The Reactivity of Borocations with Alkynes

A thesis submitted to the University of Manchester for the degree of

Doctor of Philosophy

in the Faculty of Engineering and Physical Sciences

2015

James Robert Lawson

School of Chemistry

Contents

List of Abbreviations

General

DFT	Density functional theory
FLP	Frustrated Lewis pair
NBO	Natural Bond Order
NMR	Nuclear Magnetic Resonance
ppm	parts per million
COSY	Correlation spectroscopy
NOESY	Nuclear Overhauser effect spectroscopy

Chemicals

2DMAP	2-(*N,N*-dimethylamino)pyridine
9-BBN	9-borabicyclo[3.3.1]nonane
Bn	Benzyl group
Cat	Catecholato
DCM	Dichloromethane
DMT	*N,N*-Dimethyl-*p*-toluidine

Lut	2,6-Lutidine
NHC	*N*-heterocyclic carbene
o-DCB	*ortho*-dichlorobenzene
Pin	Pinacolato
TBDMS	^{t}butyldimethylsilyl
TIPS	Triisopropylsilyl
TMP	2,2,6,6-tetramethylpiperidine
TMS	Trimethylsilyl

Abstract

It has been found that by combining various borocations or neutral electrophilic boranes with a multitude of alkynes, interesting and often highly selective borylation reactivity is observed. The reactions can be loosely categorised as de-(elemento)boration of the alkyne, haloboration and carboboration. Direct alkyne de-(elemento)boration was achieved as both dehydroboration and desilylboration, generating a selection of borylated alkynes. Other examples of more complicated alkyne borylation were also observed, such as the boroamination of TMS-ethylene.

Upon discovering that 2-*N,N*-dimethylaminopyridine ligated dichloro-boronium salt underwent selective 1,2-haloboration with a range of terminal alkynes, and that the dibromo-analogue could haloborate a limited number of internal alkynes, the more Lewis acidic borenium salt [Cl_2B(2,6-lutidine)][$AlCl_4$] was synthesised and reacted with a series of internal alkynes to give haloborated products. These included dialkyl and diaryl internal alkynes containing a range of functional groups including thioether, methoxyphenyl, vinyl and halide. Each proceeded with excellent *stereo*- and *regio*-selectivity, with the boron and the halide added mutually *cis*, and the regioselectivity determined by the electronically most stable form of the carbocation intermediate. The initial dihalovinyl borane products were esterified in-situ to provide the more stable pinacol boronate esters.

The elementoboration method was expanded via modification of the borocations to include different transfer groups that, upon reaction with trimethylsilyl-substituted alkynes, underwent 1,1-carboboration, with migration of the TMS-group. This method also provided access to a small selection of borylated dienes, resulting from reactions with excess alkyne. It was also shown that some neutral boranes reacted analogously with certain TMS-alkynes, albeit with limitations on scope. In addition to this, two types of 1,2-carboboration were discovered. The first involved intercepting products from alkyne haloboration with a TMS-alkyne, undergoing a vinylboration to produce 1-boradiene products. The second was an example of an intermolecular *trans* carboboration, where the initially formed vinyl carbocation is intercepted by a thiophene.

Declaration

No portion of the work referred to in this 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.

Copyright Statement

Acknowledgments

I would like to take this opportunity to thank a number of people, friends and colleagues, without whom this thesis would not exist. Above all others, my heartfelt thanks go out to Dr Michael Ingleson, for giving me the opportunity to undertake this research in the first place, and the support and advice he gave every day. I would also like to thank Dr Ewan Clark, not just for his tutelage and advice in the lab, and his assistance with computational studies, but for his friendship, and his unique words of advice. In a similar vein, I would like to extend my thanks to Dr Ian Cade, who sat at my right hand for years and offered an inexhaustible fountain of wisdom on all things chemistry. In addition to this, his assistance with crystallography was always greatly appreciated. Also, I would also like to thank Dr Jessica Cid for her assistance with computational studies, and her friendship.

I must also thank the University of Manchester and its support staff for the help and guidance given throughout my PhD, specifically the crystallography service staff, NMR staff and mass spectroscopy staff for assistance with the various analysis undertaken within this body of work. To all the other members of the Ingleson group, both former and current, thank you for making this an excellent environment to work in. In addition, I must express my gratitude for the support of my family throughout my PhD, along with all the friends I would not have made without this position.

Finally, I'll end as I began, with the most important person. Cheers Mike, it's been amazing.

Chapter 1: Introduction

1.1 Introduction to Borocations and Electrophilic Boranes

Borocations are generally highly electrophilic species with their reactivity dominated by their Lewis acidity, the synthetic exploitation of which was limited until recently.[1] Pre-2008; borocations were predominantly esoteric species, with studies principally limited to defining their synthesis, stability and fundamental reactivity. There have been considerably broader studies of neutral boron compounds, often highlighting their significant electrophilic character and useful reactivity. However, recent work on borocationic species has found that they can have even greater reactivity, for example, in the abstraction of halides and hydrides relative to neutral boranes. One of the first synthetic uses of borocations was derived from an oxazaborolidine, which is itself a neutral boron species and a relatively weak Lewis acid, but when activated with strong Brønsted acids, such as triflimide, it forms a borocationic species. This cation is highly active as an enantioselective catalyst for Diels-Alder reactions. [2]

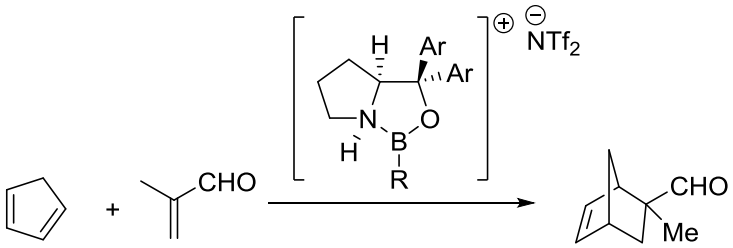


Figure 1.1: Borocation-induced Diels-Alder reactions

Studies of borocations and their reactivity have followed behind and been guided by those of neutral, but still highly electrophilic boranes. One of the earliest reactivity

studies into the borylation of π nucleophiles with neutral boranes involved the borane dimer B_2H_6, which was combined with alkenes (isobutylene and ethylene) and with benzene.[3] In the former case, trialkylboron compounds were produced, (Figure 1.2) as determined by melting point tests and mass spectrometry, whereas in the latter case a substitution reaction was observed. This reaction between diborane and benzene yielded phenylboron compounds, one of which was believed to be triphenylborane. By exposing this species to air, phenylboronic acid was isolated and verified. A wide variety of these hydroboration reactions have been reported.[4]

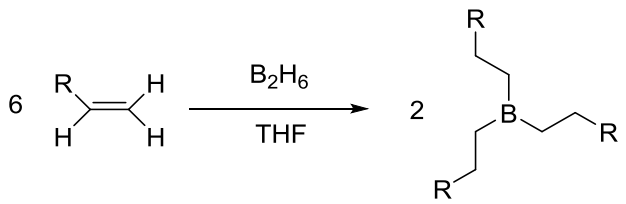


Figure 1.2: Hydroboration of alkenes with B_2H_6

Another notable early example was published in the 1960s when the reaction of the electrophilic borane BBr_3 with alkynes was demonstrated to result in a haloboration reaction.[5] Negishi and co-workers subsequently extended this reaction to haloborate propyne which produced the Z-isomer with very high selectivity. The vinyl-BBr_2 product was esterified to the pinacol boronate ester, allowing manipulation under ambient conditions. These products were subsequently used in palladium catalysed cross-coupling reactions by Negishi and co-workers.[6]

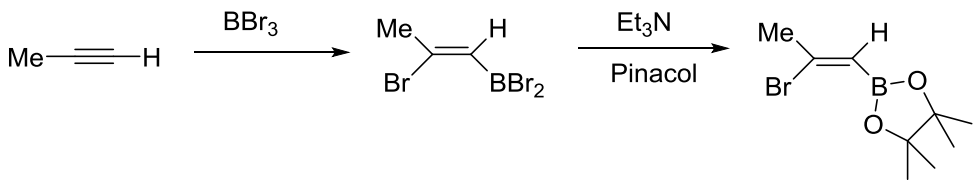


Figure 1.3: Synthesis of dimeric hydride-bridged dication

Boron containing aryl, alkynyl and vinyl species are of significant importance in a number of fields, perhaps most notably in the synthesis of drug/natural products. These molecules are sought after due to the functionalisable boron group which can undergo a variety of transformations, most notably the Suzuki reaction[7] in order to generate carbon-carbon bonds, and thus the borylated species represent useful synthetic building blocks.

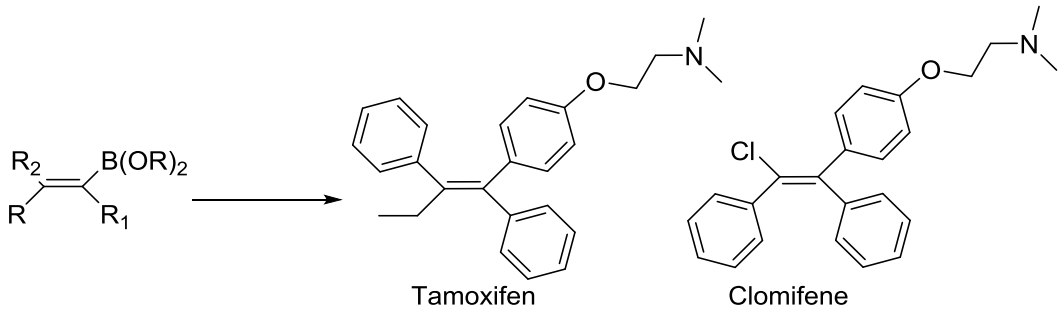


Figure 1.4: Borylated trisubstituted alkenes as building blocks to drug molecules

As such a wide range of reactions with neutral electrophilic boranes has been reported since the early reports highlighted above, select examples will be discussed further below. Since the borylations of arenes and alkynes are most relevant to this thesis, these reactions will feature predominantly.

1.2: Reactions of Electrophilic Boranes

The borylation of arenes with electrophilic boranes has been studied intensively.[8] Early work by Muetterties and by Lappert[9-12] showed that the electrophilic borylation of benzene and its derivatives was possible, but these early examples required harsh Friedel-Crafts conditions and high temperatures. The pathways to borylated arenes are shown below in Figure 1.5.

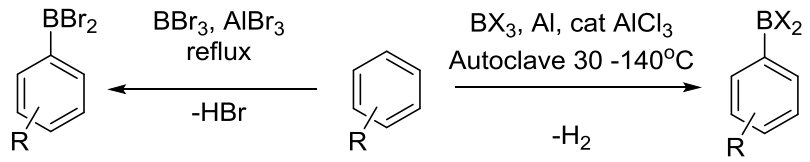


Figure 1.5: Early arene borylation using boron trihalides

Prior to our work showing that borocations can react with a range of alkyne nucleophiles, haloboration had been limited to neutral boranes. The reactivity of neutral BX_3 compounds has been far more extensively studied, and certain key examples of relevance to this thesis will be discussed below. Some haloboranes of the general formula BX_3, where X = Cl or Br, have been found to react with alkynes to give 2-halovinyl boranes as briefly discussed previously (Figure 1.6).[13] In this study, the products of borylation of four acetylenes (acetylene, phenylacetylene, ^{n}butylacetylene and diphenylacetylene) were isolated first as the haloboranes then converted by protodeborylation to the haloalkenes or alcoholysis to the dialkoxyvinylborane.

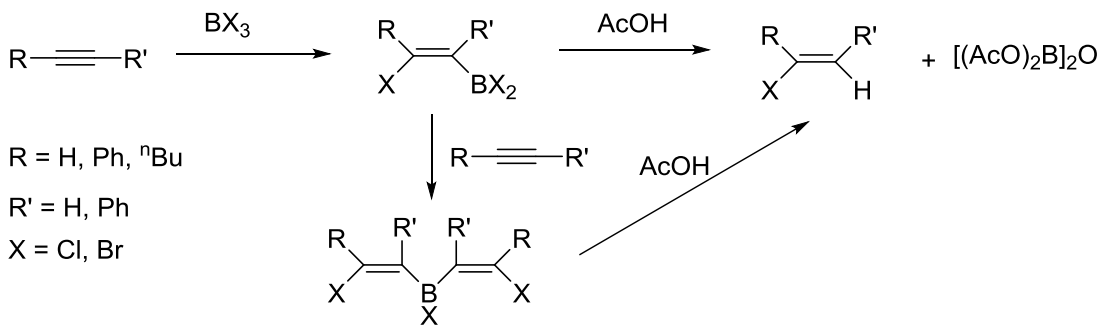


Figure 1.6: Haloboration of alkynes with neutral boranes

It was further shown that addition of a second equivalent of acetylene to the haloborane resulted in double addition, and that protodeborylation results in the same haloalkene product as the mono-haloboration. The alkenylboranes were characterised by IR spectroscopy and comparisons made between the BBr_2 containing dihalo(vinyl)borane and the alcoholysis product containing a $B(OR)_2$ group. The effect of the BBr_2 group was shown to have a greater frequency lowering effect of the C=C stretching frequency (1548 cm^{-1} compared to 1582 cm^{-1} for the $B(OR)_2$ group). Thus, as boron is less electronegative that carbon, this must be due to mesomeric rather than inductive effects. Additionally, it was shown that BCl_3 did not react with internal alkynes, as it is not Lewis acidic enough. And whilst BBr_3 reacted with internal alkynes, these reactions were slow, reversible, and gave a mixture of isomeric products. Addition of pyridine to the products from the bromoboration of internal alkynes reformed the starting alkyne and produced the BBr_3-pyridine complex. These factors combined limited the usefulness of this reaction to haloboration of terminal alkynes with BX_3.

The same studies reported the use of arylhaloboranes of the general formula BX_nPh_m (X = Cl or Br, n + m = 3), and it was observed that either haloboration, carboboration or both could occur depending on the alkyne used, and

the stoichiometry (Figure 1.7). Similar trends were observed with regards to the boron trihalides, with more nucleophilic alkynes proving more reactive, as were more Lewis acidic boranes (Br > Cl). In general, the less sterically demanding alkynes favoured carboboration, while those containing phenyl groups were more prone to haloboration. Using the carboboration reaction of certain alkynes with Ph_2BX, followed by protodeborylation, α-substituted styrenes could be synthesised, which are synthetically useful building blocks.[14]

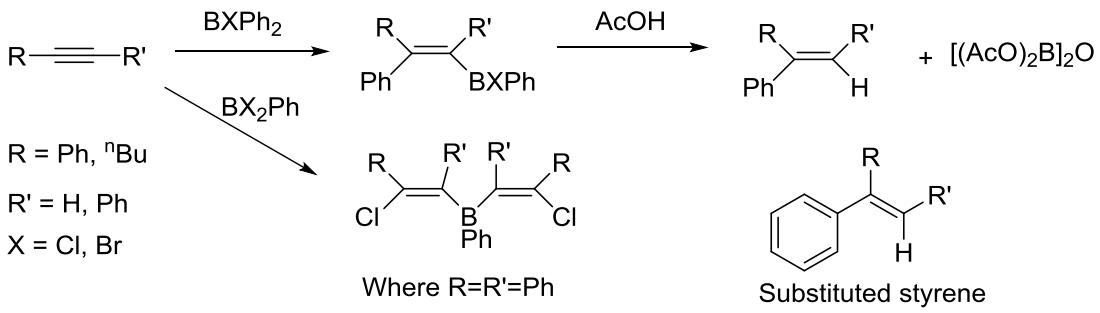


Figure 1.7: Phenylboration of alkynes with neutral boranes

Carboboration of alkynes is an area receiving much interest; as boron substituted alkenes are valuable synthetic building blocks, and regio and steroselective production is very desirable. Earlier carboborations had been of 'activated' alkynes; acetylenic substrates with a suitable migratory group at carbon such as $–SiR_3$ and $-GeR_3$.[15] Termed the Wrackmeyer reaction, combination of $B(alkyl)_3$ with activated alkynes is well established, an example of which is shown in Figure 1.8.

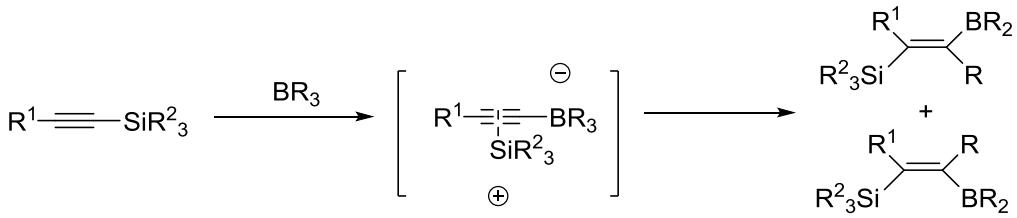


Figure 1.8: The Wrackmeyer 1,1-carboboration reaction

Subsequent work in this field showed that terminal alkynes undergo facile 1,1-carboboration with the strong boron electrophile $B(C_6F_5)_3$.[16] By modifying one of the substituents on boron, it was possible to control R group transfer, producing carboborated alkenes derived from $R\text{-}B(C_6F_5)_2$ reagents. The 1,1-carboboration of phenylacetylene with $B(C_6F_5)_3$ is shown in Figure 1.9.[17]

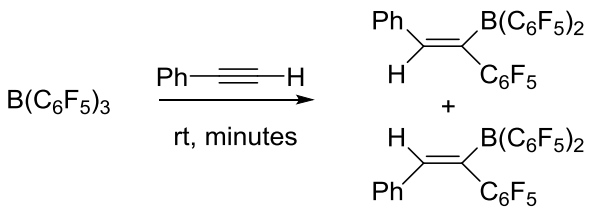


Figure 1.9: 1,1-carboboration of phenylacetylene

A more complex variation of this reactivity was also reported, wherein acetylene was reacted with $R\text{-}B(C_6F_5)_2$ in the presence of a base. The product formed is a diborylated alkene, the result of a 1,1-carboboration of acetylene and a dehydroboration to install the boron groups.[17]

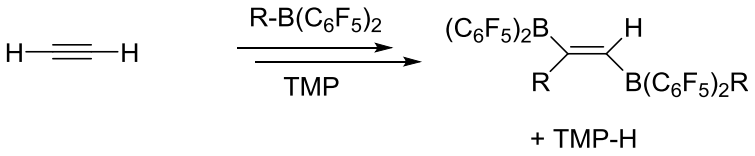


Figure 1.10: Reaction of acetylene with $R\text{-}B(C_6F_5)_3$

Recent work has expanded the 1,1-carboboration of 'non-activated' terminal alkynes. Using the Lewis acid $ClB(C_6F_5)_2$, several reagents were synthesised, such as $MeB(C_6F_5)_2$ and reacted successfully with 1-pentyne, as shown in Figure 1.11.[18] Reacting to completion at room temperature, the resulting mixture of E-/Z- isomers was subjected to photolysis, allowing the Z-isomer to be isolated

selectively in a good yield. It is a useful technique for the preparation of these highly functionalised alkenes. This work was later expanded to forgo the need for photolysis; instead heating the reaction to reflux for an extended period of time (three days, Figure 1.11) gave a single regio-and stereo-selective product.[19]

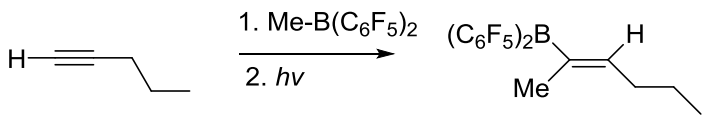


Figure 1.11: 1,1-carboboration of 1-pentyne

The 1,1-carboboration of acetylenic thioethers was reported,[20] and subsequently a range of other alkynyl substrates have now been explored. Reactions involved simply treating a doubly substituted acetylene with $B(C_6F_5)_3$ and crystallising the product. The product, seen below, features a C=C bond with the -$B(C_6F_5)_2$ group geminal to the single -C_6F_5 substituent, with a pair of –SPh groups at the other end as expected from 1,1-carboboration.

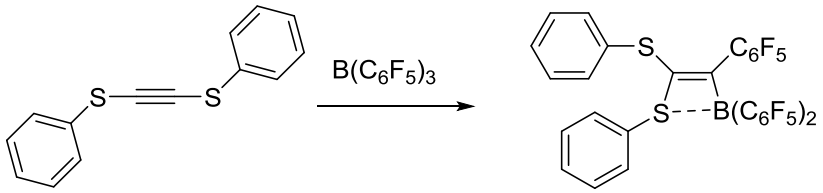


Figure 1.12: Synthesis of borylated ketene dithioacetal

More recently, 1,1-carboborations of internal alkynes have also been observed with $RB(C_6F_5)_2$.[21] The strongly electrophilic borane $B(C_6F_5)_3$ reacts cleanly with the internal alkyne 4-octyne at high temperature to give the 1,1-carboboration product in high yield (Figure 1.13). NMR spectroscopy showed that one carbon-carbon bond had broken and that one of those *n*-propyl group had migrated to the

other end of the alkyne. This, coupled with the observed transfer of a C_6F_5 group from boron to carbon, gives the product shown in Figure 1.13.

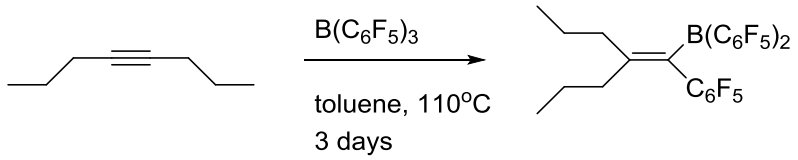


Figure 1.13: 1,1-carboboration of 4-octyne

It was also shown that other carbon groups could migrate from boron. When $MeB(C_6F_5)_2$ is treated with bis(p-tolyl)acetylene at 125˚C, a 1,1-carboboration of the internal alkyne occurs with the methyl group selectively migrating over the C_6F_5 group. The reactivity is analogous to that shown in Figure 1.13.

Borole (5 membered 4 π electron boracycles) derivatives can be also accessed from certain internal alkynes using electrophilic boranes and 1,1-carboboration. It was shown that $B(C_6F_5)_3$ and dicyclopropylacetylene can undergo 1,1-carboboration to form a dienylborane intermediate.[22] These can then undergo intramolecular cyclisation to form the dihydroboroles seen in Figure 1.14. The structural conformation of the product differs depending on how one of the cyclopropyl groups ring opens; if an enyne is generated, then the methyl group and the C_6F_5 group are observed to be *trans* to each other.

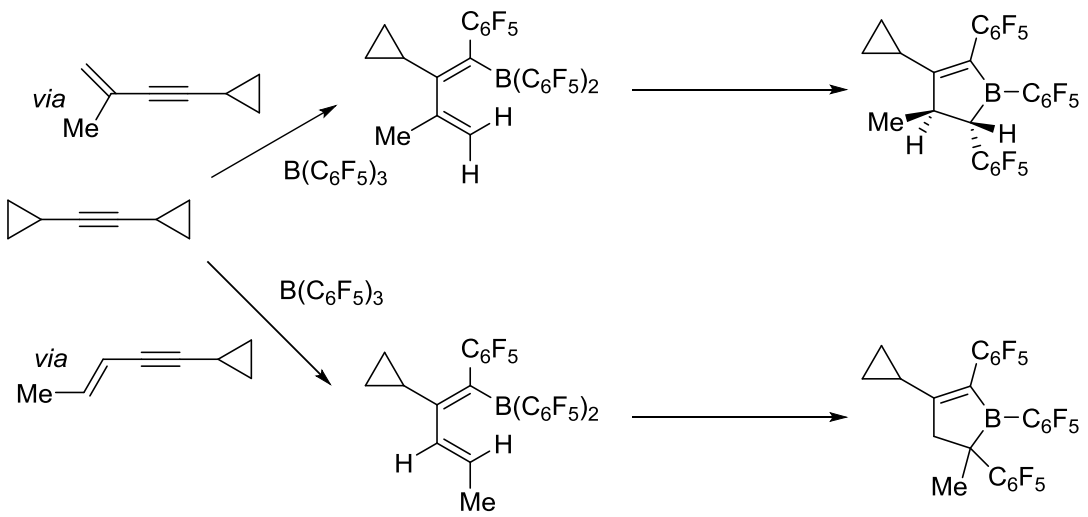


Figure 1.14: Synthesis of dihydroboroles

The process of hydroboration is extremely widespread in the literature, and one of the key uses of neutral boron containing reagents.[23] Discussion herein is limited to the use of extremely electrophilic boron reagents, such perfluorinated diaryl boranes, particularly with silylated alkynes as this is of relevance to later results. One such reagent is bis(pentafluorophenyl)borane, which was found to be a powerful hydroboration reagent, albeit for 1,2-hydroboration in contrast to the 1,1-carboboration discussed above.[24] H-B$(C_6F_5)_2$ was found to be dimeric in the solid state, but dissociated into a monomeric borane in aromatic solvents, as observed by NMR spectroscopy. H-B$(C_6F_5)_2$ was found to react very rapidly with simple alkenes and alkynes, and can be used to selectively monohydroborate terminal alkynes. Upon addition of a second equivalent of borane, a second, albeit slower, hydroboration occurred resulting in a 1,1-diborylated alkane.

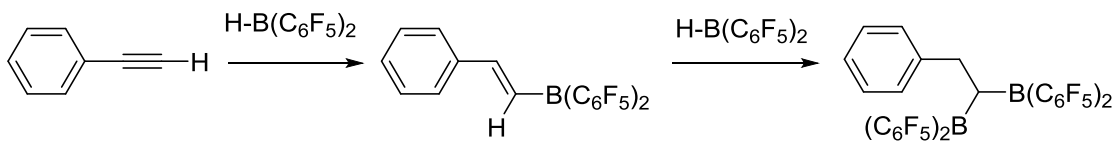


Figure 1.15: Hydroboration of phenylacetylene

It was observed that when double hydroboration of phenylacetylene was performed, the resulting product was the 1,1 diborylated isomer. However, reaction of H-B(C_6F_5)$_2$ with trimethylsilylacetylene initially yielded the 1,2 isomer as the major product, but this converted to the 1,1 isomer as the major product over time and heating. Similar selectivity is observed upon reaction of H-B(C_6F_5)$_2$ with trimethyl(vinyl)silane, the initial kinetic product is 1,2-substituted, but heating causes isomerisation, the major isomer now featuring the boron attached to the α-carbon atom. The electronic reasons for this selectivity can be explained by the β-silicon effect, where silicon groups are able to stabilise carbocations, such as the cation formed from the binding of boron in hydroborations, that are in the β-position.[24]

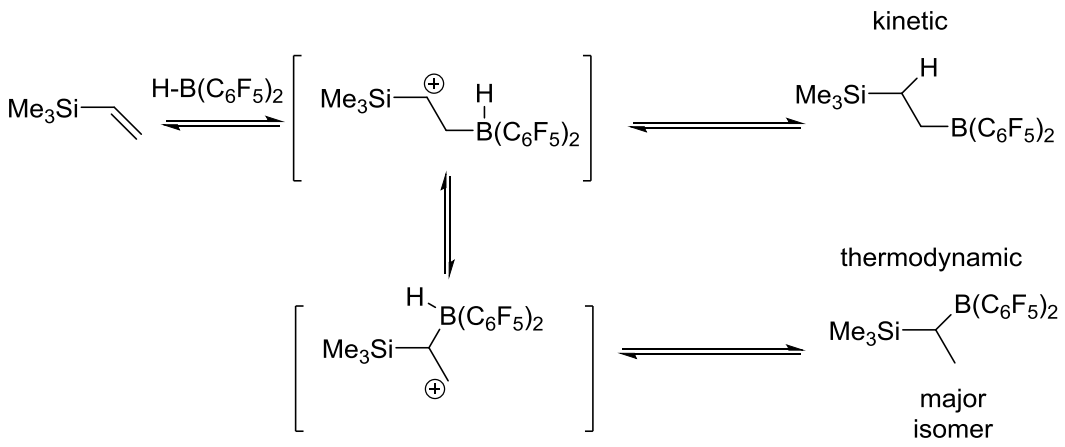


Figure 1.16: The beta-silicon effect observed during the hydroboration of trimethyl(vinyl)silane

Curran *et al.*[25,26] recently reported that the hydroboration of a variety of alkenes could be achieved utilising NHC-boranes and catalytic iodine, with reactions proposed to involve the NHC-BH_2I complex reacting via an S_N2 mechanism. Examples are shown below in Figure 1.17, where it can be seen that hydroboration

can occur not just with alkenes, but with dienes, forming cyclic NHC-boranes. It is thought that the I_2 is first activating the borane (evolving H_2), forming NHC-BH_2I, before undergoing hydroboration and a hydride transfer with another molecule of NHC-BH_3, regenerating the active boryl iodide.

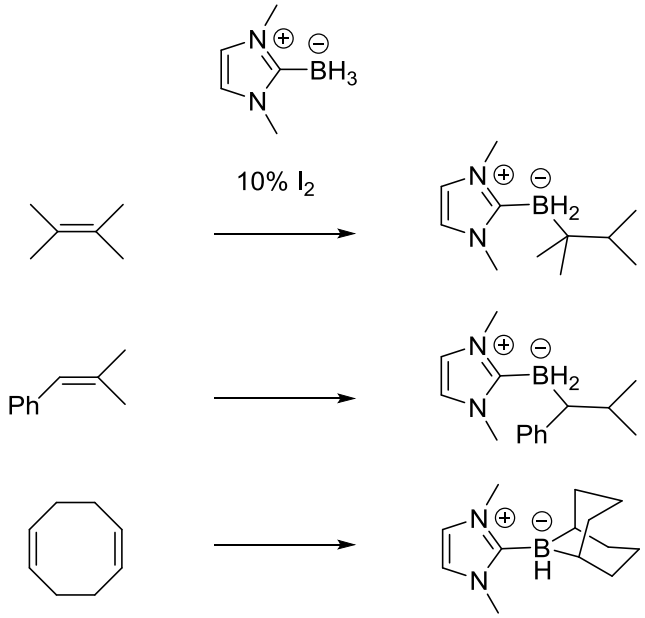


Figure 1.17: Iodine catalysed hydroboration of alkenes by NHC-boranes

The hydroborations of alkenylsilanes and alkynylsilanes were also reported, and as with the allylsilanes these reactions are typically selective for either the mono- or dihydroborated product, even when stoichiometry is manipulated to favour one over the other. Selectivity seems to be based on the structure of the alkene/alkyne. With alkenylsilanes, most gave a mixture of isomers, but one example showed that the major isomer formed was stabilised by the β-silicon effect, as shown below.

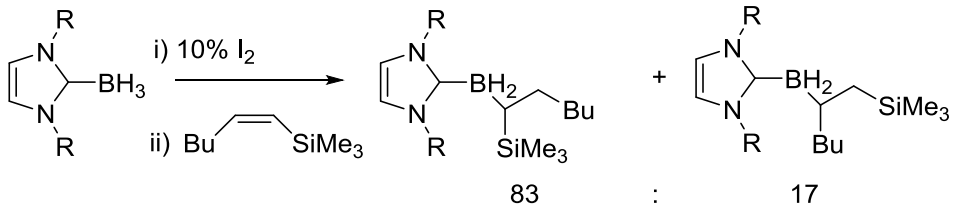


Figure 1.18: Iodide catalysed hydroboration of (Z)-1-(trimethylsilyl)-1-pentene

Diboration, wherein two boron containing groups are introduced, has been demonstrated with both terminal and internal alkynes.[27] It was shown that B_2Cl_4 can be added across acetylene, where it undergoes a diboration to generate a vinylic species. In the prescence of excess borane, the diboration was observed to occur twice, generating the species shown in Figure 1.19.[28]

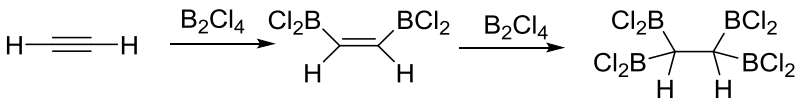


Figure 1.19: Consecutive diborations of acetylene

Diboration of alkynes using more readily accessible, more stable and less electrophilic diboron reagents (relative to B_2Cl_4) is possible but generally requires transition metal catalysis[29,30] or the addition of strong bases.[31] An example using the catechol substituted diborane Cat_2B_2 showed that alkynes could be diborylated with this, and similar $(RO)_4B_2$ species. In this specific case the diborylation required a platinum catalyst, but the reactivity was compatible with both terminal and internal alkynes. The work was extended to diynes which produced tetra-borylated dienes as shown in Figure 1.20.[32,33]

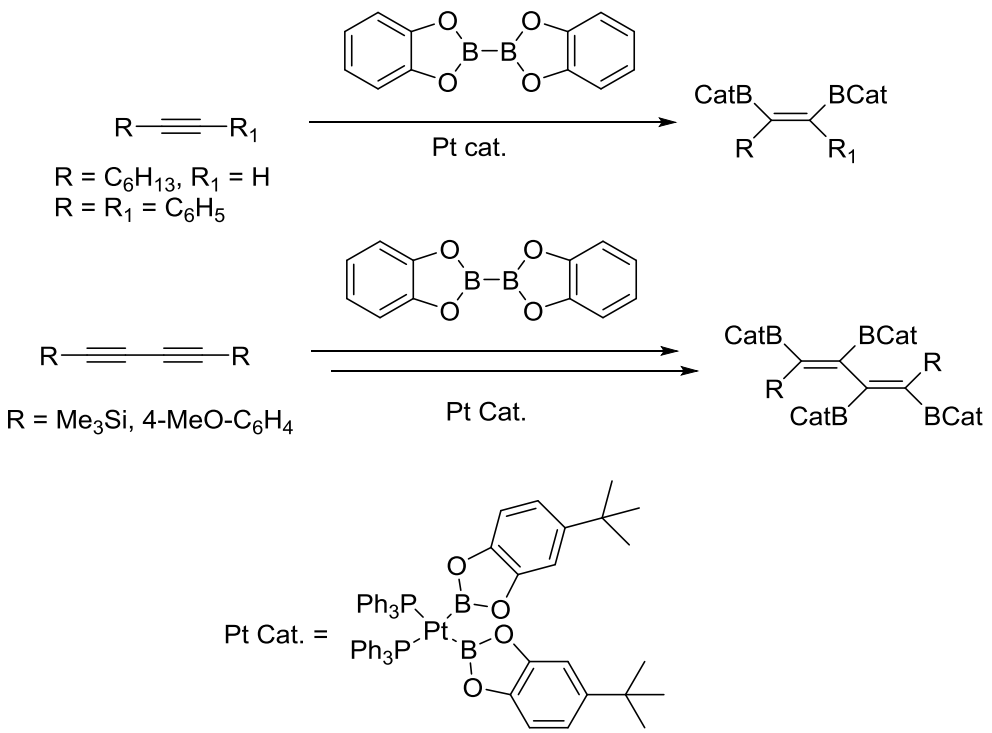


Figure 1.20: Diborylation of alkynes and diynes

Another more electrophilic diborane, shown in Figure 1.21, undergoes different reactivity with alkynes. It was reported that a borirene, the smallest aromatic boron heterocycle, which is isoelectronic with cyclopropenylium ions, can be accessed from substituted alkynes.[34] Early attempts at the synthesis of borirenes required sterically demanding substituents, while later work found that some 1-tert-butylborirenes are accessible from chloro-substituted diboranes and trimethylstannylalkynes, with Me_3SnCl observed as intermediate by-product. This process, whilst simpler than earlier routes to borirenes using photolysis, requires the synthesis of the unstable diborane B_2Cl_4 as an intermediate to generate the reagent shown below.

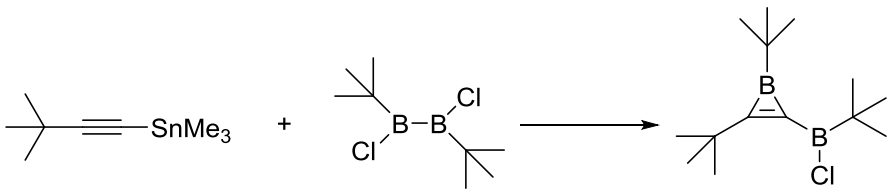


Figure 1.21: Synthesis of borirene

Despite the wealth of work showing the range of reactivity of neutral boranes with alkynes, a number of limitations arose where the electrophilicity of the neutral borane was insufficient (e.g., in the haloboration of internal alkynes). Due to this, recent investigations have begun to demonstrate the utility of borocations in this field. Select examples of the reactivity of borocations with π nucleophiles to form new C-B bonds are presented after a general introduction to borocations.

1.3 Classification and Synthesis of Borocations:

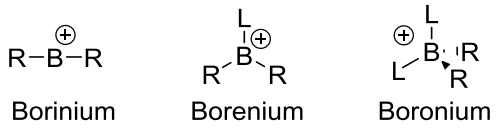


Figure 1.22: The three classes of borocation

The classification of borocations was established such that they fell into three distinct classes based on their coordination number, as shown in Figure 1.22.[35] The two-coordinate borinium cations are usually bound by two π donating substituents to reduce the electrophilicity at boron. Extremely reactive, these species often prove difficult to analyse in the condensed phase.[36] Three-coordinate borenium cations consist of a dative interaction with a ligand and two anionic substituents. The added stability provided by the donor ligand generally makes borenium cations easier to use and study in solution phase than borinium cations. Four-coordinate boroniums, easily the most common of the three classes again have two anionic substituents, but now two neutral donor ligands. With the coordination sphere now filled, these are the most stable species of borocations. The donor ligands featured in boreniums and boroniums serve to partially quench the positive charge at boron, but as boron is more electropositive than the donor atoms of the substituents used (leading to a significant polarisation of the sigma bonding framework), and as these species react as boron based electrophiles, they are drawn as having a formal positive charge on boron herein, with the ligands bound datively. Whilst we acknowledge that charge is inherently diffuse in these molecules, calculations have been performed to investigate the frontier orbital

energies and character of several borocations and support this formalism.[37] For example, it was found that the natural bond order (NBO) charges at boron were dependent upon the nature of the ligand, but with amine ligands (the predominant type studied herein), the major locus of positive charge was on boron, and correlated to the observed reactivity, i.e. boron acting as the electrophile.

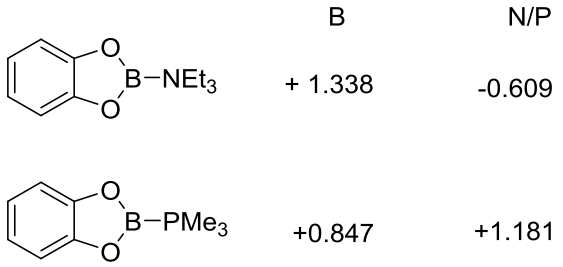


Figure 1.23: The effects of ligand on NBO charge

A strong halophilic Lewis acid is generally essential to form boreniums, as it has been shown that amine-trihaloborane adducts only undergo leaving group displacements.[38] As shown in Figure 1.24, reaction of the adduct, Me_3NBX_3 (X = Br, I), with BCl_3 occurs via a bimolecular transition state, not via a cationic borenium.

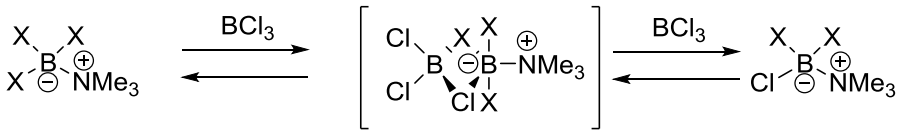


Figure 1.24: BCl_3 adducts

Only one system shows evidence for S_N1-like heterolysis, namely the BI_3-NEt_3 adduct with anionic nucleophiles (Figure 1.25).[38] For this system in the absence of other halophiles, qualitative observations imply that the reaction proceeds via a borenium ion intermediate, followed by halide exchange leading to the product.

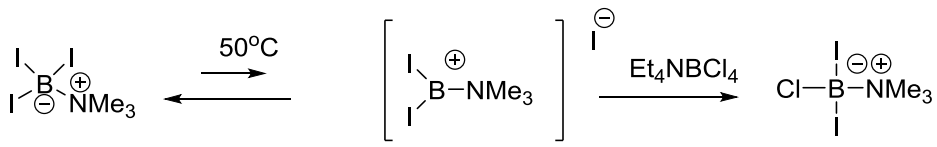


Figure 1.25: Leaving group heterolysis

Borenium cations have been synthesised with a wide range of structures, where the substituents bound to boron can be modified to attenuate the reactivity. In addition to halide abstraction, the other most common reaction route is hydride abstraction. An example of this is shown in Figure 1.26, where at first 2,3-benzazaborolidines were generated from arylboronic anhydrides, followed by hydride abstraction with trityl tetrakis(pentafluorophenyl)-borate (trityl = triphenylmethyl, Ph_3C^+).

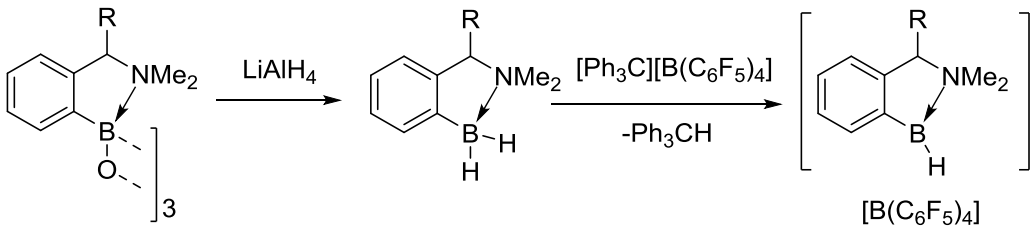


Figure 1.26: Synthesis of borenium by hydride abstraction

In another notable example, boreniums can be synthesised from monocationic hydride bridged salts via hydride abstraction. By manipulating the ligands on boron, the borenium formed could either be a borenium monocation, or a highly reactive dicationic dimer as seen in Figure 1.27 below.[39]

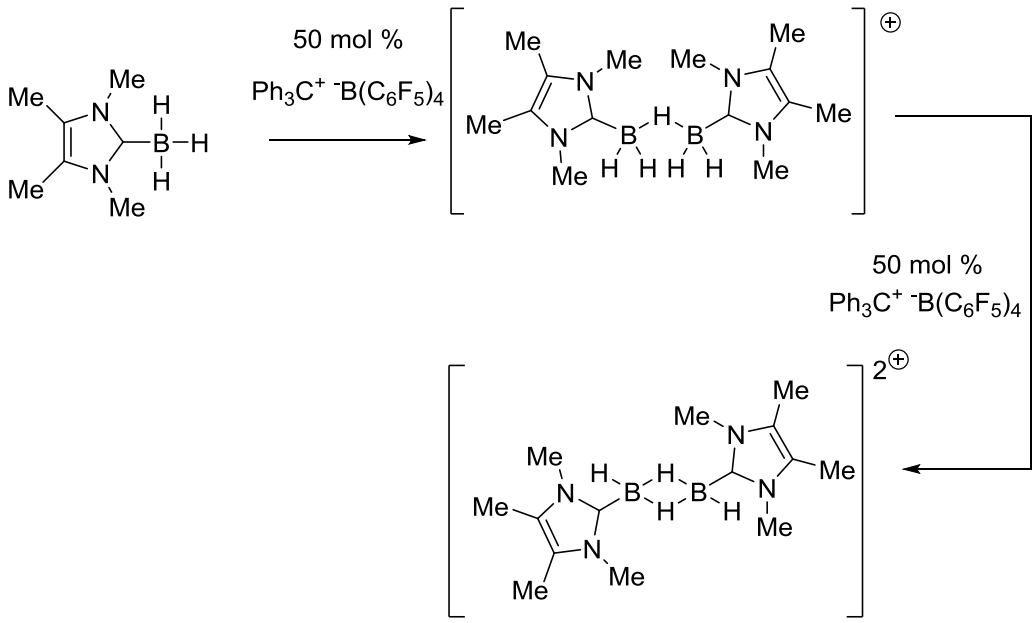


Figure 1.27: Synthesis of dimeric hydride-bridged dication

In order to access the dimeric hydride-bridged dication it was necessary to activate NHC boranes using a trityl salt ($Ph_3CB(C_6F_5)_4$) as seen above in Figure 1.27. Using this method to activate NHC-BH_3 complexes resulted in clean formation of the respective H-bridged cations, and addition of a second 50 mol % amount of the trityl salt resulted in what were at first unknown compounds, with ^{11}B NMR shifts at in the region of 8 - 12 ppm depending on the NHC. Tetrasubstituted NHC-boranes, again first formed a H-bridged cation, but on addition of the second portion of trityl salt the dication was isolated and crystallised to allow unambiguous charcterisation.

With the two most common routes to borenium cations outlined above, their applied chemistry to form C-B bonds will be the primary focus of the following section, such as reactions with arenes and alkynes, as well as examples of hydroboration, haloboration and carboboration.

1.4 Reactions of Borocations with π Nucleophiles

While it is well documented that neutral boranes, when sufficiently electrophilic, will react with a variety of nucleophiles, more recent work with highly electrophilic borocations shows that these species have a wide range of reactivity and can be modified for specific purpose by tuning the Lewis acidity. This can be achieved by changes in the groups bound to the boron centre, such as the nucleophilicity of the bound base.

Intramolecular borylations of arenes are known, initially yielding boron containing heterocycles, including an early example of the reaction running at 0˚C, as shown in Figure 1.28.[40] This implied that borenium cations (or their functional equivalent - for example where $AlCl_3$ is coordinated to the nitrogen lone pair) were able to react with π-nucleophiles, although the intermediacy of borenium cations was not definitively proven in this example.

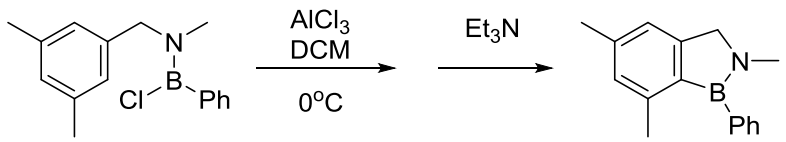


Figure 1.28: Rapid arene borylation at 0°C

A similar reaction with $AlBr_3$ has been possibly shown to proceed via a borenium ion intermediate, but is only identified by ^{1}H NMR spectroscopy (no ^{11}B NMR spectra were reported).[41] Upon warming the intermediate, the compound shown in Figure 1.29 was proposed; the N-protonation was attributed to protic contaminants in the aluminium halide reagent.

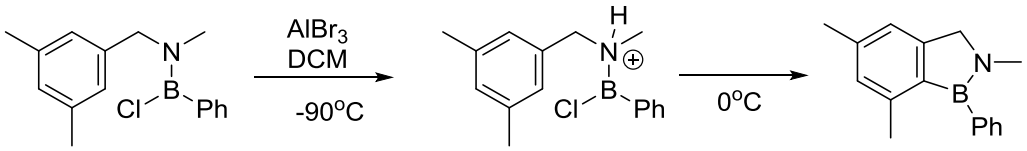


Figure 1.29: Borylation via borenium ion

An analogous cyclisation was investigated in depth with *N,N*-dimethylbenzylamine borane and a trityl salt. Initial reactions showed no cyclization with 50 mol% trityl salt, instead only forming the H-bridged dimer, but on addition of extra 40 mol% trityl salt, making the reaction effectively stoichiometric in trityl, the cyclic product formed rapidly. This is then quenched with Bu_4NBH_4 to give the more stable amine borane (Figure 1.30). This stoichiometric route has been used to prepare a range of cyclic amine boranes, showing the utility of borenium cations in electrophilic arene borylation.

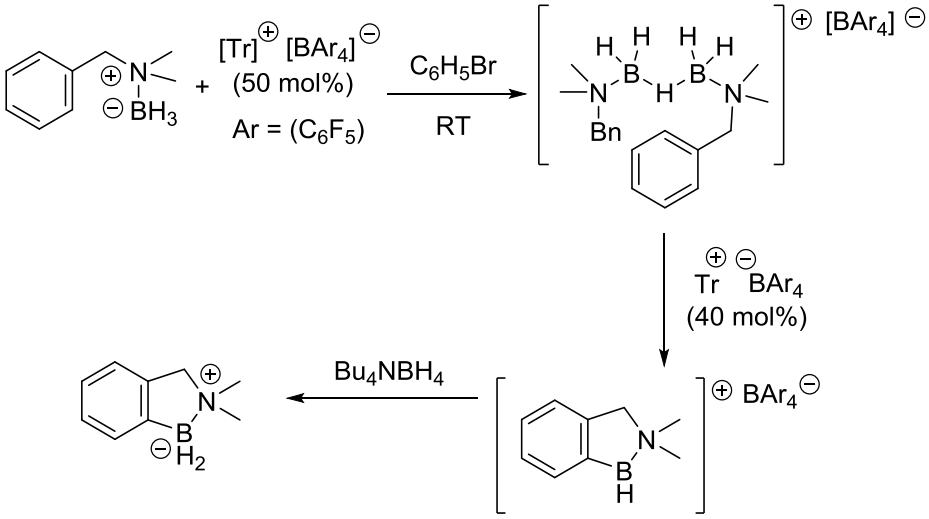


Figure 1.30: Intramolecular nitrogen-directed aromatic borylation

Intermolecular arene borylations have also been reported, with BX_3 known to react with aromatic hydrocarbons in the presence of aluminium trihalides to give

aryl dihaloboranes, and mechanisms based on borenium intermediates may be involved in this process. In the first proposed mechanism Muetterties [42] suggested the formation of a solvated BCl_2^+ species. This could of course be seen as a borenium equivalent where the neutral ligand is the arene substrate. It was also proposed by Olah [43] that the structure for the activated electrophilic intermediate was the superelectrophile $Cl_2B–(\mu\text{-}Cl)–AlCl_3$. This possible intermediate contains a borenium subunit within a neutral structure; however, the identity of the key electrophile in these borylations has not been proved, though a borenium connection is plausible.

Borenium cations are also effective for synthesising aryl boronate esters.[44] These are commonly used synthetic building blocks, due to their use in high efficacy C-X bond forming reactions.[45]

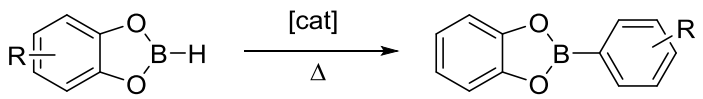


Figure 1.31: Synthesis of aryl boronate esters using borenium cations

Prior to this work, to access regioisomers controlled by electronic effects required aryl halide intermediates and then either hard organometallic and $B(OR)_3$ or metal-catalysed cross-coupling.[46] The development of a metal-free direct arene borylation via electrophillic aromatic substitution was seen as a way to increase reaction efficiency. The borenium systems developed are a boron analogue of Friedel-Crafts chemistry, and represent an alternative route to pinacol boronate esters produced under electronic control. This approach is complementary to the

recent work in iridium-catalysed direct electrophilic borylation which operates principally under steric control.[47]

Recent modification[48] of Muetterties work has suggested a more substantial connection to borenium intermediates. 2-Phenylpyridine was treated with 3 equivalents of BBr_3 and a proton scavenger, Et_2N*i*-Pr, to give the boron heterocycle product shown in Figure 1.32.

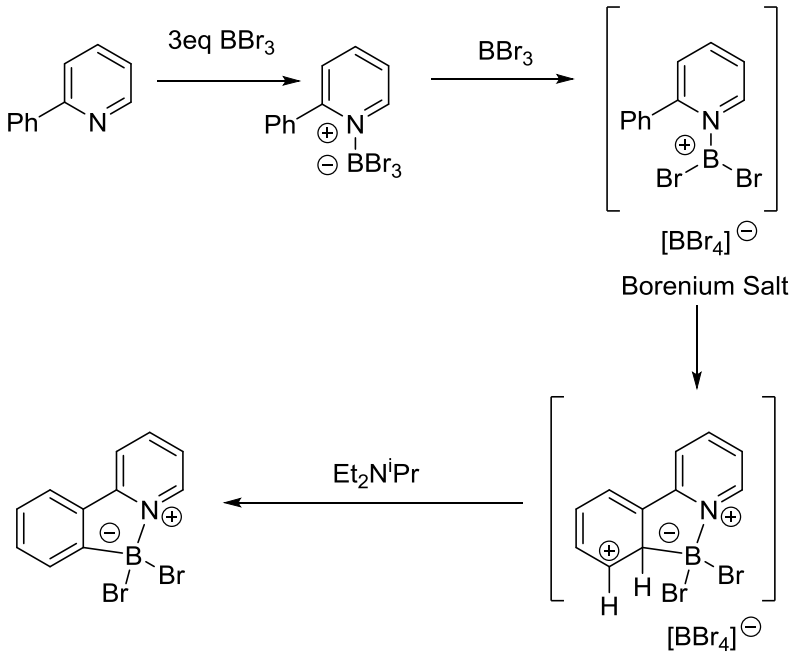


Figure 1.32: Intramolecular borylation via a postulated borenium

The proposed mechanism involves first the formation of a complex between the pyridine and BBr_3, followed by halide abstraction with excess BBr_3, giving the borenium salt shown in Figure 1.32. It is thought that electrophilic borylation via a Wheland intermediate will follow to give the observed cyclic product. This application of borocations was extended to several substituted or annulated derivatives of the starting arene.

A highly electrophilic boronium cation capable of borylating arenes was reported by Vedejs *et al.*,[49] and was synthesised from the readily available 9-borabicyclo[3.3.1]nonane (9-BBN) dimer and bis(trifluoromethanesulfonyl)imide. This is followed by the addition of 1,8-bis(dimethylamino)naphthalene, forming the borocation which exists as a 4-coordinate boronium species in solution, based upon NMR data. Successful crystallisation showed the 4-coordinate nature of boron, as well as the highly strained nature of the system (both cyclic components are distorted) which resulted in the boronium being unsymmetrical with long B-N bonds relative to non-strained boronium salts.

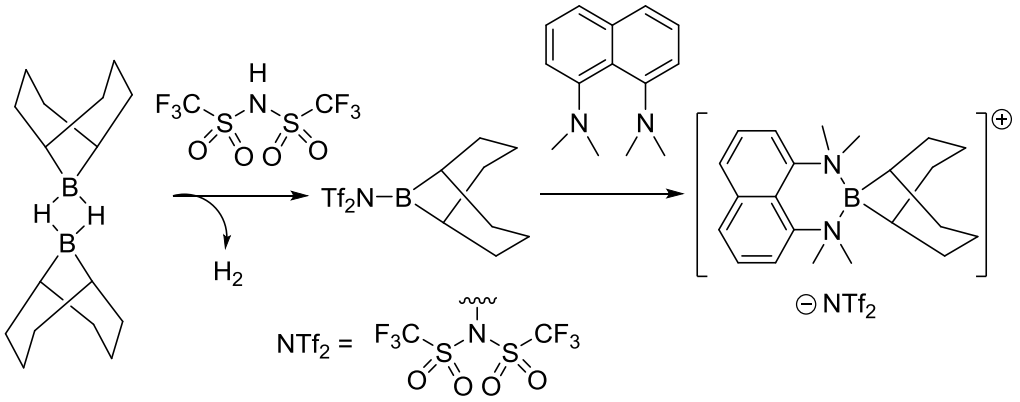


Figure 1.33: Synthesis of borocation from 9-BBN dimer, $HNTf_2$ and proton sponge

The borocation was shown to be a convenient reagent, due to the ease of synthesis in a one pot fashion and the stability of the crystallised product, which shows some tolerance to air in the solid state. When exposed to several activated arenes, this borocation was shown to undergo electrophilic borylation, possibly via a borenium intermediate formed on cleavage of one of the strained B-N bonds. A selection of nitrogen heterocycles were successfully monoborylated with excellent

yields when using one equivalent of the borocation, whilst diborylation was shown to be accessible with two equivalents.

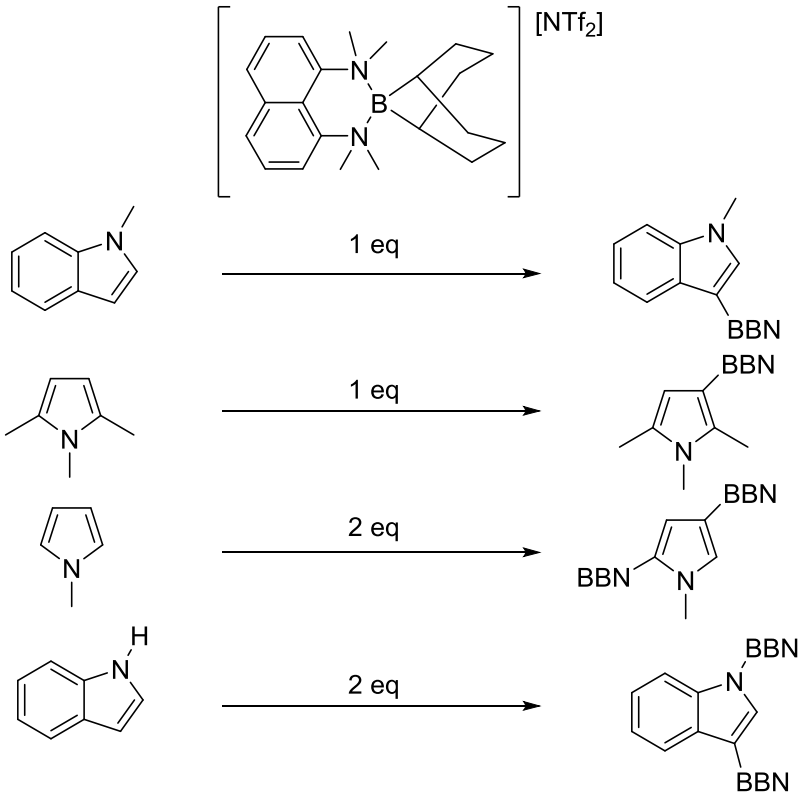


Figure 1.34: Reaction of boronium salt with N-heterocycles

It was shown through mechanistic studies that the nature of the anion partnering the borocation is important to borylation reactivity. $[CatB(NEt_3)][CbBr_6]$ and $[CatB(NEt_3)][BAr_{Cl}]$ were synthesised from the weakly coordinating anions $[closo\text{-}1\text{-}H\text{-}CB_{11}H_5Br_6]^-$ ($CbBr_6$) and $[B(3,5\text{-}C_6H_3Cl_2)_4]^-$ (BAr_{Cl}) respectively.[50] These reacted rapidly with the arenes Me_2NPh and N-Me-indole to produce borylated products in analogous reaction times to that using $[CatB(NEt_3)][AlCl_4]$. No additional base was necessary, indicating that the reaction proceeds either through early dissociation of NEt_3 to proceed via a step-wise or concerted mechanism, or unreacted arene acts as a Brønsted base, as shown in Figure 1.35.

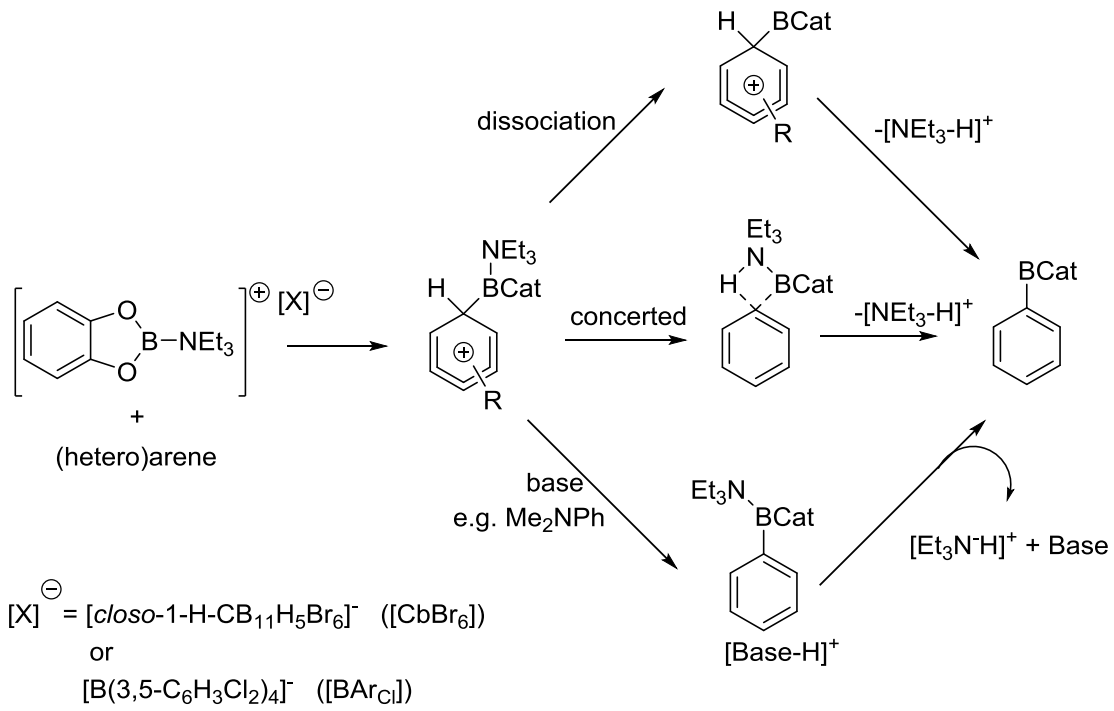


Figure 1.35: Possible borylation pathways using $[CatB(NEt_3)]^+[X]^-$

However, neither $[CatB(NEt_3)][CbBr_6]$ nor $[CatB(NEt_3)][BAr_{Cl}]$ borylated *N*-TIPS-pyrrole to any significant extent, whereas $[CatB(NEt_3)][AlCl_4]$ fully borylated it within 72 hours. The anion dependency was attributed to be an effect of the halide transfer equilibria present when using $[CatB(NEt_3)][AlCl_4]$. Therefore, there must be another compound needed for borylation present in the reaction at low concentrations (unobservable by NMR spectroscopy). It was surmised that this was either free Et_3N, to deprotonate the borylated arenium cation, or another more reactive electrophile. It was shown through reaction studies that the effective borylation of *N*-TIPS-pyrrole with $[CatB(NEt_3)][AlCl_4]$ may be attributable to a low concentration of free Et_3N generated by the various equilibria enabling deprotonation of the borylated arenium intermediate. One key reaction was the

catalysis of borylation of N-TIPS pyrrole with $[CatB(NEt_3)][CbBr_6]$ by PPh_3 which does not interact with the borocation, this forms a frustrated Lewis pair.

As well as borylations with catechol borenium cations, it has been shown that borenium cations synthesised from BCl_3, $AlCl_3$ and base are capable of intermolecular borylations in an analogous manner.[51] One such example is the $[LutBCl_2][AlCl_4]$ borocation. Successful borylations were performed on a variety of heteroarenes, such as *N*-TIPS-pyrrole, under mild reaction conditions with high isolated yields.

It has also been recently shown that borenium cations can hydroborate silyl-substituted alkenes and alkynes using a catalytic activator (e.g. $H\text{-}NTf_2$). Using a NHC-borane complex, a H-bridged NHC-borane monocation can be generated *in-situ* which can undergo rapid 1,2-hydroboration with alkenes and acts as a functional equivalent to a $[NHC\text{-}BH_2]^+$ borenium. The borenium product from hydroboration is then able to abstract a hydride from the starting material NHC-borane, leaving a neutral hydroborated product and regenerating the borenium.

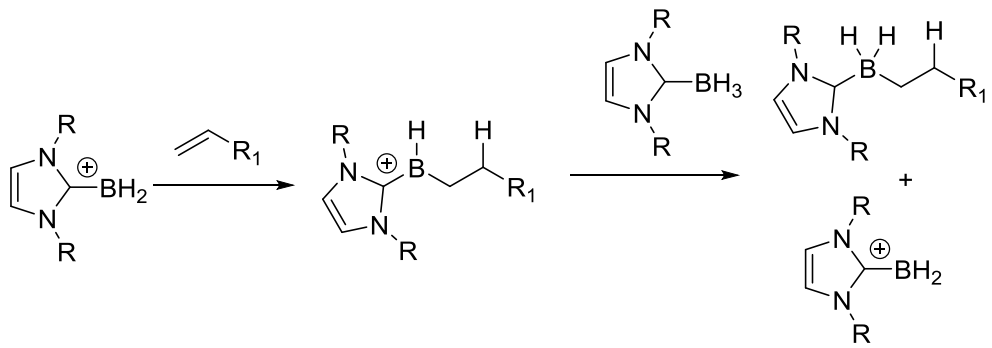


Figure 1.36: Proposed reaction for hydroboration with functional equivalents of $[NHCBH_2]^+$

Whilst beyond the scope of this report (which focuses on the functionalisation of π nucleophiles with boron electrophiles to form C-B bonds) it should also be noted that closely related borenium cations have even been shown to activate aliphatic C-H bonds.[52]

In addition to the reactions of boranes and borocations with π nucleophiles, another series of reagents and their reactivity is of importance to this body of work. The reactivity of frustrated Lewis pairs involving a neutral boron Lewis acid and a Lewis base, particularly their reactivity patterns with π nucleophiles, is often distinct to that involving just neutral boranes, therefore they are discussed next.

