclopentane and cyclohexane derivatives (Scheme 5).
Notably, the examples discussed above only describe alkyne activation by electrophiles with attack by intramolecular $\pi$-nucleophiles. Stephan reported on the activation of alkynes with BCF, which were then attacked by intermolecular carbon nucleophiles in the form of pyrroles and enamines.\[21\] These groups were chosen due to their reportedly sluggish nature in forming zwitterionic iminium borates by direct reaction with BCF.\[22-23\] As such, they could be employed in three-component reactions with BCF and an alkyne, leading to new products via 1,2-trans-carboboration.

The reaction of 1-morpholinocyclohexene with BCF in the presence of an excess of phenylacetylene led to both the desired 1,2-trans-carboboration and
an alkynylborate, produced by deprotonation of the alkyne (Scheme 6, top). When the steric bulk of the alkyne was increased (using ethynylferrocene), only deprotonation was observed. Due to the lower nucleophilicity of pyrroles, it was hypothesised that deprotonation would be precluded. Combining pyrrole, BCF and phenylacetylene led to the desired addition product, however upon standing the product degraded. Using N-methylpyrrole instead led to formation of the addition product, with electrophilic substitution occurring at both the α- and β-positions of the pyrrole (Scheme 6, bottom). 1,2,5-trimethylpyrrole was employed to obtain the addition product with S_{EAr} taking place only at the β-position. The reaction presumably proceeds via activation of the alkyne by BCF, with the intermediate sufficiently electrophilic enough for the carbon nucleophiles to attack.

2.1.2 – Aims

With a variety of main group electrophiles (particularly those in group 13) described that are able to activate alkynes to attack from π-nucleophiles, our aim was to develop the chemistry involved using the much cheaper and readily available boron electrophile, BCl$_3$ (that can also be protected subsequently to familiae boronic esters). Notably, the previous reports discussed that utilise BCF to activate alkynes revealed products that retained the boron moiety after cyclisation. This indicates that unlike electrophiles based on the heavier group 13 elements, Ga and In, protodemetallation is much less prevalent with the smaller, less polarisable boron species that form stronger bonds to carbon. With this in mind, our aim was to synthesise a variety of 1,4-disubstituted but-1ynes (and heteroatom containing analogues) and employ borocations or BCl$_3$ to induce borylative cyclisation. Borocations and BCl$_3$ were selected as BF$_3$.OEt$_2$ was previously found to be ineffective, likely due to its lower Lewis acidity (Scheme 7). Borylative cyclisation was envisaged to proceed via activation of the alkyne by the borocation or BCl$_3$ to generate a vinyl cation intermediate. This would then be sufficiently electrophilic to undergo nucleophilic attack from the pendant phenyl ring, resulting in 6-endo-dig cyclisation. Presumably, the arenium intermediate would tautomerise to give the most stabilised cation (stabilised by two aryl groups). H$^+$ is then lost as HCl, leading to the
dihydronaphthalene-BCl₂ species. The overall reaction furnishes a C-C/C-B bond concomitantly.

Scheme 7 – Proposed mechanism for the borylative cyclisation of 1,4-disubstituted but-1-ynes with BCl₃ (borocation would follow a related mechanism).

Finally, we aimed to examine further reactions of some of the generated borylated polycycles through Suzuki-Miyaura cross-coupling and oxidation reactions to obtain the corresponding naphthalene and quinoline species. Additionally, secondary cyclisations to generate boracycles with the boron atom incorporated directly in the scaffold will be examined, as there have been many developments regarding boron-doped PAHs in the field of optoelectronics and material chemistry.\cite{24}
2.2.0 – Results and Discussion - Borylated Dihyronaphthalenes from 1,4-Diarylated But-1-ynes

A variety of 1,4-diarylated but-1-ynes were synthesised via one of two reactions, a Sonogashira cross-coupling between 4-phenylbut-1-yne and an aryl bromide, or deprotonation of phenylacetylene with subsequent S_N2 on a substituted phenethyl bromide. Through these methods, a variety of alkynes were generated possessing a range of functionalities in order to examine the effects of EWGs, EDGs and Lewis basic groups (and their positions on their respective aromatic ring) on borocation and BCl_3 induced borylative cyclisation (Table 1).

Table 1 – 1,4-diarylated but-1-ynes.
Notably, due to the competitive E2 elimination reaction (to generate styrene derivatives), the yields of alkynes generated from phenethyl bromides are typically much lower than alkynes generated through cross-coupling.

Initially, 1,4-diphenylbut-1-yn-1-ene (2.1) was reacted with one equivalent of the boronium salt, [Cl₂B(2-DMAP)][AlCl₄] (given its inactivity towards haloboration of internal alkynes[25]), resulting in complete consumption of the starting material within 10 minutes. The in-situ ¹H NMR spectrum revealed a complex mixture of products (although protonated 2-DMAP was observed) and the ¹¹B NMR spectrum revealed a broad peak at 54.0 ppm, characteristic of a vinyl-BCl₂ species, suggesting that cyclisation had taken place. Upon esterification with pinacol/NEt₃, the ¹¹B NMR spectrum showed a peak at 30 ppm which indicated that a vinyl-Bpin species was present. Next, a control reaction was carried out using 2.2 equivalents of BCl₃ in the presence of a bulky base, tri-tert-butylpyridine (TBP) to examine whether BCl₃ was Lewis acidic enough to initiate the cyclisation with the TBP present to sequester the proton from the intermediate. The reaction was deemed to have gone to completion after ten minutes, as judged by the appearance of a resonance at 54 ppm in the ¹¹B NMR spectrum. This experiment reveals that BCl₃ is capable of initiating borylative cyclisation. Thus, 2.1 was reacted with just BCl₃ in DCM, resulting in complete consumption of the starting material (within 10 minutes), generating one major product. The in situ NMR spectra (Figure 2) revealed a much cleaner spectrum in the absence of a base, with a ¹H doublet at 6.79 ppm (in protio DCM with a d₆-DMSO capillary) and the broad peak around 54 ppm (¹¹B NMR spectrum), characteristic of the vinyl-BCl₂ moiety, indicating cyclisation had taken place. We reasoned that the resonance observed as a doublet at 6.79 ppm in the ¹H spectrum corresponded to H₆ (see Figure 2), which is deshielded by the presence of the neighbouring aromatic ring. H₆ presumably sits over the shielding region of the neighbouring ring A due to restricted rotation about the ring A-dihyronaphthalene bond, an observation which gains further credence from subsequent X-ray studies (on page 55). The appearance of a resonance at ca. 6.8 ppm in the products of these reactions appears to be diagnostic of cyclisation. Post-esterification, the ¹¹B NMR spectrum revealed a broad peak at 30 ppm, indicative of the vinyl-Bpin species, further suggesting that borylative
cyclisation had occurred with BCl$_3$ alone. After purification via column chromatography, borylated dihydronaphthalene 2.17 was isolated in a 91% yield (a general scheme for borylative cyclisation is shown in Scheme 8). As expected, given the lack of reactivity of BCl$_3$ with internal alkyl-aryl alkynes observed previously,$^{[25]}$ no haloboration product was observed in the crude mixture. Notably, the only product generated was from a 6-endo-dig cyclisation, with none of the 5-exo-dig cyclisation product observed. This is in-keeping with the work of Larock,$^{[26]}$ who did not observe products arising from the alternative 5-exo-dig cyclisation pathway when employing mercury based electrophiles.

Figure 2 – In situ NMR spectral data of the reaction with alkyne 2.1 and BCl$_3$.

Scheme 8 – General scheme for borylative cyclisation. See Table 2 for individual products.
Para-chloro substituted arylalkyne 2.2 reacted similarly in the presence of BCl₃. This was esterified and purified to give dihydronaphthalene 2.18 in a 95% yield, indicating that a deactivated aromatic ring bound to the alkyne does not hinder the cyclisation. The reaction was repeated with 1.3 equivalents of BCl₃ (in order to react with any moisture), using non-purified solvents in an open vessel under ambient conditions, with only a small decrease in the isolated yield of 2.18 (88%). This suggested that the borylative cyclisation of alkynes is robust and does not necessarily require rigorous air/moisture free conditions. When employing the ortho-chlorinated isomer, 2.3, the reaction proceeded analogously with BCl₃, leading to a 72% isolated yield of dihydronaphthalene 2.19. One notable observation was that post-esterification, two 6H singlets were observed (in CDCl₃) for the Bpin moiety at 1.14 ppm and 1.16 ppm. Additionally, instead of observing two triplets (corresponding to the CH₂CH₂ protons), two 2H complex multiplets were observed ranging from 2.55 - 2.73 ppm and 2.85 - 3.05 ppm, respectively (Figure 3). This suggests that a chloride substituent in the ortho-position of the alkynylphenyl provides enough steric bulk to restrict rotation of the aromatic ring/Bpin on the NMR timescale, leading to inequivalent Me and CHₐHₐ substituents.

![Figure 3](image-url)

**Figure 3** – Post-esterification spectrum of dihydronaphthalene 2.19.

With electron deficient arylalkynes 2.2 and 2.3 undergoing borylative cyclisation in high yield, pentafluorinated substrate 2.4 was employed to
examine the effect of a highly electron deficient aromatic ring on cyclisation. Pleasingly, the addition of BCl$_3$ immediately led to complete conversion of the starting material to give the cyclised product. Post-esterification/purification, the borylated dihydronaphthalene 2.20 was isolated in an 80% yield. This result suggests a hypothesised mechanistic insight to the reaction, where the formation of the vinyl cation is not the rate-limiting step, as the pentafluorinated aromatic ring did not noticeably affect the reaction time (complete < 5 minutes at 20$^\circ$C), indicating that cation stabilisation is not crucial. When a meta-trifluorotolyl group (2.5) was introduced rapid cyclisation was observed with no side-reactivity (such as C-F activation observed with stronger boron electrophiles such as borocations), and esterification with pinacol/NEt$_3$ furnished dihydronaphthalene 2.21 in a 97% yield. Pleasingly, the reaction was repeated on a gram scale, with an isolated yield of 96% (1.74 g) of 2.21, suggesting that the borylative cyclisation of 1,4-disubstituted but-1-ynes can be successfully scaled up.

With halide substituted alkynes examined, a Lewis basic nitrile-substituted aromatic (2.6) was employed with the cyano group another EWG. Initially, when BCl$_3$ was added, complete substrate and BCl$_3$ consumption was observed.

![Figure 4](in situ spectral data of the reaction between 2.6 and BCl$_3$.)
Examination by NMR spectroscopy (Figure 4) after twenty minutes revealed that the major product was the dihydronaphthalene-BCl₂ (based on the characteristic doublet at 6.57 ppm). However, a significant second product was observed, corresponding to adduct formation (based on two additional doublets at 7.91 and 7.62 ppm, diagnostic of a 1,4-disubstituted phenyl) between BCl₃ and the nitrile group. This was consistent with the $^{11}$B NMR spectrum, which revealed what presumably was the adduct of BCl₃ and the nitrile group on the cyclised product (at 12.3 ppm). The reaction was left for 12 hours at room temperature, and the cyclised product was the major species observed (> 92%) in the $^1$H NMR spectrum, indicating that the coordination of the nitrile to BCl₃ is reversible. This slows, but does not prevent borylative cyclisation. Post-esterification, the borylated dihydronaphthalene 2.22 was isolated in a 63% yield and the structure was confirmed by X-ray crystallography (Figure 5).

![Figure 5 – X-ray structure of 2.22. with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Blue: Nitrogen; Yellow: Boron; Selected Metrics: C1-B1: 1.566(4) Å; C2-C1-B1-O1: 26.5(4)$^\circ$; C1-C2-C3-C4: 107.7(3)](image)

The structural metrics of 2.22 are unremarkable, with a carbon-boron bond length of 1.566(4) Å, which is typical of a vinyl/aryl C-B species. In order to minimise non-bond interactions, both ring A and B are rotated so that they are
no longer co-planar with ring C (the Bpin moiety). In this case, the torsional angle about C1-C2-C3-C4 is 107.7(3)° and O1-B1-C1-C2 is 26.5(4)°.

Interestingly, a reaction was carried out employing the ortho-substituted isomer of 2.6, which led to unexpected reactivity. On addition of BCl₃, only one product was observed in situ, with the major peak observed in the $^{11}$B NMR spectrum at 7 ppm, inconsistent with the expected product from borylative cyclisation. Over 18 hours, solid material began to precipitate out of solution and the $^{11}$B NMR spectrum revealed a single sharp peak at 4 ppm, indicative of a four-coordinate boron species. It was proposed that instead of borylative cyclisation, a Hoesch-type reaction (between a nitrile and unsaturated $\pi$-system\[27\]) may have occurred due to spacial proximity of the alkyne and nitrile group. This would likely take place via coordination of BCl₃ to the nitrile group (likely generating the 7 ppm peak in the $^{11}$B NMR spectrum), followed by nucleophilic attack on the nitrile carbon by the alkyne to give an imine species and a vinyl cation. This would be subsequently quenched by the pendant aromatic ring with the loss of HCl restoring aromaticity leading to a polycycle possessing an imine-BCl₂ unit (Scheme 9).

Scheme 9 – Proposed mechanism for the unexpected reactivity observed with the ortho-isomer of 2.6 and BCl₃.

It was hypothesised that nitro groups may be incompatible with BCl₃ (through coordination of one of the oxygen atoms), leading to a control ‘robustness screening’ reaction, inspired by the work of Glorius et al.,\[28\] involving the borylative cyclisation of alkyne 2.2 in the presence of para-nitrobromobenzene as an additive. Pleasingly, no side-reactivity was observed, indicating that
borylative cyclisation is tolerant of nitro groups, although this result provides no data on steric or electronic effects of a substrate functionalised with a nitro group. Subsequently, nitro-substituted alkyne 2.7 was synthesised and reacted with an equivalent of BCl₃, leading to complete consumption of the starting material (within 10 minutes) to give the dihydronaphthalene as the major product. Esterification and purification led to the isolation of dihydronaphthalene 2.23 in a 70% yield.

A similar screening control was run with 2.2 in the presence of one equivalent of ethyl acetate (Figure 6, green). Notably, no cyclisation was observed, with only the BCl₃ adduct with ethyl acetate observed (indicated by the downfield shift, particularly for the quartet at 4.09 ppm moving to 4.58 ppm). Next, 2.2 equivalents of BCl₃ were used relative to 2.2 (Figure 6, red), resulting in adduct formation and cyclisation. When an excess of NEt₃ was added subsequently (Figure 6, pink), the starting ester was returned. Interestingly, the cyclised product was difficult to observe in the ¹H spectrum, perhaps due to reversible coordination of the NEt₃ to the dihydronaphthalene-BCl₂ (2.18*).

Figure 6 – In situ ¹H NMR spectra in protio DCM with a capillary of wet d₆-DMSO, showing the screening reaction of alkyne 2.2 with BCl₃ (1 or 2.2 equivalents) and one equivalent of ethyl acetate.
This reaction suggests that for ester substituted substrates, two equivalents of BCl$_3$ are required, where one coordinates to the ester and the other initiates cyclisation. During the pinacol/NEt$_3$ esterification step, any BCl$_3$ coordinated to the ester should be abstracted by NEt$_3$, indicating that the borylative cyclisation could be adapted to tolerate esters. Thus, ester-substituted alkyne 2.8 was synthesised and reacted with 2.2 equivalents of BCl$_3$, resulting in complete consumption of the starting material (within 10 minutes) with the cyclised product present as the major product. The $^1$H NMR spectrum post-esterification confirmed that dihydronaphthalene 2.24 had been generated via this adapted procedure, and was isolated in an 87% yield.

Alkyne 2.9 has an aromatic nucleophile substituted with a methoxy group positioned *meta-* to the position of nucleophilic attack, which should slow cyclisation down as MeO are actually slightly deactivating (σ$_{m^+}$ = 0.05) to *meta-*substitution.[29] Interestingly, immediate conversion to the cyclised product was observed on examination of the $^1$H and $^{11}$B NMR spectra. Additionally, a small quantity of a side product presumed to be ROBCl$_2$, indicating ether cleavage, was observed by $^{11}$B NMR, with a peak observed at 35 ppm. Pleasingly, upon esterification and subsequent purification, dihydronaphthalene 2.25 was isolated in a 79% yield.

Given the broad functional tolerance observed thus far in the investigation, 2.10, possessing a tolyl group bound to the alkyne, was initially reacted with BCl$_3$, resulting in an mixture of products that became increasingly complex over the space of 16 hours, based on the *in situ* $^1$H NMR spectrum. However, the $^{11}$B NMR spectrum revealed a large 54 ppm peak, indicating that cyclisation had taken place. It was hypothesised that the complex mixture may be due to Brønsted-acid catalysed methyl migration around the aromatic ring (*Scheme 10*).[30-31] Thus, the reaction conditions were altered, employing the sterically bulky base, tri-tert-butylpyridine (TBP) (which does not coordinate to BCl$_3$) to sequester the HCl byproduct of the reaction. This required the use of 2.2 equivalents of BCl$_3$ as one equivalent would be consumed to form the anionic component of the salt by-product, [TBPH][BCl$_4$]. Pleasingly, this change resulted in a clean cyclisation to give the desired product, which was esterified and purified to give 2.26 in a 59% yield (see page 73, *Table 2* for structure).
Scheme 10 – Proposed mechanism for Brønsted-acid catalysed methyl migration around the aromatic ring.\[30-31\]

Isomeric toylalkynes 2.11 (alkynyl-bound ortho-tolyl), 2.12 (nucleophilic toyl, methyl meta- to bond forming site) and 2.13 (nucleophilic toyl, methyl para- to bond forming site) were each subjected to the same conditions, furnishing dihydronaphthalenes 2.27, 2.28 and 2.29 in 69%, 80% and 58% yields respectively. Notably, due to the ortho-position of the methyl group in 2.27, hindered rotation on the NMR timescale was observed in the $^1$H NMR spectrum (Bpin methyl groups and aliphatic CH$_2$ protons inequivalent) as with ortho-chlorininated 2.19, due to the steric bulk of the methyl group causing restricted rotation of the aromatic ring.

Scheme 11 – The proposed isomers of 2.29 via bond rotation of alkyne 2.13.

Interestingly, the use of the meta-methyl substituted nucleophilic aromatic ring 2.13 has the potential to yield two isomers, however only 2.29 was observed, presumably due to steric hindrance around the site of C-C bond formation, making it unfavourable to form the other isomer, 2.29* (Scheme 11).

As observed in the previous examples, a destabilised vinyl cation intermediate undergoes borylative cyclisation rapidly. Para-anisole bound alkyne 2.14 was synthesised in order to observe the effects of a mesomeric donating group on
the stabilisation of the vinyl cation ($\sigma_p^+ = -0.78$) and thus the overall reaction. Initially, when BCl$_3$ was reacted with 2.14, a complex $^1$H NMR spectrum was observed, with the $^{11}$B NMR spectrum revealing two peaks, 54 ppm and 30 ppm, where the cyclised product (BCl$_2$-intermediate 2.30*) was the minor peak (Figure 7, blue). After two hours, the 54 ppm peak had decreased in relative intensity whilst the 30 ppm increased (Figure 7, red), suggesting ether cleavage was occurring to give (RO)$_2$BCl. This was confirmed by the presence of a resonance at 3.01 ppm in the $^1$H NMR spectrum, corresponding to CH$_3$Cl. Esterification of the crude mixture and attempted purification yielded very little of the desired compound.

![In situ $^{11}$B NMR spectrum of the reaction between 2.14 and BCl$_3$. The 54 ppm peak corresponds to dihydronaphthalene-BCl$_2$ 2.30* and the 30 ppm to (RO)$_2$BCl.](image)

The reaction was repeated with 2.2 equivalents of BCl$_3$ and an equivalent of TBP, however the same outcome was observed. The more electrophilic (compared to BCl$_3$) boronium salt, [Cl$_2$B(2-DMAP)][AlCl$_4$], was employed based on its greater tolerance towards methoxy groups than BX$_3$. Interestingly, the reaction between 2.14 and [Cl$_2$B(2-DMAP)][AlCl$_4$] produced no 30 ppm peak.
even over 7 hours. The *in situ* $^1$H and $^{11}$B NMR spectra looked much cleaner than when employing BCl$_3$, and was monitored from 10 minutes to 7 hours. No change was observed in the reaction beyond 1 hour (Figure 8), with complete consumption of the boronium salt also observed. The reaction was repeated and esterified after 1 hour, with subsequent purification allowing for the isolation of dihydronaphthalene-Bpin 2.30 in a 36% yield. The origin of the lower yield than expected, based on the in-situ conversion is currently unclear.

![Figure 8](image)

Figure 8 – Time monitored *in situ* NMR spectral data of the reaction between 2.14 and [Cl$_2$B(2-DMAP)][AlCl$_4$]. Asterisked peaks correspond to protonated 2-DMAP.

Given the successful *in situ* reactivity of the methoxy group *meta-* to the site of electrophilic substitution (2.9), it was hypothesised a methoxy group in the *para-* position would lead to rapid cyclisation due to increased electron density at the appropriate position. However, reactions between alkyne 2.15 and BCl$_3$ or BCl$_3$/TBP led to mixtures of products and subsequent low yields of dihydronaphthalene, as observed with alkyne 2.14. Pleasingly, the use of the boronium salt led to a much cleaner reaction, with subsequent esterification/purification leading to dihydronaphthalene 2.31 being isolated in a
57% yield. Notably, as with the para-tolyl alkyne 2.13, only one regioisomer was observed. The difference in reactivity between the BCl₃ and [Cl₂B(2-DMAP)][AlCl₄] may be due to the lower nucleophilicity of [AlCl₄]⁻ compared the Cl⁻ (produced during the cyclisation with BCl₃). This would lead to lower levels of ether cleavage by attack of the δ⁺ methyl on the ArO(Me)→BCl₃ adduct by the less nucleophilic anion.

Alkyne 2.16 possessed a chloride para- to the site of electrophilic substitution, and the cyclisation reaction was significantly affected, with reactions of 2.16 and BCl₃ or BCl₃/TBP each showing effectively no consumption of starting material, even after prolonged periods (>18h) at 60°C. Using the more electrophilic species, [Cl₂B(2-DMAP)][AlCl₄], resulted in complete consumption of 2.16 after 2.5 hours at 60°C to form the desired cyclised product. The slower reactivity (relative to the unfunctionalised analogue 2.1) is consistent with an electron deficient nucleophile affecting the rate of cyclisation, and is comparable to observations by Murai and co-workers when employing analogous chlorinated substrates. Esterification and purification allowed dihydronaphthalene 2.32 to be isolated in an 83% yield. Again, only one regioisomer was observed, indicating that overall, the borylative cyclisation reaction is particularly regioselective, with steric effects likely being a key factor controlling the high selectivity. Notably, two similar electron deficient nucleophiles were examined, one bearing a fluoride group (σₘ⁺ = +0.35), and one bearing a bromide group (σₘ⁺ = +0.41) each meta- to the site of electrophilic substitution. Neither of these reacted with any conditions discussed here, even at 60°C for 48 hours. This is attributed to both substitutents exerting a strong inductive withdrawing effect on the site of SₑAr with no mesomeric donation (Scheme 12).

Scheme 12 – Unsuccessful reactivity of electron deficient aromatic nucleophiles
2.2.1 – Cyclisation of Alkynes Without Arylalkynyl Moieties

Having synthesised a range of alkynes bearing a terminal aromatic substituent (2.1-2.16), the investigation focused on examining alkynes possessing alkyl (2.33), halide (2.34), vinyl (2.35) and naphthyl (2.36) substituents (Figure 9), with the former three chosen to observe whether an aromatic group is necessary for cation stabilisation during the cyclisation. Methyl substituted 2.33, which was synthesised via a simple deprotonation (n-BuLi)-alkylation (MeI) sequence of but-3-yn-1-ylbenzene, was reacted with BCl₃ to give one major product in situ by ¹H NMR spectroscopy. The ¹¹B NMR spectrum showed a 54 ppm peak as the major product, indicating cyclisation had taken place.

![Figure 9 – Non-phenyl substituted alkynes 2.33-2.36](image)

The reaction mixture was esterified, however after purification via column chromatography, a mixture of dihydronaphthalene 2.37 and the corresponding naphthalene was isolated from one band in a ratio of 4 : 1. This was confirmed by ¹H and ¹³C{¹H} NMR spectroscopy, as well as GC-MS. The mixture of products was presumed to be due to in situ transfer hydrogenation, based on the greater Lewis acidity towards hydride of the methyl substituted carbocation, compared to the previously examined aryl substituted carbocations (hence this reactivity not being observed previously). To examine this further, a reaction was carried out using 3 equivalents of BCl₃ over a period of 18 hours. Within 5 minutes, the dihydronaphthalene was observed in situ in the ¹H NMR spectrum as a single major product. However, overnight, this initial product had been consumed, resulting in a complex spectrum, particularly in the aliphatic region, where many multiplets were observed (Figure 9).
It was proposed that due to the Brønsted acidic environment generated, an equilibrium between the dihydronaphthalene and a hydridophilic tertiary carbocation intermediate was established, the latter of which could abstract a hydride from the dihydronaphthalene, thus leading to a hydrogenated tetralin and a naphthalene (Scheme 13).

Figure 9 – Reaction of 2.33 with 3 equivalents of BCl₃.

Scheme 13 – Proposed transfer hydrogenation mechanism to account for the reactivity observed when reacting 2.33 with BCl₃.

To preclude the Brønsted acidic environment, the reaction was carried out with 2.2 equivalents of BCl₃ and an equivalent of TBP (Scheme 14), leading to the desired cyclisation with no transfer hydrogenation observed. Post-esterification and purification, dihydronaphthalene 2.37 was isolated in a 67% yield with no naphthalene product observed, indicating that TBP sequesters the protic by-product and prevents transfer hydrogenation from proceeding.
Scheme 14 – Synthesis of alkyne 2.33 and borylative cyclisation to give dihydronaphthalene 2.37

As a control reaction, the commercially available terminal alkyne, 4-phenylbut-1-yne, was reacted with one equivalent of BCl₃. However, with this terminal alkyne, quantitative conversion to the product from cis-haloboration was observed, with esterification leading to the isolation of borylated alkene 2.38 in a 95% yield (Scheme 15). Given the propensity of BCl₃ to haloborate terminal alkynes, this result was expected.

Scheme 15 – Haloboration of 4-phenylbut-1-yne with BCl₃ to give alkene 2.38.

In contrast, bromo-alkyne 2.34 was reacted with BCl₃ (Scheme 16, top), converting to a mixture of two products (within 10 minutes), where the major product was assigned, on the basis of its ¹¹B NMR spectrum, to the cyclised compound. A minor resonance at 51 ppm in the ¹¹B NMR spectrum was also observed, presumably due to haloboration (and is consistent with the in situ chemical shift of the haloboration product from 4-phenylbut-1-yne). Following esterification and purification via silica gel column chromatography, the isolated yield of dihydronaphthalene 2.39 was found to be low (based on in-situ conversion) at 34%. This was presumably due to degradation on the silica. Nevertheless, the generation of 2.37 and 2.39 confirm that stabilisation of the cation intermediate by a delocalised π-system is not required.
Scheme 16 – Synthesis of bromo-alkyne 2.34 and subsequent reactions to generate dihydronaphthalene 2.37 (top) and vinyl-alkyne 2.35 (bottom).

Next, 2.34 was reacted with (E)-styrylboronic acid in a Suzuki-Miyaura cross coupling reaction to yield vinyl-alkyne 2.35 in a 35% yield (Scheme 16, bottom). Cyclisation of alkyne 2.35 was attempted using three sets of reagents (BCl₃ / BCl₃ + TBP and boronium), with BCl₃/TBP found to give the cleanest in situ mixture (Scheme 16, bottom right). This was esterified and purified via silica gel column chromatography to give dihydronaphthalene 2.40 in a 54% yield.

To explore the compatibility of an aromatic-alkyne able to undergo a subsequent C–B bond forming step post cyclisation (see section 2.2.4), naphthyl-alkyne 2.36 was synthesised via Sonogashira coupling and tested with all three conditions, each producing a mixture of products with the dihydronaphthalene-BCl₂ being the major component.

Scheme 17 – Synthesis of naphthyl-alkyne 2.36 and dihydronaphthalene 2.41.

With all conditions, it took ca. 1 hour to observe complete consumption of the starting material, potentially due to the steric bulk around the alkyne, resulting in
a slower rate of cyclisation. It was observed in situ that the use of BCl₃/TBP produced the cleanest mixture (Scheme 17), and upon esterification/purification, dihydronaphthalene 2.41 was isolated in a 75% yield.

Additionally, within our group the borylative cyclisation methodology was also found to be applicable to the synthesis of alternative carbocycles. A borylated phenanthrene was generated in a 60% yield from a biphenyl substituted alkyne using BCl₃/TBP, although extended reaction times were required (24 h) at 60°C (reaction performed by Valerio Fasano, Scheme 18).

Scheme 18 – Extending the scope of cyclisation towards a borylated phenanthrene (by Valerio Fasano).

Furthermore, subjecting 1,7-diphenylhepta-1,6-diyne to the borylative cyclisation conditions led to the generation of a borylated dihydro-1H-fluorene (reaction performed by James Lawson, Scheme 19).

Scheme 19 – Extending the scope of cyclisation towards a borylated dihydro-1H-fluorene (by James Lawson)
2.2.2 – Borylative Cyclisation Towards Heteroaromatic Scaffolds

With a variety of borylated dihydronaphthalenes synthesised, our attention turned towards furnishing alkynes with a heteroatom link between the aromatic nucleophile and the alkyne. The first goal was to include a nitrogen based linker in order to synthesise a borylated dihydroquinoline. It was hypothesised that a nitrogen atom with low Lewis basicity would facilitate borylative cyclisation as there would be less competitive adduct formation between the amine and BCl₃. This was first examined via a screening reaction, employing alkyne 2.2 and N-tosylindoline (as an additive) in a cyclisation with BCl₃ (Scheme 20). Pleasingly, the cyclisation was successful with no consumption of the additive observed, indicating that the reaction is tolerant of N-tosyl moieties.

Scheme 20 – A screening reaction to examine the tolerance of borylative cyclisation towards N-tosyl moieties.

Next, an appropriate N-linked alkyne, 2.42, was synthesised via an S_N2 reaction between N-tosylaniline and 1-phenyl-3-chloroprop-1-yne. When 2.42 was reacted with BCl₃, immediate consumption of the alkyne was observed (within 10 minutes), leading to a single major product and a number of minor products based on the ¹H NMR spectrum. The ¹¹B NMR spectrum revealed the major peak to be at 51 ppm, which was attributed to the desired dihydroquinoline-BCl₂ species. Upon esterification and purification via silica gel column chromatography, dihydroquinoline 2.43 was isolated in a 74% yield (Scheme 21). This result indicates that borylative cyclisation can take place when a suitably protected Lewis basic nitrogen atom is present within the alkyne substrate. This suggests that other heteroatoms, and thus other borylated heteroaromatics, may be obtainable through this methodology. The next goal was to examine an O-linked analogue of 2.42 in the interest of
generating a borylated 2H-chromene. Through a Sonogashira coupling of 4-phenyl propargyl ether and bromobenzene, O-linked alkyne 2.44 was synthesised (Scheme 22). Upon reaction with BCl₃, immediate quantitative consumption of 2.44 was observed in the ¹H NMR spectrum (Figure 10).

Scheme 21 – Synthesis of N-linked alkyne 2.42 and subsequent cyclisation to generate dihydroquinoline 2.43.

Figure 10 – In situ ¹H and ¹¹B NMR spectral data for the reaction of 2.44 and BCl₃ after 10 minutes. Asterisked peak at 4.30 ppm corresponds to 1-phenyl-3-chloroprop-1-ynel.

However, the major peak observed in the ¹¹B NMR spectrum was at 35.8 ppm, attributed to PhOBCl₂, derived from ether cleavage (1-phenyl-3-chloroprop-1-ynel was also observed at 4.30 ppm (in DCM with a d₆-DMSO capillary)) (in CDCl₃, observed at 4.39 ppm[32]). After an hour, a significant peak at 31 ppm was observed, presumed to be attributed to (PhO)₂BCl due to a second ether...
cleavage (or substituent scrambling). A much more complex mixture was observed in the in situ $^1$H NMR spectrum when BCl$_3$/TBP was reacted with 2.44, with the only peak in the $^{11}$B NMR spectrum observed at 35 ppm.

Interestingly, when [Cl$_2$B(2-DMAP)][AlCl$_4$] was employed, the initial $^{11}$B NMR spectrum taken at 15 minutes showed a mixture of three species, where the major resonance was observed at 51 ppm, indicative of the cyclisation and formation of a vinyl-BCl$_2$, and the two minor resonances were observed at 35 ppm and 31 ppm (Figure 11). However, after one hour, only the peaks at 35 ppm and 31 ppm were observed, suggesting that the cyclisation to form the 2H-chromene-BCl$_2$ was possible, however the heterocycle was also susceptible to ether cleavage. This disparity in reactivity is likely due to the higher nucleophilicity of the Cl$^-$ compared to [AlCl$_4$]$^{-}$, as observed earlier during the cyclisation of alkyne 2.14.

Based on the high yielding cyclisation of C$_6$F$_5$-substituted alkyne 2.4, an oxygen linked analogue 2.45 was synthesised in order to examine any difference in reactivity compared to that of 2.44. Upon the addition of BCl$_3$ (Scheme 23), the $^1$H NMR spectrum revealed a major product and only the 51 ppm peak was observed in the $^{11}$B NMR spectrum. When left for an hour, no changes were observed, suggesting ether cleavage was not occurring in this case.
Scheme 23 – Synthesis of O-linked 2.45 and subsequent cyclisation with BCl₃ to furnish 2H-chromene 2.46.

Figure 11 - *In situ* $^{11}$B NMR spectral data for the reaction of 2.44 and [Cl₂B(2-DMAP)][AlCl₄] after 15 minutes and 1 hour.

This may be due to lower nucleophilicity of the ether moiety disfavouring interaction with BCl₃ (or vinyl-BCl₂). The reaction was successfully esterified with pinacol and purified via chromatography to give 2H-chromene 2.46 in a 77% yield.

Based on the success in the synthesis of 2.46, it was of interest to examine whether heavier chalcogen analogues would be tolerated in the borylative cyclisation reaction. To this end, an S-linked analogue of 2.44 was synthesised in a 53% yield (Scheme 24) through a similar fashion to N-linked 2.42, but by employing thiophenol as the nucleophile instead of N-tosylaniline. Upon the reaction of S-linked 2.47 with BCl₃, a highly complex mixture was observed in the *in situ* $^1$H NMR spectrum. However, two major products were observed in
the $^{11}$B NMR spectrum, at 53 ppm and 16 ppm, where the former is consistent with the presence of a 2H-thiochromene-BCl$_2$ species. The latter may be attributable to adduct formation of R$_2$S.BCl$_3$. The use of [Cl$_2$B(2-DMAP)][AlCl$_4$] (Scheme 24) resulted in a lower quantity of the 16 ppm peak in the in situ $^{11}$B NMR spectrum, however the $^1$H NMR spectrum was still highly complex.

Scheme 24 – Synthesis of S-linked 2.47 and subsequent cyclisation attempts to obtain 2H-thiochromene 2.48.

Esterification of the crude mixtures led to a 30 ppm peak observed in the $^{11}$B NMR spectrum, indicating the 2H-thiochromene 2.48 was formed. However, the pure product could not be isolated in our hands, with silica gel column chromatography leading to impure mixtures. Further efforts to expand the scope led us to oxidise sulfide 2.47 to sulfone 2.49, as sulfones are much more prevalent in pharmaceuticals (based on the oxidising conditions typically observed in vivo) such as Dapsone, an antibiotic and dermatologically active compound.[33] Furthermore, the compatibility of tosyl groups indicated that R$_2$SO$_2$ would be tolerated, possibly more so than dialkylsulfide groups. However, the inclusion of an SO$_2$ group significantly decreased the nucleophilicity of the phenyl ring due to its electron withdrawing ability, leading to minimal reactivity, even at elevated temperatures (60°C) over 30 hours with BCl$_3$ (Scheme 25).

Scheme 25 – Oxidation of 2.47 to sulfone 2.49 and lack of subsequent reactivity.
The entirety of the alkynes and cyclisations discussed thus far have utilised a phenyl ring as the $\pi$-nucleophile. These are summarised below in Table 2.

<table>
<thead>
<tr>
<th>Y = CH$_3$, NTs, O</th>
<th>R$^1$ = EWG, EDG, R$^2$ = aryl, alkyl, vinyl, Br</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Reaction conditions" /></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2 – Borylative cyclisation to produce dihydronaphthalenes and derivatives.** [a] Condition A: 1) BCl$_3$ (1.1 eq.); 2) Pinacol (1.1 eq.)/NEt$_3$ (15 eq.); [b] Conditon B: 1) BCl$_3$ (2.1 eq.), TBP (1 eq.); 2) Pinacol (1.1 eq.)/NEt$_3$ (15 eq.); [c] Condition C: 1) [Cl$_2$B(2-DMAP)]AlCl$_4$ (1 eq.); 2) Pinacol (2.1 eq.)/NEt$_3$(15 eq.); [d] Using unpurified CH$_2$Cl$_2$ and 2 eq. BCl$_3$ in air; [e] Carried out on a 1.2 g scale; [f] Reaction time of 12h; [g] 2 eq. of BCl$_3$; [h] 2.5h at 60°C in a sealed vessel.
Next, the use of a heteroaromatic nucleophile was investigated. Basing the choice of substrate on potential applications, an N-(2-alkynylphenyl)pyrrole substituted alkyne was selected (Scheme 26), with the aim of forming either borylated pyrrolo-quinolines (useful for pharmaceutical applications) or precursors for dye-sensitised solar cells (e.g. targeting ullazine).[34]

Scheme 26 – Synthesis of heteroaromatic alkyne 2.50.

Based on the optimal conditions to cyclise alkyl-substituted alkyne 2.33, BCl₃/TBP was employed in the reaction with 2.50, leading to almost complete consumption of the starting material after 15 minutes to generate a mixture of products. After an hour, the major product observed was attributable to the cyclised product, based on the in situ ¹¹B NMR spectrum, which revealed a broad peak at 59 ppm. Esterification of the crude product and purification afforded pyrroloquinoline 2.51 in a 58% yield (Scheme 27), indicating that borylative cyclisation can be applied to heteroaromatic nucleophiles.

Scheme 27 – Borylative cyclisation of heteroaromatic 2.50 to yield pyrroloquinoline 2.51.
2.2.3 – Attempts to Generate Five- and Seven- Membered Carbocycles

An additional focus was to synthesise borylated indenes and dihydro-5H-benzo[7]annulenes from alkynes with aliphatic chain lengths of one and three carbons, respectively (Scheme 28). The precursors 2.52 and 2.53 were synthesised via a standard Sonogashira coupling methodology. 2.52 was reacted with BCl$_3$ and TBP, which led to very slow consumption of the alkyne, with a complex mixture of products observed in the aromatic region of the in situ $^1$H NMR spectrum. The reaction was monitored periodically for 6 days at room temperature, after which time the starting material still was not fully consumed, with only a minor 56 ppm peak observed in the $^{11}$B NMR spectrum. Additionally, the aliphatic region showed three new singlets, indicating the generation of multiple products. No increased intensity of the 56 ppm peak was observed, suggesting the cyclisation was not occurring. Upon esterification, the only observed compound was starting material with no borylated indene isolated. Repeating the reaction with [Cl$_2$B(2-DMAP)][AlCl$_4$] resulted in low levels of conversion of 2.52, with a highly complex $^1$H NMR spectrum observed corresponding to converted material. No trace of a 56 ppm peak was observed in the $^{11}$B NMR spectrum.

![Scheme 28 – Proposed cyclisations to obtain five- and seven- membered rings.](image)

A similar result was observed when alkyne 2.53 was reacted with BCl$_3$/TBP or [Cl$_2$B(2-DMAP)][AlCl$_4$], where full consumption of the alkyne was not observed, even after 6 days. Additionally, only trace amounts of a 56 ppm peak were observed, again indicating that cyclisation was not the major product of the reaction. Interestingly, when the borenium salt, [Cl$_2$B(2,6-lutidine)][AlCl$_4$], was
employed, a significant new peak was observed in the $^{11}$B NMR spectrum at 50 ppm. The reaction was monitored for 18 hours, after which the $^1$H NMR spectrum revealed full consumption of the borenium salt, yet unconverted 2.53 still remained. The crude mixture was esterified, which led to a major resonance at 30 ppm in the $^{11}$B NMR spectrum. Attempts to purify the sample via column chromatography were unsuccessful, with two compounds observed in one band. GC-MS was utilised to identify the products, where the minor compound was assigned as the cyclised product, and the major product of the reaction was assigned as haloboration (Scheme 29), based on relative m/z values of 346.2 g mol$^{-1}$ and 382.2 g mol$^{-1}$ respectively. As $[\text{Cl}_2\text{B}(2,6\text{-lutidine})][\text{AlCl}_4]$ has been previously shown to haloborate internal alkynes, this reaction indicates that the cyclisation pathway is unfavourable in comparison to haloboration.

![Scheme 29](image)

Scheme 29 – The two products (cyclisation and haloboration) obtained through the reaction of alkyne 2.53 and the borenium salt, $[\text{Cl}_2\text{B}(2,6\text{-lutidine})][\text{AlCl}_4]$.

Notably, Larock’s early work involving the electrophilic cyclisation of alkynes using mercuric acetate$^{[35]}$ revealed that attempts to generate five- and seven-membered carbocycles were not successful. This suggests that 5-endo-dig and 7-endo-dig cyclisations are disfavoured when utilising...
π-nucleophiles, despite Baldwin’s rules indicating these are favoured. This also contrasts with heteroatomic nucleophiles possessing a lone pair, which readily undergo 5-endo-dig cyclisations with activated alkynes.\textsuperscript{[36]} The reactivity of these substrates towards BCl\textsubscript{3} will be discussed in depth in Chapter 3. Based on the slow and complex reactivity observed, these reactions were abandoned, and our attention turned onto further reactivity of the cyclised products that had been isolated.

2.2.4 – Examining Further Reactivity – Couplings, Oxidations and Secondary Cyclisations

A common application of boronic acids and esters is the Suzuki-Miyaura cross-coupling reaction, where a new C-C bond can be furnished from a RB(OR)\textsubscript{2} and aryl/vinyl halide. With a successful gram scale reaction to generate dihydronaphthalene 2.21, it was selected to be subjected to typical Suzuki-Miyaura conditions in the presence of 4-bromotoluene, which generated the desired diarylated dihydronaphthalene 2.54 in a 75% yield (Scheme 30, middle). Next, 3.3 equivalents of a hydride abstracting reagent, [Ph\textsubscript{3}C][BF\textsubscript{4}], was employed in order to generate the corresponding naphthalene. After 3 hours at reflux (in 1,2-dichloroethane (DCE)), the in situ \textsuperscript{1}H NMR spectrum revealed that the triplets corresponding to the aliphatic methylene groups were not present, and a new 1H peak at 5.51 ppm corresponding to Ph\textsubscript{3}CH was observed, indicating that the oxidation had taken place. The reaction was worked up and purified via silica gel column chromatography to give naphthalene 2.55 in a 75% yield (Scheme 30, right).

