SYNTHESIS AND REACTIONS OF ALKYL- AND ARYL- SUBSTITUTED N-HETEROCYCLIC CARBENE BORANES

by

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Synthesis and applications of alkyl- and aryl-substituted NHC-boranes has been demonstrated. Chapter 1 shows the synthesis of methyl- and phenyl-substituted NHC-boranes by using organolithium reagents. Other alkyl- and aryl-substituted NHC-boranes have been prepared by hydroboration of alkenes and arynes respectively. The prepared substituted NHC-boranes were converted to Suzuki coupling precursors such as boronic acids, trifluoroborate salts, pinacol boronate esters and MIDA boronates. Fluorinated NHC-boranes were made by electrophilic fluorination of NHC-boranes with Selectfluor. The diMe-Imd-BF_2H has been synthesized via the use of a nucleophilic fluorination source (TBAF). The corresponding boryl radical has been generated and its properties have been compared to the boryl radical of the parent diMe-Imd-BH_3.

Chapter 2 describes the use of B-halo substituted NHC-boranes in the Suzuki coupling reactions. The NHC-(dibromo)arylboranes are converted to the boronic acids in-situ while the NHC-(difluoro)arylboranes are analogous to potassium trifluoroborate salts and used directly in the Suzuki coupling reaction. The potential for the use of NHC-(difluoro)arylboranes as a boron masking partner has been demonstrated. NHC-(difluoro)pinylborane has been used in the Minisci reaction showcasing the utility of NHC-boranes as a new boron partner in the C-C bond formation reactions.

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LIST OF ABBREVIATIONS

AAM	anthranilamide
Ac	acetate
BDE	bond dissociation energy
Bn	benzyl
Bu	n-butyl
Cp	cyclopentadienyl
DAN	1,8-diaminonaphthalene
DAST	diethylaminosulfur trifluoride
DCM	dichloromethane
dipp	2,6-diisopropylphenyl
DMAP	4-dimethylamino pyridine
DMF	dimethylformamide
Dppf	1,1'-bis(diphenylphosphino)ferrocene
equiv	equivalents
Et	ethyl
HMDS	hexamethyldisilazane
HRMS	high resolution mass spectrometry
iPr	isopropyl
Imd	imidazole-2-ylidene
LDBB	lithium4,4’-di-*tert*-butylbiphenylide
Me	methyl

MeCN	acetonitrile
mes	2,4,6-trimethylphenyl
MIDA	N-methyliminodiacetic acid
NBS	*N*-bromosuccinimde
NCS	*N*-chlorosuccinimde
NFSI	N-fluorobenzenesulfonimide
NHC	N-heterocyclic carbene
NIS	*N*-iodosuccinimide
NMP	N-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NaHMDS	sodium-bis(trimethylsilyl)amide
Ph	phenyl
pin	pinacol
PZA	2-(pyrazol-5-yl)aniline
$Rh_2(esp)_2$	bis[rhodium(α,α,α',α'-tetramethyl-1,3-benzenedipropionic acid)]
rt	room temperature
Sphos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
TBAF	tetrabutylammonium fluoride
TBAT	tetrabutylammonium difluorophenylsilicate
Tf	trifluoromethylsulfonyl (triflyl)
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	trimethylsilyl

TLC	thin layer chromatography
TPPTS	3,3',3''-phosphanetriyltris(bezenesulfonic acid) trisodium salt

PREFACE

First, I would like to express my sincere gratitude to my supervisor Prof. Dennis Curran for supporting me over the past five and half years, for his patience, motivation, enthusiasm, and immense knowledge. I appreciate all his contributions of time, ideas, and funding to make my Ph.D. experience productive. I am grateful for the freedom of the scientific research he granted and his guidance in improving my writing skills. I could not be prouder of my getting my education under his mentorship and will strive to continue using his philosophies in my future endeavors. I am grateful to my thesis committee members Prof. Paul Floreancig, Prof. Seth Horne, and Prof. Andrew VanDemark for their time and suggestions on my comprehensive exam, research proposal, and thesis writing. I would also thank Prof. Kazunori Koide for guiding me through the proposal writing.

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I especially thank my parents, Sanjay Nerkar and Shobha Nerkar. Without their unconditional love and support, I could not go through all these years to pursue true knowledge

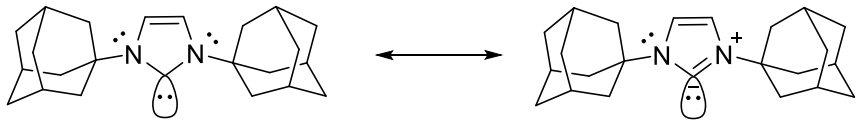
and career paths. Heartfelt thanks to my family for everything they have done for me, and this thesis is dedicated to them.

1.0 SYNTHESIS AND FLUORINATION OF SUSBTITUTED NHC-BORANES

1.1 INTRODUCTION

1.1.1 N-Heterocyclic carbene boranes

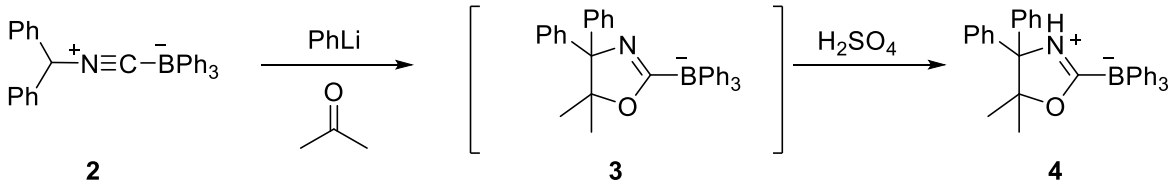
The first isolation and crystal structure analysis of a stable N-heterocyclic carbene (NHC), 1,3-bis(adamantyl)imidazole-2-ylidene **1** was reported by Arduengo in 1991 (Figure 1).[1] The chemistry of NHC's have been developed widely over the last 2 decades with their use becoming ubiquitous as ligands for metal catalyzed transformations and as organocatalysts themselves.[2]



Resonance structures diAd-Imd carbene **1**

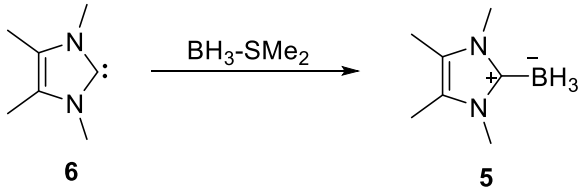
Figure 1. First stable N-heterocyclic carbene 1 isolated by Arduengo

N-heterocyclic carbene boranes (NHC-boranes) are complexes of an N-heterocyclic carbene (Lewis base) with a borane (Lewis acid). The first NHC-borane complex synthesized was by Bittner well before the isolation of free NHC's. He reacted the in-situ generated isonitrile-triphenylborane complex **2** with base and acetone to give the borate anion **3**. This was treated with H_2SO_4 to give the oxazolidine-2-ylidene triphenylborane **4** (Scheme 1).[3] Complex 4 is a protonated species and it can revert to **3** via an acid-base reaction.



Scheme 1. Synthesis of first NHC-borane **4** complex by Bittner

Despsite the discovery of stable NHC's, only isolated reports on synthesis and structure of NHC-boranes appeared in literature from 1993 to 2007. Kuhn prepared the first stable N.N-dialkylated imadozol-2-ylidine NHC-borane complexes **5** in 1993 (Scheme 2) by the complexation of the free carbene **6** with BH_3-SMe_2.[4]



Scheme 2. Synthesis of tetramethylimidazol-2-ylidine NHC-borane **5** by Kuhn

Figure 2 shows some other NHC-boranes synthesized before 2007. Compound **7** was prepared by Kuhn using a similar procedure as that for compound **5**. Compound **8** was made by Bertrand when the transient carbene was trapped with lewis acidic BF_3.[5] Robinson reported the synthesis of diborene **9** in 2007.[6]

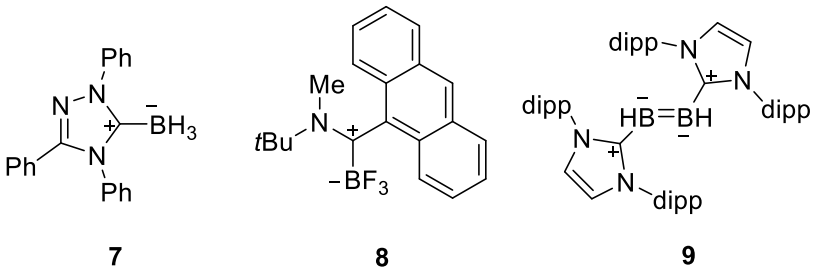
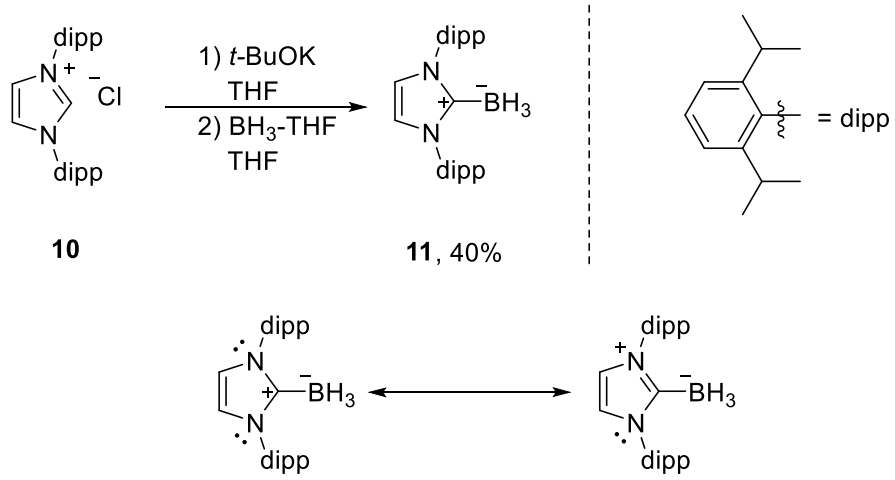


Figure 2. Selected structures of early NHC-boranes

Since 2007, studies of NHC-boranes have been reported rapidly with research on both the reactivity of NHC-boranes and on making new functionalized NHC-boranes.[7] NHC-boranes are

structurally related to complexes of other boranes with other neutral Lewis bases such as amines, phosphines and ethers. Despite this, they have unique reactivity due to the unusual electronic influence of the carbene.[8] The carbene carbon has a formal positive charge and the boron atom has a formal negative charge, resulting in a net zero charge on the NHC-borane. Scheme 3 shows the synthesis and resonance structures of a representative structure of 1,2-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene borane **11** (dipp-Imd-BH_3). Dipp-Imd-BH_3 **11** was synthesized by deprotonation of the imidazolium salt **10** with a strong base *t*-BuOK to form the carbene (Scheme 3). Addition of a borane source such as BH_3-THF gives dipp-Imd-BH_3 **11** in 40% yield.[6]



Scheme 3. Synthesis of representative dipp-Imd-BH_3 **11** and its resonance structures

A variety of NHC-boranes have been synthesized with different substituents on the nitrogen (Figure 3. **12**, **13**, **14**). Substituents on the imidazolium ring have also been incorporated along with NHC-boranes having fused alkyl or aryl rings (Figure 3. **15**, **16**, **17**).[7] These NHC-boranes are stable crystalline solids and can be purified by flash chromatography. They can be stored on the bench for months without decomposition. Unlike amine-boranes, NHC-boranes are reluctant to dissociate even on heating.

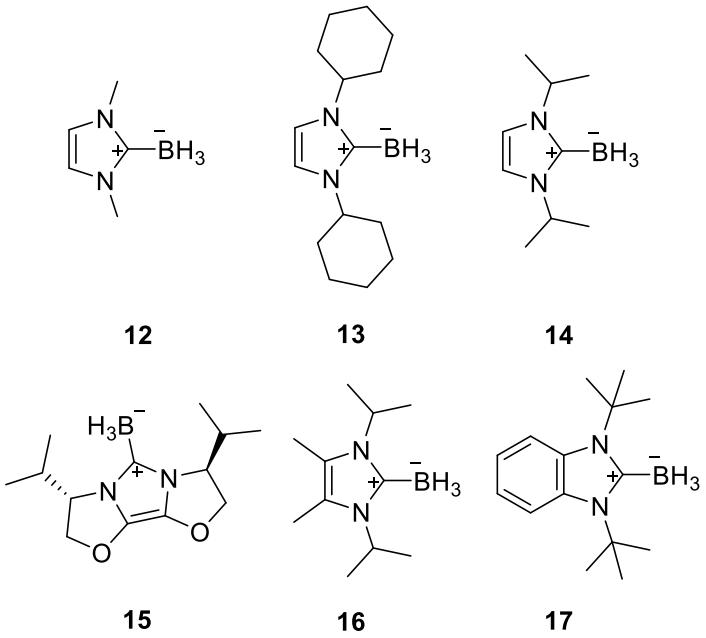
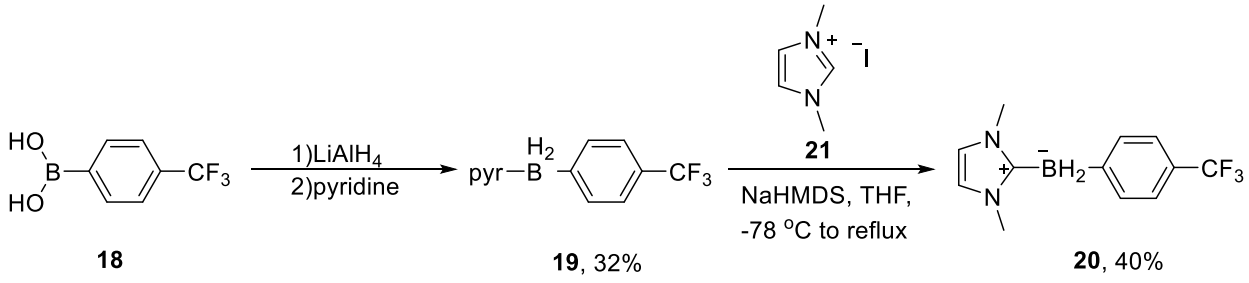


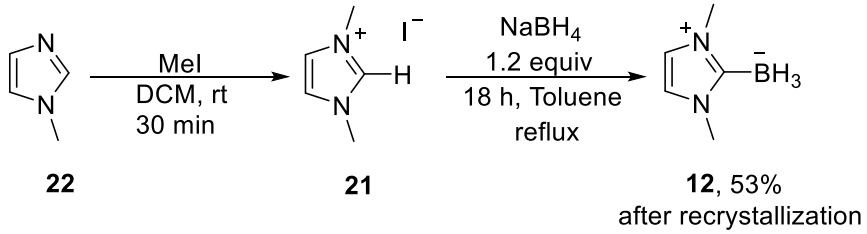
Figure 3. Structures of some selected NHC-boranes synthesized by addition of borane to NHC

NHC-boranes can also be made by ligand exchange with other stable ligated boranes. In 2010, Curran reported that NHC's exchange with amine-boranes and pyridine-boranes to make NHC-boranes.[9] Amine-boranes are readily available, safer and more convenient to use than commercial solutions of reactive boranes. This method is useful to prepare functionalized NHC-boranes, especially aryl boranes. For example (Scheme 4), aryl boronic acid **18** was reduced by $LiAlH_4$ followed by addition of pyridine to give pyridine-borane **19**. The corresponding NHC-borane **20** was obtained in 40% yield by heating **19** with a solution of in-situ generated free carbene (prepared from imidazolium salt **21**).



Scheme 4. Synthesis of NHC-borane by lewis base exchange with pyridine-borane

The Curran group has recently developed a synthesis of NHC-boranes from the imidazolium salts and inexpensive $NaBH_4$ without the use of a strong base.[10] For example, the imidazolium salt **21** was prepared in-situ by addition of methyl iodide to *N*-methyl imidazole **22**. Toluene was then added along with $NaBH_4$ and the reaction mixture was heated to reflux for 18 h. After evaporation of the solvent, the diMe-Imd-BH_3 **12** was purified by recrystallization from water (Scheme 5).