1.5: FLP Reactivity with Alkynes

Ordinarily, when a Lewis acid and a Lewis base are combined, neutralization occurs forming an adduct. Such chemistry was first described by Lewis in 1923.[53] However, it was discovered over the years that some combinations of Lewis acids and bases do not follow this general reactivity mode, such as the observation by Brown[54] that, whilst the Lewis base 2,6-lutidine forms the expected adduct with BF_3, no reactivity was observed with the sterically larger BMe_3. When the two components are sufficiently bulky, such as in the latter case, a frustrated Lewis pair (FLP) is formed.[55] For example in Figure 1.37 the boron and phosphorous centres are sufficiently sterically congested to prevent dative bond formation. This results in interesting reactivity when exposed to another reagent, such as molecular hydrogen, which gives heterolytic dihydrogen activation to yield $[HB(C_6F_5)_3][HP^tBu_3]$.[55] Recent work has extended this chemistry, and shown H_2 activation by borenium cation containing FLPs.[56]

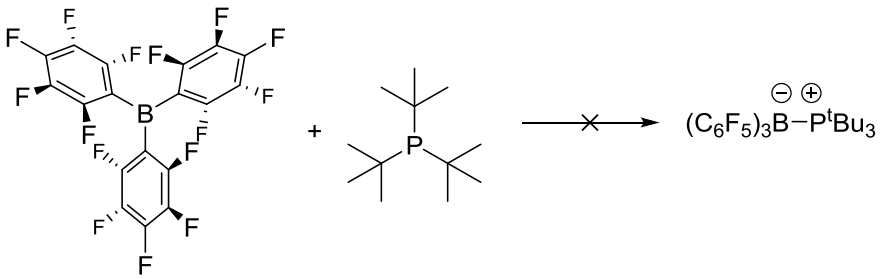


Figure 1.37: Steric properties of FLPs

Reactions of borane Lewis acids with alkenes and alkynes has been widely investigated (as discussed above),[57] but it has been shown that FLPs not only react with alkenes and alkynes, but the observed reactivity can be very different dependent on the Lewis base used. The reactivity of phosphine/Lewis acid FLPs has been demonstrated, leading to the formation of boron-substituted alkynes.[58]

Frustrated Lewis pairs were generated from $B(C_6F_5)_3$ or (PhMe).$Al(C_6F_5)_3$ and $^tBu_3P$. Addition of phenylacetylene afforded dehydroboration/dehydroalumination products in high yield, for the B and Al reactions, respectively. NMR spectroscopy studies suggested that the products were alkynyl boronates and aluminates, and this was confirmed by single crystal X-ray crystallography.

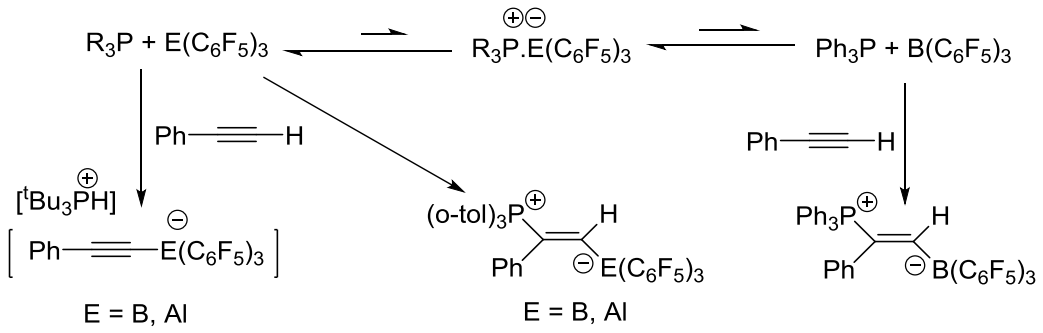


Figure 1.38: FLPs and their reactions with alkynes

FLPs were also generated from $B(C_6F_5)_3$ / (PhMe).$Al(C_6F_5)_3$ and (*o*-$C_6H_4Me)_3P$ and reacted with phenyl acetylene in the same fashion to give 1,2-addition products in good yields. These were shown by X-ray crystallographic studies to be zwitterionic species as shown in Figure 1.38, centre. Unlike the formation of the alkynyl boronates and aluminates, these FLPs react with the acetylene to give an alkene, with the boron (or aluminium) *E* to the phosphine. In contrast, the classic Lewis acid-base adduct $Ph_3P.B(C_6F_5)_3$ shows no evidence of dissociation, but reacts with phenylacetylene to give the *trans*-1,2-addition product in a high yield. This product implies that there must be an equilibrium with some degree of dissociation of PPh_3 from the borane, which is consumed by the acetylene to form the observed alkene product. The formation of this product shows that frustrated and classical Lewis pair reactivity are not mutually exclusive, and also suggest that a wide range

of FLP reactivity maybe accessible from what were previously thought to be classical Lewis adducts only. The control of whether dehydroboration or FLP addition occurs comes from the nature of the Lewis base.[59] The work carried out by Stephan and co-workers suggested that addition and deprotonation pathways are competitive, and it was observed that FLP-alkyne addition products are favoured by less bulky and less basic phosphines (and other Lewis bases).

In addition to the 1,1-carboboration work with neutral boranes mentioned earlier, Erker and co-workers also studied reactions of FLPs with terminal alkynes.[37] Using FLPs generated from $B(C_6F_5)_3$ and several phosphorus Lewis bases, they also found that the mode of reaction changed significantly with varying the strength of the Lewis base.[60] 1,2-Diethynylbenzene reacts as shown in Figure 1.39; with P^tBu_3 as the Lewis base dehydroborylation occurs, yielding the dialkynyl salt. By exchanging the Lewis base for the weaker base triarylphosphine, the alkyne undergoes cooperative 1,2-FLP addition to give the zwitterionic product. With the even weaker Lewis base $P(C_6F_5)_3$ the preferred reaction pathway changes again, yielding the cyclic product. This is thought to form via a 1,1-carboboration followed by a 1,2-FLP addition to the second carbon-carbon triple bond. This second mode of reactivity can occur due to the intermediate (top right, Figure 1.39) retaining its FLP activity with alkynes.

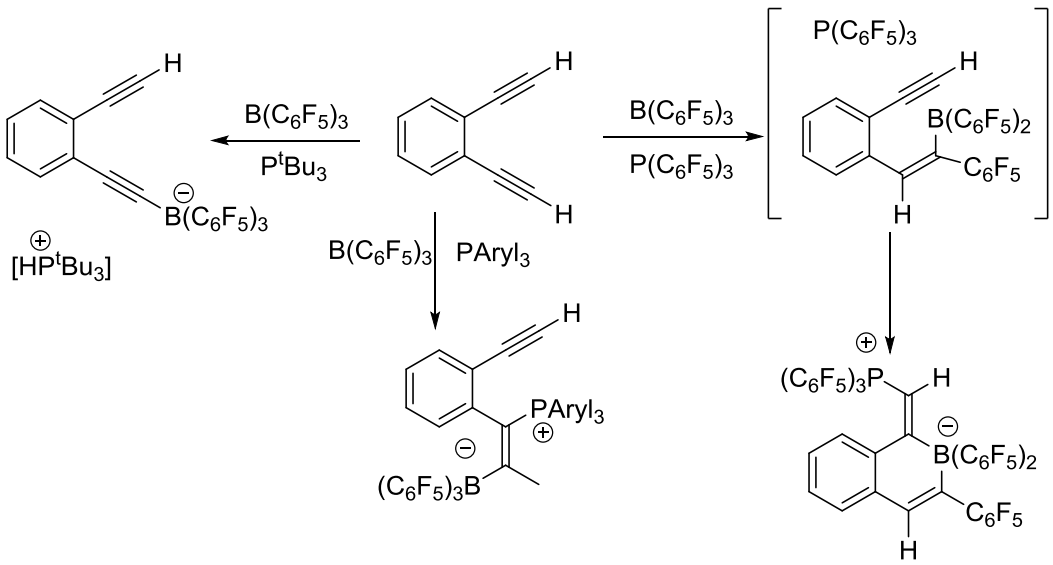


Figure 1.39: Reactions of FLPs with 1,2-diethynylbenzene

Recent work has been performed to extend the reactivity of FLPs to borometalation of terminal alkynes.[61] Work which followed from the same group showed that FLPs can activate terminal alkynes to form alkynylborates. A FLP formed from $HBAr^F_2$ and DABCO was generated and reacted with phenylacetylene (Figure 1.40). Initially $HBAr^F_2$ was mixed with phenylacetylene at room temperature to give a 1,2-hydroboration product over 5 hours. It was shown that at 0˚C, the ammonium alkynylhydridoborate salt was formed *via* the deprotonation of the vinyl cation intermediate. It was observed that upon heating of this species to 55˚C, the ammonium alkynylhydridoborate salts would convert to the 1,2-hydroboration product and regenerate free DABCO, as shown In Figure 1.40.

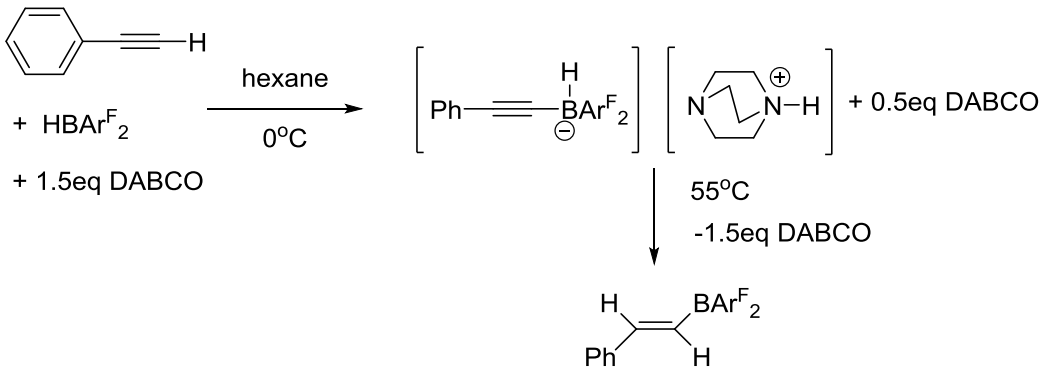


Figure 1.40: Reactivity of FLP of $HBAr^F_2$ and DABCO with phenylacetylene

Frustrated Lewis pairs have also been discovered to undergo cyclisations with terminal diacetylenes.[62] Of note to this work is that varying the length of the alkyl chain between the two alkynes can drastically alter the reactivity, resulting in different cyclic products. In the presence of terminal alkynes, FLP's usually react to from either the dehydroborylation product, or undergo a 1,2-addition of the Lewis acid/base components. When the FLP $PPh_2[C_6H_3(CF_3)_2]/(B(C_6F_5)_3)$ reacts with 1 equivalent of di(propargyl)ether, the latter is observed. However, it has been observed that when another FLP, $(o\text{-tolyl})_3P/(B(C_6F_5)_3)$ is reacted with diynes 1,6-heptadiyine and 1,7-octadiyne, neither of the two aforementioned reaction pathways occur.

The reaction with 1,7-octadiyne resulted in addition of the Lewis acid and Lewis base to the terminal positions of separate alkynes, concomitant with a new carbon-carbon bond being formed. The resulting product is an exocyclic conjugated diene, which is zwitterionic due to the newly introduced boron and phosphorous moieties. Successful crystallisation and analysis by X-ray crystallography showed that the bulky boron and phosphorous groups are orientated anti to each other.

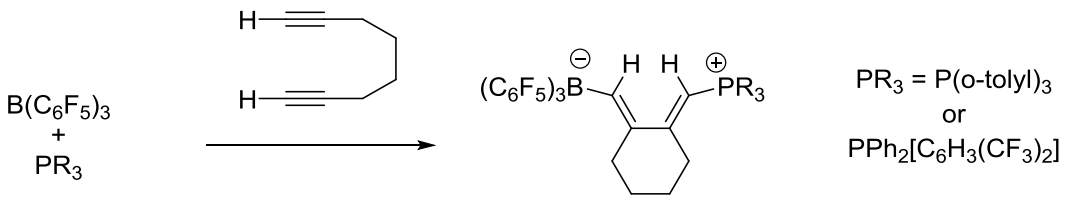


Figure 1.41: Reactivity of $B(C_6F_5)_3$ / PR_3 FLP with 1,7-octadiyine

The reaction of the same FLP with 1,6-heptadiyne shows that changing the chain length can have a notable impact on the reaction pathway. The isolated product of this reaction was revealed, by X-ray crystallography, to be the zwitterionic eight membered heterocycle. The boron atom inside the newly formed boracycle bears two of its original ligands, while the third has migrated to an adjacent vinylic carbon atom. The phosphorous moiety is bound to the other alkene in the molecule, as shown in Figure 1.42. It is theorised that this product is the result of an initial 1,1-carboboration involving a formal shift of the hydrogen to the 2-position of the alkene, allowing C-B bond formation. Cooperative addition of the phosphine could then cause ring closure, resulting in the cyclic product.

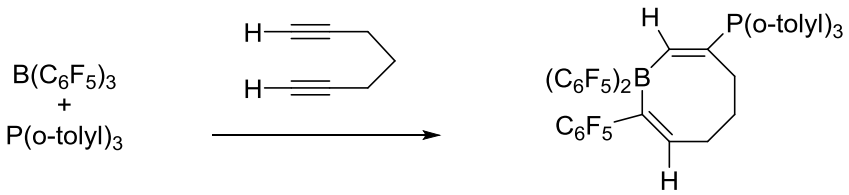


Figure 1.42: Reaction of an FLP with 1,7-octadiyne

Although only a selection of examples have been shown above, the reactivity of neutral boranes with alkynes is highly complex. The reactivity can be greatly altered resulting in a range of different outcomes depending on the borane

used, the nature of the alkyne, and whether a Lewis base is present or not, which can also result in FLP type reactivity.

It has been demonstrated that certain FLPs closely related to compounds discussed in this thesis can be used for H_2 activation and as catalysts in the hydrogenation of alkynes to *cis*-alkenes.[63] The generalised reaction shown in Figure 1.43, below, was found to be highly chemo- and stereoselective; cis-alkenes were the major product, with only traces of other products detected by NMR spectroscopy. The catalyst itself is an intramolecular Lewis adduct, synthesised as one example of thermally accessible frustrated B/N Lewis pairs.[64]

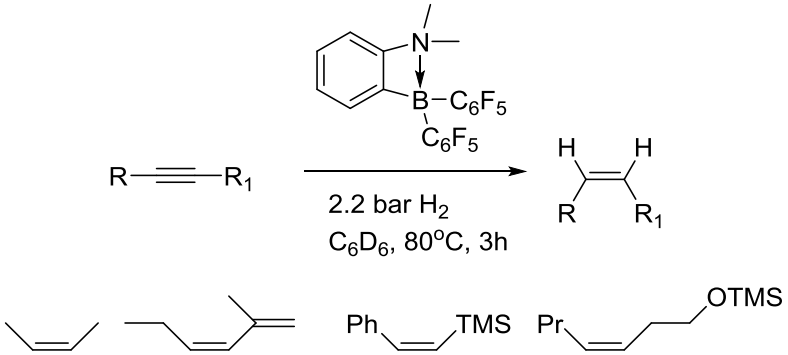


Figure 1.43: Hydrogenation of alkynes with a FLP

The postulated catalytic cycle, shown below in Figure 1.44, proceeds first by production of the active catalyst by H_2 activation and loss of HC_6F_5. The active catalyst then undergoes hydroboration of the alkyne, heterolytic H_2 cleavage with the vinylborane intermediate, and intramolecular protodeborylation releasing both the catalyst and the cis-alkene product. The selectivity is attributed to exclusive *syn*-hydroboration and stereoretentive protodeboronation. In support of this

mechanism was the isolation of some intermediates, such as the active catalyst species.

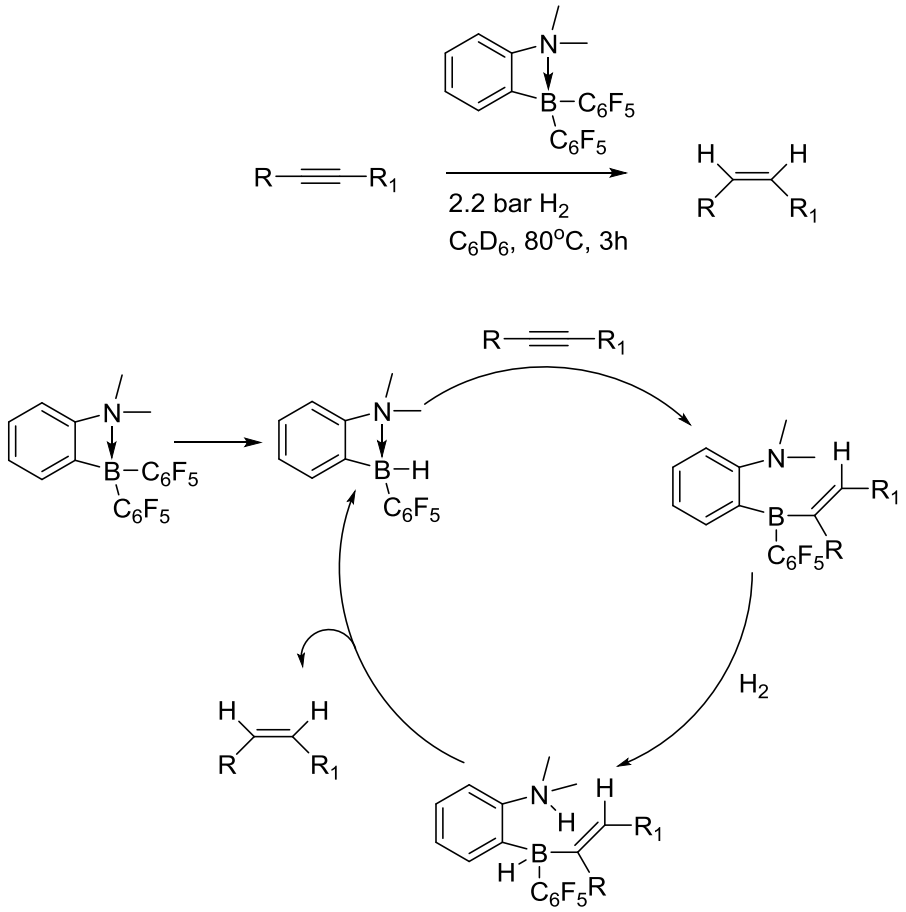


Figure 1.44: Proposed catalytic cycle

1.6 Summary and Scope of Thesis

Although not as expansively studied as reactions with neutral boranes, borocations already have shown tremendous promise for wide-reaching reactivity with π nucleophiles. The existing work with borocations in synthesis has shown that the strongly Lewis acidic borenium ions are of great interest. As the main target of this project was to study the reactivity of borocations with alkynes (with and without an additional base), a selection of borocations was required so that each may be studied in turn to observe both similarities and differences when reacted with a wide variety of alkynes. Several borocations have been previously studied within the group, and were synthesised and isolated as needed for this project, along with novel species. The borocations studied were designed to possess a range of Lewis acidities at boron, determined by the groups ligated to them, in order to provide sufficient scope for reactions with alkynes.

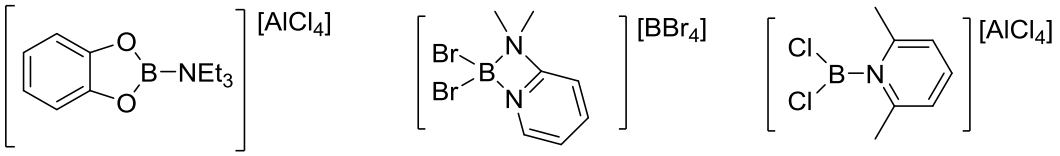


Figure 1.45: Examples of borenium and boronium borocations

In order to investigate the reactivity of borocations, a broad selection of alkynes were investigated. Whilst most were purchased, making the borylated products more desirable due to readily available starting materials, some were synthesised to allow greater variance in substrate scope. Borylation of these would allow for a wide range of functionally diverse boron containing molecules, which

may have use as building blocks in synthetic chemistry, such as natural product synthesis and drug discovery.

The three main reaction types to be studied are de(elemento)boration, haloboration and carboboration of alkynes. Borylated alkynes are one of the first targets of the project, as they represent a useful group that can be introduced into the structure of larger molecules (e.g., by benzannulation).[65] Haloboration of alkynes has proved elusive outside of using boron trihalides and dialkylB-X with both limited in scope. One of the key aims of the project is to expand this reactivity to a wider range of alkynes, as 1,2-haloborated alkene products represent highly functionalisable building blocks in synthesis. Finally, the scope of carboboration reactions with borocations will be probed to see if it can be used as an alternative to haloboration; essentially removing one cross-coupling step if the desired group can be installed directly at the same time as the boron.

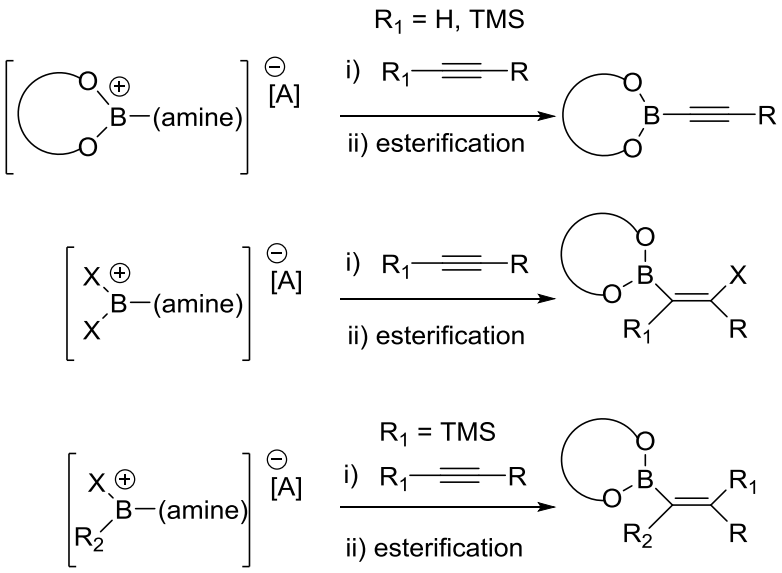


Figure 1.46: Dehydroboration, haloboration and carboboration of alkynes

1.7 References

1. Kölle, P. and Nöth, H. *Chem. Rev*., **1985**, 85, 399
2. Corey, E. J., Shibata, T., Lee, T. W. *J. Am. Chem. Soc*., **2002**, 124, 3808
3. Hurd, D. T. *J. Am. Chem. Soc*., **1948**, 70, 2053
4. Brown, H. C. *Tetrahedron*, **1961**, 12, 117
5. Lappert, M. F., Prokai, B. *J. Organometal. Chem*., **1964**, 1, 384
6. Wang, C., Tobrman, T., Xu, Z., Negishi, E. *Org. Lett*., **2009**, Vol. 11, 4092
7. Miyaura, N., Yamada, K., Suzuki, A. *Tetrahedron Letters*, **1979**, 20, 3437
8. Prokofjevs, A., Kampf, J. W., Vedejs, E. *Angew. Chem. Int. Ed*., **2011**, 50, 2098
9. Muetterties, E. L. *J. Am. Chem. Soc*., **1959**, 81, 2597
10. Bujwid, Z. J., Gerrard W., Lappert, M. F. *Chem. Ind*., **1959**, 1091
11. Muetterties, E. L. *J. Am. Chem. Soc*., 1960, 82, 4163
12. Muetterties, E. L., Tebbe, F. N. *Inorg. Chem*., 1986, 7, 2663
13. Lappert, M. F., Prokai, B. J. *Organometal. Chem*., **1964**, 1, 384
14. Yoshida, K., Shishikura,Y., Takahashi, H. Imamoto, T. *Org. Lett*., **2008**, 10, 2777
15. Köster, R., Seidel, G., Wrackmeyer, B. *Chem. Ber*., **1989**, 122, 1825
16. Jiang, C., Blacque, O., Berke, H. *Organometallics*, **2010**, 29, 125
17. Chen, C., Eweiner, F., Wibbeling, B., Fröhlich, R., Senda, S., Ohki, Y., Tatsumi, K., Grimme, S., Kehr, G., Erker, G. *Chem. Asian J*., **2010**, 5, 2199
18. Chen, C., Voss, T., Fröhlich, R., Kehr, G., Erker, G. *Org. Lett*., **2011**, 13, 62
19. Chen, C., Kehr, G., Fröhlich, R., Erker, G. *J. Am. Chem. Soc*., **2010**, 132, 13594

20. Eller, C., Kehr, G., Daniliuc, C. G., Fröhlich, R., Erker, G. *Organometallics*, **2013**, 32, 384

21. Erker, G., Kehr, G. *Chem. Commun*., **2012**, 48, 1839

22. Feldmann, A., Iida, A., Fröhlich, R., Yamaguchi, S., Kehr G., Erker, G. *Organometallics*, **2012**, 31, 2445

23. Brown, H. C. *Hydroboration*, W. A. Benjamin: New York, **1962**, 604

24. Parks, D. J., Spence, R. E. von H., Piers, W. E. *Angew. Chem. Int. Ed. Engl*., **1995**, 34, 809

25. Pan X., Boussonniere, A., Curran, D. P. *J. Am. Chem. Soc*., **2013**, 135, 14433

26. Boussonniere, A., Pan, X., Geib, S. J., Curran, D. P. *Organometallics*, **2013**, 32, 7445

27. Morrison, J. A. *Chem. Rev*., **1991**, 91. 35

28. Chambers, C., Holliday, A. K., Walker, S. M. *Proc. Chem*. Soc., **1964**, 286

29. Guo, X., Nelson, A.K., Slebodnick, C., Santos, W.L. *ACS Catal*., **2015**, 5, 2172

30. Lee, Y., Jang, H., Hoveyda A. H. *J. Am. Chem. Soc*., **2009**, 131, 18234

31. Bonet, A., Pubill-Ulldemolins, C., Bo, C., Gulyás, H., Fernández, E. *Angew. Chem. Int. Ed*., **2011**, 50, 7158

32. Vedejs, E., Nguyen, T., Powell, D. R., Schrimpf, M. R. *Chem. Commun*., **1996**, 2721

33. Zhang, X., Zhang, W. Z., Ren, X., Zhang, L. L., Lu, X. B. *Org. Lett*., **2011**, 13, 2402

34. Pues, C., Berndt, A. *Angew. Chem. Int. Ed. Engl*., **1984**, 23, 313

35. Nöth, H. Weber, S., Rasthofer, B., Narula, C. K., Konstantinov, A. *Pure Appl. Chem.,* **1983**, 55, 1453

36. Piers, W. E., Bourke, S. C., Conroy, K. D. *Angew. Chem. Int. Ed*., **2005**, 44, 5016

37. Solomon, S. A., Del Grosso, A., Clark, E. R., Bagutski, V., McDouall, J. J. W., Ingleson, M. J. *Organometallics*, **2012**, 31, 1908

38. Benton, B. W. and Miller, J. M. *Can. J. Chem*., **1974**, 52, 2866

39. Prokofjevs, A., Kampf, J. W., Solovyev, A., Curran, D. P., Vedejs, E. *J. Am. Chem. Soc.*, **2013**, 135, 15686

40. Vedejs, E., Nguyen, T., Powell, D. R., Schrimpf, M. R. *Chem. Commun*., **1996**, 2721

41. Genaev, A. M., Nagy, S. M., Salnikov, G. E., Shubin, V. G. *Chem. Commun*., **2000**, 1587

42. Muetterties, E. L. *J. Am. Chem. Soc*., **1960**, 82, 4163

43. Olah, G. A., *Angew. Chem. Int. Ed*., **1993**, 32, 767

44. Del Grosso, A., Pritchard, R. G., Muryn, C. A., Ingleson, M. J. *Organometallics,* **2010**, 29, 241

45. Dennis G. Hall; *Boronic Acids - Preparation, Applications in Organic Synthesis and Medicine*, 2nd Edition, Wiley-VCH:Weinheim (Germany), **2011**

46. Ishiyama, T., Murata, M., Miyaura, N. *J. Org. Chem*., **1995**, 60, 7508

47. Mkhalid, I. A. A., Barnard, J. H., Marder, T. B., Murphy, J. M., Hartwig, J. F. *Chem. Rev*., **2010**, 110, 890

48. Ishida, N., Moriya, T., Goya, T., Murakami, M. *J. Org. Chem*., **2010**, 75, 8709

49. Prokofjevs, A., Kampf, J. W., Vedejs, E. *Angew. Chem. Int. Ed*., **2011**, 50, 2098

50. Bagutski, V., Del Grosso, A., Singleton, P. J., Helm, M. D., Solomon, S. A., Lawson, J. R., Marcelli, T., Ingleson, M. J. *J. Am. Chem. Soc*., **2013**, 135, 474

51. Del Grosso, A., Singleton, P. J., Muryn, C. A., Ingleson, M. J. *Angew. Chem. Int. Ed.*, **2011**, 50, 2102

52. Prokofjevs, A., Vedejs, E. *J. Am. Chem. Soc*., **2011**, 133, 20056

53. Lewis, G. N., *Valence and the Structure of Atoms and Molecules*, Chemical Catalogue Company, Inc., New York, **1923**

54. Brown, H.C., Schlesinger, H.I., Cardon, S.Z. *J. Am. Chem. Soc*., **1942**, 64, 325

55. Stephan, D. W. *Org. Biomol. Chem*., **2008**, 6, 1535

56. Farrell, J. M., Hatnean, J. A., Stephan, D. W. *J. Am. Chem. Soc*., **2012**, 134, 15728

57. Aubin, S., Le Floch, F., Carrie, D., Guegan, J. P., Vaultier, M. *ACS Symp. Ser*., **2002**, 818, 334

58. Dureen, M. A., Stephan, D. W. *J. Am. Chem. Soc*., **2009**, 131, 8396

59. Dureen, M. A., Brown, C. C., Stephan, D. W. *Organometallics*, **2012**, 29, 6594

60. Liedtke, R., Fröhlich, R., Kehr, G., Erker, G. *Organometallics*, **2011**, 30, 5222

61. Ye, H., Lu, Z., You, D., Chen, Z., Li, Z. H. and Wang, H. *Angew. Chem. Int. Ed*., **2012**, 51, 12047

62. Chen, C., Fröhlich, R., Kehr, G., Erker, G. *Chem.Comm*., **2010**, 46, 3580

63. Chernichenko, K. K., Madarász, A., Pápai, I., Nieger, M., Leskelä, M., Repo, T. *Nat. Chem*., **2013**, 5, 718

64. Chernichenko, K. K., Nieger, M., Leskelä, M., Repo, T. *Dalton Trans*., **2012**, 41, 9029

65. Kirkham, J. D., Butlin, R. J., Harrity, J. P. A. *Angew. Chem. Int. Ed.,* **2012**, 51, 6402

Chapter 2: Synthesis and Characterisation of Borocations

2.1 Introduction

The synthesis of catechol ligated borocations often begins with the coordination of a Lewis base to boron, followed by either halide or hydride abstraction from the Lewis adduct of CatB-Cl or CatB-H, respectively. However, the coordination of Lewis bases to catecholborane can lead to complications, with Marder and co-workers reporting that adducts formed between CatBCl and tertiary phosphines are prone to redistribution, forming Cat_3B_2 and $Cl_3B.PR_3$.[1] It was proposed that an equilibrium existed between the CatBCl(L) adduct and the starting materials, resulting in the redistribution. By coordinating a Lewis base to boron, both of the oxygen atoms in catechol become more nucleophilic, due to the loss of π-character between boron and oxygen. Thus, the oxygen atoms present in the adduct are able to attack the boron of the free CatBCl, as shown below in Figure 2.1.

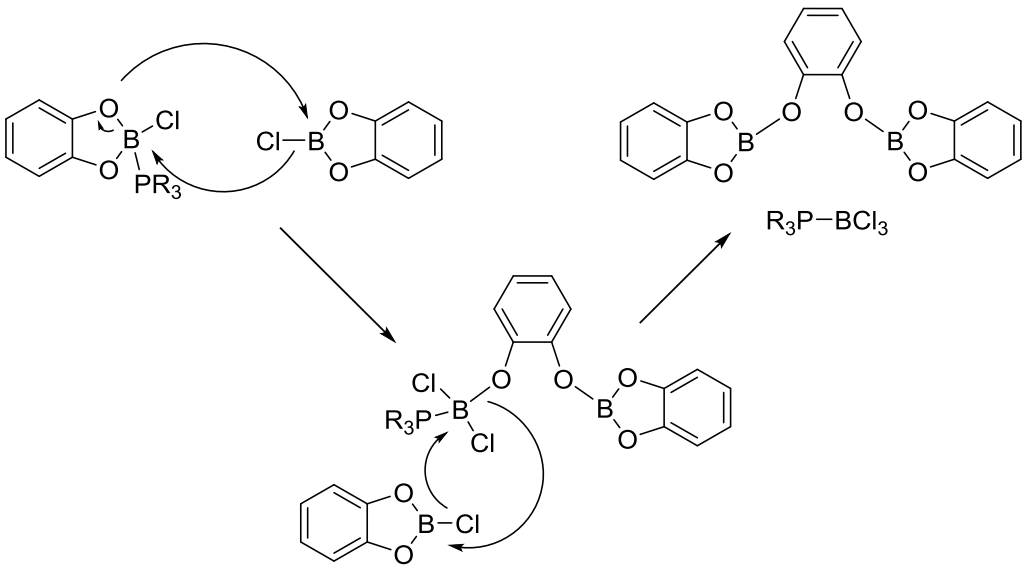


Figure 2.1: Proposed mechanism of formation of Cat_3B_2 and $R_3P.BCl_3$

The same report noted that certain amines, unlike tertiary phosphines, form stable adducts with CatBCl. Pyridine and triethylamine were both shown to form these adducts with no substituent redistribution. This is thought to be because of the stronger binding between amines and boron which shifts the equilibrium towards the adduct, precluding the unwanted redistribution reactivity by minimising the concentration of CatBCl.

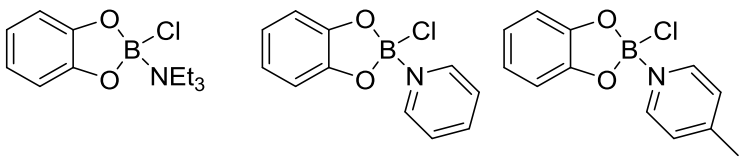


Figure 2.2: Examples of stable to ligand disproportionation CatBCl-amine adducts

It was shown that amine and phosphine ligated catechol boranes can be used as precursors for the generation of boreniums, particularly when the halide/hydride is abstracted rapidly after addition of the Lewis base (to minimise redistribution).[2] It was shown by Stephan *et al*. that catecholborane (CatB-H) can undergo B-H bond activation by a frustrated Lewis pair to form a cationic product.[3] Utilising the FLP, $B(C_6F_5)_3$ and $^tBu_3P$, wherein the phosphine, as the Lewis base, coordinates to the boron of CatBH, increasing the hydridic character of the B-H bond. This allows the BCF Lewis acid to abstract the hydride, resulting in the salt shown below in Figure 2.3. It was demonstrated that the cooperative effects of the acid and base are required for the B-H bond activation, as treatment of CatBH with only $^tBu_3P$ showed no adduct by NMR spectroscopy. Although the product can be viewed as a borenium, DFT studies suggested it was better described as a boryl-phosphonium cation.

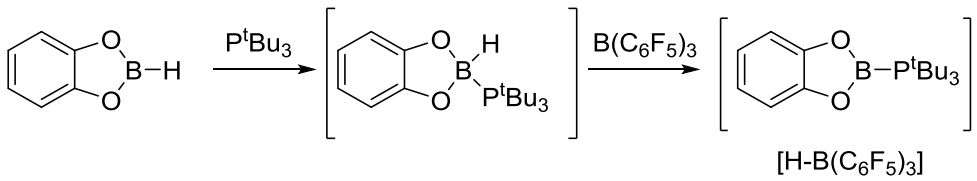


Figure 2.3: Proposed reaction pathway to borenium/ boryl-phosphonium cation

Figure 2.2: Examples of stable CatB-amine adducts

It has been shown that B-chlorocatechol borane (CatBCl) does not react with $AlCl_3$ by halide abstraction at room temperature, although there is some degree of O-$AlCl_3$ interaction (as prolonged heating leads to $\{Cat_y\text{-}Al\}_x$ species and BCl_3). However, the amine adducts CatBCl(L), when combined with one equivalent of $AlCl_3$, undergo a rapid reaction to form the borenium cation, shown below in Figure 2.4.[4]

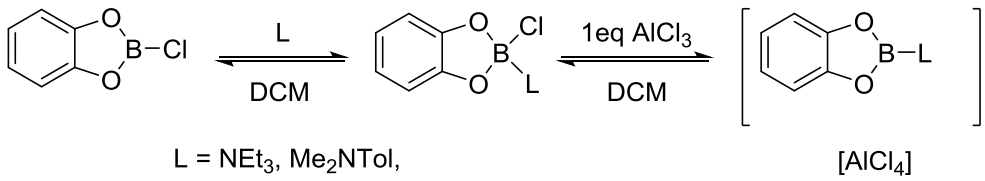


Figure 2.4: Synthesis of boreniums via CatBCl-amine adducts

The borocations of general formula [CatB(L)][$AlCl_4$] were subjected to spectroscopic and reactivity studies that showed the presence of an equilibrium between the borocation and the neutral adducts, along with equilibria between CatBCl, with $AlCl_3$-NEt_3, and the borocation.[5] The borenium cations are thus highly electrophilic, with Lewis acidity towards chloride approaching that of $AlCl_3$. This is important for its role in electrophilic aromatic substitution as a strong boron electrophile.

Two of the most common ways to generate boreniums involve forming an adduct with a neutral donor, whilst a halide/hydride is displaced by an appropriate abstracting agent. The examples already shown above represent the pathway where a neutral ligand is first added to boron, forming a neutral adduct, followed by halide/hydride abstraction to form a cationic boron species, of which several more examples are reported.[6-16] The other way is displacement of the halide/hydride by the neutral donor in the presence of an abstracting agent, such as AlX_3.[17-19]

More recently Vidovic *et al.* have synthesised catechol borocations via a number of routes, among them the exchange of halides for catechol in dihaloboreniums with loss of HCl.[20] This recent work in the synthesis of catechol boreniums proceeds via ligand substitution of N-heterocyclic carbene (NHC) coordinated boron dihalide cation.[21] Whereas prior methods mentioned earlier relied on either halide/hydride displacement or abstraction from boron by a neutral donor, this work focused on the ligand substitution of two halides for a catechol group. Using a variety of NHC-stabilised dichloro-boreniums, several catcholato-borenium products were isolated and examined via single crystal X-ray diffraction.

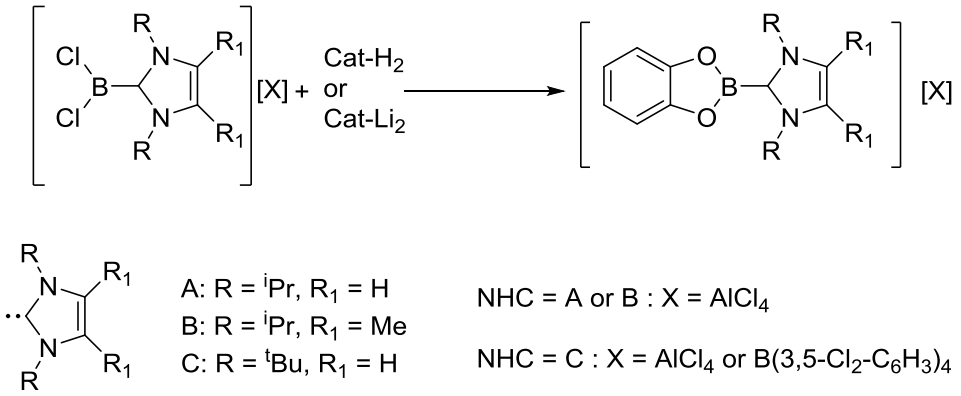


Figure 2.5: Synthesis of CatB boreniums via ligand exchange

The results of the analysis of the catechol boreniums suggested that the Lewis acidity at boron towards [$AlCl_4$] had increased with respect to the dichloro precursors. This is based on the distance between the boron and the nearest Cl of the counterion observed in the solid state, thus may be an artefact of packing effects as well. While the ligand exchange did not affect the NHC-B fragment of the structure in any notable way, it was observed that the distance between the boron centre and the counterions was reduced, again with respect to the precursors. In addition, the reaction involving the ^{t}Butyl-substituted NHC resulted in an observed shortening of the distance between the boron centre and the nearest methyl of the ^{t}Butyl-groups, again suggesting a reduction in electron density at boron following ligand substitution.

In addition to those mentioned above, many borocations that do not feature chelating ligands such as catechol have been synthesised. Dihalo-borenium cations were first observed by Ryschkewitsch *et al*. [22] An adduct of BCl_3 and 4-picoline was synthesised and treating this with aluminium trichloride, they obtained an equilibrium mixture containing the three coordinate borocation, as indicated by ^{11}B NMR spectroscopy.

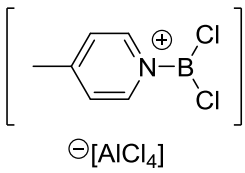


Figure 2.6: Ryschkewitsch's borenium observed by NMR spectroscopy

This borenium became a benchmark in the spectroscopic characterisation of borocations, and also set a precedent for the generation of borenium cations in the

presence of halophilic Lewis acids by B-X heterolysis. Since then this route has been used to access a wide range of dihaloborocations with halide abstractors including EX_3 Lewis acids and M[Anion] salts. Several recent examples use NHC-BX_3 adducts to generate NHC-BCl_2^+ boreniums. One such study showed that the cation-anion interaction between the boron and the $AlCl_4^-$ counterion was dependent on the steric encumbrance of the bound NHC, as observed by ^{11}B NMR spectroscopy and single crystal X-ray crystallography.[13] Another report showed that both dichloro- and dibromo-borenium cations could be synthesised, in this case stabilized by a four-membered NHC containing a P atom in its endocyclic backbone.[23]

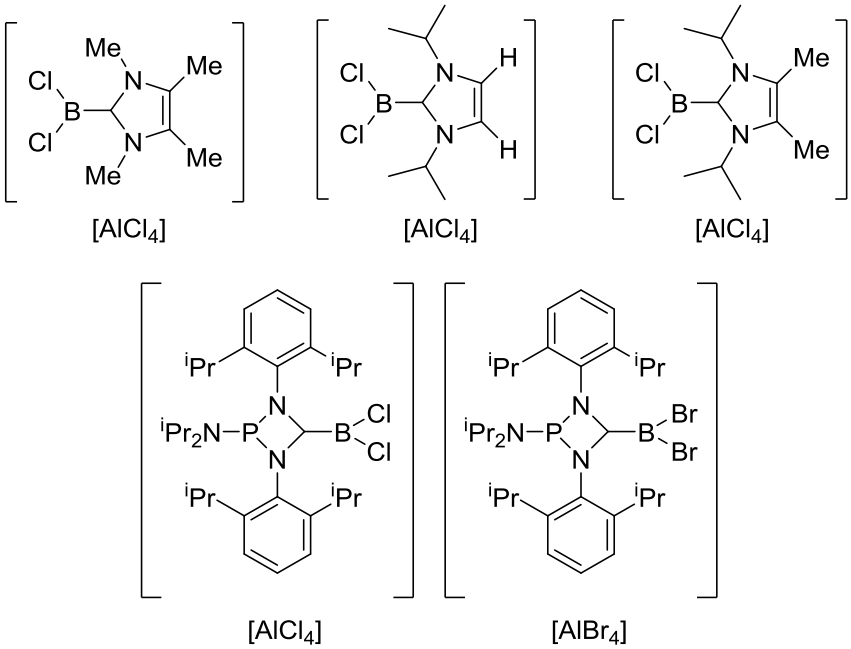


Figure 2.7: Examples of borenium cations

This approach, involving the binding of a neutral ligand, such as an amine, followed by halide abstraction with $AlCl_3$, is the general method used to access borocations in this thesis. The synthesis of all borocations relevant to the project is discussed herein.

2.2 Synthesis of Catechol Ligated Borocations

In order to investigate dehydroboration reactions of terminal alkynes, catechol ligated borocations were targeted for synthesis. While early attempts to generate borocations by halide abstraction from CatBCl with $AlCl_3$ failed, it was found that forming an adduct of boron with an amine will allow halide abstraction on addition of MX_3.[4] This can be explained by the coordination of a Lewis base to boron labilising the B-X bond and stabilising the resultant borocation, making halide abstraction thermodynamically favoured. Thus, $[CatBNEt_3][AlCl_4]$ (**2i**) was synthesised by successive addition of one equivalent of NEt_3 and $AlCl_3$ as shown below in Figure 2.8, following the established reported synthesis.[3]

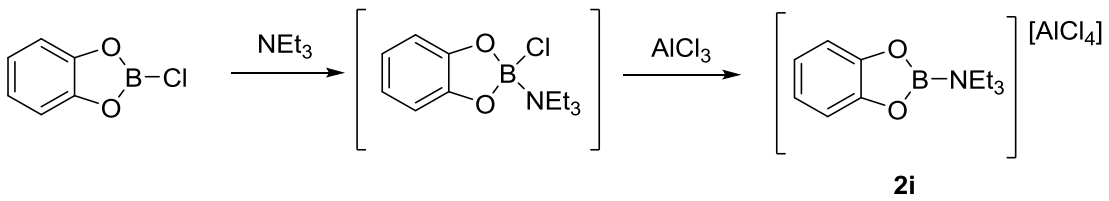


Figure 2.8: Synthesis of $[CatB(NEt_3)][AlCl_4]$

To this, it is possible to add a moderately bulky Lewis base, in this case triphenylphosphine, with no reaction observed. Hence, $[CatBNEt_3][AlCl_4].PPh_3$ can be considered a frustrated Lewis pair, disfavoured from Lewis adduct formation due to the steric bulk surrounding the Lewis acid and the Lewis base. In contrast, when more nucleophilic bases are added to **2i** it is observed that CatBCl(amine) and amine-$AlCl_3$ are generated.[4]

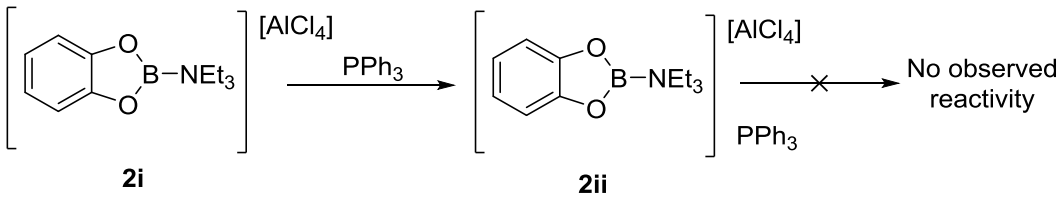


Figure 2.9: Formation of $[CatB(NEt_3)][AlCl_4].PPh_3$ FLP

A novel catechol ligated borenium was synthesised with 2-N,N-dimethylaminopyridine (2DMAP). CatBCl was combined with 2DMAP in DCM (Figure 2.10), and from ^{11}B NMR spectroscopy it was determined that a 4-coordinate boron species had been formed, with a resonance at 9.7 ppm observed. It was surmised that the two molecules had formed an amine-borane adduct, observed as the only product. Subsequent addition of equimolar $AlCl_3$ generated the borocation species via halide abstraction. Thus [CatB(2DMAP)][$AlCl_4$] (**2iii**) was successfully crystallised and its structure studied using X-ray crystallography, as shown in Figure 2.11, which revealed it is three coordinate at boron and thus a borenium ion. This is consistent with the ^{11}B NMR spectrum of **2iii** which shows a single resonance at 25.3 ppm observed in DCM solutions.

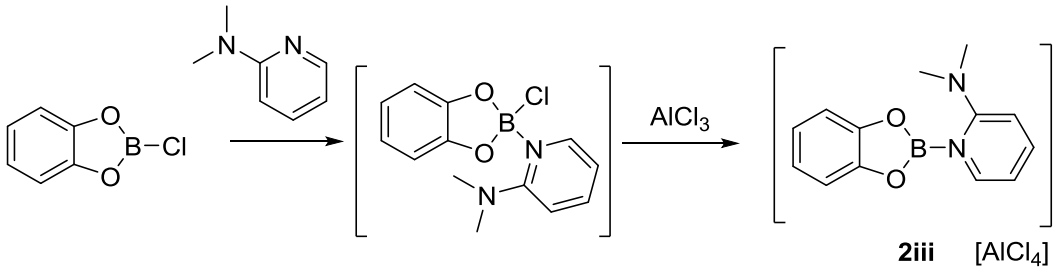


Figure 2.10: Synthesis of [CatB(2DMAP)][$AlCl_4$] (**2iii**)

Table 2.1	
Metric	**(2iii)**
B1-N1	1.472(5) Å
B1-O1	1.373(4) Å
B1-O2	1.383(4) Å
N1-C1	1.387(4) Å
N1-C5	1.386(4) Å
N2-C5	1.340(4) Å
N2-C6	1.473(4) Å
N2-C7	1.464(4) Å
O1-B1-O2	114.4(3)˚
O1-B1-N1	122.1(3)˚
O2-B1-N1	123.5(3)˚
C1-N1-C5	120.0(3)˚
N1-C5-N2	119.5(3)˚
O1-B1-N1-C5	45.3(5)˚

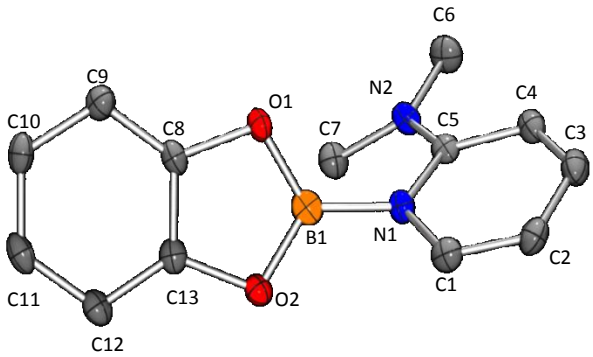


Figure 2.11: Structure and bond metrics of **2iii** (Thermal ellipsoids at 50% probability, anion and hydrogens omitted for clarity. Full crystal data and structure refinements listed in Appendix)

From the solid state structure, it can be seen that the B-N bond is slightly shorter than that of comparable amine ligated boreniums (e.g., 1.472(5) Å in **2iii** compared to 1.505(3) Å ($[Cl_4CatB(NEt_3)][AlCl_4]$)[21]); this is due to resonance from the NMe_2 side arm. Whilst the -NMe_2 is not perfectly coplanar to the aromatic ring, as the torsion angle C4-C5-N2-C6 is 7.25˚, whereas the N1-C5-N2-C7 torsion angle is 18.81˚, this conformation still allows stabilisation through resonance, as shown in Figure 2.9. The distortion on the NMe_2 side arm is probably due to the C7 atoms close proximity to the boron (2.752 Å), as such C7 is bent away from the plane of

the ring. Through this resonance, the B-N bond has some double bond character, which would actually serve to lower the Lewis acidity of the boron complex.

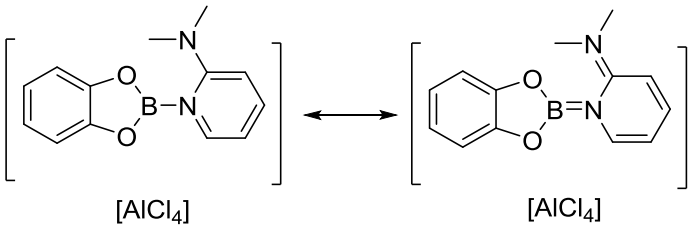


Figure 2.12: Resonance forms of [CatB(2DMAP)][$AlCl_4$]

However, it is also of note that the pyridine ring and the catechol ring are not coplanar, due to the presence of the side arm. The torsion angle of O1-B1-N1-C5 was observed as 45.3(5)˚, which lowers the degree of π bonding in a B=N bond due to the CatB and 2DMAP components not being co-planar, preventing optimal orbital overlap. So although the electrophilicity of boron has been lowered somewhat by the B=N character, the increase of local base concentration provided by the proximal NMe_2 group may be beneficial for deprotonation steps. The distance between the boron atom and the closest aluminium-bound chloride is 3.991 Å, which is long and consistent with ionic species.

2.3 Synthesis of Dihalo-borocations

Following the synthesis of [CatB(2DMAP)][$AlCl_4$], more electrophilic borocations were targeted. Hence the bidentate catechol ligand was replaced by halides, targeting an increase in the Lewis acidity at boron. The first of these species synthesised, [Cl_2B(2DMAP)][$AlCl_4$] (**2iv**) was successfully synthesised in high yield (Figure 2.13). The X-ray crystal structure was determined (single crystals suitable for X-ray diffraction were grown by Dr. S. A. Solomon), and it was found that the NMe_2 side arm had bound to boron, forming a highly strained 4-membered ring. This shows that the boron is more electrophilic than in the catechol analogue, being able to bind the side arm in spite of the distortion in the boracycle. This presented a problem, however; with boron bound to both nitrogen atoms, and now 4-coordinate, the electrophilicity is reduced considerably. It was also observable by solution ^{11}B NMR spectroscopy that the borocation was 4-coordinate, with a single resonance observed at 12.2 ppm.

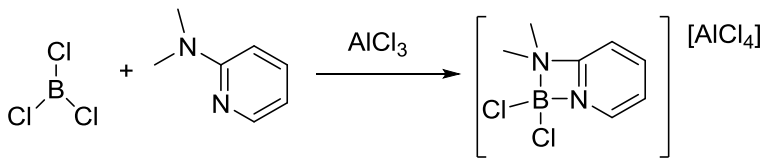


Figure 2.13: Synthesis of [BCl_2 (2DMAP)][$AlCl_4$] (**2iv**)

In order to study this compound further, DFT studies were carried out by Dr Ewan Clark at the M06-2X/6-311G(2d,2p) level. It was shown that the barrier to ring opening was low at 12.6 kcal mol^{-1}, with the ring opened form only 12.3 kcal mol^{-1} higher in energy, and so would easily ring open into the reactive borocation FLP at room temperature. This was shown to be the case as it reacted with Lewis bases

rapidly without the need for heating. However, currently we have not distinguished between S_N2 and S_N1 mechanisms for this reaction.

Table 2.2	
Metric	**(2iv)**
B1-N1	1.567(4) Å
B1-N2	1.697(4) Å
N2-C6	1.500(3) Å
N2-C7	1.496(3) Å
N1-C5	1.337(3) Å
N1-B1-N2	81.75(18)˚
N1-C5-N2	99.1(2)˚

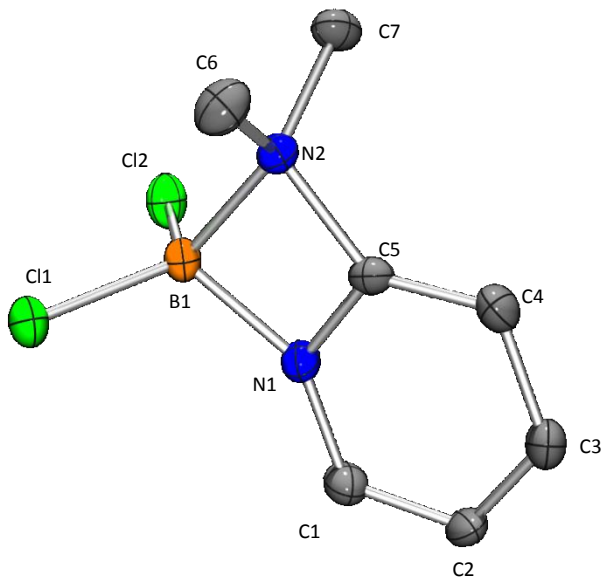


Figure 2.14: Structure and bond metrics of **2iv** (Thermal ellipsoids at 50% probability, anion and hydrogens omitted for clarity. Full crystal data and structure refinements listed in Appendix)

The X-ray crystal structure shown in Figure 2.14 demonstrates the strained ring, with the C4-C5-N2 bond angle of 136.6˚. In comparison to the structure of [CatB(2DMAP)][$AlCl_4$], The N2-C5 bond length in [Cl_2B(2DMAP)][$AlCl_4$] is longer by over 0.1 Å. This is due to the absence of resonance from the N-Me_2 side arm, as the nitrogen is now bound to boron, no N=C bond character can form. As such, a comparable resonance from to that of [CatB(2DMAP)][$AlCl_4$] shown in Figure 2.9 cannot exist, so B-N double bond characteristic is also not present. As the NMe_2 is now bound to boron in the solid state, this serves to lower the Lewis acidity at

boron. The ring itself is also distorted, with the B1-N2 bond noticeably longer that the N1-C5 bond.

As part of a previous investigation, **2iv** was combined with PPh_3 by Dr Ewan Clark, the results of which are relevant to this report in order to compare reactivity of PPh_3 with previously synthesised amine-ligated borocations. As such, the reaction was carried out and NMR spectra obtained immediately. The ^{27}Al NMR spectrum retained a single sharp peak at 103.2 ppm, indicating that the anion $[AlCl_4]$ remains the major ^{27}Al containing species in solution, and thus that halide transfer from aluminium to boron had not occurred. The ^{11}B NMR spectrum showed some residual $[Cl_2B(2DMAP)][AlCl_4]$ at 12.1 ppm, and two new signals which featured B-P coupling. The minor signal at 3.24 ppm ($^1J_{B\text{-}P}$ = 155.3 Hz) was the $Cl_3B\text{-}PPh_3$ adduct, whilst the major signal at 3.85ppm ($^1J_{B\text{-}P}$ = 153.1 Hz) was attributed to the boronium species $[(2DMAP)BCl_2(PPh_3)][AlCl_4]$, as shown below in Figure 2.12. After standing overnight, the neutral adduct $Cl_3B\text{-}PPh_3$ was the only B-P containing species in solution. The neutral adduct and borenium signals are found at -1.68 ppm and 1.48 ppm respectively in the $^{31}P\{^1H\}$ NMR.

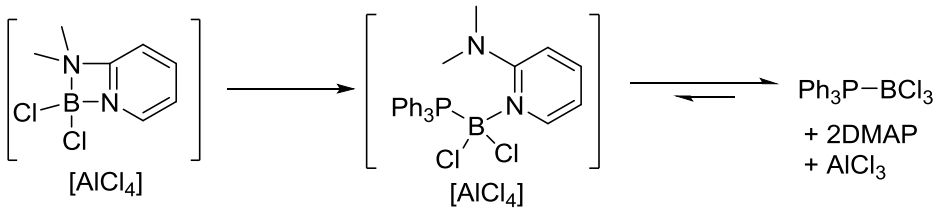


Figure 2.15: Reaction of $[Cl_2B(2DMAP)][AlCl_4]$ with PPh_3

The disparate reactivity observed between $[Cl_2B(2DMAP)][AlCl_4]$ and $[CatB(NEt_3)][AlCl_4]$ with PPh_3 can be attributed to steric and electronic effects. The

replacement of the catechol with two chlorides has served to increase the Lewis acidity at boron. Combined with the knowledge that the 4-membered ring has a low barrier to ring open to produce a highly electrophilic borenium, it is not surprising that **2iv** reacts rapidly with PPh_3, whereas the greater steric bulk and lower Lewis acidity of the catechol borenium precludes PPh_3 coordination. Therefore, both borocations can be thought of as FLPs, with $[CatB(NEt_3)][AlCl_4]$ / PPh_3 representing an intermolecular FLP, and $[BCl_2(2DMAP)][AlCl_4]$, in its ring opened form, an intramolecular FLP. Both are utilised in various reactions in the following chapters.

With **2iv** successfully synthesised and its structure and nature elucidated, a second 2DMAP ligated borocation was prepared. The bromo-analogue of $[Cl_2B(2DMAP)][AlCl_4]$ was synthesised from BBr_3 (2 equivalents) and 2DMAP to generate $[Br_2B(2DMAP)][BBr_4]$ (**2v**) (Figure 2.16). The counter ion was changed to a bromine containing species to prevent halide scrambling (which occurs if $AlCl_3$ is used with BBr_3/2DMAP). Borocation **2v** was synthesised to represent a more electrophilic version of $[Cl_2B(2DMAP)][AlCl_4]$, as it was theorised that if the former borocation is not electrophilic enough to react with the target alkynes, then replacing the chlorides on boron for bromides would lower the π overlap between boron and the halide in the ring opened FLP form. Thus, the increased electrophilicity at boron and the weakened B-X bond should also promote reactivity with alkynes. The extremely low solubility of **2v** frustrated full characterisation.

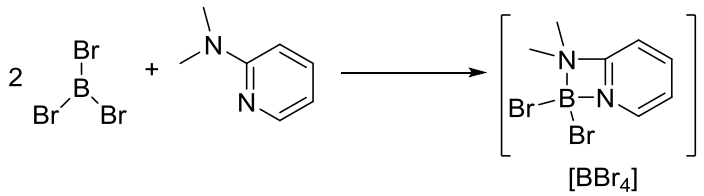


Figure 2.16: Synthesis of $[Br_2B(2DMAP)][BBr_4]$ (**2v**)

Another dihalo-borocation synthesised was the 2,6-lutidine-bound $[LutBCl_2][AlCl_4]$ (**2vi**) following the previously reported procedure where the lutidine-BCl_3 adduct which was first generated by stoichiometric addition of 2,6-lutidine to BCl_3.[5] To generate the borenium, equimolar $AlCl_3$ was added *in-situ*, and the generation of the borocation confirmed by NMR spectroscopy, with a resonance at δ^{11}B 45.4 ppm. This borenium was used extensively in haloboration reactions, documented in Chapter 4.

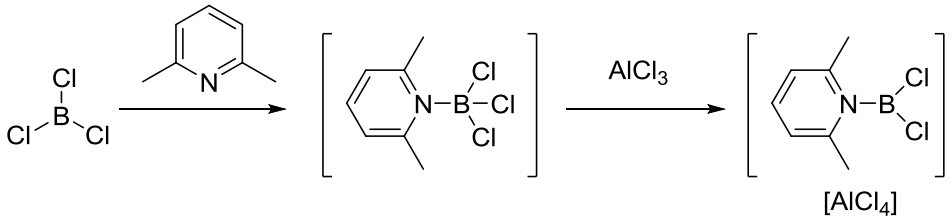


Figure 2.17: Synthesis of $[LutBCl_2][AlCl_4]$ (**2vi**)

2.4 Synthesis of aryl-substituted borocations

Following the synthesis of the dihalo-borocations, several aryl-substituted monohalo-boroniums were synthesised. The first was synthesised in a similar way to $[Cl_2B(2DMAP)][AlCl_4]$ using BCl_2Ph, 2DMAP and $AlCl_3$ so as to incorporate a phenyl ring, the synthesis of which is shown below in Figure 2.18. Successful crystallisation of $[PhClB(2DMAP)][AlCl_4]$ (**2vii**) allowed its structure to be confirmed by single crystal X-ray crystallography, as shown in Figure 2.19.

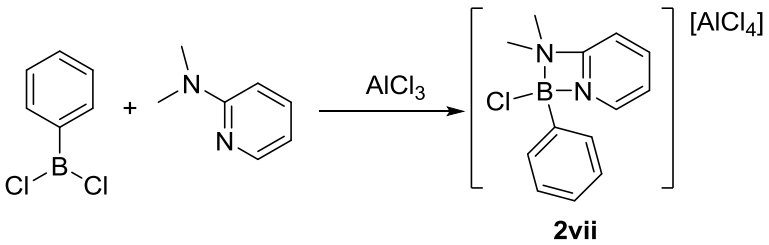


Figure 2.18: Synthesis of [PhBCl (2DMAP)][$AlCl_4$] (**2vii**)

Table 2.3	
Metric	**(2vii)**
B1-N1	1.588(2) Å
B1-N2	1.726(2) Å
B1-Cl1	1.8108(19) Å
B1-C8	1.572(2) Å
N2-C6	1.498(2) Å
N2-C7	1.495(2) Å
N1-C5	1.337(2) Å
N1-B1-N2	80.56(11)˚
N1-C5-N2	100.37(14)˚

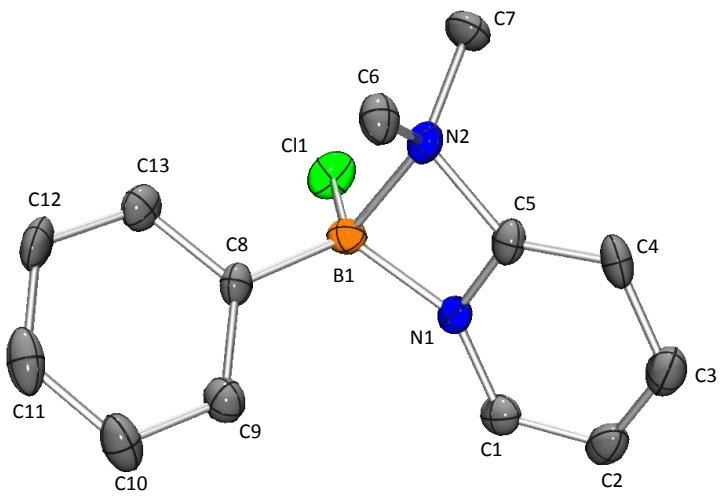


Figure 2.19: Structure and bond metrics of **2vii** (Thermal ellipsoids at 50% probability, anion and hydrogens omitted for clarity. Full crystal data and structure refinements listed in Appendix)

The structure is very similar to $[Cl_2B(2DMAP)][AlCl_4]$, a 4-membered boracycle is once again formed containing high levels of ring strain. Both B-N bond lengths in each borocation (dichloro- and chloro-phenyl boronium) are closely comparable to each other, suggesting similar strain in the 4-membered rings. It was assumed these properties would again allow rapid reaction with nucleophiles with via a S_N2 mechanism or by boracycle ring opening, generating a highly reactive borenium FLP. The 4-coordinate nature of boron was again shown to persist in solution by ^{11}B NMR spectroscopy (16.4 ppm).