Scheme 30 – Suzuki-Miyaura coupling of 2.21 to generate diarylated dihydronaphthalene 2.54, with subsequent dehydrogenation to naphthalene 2.55.
Next, the oxidation of dihydronaphthalene 2.21 was investigated. The success of this endeavour would provide a significant scope expansion and facilitate the installation of alternative functional groups that may not be tolerant of oxidation. Initially, the reaction was carried out using the same conditions for forming 2.55, however 2.21 was found to be much less robust than 2.54, leading to the generation of multiple products, where the major compounds observed were borylated naphthalene 2.56 and the corresponding protodeborylated naphthalene (Scheme 31, left). It was hypothesised these conditions were generating strong Brønsted acids after hydride abstraction, leading to protodeborylation. A reaction was carried out reducing the excess of [Ph₃C][BF₄] to just 1.3 equivalents, with an equivalent of TBP added to sequester any Brønsted acidic byproducts. Additionally, the reaction was run at room temperature. The reaction was notably slower, taking 12 hours for full substrate consumption to occur. Post purification, borylated naphthalene 2.56 was isolated in a 93% yield (Scheme 31, right).

Scheme 31 – Oxidation of 2.21 with initial (left) and adapted (right) conditions to yield borylated naphthalene 2.56.

The next investigation into further reactivity was the possibility of a second cyclisation in situ to generate a product with the boron atom incorporated within a new ring system as the key properties of PAHs can be governed by doping of the organic scaffold with other atoms.³⁷ For example, nitrogen doped scaffolds tend to possess higher HOMO energy levels³⁸ than their undoped counterparts, and boron doped scaffolds typically possess lower LUMO levels. B-doped PAHs are of high interest due to their effect on the electronics of a system (generating n-type systems). The synthesis of B-doped PAHs typically requires multistep syntheses involving some sort of transmetallation with organometallic compounds. For an overview on B-doped PAHs, see the review
articles by Ingleson\textsuperscript{[39]} and Marder.\textsuperscript{[40]} To date, examples of generating B-doped PAHs via electrophilic borylation are rare (in contrast to B-N doped PAHs that are more readily synthesised in this fashion\textsuperscript{[41-44]} (see Scheme 32 for specific examples by Nakamura\textsuperscript{[41]} (Scheme 32, top) and Ingleson\textsuperscript{[42]} (Scheme 32, bottom)), hence our interest in inducing a second electrophilic cyclisation.

Nakamura 2011

![Scheme 32 - Examples by Nakamura\textsuperscript{[41]} (top) and Ingleson\textsuperscript{[42]} (bottom) of B-N doped PAHs generated via electrophilic borylation.](image)

Alkyne 2.36 was selected due to the proximal position between the BCl\(_2\) moiety and the naphthale in the borylative cyclisation product, which is arranged to furnish a six-membered boracycle on S\(_{EAr}\). The borylative cyclisation step was carried out using the optimum conditions of BCl\(_3\)/TBP, to give the dihydronaphthalene-BCl\(_2\) intermediate. Based on the work from Ingleson\textsuperscript{[42]} (Scheme 32, bottom), the optimal conditions for subsequent intramolecular borylation were a combination of AlCl\(_3\) and 2,6-dichloropyridine to generate an electrophilic borenium species. This would then undergo S\(_{EAr}\) on the proximal naphthyl position. Upon cyclisation, the 2,6-dichloropyridine dissociates and abstracts a proton to re-aromatise the system to give a R\(_2\)BCl species (Scheme 33).
Scheme 33 – Proposed mechanism for the second cyclisation to generate the boracycle.

The $^1$H NMR spectrum at each stage was complex, therefore $^{11}$B NMR spectroscopy was used to follow the reaction. Notably, at the dihydronaphthalene-BCl$_2$ stage (Figure 12, blue), there was an equivalent of [TBPH][BCl$_4$] present, therefore two equivalents of AlCl$_3$ were required, where the first abstracts a chloride from [BCl$_4$] (Figure 12, green), (generating...)

Figure 12 – In situ $^{11}$B NMR spectra for each stage of the reaction starting from the first cyclisation (blue), leading to the second cyclisation (pink). Sharp resonance at 6.2 ppm is due to [BCl$_4$]$^-$.
[TBPH][AlCl₄] and BCl₃) and the second initiates the cyclisation in combination with 2,6-dichloropyridine.

Pleasingly, upon workup, the compound was found to be stable to air/moisture, and to purification via silica gel column chromatography which gave boracycle 2.57 in an 83% yield (Scheme 34). The structure was confirmed through X-ray crystallography (Figure 13).

Scheme 34 – Sequential cyclisations to generate boracycle 2.57.

Figure 13 – X ray structure of 2.57 with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Yellow: Boron; Selected Metrics: C1-B1: 1.537(3) Å; C6-B1: 1.547(3) Å; C7-B1: 1.580(3) Å; C6-B1-C7-C8: 94.1(2)°; C5-C2-C3-C4: 34.3(3)°; C5-C2-C1-B1: 16.2(3)°.
The metrics for 2.57 are unremarkable in regards to the three C-B bonds, with each of them typical lengths of C(aryl)-B bonds at 1.537(3) Å, 1.547(3) Å and the C(Mes)-B a little longer at 1.580(3) Å. To minimise non-bond interactions, the mesityl group (ring A) is twisted out of plane of the naphthalene moiety (ring system B) (C6-B1-C7-C8 = 94.1(2)°) due to its large steric bulk. Interestingly, with the pucker of the aliphatic carbons present in ring C, the phenyl group (ring D) is actually twisted 34.3(3)° out of the plane of ring system B, which is to reduce the non-bonding interaction between the C4-proton and the naphthalene proton in the cove region. Additionally, the six-membered ring (ring E) that contains the boron atom is not fully co-planar with the naphthalene moiety, where it is twisted by 16.2(3)° out of plane.

Next, boracycle 2.57 was subjected to the conditions employed to oxidise dihydronaphthalene 2.21. It was observed that the reaction was quite slow, requiring 18 hours at 80°C. As expected, the aliphatic resonances disappeared, and a resonance at 5.51 ppm grew in, corresponding to Ph₃CH. The reaction was purified via silica gel column chromatography to give the oxidised boracycle 2.58 in a 74% yield. (Scheme 35). The reaction was further optimised by Dr Daniel Crossley and the structure of 2.58 confirmed subsequently by X-ray crystallography (also grown by Dr. Daniel Crossley).

![Scheme 35 – Oxidation of boracycle 2.57 to boracycle 2.58.](image-url)

This approach was also applied to both alkyne 2.1 and N-methyl-2-phenylindole (Scheme 36) in an attempt to generate borole (boron analogues of pyrrole) containing species. The latter example was attempted to try and generate an indoloborole product similar to that reported by Yamaguchi who...
used a conventional halogenation/lithiation/borylation sequence to access boroles.\textsuperscript{[45]} 2.1 was cyclised with BCl\textsubscript{3} to generate the dihydronaphthalene-BCl\textsubscript{2}, whilst N-methyl-2-phenylindole was borylated with [Cl\textsubscript{2}B(2,6-lutidine)][AlCl\textsubscript{4}]. However, in both cases, on reaction with AlCl\textsubscript{3} and 2,6-dichloropyridine, no trace of a borole product was observed \textit{in situ} in the \textsuperscript{11}B NMR spectrum, and highly complex mixtures were observed in the \textsuperscript{1}H NMR spectra, therefore the investigation was not continued.

\begin{align*}
\text{Scheme 36} & \quad \text{Attempted syntheses of boroles.}
\end{align*}

\textbf{2.2.5 – Alkyne Activation with BCl\textsubscript{3} Towards 1,2-\textit{Trans}-Carboboration}

Based on Stephan’s work utilising BCF to induce 1,2-\textit{trans}-carboboration of alkynes with intermolecular heteroaryl nucleophiles,\textsuperscript{[21]} the focus of the investigation turned towards applying BCl\textsubscript{3} to the same goal. Whilst 1-phenylprop-1-yne exhibited no reactivity with either BCl\textsubscript{3} or 2-methylthiophene alone (Scheme 37, left), the combination of the three in the presence of TBP (Table 3, entry 1) led to the generation of a 55 ppm resonance in the \textit{in situ} \textsuperscript{11}B NMR spectrum, indicating formation of a vinyl-BCl\textsubscript{2} species. After 18 hours at room temperature, all the starting materials had been consumed, and the reaction was esterified and purified, with alkene 2.59 isolated in a 41\% yield (Scheme 37, right). Notably, the major stereoisomer of the reaction is from \textit{trans}-carboboration, which was confirmed by 2D NOE spectroscopy. Irradiation of the resonance at 7.27 ppm (corresponding to the phenyl protons) resulted in a NOE enhancement in the resonance at 2.46 ppm (corresponding to the methyl group on the thiophene ring). Irradiation of the resonance at 2.04 ppm
corresponding to vinyl-CH₃) resulted in a NOE enhancement of the resonances at 0.99 ppm (corresponding to the methyl groups on the Bpin moiety) and 6.57 ppm (corresponding to the thiophene protons).

Scheme 37 — 1,2-trans-carboboration of 1-phenylprop-1-yn with BCl₃/TBP and 2-methylthiophene.

This indicates that the methyl is on the same side of the alkyne as the thiophene, which is expected of the trans-carboboration product. Next, a variety of nucleophiles were examined with diphenylacetylene (whilst Dr. James Lawson examined a variety of nucleophiles with 1-phenylprop-1-yn.) towards expanding the scope of the carboxoration reactivity, with the reaction observations summarised in Table 3. Diphenylacetylene was reacted with toluene and BCl₃/TBP (Table 3, entry 2), however no reaction was observed, even with heating at 60°C for 2 days, likely due to the less nucleophilic nature of the alkyne, resulting in less electrophilic attack by BCl₃ and no subsequent attack of the vinyl cation by the toluene. Next, N-methylpyrrole (Table 3, entry 3) was employed as a stronger nucleophile. However, no peak was observed at 55 ppm in the ¹¹B NMR spectrum in situ, indicating no vinyl-BCl₂ had formed, with no alkyne consumption observed in the ¹H NMR spectrum. Both N-methylindole (Table 3, entry 4) and N-tosylindole (Table 3, entry 5) resulted in no observable reaction with diphenylacetylene.

Overall, it can be concluded that diphenylacetylene appears too unreactive to be applicable to this chemistry regardless of the nucleophile employed, with every examined reaction revealing no consumption of the starting material.
Table 3 – A summary of the results of the trans-carboboration investigation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkyne</th>
<th>Nucleophile</th>
<th>Trans-carboboration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-phenylprop-1-yne</td>
<td>2-methylthiophene</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Diphenylacetylene</td>
<td>Toluene</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Diphenylacetylene</td>
<td>N-methylpyrrole</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Diphenylacetylene</td>
<td>N-methylindole</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Diphenylacetylene</td>
<td>N-tosyliindole</td>
<td>No</td>
</tr>
</tbody>
</table>

2.2.6 – Conclusions and Future Work

In conclusion, it has been shown that the borylative cyclisation of alkynes possessing an appropriate π-nucleophile to generate C3-borylated dihydronaphthalene derivatives can be initiated by employing the simple and commercially available boron electrophile, BCl3, under mild conditions. The reaction was found to be tolerant of a wide range of functionalities and with aryl, alkyl, halo and vinyl substituted alkynes, indicating that only minimal stabilisation of the cationic intermediate is necessary for cyclisation to occur. Some products of borylative cyclisation have been reacted further, and oxidation of the dihydronaphthalene to the corresponding naphthalene has been demonstrated at both the pre- and post-cross coupled stage. Additionally, naphthyl-substituted alkyne 2.36 can undergo two cyclisation steps to generate a new six-membered boracycle.

This methodology facilitates the production of a variety of carbo/heterocycles possessing a synthetically versatile boronic ester moiety without the use of expensive transition metal catalysts. This work could provide new routes to established drugs such as Nafoxidine and Pitavastatin, as well as offering new tools to the synthetic chemist’s toolbox towards the discovery of novel pharmaceuticals. Additionally, the generation of boracycles could lead to development within the field of material chemistry. This approach could be expanded further in a number of directions (see Chapters 3 and 4 for two of
them). It would be beneficial to develop the methodology towards the generation of borylated cyclopentenes.\textsuperscript{[46]} The literature shows that tertiary groups can be used in cyclisations of appropriate alkynes involving a 1,5-hydride shift to the vinyl cation intermediate after activation of the alkyne. Thus, it may be applicable to boron electrophiles (\textbf{Scheme 38}).

\begin{center}
\begin{tikzpicture}
% Diagram code here
\end{tikzpicture}
\end{center}

\textit{Scheme 38 – Proposed generation of borylated cyclopentene inspired by work by Gaunt et al.}\textsuperscript{[46]}
2.3.0 – Experimental - General Considerations

All manipulations of air and moisture sensitive species were performed under an atmosphere of argon or nitrogen using standard Schlenk and glovebox techniques unless otherwise stated. Glassware was dried in a hot oven overnight and heated under vacuum before use. Triethylamine was dried over calcium hydride and distilled under vacuum. Pentane and dichloromethane were dried by passing through an alumina drying column incorporated into an MBraun SPS800 solvent purification system. Tetrahydrofuran was dried by refluxing over potassium metal. All solvents were degassed and stored over molecular sieves (3Å) under inert atmosphere. All other materials were purchased from commercial vendors and used as received. NMR spectra were recorded with a Bruker AV-400 spectrometer (400 MHz \( ^1\)H; 100 MHz \( ^{13}\)C; 128 MHz \( ^{11}\)B; 376.50 MHz \( ^{19}\)F; 104 MHz \( ^{27}\)Al). \( ^1\)H NMR chemical shifts are reported in ppm relative to protio impurities in the deuterated solvents and \( ^{13}\)C NMR using the solvent resonances unless otherwise stated. \( ^{11}\)B NMR spectra were referenced to external BF\(_3\)Et\(_2\)O, \( ^{27}\)Al to Al(NO\(_3\))\(_2\) in D\(_2\)O (Al(D\(_2\)O)\(_6\))\(^{3+}\) and \( ^{19}\)F to external C\(_6\)F\(_6\). Resonances for the carbon directly bonded to boron are not observed in the \( ^{13}\)C\\{\( ^1\)H\} NMR spectra due to quadrupolar relaxation effects. For obtaining mass spectrometry data for all compounds, ca. 2-5 mg of material was submitted for analysis.

4-phenylbut-1-yne and hepta-1,6-diyne were purchased from Sigma Aldrich and used without further purification. Some carbon signals in compounds 2.9, 2.43, 2.46, 2.54 and 2.56 are not observed due to coincident peaks. The ionisation mode used in GC-MS was electron ionisation. All small scale cyclisation reactions were carried out in J. Young NMR tubes to facilitate \textit{in situ} reaction monitoring. A number of samples are analysed \textit{in situ} in protio solvent with a capillary insert containing wet deuterated d\(_6\)-DMSO, this leads to a residual H\(_2\)O resonance being observed at 3.95 ppm in the \( ^1\)H NMR spectra.
2.3.1 – General Syntheses

**General Procedure A**[^47]

![Diagram of reaction](attachment:image.png)

A Schlenk was charged with *tetrakis*-(*triphenylphosphine*)palladium(0) (0.02 eq.) and copper(I) bromide (0.04 eq.). Tetrahydrofuran was added and the suspension was stirred for five minutes, followed by the addition of the aryl bromide (1 eq.) and triethylamine. After five minutes more stirring, the alkyne (1.1 eq.) was added and the solution was stirred and refluxed at 90°C for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ or silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed *in vacuo* and the crude material was purified via column chromatography to yield the corresponding alkyne.

**General Procedure B**[^47]

![Diagram of reaction](attachment:image.png)

In a Schlenk, phenylacetylene (1 eq.) was added to THF (20 mL) and cooled to -78°C. With stirring, nBuLi (1.6M in hexane, 1.2 eq.) was added dropwise and the mixture was stirred for 30 minutes. The solution was warmed to room temperature and sodium iodide was added (0.05 eq.), followed by cooling back to -78°C. Substituted phenethyl bromide (1.1 eq.) was added and the reaction mixture was allowed to warm to room temperature and refluxed over 12 h. The reaction was quenched with aqueous NH₄Cl (50 mL) and washed with brine (2 x 50 mL) and distilled water (1 x 50 mL) then extracted into diethyl ether (2 x 10 mL). The organic layers were combined, dried over MgSO₄ and the solvent...
removed in vacuo. The product was purified via column chromatography to yield the corresponding alkyne.

**Borylative Cyclisation of 1,4-Disubstituted But-1-ynes**

Due to the variable molarity of commercial BCl₃ solutions an excess of BCl₃ was formally used. All commercial BCl₃ solutions from various vendors labelled as 1M in DCM were actually found to be lower than 1M by varying amounts (by NMR titration experiments with PPh₃). Therefore between 1.1 – 1.4 equivalents of “1M” BCl₃ are used, which really approximates to a 1:1 ratio between alkyne and BCl₃. To minimise the gradual decrease in molarity of BCl₃ solutions over time due to the high volatility of BCl₃ the BCl₃ solutions are transferred to Schlenks sealed with J. Youngs valves after first use.

**General Procedure A**

\[
\begin{align*}
&\text{R}^1\text{C}≡\text{C}\text{R}^2 \\
\xrightarrow{\text{1. BCl}_3 (1.1 \text{ eq.})} \\
&\text{DCM, } 20^\circ\text{C,} \\
&< 1 \text{ hour} \\
\xrightarrow{\text{2. Pinacol (1.05 eq.)}} \\
&\text{NEt}_3 (15 \text{ eq.}) \\
&(Y = \text{CH}_2, \text{NTs}, \text{O}) \\
&\text{Bpin}
\end{align*}
\]

The alkyne (1 eq.) was dissolved in DCM and boron trichloride (“1M” in DCM, 1.1-1.4 eq) was added. The reaction was stirred at room temperature for the specified time until reaction completion and the solvent was removed in vacuo to remove any unreacted BCl₃. The resulting oil was then re-dissolved in DCM, and transferred via cannula to a 0-5°C solution of pinacol (1.1 eq.) and NEt₃ (approx. 15 eq.) in DCM (Caution: the esterification is highly exothermic!). All subsequent steps were performed under air with non-purified solvents. The solvent was removed in vacuo and the product was extracted into pentane and filtered. The filtrate was collected and the solvent removed in vacuo. The resulting material was purified via column chromatography to yield the corresponding boronate ester.
General Procedure B

The alkyne (1 eq.) and 2,4,6-tri-tert-butylpyridine (1 eq.) were dissolved in DCM and boron trichloride (“1M” in DCM, 2.1 eq) was added. The reaction was stirred at room temperature for the specified time until reaction completion and the solvent was removed in vacuo. The resulting oil was then re-dissolved in DCM, and transferred via cannula to a 0-5°C solution of pinacol (1.1 eq.) and NEt₃ (approx. 15 eq.) in DCM (Caution: the esterification is highly exothermic!). All subsequent steps were performed under air with non-purified solvents. The solvent was removed in vacuo and the product was extracted into pentane and filtered. The filtrate was collected and the solvent removed in vacuo. The resulting material was purified via column chromatography to yield the corresponding boronate ester.

General Procedure C

The alkyne (1 eq.) and [Cl₂B(2-DMAP)][AlCl₄] (1 eq.) were dissolved in DCM. The reaction was stirred at room temperature for the specified time until reaction completion. The mixture was then transferred via cannula to a 0-5°C solution of pinacol (2.1 eq.) and NEt₃ (approx. 15 eq.) in DCM (Caution: the esterification is highly exothermic!). All subsequent steps were performed under air with non-purified solvents. The solvent was removed in vacuo and the product was extracted into pentane and filtered. The filtrate was collected and the solvent removed in vacuo. The resulting material was purified via column chromatography to yield the corresponding boronate ester.
2.3.2 - Alkynes

1,4-diphenylbut-1-yne 2.1

Prepared according to general procedure A. 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), bromobenzene (0.69 mL, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 2.1 (970 mg, 73%) obtained as a colourless oil.

Data is in accordance with the literature.\(^\text{[47]}\)

1-(p-chlorophenyl)-4-phenylbut-1-yne 2.2

Prepared according to general procedure A. 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), 4-bromochlorobenzene (1.24 g, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 2.2 (1.19 g, 76%) obtained as a colourless oil. Data is in accordance with the literature.\(^\text{[48]}\)

1-(o-chlorophenyl)-4-phenylbut-1-yne 2.3

Prepared according to general procedure A. 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), 2-bromochlorobenzene (1.24 g, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 2.3 (1.29 g, 83%) obtained as a colourless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.76 (2H, t, \(J = 7.5\) Hz, PhCH\(_2\)CH\(_2\)CCPh); 2.96 (2H, t, \(J = 7.5\) Hz, PhCH\(_2\)CH\(_2\)CCPh); 7.12-7.26 (3H, m, Ar-H); 7.27-7.43 (6H, m, Ar-H); \(^{13}\)C\(^{\text{\textsuperscript{\text{1}}H}}\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 21.9, 35.0, 78.3, 95.2, 123.7, 126.3, 126.4, 128.5, 128.6, 128.7, 129.2, 133.4, 135.8, 140.6; [ESI-MS] ([M+H]\(^+\) 10%
241.0 g mol\(^{-1}\)); [Acc. Mass] Calculated: [M+K]\(^{+}\) 279.0337 g mol\(^{-1}\); Observed: [M+K]\(^{+}\) 279.0343 g mol\(^{-1}\)

1-(2,3,4,5,6-pentafluorophenyl)-4-phenylbut-1-yn 2.4

**Prepared according to general procedure A.** 4-phenylbut-1-yn (1 mL, 7.11 mmol, 1.1 eq.), (2,3,4,5,6-pentafluorobromobenzene (0.8 mL, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). *Column chromatography eluent: 20% DCM in 40-60 petroleum ether.* 2.4 (706 mg, 50%) obtained as a yellow oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.81 (2H, t, \(J = 7.3\) Hz, PhCH\(_2\)CH\(_2\)CCPhF\(_5\)); 2.97 (2H, t, \(J = 7.3\) Hz, PhCH\(_2\)CH\(_2\)CCPhF\(_5\)); 7.22-7.38 (5H, m, Ar-H); \(^{13}\)C\({^1}\)H NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 22.1, 34.5, 65.5, 100.4 (td, \(J = 18.1, 3.9\) Hz), 102.9, 126.5, 128.50, 128.53, 137.6 (m, C-F coupling), 140.0, 141.0 (m, C-F coupling), 147.5 (m, C-F coupling); \(^{19}\)F NMR (376.50 MHz, CDCl\(_3\)): \(\delta\) -162.3 (2F, m); -154.0 (1F, t, \(J = 21.0\) Hz, Ph(C\(_4\))-F); -136.9 (2F, dd, \(J = 21.8\) Hz); [GC-MS] m/z calculated for C\(_{16}\)H\(_9\)F\(_5\), 296.1; found 296.1. GC-MS retention times of analyte: 10.75 minutes (1-(pentafluorophenyl)-4-phenylbut-1-yn); [Acc. Mass] Calculated: [M+H]\(^{+}\) 297.0697 g mol\(^{-1}\); Observed: [M+H]\(^{+}\) 297.0703 g mol\(^{-1}\)

1-(m-trifluoromethylphenyl)-4-phenylbut-1-yn 2.5

**Prepared according to general procedure A.** 4-phenylbut-1-yn (1 mL, 7.11 mmol, 1.1 eq.), (3-(trifluoromethyl)bromobenzene (0.9 mL, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). *Column chromatography eluent: 20% DCM in 40-60 petroleum ether.* 2.5 (1.54 g, 87%) obtained as a colourless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.74 (2H, t, \(J = 7.5\) Hz, PhCH\(_2\)CH\(_2\)CCPh); 2.96 (2H, t, \(J = 7.5\) Hz, PhCH\(_2\)CH\(_2\)CCPh); 7.24-7.62 (6H, m, Ar-H); 7.51-7.58 (2H, m, Ar-H); 7.65 (1H, CC-Ph(C\(_2\)-H)); \(^{13}\)C\({^1}\)H NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 21.6, 35.0,
80.1, 91.4, 124.2 (q, J = 3.7 Hz, HC-CCF₃) 124.8, 125.2, 126.4, 128.4 (q, ³J = 3.7 Hz, HC-CCF₃), 128.45, 128.53, 128.7, 130.1, 134.6, 140.5; ¹⁹F NMR (376.50 MHz, CDCl₃): δ -62.94 (PhCF₃); [GC-MS] m/z calculated for C₁₇H₁₃F₃, 274.1; found 274.1 GC-MS retention times of analyte: 12.67 minutes (1-(m-trifluoromethylphenyl)-4-phenylbut-1-yn); [Acc. Mass]: Calculated: [M+H]^+ 275.1042 gmol⁻¹; Observed: [M+H]^+ 275.1048 gmol⁻¹

1-(p-cyanophenyl)-4-phenylbut-1-ynе 2.6 and 1-(o-cyanophenyl)-4-phenylbut-1-ynе 2.6*  

Prepared according to general procedure A. 4-phenylbut-1-ynе (1 mL, 7.11 mmol, 1.1 eq.), 4-bromobenzonitrile (1.18 g, 6.46 mmol, 1 eq.), Pd(PPh₃)₄ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 50% DCM in 40-60 petroleum ether. 2.6 (970 mg, 69%) obtained as an orange solid. Data corresponds with previously published data. [49]

Prepared according to general procedure A. 4-phenylbut-1-ynе (1 mL, 7.11 mmol, 1.1 eq.), 2-bromobenzonitrile (1.18 g, 6.46 mmol, 1 eq.), Pd(PPh₃)₄ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 50% DCM in 40-60 petroleum ether. 2.6* (970 mg, 90%) obtained as an orange solid.

¹H NMR (400 MHz, CDCl₃): δ 2.77 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 2.96 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 7.19-7.25 (1H, m, Ar-H); 7.26-7.34 (5H, m, Ar-H); 7.41-7.49 (2H, m, Ar-H); 7.55-7.59 (1H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 20.8, 33.7, 76.8, 95.8, 114.1, 116.8, 125.4, 126.7, 127.4, 127.5, 131.2, 131.3, 131.5, 139.2; [ESI-MS]: [M+H]^+ 232.2 gmol⁻¹; [Acc. Mass]: Calculated: [M+H]^+ 232.1121 gmol⁻¹; Observed: [M+H]^+ 232.1126 gmol⁻¹
1-(p-nitrophenyl)-4-phenylbut-1-yn 2.7

Prepared according to general procedure A. 4-phenylbut-1-yn (1 mL, 7.11 mmol, 1.1 eq.), 4-nitrobromobenzene (1.31 g, 6.46 mmol, 1 eq.), Pd(PPh₃)₄ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 30% DCM in 40-60 petroleum ether. 2.7 (1.13 g, 70%) obtained as a yellow solid.

1H NMR (400 MHz, CDCl₃): δ 2.74 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 2.94 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 7.21-7.36 (3H, m, Ar-H); 7.46 (2H, dt, J = 8.8 Hz, 2.1 Hz, Ph(C₆H₅)NO₂); 8.13 (2H, td, J = 8.8 Hz, 2.1 Hz, Ph(C₆H₅)NO₂);

13C{¹H} NMR (100.6 MHz, CDCl₃): δ 21.8, 34.7, 80.1, 95.7, 123.5, 126.5, 128.49, 128.50, 130.9, 132.2, 140.2, 146.7; [GC-MS] m/z calculated for C₁₆H₁₃NO₂, 251.1; found 251.1. GC-MS retention times of analyte: 15.28 minutes (1-(p-nitrophenyl)-4-phenylbut-1-yn); [Acc Mass] Calculated [M+H]^+ 252.1019 g mol⁻¹; Observed [M+H]^+ 252.1034 g mol⁻¹

Ethyl 4-(4-phenylbut-1-yn-1-yl)benzoate 2.8

Prepared according to general procedure A. 4-phenylbut-1-yn (1 mL, 7.11 mmol, 1.1 eq.), ethyl-4-bromobenzoate (1.05 mL, 6.46 mmol, 1 eq.) Pd(PPh₃)₄ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 50% DCM in 40-60 petroleum ether. 2.8 (1.69 g, 98%) obtained as a dark orange/red oil.

1H NMR (400 MHz, CDCl₃): δ 1.42 (3H, t, J = 7.2 Hz, OCH₂CH₃); 2.75 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 2.97 (2H, t, J = 7.4 Hz, PhCH₂CH₂CCPh); 4.40 (2H, q, 7.2 Hz, OCH₂CH₃); 7.24-7.38 (5H, m, Ar-H); 7.45 (2H, dt, J = 8.4 Hz, 1.8 Hz, Ph(C₂H₅)COOEt); 7.99 (2H, dt, J = 8.4 Hz, 1.8 Hz, Ph(C₃H₅)COOEt);

13C{¹H} NMR (100.6 MHz, CDCl₃): δ 14.3, 21.8, 35.0, 61.1, 80.9, 92.9, 126.4, 128.45, 128.53, 129.3, 129.4, 131.4, 140.5, 166.2; [GC-MS] m/z calculated for C₁₉H₁₈O₂, 278.1; found 278.1. GC-MS retention times of analyte: 15.66 minutes
(ethyl 4-(4-phenylbut-1-yn-1-yl)benzoate); [Acc. Mass]: Calculated [M+H]$^+$ 279.1380 gmol$^{-1}$; Observed [M+H]$^+$ 279.1379 gmol$^{-1}$

1-phenyl-4-(p-methoxy)but-1-yne 2.9

Prepared according to general procedure B. (4-methoxy)phenethylbromide (2.00 g, 9.3 mmol, 1.1 eq.), phenylacetylene (0.93 mL, 8.45 mmol, 1 eq.), nBuLi (1.6M in hexane) (7 mL, 11 mmol, 1.3 eq.), NaI (127 mg, 0.845 mmol, 0.1 eq.), THF (25 mL). Column chromatography eluent: 25% DCM in 40-60 petroleum ether. 2.9 (765 mg, 38%) obtained as a colourless oil. Data is in accordance with the literature.$^{[50]}

1-(p-tolyl)-4-phenylbut-1-yne 2.10

Prepared according to general procedure A. 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), 4-bromotoluene (1.11 g, 6.46 mmol, 1 eq.), Pd(PPh$_3$)$_4$ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 50% DCM in pentane. 2.10 (495 mg, 35%) obtained as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.32 (3H, s, Ar-CH$_3$); 2.68 (2H, t, J = 7.6 Hz, PhCH$_2$CH$_2$CCPh); 2.91 (2H, t, J = 7.6 Hz, PhCH$_2$CH$_2$CCPh); 7.08 (2H, d, J = 8.0Hz, CC-Ph(C$_{3,5}$-H)); 7.19-7.34 (7H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 21.5, 21.8, 35.3, 81.4, 88.8, 120.8, 126.4, 128.4, 128.6, 129.0, 131.5, 137.7, 140.8; [ESI-MS] ([M+H]$^+$ 30% 221.2 gmol$^{-1}$); [Acc. Mass]: Calculated [M+H]$^+$ 221.1325 gmol$^{-1}$; Observed [M+H]$^+$ 221.1330 gmol$^{-1}$

1-(o-tolyl)-4-phenylbut-1-yne 2.11

Prepared according to general procedure A. 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), 2-bromotoluene (1.11 g, 6.46 mmol, 1 eq.), Pd(PPh$_3$)$_4$ (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 50% DCM in pentane. 2.11 (706 mg, 50%) obtained as a colourless oil.
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.36 (3H, s, Ar-CH\(_3\)); 2.78 (2H, t, J = 7.5 Hz, PhCH\(_2\)CH\(_2\)CCPh); 2.97 (2H, t, J = 7.5 Hz, PhCH\(_2\)CH\(_2\)CCPh); 7.08-7.15 (1H, m, Ar-H); 7.16-7.20 (2H, m, Ar-H); 7.21-7.28 (1H, m, Ar-H); 7.28-7.39 (5H, m, Ar-H);

\(^{13}\)C{\(^1\)H} NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 20.7, 21.8, 35.3, 80.2, 93.4, 123.6, 125.4, 126.3, 127.6, 128.4, 128.6, 129.3, 131.8, 140.0, 140.7; [ESI-MS] ([M+H]\(^+\) 35% 221.3 gmol\(^{-1}\)); [Acc. Mass]: Calculated [M+H]\(^+\) 221.1325 gmol\(^{-1}\); Observed [M+H]\(^+\) 221.1332 gmol\(^{-1}\)

1-phenyl-4-(\(p\)-tolyl)but-1-yne 2.12

[Diagram]

Prepared according to general procedure B. (4-methyl)phenethylbromide (0.54 mL, 3.52 mmol, 1.1 eq.), phenylacetylene (0.35 mL, 3.20 mmol, 1 eq.), \(^n\)BuLi (1.6M in hexane) (2.4 mL, 3.84 mmol, 1.2 eq.), NaI (48 mg, 0.320 mmol, 0.1 eq.), THF (15 mL). Column chromatography eluent: 10% DCM in 40-60 petroleum ether. 2.12 (477 mg, 68%) obtained as a pale yellow oil. Data corresponds with previously published data.\(^{[50]}\)

1-phenyl-4-(\(m\)-tolyl)but-1-yne 2.13

[Diagram]

Prepared according to general procedure B. (2-methyl)phenethylbromide (0.45 mL, 2.950 mmol, 1.1 eq.), phenylacetylene (0.30 mL, 2.609 mmol, 1 eq.), \(^n\)BuLi (1.6M in hexane) (2 mL, 3.22 mmol, 1.2 eq.), NaI (40 mg, 0.270 mmol, 0.1 eq.), THF (15 mL). Column chromatography eluent: 10% DCM in 40-60 petroleum ether. 2.13 (352 mg, 60%) obtained as a pale yellow oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.37 (3H, s, PhCH\(_3\)); 2.71 (2H, t, J = 7.6 Hz, ArCH\(_2\)CH\(_2\)CCPh); 2.92 (2H, t, J = 7.6 Hz, ArCH\(_2\)CH\(_2\)CCPh); 7.04-7.14 (3H, m, Ar-H); 7.23 (1H, t, J = 7.6 Hz, Ar-H); 7.28-7.32 (3H, m, Ar-H); 7.38-7.43 (2H, m, Ar-H); \(^{13}\)C{\(^1\)H} NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 21.4, 21.8, 35.2, 81.3, 89.7, 123.9, 125.6, 127.1, 127.6, 128.2, 128.3, 129.4, 131.6, 138.0, 140.7; [GC-MS] m/z calculated for C\(_{17}\)H\(_{16}\), 220.1; found 220.1. GC-MS retention times of analyte:
13.52 minutes (1-phenyl-4-(m-tolyl)but-1-yne); [Acc. Mass]: Calculated [M+H]^+ 221.1325 gmol\(^{-1}\); Observed [M+H]^+ 221.1326 gmol\(^{-1}\)

1-(p-methoxyphenyl)-4-phenylbut-1-yne 2.14

![Structure of 1-(p-methoxyphenyl)-4-phenylbut-1-yne](image)

**Prepared according to general procedure A.** 4-phenylbut-1-yne (1 mL, 7.11 mmol, 1.1 eq.), 4-bromoanisole (0.81 mL, 6.46 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (149 mg, 0.129 mmol, 0.02 eq.), copper(I) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). *Column chromatography eluent: 30% DCM in 40-60 petroleum ether. 2.14* (495 mg, 32%) obtained as an orange oil. Data is in accordance with the literature.\(^{[47]}\)

1-phenyl-4-(p-methoxy)but-1-yne 2.15

![Structure of 1-phenyl-4-(p-methoxy)but-1-yne](image)

**Prepared according to general procedure B.** (2-methoxy)phenethylbromide (2.00 g, 9.3 mmol, 1.1 eq.), phenylacetylene (0.93 mL, 8.45 mmol, 1 eq.), \(^n\)BuLi (1.6M in hexane) (7 mL, 11 mmol, 1.3 eq.), NaI (127 mg, 0.845 mmol, 0.1 eq.), THF (25 mL). *Column chromatography eluent: 25% DCM in 40-60 petroleum ether. 2.15* (587 mg, 29%) obtained as a colourless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.73 (2H, t, J = 7.5 Hz, ArCH\(_2\)CH\(_2\)CCPh); 2.94 (2H, t, J = 7.5 Hz, ArCH\(_2\)CH\(_2\)CCPh); 3.83 (3H, s, OCH\(_3\)); 6.79-6.84 (1H, m, Ar-H); 6.86-6.93 (2H, m, Ar-H); 7.24-7.35 (4H, m, Ar-H); 7.39-7.44 (2H, m, Ar-H); 13C\(\{\)1H\}\(\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 21.7, 35.3, 55.2, 81.4, 89.5, 111.7, 114.3, 120.9, 123.8, 127.7, 128.2, 129.4, 131.6, 142.3, 159.7 [ESI-MS] ([M+H]^+ 100% 237.2 gmol\(^{-1}\)); ([M+Na]^+ 10% 259.2 gmol\(^{-1}\)); [Acc. Mass]: Calculated [M+H]^+ 237.1274; Observed [M+H]^+ 237.1279 gmol\(^{-1}\) [M+H]^+

1-phenyl-4-(m-chloro)but-1-yne 2.16

![Structure of 1-phenyl-4-(m-chloro)but-1-yne](image)

**Prepared according to general procedure B.** (2-chloro)phenethylbromide (1 mL, 7.00 mmol, 1.1 eq.), phenylacetylene (0.70 mL, 6.37 mmol, 1 eq.), \(^n\)BuLi (1.6M in hexane) (4 mL, 6.37 mmol, 1 eq.), NaI (96 mg, 0.64 mmol, 0.1 eq.), THF (25 mL). *Column chromatography eluent: 20% DCM
in 40-60 petroleum ether. **2.16** (165 mg, 11%) obtained as an orange oil.

Data corresponds with previously published data.\(^{[50]}\)

**1-phenylpent-3-yne 2.33**

\[ \text{Synthesised via a literature procedure.}^{[51]} \]

4-phenylbut-1-yne (0.25 mL, 1.78 mmol, 1 eq.), methyl iodide (0.22 mL, 3.56 mmol, 2 eq.), nBuLi (1.34 mL, 2.14 mmol, 1.2 eq.), THF (10 mL). **2.33** (220 mg, 86%) obtained as a pale yellow oil. Data corresponds with previously published data.\(^{[51]}\)

**\(4\)-bromobut-3-yn-1-yl)benzene 2.34**

\[ \text{Synthesised via a literature procedure.}^{[52]} \]

4-phenylbut-1-yne (1 mL, 7.11 mmol, 1 eq.), N-bromosuccinimide (1.47 g, 8.25 mmol, 1.2 eq.), AgNO\(_3\) (121 mg, 0.711 mmol, 0.1 eq.), acetone (40 mL). **2.34** (1.28 g, 86%) obtained as a dark yellow oil. Data is in accordance with the literature.\(^{[52]}\)

**1-(E)-styryl-4-phenylbut-1-yne 2.35**

\[ \text{Synthesised via a literature procedure.}^{[47]} \]

Alkyne **2.34** (800 mg, 3.83 mmol, 1.5 eq.), (E)-styrylboronic acid (378 mg, 2.55 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (148 mg, 0.128 mmol, 0.05 eq.), 3M NaOH\(_{[\text{aq}]}\) (10 mL), dioxane (20 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. **2.35** (207 mg, 35%) obtained as a yellow oil. Data is in accordance with the literature.\(^{[47]}\)
1-naphthyl-4-phenylbut-1-yn 2.36

Prepared according to general procedure A. 4-phenylbut-1-yn (1 mL, 7.11 mmol, 1.1 eq.), ethynynaphthalene (0.9 mL, 6.46 mmol, 1 eq.), Pd(PPh\textsubscript{3})\textsubscript{4} (149 mg, 0.129 mmol, 0.02 eq.), copper(l) bromide (37 mg, 0.258 mmol, 0.04 eq.), triethylamine (7 mL), THF (30 mL). Column chromatography eluent: 10% DCM in 40-60 petroleum ether. 2.36 (1.07 g, 64%) obtained as a white solid. Data is in accordance with the literature.\textsuperscript{[50]}

4-methyl-N-phenyl-N-(3-phenylprop-2-yn-1-yl)benzenesulfonamide 2.42

3-phenyl propargyl chloride (580 mg, 3.85 mmol, 1 eq.), 4-methyl-N-phenylbenzenesulfonamide (1 g, 4.04 mmol, 1.05 eq.), potassium carbonate (559 mg, 4.04 mmol, 1.05 eq.) and potassium iodide (250 mg, 1.50 mmol, 0.39 eq.) were dissolved in MeCN and stirred under reflux at 90°C for 12 hours. The resulting mixture was purified via column chromatography (15% EtOAc in hexane) to give product 2.42 (876 mg, 63%) as a yellow solid. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 2.28 (3H, s, SO\textsubscript{2}PhCH\textsubscript{3}), 4.58 (2H, s, PhN(Ts)CH\textsubscript{2}CCPh), 7.05-7.26 (12H, m, Ar-H), 7.51 (2H, d, J = 8.3 Hz, Ar-H); \textsuperscript{13}C\textsuperscript{1}H NMR (100.6 MHz, CDCl\textsubscript{3}): \(\delta\) 21.4, 42.1, 83.7, 85.6, 122.4, 128.1, 128.2, 128.5, 128.5, 129.0, 129.3, 131.5, 136.0, 139.8, 143.6; [ESI-MS] ([M+H]\textsuperscript{+} 100% 362.3 gmol\textsuperscript{-1}); ([M+Na]\textsuperscript{+} 40% 384.3); [Acc. Mass]: Calculated [M+Na]\textsuperscript{+} 384.1029 gmol\textsuperscript{-1}; Observed [M+Na]\textsuperscript{+} 384.1021 gmol\textsuperscript{-1}

(3-phenoxyprop-1-yn-1-yl)benzene 2.44

Prepared according to general procedure A. Phenyl propargylether (0.76 mL, 5.89 mmol, 1.1 eq.), bromobenzene (0.56 mL, 5.35 mmol, 1 eq.), Pd(PPh\textsubscript{3})\textsubscript{4} (124 mg, 0.107 mmol, 0.02 eq.), copper(l) bromide (31 mg, 0.214 mmol, 0.04 eq.), NEt\textsubscript{3} (6 mL), THF (25 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 2.44 (70 mg, 6%) obtained as a white solid. Data is in accordance with the literature.\textsuperscript{[53]}
1-(2,3,4,5,6-pentafluorophenyl)propargyl-3-phenylether 2.45

Prepared according to general procedure A. Phenyl propargyl ether (1.94 mL, 15.13 mmol, 1.1 eq.), 2,3,4,5,6-pentafluorobromobenzene (1.71 mL, 13.76 mmol, 1 eq.), Pd(PPh₃)₄ (350 mg, 0.303 mmol, 0.02 eq.), copper(I) bromide (87 mg, 0.606 mmol, 0.04 eq.), NEt₃ (7 mL), THF (30 mL).