Scheme 5. Synthesis of diMe-Imd-BH_3 **12** using sodium borohydride

1.1.2 Use of NHC-boranes as reducing agents

Figure 4 summarizes the use of NHC-boranes as both radical and ionic reducing reagent.[11-14] Radical reductions of alkyl and aryl halides were performed with the help of polarity reversal catalysis using thiols.[15] These experiments have established the use of NHC-boranes as substitutes for the otherwise toxic $SnBu_3H$ in radical reductions. Also, NHC-boranes **11** and **12** are among the most nucleophilic neutral hydride donors based on Mayr's scale.[12]

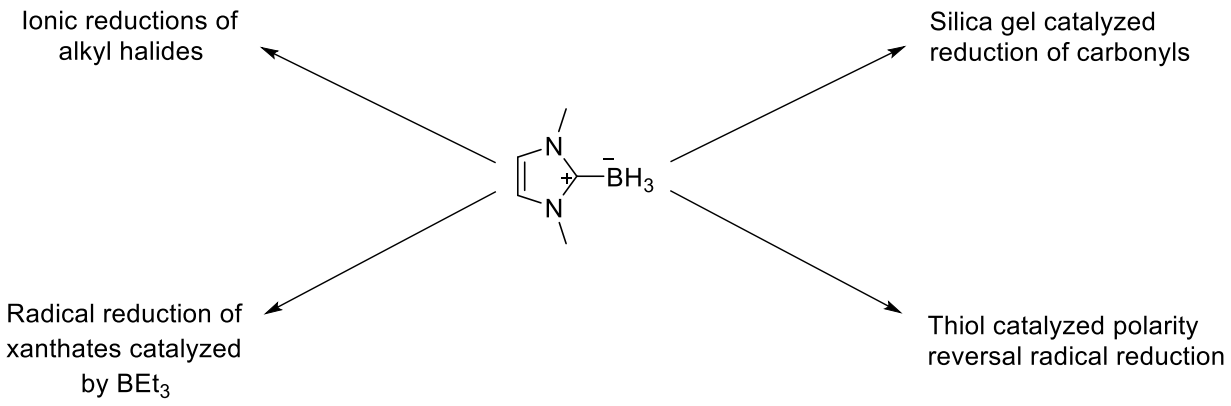
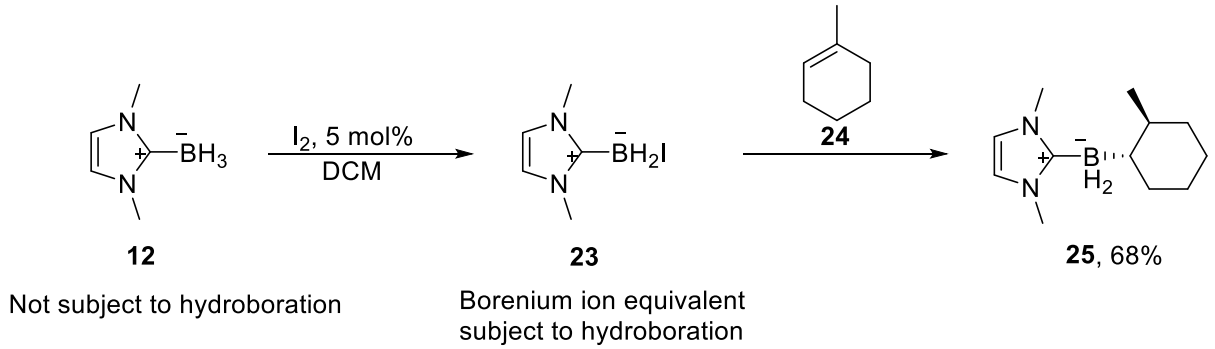


Figure 4. Reactions using NHC-boranes as reagents

1.1.3 C-Functionalized NHC-boranes

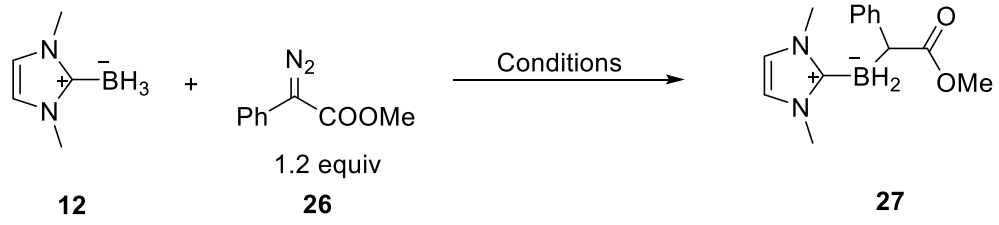
Use of NHC-boranes as reagents has led to synthesis of new boron compounds with different bonding partners. Functionalized trivalent boranes (BH_2R^1 and BHR^1R^2) can be directly complexed to NHC's to give the required NHC-boranes.[9] Many functionalized R groups however are not compatible to the Lewis acidic nature of trivalent boranes often making this route impractical. The other route to making these compounds is to functionalize the boron atom of NHC-boranes.

NHC-boranes are generally inert to direct hydroboration. However, similar to other ligated boranes like pyridine-borane[16], hydroboration with NHC-boranes can be affected by use of activating agents like iodine[17] and triflimide.[18] For example, Curran reacted diMe-Imd-BH_3 **12** with 10 mol% I_2 followed by addition of alkene **24** which led to the formation of hydroboration product **25** in 68% yield. Addition of I_2 results in the formation of boryl iodide **23**, a borenium ion equivalent that acts as a hydroboration catalyst. The alkene **24** attacks the electrophilic boryl iodide **23** and a hydride transfer from **12** gives the corresponding hydroboration product **25**.



Scheme 6. Hydroboration of alkenes by transient borenium ions

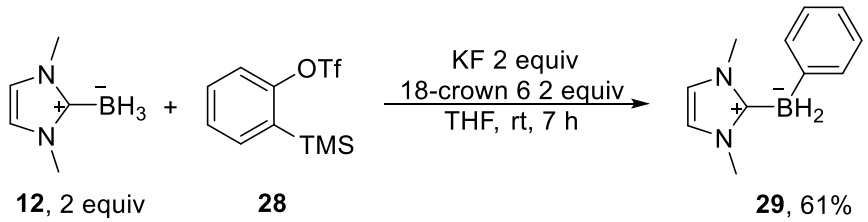
NHC-boranes are good hydride donors[12] and can be considered as carbenophiles, thus reacting with transient metal carbenes. Recently, Curran published the insertion of rhodium-carbenes into B-H bond of NHC-boranes using readily available rhodium salts.[19] For example (Scheme 7), diazo compound **26** was added to diMe-Imd-BH_3 **12** with $Rh_2(esp)_2$ as the catalyst to give the insertion product **27** in 74% yield. This is a reliable method to form boron-carbon bonds. The same transformation can be achieved with the use of borenium ion equivalents generated by reaction of NHC-borane with catalytic I_2 (Scheme 7).[20] For example, 10 mol% I_2 was added to diMe-Imd-BH_3 **12** followed by addition of the diazo compound **26** to give insertion product **27** in 64% isolated yield.



Entry	Catalyst	yield **27**
1	$Rh_2(esp)_2$ 1 mol%	74%
2	I_2, 10 mol%	64%

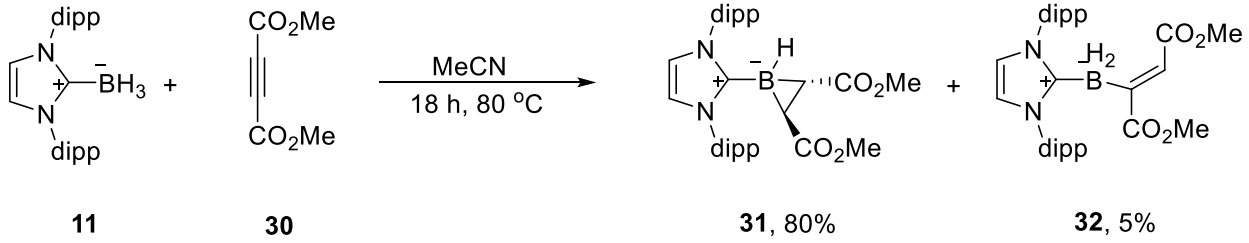
Scheme 7. Reaction of NHC-borane with diazocarbonyl compound catalyzed by rhodium and iodine

Curran and Taniguchi recently reported hydroboration of in-situ generated aryne by NHC-borane to give aryl-substituted NHC-boranes.[21] In a typical reaction (Scheme 8), 2 equiv of diMe-Imd-BH_3 **12** was reacted ortho-silyl triflate **28** in the presence of KF and 18-crown-6 to give the B-phenyl NHC-borane **29** in 61% yield. The benzyne was generated in-situ by fluoride displacement of the trimethylsilyl group.[22]



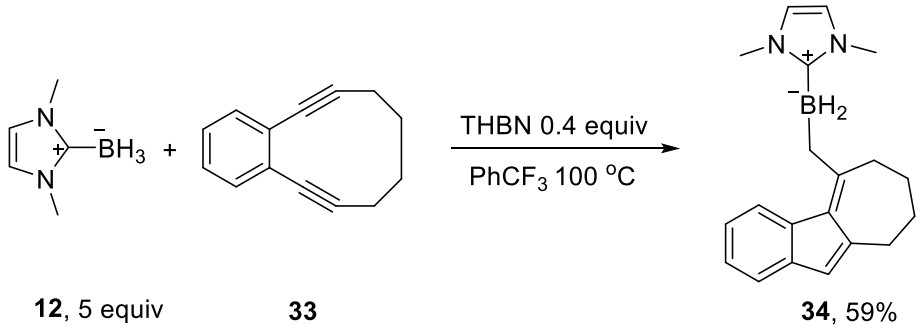
Scheme 8. Hydroboration of benzyne by diMe-Imd-BH_3 **12**

Another interesting reaction of NHC-boranes is the formal double hydroboration of acetylenedicarboxylate esters to boracyclopropanes (boriranes).[23] For example, the dipp-Imd-BH_3 **11** was heated with 2 equiv of dimethyl acetylenedicarboxylate **30** in acetonitrile at 80 °C for 18 h (Scheme 9). The borirane **31** was isolated in 80% yield along with 5% of the E-alkenyl borane **32**.



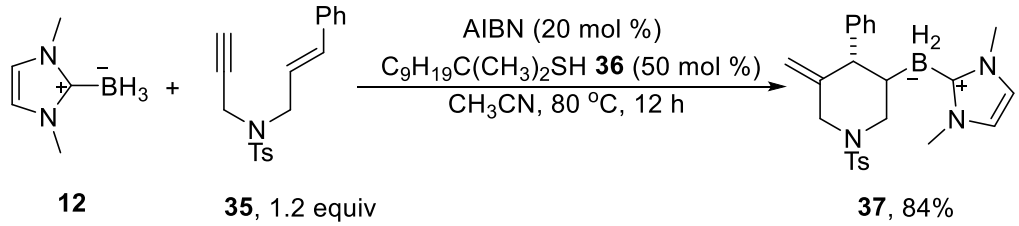
Scheme 9. Synthesis of boriranes by hydroboration of acetylene dicarboxylates

Taniguchi and Curran have recently reported radical cyclizations of 1,5-diynes and NHC-boranes to give 5-borylated azulenes.[24] For example, the diyne **33** was heated with 5 equiv of diMe-Imd-BH_3 **12** with 40 mol% of THBN at 100 °C to give the substituted NHC-borane **34** in 59% yield (Scheme 10).



Scheme 10. Reaction of diMe-Imd-BH_3 **12** with 1,5-diynes

Similarly, the Wang group has also shown radical cyclizations of NHC-boranes with 1,6-enynes to give various boron-handled carbocycles and heterocycles(Scheme 11).[25] For example, reaction of diMe-Imd-BH_3 **12** with enyne **35** in the presence of AIBN and tert-dodecanethiol **36** to give the cyclized product **37** in 84% yield.



Scheme 11. Functionilization of NHC-boryl radicals with 1,6 enynes

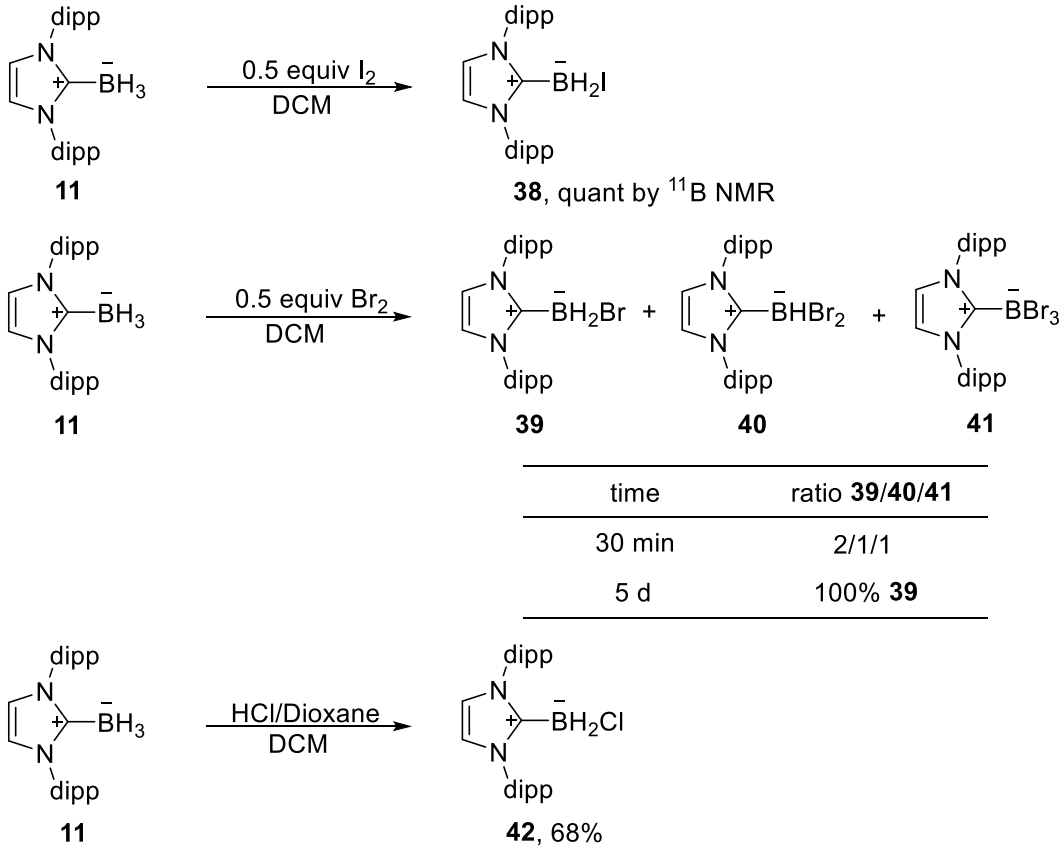
1.2 HALOGEN SUBSTITUTED NHC-BORANES

1.2.1 *B*-Chloro, *B*-bromo and *B*-iodo NHC-boranes

NHC-boranes are weak bases that are similar to amine- and phosphine-boranes. NHC-boranes react with strong acids like HCl, HBr and HI.[26] They also react with strong electrophiles including halogenating agents like *N*-bromosuccinimide (NBS), *N*-iodosuccinimide (NIS), iodine (I_2) and

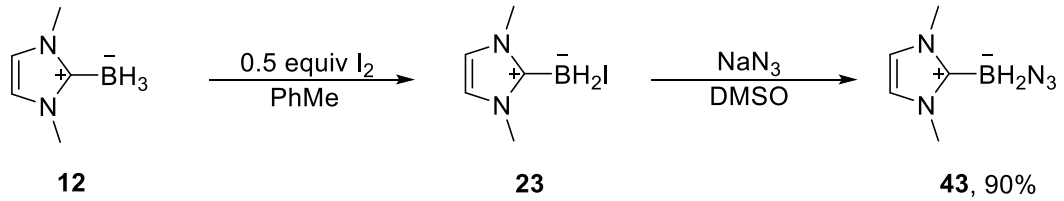
bromine (Br_2).[27] These reactions give *B*-halo mono-, di- and tri- substituted products with variable selectivities. Reaction of an NHC-boranes with 0.5 equiv of I_2 typically gives the mono-iodide exclusively. For example, dipp-Imd-BH_3 **11** reacts with 0.5 equiv I_2 to give boryl iodide **38** (Scheme 12).[27] Dipp-Imd-BH_3 **11** first reacts with I_2 in a nucleophile/electrophile reaction to give **38** and HI. The remaining dipp-Imd-BH_3 **11** reacts with HI in an acid/base reaction to give **38**. However, the reaction of dipp-Imd-BH_3 **11** with 0.5 equiv of Br_2 is not selective and gives the three products **39**, **40** and **41** (Scheme 12) in a 2:1:1 ratio.[27] These products equilibrate to give boryl bromide **39** when stirred at rt for over 5 days.

Dipp-Imd-BH_3 **11** reacts with HCl to give the mono-substituted chloride **42**(Scheme 12).[27] The dichloro NHC-borane is not observed even when excess hydrochloric acid is used suggesting that HCl is not acidic enough to react with the hydride of the boryl chloride **42**. Apart from the boryl chloride **42**, none of the above-mentioned halo-substituted NHC-boranes are fully stable to flash chromatography. Boryl bromide **39** can be recovered from chromatography but with significant loss of mass. Boryl iodide **38** is not recovered at all. Typically, such *B*-halo boranes are generated and used in situ.



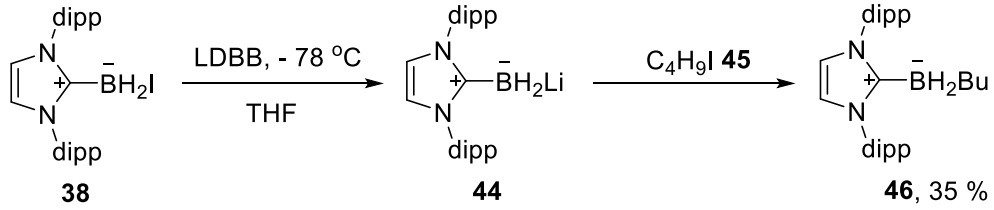
Scheme 12. Reaction of dipp-Imd-BH_3 **11** with halogens and electrophilic halogenation agents

Halo-substituted NHC-boranes can be used to prepare various B-substituted boranes via nucleophilic substitution. The halo-substituted NHC-boranes undergo nucleophilic substitution reactions despite having a formal negative charge on the boron atom. Various B-substituted NHC-boranes have been prepared including boron azides, cyanides, isocyanates, nitro compounds and nitrous esters.[27] For example, NHC-boryl azide **43** was prepared in 90% yield by addition of sodium azide to in-situ prepared NHC-boryl iodide **23** (Scheme 13).