Whilst $[PhClB(2DMAP)][AlCl_4]$ was synthesised from $PhBCl_2$, a commercially available product, in order to utilise other arene and heteroarene groups, the new borocations would have to be made from borylated arenes of the form $arylBCl_2$ preferably. Following borylation to form $arylBCl_2$, base coordination and halide abstraction was used to generate novel aryl-substituted borocations. To begin, a range of borylated arenes was required, featuring dichloro-borane groups to allow boronium formation via base association and halide abstraction. It was found that 2-methylfuran could be borylated by the borocation $[Cl_2B(2DMAP)][AlCl_4]$ in an equimolar reaction that was extremely rapid; ^{11}B NMR spectroscopy confirmed the production of a 3-coordinate $arylBCl_2$ boron species nearly instantaneously ($\delta^{11}B$ = 43.9 ppm). This reactivity was then extended to thiophenes; both 2-methyl- and 2-hexylthiophene were fully borylated within 18 hours (room temperature) or under 1 hour (60°C) forming the thienyl-BCl_2 products, as monitored by multinuclear NMR spectroscopy. The variance in reaction times can be attributed to the difference in nucleophilicity between the heteroarenes. One further heteroarene was borylated

in this process, 1-methylindole, which was borylated at the 3-position as expected for an electrophilic aromatic substitution reaction.

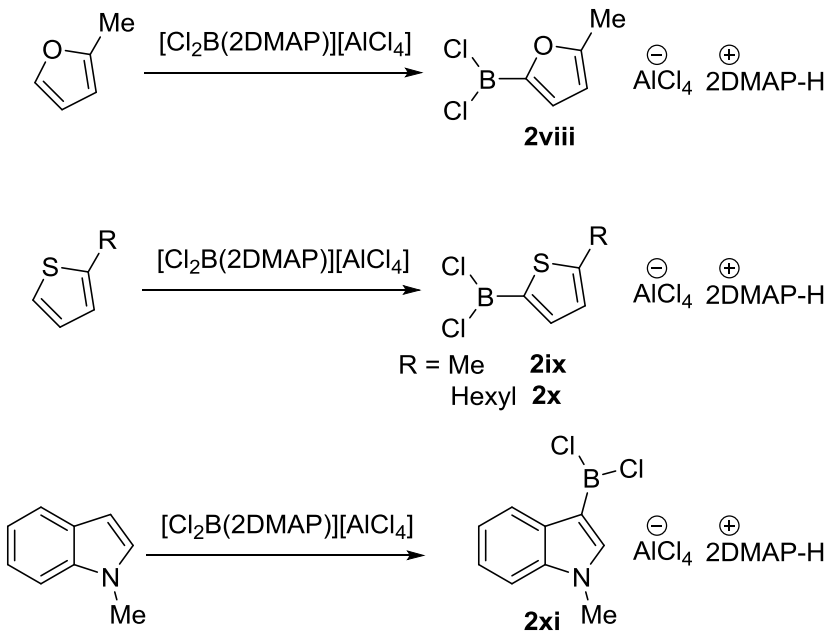


Figure 2.20: Synthesis of borylated heteroarenes (**2viii**)-(**2xi**)

In addition to these, other borylated arenes were generated by different methods, briefly described herein. Triphenylamine was monoborylated at the para-position of one of the phenyl rings using [LutBCl$_2$][AlCl$_4$]. Both benzene and chlorobenzene were borylated by using BCl$_3$-DMT and 2.1 equivalents of AlCl$_3$. These latter two reactions required temperatures of 100°C in order to achieve borylation.[24]

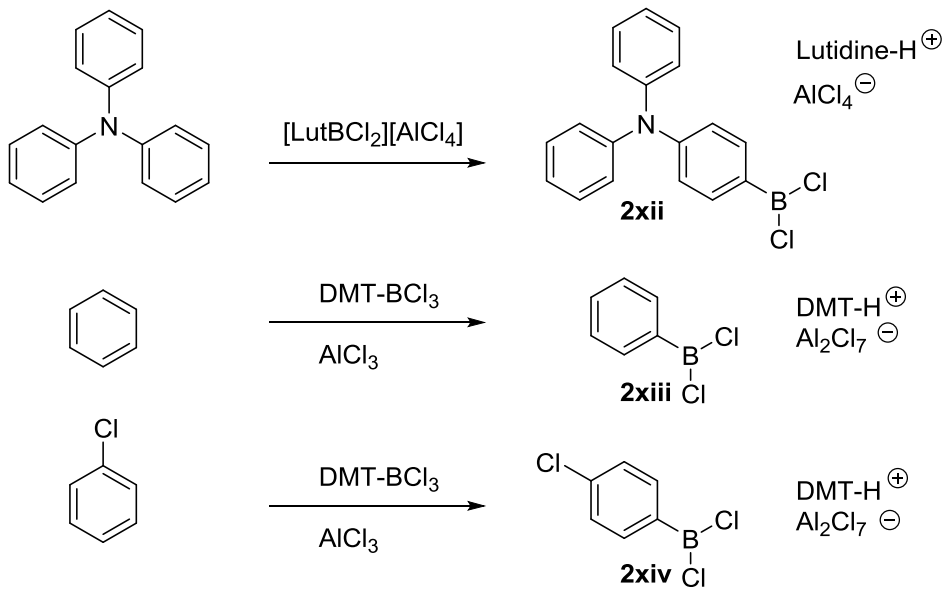


Figure 2.21: Synthesis of borylated arenes (**2xii**)-(**2xiv**)

The formation of each dihaloarylborane species was observed by multinuclear NMR spectroscopy, with protonated base present in the ^{1}H spectra and the borylation confirmed by the ^{11}B spectra. In each case the borylated species was reacted on *in-situ* with other reagents, the chemistry of which is covered in-depth in Chapter 5, wherein the carboboration of alkynes is documented. In addition to this, select borylated heteroarenes were converted into boronium salts similar to [PhClB(2DMAP)][$AlCl_4$]. This was achieved by the subsequent addition of one equivalent of 2DMAP and $AlCl_3$, generating a boronium species featuring different heteroaryl substituents, such as 2-methylthiophene (Figure 2.22, below).

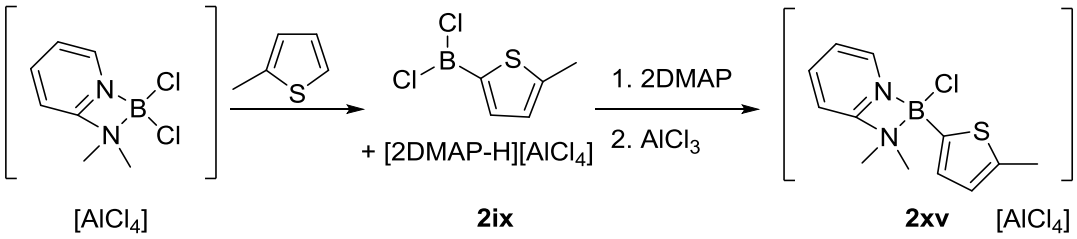
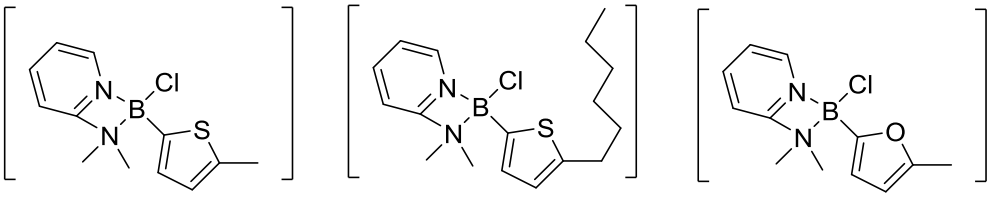


Figure 2.22: Borylation of 2-methylthiophene and subsequent formation of boronium (**2xv**)



2xv [$AlCl_4$] **2xvi** [$AlCl_4$] **2xvii** [$AlCl_4$]

Figure 2.23: Structures of boroniums (**2xv**) – (**2xvii**)

As mentioned, the aryl-BCl_2 products were difficult to isolate, so these borocations were synthesised in a 'one-pot' process without removal of by-products. Additionally, once synthesised, borocations **2xv** – **2xvii** also proved difficult to isolate as analytically pure material from the other ionic species present in the reaction mixtures. As such, isolated yields and clean NMR spectra were not obtained, and the borocations were further reacted in a 'one-pot' fashion with alkynes, the results of which are discussed in Chapter 5.

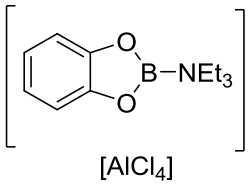
The borocations synthesised in this chapter proved to be useful in a wide range of reactions. Predominantly, they were reacted with various alkynes and, where necessary, the primary products were esterified by addition of pinacol/Et_3N to produce synthetically useful, and significantly more stable to ambient conditions, vinyl pinacol boronate esters. The main reactivity types observed were de-elementoboration, haloboration and carboboration, which are discussed in detail in chapters 3, 4 and 5, respectively.

2.5: Experimental

General Considerations

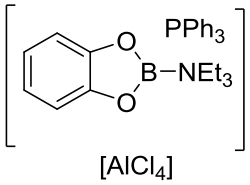
All manipulations of air and moisture sensitive species were performed under an atmosphere of argon or nitrogen using standard Schlenk and glovebox techniques. Glassware was dried in a hot oven overnight and heated before use. Hexane, *ortho* -dichlorobenzene, d_1-chloroform, d_2-dichloromethane, 2,6-lutidine, Et_3N and were 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. All solvents were degassed and stored over molecular sieves (3 Å) under an 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; 104.3 MHz ^{27}Al; 79.5 MHz ^{29}Si; 162 MHz ^{31}P). ^{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 $BF_3{:}Et_2O$, ^{19}F to Cl_3CF, ^{27}Al to $Al(NO_3)_2$ in D_2O ($Al(D_2O)_6^{3+}$), ^{29}Si to TMS, and ^{31}P to H_3PO_4. Resonances for the carbon directly bonded to boron are not observed in the $^{13}C\{^{1}H\}$ NMR spectra. Elemental analysis of air sensitive compounds were performed by London Metropolitan University service.

(**2i**) - [CatB(NEt_3)][$AlCl_4$]



Chlorocatecholborane (50 mg, 0.3 mmol) was added to a solution of triethylamine (0.45 µl, 0.3 mmol) in DCM (0.8 ml) in a J. Youngs NMR tube, generating a yellow solution. To this, $AlCl_3$ (43 mg, 0.3 mmol) was added and NMR spectroscopy used to confirm borenium formation. The borocation was then reacted with substrates *in situ*. This synthesis has been previously reported.[6]

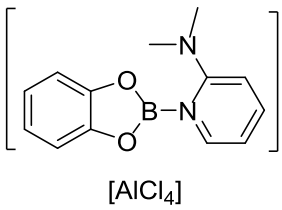
(**2ii**) - [CatB(NEt_3)][$AlCl_4$].PPh_3



To a solution of **2i**, equimolar triphenylphosphine (85 mg, 0.3 mmol) was added. NMR spectroscopy showed no reaction between the borocation and the PPh_3, and the FLP **2ii** was further reacted *in situ*.

^{1}H NMR (400 MHz, CH_2Cl_2): δ 7.50 – 7.47 (m, 2H), 7.40 – 7.33 (m, 17H), 3.73 (q, 6H), 1.43 (t, 9H); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 27.8 (s); **^{27}Al NMR** (104 MHz, CH_2Cl_2): δ 104.0 (s); **^{31}P{^{1}H} NMR** (162 MHz, CH_2Cl_2): δ -6.7 ppm.

(**2iii**) - [CatB(2DMAP)][$AlCl_4$]



2DMAP (0.13 ml, 1 mmol) was added to a solution of chlorocatecholborane (154 mg, 1 mmol) in DCM (2 ml) in a Schlenk, generating a yellow solution. The solvent was removed *in vacuo*, and $AlCl_3$ (133 mg, 1 mmol) was added. The solid mixture was dissolved in *o*DCB (3 ml) and stirred until dissolution occurred to give a bright yellow solution. The mixture was layered with ^{n}hexane and crystals grown over 5

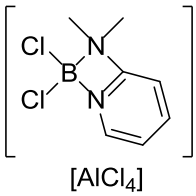
days. The crystals were isolated by filtration, washed with *o*DCB (3 ml) and ^{n}hexane (2x5 ml) and dried in vacuo to give **2iii** as yellow plates (218 mg, 0.53 mmol, 53%)

^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.15 (d, 1H), 8.02 (t, 1H), 7.45 – 7.43 (m, 2H), 7.31 – 7.29 (m, 3H), 7.09 (t, 1H), 3.35 (s, 6H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 159.38, 147.08, 145.87, 139.10, 125.32, 116.26, 115.18, 114.07, 43.51 ppm; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 25.3 (s); **^{27}Al NMR** (104 MHz, CD_2Cl_2): δ 103.4 (s) ppm.

Elemental Analysis

Calculated: C 38.10; H 3.44; N 6.83. Observed: C 38.14; H 3.44; N 6.75.

(**2iv**) - $[Cl_2B(2DMAP][AlCl_4]$



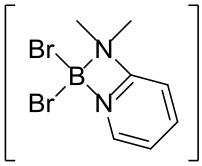
To a 1M solution of BCl_3 (10 ml, 10 mmol) in anhydrous CH_2Cl_2, 2-dimethylaminopyridine (1.24 ml, 10 mmol) was added and then aluminium trichloride (1.33 g, 10 mmol) was added. A solid precipitated out of solution, and the solvent was removed under reduced pressure, leaving a white solid. This was washed with CH_2Cl_2 (10 ml, ×3) and **2iv** was isolated as a white powder (3.03 g, 8.12 mmol, 81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88 (td, 1H, ^{3}J(H,H) = 8.2, ^{3}J(H,H) = 1.5), 8.67 (d, 1H, ^{3}J(H,H) = 5.3), 8.43 (d, 1H, ^{3}J(H,H) = 8.6), 8.24 (dd, 1H, ^{3}J(H,H) = 7.8, ^{3}J(H,H) =5.8), 3.48 (s, 6H, NMe_2) ppm; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 12.22 (s) ppm. **^{27}Al NMR** (104 MHz, $CDCl_3$): δ 103.45 (s) ppm.

Elemental Analysis

Calculated: C 22.71; H 2.72; N 7.57. Observed: C 22.64; H 2.89; N 7.56.

(**2v**) - $[Br_2B(2DMAP)][BBr_4]$



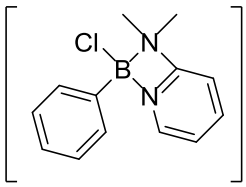
$[BBr_4]$

BBr_3 (1.0M solution in heptanes, 0.2 ml, 0.2 mmol) was added to 2DMAP (24 µl, 0.194 mmol) dissolved in DCM (5 ml), producing a colourless precipitate. The solvent was removed *in vacuo* and the resulting power redissolved in DCM (5 ml) and this solution then frozen by immersion in N_2(l). Additional BBr_3 solution (0.2ml as before) was layered upon the frozen reaction mixture, which was then sealed and allowed to slowly attain room temperature. This slow diffusion-limited reactivity grew crystals yielding **2v** as colourless blocks (60 mg, 0.096 mmol, 51%). The resulting crystals were insoluble in common chlorinated solvents and no NMR data is available.

Elemental Analysis

Calculated: C 13.490; H 1.617; N 4.494. Observed: C 13.63; H 1.72; N 4.61.

(**2vii**) - $[PhClB(2DMAP)][AlCl_4]$



$[AlCl_4]$

To a solution of $PhBCl_2$ (0.83 ml, 6.33 mmol) in anhydrous CH_2Cl_2, 2-dimethylaminopyridine (79 ml, 6.33 mmol) was added. NMR spectroscopy was used to confirm the reaction, to which aluminium trichloride (0.84 g, 6.33 mmol) was added. A solid precipitated out of solution, and the solvent was removed under reduced pressure, leaving a white solid. This was washed with CH_2Cl_2 (10 ml, x3) and **2vii** was isolated as a white powder (2.02 g, 4.89 mmol, 77%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.84 (td, 1H, ^3J(H,H) =8.2, ^3J(H,H) = 1.5), 8.62 (d, 1H, ^3J(H,H) =5.3), 8.32 (d, 1H, ^3J(H,H) =8.6), 8.21 (dd, 1H, ^3J(H,H) =7.8, ^3J(H,H) =5.8), 7.46-7.36 (m, 3H), 7.24 (d, 2H, ^3J(H,H) =6.8), 3.08 (s, 6H) ppm; **^{13}C NMR** (100.6 MHz,

CD_2Cl_2): δ 155.03, 149.69, 140.59, 131.22, 130.22, 129.24, 127.78, 118.17, 46.88 ppm; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 16.36 (s); **^{27}Al NMR** (104 MHz, CD_2Cl_2): δ 103.35 (s) ppm.

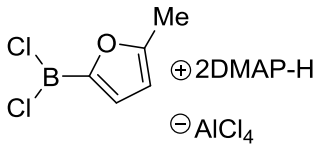
Elemental Analysis

Calculated: C 37.68; H 3.65; N 6.76. Observed: C 37.56; H 3.72; N 6.76.

Borylation of heteroarenes using [Cl_2B(2DMAP)][$AlCl_4$]

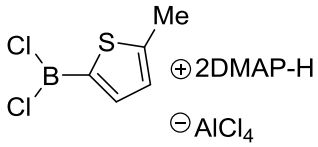
To a suspension of [Cl_2B(2DMAP)][$AlCl_4$] (50 mg, 0.14 mmol) in anhydrous CH_2Cl_2 in a J.Young's NMR tube, equimolar heteroarene was added. NMR spectroscopy was used to confirm borylation, and products were utilised in further reactions without purification or isolation. (Protonated amine[$AlCl_4$] resonances by-products have been omitted).

(**2viii**) – Cl_2B-2-methylfuran



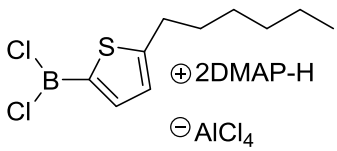
^{1}H NMR (400 MHz, CH_2Cl_2): δ 7.53 (d, 1H, ^{3}J(H,H) = 3.5 Hz), 6.26 (d, 1H, ^{3}J(H,H) = 3.5 Hz), 2.41 (s, 3H); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 43.9 (s);

(**2ix**) – Cl_2B-2-methylthiophene



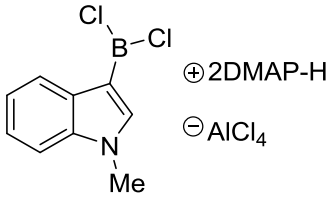
^{1}H NMR (400 MHz, CH_2Cl_2): δ 7.83 (d, 1H, ^{3}J(H,H) = 3.5 Hz), 6.99 (d, 1H, ^{3}J(H,H) = 3.5 Hz), 2.58 (s, 3H); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 47.1 (s);

(**2x**) – Cl_2B-2-hexylthiophene



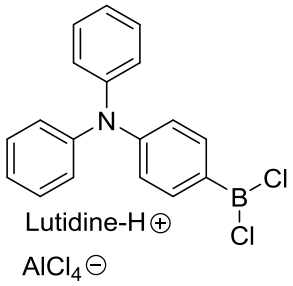
^{1}H NMR (400 MHz, CH_2Cl_2): δ 7.85 (d, 1H, ^3J(H,H) = 3.7 Hz), 7.02 (d, 1H, ^3J(H,H) = 3.7 Hz), 2.89 (t, 2H, ^3J(H,H) = 7.6 Hz), 1.74-1.66 (m, 2H), 1.31-1.29 (m, 5H), 0.89-0.86 (m, 4H); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 47.2 (s);

(**2xi**) – Cl_2B-N-methylindole



^{1}H NMR (400 MHz, CH_2Cl_2): δ 8.22 (d, 1H, ^3J(H,H) = 7.5 Hz), 7.93 (t, 1H, ^3J(H,H) = 7.5 Hz), 7.40 (d, 1H, ^3J(H,H) = 7.5 Hz), 7.35-7.27 (m, 2H), 3.84 (s, 3H); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 47.1 (s);

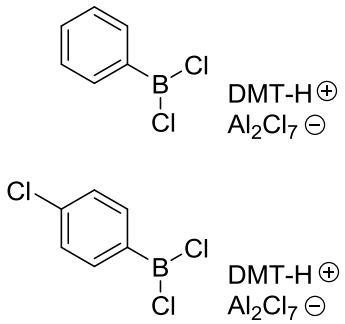
(**2xii**) – Cl_2B-C_6H_4-NPh_2



$LutBCl_3$ (50 mg, 0.22 mmol) was suspended in anhydrous *o*-CH_2Cl_2 in a J.Young's NMR tube, to which $AlCl_3$ (30 mg, 0.22 mmol) was added, causing dissolution to a clear yellow solution. To this [$LutBCl_2$][$AlCl_4$], triphenylamine (55 mg, 0.22 mmol) was added, turning first green, then to yellow. The reaction mixture was then stirred at room temperature for 2 hours, turning dark brown, and NMR spectroscopy confirmed reaction completion.

^{1}H NMR (400 MHz, CH_2Cl_2): δ 7.64 (m, 3H), 7.36 (m, 4H), 7.20 (m, 5H), 6.91 (d, 2H, ^3J(H,H) = 8.3 Hz); **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 51.4 (s);

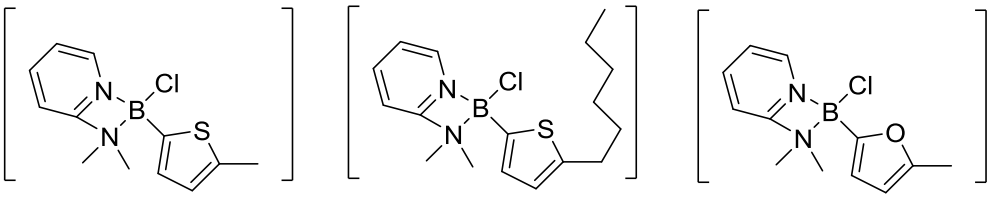
(**2xiii**) – Cl_2BPh and (**2xiv**) – $Cl_2B\text{-}C_6H_4\text{-}Cl$



For the borylation of these two arenes, an existing method was used. NMR matched those reported previously.[7]

Heteroarene boronium synthesis

To the solution of borylated heteroarene previously synthesised (also containing the protonated amine[AlCl4] salt), sequential addition of equimolar 2DMAP and $AlCl_3$ afforded the boronium analogue, as confirmed by NMR spectroscopy. These species proved difficult to isolate and purify from ammonium by-products, and as such were reacted without purification.



2xv [$AlCl_4$] **2xvi** [$AlCl_4$] **2xvii** [$AlCl_4$]

2.6: References

1. Coapes, R. B., Souza, F.E.S., Fox, M. A., Batsanov, A. S., Goeta, A. E., Yufit, D. S., Leech, M. A., Howard, J. A. K., Scott, A. J., Clegg, W., Marder, T. B. *J. Chem. Soc., Dalton Trans*., **2001**, 1201
2. Bagutski, V., Del Grosso, A., Ayuso Carrillo, J., Cade, I. A., Helm, M. D., Lawson, J. R., Singleton, P. J., Solomon, S. A., Marcelli, T., Ingleson, M. J. *J. Am. Chem. Soc.,* **2013**, 135, 474
3. Dureen, M. A., Lough, A., Gilbert, T. M., Stephan, D. W. *Chem. Commun*., **2008**, 4303
4. Del Grosso, A., Muryn, C. A., Pritchard, R. G., Ingleson, M. J. *Organometallics,* **2010**, 29, 241
5. Del Grosso, A., Helm, M. D., Solomon, S. A., Caras Quintero, D., Ingleson, M. J. *Chem. Commun*., **2011**, 47, 12459
6. Ghesner, I., Piers, W. E., Parveza, M., McDonald, R. *Chem. Commun*., **2005**, 2480
7. Bonnier, C., Piers, W. E., Parvez, M., Sorensen, T. S. *Chem. Commun*., **2008**, 4593
8. Vidović, D., Reeske, G., Findlater, M., Cowley, A. H. *Dalton Trans*., **2008**, 2293
9. Jones, C., Mills, D. P., Stasch, A., Woodul, W. D. *Main Group Chem*., **2010**, 9, 23
10. Tsurumaki, E., Hayashi, S., Tham, F. S., Reed, C. A., Osuka, A. *J. Am. Chem. Soc*., **2011**, 133, 11956

11. McArthur, D., Butts, C. P., Lindsay, D. M. *Chem. Commun*., **2011**, 47, 6650

12. Solovyev, A., Geib, S. J., Lacôte, E., Curran, D. P. *Organometallics,* **2012**, 31, 54

13. Muthaiah, S., Do, D. C. H., Ganguly, R., Vidović, D. *Organometallics,* **2013**, 32, 6718

14. Clark, E. R., Ingleson, M. J. *Organometallics,* **2013**, 32, 6712

15. Clark, E. R., Del Grosso, A., Ingleson, M. J. *Chem. Eur. J.,* **2013**, 19, 2462

16. Prokofjevs, A., Kampf, J. W., Solovyev, A.; Curran, D. P., Vedejs, E. *J. Am. Chem. Soc.,* **2013**, 135, 15686

17. Chiu, C. W., Gabbaï, F. P. *Organometallics,* **2008**, 27, 1657

18. Matsumoto, T., Gabbaï, F. P. *Organometallics,* **2009**, 28, 4252

19. Mansaray, H. B., Rowe, A. D. L., Phillips, N., Niemeyer, J., Kelly, M., Addy, D. A., Bates, J. I., Aldridge, *S. Chem. Commun*., **2011**, 47, 12295

20. Do, D. C. H., Muthaiah, S., Ganguly, R., Vidović, D. *Organometallics*, **2014**, *33***,** 4165

21. Del Grosso, A., Singleton, P. J., Muryn, C. A., Ingleson, M. J. *Angew. Chem. Int. Ed,* **2011**, 50, 2102

22. Ryschkewitsch, G. E. and Wiggins, J. W. *J. Am. Chem. Soc*., **1970**, 92, 1790.

23. Tay, M. Q. Y., Murugesapandian, B., Lu, Y., Ganguly, R., Rei, K., Vidović, D. *Dalton Trans*., **2014**, 43, 15313

24. Del Grosso, A., Ayuso Carrillo, J., Ingleson, M. J. *Chem. Commun*., **2015**, 51, 2878

Chapter 3: De-elementoboration of Alkynes

3.1 Introduction

De-elementoboration, the direct transformation of a C-E bond into a C-B bond, represents an attractive method for the introduction of a boron-containing group to a compound with minimal disruption of the structure, and the boronate ester products represent useful synthetic building blocks.[1-4] For example, dehydroborations allow the boron group to be introduced in place of hydrogens, which are obviously ubiquitous in (hetero)aromatic rings, alkenes and alkynes. Being able to selectively dehydroborylate at a specific site would allow for complex structures to be synthesised through subsequent cross-coupling reactions. Herein are presented select examples of previously reported de-elementoboration reactions to exemplify the utility of this approach.

Arene dehydroboration studies have been carried out using boron electrophiles,[5] and the resulting reactions showed that these borenium cations reacted with a wide scope of activated arenes,[6] a selection of which is shown below in Figure 3.1.[7] It was observed that direct borylation of the arenes occurred regioselectively (under electronic control) and produced the expected by-product $[Base\text{-}H]^+[AlCl_4]^-$. The sequestering of the proton prevents the superacid $[AlCl_4]H$ from forming and facilitating competing protodeborylation and heteroarene decomposition pathways. In order to isolate the aryl boronate esters, the catechol boronate esters, which are susceptible to protodeboronation and hydrolysis in the

presence of ROH, were transesterified *in situ* to the pinacol boronate esters. This proved vital for isolating the products in high yields.

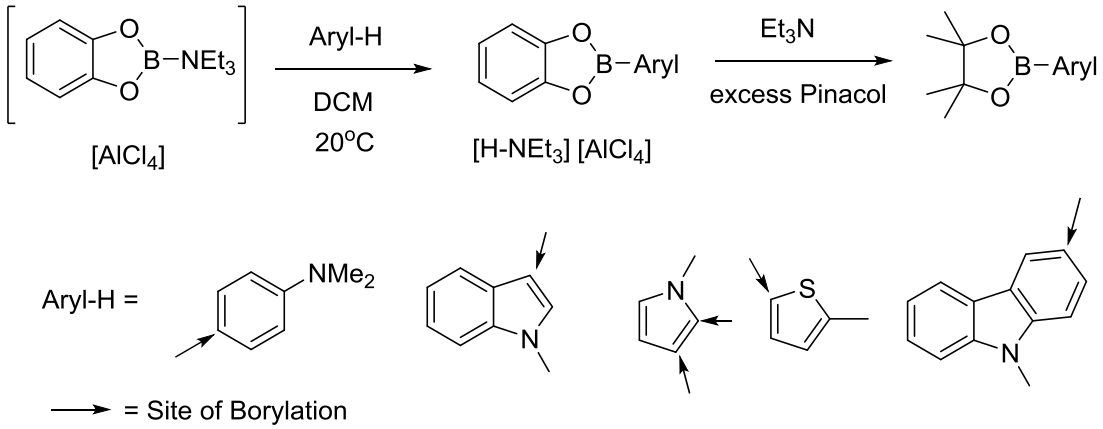


Figure 3.1: Borylation of a selection of arenes

In contrast to arenes, the non-catalysed direct dehydroboration of alkynes using boron electrophiles has not been reported. However, several routes to alkynylboron species have been reported, which although are not direct dehydroboration reactions, afford the alkynylboronate ester products. The most recent examples are one-step dehydroborations, involving transition metal catalysis. A selection of reactions to produce alkynyl boronate esters is reported below.

Among the earliest examples of borylated alkynes, Brown *et al.* demonstrated that trialkoxyboranes could be utilised for the borylation of a variety of lithiated organic species,[8] including alkynes.[9] These early reactions were multistep, with the deprotonation of the alkynes necessary before quenching with trialkoxyboranes. The starting materials were synthesised from terminal alkynes, which were lithiated with BuLi. A variety of 1-alkynyldiisopropoxyboranes were synthesised using this method, as summarised in Figure 3.2, below.

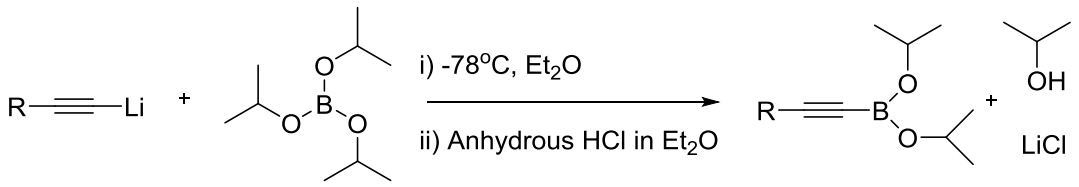


Figure 3.2: Borylation of alkynes

Attempts to transesterify the 1-alkynyldiisopropoxyboranes products with 1,3-propanediol failed, and resulted in cleavage of the C-B bond, regenerating the alkyne and re-forming the borate ester. This was overcome by changing the borate to generate different 1-alkynylboron esters. An example given was the reaction of I-lithio-1-octyne with 2-methoxy-1,3,2-dioxaborinane, generating the 1-alkynylboronate shown in Figure 3.3, below.

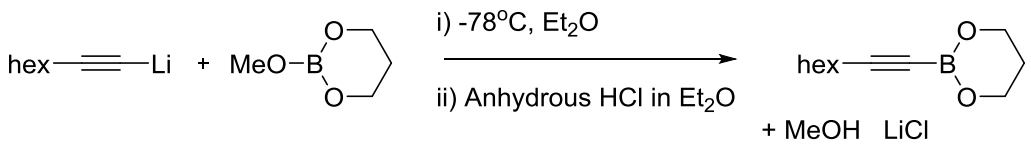


Figure 3.3: Synthesis of an alkynyl boronate ester

Another early method for the generation of 1-alkynylboranes involved using silylated and stannylated alkynes with BX_3, (X = Cl, Br) which represents desilylboration[10] and destannylboration,[11] respectively. One such example involved the transmetallation of alkynyltin reagents with bromoboranes.[11,12] One such example is shown below, utilising a tributyltin-alkyne. The subsequently synthesised 1-alkynylboranes are then used in further reactions, such as dienophiles in Diels-Alder reactions or as alkynylating reagents.[13]

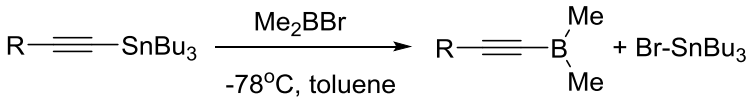


Figure 3.4: Alkyne borylation using tributyltin reagent

More recent reported methods of de-elementoboration of alkynes rely on a transition metal catalyst. One such example utilises a silver(I) catalyst, allowing access to alkynyl-boronates.[14] Inspired by, and developed as an analogue of the carboxylation of terminal alkynes using Ag(I)X,[15] it was shown that a range of terminal alkynes could be borylated in good yields on gram scale. Selected examples are shown in Figure 3.5, below.

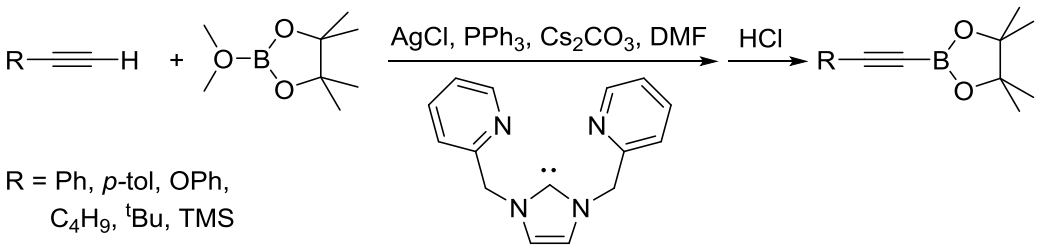


Figure 3.5: Borylation of terminal alkynes using Ag(I)

Iridium catalysis has proven useful for direct arene borylation,[16,17] and Ozerov *et al.* expanded on this by demonstrating the dehydroboration of terminal alkynes with an iridium-pincer complex.[18] The iridium catalyst promoted the dehydrogenation reaction between pinacolborane and alkyl, aryl, and silyl-substituted terminal alkynes, as shown in Figure 3.6, below. The reactions reported proceeded rapidly (≤10 min) at ambient temperature and gave nearly quantative conversions by NMR spectroscopy, and very high isolated yields in several cases.

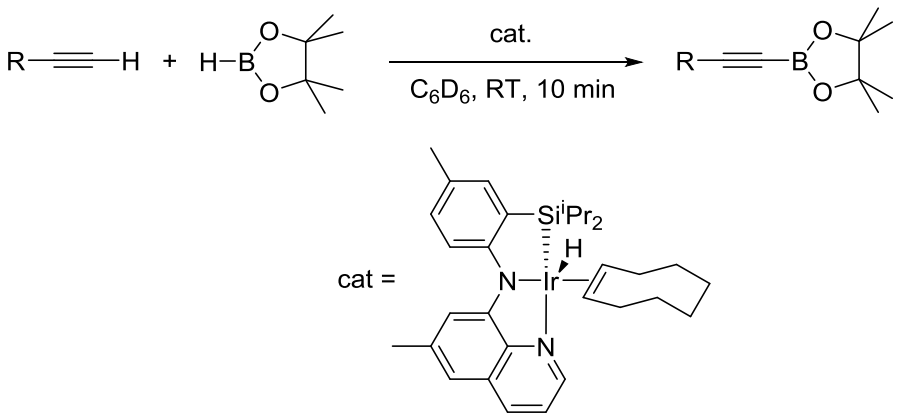


Figure 3.6: Borylation of terminal alkynes using iridium catalysis

Given the scarcity of direct electrophilic dehydroboration of alkynes in the literature, investigations were undertaken to determine if strong boron electrophiles, such as the borocations described in chapter 2, would undergo this reactivity. The results are reported herein.

3.2 Dehydroboration of Arenes

The preliminary studies of dehydroboration were undertaken with acid sensitive heteroarenes, specifically furans, which were chosen due to their significantly reduced aromatic character when compared with other simple aromatic substrates, such as benzene. This makes them a challenging substituent for selective dehydroboration with no competitive addition reactions, and serve as a good precursor for further studies on alkynes due to a mutual tendency to undergo polymerisation when reacted with electrophiles.[19] 2-Methylfuran and 2-methoxyfuran were each combined with the borocation $[CatBNEt_3][AlCl_4]$, in an attempt to borylate at the 5-position on the ring (Figure 3.7). These reactions were found not to proceed to the desired products, akin to similar reactions with other arenes;[20] instead more complex reactivity had occurred.

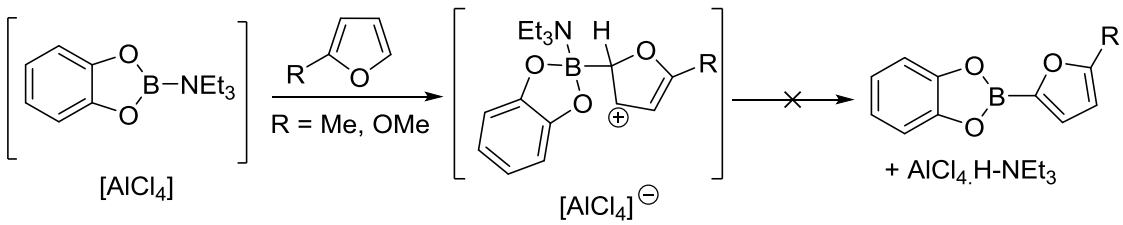


Figure 3.7: Attempted borylation of 2-methyl- and 2-methoxyfuran

It is likely that polymerisation of the furans had occurred, as indicated by large amounts of solid precipitating inside the reaction vessel that could not be redissolved in a range of common organic solvents. In order to expedite the desired reactivity, it was decided to add a base that did not react with the borenium cation. This was in order to facilitate deprotonation of the borylated furan arenium cation intermediate, as it was known that NEt_3 dissociation from these cations is slow.[5] On

addition of 1 equivalent of triphenylphosphine to $[CatBNEt_3][AlCl_4]$, a borenium frustrated Lewis pair was generated (Figure 3.8, left) as previously discussed.

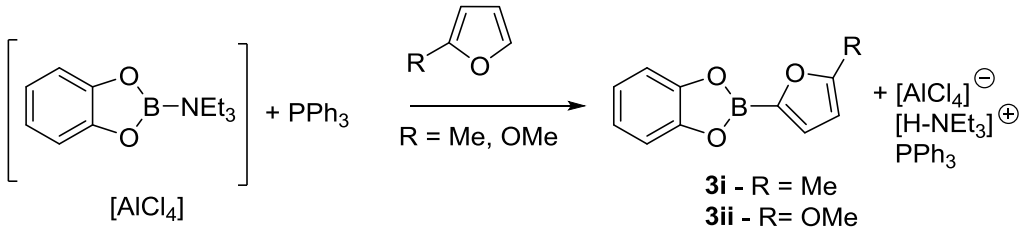


Figure 3.8: Reaction of borocation FLP with furans

This FLP reacted with both furan substrates to give the desired products.[7] It was inferred that the reactivity of an FLP was required to generate the desired product. There exists an equilibrium between the starting materials and the initial boron addition product (the borylated arenium cation, Figure 3.9). During this stage the intermediate is susceptible to polymerisation and other unwanted reactions, but, with the additional PPh_3 present in the FLP system, deprotonation is rapid and results in the formation of the desired product in good yield.

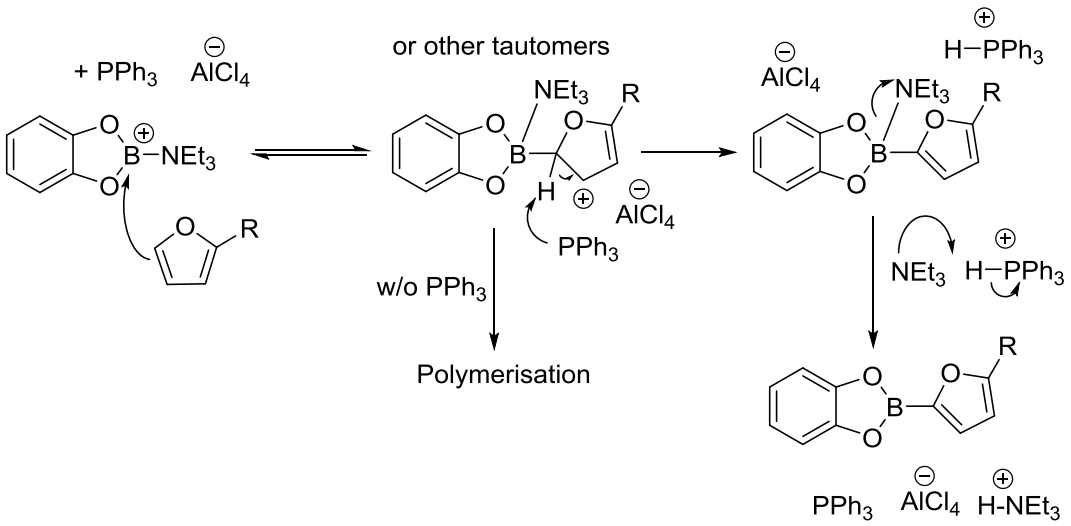


Figure 3.9: Proposed mechanism of dehydroboration of furans

Through multiple experiments, it was found that 2-methoxyfuran could be cleanly dehydroborated with only 0.2 equivalents of PPh_3 in order to react to completion, which implies that the reaction is catalytic in regards to PPh_3. This fits with the fact that $[H\text{-}PPh_3]^+$ is never observed by $^{31}P\{^1H\}$ NMR spectroscopy, and allows us to postulate a mechanism. In this, the protonated PPh_3 is rapidly deprotonated by newly liberated triethylamine (which binds weakly to the neutral CatB-furanyl moiety), regenerating PPh_3 which can be thought of as a proton shuttle. One other such mechanism is possible where the PPh_3 acts as a nucleophilic catalyst, binding to boron to allow base dissociation and subsequent deprotonation.

However, it was also observed that in the case of methylfuran, 1 equivalent of PPh_3 was required for a clean reaction; reactions with lower amounts gave poor yields of dehydroborated products and insoluble, presumably polymerisation derived, by-products. This implies that the nature of the arene is also important, with the more nucleophilic methoxyfuran reacting faster and with less PPh_3. Presumably, the borylated arenium cation generated can be stabilised through resonance from the methoxy group, lowering the electrophilicity and making it less susceptible to attack from additional molecules of furan and polymerisation.

3.3 Dehydroboration of Terminal Alkynes

With two furans successfully borylated using borocation FLPs and the products fully characterised, work moved on to the main focus of the investigation; dehydroboration of terminal alkynes. With the $[CatBNEt_3][AlCl_4]$ + PPh_3 FLP, dehydroboration was observed to occur with phenylacetylene and ^{t}butylacetylene, but the yields were low and product isolation was problematic due to competing reactions. For both of these reactions it was observed by ^{31}P NMR spectroscopy that a second new phosphorous containing species had been synthesised, with a singlet peak observed at 26 ppm in the $^{31}P\{^1H\}$ NMR spectrum, consistent with a phosphonium cation attributed to an addition product resembling that shown in Figure 3.10 based on other established FLP reactivity.[21]

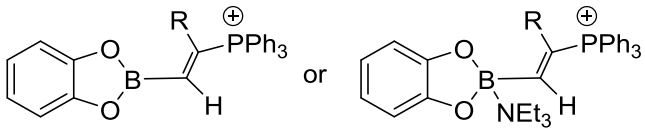


Figure 3.10: Possible structures of the addition product

In the example of the above reactivity with phenylacetylene, the ^1H NMR spectrum after 22 hours showed more complex resonances for the aliphatic protons of the NEt_3, most likely several similar species that were almost coincident. The aromatic region contained several resonances attributed to the PPh_3, catechol and phenylacetylene, but most diagnostically relevant were singlets that were observed amongst the aromatic resonances. These may have been indicative of vinyl protons, such as in the species shown above in Figure 3.10, as none of the aromatics associated with the other groups present should give rise to a singlet. As

there was more than one observed, there may have been a mixture of the isomers, although as these singlet resonances were amongst the aromatics, full characterisation remained elusive. There was also evidence for protonated Et_3N; although the aliphatic region showed several resonances for different Et_3N species, a broad singlet at 6.19 ppm (consistent with Et_3NH in dry DCM) indicated one of these species was protonated. This would account for the small amount of alkynylboronate product isolated post-transesterification.

The ^{11}B NMR spectrum showed, in addition to unreacted borenium, two new resonances at 19.1 and 13.4 ppm. As these represent 3- and 4-coordinate boron environments, respectively, it is difficult to know whether NEt_3 was still coordinated to boron in the postulated phosphorous addition product. Indeed, it may be that both were formed, or that they were in equilibrium. Attempts to transesterify this species with pinacol only ever gave small amounts of the dehydroboration product.

In order to access the desired alkynyl boronate esters, the novel borocation [CatB(2DMAP)][$AlCl_4$] was utilised. It was discussed in Chapter 2 that this borenium represents an intramolecular FLP, with the NMe_2 side-arm of 2DMAP functioning as the Lewis base. The NMe_2 represents a fixed source of base for deprotonation, increasing the local concentration, and potentially preventing the competing addition reaction observed with the external base, such as the above example with PPh_3.

It was thought that the selectivity of reaction could be increased by having the base attached to the ligand, so that it would always be close in space to the

newly generated vinyl proton of the carbocationic intermediate to facilitate rapid deprotonation. Following the deprotonation of the vinyl cation intermediate, and subsequent reformation of the alkyne, the protonation of the 2DMAP would weaken the B-N bond allowing it to dissociate, generating the final neutral boronate ester product. An alternative hypothesis is that the 2DMAP dissociates rapidly from the vinyl cation intermediate, facilitating deprotonation, as shown in Figure 3.11, although this is inconsistent with arene dehydroboration studies where strong amine nucleophiles dissociate slowly from borylated carbocationic intermediates.[7]

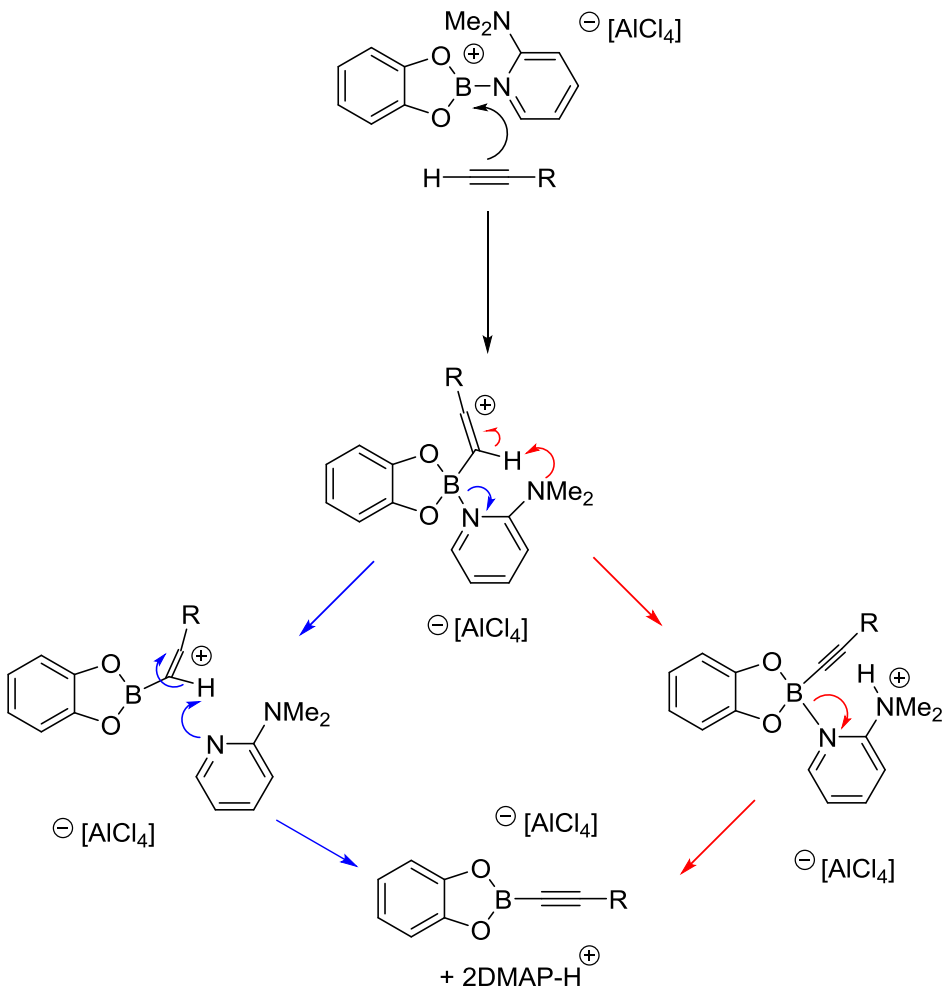


Figure 3.11: Possible mechanisms of dehydroboration

Thus, [CatB(2DMAP)][$AlCl_4$] was combined with 1 equivalent of phenylacetylene in DCM at room temperature. It was shown by ^{1}H NMR spectroscopy that, at room temperature, the dehydroboration reaction did proceed, but very slowly. Hence the reaction was heated to 60˚C (in a sealed J. Youngs NMR tube), where it was found to go cleanly to completion within 48 hours, as monitored by NMR spectroscopy. The ^{1}H NMR spectrum showed complete consumption of the alkynyl proton, and a shift of the 2DMAP peaks consistent with protonation. Attempts to isolate the product as a pinacol boronate ester via transesterification gave very low yields. In order to achieve complete transesterification $\geq$ 2 equivalents of pinacol are required, due to competitive reaction with [$AlCl_4$]$^-$.[7] Normally, these aluminium-pinacol by-products can be removed by filtration through a silica plug, but the alkynyl pinacol boronate esters also react with silica (by protodeboronation), leading to the low yields encountered. The pinacol boronate ester was isolated, and found to be pure by ^{1}H and ^{11}B NMR spectroscopy, but it was desirable to avoid this purification step to achieve acceptable isolated yields. Therefore, the product was instead isolated as the alkynyl catechol boronate ester by removal of solvent and a simple pentane extraction to separate it from the ammonium[$AlCl_4$]. The phenylacetylene dehydroboration product was produced in a moderate isolated yield of 60%, whilst the *in-situ* yield shown by ^{1}H NMR spectroscopy was > 95%. Therefore, some product is still lost during this extraction procedure, but the yield was reasonable enough to proceed to substrate scoping.

The dehydroboration reaction was extended to a range of aromatic and aliphatic acetylenes, as shown in the Table 3.1. Also shown are terminal alkynes with varying functional groups, which reacted with mixed success. The reactions of [CatB(2DMAP)][$AlCl_4$] with ^{t}butylacetylene, 1-pentyne, 1,4-diethynylbenzene, 4-methylphenylacetylene and 3-phenylpropyne gave the desired products in good to high yields within a 24 – 72 hour timescale at 60°C (in DCM in a sealed tube). The products of these reactions were isolated as the catechol boronate esters and have been fully characterised by multinuclear NMR spectroscopy and elemental analysis. Transesterification with pinacol and triethylamine was attempted on several of these alkynes, with comparable low yields as seen with phenylacetylene.

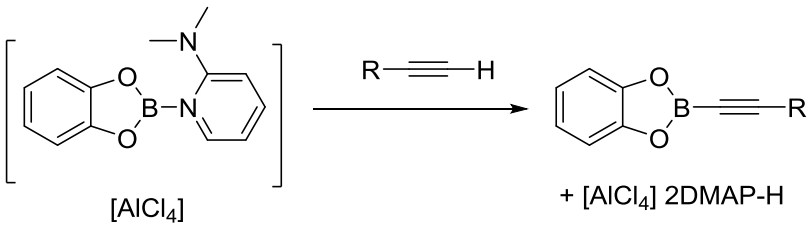
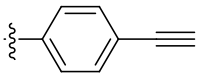
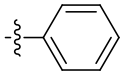
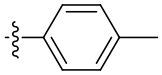
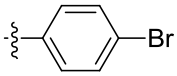
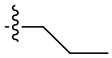
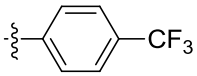
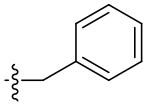


Figure 3.12: The general reaction of [CatB(2DMAP)][$AlCl_4$] with alkynes

Table 3.1					
	Substrate R-Group	**Isolated Yield %**		**Substrate R-Group**	**Isolated Yield %**
3iii		72	**3viii**		74
3iv		60	**3ix**		77
3v		88	**3x**		12
3vi		69			--
3vii		74			--

The same reaction conditions were applied with propargyl chloride, in an attempt to demonstrate some functional group tolerance. If attempting to make this alkynyl boronate ester with a lithium reagent, for example, then the chloride group may react preferentially and the borylation would fail. Using the borocation FLP, this was not observed and the reaction proceeded cleanly to the dehydroboration product in high yield. To further probe tolerance to halide groups, the alkyne 4-bromoethynylbenzene was investigated. While the desired product was observed, the yield was very low (12%). The reaction also took a very long time and did not proceed to completion. Monitoring progress by ^{11}B NMR spectroscopy, the product was seen to grow in (δ_B 25 ppm) as the starting material was consumed, but only to approximately 50% after seven days, presumably due to the low nucleophilicity of the alkyne.

Two other terminal alkynes were reacted with the borocation system, namely TMS-ethyne and trifluoromethyl phenylacetylene. In the case of the latter, the alkyne itself is electron deficient due to the electron withdrawing CF_3 group, deactivating the alkyne to borylation. It was observed by ^{19}F NMR spectroscopy that there was possible C-F activation (a new species observed in the ^{19}F NMR spectrum at -50.07 ppm). Due to this electron deficiency slowing the rate of the dehydroboration reaction, it is possible that the boron was reacting exclusively with the fluorine on the CF_3 group instead. This is most likely due to the high fluorophilicity of borocations. It was observed by ^{1}H NMR spectroscopy that the alkynyl proton remained during the reaction, whilst the ^{11}B NMR spectrum showed slow consumption of the starting material, and new peaks growing in at 21.8 and 20.8 ppm. It is possible that one of these species was CatB-F, although no known spectra are available to confirm this unambiguously. However, the majority of the alkyne remained unreacted in solution, as observed by ^{1}H and ^{19}F NMR spectroscopy, even when heated to 60°C for 64 hours. Yet the borocation was entirely consumed, therefore it is probable that the borocation was decomposing due to adventitious water and leaching of water from glassware over time under harsh reaction conditions, forming CatBOR.

The alkyne TMS-ethyne was chosen to see if the borocation would selectively borylate the alkyne at either the terminal proton or via replacement of the silyl group, or if it would borylate both ends. Reactions showed a mixture of products with no clear indication of the desired compound, even when two equivalents of [CatB(2DMAP)][$AlCl_4$] were used. Attempts to isolate the synthesised

products ultimately failed, although future reactions of this alkyne with other borocations proved to yield more tangible results.

Although internal alkynes do not feature an alkynyl proton, and are thus unable it undergo dehydroboration of an alkynyl C-H, it was postulated that [CatB(2DMAP)][$AlCl_4$] may undergo different reactivity with this type of alkyne, potentially to deprotonate a carbocationic intermediate to form allenylboronate esters, similar to those synthesised by Sawamura and co-workers, shown below.[22]

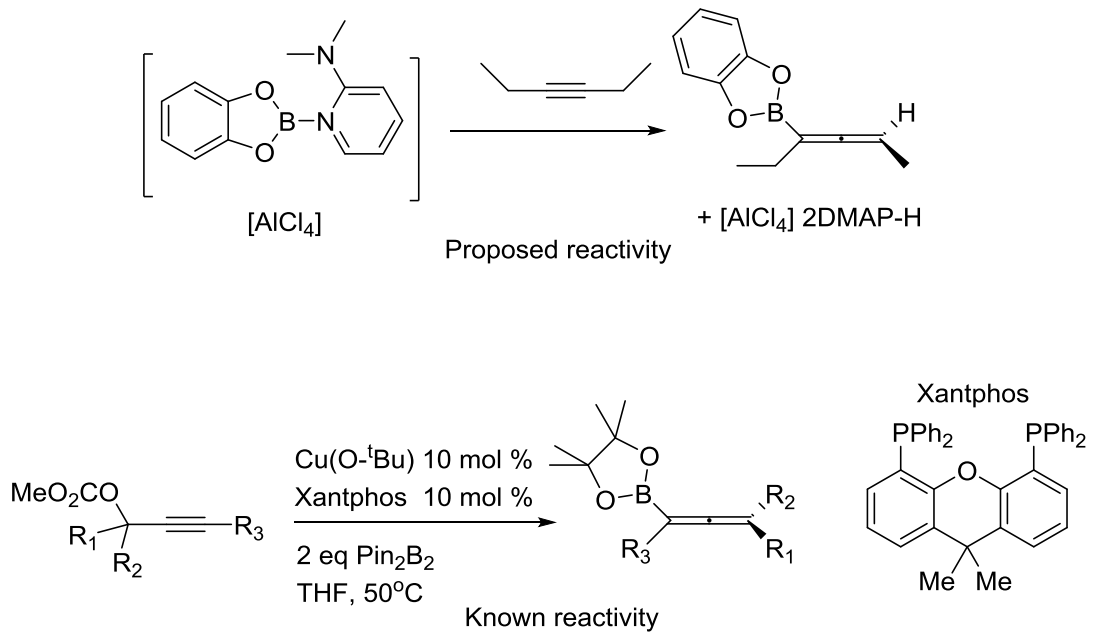


Figure 3.13: Proposed and known syntheses of allenylboronates

[CatB(2DMAP)][$AlCl_4$] was combined with equimolar 3-hexyne, but ^{1}H and ^{11}B NMR spectroscopy did not show any reactivity between the two. Over several days, the alkyne remained untouched, whilst the borocation slowly decayed to CatBOR (22 ppm) and protonated base, possibly due to small amounts of adventitious water and leaching of water from glassware over time.

3.4 Desilylboration of R_3Si-Alkynes

Later in the project, R_3Si-substituted alkynes were revisited, as largely documented in Chapter 5. Trimethylsilylacetylenes are defined as alkynes featuring the TMS group as one of the two substituents. While commonly used as an alkynylating agent, such as in the Sonogashira reaction,[23] the purpose of this body of work was to study the reactivity of Cl_2B(amine) borocations with these species. The major question was would TMS-Cl evolution take place at some point during borylation to form an alkynyl-BCl(amine) borocation or more exotic species such as a borirene (as per the stannyl examples from Pues and Bernst)[24] or a borata-allene.[26,27] Possible outcomes of this reaction are shown below in Figure 3.14 for the combination of TMS alkynes with $[Cl_2B(2DMAP)][AlCl_4]$.

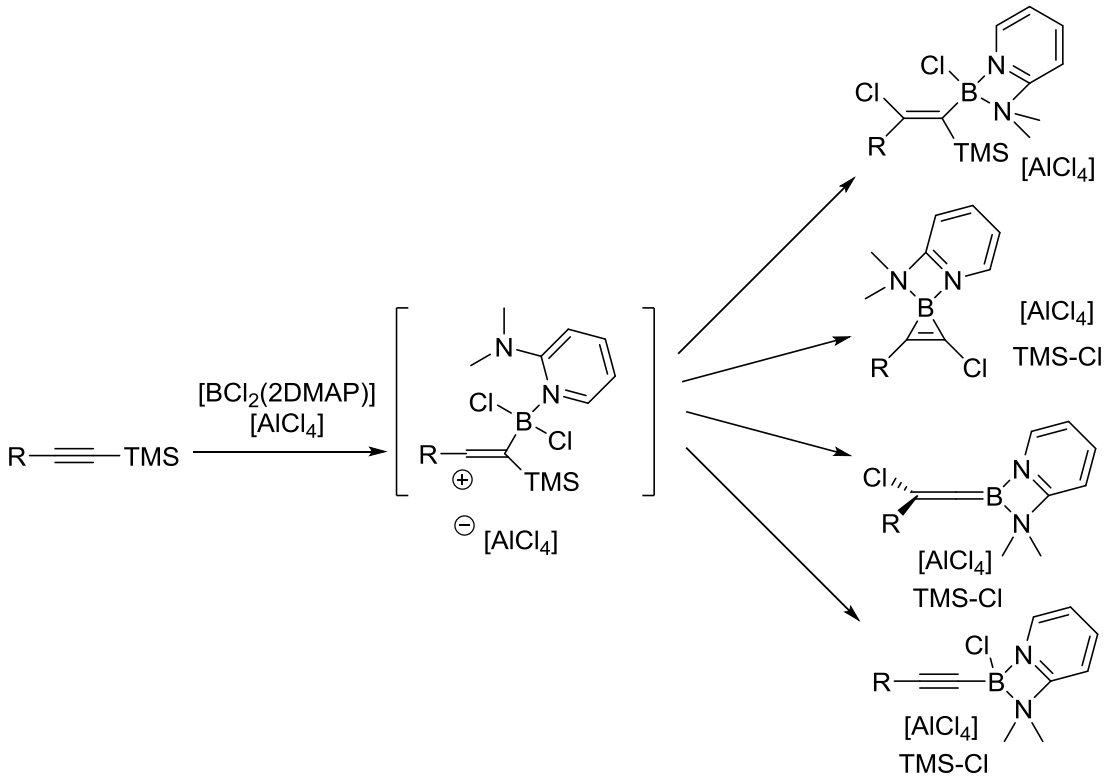


Figure 3.14: Possible outcomes of the borylation of TMS alkynes

1-(Trimethylsilyl)propyne was reacted with stoichiometric $[Cl_2B(2DMAP)][AlCl_4]$ at room temperature. After agitation for 24 hours, ^{1}H NMR spectroscopy showed new resonances; there were two alkynyl methyl resonances; the original at 1.84 ppm and a new one growing in over time at 1.95 ppm. The TMS region showed a new peak at 0.41 ppm, which is consistent with TMS-Cl. Indeed, ^{29}Si NMR spectroscopy showed a peak at 31.1 ppm, consistent with TMS-Cl formation. Finally, the ^{11}B NMR spectrum showed a new peak growing in at 6.5 ppm, along with starting material $[Cl_2B(2DMAP)][AlCl_4]$ at 12.2 ppm. An alkyne haloboration in line with all previous results would produce a vinyl-borocation species, and give a resonance around 12 ppm (see Chapter 4); the peak at 6.5 ppm was sufficiently different that the product may be an entirely new species and not simply due to haloboration, which is consistent with the evolution of TMS-Cl.

After the sample was left stirring for 72 hours at 20°C, almost all the starting TMS-propyne (>90% by NMR analysis) had been consumed with new product described above being the dominant species, along with TMSCl. The $^{13}C\{^{1}H\}$ NMR spectrum reveals little new information; resonances associated with 2DMAP, the methyl group and TMS-Cl were observed. There was no indication of a vinylic carbon species in the product, while a single vinyl resonance around 87 ppm was seen in the case of borattaallenes for the carbon not bound to boron.[25,26] Upon esterification with pinacol and triethylamine, the product was revealed to be a borylated alkyne **3xi**, with the reaction between $[Cl_2B(2DMAP)][AlCl_4]$ and TMS-propyne proceeds as desilylboration. The ^{11}B NMR spectrum of the post-esterification product showed a single peak at 24.5 ppm, consistent with alkynyl-

pinacolboronate esters. The ^{1}H NMR spectrum showed a pinacol resonance and the alkynyl methyl group only.

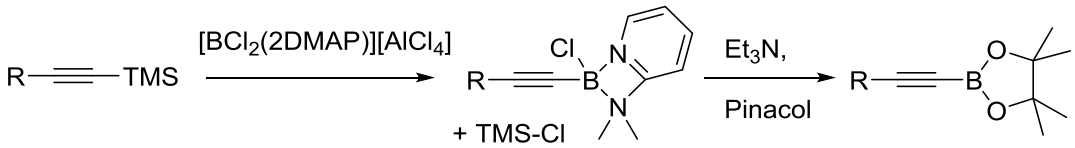


Figure 3.15: Desilylboration of a TMS-alkyne

In order to determine if the desilylboration reaction occurs with other TMS-alkynes, a small substrate scope study was performed. It was subsequently found that both 1-TMS-phenylacetylene and 1-TMS-1-hexyne reacted analogously, with TMS-Cl evolution observed by both ^{1}H and ^{29}Si NMR spectroscopy. Esterification with pinacol gave similar alkynyl-pinacol boronate esters, although full purification and characterisation was not pursued due to poor crude post-esterification yields, the crude NMR data were comparable to the reported compounds made via lithiation of alkynes and subsequent reaction with PinB(O^{i}Pr).[27] Protodeboronation was observed as a competing reaction to the esterification, similar to difficulties when attempts at transesterification of alkynyl-catecholboronates (**3iii**) – (**3x**). The fourth TMS-alkyne investigated, TMS-ethylene, underwent completely different reactivity than the others, as documented in the next section.