Column chromatography eluent: 20% DCM in 40-60 pentane.

2.45 (1.44 g, 32%) obtained as a pale yellow oil.

^1H NMR (400 MHz, CDCl₃): δ 4.98 (2H, s, PhOCH₂CCPhF₅); 7.00-7.08 (3H, m, Ar-H); 7.31-7.38 (2H, m, Ar-H); ^13C{^1H} NMR (100.6 MHz, CDCl₃): δ 56.3, 71.2, 96.7, 99.2 (td, J = 18.0 Hz, 3.7 Hz, C-F coupling) 115.0, 121.8, 129.6, 137.6 (m, C-F coupling), 141.9 (m, C-F coupling), 147.6 (m, C-F coupling), 157.4; ^19F NMR (376.5 MHz, CDCl₃): δ -161.5 (2F, m, (Ar-F); -151.5 (1F, t, J = 20.9 Hz, Ph(C₄-F); -135.5 (2H, dd, J = 21.8 Hz, 7.5 Hz); [GC-MS] m/z calculated for C₁₅H₁₇F₅O, 298.0; found 298.1 GC-MS retention times of analyte: 10.83 minutes (1-(pentafluorophenyl)propargyl-3-phenyl ether); [Acc. Mass]: Calculated [M+H]^+ 299.0490 gmol⁻¹; Observed [M+H]^+ 299.0488 gmol⁻¹

Phenyl(3-phenylprop-2-yn-1-yl)sulfane 2.47

3-phenyl propargyl chloride (1.19 mL, 8.64 mmol, 1 eq.), thiophenol (0.93 mL, 9.08 mmol, 1.05 eq.), potassium carbonate (1.25 g, 9.08 mmol, 1.05 eq.) and potassium iodide (250mg, 1.50 mmol, 0.39 eq.) were dissolved in MeCN and stirred under reflux at 90°C for 12 hours. The resulting mixture was purified via column chromatography (5% DCM in pentane) to give product 2.47 (1.04 g, 53%) as an orange oil. Data was in accordance with the literature.^[54]
Phenyl(3-phenylprop-2-yn-1-yl)sulfane 2.49

Prepared via a known procedure.\[54\] Alkyne 2.47 (224 mg, 1 mmol, 1 eq.), acetic acid (0.5 mL, 8.74 mmol, 8.7 eq.), H$_2$O$_2$ (30\% w/v) (0.7 mL, 6.2 mmol, 6.2 eq.). Data was in accordance with the literature.

1-(2-bromo-6-(oct-1-yn-1-yl)phenyl)-1H-pyrrole 2.50

Adapted from a procedure in the literature.\[55\] A Schlenk tube was charged bis(triphenylphosphine)palladium(II)dichloride (0.06 eq.) and copper(I) iodide (0.04 eq.). Tetrahydrofuran (5 mL) was added and the suspension was stirred for five minutes, followed by the addition of the aryl bromide (1 eq.) and triethylamine. After five minutes more stirring, oct-1-yne (1.1 eq.) was added and the solution was stirred and refluxed at 90°C for 12h. The solution was cooled to room temperature, filtered through Celite\textsuperscript{TM} and silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography to yield 2.50 as a colourless oil. Due to the high difficulty associated with the separation, there was not enough pure material to get conclusive $^{13}$C NMR spectral data, and the entirety of material (<10 mg) was used up in the cyclisation reaction. (\textsuperscript{1}H attached for clarification)
$^1$H NMR (400 MHz, CDCl$_3$) δ 0.90 (3H, t, J = 7.0 Hz, hexyl); 1.19-1.45 (8H, m, hexyl); 2.24 (2H, t, J = 7.0 Hz, hexyl); 6.32 (2H, t, J = 2.1 Hz, Pyr-H); 6.75 (2H, t, J = 2.1 Hz, Pyr-H); 7.17 (1H, t, J = 7.9 Hz, Ar-H (para to pyrrole)); 7.43 (1H, dd, J = 7.7, 1.3 Hz, Ar-H); 7.59 (1H, dd J = 7.7, 1.3 Hz, Ar-H);

1,3-diphenylprop-1-yne 2.52

Prepared according to general procedure A. 3-phenylprop-1-yne (0.73 mL, 5.89 mmol, 1.1 eq.), bromobenzene (0.56 mL, 5.35 mmol, 1 eq.), Pd(PPh)$_3$$_4$ (124 mg, 0.107 mmol, 0.02 eq.), copper(I) bromide (31 mg, 0.214 mmol, 0.04 eq.), NEt$_3$ (5.5 mL), THF (30 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 2.52 (733 mg, 72%) obtained as a colourless oil. Data was in accordance with the literature.$^{[56]}$

1,5-diphenylpent-1-yne 2.53

Prepared according to general procedure A. 5-phenylpent-1-yne (0.89 mL, 5.89 mmol, 1.1 eq.), bromobenzene (0.56 mL, 5.35 mmol, 1 eq.), Pd(PPh)$_3$$_4$ (124 mg, 0.107 mmol, 0.02 eq.), copper(I) bromide (31 mg, 0.214 mmol, 0.04 eq.), NEt$_3$ (5.5 mL), THF (30 mL). Column
chromatography eluent: 5% DCM in 40-60 petroleum ether. 2.53 (673 mg, 57%) obtained as a colourless oil. Data was in accordance with the literature.\textsuperscript{[57]}

### 2.3.3 – Borylated Carbocycles

4,4,5,5-tetramethyl-2-(1-phenyl-3,4-dihyronaphthalen-2-yl)-1,3,2-dioxaborolane 2.17

**Prepared according to general procedure A.** 2.1 (200 mg, 0.97 mmol) and boron trichloride (1.16 mL, 1.1 mmol) were stirred in DCM for 20 minutes. The reaction mixture was transferred to a cooled solution of pinacol (241 mg, 2 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.17 (293 mg, 91%) as a yellow crystalline solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.10 (12H, s, Bpin); 2.49 (2H, t, $J = 7.8$ Hz, CH$_2$CH$_2$CBPin); 2.84 (2H, t, $J = 7.8$ Hz, CH$_2$CH$_2$CBPin); 6.79 (1H, d, $J = 7.8$ Hz, HCCC(Ph)CBPin); 7.03-7.09 (1H, m, Ar-H); 7.12-7.20 (2H, m, Ar-H); 7.22-7.28 (2H, m, Ar-H); 7.29-7.38 (3H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 23.4, 25.1, 27.0, 82.0, 125.1, 125.4, 125.8, 126.2, 126.4, 126.6, 128.8, 134.8, 136.3, 140.3, 147.5; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.8 (s); [ESI-MS] ([M+H]$^+$ 100% 333.2 gmol$^{-1}$); ([M-Bpin+2H]$^+$ 50% 207.2 gmol$^{-1}$); Anal. Calcd. for C$_{22}$H$_{25}$BO: C, 79.53; H, 7.58; Found: C, 79.21; H, 7.58; [Acc. Mass]: 333.2020 gmol$^{-1}$ [M+H]$^+$

2-(1-(4-chlorophenyl)-3,4-dihyronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.18

**Prepared according to general procedure A.** 2.2 (200 mg, 0.83 mmol) and boron trichloride (1 mL, 1 mmol) were stirred in DCM for 20 minutes. The reaction mixture was transferred to a cooled solution of pinacol (118 mg, 1 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.18 (289 mg, 95%) as a white crystalline solid.
1H NMR (400 MHz, CDCl3): 1.12 (12H, s, Bpin); 2.49 (2H, t, J = 7.8 Hz, CH2CH2CBPin); 2.83 (2H, t, J = 7.8 Hz, CH2CH2CBPin); 6.74(1H, d, J = 7.8 Hz, HCCC(Ph)CBPin); 7.05-7.11 (1H, m, Ar-H); 7.13-7.23 (4H, m, Ar-H); 7.33 (2H, d, J = 8.3 Hz, Ar-H); 13C{1H} NMR (100.6 MHz, CDCl3): δ 24.5, 26.1, 27.9, 83.3, 126.2, 126.3, 127.4, 127.7, 127.8, 130.1, 131.3, 132.8, 135.5, 137.5, 139.9, 147.6; 11B NMR (128.4 MHz, CDCl3): δ 31.0 (s); [ESI-MS] ([M-Bpin]+ 100% 239.4 gmol⁻¹); Acc. Mass: (241.2038 gmol⁻¹ – [M-Bpin+2H]+). Mass reported involves 35Cl isotope.

2-(1-(2-chlorophenyl)-3,4-dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.19

Prepared according to general procedure A. 2.3 (200 mg, 0.83 mmol) and boron trichloride (1 mL, 1 mmol) were stirred in DCM for 20 minutes. The reaction mixture was transferred to a cooled solution of pinacol (98 mg, 0.87 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.19 (220 mg, 72%) as a colourless oil.

1H NMR (400 MHz, CDCl3): δ 1.14 (6H, s, Bpin); δ 1.16 (6H, s, Bpin); 2.55-2.73 (2H, m, CH2CH2CBPin); 2.85-3.05 (2H, m, CH2CH2CBPin); 6.73 (1H, d, J = 7.6 Hz, HCCC(Ar)CBPin); 7.14 (1H, t, J = 7.3 Hz, Ar-H); 7.20-7.38 (5H, m, Ar-H); 7.44-7.51 (1H, m, Ar-H); 13C{1H} NMR (100.6 MHz, CDCl3): δ 23.5, 24.6, 26.7, 81.9, 124.6, 125.0, 125.2, 126.3, 126.6, 127.1, 127.8, 130.8, 133.0, 133.7, 136.1, 139.1, 145.8; 11B NMR (128.4 MHz, CDCl3): δ 30.5 (s); [ESI-MS] ([M+H]+ 40% 367.1 gmol⁻¹); [Acc. Mass]: (367.1638 gmol⁻¹ [M+H]+). Mass reported involves 35Cl isotope.
4,4,5,5-tetramethyl-2-(1-(perfluorophenyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane 2.20

Prepared according to general procedure A. 2.4 (110 mg, 0.37 mmol) and boron trichloride (0.5 mL, 0.5 mmol) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (44 mg, 0.37 mmol) and excess triethylamine in DCM. The mixture was filtered through a silica plug with pentane to give 2.20 (125 mg, 80%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.19 (12H, s, Bpin); 2.64 (2H, t, J = 7.8Hz, CH$_2$CH$_2$CBpin); 2.90 (2H, t, J = 7.8Hz, CH$_2$CH$_2$CBpin); 6.76 (1H, d, J = 7.6Hz, HCCC(Ar)CBpin); 7.12-21 (1H, m, Ar-H); 7.21-7.29 (2H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 23.5, 24.7, 26.3, 82.4, 114.2 (td, C-F coupling), 123.7, 125.6, 126.7, 127.6, 132.6, 134.2, 136.3 (m, C-F coupling), 136.3, 139.4 (m C-F coupling), 143.7 (m, C-F coupling); $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 29.7 (s); $^{19}$F NMR (376.50 MHz, CDCl$_3$): $\delta$ -164.19 (2F, td, J = 5.8Hz, Ar-F); -157.21 (1F, t, J = 20.5Hz, Ph(C$_4$-F); -140.94 (2F, dd, J = 7.6Hz, 7.8Hz, Ar-F); [ESI-MS] ([M+F] 100% 441.2gmol$^{-1}$); [Acc. Mass]: (423.1548 gmol$^{-1}$ [M+H]$^+$)

4,4,5,5-tetramethyl-2-(1-(3-(trifluoromethyl)phenyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane 2.21

Prepared according to general procedure A. 2.5 (100 mg, 0.365 mmol) and boron trichloride (0.4 mL, 0.4 mmol) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (44 mg, 0.37 mmol) and excess triethylamine in DCM. The mixture was filtered through a silica plug with pentane to give 2.21 (141 mg, 97%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.10 (12H, s, Bpin); 2.54 (2H, t, J = 7.8Hz, CH$_2$CH$_2$CBpin); 2.86 (2H, t, J = 7.8Hz, CH$_2$CH$_2$CBpin); 6.70 (1H, d, J = 7.6Hz, HCCC(Ar)CBpin); 7.06-7.12 (1H, m, Ar-H); 7.16-7.24 (2H, m, Ar-H); 7.40-7.52 (2H, m, Ar-H); 7.55 (1H, s, Ph(C$_2$-H)); 7.61 (1H, d, J = 7.6Hz, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 24.5, 26.1, 27.9, 83.3, 123.7 (q, $^3$J$_{C-F}$ = 3.7 Hz, HC-
CCF₃), 124.3 (q, ¹J_C-F = 272.2 Hz, CF₃), 126.3, 126.4, 127.0 (q, ³J_C-F = 3.7 Hz, HC-CF₃), 127.5, 127.9, 128.0, 130.1 (q, ²J_C-F = 32.0 Hz, CCF₃), 133.2, 135.4, 137.5, 142.2, 147.9; ¹¹B NMR (128.4 MHz, CDCl₃): δ 30.6 (s); [GC-MS] m/z calculated for C₂₃H₂₄BF₃O₂, 400.2; found 400.2. GC-MS retention times of analyte: 14.58 minutes (4,4,5,5-tetramethyl-2-(1-(3-(trifluoromethyl)phenyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane); [Acc. Mass]: ([M+H]⁺ 401.1885 gmol⁻¹)

4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydronaphthalen-1-yl)benzonitrile 2.22

Prepared according to general procedure A. 2.6 (100 mg, 0.432 mmol) and boron trichloride (0.9 mL, 0.9 mmol) were stirred in DCM for 12h. The reaction mixture was transferred to a cooled solution of pinacol (118 mg, 1 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (50% dichloromethane in petroleum ether 40-60) to give 2.22 (98 mg, 63%) as a white crystalline solid.

¹H NMR (400 MHz, CDCl₃): δ 1.10 (12H, s, Bpin); 2.51 (2H, t, J = 7.8 Hz, CH₂CH₂CBPin); 2.83 (2H, t, J = 7.8 Hz, CH₂CH₂CBPin); 6.62 (1H, d, J = 7.7 Hz, HCCC(Ar)CBPin); 7.04-7.10 (1H, m, Ar-H); 7.15-7.23 (2H, m, Ar-H); 7.35 (2H, d, J = 8.3 Hz, Ph(C₂₆-H)); 7.65 (2H, d, J = 8.3 Hz, Ph(C₃₅-H)); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.5, 26.0, 27.7, 83.4, 110.6, 119.3, 126.2, 126.3, 127.6, 128.1, 130.8, 131.5, 134.9, 137.4, 146.7, 147.7; ¹¹B NMR (128.4 MHz, CDCl₃): δ 30.9 (s); [ESI-MS] ([M+H]⁺ 25% 358.4 gmol⁻¹); ([M+Na]⁺ 100% 380.2 gmol⁻¹); [Acc. Mass]: (358.198 gmol⁻¹ [M+H]⁺)

4,4,5,5-tetramethyl-2-(1-(4-nitrophenyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane 2.23

Prepared according to general procedure A. 2.7 (80mg, 0.318 mmol, 1 eq.) and boron trichloride (0.45 mL, 0.446 mmol, 1.4 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (41 mg, 0.350 mmol, 1.1 eq.) and excess triethylamine
in DCM. The mixture was purified via column chromatography (50% DCM in 40-60 petroleum ether) to give 2.23 (84 mg, 70%) as an orange solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.10 (12H, s, Bpin); 2.53 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 2.85 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 6.62 (1H, d, J = 7.6 Hz, HCCC(Ar)CBPin); 7.05-7.10 (1H, m, Ar-H); 7.17-7.24 (2H, m, Ar-H); 7.40 (2H, dt, J = 8.8 Hz, 2.1 Hz, Ph(C\(_{2,6}\)-H)); 8.23 (2H, dt, J = 8.8 Hz, 2.1 Hz Ph(C\(_{3,5}\)-H)); \(^13\)C\(^{\{1\}}\)H NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 24.5, 26.1, 27.7, 83.4, 122.9, 126.2, 126.4, 127.6, 128.2, 131.0, 134.9, 137.5, 147.0, 147.5, 148.8; \(^{11}\)B NMR (128.4 MHz, CDCl\(_3\)): \(\delta\) 30.2 (s); [GC-MS] m/z calculated for C\(_{22}\)H\(_{24}\)BNO\(_4\), 377.2; found 377.2 GC-MS retention times of analyte: 18.56 minutes (1-(4,4,5,5-tetramethyl-2-(1-(4-nitrophenyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane); [Acc. Mass]: (377.1791 gmol\(^{-1}\) [M]+)

**Ethyl 4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydronaphthalen-1-yl)benzoate 2.24**

Prepared according to general procedure A. 2.8 (55 mg, 0.207 mmol, 1 eq.) and boron trichloride (0.43 mL, 0.43 mmol, 2.1 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (52 mg, 0.44 mmol, 2.13 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (60% dichloromethane in pentane) to give 2.24 (73 mg, 87%) as a white solid.

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.10 (12H, s, Bpin); 1.44 (3H, t, J = 7.2 Hz, COOCH\(_2\)CH\(_3\)); 2.51 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 2.84 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 4.42 (2H, q, J = 7.2 Hz); 6.68 (1H, d, J = 7.6 Hz, HCCC(Ar)CBPin); 7.02-7.09 (1H, m, Ar-H); 7.13-7.22 (2H, m, Ar-H); 7.33 (2H, dt, J = 8.5 Hz, 2.0 Hz, Ph(C\(_{2,6}\)-H)); 8.05 (2H, dt, J = 8.5 Hz, 2.0 Hz, Ph(C\(_{3,5}\)-H)); \(^13\)C\(^{\{1\}}\)H NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 14.4, 24.5, 26.1, 27.9, 60.9, 83.3, 126.2, 126.4, 127.4, 127.8, 128.99, 129.01, 130.0, 135.4, 137.4, 146.4, 148.0, 166.8; \(^{11}\)B NMR (128.4 MHz, CDCl\(_3\)): \(\delta\) 30.8 (s); [GC-MS] m/z calculated for C\(_{25}\)H\(_{29}\)BO\(_4\), 404.2; found 404.2 GC-MS retention times of analyte: 18.50
minutes (ethyl 4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,4-dihydropyran-1-yl)benzoate); [Acc. Mass]: (404.2148 gmol\(^{-1}\) [M]+)

2-(7-methoxy-1-phenyl-3,4-dihydropyran-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.25

Prepared according to general procedure A. 2.9 (30 mg, 0.127 mmol, 1 eq.) and boron trichloride (0.14 mL, 0.14 mmol, 1.1 eq.) were stirred in DCM for 20 minutes. The reaction mixture was transferred to a cooled solution of pinacol (15 mg, 0.128 mmol, 1.01 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (50% dichloromethane in petroleum ether 40-60) to give 2.25 (36 mg, 79%) as a white solid.

\(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.10 (12H, s, Bpin); 2.47 (2H, t, \(J = 7.8\)Hz, CH\(_2\)CH\(_2\)CBPin); 2.77 (2H, t, \(J = 7.8\)Hz, CH\(_2\)CH\(_2\)CBPin); 3.65 (3H, s, OCH\(_3\)); 6.38 (1H, d, \(J = 2.6\)Hz, Ar-H (proton ortho to OMe); 6.71 (1H, dd, \(J = 8.1\) Hz, 2.6 Hz, para to new C-C bond); 7.10 (1H, d, \(J = 8.1\) Hz, Ar-H (meta to OMe); 7.21-7.27 (2H, m, Ar-H); 7.29-7.36 (3H, m Ar-H); \(^{13}\)C\(^{\text{1}}\)H NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 24.5, 26.5, 27.1, 55.2, 83.2, 112.0, 113.0, 127.0, 127.7, 129.7, 129.9, 136.8, 141.2, 148.3, 158.0; \(^{11}\)B NMR (128.4 MHz, CDCl\(_3\)): \(\delta\) 30.6 (s); [ESI-MS] ([M+H]\(^{+}\) 50% 363.5 gmol\(^{-1}\)); ([M+Na]\(^{+}\) 20% 385.4 gmol\(^{-1}\)); [Acc. Mass]: (385.1949 gmol\(^{-1}\) [M+Na]\(^{+}\))

4,4,5,5-tetramethyl-2-(1-(p-tolyl)-3,4-dihydropyran-2-yl)-1,3,2-dioxaborolane 2.26

Prepared according to general procedure B. 2.10 (75 mg, 0.345 mmol), 2,4,6-tri-tert-butylpyridine (85.4 mg, 0.345 mmol) and boron trichloride (0.73 mL, 0.73 mmol) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (43 mg, 0.362 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.26 (70 mg, 59%) as a colourless oil.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.13 (12H, s, Bpin); 2.41 (3H, s, PhCH$_3$); 2.49 (2H, t, J = 7.8 Hz, CH$_2$CH$_2$CBpin); 2.84 (2H, t, J = 7.8 Hz, CH$_2$CH$_2$CBpin); 6.83 (1H, d, J = 7.6 Hz, HCCC(Ar)CBpin); 7.07 (1H, t, J = 7.3 Hz, Ar-H); 7.13-7.22 (6H, m, Ar-H); $^{13}$C{$^1$H} NMR (100.6 MHz, CDCl$_3$): $\delta$ 21.3, 24.5, 26.2, 28.0, 83.1, 126.1, 126.5, 127.2, 127.4, 128.4, 129.8, 136.0, 136.4, 137.5, 138.4, 148.3; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.8 (s); [ESI-MS] ([M+Na]$^+$ 5% 369.4 gmol$^{-1}$); ([M+H]$^+$ 10% 347.4 gmol$^{-1}$); ([M-Bpin]$^+$ 5% 221.3 gmol$^{-1}$); [Acc. Mass]: 347.2182 gmol$^{-1}$ [M+H]$^+$

4,4,5,5-tetramethyl-2-(1-(o-tolyl)-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane 2.27

Prepared according to general procedure B. 2.11 (100 mg, 0.46 mmol), 2,4,6-tri-tert-butylpyridine (114 mg, 0.46 mmol) and boron trichloride (0.5 mL, 0.50 mmol) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (55 mg, 0.46 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.27 (110 mg, 69%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.05 (6H, s, Bpin); 1.08 (6H, s, Bpin); 2.15 (3H, s, PhCH$_3$); 2.51-2.59 (2H, m, CH$_2$CH$_2$CBpin); 2.89 (2H, t, J = 7.8 Hz, CH$_2$CH$_2$CBpin); 6.66 (1H, d, J = 7.6 Hz, HCCC(Ar)CBpin); 7.07 (1H, t, J = 7.4 Hz, Ar-H); 7.11-7.30 (6H, m, Ar-H); $^{13}$C{$^1$H} NMR (100.6 MHz, CDCl$_3$): $\delta$ 19.6, 24.4, 24.5, 25.6, 28.0, 82.9, 125.1, 125.7, 126.4, 126.9, 127.3, 127.4, 129.3, 130.3, 135.3, 136.8, 137.1, 140.7, 147.9; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.5 (s); [ESI-MS] ([M+Na]$^+$ 30% 369.2 gmol$^{-1}$); ([M+H]$^+$ 5% 347.2 gmol$^{-1}$); [Acc. Mass]: 347.2182 gmol$^{-1}$ [M+H]$^+$
4,4,5,5-tetramethyl-2-(7-methyl-1-phenyl-3,4-dihyronaphthalen-2-yl)-1,3,2-dioxaborolane 2.28

Prepared according to general procedure B. 2.12 (50 mg, 0.227 mmol), 2,4,6-tri-tert-butylpyridine (57 mg, 0.230 mmol) and boron trichloride (0.34 mL, 0.34 mmol) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (30 mg, 0.46 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.28 (63 mg, 80%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.09 (12H, s, Bpin); 2.18 (3H, s, PhCH$_3$); 2.46 (2H, m, CH$_2$CH$_2$CBPin); 2.79 (2H, t, $J = 7.8$ Hz, CH$_2$CH$_2$CBPin); 6.60 (1H, d, $J = 7.6$ Hz, HCCC(Ph)CBPin); 6.97 (1H, m, Ar-H); 7.08 (1H, d, $J = 7.6$ Hz, Ar-H); 7.23-7.26 (2H, m, Ar-H); 7.32-7.36 (3H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 21.2, 24.5, 26.3, 27.6, 83.1, 126.8, 127.1, 127.2, 127.7, 128.1, 129.9, 134.5, 135.5, 135.7, 141.5, 148.6; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.9 (s); [ESI-MS] ([M+Na]$^+$ 100% 369.3 gmol$^{-1}$); ([M+H]$^+$ 100% 347.4 gmol$^{-1}$); [Acc. Mass]: 369.1981 gmol$^{-1}$ [M+Na]$^+$

4,4,5,5-tetramethyl-2-(6-methyl-1-phenyl-3,4-dihyronaphthalen-2-yl)-1,3,2-dioxaborolane 2.29

Prepared according to general procedure B. 2.13 (55 mg, 0.25 mmol), 2,4,6-tri-tert-butylpyridine (62 mg, 0.25 mmol) and boron trichloride (0.52 mL, 0.52 mmol) were stirred in DCM for 30 minutes. The reaction mixture was transferred to a cooled solution of pinacol (31 mg, 0.26 mmol) and excess triethylamine in DCM. The product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.29 (50 mg, 58%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.12 (12H, s, Bpin); 2.34 (3H, s, PhCH$_3$); 2.50 (2H, m, CH$_2$CH$_2$CBPin); 2.82 (2H, t, $J = 7.8$ Hz, CH$_2$CH$_2$CBPin); 6.70 (1H, d, $J = 7.8$ Hz, HCCC(Ph)CBPin); 6.90 (1H, t, $J = 7.4$ Hz, Ar-H); 7.03 (1H, s, Ar-H);
7.24-7.29 (2H, m, Ar-H); 7.32-7.39 (3H, m, Ar-H); \(^{13}\)C\(^{1}\)H\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 21.2, 24.5, 26.2, 28.1, 83.1, 126.5, 126.7, 126.8, 127.6, 128.2, 129.9, 133.3, 137.4, 137.5, 141.6, 148.6; \(^{11}\)B NMR (128.4 MHz, CDCl\(_3\)): \(\delta\) 30.9 (s); [ESI-MS] [M+H]\(^{\text{+}}\) 5% 347.3 gmol\(^{-1}\); [Acc. Mass]: 369.2099 gmol\(^{-1}\) [M+Na]\(^{+}\)

2-(1-(4-methoxyphenyl)-3,4-dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.30

[Diagram of 2.30]

Prepared according to general procedure C. 2.14 (70 mg, 0.296 mmol, 1 eq.) and [Cl\(_2\)B(2-DMAP)][AlCl\(_4\)] (110 mg, 0.296 mmol, 1 eq.) were stirred in DCM for 1h. The reaction mixture was transferred to a cooled solution of pinacol (74 mg, 0.622 mmol, 2.1 eq.) and excess triethylamine in DCM. The product was purified via column chromatography (50% dichloromethane in petroleum ether 40-60) to give 2.30 (38 mg, 36%) as an off white solid.

\(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.13 (12H, s, Bpin); 2.47 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 2.82 (2H, t, J = 7.8 Hz, CH\(_2\)CH\(_2\)CBPin); 3.86 (3H, s, OCH\(_3\)); 6.81 (1H, d, J = 7.6 Hz, HCCC(Ar)CBPin); 6.89 (2H, d, J = 8.6 Hz Ar-H); 7.04-7.10 (1H, m, Ar-H); 7.12-7.20 (4H, m, Ar-H); \(^{13}\)C\(^{1}\)H\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta\) 23.5, 25.2, 27.0, 54.3, 82.1, 112.1, 125.1, 125.4, 126.2, 126.3, 130.0, 132.8, 135.0, 136.6, 147.0, 157.7; \(^{11}\)B NMR (128.4 MHz, CDCl\(_3\)): \(\delta\) 30.9 (s); [ESI-MS] ([M+H]\(^{\text{+}}\) 70% 361.2 gmol\(^{-1}\); ([M+Na]\(^{+}\) 50% 385.3 gmol\(^{-1}\); [Acc. Mass]: 385.194 gmol\(^{-1}\) [M+Na]\(^{+}\]

2-(6-methoxy-1-phenyl-3,4-dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.31

[Diagram of 2.31]

Prepared according to general procedure C. 2.15 (38 mg, 0.161 mmol, 1 eq.) and [Cl\(_2\)B(2-DMAP)][AlCl\(_4\)] (60 mg, 0.161 mmol, 1 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (40 mg, 0.338 mmol, 2.1 eq.)
and excess triethylamine in DCM. The mixture was purified via column chromatography (50% dichloromethane in petroleum ether 40-60) to give 2.31 (33 mg, 57%) as a colourless oil.

\[^1\text{H}\] NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 1.10 (12H, s, Bpin); 2.48 (2H, t, J = 7.7 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 2.81 (2H, t, J = 7.7 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 3.80 (3H, s, OC\textsubscript{6}H\textsubscript{3}); 6.59 (1H, d, J = 8.6 Hz, Ar-H); 6.69-6.78 (2H, m, Ar-H); 7.20-7.26 (2H, m, Ar-H); 7.29-7.37 (3H, m, Ar-H);

\[^{13}\text{C}\{^1\text{H}\}]\) NMR (100.6 MHz, CDCl\textsubscript{3}): \(\delta\) 26.1, 55.2, 83.0, 110.8, 113.2, 126.8, 127.6, 128.0, 129.3, 129.8, 139.5, 141.6, 148.6, 158.9; \[^{11}\text{B}\] NMR (128.4 MHz, CDCl\textsubscript{3}): \(\delta\) 30.8 (s); GC-MS: m/z calculated for C\textsubscript{23}H\textsubscript{27}BO\textsubscript{4}, 362.2; found 362.2. GC-MS retention times of analytes: 16.86 minutes 2-(6-methoxy-1-phenyl-3,4-dihydmoronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass]: [(M+H)]\+ 363.2246 gmol\(^{-1}\)

2-(6-chloro-1-phenyl-3,4-dihydmoronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.32

Prepared according to general procedure C. 2.16 (50 mg, 0.208 mmol, 1 eq.) and [Cl\textsubscript{2}B(2-DMAP)][AlCl\textsubscript{4}] (80 mg, 0.208 mmol, 1 eq.) were stirred in DCM and heated in a sealed tube in a 60°C oil bath for 2.5 h. The reaction mixture was cooled and transferred to a cooled solution of pinacol (54 mg, 0.458 mmol, 2.2 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.32 (63 mg, 83%) as a colourless oil.

\[^1\text{H}\] NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 1.09 (12H, s, Bpin); 2.47 (2H, t, J = 7.8 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 2.81 (2H, t, J = 7.8 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 6.70 (1H, d, J = 8.3 Hz, Ar-H (meta to Cl)); 6.93 (1H, dd, J = 8.3 Hz, 2.3 Hz, Ar-H (ortho to Cl, meta to new C-C bond)); 7.08 (1H, d, J = 2.3 Hz, Ar-H (ortho to Cl and alkyl chain); 7.11-7.15 (2H, m, Ar-H); 7.22-7.29 (3H, m, Ar-H); \(^{13}\text{C}\{^1\text{H}\}]\) NMR (100.6 MHz, CDCl\textsubscript{3}): \(\delta\) 24.5, 25.9, 27.9, 83.2, 126.1, 127.1, 127.3, 127.7, 127.8, 129.8, 132.8, 134.3, 139.3, 140.9, 147.6; \[^{11}\text{B}\] NMR (128.4 MHz, CDCl\textsubscript{3}): \(\delta\) 29.1 (s); GC-MS: m/z calculated for C\textsubscript{22}H\textsubscript{24}BO\textsubscript{2}Cl, 366.1; found 366.1 - GC-MS retention
times of analytes: 16.46 minutes (2-(6-chloro-1-phenyl-3,4-dihyronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane); [Acc. Mass]: ([M+H]$^+$ 367.1647 g mol$^{-1}$). Mass reported involves $^{35}$Cl isotope.

4,4,5,5-tetramethyl-2-(1-methyl-3,4-dihyronaphthalen-2-yl)-1,3,2-dioxaborolane 2.37

Prepared according to general procedure B. 2.33 (31 mg, 0.215 mmol, 1 eq.), 2,4,6-tri-tert-butylpyridine (53 mg, 0.215 mmol, 1 eq.) and boron trichloride (0.47 mL, 0.47 mmol, 2.2 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (28 mg, 0.237 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via washing with 6M aqueous HCl and extraction into pentane. The pentane solution was dried over MgSO$_4$ and filtered and the solvent removed in vacuo to give 2.37 (39 mg, 67%) as a colourless oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.34 (12H, s, Bpin); 2.31-2.40 (5H, overlapped singlet and triplet); 2.68 (2H, t, J = 7.5 Hz, CH$_2$CH$_2$CBPin); 7.12-7.26 (3H, m, Ar-H); 7.39 (1H, br d, J = 7.6 Hz, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 18.1, 24.9, 25.8, 28.2, 83.1, 123.9, 126.2, 127.1, 127.4, 136.6, 138.1, 145.0; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.6 (s); [GC-MS] m/z calculated for C$_{17}$H$_{23}$BO$_2$, 270.2; found 270.1 - GC-MS retention times of analytes: 13.6 minutes 4,4,5,5-tetramethyl-2-(1-methyl-3,4-dihyronaphthalen-2-yl)-1,3,2-dioxaborolane; [Acc. Mass]: ([M]$^+$ 270.1775 g mol$^{-1}$)

2-(1-bromo-3,4-dihyronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 2.39

Prepared according to general procedure A. 2.34 (100mg, 0.478 mmol, 1 eq.) and boron trichloride (0.62 mL, 0.620 mmol, 1.3 eq.) were stirred in DCM for 20 minutes. The reaction mixture was transferred to a cooled solution of pinacol (62 mg, 0.53 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.39 (55 mg, 34%) as a brown oil.
1H NMR (400 MHz, CDCl₃): δ 1.37 (12H, s, Bpin); 2.44 (2H, t, J = 7.9 Hz, CH₂CH₂CBPin); 2.78 (2H, t, J = 7.9 Hz, CH₂CH₂CBPin); 7.10 (1H, d, J = 7.6 Hz, HCC(C(Br)CBPin); 7.17-7.28 (2H, m, Ar-H); 7.69 (1H, dd, J = 7.6 Hz, 1.3 Hz, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.8, 27.6, 28.3, 84.0, 126.7, 127.0, 127.5, 128.7, 133.8, 137.6; ¹¹B NMR (128.4 MHz, CDCl₃): δ 30.4 (s); [GC-MS] m/z calculated for C₁₆H₂₀BrBO₂, 334.1; found 334.1 GC-MS retention times of analyte: 14.66 minutes (2-(1-bromo-3,4-dihydronaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane); [Acc. Mass]: (334.0722 gmol⁻¹ [M]+). Mass reported involves ⁷⁹Br isotope.

(E)-4,4,5,5-tetramethyl-2-(1-styryl-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane 2.40

Prepared according to general procedure B. 2.35 (34 mg, 0.146 mmol, 1 eq.), 2,4,6-tri-tert-butylpyridine (36 mg, 0.146 mmol, 1 eq.) and boron trichloride (0.32 mL, 0.32 mmol, 2.2 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (19 mg, 0.16 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (graduating 10% dichloromethane in petroleum ether 40-60 to 20% dichloromethane in petroleum ether 40-60) to give 2.40 (28 mg, 54%) as a light yellow film.

1H NMR (400 MHz, CDCl₃): δ 1.33 (12H, s, Bpin); 2.41 (2H, t, J = 7.6 Hz, CH₂CH₂CBPin); 2.69 (2H, t, J = 7.6 Hz, CH₂CH₂CBPin); 6.77 (1H, d, J = 16.4 Hz, RC(H)=C(H)Ph); 7.21-7.25 (3H, m, Ar-H); 7.25-7.29 (1H, m, Ar-H); 7.36 (2H, t, J = 7.5 Hz); 7.47-7.52 (2H, m, Ar-H); 7.53-7.58 (1H, m, Ar-H); 7.74 (1H, d, J = 16.4 Hz, RC(H)=C(H)Ph); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.9, 26.3, 28.3, 83.4, 126.0, 126.5, 126.5, 127.3, 127.4, 127.6, 128.6, 128.6, 132.4, 134.4, 138.0, 139.1, 147.3; ¹¹B NMR (128.4 MHz, CDCl₃): δ 31.0 (s); GC-MS: m/z calculated for C₂₄H₂₂BO₂, 358.2; found 358.2. GC-MS retention times of analytes: 17.72 minutes ((E)-4,4,5,5-tetramethyl-2-(1-styryl-3,4-dihydronaphthalen-2-yl)-1,3,2-dioxaborolane; [Acc. Mass]: 359.2128 gmol⁻¹ [M+H]⁺)
2-(3,4-dihydro-[1,1'-binaphthalen]-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

2.41

Prepared according to general procedure B. 2.36 (68 mg, 0.265 mmol, 1 eq.), 2,4,6-tri-tert-butylpyridine (66 mg, 0.265 mmol, 1 eq.) and boron trichloride (0.58 mL, 0.58 mmol, 2.2 eq.) were stirred in DCM for 30 minutes. The reaction mixture was transferred to a cooled solution of pinacol (35 mg, 0.292 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (30% dichloromethane in petroleum ether 40-60) to give 2.41 (76 mg, 75%) as a white solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.74 (6H, s, Bpin); 0.86 (6H, s, Bpin); 2.52-2.73 (2H, m, CH$_2$CH$_2$CBpin); 2.88-3.04 (2H, m, CH$_2$CH$_2$CBpin); 6.59 (1H, d, J = 7.7 Hz, Ar-H); 6.95 (1H, t, J = 7.5 Hz, Ar-H); 7.15 (1H, t, J = 7.3 Hz, Ar-H); 7.23 (1H, d, J = 7.3 Hz, Ar-H); 7.31-7.38 (2H, m, Ar-H); 7.43 (1H, t, J = 7.3 Hz, Ar-H); 7.49 (1H, t, J = 7.5 Hz, Ar-H); 7.76 (1H, d, J = 8.4 Hz, Ar-H); 7.84 (2H, t, J = 8.6 Hz, Ar-H); $^{13}$C{$^1$H} NMR (100.6 MHz, CDCl$_3$): $\delta$ 24.2, 26.0, 28.0, 82.8, 125.2, 125.4, 125.7, 126.4, 126.4, 127.1, 127.3, 127.5, 127.9, 133.3, 133.51, 136.0, 137.0, 139.1, 146.9; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 30.8 (s); [GC-MS] m/z calculated for C$_{28}$H$_{27}$BO$_2$, 382.2; found 382.2 - GC-MS retention times of analytes: 17.89 minutes 2-(3,4-dihydro-[1,1'-binaphthalen]-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass]: ([M]$^+$ 382.2105 gmol$^{-1}$)
2.3.4 – Borylated Heterocycles

4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosyl-1,2-dihydroquinoline 2.43

Prepared according to general procedure A. 2.42 (67 mg, 0.185 mmol, 1 eq.) and boron trichloride (0.2 mL, 0.203 mmol, 1.1 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (24 mg, 0.203 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (25% 40-60 petroleum ether in DCM) to give 2.43 (67 mg, 74%) as an orange solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.08 (12H, s, Bpin); 2.38 (3H, s, SO$_2$Ar-CH$_3$); 4.63 (2H, s, NCH$_2$C-Bpin); 6.45-6.49 (2H, m, Ar-H); 6.66 (1H, dd, J = 7.8 Hz, 1.5 Hz, Ar-H); 7.05-7.11 (3H, m, Ar-H); 7.13-7.19 (2H, m, Ar-H); 7.20-7.26 (1H, m, Ar-H); 7.32 (1H, td, J = 7.6 Hz, 1.6 Hz, Ar-H); 7.41 (2H, d, J = 8.3 Hz, Ar-H); 7.80 (1H, dd, J = 8.1 Hz, 1.0 Hz, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 21.4, 24.5, 47.6, 83.3, 126.3, 127.0, 127.1, 127.1, 127.8, 128.7, 129.1, 129.5, 131.5, 135.9, 136.8, 138.6, 143.2, 147.9; $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 29.9 (s); [ESI-MS] ([M+H]$^+$ 20% 488.4 gmol$^{-1}$); ([M+NH$_4$]$^+$ 50% 505.4 gmol$^{-1}$); ([M+Na]$^+$ 50% 510.4 gmol$^{-1}$); ([M+K]$^+$ 50% 547.5 gmol$^{-1}$); [Acc. Mass]: (510.1911 gmol$^{-1}$ [M+Na]$^+$)

4,4,5,5-tetramethyl-2-(4-(perfluorophenyl)-2H-chromen-3-yl)-1,3,2-dioxaborolane 2.46

Prepared according to general procedure A. 2.45 (400 mg, 1.34 mmol, 1 eq.) and boron trichloride (1.5 mL, 1.5 mmol, 1.1 eq.) were stirred in DCM for 15 minutes. The reaction mixture was transferred to a cooled solution of pinacol (175 mg, 1.5 mmol, 1.1 eq.) and excess triethylamine in DCM. The resulting crude product was purified via column chromatography (50% dichloromethane in 40-60 petroleum ether) to give 2.46 (440 mg, 77%) as a colourless oil.
Prepared according to general procedure C, 2.45 (30 mg, 0.1 mmol) and [Cl₂B(2-DMAP)][AlCl₄] (37.5 mg, 0.1 mmol) were stirred in DCM (1mL) for 10 minutes after complete dissolution of the boronium salt. The reaction mixture was transferred to a cooled solution of pinacol (25 mg, 0.21 mmol) and excess triethylamine in DCM. The mixture was filtered through a silica plug to give 2.46 (42 mg, 60%) as a colourless oil.

1H NMR (400 MHz, CDCl₃): δ 1.15 (12H, s, BPin), 4.98 (2H, OC₆H₄C(Bpin)C(C₆F₅)), 6.67 (1H, d, J = 7.8 Hz, HCCC(Ar)CBPin), 6.71-7.24 (1H, m, Ar-H); 13C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.6, 67.2, 83.7, 116.5, 121.5, 122.5, 125.3, 131.1, 133.6, 155.3; ¹⁹F NMR (376.50 MHz, CDCl₃): δ -163.55 (2F, td, J = 23.2Hz, 6.1Hz, Ar-F); -155.82 (1F, t, J = 20.8Hz, Ph(C₄-F); -140.16 (2F, dd, J = 23.2Hz, 8.2 Hz, Ar-F); ¹¹B NMR (128.4 MHz, CDCl₃): δ 29.1 (s); [ESI-MS] ([M] -100% 424.3 gmol⁻¹); [Acc. Mass]: 424.1253 gmol⁻¹ [M+H]⁺

9-bromo-4-hexyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolo[1,2-a]quinoline 2.51

In a J Young’s NMR tube, 2.50 (10 mg, 0.0302 mmol, 1 eq.) and TBP (7.5 mg, 0.0302 mmol, 1 eq.) were dissolved in DCM (0.5 mL). BCl₃ (0.063 mL, 0.063 mmol, 2.1 eq.) was added. After 45 minutes, the reaction mixture was transferred to a cooled solution of pinacol (4 mg, 0.0332 mmol, 1.1 eq.) and excess triethylamine in DCM. The mixture was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.51 (8 mg, 58%) as a colourless oil.