Scheme 13. Reaction of NHC-boryl iodide with a nucleophile

Boryl iodides are also precursors of boryl anions. For example, reductive metalation of boryl iodide **38** with lithium di-*tert*-butylbiphenyl (LDBB) followed by addition of electrophile butyl iodide **45** gives a stable butyl substituted NHC-borane **46** in 35% overall yield (Scheme 14). Addition of LDBB results in the formation of an unstabilized boryl anion **44** which can be observed in the ^{11}B NMR spectrum at low temperatures.[28]



38 **44** **46**, 35 %

Scheme 14. Preparation of NHC-boryl anion and reaction with electrophiles

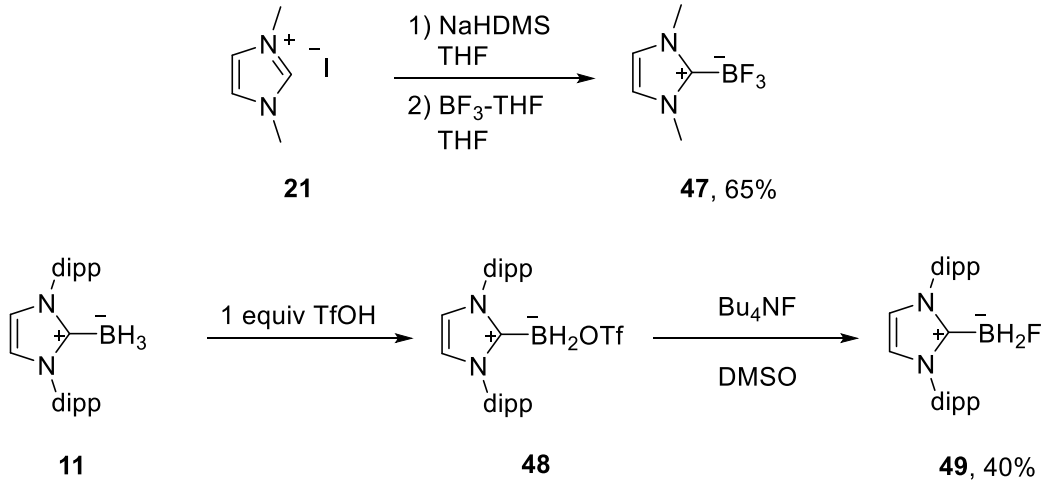
1.2.2 *B*-Fluoro NHC-boranes

Compared to other halo substituted NHC-boranes mentioned in Section 1.2.1, fluorinated NHC-boranes are generally bench-stable and can be isolated via column chromatography. The synthesis of chloro-, bromo- and iodo- NHC-boranes is different from the synthesis of B-fluoro NHC-boranes.

1.2.3 Synthesis of fluoro-substituted NHC-boranes

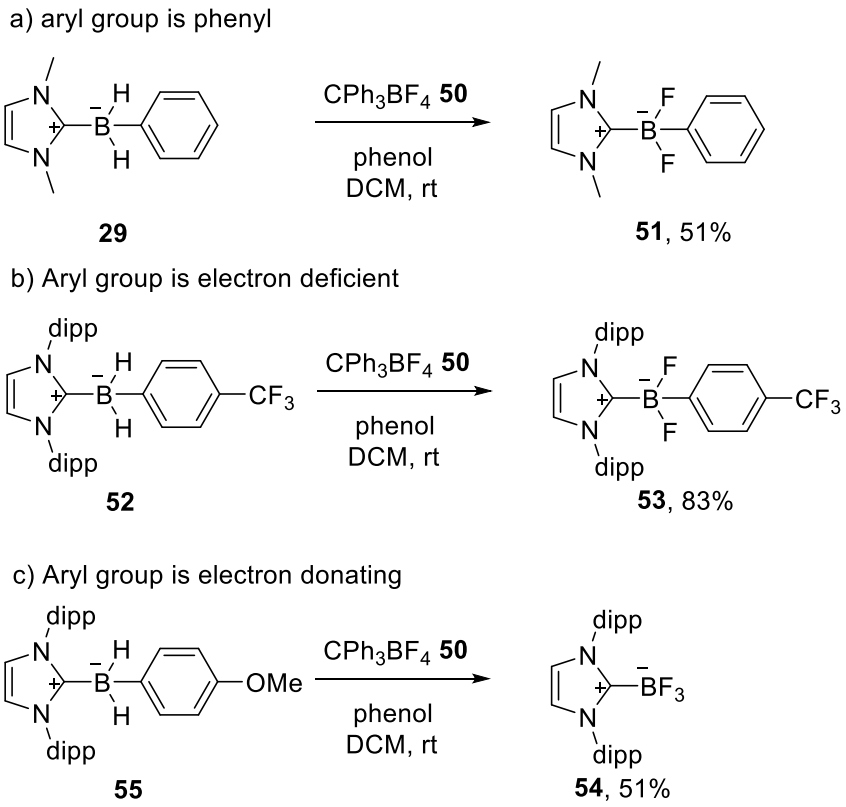
Tri-fluoro substituted NHC-boranes have been prepared by complexation of free carbenes with lewis acidic BF_3 (Scheme 8).[7] The imidazolium salt **21** was deprotonated using sodium hexamethyldisilazide (HMDS) followed by addition of BF_3-THF to give the diMe-Imd-BF_3 **47** in 65% yield.[7]

Mono- or di-fluorinated NHC-boranes have been synthesized selectively by nucleophilic substitution on NHC-boryl triflate or NHC-boryl iodide. For example, NHC-boryl triflate **48** was prepared by acid base reaction of dipp-Imd-BH_3 **11** with triflic acid. Reaction of **48** with Bu_4NF gave mono-fluoro NHC-borane **49** in 40 % yield (Scheme 15).[27] Fluorinated NHC-boranes like **47** and **49** could be purified by chromatography and stored without special precautions.



Scheme 15. Synthesis of fluorinated NHC-boranes

Lacôte has made B-fluoro substituted NHC-boranes from aryl substituted NHC-boranes.[29] For example, B-phenyl NHC-borane **29** was treated with trityl tetrafluoroborate **50** followed by addition of phenol to give the difluoro NHC-borane **51** in 51 % yield (Scheme 16a). However, the course of this reaction depends on the nature of the aryl ring substituent. When B-(4-trifluoromethyl) phenyl NHC-borane **52** is used, target difluoro NHC-borane was isolated in 83 % yield (Scheme 16b). However, trifluoro NHC-borane **54** was the sole product when B-(4-methoxy) phenyl NHC-borane **55** was employed as the substrate under identical reaction conditions (Scheme 16c).



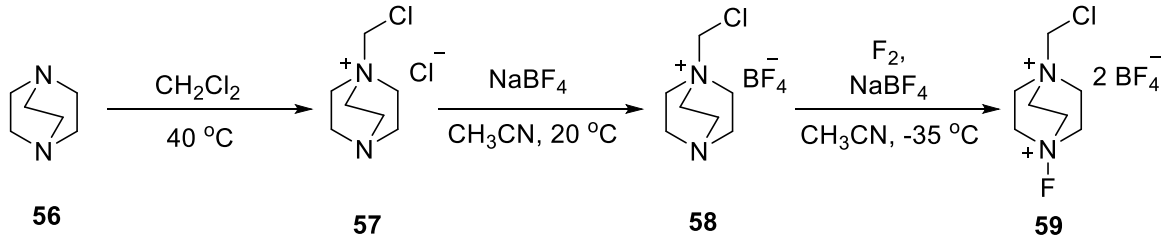
Scheme 16. Reaction of B-aryl substituted NHC boranes with trityl tetrafluoroborate **50**

1.2.4 Electrophilic fluorination with Selectfluor

Replacement of hydrogen by fluorine in a molecule alters its physical, chemical and biological properties.[30-31] This makes the synthesis of fluorinated compounds important in drug discovery, agriculture and other areas. Fluorine can be incorporated in a molecule using both nucleophilic and electrophilic sources. The most common source of nucleophilic fluorine is (diethylamino)sulfur trifluoride (Et_2NSF_3, DAST).[32] Molecular fluorine (F_2) was the first source of electrophilic fluorine but dilute solutions are needed because of its high reactivity. This coupled with other dangerous properties such as toxicity necessitated development of other reagents.

Popular electrophilic fluorinating reagents include perchloryl fluoride ($FClO_3$)[33], xenon difluoride (XeF_2)[34], and fluoroxy compounds (CF_3OF, $CsSO_4F$).[35]

Many of today's most popular electrophilic fluorinating agents contain N-F bonds. Among these, Selectfluor® **59** has emerged as a reagent of choice for many transformations.[36] Selectfluor is easily prepared on large scale (Scheme 17), commercially available and cheaper than other N-F fluorinating agents.[37] The synthesis (Scheme 17) begins with reaction of DABCO **56** with dichloromethane to give salt **57**. The chloride counterion is then exchanged with tetrafluoroborate to give **58** which is reacted with fluorine and sodium tetrafluoroborate at $-35\ ^oC$ to give Selectfluor **59**. It is a stable, non-hygroscopic crystalline solid that is safer than other electrophilic fluorinating agents.[38] It is significantly less toxic than molecular fluorine. Environmentally, the effects of Selectfluor on algal growth, sewage-sludge respiration were found to be within acceptable levels.[37]



Scheme 17. Large scale synthesis of Selectfluor

Various analogs of Selectfluor used in synthesis. Selectfluor itself has BF_4^- as the counterion, but OTf^- and PF_6^- analogs can be made via anion exchange.[36] The counterion in Selectfluor has an impact on reactivity as it can alter the solubility of the compound in various solvents. Other commonly used N-F fluorinating agents include N-fluoropyridinium triflate **60** and N-benzenesulfonimide **61**(Figure 5).

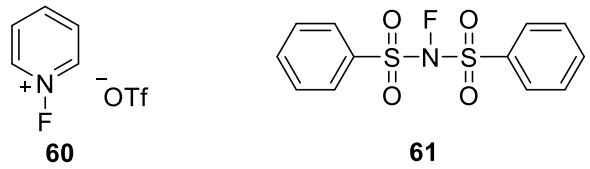
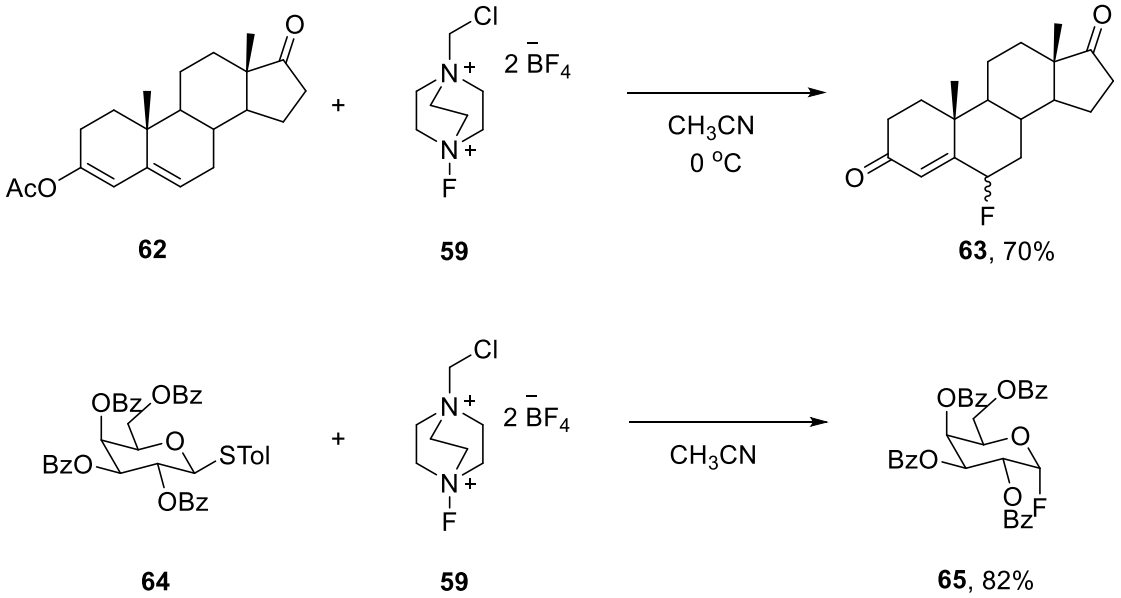


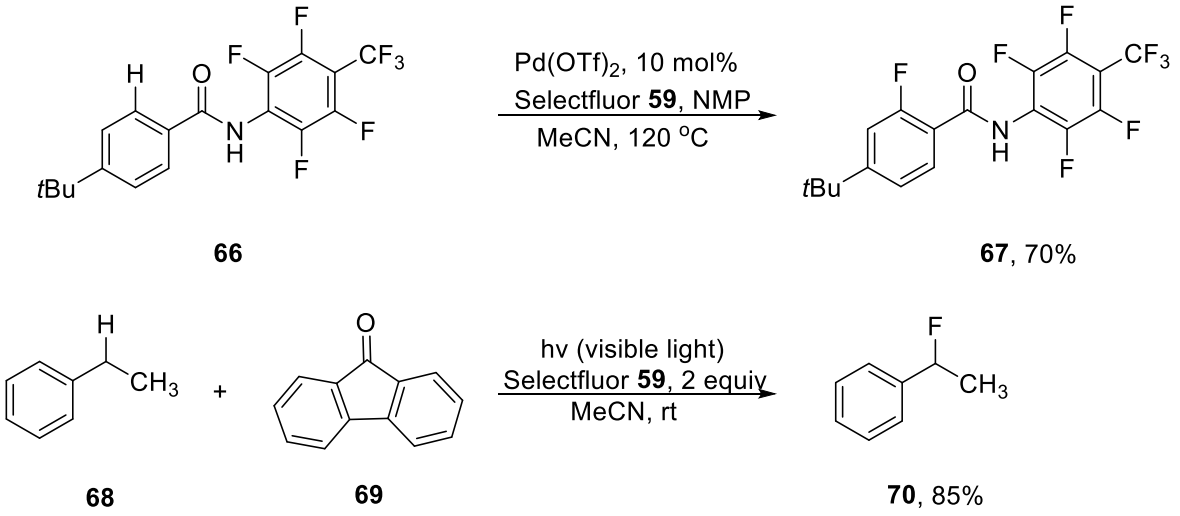
Figure 5. Commonly used N-F fluorinating agents apart from Selectfluor

The α-fluorination of carbonyl compounds or silyl enol ethers is one of the most common reactions of Selectfluor. For example, Herrington and coworkers reported that Selectfluor was the preferred reagent for converting dienolacetate **62** to γ-fluoroketone **63** in 70 % yield (Scheme 18)[39]. Selectfluor can be used to make fluoroglycosides from thioglycosides[40]. For example, thioglycoside **64** was reacted with Selectfluor to give α-glycosyl fluoride **65** in 82 % yield (Scheme 18). This reaction occurs by electrophilic fluorination at sulfur, followed by displacement. The yields obtained were better than reactions where nucleophilic fluorine sources such as DAST were used due to thiophilic nature of electrophilic fluorine.



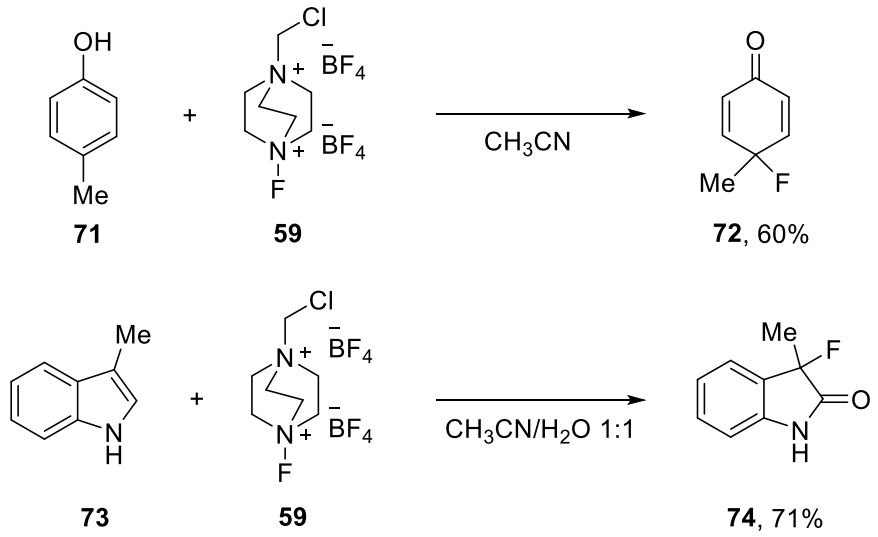
Scheme 18. Fluorination of carbonyls and conversion of thioglycosides to α-fluoro sugars

Selectfluor has also been used with metal catalysts to perform C-H fluorinations. The Yu group reacted Selectfluor with the aromatic amide **66** using $Pd(OTf)_2$ as the catalyst to selectively activate the ortho C-H bond to give fluorinated product **67** in 70 % yield (Scheme 9)[41]. The Chen group selectively fluorinated benzylic C-H bonds. They used visible light along with a diarylketone catalyst **69** to selectively abstract the benzylic hydrogen of compound **68** which is then fluorinated to give **70** in 85% yield (Scheme 19)[42].



Scheme 19. Examples of C-H fluorination with Selectfluor

Electrophilic aromatic substitution incorporating a fluorine is also possible using Selectfluor. Highly reactive analogue of Selectfluor (where the R group is CF_3CH_2) can fluorinate benzene.[36] Aromatic compounds bearing electron donating groups and electron rich heteroaromatics like indoles undergo fluorination readily with Selectfluor **59.**[43] For example, *p*-cresol **71** was reacted with Selectfluor **59** to give compound **72** in 52% yield. 3-Methylindole **73** gave fluorooxindole **74** in 1:1 acetonitrile water mixture in 71% yield (Scheme 20).[44]



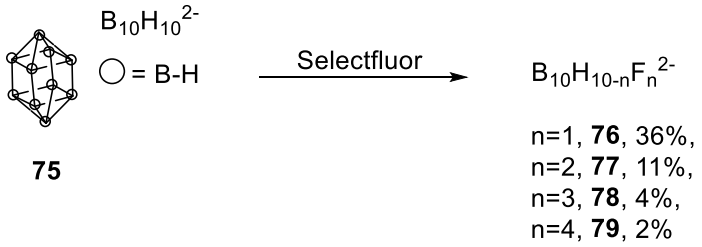
Scheme 20. Reaction of Selectfluor **59** electron rich aromatics and indoles

Selectfluor has been utilized to react with alkenes and alkynes regioselectively to give 1,2 -difluoroethers and α,α-difluoroketones respectively.[38] Enantioselective fluorinations have been achieved with limited success with the use of N-fluoroammonium derivatives of cinchona alkaloids.[45] Organocatalytic fluorination can is possible with the use of chiral BINOL-derived phosphoric acids to synthesize compunds with quaternary stereocenters. Selectfluor mediates electrophilic addition of anions to aromatic substrates and is also used to cleave protecting groups such as tetrahydropyranyl (THP) and dithianes.[46]

1.2.5 B-H fluorination using electrophilic agents

While the use of electrophilic reagents to fluorinate C-H bonds is well established, fluorinations of B-H bonds has only been reported for carboranes. In 1995, the Solnstev and Strauss groups reported fluorination of carborane $B_{10}H_{10}^{2-}$ dianion with Selectfluor in water.[47] Mono and polyfluorinated products were formed and the ratios were determined by mass spectroscopy. For example (Scheme 21), carborane $B_{10}H_{10}^{2-}$ **75** was reacted with 1 equiv of Selectfluor to give

monofluorinated carborane **76** (36%), difluorinated carborane **77** (11%), trifluorinated carborane **78** (4%), tetrafluorinated carborane **79** (2%) and unreacted carborane **75** (46%).