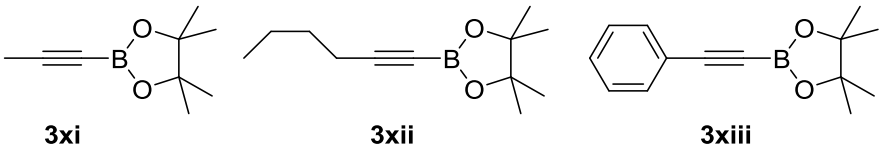


Figure 3.16: Desilylboration products derived from TMS-alkynes

3.5 Boroamination of TMS-Ethylene

During the investigation into the desilylboration of TMS-alkynes it was discovered that, unlike the other TMS-alkynes tested, TMS-ethylene did not lead just to desilaboration. When reacted with $[Cl_2B(2DMAP)][AlCl_4]$, it was observed via NMR spectroscopy that multiple products had formed. Desilylboration was still occurring, but a second product containing a vinyl singlet in the ^1H NMR spectrum was observed also. In addition to this, an insoluble third product precipitated out of solution and thus was not observed by NMR spectroscopy in CD_2Cl_2.

The DCM insoluble product was successfully crystallised and its structure determined by single crystal X-ray diffraction. It was found to be borate **3xv** shown below in Figure 3.18, wherein reaction between the boronium and the TMS-ethylene proceeded in a hitherto unreported 'boroamination' reaction. The compound isolated was shown to contain a five membered heterocycle where the boron and the nitrogen of the NMe_2 of 2DMAP were bound to a newly formed alkene carbon. The TMS group had migrated, similar to Wrackmeyer's carboborations of TMS-alkynes with BEt_3,[28] to the other end of the alkene, geminal to the vinylic proton, generating the proposed intermediate **3xiv**, which was subsequently exposed to a further source of boron (most likely due to a slight excess of boronium) allowing for a desilaborationreaction (Figure 3.17). This occured four times around a single boron atom forming a tetra-substituted borate which precpitates from solution. The crystal structure of the borate showed three $[AlCl_4]$ counter ions in the unit cell, to charge balance the compound.

Table 3.2		
Metric	**(3xv)**	**[BCl_2(2DMAP)] [$AlCl_4$]**
B1-N1	1.57(2) Å	1.567(4) Å
C5-N2	1.50(2) Å	1.471(3) Å
C5-N1	1.34(2) Å	1.337(3) Å
C8-C9	1.32(2) Å	-
C6-Cl1	4.978 Å	3.122 Å
C7-Cl2	3.733 Å	3.142 Å
N1-C5-N2	114.9(14) ˚	99.1(2) ˚
B1-C8-C9	138.5(15) ˚	-
B1-C8-C9-B2	1.29 ˚	-

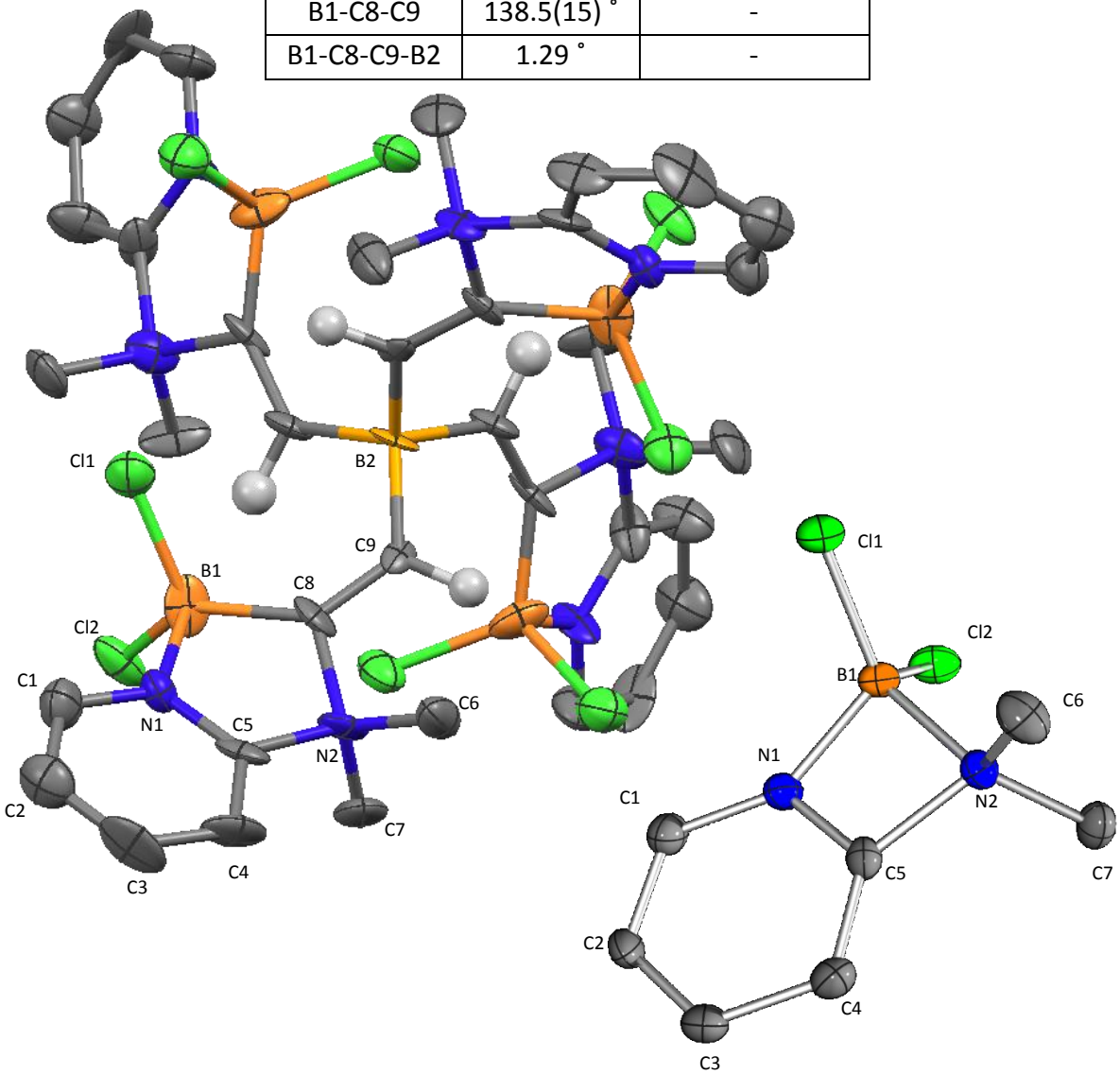


Figure 3.17: Single crystal X-ray structures of (**3xv**) and [Cl_2B(2DMAP][$AlCl_4$], for comparison (thermal ellipsoids at 50% probability, counterions and non-diagnostically relevant hydrogens omitted for clarity. Full crystal data and structure refinements listed in Appendix)

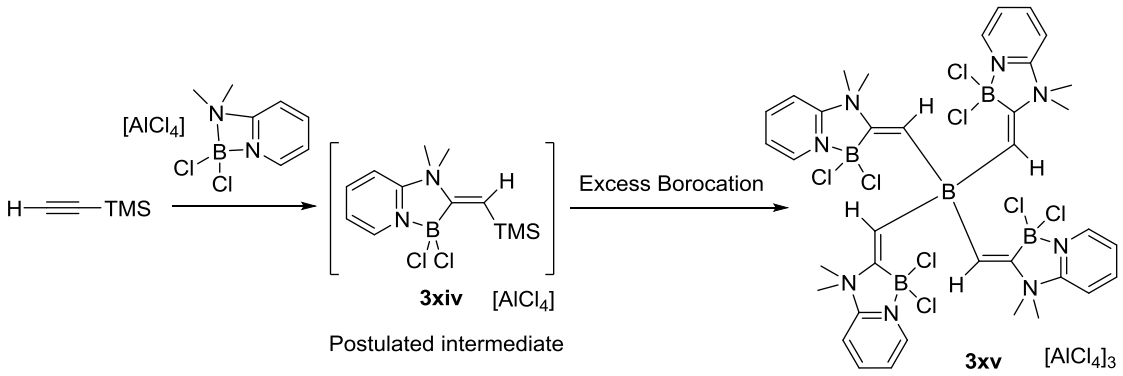


Figure 3.18: Formation of tricationic borate (**3xv**)

The bond lengths common to both $[Cl_2B(2DMAP][AlCl_4]$ and the tri-cationic borate show no significant difference. Indeed, even the change of a four-membered ring to a five-membered one only affects the bond angles associated with the ring, and shows a very minor lengthening of the N1-B and C5-N2 bonds. The C8-C9 bond is in the region expected (ca. 1.34 Å) for an alkene, and the atoms arranged around the central boron are in a tetrahedral conformation. The torsion angle of B1-C8-C9-B2 is close to 0°, as both boron atoms mutually *cis* arranged in the alkene.

Although insoluble in DCM, it was found that **3xv** was soluble and stable enough in acetonitrile to obtain NMR spectra. Based on the nOe spectrum of **3xv**, the vinyl proton is *cis* to the NMe_2 group. The ^{11}B NMR spectrum of **3xv** showed two boron environments at 3.90 and -15.44 ppm, consistent with the solid state structure, and the ^{1}H NMR spectrum showed a vinyl singlet and four aromatic resonances. However, the expected peak of the NMe_2 presented as a broad resonance at 3.75-3.50 ppm. Variable temperature NMR techniques were employed, and at -40 °C the broad resonance resolved to two 3H singlet

resonances, indicating the inequivalent environments of the methyl groups bound to nitrogen.

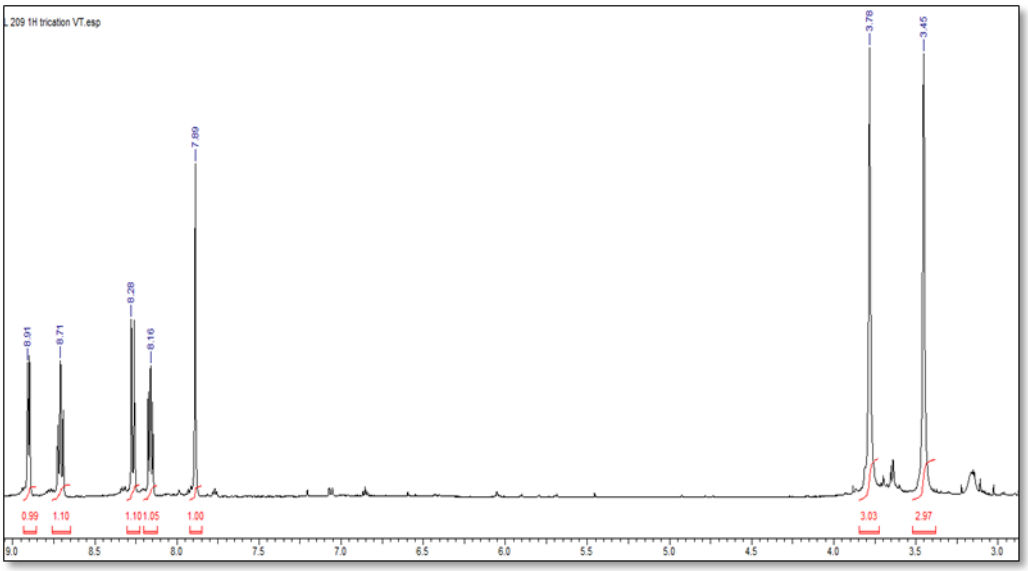


Figure 3.19 ^{1}H NMR spectrum of **3xv** (-40°C)

In order to determine the cause of the inequivalency, the solid-state structure was re-examined, and alludes that the reason for this may be proximity between the methyl-groups and the chloride atoms within the structure. The distance of C6 to Cl1 and C7 to Cl2 is not equal, the latter are closer by over 1 Å. This is most likely due to the four boroamination 'units' of the structure exerting steric pressure on each other, accounting for this distortion. As the mechanism for making the two methyl-groups equivalent is unknown, a number of possibilities may be postulated. If the equivalency is due to the low energy barrier to ring opening via B-N bond cleavage (as is the case with the boronium), which allows rotation about the C-N bond, then it may be the case that, for **3xv** either the barrier to ring opening is larger (as expected on going from a four membered to a five membered ring), due to the increased Lewis acidity of the trication, or steric

crowding prevents the C-N bond rotation. An alternative is steric crowding producing a non-negligable barrier to interconversion of the C_s-envelope configurations (as per hindered cyclopentanes).

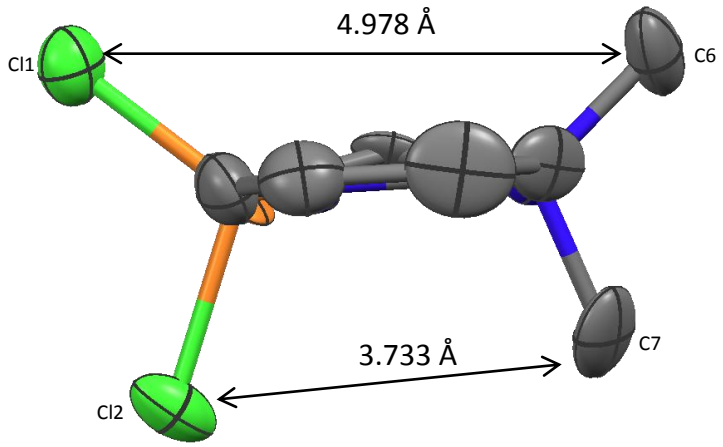


Figure 3.20: Single boroamination 'unit' of (**3xv**), viewed in the plane of the ring (thermal ellipsoids at 50% probability, counterions and hydrogens omitted for clarity)

In the initial reaction, **3xv** was observed as a minor product, and is thought to occur due to a slight excess of the borocation relative to alkynes, thereby providing the central boron atom. Indeed when the reaction was repeated with a 5:4 ratio of $[Cl_2B(2DMAP][AlCl_4]$ to TMS-acetylene it was observed that a larger quantity of solid precipitated out of solution, which was subsequently confirmed as **3xv** by NMR spectroscopy (CD_3CN). NMR analysis of the remaining solvent showed only small amounts of unreacted starting materials and TMS-Cl, the by-product of the formation of the borate.

In order to investigate the mechanism of the formation of **3xv**, the DCM soluble product was extracted from the reaction mixture in order to investigate its structure. It was found through NMR studies that the proposed intermediate in the formation of **3xv**, with TMS still bound to the vinyl backbone, is **3xiv**. Unfortunately,

the sample still contained protonated base (presumably from adventitious water / minor dehydroboration reaction), and these two charged species proved very difficult to separate, it is still possible to observe the boroamination product **3xiv** clearly by ^{1}H NMR spectroscopy.

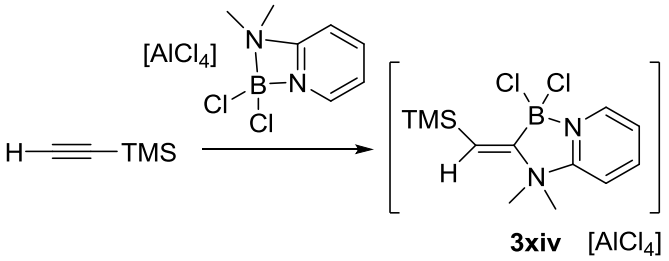


Figure 3.21: Boroamination of TMS ethylene

The spectrum showed four aromatic protons corresponding to the 2DMAP ring, a vinyl proton at 6.65 ppm, and a 6H singlet at 3.80, caused by the NMe_2 methyl groups on the 2DMAP. Also observed was a 9H singlet at 0.38 ppm, which corresponds to a trimethylsilyl-group bound to the product. Although the sample proved too weak to provide a ^{29}Si NMR spectrum, based on **3xv**, it can be postulated that this was a vinyl TMS group bound geminal to the vinyl proton.

The stereochemistry of **3xiv** was elucidated by nOe spectroscopy, wherein it was shown that the vinyl proton was mutually *cis* to the NMe_2 side-arm, which indicated that the silicon and boron atoms are also *cis* on the opposite side of the double bond. No other nOe interactions were observed.

It is postulated that this reactivity begins with either the borocation ring-opening into the reactive borenium form and is then subject to nucleophilic attack by the TMS-alkyne, or this occurs via an S_N2 mechanism. The TMS-group then migrates to the other end of the vinylcation intermediate. With the carbocation

now proximal to the NMe_2 side-arm, it is susceptible to attack forming a new C-N bond and, simultaneously, a 5-membered cyclic species, as shown in Figure 3.22.

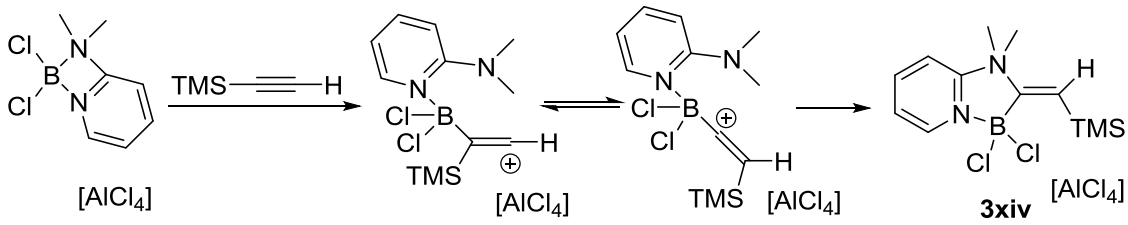


Figure 3.22: Proposed reaction pathway of boroamination of TMS-ethylene

Whilst only a single boroamination product was observed by NMR analysis, it is conceivable that **3xiv** is a 5-membered species, consistent with being the precursor to **3xv**, or a 6-membered cyclic species, where instead of TMS migration, the NMe_2 side arm would attack the initially formed vinyl carbocation, forming the 6-membered cyclic species, as per Figure 3.23, below. These would both give very similar NMR spectroscopic results and the identification of the product as the 5-membered species is reliant on the crystal structure of (**3xv**).

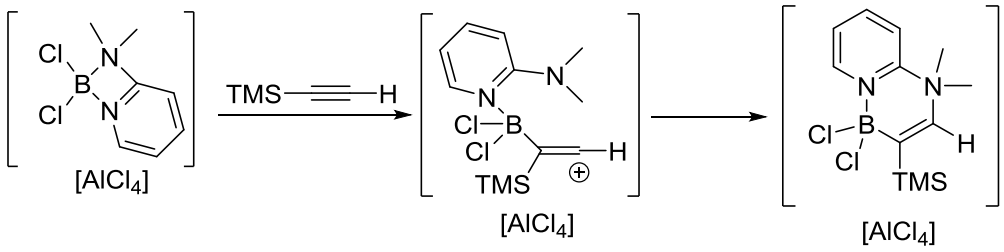


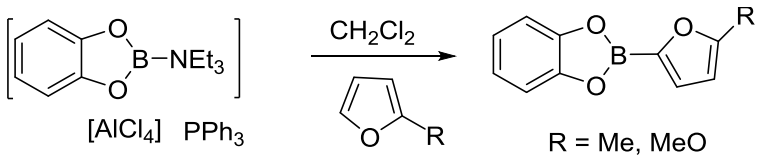
Figure 3.23: Proposed reaction pathway of boroamination of TMS ethylene forming hypothetical 6-membered cyclic product

3.6 Conclusions

The borenium [CatB(2DMAP)][$AlCl_4$] shows useful dehydroboration reactivity with a range of terminal alkynes. Although the alkynyl-catecholboronates are unstable towards ambient atmosphere, they can be isolated under inert conditions. Another route to borylated alkynes investigated was by starting from TMS-alkynes. Desilylboration was shown to occur when using the borocation [Cl_2B(2DMAP][$AlCl_4$] with TMS-alkyl/aryl alkynes. However, when using TMS-acetylene, it was shown to undergo new reactivity, namely boroamination followed by desilylboration. By modifying the stoichiometry of the reaction it was also possible to synthesise and crystallise a tricationic four-coordinate borate species.

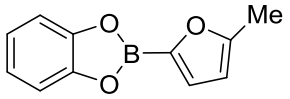
3.7 Experimental

General procedure for the borylation of furans with [CatB(NEt$_3$)][AlCl$_4$]



To a solution of Et_3N (90 µl, 0.65 mmol) in anhydrous CH_2Cl_2 in a J.Young's NMR tube, chlorocatecholborane (100 mg, 0.65 mmol) was added under an atmosphere of argon. Once dissolved, $AlCl_3$ (86 mg, 0.65 mmol) and PPh_3 (170 mg, 0.65 mmol for 2-methylfuran, 34 mg, 0.13 mmol for 2-methoxyfuran) were added sequentially, giving a clear, colourless solution. To the reaction mixture, 2-methylfuran (58 µl, 0.65 mmol) or 2-methoxyfuran (60 µl, 0.65 mmol) was added, turning pale yellow/ orange, respectively. The 2-methylfuran reaction was then heated to 60 °C for 38 hours, during which time it turned a darker shade of yellow, whilst the 2-methoxyfuran reaction was stirred at ambient temperature for 18 hours, during which time it turned a darker shade orange/brown. NMR spectroscopy was used to confirm reaction completion, and the solution was transferred to a Schlenk flask via cannula transfer under argon. The solvent was removed under reduced pressure, leaving an orange oil. Anhydrous pentane was added and the soluble component extracted. MeI (1.1 eq/0.25 eq) was added to convert the PPh_3 into the corresponding phosphonium salt, which precipitated out of solution. The solution was then filtered into another flask where the solvent was removed, affording the product as a white solid.

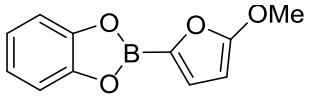
(**3i**) - 2-(5-methylfuran-2-yl)benzo[d][1,3,2]dioxaborole



(87 mg, 4.36 mmol, 67%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 7.29 (d, 1H, ^{3}J(H,H) = 1.0 Hz), 7.26 (dd, 2H), 7.12 (dd, 2H), 6.17 (d, 1H, ^{3}J(H,H) = 1.0 Hz), 2.41 (s, 3H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 158.32, 147.00, 125.83, 121.73, 111.33, 106.41, 12.56; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 27.7 (s) ppm.

Elemental Analysis – Despite multiple attempts to obtain using air sensitive techniques, we were unable to obtain satisfactory elemental analysis of compound (**3i**).

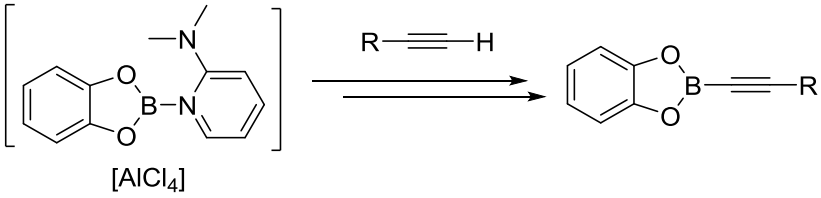
(**3ii**) - 2-(5-methoxyfuran-2-yl)benzo[d][1,3,2]dioxaborole



(88 mg, 0.35 mmol, 63%). **^{1}H NMR** (400 MHz, CD_2Cl_2): δ 7.25 (d, 1H, ^{3}J(H,H) = 3.3 Hz), 7.16 (dd, 2H), 7.02 (dd, 2H), 5.30 (d, 1H, ^{3}J(H,H) = 3.3 Hz), 3.86 (s, 3H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 166.91, 148.57, 129.20, 123.14, 112.74, 82.51, 58.40; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 28.3 (s) ppm.

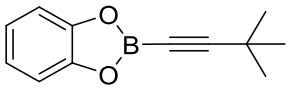
Elemental Analysis Calculated: C 61.20; H 4.21. Observed: C 60.99; H 4.27.

General reaction of [CatB(2DMAP)][$AlCl_4$] with terminal alkynes



To a solution of [CatB(2DMAP)][$AlCl_4$] (100 mg, 0.24 mmol) in anhydrous CH_2Cl_2 (0.5 ml) in a J. Young's NMR tube, equimolar terminal alkyne (0.24 mmol) was added, with the reaction remaining a clear orange solution. The reaction mixture was then heated at 60˚C for 72 hours, during which time the reaction mixture turned a darker shade of orange/brown. NMR spectroscopy was used to confirm reaction completion, and the solution was transferred to a Schlenk flask via cannula transfer. The solvent was removed under reduced pressure, and anhydrous pentane (10 ml) used to extract the product into another Schlenk flask, where solvent removal *in vacuo* afforded the alkynyl-pinacol boronate. (In the ^{13}C NMR spectra of these compounds, neither alkynyl-carbons are observed despite a large number of scans).

(**3iii**) - 2-(3,3-dimethylbut-1-yn-1-yl)benzo[d][1,3,2]dioxaborole

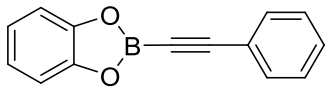


White solid (35 mg, 0.18 mmol, 72%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.14 (dd, 2H, ^3J(H,H) = 8.3), 7.04 (dd, 2H, ^3J(H,H) = 8.3), 1.26 (s, 9H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.76, 123.01, 112.51, 30.34, 28.26; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.1 ppm.

Elemental Analysis Calculated: C 72.04; H 6.55. Observed: C 71.91; H 6.67.

(**3iv**) - 2-(phenylethynyl)benzo[d][1,3,2]dioxaborole

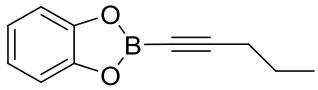


Pale white solid (32 mg, 0.15 mmol, 60%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.55 (d, 2H, ^{3}J(H,H) = 7.6 Hz), 7.38-7.29 (m, 3H), 7.19 (dd, 2H, ^{3}J(H,H) = 8.3), 7.08 (dd, 2H, ^{3}J(H,H) = 8.3); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.83, 132.79, 130.10, 128.51, 123.22, 121.18, 112.68; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.9 ppm.

Elemental Analysis Calculated: C 76.44; H 4.12. Observed: C 76.32; H 4.17.

(**3v**) - 2-(pent-1-yn-1-yl)benzo[d][1,3,2]dioxaborole

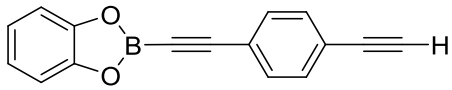


White solid (31 mg, 0.17 mmol, 69%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.14 (m, 2H, ^{3}J(H,H) = 8.3), 7.04 (m, 2H, ^{3}J(H,H) = 8.3) 2.30 (t, 2H, ^{3}J(H,H) = 7.1 Hz), 1.58 (sextet, 2H, ^{3}J(H,H) = 7.3 Hz), 0.98 (t, 3H, ^{3}J(H,H) = 7.4 Hz); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.76, 123.02, 112.53, 21.68, 21.48, 13.48; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.1 ppm.

Elemental Analysis Calculated: C 71.06; H 5.96. Observed: C 70.89; H 5.89.

(**3vi**) - 2-((4-ethynylphenyl)ethynyl)benzo[d][1,3,2]dioxaborole

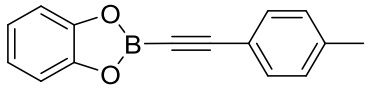


White solid (44 mg, 0.18 mmol, 74%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.52 (d, 2H, ^{3}J(H,H) = 8.1 Hz), 7.44 (d, 2H, ^{3}J(H,H) = 8.1 Hz), 7.21 (dd, 2H), 7.08 (dd, 2H), 3.16 (s, 1H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 146.75, 131.58, 131.15, 130.99, 122.27, 111.70, 78.92, 78.05; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.5 ppm.

Elemental Analysis Calculated: C 78.76; H 3.72. Observed: C 78.82; H 3.64.

(**3vii**) - 2-(p-tolylethynyl)benzo[d][1,3,2]dioxaborole

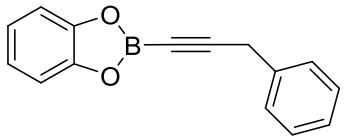


White solid (50 mg, 0.21 mmol, 88%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.44 (d, 2H, ^{3}J(H,H) = 8.1 Hz), 7.20 (dd, 2H, ^{3}J(H,H) =8.3), 7.12 (d, 2H, ^{3}J(H,H) = 7.8 Hz), 7.07 (dd, 2H, ^{3}J(H,H) =8.3), 2.32 (s, 3H, Methyl); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.85, 140.63, 132.76, 129.29, 123.16, 118.09, 112.66, 21.72 ppm; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.8 (s) ppm.

Elemental Analysis Calculated: C 76.97; H 4.74. Observed: C 76.93; H 4.73.

(**3viii**) - 2-(3-phenylprop-1-yn-1-yl)benzo[d][1,3,2]dioxaborole

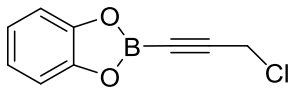


Off-white solid (42 mg, 0.18 mmol, 74%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.34-7.19 (m, 5H), 7.16 (dd, 2H, ^{3}J(H,H) =8.2), 7.08 (dd, 2H, ^{3}J(H,H) =8.2), 3.74 (s, 2H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.73, 134.75, 128.76, 128.04, 127.06, 123.13, 112.61, 26.11 ppm; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.2 (s) ppm.

Elemental Analysis Calculated: C 77.64; H 3.91. Observed: C 77.59, H 3.90.

(**3ix**) - 2-(3-chloroprop-1-yn-1-yl)benzo[d][1,3,2]dioxaborole

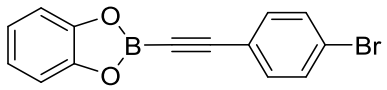


White solid (17 mg, 0.09 mmol, 77%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.19 (dd, 2H, ^{3}J(H,H) =7.9), 7.07 (dd, 2H, ^{3}J(H,H) =7.9), 4.19 (s, 2H); **^{13}C NMR** (100.6 MHz, CD_2Cl_2): δ 147.56, 123.40, 112.78, 29.78; **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 23.5 (s) ppm.

Elemental Analysis Calculated: C 58.76; H 2.96. Observed: C 58.69; H 2.90.

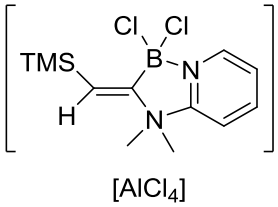
(**3xii**) - 2-((4-bromophenyl)ethynyl)benzo[d][1,3,2]dioxaborole



In this case, the reaction did not go to completion, and was esterified after 7 days, yielding a very small amount of clear colourless oil (8.6 mg, 0.03 mmol, 12%). The sample proved too weak to give viable ^{13}C NMR spectrum .

^{1}H NMR (400 MHz, CD_2Cl_2): δ 7.46 (d, 2H, ^{3}J(H,H) = 8.6 Hz), 7.41 (d, 2H, ^{3}J(H,H) = 8.6 Hz), 7.21 (dd, 2H, ^{3}J(H,H) =8.3), 7.08 (dd, 2H, ^{3}J(H,H) =8.3); **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 24.9 (s) ppm.

(**3xiv**) - Boroamination of 1-(trimethylsilyl)acetylene



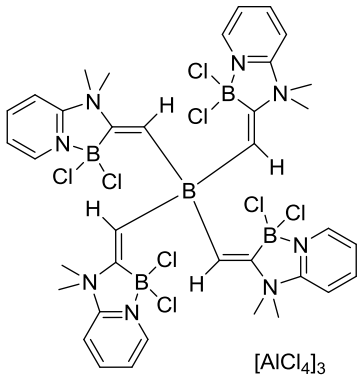
To a suspension of $[BCl_2(2DMAP)][AlCl_4]$ (100 mg, 0.27 mmol, 1 eq) in anhydrous CH_2Cl_2 in a J.Young's NMR tube, trimethylsilylacetylene (38 µl, 0.27 mmol, 1eq) was added, and the reaction mixture was then stirred at room temperature for 18 hours. NMR spectroscopy was used to confirm reaction completion, and the solvent was removed under reduced pressure, and the product redissolved in DCM.

^{1}H NMR (400 MHz, CH_2Cl_2): δ 8.99 (d, 1H), 8.88 (t, 1H), 8.56 (d, 1H), 8.25 (t, 1H), 6.65 (s, 1H), 3.80 (s, 6H), 0.38 (s, 9H); δ **^{11}B NMR** (128.4 MHz, CH_2Cl_2): δ 2.5 (s); **^{29}Si NMR** (MHz, CH_2Cl_2) δ -3.6 ppm.

Due to difficulties in purifiying this compound, the ^{13}C NMR spectrum was complicated by the numerous species present, making accurate interpretation difficult.

nOe spectroscopy showed through space interaction between the vinyl proton and the NMe_2 methyl groups. Elemental analysis could not be obtained due to the impure nature of each attempt to isolate this product.

(**3xv**) – Boroamination complex



Utilising a 5:4 ratio of $[BCl_2(2DMAP)][AlCl_4]$ (50 mg, 0.14 mmol, 5 eq), to trimethylsilylacetylene (16 µl, 0.11 mmol, 4 eq) dissolved in anhydrous CH_2Cl_2 in a J.Young's NMR tube, a crystalline solid rapidly precipitated out of solution. Removal of the solvent under reduced pressure allowed isolation of the crystals, which proved soluble in anhydrous acetonitrile.

^{1}H NMR (400 MHz, CD_3CN, -40°C): δ 8.91 (d, 1H), 8.71 (t, 1H), 8.28 (d, 1H), 8.16 (t, 1H), 7.89 (s, 1H), 3.78 (s, 3H), 3.45 (s, 3H); **^{11}B NMR** (128.4 MHz, CD_3CN): δ 3.90, -15.44; **^{13}C NMR** (100.6 MHz, CD_3CN): δ 154.09, 150.15, 143.80, 130.47, 119.85 ppm

Elemental Analysis Calculated: C 30.18; H 3.10; N 7.82. Observed: C 29.94; H 2.97; N 7.65.

nOe spectroscopy showed through space interaction between the vinyl proton and the NMe_2 methyl groups. Multiple attempts at elemental analysis were undertaken, but satisfactory analysis could not be obtained due to possible trace impurities of 2DMAP-H.

3.8: References

1. Hansen E. C., Lee, D. *J. Am. Chem. Soc*., **2005**, 127, 3252
2. Browne, D. L., Vivat, J. F., Gomez-Bengoa E., Harrity, J. P. A. *J. Am. Chem. Soc*., **2009**, 131, 7762
3. Auvinet, A. L., Harrity, J. P. A., Hilt, G. *J. Org. Chem.*, **2010**, 75, 3893
4. Gandon, V., Leboeuf, D., Amslinger, S., Vollhardt, K. P. C., Malacria M., Aubert C. *Angew. Chem. Int. Ed.*, **2005**, 44, 7114
5. Del Grosso, A., Muryn, C. A., Pritchard, R. G., Ingleson, M. J. *Organometallics,* **2010**, 29, 241
6. Del Grosso, A., Helm, M. D., Solomon, S. A., Caras Quintero, D., Ingleson, M. J. *Chem. Commun.,* **2011**, 47, 12459
7. Bagutski, V., Del Grosso, A., Singleton, P. J., Helm, M. D., Solomon, S. A., Lawson, J. R., Marcelli, T., Ingleson, M. J. *J. Am. Chem. Soc.,* **2013**, 135, 474
8. Brown, H. C., Cole, T. E. *Organometallics*, **1983**, 2, 1316
9. Brown, H. C., Bhat, N. G., Srebnik, M. *Tetrahedron Lett*., **1988**, 29, 2631
10. D. A. Singleton and S. -W. Leung, *J. Organomet. Chem*., **1997**, 544, 157
11. Singleton, D. A. Leung, S. W. *J. Org. Chem*., **1992**, 57, 4796
12. Corey, E. J. Cimprich, K. A. *J. Am. Chem. Soc*., **1994**, 116, 3151
13. Leung, S. -W., Singleton, D. A. *J. Org. Chem*., **1997**, 62, 1955
14. Hu, J. R., Liu, L. H., Hu, X., Hong-De Ye, H. D. *Tetrahedron,* **2014**, 70, 5815
15. Zhang, X.; Zhang, W. Z.; Ren, X.; Zhang, L. L.; Lu, X. B. *Org. Lett*., **2011**, 13, 2402

16. Mkhalid, I. A. I., Barnard, J. H., Marder, T. B., Murphy J. M., Hartwig, J. F. *Chem. Rev*., **2010**, 110, 890

17. Hartwig, J. F. *Chem. Soc. Rev*., **2011**, 40, 1992

18. Lee, C.-I., Zhou, J., Ozerov, O. V. *J. Am. Chem. Soc.,* **2013**, 135, 3560–3566

19. Gandini, A. *Adv. Polym. Sci*., **1977**, 25, 47

20. Del Grosso, A., Singleton, P. J., Muryn, C. A., Ingleson, M. J. *Angew. Chem. Int. Ed*., **2011**, 50, 2102

21. Dureen, M. A., Stephan, D. W. *J. Am. Chem. Soc*., **2009**, 131, 8396

22. Ito, H., Sasaki, Y., Sawamura, M. *J. Am. Chem. Soc.,* **2008**, 130, 15774

23. Sonogashira, K., Tohda, Y., Hagihara, N. *Tetrahedron Lett*., **1975**, 4467

24. Pues, C., Berndt, A. *Angew. Chem. Int. Ed. Engl*., **1984**, 23, 825

25. Pilz, M., Allwohn, J., Willershausen, P., Massa W., Berndt, A. *Angew. Chem., Int. Ed. Engl*., **1990**, 29, 1030

26. Bertermann, R., Braunschweig, H., Brown, C. K. L., Damme, A., Dewhurst, R. D., Hçrl, C., Kramer, T., Krummenacher, I., Pfaffinger, B., Radacki, K. *Chem. Commun.,* **2014**, 50, 97

27. Gandon, V., Leca, D., Aechtner, T., Vollhardt, K. P. C., Malacria, M., Aubert, C. *Org. Lett*., **2004**, 6, 3405

28. Köster, R., Seidel, G., Wrackmeyer, B. *Chem. Ber*., **1989**, 122, 1825

Chapter 4. Haloboration of Alkynes

4.1 Introduction

The haloboration of alkynes is a relatively rare reaction with only a few reported examples, which will be discussed in turn below. As stated in Chapter 1, Lappert[1,2] showed that the reaction between BX_3 (X = Cl, Br) and terminal alkynes yielded a 1,2-haloboration product, with the *syn* addition of boron and a halide across the alkyne generating a borylated alkene. It was shown that haloborated alkenes can also be synthesised using different boron reagents by Suzuki,[3] wherein it was reported that the haloboration of terminal alkynes was achieved with B-bromo- or B-iodo-9-BBN (9-BBN = 9-Borabicyclo[3.3.1]nonane) boranes generating, 1,2-haloborated alkenes. This procedure was shown to proceed with high *regio*- and *stereo*-selectively (>98%) to afford the *syn* adducts, as shown in Figure 4.1.

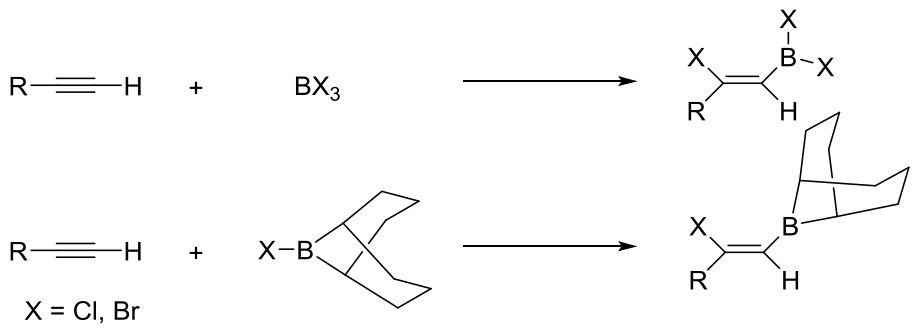


Figure 4.1: Haloboration of terminal alkynes with haloboranes

These haloborated alkenes can be subsequently used in a range of reactions, such as addition reaction with *α,*β-enones to generate (Z)-*δ*- halo-*γ,δ*-unsaturated ketones.[4] Through optimising the reaction conditions for the addition reaction, it was found that the haloalkenylboranes are far less reactive to conjugate

addition reactions with α,β-enones than simple alkenylboranes, such as those obtained by hydroboration of terminal alkynes.[5] This is presumably owing to the electronegative halogen substituent of the vinylboranes, so the reactions were run under Lewis acidic conditions (100% excess of 9BBN-X).

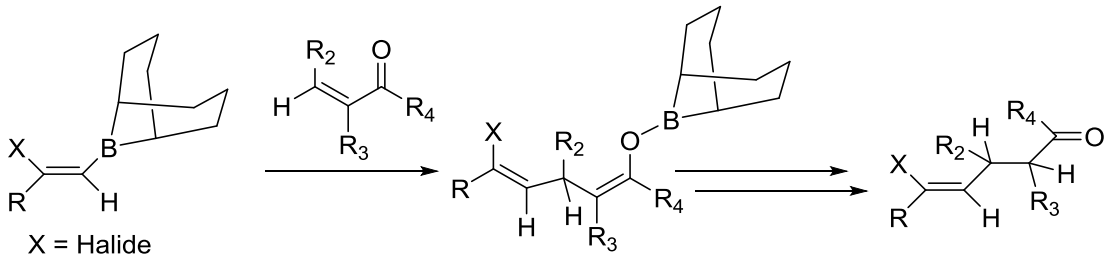


Figure 4.2: Synthesis of (Z)-δ- halo-γ,δ-unsaturated ketones from haloboration products

Later developments in haloboration showed that the bromoboration of the terminal alkyne propyne was possible using boron tribromide.[6] It was found that the reaction proceeded in >98% *syn* selectivity to produce the (Z)-bromo-boryl-alkene, as shown in Figure 4.3. Subsequent esterification with pinacol yielded products stable to stereoisomerisation, which could then be utilised in a wide variety of cross-coupling reactions to build larger, more complex molecules.

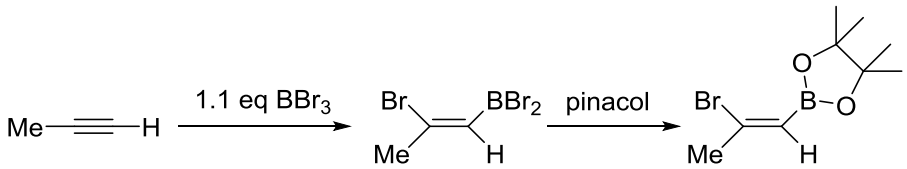


Figure 4.3: Bromoboration of 1-propyne

BBr_3 was also shown to react with acetylene in a haloboration reaction, generating the (*E*) bromovinylborane isomer.[1] Following the initial report of this reaction, (*E*)-(2-bromoethenyl)dibromoborane was subjected to sequential cross-

coupling reactions to generate a range of (*E*)-1,2-disubstituted ethenes, as shown in Figure 4.4.[7] Substitution of the bromo moiety of the alkene was carried out by the cross-coupling with an organozinc chloride and a palladium catalyst which was followed by substitution at the boron position achieved by the addition of base and an organohalide.

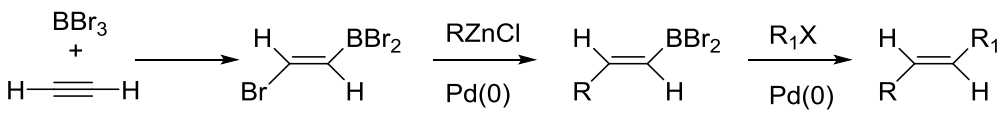


Figure 4.4: Haloboration and subsequent cross-coupling reactions of acetylene

The boron tribromide mediated deprotection of aryl propargyl ethers was found to proceed via a haloboration reaction (Figure 4.5).[8] It was proposed that the mechanism of this reaction began with the addition of boron tribromide to the terminal alkyne, generating a vinylboron dibromide intermediate. Subsequent C-O bond cleavage would afford an intermediate featuring a B-O bond, and hydrolysis would then give the observed products of phenol and bromovinylboronic acid. The bromovinylboronic acid was converted to an organotrifluoroborate, allowing it to be isolated and identified using NMR spectroscopy, supporting this proposed mechanism.

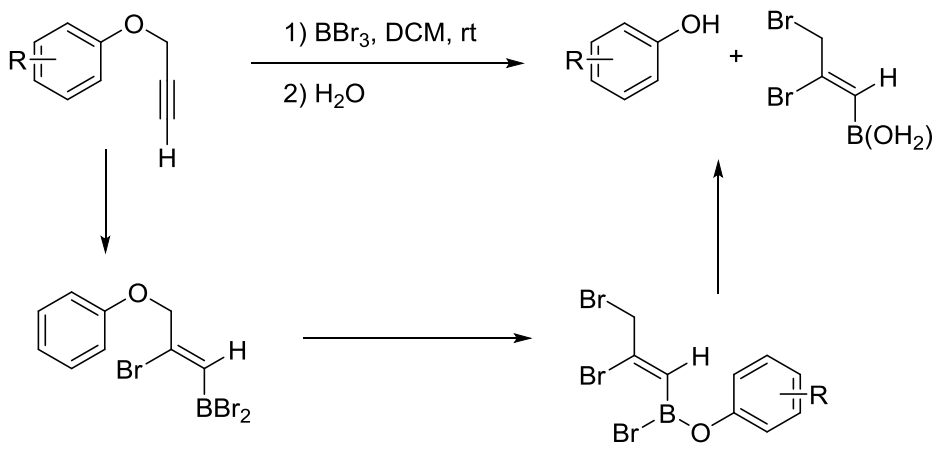


Figure 4.5: Deprotection of aryl propargyl ethers

The haloboration of alkynes has been studied computationally with calculations carried out at the MP2/631SVP level.[9] This study probed important aspects of the reaction, such as reaction mechanism, energetics and stereoconversion pathways. The calculations suggested that chloroboration and bromoboration can proceeded via four-centred polarised transition states (Figure 4.6, below) without the need for the π complex. The nature of the halides bound to boron, and the alkyne used, govern the stability of both the transition state and the product formed, and ultimately control the reactivity and stereo/regioselectivity. It was also shown that the haloboration of internal alkynes is an endergonic reaction; whilst following similar reaction pathways and possessing similar activation barriers as terminal alkynes, the products were thermodynamically unfavourable.

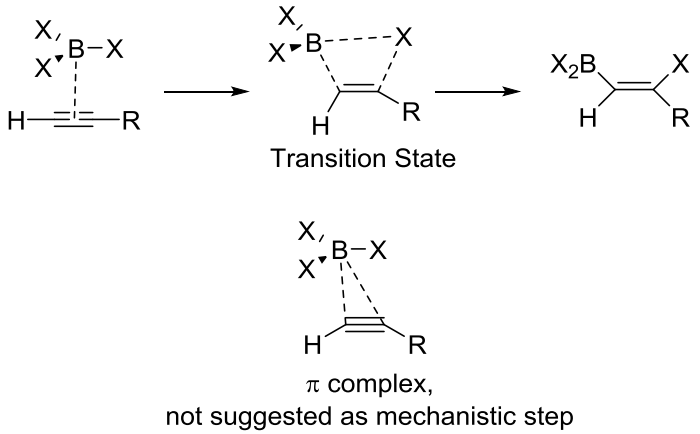


Figure 4.6: Proposed reaction route for the haloboration of alkynes

It was also shown that the *cis*-haloboration product was able to undergo conversion to the *trans*-isomer via a BX_3 mediated pathway. Whilst several other possible pathways were investigated, such as the Nazarov type *cis/trans* conversion shown in Figure 4.7, they involved very high (50 kcalmol^{-1} or more) energy barriers, indicating that isomerisation through direct rearrangement of the product is unlikely.

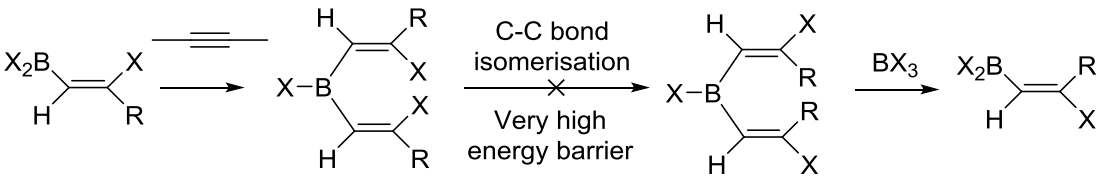


Figure 4.7: Unfavourable *cis*/*trans* isomerisation pathway

The BX_3 mediated mechanism for *cis/trans* was proposed to go via haloboration of the alkene, which allows access to the *trans*-isomer due to the relatively lower activation energy of the C-C bond rotation in the transition state shown in Figure 4.8. This is followed by elimination of the BX_3 in a retrohaloboration reaction, affording the *trans*-isomer. Whilst the stereostructure

of the product is controlled by thermodynamics, the nature of BX_3, specifically the halides, affects the kinetics. The chloroboration of the haloborated alkene is unfavourable due to a high energy barrier, but the bromo- and iodoboration have lower energy barriers, consistent with experimentally observed data that less Lewis acidic boron trihalides under milder conditions supress this isomerisation and the trans-isomer is not observed.

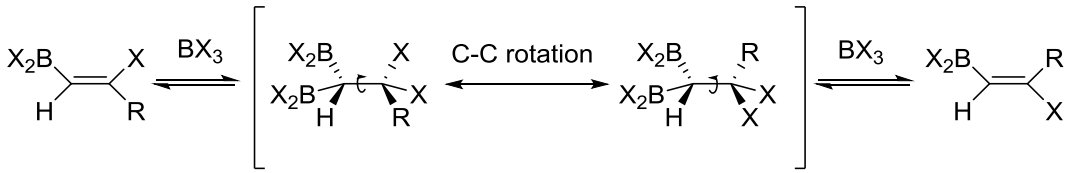


Figure 4.8: *cis*/*trans* Isomerisation of the haloboration reaction

In addition, theoretical studies compared haloboration to haloalumination and halosilation of a terminal alkyne. The hypothetical haloalumination reaction with Al_2Cl_6 was found to be energetically unfavourable, with the haloaluminated alkene being far less stable than the comparable haloborated product, most likely due to the comparatively reduced C-Al bond strength. With the halosilyation, the reaction was shown to proceed in a similar pathway to haloborations, but a high activation barrier ($\Delta E^{\ddagger}$ = 44.1 kcal mol^{-1} and $\Delta G^{\ddagger}$ = 48.5 kcal mol^{-1}, starting material set to zero) makes the reaction kinetically unfavourable. This suggests that haloboration is superior in regards to other (proposed) non-catalysed element-metalation reactions due to its favourable kinetics and thermodynamics, albeit limited to terminal alkynes currently.

4.2 Haloboration of Terminal Alkynes with borocations

Following the discovery that the [CatB(2DMAP)][$AlCl_4$] system underwent dehydroboration with terminal alkynes, related borocations were investigated initially to expand the scope of reactivity and avoid the necessity of heating and long reaction times. In order to make the borocation more electrophilic, the catechol ligand was exchanged for two chloride groups. As a third row element, chlorine has a poorer π overlap with boron compared to the oxygens of catechol. The resultant increased electrophilicity was expected to increase the rate of reaction, and allow expansion of the substrate scope to more π nucleophiles. However, the question remained as to whether the dehydroborylation or a haloboration[10] product would be kinetically preferred.

The borocation [Cl_2B(2DMAP)][$AlCl_4$] was synthesised readily (as described in Chapter 2) and first reacted with ^{t}butylacetylene at room temperature in DCM. While the reaction proceeded swiftly and cleanly to a single product, NMR spectroscopy showed that dehydroboration had not occurred. The ^{1}H NMR spectrum showed a vinylic proton at δ_H 5.7 ppm, and the loss of the alkynyl resonance, confirming that the C-H bond was retained, but its chemical environment had changed. The product **4i**, prior to pinacol esterification, was successfully isolated and its crystal structure elucidated by single crystal X-ray diffraction, as shown in Figure 4.9. The observed product comes from the 1,2 haloboration reaction, with chloride migrating from boron to carbon.

Table 4.1	
Metric	(**4i**)
B1-C8	1.576(6) Å
B1-Cl1	1.817(5) Å
B1-N1	1.594(5) Å
B1-N2	1.722(5) Å
N1-C5	1.327(5) Å
N2-C5	1.457(5) Å
C8-C9	1.299(5) Å
C9-Cl2	1.779(4) Å
N1-B1-N2	79.9(2)°
B1-C8-C9-Cl2	-6.7(4)°

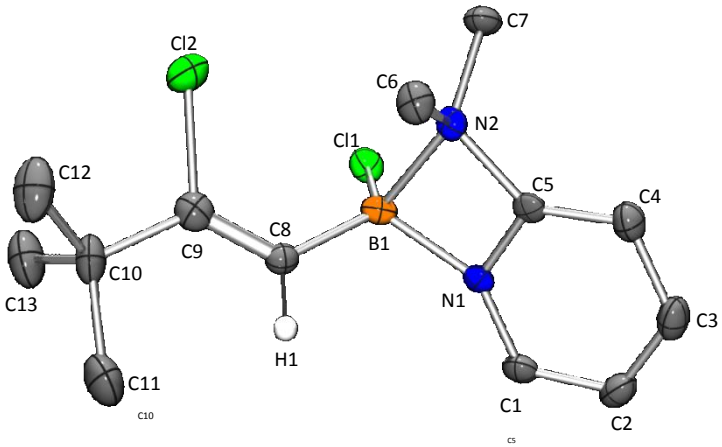


Figure 4.9: Structure of the product formed from $[Cl_2B(2DMAP)][AlCl_4]$ and ^{t}butylacetylene (**4i**) (thermal ellipsoids at 50% probability, anion and all protons bar H1 omitted for clarity. Full crystal data and structure refinements listed in Appendix)

The crystal structure showed that a *cis*-1,2-haloboration had occurred, and the product features a four-coordinate boron bound to the alkene. It was observed that the boron is bound to what was the terminal end of the alkyne, with the chloride migrated across the C=C bond, which is now 1.299(5) Å, in keeping with the expected length of an alkene. The B-C=C-Cl torsion angle is -6.7(4)°, the slight deviation from planarity may be due to steric interactions between the boron centre and the migrated halide. There is also a slight lengthening of both B-N bonds, compared to $[Cl_2B(2DMAP)][AlCl_4]$, most probably due to the reduction in Lewis acidity at boron due to the replacement of a chloride for a vinyl group.

As shown in Figure 4.10, the isolated intermediate can undergo esterification, yielding a pinacol boronate ester, which can be subsequently easily purified by filtration through silica to remove by-products, and dried *in vacuo* to remove solvent and excess base. This is advantageous, as the pinacol boron ester products are much more tolerant to ambient conditions and as such easier to handle. The borocation $[Cl_2B(2DMAP)][AlCl_4]$ was subsequently reacted with a range of terminal alkynes, giving haloboration products in good yields, as shown in Table 4.2.

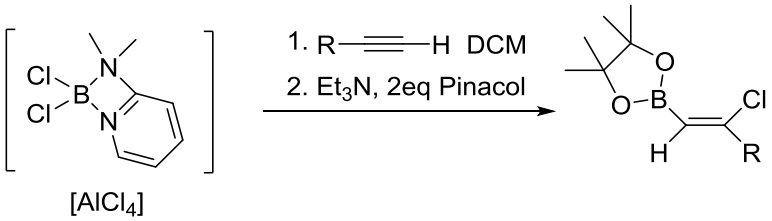
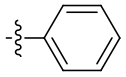
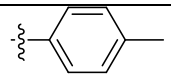
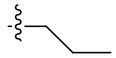
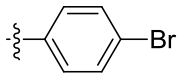


Figure 4.10: General reaction scheme of the haloboration of terminal alkynes with $[Cl_2B(2DMAP)][AlCl_4]$

Table 4.2		
Entry	**Substrate R-Group**	**Isolated Yield %**
4ii		63
4iii		88
4iv		65
4v		73
4vi		68

Reaction conditions were found to be mild, proceeding rapidly to completion at room temperature, and there were virtually no competing reactions observed by NMR spectroscopy, allowing isolation of pure products in good yields. It was observed in one reaction, that there was an additional vinylic resonance in the ^{1}H NMR spectrum. It was reasoned that double haloboration was occurring, with each molecule of $[Cl_2B(2DMAP)][AlCl_4]$ reacting with two molecules of alkyne, thanks to the two chloride groups present on boron. As there was a mixture of mono- and double haloborated products *in situ*, it was speculated that the other vinylic resonance associated with double haloboration was coincident with the monohaloboration species.

By modifying the reaction conditions to include an extra equivalent of alkyne, the second vinylic resonance in the ^{1}H NMR spectrum became more prevalent. This reactivity is similar to that reported by Lappert for the reaction between boron trihalides and terminal alkynes.[1] The double addition product, once subjected to esterification conditions, was no longer observed. This is most likely due to one of the B-C bonds being cleaved and loss of a volatile vinylmoiety.

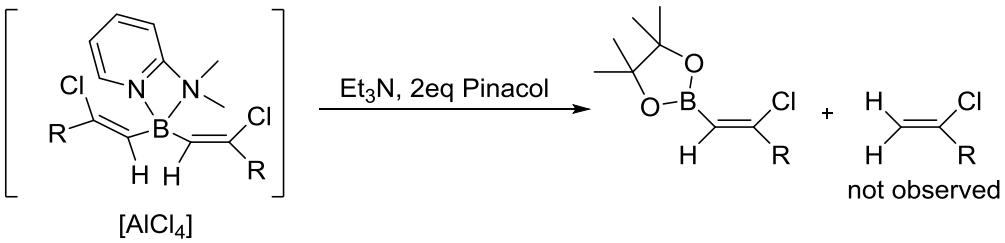


Figure 4.11: Esterification of the double addition product

During the expansion of the substrate scope it was discovered that diynes 1,6-heptadiyne and 1,7-octadiyne were incompatible with $[BCl_2(2DMAP)][AlCl_4]$ and

the haloboration reaction, leading to completely intractable mixtures. These diynes were initially chosen to investigate if haloboration or if cyclisation would occur, as there is literature precedence for these diynes to undergo cyclisation reactions with boron Lewis acid FLPs, as shown in Figure 4.12.[11] More successful reactions involving diynes are discussed later in this chapter.

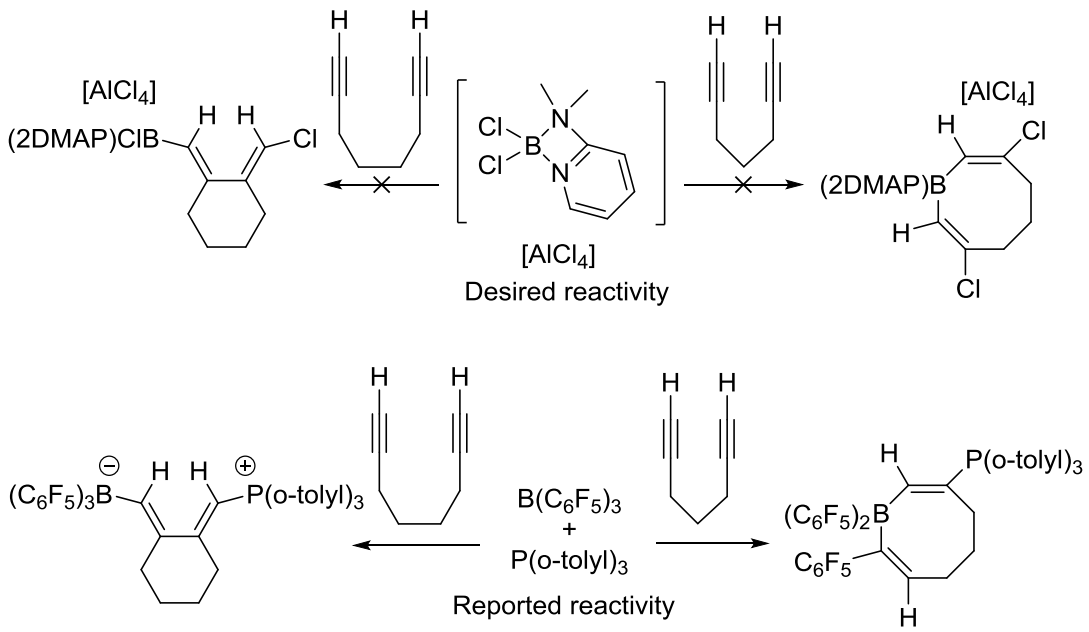


Figure 4.12: Desired and reported cyclisations of diynes with FLPs

Whilst $[Cl_2B(2DMAP)][AlCl_4]$ represents a new way to access haloborated alkenes from terminal alkynes, BCl_3 can also be used to achieve the same products. The borocation possesses some advantageous properties compared to BCl_3, chiefly being more tolerant to ambient conditions. Allowing a sample of $[Cl_2B(2DMAP)][AlCl_4]$ to be exposed to air when weighed using normal laboratory equipment, it was shown by both ^{1}H and ^{11}B NMR spectroscopy that the borocation was unchanged. The same sample was then stored in a sample vial overnight under ambient atmosphere not inert atmosphere, and NMR spectra run again. A small

quantity (~5%, observed by ^{11}B NMR spectroscopy) had decayed from exposure to moisture in the air. Thus, $[Cl_2B(2DMAP)][AlCl_4]$ was shown to be sufficiently air stable to be used in ambient atmosphere for short periods of time, but should be stored under inert atmosphere when not in use. A sample of the borocation was also heated to 60°C in DCM in a sealed tube for one week, and NMR spectroscopy showed virtually no decay of the reagent, demonstrating its thermal stability over extended periods of time.

In order to see why the reactions of $[Cl_2B(2DMAP)][AlCl_4]$ with alkynes was yielding 1,2-addition products, and to compare the mechanism to that of BCl_3, computational studies were performed on the haloboration reaction of phenylacetylene. These were performed at the (M06-2X/6-311G(d,p))(PCM, DCM) level by Dr Ewan Clark, and were useful in seeing if the reaction was concerted (concomitant B-C and C-Cl formation) or step-wise. The results are shown in the energy level diagram in Figure 4.13.

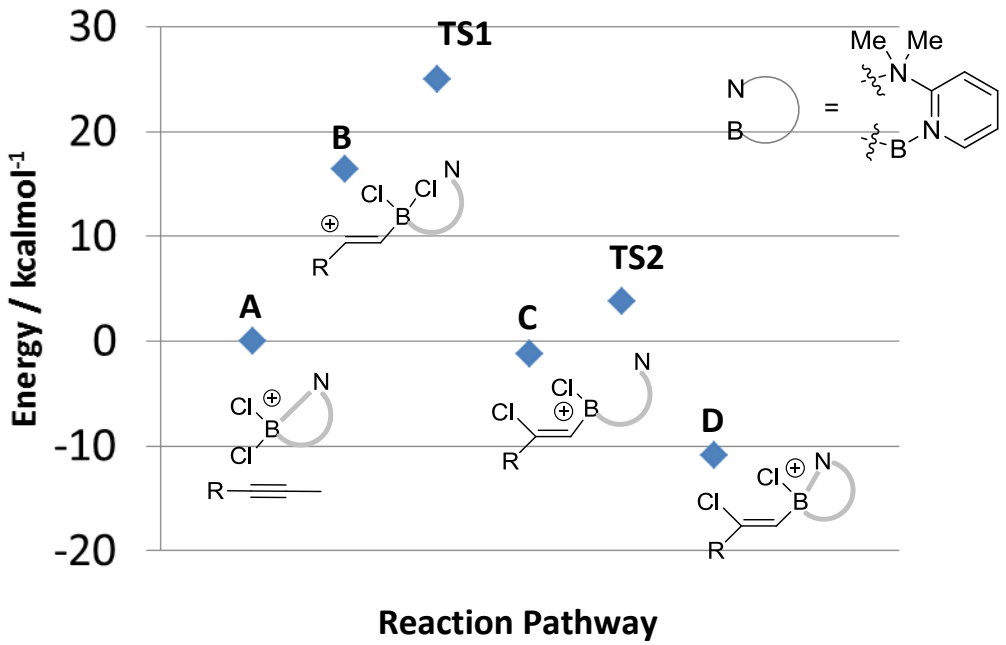


Figure 4.13: Energy level diagram of the reaction pathway of haloboration

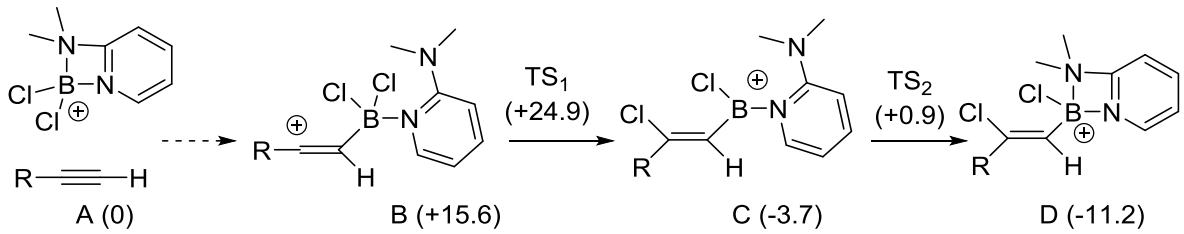


Figure 4.13: Energy level diagram of the reaction pathway of haloboration

The reaction was found to be step-wise, in contrast to the BCl_3 haloboration. It begins with a concerted ring opening and initial complexation of boron to the alkyne to form the vinyl cation. From here, the halide migrates, followed by a separate ring-closing step to give the 1,2 haloboration product. These studies showed that the reaction was indeed likely to be stepwise, with no alternate pathways featuring concerted C-Cl or B-N bond formation found.