1H NMR (400 MHz, CDCl₃) δ 0.91 (3H, m, CCCH₂(CH₂)₄CH₃); 1.34 (4H, m, hexyl-H); 1.46 (2H, m, hexyl-H); 1.46 (12H, s, Bpin); 1.74 (2H, m, hexyl-H); 2.93 (2H, m, CCCH₂(CH₂)₄CH₃); 6.69 (1H, dd, J = 3.8, 1.5 Hz, Pyrr-H); 6.77 (1H, m, Pyrr-H); 7.09 (1H, t, J = 7.9 Hz, Ar-H (para to pyrrole)); 7.68 (1H, dd, J = 7.9, 1.5 Hz, Ar-H); 7.90 (1H, dd, J = 7.9, 1.5 Hz, Ar-H); 9.32 (1H, dd, J = 3.0, 1.5 Hz); ¹³C{¹H} NMR (100.06 MHz, CDCl₃): δ 14.1, 22.7, 25.1, 30.0, 30.9, 31.8, 33.2, 84.0, 102.7, 108.9, 111.3, 119.3, 123.8, 128.1, 130.5, 130.7, 132.8, 133.4,
140.5 ; \textsuperscript{11}B NMR (128.4 MHz, CDCl\textsubscript{3}): $\delta$ 32.2 (s); [GC-MS] m/z calculated for C\textsubscript{24}H\textsubscript{31}BBrNO\textsubscript{2}, 455.2; found 455.2. GC-MS retention times of analyte: 24.91 minutes (9-bromo-4-hexyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolo[1,2-a]quinoline); [Acc. Mass]: ([M]\textsuperscript{+} 455.1635 gmol\textsuperscript{-1}). Mass reported involves \textsuperscript{79}Br isotope.

2.3.5 – Further Reactivity – Cross Coupling, Oxidation and Boracycle Formation

3-(p-tolyl)-4-(3-(trifluoromethyl)phenyl)-1,2-dihydronaphthalene 2.54

Adapted from a previously reported procedure.\textsuperscript{[25]}

2.21 (150 mg, 0.375 mmol, 1 eq.) and tri-tert-butylphosphine (16 mg, 0.075 mmol, 0.2 eq.) were dissolved in THF (10 mL), and 3M NaOH (375 µL), 4-bromotoluene (64 mg, 0.375 mmol, 1 eq.) and Pd\textsubscript{2}(dba)\textsubscript{3} (18 mg, 0.0187 mmol, 0.05 eq.) added. The resulting mixture was refluxed under nitrogen in a Schlenk with water condenser attached for 12 h. The reaction was quenched with aqueous NH\textsubscript{4}Cl (25 mL) and extracted with ether (3 x 20 mL). The organic layer was washed with water (2 x 25 mL) and dried over MgSO\textsubscript{4}. The solvent was removed \textit{in vacuo}. The resulting crude oil was purified via column chromatography (5% dichloromethane in petroleum ether 40-60) to give 2.54 (89 mg, 75%) as a white solid.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): $\delta$ 2.30 (3H, s, Ar-CH\textsubscript{3}); 2.86 (2H, t, J = 7.7 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 3.05 (2H, t, J = 7.7 Hz, CH\textsubscript{2}CH\textsubscript{2}CBPin); 6.74 (1H, d, J = 7.8 Hz, Ar-H); 6.92 (2H, d, J = 8.3 Hz, Ar-H); 6.98 (2H, d, J = 8.3 Hz, Ar-H); 7.13 (1H, td, J = 7.6 Hz, 1.5 Hz, Ar-H); 7.22 (1H, td, J = 7.3 Hz, 1.3 Hz, Ar-H); 7.26-7.32 (2H, m, Ar-H); 7.38 (1H, t, J = 7.6 Hz, Ar-H); 7.44 (1H, br s, Ar-H); 7.52 (1H, d, J = 7.8 Hz, Ar-H); \textsuperscript{13}C\textsuperscript{1}H NMR (100.6 MHz, CDCl\textsubscript{3}): 21.1, 28.4, 30.9, 123.3 (q, $^3$J\textsubscript{C-F} = Hz 3.9 Hz HCCC\textsubscript{F}; 124.2 (q, $^1$J\textsubscript{C-F} = 272.0 Hz, CF\textsubscript{3}) 125.8, 126.5, 127.1, 127.3, 128.1 (q, $^3$J\textsubscript{C-F} = Hz 3.9 Hz HCCC\textsubscript{F}), 128.1, 128.5, 128.6, 130.4 (q, $^2$J\textsubscript{C-F} = 31.9 Hz, HCCC\textsubscript{F}), 134.0, 134.7, 135.8, 136.1, 136.5, 138.6, 139.3, 140.8; \textsuperscript{19}F NMR (376.50 MHz, CDCl\textsubscript{3}): $\delta$ -62.54 (s, CF\textsubscript{3}); GC-MS: m/z calculated for C\textsubscript{24}H\textsubscript{19}F\textsubscript{3}, 364.1; found 364.2 - GC-MS retention times of analytes: minutes 3-
Adapted from a previously reported procedure \cite{58}
dihydronaphthalene 4 (12 mg, 0.0329 mmol, 1 eq.) and [Ph₃C][BF₄] (37 mg, 0.112 mmol, 3.4 eq.) were dissolved in 1,2-dichloroethane (DCE) and refluxed in a sealed vessel at 90°C for 3 h. The mixture was then concentrated in vacuo and extracted into pentane. The resulting crude product was purified via preparative Thin Layer Chromatography (TLC) SiO₂ plate (5% dichloromethane in petroleum ether 40-60) to give the corresponding naphthalene (9 mg, 75%) as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 2.30 (3H, s, Ar-C₃H₃); 6.97- 7.04 (4H, m, Ar-H); 7.34-7.48 (3H, m, Ar-H); 7.49-7.61 (5H, m, Ar-H); 7.93-7.99 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 21.1, 123.5 (q, ³J_C-F = 3.7 Hz HCCCF₃); 128.4, 128.5, 128.9, 130.2 (q, ²J_C-F = 32.2 Hz, CCF₃); 132.3, 132.7, 134.75, 134.76, 135.8, 136.2, 138.4, 138.8, 140.1; ¹⁹F NMR (376.50 MHz, CDCl₃): δ -62.58 (s, CF₃); GC-MS: m/z calculated for C₂₄H₁₇F₃, 362.1; found 362.1 - GC-MS retention times of analytes: 15.56 minutes (2-(p-tolyl)-1-(3-(trifluoromethyl)phenyl)naphthalene); [Acc. Mass]: ([M+H]⁺ 363.1349 gmol⁻¹)

4,4,5,5-tetramethyl-2-(1-(3-(trifluoromethyl)phenyl)naphthalen-2-yl)-1,3,2-dioxaborolane 2.56

Borylated dihydronaphthalene 2.21 (90 mg, 0.247 mmol, 1 eq.), [Ph₃C][BF₄] (106 mg, 0.321 mmol, 1.3 eq.) and tri-tert-butylpyridine (61 mg, 0.247 mmol, 1 eq.) were dissolved in 1,2-dichloroethane (DCE) and stirred for 12 h. The mixture was then concentrated in vacuo and extracted into pentane. The resulting crude product was purified via column chromatography (20% dichloromethane in petroleum ether 40-60) to give 2.56 (83 mg, 93%) as a colourless oil.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.14 (12H, s, Bpin); 7.38-7.45 (1H, m, Ar-H); 7.48-7.59 (4H, m, Ar-H); 7.64 (1H, s, Ar-H); 7.67-7.73 (1H, m, Ar-H); 7.85 (1H, d, J = 8.32 Hz, Ar-H); 7.88-7.93 (2H, m, Ar-H); $^{13}$C$^1$H NMR (100.6 MHz, CDCl$_3$): $\delta$ 24.54, 83.6, 123.7 (q, $^3$J$_{C-F}$ = 3.7 Hz, HCCF$_3$), 124.4 (q, $^3$J$_{C-F}$ = 272.0 Hz, CF$_3$-), 126.1, 126.6, 126.7, 127.1, 127.4 (q, $^3$J$_{C-F}$ = 3.7 Hz, HC-CCF$_3$), 127.8, 128.1, 129.9 (q, $^2$J$_{C-F}$ = 31.9 Hz, CCF$_3$), 130.1, 131.8, 133.8, 142.0, 145.3; $^{19}$F NMR (376.50 MHz, CDCl$_3$): $\delta$ -62.40 (s, CCF$_3$); $^{11}$B NMR (128.4 MHz, CDCl$_3$): $\delta$ 31.2 (s); GC-MS: m/z calculated for C$_{23}$H$_{22}$BF$_3$O$_2$, 398.2; found 398.2; GC-MS retention times of analytes: 12.88 minutes (4,4,5,5-tetramethyl-2-(1-(3-(trifluoromethyl)phenyl)naphthalen-2-yl)-1,3,2-dioxaborolane); [Acc. Mass]: ([M+H]$^+$ 399.1732 gmol$^{-1}$)

7-mesityl-8,9-dihydro-7H-dinaphtho[1,8-bc:1’,2’-e]borinine 2.57

Alkyne 2.36 (82 mg, 0.325 mmol, 1 eq.) and TBP (80 mg, 0.325 mmol, 1 eq.) were dissolved in DCM (1 mL) in an ampoule. BCl$_3$ (0.68 mL, 0.680 mmol, 2.1 eq.) was added and the reaction was stirred for an hour before adding AlCl$_3$ (43 mg, 0.325 mmol, 1 eq.). The solvent was removed in vacuo and 2,6-dichloropyridine (48 mg, 0.325 mmol, 1 eq.) was added. The solids were redissolved in DCM (1 mL), and AlCl$_3$ (43 mg, 0.325 mmol, 1 eq.) was added, leading to a deep green solution. The solvent was removed in vacuo and the resulting solid was suspended in toluene (2 mL). Copper(I) mesitylene (233 mg, 1.280 mmol, 4 eq.) was added and the reaction mixture was heated at 90°C for one hour. The solvent was removed in vacuo, and the solid was extracted into pentane (3 x 10 mL). The organic extract was concentrated in vacuo. Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 2.57 (102 mg, 83%) was obtained as a bright yellow solid that fluorescent green under UV light.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.04 (6H, s, (CH$_3$)$_2$Ph(CH$_3$)); 2.40 (3H, s, (CH$_3$)$_2$Ph(CH$_3$)); 2.50 (2H, br t, J = 7.0 Hz, BC-CH$_2$CH$_2$Ph); 2.73 (2H, t, J = 7.0 Hz, J = 7.0 Hz, BC-CH$_2$CH$_2$Ph); 6.93 (2H, s, Ar-H); 7.19-7.34 (3H, m, Ar-H); 7.62-7.67 (1H, m, Ar-H); 7.67-7.74 (2H, m, Ar-H); 8.08-8.13 (2H, m, Ar-H); 8.28 (1H, dd, J = 8.1 Hz, 1.3 Hz, Ar-H); 8.38 (1H, dd, J = 7.3 Hz, 1.0 Hz, Ar-H); $^{13}$C
NMR (100.6 MHz, CDCl₃): δ 21.9, 35.0, 78.3, 95.2, 123.7, 126.3, 126.4, 128.5, 128.6, 128.7, 129.2, 133.4, 135.8, 140.6; ¹¹B NMR (128.4 MHz, CDCl₃): δ 58.5 (br s); GC-MS: m/z calculated for C₉₉H₂₂₅B, 384.2; found 384.2. GC-MS retention times of analytes: 31.74 minutes: 7-mesityl-8,9-dihydro-7H-dinaphtho[1,8-bc1',2'-e]borinine; [Acc. Mass]: [M+H]+ 385.2133 gmol⁻¹

7-mesityl-7H-dinaphtho[1,8-bc1',2'-e]borinine 2.58

In a J. Young’s NMR tube, 2.57 (15 mg, 0.0390 mmol), [Ph₃C][BF₄] (16 mg, 0.0485 mmol) and TBP (12 mg, 0.0485 mmol) were dissolved in 1,2-dichloroethane (DCE) (0.5 mL) and heated at 80°C for 18 hours. Following this, the solvent was removed in vacuo and the crude product was extracted into pentane and concentrated in vacuo. The resulting solid was heated at 85°C at reduced pressure, to remove the triphenylmethane impurity via sublimation. The remaining yellow solid was purified via preparative Thin Layer Chromatography (prep. TLC) using 20% DCM in petroleum ether 40-60 as an eluent to give 7-mesityl-7H-dinaphtho[1,8-bc1',2'-e]borinine 2.58 as a yellow solid (11 mg, 74%).

¹H NMR (400 MHz, CDCl₃): δ 2.00 (6H, s, (CH₃)₂Ph(CH₃)); 2.44 (3H, s, (CH₃)₂Ph(CH₃)); 6.98 (2H, s, Ar-H); 7.61-7.67 (2H, m, Ar-H); 7.70-7.85 (4H, m, Ar-H); 7.95-8.00 (1H, m, Ar-H); 8.13 (1H, d, J = 7.6 Hz, Ar-H); 8.20 (1H, dd, J = 6.8 Hz, 1.5 Hz, Ar-H); 8.34 (1H, dd, J = 8.1 Hz, 1.3 Hz, Ar-H); 8.67 (1H, d, J = 7.6 Hz, Ar-H); 8.70-8.76 (1H, m, Ar-H); ¹³C NMR (100.6 MHz, CDCl₃): δ 21.4, 23.4, 125.2, 125.7, 126.2, 126.7, 126.9, 127.1, 128.4, 130.4, 130.5, 130.7, 131.1, 132.5, 132.6, 132.7, 133.7, 136.1, 136.8, 137.9, 139.0, 141.5, 143.8; ¹¹B NMR (128.4 MHz, CDCl₃): Not observed; GC-MS: m/z calculated for C₂₉H₂₂₅B, 382.2; found 382.2. GC-MS retention times of analytes: 22.93 minutes: 7-mesityl-7H-dinaphtho[1,8-bc1',2'-e]borinine; [Acc. Mass]: [M]+ 382.1878 gmol⁻¹
2.3.6 – Intermolecular 1,2-Trans-Carboboration

(Z)-4,4,5,5-tetramethyl-2-(1-(5-methylthiophen-2-yl)-1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane 2.59

1-phenyl-1-propyne (36 µL, 1 eq. 0.2 mmol) and 2,4,6-tri-tert-butylpyridine (50 mg, 1 eq., 0.2 mmol) were dissolved in DCM. 2-methylthiophene (19 µl, 1 eq., 0.2 mmol) and BCl₃ (420 µl, 2.1 eq. 0.42 mmol) were then added. After 18 hours, the mixture was added to a cooled solution of excess triethylamine and pinacol (24 mg, 1 eq. 0.2 mmol) in DCM. The mixture was purified via column chromatography (50% dichloromethane in 40-60 petroleum ether) to give 2.59 as a yellow oil (28 mg, 41%).

¹H NMR (400 MHz, CDCl₃) δ 1.08 (12H, s, Bpin); 2.14 (3H, s, C=C(CH₃)Bpin); 2.46 (3H, s, H₃C-thiophene); 6.66 (2H, s, thiophene-C₂,₄-H coincident singlet due to second order effects in the BCl₂ complex prior to pinacol protection these resonances are inequivalent and visible as two doublets); 7.27 (5H, s, Ar-H); 13C{¹H} NMR (100.06 MHz, CDCl₃) δ 15.4, 19.3, 24.5, 83.2, 124.8, 127.2, 127.7, 128.6, 129.6, 140.7, 142.1, 144.0, 144.7; ¹¹B NMR (128.4 MHz, CDCl₃): δ 31.1 (s); GC-MS: m/z calculated for C₂₀H₂₅BO₂S, 340.1; found 340.1; GC-MS retention times of analytes: 14.71 minutes ((Z)-4,4,5,5-tetramethyl-2-(1-(5-methylthiophen-2-yl)-1-phenylprop-1-en-2-yl)-1,3,2-dioxaborolane); [Acc. Mass]: ([M]⁺ 340.1662 gmol⁻¹)

NOE spectroscopy: Irradiation at 7.27 ppm (Ar-H) produced enhancement at 2.46 (H₃C-thiophene); Irradiation at 2.04 ppm (C=C(CH₃)Bpin) produced enhancements at 0.99 ppm (Bpin) and 6.57 (thiophene-C₂,₄-H);
### 2.3.7 – Crystal Data

Crystal structure of 2.22, CCDC No: 1408578

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Crystal structure of 2.57, CCDC No: 1537995

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2.4.0 – References

1. Legha, S. S; Slavik, M.; Carter, S. K. *Cancer*, 1976, 38, 1535
30. _Friedel Crafts Chemistry_, Wiley, Hoboken, **1973**
57. Xu, G.; Li, X.; Sun, H. J. Org. Chem., 2011, 696, 3011
Chapter 3:
Borylative Cyclisation of 2-Alkynylanisoles and 2-Alkynylthioanisoles
3.1.0 – Introduction

Heteroaromatic scaffolds such as benzofurans, benzothiophenes and indoles are prevalent in the pharmaceutical sector, found in a variety of drugs (Figure 1) including those with anti-arrhythmic,[1] anti-cancer,[2] selective estrogen receptor modulator,[3] anti-hyperglycemic[4] and anti-viral[5] applications.

Figure 1 – Three examples of pharmaceuticals involving a benzofuran (left), benzothiophene (middle) and indole (right) scaffold.

With these oxygen, sulphur and nitrogen heterocycles so ubiquitous across a number of applications, numerous investigations into their synthesis have been reported, including transition metal catalysed reactions[6-10] and main-group initiated cyclisations.[11-12] This introduction however, will focus specifically on the generation of borylated heterocycles via the electrophilic cyclisation of 2-alkynylanisoles, 2-alkynythioanisoles and 2-alkynylanilines initiated by boron electrophiles proceeding through 1,2-elementoborations across the triple bond. Firstly, a few examples of these transformations involving transition metal catalysis to give borylated cycles will be explored, followed by transformations initiated purely by boron electrophiles. For a more in-depth overview of borylative cyclisation, see the recent reviews from Cardenas[13] and Melen.[14]

3.1.1 – Select Transition Metal Catalysed 1,2-Elementoboration of Alkynes

Harrity et al. developed a palladium catalysed synthesis of 3-borylated indoles via Pd initiated cyclisation and then a Miyaura type borylation, utilising 2-alkynylaniline derivatives and B$_2$Pin$_2$.[15] It was discovered during optimisation of the reaction that Ph$_3$As was necessary as an additive to preclude the formation of 3H-indole as the major product through a hypothesised palladium catalysed hydroamination.[16] Interestingly, it was later observed that the conditions
employed for borylative cyclisation additionally catalysed the protodeborylation of the newly formed 3-borylated indole.[17] Addressing this, a diboron reagent reported by Suginome,[19] pinB-Bdan, was utilised in the interest of generating more stable borylated indoles. The use of this diboron reagent led to 3-Bdan substituted indoles, which were shown to be much more stable towards protodeborylation than the previously reported pinacol boronate esters (Scheme 1).

Scheme 1 – Highlighting the difference in quantity of protodeborylation of the 3-borylated indoles based on the diboron reagent used.[17]

Building on Larock’s work in the area using main group electrophiles,[11-12] Blum and co-workers reported a gold catalysed electrophilic cyclisation to generate borylated benzofurans from 2-alkynylphenols and B-chlorocatecholborane (CatBCl) with a linear gold-NHC complex, IPrAuCl, in the presence of sodium trifluoroacetate (NaTFA) (Scheme 2).[19]

Scheme 2 – General reaction scheme for Blum’s work using bifunctional gold catalysis to generate 3-borylated benzofurans.[19]

The initial alkynyl phenol is converted to the corresponding boric ester before addition of the catalyst. The NaTFA was utilised to convert the IPrAuCl catalyst into a bifunctional Lewis acid/Lewis base catalyst, IPrAuTFA, in which the Lewis
acidic gold moiety activates the alkyne to generate a suitable electrophile, whilst the TFA converts the electrophilic boric ester into a nucleophilic borate. Nucleophilic attack by the phenolic B-O bond on the activated alkyne then generates two neutral species, the electrophilic CatBTFA and the nucleophilic organogold species. These species react together, releasing the CatB-benzofuran and regenerating the bifunctional catalyst (Scheme 4, $X = O$). The CatB-benzofuran derivatives were subsequently converted to organotrifluoroborates (RBF$_3$K) and N-methyliminodiacetic acid (MIDA) boronates to generate air-stable products. The following year, Blum applied this chemistry to the generation of a variety of borylated indoles through methodology adapted from that of the benzofuran synthesis (Scheme 3).[20] Secondary amines were found to undergo deprotonation with a weaker base, NEt$_3$, than previously required for the phenols.

![Scheme 3](image)

Scheme 3 – General reaction scheme for Blum’s work using bifunctional gold catalysis to generate 3-borylated indoles.[20]

CatBCl was again employed to generate the initial borane after initial attempts with simple CatBH resulted in moderate yields due to the degradation of the boron reagent via ligand redistribution to give Cat$_3$B$_2$.[21] Although proposed to proceed via the same mechanistic pathway (Scheme 4, $X = NR$), it was observed that the reaction did not work with just IPrAuTFA alone, and that the NaTFA additive was required, presumably to overcome catalyst inhibition by the [HNEt$_3$][Cl] generated during the B-N forming step.

Whilst notable, these reports and others require the use of precious metal catalysts and the ability to perform borylative cyclisation initiated by a simple boron electrophile is more attractive.
Scheme 4 – Proposed catalytic cycle of the bifunctional gold catalysis mechanism to generate 3-borylated benzofurans and indoles \((X = O\) or \(NR\)).\(^{19-20}\)

3.1.2 – 1,2-Elementoboration of Alkynes Using Boron Electrophiles

An early example of a 1,2-elementoboration of an alkyne comes from Stephan\(^{22}\) utilising \(N,N\)-dimethylanilines with an adjacent prop-2-ene group, in which the utilisation of BCF resulted in a 5-exo-trig cyclisation to generate a zwitterionic indolinium with an external methyl-B(C\(_6\)F\(_5\))\(_3\) moiety (Scheme 5, top left). This was also applied to four different substrates: 2-(but-3-ene)aniline (Scheme 5, top right), \(o\)-(2-prop-2-eny1)-\(N,N\)-dimethylbenzylamine (Scheme 5, bottom left), \(o\)-(pent-1-ynyl)-\(N,N\)-dimethyltoluidine and \(o\)-(phenylethynyl)-\(N,N\)-dimethyltoluidine (Scheme 5, bottom right). The former two reagents proceeded via a 6-exo-trig cyclisation, generating a tetrahydroquinolinium and a tetrahydroisoquinolinium respectively, each with methyl borates. The latter two
proceeded via a 5-endo-dig cyclisation to generate zwitterionic 3-borylated indolium species.

\[
\begin{align*}
\text{Me}_2\text{N}^- & \quad \text{BCF} \quad \text{5-exo-trig} \\
[\text{C}_8\text{F}_5]_3\text{B} & \quad \text{Indolinium borate} \\
\text{NMe}_2 & \quad \text{BCF} \quad \text{6-exo-trig} \\
\text{Me}_2\text{N}^- & \quad \text{BCF} \quad \text{6-exo-trig} \\
[\text{C}_8\text{F}_5]_3\text{B} & \quad \text{Tetrahydroisoquinolinium borate} \\
\end{align*}
\]

Scheme 5 – Synthesis of various zwitterionic N-heterocycles obtained via BCF-initiated 1,2-aminoboration of unsaturated C-C bonds.\[^{22}\]

This approach has been more recently extended by Paradies et al. in a BCF-catalysed hydroaminative method to form indoles and tetrahydroisoquinolines (Scheme 6).\[^{23}\]

\[
\begin{align*}
\text{BCF (20 mol\%)} \quad \text{H}_2 \quad (80 \text{ bar}) \\
\text{Toluene, 100}^\circ \text{C} & \quad \text{Ph} \\
\end{align*}
\]

Scheme 6 – BCF catalysed hydroamination of alkynes to form tetrahydroisoquinolines.\[^{23}\]

Stephan et al. also reported a transition metal free synthesis of borylated oxazolium products via 1,2-oxyboration of propargyl amides initiated by BCF.\[^{24}\]

Initially, tertiary amides were employed, leading to adduct formation. Heating these adducts to 45°C led to the dissociation of BCF, facilitating activation of the alkyne and subsequent 5-exo-dig cyclisation, generating zwitterionic borates in good yields (Scheme 7), in which the exocyclic alkene had exclusive Z-stereochemistry. The rates of reaction increased when the substituent adjacent to the carbonyl was more electron withdrawing, due to the diminished Lewis basicity of the carbonyl group, promoting release of the BCF group. This hypothesis was supported when
substituted aromatic groups were used, with the observed trend in the rate of reaction being $p$-NO$_2 > p$-H > $p$-OMe.

Scheme 7 – 5-exo-dig cyclisation of alkynyl amides initiated by BCF to generate zwitterionic borylated oxazolium products.$^{[24]}$

Additionally, using secondary amides resulted in no heating being required to induce the cyclisation step. Interestingly, when aryl-substituted secondary amides were employed and the reaction was heated to 45°C, the borane adducts of the corresponding oxazoles were observed, indicating that proton migration from the nitrogen could induce protodeborylation to aromatise the oxazolium (Scheme 8).

Scheme 8 – 5-exo-dig cyclisation of alkynyl amides initiated by BCF to generate zwitterionic borylated oxazolium products.$^{[24]}$

Very recently, Blum reported the transition metal free synthesis of a variety of borylated isocoumarins and 2-pyrones, formed *via* a 6-endo-dig cyclisation/1,2-oxyboration using CatBCI and 2-(alkynyl)methylbenzoates$^{[25]}$ (Scheme 9). Based on our previous work$^{[26]}$ (*see* Chapter 2), BCl$_3$ and BBr$_3$ were initially tested to induce cyclisation of 2-(ethynylphenyl)methylbenzoate, however no isocoumarin product was observed. When CatBCI was employed at 45°C, a 25% yield of desired product was observed, increasing to 75% when repeated at 100°C. The resulting RBCat species were converted to Bpin, B(OH)$_2$ and BF$_3$K to increase air/moisture stability and the ease of handling. Notably, the only regioisomer observed was the product arising from a 6-endo-dig cyclisation pathway; cyclisation *via* the alternate 5-exo-dig pathway was not observed. It is additionally interesting to note that although an increase in reactivity was
observed with an increase in temperature, BCl$_3$ was not re-examined at raised temperatures.

Scheme 9 – Reaction scheme highlighting the generation of borylated isocoumarins via 1,2-oxyboration of alkynes using CatBCl.$^{[28]}$

The reaction was shown to be tolerant of a wide variety of functional groups including esters, nitriles, aryl bromides/chlorides and thiophenes, each of which are not compatible with standard lithiation/borylation$^{[27]}$ sequences and/or Pd catalysed borylation routes.$^{[28]}$ However, it is notable that due to the reactivity of CatBCl, ethers were not tolerated, which prevents this methodology from being applied to the transition metal free synthesis of borylated benzofurans.

Scheme 10 – Reaction scheme highlighting the two proposed potential pathways to 1,2-oxyboration of alkynes.$^{[29]}$

This transformation could proceed via two different reaction pathways, which ultimately lead to the expulsion of chloromethane. Next, the oxyboration/cyclisation step would take place to generate the isocoumarin. The second, and more likely pathway (Scheme 10, bottom) is proposed to proceed
via boron mediated electrophilic cyclisation to generate an ionic species, followed by rapid demethylation to generate the isocoumarin. It was expected that the demethylation step would be much faster through pathway 2, as the formal positive charge on the oxygen atom would enhance electrophilicity of the methyl substituent. Notably, it was observed that different esters effected the outcome of the reaction, with decreases in yield observed as the bulk of the alkoxy group increased (OMe > OEt > OPr >> OtBu (0% yield when using tBu)).

Most closely related to the work in this chapter, and published concomitantly to our studies\textsuperscript{[29]} is the CatBCI induced borylative cyclisation of a variety of 2-alkynylthioanisoles, generating 3-borylated benzothiophenes in high yield (Scheme 11).\textsuperscript{[30]} A wide number of functional groups were tolerated by this reaction including esters, alkyl halides, amines, nitriles, silyl ethers and heterocycles. This represented a rare example of thioboration of alkynes, with only two notable reports published earlier.\textsuperscript{[31-32]}

![Scheme 11](image)

Scheme 11 – Reaction scheme for the 1,2 thioboration/cyclisation of 2-alkynylthioanisoles to generate 3-borylated benzothiophenes.\textsuperscript{[30]}

To highlight the synthetic utility of this methodology, \textit{in-situ} borylative cyclisation/functionalisations were carried out without the isolation of any organoboron intermediates. Reactions reported included oxidative workups and conjugate addition, as well as trifluoromethylation and Suzuki-Miyaura cross-couplings to give a wide variety of complex products. An interesting addition to this report is the use of thioacetate groups (Scheme 12, bottom) as well as thioethers (Scheme 12, top) during an investigation into dihydrothiophene synthesis. Presumably, instead of losing chloromethane as a by-product (as with the thioethers), acetyl chloride would be the likely by-product.
Scheme 12 – The use of different leaving groups during a synthesis of dihydrothiophenes via borylative cyclisation of alkynes with CatBCl.[30]

Three mechanistic pathways were proposed for this reactivity: thiophilic activation (Scheme 13, top), in which the CatBCl coordinates to the sulfur over the alkyne, followed by thioboration of the alkyne. However, no sulfur coordination was observed in $^1$H and $^{11}$B NMR spectra when utilising 2-(hex-1-ynyl)thioanisole. Additionally, no coordination was observed in the control reaction involving 2-iodothioanisole, ruling this pathway out. The second

Scheme 13 – Proposed mechanistic pathways for benzothiophene synthesis from alkynes and CatBCl.[30]
pathway was proposed to be carbophilic activation (Scheme 13, middle), in which 1,2-cis-chloroboration occurs across the alkyne, followed by nucleophilic attack from the sulfur atom. This induces the loss of a chloride ion, generating an ionic intermediate, which is demethylated by the chloride ion to give the desired product. Haloboration was not observed in a control reaction with diphenylacetylene (a non-sulfur analogue), making it an unlikely pathway in this reaction. The third pathway (Scheme 13, bottom) is analogous to that described by Stephan for generating indolium species,\textsuperscript{[22]} in which the boron electrophile activates the alkyne and the sulfur attacks, generating a zwitterionic or ionic (if chloride dissociates from boron as shown) intermediate. Demethylation then occurs to furnish the benzothiophene. However, it is notable that the mechanism is not fully elucidated in this report.

3.1.3 – Aims

Due to the utility of 3-borylated heteroaromatic derivatives in the literature, our goal was to apply BCl\textsubscript{3} induced borylative cyclisation towards new heteroaromatic scaffolds. The significance of this work was to achieve the borylative cyclisation of aryl-alkynes possessing suitable heteroatom substituents using cheap, commercially available, easy-to-handle BCl\textsubscript{3} (in comparison to the BCF and CatBCl), without the use of expensive and highly toxic transition metal catalysts.\textsuperscript{[17]-[19-20]} This would facilitate the generation of a wide variety of borylated heteroaromatics that have applications within the pharmaceutical sector.\textsuperscript{[1-5]}

The proposed mechanism of borylative cyclisation in this investigation would proceed in a similar manner to that described in Chapter 2, in which the C-C triple bond would be activated by BCl\textsubscript{3}, generating a vinyl cation intermediate. However, in this case instead of a carbon nucleophile (e.g S\textsubscript{E}Ar from a pendant aromatic group), a heteroatomic moiety would attack the activated alkyne instead, leading to the generation of a zwitterionic intermediate. To furnish the neutral 3-BCl\textsubscript{2} heterocycle, an equivalent of CH\textsubscript{3}Cl would be lost. Subsequently, an esterification step using pinacol and NEt\textsubscript{3} would be undertaken in order to generate products that are air/moisture stable (Scheme 14).
Scheme 14 – Proposed reaction mechanism for the borylative cyclisation of aryl-alkynes with an ortho-substituted heteroatomic moiety.

3.2.0 – Results and Discussion – N-directed Trans-Haloboration

Scheme 15 – Sonogashira coupling to form N,N-dimethyl-2-(phenylethynyl)aniline 3.1.

For comparison to the work of Stephan using BCF, the alkyne substrate N,N-dimethyl-2-(phenylethynyl)aniline 3.1 was synthesised (Scheme 15). It was hypothesised that with BCl₃, this would follow the proposed mechanism (Scheme 14) with loss of MeCl to give a neutral species, as opposed to the zwitterionic indolium observed previously (Scheme 5).[22] Alkyne 3.1 was reacted with 1.1 equivalents of BCl₃ at 20°C, and after 20 minutes, the expected ¹¹B NMR resonance associated with an aryl-BCl₂ (ca. 52 ppm) due to the cyclised product was not observed, and instead a major resonance at ca. 10 ppm was observed. The ¹H NMR spectral data was obtained in d₂-DCM (Figure 3, bottom) as dissolving the crystals in d₁-chloroform led to protodeborylation (over the course of 24 hours).
Figure 2 – In situ $^1$H and $^{11}$B NMR spectra after 20 minutes from the reaction of 1 and 1.1 eq. BCl$_3$ (in DCM with a $d_6$-DMSO capillary). Resonance at 3.6 ppm attributed to protonated NMe$_2$ moiety.

The structural metrics of 3.2 show that the C-B and B-N bonds are of a comparable length to a similar compound possessing a five-membered ring with an internal B-N bond$^{[33]}$ at 1.597(5)Å, and 1.642(4)Å. The five membered B-N ring (ring A) is twisted 30.5(3)$^\circ$ out of plane with the fused benzene ring (ring B) and the phenyl group (ring C) is twisted 129.6(3)$^\circ$ out of plane with the vinyl moiety, most likely in order to minimise non-bonding interactions. Although the exact mechanism is not known, it was proposed that the NMe$_2$ moiety forms an adduct with the BCl$_3$ enabling intramolecular nucleophilic attack by the alkyne (possibly assisted by a second equivalent of BCl$_3$), followed by a subsequent chloride loss (possibly as BCl$_4$) and chloride transfer to the opposite face of vinyl cation (Scheme 16).

Scheme 16 – Proposed mechanism for N-directed trans-haloboration of 3.1 with BCl$_3$. 

140
Figure 3 – Top: X-ray structure of 3.2 with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Blue: Nitrogen; Yellow: Boron; Green: Chlorine; Selected metrics: C9-B1: 1.597(5) Å; B1-N1: 1.642(4) Å; B1-Cl1: 1.864(3) Å; C10-Cl3: 1.764(3) Å; C8-C9-B1-N1: 30.5(3)°; C9-C10-C11-C16: 129.6(3)°

Bottom: $^1$H and $^{11}$B NMR spectral data obtained from the crystals of N-directed trans-haloboration product 3.2 (CD$_2$Cl$_2$).
The reactivity disparity to $\text{B(C}_6\text{F}_5)_3$ is then attributed to the greater bulk of BCF disfavouring adduct formation, along with the lack of a suitable leaving group in BCF (compared to Cl in BCl$_3$). The reaction was repeated and the product was isolated as off-white crystals in a 67% yield, and the solid was found to be air/moisture stable. Although 1,2-cis-haloboration of alkynes using boron trihalides is well preceded,[34-36] 1,2-trans-haloboration is scarce in the literature, and outside of the work reported herein,[29] there are only a few examples to be found, including a very recent report on the generation of borazaronaphthalenes[37] and the cyclisation/demethylation of a bis-ortho-anisoleacetylene (A) derivative using BBr$_3$ (Scheme 17).[36] A similar intramolecular 1,2-trans-hydroboration was recently reported involving pyridyl directing groups, however this was proposed to proceed via initial hydride transfer from boron to carbon and formation of a vinyl anion.[33]

Scheme 17 – Bottom: 1,2-trans-haloboration via cyclisation/demethylation using a bis-ortho-anisoleacetylene derivative A and BBr$_3$.[38]

In order to examine if the indole product could be obtained, the reaction was repeated in o-DCB and heated at 100°C for 8 hours. However, this led to the same product, with no borylative cyclisation observed. It is feasible that modification of steric bulk at N or the electronics of the aryl residue could lead to borylative cyclisation being preferred over trans-haloboration, though due to time constraints this has not been explored herein.
3.2.1 – O-alkynylanisoles: Borylative Cyclisation or Trans-Haloboration?

We focused our attention next on the generation of 3-borylated benzofurans in the absence of transition metal catalysts.[19] Before examining substrates for borylative cyclisation, it is worth considering that based on Yamato’s work, 1,2-trans-haloboration of ortho-alkynylanisoles is clearly possible.[38] However, in their report, it is proposed that the mechanism proceeds via initial demethylation of the ether moieties with BBr₃, a reagent widely used for ether cleavage. Our investigation into the generation of borylated dihydronaphthalenes (Chapter 2) revealed that ether cleavage was a minor issue when employing BCl₃. Furthermore, computational studies into the mechanism of ether cleavage propose that two molecules of ether are required, thus Yamato’s compound may well be preorganised to favour ether cleavage. Thus it was hypothesised that borylative cyclisation should be viable with other substrates using BCl₃.

Furthermore, as a control, equimolar quantities of anisole and BCl₃ were combined (Figure 4), resulting in the appearance of a resonance at 30 ppm in the ¹¹B NMR spectrum, indicative of an equilibrium between the Lewis adduct and free anisole/BCl₃ with no MeCl observed, indicating that ether cleavage is not rapid under these conditions.

![Figure 4 – In situ ¹H and ¹¹B NMR spectra 1 hour after the combination of anisole and BCl₃ (in DCM with a d₆-DMSO capillary).](image)

After 30 hours at 20°C, only ca. 2.5% of CH₃Cl (3.01 ppm) was generated, based on the in situ ¹H NMR spectrum. This result indicates that Lewis adduct
formation is reversible and the quantity of ether cleavage is insignificant, even at prolonged periods at 20°C.

To probe if borylative cyclisation was viable, a variety of ortho-alkynylanisoles were synthesised via palladium-catalysed Sonogashira couplings starting from either 2-bromoanisole (Table 1, Procedure A) or 2-ethynylanisole (Table 1, Procedure B) with the exception of 3.10, which was synthesised via deprotonation of 2-ethynylanisole using n-butyllithium followed by methylation using iodomethane (Table 1, Procedure C).

Table 1 – Ortho-alkynylanisoles synthesised in order to examine their propensity towards borylative cyclisation in the presence of BCl$_3$. 

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Isolated Yield</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>84%</td>
</tr>
<tr>
<td>A</td>
<td>77%</td>
</tr>
<tr>
<td>A</td>
<td>98%</td>
</tr>
<tr>
<td>A</td>
<td>71%</td>
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<tr>
<td>A</td>
<td>19%</td>
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<td>B</td>
<td>75%</td>
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<tr>
<td>B</td>
<td>35%</td>
</tr>
<tr>
<td>C</td>
<td>89%</td>
</tr>
<tr>
<td>A</td>
<td>68%</td>
</tr>
<tr>
<td>A</td>
<td>63%</td>
</tr>
</tbody>
</table>
Alkynes 3.3-3.8 were synthesised in order to examine the effects of EDG and EWG, where 3.3-3.5 differ in regards to functionality on the core anisole ring with substitutions para- to the methoxy group. Alkyne 3.7 was synthesised to observe the change in reactivity when steric bulk is introduced adjacent to the alkyne. In order to expand the potential scope beyond aryl-substituted alkynes, 3.9-3.10 were synthesised. Alkyne 3.11 possessed a nitro group on the anisole ring, which was expected to severely affect the nucleophilicity of the alkyne moiety. Finally, alkyne 3.12 was synthesised not only to test if it was viable in borylative cyclisation, but also to provide an appropriate moiety for a second cyclisation with the aim of generating a six-membered boracycle (Scheme 18), similar to the reactivity described in Chapter 1.

![Scheme 18 – Proposed reaction to generate a boracycle starting from alkyne 3.12.](image)

With a variety of alkynes synthesised, unsubstituted arylalkynylanisole 3.3 was combined with 1.1 equivalents of BCl₃ (to ensure at least 1 equivalent was used in case of variation in the concentration of the 1M BCl₃ in DCM), resulting in complete consumption of the starting material within 10 minutes. The \textit{in situ} \textsuperscript{1}H NMR spectrum (in DCM with a d₆-DMSO capillary) revealed a peak at 3.01 ppm (Figure 5), indicative of CH₃Cl formation. Additionally, a peak corresponding to a minor product of the reaction was observed at 4.45 ppm. A major peak was observed at 51 ppm in the \textsuperscript{11}B NMR spectrum, consistent with the formation of heteroaryl-BCl₂ species, with a minor peak observed at 14 ppm. The post-esterification \textsuperscript{11}B NMR spectral data revealed a 30 ppm resonance, indicative of an aryl-Bpin species. The crude mixture was filtered through silica, allowing benzofuran 3.13 to be isolated in 56% yield.
Based on the control reaction of anisole and BCl₃, alkyne activation and cyclisation presumably took place first before demethylation. A non-linked analogue (B) of the bisanisoleacetylene A (Scheme 17) was synthesised and reacted with both BCl₃ and BBr₃ to investigate whether the difference in reactivity observed between compound A and B was due to the different boron trihalides employed. Interestingly, both BCl₃ and BBr₃ led to immediate consumption (< 10 minutes) of the starting material, where the use of BCl₃ furnished the 1,2-trans-haloborated product almost quantitatively (Scheme 19, right). This was indicated by a single major resonance in the $^{11}$B NMR spectrum at 34 ppm (Figure 6, blue), characteristic of a vinyl-B(OR)₂ species, and a 6H resonance in the $^1$H NMR spectrum at 3.01 ppm, attributable to the loss of two equivalents of CH₃Cl. This indicates that presumably the two proximal ether moieties result in rapid demethylation prior to cyclisation and trans-haloboration. Notably, in the case of BBr₃, two major resonances were observed in the $^{11}$B NMR spectrum, at 33.91 ppm and 6.68 ppm, indicating that the double demethylation/cyclisation was not quantitative (Scheme 19, left).
Scheme 19 – A control reaction to examine if the choice of boron trihalides affects the outcome of the reaction using bis-anisoleacetylene B.

Figure 6 – In situ $^{11}$B NMR spectra for the reaction of B with both BCl$_3$ and BBr$_3$.