Scheme 21. B-H fluorination of $B_{10}H_{10}$ dianion using Selectfluor

We envision that fluorinated NHC-boranes could be potential Suzuki coupling precursors. Analogous to the reaction of NHC-boranes with electrophilic halogenating agents such as *N*-chlorosuccinimide, we envisioned that N-F fluorinating agents can be used to give target fluorinated NHC-boranes. We chose Selectfluor **59** and NFSI **61** (Figure 6) due to their low cost compared to the other commercially available reagents.

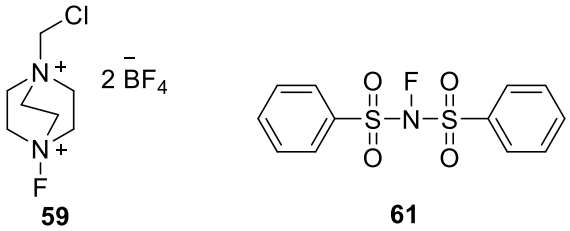


Figure 6. N-F fluorinating agents to be attempted for fluorination of NHC-boranes

Reactions of ligand exchange[9], borenium ions, carbene insertions[19-20] and hydroborations[17-18] provide access to many new B-substituted NHC-boranes. However, at present there are few methods to use these NHC-boranes as substrates in Suzuki coupling[48] similar to that of pinacol boronates or the trifluoroborate salts.

The goals of this study are i) to develop efficient methods to synthesize alkyl/aryl substituted NHC-boranes ii) to convert them to other Suzuki cross-coupling precursors and iii) to

convert the NHC-boranes to NHC-BX_2R, especially where X = F which could possibly be used directly in Suzuki coupling reactions.

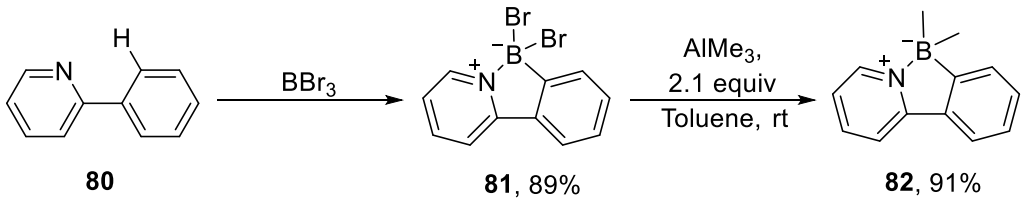
1.3 RESULTS AND DISCUSSION

1.3.1 Synthesis of B-alkyl and B-aryl NHC-boranes

The methods described to make aryl and alkyl mono-substituted NHC-boranes in Section 1.1 have certain limitations. Synthesis of NHC-boranes via complexation of the free carbene with corresponding mono-substituted amine-boranes is a multi-step process.[9] The benzyne hydroboration method is limited to aryl boranes.[21] To test the use of substituted NHC-boranes in reactions such as Suzuki coupling, we needed a quick and efficient method to prepare aryl- and alkyl- substituted NHC-boranes on gram scale. We first decided to attempt substitution reactions of NHC-boryl iodides and NHC-boryl chlorides to make the target substituted NHC-boranes.

1.3.2 Substitution of a boryl iodide by $AlMe_3$

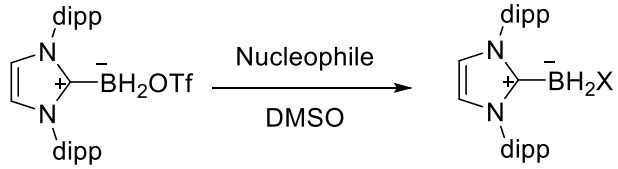
Murakami and coworkers published synthesis of 2-phenylpyridine-borane complexes by borylation of 2-phenylpyridine with tribromoborane followed by addition of organometallic reagents to substitute the bromine atom on boron.[49] In a typical example (Scheme 22), 2-phenyl-pyridine **80** was reacted with 3 equiv of BBr_3 to give the dibromo-borane **81** in 89% yield. Addition of slight excess of $AlMe_3$ to **81** in toluene at room temperature gave the corresponding dimethyl-substituted borane **82** in 91% yield.



80 **81**, 89% **82**, 91%

Scheme 22. Reaction of organometallics with B,B-dibromo pyridine-boranes

Similarly, organometallic reagents like $AlMe_3$ could potentially be used to substitute halogen atoms on NHC-boranes. Dr. Andrey Solovyev described the substitution reactions on boron atom with various nucleophiles reagents with NHC-boryl iodide **38** and NHC-boryl triflate **48** as the substrates (Scheme 23).[27] This reaction was limited to the use of heteroatom nucleophiles, and attempted substitution reactions with carbon nucleophiles like phenyl magnesium bromide gave bromo-substituted NHC-boranes. For example, when PhSLi was added to NHC-boryl triflate **48**, NHC-boryl sulfide **83** was isolated in 82% yield. However, when phenylmagnesium bromide was used as the nucleophile, the only product observed was NHC-boryl bromide **39**.



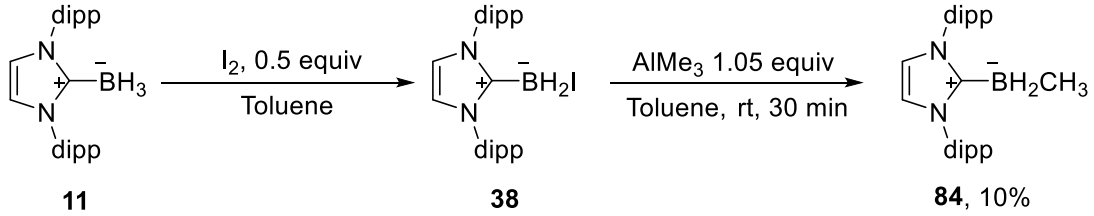
48

nucleophile	dipp-Imd-BH_2X	yield
PhSLi	X = SPh, **83**	58%
PhMgBr	X = Br, **39**	-

Scheme 23. Substitution on boron atom of NHC-boranes

We initially used NHC-boryl iodide **39** for the reaction with organometallic reagents because substituted dipp-NHC-boranes are generally more stable than the corresponding *N,N'*- di-Me analogs. The progress of the substitution reactions was monitored by ^{11}B NMR spectroscopy.

In a typical experiment, the NHC-boryl iodide **38** was prepared by slow addition of 0.5 equiv of I_2 to NHC-borane **11** (Scheme 24). A slight excess of $AlMe_3$ (1.05 equiv) was added inducing the formation of a white precipitate. After 30 min, the reaction was quenched with water. An ^{11}B NMR spectrum of the organic layer showed the presence of the methyl substituted NHC-borane **84** (a triplet at –28 ppm as the major peak) along with an unknown product (small sharp singlet at –18 ppm) and dipp-Imd-BH_3 **11** (quartet at –36 ppm). After chromatography, the product **84** was obtained in 10 % yield in approximately 80 % purity. The impurity was dipp-Imd-BH_3 **11**. The spectra of the compound **84** were identical to those reported by Dr. Andrey Solovyev.[28]



11 **38** **84**, 10%

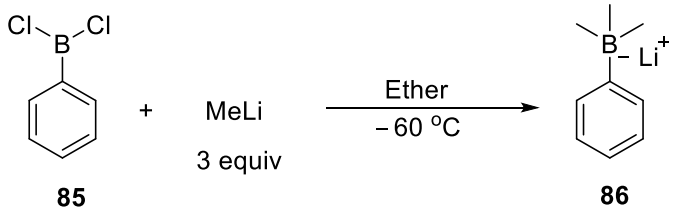
Scheme 24. Reaction of $AlMe_3$ with dipp-Imd-BH_2I **38**

We tried to improve this reaction by using various organometallic reagents, workup procedures and other NHC-substrates like boryl chloride **42**, but without success. Although this route is not feasible to prepare compound **83**, the moderate success encouraged us to try reactions of other organometallic reagents with boryl halides.

1.3.3 Substitution on NHC-boryl chlorides by organolithium reagents

Pietrzak made phenyltrialkylborate salts by adding alkyllithium reagents to dichlorophenylborane.[50] For example, 3 equiv of methyllithium (MeLi) was added to dichorophenylborane **85** to cleanly give the corresponding lithium trimethylphenylborate salt **86**

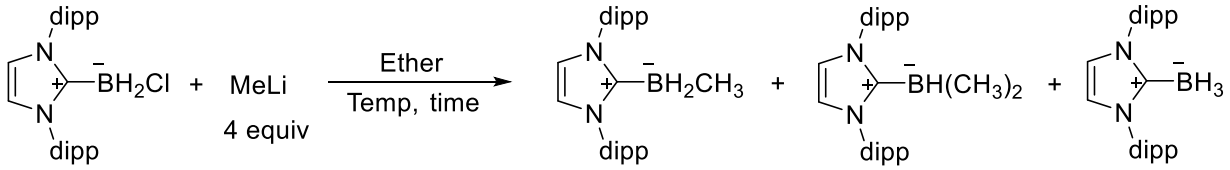
(Scheme 25). The lithium salt was not stable to chromatography, so it was converted to the tetramethylammonium salt to be isolated.



Scheme 25. Reaction of methyllithium with dichlorophenylborane

Following this precedent, we envisioned that organolithium reagents could be used to substitute the chlorine atom in NHC-boryl chlorides to yield substituted NHC-boranes. NHC-boryl chloride **42** was prepared following the procedure developed by Dr. Andrey Solovyev[27]. HCl (2.1 equiv, 4 M in dioxane) was added to dipp-Imd-BH_3 **11** in chloroform and NHC-boryl chloride **42** was isolated in 75% yield after flash chromatography. To test the substitution reaction, methyllithium (4 equiv) was added to NHC-boryl chloride **42** in ether at –78 °C (Scheme 26). After 15 min, an ^{11}B NMR spectrum of an aliquot showed the presence of the methylated product **84** along with small amounts di-methylated product **87** (doublet at –22 ppm) and reduced dipp-Imd-BH_3 **11** (quartet at –36 ppm). Surprisingly, quenching of this reaction at –78 °C yielded dipp-Imd-BH_3 **11**. This indicated that the reaction proceeded in the NMR tube upon warming.

We then carried similar reactions at 0 °C and 15 °C to determine a convenient temperature (Scheme 26). The reaction at 0 °C was completed in 2.5 h (^{11}B NMR spectral analysis) and **84** was isolated in 40 % yield. The reaction proceeded smoothly at 15 °C in 30 min giving **84** in 60 % yield after chromatography.



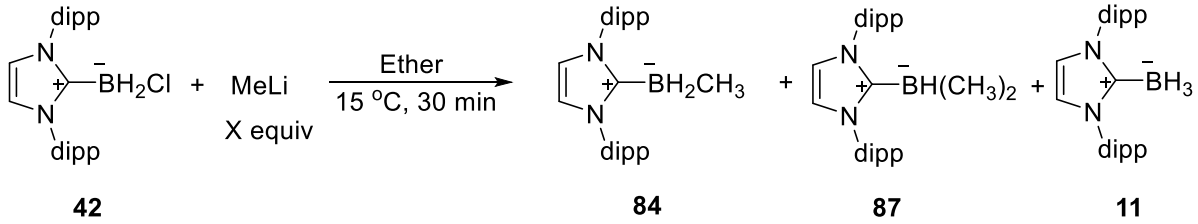
42 **84** **87** **11**

temp	time	yield **84**
−78 °C	30 min	0%
0 °C	2.5 h	40%
15 °C	30 min	60%

Scheme 26. Substitution reaction of NHC-boryl chloride **42** with methyllithium

Based on the above results, we decided to conduct further optimization of reaction conditions at 15 °C. The results for these reactions are summarized in Table 1. In the reaction with 3 equiv of methyllithium (Table 1, entry 1), dimethylated product **87** (~20%) and reduced dipp-Imd-BH_3 **11** (~20%) were observed in the crude ^{11}B NMR spectroscopy. In the reaction with 4 equiv of methyllithium (Table 1, entry 2), dimethylated product **87** and reduced product dipp-Imd-BH_3 **11** (~10 % each) were detected in the crude ^{11}B NMR spectrum and the methyl substituted NHC-borane **84** was isolated in 60 % yield. When 5 equiv of methyllithium was used, the amounts of dimethylated product **87** and dipp-Imd-BH_3 **11** were low (< 10 %) and methyl substituted NHC-borane **84** was isolated in 87 % yield (Table 1, entry 3).

Table 1. Varying the equivalents of the methyllithium in substitution reaction of **43** at 15 °C



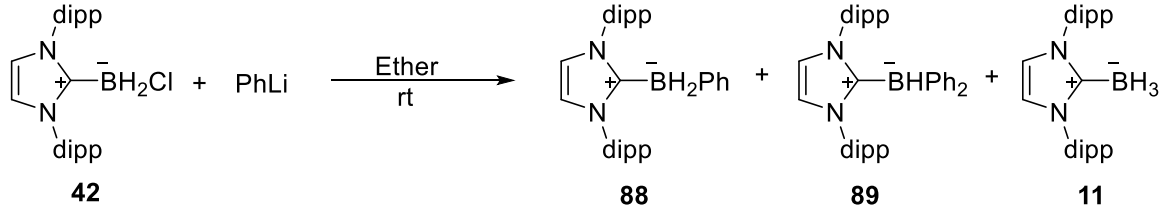
42 **84** **87** **11**

entry	methyllithium	% **84**[a]	% **87**[a]	% **11**[a]	yield **84**[b]
1	3 equiv	61	18	19	N.D.[c]
2	4 equiv	>90	<10	<10	60%
3	5 equiv	>90	<10	<10	87%

[a] product ratio determined by crude ^{11}B NMR spectrum [b] after flash chromatography [c] purification not attempted

We tried reactions of phenyllithium (PhLi) with NHC-boryl chloride **42** next and the results are summarized in Table 2. The initial procedure involved addition of excess phenyllithium (5 equiv) to a solution of the NHC-boryl chloride **42** (normal addition mode) in ether at room temperature (Table 3, entry 1). After 15 min, the ^{11}B NMR spectrum showed formation of B-phenyl NHC-borane **88** (triplet at –24 ppm), diphenylated NHC-borane **89** (doublet at –13 ppm) and dipp-Imd-BH_3 **11** (quartet at –36 ppm) in ratio of 51/22/27 (entry 1).

Table 2. Substitution of NHC-boryl chloride **42** by phenyllithium

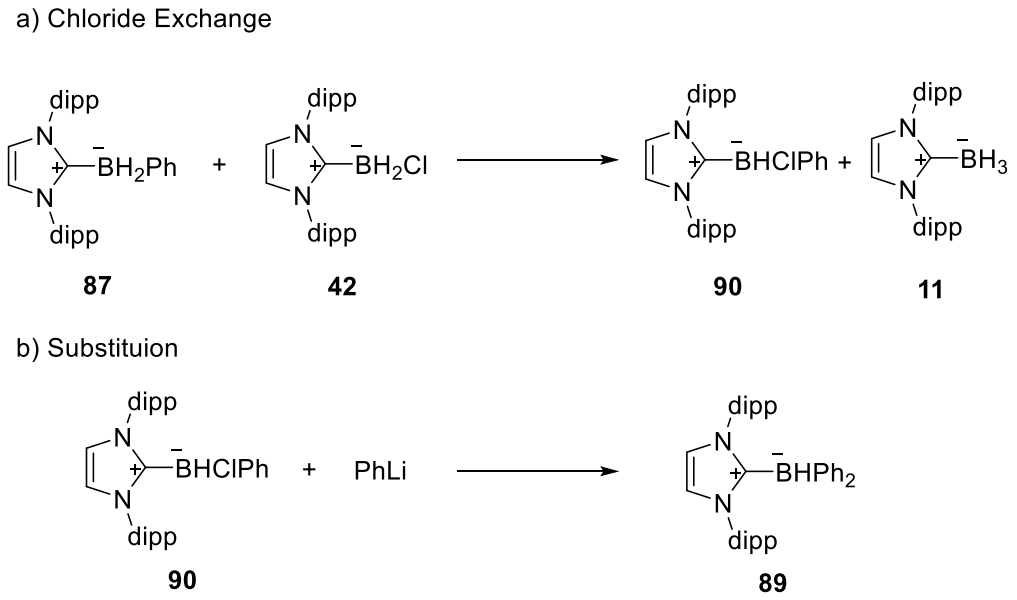


42 **88** **89** **11**

entry	addition mode	phenyllithium	% **88**[c]	% **89**[c]	% **11**[c]	yield **88**[d]
1	Normal[a]	5 equiv	51	22	27	N.D[c]
2	Reverse[b]	5 equiv	> 90	< 10	< 10	73%
3	Reverse[b]	4 equiv	76	13	11	50%[e]
4	Reverse[b]	2.5 equiv	60	19	21	N.D[a]

[a] phenyllithium is added to NHC-boryl chloride [b]NHC-boryl chloride is added to phenyllithium [c]product ratio determined by ^{11}B NMR spectroscopy [d]after flash chromatography [e]purified by recrystallization

The side products are presumably formed by a disproportionation reaction between the NHC-boryl chloride **42** and the B-phenyl NHC-borane **88** to give the chlorinated product **90** along with dipp-Imd-BH_3 **11** as shown in Scheme 27a. Reaction of chlorinated product **90** with phenyllithium yields diphenylated NHC-borane **89** (Scheme 27b).