It can be seen on the energy level diagram that **A** and the chloro-migrated, ring open intermediate **C** are almost the same in energy (0 and -3.7 kcalmol^{-1}, respectively). Thus, it may be the case that they exist in equilibrium, and that the final step of ring closing is needed to trap the product in a more stable form. It is also worth noting the energy of the first transition state, 24.2 kcal mol^{-1} which, assuming the reaction is first order, equates to a half-life of ~18 hours, consistent with each reaction being observed to proceed to completion within 24 hours.

It was postulated that an alternative mechanism may exist where the halide transfer step of the reaction may be via a halide shuttling agent, such as the [$AlCl_4$] counterion. Although during the course of haloboration reactions with [$Cl_2B(2DMAP)$][$AlCl_4$] the ^{27}Al NMR spectrum exclusively shows $AlCl_4$, this does not preclude the reactivily entirely. In order to demonstrate the anion independence of the haloboration reaction, [$Cl_2B(2DMAP)$][BArCl] was synthesised and reacted with

1-pentyne. The reaction pathway shown in Figure 4.14 is based on consumption of alkynyl peak and growth of vinylic peak in the ^{1}H NMR spectrum over time, expressed as a percentage. The rates of reaction are almost analogous, suggesting that the anion plays a minimal part in the reaction.

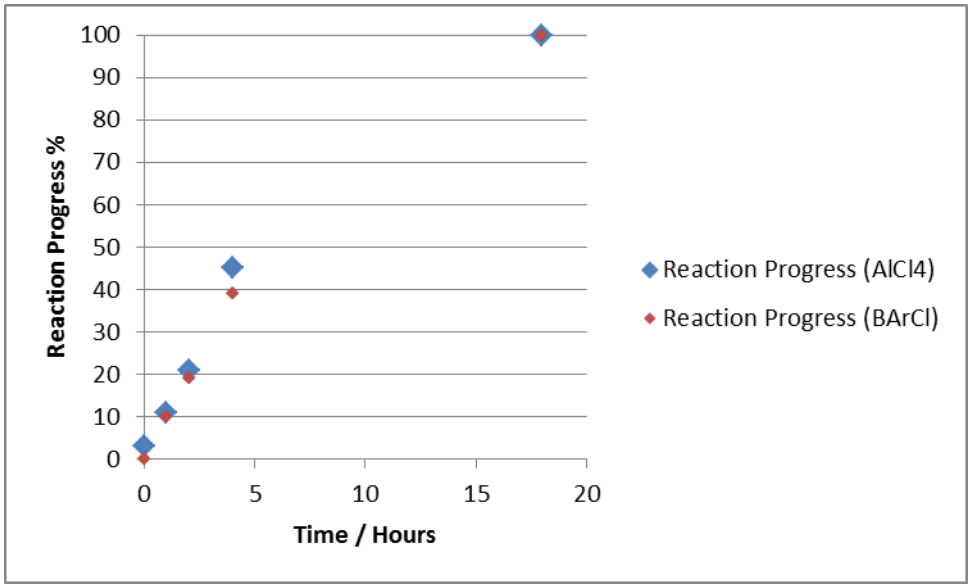


Figure 4.14: Reactivity of 1-pentyne with $[Cl_2B(2DMAP)][AlCl_4]$ versus $[Cl_2B(2DMAP)][BArCl]$

With $[Cl_2B(2DMAP)][AlCl_4]$ successfully undergoing haloboration with several terminal alkynes, it was wondered if modification of the borocation would allow carboboration, with an aliphatic or aromatic group migrating instead of chlorine. There is precedent for this, with phenylboration of a small number of alkynes with Ph_2BCl.[1] Thus, $[PhClB(2DMAP)][AlCl_4]$ was synthesised, with its structure and desired reactivity is shown in Figure 4.15.

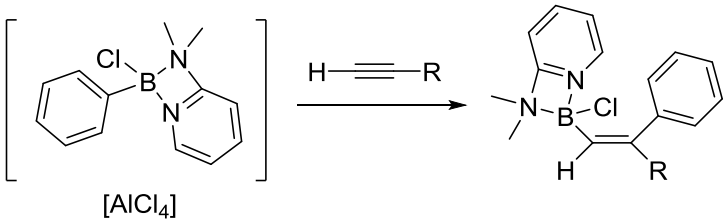


Figure 4.15: Structure and desired carboboration reactivity of [PhClB(2DMAP)][$AlCl_4$]

Upon reaction of [PhClB(2DMAP)][$AlCl_4$] with ^{t}butylacetylene, it was found that the B-Ph bond did not break as hoped, and haloboration occurred exclusively. Upon addition of a second equivalent of ^{t}butylacetylene, there was no observed phenylboration either, possibly as a result of reduced Lewis acidity at boron, which has no remaining halides bound. It was also found that the haloborated alkyne could not be isolated as a pinacol boronate ester. On esterification, the halogenated alkene was lost preferentially by protodeborylation and the product isolated was PinBPh, as shown below in Figure 4.16. More successful uses of this boronium are documented in Chapter 5.

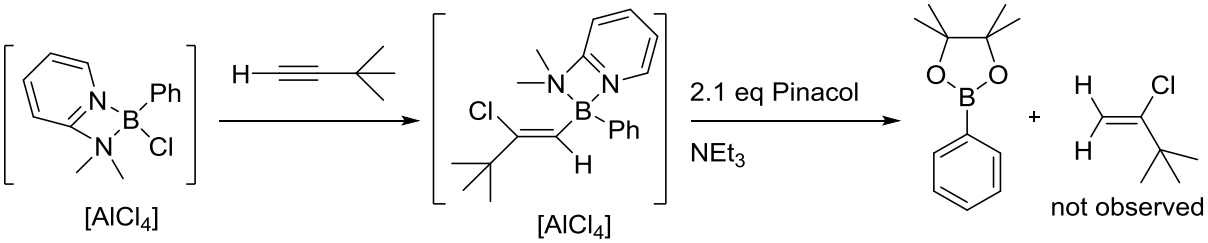


Figure 4.16:Reactivity of [PhBCl(2DMAP)][$AlCl_4$] with ^{t}butylacetylene

With the 2DMAP ligated boroniums undergoing haloboration with terminal alkynes, it was postulated that modification of the borocation would allow the reactivity to be extended to internal alkynes. With the [Cl_2B(2DMAP)][$AlCl_4$] boronium forming the 1,2-haloboration products, internal alkynes represented the

next step in the investigation, as these were previously not reported to undergo haloboration. It was hoped that increasing electrophilicity at boron would improve substrate scope compared to haloborations with BCl_3 and BBr_3.

To begin with, control reactions were performed between $[Cl_2B(2DMAP)][AlCl_4]$ and both 3-hexyne and diphenylacetylene, using the same conditions as with terminal alkynes. Neither reaction proceeded to the intended haloborated product. By monitoring the reaction progress by NMR spectroscopy, it was observed that over time the ^{1}H NMR spectra showed desymmeterisation of the ethyl groups on 3-hexyne, but instead of the four expected aliphatic resonances consistent with a single haloborated product, many were present. The ^{11}B NMR spectra also showed a majority of starting material, with several smaller resonances growing in. After five days no more changes were present in either spectrum. It was concluded that the borocation was not electrophilic enough to react to completion with the internal alkynes, instead forming a small amount of multiple products. Hence the chlorides on boron were substituted with bromides, as the π overlap between boron and bromine is even lower than that between boron and chlorine, providing a weakened B-X bond so as to promote halide transfer. Thus the reactivity of the bromo-analogue of $[Cl_2B(2DMAP)][AlCl_4]$, $[Br_2B(2DMAP)][BBr_4]$ was examined.

$[Br_2B(2DMAP)][BBr_4]$ was first reacted with the terminal alkyne 1-pentyne, in order to test if analogous haloboration reactivity occurred. Unsurprisingly, the 1,2-bromo-boronate ester **4vii** was successfully synthesised in high yield (78%) post esterification with the structure confirmed by NMR spectroscopy. Following this,

further reactions were conducted with the same two internal alkynes. With 3-hexyne, the reaction produced a major product consistent with the desired haloborated species, but other minor resonances were also present in the ^{1}H NMR spectra. When the crude product was separated by column chromatography, the major fraction isolated was shown to be the 1,2-haloboration product **4viii**, isolated in 62% yield, as shown in Figure 4.17.

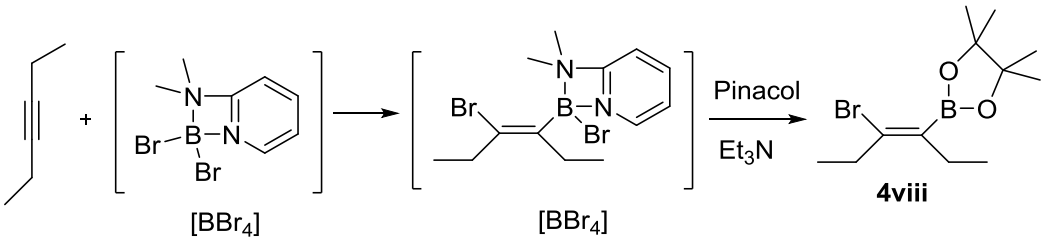


Figure 4.17: Reaction of $[Br_2B(2DMAP)][BBr_4]$ with 3-hexyne

Additionally, it was shown that the internal alkyne 2-methyl-4-pentyne was susceptible to haloboration with $[Br_2B(2DMAP)][BBr_4]$, resulting in **4ix**, isolated in 52% yield) shown below in figure 4.16. Although the product still had to be purified by column chromatography, only a single major product was isolated. The other possible *cis*-haloboration product was not observed, with nOe spectroscopy confirming the stereo- and regiochemistry of **4ix**. The selectivity observed is attributed to both sterics and electronics, where the boron containing group is further away from the bulky isopropyl group, and the electronic stabilisation of the carbocation formed prior to halide transfer is maximised. The most stable vinyl carbocation is adjacent to the isopropyl group, as it is stabilised by a greater degree of hyperconjugation.

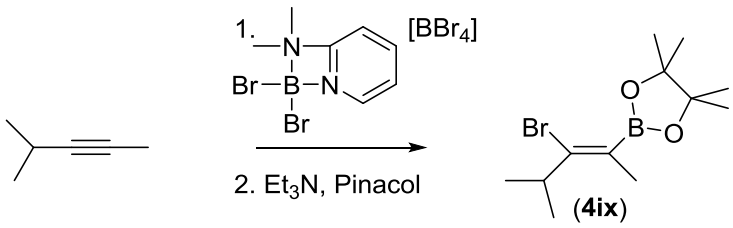


Figure 4.18: Reaction of $[Br_2B(2DMAP)][BBr_4]$ with 2-methyl-4-pentyne

It has been documented that BCl_3 does not react with internal alkynes,[8] because it is not Lewis acidic enough. BBr_3 has been shown to react with some internal alkynes, but slowly, and forming a mixture of products. $[Br_2B(2DMAP)][BBr_4]$ represents a novel borocation that can access these orthogonally functionalised alkenes, in good yields, which have a wide application in synthesis, such as in the synthesis of drug molecules. As shown in Figure 4.19, both Clomifene and Tamoxifen share a tetra-substituted alkene backbone, and using the correct internal alkyne with a haloboration reagent followed by two Suzuki-Miyaura[12] cross-couplings could represent a new way to these drugs.

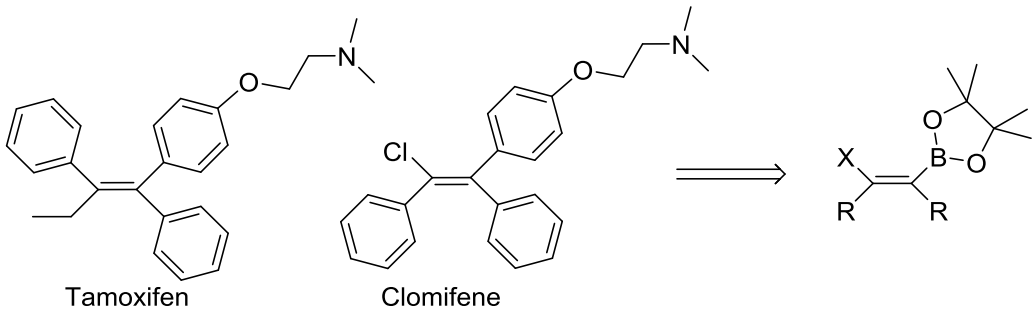


Figure 4.19: Proposed retrosynthesis of drug molecules featuring tetra-substituted alkene backbone

It was discovered through attempted reactions with diphenylacetylene that $[Br_2B(2DMAP)][BBr_4]$ was unable to react with this diarene substituted alkyne, as NMR spectroscopy showed only starting materials after 72 hours. It was surmised

that $[Br_2B(2DMAP)][BBr_4]$ is electrophilic enough to react with the most nucleophilic alkynes,[13] such as 3-hexyne, but is limited to a small scope of internal alkynes. Thus, a new borocation reagent was required. With computational studies showing that the NMe_2 side-arm of 2DMAP was not necessary for the reaction, and merely served to reduce the electrophilicity of boron in the ring opened form by enhancing the N→B π donation, the amine base was swapped.

4.3 Haloboration of Internal Alkynes

In the search for a borocation capable of undergoing haloboration with a wide range of internal alkynes, it was decided to replace the 2DMAP with a new base to increase Lewis acidity at boron. Initial attempts using *N,N*-dimethyl-*p*-toluidine (DMT) ligated borocations resulted in polymerisation of the alkyne, which may be due to a different equilibrium position of the DMT-BCl_3 and $AlCl_3$ mixture, resulting in aluminium Lewis acids causing the unwanted reactivity. A bulkier and more nucleophilic Lewis base was therefore required to shift the equilibrium towards the borocation, and so 2,6-lutidine was chosen, as a bulky mild base and weak nucleophile.

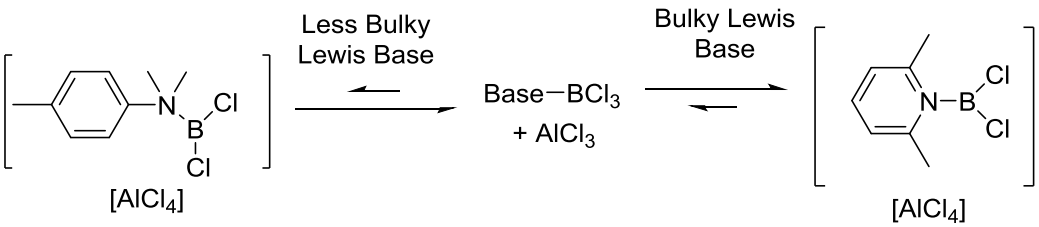


Figure 4.20: Equilibrium of boroactions and adducts

As discussed in Chapter 2 the $LutBCl_3$ adduct was first readily isolated as an easily handled solid, allowing exact control of stoichiometry, then the borenium $[LutBCl_2][AlCl_4]$ was generated by addition of one equivalent of $AlCl_3$ in a solution of DCM, forming the active species. When combined with phenylacetylene, the borocation reacted rapidly, with complete consumption of the alkyne within 4 hours at room temperature, as monitored by ^{1}H and ^{11}B NMR spectroscopy (the ^{27}Al spectra remained unchanged throughout, showing only $[AlCl_4]^-$). The result was once again the 1,2-haloboration product in comparable yield to that with

$[Cl_2B(2DMAP)][AlCl_4]$, and was slightly easier to purify due to 2,6-lutidine's lower boiling point compared to 2DMAP, facilitating quicker removal *in vacuo* post esterification.

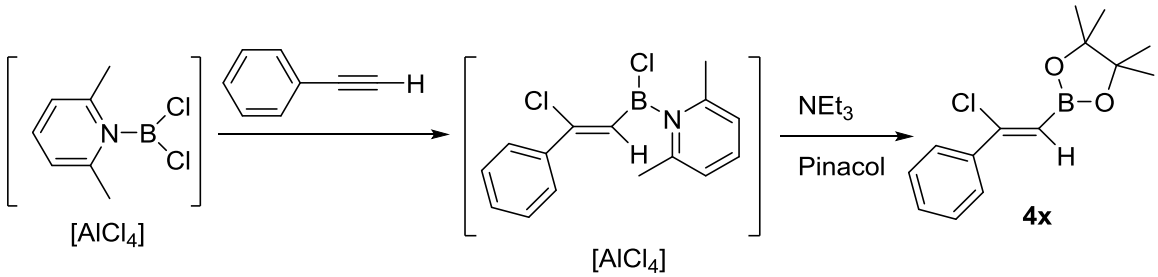


Figure 4.21: Haloboration of phenylacetylene using $[LutBCl_2][AlCl_4]$

In addition to this, the reaction between $[LutBCl_2][AlCl_4]$ and phenylacetylene was repeated, but instead of esterification with pinacol once haloboration was complete (as determined by multinuclear NMR spectroscopy), the reaction mixture was heated in a sealed tube at 60°C for 85 hours. NMR spectroscopy showed almost no change, indicating a high level of thermal stability of the haloboration product. It also suggests that the haloboration product is the thermodynamic, and not the kinetic product.

To begin probing the substrate scope, and the feasibility of the haloboration of internal alkynes, $[LutBCl_2][AlCl_4]$ was then reacted with 3-hexyne, which pleasingly gave the 1,2-haloboration product. Unlike the reaction between $[Br_2B(2DMAP)][BBr_4]$ and 3-hexyne, purification by column chromatography was not necessary, as a single product was formed within 24 hours stirring at room temperature. Following this, the reaction of $[LutBCl_2][AlCl_4]$ with other internal alkynes was probed.

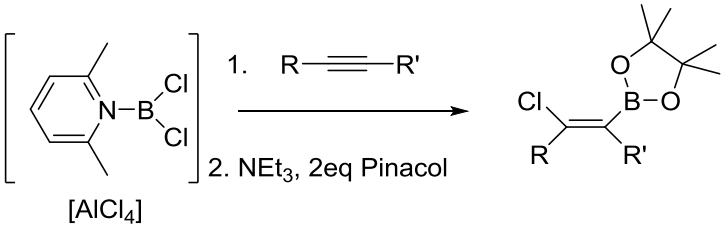
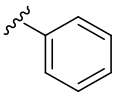


Figure 4.22: General haloboration of internal alkynes

Table 4.3				
Entry	**R**	**R'**	**t [h]**	**Isolated Yield [%]**
4x			4	71
4xi			24	81
4xii			48	83
4xiii			n/a	n/a

As seen in Table 4.3, the $[LutBCl_2][AlCl_4]$ borenium will undergo haloboration with internal alkynes featuring linear alkyl groups, and the branched isopropyl group. However, multiple attempts at the clean haloboration of an internal alkyne featuring a ^{t}butyl group failed (Entry **4xiii**). Whilst reactivity was observed, it was not clean haloboration, as after 18 hours several new aliphatic resonances were observed, along with at least four resonances in the ^{11}B NMR spectrum. Attempts to esterify this mixture gave an intractable mixture of products. This could imply that the steric bulk of the ^{t}butyl group is inhibiting the initial reaction between the alkyne and the borocation, or that there is loss of a relatively stable $^{t}Bu^{+}$ cation, and more complex reactivity associated with this event. The unidentified reactivity persisted when the reaction was left longer than the usual time window (>72 h),

generating several boron-containing species. Efforts to identify these compounds proved unsuccessful, as attempts at isolation both prior and post-esterification failed.

Following this, alkynes that were previously not amenable to haloboration with the $[Br_2B(2DMAP)][BBr_4]$ boronium were investigated, beginning with internal alkynes featuring aryl groups. As shown in Table 3.3, alkyl-aryl alkynes were reacted with $[LutBCl_2][AlCl_4]$ and gave the desired 1,2-haloboration product. The greater Lewis acidity of the borocation was apparent here, and haloboration occured with diphenylacetylene, which was shown to be unreactive towards previous borocations. Also demonstrated was the selectivity of the borocation; it reacted in preference with the alkyne over the arene substituents investigated.

As with the previous internal alkynes, selectivity was excellent, as both in situ and post esterification only a single major product is observed. Indeed, after a simple purification of flushing the product through a silica plug, only one compound was observed by NMR spectroscopy. The regio- and stereochemistry of the product was determined by electronic effects, with the most stable vinyl cation formed exclusively prior to halide transfer.

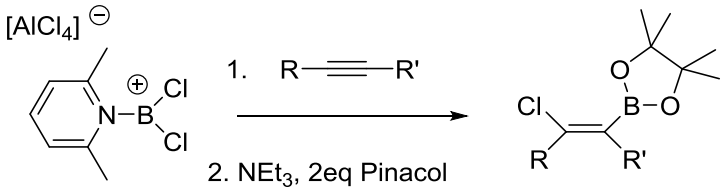
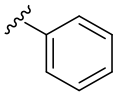
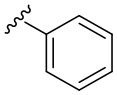
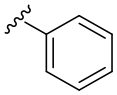
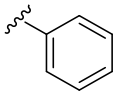


Table 4.4				
Entry	**R**	**R'**	**t [h]**	**Isolated Yield [%]**
4xiv			8	62
4xv			24	72
4xvi			48	43

Tolerance of functional groups was next explored, generating more complex haloborated products, as shown below in Table 4.5. 1-Bromo-2-phenylacetylene successfully underwent haloboration, forming an alkene with two different halogen substituents, allowing even more options for future functionalization via cross-coupling reactions. The conditions of C-C bond forming reactions could be modified to allow selective functionalization of the two halides, adding rich functionality. The remaining two entries are terminal alkynes, but were chosen to investigate if these functional groups were tolerant to reaction conditions.

The reaction of $[LutBCl_2][AlCl_4]$ with 2-ethynylthiophene proceeded at room temperature within 48 hours. The reaction was monitored by NMR spectroscopy which showed no reaction between the borocation and the thiophene moiety;

indeed the only product isolated was the desired 1,2-haloborated alkene. This further demonstrated the tolerance of the haloboration to activated heteroarenes. It was also decided to observe the tolerance of the borocation to a methoxy group, as aryl-ether groups are common in various drug molecules (e.g. Tamoxifen), hence 4-ethynyl anisole was chosen as a substrate. There existed the possibility that B-O bond formation may be one of the outcomes of this reaction; pleasingly the only isolated species post esterification was the haloboration product, albeit with minor ether cleavage products observed *in-situ*.

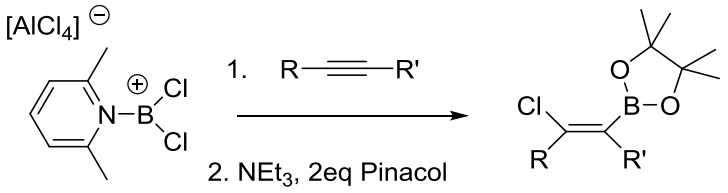
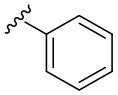
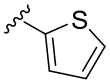
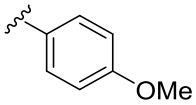


Table 4.5				
Entry	**R**	**R'**	**t [h]**	**Isolated Yield [%]**
4xvii			48	71
4xviii			48	65
4xix			4	52

Another family of alkynes that was investigated posessed alkenes within their structure, as shown in Table 4.6. An example of a non-conjugated skipped enyne and both a terminal and an internal conjugated enyne were utilised in order to probe the selectivity of $[LutBCl_2][AlCl_4]$ in regards to alkynes and alkenes. In all three reactions, there was no observable reaction between the borocation and the alkene; the corresponding vinylic protons remained intact in the ^1H NMR spectra recorded throughout the reaction, and single products were formed from 1,2-addition to each alkyne, with no 1,4-addition observed with conjugated enynes.

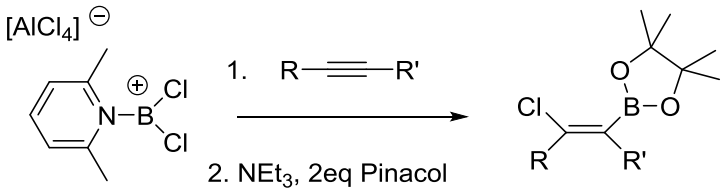
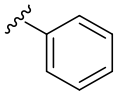
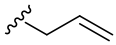


Table 4.6				
Entry	**R**	**R'**	**t [h]**	**Isolated Yield [%]**
4xx			48	61
4xxi			1	90
4xxii			4	53

The high selectivity observed in reactions of $[LutBCl_2][AlCl_4]$ with internal alkynes allows specific products to be isolated. Throughout all of the work on haloboration, the reaction has always proceeded *syn* in regard to addition of boron

and the halide, resulting in a 1,2-substituted alkene. The regioselectivity of the product is determined by the electronic effects maximising the stability of the vinylic carbocation intermediate. In the example of Table 4.6, Entry **4xx**, borylation occurs at the alkynyl carbon bound to the alkene. It was postulated that steric interactions between the methyl and ethyl group of the newly formed diene would force the two C=C bonds out of plane with each other. Computational studies performed by Dr Jessica Cid suggested that this is the case. Furthermore, if haloboration is reversible (see subsequent discussion for evidence to support this) the reaction allows the 2-boradiene to be isolated as a single product, as the right-hand pathway shown in Figure 4.23 is more energetically favourable as this haloboration product is lower in energy by 2.74 kcalmol^{-1}, as calculated at the M06-2X/6-311G(d,p)(PCM:DCM) level.

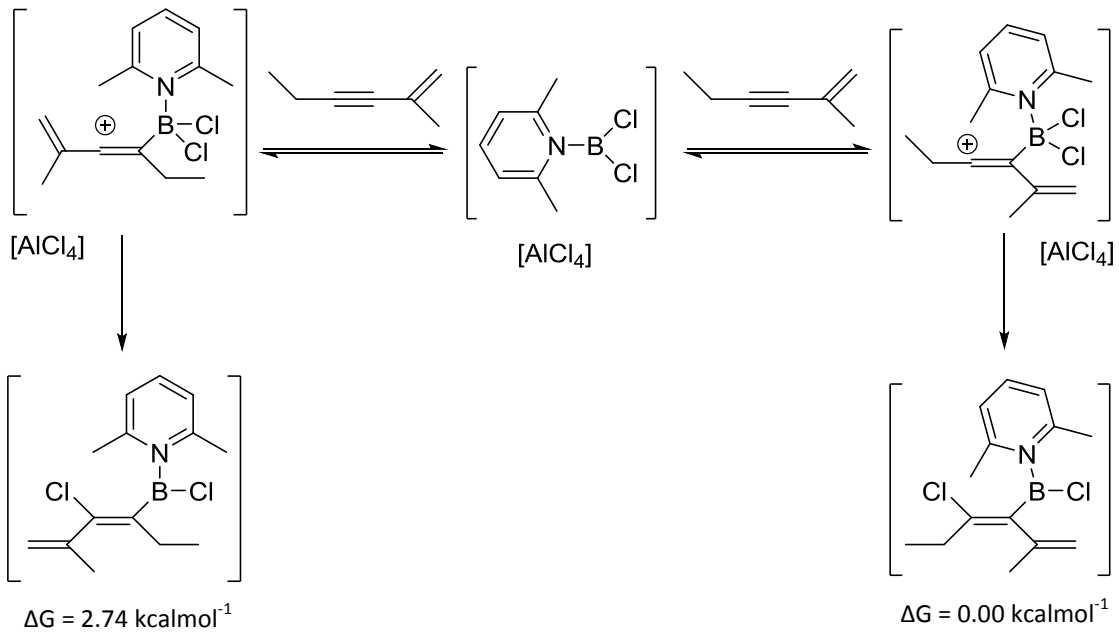


Figure 4.23: Haloboration of enyne 2-methylhex-1-en-3-yne

There is also a degree of steric control in haloboration, where boron can be observed at the least hindered end of the alkene formed. As mentioned above another interesting feature of this reaction is that haloboration may be reversible. After reaction with an internal alkyne (but before isolation via esterification), an equivalent of a more nucleophilic alkyne can be introduced. Within 6 hours at room temperature, there was observed by NMR spectroscopy complete displacement of the less nucleophilic alkyne, as shown in Figure 4.24. At no point was double haloboration observed, although it cannot be precluded completely, in contrast to the reaction of $[Cl_2B(2DMAP)][AlCl_4]$ where the double haloboration product was observed by NMR spectroscopy. The absence of spectroscopic evidence for a second haloboration indicates it is endergonic, possibly due to the lower nucleophilicity of the internal alkynes; upon the first haloboration, the boron is no longer Lewis acidic enough to react with a further equivalent of alkyne. It is also possible that the bulky 2,6-lutidine causes enough steric crowding around boron disfavouring a second haloboration reaction. Therefore, the observed reactivity in Figure 4.2.4 may be due to (i) a retrohaloboration and haloboration of a different alkyne or (ii) a haloboration to form a doubly haloborated product followed by a retro-haloboration.

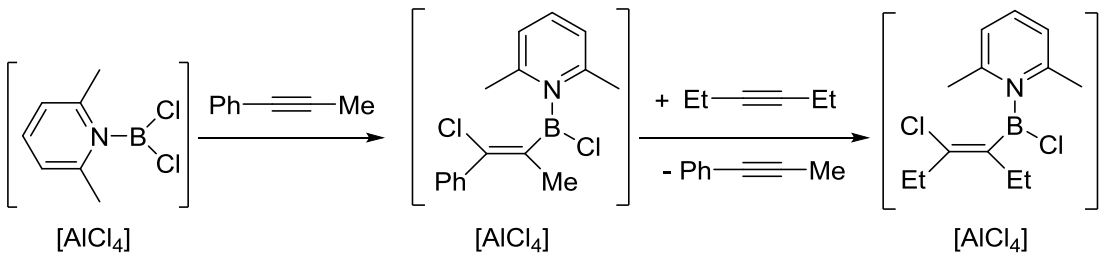


Figure 4.24: 'Reversibility' of haloboration

With a range of various 1,2-haloborated products now readily accessible, the use of the $[LutBCl_2][AlCl_4]$ borocation represents a new route to highly functionalised alkenes. Test reactions were also performed to investigate the versatility of the borocation. Scaling up the reaction by factors of 4 and 10 resulted in comparable yields of the 1,2-haloborated product, whilst the entire reaction (including synthesis of the borenium) can be carried out without use of a glovebox, with no observable impact on yield.

In order to demonstrate the utility of these 1,2-haloborated alkenes, cross-coupling reactions were undertaken to introduce new groups to the alkene. First, the boron group was targeted in a Suzuki-Miyaura reaction with 4-iodotoluene, which proceeded in excellent yield with no observable isomerisation, just replacement of BPin with the tolyl group, as shown in Figure 4.25.

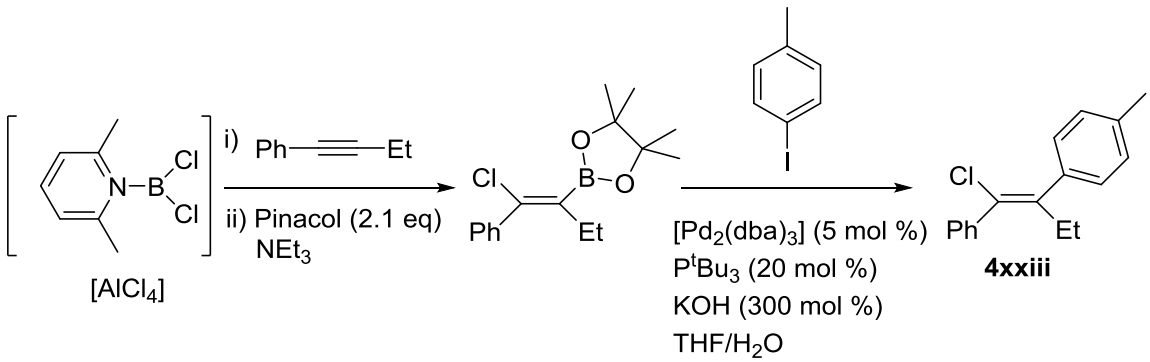


Figure 4.25: Cross-coupling reaction of vinyl boronate ester (**4xxiii**)

The alkene product was formed readily in 92% isolated yield, and represents a structural analogue of the anti-cancer drug, zuclomifene (Figure 4.26). It is, therefore, conceivable that this represents a simple, high-yielding, route to a single isomer of clomifene from an internal alkyne.

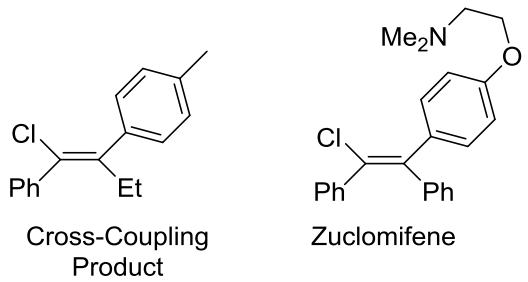


Figure 4.26: Structures of Tamoxifen and Zuclomifene

In order to see if both sites on the haloborated alkene could be functionalised, successive cross-coupling reactions were performed. Following the same procedure shown above in Figure 4.26, a Suzuki-Miyaura cross-coupling with 4-iodotoluene was first performed, followed by subsequent cross-coupling of the initial product with 4-fluorophenylboronic acid. This was performed without purification of the intermediates to see if the reaction could be undertaken in a 'one-pot' fashion. While these conditions remain unoptimised, due to the proof-of-concept nature of this reaction, the second coupling proceeded well, but with a minor side-product consisting of a second isomer. Using column chromatography, it was found that the ratio of product isomers was around 6:1, it is theorised that the second isomer forms as a result of the steric demand of the P^tBu_3 which may be inducing *cis-trans* isomerisation during the cross-coupling. A similar observation was reported by Suginome and co-workers in the coupling of chloroborane-tethered alkynes to make cyclic species, where the nature of the phosphine was used to control the stereochemical outcome of the reaction.[14] The choice of 4-iodotoluene and 4-fluorophenylboronic acid as cross-coupling reagents was purely to introduce groups that are easily identifiable by ^{1}H and ^{19}F NMR spectroscopy.

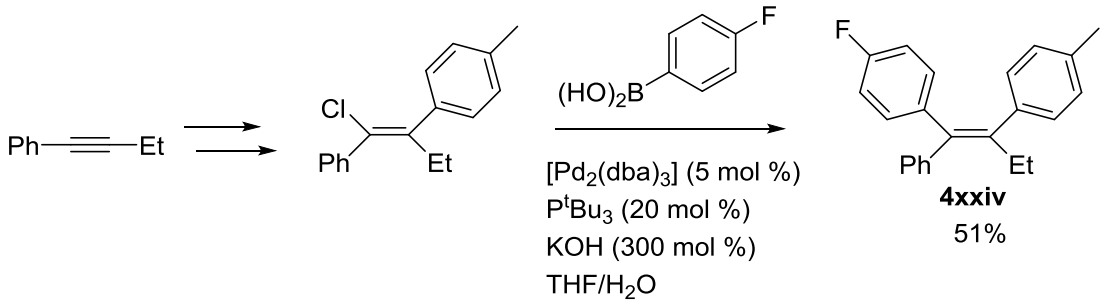


Figure 4.27: One-pot synthesis of a tetrasubstituted alkene

There were several examples of alkynes that did not react to give the expected haloboration product, but led, in some cases, to other interesting products. It has been demonstrated by Andrew Warner that using BCl_3 or some borocations, that cyclisations of alkynes of the general formula R-C≡C-$(CH_2)_2$-aryl can be accomplished, with an example shown below (Figure 4.28).[15] These form six-membered rings exclusively via 6-endo-dig cyclisations, and attempts to generate five- and seven-membered species with BCl_3 proved unfruitful.

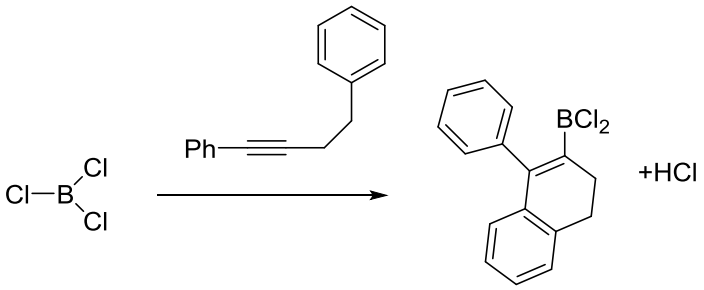


Figure 4.28: Cyclisation reactions with BCl_3

During the course of expanding the substrate scope of the haloboration reaction, it was proposed that the benzyl alkyne shown above could conceivably undergo cyclisation to generate five-membered cyclic products instead of haloboration.

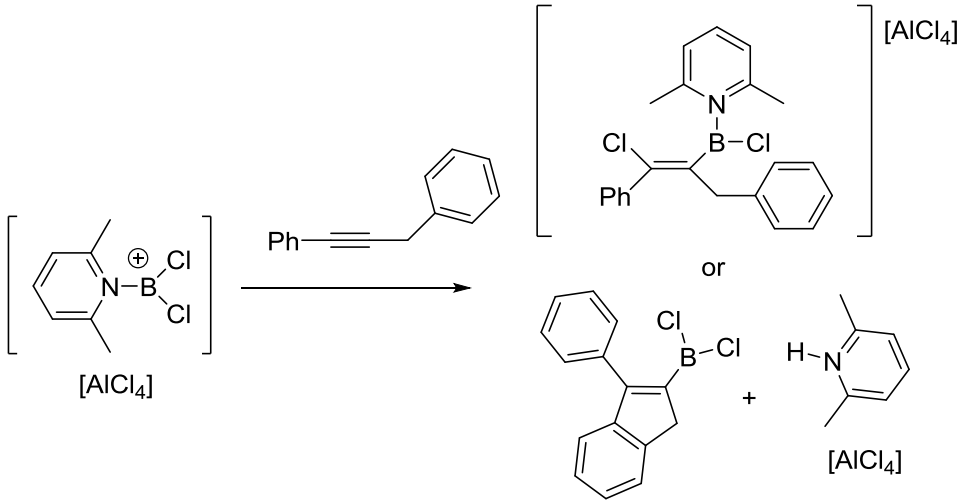


Figure 4.29: Proposed haloboration and cyclisation products

Upon reaction and esterification, a single Pin-B-vinyl species was observed by NMR spectroscopy. However, NMR spectroscopy was inconclusive as to whether the cyclisation product or the haloboration product had formed (Figure 4.29), but mass spectroscopy confirmed that the product observed was the cyclic species. The product proved difficult to purify, and optimisation of the reaction was discontinued.

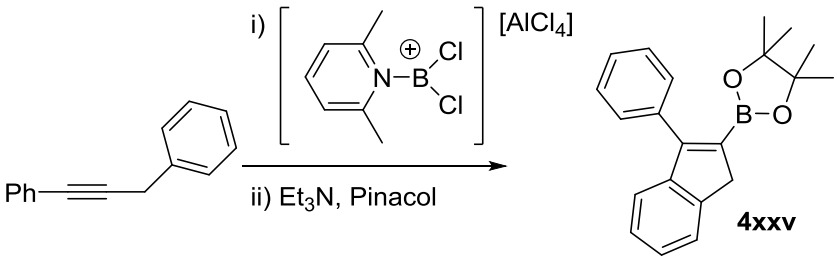


Figure 4.30: Cyclisation of internal benzyl alkyne

As previously mentioned in Chapter 4.2, the terminal diynes 1,6-heptadiyne and 1,7-octadiyne were reacted with $[Cl_2B(2DMAP)][AlCl_4]$, and gave complex mixtures of products as observed by NMR spectroscopy. The reaction of

$[LutBCl_2][AlCl_4]$ with 1,6-heptadiyne was very rapid, with complete dissolution of the borenium and a colour change to dark brown observed instantly. The ^{1}H NMR spectrum showed that all of the diyne was consumed, but multiple vinyl peaks are now observed, and the aliphatic region becomes broad with multiple signals. The ^{11}B NMR spectrum showed a single broad resonance at 50.0 ppm, inconsistent with haloboration which generates a resonance in the region of 46 ppm. Esterification with pinacol and triethylamine gave a mixture of products, with at least nine distinct vinyl resonances. Attempts at separation via column chromatography proved unsuccessful, with no specific products isolated.

Switching the alkyne to 1,7-octadiyne showed a comparable reaction, albeit at a slower rate. The ^{1}H NMR spectrum presents a broad and ill-defined aliphatic region, making it difficult to determine if all the diyne has been consumed. The ^{11}B spectrum meanwhile shows a new resonance at 50.5 ppm, similar to that of the previous reaction. After 18 hours the reaction had ceased, before complete consumption of the borocation. When the sample was esterified and purified via column chromatography, a very small amount of a single product was obtained. The ^{11}B spectrum shows predominantly a major peak at 29.1 ppm, roughly consistent with vinylBPin products obtained using $[LutBCl_2][AlCl_4]$ (~30 ppm). The ^{1}H NMR spectrum now shows two separate vinylic resonances. Further analysis proved difficult as the product was unstable. Whilst the reaction was repeated to obtain the mixture of crude products, repeated purifications did not give a single product again.

Whilst investigating the reactivity of diynes with borocations, control reactions between BCl_3 and both 1,6-heptadiyne and 1,7-octadiyne were carried out. It was found that the reaction with 1,6-heptadiyne initially gave a single product by NMR spectroscopy. Two vinylic protons were present, which each integrated as 1H to a new set of aliphatic protons corresponding to the three CH_2 groups of the molecule. It was found that if left overnight new products are formed in a complex mixture, so the initial product was isolated via esterification and examined. The ^{1}H NMR spectrum showed that the species observed *in-situ* had been successfully pinacolated, as the vinylic and aliphatic resonances persisted. In addition to them, a new peak at 1.27 ppm indicated a pin-B group, with a resonance in the ^{11}B spectrum at 29.8 ppm supporting this. The ^{13}C spectrum showed two resonances consistent with pinacol, along with three additional aliphatic carbons associated with the three CH_2 carbons. In addition to these three distinct vinyl carbons are observed, and it was initially thought that, as with previous borylated alkenes, the carbon bound to boron is not observed due to quadrapolar relaxation. However, upon inspection of the HMQC spectrum the fourth vinyl carbon is observed as a broad peak at 115.3 ppm, correlating to the vinyl proton peak at 5.01 ppm in the ^{1}H NMR spectrum.

Further analysis by GC/MS showed that a chloride had been incorporated into the structure; however the presence of two vinyl and absence of any alkynyl protons in the ^{1}H NMR spectrum precludes a simple haloboration reaction, while the mass spectroscopy indicates that it is also not a double haloboration. Instead it was reasoned that a cyclisation had occurred. COSY NMR analysis confirmed the

stereo- and regioconformation of **4xxvi**, in combination with nOe, HMQC and HMBC data.

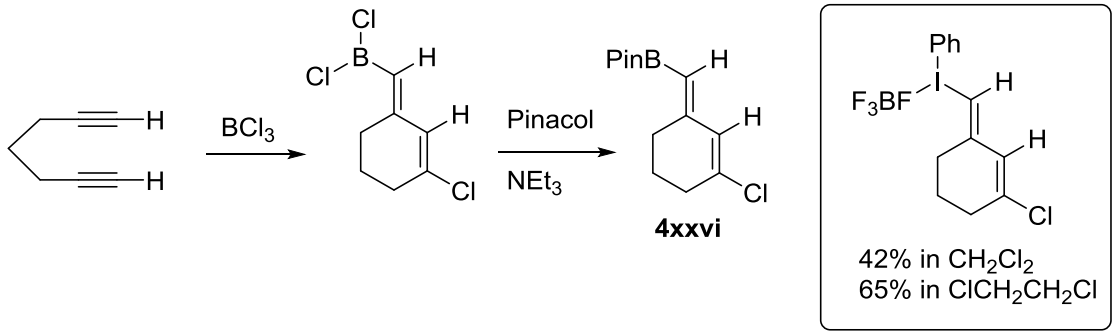


Figure 4.32: Cyclisation of 1,6-heptadiyne

Precedence for this reactivity was found, wherein 1,6-heptadiyne was exposed to iodosylbenzene in the presence of BF_3-Et_2O in DCM, which afforded a similar cyclic diene product containing a vinyl chloride moiety, insert Figure 4.31.[16] In this reaction it was surmised that the chloride was delivered to the vinyl carbocation from the halogenated solvent; indeed, when the reaction was repeated in the more nucleophilic dichloroethane the yield of the cyclisation product increased (Figure 4.32, inset).

In order to see if the halide transfer was solvent mediated in the case of 1,6-heptadiyne and BCl_3, the reaction was repeated with the BCl_3 used now as a 1M solution in heptanes and the solvent o-DCB. Obtaining useful *in situ* NMR data proved difficult due to solubility issues, but after esterification it was observed that, whilst the cyclisation product was still obtained, it was a very minor product, with other new products observed instead. These multiple products proved intractable, although both featured a vinyl-Bpin group according to ^{1}H and ^{11}B NMR spectroscopy. It is reasonable to assume that the vinyl carbocation, unable to readily receive a halide from solvent, is intercepted by another species.

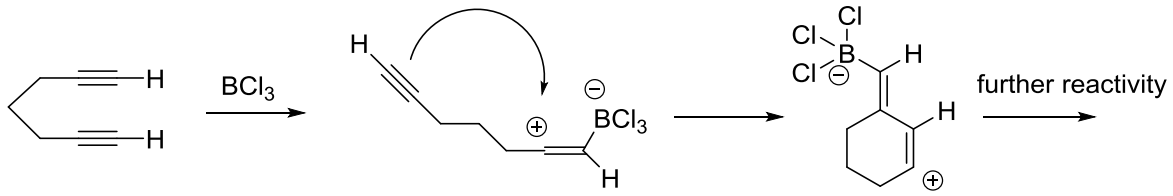


Figure 4.32: Proposed mechanism for the cyclisation of 1,6-heptadiyne

The reactivity of BCl_3 with diynes was extended to 1,7-octadiyne, but instead of a single product being formed as with 1,6-heptadiyne, NMR data suggested several were forming. The *in situ* ^{11}B NMR spectrum taken after one hour showed a new broad peak at 50.1 ppm, whilst in the ^{1}H spectrum the previously clearly defined aliphatic CH_2 resonances collapsed into a broad, complex series of peaks. In addition, two vinylic resonances were observed at 6.32 and 6.16 ppm; their inequivalent integrals indicating that they belong to separate molecules.

The reaction was repeated with esterification performed immediately. Following work up the NMR spectra showed a broad resonance at 29.4 ppm, and whilst this is consistent with a vinyl-Bpin species, the ^{1}H NMR spectrum showed extremely broad, undefined resonances in the aliphatic region and at least five distinct vinylic species. Attempts to separate these species by column chromatography proved unsuccessful. It is probable that there are multiple reaction pathways that can be followed.

Following this, two new diynes were synthesised from 1,6-heptadiyne and 1,7-octadiyne via a Sonogashira reaction.[17] This produced 1,7-diphenyl-1,6-heptadiyne and 1,8-diphenyl-1,7-octadiyne, as shown in Figure 4.33 below, and both of these new internal diynes were reacted with several boron reagents.

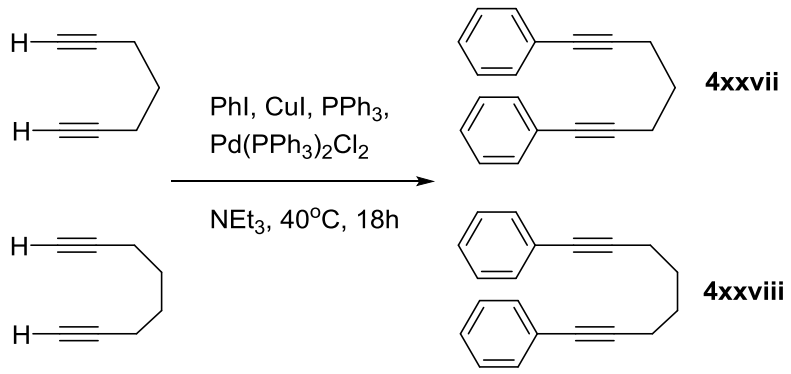


Figure 4.33: Synthesis of diphenyl-diynes

When BCl_3 was reacted with 1,7-diphenyl-1,6-heptadiyne, a rapid reaction was observed by NMR spectroscopy, with complete consumption of the diyne within 1 hour, with additional resonances growing in over extended periods. The ^{11}B NMR spectrum showed a new resonance at 58.0 ppm, indicative of a vinyl-BCl_2 species. It was proposed that an electrophilic aromatic substitution was occurring, generating HCl, which may be the cause of the additional resonances growing in over time in the ^{1}H spectrum (e.g., protodeboronation due to HCl remaining in the sealed tube). Subsequently, the reaction was modified to sequester HCl by the addition of the non-coordinating base, 2,4,6-tri-*tert*-butylpyridine.

When the reaction was repeated in the presence of base, the ^{1}H NMR spectrum showed complete consumption of the diyne within 1 hour, as before, but also that the majority of the 2,4,6-tri-*tert*-butylpyridine was now protonated. Hence the reaction was esterified with pinacol and purified by filtration through a silica plug. It was found that an acid wash was also necessary to remove by-products derived from the base. NMR analysis of the esterified product showed that a vinyl-BPin species was present, as indicated by a peak at 31.2 ppm in the ^{11}B NMR spectrum and a 12H peak at 1.32 ppm in the ^{1}H spectrum. In addition to this, three

2H aliphatic resonances at 2.61, 2.53 and 1.72 ppm were observed for the $–CH_2$-CH_2-CH_2- chain. The aromatic region showed nine protons present, whilst eight of these resonances occur between 7.40 and 7.00 ppm, a single doublet occurs downfield of all the other peaks at 8.21 ppm. Performing nOe spectroscopy studies shows a through-space interaction between the pinacol and the aromatic proton doublet at 8.21 ppm, this is presumably the proton highlighted in Figure 4.34, below. Close proximity to the Pin-B group would seem to be responsible for the significant downfield shift of the ^{1}H resonance. Based on the spectroscopic data it was concluded that the product of the reaction was a borylated annulated indene.

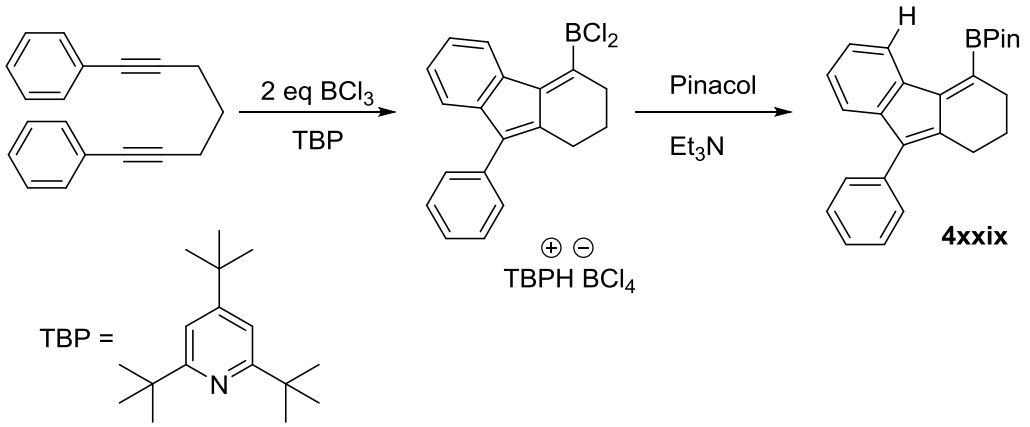


Figure 4.34: Synthesis of annulated indene (**4xxix**)

It is postulated that this reaction proceeds via the mechanism shown below in Figure 4.35. It begins with borylation of one of the alkyne moieties, forming the more stable carbocation adjacent to the phenyl ring. This carbocation is subsequently attacked by the remaining alkyne forming a six-membered ring in a 6-*exo*-dig reaction, with the carbocation once again stabilised by a phenyl group. This is followed by a second cyclisation with deprotonation of an aryl proton, forming a five-membered ring. A chloride can be abstracted from the boron to give a neutral

vinyl-BCl_2 species and BCl_4^- to charge balance the newly protonated base. Finally esterification and purification give the pinacolated final product.

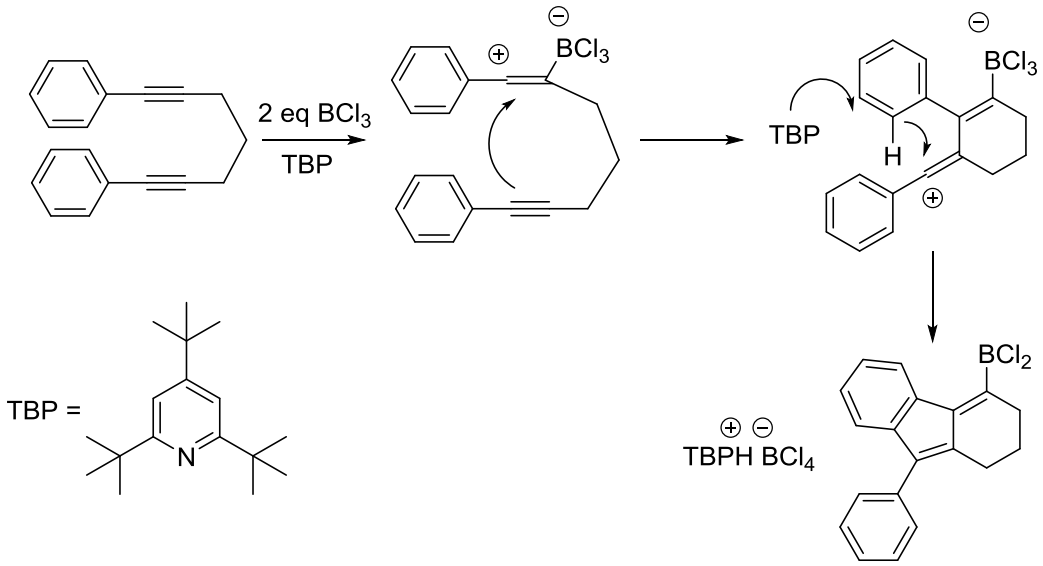


Figure 4.35: Proposed reaction mechanism for the synthesis of (**4xxix**)

A similar reaction has been observed, wherein unactivated diynes can undergo intramolecular cycloadditions catalysed by $AuPPh_3SbF_6$, as shown below in Figure 4.33.[18] The study contained a comparable example; the cyclisation of 1,7-diphenyl-1,6-heptadiyne, which gives a related product to the one formed by the reaction with BCl_3. It is worth noting that our products contain a borylated site, allowing subsequent functionalizations e.g., through cross-coupling reactions, and that the reaction does not require a metal catalyst as the reaction shown in Figure 4.36 does.

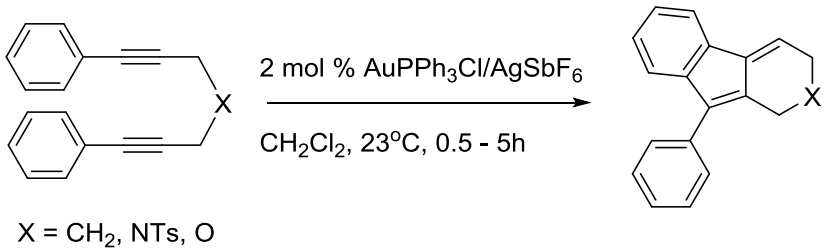


Figure 4.36: Cycloaddition reaction of diphenyl-diynes

The reaction between 1,7-diphenyl-1,6-heptadiyne and $[Cl_2B(2DMAP)][AlCl_4]$ proceeds analogously to the above reaction with BCl_3. *In situ* NMR spectroscopy showed protonation of the 2DMAP, and comparable resonances in the aliphatic and aromatic region. Upon esterification, the same product was isolated. This represents an internal alkyne that reacts with $[Cl_2B(2DMAP)][AlCl_4]$, albeit via a cyclisation reaction, not a haloboration.

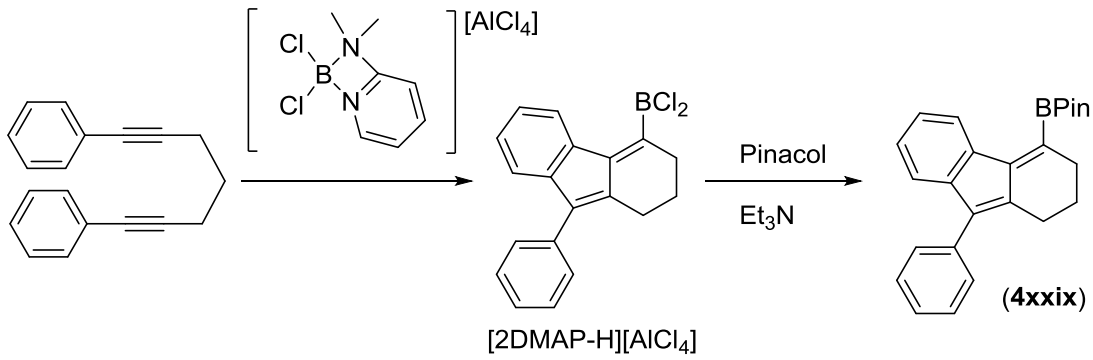


Figure 4.37: Synthesis of (**4xxix**) using $[BCl_2(2DMAP)][AlCl_4]$

When BCl_3 was reacted with 1,8-diphenyl-1,7-octadiyne in the presence of TBP, the *in situ* NMR data showed multiple species present. After esterification and workup, it was surmised from NMR data that there were two main products present in a roughly 4:1 ratio. Analysis of the mixture by GC/MS lent credibility to this theory, with molecular ion peaks at 384.2 and 420.2 $gmol^{-1}$. These masses correspond to a cyclisation product (with the loss of a proton) and a haloboration (inclusion of a chloride and retention of the proton) respectively. Attempts to preclude the haloboration product were unsuccessful, however by repeating the reaction in the absence of base the haloboration product was formed almost exclusively.

The NMR spectrum post esterification showed a 10H multiplet between 7.13 and 7.00 ppm, concurrent with the retention of all aromatic protons on the phenyl rings. The four aliphatic CH_2 groups present as separate distinct peaks, most of which are broad, the multiplicity of which could not be identified. A 12H singlet at 1.30 ppm indicated the installation of a PinB group, with the ^{11}B spectrum confirming with a peak at 31.1 ppm. Given that the nOe spectrum showed through space interactions between the pinacol and a 2H aromatic proton resonance, the structures below in Figure 4.38 are the most likely outcomes of this reaction, although they were indistinguishable using the aforementioned data.

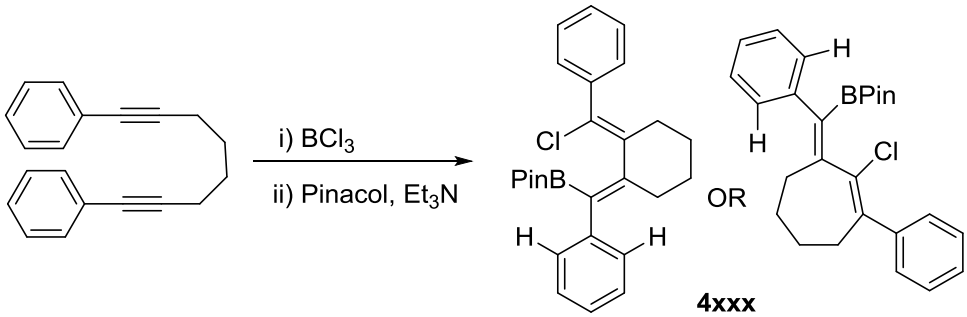


Figure 4.38: Cyclisation of 1,8-diphenyl-1,7-octadiyne with BCl_3

Thus, several attempts were made to confirm the structure of this product, so the reaction was first scaled up four-fold, showing reproducibility at higher quantities with a comparable yield, and giving enough pure **4xxx** to allow multiple experiments. One such experiment was the attempted Diels-Alder reaction of (4xxx) with N-phenylmaleimide. It was postulated that if the structure of **4xxx** was the 6-membered ring, then it could act as a diene in a 4+2 addition. However, the reaction was observed to not occur, even under harsh reaction conditions (toluene, 100°C, 4 days. Thus, it may be that if **4xxx** is the 6-membered structure, the two

alkenes are in the wrong conformation; each bent away from the other due to the steric bulk of the substituents.

Another attempt was made where a sample of **4xxx** was dissolved in THF, to which aqueous HCl was added. After stirring for 24 hours at room temperature, an aliquot was removed and the reaction quenched, and extracted into ether. NMR analysis showed no reaction, with **4xxx** untouched. At longer reaction times, it was shown that the coumpound began to decompose, with several smaller new resonances present in the ^{1}H NMR spectrum. It would appear that the pinacol boronate ester is too stable to be cleanly protodeboronated. Pd catalysed cross coupling reactions and catalysed protodeboronations were also attempted,[20] however these were all inconclusive. In light of the difficulties identifying this compound, we are more inclined to believe that it is the 6-membered cyclic species shown in Figure 4.38, due to the stability associated with the formation of 6-membered species from octadiynes in the literature,[11] as well as observations made during the study of other diynes during this report.

4.4 Conclusions

By utilising borocations, it has been shown that haloboration of both terminal and internal alkynes is now possible. Analysis of the products has shown that the reaction proceeds with a high degree of regio/stereo-control; a single product is always formed with excellent *in situ* conversions, and moderate to high isolated yields of the pinacol bononate esters.

Furthermore, it has been demonstrated that the haloboration products represent viable synthetic building blocks to more complex tetra-substituted alkenes. Modification through cross-coupling reactions of both the boron and halide site allows this, and each are tolerant enough to allow consecutive cross-coupling reactions without competing pathways.

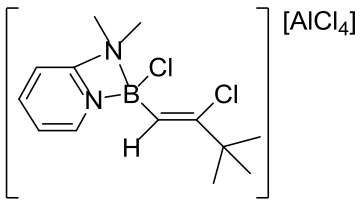
Finally, it has been demonstrated that certain alkynes can undergo cyclisation reactions with electrophilic boron reagents. Both 1,7-diphenyl-1,6-heptadiyne and 1,6-heptadiyne cyclise in different ways to give useful borylated cyclic species. It is apparent that heptadiyne species react far more cleanly than their octadiyne counterparts, most probably due to being able to form a stable six-membered ring system more readily.

4.5 Experimental

General procedure for the haloboration of terminal alkynes with $[BCl_2(2DMAP)][AlCl_4]$

To a suspension of $[Cl_2B(2DMAP)][AlCl_4]$ (50 mg, 0.14 mmol) in anhydrous CH_2Cl_2 in a J.Young's NMR tube, alkyne (1 eq, 0.14 mmol) was added, turning light yellow and dissolving some of the precipitate. The reaction mixture was then stirred at room temperature for x hours, during which time the precipitate fully dissolved. NMR spectroscopy was used to confirm reaction completion, and the solution was esterified with excess triethylamine and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving a yellow oil. Pentane was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities.

(**4i**) Initial haloboration product from $[Cl_2B(2DMAP)][AlCl_4]$ and ^{t}butylacetylene

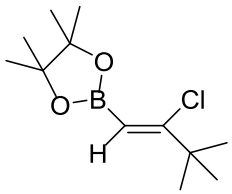


To a suspension of $[Cl_2B(2DMAP)][AlCl_4]$ (50 mg, 0.14 mmol) in anhydrous oDCB in a J.Young's NMR tube, ^{t}Butylacetylene (17 µl, 0.14 mmol) was added, and the reaction mixture was then heated to 100°C until dissolution of the boronium. This was then cooled to room temperature over 6 hours, affording a grey solution with

large, colourless crystals. The supernatant was removed and the crystals washed with oDCB, a portion of which was dissolved in CD_2Cl_2 for NMR data.

^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.77 (t, 1H, ^{3}J(H,H) = 8 Hz), 8.67 (d, 1H, ^{3}J(H,H) = 8 Hz), 8.26 (d, 1H, ^{3}J(H,H) = 8 Hz), 8.15 (t, 1H, ^{3}J(H,H) = 8 Hz), 5.81 (s, 1H), 3.36 (s, 6H), 1.21 (s, 9H); **^{11}B NMR** (128.4 MHz, CD_2Cl_2): δ 12.2 (s) ppm.

(**4ii**) (Z)-2-(2-chloro-3,3-dimethylbut-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

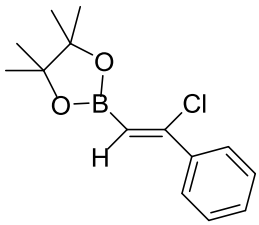


The product was isolated as a colourless oil (20 mg, 0.08 mmol, 63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.47 (s, 1H), 1.24 (s, 12H), 1.12 (s, 9H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 162.36, 83.57, 40.71, 28.82, 24.81; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.8 (s) ppm.

Elemental Analysis Calculated: C 62.52; H 9.07. Observed: C 62.49; H 9.11.

(**4iii**) (Z)-2-(2-chloro-2-phenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

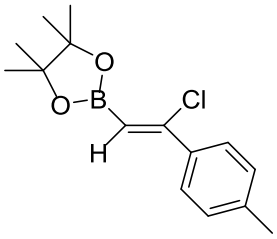


The product was isolated as a yellow oil (30 mg, 0.12 mmol, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.58 (m, 2H), 7.29-7.28 (m, 3H), 6.04 (s, 1H), 1.27 (s, 12H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 149.06, 138.99, 129.46, 128.26, 126.82, 83.74, 24.84; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.7 (s) ppm.