Notably, CH$_3$Br was observed in the $^1$H NMR spectrum at 2.64 ppm. After 7 hours, no change was observed in the $^{11}$B NMR spectrum, indicating no further conversion to the double demethylated product. Based on the observed $^{11}$B resonance (ca. 10 ppm) of the N-directed trans-haloboration product 3.2, it is feasible that the 6.68 ppm resonance observed in the $^{11}$B NMR spectrum during the reaction of B with BBr$_3$ is attributable to an analogous reaction, furnishing a non-demethylated five-membered ring (Figure 6, 6.68 ppm). Notably, a peak
was also observed at 4.55 ppm in the $^1$H NMR spectrum, which is characteristic of an aryl-OMe unit coordinated to a Lewis acid.

Returning to the substrate exploration next, para-methyl (to the methoxy group) substituted anisole 3.4 was subjected to the same conditions as 3.3, again resulting in complete consumption of the alkyne within 10 minutes. The appearance of both a 3.01 ppm peak in the $^1$H NMR spectrum and a 51 ppm peak in the $^{11}$B NMR spectrum indicated the loss of CH$_3$Cl, and formation of the corresponding benzofuran-BCl$_2$. Peaks at 4.41 ppm and 14 ppm in $^1$H/$^{11}$B spectrum respectively, were also observed and attributed to a minor product, presumably analogous to that observed in the reaction of 3.3. Notably, with the more electron rich anisole, a lower quantity of the minor product was formed in situ compared to the cyclisation product. The intermediate product was esterified and purified via chromatography, where benzofuran 3.14 was isolated in an 89% yield.

When chlorinated anisole 3.5 was reacted with BCl$_3$, the reaction was much slower than previously observed with alkynes 3.3 and 3.4. The starting material was consumed after two hours of heating at 60°C. Presumably, the chloride lowers the nucleophilicity of both the alkyne and methoxy positions, therefore retarding reaction. Interestingly, the in situ NMR data revealed a ratio between the borylated benzofuran 3.15* and the side product (comparing the 3.01 ppm (CH$_3$Cl) resonance to that at 4.45 ppm) of approximately 1 : 1 before heating (Figure 7, green), and 1 : 2 after heating for two hours (Figure 7, red).

![Scheme 20](image)

Scheme 20 – Proposed explanation for the 4.45 ppm product in the $^1$H NMR spectrum.

It was hypothesised that the resonance at 4.45 ppm may be due to the non-demethylated zwitterionic intermediate, which is converted through to
benzofuran-BCl$_2$ 3.15* by halide abstraction by BCl$_3$ to form a more electrophilic methylated benzofuran-BCl$_2$, which then methylates BCl$_4$ or arylBCl$_3$ (Scheme 20).

Thus, an extra equivalent of BCl$_3$ was added, but this didn’t affect the ratio (Figure 7, pink). Heating for a further 12 hours (Figure 7, yellow) resulted in a minor change in the ratio. Most notably, after esterification and purification, benzofuran 3.15 was isolated in a 72% yield.

Figure 7 – A comparison of in situ $^1$H NMR spectra of the reaction of 3.5 with BCl$_3$. $^{11}$B NMR spectrum of the reaction heated at 60°C for 12 hours after addition of extra BCl$_3$.

This potentially suggests that the formation of the side product is reversible, and that the esterification traps the product of borylative cyclisation. Another
explanation is that the 14.58 ppm peak in the $^{11}$B NMR spectrum is attributable to the hypothesised non-demethylated zwitterionic benzofuran-BCl$_3$ product, which is converted to the desired benzofuran product 3.15 by demethylation/dechlorination on addition of pinacol/base. This may explain a yield of greater than ca. 30%, which would be the maximum expected when a 1 : 2.2 ratio of products is encountered.

It was expected that fluorinated alkyne 3.6 would lead to extended reaction times due to its strong inductively withdrawing effect on the meta positioned alkyne. Surprisingly, 15 minutes after BCl$_3$ was added to it, almost all of the starting material had been consumed, with complete consumption observed after an hour at room temperature (Figure 8).

Figure 8 – Comparison of in situ $^1$H, $^{11}$B and $^{19}$F NMR spectra of the reaction between fluorinated alkyne 3.6 and BCl$_3$. 
The ratio of products observed was approximately 3:2 in favour of the borylated benzofuran (BCl₂-intermediate 3.16*). As observed during the reaction of 3.5, the isolated yield of esterified product 3.16 was higher than the maximum yield based on the measured in situ ratio (therefore roughly 60%), with a 79% yield.

It was predicted that increasing the steric bulk around the alkyne moiety would lead to reduced yields of the borylated benzofuran. After the initial addition of BCl₃ to alkyne 3.7, a complete consumption of starting material was observed to give one product. However no trace of the ¹¹B resonance at 51 ppm (associated with heteroaryl-BCl₂), or 3.01 ppm ¹H resonance (associated with the production of CH₃Cl), indicative of borylative cyclisation was observed (BCl₂-intermediate 3.17*). The ¹¹B NMR spectrum revealed only one peak at 41 ppm.

Figure 9 – Comparison of in situ ¹H and ¹¹B spectra of the reaction between alkyne 3.7 and BCl₃.

With the resonance for anisole-BCl₃ adduct known to be around 30 ppm (in DCM with a d₆-DMSO capillary) and BCl₃ to be at 46 ppm, it is possible that the
resonance at 41 ppm is simply showing an equilibrium between free BCl₃ and the BCl₃ adduct with 3.7 (which this more hindered anisole favours free BCl₃). This result is attributed to the greater steric bulk around the alkyne slowing the cyclisation. When the reaction was left overnight, multiple products were observed in the NMR spectra, including the peaks relevant to borylative cyclisation. Notably, the ¹¹B NMR spectrum revealed a peak at 57 ppm instead of the usual 51 ppm, which given the adjacent methyl group, may be due to a change in conformation of the boron moiety, potentially resulting in a twist out of the plane of the aromatic ring reducing mesomeric delocalisation. Leaving the reaction for prolonged times (>60 hours) led to more of the borylative cyclisation product, but a much more complex mixture of products overall (Figure 9). Notably, the 41 ppm peak in the ¹¹B spectrum shifts downfield over time (ca. 43 ppm) as the reaction slowly progressed, suggesting it is associated with the equilibrium of free BCl₃ and BCl₃:3.7 adduct. The reaction was repeated, esterified after 18 hours and purified via chromatography to give benzofuran 3.17 in a 33% yield.

It was hypothesised that utilising a substrate with a mesomeric withdrawing group such as an ester para- to the alkyne (on the pendant alkynylbenzene ring) would lead to lower rates of cyclisation due to competitive binding of the boron electrophile to the ester moiety as well as simultaneous deactivation of the alkyne nucleophile and the methoxy group (Scheme 21).

![Scheme 21](image)

Scheme 21 – Resonance forms of 8, highlighting the decreased nucleophilicity of the alkyne and methoxy group due to the mesomeric withdrawing effect of the ester.

Following a procedure from our earlier work (Chapter 2) regarding the use of carbonyls, 2.2 equivalents of BCl₃ were reacted with ester-possessing alkyne 3.8, where one equivalent of BCl₃ coordinates to the carbonyl (which can be
cleaved later by NEt₃ during the esterification step) and one initiates borylative cyclisation.[26] Initially, as expected complete consumption of the starting material (within 10 minutes) was observed in the ¹H and ¹¹B NMR spectra, with the new major product presumably the carbonyl:BCl₃ adduct (based on a 33 ppm peak in the ¹¹B spectrum). Additionally, a small quantity of the heteroaromatic-BCl₂ peak (¹¹B: 51.0 ppm) was observed alongside the CH₃Cl peak (¹H: 3.01 ppm), indicating cyclisation was taking place. The reaction was heated overnight at 60°C, leading to an increased quantity of the cyclised product, as well as a minor amount of the previously observed side product, indicated by a broad resonance in the ¹¹B NMR spectrum at 14 ppm. The reaction was esterified and benzofuran 3.18 was isolated in a 35% yield after purification via column chromatography. It was observed during a second reaction utilising an equivalent of TBP and 3.3 equivalents of BCl₃ that the reaction could be carried out overnight at room temperature, with fewer side products observed. Presumably, TBP sequesters any protic impurities, reducing the amount of side products. However, after esterification and purification, only a 46% isolated yield was observed. These lower yields are consistent with our earlier hypothesis on the decreased rates of cyclisation due to the electron withdrawing nature of the ester.

With a number of aryl substituted alkynes examined, we employed benzyl (3.9) and methyl (3.10) substituted alkynes to observe whether similar reactivity takes place in the absence of mesomeric stabilisation of the vinyl cation into the aromatic ring. When 3.9 was reacted with an equivalent of BCl₃, the in situ ¹H NMR spectrum showed one major product, combined with CH₃Cl, indicating borylative cyclisation (BCl₂-intermediate 3.19*). However, it was interesting that although the ¹H NMR spectrum looked reasonably clean, the ¹¹B NMR spectrum showed two peaks other than the major 51 ppm peak, at 40 ppm and 26 ppm. The resonance at 40 ppm may be associated with equilibrium between free BCl₃ and BCl₃:3.9 adduct. The generation of these undetermined products may contribute to the moderate yield of 57% (given the in situ ¹H NMR spectrum, (Figure 10)) of benzofuran 3.19 observed post esterification.
Figure 10 – Comparison of in situ $^1$H, and $^{11}$B NMR spectra of the reaction between alkyne 3.9 and BCl$_3$.

The employment of methylated alkyne 3.10 with an equivalent of BCl$_3$ resulted in quantitative conversion to the borylated benzofuran within 10 minutes. Esterification and subsequent purification facilitated the isolation of benzofuran 3.20 in an 89% yield. The reaction was successfully repeated on a gram scale, where 1.16 g (76%) of 3.20 was isolated, indicating that this chemistry could be scaled up. Additionally, with the clean reactivity observed in this reaction, a control utilising ambient conditions was carried out. Instead of employing Schlenk techniques and ensuring an air/moisture free environment, an open vessel was used, with 1.1 equivalents of BCl$_3$. In addition, non-purified solvents were used directly from the bench. Post esterification, the isolated yield of 3.20 was 81%, indicating that this chemistry is particularly robust, and has some
degree of air/moisture tolerance. The structure of 3.20 was confirmed by X-ray crystallography (Figure 11). The structural metrics of 3.20 are unremarkable with a B-C bond distance of 1.543(4)Å, a typical length for an aryl-Bpin moiety. The benzofuran (ring system A) is planar, and presumably due to the lower steric bulk of the methyl group compared to the phenyl group, the non-bonding interactions are much lower by comparison, thus the Bpin moiety (ring B) is only twisted 2.7(4)° out of the plane of A. The results of each of the borylative cyclisations can be found summarised below in Table 2.

Figure 11 - X-ray structure of 3.20 with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Red: Oxygen; Yellow: Boron; Selected Metrics: C1-B1: 1.543(4)Å; O1-C3-C4-C5: 180.0(2)°; C2-C1-B1-O2: 2.7(4)°
A slight excess of the 1M BCl$_3$ (in DCM) solution was used to ensure at least 1 eq. was added in case of variation in the concentration of BCl$_3$ on storage / handling;

Employing the standard conditions in a Young's NMR tube;

Carrying out the reaction on a gram scale to yield 1.16 g of 3.20 (76%),

Employing ambient conditions, using an open vessel and non-purified solvents;

Table 2 – A table displaying the standard 3-borylated benzofurans obtained via borylative cyclisation using BCl$_3$. 

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3.2.2 - Elucidating the Trans-Haloboration of O-Alkynylanisoles

Throughout this investigation into the borylative cyclisation of heteroatom possessing alkynes, a second resonance around 14 ppm in the $^{11}\text{B}$ NMR spectrum was observed in varying quantities across the majority of alkynes examined, particularly in the electron deficient alkynes (3.5, 3.6 and 3.8), with larger quantities of this side-product observed for 3.5 and 3.6, where the EWG are located on the anisole moiety. The corresponding peaks of this product observed at around 4.45 ppm in the $^1\text{H}$ NMR spectrum are consistent with an aryl-OMe unit coordinated to a Lewis acid. Notably, the product derived from N-directed $\text{trans}$-chloroboration produced an $^{11}\text{B}$ resonance of around 10 ppm, which would be expected as nitrogen is a better electron donor, so a peak of around 14 ppm for the O-directed $\text{trans}$-chloroboration is feasible. Additionally, the absence of CH$_3$Cl associated with this product suggested that the methyl was still bound to the oxygen and that a chlorine atom had not been lost in the reaction as observed with borylative cyclisation (Scheme 22, top). Overall, these observations led to our hypothesis that the resonance around 14 ppm may be indicative of $\text{1,2-trans}$-chloroboration with the anisole moiety coordinating to the RBCl$_2$, thus generating the upfield shift (Scheme 22, bottom).

![Scheme 22](image)

Scheme 22 – Comparing the difference in reactivity between borylative cyclisation and the proposed $\text{trans}$-haloboration of 2-alkynylanisoles.

$\text{Para}$-nitro substituted alkyne 3.11 was employed to examine the effect of a strong mesomeric withdrawing group on the anisole ring $\text{para}$- to the alkyne on
the reaction pathway observed. As less cyclisation was observed with ester substituted 3.8, it was hypothesised that the inclusion of a nitro group would severely hinder the cyclisation and lead to more of the by-product at 14 ppm. As expected, upon addition of BCl₃ to 3.11, the ¹H NMR spectrum revealed that only a small quantity of the starting material had been consumed, with the major new product showing clear peaks, the expected singlet at 4.56 ppm as well as a doublet at 6.59 ppm that integrated to 3 protons and 1 proton respectively. The ¹¹B NMR spectrum revealed a major peak at 15 ppm with trace quantities of a 51 ppm resonance, corresponding to the cyclised product (alongside trace CH₃Cl in the ¹H NMR spectrum).

Figure 12 – Comparison of in situ ¹H, and ¹¹B NMR spectra of the reaction between alkyne 3.11 and BCl₃ at 10 minutes, 2 hours, 5 hours and 18 hours.
Over 18 hours, the 15 ppm product significantly increased in quantity whereas only a trace of the cyclisation product was observed (Figure 12). Notably, the $^1$H NMR spectrum revealed that post-esterification, the major product was returned starting material with a complex mixture of minor products also observed. Additionally, the $^{11}$B NMR spectrum showed only a very minor peak at 30 ppm, indicative of an aryl/vinyl-Bpin species with other peaks at 22.5 ppm and 9.5 ppm, which correspond to pinacol boron derivatives $\text{Pin}_3\text{B}_2$ and $[\text{Pin}_2\text{B}]^-$ respectively. This suggested that the proposed trans-haloboration product 3.11* can be converted back to starting material potentially via base initiated (by the $\text{NEt}_3$ from the esterification step) E2 elimination (Scheme 23).

![Scheme 23](image)

Scheme 23 – Proposed E2 elimination of the trans-haloboration intermediate 3.11* by $\text{NEt}_3$.

Next, the reaction was attempted using $\text{BCl}_3$ (1M in heptane) and $\alpha$-DCB. Interestingly, the same resonances of 15 ppm ($^{11}$B) and 4.50 ppm ($^1$H) were initially observed, however upon heating 18 hours at 100°C, the major product observed in the $^{11}$B NMR spectrum was a peak at 40 ppm. In addition, a small quantity of starting material remained, and the $^1$H resonance at 4.50 ppm was significantly smaller, whilst a new major CH$_3$Cl peak was observed (Figure 13). Notably, there was only a trace quantity of the of the aryl-BCl$_2$ product (at 51 ppm) observed in the $^{11}$B spectrum, which indicated that retro-haloboration followed by cyclisation had not taken place (Figure 13).

Post-esterification of the 40 ppm product, the $^1$H NMR spectrum revealed that the major product of the reaction was demethylated alkyne starting material. It was proposed that the initial trans-haloboration product (3.11*) loses an equivalent of MeCl with heating (to give intermediate 3.11**), resulting in a stronger covalent B-O bond (ArylO-BCl(R)) compared to the dative bond of ArylO(Me)BCl$_2$(R)), and upon esterification, the weaker C-B bond is broken to
furnish ArylO-Bpin. This then undergoes protodeborylation during the purification steps (Scheme 24).

Figure 13 – Comparison of in situ $^1$H, and $^{11}$B NMR spectra of the reaction between alkyne 3.11 and BCl$_3$ at 10 minutes, and 18 hours at 100°C.

Scheme 24 – Proposed pathway of 3.11 and BCl$_3$ when heated at 100°C in o-DCB.
Alternative alkynes possessing electron withdrawing substituents on the anisole moiety para- to the alkyne including bromide and methyl esters were examined for similar reactivity. Although the major components of the converted material were presumed to be the trans-haloboration product (major product around 14 ppm in the $^{11}$B NMR spectrum), the reactions required extended reaction times (>5 days) and heating (60-100°C) to consume significant quantities of the starting material. Additionally, these were less selective for cyclisation / haloboration (although haloboration was still the major product) and as such were not studied in-depth as utilising 3.11 led selectively to haloboration, making it more appropriate for study. However, these reactions did support the results of earlier reactions (e.g using 3.5, 3.6 and 3.8), indicating that electron withdrawing groups tend to disfavour the borylative cyclisation pathway.

Interestingly, when utilising naphthalene substituted alkyne 3.12 (in the interest of obtaining a benzofuran-fused boricycle), it was observed to be highly selective towards the trans-haloboration pathway. Fortunately, the reaction between 3.12 and BCl$_3$ proceeded more rapidly than with 3.11, with the starting material consumed within 10 minutes at room temperature to give the initial trans-haloboration product. As observed during the investigation using 3.11, the esterification step with NEt$_3$ led to 3.12 being returned as the major product with no vinyl-Bpin resonance observed in the $^{11}$B NMR spectrum. To preclude the proposed E2 elimination step, the reaction was repeated and the work up was performed base free, where water was added after formation of the trans-haloboration product, resulting in a sole peak of 29 ppm in the $^{11}$B NMR spectrum, corresponding to a vinyl-B(OH)$_2$. This was subsequently followed by esterification with pinacol to furnish O-directed trans-haloboration product 3.22 (Scheme 25), which was stable to column chromatography with GC-MS confirming it was the major product (with an m/z of 421.2 g mol$^{-1}$). Notably, two minor products (with very similar Rf values), alkyne 3.12 and benzofuran 3.21 (from the borylative cyclisation pathway) were also observed and could not be separated from 3.22 in our hands by column chromatography.
Compound 3.22 was subjected to acidic conditions for a prolonged period (>24 hours) at 100°C to induce protodeborylation in an attempt to use 2D NMR spectral data to confirm the stereochemistry. However the obtained data was inconclusive. Given that internal alkynes do not undergo cis-haloboration with BCl₃, and based on the trans-haloboration of 2-alkynylaniline 3.1, it can be presumed that the reaction of 3.12 with BCl₃ proceeded via trans-haloboration.

Overall, it can be concluded from the data obtained on the reactions of 2-alkynylanisoles with BCl₃ that borylative cyclisation is the most favoured pathway for electron rich substrates, whereas severely electron deficient substrates and substrates possessing steric bulk around the alkyne disfavour the cyclisation pathway, and facilitate an alternative pathway of O-directed trans-haloboration, analogous to the reactivity observed when reacting 2-alkynyl-N-N-dimethylaniline 3.1 with BCl₃. Although in situ conversion suggested lower yields of cyclisation, the proposed chemistry in Scheme 20 may provide a possible explanation to the higher yields of borylated benzofurans isolated.

### 3.2.3 – O-alkynylanisoles: Further Reactivity and Investigation

After factors affecting the competing pathways of borylative cyclisation and trans-haloboration were elucidated, it was important to investigate further substrates the methodology could be applied to. Firstly, 3.23, a bis-alkynyl benzene possessing two methoxy groups was synthesised (via Sonogashira
coupling) in order to obtain an appropriate substrate to examine a double borylative cyclisation reaction (Scheme 26). Alkyne 3.23 was reacted with 2.2 equivalents of BCl₃, leading to almost complete consumption of the starting material within 10 minutes. Due to the formation of precipitated material, the in situ ¹H NMR spectrum was broad and unresolved. However, the two major products were assigned based on the ¹¹B NMR spectrum as the borylative cyclisation (51 ppm, major) and trans-haloboration (14 ppm, minor) products. Post-esterification, the ¹H and ¹¹B NMR spectra confirmed the production of diborylated benzodifuran 3.24, which was purified via column chromatography, yielding 3.24 in an 88% yield. Interestingly, there was only a small quantity (compared to 3.24) of the starting material observed post-esterification before purification. This is again consistent with the trans-haloboration product undergoing retrohaloboration on addition of base leading to further alkyne cyclisation. This result overall is significant as there is no precedence in the literature towards generating 3,7-diborylated benzodifurans. These have potential applications as versatile precursors to 2,3,6,7-tetraarylbenzo[1,2-b:4,5-b']difurans, which are of high interest as hole transport materials.[39]

Scheme 26 – A scheme showing the double cyclisation of dyne 3.23 to generate doubly borylated 2,6-diphenylbenzo[1,2-b:4,5-b']difuran 3.24.

Next, in order to observe whether the 3-borylated benzofurans were employable in cross-coupling reactions, benzofuran 3.20 was subjected to standard Suzuki-Miyaura coupling conditions (Scheme 27). The reaction was successful in generating the desired 3-arylated benzofuran 3.25, albeit in a moderate yield. This was most likely due to protodeborylation during the reaction, although the 3H-benzofuran was not isolated. It was next hypothesised that both the borylative cyclisation and cross coupling reactions could be carried out in one pot (Scheme 28). Given the lower yield observed during the reaction to generate 3.25 due to protodeboronation under cross
coupling conditions, an excess of alkyne 3.4 (1.5 equivalents) was employed in order to produce an appropriate small excess of the boron coupling component in situ.

Scheme 27 – A scheme highlighting a Suzuki cross-coupling utilising benzofuran 3.20.

The borylative cyclisation was complete in minutes, and the resulting mixture was dried in-vacuo and the intermediate was dissolved in wet THF and subjected to standard Suzuki-Miyaura conditions, which furnished 3-arylated benzofuran 3.26 in a 72% yield (yield based on the electrophile). This result indicates that the borylated compounds from these reactions need not be pinacol protected and isolated prior to further functionalisation. Therefore a wide variety of 2,3-substituted benzofurans could potentially be synthesised in one-pot from appropriate starting alkynes using this methodology.
3.2.4 – Functionality Screening

As observed during the investigation into substituent effects on reaction outcome, EDG groups tended to promote borylative cyclisation whilst EWG, particularly para- to the alkyne promoted trans-haloboration. However, as these effects were observed to typically rely on their position in each substrate, it was important to examine the functional group tolerance of the reactions by carrying out a ‘robustness screen’, involving the examination of a reliable high-yielding cyclisation in the presence of a variety of additives possessing different functional groups. Adapted from the procedure\(^{[40]}\) reported by Glorius et al., the goal was to observe any changes to yield *in situ* by employing an equivalent of mesitylene as internal standard to compare products and reactants against (Scheme 29).

Scheme 29 – A general scheme illustrating the functional group screening, employing mesitylene as an internal standard.

As the initial benchmark, the reaction of alkyne 3.4 and ca. 1 equiv. of BCl\(_3\) was carried out in the absence of an additive (Table 3, entry 1), with only the mesitylene standard present, which resulted in a 96% *in situ* yield of the corresponding benzofuran-BCl\(_2\) intermediate. Repeating the reaction in the presence of nitromethane (Table 3, entry 2), hex-1-ene (Table 3, entry 3) and trifluorotoluene (Table 3, entry 4) resulted in very little to no effect, with observed yields of the RBCl\(_2\) intermediate at 84%, 91% and 90%, respectively (based on integration of the singlet resonance at 8.02 ppm relative to the Ar-H signal of mesitylene at 6.79 ppm (in DCM with d\(_6\)-DMSO capillary)). This indicates that the cyclisation is tolerant of nitro, vinyl and trifluoromethyl groups.

Conversely, when acetone (Table 3, entry 5) and benzaldehyde (Table 3, entry 6) were employed as additives, the resulting yields of the desired
benzofuran-BCl$_2$ were 38% and 17%, respectively, with complete substrate and additive consumption. This may be due to coordination of BCl$_3$ to the oxygen atom, which significantly enhances the electrophilicity of the carbonyl carbon, leading to side reactions. When para-bromobenzonitrile (Table 3, entry 7) was employed as the additive, coordination to the BCl$_3$ was immediately observed, however after 24 hours, the desired intermediate was observed in a 72% yield, indicating the adduct formation was reversible. Subsequently, a repeat reaction with 2.2 equivalents of BCl$_3$ was carried out (Table 3, entry 8), where the intermediate benzofuran-BCl$_2$ was observed in a 94% yield within 30 minutes. Thus, 2.2 equivalents of BCl$_3$ were used for screening reactions employing other basic functionalities including 2-bromopyridine (Table 3, entry 9), N,N-dimethylaniline (Table 3, entry 10), and N,N-dimethylbenzamide (Table 3, entry 11), leading to in situ yields of 84%, 74% and 72%, respectively within 30 minutes. The addition of excess NEt$_3$ during the esterification step abstracts BCl$_3$ from these less Lewis basic groups, indicating that overall the borylative cyclisation is tolerant of these Lewis basic groups (Scheme 30).

Scheme 30 – A scheme to illustrate the proposed initial coordination of BCl$_3$ to the Lewis basic functionality followed by a second equivalent of BCl$_3$ inducing cyclisation.

Overall, it can be concluded from this ‘robustness screen’ that the borylative cyclisation reaction of 2-alkynylanisoles is tolerant to a variety of useful functionalities. This study reveals that the reaction offers an alternative pathway to form 3-borylated-2-substituted benzofurans than the established routes involving 3-halo-2-substituted benzofurans and either metalation/quenching with B(OR)$_3$ or palladium catalysed Miyaura borylation,[41] as these routes are typically incompatible with some of the functionalities screened, including amides and nitriles. However, it is imperative to note that these observations merely indicate that the reaction is tolerant of these functionalities, and does not
reveal any steric or electronic effects when these groups are bound to the alkynylanisole. The screening is highly useful for designing new substrates relevant to this investigation in an efficient manner, without having to spend time synthesising substrates with very little prior knowledge regarding their compatibility with cyclisation.

![Borylative Cyclisation](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>BCl₃ Equivalents</th>
<th>Additive</th>
<th>NMR Yield of RBCl₂ (%)</th>
<th>Time (h)</th>
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<td>&lt; 0.5</td>
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<td>17</td>
<td>&lt; 0.5</td>
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<tr>
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<td>1.2</td>
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<td>24</td>
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</tr>
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<td>84</td>
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<td>2.2</td>
<td>N,N-dimethylbenzamide</td>
<td>72</td>
<td>&lt; 0.5</td>
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ᵃ = starting alkyne fully consumed

Table 3 – Results of the ‘robustness screening’ from the borylative cyclisation of alkyne 3.4.

3.2.5 – Borylative Cyclisation of O-alkynylothioanisoles

With a range of 3-borylated benzofurans successfully isolated via borylative cyclisation, our attention was focused on applying the methodology to 2-alkynylothioanisoles. Four alkynes were synthesised via Sonogashira coupling (adapted from Procedure A, Table 1) to yield alkynes with pendant phenyl (3.27), naphthyl (3.28) (3.27 and 3.28 synthesised by Anna Churn as part of her
MChem project), 3-thienyl (3.29) and mesityl (3.30) groups. 3.27 and 3.28 were intended to serve as direct comparisons between their corresponding oxygen analogues (3.3 and 3.12) whereas 3.29 and 3.30 were synthesised to examine whether this methodology was tolerant of pendant heteroaromatic groups and sterically bulky aromatics, respectively. As an initial control, thioanisole was combined with equimolar BCl$_3$, resulting in adduct formation, indicated by a peak at 7.9 ppm in the $^{11}$B NMR spectrum. Notably, no demethylation was observed, which suggests that under the standard conditions employed for borylative cyclisation, thioether cleavage would not be an issue.

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>Isolated Yield</th>
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<td><img src="structure" alt="3.27" /></td>
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<tr>
<td><img src="structure" alt="3.30" /></td>
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</tr>
</tbody>
</table>

Table 4 – 2-alkynylthioanisoles synthesised for this investigation.

When alkyne 3.27 was reacted with an equivalent of BCl$_3$, complete consumption of the starting material was observed (< 10 minutes) and a precipitate formed, with the $^{11}$B NMR spectrum revealing the major peak centred at 4 ppm (in DCM with a d$_6$-DMSO capillary) with a minor sharp peak at 6.5 ppm. Notably, the expected benzothiophene-BCl$_2$ species was expected to generate a resonance at ca. 52 ppm, suggesting it had not been furnished. This correlated with the fact that no CH$_3$Cl was observed in the $^1$H NMR spectrum, indicating that demethylation had not taken place. Upon esterification of the reaction mixture, a peak at 30 ppm was observed in the $^{11}$B NMR spectrum corresponding to an aryl-Bpin species. Purification via column chromatography provided benzothiophene 3.31 in a 38% yield. It was interesting that the in situ $^1$H NMR spectrum was reasonably clean (Figure 14), showing one major product, yet the final isolated yield was low.
A very similar result was observed when utilising naphthyl substituted thioanisole 3.28, in which the 4 ppm resonance was observed once more with conversion to almost a single major product in situ. Esterification of the reaction mixture again led to the generation of a 30 ppm peak observed in the $^{11}$B NMR spectrum, with purification yielding the desired benzothiophene, 3.32 in a 48% yield. This is in stark contrast to the oxygen analogue 3.21, where only trace amounts of the cyclised benzofuran product were observed. This suggests that when employing sulfur as the heteroatom, the reaction is more selective towards borylative cyclisation and the alternative trans-haloboration pathway is disfavoured.
Given that no demethylation was observed in either reaction (based on the absence of CH$_3$Cl), it was hypothesised that as methylsulfonylum cations are significantly weaker methylating agents compared to their methyloxonium counterparts,$^{[42]}$ the intermediate observed was actually a zwitterionic benzo thiophenium-BCl$_3$ species (which potentially was attributable to the formed precipitate in both reactions). These will be more susceptible to protodeborylation than benzothiophene-BCl$_2$ due to the anionic heteroaryl-BCl$_3$ moiety being more nucleophilic than the corresponding benzothiophenyl-BCl$_2$ species, and as such would likely result in low yields post-esterification as observed. The presence of a four-coordinate boron species in situ would also account for the upfield 4 ppm peak observed in the $^{11}$B NMR spectrum (Figure 15 bottom, blue). Subsequently, a reaction in which NEt$_3$ was added (after 10 minutes) to the combination of 3.27 and BCl$_3$ was examined in order to induce demethylation of the zwitterionic intermediate. This resulted in a shift of the 4 ppm peak to around 6 ppm in the $^{11}$B NMR spectrum (Figure 15 bottom, green), and an equivalent of [MeNEt$_3$]$^+$ was observed in the $^1$H NMR spectrum (Et$_3$NCH$_3$ = 2.90 ppm in DCM with a d$_6$-DMSO capillary) (Figure 15 top, grey). The 6 ppm peak was therefore presumed to correspond to the product of demethylation of the zwitterion. When an equivalent of AlCl$_3$ was added subsequently, chloride abstraction from the anionic RBCl$_3$ moiety took place, resulting in the expected benzothiophene-BCl$_2$ peak at 53 ppm (Figure 15 bottom, red).$^{[43]}$ A broad minor resonance at ca. 57 ppm was also observed, which was tentatively attributed to the borenium species, [benzothienyl-B(NEt$_3$)Cl][AlCl$_4$]. Upon esterification and purification of this reaction mixture, an improved yield of 68% of 3.31 was isolated (Scheme 31).
Figure 15 – *In situ* $^1$H and $^{11}$B NMR spectral data of the reaction between 3.27 and BCl$_3$ with NEt$_3$/AlCl$_3$ addition.
Scheme 31 – A scheme illustrating how the addition of NEt₃ and AlCl₃ facilitates demethylation and halide abstraction post-cyclisation of 3.27 with BCl₃.

Notably the same benzothiophene-BCl₂ species was observed ultimately if AlCl₃ was added first followed by NEt₃. This adapted procedure was applied to the cyclisation of naphthalene substituted 3.28, which provided an improved yield of 73%.

When 3-thienyl alkyne 3.29 was reacted with BCl₃, the starting material was completely consumed within 10 minutes, leading to one major product in the ¹H NMR spectrum, with a corresponding peak at 4.5 ppm in the ¹¹B NMR spectrum. Based on the reactions with 3.27 and 3.28, this was presumed to be the zwitterionic benzothiophenium-BCl₃ species. Esterification and purification provided borylated benzothiophene 3.33 in a 55% yield. Notably, when the adapted procedure with NEt₃/AlCl₃ was applied in order to increase the yield via formation of the neutral benzothiophene-BCl₂ intermediate, a complex mixture of products was observed. It is possible that formation of any [benzothiopheneBCl(NEt₃)]⁺ could lead to borylation of the alpha C-H position and thus complex mixtures.

Based on the reactions of alkynes 3.6 and 3.12 with increased steric bulk, it was hypothesised that the reaction of mesityl substituted alkyne 3.30 would be very slow, or potentially follow the pathway of trans-haloboration. Interestingly, upon combination of 3.30 and BCl₃, a white precipitate immediately formed, making spectral data very difficult to obtain. Fortunately, upon the addition of NEt₃, the solid rapidly dissolved, which may potentially be due to demethylation of the intermediate by NEt₃, generating a more soluble salt, [RBCl₃][MeNEt₃]. Pinacol was added and the post-esterification ¹H NMR spectrum was obtained. This revealed that the major product of the reaction was from borylative cyclisation, and benzothiophene 3.34 was isolated in an 82% yield. The reaction was not attempted using the adapted procedure due to the large quantity of
precipitate generated in situ, combined with the already high yield obtained simply using BCl₃. Presumably, the higher yield observed for 3.34 is due to the greater bulk of the mesityl group, retarding protodeboronation (by disfavouring pyramidalisation at B).

A Standard cyclisation conditions; B Adapted conditions to ensure demethylation/halide abstraction before esterification.

Table 5 – 3-borylated benzothiophenes synthesised via borylative cyclisation of 2-alkynyl thioanisoles.

3.2.6 – Attempted Borylative Cyclisation to Produce Isocoumarins

Scheme 32 – Proposed reaction scheme for the formation of an isocoumarin from the reaction of alkyne 3.35 with BCl₃.

Next, the investigation was focused on the generation of a borylated isocoumarin from 2-(phenylethynyl)methylbenzoate 3.35 and BCl₃ (Scheme 32). An initial reaction of 3.35 with 2.2 equivalents of BCl₃ immediately led to complete conversion to one product based on the in situ NMR spectra, with a resonance observed at 8.7 ppm in the ¹¹B spectrum (Figure 16). This did not
seem attributable to adduct formation between the ester carbonyl and BCl$_3$ as the previous cyclisation of ester substituted alkyne 3.8 produced an adduct peak (in equilibrium with free BCl$_3$) around 33 ppm. However, upon esterification of the *in situ* mixture, no trace of cyclised product was observed in the NMR spectra, with the major component observed to be returned starting material. It was hypothesised that a zwitterionic intermediate similar to that observed in the reaction of 2-alkynylthioanisole 3.27 and BCl$_3$ may have been generated, so the reaction was repeated employing an equivalent of NEt$_3$ and AlCl$_3$ in an attempt to generate a neutral borylated isocoumarin. However, this led to a mixture of products in the *in situ* $^1$H NMR spectrum. The post-esterification $^{11}$B NMR spectrum of this mixture unfortunately revealed no trace of a vinyl-Bpin moiety, although the major product in the $^1$H NMR spectrum was not attributed to returned starting material. Notably, the work of Blum et. al involving the transition metal free oxyboration of alkynes with CatBCl to furnish borylated isocoumarins was published during the course of this investigation and as such it was discontinued.\cite{25}

Figure 16 – *In situ* $^1$H and $^{11}$B NMR spectra of the initial reaction between 3.35 and 2.2 equivalents of BCl$_3$. 

![NMR spectra](image-url)
3.2.7 – Conclusions and Future Work

In conclusion, it has been shown that the borylative cyclisation of phenylalkynes possessing an ortho-heteroatomic component can be initiated by employing the simple, commercially available boron electrophile, BCl$_3$, under mild conditions. Notably, there are two distinct reaction pathways, borylative cyclisation and trans-haloboration, depending on the heteroatom employed. When 2-(phenylethynyl)-N,N-dimethylaniline was utilised, trans-haloboration was the only pathway observed, albeit with only one substrate explored. Conversely, 2-alkynylthioanisoles exhibited complete selectivity towards borylative cyclisation for all four substrates. Most interestingly, the employment of 2-alkynylanisoles resulted in both pathways being observed, which was based on the steric and electronics of the substrate. In the presence of electron withdrawing groups, particularly para- to the alkyne, or sufficient steric bulk around the alkyne, trans-haloboration is the dominant pathway. Conversely, when electron donating groups are present, or the steric bulk is reduced, borylative cyclisation is the major observed pathway.

Overall, the goals of this investigation were achieved and this methodology offers a transition-metal free route to a variety of 3-borylated benzoquinones and benzoquinones. In addition, we provided a rare example of trans-haloboration a reaction which is particularly scarce in the literature. The facile nature in which borylative cyclisation takes place, combined with the tolerance of a wide range of useful functional groups potentially points towards very simple syntheses of a myriad of heteroarenes under mild conditions, which have major applications in the pharmaceutical sector.

To expand this study further, a number of reactions could be examined to utilise this methodology in other areas, such as material chemistry. As stated in our initial aims, oxygen-possessing alkyne 3.12 was originally designed in order to attempt a secondary cyclisation to generate a benzoquinone-fused six-membered boracyle. However, this idea was abandoned once trans-haloboration had been established as the dominant pathway. Notably, as only borylative cyclisation was observed with sulfur-possessing alkyne 3.28, it may
be feasible to induce the second cyclisation, generating a benzothiophene-fused six-membered boracycle (Scheme 33)

Scheme 33 – Scheme illustrating the application of a second borylative cyclisation to furnish a benzothiophene-fused six-membered boracycle.

An important development towards this chemistry would be the successful synthesis of borylated indoles. As only one alkynylaniline (3.1) was tested (resulting in trans-haloboration), it is important to vary the substituents in order to tune the electronics of the substrate and potentially favour the borylative cyclisation pathway over haloboration. Methyl-substituted alkynylanisole 3.10 showed quantitative conversion to the benzofuran species with no haloboration observed, thus a methyl-alkynylaniline substrate would be an ideal starting point of scope exploration. Additionally, based on the reactivity observed with the anisole substrates, EDG-substituted anilines should also be more likely to undergo borylative cyclisation (Scheme 34).

Scheme 34 – Proposed formation of borylated indoles.

Finally, based on the observations ($^{11}$B: 8 ppm) from the reaction of methyl benzoate 3.35, it would be worth applying the reaction conditions used to generate and isolate the trans-haloboration product 3.22. As the major component in the post-esterification $^1$H NMR spectrum of the reaction of 3.35 with BCl$_3$ was starting material, it may be possible that a trans-haloboration was taking place due to the electron withdrawing nature of the ester (Scheme 35).
Scheme 35 – Proposed scheme for a trans-haloboration of 3.35 instead of borylative cyclisation.
3.3.0 – Experimental – General Considerations

Some carbon signals in compounds 3.13, 3.14, 3.18 and 3.26 are not observed due to coincident peaks. The ionisation mode used in GC-MS was electron ionisation. All small scale cyclisation reactions were carried out in J. Young NMR tubes to facilitate in situ reaction monitoring. A number of samples are analysed in situ in protio solvent with a capillary insert containing wet deuterated d6-DMSO, this leads to a residual H2O resonance being observed at 3.95 ppm in the 1H NMR spectra.

3.3.1 – General Syntheses

**Synthesis of Alkynes - General Procedure A**[^44]

\[
\text{R} - \text{YMe} + \text{H} \equiv \text{Ar} \xrightarrow{\text{Pd(PPh}_3\text{)}_4 (0.02 \text{ eq.})} \xrightarrow{\text{CuX (0.04 \text{ eq.})}} \xrightarrow{\text{NEt}_3, \text{THF}} \xrightarrow{12 \text{h, reflux}} \text{R} - \text{XMe} \equiv \text{Ar}
\]

Y = O, NMe, X = Br
Y = S, X = I

A Schlenk fitted with a J. Young’s valve was charged with tetrakis-(triphenylphosphine)palladium(0) (0.02 eq.) and copper(I) halide (0.04 eq.). Tetrahydrofuran was added and the suspension was stirred for five minutes, followed by the addition of the aryl bromide (1 eq.) and triethylamine. After five minutes more stirring, the alkyne (1.1 eq.) was added and the solution was stirred and refluxed in the sealed vessel for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography to yield the corresponding alkyne.
Synthesis of Alkynes - General Procedure B

A Schlenk fitted with a J. Young’s valve was charged with tetrakis-(triphenylphosphine)palladium(0) (0.02 eq.) and copper(I) bromide (0.04 eq.). Tetrahydrofuran was added and the suspension was stirred for five minutes, followed by the addition of the aryl bromide (1 eq.) and triethylamine. After five minutes more stirring, the alkyne (1.1 eq.) was added and the solution was stirred and refluxed in the sealed vessel for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography to yield the corresponding alkyne.

Borylative Cyclisation of 2-alkynylanisoles and 2-alkynylthioanisoles

Due to the variable molarity of commercial BCl₃ solutions an excess of BCl₃ was formally used. All commercial BCl₃ solutions from various vendors labelled as 1M in DCM were actually found to be lower than 1M by varying amounts (by NMR titration experiments with PPh₃). Therefore between 1.1 – 1.4 equivalents of “1M” BCl₃ are used, which really approximates to a 1:1 ratio between alkyne and BCl₃. To minimise the gradual decrease in molarity of BCl₃ solutions over time due to the high volatility of BCl₃ the BCl₃ solutions are transferred to ampoules sealed with J. Young’s valves after first use. An excess of BCl₃ can be used rather than determining the molarity of BCl₃, with removal of solvent in vacuo also removing any excess of BCl₃.
The alkyne (1 eq.) was dissolved in DCM and boron trichloride ("1M" in DCM, 1.1-1.4 eq) was added. The reaction was stirred (or rotated at 10 revolutions per minute if performed in a J. Youngs NMR tube) at room temperature for the specified time until reaction completion and the solvent was removed in vacuo (also removing any unreacted BCl$_3$). The resulting oil was then re-dissolved in DCM, and transferred via cannula to a 0-5°C solution of pinacol (1.1 eq.) and NEt$_3$ (approx. 15 eq.) in DCM (Caution: the esterification is highly exothermic!). All subsequent steps were performed under air with non-purified solvents. The solvent was removed in vacuo and the product was extracted into pentane and filtered. The filtrate was collected and the solvent was removed in vacuo. If necessary the resulting material was purified further via column chromatography to yield the corresponding boronate ester. It should be noted the majority of boronate esters did not require column chromatography, with a simple filtration through a plug of silica sufficient to yield pure material.