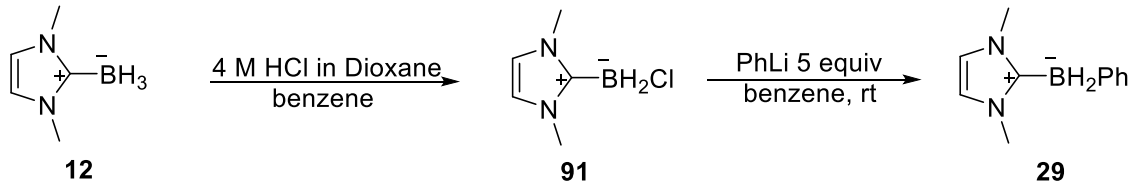
Scheme 27. Proposed side reactions during substitution with phenyllithium

This chloride exchange could possibly be minimized if the mode of addition is reversed. To test this notion, NHC-boryl chloride **42** was added to a phenyllithium solution (reverse addition mode) over a period of 45 min by syringe pump (Table 3, entry 2). The crude ^{11}B NMR spectrum showed the amount of diphenylated product **89** and dipp-Imd-BH_3 **11** had reduced significantly (<10 %). After workup and purification by flash chromatography, the B-phenyl NHC-borane **88** was obtained in 73 % yield. Reducing the amount of phenyllithium in the reaction led to increase in the amount of diphenylated product **89** and reduced dipp-Imd-BH_3 **11**. When 4 equiv of phenyllithium were used (entry 3), diphenylated product **88** and dipp-Imd-BH_3 **11** were observed in 13% and 11% respectively along with 76% of the B-phenyl NHC-borane **87**. Column chromatography was attempted to purify **88**, but only a mixture of diphenylated product **89** and **88** was isolated. Recrystallization was then used to purify B-phenyl NHC-borane **88** lowering the isolated yield to 50%. Reducing the equivalents of phenyllithium to 2.5 (entry 4) increased amount of diphenylated product **89** and dipp-Imd-BH_3 **11** (19% and 21% respectively). Based on the poor results, flash chromatography was not attempted.

We tried the reaction of phenyllithium with NHC-boryl chloride **91** which was prepared by addition of 1 equiv of HCl (4 M in dioxane) to diMe-Imd-BH_3 **12** in benzene. Some of the NHC-boryl chloride **91** precipitated out due to its low solubility. To repeat the reaction conditions established for the NHC-boryl chloride **38**, benzene was evaporated and ether was added. NHC-boryl chloride **91** was not soluble in ether so the reaction was stopped.

We then attempted to use benzene as the solvent for the substitution reaction. The NHC-boryl chloride **91** was prepared by addition of 1 equiv HCl (4 M in dioxane) to NHC-borane **12** (50 mg, 0.5 mmol) in benzene (5 mL). After the reaction, fresh benzene (15 mL) was added but all the precipitate again did not dissolve. The supernatant liquid was added to a solution of phenyllithium (5 equiv) by syringe pump. After workup and flash chromatography B-phenyl NHC-borane **29** was obtained in 28 % yield (Table 3, entry 1). The yield of the reaction is lower compared to the reaction for making B-phenyl product **88**. Increasing the amount of benzene (total 35 mL to dissolve all the precipitate) (Table 3, entry 2) gave a slight increase in yield of **29** to 34%. Benzotrifluoride (total 20 mL) was tried as the solvent for the reaction (Table 3, entry 3) and the solution was still cloudy. After workup and flash chromatography, B-phenyl NHC-borane **29** was obtained in 47 % yield. Repeating the reaction several times using benzotrifluoride as the solvent gave yields ranging from 30-47%. These results suggest that the reaction is not reproducible mainly due to low solubility of the NHC-boryl chloride **91**.

Table 3. Substitution by using phenyllithium on boryl chloride **91**



12 **91** **29**

entry	solvent (quantity)	yield **29**[a]
1	benzene (20 mL)	28%
2	benzene (35 mL)	34%
3	benzotrifluoride (20 mL)[b]	47%

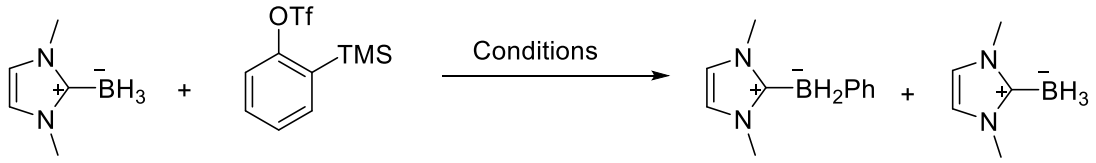
[a] after flash chromatography [b] benzotrifluoride is $C_6H_5CF_3$.

Based on the above results, organolithium reagents can be used synthesize substituted NHC-boranes when a bulky NHC such as dipp-Imd is used. But, the reaction is not very efficient when more atom economical NHC di-Me is employed. So, we decided use Taniguchi's new hydroboration procedure for making the substituted NHC-boranes.[21]

1.3.4 Hydroboration of benzyne precursors with NHC-boranes

As shown in Section 1.1.3 (Scheme 8), Taniguchi and Curran had shown that NHC-boranes are competent reagents for hydroboration of benzynes. In a repeat of one of their experiments (Scheme 28), diMe-NHC-BH_3 **12** (2 equiv), cesium fluoride (2 equiv) and α-silyltriflate **28** (1 equiv) were added to acetonitrile at room temperature under argon. After 6 h, the solvent was evaporated and flash chromatography gave the B-phenyl NHC-borane **29** in 58% yield. About 10% of the diphenylated product **92** was formed (seen in crude ^{11}B NMR spectrum, the product was not isolated) along with unreacted diMe-NHC-BH_3 **12**. When TBAF (2 equiv) was used as the fluoride source with THF as the solvent (Scheme 16, condition B), the reaction was complete in 2 h and

the B-phenyl NHC-borane **29** was isolated in 55% yield. Use of KF as the fluoride source with crown ether gave the B-phenyl NHC-borane **29** (Scheme 16, condition C) in 60% yield.

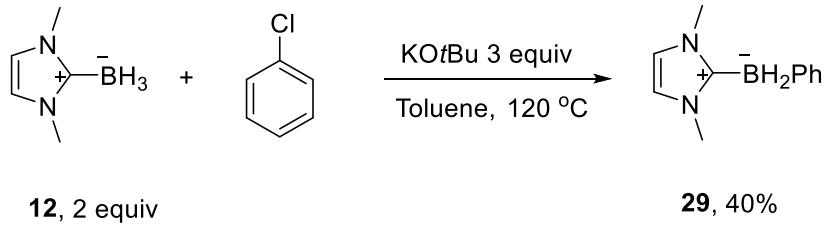


12, 2 equiv **28** **29** **12**

Conditions	Fluoride Source	Solvent	time	yield **29**	recovered **12**
A	CsF	MeCN	6 h	58%	50%
B	TBAF	THF	2 h	55%	53%
C	KF, crown ether	THF	6 h	60%	47%

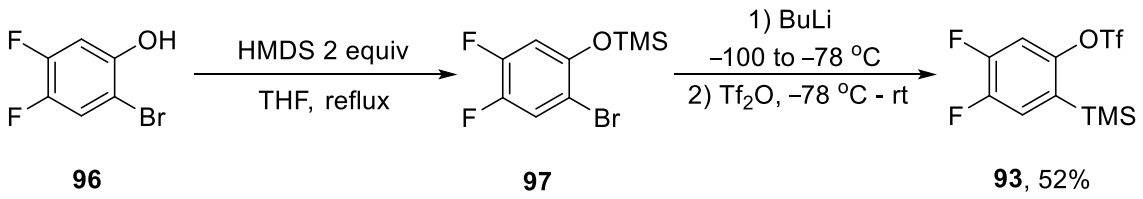
Scheme 28. Reaction of diMe-Imd-BH_3 **12** with benzyne precursor

B-phenyl NHC-borane **29** was also prepared using the procedure established by Dr Takuji Kawamoto which uses chlorobenzene as the benzyne precursor. DiMe-Imd-BH_3 **12** (2 equiv) was added to a solution of chlorobenzene in toluene and 3 equiv of potassium *tert*-butoxide was added as a base (Scheme 29). After 16 h, the solvent was evaporated and the B-phenyl NHC-borane **29** was isolated in 40% yield after flash chromatography. Despite the lower yield obtained compared to the reaction with α-silyltriflate **28**, the chlorobenzene method was chosen for large scale preparation of the B-phenyl NHC-borane **29**. This is due of the lower cost and easy of availability of the reagents.

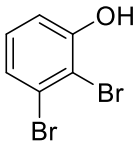
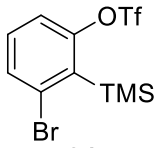
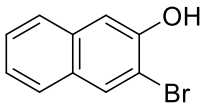
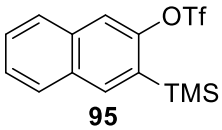


Scheme 29. Synthesis of B-phenyl NHC-borane **29** using chlorobenzene

We next made some other substituted NHC-boranes with different substituents on the aryl ring. Here, Taniguchi's method was used because the benzyne precursors **93-95** The benzyne precursors **93**, **94** and **95** were prepared by Castedo.[51] Following the procedure by Castedo, 4,5-difluoro-2-bromophenol **96** was reacted with 2 equiv of HMDS in refluxing THF for 2 h. The solvent was then evaporated and a crude ^{1}H spectrum showed complete conversion to the phenoxy trimethylsilane **97**. This product was used immediately in the next reaction. BuLi was added dropwise to the solution of **97** in THF at –100 °C over 30 min. Warming the reaction mixture to –78 °C leads to exchange of TMS group with the Li, which followed by the addition of triflic anhydride gives the benzyne precursor **93** in 52 % overall yield after flash chromatography (Scheme 30). Benzyne precursors **94** and **95** were prepared using the same procedure from the corresponding bromophenol and naphthol in 29% and 86% yields respectively (Scheme 30).

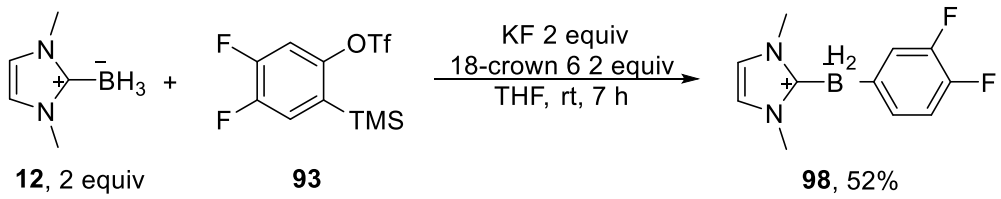


96 **97** **93**, 52%

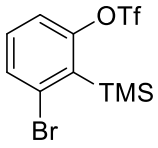
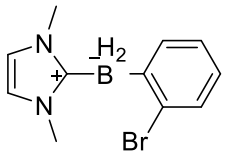
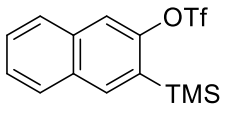
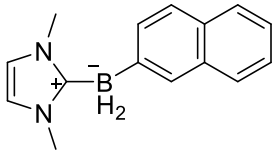
entry	phenol	benzyne precursor	yield
1)		 **94**	29%
2)		 **95**	86%

Scheme 30. Synthesis of benzyne precursors **93-95**

The prepared benzyne precursors **93-95** were subjected to hydroboration conditions to make the substituted NHC-boranes. For example (Scheme 31), KF and crown ether (2 equiv) were added to a flame dried flask followed by THF. DiMe-Imd-BH_3 **12** (2 equiv) was then added followed by the addition of the benzyne precursor **93**. After 6 h, the solvent was evaporated and the difluorophenyl-substituted NHC-borane **98** was isolated in 52% yield. For the 2-bromophenyl-substituted NHC-borane **99**, the same procedure was followed but the reaction time was increased to 16 h (to increase conversion). The product **99** was isolated in 42% yield after flash chromatography. The 2-naphthyl substituted NHC-borane **100** was isolated in 55% yield.

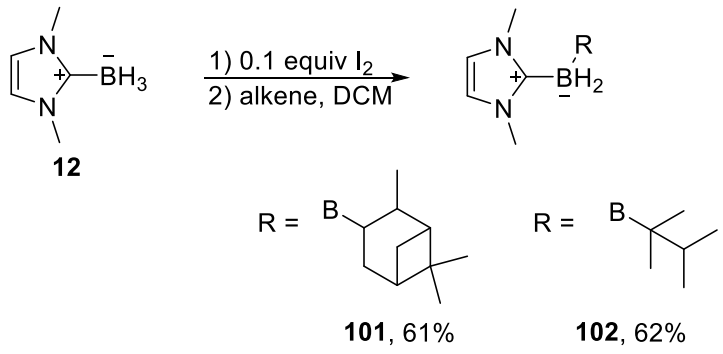


12, 2 equiv **93** **98**, 52%

entry	benzyne precursor	NHC-borane	yield
1)	 **94**	 **99**	42%
2)	 **95**	 **100**	55%

Scheme 31. Substituted NHC-boranes prepared by hydroboration of benzynes

Along with aryl-substituted NHC-boranes, we also wanted to prepare alkyl-substituted NHC-boranes and convert them to other Suzuki coupling precursors. The pinyl and thexyl substituted NHC-boranes **101** and **102** were prepared by iodine catalyzed hydroboration of α-pinene and 2,3-dimethyl-2-butene (Scheme 32).[17]



12 **101**, 61% **102**, 62%

Scheme 32. Synthesis of alkyl-substituted NHC-boranes vis hydroboration

1.4 CONVERSION OF NHC-BORANES TO SUZUKI SUBSTRATES

The Suzuki cross-coupling is one of the most common reactions boranes and many boron substrates have been developed.[52] However, there is currently no link between NHC-borane chemistry and Suzuki chemistry. So, we studied the transformation of substituted NHC-boranes to other Suzuki cross-coupling precursors. We focused on the most common precursors, boronic acids, pinacol boronate esters, MIDA boronates and trifluoroborates (Figure 7).

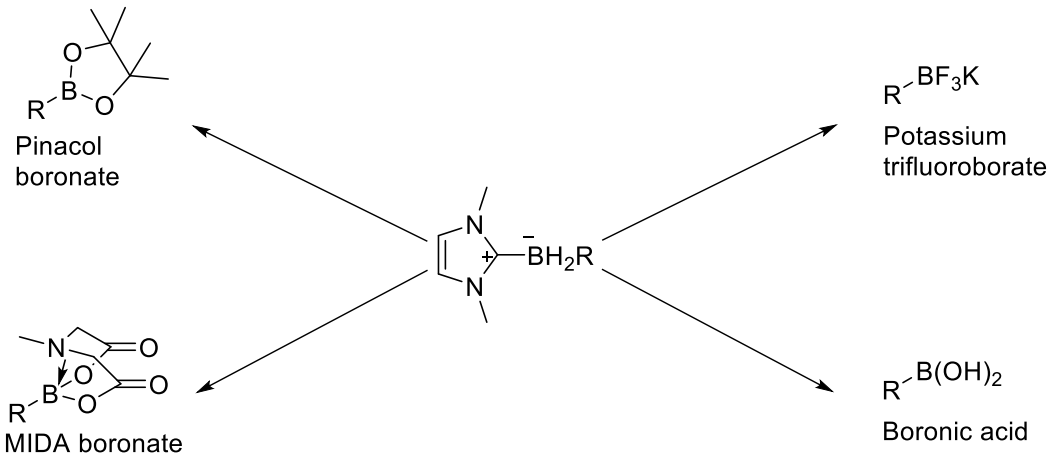
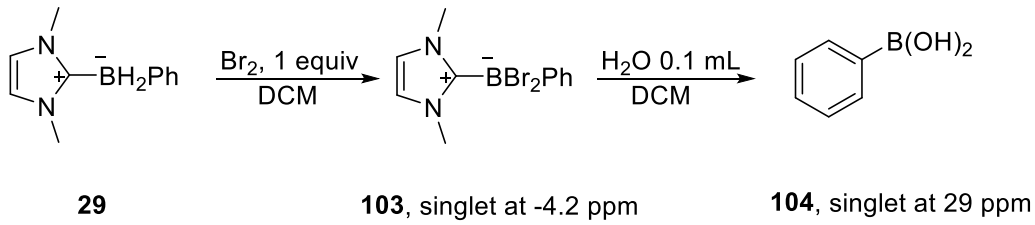


Figure 7. Projected conversion of NHC-boranes to other Suzuki coupling precursors

1.4.1 Conversion of NHC-boranes to other pinacol boronates

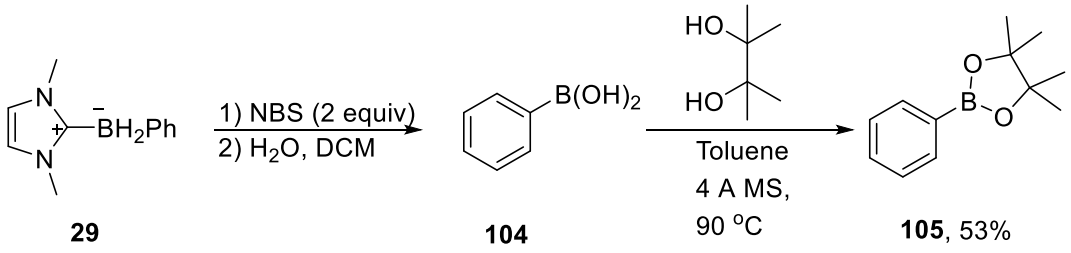
To begin, we attempted conversion of the substituted NHC-boranes to boronic acids (Scheme 33). Br_2 (1 equiv) was added to a solution of phenyl NHC-borane **29** in DCM. The ^{11}B NMR spectrum showed the presence of the dibrominated product **103** (singlet at 4 ppm). Water (0.1 mL) were added to the reaction mixture. After 30 min, the ^{11}B NMR spectrum showed formation of phenylboronic acid **104** (singlet at 29 ppm). This shows clean formation of boronic acids from

substituted NHC-boranes. The in-situ prepared boronic acids would be converted to other cross-coupling precursors.