Elemental Analysis Calculated: C 63.56; H 6.86. Observed: C 63.52; H 6.90

(**4iv**) (Z)-2-(2-chloro-2-(p-tolyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

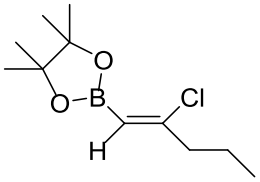


The product was isolated as a yellow oil (24 mg, 0.09 mmol, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, 2H, $^{3}J(H,H)$ = 8 Hz), 7.08 (d, 2H, $^{3}J(H,H)$ = 8 Hz), 2.28 (s, 3H), 1.24 (s, 12H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ152.53, 140.12, 132.77, 131.89, 129.96, 84.77, 21.89, 21.81; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.6 (s) ppm.

Elemental Analysis Calculated: C 64.67; H 7.24. Observed: C 64.72; H 7.30

(**4v**) (Z)-2-(2-chloropent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

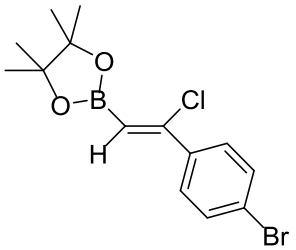


The product was isolated as a colourless oil (26 mg, 0.11 mmol, 73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (s, 1H), 2.31 (t, 2H, alkyl), 1.53 (sextet, 2H, alkyl), 1.23 (s, 12H, pinacol), 0.85 (t, 3H, alkyl); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 153.89, 83.64, 38.39, 24.54, 21.75, 13.08; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.5 (s) ppm.

Elemental Analysis Calculated: C 57.31; H 8.75. Observed: C 57.36; H 8.77.

(**4vi**) (Z)-2-(2-(4-bromophenyl)-2-chlorovinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



The product was isolated as a yellow oil (63 mg, 0.18 mmol, 68%).

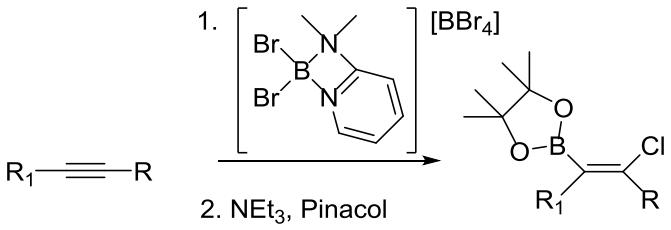
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, 2H, ^{3}J(H,H) = 8.6 Hz), 7.31 (d, 2H, ^{3}J(H,H) = 8.6 Hz), 5.61 (s, 1H), 1.27 (s, 12H, pinacol); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 149.32, 139.59, 134.90, 132.54, 129.89, 83.69, 24.93; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.3 (s) ppm.

Elemental Analysis Calculated: C 48.96; H 4.98. Observed: C 48.96; H 4.97

Reaction of [LutBCl$_2$][AlCl$_4$] with phenylacetylene - Thermal stability test

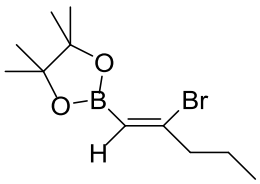
A J. Young's NMR tube fitted with a d_6-DMSO capillary was charged with Lutidine-BCl_3 adduct (40 mg, 0.18 mmol) and $AlCl_3$ (24 mg, 0.18 mmol) and DCM (0.5 ml) added, the tube then gently inverted until dissolution was complete. Phenylacetylene (20 μl, 0.18 mmol) was added and a red colour formed immediately. Formation of the haloborated alkylborenium was quantitative. The reaction mixture was heated in a sealed tube at 60°C for 85 hours, after which the NMR spectra were found to be largely unchanged with no evidence for dehydroboration and alkynyl-BCl_2 formation.

General procedure for the haloboration of alkynes with [BBr_2(2DMAP)][BBr_4]



To a suspension of [Br_2B(2DMAP)][BBr_4] (100 mg, 0.16 mmol) in anhydrous CH_2Cl_2 in a J.Young's NMR tube, an alkyne (e.g., 1-pentyne 16 µl, 0.16 mmol) was added, turning light yellow and dissolving some of the precipitate. The reaction mixture was then stirred at room temperature for 18 hours, during which time the precipitate fully dissolved. NMR spectroscopy was used to confirm reaction completion, and the solution was esterified with excess triethylamine and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving a pale yellow oil. Pentane was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities. Further purification by column chromatography was required for some products.

(**4vii**) (Z)-2-(2-bromopent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

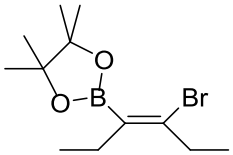


The product was isolated as a yellow oil (34 mg, 0.12 mmol, 78%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87 (t, 1H, ^4J(H,H) = 0.8 Hz), 2.49 (td, 2H, ^3J(H,H) = 7.3 Hz, ^4J(H,H) = 0.8 Hz), 1.61 (sextet, 2H, ^3J(H,H) = 7.3 Hz), 1.30 (s, 12H, pinacol), 0.92 (t, 3H, ^3J(H,H) = 7.3 Hz); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.4 (s) ppm.

Elemental Analysis Calculated: C 48.04; H 7.33. Observed: C 48.14; H 7.37

(**4viii**) (*E*)-2-(4-bromohex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

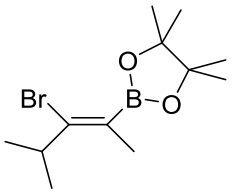


Purification via column chromatography (1:1 DCM:petroleum ether) afforded a yellow oil (29 mg, 0.10 mmol, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (q, 2H, ^{3}J(H,H) = 7.3 Hz), 2.10 (q, 2H, ^{3}J(H,H) = 7.6 Hz), 1.25 (s, 12H), 1.04 (t, 3H, ^{3}J(H,H) = 7.3 Hz), 0.94 (t, 3H, ^{3}J(H,H) = 7.7 Hz); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 134.43, 83.91, 30.73, 25.60, 24.78, 14.03, 13.24; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.2 (s) ppm.

Elemental Analysis Calculated: C 49.69; H 7.65. Observed: C 49.72; H 7.69

(**4ix**) (*E*)-2-(3-bromo-4-methylpent-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



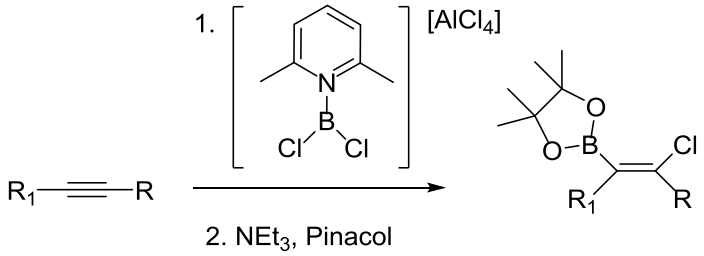
The product was isolated as a colourless oil (24 mg, 0.08 mmol, 52 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.97 (septet, 1H, ^{3}J(H,H) = 6.5 Hz), 1.76 (s, 3H,), 1.33 (s, 12H), 1.04 (d, 6H, ^{3}J(H,H) = 6.5 Hz); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 141.75, 83.88, 32.12, 24.69, 21.22, 17.12 ppm; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.1 (s) ppm.

Elemental Analysis Calculated: C 49.87; H 7.67. Observed: C 49.98; H 7.69.

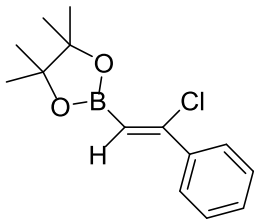
nOe spectroscopy shows through space interaction between resonances at 2.97 and both 1.76 and 1.04, but not with 1.33 ppm.

General procedure for the haloboration of alkynes with [LutBCl$_2$][AlCl$_4$]



LutBCl$_3$ (50 mg, 0.22 mmol) was suspended in anhydrous CH_2Cl_2 in a J.Young's NMR tube, to which $AlCl_3$ (30 mg, 0.22 mmol) was added, causing dissolution to a clear yellow solution. To this [LutBCl$_2$][AlCl$_4$], alkyne (1 eq, 0.22 mmol) was added, turning dark brown. The reaction mixture was then stirred at room temperature for 4 - 48 hours, NMR spectroscopy confirmed reaction completion, and the solution was esterified with excess triethylamine and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving an orange/brown oil. Pentane was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities.

(**4x**) (Z)-2-(2-chloro-2-phenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



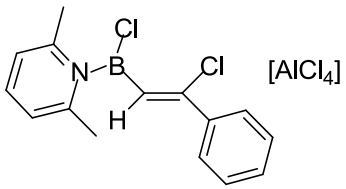
Reaction time 4 hours, the product was isolated as a yellow/orange oil (40 mg, 0.16 mmol, 71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.67 (m, 2H, phenyl), 7.37-

7.35 (m, 3H, phenyl), 6.13 (s, 1H, vinylic), 1.36 (s, 12H, pinacol); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 149.07, 138.99, 129.47, 128.27, 126.82, 83.74, 24.85; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.6 (s) ppm.

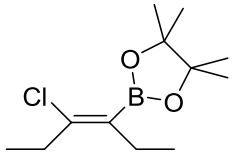
Elemental Analysis Calculated: C 63.56; H 6.86. Observed: C 63.54; H 6.89.

Initial product of (4x) (pre-esterification)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (t, 1H, ^{3}J(H,H) = 8 Hz), 7.92 (d, 2H, ^{3}J(H,H) = 8 Hz), 7.86 (d, 2H, ^{3}J(H,H) = 8 Hz), 7.64 (t, 1H, ^{3}J(H,H) = 8 Hz), 7.53 (t, 2H, ^{3}J(H,H) = 8 Hz), 7.23 (s, 1H), 2.85 (s, 6H); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 46 (broad); **^{27}Al NMR** (104 MHz, CD_2Cl_2): δ 103.4 (s) ppm.

(**4xi**) (*E*)-2-(4-chlorohex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Reaction time 24 hours, the product was isolated as a yellow/orange oil (44 mg, 0.18 mmol, 81 %).

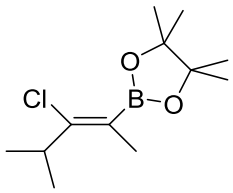
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (q, 2H, ^{3}J(H,H) = 7.3 Hz), 2.18 (q, 2H, ^{3}J(H,H) = 7.6 Hz), 1.31 (s, 12H), 1.12 (t, 3H, ^{3}J(H,H) = 7.3 Hz), 1.00 (t, 3H, ^{3}J(H,H) = 7.7 Hz); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 142.69, 83.73, 28.63, 14.28, 12.54; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.3 (s) ppm.

Elemental Analysis Calculated: C 58.93; H 9.07. Observed: C 59.00; H 9.09

Mass Spectrum Calculated 244.57; Found 244.19 $gmol^{-1}$

nOe spectroscopy shows through space interaction between resonances at 1.12 and 1.00 ppm.

(**4xii**) (*E*)-2-(3-chloro-4-methylpent-2-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



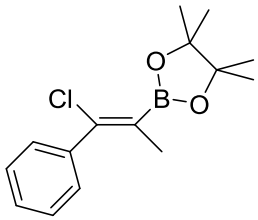
Reaction time 18 hours, the product was isolated as a brown/orange oil (40 mg, 0.19 mmol, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (septet, 1H, ^{3}J(H,H) = 6.7 Hz), 1.76 (s, 3H), 1.32 (s, 12H), 1.07 (d, 6H, ^{3}J(H,H) = 6.7 Hz); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 148.09, 83.72, 31.24, 24.69, 20.19, 16.07; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ (s) 30.3 ppm.

Elemental Analysis Calculated: C 58.93; H 9.07; Observed: C 59.01; H 9.14;

nOe spectroscopy shows through space interaction between resonances at 1.76 (the methyl) and the other three; 3.11, 1.32 and 1.07.

(**4xiv**) (*E*)-2-(1-chloro-1-phenylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



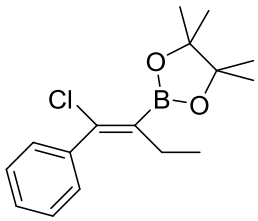
Reaction time 4 hours, the product was isolated as a yellow/orange oil (38 mg, 0.14 mmol, 62 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.23 (m, 3H, phenyl), 7.15-7.11 (m, 2H, phenyl), 2.06 (s, 3H, methyl), 1.22 (s, 12H, pinacol); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 132.58, 130.55, 128.37, 127.73, 84.04, 24.63; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.4 (s) ppm.

Elemental Analysis Calculated: C 64.67; H 7.18. Observed: C 64.73; H 7.19

nOe spectroscopy shows through space interaction between resonances 7.23 (part of the multiplet corresponding to an *ortho* proton) and 2.06. Also shown between 2.06 and 1.22 resonances.

(**4xv**) (*E*)-2-(1-chloro-1-phenylbut-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



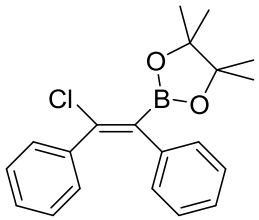
Reaction time 18 hours, the product was isolated as a yellow oil (46 mg, 0.16 mmol, 72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.08 (m, 5H, phenyl), 2.31 (q, 2H, ^{3}J(H,H) = 7.4 Hz), 1.22 (s, 12H, pinacol), 1.06 (t, 3H, ^{3}J(H,H) = 7.4 Hz); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 144.52, 137.85, 129.50, 125.62, 83.08, 44.74, 28.28, 11.75; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.8 (s) ppm.

Elemental Analysis Calculated: C 65.68; H 7.58. Observed: C 65.64; H 7.57

nOe spectroscopy shows through space interaction between resonances at 7.09 (part of the multiplet corresponding to an *ortho* proton) and 2.31 ppm. Also shown between 1.22 and both 2.31 and 1.06 ppm.

(**4xvi**) (*E*)-2-(2-chloro-1,2-diphenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

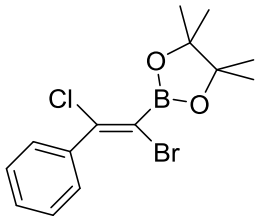


Reaction time 24 hours, the product was isolated as a brown oil (32 mg, 0.09 mmol, 43 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.45 (m, 4H, phenyl), 7.29-7.24 (m, 6H, phenyl), 1.24 (s, 12H, pinacol); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.4 (s) ppm.

Elemental Analysis Calculated: C 64.67; H 7.18. Observed: C 64.73; H 7.19

(**4xvii**) (*E*)-2-(1-bromo-2-chloro-2-phenylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



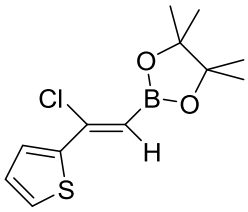
Reaction time 18 hours, the product was isolated as a brown/orange oil (54 mg, 0.16 mmol, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.41 (m, 2H, phenyl), 7.32-7.31 (m, 3H, phenyl), 1.31 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 138.64, 137.91, 129.37, 128.69, 128.18, 85.19, 24.55; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ28.4 (s) ppm.

Elemental Analysis Calculated: C 48.96; H 4.99; Observed: C 48.99; H 5.04;

nOe shows no through space interaction between phenyl and pinacol resonances

(**4xviii**) (*Z*)-2-(2-chloro-2-(thiophen-2-yl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Reaction time 18 hours, the product was isolated as a brown/orange oil (39 mg, 0.15 mmol, 65%).

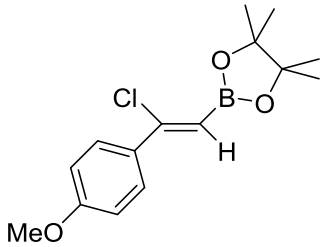
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, 1H, ^{3}J(H,H) = 3.7 Hz, ^{4}J(H,H) = 1.2 Hz), 7.24 (dd, 1H, ^{3}J(H,H) = 3.7 Hz, ^{4}J(H,H) = 1.2 Hz), 6.93 (dd, 1H, ^{3}J(H,H) = 3.7 Hz), 5.99 (s, 1H), 1.26 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 141.7, 132.65, 130.87, 127.87, 127.72, 83.70, 24.83; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.5 (s) ppm.

Elemental Analysis Calculated: C 53.27; H 5.96; Observed: C 53.24; H 6.00;

Mass Spectrum Calculated 270.58; Found 270.22

nOe spectroscopy shows through space interaction between resonances at 7.24 and 5.99 ppm.

(**4xix**) (*Z*)-2-(2-chloro-2-(4-methoxyphenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



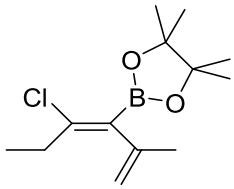
Reaction time 4 hours, the product was isolated as a colourless oil (30 mg, 0.12 mmol, 52%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 2H, ^{3}J(H,H) = 9 Hz), 6.80 (d, 2H, ^{3}J(H,H) = 9 Hz), 5.94 (s, 1H), 3.76 (s, 3H), 1.27 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 160.66, 148.94, 128.32, 113.55, 83.62, 55.13, 24.85; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ30.4 (s) ppm.

Elemental Analysis Calculated: C 61.16; H 6.84; Observed: C 61.14; H 6.80;

(nOe shows through space interaction between the vinylic proton (5.94 ppm) and phenyl (7.56 ppm) resonances, but no interaction between phenyl and pinacol resonances)

(**4xx**) (*E*)-2-(4-chloro-5-methylhexa-3,5-dien-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



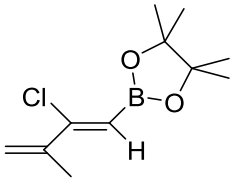
Reaction time 6 hours, the product was isolated as a light yellow oil (35 mg, 0.14 mmol, 61%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (m, 1H), 4.64 (m, 1H), 2.40 (q, 2H, ^{3}J(H,H) = 7.3 Hz), 1.76 (dd, 3H, ^{4}J(H,H) = 1.6 Hz), 1.24 (s, 12H), 1.06 (t, 3H, ^{3}J(H,H) = 7.3 Hz); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 144.50, 143.53, 113.43, 83.96, 29.70, 24.64, 13.14; **^{11}B NMR** (128.4 MHz, CDCl3): δ30.0 (s) ppm.

Elemental Analysis Calculated: C 60.85; H 8.64; Observed: C60.89; H 8.67;

nOe spectroscopy shows through space interaction between resonances at 4.64 and 2.40 ppm, also shows interaction between 1.24 and 1.76 ppm. Interaction between 4.87 and both 4.64 and 1.76 ppm is observed.

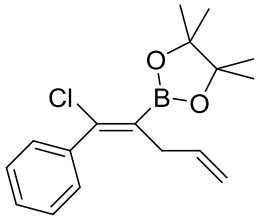
(**4xxi**) (*Z*)-2-(2-chloro-3-methylbuta-1,3-dien-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Reaction time 1 hour, the product was isolated as a light yellow oil (46 mg, 0.2 mmol, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (s, broad, 1H), 5.70 (s, broad, 1H), 5.24 (s, broad, 1H), 1.98 (s, 3H), 1.32 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 149.05, 140.81, 119.39, 83.71, 24.80, 20.67; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.6 ppm.

(**4xxii**) (*E*)-2-(1-chloro-1-phenylpenta-1,4-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



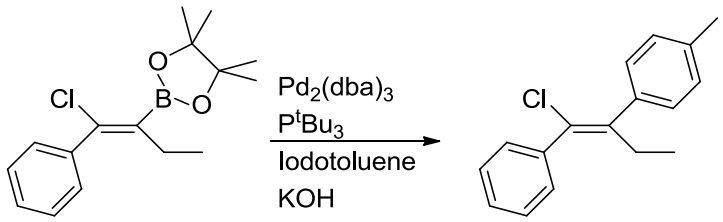
Reaction time 4 hours, the product was isolated as a colourless oil (35 mg, 0.12 mmol, 53%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.12 (m, 5H), 5.76-5.69 (m, 1H) 5.02-4.98 (dq, 1H), 4.97-4.94 (dq, 1H), 2.80 (dt, 2H), 1.27 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 138.57, 138.04, 136.00, 128.40, 116.11, 84.14, 37.25, 24.77; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.3 (s) ppm.

Elemental Analysis Calculated: C 67.03; H 7.28; Observed: C 67.00; H 7.27;

(nOe shows through space interaction between the alkyl CH_2 protons (2.80 ppm) and pinacol (1.27 ppm) resonance, but no interaction between pinacol and any phenyl resonances)

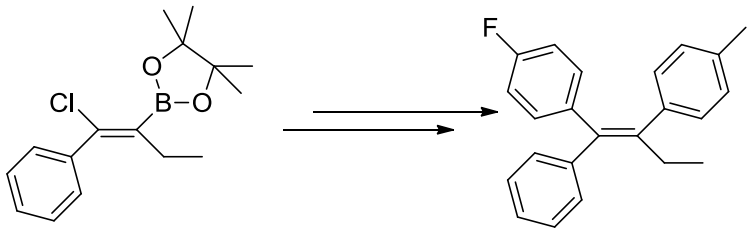
(**4xxiii**) (*Z*)-1-(1-chloro-1-phenylbut-1-en-2-yl)-4-methylbenzene



Under an inert atmosphere, $Pd_2(dba)_3$ (21 mg, 0.05 eq), P^tBu_3 (18 mg, 0.2 eq), vinylboronate (**4xv**) (133 mg, 1 eq) and 4-iodotoluene (99 mg, 1 eq) were combined in THF (10 ml). To this, 3M KOH (454 µl, 3 eq) was added and the reaction stirred for 18 hours. The reaction was quenched with aqueous ammonium chloride (10 ml) and extracted with ether (20 ml). The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to yield a dark yellow oil. This crude product was purified with column chromatography using 3:1 hexane:DCM eluent. The product has an R_f value of 0.74, and presented as a light yellow oil (55 mg, 92 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 – 7.22 (m, 3H), 7.10 – 7.04 (m, 6H), 2.38 (q, 2H), 2.26 (s, 3H), 1.13 (t, 3H); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ 137.96, 136.86, 134.12, 128.47, 128.30, 128.01, 127.63, 126.10, 123.16, 122.36, 29.27, 20.23, 12.11 ppm.

(**4xxiv**) (*Z*)-1-fluoro-4-(1-phenyl-2-(p-tolyl)but-1-en-1-yl)benzene



Under an inert atmosphere, $Pd_2(dba)_3$ (21 mg, 0.05 eq), P^tBu_3 (18 mg, 0.2 eq), vinylboronate (**4xv**) (133 mg, 1 eq) and 4-iodotoluene (99 mg, 1 eq) were combined in THF (10 ml). To this, 3M KOH (454 µl, 3 eq) was added and the reaction stirred for 18 hours. The reaction was quenched with aqueous ammonium chloride (10 ml) and extracted with ether (20 ml). The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to yield a yellow oil, which was immediately used in the next step.

To the product, $Pd_2(dba)_3$ (24 mg, 0.05 eq), P^tBu_3 (21 mg, 0.2 eq), 4-fluorophenyl boronic acid (73 mg, 1 eq) were added in THF (10 ml). To this, 3M KOH (518 µl, 3 eq) was added and the reaction stirred for 18 hours. The reaction was quenched with aqueous ammonium chloride (10 ml) and extracted with ether (20 ml). The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to yield a yellow/brown oil. This crude product was purified with column chromatography using 2:1 hexane:DCM eluent. The product shows an R_f value of 0.60, and presented as a colourless oil (79 mg, 53 %)

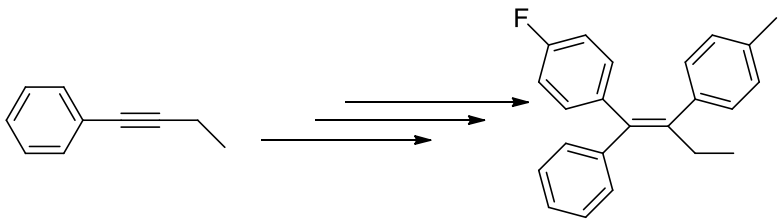
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.35 (m, 2H), 7.25-7.15 (m, 4H), 7.11-7.01 (m, 7H), 2.37 (q, 2H, alkyl CH_2), 2.25 (s, 3H, methyl), 1.12 (t, 3H, alkyl CH_3); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 140.14, 137.33, 136.86, 135.74, 134.11, 128.31, 128.00, 127.64,

127.27, 126.10, 114.76, 114.55, 29.28, 20.22, 12.10; **^{19}F NMR** (376.50 MHz, $CDCl_3$) δ -115.70 ppm.

Minor Product (9 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.30 (m, 13H), 2.75 (q, 2H, alkyl CH_2), 2.56 (s, 3H, methyl), 1.49 (t, 3H, alkyl CH_3); **^{19}F NMR** (376.50 MHz, $CDCl_3$) δ -116.27 ppm.

Synthesis of (4xxiv) (*Z*)-1-fluoro-4-(1-phenyl-2-(p-tolyl)but-1-en-1-yl)benzene



Under an inert atmosphere, 2,6-lutidine (261 µl, 1 eq) in hexane was added dropwise to boron trichloride (1M solution in heptanes, 2.24 ml, 1.2 eq) at 0˚C. This caused a precipitation of pale yellow-white solid; the Lut-BCl_3 adduct. After 20 minutes the solvent was removed under reduced pressure and the adduct suspended in dichlorobenzene. To this, aluminium trichloride (500 mg, 1 eq) was added to generate the desired borocation. After 20 minutes of stirring, the internal alkyne 1-phenyl-1-butyne (320 µl, 1 eq) was added dropwise, causing the suspention to go into solution, turning a yellow colour. The reaction was stirred for 18 hours, turning a dark orange, before transesterification with a solution of pinacol (2.1 eq) in excess triethylamine. Extraction with pentane and subsequent filtration

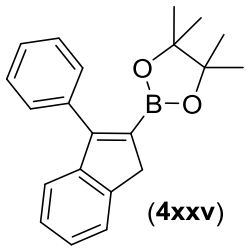
through silica removed impurities to generate the pinacol boronate ester. (yield = 69%)

Under an inert atmosphere, $Pd_2(dba)_3$ (0.05 eq), P^tBu_3 (0.2 eq), vinylboronate (**4xv**) (1 eq) and 4-iodotoluene (1 eq) were combined in THF. To this, 3M KOH (3 eq) was added and the reaction stirred for 18 hours. The reaction was quenched with aqueous ammonium chloride and extracted with ether. The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to yield a yellow oil, which was immediately used in the next step.

To the product, $Pd_2(dba)_3$ (0.05 eq), P^tBu_3 (0.2 eq), 4-fluorophenyl boronic acid (1 eq) were added in THF. To this, 3M KOH (3 eq) was added and the reaction stirred for 18 hours. The reaction was quenched with aqueous ammonium chloride and extracted with ether. The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to yield a yellow/brown oil. This crude product was purified with column chromatography using 2:1 hexane:DCM eluent. The product shows an R_f value of 0.60, and presented as a colourless oil (249 mg, 51 %) NMR data is consistent with previous synthesis of (**4xxiv**).

Major product : Minor Product (6:1 ratio, 249 : 41 mg)

(**4xxv**) 4,4,5,5-tetramethyl-2-(3-phenyl-1H-inden-2-yl)-1,3,2-dioxaborolane



(**4xxv**)

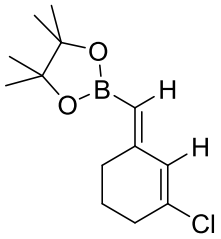
$LutBCl_3$ (50 mg, 0.22 mmol) was suspended in anhydrous *o*-$C_6H_4Cl_2$ in a J.Young's NMR tube, to which $AlCl_3$ (30 mg, 0.22

mmol) was added, causing dissolution to a clear yellow solution. To this [LutBCl$_2$][AlCl$_4$], prop-1-yne-1,3-diyldibenzene (43 mg, 0.22 mmol) was added, turning dark brown. The reaction mixture was then stirred at room temperature for 18 hours, NMR spectroscopy confirmed reaction completion, and the solution was esterified with excess triethylamine and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving a yellow oil. Hexane was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities. The product was isolated as a colourless oil (30 mg, 0.12 mmol, 52%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.28-7.12 (m, 9H), 3.66 (s, 2H), 1.22 (s, 12H); **^{13}C NMR** (100.06 MHz, CDCl$_3$) δ 140.93, 138.65, 137.34, 128.81, 128.58, 128.42, 128.03, 126.99, 126.57, 84.25, 41.63, 24.61; **^{11}B NMR** (128.4 MHz, CDCl$_3$): δ30.2 (s) ppm.

GC/MS: 318.2 gmol^{-1} **MS**: Theoretical = 318.1786 gmol^{-1}, Measured = 318.1794 gmol^{-1}

(**4xxvi**) (*Z*)-2-((3-chlorocyclohex-2-en-1-ylidene)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



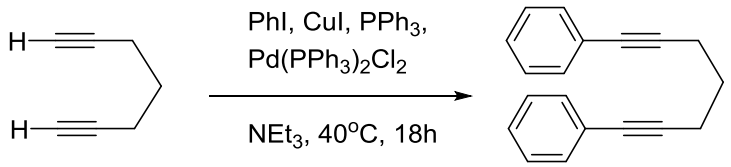
To a solution of 1,6-heptadiyne (21 µl, 0.18 mmol, 1 eq) in DCM in a J. Youngs tube, BCl_3 (1M, 200 µl, 1.1 eq) was added. After 1 minute of inversion to mix, the reaction mixture was esterified with sequential addition of excess trimethylamine and pinacol (26 mg, 0.22 mmol, 1.2 eq). The crude material was extracted into pentane and filtered through a plug of silica, before addition of 1M HCl (5 ml) to the pentane extracts. The organic layer was subsequently decanted away from the aqueous layer, dried with $MgSO_4$, and the solvent removed under reduced pressure to give (**4xxvi**) as an orange oil (37 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.28 (m, 1H), 5.08 (m, 1H), 2.63 (td, 2H), 2.43 (td, 2H), 1.81 (quintet, 2H), 1.27 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 155.55, 138.81, 130.90, 115.03 (broad), 82.87, 33.41, 27.54, 24.85, 23.40; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ29.8 (s) ppm.

GC/MS 254.1 gmol^{-1}

nOe shows through space interaction between the resonances at 5.08 and 1.27 ppm, as well as between 5.08 and 6.28 ppm.

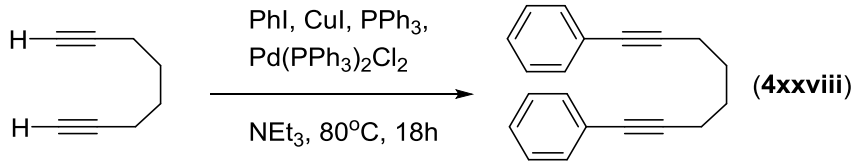
(**4xxvii**) 1,8-diphenyl-1,7-octadiyne



(**4xxviii**)

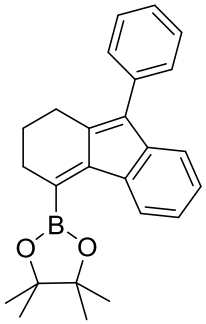
To a solution of 1,6-heptadiyne (182 µl, 1.6 mmol, 1 eq) and PhI (534 µl, 4.8 mmol, 3 eq) in NEt_3 (20 ml) $Pd(PPh_3)_2Cl_2$ (70 mg), CuI (30 mg) and PPh_3 (29 mg) were added under inert conditions at ambient temperature. The reaction mixture was heated to 40°C for 18 hours, and after cooling to room temperature, the suspension filtered through celite and rinsed with Et_2O (100 ml). the solvent was removed under reduced pressure to give the crude product, which was purified on silica gel, wherein the crude mixture was first flushed with neat hexane to remove excess PhI, then with DCM to extract the cross coupling product. The NMR spectra were comparable to that previously reported.[19]

(**4xxviii**) 1,8-diphenyl-1,7-octadiyne



To a solution of 1,7-octadiyne (625 µl, 4.8mmol, 1 eq) and PhI (1.60 ml, 14.3 mmol, 3 eq) in NEt_3 (20 ml) $Pd(PPh_3)_2Cl_2$ (210 mg), CuI (90 mg) and PPh_3 (87 mg) were added under inert conditions at ambient temperature. The reaction mixture was heated to 80°C for 18 hours, and after cooling to room temperature, the suspension filtered through celite and rinsed with Et_2O (100 ml). the solvent was removed under reduced pressure to give the crude product, which was purified on silica gel, wherein the crude mixture was first flushed with neat hexane to remove excess PhI, then with DCM to extract the cross coupling product. The NMR spectra were comparable to that previously reported.[19]

(**4xxix**) 4,4,5,5-tetramethyl-2-(9-phenyl-2,3-dihydro-1H-fluoren-4-yl)-1,3,2-dioxaborolane

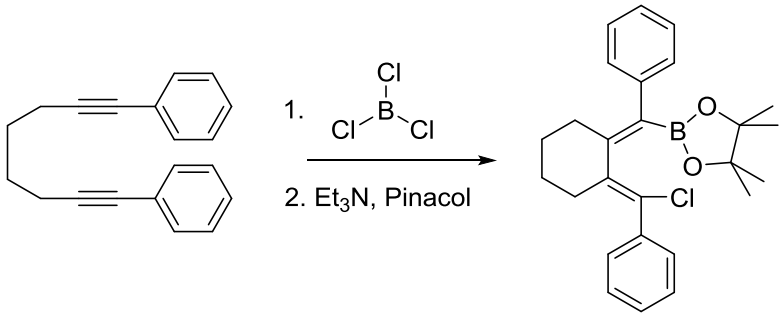


To a solution of 1,7-diphenyl-1,6-heptadiyne (25 mg, 0.1 mmol, 1 eq) and 2,4,6-tri^{t}butylpyridine (25 mg, 0.1 mmol, 1 eq) in DCM in a J. Youngs tube, BCl_3 (1M, 200 µl, 2 eq) was added. Within 1 hour the reaction was complete, as monitored by ^{1}H NMR spectroscopy showing complete consumption of the diyne, and the reaction mixture was then esterified with sequential addition of excess trimethylamine (0.1 ml) and pinacol (105 mg, 0.3 mmol, 3 eq). The crude material was extracted into pentane and filtered through a plug of silica, before addition of 5M HCl (5 ml) to the pentane extracts. The organic layer was subsequently decanted away from the aqueous layer, dried with $MgSO_4$, and the solvent removed under reduced pressure. This was then redissolved in a 3:1 Hexane:DCM solution and filtered through a 1 inch plug of silica to remove the remaining impurities. This afforded (**4xxix**) as a yellow oil (31 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, 1H, ^{3}J (H,H) = 7 Hz), 7.27 (m, 4H), 7.14 (m, 1H), 7.05 (d, 1H), 6.99 (td, 1H), 6.94 (td, 1H), 2.51 (t, 2H), 2.43 (t, 2H), 1.62 (quintet, 2H), 1.22 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 147.83, 143.90, 136.78, 135.50, 135.06, 134.63, 128.90, 128.30, 127.29, 127.11, 124.41, 122.86, 118.71, 84.01, 30.41, 24.98, 24.40, 24.17; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ31.2 (s) ppm.

GC/MS: 370.2 gmol^{-1} **MS**: Theoretical = 370.2104 gmol^{-1}, Measured = 370.2106 gmol^{-1}

(**4xxx**) BCl_3 + 1,8-diphenyl-1,7-octadiyne



To a solution of 1,8-diphenyl-1,7-octadiyne (46 mg, 0.18 mmol, 1 eq) in DCM in a J. Youngs tube, BCl_3 (1M, 200 µl, 1.1 eq) was added. After stirring for 24 hours, the reaction mixture was transesterified with sequential addition of excess trimethylamine and pinacol (26 mg, 0.22 mmol, 1.2 eq). The crude material was extracted into pentane and filtered through a plug of silica, then purified via column chromatography using 1:1 DCM:Hexane solution. This afforded (**4xxx**) as a yellow oil (27 mg, 36%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.00 (m, 10H), 2.48 (t(br), 2H), 2.16 (broad, 2H), 1.78 (quintet, 2H), 1.61 (broad, 2H), 1.30 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 150.91, 141.27, 138.99, 138.58, 129.86, 129.81, 127.83, 127.70, 127.42, 127.00, 125.79, 83.44, 33.97, 30.44, 24.73, 23.95, 22.35; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 31.1 ppm;

GC/MS: 420.2 $gmol^{-1}$ **MS**: Theoretical =420.2027 $gmol^{-1}$, Measured = 420.2142 $gmol^{-1}$

nOe shows through space interaction between the pinacol resonance (1.30 ppm) and a single aromatic resonance (7.02 ppm)

4.6 References

1. Lappert, M. F., Prokai, B. J. *Organometal. Chem*., **1964**, 1, 384
2. Joy, F., Lappert, M. F., Prokai, B. *J. Organometal. Chem.*, **1966**, 5, 506
3. Hara, S., Dojo, H., Takinami, S., Suzuki, A. *Tetrahedron Lett*., **1983**, 24, 731
4. Satoh, Y., Serizawa, H., Hara, S., Suzuki, A. *J. Am. Chem. Soc*., **1985**, 107, 5225
5. Suzuki, A., Arase, A., Matsumoto, H., Itoh, M., Brown, H. C., Rogic, M. M., Rathke, M. W. *J. Am. Chem. Soc*., **1967**, 89, 5708
6. Wang, C., Tobrman, T., Xu, Z., Negishi, E. *Org. Lett*., **2009**, 11, 4092
7. Hyuga, S., Chiba, Y., Yamashina, N., Hara, S., Suzuki, A. *Chem. Lett*., **1987**, 1757
8. Yao, M.-L., Reddy, M. S., Zeng, W., Hall, K., Walfish, I., Kabalka, G. W. *J. Org. Chem*., **2009**, 74, 1385
9. Wang, C., Uchiyama, M. *Eur. J. Org. Chem*., **2012**, 33, 6548
10. Parks, D. J., Spence, R. E. von H., Piers, W. E. *Angew. Chem. Int. Ed. Engl*., **1995**, 34, 809
11. Chen, C., Fröhlich, R., Kehr, G., Erker, G. *Chem.Comm*., **2010**, 46, 3580
12. Stephan, D. W. *Org. Biomol. Chem*., **2008**, 6, 1535
13. Mayr, H., Patz, M. *Angew Chem. Int. Ed*. Engl., **1994**, 33, 938
14. Daini, M., Yamamoto, A., Suginome, M. *J. Am. Chem. Soc.,* **2008**, 130, 2918
15. Warner, A. J., Lawson, J. R., Fasano, V., Ingleson, M. J. Submitted
16. Ochiai, M., Hirobe, M., Yoshimura, A., Nishi, Y., Miyamoto, K., Shiro, M. *Org. Lett*., **2007**, 9, 3335

17. Yang, J.-M., Tang, X.-Y., Wei, Y. and Shi, M. *Adv. Synth. Catal*., **2013**, 355, 3545

18. Lian, J-J., Chen, P-C., Lin,Y-P., Ting, H-C., Liu, R-S. *J. Am. Chem. Soc.*, **2006**, *128*, 11372

19. Cheng, C-C., Change, C-S., Hsu, Y-L., Lee, T-Y., Chang, L-C.,; Liu, S-H.,; Wu, Y-T. *European Journal of Organic Chemistry*, **2010**, 4, 672

20. Miyaura, N., Yamada, K., Suzuki, A. *Tetrahedron Letters*, **1979**, 20, 3437

Chapter 5. Carboboration of Alkynes

5.1 Introduction

As a way of accessing desirable vinylboronate esters from alkynes, carboboration reactions, where an alkyne formally inserts into a C-B bond, are an efficient way to access a wide variety of different molecules. Before the first reported carboborations, vinylboranes could be accessed via the reaction between trialkyl(alkynyl)borate salts and electrophilic tin and silicon halide reagents. This resulted in a vinylborane where an R-group previously bound to boron has migrated, and is now germinal to boron, as shown below in Figure 5.1.[1] Following this, a variety of mechanistically related 1,1-carboboration reactions were discovered, select examples are documented below. [2-20]

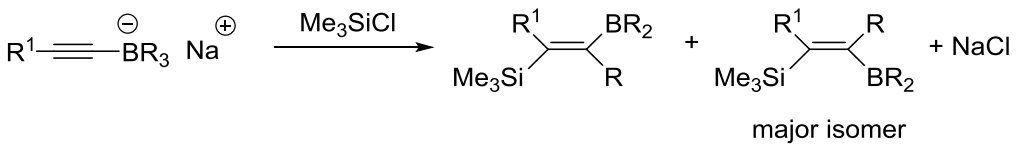


Figure 5.1: Carboboration of trialkyl(alkynyl)borate salts

Early carboborations had been of 'activated' alkynes featuring a suitable migratory group such as $–SiR_3$. Here, alkynes featuring such groups would generate vinylboranes similar to those featured above when reacted with trialkylboranes. Mechanistically, this 'Wrackmeyer' reaction begins with the activation of the E-C≡ bond (E = SiR_3, for example) by the electrophilic borane, ultimately leading to the cleavage of the C-E bond, forming the alkynylboronate zwitterion shown in Figure 5.2. This is followed by the migration of an R-group from boron, generating the

vinylborane, where generally the boron and ER_3 groups are mutually *cis*. However, mixtures of isomers have been reported in some cases. [21]

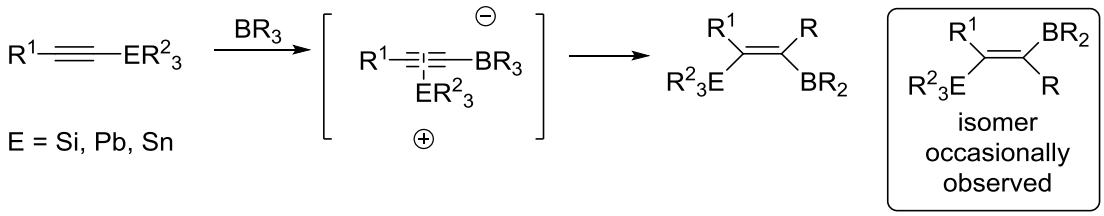


Figure 5.2: 1,1-carboboration of 'activated' alkynes

The zwitterionic intermediates in this reaction are of vital importance to the mechanism, and through multiple attempts to isolate them for structural characterisation by single crystal X-ray crystallography, an example was reported from the reaction of dimethyl-di(propyn-1-yl)lead with triisopropylborane, shown in Figure 5.3.[22] At low temperatures, the solid state structure was confirmed, and supported by multinuclear NMR spectroscopy in solution. The structure features a tri-coordinate lead atom coordinated to the alkyne.

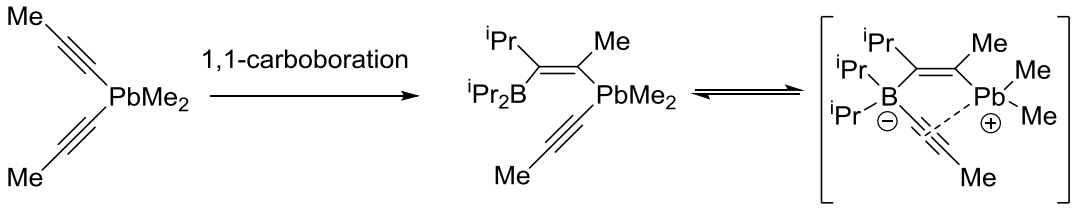


Figure 5.3: 1,1-carboboration intermediate observed in solid state

The migrating group bound to the alkyne has been varied, as in addition to –SiR_3 groups –GeR_3, –SnR_3 and –PbR_3 have been shown to react analogously. The reaction conditions for the carboborations can vary dramatically based on the groups bound to the alkyne. Temperatures can range from 120°C to -20°C simply by exchanging the silicon for tin in the reagent, which correlates to C-E bonds strength

and migratory aptitude. The nature of the borane also has an effect on the reaction, for example triallylborane was found to be more reactive than triethylborane, and reacted more readily with the activated alkynes. [23]

Wrackmeyer and co-workers utilised this reaction to make a wide range of heterocycles from dialkynyl precursors, featuring Si, Ge, Sn and Pb as the heteroatoms in the cyclic species.[24] An example of each is shown in Figure 5.4. The reported 1,1-carboborations of alkynes and cyclisations of diynes are limited to mainly trialkylboranes (such as BEt_3), and select examples with allyl- and vinylboranes. There is an absence of reported activity with simple triarylboranes such as BPh_3, placing a limitation on substrates that can be synthesised in this manner.

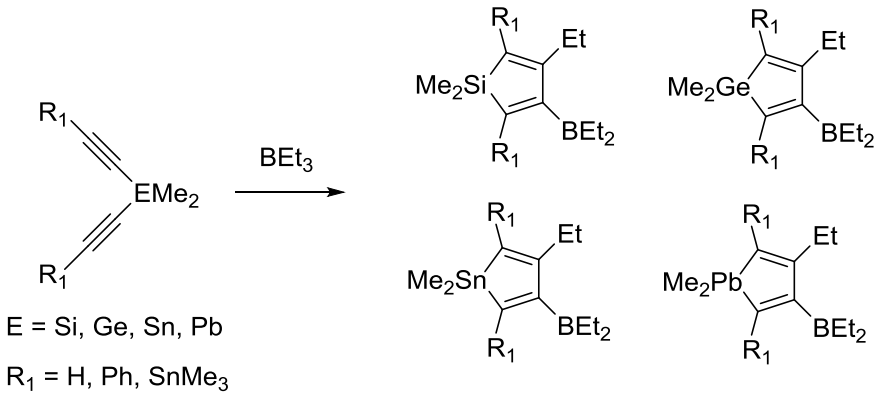


Figure 5.4: Synthesis of heteroarenes using the Wrackmeyer reaction

More recently, the strong boron electrophile tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) has been shown to be a reliable reagent for 1,1-carboboration reactions, allowing transfer of an aryl group (in this case a pentafluorophenyl-group). When exposed to activated alkynes like those mentioned above, similar products to the Wrackmeyer reaction can be obtained, though the conditions are usually milder

due to the greater Lewis acidity of the borane inducing a more rapid reaction. When dialkynylsilanes are reacted with $B(C_6F_5)_3$ the product is a boryl-substituted silole species (like those shown above from Wrackmeyer, albeit featuring an arene transfer group) as shown below in Figure 5.5. [25]

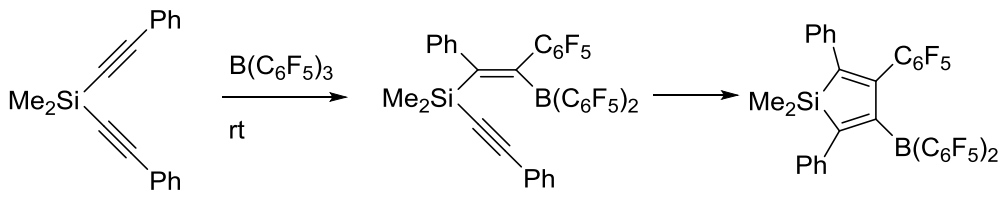


Figure 5.5: Carboboration of dialkylsilanes

Terminal alkynes also undergo facile 1,1-carboboration with $B(C_6F_5)_3$ something not possible using the less electrophilic BEt_3. When phenylacetylene is reacted the product is a 50:50 mixture of the (*E*) and (*Z*) isomers of the 1,1-carboboration product. In this case, the $B(C_6F_5)_3$ has delivered a C_6F_5 group, and the hydrogen group has migrated to the other end of the alkene. Photolysis of this mixture afforded solely the (*Z*)-isomer, which was identified by X-ray crystallography. [26]

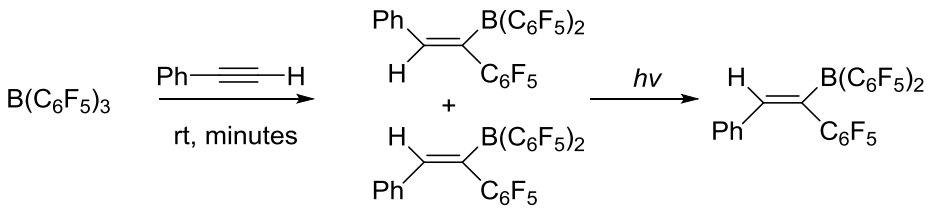


Figure 5.6: Carboboration of terminal alkynes

It was subsequently shown that 1,1-carboborations of terminal alkynes was possible through the use of electrophilic boron reagents $RB(C_6F_5)_2$, where R can be a variety of aliphatic hydrocarbyl-groups. Using this method, the borylated alkene

was generated as a mixture of stereoisomers in *E*/*Z* ratios of 1:1.2 – 1:1.9 depending on steric bulk of the R group. Subsequent photolysis of the mixture resulted in high conversion of the (*E*)-isomer to the (*Z*)-isomer, giving a single product in good yields. The reaction was found to be chemoselective with regards to the migrating group at the borane: When R ≠ C_6F_5, there is no observed migration of the C_6F_5 groups bound to boron. [27]

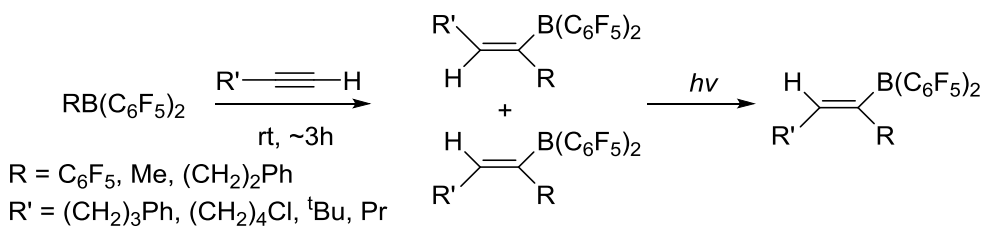


Figure 5.7: Carboboration of terminal alkynes using $RB(C_6F_5)_2$

In addition to this, a method to selectively produce the (*E*)-isomer of the carboboration product was discovered. Using $B(C_6F_5)_3$, the 1,1-carboboration of terminal alkynes featuring an ether substituent proceeds as expected to afford the mixture of isomers, as with other terminal alkynes. However, photolysis returns primarily the (*E*)-isomer instead of the (*Z*)-isomer, as was the case with phenylacetylene. This is due to internal oxygen to boron coordination between the ether and boryl groups, which results in a more stable and favourable isomer.

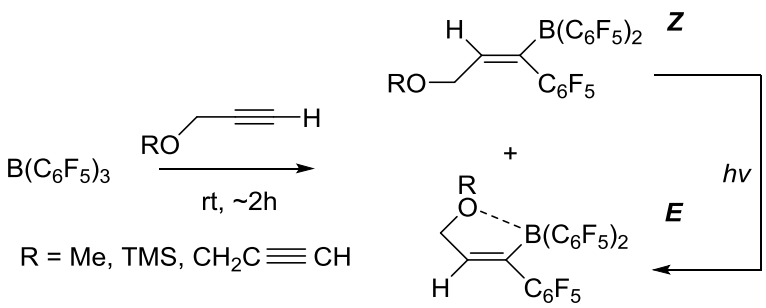


Figure 5.8: Carboboration of ether-substituted alkynes with $B(C_6F_5)_3$

$B(C_6F_5)_3$ also reacts with internal alkynes to undergo 1,1-carboboration. Whilst the reaction conditions are harsher than those with terminal alkynes, no doubt due to the cleaving of a strong, non-activated C-C bond, the reaction proceeds analogously at the elevated temperatures. By using the symmetrical alkyne 3-octyne, only a single isomer is obtained from the reaction.[28,29] More recently, Berke *et al.*[30] demonstrated a 1,1-addition of frustrated Lewis pairs featuring $B(C_6F_5)_3$ across a terminal alkyne, in a similar manner.

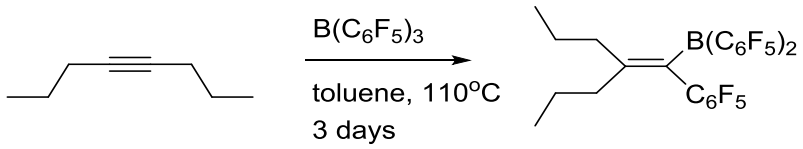


Figure 5.9: Carboboration of internal alkynes

Besides generating products useful for cross-coupling reactions, 1,1-carboboration reactions can have other uses. One such is the synthesis of alkenyl-bridged intramolecular FLPs, which are interesting species in catalysis. [31] These can be generated by the reaction of $B(C_6F_5)_3$ with phosphinyl substituted alkynes, as shown below in Figure 5.10. In this case, the $-PPh_2$ group migrates during the 1,1-carboboration. [32]

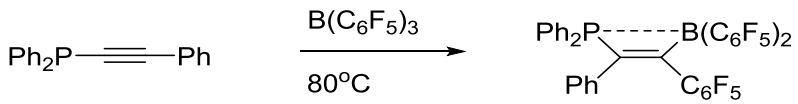


Figure 5.10: Carboboration of phosphinyl substituted alkynes

1,2-Carboborations of alkynes are rarer in literature than the 1,1-carboborations, and whilst there are several reported transition metal-catalysed examples,[33] there are few examples of metal-free examples available. One example

of transition metal catalysed 1,2-carboboration was demonstrated by Suginome *et al*.[34] where alkynylboranes were utilised with a nickel catalyst. It was observed that the stereochemical outcome of the reaction is a *cis* addition.

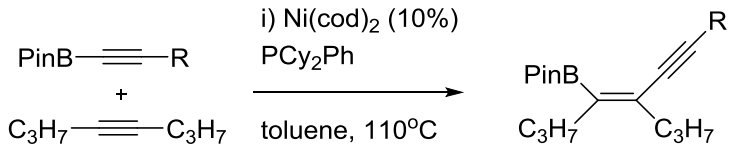


Figure 5.11: Metal catalysed carboboration of alkynes

Lappert and Prokai demonstrated metal-free carboboration wherein certain aryl-haloboranes would undergo 1,2-carboboration with select alkynes, although mixtures of haloboration and carboboration were sometimes observed.[35] In fact, it was demonstrated that haloboration was the dominant reaction pathway, showing the rarity of 1,2-carboborations in literature.

One example of 1,2-carboboration using borocations is through the use of quinolato-borenium salts, and a selection of internal alkynes. Whilst the 1,2-carboboration products were isolated, the reaction was complicated by the tendency of alkynes to oligomerise in the presence of Lewis acids, such as $AlCl_3$. [36]

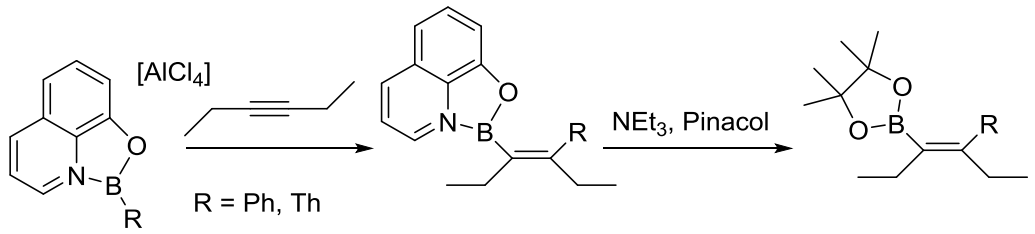


Figure 5.12: 1,2-Carboboration internal alkynes

A rare example of an anti-carboboration exists, where the two groups are added *trans* across the alkyne, in the reaction of alkynyloates with alkyl, aryl, and alkenylboranes. The reaction is a 1,2-carboboration, but where the boron and the group transferred from boron are positioned *trans* to each other on the newly formed alkene. As shown below in Figure 5.13, these reactions require trialkylphosphines as a catalyst. [37]

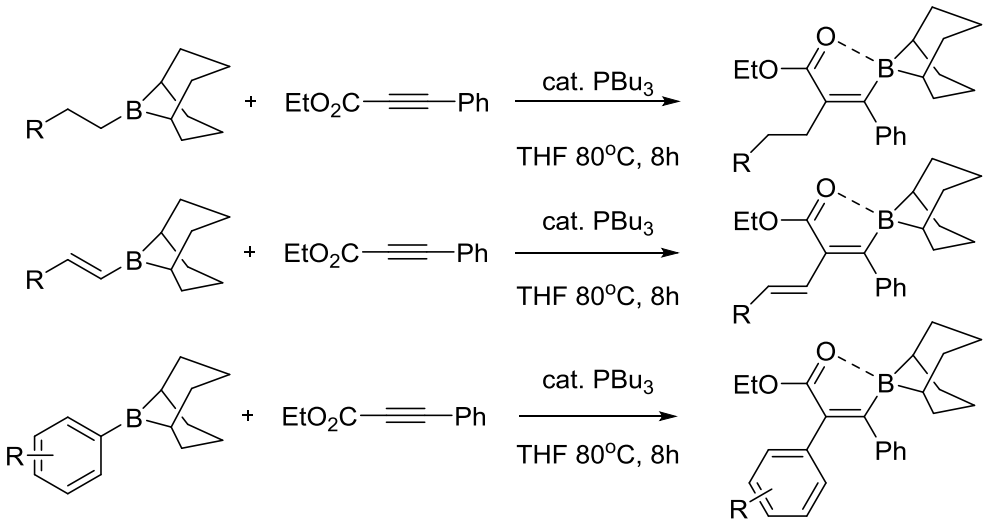


Figure 5.13: The *anti* 1,2-carboboration of alkynoates

The proposed catalytic cycle involves carbonyl activation via B-O binding allowing the addition of the phosphine to the alkynoate, forming a zwitterionic allenoate intermediate. This allows the R-group bound to boron to migrate to the central allene carbon, forming a phosphonium ylide. After isomerisation, the ylide carbon binds to boron, followed by the elimination of PBu_3 in conjunction with B-O bond cleavage yields the vinylboronate and regenerates the catalyst. The B-O interaction and concerted nature of the final elimination determines the unusual stereochemistry observed.

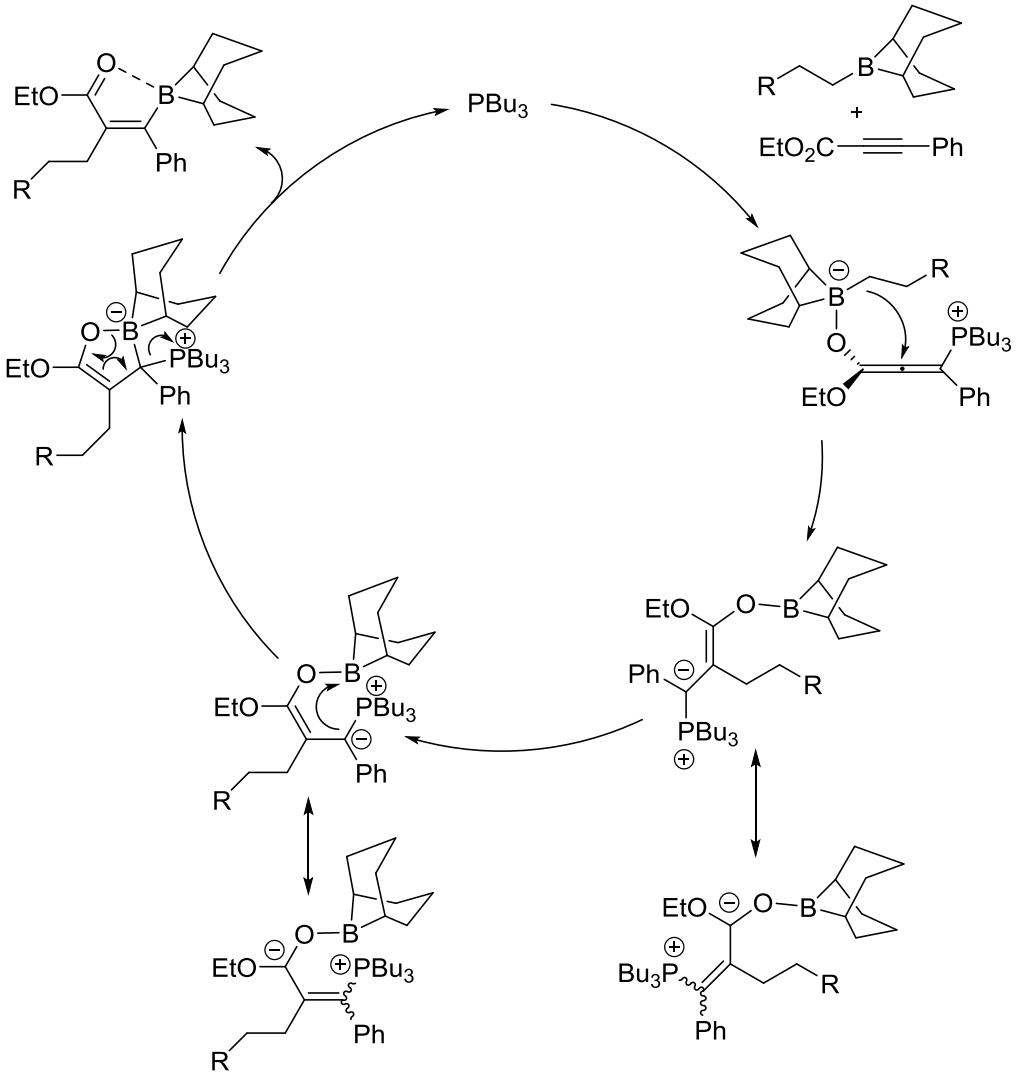


Figure 5.14: Proposed catalytic cycle of *anti* 1,2-carboboration

Recently Bourissou *et al*. [38] demonstrated the 1,2-carboboration of 3-hexyne using a borenium salt. The phosphorous coordinated borenium shown in Figure 5.15 reacted rapidly with 3-hexyne at room temperature, with the reaction judged to be complete within 2 hours by multinuclear NMR spectroscopy. The product is a vinyl borenium where the mesityl-group was found to be *cis* to the boron.

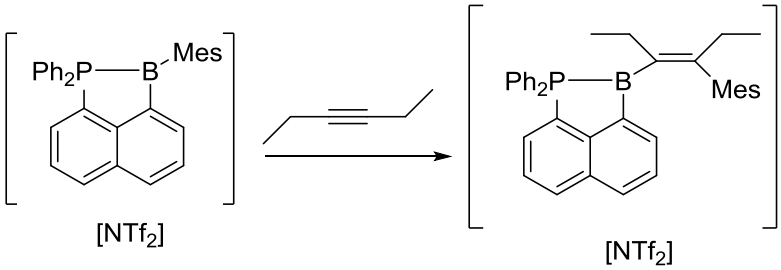


Figure 5.15: 1,2-carboboration of 3-hexyne

With the carboboration of alkynes using B-aryl and B-vinyl containing compounds (due to the π donation lowering electrophilicity at boron in the neutral boranes) so scarsely reported, we decided to explore borocations containing these substituents as migratory groups. The transfer of more diverse arenes and heteroarenes to alkynes represents an attractive route to more complex vinyl boronate species.

5.2: 1,1-carboboration of activated alkynes

As mentioned in Chapter 2, the borocation [PhClB(2DMAP)][$AlCl_4$] was synthesised to mirror the reactivity of [Cl_2B(2DMAP)][$AlCl_4$] with terminal alkynes, but to undergo 1,2-carboboration instead of haloboration. While this ultimately proved unsuccessful, with haloboration the only observed reactivity, it was postulated that this aryl containing borocation may undergo 1,1-carboboration with activated alkynes, similar to the Wrackmeyer reaction.[21] Trimethylsilyl- substituted alkynes were chosen, due to the relative availability and precedence to readily undergo 1,1-carboboration.

[PhClB(2DMAP)][$AlCl_4$] was reacted with equimolar TMS-propyne at room temperature in DCM under inert conditions. The NMR spectra at t = 10 minutes showed that the alkyne was being slowly consumed; new peaks in the ^{1}H NMR spectrum corresponding to new methyl and TMS environments were present, as was a new peak in the ^{29}Si spectrum at -6.05 ppm consistent with the product containing a vinyl TMS group. The unreacted boronium was very poorly soluble in DCM, possibly inhibiting the reaction, so brief heating to 60°C in a sealed tube was used to accelerate reactivity. Upon cooling to room temperature, any unreacted boronium crystallised out of solution. Heating times were optimised to 30 minutes; although some unreacted boronium persisted it was found that extended periods of heating generated other species, so the reaction was esterified with pinacol / NEt_3 after 30 minutes of heating.

Esterification of the reaction mixture gave two major products; 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (PinBPh) which is the result of esterifying

unreacted boronium, and a second product. Isolation of this new product by column chromatography allowed it to be analysed and identified. The ^{1}H NMR spectrum showed five aromatic protons, indicating that the phenyl group from the boronium was part of the product. Also present were peaks at 1.68, 1.23 and 0.23 ppm, corresponding to a methyl, pinacol and TMS group, respectively. Given this data alone, it is possible to infer that this new product is the result of a carboboration reaction. The remaining NMR evidence supports this; the ^{11}B NMR spectrum shows a single peak at 30.2 ppm, indicative of a vinyl-boronate ester, and the ^{29}Si NMR spectrum shows a single peak at -4.22 ppm, which corresponds to a vinyl TMS group.

To confirm the structure of the product, nOe spectroscopy experiments were undertaken, the results of which showed through-space interaction between the pinacol group and the TMS-group, whilst the methyl group showed interaction with an aromatic proton of the phenyl ring, as well as the TMS-group. Thus, the structure was confirmed as the product of a 1,1-carboboration of a TMS-alkyne, the result of migration of the TMS group, which itself is *cis* to the boron group. Unlike the products of previous 1,1-carboborations, only a single isomer was isolated.