**Adapted Procedure for Borylative Cyclisation of 2-alkynylthioanisole**

Further investigations into the reaction involved the direct comparison of the in-situ NMR spectra between the sulphur and oxygen analogues. It was concluded that the thioanisole moiety was not demethylated in-situ, leading to the generation of a zwitterionic sulphonium intermediate.

Into a J. Young's NMR tube, alkyne (1 eq.), DCM (0.4 mL), BCl$_3$ (2.2 eq) were added. An equivalent of AlCl$_3$ (1 eq.) was added to abstract the chloride, followed by demethylation with an excess of NEt$_3$ (0.5 mL) to generate the neutral benzothiophene-BCl$_2$ compound (presumably as the Et$_3$N adduct) and
[MeNEt₃][AlCl₄]. Pinacol (3 eq.) was added with an excess used to ensure complete esterification of the borylated species (as pinacol also reacts with the AlCl₄). (Caution: the esterification is highly exothermic!). This was purified via chromatography to give the desired compound.

### 3.3.2 – Alkynes

#### N,N-dimethyl-2-(phenylethynyl)aniline 3.1

![Chemical structure](image)

**Prepared according to general procedure A.** 2-bromo-
N,N-dimethylaniline (0.8 g, 4.00 mmol, 1 eq.), phenylacetylene (0.66 mL, 6.00 mmol, 1.5 eq), Pd(PPh₃)₄ (139 mg, 0.120 mmol, 0.03 eq.), copper(I) bromide (34 mg, 0.240 mmol, 0.06 eq.), triethylamine (8 mL) and THF (10 mL). *Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 3.1 (0.42 g, 47%) obtained as an orange oil. Data is in accordance with the literature.*

#### 1-methoxy-2-(phenylethynyl)benzene 3.3

![Chemical structure](image)

**Prepared according to general procedure A.** 2-bromoanisole (0.67 mL, 5.35 mmol, 1 eq.), phenylacetylene (0.70 mL, 6.42 mmol, 1.2 eq.), Pd(PPh₃)₄ (124 mg, 0.107 mmol, 0.02 eq.), copper(I) bromide (31 mg, 0.214 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). *Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 3.3 (0.93 g, 84%) obtained as a dark orange oil. The data was in accordance with the literature.*

#### 1-methoxy-4-methyl-2-(phenylethynyl)benzene 3.4

![Chemical structure](image)

**Prepared according to general procedure A.** 2-bromo-1-methoxy-4-methylbenzene (1.08 mL, 7.46 mmol, 1 eq.), phenylacetylene (1.00 mL, 8.95 mmol, 1.2 eq.), Pd(PPh₃)₄ (172 mg, 0.150 mmol, 0.02 eq.), copper(I) bromide (43 mg, 0.300 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). *Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 3.4 (1.28 g, 77%) obtained as an orange oil. The data was in accordance with the literature.*
4-chloro-1-methoxy-2-(phenylethynyl)benzene 3.5

Prepared according to general procedure A. 2-bromo-1-methoxy-4-chlorobenzene (0.92 mL, 6.77 mmol, 1 eq.), phenylacetylene (0.90 mL, 8.13 mmol, 1.2 eq.), Pd(PPh₃)₄ (156 mg, 0.135 mmol, 0.02 eq.), copper(I) bromide (39 mg, 0.271 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 

3.5 (1.62 g, 98%) obtained as an orange oil. ¹H NMR (400 MHz, CDCl₃): δ 3.91 (3H, s, OC₃H₃); 6.83 (1H, d, J = 9.1 Hz, Ar-H); 7.26 (1H, dd, J = 8.8 Hz, 2.5 Hz, Ar-H); 7.33-7.39 (3H, m, Ar-H); 7.48 (1H, d, J = 2.5 Hz, Ar-H); 7.54-7.58 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 56.2, 84.4, 94.5, 111.8, 114.1, 123.1, 125.2, 128.3, 128.5, 129.5, 131.7, 132.9, 158.6; [GC-MS] m/z calculated for C₁₅H₁₁ClO, 242.1; found 242.1. GC-MS retention times of analytes: 11.96 minutes: 4-chloro-1-methoxy-2-(phenylethynyl)benzene; [Acc. Mass] Calculated [M+H]^+: 243.0571 gmol⁻¹, Observed: [M+H]^+ 243.0571 gmol⁻¹.

1-(phenylethynyl)-2-methoxy-3-fluorobenzene 3.6

Prepared according to general procedure A. 1-bromo-2-methoxy-3-fluorobenzene (0.65 mL, 4.88 mmol, 1 eq.), phenylacetylene (0.54 mL, 4.88 mmol, 1.2 eq.), Pd(PPh₃)₄ (113 mg, 0.098 mmol, 0.02 eq.), copper(I) bromide (28 mg, 0.196 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). Column chromatography eluent: 25% DCM in 40-60 petroleum ether. 

3.6 (0.77 g, 71%) obtained as a brown solid. ¹H NMR (400 MHz, CDCl₃): δ 4.09 (3H, s, OCH₃); 6.96-7.03 (1H, m, Ar-H); 7.05-7.12 (1H, m, Ar-H); 7.28 (1H, dt, J = 7.8 Hz, 1.5 Hz, Ar-H); 7.34-7.41 (3H, m, Ar-H); 7.54-7.60 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 61.6 (d, ⁴J_CF = 4.4 Hz, OMe); 84.6 (d, ⁴J_CF = 5.2 Hz, C₁-C=); 94.3 (C₁-C=C); 117.2 (d, ²J_CF = 19.2 Hz, C₄); 118.7 (d, ³J_CF = 3.7 Hz, C₇); 123.1, 123.4 (d, ²J_CF = 19.2 Hz, C₄); 128.4, 128.56, 128.62 (d, ⁴J_CF = 3.7 Hz, C₆); 131.7, 148.6 (d, ²J_CF = 11.8 Hz, C₂); 155.4 (d, ¹J_CF = 247.0 Hz, C₃); ¹⁹F NMR (376.50 MHz, CDCl₃): δ -130.79 (1F, Ar-F); [GC-MS] m/z calculated for C₁₅H₁₁FO, 226.1; found 226.1. GC-MS retention times of analytes:

1-methoxy-3-methyl-2-(phenylethynyl)benzene 3.7

\[
\text{OMe} \quad \text{H} \quad \text{CH} = \text{C} \quad \text{Ph}
\]

**Prepared according to general procedure A.** 2-bromo-1-methoxy-3-methylbenzene (1 g, 4.97 mmol, 1 eq.), phenylacetylene (0.55 mL, 4.97 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (115 mg, 0.099 mmol, 0.02 eq.), copper(I) bromide (28 mg, 0.198 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). **Column chromatography eluent:** 30% DCM in 40-60 petroleum ether. 3.7 (0.22 g, 19%) obtained as a brown oil. Data is in accordance with the literature.\[^{[48]}\]

Ethyl 4-((2-methoxyphenyl)ethynyl)benzoate 3.8

\[
\text{OMe} \quad \text{H} \quad \text{CH} = \text{C} \quad \text{Ph} \quad \text{OEt}
\]

**Prepared according to general procedure B.** 2-ethynylanisole (0.98 mL, 7.57 mmol, 1.2 eq.), ethyl-4-bromobenzoate (1.03 mL, 6.31 mmol, 1 eq.), Pd(PPh\(_3\))\(_4\) (146 mg, 0.126 mmol, 0.02 eq.), copper(I) bromide (36 mg, 0.252 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). **Column chromatography eluent:** 30% DCM in 40-60 petroleum ether. 3.8 (1.33 g, 75%) obtained as an orange oil. Data is in accordance with the literature.\[^{[46]}\]

1-methoxy-2-(3-phenylprop-1-yn-1-yl)benzene 3.9

A Young’s ampoule was charged with tetrakis-(triphenylphosphine)palladium(0) (247 mg, 0.214 mmol, 0.02 eq.) and copper(I) bromide (61 mg, 0.428 mmol, 0.04 eq.). Tetrahydrofuran (10 mL) was added and the suspension was stirred for five minutes, followed by the addition of 2-bromoanisole (1.33 mL, 10.69 mmol, 1 eq.) and triethylamine (7 mL). After five minutes more stirring, 3-phenylprop-1-yne (1.6 mL, 12.83 mmol, 1.2 eq.) was added and the solution was stirred and refluxed in the sealed vessel for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent
was removed *in vacuo* and the crude material was purified via column chromatography (15% DCM in 40-60 petroleum ether) to yield 3.9 (0.93 g, 39%) as a brown oil. $^1$H NMR (400 MHz, CDCl$_3$): δ 3.91 (3H, s, OCH$_3$); 3.93 (2H, s, CH$_2$Ph); 6.88-6.94 (2H, m, Ar-H); 7.23-7.32 (2H, m, Ar-H); 7.36 (2H, t, J = 7.6 Hz, Ar-H); 7.42-7.51 (3H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): δ 26.1, 55.8, 78.9, 91.7, 110.5, 112.7, 120.4, 126.6, 128.0, 128.5, 129.3, 133.7, 136.9, 160.0; [GC-MS] m/z calculated for C$_{15}$H$_{11}$O, 207.1; found 207.1. GC-MS retention times of analytes: 10.81 minutes: 1-methoxy-2-(3-phenylprop-1-yn-1-yl)benzene; [Acc. Mass] Calculated [M]$^+$: 222.1045 gmol$^{-1}$, Observed: [M]$^+$ 222.1045 gmol$^{-1}$.

1-methoxy-2-(prop-1-yn-1-yl)benzene 3.10

![1-methoxy-2-(prop-1-yn-1-yl)benzene](image)

In a Young’s ampoule, 2-ethynylanisole (0.98 mL, 7.57 mmol, 1 eq.) was dissolved in tetrahydrofuran and stirred at -78°C over 20 minutes. $^9$BuLi (5.7 mL, 9.08 mmol, 1.2 eq.) was added dropwise and stirred at -78°C for a further 20 minutes. After this time, iodomethane (0.94 mL, 15.133 mmol, 2 eq.) was added dropwise and the solution was warmed to 20°C and stirred for 5 hours before being quenched with NH$_4$Cl (100 mL). The desired compound was extracted into DCM (4 x 25 mL), dried over MgSO$_4$ and the solvent was removed *in vacuo* to give 3.10 (985 mg, 89%) as an orange oil, with no further purification necessary. Data is in accordance with the literature.[49]

2-methoxy-4-nitro-1-(phenylethynyl)benzene 3.11

![2-methoxy-4-nitro-1-(phenylethynyl)benzene](image)

**Prepared according to general procedure A.** A Schlenk fitted with a J. Young’s valve was charged with tetrakis-(triphenylphosphine)palladium(0) (122 mg, 0.106 mmol, 0.02 eq.) and copper(I) bromide (30 mg, 0.212 mmol, 0.04 eq.). Tetrahydrofuran (10 mL) was added and the suspension was stirred for five minutes, followed by the addition of 2-bromo-5-nitroanisole (1.23 g, 5.3 mmol, 1 eq.) and triethylamine (7 mL). After five minutes more stirring, phenylacetylene (0.7 mL, 6.36 mmol, 1.2 eq.) was added and the solution was stirred and refluxed in the sealed vessel for 12 h. The solution was
cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography (50% DCM in 40-60 petroleum ether) to yield 3.11 (0.91 g, 68%) as a yellow solid. Data is in accordance with the literature.[50]

1-((2-methoxyphenyl)ethynyl)naphthalene 3.12

Prepared according to general procedure A. A Schlenk fitted with a J. Young’s valve was charged with tetrakis-(triphenylphosphine)palladium(0) (124 mg, 0.107 mmol, 0.02 eq.) and copper(I) bromide (31 mg, 0.214 mmol, 0.04 eq.). Tetrahydrofuran (10 mL) was added and the suspension was stirred for five minutes, followed by the addition of 2-bromoanisole (0.67 mL, 5.35 mmol, 1 eq.) and triethylamine (7 mL). After five minutes more stirring, 1-ethynynaphthalene (0.91 mL, 6.42 mmol, 1.2 eq.) was added and the solution was stirred and refluxed in the sealed vessel for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography (50% DCM in 40-60 petroleum ether) to yield 3.12 (0.88 g, 63%) as a brown oil. Data is in accordance with the literature.[51]

((2,5-dimethoxy-1,4-phenylene)bis(ethyne-2,1-diyl))dibenzene 3.23

Prepared according to general procedure A. 1,4-dibromo-2,5-dimethoxybenzene (2 g, 6.76 mmol, 1 eq.), phenylacetylene (1.71 mL, 15.55 mmol, 2.3 eq), Pd(PPh₃)₄ (312 mg, 0.270 mmol, 0.04 eq.), copper(I) bromide (78 mg, 0.541 mmol, 0.08 eq.), triethylamine (10 mL) and THF (15 mL). Column chromatography eluent: 50% DCM in 40-60 petroleum ether. 3.23 (1.196 g, 52%) obtained as an orange oil. Data is in accordance with the literature.[52]
Methyl(2-(phenylethynyl)phenyl)sulfane 3.27

Prepared according to general procedure A. 2-iodothioanisole (1 g, 4.00mmol, 1 eq.), phenylacetylene (0.66 mL, 6.00 mmol, 1.5 eq.), Pd(PPh₃)₄ (138 mg, 0.120 mmol, 0.03 eq.), copper(I) iodide (46 mg, 0.24 mmol, 0.06 eq.), triethylamine (8 mL) and THF (10 mL). Column chromatography eluent: 10% DCM in 40-60 petroleum ether. 3.27 (0.24 g, 27%) obtained as a dark orange oil. Data is in accordance with the literature.[49]

Methyl(2-(naphthalen-1-ylethynyl)phenyl)sulfane 3.28

Prepared according to general procedure A. 2-iodothioanisole (1 g, 4.00mmol, 1 eq.), 1-ethynlnaphthalene (0.85 mL, 6.00 mmol, 1.5 eq.), Pd(PPh₃)₄ (138 mg, 0.120 mmol, 0.03 eq.), copper(I) iodide (46 mg, 0.24 mmol, 0.06 eq.), triethylamine (8 mL) and THF (10 mL). Column chromatography eluent: DCM on base-treated silica (run through 5% NEt₃ in hexane before adding compound to column). 3.28 (543 mg, 50%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 2.58 (3H, s, SCH₃); 7.18 (1H, td, J = 7.5 Hz, 1.1 Hz, Ar-H); 7.22-7.26 (1H, m, Ar-H); 7.33-7.39 (1H, m, Ar-H); 7.48 (1H, dd, J = 8.3 Hz, 7.3 Hz, Ar-H); 7.52 - 7.58 (1H, m, Ar-H); 7.60-7.67 (2H, m, Ar-H); 7.83 (1H, dd, J = 7.2 Hz, 1.1 Hz); 7.84 - 7.91 (2H, m, Ar-H); 8.63 (1H, d, J = 8.3 Hz, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 15.3, 91.7, 94.1, 120.9, 121.6, 124.3, 124.4, 125.3, 126.5, 126.6, 126.9, 128.2, 128.87, 128.92, 130.6, 132.5, 133.2, 133.3, 141.7 [GC-MS] m/z calculated for C₁₉H₁₄S, 274.1; found 274.1. GC-MS retention times of analytes: 14.23 minutes: Methyl(2-(naphthalen-1-ylethynyl)phenyl)sulfane; [Acc. Mass] Calculated [M+H]^+: 275.0889 gmol⁻¹, Observed: [M+H]^+ 275.0892 gmol⁻¹.

3-((2-(methylthio)phenyl)ethynyl)thiophene 3.29

Prepared according to general procedure A. 2-iodothioanisole (1 g, 4.00mmol, 1 eq.), 3-ethynlthiophene (0.47 mL, 4.80 mmol, 1.2 eq), Pd(PPh₃)₄ (139 mg, 0.120 mmol, 0.02 eq.), copper(I) iodide (46 mg, 0.240 mmol, 0.04
eq.), triethylamine (8 mL) and THF (10 mL). **Column chromatography eluent: 20% DCM in 40-60 petroleum ether.** 3.29 (0.62 g, 68%) obtained as an orange oil. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.52 (3H, s, SCH$_3$); 7.12 (1H, td, J = 7.6 Hz, 1.3 Hz, Ar-H); 7.18 (1H, d, J = 8.1 Hz, Ar-H); 7.25 (1H, dd, J = 5.0 Hz, 1.3 Hz, Ar-H); 7.29-7.34 (2H, m, Ar-H); 7.48 (1H, dd, J = 7.6 Hz, 1.3 Hz, Ar-H); 7.58 (1H, dd, J = 3.0 Hz, 1.3 Hz, Ar-H); $^{13}$C{$^1$H} NMR (100.6 MHz, CDCl$_3$): δ 15.1, 86.3, 91.0, 121.3, 122.2, 124.1, 124.3, 125.4, 128.7, 128.8, 129.9, 132.2, 141.6; [GC-MS] m/z calculated for C$_{13}$H$_{10}$S$_2$, 230.0; found 230.0. GC-MS retention times of analytes: 12.08 minutes: 3-((2-(methylthio)phenyl)ethynyl)thiophene; [Acc. Mass] Calculated [M+H]$^+$: 231.0296 gmol$^{-1}$, Observed: [M+H]$^+$ 231.0306 gmol$^{-1}$.

(2-(mesitylethynyl)phenyl)(methyl)sulfane 3.30

Prepared according to general procedure A. 2-iodothioanisole (1.6 g, 6.30 mmol, 1 eq.), 2-ethynylmesitylene (1 g, 6.93 mmol, 1.1 eq), Pd(PPh$_3$)$_4$ (146 mg, 0.126 mmol, 0.02 eq.), copper(I) iodide (48 mg, 0.252 mmol, 0.04 eq.), triethylamine (8 mL) and THF (10 mL). **Column chromatography eluent: 15% DCM in 40-60 petroleum ether.** 3.30 (1.59 g, 95%) obtained as an orange solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.34 (3H, s, SCH$_3$); 2.54 (3H, s, Mes(p-CH$_3$)); 2.58 (6H, s, C=C-Mes(o-CH$_3$)$_2$); 6.94 (2H, s, Mes-H); 7.15 (1H, t, J = 7.6 Hz, Ar-H); 7.21 (1H, d, J = 7.8 Hz, Ar-H); 7.30-7.40 (1H, m, Ar-H); 7.54(1H, d, J = 7.8 Hz, Ar-H); $^{13}$C{$^1$H} NMR (100.6 MHz, CDCl$_3$): δ 15.1, 21.3, 21.5, 94.0, 94.4, 120.0, 121.9, 123.8, 124.2, 127.7, 128.5, 132.3, 138.0, 140.4, 141.1; [GC-MS] m/z calculated for C$_{18}$H$_{18}$S, 266.1; found 266.1. GC-MS retention times of analytes: 12.98 minutes: (2-(mesitylethynyl)phenyl)(methyl)sulfane; [Acc. Mass] Calculated [M+H]$^+$: 267.1202 gmol$^{-1}$, Observed [M+H]$^+$: 267.1198 gmol$^{-1}$.
Methyl 2-(phenylethynyl)benzoate 3.35

In a Young’s ampoule, Pd(PPh₃)₄ (176 mg, 0.153 mmol, 0.02 eq.) and Cul (58 mg, 0.306 mmol, 0.04 eq.) were stirred in THF (10 mL). 2-iodomethylbenzoate (1.12 mL, 7.63 mmol, 1 eq.) and NEt₃ (8 mL) were added followed by phenylacetylene (1.01 mL, 9.159 mmol, 1.2 eq.). The mixture was refluxed at 95°C in the sealed vessel overnight, then cooled to room temperature, and filtered through a plug of Celite™ on top of a silic plug. The resulting crude mixture was purified via column chromatography (50% pentane in DCM) to give 3.35 (1.78 g, 99%) as an orange oil. Data was in accordance with the literature.²⁵

3.3.3 - Indole Formation Versus N-directed Trans-Haloboration

N-directed trans-haloboration 3.2

In a Schlenk fitted with J. Young’s valve, alkyne 3.1 (50 mg, 0.226 mmol, 1 eq.) was dissolved in o-dichlorobenzene (2 mL) and BCl₃ (1M in heptane) (0.29 mL, 0.290 mmol, 1.3 eq.) was added. The reaction was left for an hour at room temperature. The solution was layered with hexane and stored in the freezer for a week. A colourless crystalline solid deposited on the walls of the ampoule and was collected. Upon analysis, the solid was found to be the desired trans-haloboration product 3.2 (51 mg, 67%).

¹H NMR (400 MHz, CD₂Cl₂): δ 3.02 (6H, s, NMe₂); 7.35-7.41 (4H, m, Ar-H); 7.44 (1H, t, J = 7.6 Hz, Ar-H); 7.50 (1H, t, J = 7.6 Hz, Ar-H); 7.63-7.70 (2H, m, Ar-H); 8.47 (1H, d, J = 7.8 Hz, Ar-H); ³¹C{¹H} NMR (100.6 MHz, CD₂Cl₂): δ 49.5, 117.0, 127.4, 128.1, 128.7, 128.9, 129.0, 129.5, 130.5, 136.0, 140.5, 149.1; ¹¹B NMR (128.6MHz, CD₂Cl₂); δ 10.5 (s) [GC-MS] m/z calculated for C₁₆H₁₅BCl₃N, 337.0; found 337.0. GC-MS retention times of analytes: 14.30 minutes: N-directed trans-haloboration product; [Acc. Mass] Calculated [M]⁺ 337.0363 gmol⁻¹, Observed [M]⁺ 337.0352 gmol⁻¹; Anal. Calcd for C₁₆H₁₅BCl₃N: C, 56.78; H, 4.47; N, 4.14. Found: C, 56.79; H, 4.56; N, 4.11. Mass data involves ³⁵Cl isotope.
3.3.4 – 3-Borylated Benzofurans

4,4,5,5-tetramethyl-2-(2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane 3.13

Prepared according to the general procedure. Alkyne 3.3 (130 mg, 0.630 mmol, 1 eq.), BCl₃ (0.75 mL, 0.750 mmol, 1.2 eq.), DCM (0.5 mL), NEt₃ (1.5 mL) and pinacol (78 mg, 0.660 mmol, 1.05 eq.). Filtered through silica with pentane for purification. 3.13 (112 mg, 56%) obtained as an orange film.

¹H NMR (400 MHz, CDCl₃): δ 1.40 (12H, s, Bpin); 7.21-7.33 (2H, m, Ar-H); 7.37-7.47 (3H, m, Ar-H); 7.49-7.53 (1H, m, Ar-H); 8.00-8.03 (1H, m, Ar-H); 8.13-8.19 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 23.9, 82.6, 109.5, 121.9, 122.1, 123.2, 127.1, 128.1, 130.3, 132.3, 153.6, 161.9; ¹¹B NMR (128.6 MHz, CDCl₃); δ 30.6 (s); [GC-MS] m/z calculated for C₂₀H₂₁BO₃, 320.2; found 320.2. GC-MS retention times of analytes: 16.31 minutes: 4,4,5,5-tetramethyl-2-(2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]⁺: 321.1657 gmol⁻¹, Observed [M+H]⁺: 321.1655 gmol⁻¹.

4,4,5,5-tetramethyl-2-(5-methyl-2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane 3.14

Prepared according to the general procedure. Alkyne 3.4 (44 mg, 0.198 mmol, 1 eq.), BCl₃ (0.24 mL, 0.240 mmol, 1.2 eq.), DCM (0.5 mL), NEt₃ (0.5 mL) and pinacol (28 mg, 0.240 mmol, 1.2 eq.). Filtered through silica with pentane for purification. 3.14 (59 mg, 89%) obtained as a colourless film. ¹H NMR (400 MHz, CDCl₃): δ 1.43 (12H, s, Bpin); 2.50 (3H, s, Ar-CH₃); 7.11 (1H, dd, J = 8.3 Hz, 1.8 Hz, Ar-H); 7.38-7.49 (4H, m, Ar-H); 7.76-7.79 (1H, m, Ar-H); 8.14-8.18 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 21.6, 25.0, 83.6, 110.1, 122.8, 125.5, 128.1, 129.0, 131.4, 132.4, 133.3, 153.1, 163.1; ¹¹B NMR (128.6 MHz, CDCl₃); δ 30.5 (s); [GC-MS] m/z calculated for C₂¹H₂₃BO₃: 334.2; found 334.2. GC-MS retention times of analytes: 13.44 minutes: 4,4,5,5-tetramethyl-2-(5-methyl-2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M]⁺: 334.1740 gmol⁻¹, Observed [M]⁺: 334.1733 gmol⁻¹.
2-(5-chloro-2-phenylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

Prepared according to the general procedure. Alkyne 3.5 (44 mg, 0.181 mmol, 1 eq.), BCl₃ (0.22 mL, 0.220 mmol, 1.2 eq.), DCM (0.5 mL), NEt₃ (0.5 mL) and pinacol (26 mg, 0.220 mmol, 1.2 eq.). Filtered through silica with pentane for purification. 3.15 (46 mg, 72%) obtained as a colourless film. ¹H NMR (400 MHz, CDCl₃): δ 1.42 (12H, s, Bpin); 7.25 (1H, dd, J = 8.6 Hz, 2.3 Hz, Ar-H); 7.40-7.49 (4H, m, Ar-H); 7.98 (1H, dd, J = 2.3 Hz, 0.5 Hz, Ar-H); 8.06-8.16 (2H, m, Ar-H); 13C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.9, 83.8, 111.5, 122.7, 124.4, 128.2, 128.3, 128.5, 129.5, 130.8, 134.8, 153.0, 164.4; ¹¹B NMR (128.6MHz, CDCl₃); δ 30.4 (s); [GC-MS] m/z calculated for C₂₀H₂₀BClO₃: 354.2; found 354.2. GC-MS retention times of analytes: 13.80 minutes: 2-(5-chloro-2-phenylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass] [M]+ 354.1189 gmol⁻¹ [Acc. Mass] Calculated [M]+: 354.1194 gmol⁻¹, Observed [M]+: 354.1189 gmol⁻¹. Mass data involves ³⁵Cl isotope.

2-(7-fluoro-2-phenylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

Prepared according to the general procedure. Alkyne 3.6 (91 mg, 0.402 mmol, 1 eq.), BCl₃ (0.53 mL, 0.52 mmol, 1.3 eq.), DCM (0.5 mL), NEt₃ (1 mL) and pinacol (65 mg, 0.550 mmol, 1.4 eq.). Filtered through silica with pentane for purification. 3.16 (107 mg, 79%) obtained as a colourless film. ¹H NMR (400 MHz, CDCl₃): δ 1.45 (12H, s, Bpin); 7.06 (1H, ddd, J = 10.6 Hz, 8.1 Hz, 1.0 Hz, Ar-H); 7.21 (1H, td, J = 8.1 Hz, 4.5 Hz, Ar-H); 7.43-7.53 (3H, m, Ar-H); 7.82 (1H, dd, J = 7.8 Hz, 1.0 Hz, Ar-H); 8.21-8.25 (2H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.9 ((CH₃CO)₂B), 83.8 ((CH₃CO)₂B), 110.5 (d, J = 15.5 Hz); 118.7 (d, 3.7 Hz); 123.4 (d, J = 5.9 Hz); 128.3 (d, J = 8.9 Hz); 128.9 (d, J = 13.2 Hz); 129.5, 130.7, 136.9 (d, J = 3.0 Hz); 141.6 (d, J = 11.1 Hz); 142.6 (d, J = 248.4 Hz); 163.8; ¹¹B NMR (128.6MHz, CDCl₃); δ 30.5 (s); ¹⁹F NMR (376.50 MHz, CDCl₃): δ -137.66; [GC-MS] m/z
calculated for C_{20}H_{20}BFO_3: 338.2; found 338.2. GC-MS retention times of analytes: 16.19 minutes: 2-(7-fluoro-2-phenylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M]^+: 338.1490 g mol^{-1}, Observed [M]^+: 338.1486 g mol^{-1}.

4,4,5,5-tetramethyl-2-(4-methyl-2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane 3.17

In a J. Young’s NMR tube, Alkyne 3.7 (32 mg, 0.144 mmol, 1 eq.) and 2,4,6-tri-tert-butylpyridine (TBP) (36 mg, 0.144 mmol, 1 eq.) were dissolved in DCM (0.5 mL). BCl_3 (0.53 mL, 0.52 mmol, 1.3 eq.) was added and the mixture was left for 12 hours at 20°C. After this time, the mixture was layered with NEt_3 (1 mL) and pinacol (18 mg, 0.152 mmol, 1.25 eq.) was added. The tube was inverted to mix, and the crude compound was immediately generated. This was purified via preparative TLC (Eluent: 15% DCM in 40-60 petroleum ether) to give 3.17 (16 mg, 33%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 1.41 (12H, s, Bpin); 2.66 (3H, m, Ar-CH_3); 7.02 (1H, dt, J = 7.3 Hz, 0.7 Hz, Ar-H); 7.18 (1H, t, J = 7.8 Hz, Ar-H); 7.34-7.47 (4H, m, Ar-H); 7.91-7.95 (2H, m, Ar-H); ^13C{^1H} NMR (100.6 MHz, CDCl_3): δ 20.7, 25.1, 84.3, 108.4, 123.9, 124.2, 127.8, 128.2, 128.8, 131. 4, 131.7, 132.4, 155.1.; ^11B NMR (128.6MHz, CDCl_3); δ 31.7 (s); [GC-MS] m/z calculated for C_{21}H_{23}BO_3: 334.2; found 334.2. GC-MS retention times of analytes: 13.49 minutes: 4,4,5,5-tetramethyl-2-(4-methyl-2-phenylbenzofuran-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]^+: 335.1813 g mol^{-1}, Observed [M+H]^+: 335.1811 g mol^{-1}

TBP was added to this reaction mixture as trace hydrolysis of BCl_3 generates HCl which can lead to alkyl migration as previously observed (See Chapter 2). Indeed, on addition of TBP a small quantity of protonated TBP was observed.
Ethyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzofuran-2-yl)benzoate \(3.18\)

In a J. Young’s NMR tube, alkyne \(3.8\) (20 mg, 0.071 mmol, 1 eq.) and TBP (20 mg, 0.071 mmol, 1 eq.) were dissolved in DCM (0.5 mL). BCl\(_3\) (0.24 mL, 0.240 mmol, 3.3 eq.) was added and the mixture was left for 12 hours at 20°C. After this time, the mixture was layered with NEt\(_3\) (1 mL) and pinacol (29 mg, 0.245 mmol, 3.5 eq.) was added. The tube was inverted to mix, and the crude compound was immediately generated. This was purified via preparative TLC (Eluent: 20% DCM in 40-60 petroleum ether) to give \(3.18\) (13 mg, 46%) as a white solid. 

\[\begin{align*}
\text{[H NMR (400 MHz, CDCl}_3\text{): }\delta & \quad 1.43 (12H, s, Bpin); 1.44 (3H, t, J = 7.1 Hz, COOCH}_2\text{CH}_3); 4.42 (2H, q, J = 7.1 Hz, COOCH}_2\text{CH}_3); 7.25-7.36 (2H, m Ar-H); 7.52-7.55 (1H, m, Ar-H); 8.04 (1H, m, Ar-H); 8.12 (2H, dt, J = 8.4 Hz, 1.7 Hz, Ar-H); 8.28 (2H, dt, J = 8.4 Hz, 1.7 Hz, Ar-H); 13C\{^1H\} NMR (100.6 MHz, CDCl\(_3\)): }\delta \\
& \quad 14.4, 25.0, 61.1, 83.9, 110.7, 123.2, 123.4, 124.9, 127.8, 129.4, 130.4, 133.1, 135.4, 154.8, 161.4, 166.4; ^{11}B NMR (128.6MHz, CDCl\(_3\)): }\delta \\
& \quad 30.4 (s); [GC-MS] m/z calculated for C\(_{23}\)H\(_{25}\)BO\(_5\): 392.2; found 392.2. GC-MS retention times of analytes: 15.33 minutes: Ethyl 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzofuran-2-yl)benzoate; [Acc. Mass] Calculated [M+H]\(^{+}\): 393.1868 gmol\(^{-1}\), Observed [M+H]\(^{+}\): 393.1868 gmol\(^{-1}\)
\end{align*}\]

Excess BCl\(_3\) was utilised in this case as one equivalent of BCl\(_3\) coordinates to the ester moiety (See Chapter 2).

2-(2-benzylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane \(3.19\)

Prepared according to the general procedure. Alkyne \(3.9\) (30 mg, 0.135 mmol, 1 eq.), BCl\(_3\) (0.16 mL, 0.160 mmol, 1.2 eq.), DCM (0.5 mL), NEt\(_3\) (0.5 mL) and pinacol (19 mg, 0.160 mmol, 1.2 eq.). Filtered through silica with pentane for purification. \(3.19\) (26 mg, 57%) obtained as a colourless film. 

\[\begin{align*}
\text{[H NMR (400 MHz, CDCl}_3\text{): }\delta & \quad 1.42 (12H, s, Bpin); 4.40 (2H, s, PhCH}_2); 7.20-7.27 (3H, m, Ar-H); 7.32 (2H, t, J = 7.6 Hz); 7.38-7.43 (3H, m, Ar-}
\end{align*}\]
1H NMR (400 MHz, CDCl3): δ 1.38 (12H, s, Bpin); 1.66 (3H, s, Ar-CH3); 7.18-7.25 (2H, m, Ar-H); 7.38-7.44 (1H, m, Ar-H); 7.82-7.88 (1H, m, Ar-H); 13C{1H} NMR (100.6 MHz, CDCl3): δ 14.5, 25.0, 83.1, 110.2, 122.1, 122.7, 123.2, 132.1, 154.8, 165.8; 11B NMR (128.6 MHz, CDCl3); δ 30.3 (s); [GC-MS] m/z calculated for C15H19BO3, 258.1; found 258.1. GC-MS retention times of analytes: 10.73 minutes: 2-(2,5-dimethylbenzofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 3.20

4,4,5,5-tetramethyl-2-(2-methylbenzofuran-3-yl)-1,3,2-dioxaborolane 3.20

**Small scale:** Prepared according to the general procedure using a J. Young’s NMR tube. Alkyne 3.10 (31 mg, 0.212 mmol, 1 eq.), BCl3 (0.23 mL, 0.230 mmol, 1.1 eq.), DCM (0.5 mL), NEt3 (0.5 mL) and pinacol (27 mg, 0.230 mmol, 1.1 eq.). Filtered through silica with pentane for purification. 3.20 (48 mg, 89%) obtained as a white solid.

**Larger scale:** Prepared according to the general procedure. Alkyne 3.10 (867 mg, 5.931 mmol, 1 eq.), BCl3 (7.7 mL, 7.71 mmol, 1.3 eq.), DCM (5 mL), NEt3 (5 mL) and pinacol (940 mg, 7.95 mmol, 1.3 eq.). Filtered through silica with pentane for purification. 3.20 (1.16 g, 76%) obtained as a white solid.

**Non-purified solvents under ambient conditions:** In a 100 mL round-bottomed flask open to the atmosphere, alkyne 3.10 (51 mg, 0.345 mmol, 1 eq.), BCl3 (0.41 mL, 0.410 mmol, 1.1 eq.), non-purified DCM (0.5 mL) were added. The mixture was stirred for five minutes before non-purified NEt3 (1 mL) and pinacol (49 mg, 0.41 mmol, 1.1 eq.) were added. The crude mixture was extracted and filtered through silica using pentane to give 3.20 (72 mg, 81%) as a white solid.

3.3.5 – O-directed Trans-Haloboration Product

(Z)-2-(2-chloro-1-(2-methoxyphenyl)-2-(naphthalen-1-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 3.22

In a Young’s NMR tube, alkyne 3.12 (35 mg, 0.135 mmol, 1 eq.) was dissolved in DCM (0.4 mL). BCl₃ (0.15 mL, 0.150 mmol, 1.1 eq.) was added. After five minutes, an excess of water was added and the tube was sonicated to assist with mixing. The resulting boronic acid was then stirred with pinacol (18 mg, 0.149 mmol, 1.1 eq.) in THF (5 mL) to generate the esterified product. This was purified via chromatography (20% DCM in 40-60 petroleum ether), however two very minor impurities, the starting alkyne and the borylated benzofuran (from the cyclisation pathway), were observed that could not be completely separated in our hands. Data reported for the major component, which corresponds to the haloboration product 3.22.

¹H NMR (400 MHz, CDCl₃): δ 1.39 (6H, s, Bpin); 1.41 (6H, s, Bpin); 3.74 (3H, s, OMe); 6.37 (1H, td, J = 7.6 Hz, 1.0 Hz, Ar-H); 6.62 (1H, dd, J = 7.6 Hz, 1.1 Hz, Ar-H); 6.67 (1H, d, J = 8.1 Hz, Ar-H); 6.95 (1H, td, J = 8.3 Hz, 1.7 Hz, Ar-H); 7.23-7.31 (2H, m, Ar-H); 7.42-7.51 (2H, m, Ar-H); 7.70 (1H, d, J = 7.6 Hz, Ar-H); 7.78 (1H, d, J = 7.3 Hz, Ar-H); 8.20 (1H, d, J = 8.3 Hz, Ar-H); ¹¹B NMR (128.6MHz, CDCl₃): δ 31.0 (s); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.8, 24.9, 55.1, 84.0, 109.8, 120.3, 125.1, 125.8, 126.0, 126.2, 127.3, 128.1, 128.2, 128.3, 128.8, 130.0, 130.7, 133.4, 137.2, 138.3, 156.1 [APCI] m/z calculated for [M+H]+ 421.2; found 421.1; [M-Cl]+ Calculated 385.2; found 385.2;[M+NH₄]+ Calculated 438.2; Found 438.2 [Acc.Mass] [M+H]+ Calculated 421.1736 gmol⁻¹; Found 421.1743 gmol⁻¹
3.3.6 – Further Functionalisation

Double Borylative Cyclisation

2,2’-(2,6-diphenylbenzo[1,2-b4,5-b’]difuran-3,7-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) 3.24

Prepared according to the general procedure. Alkyne 3.23 (118 mg, 0.358 mmol, 1 eq.), BCl₃ (0.79 mL, 0.790 mmol, 2.2 eq.), DCM (4 mL). Grey precipitate forms after minutes. NEt₃ (4 mL) and pinacol (91 mg, 0.790 mmol, 2.2 eq.). Filtered through silica with pentane for purification. 3.24 (176 mg, 88%) obtained as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 1.45 (24H, s, Bpin); 7.37-7.50 (6H, m, Ar-H); 8.10 (2H, s, 2(C-H) on central ring); 8.20-8.24 (4H, m, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 25.0, 83.7, 103.3, 128.12, 128.16, 129.0, 131.4, 131.5, 152.1, 163.5; ¹¹B NMR (128.6MHz, CDCl₃); δ 31.0 (s); [APCI] m/z calculated for C₃₄H₃₆B₂O₆, 563.3; found 563.3; [Acc. Mass] Calculated [M+H]⁺: 563.2771 gmol⁻¹, Observed [M+H]⁺: 563.2755 gmol⁻¹

Isolated Borylated Benzofuran Cross Coupling

2-methyl-3-(p-tolyl)benzofuran 3.25

In a Schlenk fitted with a J. Young’s valve, 4,4,5,5-tetramethyl-2-(2-methylbenzofuran-3-yl)-1,3,2-dioxaborolane 3.20 (100 mg, 0.387 mmol, 1.1 eq.), 4-bromotoluene (60 mg, 0.352 mmol, 1 eq.) and Pd(PPh₃)₄ (25 mg, 0.021 mmol, 0.06 eq) were added to a degassed solution of 1:1 THF/2M K₃PO₄(aq) (10 mL) which was sealed and stirred at 80°C for 12 hours. The mixture was then cooled to 20°C, washed with water (3 x 10 mL) and extracted into ether (3 x 10 mL). The solvent was removed in vacuo and the compound was purified via column chromatography (10% DCM in 40-60
petroleum ether) to give the cross coupled product 3.25 (43 mg, 50%) as a white solid. The data was in accordance with the literature.[53]

In this case, the moderate yield was attributed to protodeboronation of the boronate ester. Typically heteroaryl boronate esters are used in a larger excess to allow complete consumption of the aryl halide due to competitive protodeboronation (for example 1.5 eq of the alkyne (and thus boronate ester) was used in the one-pot borylative cyclisation cross coupling).

**In Situ Cross Coupling**

5-methyl-2-phenyl-3-(p-tolyl)benzofuran 3.26

![Reaction Scheme](image)

In a Schlenk fitted with a J. Young valve, BCl$_3$ (0.54 mL, 0.540 mmol, 1.7 eq.) was added to a solution of alkyne 3.4 (100 mg, 0.450 mmol, 1.5 eq.) in DCM (2 mL) and stirred for 10 minutes. After this time, the solvent and any remaining BCl$_3$ were removed *in vacuo* and Pd(PPh$_3$)$_4$ (21 mg, 0.018 mmol, 0.06 eq.) and 4-bromotoluene (51 mg, 0.298 mmol, 1 eq.) were added as solids. A solution of aqueous 2M K$_3$PO$_4$ (1.1 mL, 2.250 mmol, 7.5 eq.) in THF (10 mL) was degassed for 30 minutes and added to the ampoule. The resulting solution was stirred and refluxed for 12 hours. After this time, the solution was allowed to cool to 20°C and Et$_2$O (15 mL) was added. The crude mixture was washed with distilled water (3 x 10 mL) and the organic layer was dried over MgSO$_4$ and evaporated *in vacuo*. The resulting oil was purified via column chromatography (10% DCM / 90% 40-60 petroleum ether) to give benzofuran 3.26 (63 mg, 72% based on 4-bromotoluene) as a colourless oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.44 (3H, s, Ar-Me); 2.47 (3H, s, Ar-Me); 7.15 (1H, d, J = 8.3 Hz, Ar-H); 7.27-7.36 (6H, m, Ar-H); 7.38-7.47 (3H, m, Ar-H); 7.68 (2H, d, J = 7.3 Hz, Ar-H);
\[^{13}\text{C}(^1\text{H})\] NMR (100.6 MHz, CDCl\textsubscript{3}): \(\delta\) 21.4, 110.6, 117.3, 119.8, 125.9, 126.9, 128.2, 128.4, 129.65, 129.71, 130.0, 130.5, 131.0, 132.4, 137.3, 150.5, 152.4; [GC-MS] m/z calculated for C\textsubscript{22}H\textsubscript{18}O, 298.1; found 298.1. GC-MS retention times of analytes: 17.46 minutes: 5-methyl-2-phenyl-3-(p-toly)benzofuran; [Acc. Mass] Calculated [M+H]\(^+\) 299.1431 gmol\(^{-1}\), Observed [M+H]\(^+\) 299.1430 gmol\(^{-1}\)

3.3.7 – Functionality Screening

In a J. Young’s NMR tube, alkyne 3.4 (30mg) was dissolved in DCM (0.5 mL) with a known amount of mesitylene to act as an internal standard, and one equivalent of an additive. BCl\textsubscript{3} was added and the in-situ yields were determined within 30 minutes using NMR spectroscopy to compare the quantities of desired product and additive against the mesitylene standard.