Scheme 33. Boronic acid formation from NHC-boranes

We decided to use *N*-bromosuccinimide (NBS) in place of Br_2 to generate the boronic acid in-situ because it is easier to handle than bromine. NBS (2 equiv) was added to solution of B-phenyl NHC-borane **29** in DCM (1 M). After 15 min, 0.1 mL of water was added to the reaction mixture and it was stirred for 30 min to form the phenylboronic acid **104** (Scheme 33). The solvent was then evaporated and toluene was added. Pinacol (1.2 equiv) was added along with molecular sieves and the reaction mixture was heated to 100 ^{o}C for 6 h. An ^{11}B NMR spectrum showed the presence of phenyl pinacol boronate **105** (singlet at 32 ppm). The solvent was evaporated and the product pinacol boronate ester **105** was isolated in 53 % yield after flash chromatography (Scheme 34).

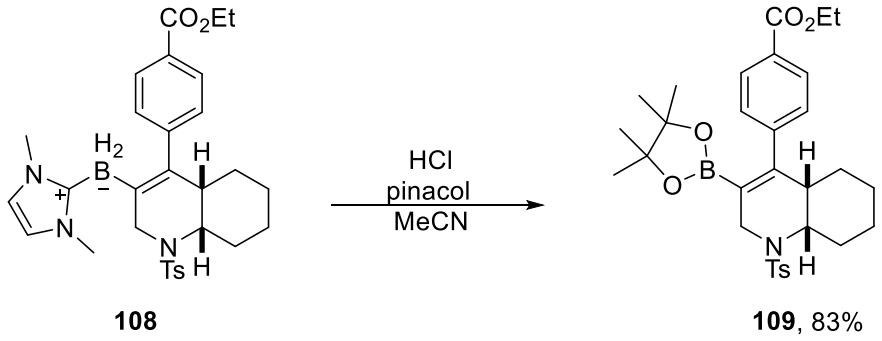


Scheme 34. One-pot synthesis of pinacol boronate from NHC-borane

The difluorophenyl-substituted NHC-borane **98** and naphthyl-substituted NHC-borane **100** were subjected to the same reaction conditions as the B-phenyl NHC-borane **29**. The

corresponding pinacol esters **106** and **107** were isolated in 45% and 52% yield, respectively. The results show that conversion of the NHC-boranes to the corresponding pinacol esters can be achieved in moderate yield.

During the course of this work, the Wang group published their work on radical borylation/cyclizations of 1,6 enynes to give boron handled heterocycles. They converted the substituted NHC-borane **108** to the corresponding pinacol ester **109** by reaction with HCl and 2 equiv of pinacol in acetonitrile (Scheme 35).[25] This is a one-pot procedure and uses less expensive reagents.



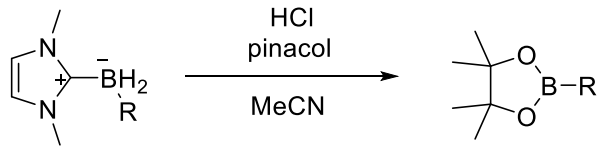
108 **109**, 83%

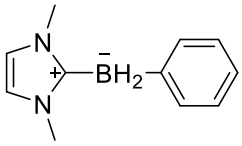
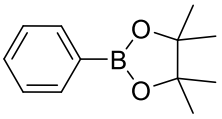
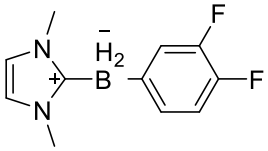
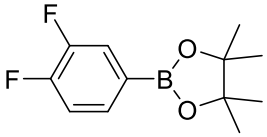
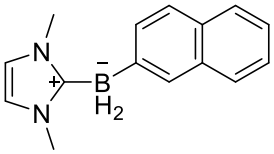
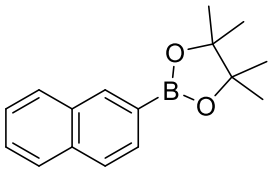
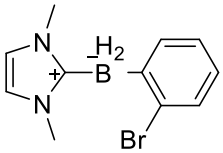
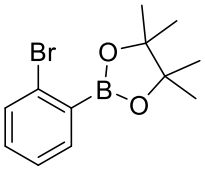
Scheme 35. Synthesis of pinacol boronates from NHC-boranes reported by Wang

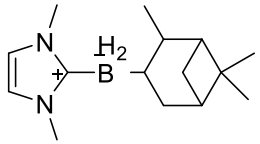
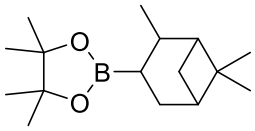
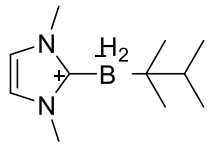
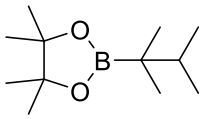
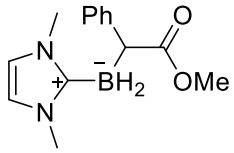
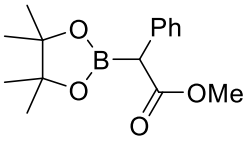
We used Wang's procedure to convert the alkyl- and aryl-substituted NHC-boranes to the corresponding pinacol boronate esters. Table 4 shows the yields obtained. In a typical example, an HCl solution (2 M in H_2O) was added to the solution of B-phenyl NHC-borane **29** and 2 equiv of pinacol in acetonitrile (Table 4, entry 1). After 3 h, ^{11}B NMR showed the presence of a single peak corresponding to the pinacol boronate ester **105** (singlet at 32 ppm). The solvent was evaporated and the pinacol boronate ester **105** was isolated by flash chromatography in 75 % yield. The difluorophenyl-substituted NHC-borane **98** (entry 2) gave the pinacol boronate ester **106** in 69% yield, while the naphthyl-substituted pinacol boronate ester **107** (entry 3) was isolated in 72% yield. The 2-bromo substituted pinacol boronate ester **110** (entry 4) was isolated in 78% yield.

Alkyl substituted NHC-boranes (entry 5-6) also gave the corresponding pinacol boronate esters in good yields (78% and 81% respectively for the pinene substituted boronate ester **111** and thexyl substituted boronate ester **112**).

Table 4. Synthesis of pinacol boronate esters from NHC-boranes



entry	NHC-borane	product	yield[a]
1	 **29**	 **105**	75%
2	 **98**	 **106**	69%
3	 **100**	 **107**	72%
4	 **99**	 **110**	78%

5	 **101**	 **111**	78%
6	 **102**	 **112**	81%
7	 **27**	 **113**	-

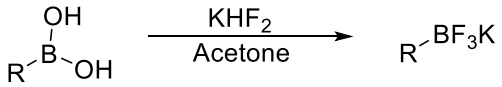
[a]isolated yield after flash chromatography

Next, we tried the reaction for the α-boryl ester **27** (entry 7) which was prepared by the iodine catalyzed insertion reactions of diMe-Imd-BH_3 **12** with diazocarbonyl compound **26** (Section 1.1.3, Scheme 7).[20] Boronic acids or pinacol boronate esters with a carbonyl group on the α-carbon have not been isolated before.

The α-boryl ester **27** was treated with HCl and pinacol in acetonitrile. The ^{11}B NMR spectrum after 1.5 h showed the presence of two products, pinacol boronate ester (singlet at 22.4 ppm), protodeborylated product (singlet at 20 ppm) along with a small amount of starting α-boryl ester **27** (triplet at −24 ppm, about 10% by integration). Flash chromatography was attempted to purify the reaction mixture but the product **113** was not isolated suggesting that the pinacol boronate ester **113** is completely protodeborylated on silica gel.

1.4.2 Conversion of NHC-boranes to trifluoroborates

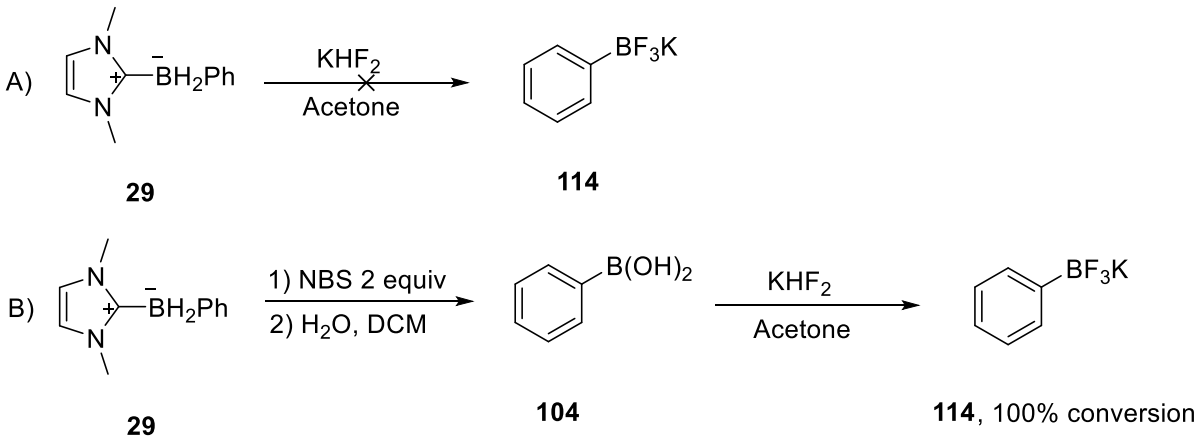
After establishing the conversion of NHC-boranes to pinacol boronates, the next step was to attempt their conversion to trifluoroborates. Synthesis of trifluoroborates from boronic acids by treatment with KHF_2 is straightforward (Scheme 36).[53]



Scheme 36. Synthesis of trifluoroborate salts from boronic acids

Initially we tried a direct reaction between B-phenyl NHC-borane **29** and KHF_2 in acetone (Scheme 37a). A ^{11}B NMR spectrum after 6 h of stirring at rt showed no conversion to phenyl trifluoroborate **114** (quartet at 3.4 ppm). Apparently, KHF_2 is not a strong enough acid to react with B-phenyl NHC-borane **29**.

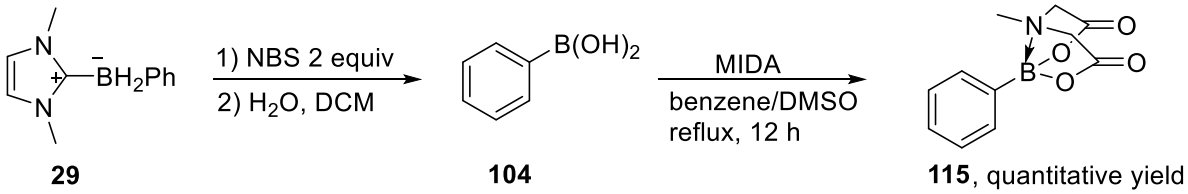
Based on this result, we decided to follow the procedure described in Scheme 33 to first make the phenylboronic acid and then add KHF_2 (Scheme 37b). NBS was added to B-phenyl NHC-borane **29** in DCM followed by addition of water. After checking the crude ^{11}B NMR spectrum for complete formation of $PhB(OH)_2$ **104**, the DCM was evaporated and KHF_2 (3 equiv) and acetone were added. After 15 min, the ^{11}B NMR spectrum showed complete conversion to the target product **114** (quartet at 3.4 ppm) (Scheme 37b). The solvent was evaporated and recrystallization was attempted. The ^{1}H NMR spectrum of the recrystallized product still showed the presence of the imidazolium salt peaks. Due to this result, we did not pursue conversion of other substituted NHC-boranes to trifluoroborates. But in principle, the conversion is a viable reaction to prepare the salts if they need to be used in-situ.

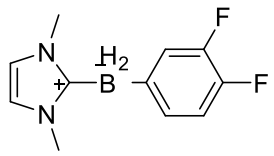
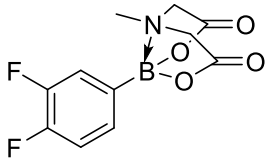
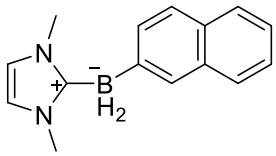
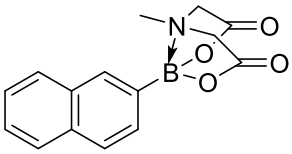


Scheme 37. Synthesis of phenyl trifluoroborate salt **114** from B-phenyl NHC-borane **29**

1.4.3 Conversion of NHC-boranes to MIDA boronates

The conversion of NHC-boranes to the corresponding MIDA boronates was performed by Mr. Owen Budawich in our group. B-phenyl NHC-borane **29** was reacted with NBS (2 equiv) in DCM followed by addition of water to give phenylboronic acid **104** (Scheme 38). The solvent was then evaporated and a 1:1 mixture of benzene/DMSO was added as the solvent along with N-methyliminodiacetic acid (MIDA). The reaction mixture was refluxed for 12 h. After verifying that the reaction was complete by ^{11}B NMR spectroscopy, water was added and the MIDA boronate **115** was extracted using DCM 3 times. The solvent was evaporated and MIDA boronate was obtained in quantitative yield after flash chromatography (Scheme 38). The difluorophenyl substituted NHC-borane **98** was subjected to the same reaction conditions and the MIDA boronate **116** was isolated in 89% yield after flash chromatography. MIDA boronate **117** was prepared from naphthylsubstituted NHC-borane **100** and isolated in 50% yield after flash chromatography.



entry	NHC-borane	MIDA boronate	yield
1)	 **98**	 **116**	89%
2)	 **100**	 **117**	50%

Scheme 38. Synthesis of MIDA boronates from aryl-substituted NHC-boranes

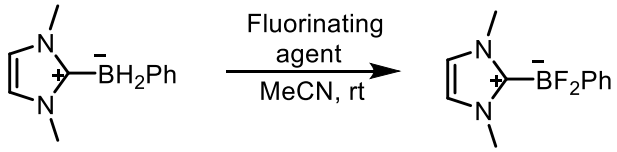
To summarize, we have prepared alkyl- and aryl-substituted dipp-Imd bornaes by addition of organolithium reagents to the NHC-boryl chloride. This method was not very efficient when diMe-Imd was the NHC employed, so the corresponding aryl-substituted diMe-Imd boranes were prepared by aryne hydroboration established by Taniguchi and Curran. The prepared alkyl- and aryl-substituted NHC-boranes were converted to the boronic acids by addition with brominating agents (Br_2 or NBS) followed by water or by reaction with HCl. The in-situ prepared boronic acids were converted to pinacol boronate esters, trifluoroborate salts and MIDA boronates. The next step was to develop efficient fluorination of the NHC-boranes to fluorinated NHC-boranes which can potentially be used directly in the Suzuki cross-coupling reaction.

1.5 FLUORINATION OF SUBSTITUTED NHC-BORANES

1.5.1 Reaction of Selecfluor with aryl-substituted NHC-boranes

With the goal to use difluoro NHC-boranes for Suzuki coupling, we first studied the fluorination of arylsubstituted NHC-boranes. B-phenyl NHC-borane **29** was treated with 2 equiv of Selectfluor **59** in acetonitrile (0.01 M with respect to the borane) at rt and the reaction progress was followed by ^{11}B NMR spectroscopy (Scheme 39). After 1 h, a ^{11}B NMR spectrum of an aliquot showed two new peaks, a triplet at 4.6 ppm (70% by integration) and a triplet at −24 ppm for the B-phenyl NHC-borane **29** (30%). After 2 h, a ^{11}B NMR spectrum showed only one major peak (triplet at 4.6 ppm, $J_{B\text{-}F}$ = 62.4 Hz). The solvent was then evaporated and the residue was purified by flash chromatography to give the B-phenyl NHC-difluoroborane **51** in 83 % yield (Scheme 38). The NMR spectra (^{1}H, ^{13}C, ^{11}B and ^{19}F) of the isolated product were identical to those of the B-phenyl NHC-difluoroborane **51** reported by Lacôte.[29]

The reaction was then attempted under similar conditions with NFSI **61** as the fluorination source. A ^{11}B NMR spectrum after 1 h showed the triplet at 4.6 ppm as the only major peak. Workup followed by flash chromatography gave the B-phenyl NHC-difluoroborane **29** in 77% yield (Scheme 39). While these two reactions gave comparable results, we decided to go ahead with Selectfluor since it is cheaper than NFSI.



29 **51**

fluorinating agent	time	yield
Selectfluor **59**	2 h	83%
NFSI **61**	1 h	77%

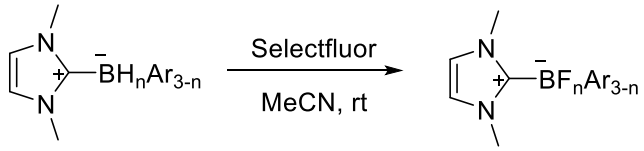
Scheme 39. Fluorination of B-phenyl NHC-borane **29** with Selectfluor and NFSI

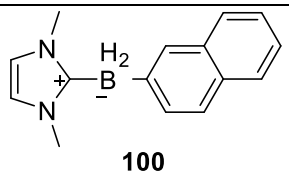
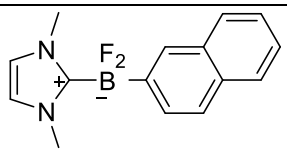
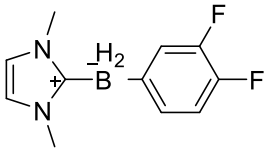
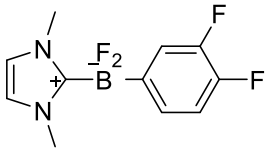
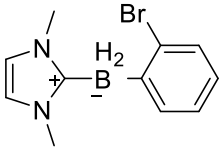
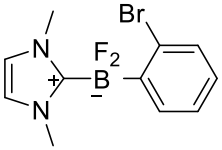
The scope of the fluorination reaction was studied with different aryl substituted NHC-boranes and other NHC's. Table 5 (entries 1-4) shows the structures and yields of the different fluorinated aryl substituted NHC-boranes synthesized. All reactions were run on 0.5 mmol scale at 0.01 M concentration with respect to the NHC-borane. The reactions were monitored by periodic ^{11}B NMR spectroscopic analysis. The ^{11}B NMR spectrum of the reaction mixture with naphthyl-substituted NHC-borane **100** (entry 1) naphthyl-substituted NHC-difluorborane **118** (broad peak at 4.75 ppm) as the major product after 1 h. Workup and flash chromatography gave **118** in 68% yield (entry 1).