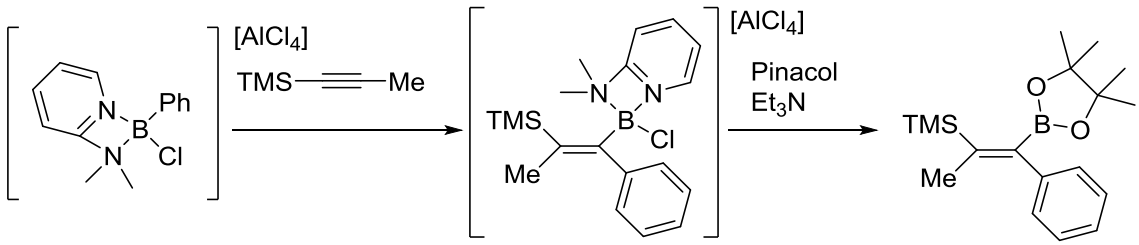


Figure 5.16: 1,1-Carboboration of TMS-Propyne

The mechanism of this 1,1-carboboration reaction is postulated as shown below in Figure 5.17 (based on its similarity to 'Wrackmeyer' carboborations with BEt_3).[21] Initial borylation of the nucleophilic alkyne results in the formation of a carbocation, in reactivity analogous to that of 1,2-haloboration (Chapter 4.2). Subsequent migration of the TMS group results in a carbocation *alpha* to the boron, stabilised through the *beta* silicon effect. This is followed by a migration of the phenyl group from boron to the carbocation, generating the 1,1-carboborated alkene.

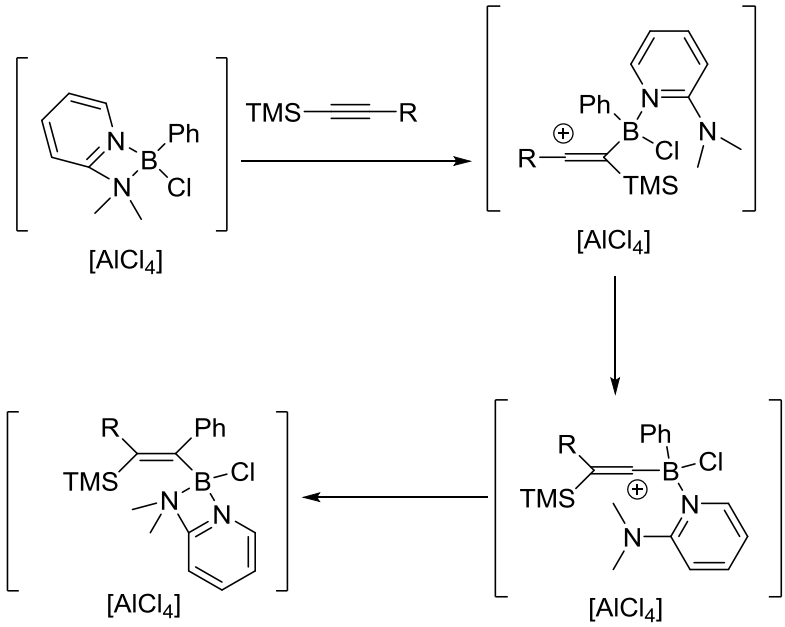


Figure 5.17: Postulated mechanism of 1,1-carboboration – carbocationic intermediates shown classically as vinyl cations, π complex TMS is also a possibility

Following the successful carboboration of TMS-propyne, other TMS-alkynes were investigated, as shown in Table 5.1, below, and all underwent the 1,1-carboboration reaction, giving single products (regio- and stereo-chemistry confirmed by nOe spectroscopy) in comparable yields to **5i**.

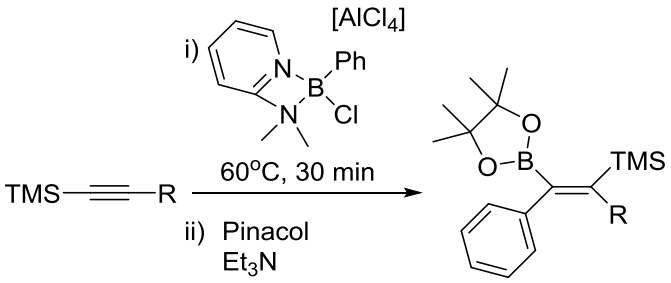
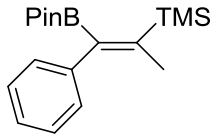
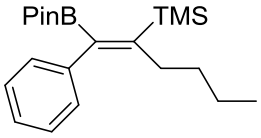
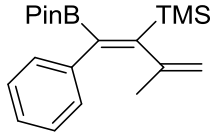
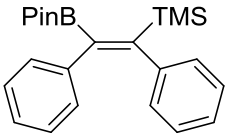
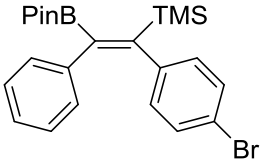


Table 5.1		
Entry	**Compound**	**Isolated Yield (%)**
5i		63
5ii		61
5iii		55
5iv		65
5v		56

Whilst only a single isomer of the 1,1-carboboration product was observed after purification, competing reactivity was also observed which prevented the yields from being higher, which will be discussed shortly in section 5.3. As mentioned, the reactions were quenched by esterification after 30 minutes, as this

represented the best balance of maximising the desired product and minimising the additional, unidentified product or products. However, this also meant that there was unreacted [PhClB(2DMAP)][$AlCl_4$] in solution, which when esterified produces PinBPh, which must be seperated by column chromatography. Heating the reaction for longer periods of time, whilst decreasing the amount of unreacted boronium, increases the amount of by-products. For example, when the reaction mixture of [PhClB(2DMAP)][$AlCl_4$] and TMS-propyne was heated for 18 hours at 60°C, the ^{1}H NMR spectrum shows at least 12 aliphatic resonances, corresponding to various methyl and TMS-groups. In addition to this, large quantities of protonated 2DMAP were present, and it was possible that this proton was derived from the methyl group of TMS-propyne. This would form allene-like species, which may correspond to new peaks between 6.5 and 7.0 ppm. The ^{11}B NMR spectrum shows broad peaks around 66 and 58 ppm, indicating 3-coordinate boron species, consistent with the generation of 2DMAP-H. The ^{29}Si NMR spectrum shows at least 4 vinyl TMS resonances between -4 and -7 ppm, again consistent with the multiple TMS resonances in the ^{1}H NMR spectrum. In addition to this, a ^{29}Si resonance is observed at 10.85 ppm. No literature precedence has been found for silicon in this environment, although heating can result in exchange of groups bound to boron and silicon, in this case possibly forming Si-Cl and B-Me, the latter of which would be consistent with the downfield shift observed in the ^{11}B NMR spectrum.

Another TMS alkyne was utilised in substrate scope expansion, but did not undergo 1,1-carboboration. When trimethyl(3-methylbut-1-yn-1-yl)silane, shown in Figure 5.18, was combined with [PhClB(2DMAP)][$AlCl_4$], no reaction was observed

due to the poor solubility of the boronium, but when the reaction was heated to 60°C, after 5 hours reactivity was observed, though NMR spectroscopy suggested that the 1,1-carboboration was not occurring.

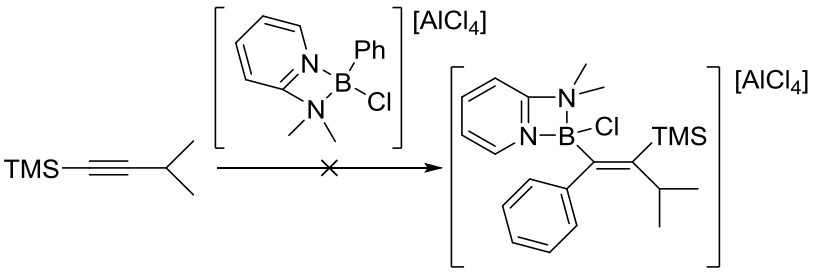


Figure 5.18: 1,1-carboboration was not observed with trimethyl(3-methylbut-1-yn-1-yl)silane

Instead, the ^{1}H NMR spectrum showed a new set of resonances associated with the isopropyl and TMS groups, in similar positions to the (still present) unreacted starting material. However, it was observed that the new doublet, from the two isopropyl methyl groups, and the new TMS resonance integrated 1:1, instead of the 6:9 ratio expected. The ^{11}B NMR spectrum also showed, besides unreacted boronium, new peaks at 66.2 and 54.3 ppm. The latter may be a small amount of $PhBCl_2$, generated from loss of 2DMAP, but the downfield shifted peak at 66.2 ppm is a new species entirely. The ^{29}Si NMR spectrum shows that instead of the expected vinyl-TMS resonance, previously observed ~-4 ppm, two new resonances are observed at 9.74 and 6.82 ppm.

When heated for 1 week, the NMR spectra show that the 1:1 ratio isopropyl:TMS group species is the major product formed, along with the peak at 66 ppm in the ^{11}B spectrum and the 6.8 in the ^{29}Si spectrum. In order to try and isolate this species, $ZnPh_2$ was added to the reaction mixture, to install a phenyl ring on the

boron. As it was expected that the product was a neutral species, it was extracted into toluene to separate it from the ionic remnants, such as 2DMAP-H and $AlCl_4$. The toluene was removed *in vacuo* and the new product was redissolved in DCM, NMR analysis of which showed primarily a single product which frustrated all attempts at crystallisation. The ^{1}H NMR shows a wealth of overlapping aromatic resonances integrating to 14H. In addition, the isopropyl septet is observed at 2.89 ppm, along with the corresponding doublet at 1.05 ppm. As previously seem, the major silicon-bound methyl resonance now integrates to 6H instead of 9H, possibly indicating the loss of, or migration of, one of the methyl groups. The ^{11}B and ^{29}Si also indicate one major product, with peaks at 70 ppm and 6.98 ppm, respectively.

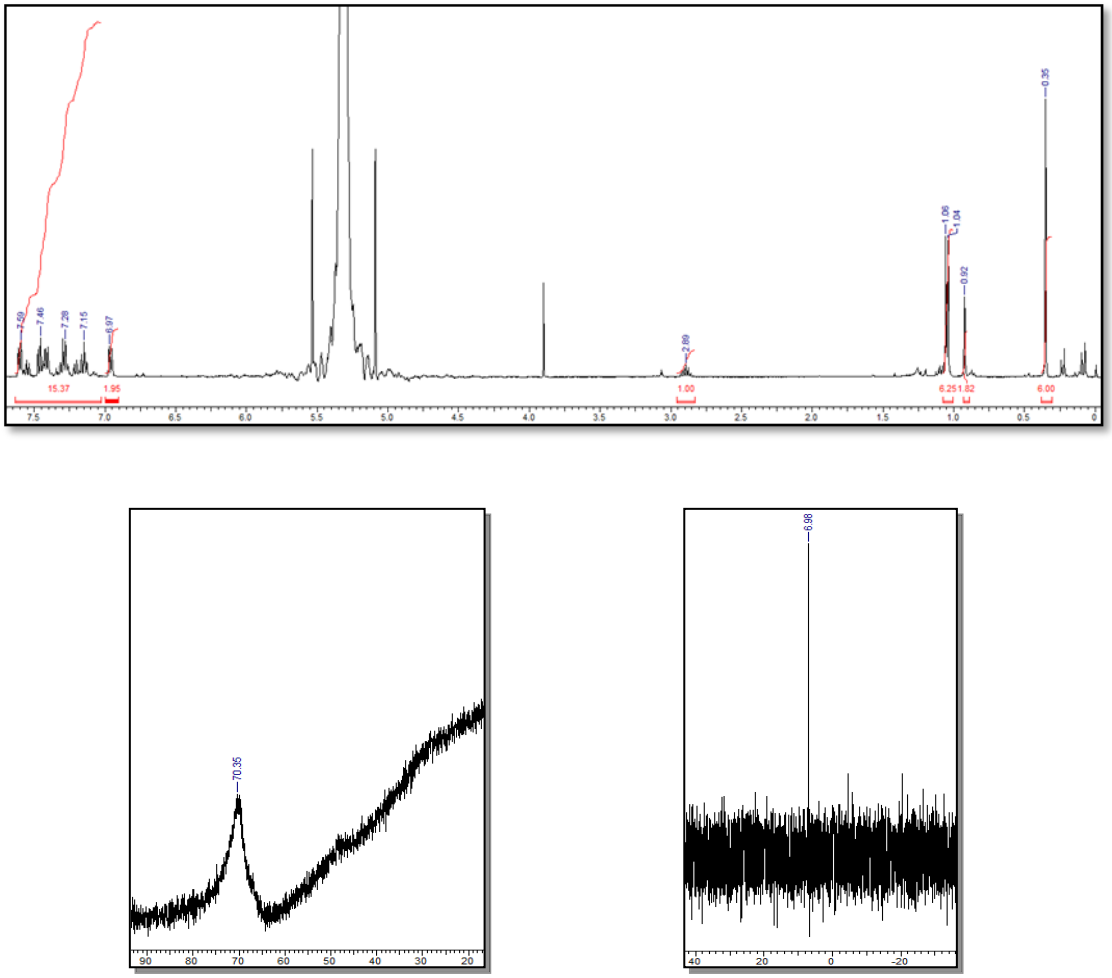


Figure 5.19: ^{1}H, ^{11}B and ^{29}Si NMR spectra of unknown product

This product remains unidentified, and is sensitive to atmospheric conditions which hampered further identification. It is uncertain why this reactivity is only observed with a TMS-alkyne featuring an isopropyl-group, although the enhanced sterics of iPr may be disfavouring TMS migration leading to other reactivity. One possibility of the outcome of this reaction, accounting for the downfield ^{11}B NMR resonance and the 6H singlet in the ^{1}H NMR spectrum would be, during the course of the reaction, exchange of Cl and methyl groups from boron and silicon, respectively.

As such, whilst the reaction of [PhClB(2DMAP)][$AlCl_4$] and TMS-alkynes does give synthetically useful 1,1-carboboration products, the associated limitations of the reaction conditions are undesirable. During attempts to optimise the reaction conditions, a control reaction was carried out between dichlorophenylborane ($PhBCl_2$) and TMS-propyne. It was found that a reaction occurs rapidly, and is complete (as monitored by NMR spectroscopy, based on consumption of the alkyne) within 1 hour. The ^{29}Si NMR spectrum indicated that the TMS group was now in a vinylic environment, as denoted by a shift of -3.88 ppm. The ^{11}B NMR spectrum showed a new peak at 56.0 ppm which is indicative of a vinyl-BCl_2 species.

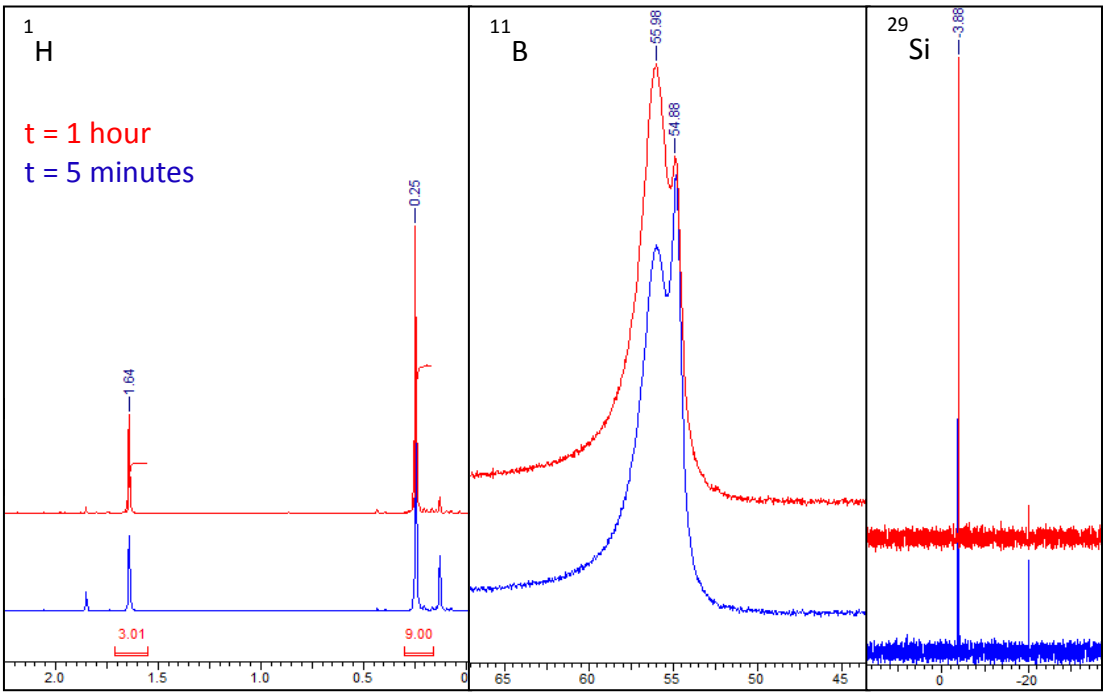


Figure 5.20: NMR spectra for the reaction between $PhBCl_2$ and TMS-propyne, t = 5 min and t = 1h

Whilst the spectroscopic data was identical to the product of the reaction with the borocation, the yield was noticeably better at 88% compared to 63%. With mass spectroscopy and additional NMR data (nOe, Cosy, HMQC, HMBC) confirming the 1,1-carboboration reaction, the substrate scope was expanded to all of the TMS-alkynes previously tested with the borocation.

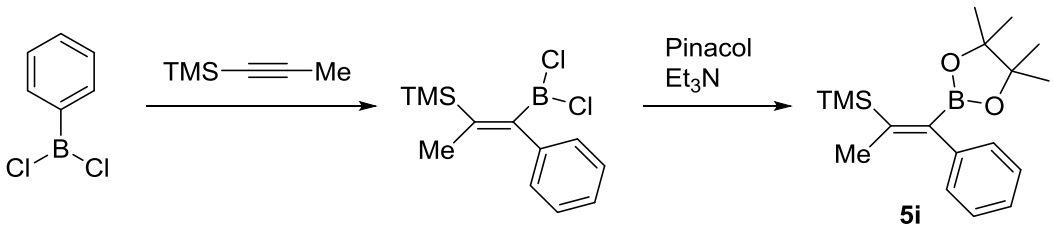


Figure 5.21: 1,1-Carboboration of TMS-propyne using $PhBCl_2$

Pleasingly, reactions between $PhBCl_2$ and multiple TMS-alkynes proceeded well, as summarised below in Table 5.2, with increased yields and fewer by-products from competing reactions. As there does not seem to be a competing

pathway with desilylboration, as found with BCl_3, as no consequential amount of TMS-Cl was observed by NMR spectroscopy, the resulting higher conversions to the carboboration product allowed for higher yields. The lack of associated by-products generated upon esterification was most likely also a factor in the higher yields.

In addition, the alkyne trimethyl(3-methylbut-1-yn-1-yl)silane underwent carboboration readily with $PhBCl_2$, forming **5vi**, whereas with the borocation [PhClB(2DMAP)][$AlCl_4$] the outcome was unidentified. This was due to the unidentified reactivity discussed earlier, which does not occur when using $PhBCl_2$, suggesting that the higher electrophilicity of the borocation is necessary to access the other reaction pathway.

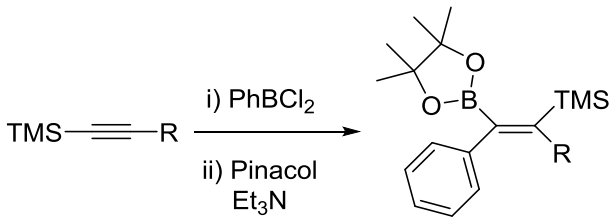
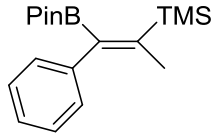
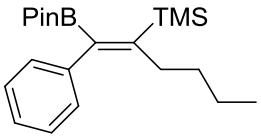
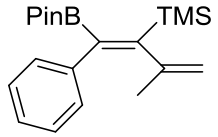
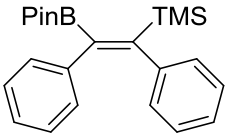
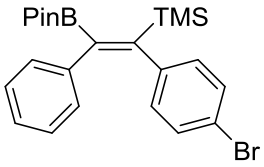
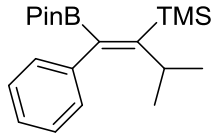


Figure 5.22: General 1,1-carboboration of TMS-alkynes using $PhBCl_2$

Table 5.2			
Entry	**Compound**	**Time (h)**	**Isolated Yield (%)**
(**5i**)		1	88
(**5ii**)		6	79
(**5iii**)		24	77
(**5iv**)		20	85
(**5v**)		20	68
(**5vi**)		2	76

Several of the products obtained were crystalline solids, which were successfully recrystalised to produce crystals suitable for single crystal X-ray diffraction, and their solid state structures subsequently confirmed. In all three structures obtained, the conformation of groups on the alkene backbone corresponded with the NMR data, showing that 1,1-carboboration was taking place. Varying degrees of disorder in the pinacol groups was observed in each structure, one of which, for **5v**, is shown below in Figure 5.23. For clarity, the methyl groups of the pinacol have been omitted.

Table 5.3	
Metric	(**5v**)
C7-C8	1.348(5) Å
B1-Cl7	1.573(5) Å
C1-C7	1.508(4) Å
C8-Si1	1.911(3) Å
C8-C9	1.500(4) Å
B1-C7-C1	114.6(3)°
Si1-C8-C9	113.0(2)°
B1-C7-C8-Si1	6.1°

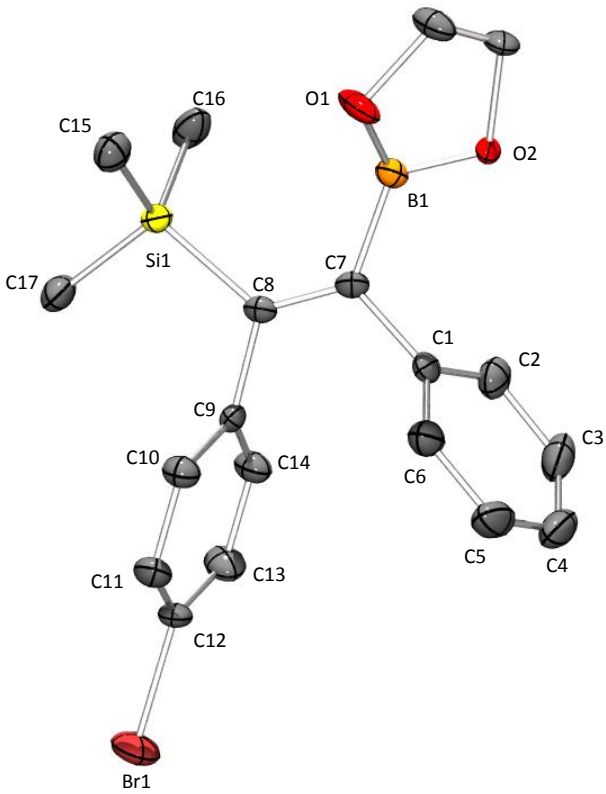


Figure 5.23: Single crystal X-ray structure of (**5v**) (thermal ellipsoids at 50% probability, counterions, hydrogens and disordered pinacol methyls omitted for clarity. Full crystal data and structure refinements listed in Appendix)

The structure of **5v** shows the 1,1-carboboration of trimethylsilyl(4-bromophenylacetylene). The disorder in the pinacol group may be due to steric interactions with the bulky TMS-group that is mutually *cis* on the alkene, or due to the non-planar nature of the 5-membered ring in different structural conformations. The C7-C8 bond length is consistent with a C=C bond, with the substituents trigonal planar around both (sp^2) carbons, as expected.

In addition to TMS-substituted alkynes, examples of other R_3Si-alkynes were investigated, to see if 1,1-carboboration could be extended. Dimethyl(pent-1-yn-1-yl)(phenyl)silane was synthesised from 1-pentyne and $Me_2PhSiCl$, as this represented increased steric bulk about the silicon, in order to investigate this effect of reactivity. The $Ph(Me_2)Si$- group is also synthetically important as a functional equivalent of a hydroxyl group, and can be converted using Tamao-Fleming oxidation reactions.[39] When dimethyl(pent-1-yn-1-yl)(phenyl)silane was reacted with [PhBCl(2DMAP)][$AlCl_4$] using previously optimised conditions, in-situ ^{29}Si NMR spectroscopy showed a mixture of products, among them a resonance consistent with a vinyl-$SiMe_2Ph$ group. Whilst esterification of this crude mixture afforded the product **5vii**, which was isolated after purification by column chromatography, the yield was very low (8%). When left for 18 hours at 60°C, it was observed that the major ^{29}Si NMR resonance was attributed to $Ph(Me)_2Si$-Cl, possible indicating a desilylboration akin to those reported in Chapter 3. This alkynyl-boron species would also be protodeboronated upon esterification, with PinBPh obtained instead with loss of the alkynyl fragment.

However, the ^{11}B NMR spectrum also shows downfield 3-coordinate boron resonances at 45.4 and 59.8 ppm, which in tandem with the presence of protonated 2DMAP, hint at more complex reactivity. These competing reaction pathways help to explain why the 1,1-carboboration product was obtained in such a low yield, as the generation of other products preclude the formation of the desired one. Attempts to identify the other products were unsuccessful.

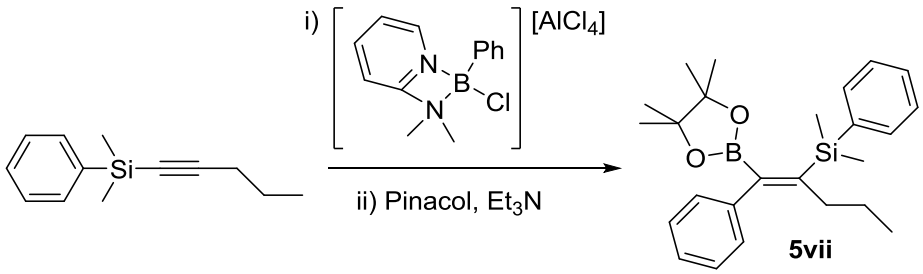


Figure 5.24: 1,1-carboboration of dimethyl(pent-1-yn-1-yl)(phenyl)silane

When dimethyl(pent-1-yn-1-yl)(phenyl)silane was reacted with $PhBCl_2$, the reaction proceeded swiftly at room temperature, and all the alkyne was quickly consumed by NMR spectroscopy. The ^{11}B NMR spectrum showed a very broad resonance centred at 59.9 ppm, similar to one on the unidentified products of the reaction of this alkyne with the boronium. The ^{29}Si spectrum, in concert with the ^{1}H spectrum, showed that the major silicon environment was $Ph(Me)_2Si$-Cl, indicating that the desired 1,1-carboboration had not occurred. Esterification of this reaction gave PinBPh as the major product, indicating that the major product at 59.9 ppm in the ^{11}B NMR spectrum may be an alkynyl or dialkynylborane (hence prone to protodeboronation of the B-alkynyl moiety), maintaining the Ph-B bond in each case, as shown in Figure 5.25.

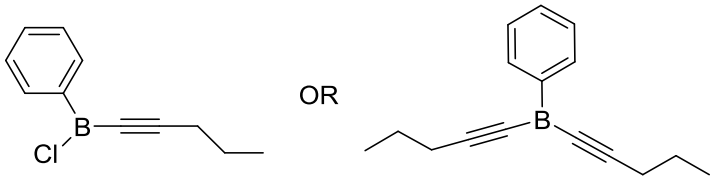


Figure 5.25: Possible outcomes of reaction between $PhBCl_2$ and dimethyl(pent-1-yn-1-yl)(phenyl)silane

The next R_3Si-alkyne investigated was 1-triisopropylsilylpropyne, representing a significant increase in steric bulk around silicon. Under the optimised reaction conditions of heating to 60°C for 30 minutes with the boronium, there was no observed reactivity by NMR spectroscopy. Extending the time to 24 hours showed still no reaction, with both the alkyne and the boronium persisting. This would suggest that there is a limit to the size of the silyl-group in this reaction, which in this case prevents formation of the first proposed intermediate, shown in Figure 5.26.

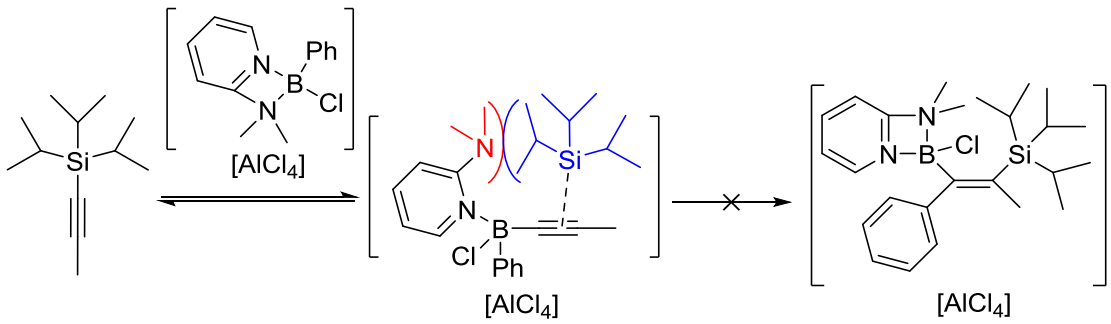


Figure 5.26: Proposed steric interactions of triisopropylsilyl-group

Following this work, it was postulated that modification of the borane, specifically replacing the phenyl group with other arenes, would allow access to additional 1,1-carboboration products. As such, four new boranes of the general structure $RBCl_2$ were generated by electrophilic arene borylation (see Chapter 2 for details) and reacted with TMS-propyne *in situ*.

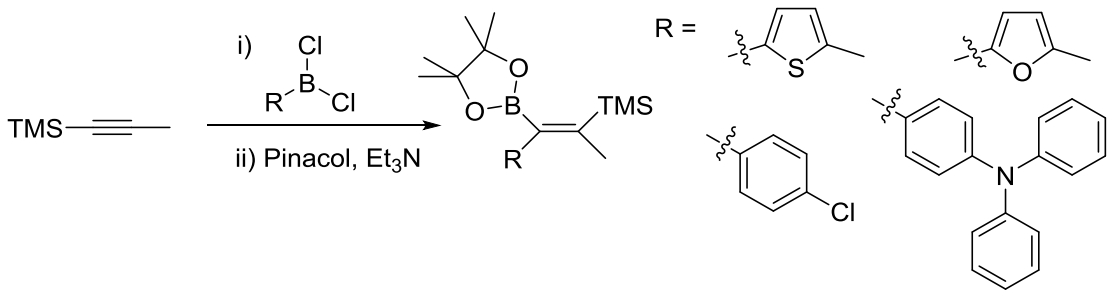
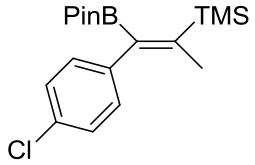
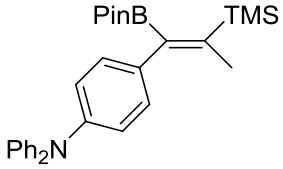
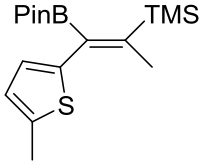
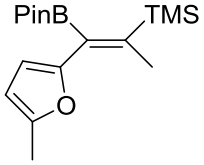


Table 5.4			
Entry	**Compound**	**Time (min)**	**Isolated Yield (%)**
(**5viii**)		40	61
(**5vix**)		30	65
(**5x**)		60	77
(**5xi**)		30	65

In each case the reaction was rapid, and the initial products were all esterified within an hour. Each product gave comparable NMR data to (**5i**), with the only variance the different arene groups. This showed that 1,1-carboboration of TMS alkynes can be achieved with the transfer of other groups besides phenyl,

obtained in good yields considering these are multistep reactions, starting with the borylation of the (hetero)arene.

However, limitations of this reaction were uncovered during expansion of the substrate scope of TMS-alkynes besides TMS-propyne. Each of the (hetero)arene bound boranes $RBCl_2$ were reacted with both TMS-phenylacetylene and trimethyl(3-methylbut-1-yn-1-yl)silane, but rather that the relatively clean reaction observed with TMS-propyne, the primary product generated was TMS-Cl in each case. This would imply that TMS-propyne is the limit of the reactivity, as inreasing the steric bulk of the alkyne precludes the desired reactivity, presumably allowing the competing desilylboration pathway to take prominence.

In addition, concerns were raised that the broader scope of 1,1-carboboration reactions with commercially sourced $PhBCl_2$ may be catalysed by trace impurities of metal in the starting reagent. Since this was most likely to be tin, due to the common preparation of $PhBCl_2$ by transmetalation reaction between BCl_3 and Ph_4Sn,[40] ^{119}Sn NMR spectroscopy was used on our $PhBCl_2$ reagent. Pleasingly, no trace of tin was observed, but to further prove this reactivity was not caused by undetectable traces of Sn, $PhBCl_2$ was synthesised using electrophilic borylation to use in a control reaction. DMT-BCl_3 and 2 equivalents of $AlCl_3$ were dissolved in benzene/*o*-DCB and heated to 60°C for 24 hours. NMR spectroscopy confirmed the generation of $PhBCl_2$, to the solution of which was added hexane, which caused the ionic by-products to precipitate. By careful decanting of the solvent, $PhBCl_2$ was isolated. In order to assess the viability of the independently synthesised $PhBCl_2$, it was reacted with trimethyl(3-methylbut-1-yn-1-yl)silane,

which was chosen because: i) previous reaction with $PhBCl_2$ was swift (2 hours); and ii) this alkyne did not react by 1,1-carboboration with other aryl-BCl_2 reagents synthesised and used *in situ*. Pleasingly, NMR spectroscopy showed formation of the vinylborane species from 1,1-carboboration predominantly, as indicated by the ^{11}B and ^{29}Si spectra.

With $PhBCl_2$ reacting with a range of TMS-alkynes, this methodology allows access to a selection of 1,1-vinylboronate products. Modification of the phenyl group on boron to feature substituted arenes and heteroarenes allows access to certain vinylboronates featuring these groups geminal to boron, albeit with limited TMS-alkyne scope. The reactions proceeded with excellent stereo-and regiochemistry control, with only a single isomer isolated post esterification.

5.3 Synthesis of 2-boradienes

As mentioned in section 5.2, during 1,1-carboboration reactions with [PhClB(2DMAP)][$AlCl_4$], it was observed that over extended periods of time, or when the reaction mixture was heated to 60°C, other products were observed by NMR spectroscopy. When the reaction mixture from the reaction with TMS-propyne was esterified with pinacol, one of these new products persisted, resulting in a crude mixture containing itself, the 1,1-carboboration product, and a small quantity of PhBPin. This new product was isolated via column chromatography, and its structure elucidated. Analysis by ^{1}H NMR spectroscopy showed that there was a phenyl group (as indicated by a 5H multiplet from 7.24 – 7.15 ppm), , whilst further upfield were two 3H singlets at 1.98 and 1.85 ppm, indicating two distinct methyl-groups and two 9H singlets at 0.09 and -0.15 ppm, which are consistent with two distinct TMS-groups. The final resonances were two 6H singlets at 1.16 and 1.11 ppm. Owing to the fact that the ^{11}B NMR spectrum showed only a single peak at 30.3 ppm, indicating a vinyl pinacolate ester, these two peaks are consistent with a pinacol group subject to hindered rotation around the C-B bond so as to differentiate its two sets of two methyl-groups into two distinct resonances. Similar phenomena have been reported previously in hindered pinacol boronate esters.[41]

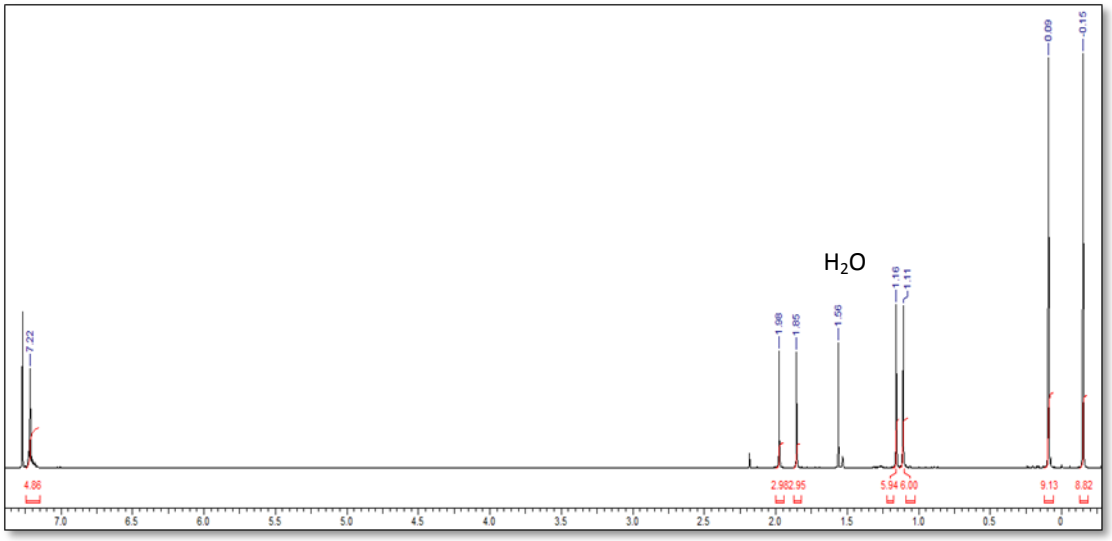


Figure 5.27: ^{1}H NMR Spectrum for Compound (**5xii**)

The ^{29}Si NMR spectrum shows a single peak at -6.00 ppm, which is in the region of a vinyl TMS-group, presumably the two distinct TMS groups are coincident. The ^{13}C NMR spectrum shows seven resonances between 144.00 and 125.59 ppm, indicating the prescence of the phenyl ring (4 resonances) and three of the 4 vinyl resonances of a borylated diene (the carbon bound directly to boron is not observed). In addition, resonances associated with pinacol are observed, along with two other aliphatic resonances, most likely methyl groups, and a single TMS resonance at 0.01 ppm (if there are two TMS-groups, presumably the methyl groups bound to silicon are coincident). The NMR data suggested that either following, or in addition to, a 1,1-carboboration, secondary reactivity with another molecule of unreacted TMS-propyne had led to this new product, which seemed to be a borylated diene. Mass spectroscopy supported this hypothesis, with a measured accurate mass of 429.2812 gmol^{-1} consistent with **5xii** (Figure 5.28).

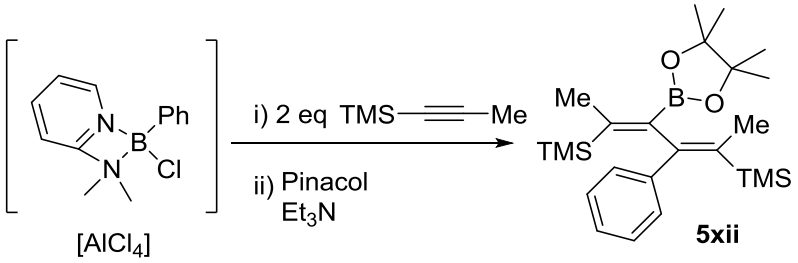


Figure 5.28: Synthesis of 2-boradiene (**5xii**)

Using nOe spectroscopy, it was shown that the methyl resonance at 1.85 ppm showed interaction with both TMS resonances, but the methyl resonance at 1.98 only saw this interaction with one of the TMS resonances. However, this methyl did interact with the pinacol resonance at 1.16 ppm, whilst the methyl at 1.85 did not. The 5H aromatic multiplet saw interaction with both TMS groups, as well as the pinacol. In order to postulate a structure based on this data, we needed to assume that the diene was not planar due to steric crowding. This way, the highlighted methyl group in Figure 5.29 can have through-space interactions with both TMS groups, whilst the other methyl cannot, and the highlighted diene-backbone is non-planar. However, steric interactions probably prevent free rotation about this bond.

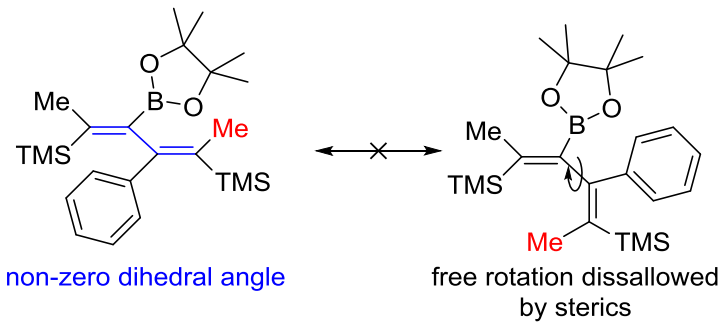


Figure 5.29: Speculated structure of (**5xi**) based on nOe spectroscopy data

To probe the non-planar nature, computational studies were undertaken as single crystals were not obtainable in our hands. Calculations performed by Dr. Jessica Cid at the M06-2X/6-311G(d,p)(PCM:DCM) level suggested that the diene is non-planar, with a C1-C2-C3-C4 dihedral angle of 60.24°. This structure is consistent with the observed nOe interaction of one of the methyl groups with both TMS groups.

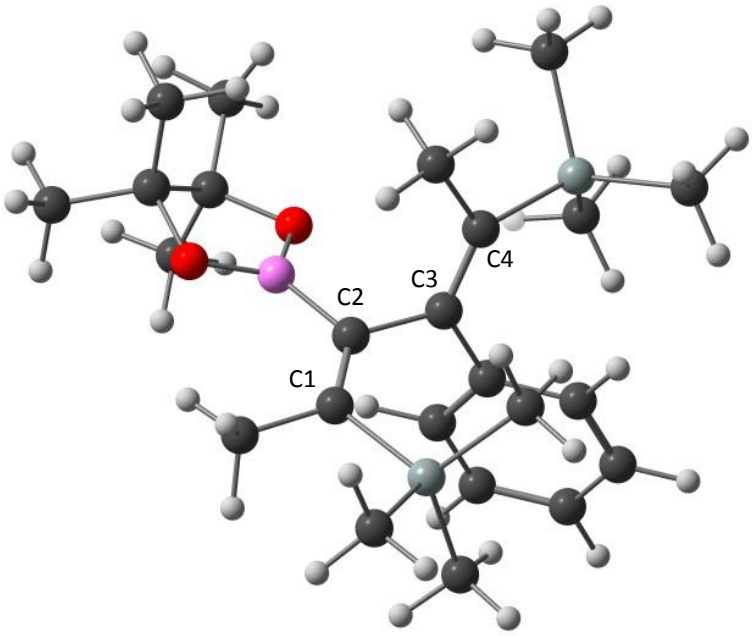


Figure 5.30: Calculated structure of (**5xii**) (M06-2X/6-311G(d,p)(PCM:DCM))

In order to investigate the reaction further, and to try and maximise the yield of the 2-boradiene, the reaction conditions were optimised to allow total conversion of the 1,1-carboboration product into the diene. It was found that using a large excess of TMS-propyne (10 eq) did increase the amount of diene observed in situ, however the NMR spectra always showed a mixture of 1,1-carboboration and diene formation; conversion was never quantitative (in boron). Attempts at heating

for longer, and at higher temperatures, did not give any noticeable increase in diene formation.

The proposed mechanism for diene formation is shown in Figure 5.31, and involves the initial migration of the TMS group, as with the previous 1,1-carboborations, forming vinylcation 1, which is then intercepted by another equivalent of TMS-propyne. After attack by alkyne, another TMS migration occurs in conjunction with migration of the boron group, creating a new less sterically crowded vinylcation 2 less proximal to boron, but still stabilised by the beta silicon effect. The phenyl group is now able to migrate to this cation, forming the product.

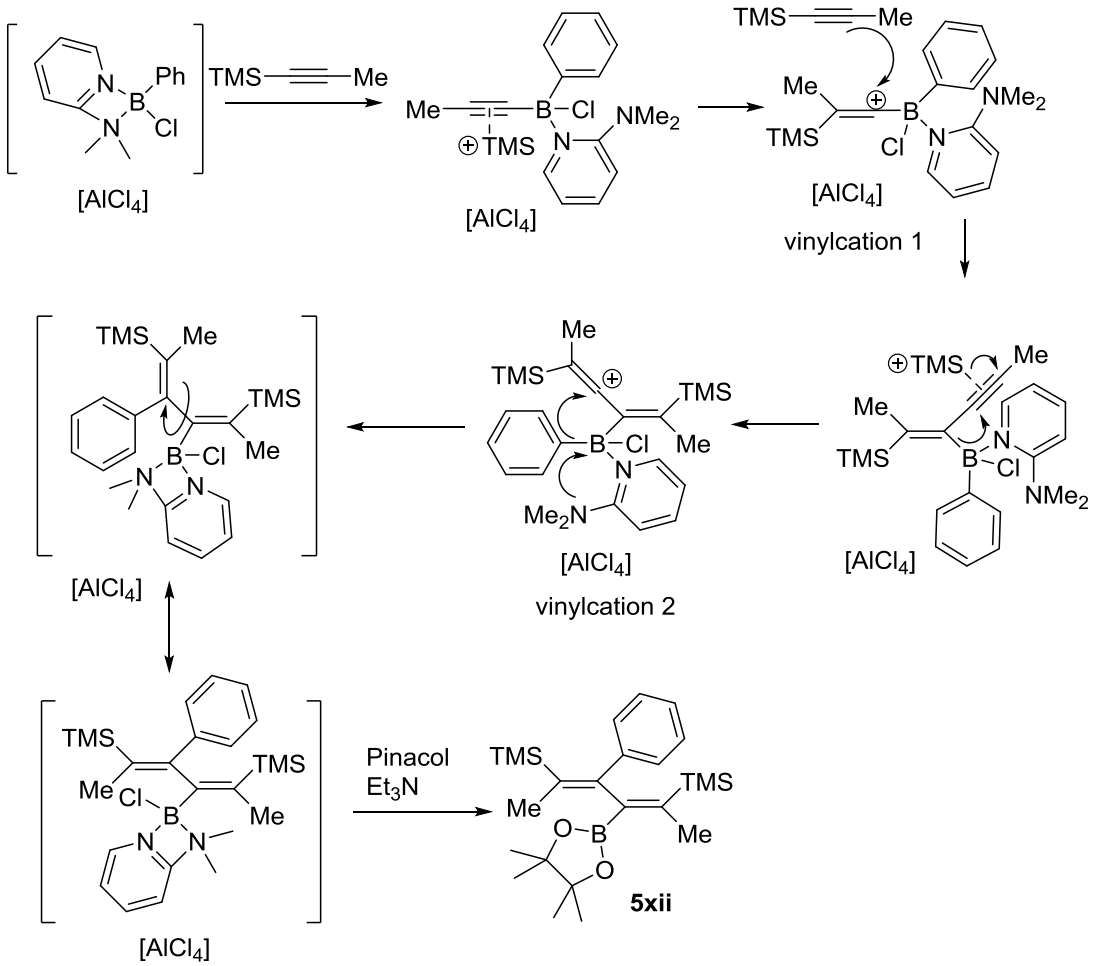


Figure 5.31: Proposed mechanism of the formation of the 2-boradiene (**5xi**)

The formation of the 2-boradienes, such as **5xii**, proved to be very limited when preliminary substrate scope expansion was probed. The synthesis of [Cl_2B-2-methylthiophene(2DMAP)][$AlCl_4$] was discussed in Chapter 2, and herein it was utilised to see if a borylated diene could be synthesised featuring a heteroarene at the 3-position of the 2-boradiene backbone, instead of the phenyl group featured in **5xii**. Subsequently [Cl_2B-2-methylthiophene(2DMAP)][$AlCl_4$] was reacted with TMS-propyne at room temperature. The reaction was monitored by multinuclear NMR spectroscopy, where once again a mixture of 1,1-carboboration and the diene were formed. In addition, over extended periods of time, 2DMAP-H was produced, as with previous reactions of these arene bound borocations with TMS-alkynes. Upon esterification, a mixture of products was formed; a combination of the 1,1-carboboration product, PinB-2-methylthiophene from unreacted boronium, and the desired diene product, which was isolated via column chromatography. The ^{1}H NMR spectrum of diene **5xiii** is shown below in Figure 5.32, and is similar to that of the diene **5xii**; both feature the splitting of the pinacol peak into two 6H singlets, along with two methyl resonances and two TMS resonances derived from the two equivalents of TMS-propyne. The resonances associated with the incorporated 2-methylthiophene are now present as well.

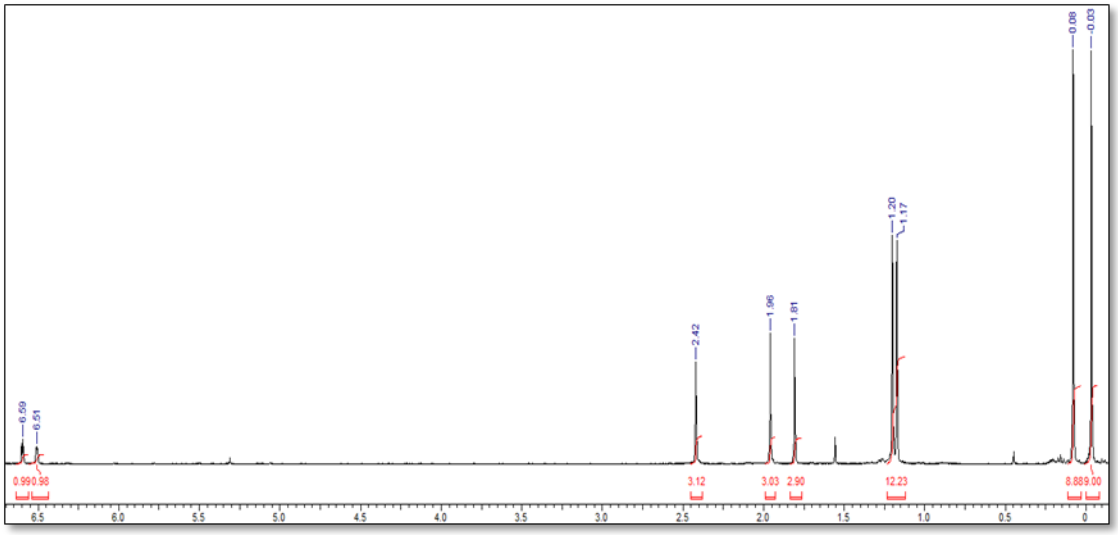


Figure 5.32: ^{1}H NMR Spectra for Compound (**5xiii**)

The ^{11}B NMR spectrum showed a single peak at 29.4 ppm, whilst the ^{29}Si NMR spectra showed only a peak at – 5.98 ppm, both comparable with the previous borylated diene. In addition to this, the ^{13}C NMR spectrum showed two resonances for the TMS carbons at -0.13 and -0.54 ppm, along with the remaining expected peaks for the proposed structure. Careful inspection of the spectrum showed that the pinacol carbons are in slightly different environments, with resonances at 24.65 and 24.59 ppm. Analysis using nOe spectroscopy showed results very similar to product **5xii**, with the aromatic protons on thiophene showing through-space interaction with both the TMS groups and the pinacol, and similar interactions between the vinyl-methyls observed. The methyl group bound to thiophene is too distant to see any interaction except with the closest aromatic H.

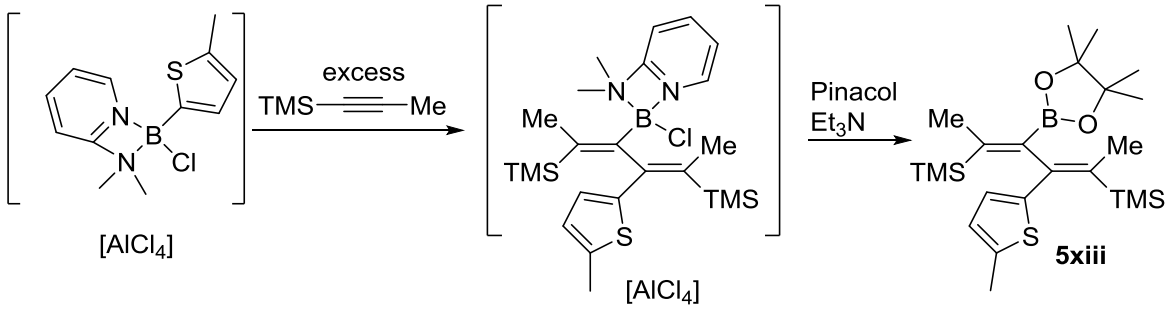


Figure 5.33: Synthesis of 2-boradiene (**5xiii**)

Whilst these 2-boradiene species are coveted for their relative rarity in the literature, and this represents a new way to access them, the reaction is still hampered by the same problems as the 1,1-carboboration with borocations, namely not achieving full, clean conversion, and competitive reaction pathways occurring. Thus far, the reaction is limited to TMS-propyne and only 2 borocations, though other alkynes and borocations have been explored but did lead to intractable mixtures of products.

5.4: Vinylboration of Alkynes

Following the observed reactivity between $[LutBCl_2][AlCl_4]$ and TMS-alkynes, which resulted in desilylboration as covered in Chapter 3, this new reactivity was probed further. It was postulated that the reactivity shown in Figure 5.34 may occur if a borocation was exposed to 1 equivalent of alkyne and 1 equivalent of TMS-alkyne. However, since we have no evidence that $[LutBCl_2][AlCl_4]$ undergoes double haloboration of alkynes, possibly due to steric hindrance around boron in the expected divinyl(lutidine) borenium cation product, other reactivity may occur instead that does not involve formation of diorganoB(lut) cations.

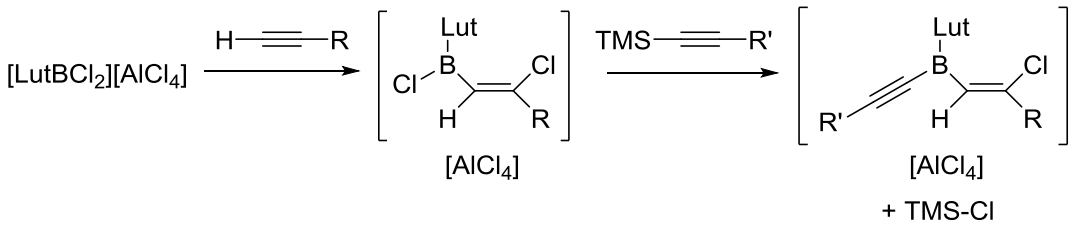


Figure 5.34: Possible Reactivity of Haloborated alkene and TMS-Alkyne

A terminal alkyne, phenylacetylene, was haloborated with $[LutBCl_2][AlCl_4]$, (confirmed by ^{1}H and ^{11}B NMR spectroscopy as discussed in Chapter 4). Instead of performing the esterification with pinacol, one equivalent of trimethylsilyl-propyne was added. Immediately, the ^{1}H NMR spectrum showed that while the vinyl resonance associated with haloborated phenylacetylene remained at 7.12 ppm, a new vinylic species grew in at 6.41 ppm.

While it was difficult to glean anything from the ^{11}B NMR spectrum, which gave a resonance too broad to observe at 20°C, the ^{29}Si NMR spectrum was far more telling. The starting material, namely TMS-propyne, was observed at -20.71 ppm, along with a new peak at -4.71 ppm. It was known from previous

carboboration reactions with TMS-alkynes, that vinyl-TMS resonances occurred in this region, however, TMS-propyne haloboration was disfavoured as the product would be sterically crowded at boron.

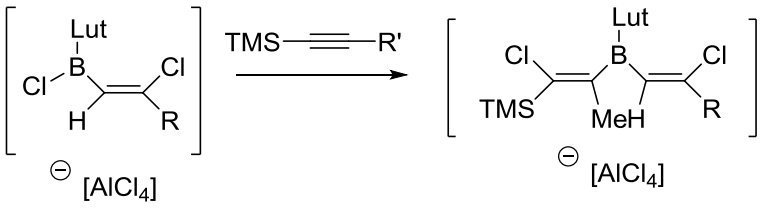


Figure 5.35: Proposed di-haloboration of alkynes

Upon esterification of the product with pinacol, a light yellow oil was produced and filtration through silica gave a crude mixture of two products by NMR spectroscopy. The ^{11}B NMR spectrum showed only a broad peak at 29.3 ppm, which is consistent with vinyl pin-B species in the structure of the products. The ^{29}Si NMR spectrum also showed only a single peak, at -4.17, again indicative of a vinyl-TMS species. The ^{1}H NMR spectrum proved most telling: present were resonances that corresponded to haloborated phenylacetylene (from left over starting material), but this was the minor product (approximately 20%). The major product showed peaks corresponding to the phenyl ring, a vinyl proton with a different chemical shift compared to the haloborated phenylacetylene product (6.89 and 6.08, respectively), methyl, pinacol and TMS groups. Whilst the aromatic peaks overlapped with the haloborated minor product, the other peaks displayed consistent integration, strongly suggesting that they all belonged to a single molecule. This data suggests that a form of carboboration has occurred between the haloborated alkene intermediate and the TMS alkyne. This 'vinylborated'

product could be in one of several possible configurations, depending if 1,1- or 1,2-carboboration occurs.

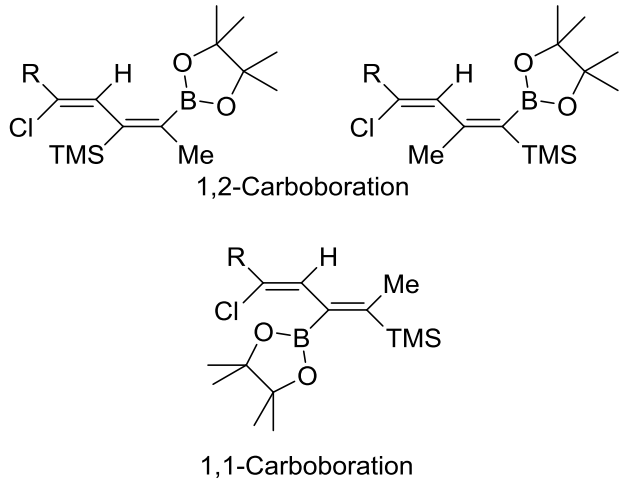


Figure 5.36: Possible conformations of the vinylboration product

Further evidence was required to elucidate the structure of this product, so the reaction was repeated, but using ^{t}butylacetylene instead of phenylacetylene in the initial haloboration step. One reason for this was to make the ^{13}C NMR spectrum easier to assign, as without the aromatic group the vinylic carbon resonances will be easier to observe, and if vinylboration is occurring then three or four resonances will be present (depending on whether the carbon bound to boron is observed). The reaction was carried out in a similar manner to the previous one, with a crude post-esterification products once again presenting as a pale yellow oil. NMR spectroscopy showed a similar mixture of products; a small amount of haloborated ^{t}butylacetylene and the vinylboration product.

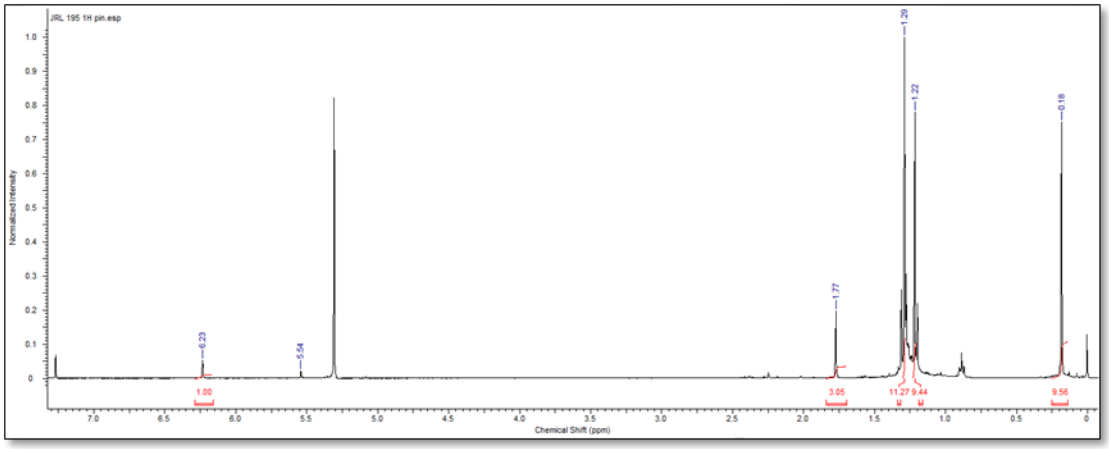


Figure 5.37: ^{1}H NMR spectrum of the crude mixture in $CDCl_3$

A series of thin layer chromatography experiments determined that a solvent mixture of hexane and DCM 2:1 provided adequate separation of the crude mixture. The ^{1}H NMR spectrum of the new species showed a 1H singlet at 6.24 ppm, the methyl derived from TMS-propyne presented as a 3H singlet at 1.78 ppm, pinacol gave a resonance at 1.29 ppm, the ^{t}butyl group at 1.22 ppm and the TMS group at 0.19 ppm. The ^{11}B and ^{29}Si NMR spectra gave similar data to the previous experiment with phenylacetylene, with peaks at 29.4 ppm and -4.62 ppm, respectively. The ^{13}C NMR spectrum of the pure compound further validated the vinylboration theory. Three peaks were visible in the vinyl region, at 153.22, 144.49 and 123.44 ppm. This was consistent with a borylated diene species, wherein the resonance for the fourth vinyl carbon, bound to boron, was not observed due to quadrupolar relaxation.

To confirm the structural conformation, COSY and NOESY spectroscopy was performed on the pure sample. Upon closer inspection of the ^{1}H NMR spectrum, a ^{4}J coupling was visible, as the methyl groups present as doublet from coupling to

the vinylic proton with a very small coupling constant (1 Hz). This data would preclude any structures where the methyl group and the vinylic proton are further apart, indicating that they were most likely bound at the 2- and 3-positions of the diene. This also precludes a 1,1-carboboration of the TMS-alkyne.

By using nOe spectroscopy, it was possible to observe through space interactions between the methyl and the vinyl C-H, which suggested that the diene was not conjugated but steric demand led to a non-zero C-C-C-C dihedral angle. The methyl group and the TMS group also showed a through space interaction, but the methyl and the pinacol do not. Hence, it can be assumed that the methyl and the TMS group were *cis* on the alkene, and that the product of vinylboration was a 1-boradiene. From this, a structure for the product can be postulated, as shown in Figure 5.38.

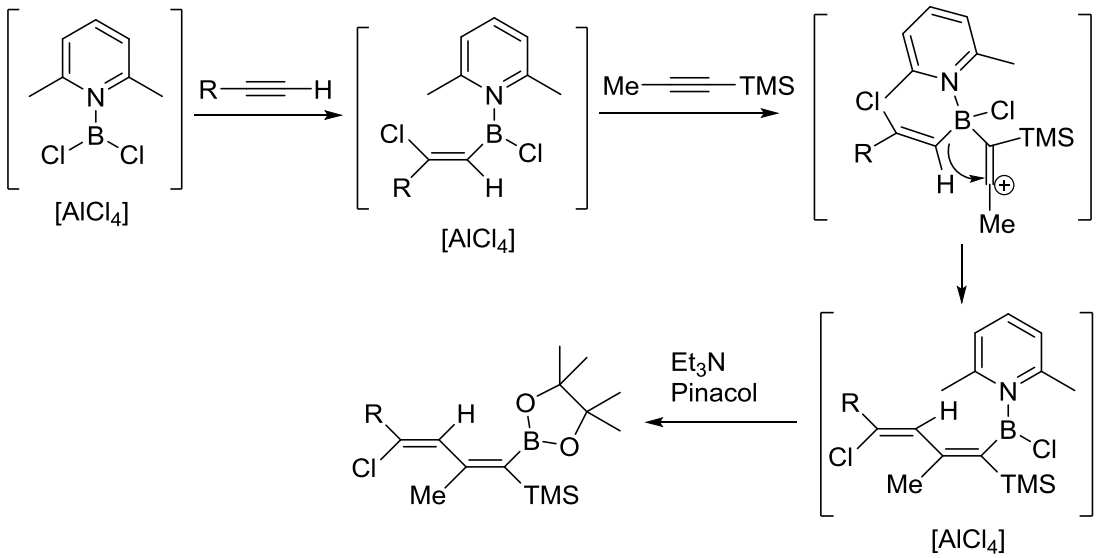


Figure 5.38: Proposed synthesis of a diene product

In order to investigate the product further, computational studies were undertaken. When the calculation were run at the M06-2X/6-311G(d,p)(PCM:DCM) level by Dr. Jessica Cid, The C1-C2-C3-C4 dihedral angle was found to be 39.93°, further corroborating the hypothesis that the 1-boradienes diene backbone are not planar.

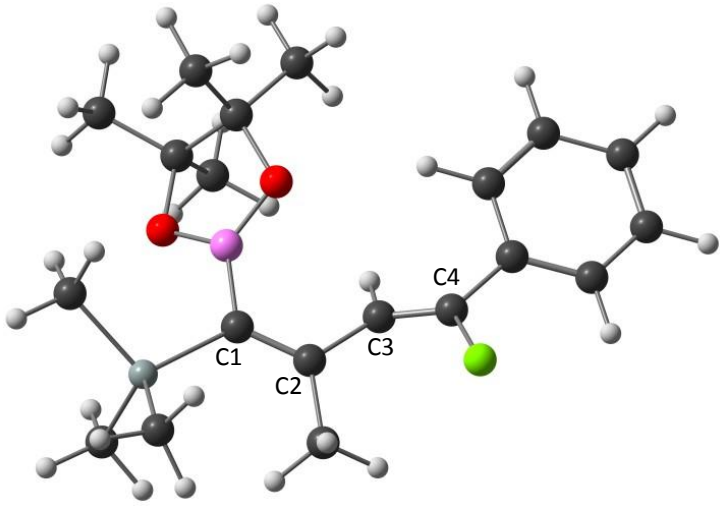


Figure 5.39: Calculated structure of (**5xiv**) (M06-2X/6-311G(d,p)(PCM:DCM))

In order to understand this new reactivity, a control reaction was carried out to see if vinylboration required the TMS-alkyne, as TMS is not migrating in the above reaction. $[LutBCl_2][AlCl_4]$ was used to haloborate phenylacetylene, and to this reaction mixture 1 equivalent of 3-hexyne was added. 3 Hexyne was chosen to prevent haloboration transfer, as a more nucleophilic alkyne would be haloborated instead, regenerating the phenylacetylene (see section 4.3). ^{1}H NMR spectroscopy showed no desymmetrisation of the alkyl chains of 3-hexyne, indicating that it remained unreacted even after 24 hours. As a test, the reaction mixture was esterified with pinacol; post work up the only product isolated was haloborated phenylacetylene.