3.3.8 – 3-Borylated Benzothiophenes

4,4,5,5-tetramethyl-2-(2-phenylbenzo[b]thiophen-3-yl)-1,3,2-dioxaborolane 3.31

Prepared according to the general procedure. Alkyne 3.27 (100 mg, 0.446 mmol, 1 eq.), BCl\textsubscript{3} (0.56mL, 0.560 mmol, 1.2 eq.), DCM (1 mL), NEt\textsubscript{3} (1 mL) and pinacol (70 mg, 0.592 mmol, 1.3 eq.). Filtered through silica with pentane for purification. 3.31 (57 mg, 38%) obtained as a white solid. \(^1\text{H}\) NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 1.35 (12H, s, Bpin); 7.30 - 7.37 (1H, m, Ar-H); 7.37 - 7.47 (4H, m, Ar-H); 7.60 - 7.68 (2H, m, Ar-H); 7.82 - 7.89 (1H, m, Ar-H); 8.22 - 8.29 (1H, m, Ar-H); \(^{13}\text{C}(^1\text{H})\) NMR (100.6 MHz, CDCl\textsubscript{3}): \(\delta\) 24.8, 83.6, 121.6, 124.0, 124.4, 125.2, 127.9, 128.4, 129.8, 135.4, 140.5, 144.8, 154.9; \(^{11}\text{B}\) NMR (128.6MHz, CDCl\textsubscript{3}); \(\delta\) 30.32 (s); [GC-MS] m/z calculated for C\textsubscript{20}H\textsubscript{21}BO\textsubscript{2}S, 336.2; found 336.2. GC-MS retention times of analytes: 13.56 minutes: 4,4,5,5-tetramethyl-2-(2-
phenylbenzo[b]thiophen-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]+: 337.1428 gmol⁻¹, Observed [M+H]+: 337.1425 gmol⁻¹

Modified procedure – with addition of NEt₃/AlCl₃

Further investigations into the reaction involved the direct comparison of the in-situ NMR spectra between the sulphur and oxygen analogues. It was concluded that the thioanisole moiety was not demethylated in-situ, leading to the generation of a zwitterionic sulphonium intermediate.

Adapted procedure – NEt₃ followed by AlCl₃

In a J. Young’s NMR tube, alkyne 3.27 (56 mg, 0.249 mmol, 1 eq.), DCM (0.4 mL), BCl₃ (0.55mL, 0.55 mmol, 2.2 eq.) were added. An equivalent of AlCl₃ (33 mg, 1 eq. 0.249 mmol) was added to abstract the chloride, followed by demethylation with an excess of NEt₃ (0.5 mL) to generate the neutral thiophene-BCl₂ compound (presumably as the Et₃N adduct) and [MeNEt₃][AlCl₄]. 3 equivalents of pinacol (88 mg, 0.747 mmol) were added with an excess used to ensure complete esterification of the borylated species (as pinacol also reacts with the AlCl₄). This was purified via chromatography (20% DCM in 40-60 petroleum ether) to give the desired compound 3.31 (57 mg, 68%).

4,4,5,5-tetramethyl-2-(2-(naphthalen-1-yl)benzo[b]thiophen-3-yl)-1,3,2-dioxaborolane 3.32

Prepared according to the general procedure using a J. Young’s NMR tube. Alkyne 3.28 (10 mg, 0.036 mmol, 1 eq.), BCl₃ (0.44 mL, 0.440 mmol, 1.2 eq.), DCM (0.5 mL), NEt₃ (0.5 mL) and pinacol (5 mg, 0.042 mmol, 1.2 eq.). Purified via preparative TLC (Eluent: 30% DCM in 40-60 petroleum ether). 3.32 (7 mg, 48%) obtained as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 0.98 (12H, s, Bpin); 7.34 - 7.55 (5H, m, Ar-H); 7.61 (1H, dd, J = 6.9 Hz, 1.1 Hz, Ar-H); 7.87-7.93 (4H, m, Ar-H); 8.32 (1H, d, J = 7.9 Hz, Ar-H); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.5, 83.1, 121.6, 124.1, 124.5, 124.7, 125.2, 125.6, 126.16, 126.21, 127.9, 128.2, 128.6, 133.1, 133.3, 133.6, 140.9,
144.0, 152.8; $^{11}$B NMR (128.6MHz, CDCl$_3$); δ 30.2 (s); [GC-MS] m/z calculated for C$_{24}$H$_{23}$BO$_2$S, 386.2; found 386.2. GC-MS retention times of analytes: 15.22 minutes: 4,4,5,5-tetramethyl-2-(2-(naphthalen-1-yl)benzo[b]thiophen-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]$^+$: 387.1585 gmol$^{-1}$, Observed [M+H]$^+$: 387.1585 gmol$^{-1}$

Following the previously described adapted procedure (AlCl$_3$ followed by NEt$_3$), Alkyne 3.28 (29 mg, 0.106 mmol, 1 eq.), DCM (0.4 mL), BCl$_3$ (0.23 mL, 0.23 mmol, 2.2 eq.), AlCl$_3$ (14 mg, 0.106 mmol, 1 eq.), NEt$_3$ (0.5 mL), pinacol (38 mg, 0.318 mmol, 3 eq.). Purified via chromatography (20% DCM in 40-60 petroleum ether) to give a higher yield of 3.32 (30 mg, 73%).

4,4,5,5-tetramethyl-2-(2-(thiophen-3-yl)benzo[b]thiophen-3-yl)-1,3,2-dioxaborolane 3.33

Prepared according to the general procedure. Alkyne 3.29 (62 mg, 0.269 mmol, 1 eq.), BCl$_3$ (0.33 mL, 0.330 mmol, 1.2 eq.), DCM (1 mL), NEt$_3$ (1 mL) and pinacol (34 mg, 0.287 mmol, 1.2 eq.). Filtered through silica with pentane for purification. 3.33 (49 mg, 55%) obtained as a white solid. $^1$H NMR (400 MHz, CDCl$_3$): δ 1.39 (12H, s, Bpin); 7.28-7.42 (3H, m, Ar-H); 7.44 (1H, dd, J = 5.0 Hz, 1.3 Hz, Ar-H); 7.69 (1H, dd, J = 3.0 Hz, 1.3 Hz, Ar-H); 7.81 (1H, d, J = 7.8 Hz, Ar-H); 8.25 (1H, d, J = 8.3 Hz, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): δ 24.9, 83.7, 121.5, 124.1, 124.5, 124.7, 124.9, 125.2, 129.3, 135.9, 139.8, 144.9, 148.9; $^{11}$B NMR (128.6MHz, CDCl$_3$); δ 30.0 (s); [GC-MS] m/z calculated for C$_{18}$H$_{19}$BO$_2$S$_2$, 342.1; found 342.1. GC-MS retention times of analytes: 13.75 minutes: 4,4,5,5-tetramethyl-2-(2-(thiophen-3-yl)benzo[b]thiophen-3-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]$^+$: 343.0992 gmol$^{-1}$, Observed [M+H]$^+$: 343.0991 gmol$^{-1}$

Attempts using the adapted procedure involving addition of AlCl$_3$ / Et$_3$N prior to pinacol led to complex mixtures containing intractable material, this is attributed to AlCl$_3$ reacting with the alpha thieryl positions.
2-(2-mesitylbenzo[b]thiophen-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 3.34

Prepared according to the general procedure. Alkyne 3.30 (26 mg, 0.098 mmol, 1 eq.), BCl₃ (0.12 mL, 0.120 mmol, 1.2 eq.), DCM (0.5 mL), NEt₃ (0.5 mL) and pinacol (14 mg, 0.120 mmol, 1.2 eq.). Filtered through silica with pentane for purification. 3.34 (30 mg, 82%) obtained as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 1.17 (12H, s, Bpin); 2.11 (6H, s, Ar-Ph(o-CH₃)₂); 2.36 (3H, s, Ar-Ph(p-CH₃)); 6.92 (2H, s, Mes-H); 7.31-7.37 (1H, m, Ar-H); 7.39-7.44 (1H, m, Ar-H); 7.86 (1H, dt, J = 8.1 Hz, 0.8 Hz, Ar-H); 8.30 (1H, dq, J = 7.3 Hz, 0.8 Hz); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 20.4, 21.2, 24.6, 82.9, 121.7, 123.7, 124.1, 125.1, 127.4, 132.1, 137.4, 141.1, 144.2, 154.7; ¹¹B NMR (128.6 MHz, CDCl₃): δ 29.2 (s); [GC-MS] m/z calculated for C₂₃H₂₇BO₂S, 378.3; found 378.3. GC-MS retention times of analytes: 16.8 minutes: 2-(2-mesitylbenzo[b]thiophen-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M]⁺: 378.1825 g mol⁻¹, Observed [M]⁺: 378.1824 g mol⁻¹
3.3.9 – Crystal Data

Crystal structure of 3.2, CCDC No: 1497854

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Crystal structure of 3.20, CCDC No: 1497853

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3.4.0 – References

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203
32. Eller, C.; Kehr, G.; Daniliuc, C. G.; Frölich, R.; Erker, G. *Organometallics*, **2013**, *32*, 384
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Chapter 4:

Borylative Cyclisation of

1,2-Bis(alkynyl)benzenes
4.1.0 – Introduction

Dibenzopentalenes are polyaromatic hydrocarbons (PAHs) consisting of benzene rings fused either side of a pentalene scaffold, which in itself is an 8π anti-aromatic system, comprised of two fused cyclopentadienes. With two fused benzene rings, dibenzopentalenes are termed as extended anti-aromatic systems, as they still adhere to the 4n \( \pi \)-electron rule, possessing 16\( \pi \) electrons in their skeleton. This allows for the facile formation of dianions and dications\[^1\] to form 18\( \pi \) and 14\( \pi \) aromatic scaffolds (Scheme 1).

![Scheme 1](image1.png)

Scheme 1 – A reaction scheme highlighting known routes to both the aromatic dianion and dication.\[^1\]

Since the first synthesis of a dibenzopentalene (specifically the 5,10-diphenyldibenzopentalene) reported in 1912 by Brand (Scheme 2) starting from diphenylsuccindanedione, and utilising Grignard reagents including phenyl and tolyl magnesium bromide,\[^2\] there have been a wide variety of developments in the area as new facile methodologies are discovered, facilitating the synthesis of varied and extended \( \pi \) systems.

![Scheme 2](image2.png)

Scheme 2 – A reaction scheme highlighting the first route to dibenzopentalenes as described by Brand in 1912.\[^2\]
Whilst many routes to dibenzopentalenes are known, such as subjecting various \( \pi \) systems to high temperatures (>350°C)\(^{[3-5]} \) or transition metal catalysts,\(^{[6-7]} \) this introduction focuses on the reactions of 1,2-bis(alkynyl)benzene derivatives to form PAH systems including annulated pentalenes due to the direct relevance to the results discussed in section 4.2.0 onwards. A few examples of the reactivity of similar alkynes using transition metals will be highlighted, however the major focus will be on reactions of the 1,2-bis(alkynyl)benzenes with main group electrophiles.

4.1.1 – Transition Metal Catalysed Routes to Dibenzopentalenes From Bisalkynylarenes

One reaction of interest is the employment of a Stille-type cross coupling of two acetylenes in work undertaken by Tilley et al.\(^{[8]} \) Using two diphenylacetylene species, one possessing an SnBu\(_3\) group and the other a halide, resulted in the formation of the desired dibenzopentalene in high yield (Scheme 3, left). Interestingly, at higher temperatures, hetero-coupling and homocoupling of the halo-substituted diphenylacetylene both led to dibenzopentalene products suggesting the chemistry could be applied using just haloarene substrates, but in the absence of a tin reagent, which would lower the overall risk and toxicity of the reaction (Scheme 3, right). Hydroquinone was added as a reducing agent based on a previous report of palladium catalysed homocoupling.\(^{[9]} \)

![Scheme 3](image)

Scheme 3 – A scheme highlighting dibenzopentalene formation through a Stille cross-coupling reaction (left) and a homocoupling reaction (right).\(^{[8]} \)

Utilising comparable 1,2-bis(alkynyl)benzene derivatives to that utilised in our
work in section 4.2.0 onwards, Müller et al. reported the platinum catalysed generation of dibenzopentalenes in the 1960s\cite{10}. This proceeded via a cyclisation reaction with PtCl$_4$ as the catalyst to give an unstable platinum complex of the dibenzopentalene, which demetallated during purification to give a mono substituted dibenzopentalene product in an 85% yield.

\begin{center}
\begin{tikzpicture}
\node (1) at (0,0) {\includegraphics[width=0.8\textwidth]{dibenzopentalene.png}};
\end{tikzpicture}
\end{center}

Scheme 4 – A scheme showing the formation of the monosubstituted dibenzopentalene proceeding via a metal complex intermediate\cite{10-12}.

A palladium catalysed analogue of this reaction using PdCl$_2$ facilitated the isolation of the analogous palladium complex of the dibenzopentalene, which when reacted with PPh$_3$, led to the monosubstituted scaffold in low yield\cite{11}. This work was continued decades later by Blum et al. who employed an alternative platinum catalyst, H$_2$PtCl$_6$.6H$_2$O in conjunction with methyltrioctylammonium chloride (Aliquat 336) to also give high yields of dibenzopentalene products\cite{12} (Scheme 4). Aside from platinum and palladium catalysts, gold catalysts have also been employed as $\pi$-electrophiles in work by Hashmi et al. to cyclise diynes to generate dibenzopentalene scaffolds\cite{13-15}. For an overview of gold catalysed cyclisations of diynes, see the review by Hashmi\cite{16}.

It is clear that the use of large soft $\pi$-electrophiles such as platinum, palladium and gold lead to facile cyclisation. The formed C-M bonds undergo facile protodemetallation which can be beneficial in enabling turnover. Using main
group electrophiles that form stronger C-M (or C-metalloid) bonds and that are highly covalent should enable the C-M to remain intact. Notably, main group electrophiles will not form analogous vinylidene species as observed when employing Au catalyst chemistry,\textsuperscript{[15]} where vinylidene intermediates are often proposed.\textsuperscript{[17]} Hence, main group electrophiles will initiate the reaction differently and proceed through an alternative cyclisation mechanism.

### 4.1.2 – Dibenzopentalene Synthesis via Main Group Electrophiles

Recent reactions to generate the dibenzopentalene scaffold have been developed in the absence of transition metals. An example of this was reported by Otera et al.,\textsuperscript{[18]} starting from highly strained 5,6,11,12-tetrahydrodibenzo[a,e]cyclooctene (easily synthesised in high yield from ortho-(phenylsulfonylmethyl)benzaldehyde in the presence of ClP(O)(OEt)\textsubscript{2} and LiHMDS, followed by LDA\textsuperscript{[19]}). The addition of I\textsubscript{2} or IBr resulted in the conversion of the highly strained cyclic diynes to highly functionalisable dihalogenated dibenzopentalenes in good yields which could be used for multiple subsequent cross-couplings (Scheme 5).

![Scheme 5](image)

**Scheme 5** – A scheme highlighting the production of complex dibenzopentalenes from the 1,2-diyne derivative, 5,6,11,12-tetrahydrodibenzo[a,e]cyclooctene.\textsuperscript{[18]}

Another interesting method of generating dibenzopentalenes was discovered by Blum et al. in the mid-1990s.\textsuperscript{[20]} Refluxing a number of 1,2-bis(phenylethynyl)benzenes for 24 hours with a catalytic quantity of tellurium in pentachloroethane (PCE) resulted in the formation of a chlorinated dibenzopentalene as the major product in good yield via halogen transfer from the solvent \textit{in-situ}. The minor product of this reaction was a chlorinated benzofulvene. Interestingly, if 1,1’,2,2’-tetrachloroethane (TCE) was employed as the solvent and refluxed then the only isolated product was the
benzofulvene. The reaction was extended to substrates possessing one substituent on the core benzene ring, namely a methyl and chloride group. These were refluxed in PCE to give 1:1 isomeric mixtures, albeit in high overall yields (>75%) (Scheme 6). The formation of the dibenzopentalenes was proposed to proceed via thermal dehydrohalogenation of the dihalide intermediate.

Scheme 6 – A scheme highlighting the tellurium catalysed cyclisation of 1,2-bis(alkynyl)benzene derivatives.[20]

There is early precedence for the benzofulvene products, where Whitlock et al. reported the reaction of 1,2-bis(phenylethynyl)benzene with HBr, Br₂ and I₂, yielding both stereoisomers of the respective benzofulvene with no dibenzopentalene reported (Scheme 7).[21] This is presumably due to the lack of facile discrimination in the quenching of the vinyl cation by halide addition.
Scheme 7 – The benzofulvene isomers isolated through the reaction of 1,2-bis(phenylethynyl)benzene with HBr or Br₂/I₂.\[21\]

It was initially hypothesised that tellurium as a heavier congener of sulfur would lead to an organotellurium analogue of the organosulfur compounds reported in Blum’s earlier work in the area, involving the reaction of 1,2-bis(phenylethynyl)benzene with elemental sulfur.\[22\] However, the isolated product consisted of a dibenzopentalene derivative, where the sulfur atom had inserted into one of the five-membered rings (Scheme 8). A secondary product, two of the sulfur containing scaffolds linked by an S₂ unit, was also isolated.

Scheme 8 – A scheme highlighting the reactivity cyclisation of 1,2-bis(phenylethynyl)benzene with elemental sulfur.\[22\]
4.1.3 – Dibenzopentalene Synthesis via Boron Electrophiles

More recently, and much closer to the work undertaken in this chapter, Erker et al. reacted a variety of 1,2-bis(phenylethynyl)benzene derivatives with BCF.[23] This was proposed to proceed via activation of the alkyne by BCF, which would facilitate a 5-endo-dig cyclisation to generate a vinylic cationic intermediate, which would be quenched in-situ by the neighbouring aromatic ring via \( \text{S}_\text{E} \text{Ar} \) to generate the zwitterionic dibenzopentalene species with a pendant \( \text{B}([\text{C}_6\text{F}_5])_3 \) anion. The rearomatisation step results in the deborylation of the system, to generate neutral dibenzopentalene. The major success in this reaction lies in the first diyne, where the central benzene core is tetrafluorinated, leading to a complete conversion to dibenzopentalene \( A \) at room temperature, albeit after two days, in a good yield (Scheme 9).

![Proposed mechanism for the formation of the tetrafluorinated dibenzopentalene A.][23]

With two other diynes, a non-substituted benzene core and a dimethylated core, secondary products are observed (Scheme 10, top).[24] This is due to the migration of the \( \text{C}_6\text{F}_5 \) groups to the dibenzopentalene skeleton, converting the compound from a zwitterion to a neutral molecule. Then re-aromatisation occurs and \( \text{HB}([\text{C}_6\text{F}_5])_2 \) is lost to give the arylated dibenzopentalene \( B \). (Scheme 10,
Interestingly, Erker and co-workers also used BCl$_3$ to initiate the cyclisation of the tetrafluorinated diyne, yielding a BCl$_2$-substituted dibenzopentalene.$^{[23]}$ However, this was deborylated with acetic acid to give the same dibenzopentalene obtained using BCF, albeit in very low yield. They did not isolate the borylated form of the dibenzopentalene.

Scheme 10 – Secondary products obtained from the reaction of 1,2-bis(alkynyl)benzenes and BCF (top). Proposed mechanism for the formation of arylated dibenzopentalene B (bottom).$^{[24]}$

Furthermore, other diynes successfully cyclised with BCF were reported to not undergo cyclisation with BCl$_3$, for reasons that were not discussed. The BCF reactivity was also applied to diynes possessing naphthalenes (Scheme 11, right) and thiophenes, which led to the isolation of more complex PAHs. The thiophene derivative of the pentalene was particularly interesting, as the -B(C$_6$F$_5$)$_2$ moiety actually migrates to the junction of the thiophene framework,
with the sulfur atom coordinating to the boron centre. (Scheme 11, left).

Scheme 11 – A scheme highlighting the products using derivatives of 1,2-bis(alkynyl)benzene possessing naphthalene and thiophene groups.\textsuperscript{[24]}

An interesting set of cyclisation reactions of 1,2-diyne derivatives were observed in reports from Erker and Kehr. When the alkyne moieties are substituted with TMS groups\textsuperscript{[25]} and reacted with RB(C$_6$F$_5$)$_2$, a –B(C$_6$F$_5$)$_2$ substituted naphthalene is the observed product, formed \textit{via} a two-step process involving 1,1-carboboration (Scheme 12, right top). This reactivity follows a similar 1,1-carboboration when using unsubstituted alkynes (in the presence of a phosphine), with the major difference being that the resulting naphthalene derivative possesses the boron atom within the ring structure \textit{via} a subsequent 1,2 addition of the borane and a phosphine across the remaining alkyne (Scheme 12, right bottom).\textsuperscript{[26]}

Scheme 12 – A scheme highlighting the different reactivity between unsubstituted and silyl or phosphine substituted alkynes.\textsuperscript{[25-27]}
Alternatively, with bulky phosphine substituted alkynes, different reactivity is observed, in which borylative cyclisation initiated by the BCF takes place, followed by migration of a C₆F₅ group from boron to phosphorus, and mesityl from phosphorus to carbon with no 1,1-carboboration involved. (Scheme 12, left)[27]

An interesting study into the difference of reactivity exhibited by hard and soft main group electrophiles was carried out by Melen et al.[28] This involved the reaction of BCF or PhSeCl with 1,2-bis(phenylethynyl)benzene derivatives possessing an ester functionality on one of the aromatic rings. When the soft selenium reagent was used, 1,2-oxoselenation cyclisation of one of the alkynes was observed to give a neutral compound possessing an isocoumarin scaffold (Scheme 13, top right), with excess selenium leading to a 1,2-diselenation of the second alkyne, generating an ionic tetracycle (Scheme 13, bottom right). When the much harder and bulkier electrophile BCF was employed (Scheme 13, left), a benzofulvene bound to an isobenzofuran scaffold via the external double bond was the observed product. Notably, if BCF was added after selenium, only the BCF/carbonyl Lewis adduct was formed.

Scheme 13 – A scheme highlighting the different reactivity between hard and soft electrophiles with a carbonyl possessing diyne.[28]

4.1.4 Aims

With the overall aim of widening the scope of BCl₃ and borocation induced borylative cyclisation, our attention was focused on exploring the reactivity of 1,2-diynes in order to obtain new polycyclic scaffolds containing pinacol boronic
esters. The significance of this goal was to be able to build complex polycycles containing a versatile functional group (BPin) in positions previously observed to be synthetically difficult to obtain in high yields without the use of highly toxic, expensive transition metal catalysts.\textsuperscript{[6-8][10-12][14]} This would facilitate the generation of a wide scope of complex PAHs, with applications in materials chemistry (e.g. optoelectronics\textsuperscript{[29]}).

**Proposed Mechanism for Borylative Dibenzopentalene Synthesis**

![Scheme 14](image)

**Competitive Pathways**

Scheme 14 – Proposed outcomes and key mechanistic steps for the borylative cyclisation of 1,2-bis(phenylethynyl)benzene.

It was hypothesised that the borylative cyclisation of 1,2-bis(arylethynyl)benzenes would follow initially the mechanism proposed during the synthesis of dibenzopentalenes and benzofulvenes utilising BCF.\textsuperscript{[23][30]} The 5-endo-dig mechanism will proceed via initial activation of one of the alkynes by BCl\textsubscript{3} or a borocation, followed by a subsequent nucleophilic attack from the second alkyne to generate a zwitterionic benzofulvene intermediate possessing
an external vinyl cation. This cation can then be quenched via a number of routes, e.g., quenched via an internal Friedel-Crafts reaction (Scheme 14, top) by the pendant aromatic group, generating the borylated dibenzopentalene. Possible competitive pathways would generate other scaffolds such as benzofulvenes in the presence of chloride nucleophiles (Scheme 14, bottom right). Notably, an alternative 6-endo-dig pathway (Scheme 14, bottom left) would be expected to be the highly unfavoured due to the generation of a phenyl cation over an aryl-stabilised vinylic cation.
4.2.0 - Results and Discussion

The initial task was to synthesise a number of 1,2-bis(arylethynyl)benzene derivatives with variations in electronic properties to observe their influence over the reactions with BCl₃ and borocations. This was achieved by syntheses involving the Sonogashira cross coupling of dibromobenzene derivatives and the desired substituted terminal alkynes, with the resulting 1,2-bis(arylethynyl)benzenes shown below in Table 1. Diynes 4.1-4.4 were prepared in order to explore the effects of EDG and EWG on reactivity, where the core diyne possessed unsubstituted 4.1, p-methyl- 4.2, p-methoxy- 4.3, and m-chloro- 4.4 phenyl groups. The choice to use the meta-substituted

![Chemical structure](attachment:structure.png)

Table 1 – 1,2-bisethynyl benzene derivatives synthesised during this investigation.
phenyl for 4.4 was due to a combination of factors including price, availability and inherent electron deficiency, where *meta*-chloro offers only inductive withdrawing effects with no mesomeric donation. Fluorinated diyne 4.5 was synthesised from an adapted procedure by Erker et al.\textsuperscript{[23]} in order to observe any differences in reactivity between the use of BCl\textsubscript{3}, borocations and their BCF methodology. 3-thienyl 4.6 and alkyl 4.7 were synthesised in order to observe any differences in reactivity. In the case of 4.7 the dibenzopentalene pathway illustrated in Scheme 14 would be inaccessible due to the absence of an appropriate aromatic nucleophile and so only the generation of a borylated benzofulvene via quenching of the cationic intermediate with chloride ions was hoped for. In some of the substrate syntheses, low to moderate yields were observed, likely due to a much slower secondary alkynylation (mono-coupled products are observed in all cases).

4.2.1 Borylative Cyclisation of 1,2-bis(alkynyl)benzenes with Boron Electrophiles

With a variety of diynes in hand, the investigation began by utilising our standard methodology reported earlier with the simplest diyne, 4.1. The addition of approximately (due to the variable molarity of BCl\textsubscript{3}) one equivalent of BCl\textsubscript{3} (Table 2, entry 1) resulted in complete consumption of the substrate within 10 minutes, leading to a mixture of products. The *in-situ* \textsuperscript{1}H NMR spectrum (Figure 1) showed a complex aromatic region, providing little information to assist in determining what had occurred. However, further downfield from the normal aromatic region, a doublet was observed at 8.58 ppm (in DCM with a d\textsubscript{6}-DMSO capillary). This signal was of lower intensity compared to other resonances observed within the aromatic region, suggesting it was a minor compound generated in the reaction. The \textsuperscript{11}B NMR spectrum provided more insight, with a broad peak observed around 52 ppm, indicative that an aryl- or vinyl-BCl\textsubscript{2} moiety had been generated. The reaction mixture was esterified with the conditions used throughout this work to generate the corresponding pinacol boronate esters of the RBCl\textsubscript{2} *in-situ* products, and the resulting \textsuperscript{1}H NMR spectrum revealed two clearly resolved doublets downfield of the main aromatic region at 7.71 ppm and 8.58 ppm (in CDCl\textsubscript{3}) in a 3 : 2 ratio respectively.
Supporting the generation of aryl/vinyl Bpin products was a broad resonance at around 30 ppm in the $^{11}$B NMR spectrum. The GCMS data of the crude mixture showed two products in roughly a 2:3 ratio. The major compound showed a parent ion $[M]^+$ peak of 404 Da whereas the minor showed a parent ion $[M]^+$ peak of 440 Da with an isotopic distribution consistent with Cl incorporation. Using this data, we assigned the doublet at 7.71 ppm to be characteristic of the borylated dibenzopentalene product 4.8 and the doublet at 8.58 ppm to be characteristic of the borylated benzofulvene 4.9 obtained via in-situ vinyl-cation quenching by a chloride ion. However, it is noteworthy that this data could not help elucidate the identity of the isomer of the borylated benzofulvene as they possess the same molecular weight. In the majority of cases in Table 2 (and for later examples), the crude mixture consisted of the desired borylated polycycles with impurities including derivatives of Bpin (pin$_3$B$_2$ and [pin$_2$B]$^-$) and salts such as protonated bases, which just required a simple acidic aqueous wash (6M HCl) procedure to remove. It should be noted that the separation of the borylated products via column chromatography was not feasible in our hands as the compounds were observed to degrade on silica as well as having similar Rf values.
Table 2 - Conditions tested for the borylative cyclisation of diyne 4.1.

The poor selectivity of the reaction was unsatisfactory and other conditions were tested in order to see if the selectivity could be improved. Following our previous work on borylative cyclisation, approximately two equivalents of BCl$_3$ and an equivalent of 2,4,6-tri-tert-butylpyridine were reacted with 4.1 (Table 2, entry 2). The addition of a base was hoped to favour the Friedel-Crafts step as this is possibly reversible until deprotonation occurs, however this resulted in very similar selectivity to that in the absence of base. Next, the use of [Cl$_2$B(2-DMAP)][AlCl$_4$] was employed (Table 2, entry 3), and the starting diyne material was consumed within 10 minutes on mixing, and peaks corresponding to protonated 2-DMAP were observed, suggesting deprotonation to achieve re-aromatisation following the S$_E$Ar step. It was observed post-esterification that using [Cl$_2$B(2-DMAP)][AlCl$_4$] had a positive effect on the selectivity, resulting in a product ratio of 3 : 1 with 4.8 being the major product.

<table>
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<th>Entry</th>
<th>Conditions</th>
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<td>DCM</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>[Cl$_2$B(2-DMAP)][AlCl$_4$] (1 eq.)</td>
<td>DCM</td>
<td>3</td>
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<tr>
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<td>-</td>
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<td>[Br$_2$B(2-DMAP)][BrBr$_4$] (1 eq.)</td>
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<td>-$^b$</td>
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<td>7</td>
<td>[Cl$_2$B(2,6-lutidine)][AlCl$_4$] (1 eq.)</td>
<td>DCM</td>
<td>7</td>
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</table>

a) A slight excess of the 1M BCl$_3$ (in DCM) solution was used to ensure at least 1 eq. was added in case of variation in the concentration of BCl$_3$; b) Products not observed in-situ or post-esterification. Product ratios are based on $^1$H NMR spectroscopy and are consistent with GC-MS data (indicating comparable response factors).
It was hypothesised that the generation of 4.9 may involve the DCM solvent. However, when switching solvents from DCM to DCE (Table 2, entry 4), and more importantly to o-DCB, a solvent not able to donate chloride (Table 2, entry 5), no changes in selectivity were observed. This indicates that the chloride ion quenching the vinyl cation intermediate is not provided by the solvent and therefore originates from the B-Cl electrophile or [AlCl₄]. The use of an alternative boronium salt, [Br₂B(2-DMAP)][BBr₄] (Table 2, entry 6), was tested in order to generate a borylated polycycle possessing a bromine atom. This however led to a very complex mixture of products, and incomplete consumption of the starting boronium. The ¹H and ¹¹B NMR spectra showed inconclusive in-situ data regarding the identities of any generated products, even with a reaction time of 48 hours.

The last conditions explored with diyne 4.1 involved using the borenium salt, [Cl₂B(2,6-lutidine)][AlCl₄] (Table 2, entry 7), although alkyne 1,2-haloboration[^31] may take place and add another competitive reaction pathway.

![Figure 2 - Post-esterification comparison of the ¹H NMR spectra of entries 1, 3 and 7 from Table 2. Resonance at 8.2 ppm in the green trace produced by the presence of remaining 2-DMAP after esterification.](image-url)
A complex *in-situ* $^1$H NMR spectrum was observed, but it was notable that the majority of the 2,6-lutidine had been protonated, again suggesting the formation of the BCl$_2$ analogue of 4.8, however the doublet at 8.59 ppm (in DCM with a $d_6$-DMSO capillary) corresponding to the benzofulvene-BCl$_2$ analogue of 4.9 was again observed. After conversion to the pinacol ester, the overall yield of the reaction was ca. 85%, where the ratio of products was observed to be ca. 7 : 1 dibenzopentalene 4.8 : benzofulvene 4.9. Pleasingly, the combined NMR and GCMS data showed no trace of any other products (e.g., 1,2-haloboration) in the crude mixture. To highlight the most contrasting conditions, a comparison of the aromatic region of the post-esterification $^1$H NMR spectra of entries 1, 3 and 7 from Table 2 can be seen in Figure 2.

It was postulated that the reactions utilising the boronium and borenium salts exhibited higher selectivity towards the dibenzopentalene product due to the inherently lower chloride donating ability of the initial boron species (organo-BCl$_2$(amine)) formed (Figure 3) and the [AlCl$_4$] anion (relative to [BCl$_4$]$^-$ or [RBCl$_3$]$^-$), resulting in less benzofulvene product. This is based on the expected chloride ion affinities of the conjugate Lewis acids (after Cl$^-$ loss) by analogy to similar compounds previously studied.[32] However, the presence of an amine may also facilitate the deprotonation step, although we disfavour this based on the outcome from TBP.

![Figure 3](image-url) - Highlighting the difference in chloride donor power between [RBCl$_3$]$^-$, [BCl$_4$]$^-$ and [AlCl$_4$]$^-$

After the analysis of the selectivity in the cyclisation of diyne 4.1, diyne 4.2 was explored with a more electron rich aromatic expected to a) stabilise to a greater extent the vinylic cation intermediate on the alkynyl carbon closest to the tolyl...
moiety and b) increase the rate of $S_{E}\text{Ar}$ as it is a more nucleophilic aromatic, therefore potentially improving the selectivity in favour of the dibenzopentalene. Initially, one equivalent of $\text{BCl}_3$ (Table 3, entry 1) was reacted with diyne 4.2, resulting once again in rapid consumption ($< 10$ minutes) of the starting material to generate two products possessing an $\text{RBCl}_2$ moiety. Similar to the reaction with 4.1 a doublet was observed in the $^1\text{H}$ NMR spectrum at 8.55 ppm, attributed to benzofulvene formation. A doublet of twice the integral was also observed at 7.57 ppm, attributed to the formation of the dibenzopentalene product, indicating the product ratio of the reaction was 2 : 1 in favour of the dibenzopentalene. This was supported in the $^1\text{H}$ NMR spectrum post-esterification (see Figure 4), by two 3H relative integral singlets at 2.20 ppm and 2.45 ppm (for the p-tolyl methyl groups of the major product, dibenzopentalene 4.10) and two 1.5H relative intensity singlets at 2.18 ppm and 2.19 ppm (for the p-tolyl methyl groups of the minor product, benzofulvene 4.11).

![Figure 4 - Post-esterification $^1\text{H}$ NMR spectrum of the reaction of diyne 4.2 with BCl₃ (1.1 eq.) (Table 3, entry 1)](image)
Additionally, two singlets corresponding to the Bpin groups were observed in a 2 : 1 ratio at 1.39 ppm and 1.20 ppm, respectively. These product assignments were also supported by GCMS data, where the major product had a parent ion [M]+ of 432 Da and the minor product, had a parent ion [M]+ peak of 468 Da (containing Cl). Thus, the replacement of phenyl for p-tolyl leads to very similar outcomes using just BCl3.

The reaction was repeated with the inclusion of TBP (Table 3, entry 2), however this led to the same ratio of products (as observed with 4.1). Pleasingly, the use of [Cl2B(2-DMAP)][AlCl4] (Table 3, entry 3) led to the selective formation of the borylated dibenzopentalene, where the overall yield of the reaction was 66% observed as a ratio of 11 : 1 of 4.10 : 4.11. Other boron electrophiles were tested to observe the effect on the selectivity, specifically an alternative 2-DMAP borocation, [CatB(2-DMAP)][AlCl4] (Table 3, entry 4). This was tested as anion transfer is disfavoured due to the chelating catechol structure, thus may enable improved selectivity. When [CatB(2-DMAP)][AlCl4] was tested, no reaction was observed over 18 hours at room temperature, with only trace amounts of new compounds being generated after a further 24 hours at 60°C. This low reactivity over an extended period of time compared to the [Cl2B(2-DMAP)][AlCl4] was most likely the result of the significantly decreased Lewis acidity, due to electron donation into the formally empty pz-orbital of boron from both the 2-DMAP and the catechol ligand. These issues were also encountered when switching to alternative catechol borenium cations, [CatB(2,6-lutidine)][AlCl4] (Table 3, entry 5) and [CatB(NEt3)][AlCl4] (Table 3, entry 6), in which the former led to no reaction at all over extended periods, and the latter resulted in trace amounts of multiple products. Finally, the use of neutral borane PhBCl2 or [PhBCl(2-DMAP)][AlCl4] resulted in a highly complex mixture of products, although the in-situ NMR spectrum revealed a lot of unreacted starting materials after 18 hours. Overall, it can be concluded from these two substrates that the most effective conditions to use was BCl3 alone for maximising the amount of benzofulvene, or using BCl2-based borocations to minimise the amount of benzofulvene e.g., [Cl2B(2-DMAP)][AlCl4] and if necessary [Cl2B(2,6-lutidine)][AlCl4].
A slight excess of the 1M BCl₃ (in DCM) solution was used to ensure at least 1 eq. was added in case of variation in the concentration of BCl₃; b) Complex mixtures observed; c) No/trace reaction observed. Product ratios are based on ¹H NMR spectroscopy and are consistent with GC-MS data (indicating comparable response factors)

<table>
<thead>
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<th>Entry</th>
<th>Conditions</th>
<th>Solvent</th>
<th>Product Ratios</th>
</tr>
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<tr>
<td>1</td>
<td>BCl₃ (1.1 eq.)³</td>
<td>DCM</td>
<td>2 1</td>
</tr>
<tr>
<td>2</td>
<td>BCl₃ (2.1 eq.)³/ TBP (1 eq.)</td>
<td>DCM</td>
<td>2 1</td>
</tr>
<tr>
<td>3</td>
<td>[Cl₂B(2-DMAP)][AlCl₄] (1 eq.)</td>
<td>DCM</td>
<td>11 1</td>
</tr>
<tr>
<td>4</td>
<td>[CatB(2-DMAP)][AlCl₄] (1 eq.)</td>
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<td>²² ²²</td>
</tr>
<tr>
<td>5</td>
<td>[CatB(2,6-lutidine)][BBr₄] (1 eq.)</td>
<td>DCM</td>
<td>²² ²²</td>
</tr>
<tr>
<td>6</td>
<td>[CatB(NEt₃)][AlCl₄] (1 eq.)</td>
<td>DCM</td>
<td>³³ ³³</td>
</tr>
</tbody>
</table>

Table 3 - Conditions tested for the borylative cyclisation of diyne 4.2.

Diyne 4.3 containing p-MeO groups was next utilised initially with an equivalent of [Cl₂B(2-DMAP)][AlCl₄] due to previous issues with ether cleavage occurring when generating borylated dihydronaphthalenes from substrates possessing methoxy groups.³³ Unfortunately, this resulted in a very complex mixture of products which proved intractable in our hands, and as such, BCl₃ was used instead. This resulted in complete consumption (< 10 minutes) of the starting material with no ether cleavage observed. Pleasingly, the in-situ ¹H NMR spectrum indicated the formation of the BCl₂-benzofulvene product as the major product. This assignment was based on the appearance of a doublet at 8.55 ppm (in DCM with a d₆-DMSO capillary), characteristic of the borylated benzofulvene products, with only trace amounts of the dibenzopentalene observed. ¹¹B NMR spectroscopy indicated that cyclisation had taken place, with a major resonance at 54 ppm for the aryl-BCl₂. A minor resonance at 31 ppm was also observed, typical of reversible coordination of the methoxy group.
to BCl₃. As seen in previous work using alkynes substituted with OMe, any ether coordinated BCl₃ was abstracted by the excess NEt₃ used in the esterification step and removed during the acidic aqueous workup. The post-esterification ¹H NMR spectrum revealed that the reaction generated both dibenzopentalene 4.12 and benzofulvene 4.13 in an overall yield of 85%, with a ratio of 17 : 1 favouring 4.13. Attempted reactions with other conditions showed either no change in selectivity, or led to complex mixtures of products, indicating that benzofulvene formation is preferred with this substrate.

The GCMS of the worked up reaction mixture using BCl₃ showed two products, one major and one minor which corresponded to 4.13 and 4.12 respectively, supporting the ¹H NMR spectral data. This also indicates that only one benzofulvene isomer is formed.

Figure 5 - X-ray structure of 4.13 with thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Red: Oxygen; Yellow: Boron; Green: Chlorine; Selected metrics: C1-B1: 1.555(3)Å; C1-C2-C3-C4: 64.5(3)°; C5-C1-B1-O1: 32.2(3)°.
The structure of **4.13** was confirmed by X-ray crystallography (Figure 5), showing the *trans*-isomer of the chlorovinyl product, indicating that the chloride attacks the opposite face to the new C-C bond formed *via* the nucleophilic attack of the alkyne, possibly due to this being the less sterically hindered approach. This is supported through Whitlock’s reported synthesis of benzofulvenes using 1,2-bis(phenylethynyl)benzene with HBr, Br₂ and I₂, where the isomer with the aromatic rings on the same side of the alkene was observed as the major isomer.\[21\] However it is important to note that it does not necessarily mean the same geometric selectivity of benzofulvene isomers applies across all of the diynes investigated, although it is probable based on the similar steric environment around the vinyl cation. The structural metrics of **4.13** are unremarkable with a B-C distance of 1.555(3)Å as observed for previous aryl-Bpin species.\[34\] The anisole ring (ring A) directly bound to the indene moiety (ring system B) is twisted out of the plane of the indene by 64.5(3)° and the Bpin group (ring C) is twisted 32.2(3)° out of the plane to minimise non-bonding interactions.

It was initially surprising that the reaction of **4.3** and BCl₃ was highly selective towards the benzofulvene, given the electron rich nature of the anisole moiety, which was expected to contribute towards a higher rate of S₂Ar, therefore favouring **4.12**. However, the σ⁺ values for MeO *meta* (+0.05) relative to the position of S₂Ar reveal it is slightly deactivating, in contrast methyl in the *meta*-position is slightly activating towards S₂Ar (-0.07).\[35\] This, in combination with the more stabilised vinyl cation (resulting in a longer lifetime in solution and thus more time to be quenched by intermolecular chloride delivery in an intermolecular step) derived from **4.3**, leads to the observed selectivity. The deactivation towards S₂Ar is also consistent with the borocations giving poorer outcomes as the vinyl cation may persist longer in solution (due to the less efficient chloride transfer) and undergo other undesired side reactions.

Next, it was crucial to investigate the effects of other substituents, with a m-chloro substituted phenyl selected, this will lead to a chlorine *ortho*- or *para*- to the position of S₂Ar, with the σ⁺ value (+0.11)\[35\] of the latter being comparable to that of a *meta*-methoxy substituent. However, the vinyl cation formed with a
meta-chloro will be much less stable (than the para-OMe congener) enabling the effect on selectivity of the two key factors (stability of the vinyl cation vs. nucleophilicity of the aromatic position undergoing S_eAr) to be determined (Scheme 15).

![Scheme 15](image)

Scheme 15 – Highlighting the effect on selectivity due to varying stabilisation of the vinyl cation for the reaction of BCl_3 with 4.3 or 4.4.