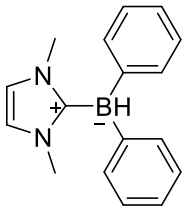
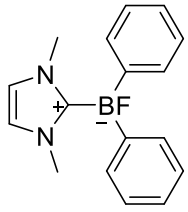
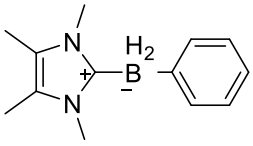
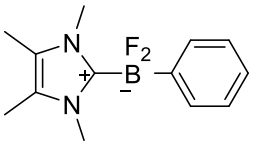
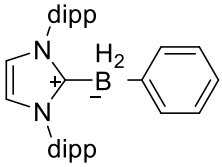
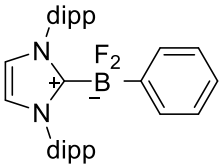
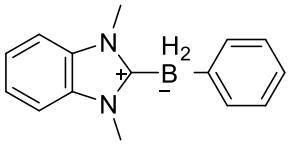
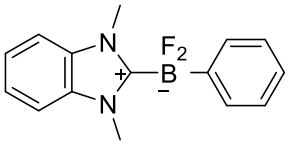
For a NHC-borane with electron withdrawing substituents (fluorine) on the phenyl group **98** (entry 2), the ^{11}B NMR spectrum after 45 min showed diMe-Imd-BF_3 **47** (quartet at 0.2 ppm) as the major product. The minor product was *B,B*-difluoroborane **119** (triplet at 3.96 ppm). An NMR scale reaction was conducted next to ascertain if shorter reaction time gave increased amount of *B,B*-difluoroborane **119**. After 15 mins, the ^{11}B NMR spectrum showed *B,B*-difluoroborane **119** as the major product (>90% by integration, triplet at 3.96 ppm) and diMe-Imd-BF_3 was the minor product (<10% by integration, quartet at 0.6 ppm). Increasing the reaction time to 30 min showed conversion of the B,B-difluroborane **119** to diMe-Imd-BF_3 **47**. The reaction was repeated on a

preparative scale and worked up after 15 min. Flash chromatography gave target *B,B*-difluoro borane **119** in 81 % yield. NHC-borane **99** (entry 3) has a bromine substituent, so theme same reaction conditions as that of NHC-borane **98** were employed. After 15 min, the ^{11}B NMR spectrum showed the major product to be *B,B*-difluoroborane **120** (triplet at 3.8 ppm) and diMe-Imd-BF_3 (quartet at 0.6 ppm) as the minor product. Workup and flash chromatography lead to isolation of *B,B*-difluoroborane **120** in 83% yield. Diphenylated NHC-borane **92** was reacted with 1 equiv of Selectfluor to give B-fluoroborane **121** in 69% yield.

Table 5. Fluorination of aryl-substituted NHC-boranes[a]



entry	starting material	product	time	yield[b]
1	 **100**	 **118**	1 h	68%
2	 **98**	 **119**	15 min	81%
3	 **99**	 **120**	15 min	83%

4[c]	 **92**	 **121**	1.5 h	69%
5	 **122**	 **123**	1 h	87%
6	 **88**	 **124**	3 h	72%
7	 **125**	 **126**	1.5 h	90%

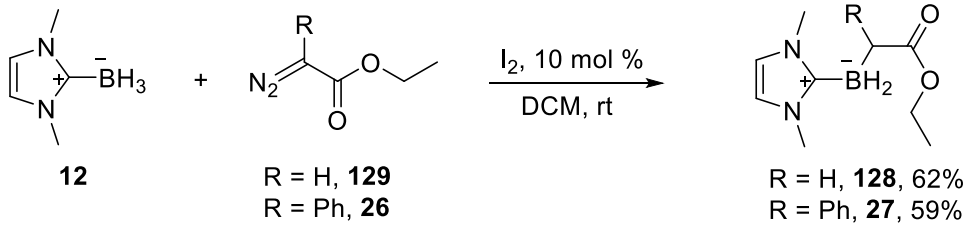
[a]Reaction conditions: Aryl NHC-borane (0.5 mmol), Selectfluor (1 mmol), MeCN (5 ml). [b]Yield obtained after flash chromatography [c]0.5 mmol (1 equiv) Selectfluor used.

Next, we attempted fluorination of B-phenyl boranes with different NHC partners (Table 5, entries 5-8). With tetramethyl NHC-phenyl borane **91** (entry 5), the ^{11}B NMR spectrum showed complete conversion to **122** (triplet at 4.6 ppm) in 1 h and **122** was obtained in 87% yield after flash chromatography. For the dipp-NHC phenylborane **88** (entry 6), an ^{11}B NMR spectrum after 1 h of the reaction showed presence of the starting material (broad triplet at −24 ppm) along with product **124** (broad triplet at 3.9 ppm). After 3 h, starting material (broad triplet at −24 ppm) was absent and the major product was **124** (broad triplet at 3.9 ppm) in the ^{11}B NMR spectrum. The

solvent was evaporated and flash chromatography gave **124** in 72% yield. The reaction takes longer time presumably due to the increased steric hindrance of the dipp group. Fluorination of benzimidazole NHC-phenyl borane **125** (entry 7) was completed in 1.5 h and *B,B*-difluoroborane product **126** was obtained in 90% yield after flash chromatography.

1.5.2 Reaction of Selectfluor with alkyl-substituted NHC-boranes

To further expand the scope, we attempted fluorination of alkyl-substituted NHC-boranes. The alkyl and alkenyl substituted NHC-boranes **101, 102** and **127** were synthesized by iodine-catalyzed hydroboration of corresponding electron rich alkenes and alkynes (Section 1.1.3, Scheme 6).[17] The α-NHC-boryl carbnonyl compunds **27** and **128** were prepared by iodine-catalyzed insertion of diazocarbonyl compunds into B-H bonds of diMe-Imd-BH_3 **12**. Reaction of diazo compound **129** with **12** in the presence of catalytic I_2 gave the insertion product **128** in 62% yield (Scheme 40).[20] With donor acceptor diazo compound **26**, compound **27** was obtained in 59% yield (Scheme 40).



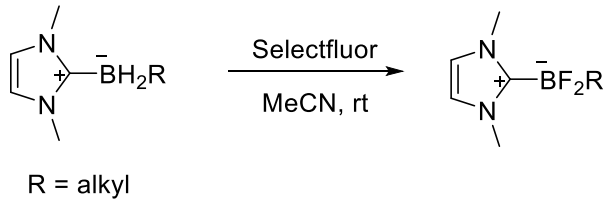
Scheme 40. Synthesis of α-NHC-boryl carbnonyl compunds

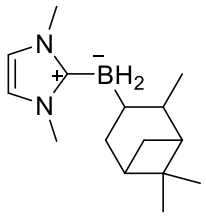
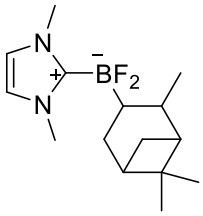
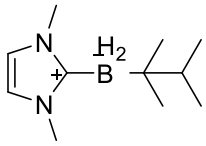
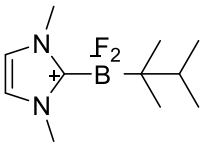
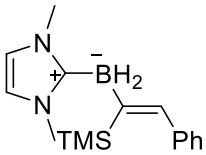
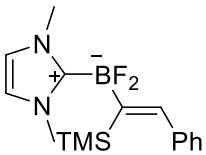
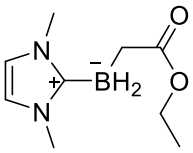
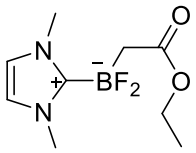
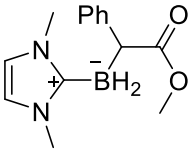
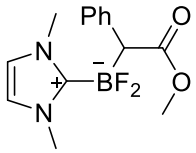
Table 6 shows the structures and yields of the different fluorinated alkyl substituted NHC-boranes synthesized by reactions of these precursors with Selectfluor. In a typical reaction, pinyl-substituted NHC-borane **101** was treated with 2 equiv of Selectfluor **59** at rt in MeCN (0.1 M with respect to NHC-borane) and the reaction progress was followed hourly by ^{11}B NMR spectroscopy. Complete conversion of pinyl-substituted NHC-borane **101** (entry 1) (triplet at −24 ppm) to

difluoro compound **130** (broad singlet at 6.28 ppm) was observed after 2 h. Workup and flash chromatography gave pinyl-substituted NHC-difluoroborane **130** in 65% yield. Thexyl-substituted NHC-borane **102** (entry 2) was converted to the difluoro borane **131** in 1 h and was isolated in 89% yield after flash chromatography.

For the alkenyl substituted NHC-borane **127** (Table 6, entry 3), the ^{11}B NMR spectrum after 1 h showed only diMe-Imd-BF_3 **47** (quartet at 0.24 ppm). Based on the results of fluorination reactions of aryl-substituted NHC-boranes bearing electron withdrawing groups (Table 4, entry 2-3), we attempted the reaction again with shorter reaction times. Initially, a small-scale reaction (0.1 mmol) was run using the same concentration as the preparative scale reaction. After 15 min, the ^{11}B NMR spectrum showed two products, alkenyl-substituted NHC-difluoroborane **132** (broad singlet at 6.42 ppm) and diMe-Imd-BF_3 **47** (quartet at 0.24 ppm) in 1:2 ratio by integration. The reaction was then repeated on a preparative scale reaction (0.5 mmol). To increase the yield of target product **132**, reaction was stopped after 5 min and the solvent immediately evaporated. The ^{11}B NMR spectrum of the aliquot showed complete conversion to a mixture of alkenyl-substituted NHC-difluoroborane **132** (broad triplet at 6.42 ppm) and diMe-Imd-BF_3 **47** (quartet at 0.24 ppm) in a 1:1 ratio. Alkenyl-substituted NHC-difluoroborane **132** was isolated in 26 % yield after flash chromatography (Table 6, entry 3). Despite the short reaction time, the yield is significantly lower than those obtained in alkyl-substituted NHC-boranes.

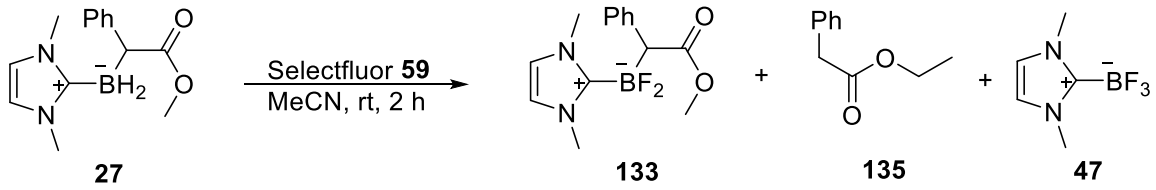
Table 6. Fluorination of alkyl substituted NHC-boranes



entry	NHC-borane	fluorination product	time	yield[a]
1	 **101**	 **130**	2 h	65%
2	 **102**	 **131**	1 h	89%
3	 **127**	 **132**	5 min	26%
4	 **128**	 **133**	5 min	56%
5	 **27**	 **134**	5 min	57%

[a]after flash chromatography

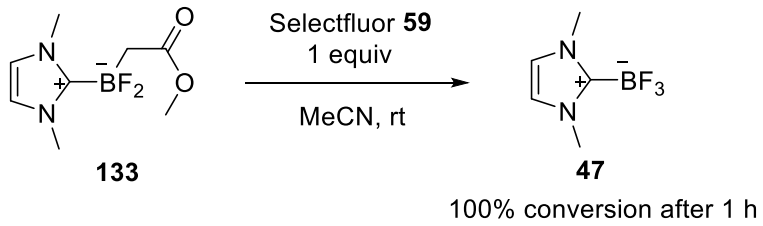
α-Boryl esters **128** and **27** were studied to check whether B-H fluorination would be faster than that of the α-carbon of the ester. An NMR scale reaction of 0.05 mmol of compound **27**, 0.1 mmol of Selectfluor and 0.5 ml of MeCN. After 30 min, the ^{11}B NMR spectrum showed the presence of only diMe-Imd-BF_3 **47**. The acetonitrile was evaporated, $CDCl_3$ was added and a crude ^{1}H NMR spectrum of the crude product was recorded. The only non-boron product was ethyl 2-phenylacetate **135** (Scheme 41). Another NMR scale reaction of compound **128** was conducted with shorter reaction time to see if *B,B*-difluoroborane **133** is observed. After 5 min, two major products were seen in the ^{11}B NMR spectrum, *B,B*-difluoroborane **133** (triplet at 4.5 ppm) and diMe-Imd-BF_3 **47** (quartet at 0.24 ppm) in a 2:1 ratio. A comparable preparative experiment was conducted for borane **128** (Table 6, entry 4). The reaction was stopped after 5 min. Workup followed by flash chromatography gave target *B,B*-difluoroborane **133** in 56% yield. NHC-borane **27** (Table 6, entry 5) was also fluorinated for 5 min to give product **134** in 57% yield after flash chromatography.



27 **133** **135** **47**

Scheme 41. Reaction of α-NHC-boryl carbonyl compound **27** with Selectfluor **59**

Both reactions showed formation of diMe-Imd-BF_3 **47**, which progressively increased with reaction time. To determine whether the trifluoroborane **47** is formed from di-fluorination product **133**, pure **133** was subjected to standard fluorination conditions in a NMR tube. The ^{11}B NMR spectra showed gradual conversion of *B,B*-difluoroborane **133** to diMe-Imd-BF_3 **47** over 1 h (Scheme 42). This result shows **133** is converted to **47**, and explains why short reaction times are required for fluorination reactions of NHC-boryl esters **27** and **128**.



Scheme 42. Reaction of pure fluorination product **133** with Selectfluor

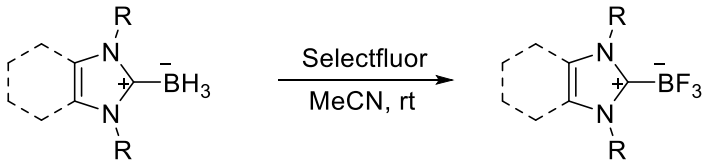
1.6 FLUORINATION OF UNSUBSTITUTED NHC-BORANES

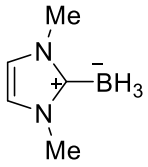
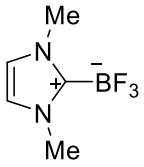
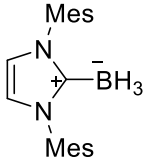
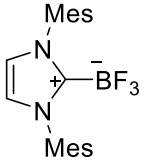
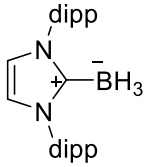
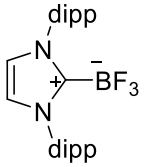
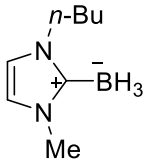
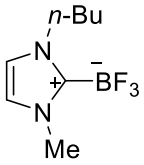
1.6.1 Fluorination of NHC-boranes to give trifluoro-NHC-boranes

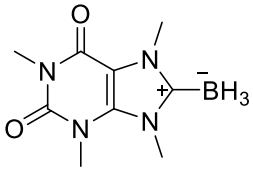
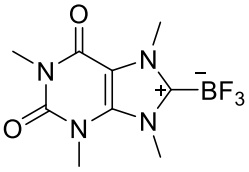
We next studied the fluorination of unsubstituted NHC-boranes with Selectfluor. In a typical example, diMe-Imd-BH_3 **12** was treated with 3 equiv of Selectfluor **59** in acetonitrile at rt (0.01 M) and the reaction progress was followed by ^{11}B NMR spectroscopy. After 3 h, starting material peak was absent and three peaks were seen in the ^{11}B NMR spectrum, a quartet at 0.24 ppm (target product diMe-Imd-BF_3 **47**), singlet at −0.5 ppm (BF_4^- peak) and a new broad peak at −12 ppm. Assuming that the peak at −12 ppm arises from a reaction intermediate, the reaction was checked periodically by ^{11}B NMR spectroscopy for complete disappearance of the broad peak. After 6 h, only two peaks were observed in the ^{11}B NMR spectrum (product quartet at 0.24 ppm and BF_4^- peak). The solvent was evaporated and diMe-Imd-BF_3 **47** was isolated by flash chromatography in 74% yield (Table 7, entry 1). The di-Mes-Imd-BH_3 **136** and dipp-Imd-BH_3 **11** required 12 h for complete conversion, and the trifluoroboranes **137** and **54** in 73% and 76% yield respectively (Table 7, entry 2-3). The MeBu-Imd-borane **138** was converted to the trifluoroborane **139** in 70%

yield in 4 h (Table 7, entry 4). Caffeine-BH_3 **140 (**made by Mr. Tim McFadden) was reacted with Selectfluor for 6 h to give the Caffeine-BF_3 **141** in 65% yield (Table 7, entry 5).

Table 7. Reaction of Selectfluor with unsubstituted NHC-boranes



entry	NHC-borane	fluorinated product	time	yield
1	 **12**	 **47**	6 h	74%
2	 **136**	 **137**	12 h	73%
3	 **11**	 **54**	12 h	76%
4	 **138**	 **139**	4 h	70%

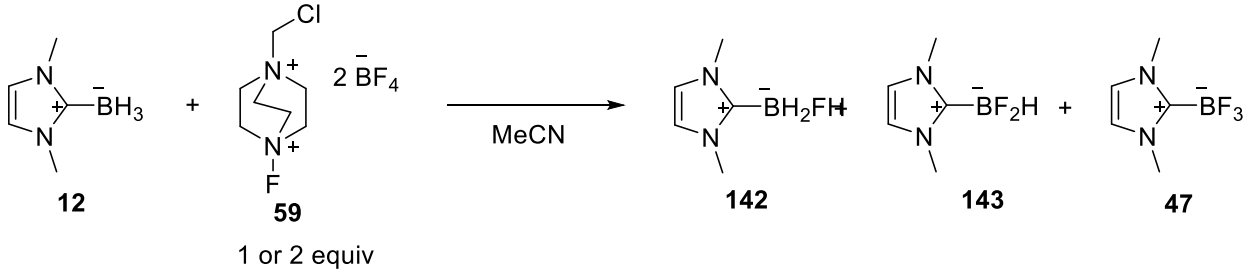
5	 **140**	 **141**	6 h	65%

The above results suggest that fluorination reactions of unsubstituted NHC-boranes are slower than the reaction of the substituted NHC-boranes. Still, the reactions are clean and yields are good. This reaction provides a viable alternative for synthesis of NHC-BF_3 as compared to direct reaction of the NHC carbene and BF_3.