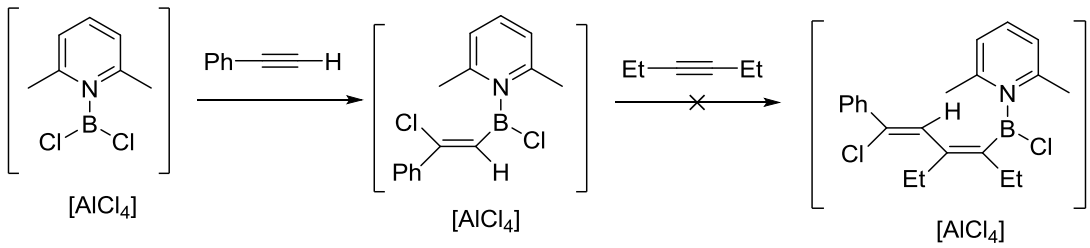


Figure 5.40: Attempted synthesis of diene without a TMS-alkyne

In light of this lack of reactivity, along with the observation that the reactions never proceed to completion, it was proposed that the 1,2-vinyl boration is close to ΔG = zero, and hence maybe in equilibrium with the haloboration product by retrocarboboration. Computational studies at the M06-2X/6-311G(d,p)(PCM:DCM) level suggested that, for the vinylboration step of TMS-propyne, ΔG = -7.67 kcalmol^{-1}. As this precludes our earlier hypothesis, it is more likely that the reason the reaction was not observed to go to completion is due to competing reaction pathways, such as desilylboration.

With this in mind, the vinylboration reaction conditions were then optimised to try and minimise by-product formation and maximise the amount of haloborated alkene converted to the diene. It was found that most haloborations of terminal alkynes with [LutBCl$_2$][AlCl$_4$] proceeded quantitatively (by *in-situ* NMR spectroscopy) extremely rapidly, as NMR spectroscopy showed total consumption of the alkyne as soon as the sample could be run. Hence, the haloboration reaction was given 5 minutes stirring at room temperature before addition of the TMS alkyne. It was observed that with 1 equivalent of TMS alkyne, there was always haloborated product present in both *in situ* and post esterification (by NMR spectroscopy), hence 2 equivalents of TMS-alkyne were used to favour the full

reaction of the haloborated product with the TMS-alkyne. Under these conditions both ^{1}H and ^{29}Si NMR spectra showed formation of TMS-Cl. This may be the result of a competing desilylboration reaction.

Further modification of the reaction conditions showed that using 1.2 equivalents of the TMS-alkyne resulted in no observable TMS-Cl formation, and minimised the amount of the initial haloborated alkene remaining *in situ*, although did not preclude it entirely.

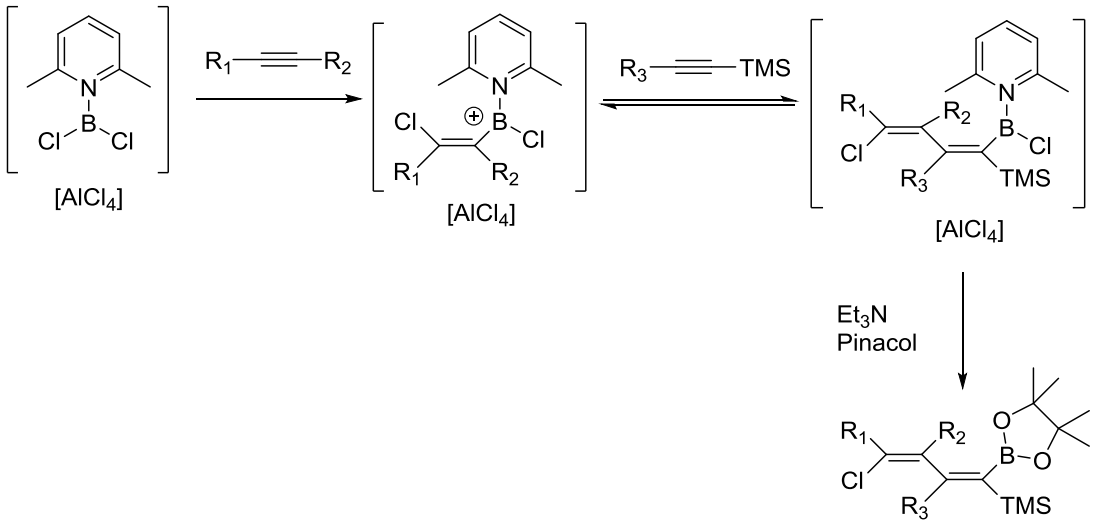
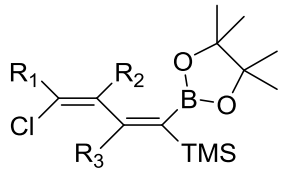


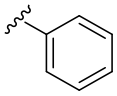
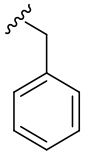
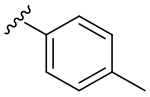
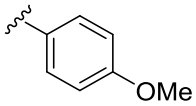
Figure 5.41: Proposed synthesis and configuration of diene product

With conditions in place, preliminary substrate scope expansion began by first varying the terminal alkyne that undergoes haloboration, whilst keeping the TMS-alkyne as TMS-propyne. As mentioned earlier, conversion to the diene is never complete, consistent with an equilibrium process, so after esterification the pinacolated haloboration product is also present. Table 5.5 below shows both the yield of the diene by NMR, using the mass of the crude mixture and calculated ratios of haloboration:diene formation via integrals, as well as the isolated yields of the dienes, post column chromatography, where possible. These are often considerably lower due to the difficulty of separating the two species. As such, in

some cases acquiring full spectroscopic analysis of clean compounds was challenging.

Table 5.5



Entry	R_1	R_2	R_3	Conversion To diene by NMR (%)	Isolated Yield [%]
(5xiv)		—H	—Me	65	23
(5xv)		—H	—Me	71	59
(5xvi)		—H	—Me	70	31
(5xvii)		—H	—Me	70	-
(5xviii)		—H	—Me	67	-

In addition to the terminal alkynes featured in Table 5.5, it was postulated that this reactivity could be extended to internal alkynes, since $[LutBCl_2][AlCl_4]$ has been shown to readily haloborate internal alkynes.[42] 3-Hexyne was haloborated using this borenium, to which 1.2 eq of TMS-propyne was added. After esterification and purification, it was determined by NMR spectroscopy that the

vinylboration had occurred, however, the yield was much lower than the examples with terminal alkynes.

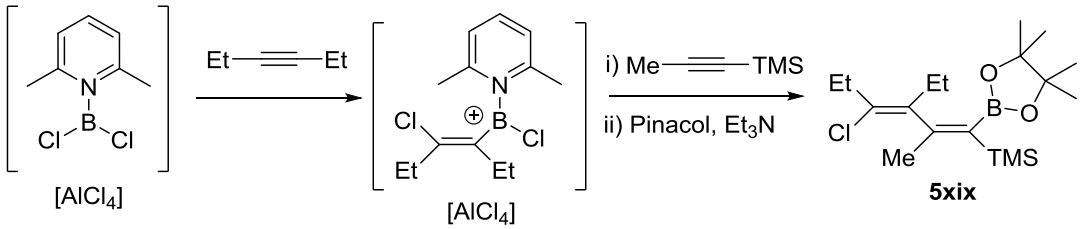


Figure 5.42: Vinylboration using internal alkyne 3-hexyne

In addition, preliminary studies into substate scope expansion via modification of the TMS-alkyne was investigated. The haloborated product from the reaction of the borenium with ^{t}butylacetylene was intercepted with both TMS-phenylacetylene and TMS-hexyne. In the first reaction, a roughly 5:1 mixture of haloboration product-to-diene is observed, ^{1}H NMR spectroscopy shows that, for the diene, a ^{t}butyl-group, phenyl-group, PinB, TMS and vinyl proton are incorporated into the structure, similar to previous vinylborations. ^{11}B and ^{29}Si NMR spectra show single resonances at 29.6 and -6.14 ppm, respectively.

The reaction with TMS-hexyne gives similar NMR data to previously discussed dienes, in a ratio of 4:1 with the haloboration product. Once again, these products proved very challenging to isolate cleanly, and thus have not been fully characterised, and represent merely a proof-of-principle that other TMS-alkynes can be incorporated into the diene structure.

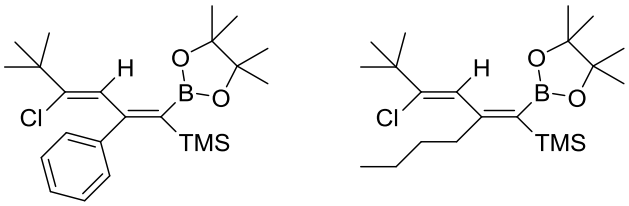


Figure 5.43: Proposed structures of vinylboration with TMS-phenylacetylene and TMS-hexyne

This represents a new and interesting reaction in the form of ‘1,2-vinylboration’ forming the synthetically useful borylated dienes, although challenging reaction conditions and the observation of a mixture of productsdetracts from the utility of this reaction. .

5.5: Intermolecular Carboboration

The reaction of some borocations, such as [CatB(2DMAP)][$AlCl_4$] with terminal alkynes results in dehydroboration as previously discussed in Chapter 3. It is speculated that this occurs stepwise, with initial binding of the alkyne to boron forming a vinylic carbocation (or its non-classical π adduct), followed by deprotonation to reform the alkyne. Early work involving an intermolecular FLP utilising [CatB-NEt_3][$AlCl_4$] and PPh_3 resulted in a mixture of products; some of the desired borylated alkyne, but also a product where PPh_3 had acted as a nucleophile and attacked the initially formed cationic intermediate. This product was observed in the ^{31}P NMR spectrum of the reaction mixture.

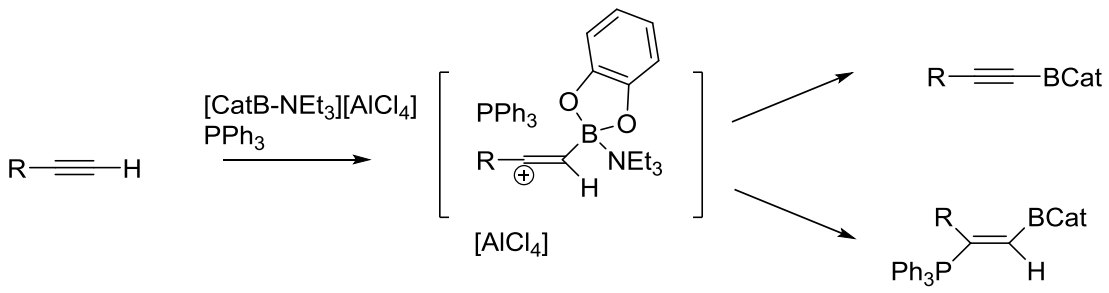


Figure 5.44: Outcomes of reaction of FLP with terminal alkynes

From this, it was postulated that the carbocationic intermediate could be intercepted by a nucleophile such as an arene, resulting in 1,2-carboboration, which has precedence from the work of Gaunt and co-workers using carbon electrophiles and by Stephan et al., using $B(C_6F_5)_3$, alkynes and *N*-heterocycles.[43,44] To begin with, [CatB(2DMAP)][$AlCl_4$] was added to 2-hexylthiophene at room temperature, and no reaction was observed. This was to check if a competing reaction pathway existed wherein the thiophene itself was rapidly borylated. To this mixture, one equivalent of 3-hexyne was added, and the reaction mixture stirred. An internal alkyne was

initially chosen to avoid the competing reactivity between the borocation and terminal alkynes which results in alkyne dehydroboration. After several days, no desired reaction was observed, so the mixture was heated to 60˚C in a sealed NMR tube for 24 hours. At this point, the NMR spectra indicated that the [CatB(2DMAP)][$AlCl_4$] had begun to react with the thiophene by dehydroborylation, leaving the alkyne intact.

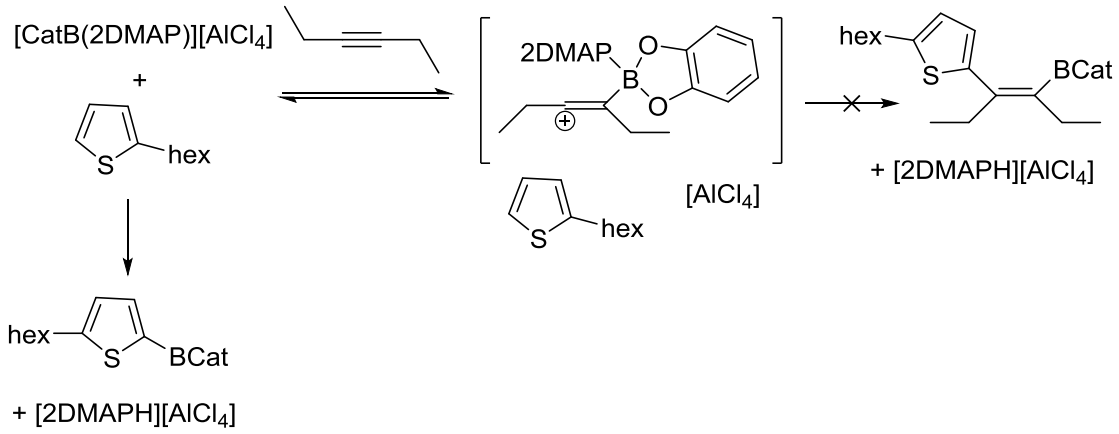


Figure 5.45: Attempted carboboration of 3-hexyne

During the course of the investigation into intermolecular carboboration, reactions using BCl_3 were carried out. It is known that BCl_3 undergoes haloboration with terminal alkynes, so internal alkynes were chosen as substrates instead. In order to probe possible competing reactions, BCl_3 was combined with 2-methylthiophene, both in the presence and absence of a base (TBP). It was found that no reaction was occurring in either case, so competing reactions would be minimal. 2-Methylthiophene, 1-phenyl-1-propyne and TBP were combined in DCM. To this, BCl_3 (2 eq) was added, and the t = 5 minutes ^{1}H NMR spectrum showed that the base was partially protonated. After 18 h, most of the base was protonated (> 90%) and when left for 72h there was no trace of unprotonated base. It is possible to observe a doublet growing in in the aromatic region over the course of the

reaction. As this occurs as the base is protonated, it can be assumed that the doublet belongs to the 2-methylthiophene as it is being functionalised at the 5 position. Presumably, the other doublet associated with this fragment is coincident with other aromatic resonances. The ^{11}B NMR spectrum shows a new broad peak at around 55 ppm, which is indicative of a vinyl-BCl_2 species. The other resonance associated with BCl_3 shifts upfield over time, moving from 45 ppm at t = 5 minutes, to 42 ppm at t = 18h, reaching 16 ppm after 96 h. This is due to the excess BCl_3 being in equilibrium with the newly generated BCl_4^- anion and in fast exchange at 20°C on the NMR timescale, hence, it can be deduced that a haloboration is not occurring, as [TBPH][BCl_4] would not be produced if this were the case. Given this data, it was postulated that an intermolecular carboboration reaction had occurred.

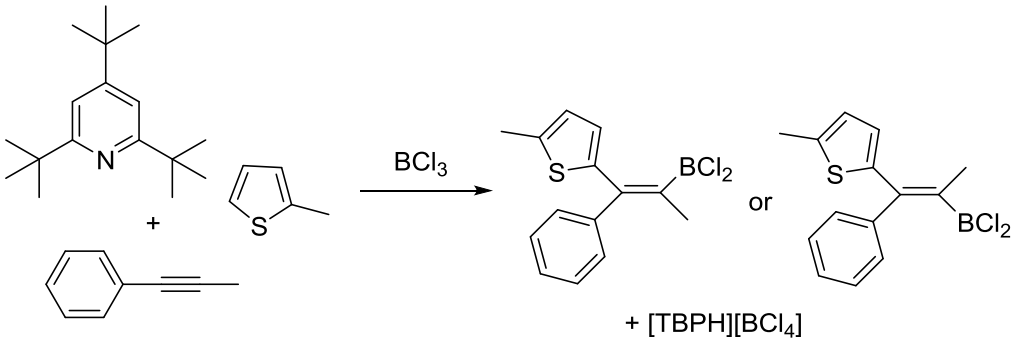


Figure 5.46: Potential isomers of carboboration reaction

After esterification, the crude product produces a ^{1}H NMR spectrum, in which both the aromatic protons from the thiophene are coincident, presenting as a 2H singlet, as are the 5 aromatic protons associated with the phenyl ring. These persist through purification via column chromatography and are associated with the major product. In addition to these resonances, 2 methyl groups present as 3H singlets at 2.37 and 2.04, which are a result of the methyls from the thiophene and

the alkyne. This, in tandem with an expected Pin-B resonance at 0.99 ppm in the ^{1}H spectrum and a resonance at 31.8 ppm in the ^{11}B spectrum, suggests that the alkyne has undergone the desired intermolecular carboboration reaction. Mass spectroscopy is consistent with this, with an accurate mass of 340.1662 $gmol^{-1}$ recorded.

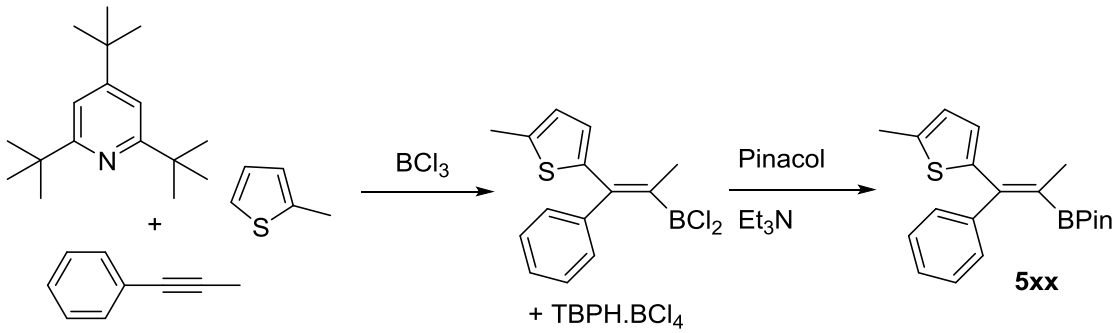


Figure 5.47: Synthesis of carboboration product **5xx**

Further NMR studies were carried out to deduce the products regio- and stereochemistry. The nOe spectrum shows through-space interaction between the methyl group derived from the alkyne and both the pinacol and the aromatic thiophene resonances. The HMQC showed that the thienyl 2H singlet corresponded to two distinct carbon environments, further showing that this is the thiophene resonance, whilst the 5H singlet corresponded to three distinct proton-bound carbon environments, as expected for a symmetrical phenyl group.

The ^{1}H NMR spectrum of **5xx** can be explained by second order effects. In the spectrum, it is observed that the five aromatic protons of the phenyl group present as a 5H singlet, and the two aromatic protons on the thiophene group have merged into a 2H singlet. If the chemical shifts between the proton resonances are

similar to the coupling constant, then second order effects are observed, resulting in the first order multiplets not being observed. In the case of the thiophene, two doublets are expected, but as chemical shifts become comparable to couplings, intensities are no longer integral ratios. The resonance away from the chemical shift of the other proton (outer lines) become smaller and resonances closer (inner lines) become larger. As such the multiplets "lean" towards each other. The leaning becomes more pronounced as the chemical shift difference between the coupled multiplets becomes smaller; this is an extreme case the multiplets have merged completely (e.g., both thiophene beta protons resonate at the same frequency).

In order to see whether this reactivity was limited to just 2-methylthiophene, the reaction was repeated using thiophene and 2-chlorothiophene. Instead of reacting cleanly to the carboboration product, these substrates produce a large quantity of different products, and upon esterification of the crude mixture, these products proved intractable. It is likely that the reaction is not as clean due to the lower nucleophilicity of these heteroarenes compared to 2-methylthiophene, slowing the rate of reaction and allowing other, more complex products to be formed, such as other isomers of carboboration product.

Preliminary substrate scope expansion of the alkyne was undertaken, first with diphenylacetylene. When reacted with 2-methylthiophene in analogous reaction conditions, it was found that, after 24 hours, the ^{1}H NMR showed a majority of protonated base, and a new methyl resonance derived from the 2-methylthiophene, similar to the reaction with 1-phenyl-1-propyne. The ^{11}B NMR

spectrum also showed a characteristic peak at 54 ppm; consistent with a vinyl-BCl_2 species, again in keeping with the reactivity with the previous alkyne.

However, after esterification the NMR spectrum became far less clean and harder to identify. There were four distinct methyl resonances in the ^{1}H spectrum, from the 2-methylthiophene, and a large quantity of peaks associated with pinacol. In addition, whilst the ^{11}B NMR spectrum showed the desired peak at 30 ppm for a vinyl-Bpin species, there was a large peak at 21.5 ppm, which is consistent with protodeborylation products such as PinBOR. Thus, it can be surmised that the initial product of this reaction is unstable to esterification conditions, and decays to several species in the process.

5.6: Conclusions

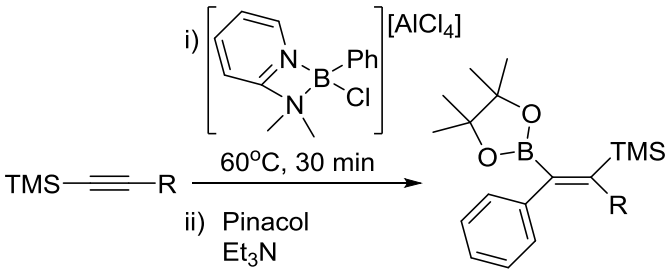
Through the course of the investigation, several novel methods of carboboration have been discovered. 1,1-carboboration of activated TMS-alkynes has been previously established, but can now be achieved using the inexpensive and readily available borane dichlorophenylborane. Only a single stereo-and regio-isomer is isolated, providing access to specific synthetically useful vinylboronate esters. It was also found that synthesis of analogues of $PhBCl_2$ was possible, and that they react in an analogous fashion with TMS-alkynes, further expanding the range of vinylboronate esters accessible.

The boronium [PhClB(2DMAP)][$AlCl_4$] was shown to react with TMS-alkynes in the same way, undergoing 1,1-carboboration. In addition to this, it was found that this borocation represents a route to accessing 2-boradienes when exposed to an excess of TMS-alkyne. Its structural analogue, [ClB-2-methylthiophene (2DMAP)][$AlCl_4$], undergoes the same reactivity, generating a 2-boradiene featuring a 2-methylthiophene at the 3-position of the 2-boradiene moiety.

By reacting haloborated alkyne products (pre-esterification) with TMS alkynes, it was found that 1-boradienes could be generated. This represents the ability to create highly customisable dienes, by varying the alkyne and the TMS-alkyne. In addition, a new method of 1,2-carboboration was discovered, where a vinyl cation is intercepted by a heteroarene, resulting in the *anti*-carboboration product.

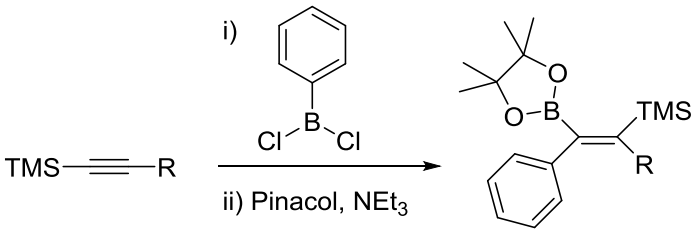
5.7: Experimental

General procedure for 1,1-carboboration with [PhBCl(2DMAP)][$AlCl_4$] (Route 1)



To a suspension of [PhBCl(2DMAP)][$AlCl_4$] (50 mg, 0.12 mmol, 1 eq) in DCM (0.5 ml) in a J. Youngs NMR tube, TMS-alkyne (0.12 mmol, 1 eq) was added. This was sealed and the mixture heated to 60°C until dissolution of the borocation, at which point NMR spectroscopy was used to confirm consumption of the alkyne. Competing reactivity occurs over extended periods of time, so after 30 minutes an excess of triethylamine (0.1 ml) and pinacol (30 mg, 0.24 mmol, 2 eq) were added, and the solvent was removed under reduced pressure, leaving an oil. Pentane was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities. Column chromatography (DCM:hexane, 1:1) was used to separate the desired product from the by-products.

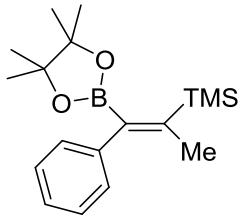
General procedure for 1,1-carboboration with $PhBCl_2$ (Route 2)



To a solution of $PhBCl_2$ (200 µl, 1.5 mmol, 1 eq) in DCM (5 ml) in a Schlenk, TMS-propyne (224 µl, 1.5 mmol, 1 eq) was added. After 1 hour, the reaction was

complete, as monitored by NMR spectroscopy, an excess of triethylamine (0.5 ml) and pinacol (350 mg, 3.0 mmol, 2 eq) were added, and the solvent was removed under reduced pressure, leaving an oil. Filtration through a 1 inch plug of silica afforded the pure product.

(**5i**) (*E*)-trimethyl(1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-2-yl)silane



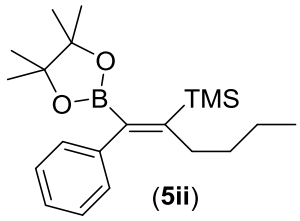
(Route 1) The product was isolated as a yellow oil (24 mg, 0.08 mmol, 63%).

(Route 2) The product was isolated as an orange oil (424 mg, 1.3 mmol, 88%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, 2H, ^{3}J(H,H) = 7.2 Hz), 7.18 (t, 1H, ^{3}J(H,H) = 7.2 Hz), 7.06 (d, 2H, ^{3}J(H,H) = 7.2 Hz), 1.68 (s, 3H), 1.23 (s, 12H), 0.23 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 150.92, 143.54, 128.42, 127.86, 125.55, 83.50, 25.05, 20.58, 0.00; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.2; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.22 ppm.

MS: (M + Na^+): Calculated = 339.1928 Found = 339.1923 $gmol^{-1}$

(**5ii**) (*E*)-trimethyl(1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-1-en-2-yl)silane



(**5ii**)

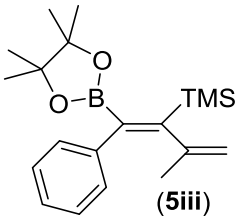
(Route 1) The product was isolated as a yellow oil (27 mg, 0.08 mmol, 61%).

(Route 2) The product was isolated as an orange oil (431 mg, 1.3 mmol, 79%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, 2H), 7.18 (t, 1H), 7.07 (d, 2H), 2.07-2.03 (m, 2H), 1.21 (s, 12H), 1.19-1.10 (m, 4H), 0.72 (t, 2H), 0.26 (9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 155.70, 143.59, 128.16, 127.67, 125.35, 83.42, 33.49, 32.49, 24.90, 22.81, 13.77, 0.81; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.4; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.60 ppm.

MS: (ES^+)(M + H^+) 359.3 $gmol^{-1}$ **MS**: (M + K^+) 397.2136 $gmol^{-1}$

(**5iii**) (*E*)-trimethyl(3-methyl-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)buta-1,3-dien-2-yl)silane



(**5iii**)

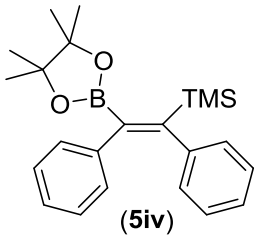
(Route 1) The product was isolated as a yellow oil (23 mg, 0.08 mmol, 55%).

(Route 2) The product was isolated as orange crystals (403 mg, 1.2 mmol, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.15 (m, 5H), 4.69 (m, 1H), 4.38 (m, 1H), 1.42 (s, 1H), 1.23 (s, 12H), 0.24 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 158.70, 147.58, 142.92, 134.70, 128.37, 127.19, 125.58, 83.72, 25.00, 24.17, 0.27; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 31.1; **^{29}Si NMR** (MHz, $CDCl_3$) δ -6.59 ppm.

MS: (ES^+)(M + Na^+) 365.3 $gmol^{-1}$

(**5iv**) (*E*)-(1,2-diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)trimethylsilane



(**5iv**)

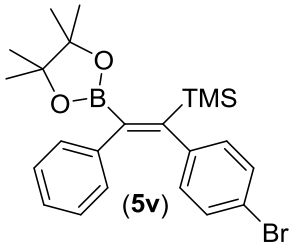
(Route 1) The product was isolated as a yellow oil (29 mg, 0.08 mmol, 65%).

(Route 2) The product was isolated as an orange oil (489 mg, 1.3 mmol, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06-7.00 (m, 4H), 6.96-6.93 (m, 4H), 6.75-6.73 (m, 2H), 1.29 (s, 12H), 0.17 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 156.92, 144.48, 142.51, 128.84, 128.10, 127.19, 127.11, 125.22, 124.57, 83.91, 25.11, 0.36; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.6; **^{29}Si NMR** (MHz, $CDCl_3$) δ -5.00 ppm.

GC/MS: 378.2 $gmol^{-1}$ **MS**: (ES^+)(M + Na^+) 401.4 $gmol^{-1}$

(**5v**) (*E*)-(1-(4-bromophenyl)-2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)trimethylsilane



(**5v**)

(Route 1) The product was isolated as a yellow oil (31 mg, 0.08 mmol, 56%).

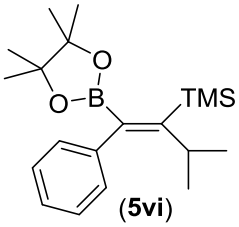
(Route 2) The product was isolated as white crystals (102 mg, 0.1 mmol, 68%). (Reaction was done on ¼ scale of general procedure)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, 2H, ^{3}J(H,H) = 8.2 Hz), 6.90-6.74 (m, 5H), 6.46 (d, 2H, ^{3}J(H,H) = 8.2 Hz), 1.28 (s, 12H), 0.16 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 155.55, 143.50, 142.16, 130.36, 129.80, 128.68, 128.08, 127.33, 125.47, 83.98,

25.08, 0.34; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.0; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.92 ppm.

GC/MS: ($M + H^+$) 458.0 $gmol^{-1}$

(**5vi**) (*E*)-trimethyl(3-methyl-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-2-yl)silane

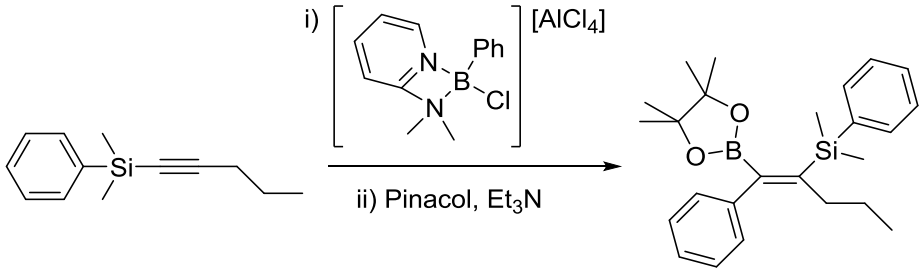


(Route 2) The product was isolated as orange crystals (100 mg, 0.3 mmol, 76%). (Reaction was done on ¼ scale of general procedure)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, 2H, $^{3}J(H,H)$ = 7.0 Hz), 7.03 (t, 1H, $^{3}J(H,H)$ = 7.0 Hz), 6.94 (d, 2H, $^{3}J(H,H)$ = 7.0 Hz), 2.57 (septet, 1H, $^{3}J(H,H)$ = 7.0 Hz), 1.02 (s, 12H), 0.81 (d, 6H, $^{3}J(H,H)$ = 7.0 Hz), 0.16 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 157.97, 143.70, 128.05, 127.89, 125.57, 83.56, 33.79, 24.92, 22.28, 2.67; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.5; **^{29}Si NMR** (MHz, $CDCl_3$) δ -5.83 ppm.

MS: (ES^+)($M + Na^+$) 367.4 $gmol^{-1}$

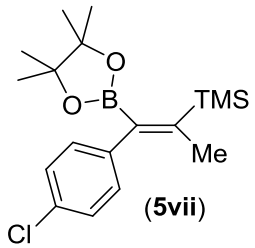
(**5vii**) (*E*)-dimethyl(phenyl)(1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-2-yl)silane



(Route 1, using dimethyl(pent-1-yn-1-yl)(phenyl)silane (24 mg, 0.12 mmol, 1 eq) heated at 60°C for 24 hours) The product was isolated as a pale yellow oil (4 mg, 0.01 mmol, 8%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, 1H, ^{3}J(H,H) = 7.0 Hz, ^{4}J(H,H) = 1.8 Hz), 7.70 (dd, 1H, ^{3}J(H,H) = 7.0 Hz, ^{4}J(H,H) = 1.8 Hz), 7.45-7.17 (m, 7H), 6.65 (s, 1H), 2.37 (m, 2H), 1.42 (m, 2H), 1.27 (s, 12H), 0.85 (t, 3H, ^{3}J(H,H) = 7.3 Hz), 0.51 (s, 6H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 145.49, 144.75, 138.77, 138.13, 135.94, 135.45, 129.61, 128.61, 127.97, 126.23, 83.72, 53.42, 33.52, 24.89, 23.28, 14.53, -0.37; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 31.9 (s); **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.96 ppm.

(**5viii**) (*E*)-(1-(4-chlorophenyl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-2-yl)trimethylsilane



(**5vii**)

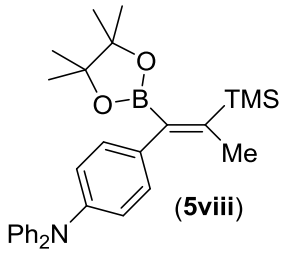
DMT-BCl_3 (100 mg, 1 eq) and $AlCl_3$ (111 mg, 2.1 eq) were combined in chlorobenzene (0.5 ml) in a J.Youngs NMR tube under inert conditions, sealed and heated to 100°C for 18h. NMR spectroscopy confirmed formation of 4-chloro-phenyl-BCl_2, which was extracted into hexane (10 ml). To this hexane solution, TMS-propyne (117 µl, 2 eq) was added, turning the solution brown. After 40 minutes, the reaction mixture was esterified with excess Et_3N (0.1 ml) and pinacol (140 mg, 3 eq). The crude product was extracted into pentane (20 ml) and filtered through a 1 inch plug of silica affording the pure product. (85 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (d, 2H, ^{3}J(H,H) = 8.2 Hz), 6.75 (d, 2H, ^{3}J(H,H) = 8.2 Hz), 1.44 (s, 3H), 1.00 (s, 12H), 0.00 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 152.57,

136.11, 131.30, 129.82, 128.03, 83.59, 24.99, 20.77, 0.00; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.0; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.04 ppm.

GC/MS: 350.1 gmol^{-1}

(**5ix**) (*E*)-N,N-diphenyl-4-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(trimethylsilyl)prop-1-en-1-yl)aniline



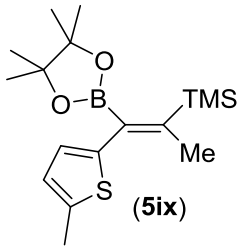
(**5viii**)

[$LutBCl_2$][$AlCl_4$] (80 mg, 2.2 mmol, 1 eq) was generated *in-situ* (from Lut-BCl_3 and $AlCl_3$) and combined with triphenylamine (55 mg, 2.2 mmol, 1 eq) in DCM (0.5 ml) in a J.Youngs NMR tube under inert conditions, and the sealed tube rotated at room temperature for 2 hours, turning from green to yellow to brown. NMR spectroscopy confirmed formation of triphenylamine-BCl_2, which was extracted into hexane (10 ml). To this, TMS-propyne (66 µl, 4.5 mmol, 2 eq) was added. The reaction was complete, as monitored by NMR spectroscopy, within 30 minutes, then the reaction mixture was esterified with excess Et_3N (0.1 ml) and pinacol (78 mg, 3 eq). The crude product was extracted into pentane (20 ml) and filtered through a 1 inch plug of silica afforded the pure product. (74 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-6.77 (m, 14H), 1.58 (s, 3H), 1.07 (s, 12H), 0.05 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 150.41, 147.97, 145.25, 137.85, 129.38, 129.08, 123.97, 123.69, 122.35, 83.49, 25.04, 20.63, -0.03; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.3; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.29 ppm.

GC/MS: 483.3 gmol^{-1}

(**5x**) (*E*)-trimethyl(1-(5-methylthiophen-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-2-yl)silane



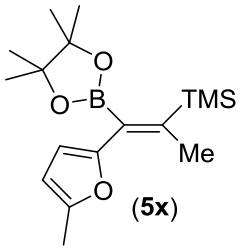
(**5ix**)

$[BCl_2(2DMAP)][AlCl_4]$ (100 mg, 2.7 mmol, 1 eq) was combined with 2-methylthiophene (26 µl, 2.7 mmol, 1 eq) in DCM (0.5 ml) in a J.Youngs NMR tube under inert conditions, and sealed and then heated at 60°C for 1 hour. NMR spectroscopy confirmed formation of 2-methylthiophene-BCl_2, which was extracted into hexane (10 ml). To this, TMS-propyne (80 µl, 5.4 mmol, 2 eq) was added, turning deep orange. The reaction mixture was esterified after 1 hour with excess Et_3N (0.1 ml) and pinacol (96 mg, 3 eq). The crude product was extracted into pentane (20 ml) and filtered through a 1 inch plug of silica afforded the pure product. (70 mg, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (m, 1H), 6.57 (d, 1H, ^{3}J(H,H) = 7.1 Hz), 2.46 (s, 3H), 1.93 (s, 3H), 1.29 (s, 12H), 0.22 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 148.27, 139.11, 135.82, 126.00, 122.91, 83.22, 25.01, 20.37, 15.86, 0.02 ppm; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.0; **^{29}Si NMR** (MHz, $CDCl_3$) δ -3.92 ppm.

GC/MS: 336.4 gmol^{-1}

(**5xi**) (E)-trimethyl(1-(5-methylfuran-2-yl)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-2-yl)silane



(**5x**)

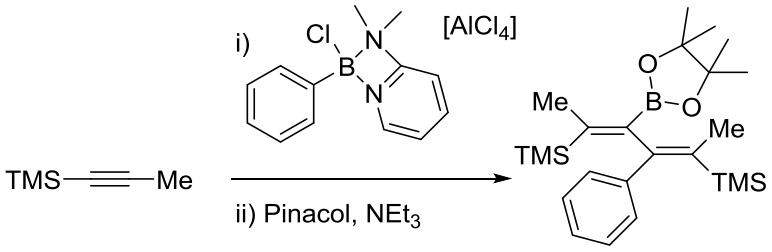
$[BCl_2(2DMAP)][AlCl_4]$ (100 mg, 2.7 mmol, 1 eq) was combined with 2-methylfuran (24 µl, 2.7 mmol, 1 eq) in DCM (0.5 ml) in a J.Youngs NMR tube under inert conditions, and NMR confirmed formation of 2-methylfuran-BCl_2 effectively instantaneously,

which was extracted into hexane (10 ml). To this, TMS-propyne (40 µl, 2.7 mmol, 1 eq) was added, turning deep orange. The reaction mixture was esterified within 30 minutes with excess Et_3N (0.1 ml) and pinacol (96 mg, 3 eq). The crude product was extracted into pentane and filtered through a 1 inch plug of silica afforded the pure product. (56 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (d, 1H, ^{3}J(H,H) = 3.2 Hz), 5.99 (m, 1H), 2.28 (s, 3H), 2.02 (s, 3H), 1.37 (s, 12H), 0.21 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 155.78, 153.22, 152.09, 109.07, 102.72, 82.98, 25.03, 21.25, 14.76, 0.98 ppm;**^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.2; **^{29}Si NMR** (MHz, $CDCl_3$) δ -3.92 ppm.

GC/MS: 320.3 gmol^{-1}

(**5xii**) ((2*Z*,4*Z*)-3-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-2,4-diene-2,5-diyl)bis(trimethylsilane)



To a suspension of [PhBCl(2DMAP)][$AlCl_4$] (50 mg, 0.12 mmol, 1 eq) in DCM (0.5 ml) in a J. Youngs NMR tube, 1-trimethylsilylpropyne (90 µl, 0.6 mmol, 5 eq) was added. This was sealed and then heated to 60°C for 18 h, after which an excess of triethylamine (0.1 ml) and pinacol (30 mg, 0.24 mmol, 2 eq) were added, and the solvent was removed under reduced pressure, leaving a yellow/orange oil. Pentane (20 ml) was used to extract the product, which was passed through a 1 inch plug of silica to remove pinacol impurities. Column chromatography (DCM:hexane, 1:1)

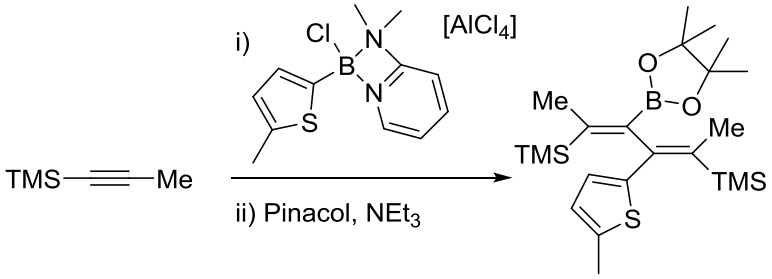
was used to separate the desired diene from the 1,1-carboboration product. The product was isolated as a yellow oil (8 mg, 0.02 mmol, 15%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.20 (m, 5H), 1.98 (s, 3H), 1.85 (s, 3H), 1.16 (s, 6H), 1.11 (s, 6H), 0.09 (s, 9H), -0.15 (s, 9H) ppm;

^{13}C NMR (100.06 MHz, $CDCl_3$) δ 144.00, 133.75, 130.67, 129.96, 127.37, 126.72, 125.59, 83.08, 24.72, 22.40, 20.86, 0.01 (TMS resonances coincident); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.6; **^{29}Si NMR** (MHz, $CDCl_3$) δ -6.00 ppm.

MS: (M + H^+): Calculated = 429.2811 $gmol^{-1}$ Measured = 429.2812 $gmol^{-1}$

(**5xiii**) ((2*Z*,4*Z*)-3-(5-methylthiophen-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-2,4-diene-2,5-diyl)bis(trimethylsilane)



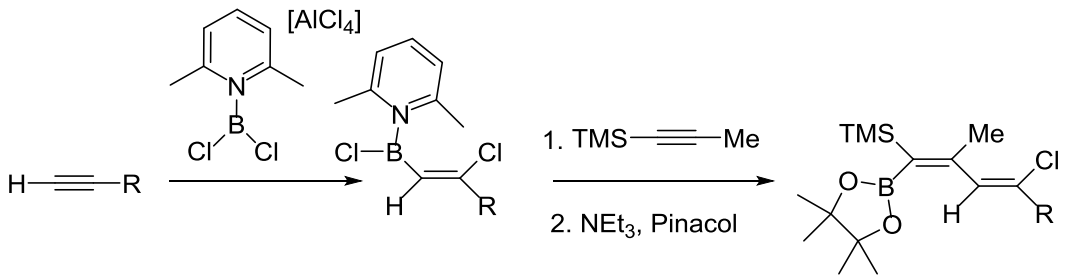
To a suspension of [Cl_2B(2-DMAP)][$AlCl_4$] (50 mg, 0.14 mmol, 1 eq) in DCM (0.5 ml) in a J. Youngs NMR tube, 2-methylthiophene (14 µl, 0.15 mmol, 1.1 eq) was added. The reaction was heated at 60°C for 1h, whereupon borylation was confirmed by NMR spectroscopy. Sequential addition of equimolar 2DMAP (17 µl) and $AlCl_3$ (18 mg) was used to generate [ClB 2-methylthiophene(2DMAP)][$AlCl_4$]. To this, 1-trimethylsilylpropyne (100 µl, 0.7 mmol, 5 eq) was added. This was sealed and then heated to 60°C for 18 h, after which an excess of triethylamine (0.1 ml) and pinacol (30 mg, 0.24 mmol, 2 eq) were added, and the solvent was removed under reduced pressure. Pentane (20 ml) was used to extract the product, which was passed through a 1 inch plug of silica. Column chromatography (DCM:hexane,

1:1) was used to separate the desired diene from the 1,1-carboboration product. The product was isolated as a yellow oil (8 mg, 0.02 mmol, 13%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (d, 1H, ^{3}J(H,H) = 3.5 Hz), 6.51 (m, 1H), 2.42 (s, 3H), 1.96 (s, 3H), 1.81 (s, 3H), 1.20 (s, 6H), 1.17 (s, 6H), 0.08 (s, 9H), -0.03 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 147.42, 146.02, 144.67, 139.85, 135.77, 126.83, 123.83, 83.06, 24.65, 24.59, 22.23, 20.49, 15.44, -0.13, -0.54; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 30.0; **^{29}Si NMR** (MHz, $CDCl_3$) δ -5.98 ppm.

GC/MS: 448.6 gmol^{-1}

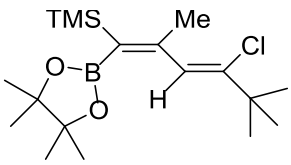
General Reaction method of vinylboration



$LutBCl_3$ (50 mg, 0.22 mmol) was suspended in anhydrous CH_2Cl_2 (0.5 ml) in a J.Young's NMR tube, to which $AlCl_3$ (30 mg, 0.22 mmol) was added, causing dissolution to form a clear yellow solution. To this $[LutBCl_2][AlCl_4]$, alkyne (1 eq, 0.22 mmol) was added. The reaction mixture was rotated at room temperature for 10 minutes, after which time (trimethylsilyl)propyne (40 µl, 0.26 mmol) was added. After rotating for a further 45 minutes, the solution was esterified with excess triethylamine (0.1 ml) and of pinacol (2 eq). The solvent was removed under reduced pressure, leaving a light yellow oil. Hexane (30 ml) was used to extract the

product, which was filtered to remove aluminium based impurities. This left a mixture of the desired diene and the haloboration by-product. NMR yields were determined using the mass of crude product in addition to the percentage of haloboration product determined by integrals, to obtain the mass of vinylboration product in each crude mixture.

(**5xiv**) ((1*E*,3*Z*)-4-chloro-2,5,5-trimethyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,3-dien-1-yl)trimethylsilane



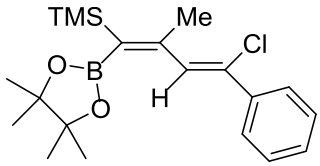
This crude product (65% yield by NMR) was then purified with column chromatography using 2:1 hexane:DCM eluent and presented as a light yellow oil (18 mg, 23%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (q, 1H, ^{4}J (H,H) = 1 Hz), 1.78 (d, 3H, ^{4}J (H,H) = 1 Hz), 1.29 (s, 12H), 1.22 (s, 9H), 0.19 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ153.77, 144.49, 123.44, 82.97, 38.43, 28.66, 25.08, 20.45, 0.00; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ29.41; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.64 ppm.

GC/MS: 356.3 gmol^{-1}

nOe shows through-space interactions between Pin – TMS, TMS – Me

(**5xv**) ((1*E*,3*Z*)-4-chloro-2-methyl-4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)buta-1,3-dien-1-yl)trimethylsilane



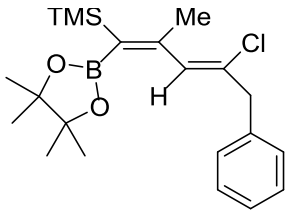
This crude product (71% yield by NMR) was then purified with column chromatography using 2:1 hexane:DCM eluent and presented as a light yellow oil (49 mg, 59%)

^{1}H NMR (400 MHz, $CDCl_3$) δ7.69 (m, 2H), 7.38-7.30 (m, 3H), 6.94 (q, 1H, ^{4}J (H,H) = 1.2 Hz), 1.91 (d, 3H, ^{4}J (H,H) = 1.2 Hz), 1.33 (s, 12H), 0.25 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 155.01, 147.37, 136.44, 129.00, 128.31, 127.32, 120.10,84.07, 24.25, 22.87, 0.41; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 29.16 **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.18 ppm.

GC/MS: 376.2 $gmol^{-1}$

nOe shows through-space interactions between Pin – TMS, TMS – Me

(**5xvi**) ((1*E*,3*Z*)-4-chloro-2-methyl-5-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)penta-1,3-dien-1-yl)trimethylsilane



This crude product (70% yield by NMR) was then purified with column chromatography using 2:1 hexane:DCM eluent and presented as a light yellow oil (27 mg, 31%)

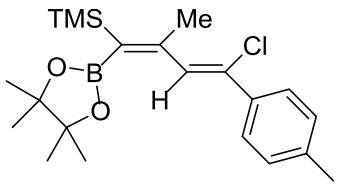
^{1}H NMR (400 MHz, $CDCl_3$) δ7.33-7.23 (m, 5H), 6.37 (q, 1H, ^{4}J (H,H) = 1 Hz), 3.74 (s, 2H), 1.84 (d, 3H, ^{4}J (H,H) = 1 Hz), 1.30 (s, 12H), 0.20 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 156.72, 138.00, 132.80, 129.37, 128.85, 128.28, 126.56, 83.41, 45.64,

25.32, 21.43, 0.36; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ29.5 ppm; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.40 ppm.

GC/MS: 390.2 $gmol^{-1}$

nOe shows through-space interactions between Pin – TMS, TMS – Me

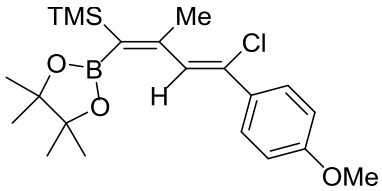
(**5xvii**) ((1*E*,3*Z*)-4-chloro-2-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(p-tolyl)buta-1,3-dien-1-yl)trimethylsilane



This crude product (70% yield by NMR) unable to isolate pure compound.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.38 (m, 2H), 7.01-6.99 (m, 2H), 6.72 (m, 1H), 1.72 (m, 3H), 1.21 (s, 3H), 1.15 (s, 12H), 0.07 (s, 9H); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ29.5; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.24 ppm.

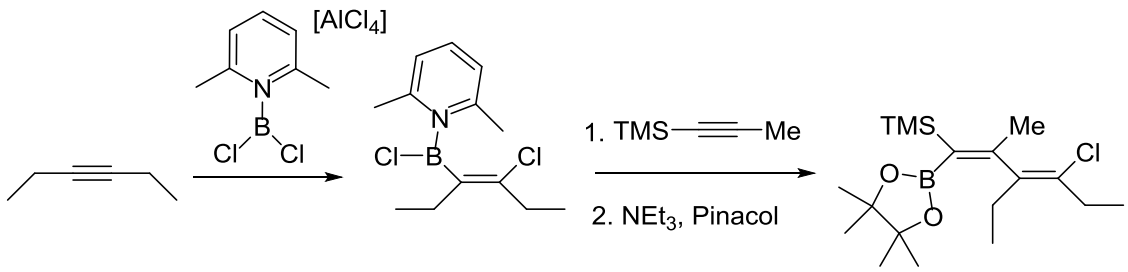
(**5xviii**) ((1*E*,3*Z*)-4-chloro-4-(4-methoxyphenyl)-2-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)buta-1,3-dien-1-yl)trimethylsilane



This crude product (67% yield by NMR) unable to isolate pure compound.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.59 (m, 2H), 6.89-6.87 (m, 2H), 6.81 (m, 1H), 3.83 (s, 3H), 1.88 (m, 3H), 1.32 (s, 12H), 0.23 (s, 9H); **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ30.0; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.28 ppm.

(**5xix**) ((1*E*,3*Z*)-4-chloro-3-ethyl-2-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,3-dien-1-yl)trimethylsilane



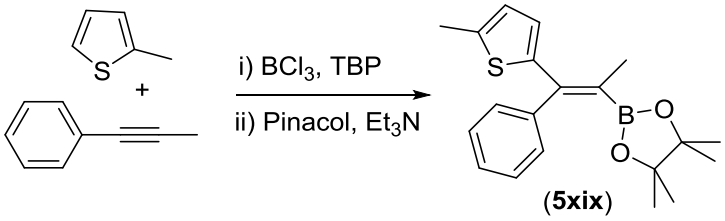
$LutBCl_3$ (50 mg, 0.22 mmol) was suspended in anhydrous CH_2Cl_2 in a J.Young's NMR tube, to which $AlCl_3$ (30 mg, 0.22 mmol) was added, causing dissolution to a clear yellow solution. To this $[LutBCl_2][AlCl_4]$, 3-hexyne (25 µl, 0.22 mmol) was added, turning dark brown. The reaction mixture was then stirred at room temperature for 4 hours, to which (trimethylsilyl)propyne (40 µl, 0.26 mmol) was added. After stirring for a further 45 minutes, the solution was esterified with excess triethylamine and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving a light yellow oil. Hexane was used to extract the product, which was filtered to remove aluminium based impurities. This crude product was then purified with column chromatography using 2:1 hexane:DCM eluent and presented as a light yellow oil (8 mg, 10%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 – 2.39 (m, 2H), 2.26 – 2.16 (m, 2H), 1.74 (s, 3H), 1.24 (s, 12H), 1.14 (t, 3H), 0.95 (t, 3H), 0.19 (s, 9H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ

153.05, 139.87, 128.54, 82.65, 27.98, 26.10, 24.62, 24.39, 20.72, 12.65, 12.30; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ29.30; **^{29}Si NMR** (MHz, $CDCl_3$) δ -4.75 ppm.

nOe shows through-space interactions between Pin – TMS, TMS – Me, triplets – quartets

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



1-phenyl-1-propyne (36 µl, 0.2 mmol, 1 eq), 2-methylthiophene (19 µl, 0.2 mmol, 1 eq) and TBP (50 mg, 0.2 mmol, 1 eq) were combined in a J. Youngs NMR tube in DCM (5 ml) under inert conditions. To this, BCl_3 (1M, 240 µl, 1.2 eq) was added, and the reaction mixture turned bright orange. After stirring at room temperature for 18 h, the reaction mixture was esterified with excess triethylamine (0.5 ml) and 2 equivalents of pinacol. The solvent was removed under reduced pressure, leaving a light orange oil. Purification by column chromatography (1:1 DCM : Hexane) afforded the product as a yellow oil (28 mg, 0.08 mmol, 41%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 5H), 6.57 (s, 2H), 2.37 (s, 3H), 2.04 (s, 3H), 0.99 (s, 12H); **^{13}C NMR** (100.06 MHz, $CDCl_3$) δ 144.65, 144.00, 142.11, 140.74, 129.62, 128.58, 127.66, 127.21, 124.76, 83.23, 24.51, 19.30, 15.35; **^{11}B NMR** (128.4 MHz, $CDCl_3$): δ 31.1 ppm.

GC/MS: 340.2 $gmol^{-1}$ **MS**: Theoretical = 340.1668 $gmol^{-1}$, Measured = 340.1662 $gmol^{-1}$

nOe spectroscopy shows through-space interaction between the vinyl methyl and both the pinacol and the aromatic thiophene resonances. Also, no interaction between the thiophene methyl and pinacol is observed.

5.8: References

1. Wrackmeyer, B., Tok, O. L., Klimkina, E., Bubnov, Y. N. *Inorg. Chim. Acta.*, **2000**, 300, 169
2. Wrackmeyer, B., Klimkina, E. V., Bubnov, Y. N. *J. Organomet. Chem.*, **2001**, 620, 51
3. Wrackmeyer, B., Zentgraf, R. *J. Chem. Soc., Chem. Commun.*, **1978**, 402
4. Wrackmeyer, B., Bihlmayer, C., Schilling, M. *Chem. Ber.*, **1983**, 116, 3182
5. Kerschl S., Wrackmeyer, B. *Z. Naturforsch.*, **1986**, 41B, 890
6. Bihlmayer, C., Abu-Orabi, T., Wrackmeyer, B. *J. Organomet. Chem.*, **1987**, 321, 25
7. Wrackmeyer, B., Abu-Orabi, T. *Chem. Ber.*, **1987**, 120, 1603
8. Wrackmeyer, B., Wagner, K., Abu-Orabi, T. *J. Organomet. Chem.*, **1988**, 346, 333
9. Wrackmeyer, B., Tok, O. L., Bhatti, M. H., Ali, S. *Appl. Organomet. Chem.*, **2003**, 17, 843
10. Wrackmeyer, B., Klimkina, E. V., Milius W., Bubnov, Y. N. *J. Organomet. Chem.*, **2003**, 687, 108
11. Wrackmeyer, B., Kenner-Hofmann, B. H., Milius, W., Thoma, P., Tok, O. L., Herberhold, M. *Eur. J. Inorg. Chem.*, **2006**, 101
12. Wrackmeyer, B., Tok, O. L. *Z. Naturforsch.*, **2007**, 62B, 1509
13. Wrackmeyer, B., Horchler, K. *Organometallics*, **1990**, 9, 1881
14. Wrackmeyer, B., Horchler, K. *Main Group Met. Chem.*, **1990**, 13, 387
15. Wrackmeyer, B., Horchler, K. *Z. Naturforsch.*, **1991**, 46B, 1207

16. Sebald, A., Wrackmeyer B. *J. Chem. Soc., Chem. Commun.*, **1983**, 309

17. Sebald, A., Wrackmeyer B. *J. Chem. Soc., Chem. Commun.*, **1983**, 1293

18. Sebald, A., Wrackmeyer B. *J. Organomet. Chem.*, **1986**, 304, 271

19. Sebald, A., Wrackmeyer B. *J. Organomet. Chem.*, **1997**, 544, 105

20. Wrackmeyer, B., Pedall A., Weidinger, J. *J. Organomet. Chem.*, **2002**, 649, 225

21. Köster, R., Seidel, G., Wrackmeyer, B. *Chem. Ber*., **1989**, 122, 1825

22. Wrackmeyer, B., Horchler, K., Boese, R. *Angew. Chem. Int. Ed*., **1989**, 28, 1500

23. Wrackmeyer, B., Pedall, A., Milius, W., Tok O. L., Bubnov, Y. N. *J. Organomet. Chem.*, **2002**, 649, 232

24. Wrackmeyer, B. *Heteroatom. Chemistry*, **2006**, 17, 188

25. Dierker, G., Ugolotti, J., Kehr, G., Fröhlich R., Erker, G. *Adv. Synth. Catal.*, **2009**, 351, 1080

26. Chen, C., Eweiner, F., Wibbeling, B., Fröhlich, R., Senda, S., Ohki, Y., Tatsumi, K., Grimme, S., Kehr G., Erker G. *Chem. Asian J.*, **2010**, 5, 2199

27. Chen, C., Voss, T., Fröhlich, R., Kehr, G., Erker, G. *Org. Lett.*, **2011**, 13, 62

28. Xu, B.-H., Kehr, G., Fröhlich, R., Grimme S., Erker, G. *J. Am. Chem. Soc.*, **2011**, 113, 3480

29. Erker, G., Kehr, G. *Chem. Commun*., **2012**, 48, 1839

30. Jiang, C., Blacque, O., Berke, H. *Organometallics*., **2010**, 29, 125

31. Fukazawa, A., Yamada, H., Yamaguchi, S. *Angew. Chem., Int. Ed*., **2008**, 47, 5582

32. Ekkert, O., Fröhlich, R., Kehr G., Erker, G. *J. Am. Chem. Soc.*, **2011**, 133, 4610

33. Suginome, M., Matsuda, T., Ohmura, T., Seki, A., Murakami, M. *Comprehensive Organometallic Chemistry III*

34. Suginome, M. *The Chemical Record*, **2010**, 10, 348

35. Lappert, M. F., Prokai, B. J. Organomet. Chem., **1964**, 1, 384

36. Cade, I. A., Ingleson, M. J. *Chem. Eur. J*., **2014**, 20, 12874

37. Nagao, K., Ohmiya, H., Sawamura, M. *J. Am. Chem. Soc.*, 2014, *136*, 10605

38. Devillard, M., Brousses, R., Miqueu, K., Bouhadir, G., Bourissou, D. *Angew. Chem. Int. Ed*., **2015**, 54, 5722

39. Fleming, I., Henning, R., Plaut, H.E. *J. Chem. Soc., Chem. Commun.*, **1984**, 29

40. Niedenzu, K., Dawson, J. W. *J. Am. Chem. Soc*., **1960**, 82, 4223

41. Schilling, B., Kaiser, V., Kaufmann, D. E. *Chem. Ber*., **1997**, 130, 923

42. Lawson, J. R., Clark, E. R., Cade, I. A., Solomon, S. A., Ingleson, M. J. *Angew. Chem. Int. Ed.,* **2013**, 52, 7518

43. Walkinshaw, A. J., Xu, W., Suero, M. G., Gaunt, M. J. *J. Am. Chem. Soc*., **2013**, *135* , 12532

44. Dureen, M. A., Brown, C. C., Stephan, D. W. *Organometallic*s, **2010**, 29, 6594

45. Bagutski, V., Del Grosso, A., Singleton, P. J., Helm, M. D., Solomon, S. A., Lawson, J. R., Marcelli, T., Ingleson, M. J. *J. Am. Chem. Soc.,* **2013**, 135, 474

Appendix

Crystal structure determinations and refinements: X-ray data were processed and reduced using CrysAlisPro suite of programs. Absorption correction was performed using empirical methods based upon symmetry-equivalent reflections combined with measurements at different azimuthal angles. The crystal structure was solved and refined against all F^2 values using the SHELXTL suite of programs. Atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions refined using idealized geometries (riding model) and assigned fixed isotropic displacement parameters. X-ray data was trimmed for **3xv** due to absence of diffraction beyond 1.1 Å. The C-C distances of the disordered ligands in **5v** were restrained to be the same using SADI and DFIX commands. The atomic displacement parameters of the disordered ligands were restrained using RIGU and SIMU commands.

Name	**2iii**	**2iv**	**2vii**	**3xv**	**4i**	**5v**
Formula	$C_{13}H_{14}BN_2O_2.AlCl_4$	$C_7H_{10}BCl_2N_2.AlCl_4$	$C_{13}H_{15}BClN_2.AlCl_4$	$C_{36}H_{44}Al_3B_5N_8Cl_{20}$	$C_{13}H_{20}BCl_2N_2.AlCl_4$	$C_{24}H_{33}O_2BSi$
CCDC Number	931220	931221	931223	1416375	931222	1416376
M_r	409.87	372.68	414.33	1432.86	454.80	457.27
Crystal Size / mm	0.70 × 0.40 × 0.10	0.35 × 0.25 × 0.20	0.60 × 0.05 × 0.05	0.40 × 0.10 × 0.10	0.41 × 0.28 × 0.28	0.10 × 0.06 × 0.03
Crystal System	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/c$	I2/a	$P2_1/n$	$P2_1/c$
T / K	100	100	100	150	100	150
***a* /Å**	9.9898(7)	12.3859(5)	9.8747(4)	22.085(4)	13.6092(8)	11.5585(7)
***b* / Å**	16.8931(18)	10.3851(4)	10.8803(5)	13.066(2)	11.0861(5)	18.4820(8)
***c* / Å**	10.4877(7)	12.6823(6)	17.5200(7)	23.157(6)	15.0265(9)	12.0048(9)
β / °	91.183(6)	101.692(4)	98.167(1)	96.49(2)	111.389(7)	115.161(8)
V / Å^3	1769.5(3)	1597.47(12)	1863.25(14)	6640(2)	2110.9(2)	2321.2(3)
Z	4	4	4	4	4	4
$D_{calc.}$ / Mg.m^3	1.538	1.549	1.477	1.518	1.431	1.31
radiation	Mo *K*α, λ = 0.71073 Å	Mo *K*α, λ = 0.71073 Å	Cu *K*α, λ = 1.54178 Å	Mo *K*α, λ = 0.71073	Mo *K*α, λ = 0.71073 Å	Mo *K*α, λ = 0.71073 Å
θ range (min-max) / °	3.0-28.6	3.2-28.4	4.5-72.8	6.16-37.692	2.9-27.4	3.4-29.0
reflns collected	7308	10889	18506	5396	7335	5066
indep reflns (R_{int})	3922 (0.056)	3669 (0.051)	3658 (0.039)	2585 (0.0697)	4073 (0.042)	5079 (0.0291)
reflns obsd I>2σ (I)	2824	2870	3314	1776	2910	3582
R, *w*R for I>2σ (I)	0.052, 0.133	0.043, 0.103	0.028, 0.071	0.0922, 0.1521	0.050, 0.054	0.0555, 0.0929
R, *w*R for all data	0.084, 0.135	0.063, 0.104	0.030, 0.071	0.2207, 0.2559	0.082, 0.084	0.1156, 0.1343
S	1.02	1.03	1.00	1.071	1.03	1.046