Using BCl_3 (Table 4, entry 1) led to a reaction and complete consumption of 4.4 within 10 minutes. The in-situ ^1H NMR spectrum revealed a variety of aromatic resonances corresponding to more than just one product, however only trace quantities of any resonances around 8.50 ppm were observed, suggesting that in this case the benzofulvene product was not formed in any significant quantity. The ^11B NMR spectrum showed a major peak at 53 ppm, indicating borylative cyclisation had still occurred. After the reaction was esterified with pinacol/NEt_3, the ^1H NMR spectral data supported the formation of two major products with resonances at 7.71 ppm and 7.80 ppm, in a ratio of 3 : 1 with trace amounts of a third, indicated by a doublet at 8.36 (in CDCl_3), presumably associated with minor amounts of the borylated benzofulvene product. The GCMS also revealed two major products in a 3 : 1 ratio, each with the same parent ion [M]^+ of 472 Da, suggesting they corresponded to isomers of the dibenzopentalene product. This outcome is due to the meta-substitution pattern of the aromatic rings, which leads to two isomers formed during the
$\text{SEAr}$ step, with the chlorine atom positioned $\text{ortho}$- or $\text{para}$- to the newly formed C-C bond (Scheme 16).

Scheme 16 - A reaction scheme proposing the generation of two isomers of the pre-esterified dibenzopentalene via rotation of the aromatic ring.

It would be expected that the minor isomer of the reaction would possess the chlorine atom situated $\text{ortho}$- to the new C-C bond, due to the greater degree of inductive electron withdrawal and steric hindrance, whereas the chlorine in the $\text{para}$- position would have significantly less inductive effect. 2D NMR spectroscopy techniques including NOESY, HSQC and HMBC were carried out in an attempt to identify each isomer in the $^1\text{H}$ NMR spectrum, however the data provided inconclusive evidence to confidently assign the major product. With both major products associated with borylated dibenzopentalene 4.14, the overall yield for the reaction was 94% with an observed ratio of 37 : 1 of 4.14 (in a 3 : 1 ratio of isomers) : benzofulvene 4.15. The stark difference observed in the outcome of the reactions of 4.3 and 4.4 is most likely due to the significant contrast in stabilisation of the respective generated vinyl cations. Since the mesomeric stabilisation by the anisole groups led to prolonged existence of the vinyl cation, facilitating higher levels of chloride quenching, presumably the opposite is the case with the vinyl cations destabilised by the $m$-chlorophenyl groups. Thus, the vinyl cation is quenched via $\text{SEAr}$, leading to significantly lower levels of chloride quenching and therefore reduced benzofulvene production.

The cyclisation of 4.4 was repeated using 2 eq. $\text{BCl}_3$/ 1 eq. TBP (Table 4, entry 2 / Figure 6, green) and surprisingly, the presence of TBP actually led to
a significant change in the reaction outcome, resulting in formation of the benzofulvene as the major product, with the post-esterification $^1$H NMR spectrum revealing the ratio between 4.15 and the combined isomers of 4.14 to be approximately 1:1. The GCMS confirmed the assignment of the product as 4.15, based on the parent ion [M]$^+$ peak of 508 Da with a [M-Cl]$^+$ peak of 472 Da. From previous work, when using TBP in the reaction, [TBPH][BCl$_4$] is generated as the by-product from SeAr, leading to the hypothesis that the BCl$_4$ anion could act as a suitable chloride donor towards the vinyl cationic intermediate, therefore generating more of the benzofulvene.

Figure 6 - Comparison of Entries 1-4 from Table 4 to highlight the differences in selectivity with varying quantities of BCl$_4$ anion.
In order to test this, a reaction was carried out using equimolar quantities of 4.4 and BCl₃ with an equivalent of [NBu₄][BCl₄] (Table 4, entry 3 / Figure 6, red) as the source of the desired anion. This resulted in another shift of the ratio in favour of 4.15, observed at around 2 : 1 against both isomers of 4.14. This indicates that the BCl₄ anion can indeed perform a role in the chlorination of the vinyl cation. A follow-up reaction was undertaken, using an excess of three equivalents of [NBu₄][BCl₄] (Table 4, entry 4 / Figure 6, pink) resulting in a ratio of almost 4 : 1 in favour of 4.15 with an overall yield of both products at 95%. A control reaction was carried out to test whether a borylative cyclisation reaction would take place in the presence of [NBu₄][BCl₄] alone (Table 4, entry 5), however no reaction was observed, even under extended reaction times at 60°C. Additionally, it was worth noting that the isomeric ratio of 4.14 remained constant at 3 : 1 regardless of the quantity of the BCl₄ anion present. A comparison of the post-esterification ¹H NMR spectra for all four reactions is shown in Figure 6 to highlight the significant changes to the ratio of products.

It should be noted that borocations were also explored in this reaction however [Cl₂B(2-DMAP)][AlCl₄] (Table 4, entry 6) very little reaction was observed at ambient temperature, and extended reaction times at 60°C led to complex ¹H NMR spectra with only a small resonance for the aryl/vinyl-BCl₂ observed in the ¹¹B spectrum. When [Cl₂B(lut)][AlCl₄] (Table 4, entry 7) was employed, the outcome was similar, requiring extended reaction times only to obtain a small quantity of a complex mixture of products with the majority of starting material remaining unreacted. It is unclear currently why these two borocations perform poorly in this reaction.
a) A slight excess of the 1M BCl₃ (in DCM) solution was used to ensure at least 1 eq. was added in case of variation in the concentration of BCl₃ on storage / handling; b) Complex mixtures observed; c) No/trace reaction observed; d) all observed dibenzopentalene was a mixture of isomers in a 3 : 1 ratio. Product ratios are based on ¹H NMR spectroscopy and are consistent with GC-MS data (indicating comparable response factors)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Solvent</th>
<th>Product Ratios</th>
</tr>
</thead>
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<td></td>
<td></td>
<td></td>
<td>4.14</td>
</tr>
<tr>
<td>1</td>
<td>BCl₃ (1.1 eq.)</td>
<td>DCM</td>
<td>37ₚ</td>
</tr>
<tr>
<td>2</td>
<td>BCl₃ (2.1 eq.) / TBP (1 eq.)</td>
<td>DCM</td>
<td>1ₚ</td>
</tr>
<tr>
<td>3</td>
<td>BCl₃ (1.1 eq.)/[NBu₄][BCl₄] (1 eq.)</td>
<td>DCM</td>
<td>1₀</td>
</tr>
<tr>
<td>4</td>
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<td>DCM</td>
<td>1₀</td>
</tr>
<tr>
<td>5</td>
<td>[NBu₄][BCl₄] (1 eq.)</td>
<td>DCM</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>[Cl₂B(2-DMAP)][AlCl₄] (1 eq.)</td>
<td>DCM</td>
<td>-₂bc</td>
</tr>
<tr>
<td>7</td>
<td>[Cl₂B(2.6-lutidine)][AlCl₄] (1 eq.)</td>
<td>DCM</td>
<td>-₂bc</td>
</tr>
</tbody>
</table>

Table 4 - Conditions tested for the borylative cyclisation of diyne 4.4.

It is interesting to note that the use of TBP with diynes 4.1-4.3 did not affect the product ratios as observed with diyne 4.4. Due to the electron deficient aromatic rings, the enhanced electrophilicity of this vinyl cation compared to the other examples may be sufficient to abstract a halide from BCl₄. Presumably, with the previous examples, benzofulvene forms via halide abstraction at the zwitterionic RBCl₃ intermediate which is a better chloride donor. However, due to its increased bulk, the reaction around a relatively hindered vinyl cation would be slower, leading to higher quantities of the dibenzopentalene.

To supplement the work from Erker et al., diyne 4.5 was reacted with BCl₃. Similar to their procedure using BCF, the reaction with BCl₃ is slow requiring an
extended period of 48 hours to achieve full conversion of the starting material. Alternatively, a repeated reaction heated over 18 hours at 60°C also resulted in complete conversion of the starting material. In both cases, only one product was observed \textit{in-situ} by \textsuperscript{1}H, \textsuperscript{11}B and \textsuperscript{19}F NMR spectroscopy (in DCM with a \textit{d}_6-DMSO capillary), the latter of which revealed four separate multiplets at -130.74 ppm, -137.58 ppm, -158.04 ppm and -158.72 ppm.

Figure 7 - X-ray structure of 4.16 with thermal ellipsoids at 50\% probability level. Hydrogen atoms are omitted for clarity. Grey: Carbon; Red: Oxygen; Yellow: Boron; Pink: Fluorine; Selected metrics: C1-B1: 1.562(3)Å; C1-C2: 1.366(4)Å; C2-C3: 1.465(3)Å; C3-C4: 1.374(4)Å; C1-C7: 1.486(4)Å; C1-C2-C3: 111.9(2)°; C2-C3-C4: 110.7(2)°; C3-C4-C5-C6: 39.8(4)°
The NMR data post-workup showed borylated dibenzopentalene 4.16, which was isolated in a 92% yield at >99.5% purity with only a trace quantity of what was presumably the benzofulvene product. The exclusive formation of 4.16 is presumably due to the high electrophilicity of the formed vinyl cation leading to rapid SEAr. The structure of 4.16 was confirmed by x-ray crystallography (Figure 7). The structural metrics of 4.16 show the C-B bond is unremarkable and that the C-C bond lengths within the pentalene moiety are as expected, based on Erker’s similar dibenzopentalene structure.\(^{[23]}\) The bond angles within the pentalene moiety (ring system A; C1-C2-C3 and C2-C3-C4) are almost identical to Erker’s dibenzopentalene. The pendant phenyl group (ring B) is twisted out of the pentalene plane by 39.8(4)° to minimise the non-bonding interactions within the system. Additionally, it is worth noting that the dibenzopentalene moiety (ring system A/rings C and D) is not completely planar, and exhibits a slight twist within the scaffold. The angle between the planes of the two fused benzene rings (rings C and D) either side of the pentalene moiety is 6.85°.

Due to the high selectivity of the reaction to form 4.16, borocation electrophiles were not tested, however based on the increased benzofulvene production observed when spiking the cyclisation of 4.4 with [NBu\(_4\)]\([\text{BCl}_4]\), it was envisaged that a similar effect during the cyclisation of 4.5 may occur. Using three equivalents of the BCl\(_4\) anion indeed resulted in an increase in the benzofulvene product 4.17, resulting in a post-esterification product ratio of 10 : 1 in favour of the dibenzopentalene, a significant difference to the 70 : 1 product ratio observed in the absence of BCl\(_4\). The higher selectivity for dibenzopentalene observed with both 4.4 and 4.5 suggests that electron deficient diynes that react via formation of a destabilised vinyl cation intermediate have a propensity towards dibenzopentalene formation, due to a faster SEAr step. However, the difference in the steric hindrance around the vinyl cations generated from 4.4 and 4.5 also may be a factor behind the significant difference in observed selectivity when each reaction is spiked with a source of chloride ions. In the case of 4.5, the tetrafluorinated aromatic has a more sterically hindered vinyl cation, hence the intermolecular quenching of the vinyl cation is slower than the SEAr step, thus a less significant change in selectivity is observed.
To further investigate the potential of benzofulvene formation via a BCl₄ anion additive, diyne 4.1 was re-examined due to its lack of selectivity towards either product. Spiking a BCl₃ reaction with three equivalents of [NBu₄][BCl₄] resulted in only a negligible ratio shift from 3:2 to 1:1. Furthermore, three equivalents of BCl₃ were added to a solution of 4.1 to observe whether a buildup of BCl₄ anion during the reaction progression would affect the overall product distribution. Notably, the ratio did not shift in favour of the benzofulvene, and actually gave a product ratio comparable to that when [Cl₂B(lut)][AlCl₄] was used (Table 2, entry 7). The ratios for the spiking reactions (and control) of 4.5 and 4.1 are summarised in Scheme 17.

Scheme 17 – Product ratios after spiking the reaction of BCl₃ and 4.5 or 4.1 with [NBu₄][BCl₄]. Control reaction of 4.1 using excess BCl₃ also shown.

The excess BCl₃ control reaction suggests that in-situ there is less zwitterionic RBCl₃ able to donate chloride as the equilibrium will shift towards RBCl₂ and BCl₄ anions. As expected, with the poorer chloride donor, less benzofulvene is produced, making the reaction more selective towards dibenzopentalene 4.8. The spiked reaction of 4.1 also supports the earlier hypothesis that the vinyl cation generated from 4.1 is not sufficiently electrophilic to abstract chloride from BCl₄ anions, hence spiking the reaction with [NBu₄][BCl₄] led to only a negligible change, suggesting the chloride transfer from BCl₄ is very slow and instead it is occurring from [RBCl₃]⁺.

In order to investigate whether heteroaromatic rings would also undergo the SₐEAr step in a similar manner (Scheme 18), diyne 4.6 was subjected to BCl₃, resulting in complete consumption of the starting material within 10 minutes.
Pleasingly, the *in-situ* $^1$H NMR spectrum revealed almost complete conversion to the dibenzopentalene, with only small amounts of the benzofulvene, indicated by a doublet at 8.50 ppm (in DCM with a $d_6$-DMSO capillary). The selectivity is attributed to the higher nucleophilicity of thiophene moieties coupled with a lower barrier to $S_{E}Ar$ on thiophenes due to their lower aromaticity (relative to benzene derivatives). Post-esterification, the product ratio was observed to be 11 : 1 of dibenzopentalene 4.18 : benzofulvene 4.19. However, the main issue encountered during the reaction was that the borylated product was susceptible to protodeborylation under a range of work up conditions. To minimise this, the product was washed with water multiple times instead of 6M HCl, in an effort to remove any of the salt by-products and pinacol impurities mentioned previously. Utilising $[\text{Cl}_2\text{B}(2\text{-DMAP})][\text{AlCl}_4]$ also resulted in high selectivity towards the dibenzopentalene, generating a product ratio of 50 : 1 which was isolated in a 48% yield, albeit with a 7% protodeborylation impurity, obtained after a water wash of the crude product.

With the outcome of the aryl-substituted diyne elucidated, we explored an alkyl-substituted diyne, allowing a controlled investigation to observe borylative cyclisation with dibenzopentalene formation precluded. The main electronic difference when using non-aromatic substituents will be the position of the vinyl cation generated upon addition of the boron electrophile, where the most stabilised position is closest to the benzene core of the molecule. The result of this change in electronics means that two 5-exo-dig cyclisation pathways may be feasible (Scheme 19).
Cyclohexyl substituted diyne 4.7 was subjected to BCl3, leading to complete consumption of the starting material within 10 minutes. The post-esterification 11B NMR spectrum revealed a resonance at 30 ppm (in CDCl3), which may suggest the presence of an aryl/vinyl-Bpin. However, the 1H NMR spectrum (Figure 8, red) revealed a complex mixture of products containing a broad unresolved multiplet at 5.50 ppm, and three doublets in the vinylic region at 5.82 ppm, 5.83 ppm, and 6.24 ppm. The GCMS provided no assistance in assigning the components of the complex mixture of generated materials. Utilising BCl3 and TBP resulted in a much cleaner reaction, most notably post-esterification (Figure 8, green), with the doublets at 5.82 ppm and 5.83 ppm (in CDCl3) not being observed but the other vinylic resonances at 5.50 and 6.24 ppm remaining. Unfortunately, the GCMS again provided no assistance in the identification of the product, however the use of 2D NMR Correlation Spectroscopy (COSY) highlighted that the doublet at 6.24 ppm coupled to a neighbouring aliphatic multiplet at 3.16 ppm consistent with a cyclohexyl C-H. These resonances may be potentially due to a product resulting from a hydride transfer during the reaction to generate a more stable carbocation, and thus on deprotonation results in a double bond over in the cyclohexyl moiety. The coupling constants of the observed doublets (using TBP) were 10 Hz, consistent with a 3JHH between a vinylic and a cyclohexyl C-H, supporting this hypothesis.
Figure 8 – Post-esterification $^1$H NMR spectra of the reactions between diyne 4.7 and BCl$_3$ (red) or BCl$_3$ and TBP (green).

Scheme 20 - Proposed mechanism for the [1,11]-hydride shift step during cyclisation of 4.7.

The cyclisation of 4.7 was also explored with [Cl$_2$B(2-DMAP)][AlCl$_4$], however the reaction was observed to be much slower, requiring extended times of 24 hours for full consumption of the starting material. This time, it was clear to see a doublet at 6.54 ppm (in DCM with a d$_6$-DMSO capillary) growing in during the reaction which may correspond to the observed vinylic resonance post-esterification. Unfortunately, a more complex aromatic region was observed in the $^1$H NMR spectrum post-esterification, although the vinylic doublet and
multiplet (6.24 / 5.50 ppm) of interest were still clearly observed. The mechanism of the reaction is worth speculating upon. Compared to the aryl-substituted diynes, the vinyl cation generated from 4.7 is less stabilised, which combined with the potential to form a highly substituted allyl cation presumably leads to the hypothesised side reaction via a hydride shift (Scheme 20).

*Condition A* spiked with 3 eq. [NBu₄][BCl₄]; **Tentatively proposed product of the reaction; a = reaction time of 18h at 60°C.

Table 5 - An overview of the products generated through the borylative cyclisation of 1,2-bis(alkynyl)benzene derivatives.
Unfortunately on no occasion was the material pure enough to isolate the major product observed. Preparative Thin Layer Chromatography was attempted, but the majority of the product degraded on the silica, resulting in this experiment being abandoned. The overall outcomes from this study are summarised in Table 5.

4.2.2 – Conclusions and Future Work

In conclusion, it has been shown that the borylative cyclisation of diynes can be initiated by a variety of boron electrophiles under mild conditions to give two significantly different scaffolds, substituted dibenzopentalenes and benzofulvenes via the same intermediate. Each diyne substrate required extensive investigation to be carried out in order to optimise the selectivity between the two products. Whilst an understanding of the factors affecting product distribution are now in hand, pure products (and thus yields) could not be stated for the majority of compounds due to impurities that could not be removed using an aqueous acidic wash (given the tendency of all of the products to degrade on silica prevented purification). The optimal conditions of each substrate investigated, combined with the most selective product ratios, have been summarised in Table 5.

Although many goals from this investigation were achieved in terms of developing methodology to obtain polycycles with boronic ester moieties, there are issues that still need solving to make this chemistry synthetically useful, particularly improving the selectivity and broadening the scope. These goals may be challenging to realise as it is clear that the propensity to form dibenzopentalenes and benzofulvenes differ from substrate to substrate. The key factors are the stabilisation of the vinyl cation intermediate by the alkyne substituents, the propensity for $S\text{E}Ar$ on the aromatic, the steric bulk found around the cation and the chloride donor power of the anions present in solution. Electron rich groups (e.g. $\text{p-MeO}$) tend to lead to unselective reactions due to the prolonged existence of the cation, leading to competing levels of chloride quenching over $S\text{E}Ar$. Electron poor groups destabilise the cation and $S\text{E}Ar$ becomes the dominant pathway. Spiking reactions with excess $[\text{NBu}_4][\text{BCl}_4]$ as a chloride source was found to give higher quantities of...
benzofulvene. Unfortunately, due these complex independent factors, the elucidation of a ‘universal’ condition to provide single products from the borylative cyclisation of diynes is unlikely.

To expand this study, a number of other substrates would be useful including para-chlorophenyl rings instead of the meta-substituted substrate 4.4, which would preclude the formation of dibenzopentalene isomers. Additionally, further development of the scope of the reaction is required, with ideal starting materials aimed at investigating the effects of steric hindrance on the reaction, as the majority of substrates reported within this chapter closely resemble one another from a steric perspective, containing substituted phenyl rings. Other alkyl substituted diynes should be explored and would hopefully confirm the hydride transfer mechanism proposed.

Lastly, it would be of interest to take a selective dibenzopentalene synthesis, such as the synthesis of 4.16, and isolate the product on gram scales. Subsequent cross-coupling could be explored enabling access to a whole new variety of materials for organic electronics and as potential ligands adding to the field of work using dianionic pentalenes as ligands for metal catalysis.\[36\]
4.3.0 - Experimental - General Considerations

For general considerations see Chapter 2. For compounds 4.13 and 4.17, not all aromatic resonances were observable, presumably due to coincidence of some resonances. For compound 4.16, due to some of the resonances being indistinguishable in the $^{13}\text{C}\{^{1}\text{H}\}$ spectrum even at 3072 scans, six carbons are not reported, four bound to fluorine, and two adjacent quaternaries. All small scale cyclisation reactions were carried out in J. Young NMR tubes to facilitate in-situ reaction monitoring. A number of samples are analysed in-situ in protio solvent with a capillary insert containing wet deuterated $d_6$-DMSO, which leads to a residual $\text{H}_2\text{O}$ resonance being observed at 3.95 ppm in the $^{1}\text{H}$ NMR spectra.

4.3.1 - Synthesis of Diynes

**General Procedure**

An ampoule fitted with a J. Young's valve was charged with tetraakis-(triphenylphosphine)palladium(0) (0.02 eq.) and copper(I) bromide (0.04 eq.). Tetrahydrofuran was added and the suspension was stirred for five minutes, followed by the addition of the aryl bromide (1 eq.) and triethylamine. After five minutes, the alkyne (2.2 eq.) was added and the solution was stirred and heated at 95°C in the sealed vessel for 12 h. The solution was cooled to room temperature, filtered through a layer of Celite™ on top of silica and eluted with diethyl ether (3 x 10 mL). The solvent was removed in vacuo and the crude material was purified via column chromatography to yield the corresponding alkyne.
1,2-bis(phenylethynyl)benzene 4.1
Prepared according to the general procedure. 1,2-dibromobenzene (1.01 mL, 8.47 mmol, 1 eq.), phenylacetylene (2.05 mL, 18.65 mmol, 2.2 eq.), Pd(PPh₃)₄ (195 mg, 0.169 mmol, 0.02 eq.), copper(I) bromide (48 mg, 0.338 mmol, 0.04 eq.), triethylamine (10 mL) and THF (20 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 4.1 (965 mg, 41%) obtained as an orange oil. Data is in accordance with the literature.[23]

1,2-bis(p-tolylethynyl)benzene 4.2
Prepared according to the general procedure. 1,2-dibromobenzene (1.01 mL, 8.47 mmol, 1 eq.), 4-ethynyltoluene (2.4 mL, 18.65 mmol, 2.2 eq.), Pd(PPh₃)₄ (195 mg, 0.169 mmol, 0.02 eq.), copper(I) bromide (48 mg, 0.338 mmol, 0.04 eq.), triethylamine (10 mL) and THF (20 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 4.2 (1.12 g, 43%) obtained as an orange oil. Data is in accordance with the literature.[37]

1,2-bis((4-methoxyphenyl)ethynyl)benzene 4.3
Prepared according to the general procedure. 1,2-dibromobenzene (1.01 mL, 8.47 mmol, 1 eq.), 4-ethynylanisole (2.42 mL, 18.65 mmol, 2.2 eq.), Pd(PPh₃)₄ (195 mg, 0.169 mmol, 0.02 eq.), copper(I) bromide (48 mg, 0.338 mmol, 0.04 eq.), triethylamine (10 mL) and THF (20 mL). Column chromatography eluent: 20% DCM in 40-60 petroleum ether. 4.3 (728 mg, 25%) obtained as a yellow solid. Data for 4.3 is in accordance with the literature.[37]
1,2-bis((3-chlorophenyl)ethynyl)benzene 4.4

Prepared according to the general procedure. 1,2-dibromobenzene (0.80 mL, 6.65 mmol, 1 eq.), 3-chloroethynylbenzene (1.8 mL, 14.64 mmol, 2.2 eq.), Pd(PPh₃)₄ (307 mg, 0.266 mmol, 0.04 eq.), copper(I) bromide (76 mg, 0.532 mmol, 0.08 eq.), triethylamine (8 mL) and THF (20 mL). Column chromatography eluent: 10% DCM in 40-60 petroleum ether. 4.4 (1.00 g, 43%) obtained as an orange solid.

1H NMR (400 MHz, CDCl₃): δ 7.25-7.36 (6H, m, Ar-H); 7.44 (2H, dt, J = 7.3 Hz, 1.5 Hz, Ar-H); 7.53-7.59 (4H, m, Ar-H); 13C{¹H} NMR (100.6 MHz, CDCl₃): δ 89.3, 92.3, 124.9, 125.5, 128.4, 128.8, 129.70, 129.72, 131.5, 131.9, 134.3; [GC-MS] m/z calculated for C₂₂H₁₂Cl₂, 346.0; found 346.0. GC-MS retention times of analytes: 21.81 minutes: 1,2-bis((3-chlorophenyl)ethynyl)benzene; [Acc. Mass] Calculated [M]+: 346.0316 gmol⁻¹, Observed: [M]+ 346.0311 gmol⁻¹. Mass data involves 35Cl isotope.

((perfluoro-1,2-phenylene)bis(ethyne-2,1-diyl))dibenzene 4.5

Prepared according to the general procedure. 1,2-dibromo-3,4,5,6-tetrafluorobenzene (1.38 mL, 10 mmol, 1 eq.), phenylacetylene (2.42 mL, 22.00 mmol, 2.2 eq.), Pd(PPh₃)₄ (462 mg, 0.40 mmol, 0.04 eq.), copper(I) bromide (153 mg, 0.80 mmol, 0.08 eq.), triethylamine (12 mL) and THF (20 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 4.5 (340 mg, 10%) obtained as a white solid. Data is in accordance with the literature.[23]

1,2-bis(thiophen-3-ylethynyl)benzene 4.6

Prepared according to the general procedure. 1,2-dibromobenzene (1.01 mL, 8.47 mmol, 1 eq.), 3-ethynyldithiophene (1.84 mL, 18.65 mmol, 2.2 eq.), Pd(PPh₃)₄ (195 mg, 0.169 mmol, 0.02 eq.), copper(I) bromide (49 mg, 0.338 mmol, 0.04 eq.), triethylamine (10 mL) and THF (20 mL). Column chromatography eluent: 10% DCM in 40-60
petroleum ether. 4.6 (500 mg, 20%) obtained as a yellow solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.24 (2H, d, J = 4.8 Hz, Ar-H); 7.30-7.35 (4H, m, Ar-H); 7.53-7.59 (4H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 87.8, 88.7, 122.4, 125.5, 125.8, 128.0, 128.8, 129.9, 131.7; [GC-MS] $m/z$ calculated for C$_{18}$H$_{10}$S$_2$, 290.0; found 290.0. GC-MS retention times of analytes: 18.51 minutes: 1,2-bis(thiophen-3-ylethynyl)benzene; [Acc. Mass] Calculated [M]$^+$: 346.0224 gmol$^{-1}$, Observed: [M]$^+$ 346.0216 gmol$^{-1}$.

1,2-bis(cyclohexylethynyl)benzene 4.7

Prepared according to the general procedure. 1,2-dibromobenzene (1.28 mL, 10.60 mmol, 1 eq.), ethynylcyclohexane (2.9 mL, 22.25 mmol, 2.1 eq.), Pd(PPh$_3$)$_4$ (490 mg, 0.424 mmol, 0.04 eq.), copper(I) bromide (122 mg, 0.848 mmol, 0.08 eq.), triethylamine (12 mL) and THF (10 mL). Column chromatography eluent: 5% DCM in 40-60 petroleum ether. 4.7 (1.20 g, 39%) obtained as a yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.31-1.45 (6H, m, Cy-H); 1.48-1.67 (6H, m, Cy-H); 1.73-1.97 (8H, m, Cy-H); 2.67 (2H, quintet, J = 4.8 Hz, (C≡C-CH(Cy)); 7.14-7.20 (2H, m, Ar-H); 7.35-7.41 (2H, m, Ar-H); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 24.8, 26.1, 29.8, 32.7, 79.6, 98.1, 126.3, 127.1, 131.8; [GC-MS] $m/z$ calculated for C$_{22}$H$_{26}$, 290.2; found 290.1. GC-MS retention times of analytes: 16.80 minutes: 1,2-bis(cyclohexylethynyl)benzene; [Acc. Mass] Calculated [M]$^+$: 290.2035 gmol$^{-1}$, Observed: [M]$^+$ 290.2027 gmol$^{-1}$. 
Experimental Considerations

The experimental report for each substrate cyclisation will contain the most selective procedure only. A table displaying all of the procedures and subsequent product ratios will feature after the experimental accounts below. BCl₃ ratios used experimentally were typically between 1.1-1.3 equivalents in order to ensure at least 1 eq. was added to counter any decrease in concentration in the “1M” solution of BCl₃ in DCM. Additionally, due to the products’ nature to degrade on silica, the dibenzopentalenes and indene products were inseparable in our hands. Ratios were determined using two easily identifiable characteristic peaks which correspond to each product and the ratios are supported by GC-MS.

General Procedure A: A vessel fitted with a J. Young’s valve was charged with the diyne (1 eq.) and DCM. BCl₃ (1.1 eq.) was added and the mixture was stirred for 5 minutes at room temperature (one exception, tetrafluorinated alkyne 4.5, required stirring for 48 hours at room temperature or heating at 60°C for 12 hours). After this time, triethylamine (≈15 eq.) was added, followed by pinacol (1.1 eq.), leading to esterification. The solvent was removed in vacuo, and the compound was extracted into pentane (3 x 20 mL). This was washed with 6M aqueous HCl (3 x 20 mL), and distilled water (2 x 20 mL) and the organic layer was dried over MgSO₄ then evaporated in vacuo to give a mixture of the two compounds.

General Procedure B: A vessel fitted with a J. Young’s valve was charged with the diyne (1 eq.), 2,4,6-tri-tert-butylpyridine (TBP) (1 eq.) and DCM. BCl₃ (2.1 eq.) was added and the mixture was stirred for 5 minutes at room temperature.
After this time, triethylamine (≈15 eq.) was added, followed by pinacol (2.1 eq.), leading to esterification. The solvent was removed *in vacuo*, and the compound was extracted into pentane (3 x 20 mL). This was washed with 6M aqueous HCl (3 x 20 mL), and distilled water (2 x 20 mL) and the organic layer was dried over MgSO₄ then evaporated *in vacuo* to give a mixture of the two compounds.

**General Procedure C:** A vessel fitted with a J. Young’s valve was charged with the diyne (1 eq.) and DCM. [Cl₂B(2-DMAP)][AlCl₄] (1 eq.) was added and the mixture was stirred for 5 minutes at room temperature. After this time, triethylamine (≈15 eq.) was added, followed by pinacol (2.1 eq.), leading to esterification. The solvent was removed *in vacuo*, and the compound was extracted into pentane (3 x 20 mL). This was washed with 6M aqueous HCl (3 x 20 mL), and distilled water (2 x 20 mL) and the organic layer was dried over MgSO₄ then evaporated *in vacuo* to give a mixture of the two compounds.

**General Procedure D:** In a vessel fitted with a J. Young’s valve, BCl₃ (1 eq.) and 2,6-lutidine (1 eq.) were dissolved in DCM and stirred for 10 minutes to ensure formation of the BCl₃-lutidine adduct. The vessel was then charged with AlCl₃ (1 eq.) and the mixture was stirred for a further 15 minutes to ensure formation of the borenium salt (1 eq.). A separate vessel fitted with a J. Young’s valve was charged with the diyne (1 eq.) and DCM. This solution was transferred *via* cannula to the vessel containing the dissolved borenium salt and the mixture was stirred for 5 minutes at room temperature. After this time, triethylamine (≈15 eq.) was added, followed by pinacol (2.1 eq.), leading to esterification. The solvent was removed *in vacuo*, and the compound was extracted into pentane (3 x 20 mL). This was washed with 6M aqueous HCl (3 x 20 mL), and distilled water (2 x 20 mL) and the organic layer was dried over MgSO₄ then evaporated *in vacuo* to give a mixture of the two compounds.
4,4,5,5-tetramethyl-2-(10-phenyldieno[2,1-a]inden-5-yl)-1,3,2-dioxaborolane 4.8 and (E)-2-(1-(chloro(phenyl)methylene)-2-phenyl-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.9

Using an adapted procedure of general procedure A (involving excess BCl₃). Diyne 4.1 (25 mg, 0.090 mmol, 1 eq.), DCM (0.4 mL), BCl₃ (0.27 mL, 0.270 mmol, 3 eq.), NEt₃ (0.3 mL) and pinacol (42 mg, 0.3592 mmol, 4 eq.). 7:1 mixture of 4.8 and 4.9 obtained as a brown film. $^{11}$B NMR (128.6 MHz, CDCl₃); δ 29.9 (s)


[GC-MS] m/z calculated for C$_{28}$H$_{26}$BClO$_2$ 4.9, 440.2; found 440.2. GC-MS retention times of analytes: 17.89 minutes: (E)-2-(1-(chloro(phenyl)methylene)-2-phenyl-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]$^+$: 441.1787 gmol$^{-1}$, Observed: [M]$^+$ 441.1782 gmol$^{-1}$. 

$^1$H(CDCl₃)
4,4,5,5-tetramethyl-2-(2-methyl-10-(p-tolyl)inden[2,1-a]inden-5-yl)-1,3,2-
dioxaborolane 4.10 and (E)-2-(1-(chloro(p-tolyl)methylene)-2-(p-tolyl)-1H-inden-
3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.11

Using general procedure C. Diyne 
4.2 (39 mg, 0.127 mmol, 1 eq.), 
[Cl₂B(2-DMAP)][AlCl₄] (52 mg, 0.140 mmol, 1.1 eq.), DCM (0.4 mL), NEt₃ 
(0.4 mL), pinacol (33 mg, 0.280 mmol, 2.2 eq). 11 : 1 mixture of 4.10 : 4.11 obtained as a brown film. 

\(^{11}\text{B NMR (128.6 MHz, CDCl}_3\); \(\delta\) 30.2 (s)


[GC-MS] \(m/z\) calculated for \(\text{C}_{30}\text{H}_{30}\text{BClO}_2\) 4.11, 468.2; found 468.2. Additionally, calculated [M-Cl]⁺, 432.2, found 432.2. GC-MS retention times of analytes: 19.14 minutes: (E)-2-(1-(chloro(p-tolyl)methylene)-2-(p-tolyl)-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.
2-(10-(4-methoxyphenyl)-2-methylindeno[2,1-a]inden-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.12 and (E)-2-(1-(chloro(4-methoxyphenyl)methylene)-2-(4-methoxyphenyl)-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.13

Using general procedure A. Diyne 4.3 (46 mg, 0.136 mmol, 1 eq.), DCM (0.4 mL), BCl₃ (0.18 mL, 0.176 mmol, 1.3 eq.), NEt₃ (0.3 mL) and pinacol (25 mg, 0.212 mmol, 1.6 eq.). 1 : 17 mixture of 4.12 and 4.13 obtained as an orange film in an 85% overall yield.

¹H NMR (400 MHz, CDCl₃) of 4.13: δ 1.21 (12H, s, Bpin); 3.69 (6H, s, 2 x OMe); 6.40-6.45 (4H, m, Ar-H); 6.80 (2H, dt, J = 8.8 Hz, 2.5 Hz, Ar-H); 7.02 (2H, dt, J = 8.8 Hz, 2.5 Hz, Ar-H); 7.24 (1H, td, J = 7.6 Hz, 1.4 Hz, Ar-H); 7.31 (1H, td, J = 7.6 Hz, 1.1 Hz, Ar-H); 7.61 (1H, d, J = 7.3 Hz, Ar-H); 8.49 (1H, d, J = 7.8 Hz, Ar-H); ¹¹B NMR (128.6 MHz, CDCl₃); δ 30.5 (s); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): δ 24.7, 55.2, 83.4, 112.3, 112.7, 122.0, 125.1, 125.4, 128.2, 130.0, 131.2, 131.5, 132.2, 137.0, 138.0, 140.8, 145.6, 151.3, 157.8, 159.9; [GC-MS] m/z calculated for C₃₀H₃₀BCIO₄ 4.13, 500.2; found 500.3. GC-MS retention times of analytes: 24.83 minutes: (E)-2-(1-(chloro(4-methoxyphenyl)methylene)-2-(4-methoxyphenyl)-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M]⁺: 500.1926 gmol⁻¹, Observed: [M]⁺ 500.1932 gmol⁻¹.

[GC-MS] m/z calculated for C₃₀H₂₉BO₄ 4.12, 464.2; found 464.2. GC-MS retention times of analytes: 38.49 minutes: 2-(10-(4-methoxyphenyl)-2-methylindeno[2,1-a]inden-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Mass data involves ³⁵Cl isotope.
2-(3-chloro-10-(3-chlorophenyl)inden-2,1-a[inden-5-yl])-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and 2-(1-chloro-10-(3-chlorophenyl)inden-2,1-a[inden-5-yl])-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.14

Using general procedure A. 
Diyne 4.4 (58 mg, 0.167 mmol, 1 eq.), DCM (0.4 mL), BCl₃ (0.20 mL, 0.200 mmol, 1.2 eq.), NEt₃ (0.3 mL) and pinacol (24 mg, 0.203 mmol, 1.2 eq.). 3:1 ratio of isomers of 4.14 obtained. Para and ortho isomer identity not assignable by ¹H NMR spectroscopy. ¹¹B NMR (128.6 MHz, CDCl₃); δ 29.6 (s)

[GC-MS] m/z calculated for C₂₈H₂₄BCl₃O₂, 472.1; found 472.1. GC-MS retention times of analytes: 46.20 minutes: Major isomeric form, identity not assignable

[GC-MS] m/z calculated for C₂₈H₂₄BCl₃O₂, 472.1; found 472.1. GC-MS retention times of analytes: 50.18 minutes: Minor isomeric form, identity not assignable by GC-MS; [Acc. Mass] Calculated [M]: 473.1241 gmol⁻¹, Observed: [M]⁺ 473.1238 gmol⁻¹. Mass data involves ³⁵Cl isotope.
(E)-2-(1-(chloro(3-chlorophenyl)methylene)-2-(3-chlorophenyl)-1H-inden-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 4.15

Using an adaption of general procedure A (spiking the reaction with [NBu$_4$][BCl$_4$]). Diyne 4.4 (32 mg, 0.092 mmol, 1 eq.), [NBu$_4$][BCl$_4$] (109 mg, 0.276 mmol, 3 eq.) DCM (0.4 mL), BCl$_3$ (0.10 mL, 0.10 mmol, 1.1 eq.). NEt$_3$ (0.3 mL) and pinacol (8 mg, 0.068 mmol, 1.2 eq.). A mixture of 4.14 and 4.15 were obtained as a brown film in a 96% yield. The observed ratio of isomers of 4.14 were 3:1. $^{11}$B NMR (128.6 MHz, CDCl$_3$); δ 30.2 (s)
4,4,5,5-tetramethyl-2-(6,7,8,9-tetrafluoro-10-phenylindenol[2,1-a]inden-5-yl)-1,3,2-dioxaborolane 4.16

Using an adaptation of general procedure A. Diyne 4.5 (20 mg, 0.054 mmol, 1 eq.), DCM (0.4 mL), BCl₃ (0.07 mL, 0.07 mmol, 1.2 eq.). The reaction was heated to 60°C for 12 hours, then cooled to room temperature before adding NEt₃ (0.3 mL) and pinacol (8 mg, 0.068 mmol, 1.2 eq.). 4.16 was obtained as an orange/red film in a 92% yield.

¹H NMR (400 MHz, CDCl₃): δ 1.42 (12H, s, Bpin); 6.88 (1H, d, J = 7.1 Hz, Ar-H); 6.94 (1H, td, J = 7.5 Hz, 1.0 Hz, Ar-H); 6.99 (1H, td, J = 7.6 Hz, 1.1 Hz, Ar-H); 7.42-7.49 (5H, m, Ar-H); 7.66 (1H, d, J = 7.1 Hz, Ar-H); ¹¹B NMR (128.6 MHz, CDCl₃): δ 29.7 (s); ¹⁹F NMR (376.5 MHz, CDCl₃); δ -158.85 (1F, dd, J = 21.5 Hz, 17.4 Hz, Ar-F); -157.49-157.34 (1F, m, Ar-F); -139.18 (1F, dd, J = 20.8 Hz, 13.6 Hz, Ar-F); -130.67 (1F, ddd, J = 21.8 Hz, 14.0 Hz, 1.7 Hz, Ar-F); ¹³C{¹H} NMR (100.6 MHz, CDCl₃): (C₆F₄ unit omitted) 24.9, 84.6, 123.5, 124.4, 127.9, 128.8, 128.95, 128.98, 129.1, 129.4, 132.8, 135.1, 146.6, 150.1, 159.5; [GC-MS] m/z calculated for C₆H₂₁BF₄O₂, 476.2; found 476.2. GC-MS retention times of analytes: 19.08 minutes: 4,4,5,5-tetramethyl-2-(6,7,8,9-tetrafluoro-10-phenylindenol[2,1-a]inden-5-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]⁺: 477.1643 g mol⁻¹, Observed: [M⁺] 477.1643 g mol⁻¹
4,4,5,5-tetramethyl-2-(4-(thiophen-3-yl)benzo[4,5]pentaleno[1,2-b]thiophen-9-yl)-1,3,2-dioxaborolane 4.18

Using general procedure B. Diyne 4.6 (39 mg, 0.127 mmol, 1 eq.), TBP (33 mg, 0.134 mmol, 1 eq.), DCM (0.4 mL), BCl$_3$ (0.3 mL, 0.300 mmol, 2.3 eq.), NEt$_3$ (0.4 mL), pinacol (33 mg, 0.280 mmol, 2.2 eq). 4.18 was isolated as a colourless film in a 48% yield.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.34 (12H, s, Bpin); 6.67-6.76 (2H, m, Ar-H); 6.89 (1H, d, J = 4.8 Hz, Ar-H); 7.03 (1H, d, J = 4.8 Hz, Ar-H); 7.04-7.07 (1H, m, Ar-H); 7.15-7.19 (1H, m, Ar-H); 7.43-7.46 (2H, m, Ar-H); 7.69-7.71 (1H, m, Ar-H); $^{11}$B NMR (128.6 MHz, CDCl$_3$): $\delta$ 29.9 (s); $^{13}$C($^1$H) NMR (100.6 MHz, CDCl$_3$): $\delta$ 25.0, 83.6, 121.2, 123.7, 125.4, 126.2, 126.5, 127.0, 127.2, 127.56, 127.57, 132.4, 134.7, 136.3, 141.1, 152.2, 152.6, 157.1 [GC-MS] m/z calculated for C$_{24}$H$_{21}$BO$_2$S$_2$ 18; 416.1; found 416.1. GC-MS retention times of analytes: 25.06 minutes: 4,4,5,5-tetramethyl-2-(4-(thiophen-3-yl)benzo[4,5]pentaleno[1,2-b]thiophen-9-yl)-1,3,2-dioxaborolane; [Acc. Mass] Calculated [M+H]$^+$: 417.1149 gmol$^{-1}$, Observed: [M]$^+ 417.1143$ gmol$^{-1}$. 

257
4.3.3 – Crystal Data

Crystal structure and data for 4.13 CCDC No: 1529716

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Crystal structure and data for **4.16** CCDC no: 1529715

![Crystal structure image]

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### References