1.6.2 Fluorination of unsubstituted NHC-boranes with limited amounts of Selectfluor

To learn whether selective mono- or di-fluorination of diMe-Imd-BH_3 **12** is possible, we reacted diMe-Imd-BH_3 **12** with 1 and 2 equiv of Selectfluor. Table 8 summarizes the key results of attempted electrophilic fluorination reactions.

Table 8. Fluorination of diMe-Imd-BH_3 **12** with 1 and 2 equiv of Selectfluor **59**



entry	Selectfluor equiv	temp	**142**[a]	**143**[a]	**47**[a]	**12**[a]
1	1	rt	0%	57%	43%	0%
2	1	−78 °C	5%	31%	44%	19%

3	2	rt	0%	19%	81%	0%

[a]ratios determined by crude ^{11}B NMR spectrum analysis

Selectfluor (1 equiv) was added to a solution of diMe-Imd-BH_3 **12** in MeCN (0.01 M at rt) and the reaction was monitored by periodic ^{11}B NMR spectrum analysis. After 10 min, the ^{11}B NMR spectroscopy showed the presence of diMe-Imd-BH_2F **142** (doublet of triplets at −6 ppm), diMe-Imd-BF_2H **143** (doublet of triplets at 2.2 ppm), diMe-Imd-BF_3 **47** (quartet at 0 ppm), diMe-Imd-BH_3 **12** (quartet at at −37 ppm) and a reaction intermediate (broad triplet at −12 ppm, 50 % by integration). Per the ^{11}B NMR spectrum, diMe-Imd-BH_2F **142** intergrates to only 5 %. After 30 min, the ^{11}B NMR spectrum showed two products, diMe-Imd-BF_2H **143** (doublet of triplets at 2.2 ppm), diMe-Imd-BF_3 **47** (quartet at 0 ppm), and the reaction intermediate (broad triplet at −12 ppm). DiMe-Imd-BH_2F **142** is not observed. The reaction was stopped and products were attempted to be isolated by flash chromatography. DiMe-Imd-BF_2H **143** and diMe-Imd-BF_3 **47** were obtained as an inseparable mixture in 35% overall yield. A second flash chromatography did not lead to any separation (Table 8, entry 1). The reaction intermediate (broad peak at −12 ppm) could not be isolated from the column.

A similar reaction was conducted at –78 °C (same concentration as rt reaction). Due to low solubility of Selectfluor in MeCN at –78 °C, this reaction mixture was cloudy. After 2 h, solvent was evaporated and crude ^{11}B NMR spectrum was taken which showed presence of 4 products (Table 8, entry 2), diMe-Imd-BH_2F **142** (5%), diMe-Imd-BF_2H **143** (31%), diMe-Imd-BF_3 **47** (44%) and diMe-Imd-BH_3 **12** (19%). Since the ratio of fluorinated products observed is greater than equivalents of Selectfluor used, some of the fluoride from the counterion (BF_4^-) of Selectfluor is being incorporated during the reaction.

When 2 equiv of Selectfluor was used, the ^{11}B NMR spectrum after 30 mins showed formation of diMe-Imd-BF_3 **47** as the major product and only a small amount of target product diMe-Imd-BF_2H **143** (< 20%) was seen (Table 8, entry 3). These reactions show that the second and third fluorinations are faster than the first and thus it is not practical to selectively synthesize mono- or di-fluorinated NHC-boranes by using limited amounts of Selectfluor.

1.6.3 Fluorination of other ligated boranes with Selectfluor

We also studied electrophilic fluorination of other ligated boranes with Selectfluor. Reactions of pyridine-borane **144**, trimethylamine-borane **145**, DMAP-borane **146** and DBU-borane **147** with 3 equiv of Selectfluor (Figure 8) were conducted and monitored by ^{11}B NMR spectral analysis. Both pyridine-borane **144** and trimethylamine-borane **145** gave complete conversion to corresponding fluorinated products **148** and **149** (^{11}B NMR spectrum of the reactions showed presence of quartets at −1.0 ppm and 0.6 ppm respectively). The peaks were identical to those reported in literature.[54-55] Workup and flash chromatography of these reactions did not lead to isolation of either product. The ^{11}B NMR spectrum of the reaction of DMAP-borane **146** showed presence of two peaks at 0.95 ppm and 0.76 ppm, neither of which matched with the literature value reported for target product **150.**[56] Reaction of DBU-borane **147** was complete in 1 h. The ^{11}B NMR spectrum showed a single peak at 0.5 ppm. This peak did not match with those observed when target product **151** was made by ligation reaction of DBU with BF_3 (reaction performed by Mr. Tim McFadden). These results suggest that the reaction with Selectfluor is not unique to NHC-boranes but cannot be applied to all ligated boranes.

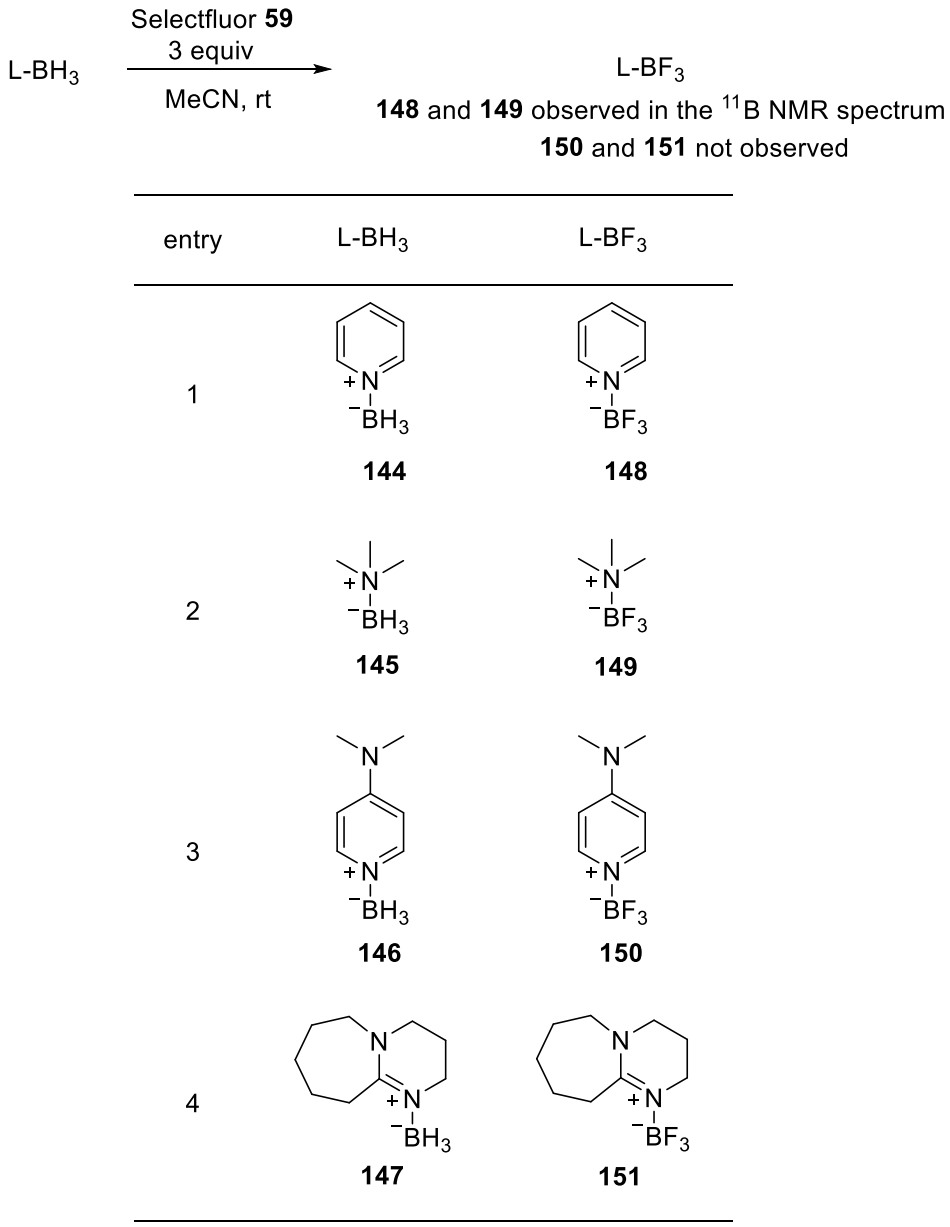


Figure 8. Ligated boranes with which fluorination reaction was attempted

1.7 MECHANISM OF ELECTROPHILIC B-H FLUORINATION

Figure 9 shows a possible ionic mechanism for the fluorination of NHC-boranes with Selectfluor based on the notion that the fluorine of Selectfluor is electrophilic. In step 1, the hydride from the

NHC-borane attacks the N-F bond to give HF and boronium ion **152**. We suggest that the broad peak observed around −12 ppm in the reaction of diMe-Imd-BH_3 **12** with Selectfluor belongs to the boronium ion **152** based on analogous chemical shifts. The HF formed then reacts with diMe-Imd-BH_3 **12** in an acid/base reaction to give diMe-Imd-BH_2F **142** and H_2 (step 2). It is also possible that intermediate **152** can react with HF to give **153** (step 3).

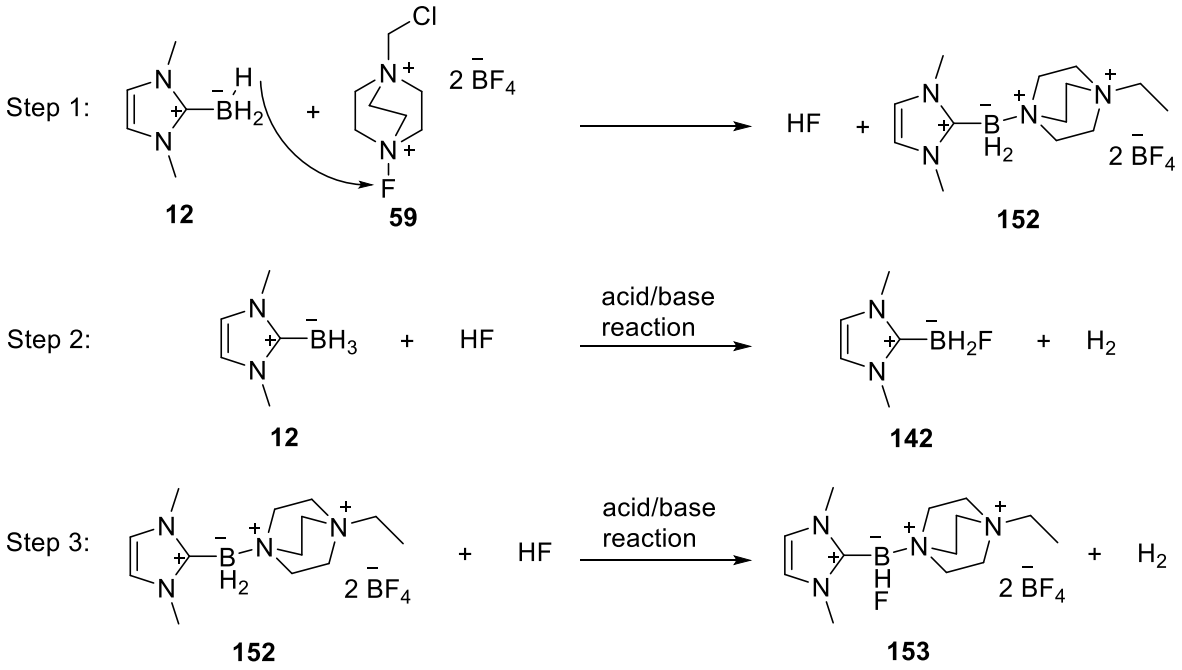
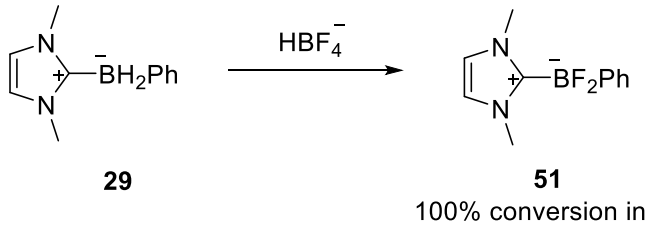


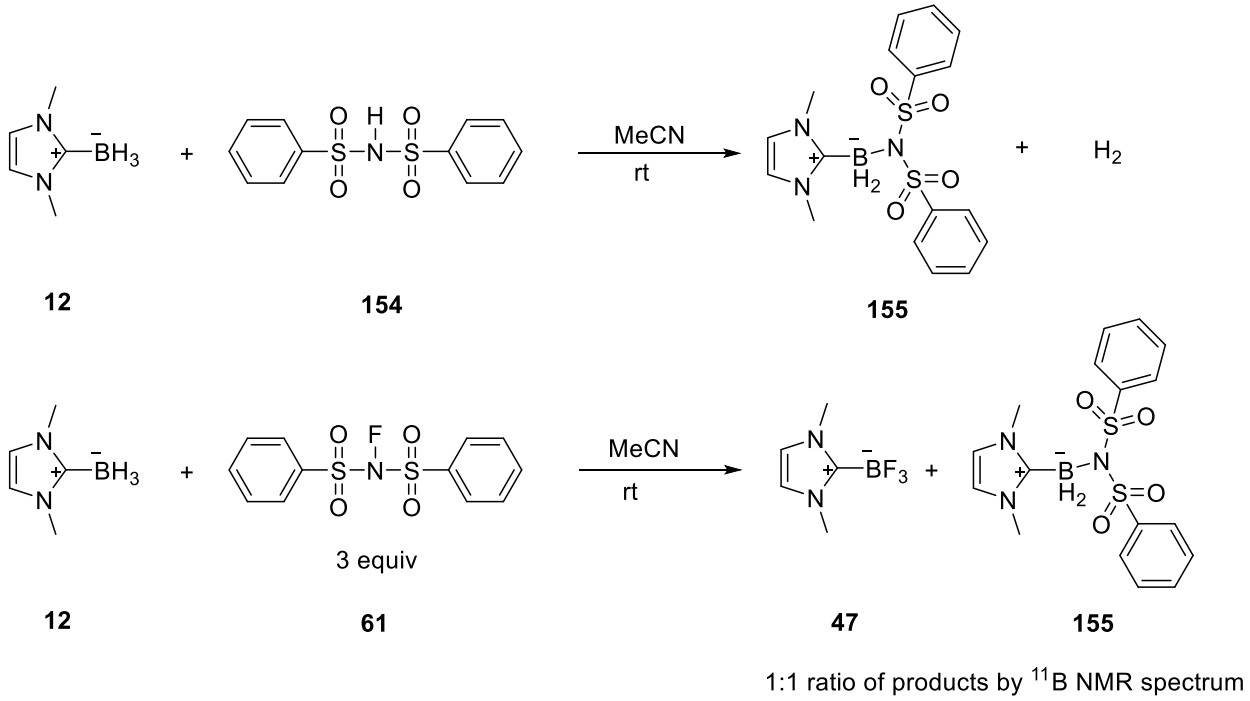
Figure 9. Suggested mechanism for fluorination of NHC-boranes with Selectfluor

To check whether HF is a strong enough acid to react with NHC-boranes, we reacted B-phenyl NHC-borane **29** with 2 equiv of HBF_4^-. After 2 h, ^{11}B NMR spectrum showed complete conversion to the target difluoroborane **51** (Scheme 43).



Scheme 43. Reaction of B-phenyl NHC-borane **29** with HBF_4^-

We then decided to react diMe-Imd-BH_3 **12** with NFSI **61** because the boronium ion formed in the reaction can be formed separately by reaction of diMe-Imd-BH_3 **12** with dibenzenesulfonimide **154**. DiMe-Imd-BH_3 **12** was reacted with dibenzenesulfonimide **154** in a NMR tube in MeCN (Scheme 44). Bubbling was observed when the reagents were mixed suggesting the release of H_2 gas. An ^{11}B NMR spectrum after 15 min showed the presence of boryl sulfonimide **155** (broad triplet at −18 ppm). Next, diMe-Imd-BH_3 **12** was reacted with 3 equiv of NFSI **61** at rt in MeCN (0.1 M). The ^{11}B NMR spectrum after 30 min showed the presence of a broad triplet at −18 ppm (Scheme 43). This suggests that a boronium ion **155** is an intermediate in fluorination of diMe-Imd-BH_3 **12** with NFSI **61**. By extension, boronium ion **152** is a likely intermediate in the reaction of diMe-Imd-BH_3 with Selectfluor **59**.



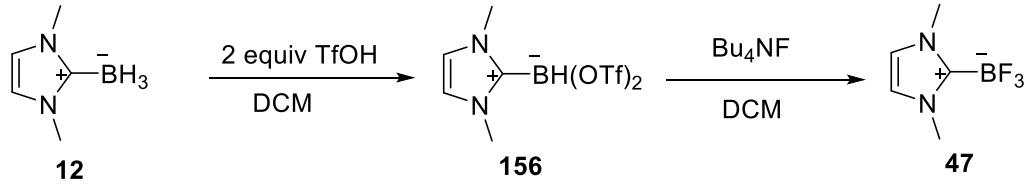
Scheme 44. Reaction of NHC-borane **12** with NFSI **78** and dibenzenesulfonamide **154**

1.8 SYNTHESIS AND REACTIONS OF DI-ME-IMD-DIFLUOROBORANE

1.8.1 Synthesis of diMe-Imd-BF_2H using nucleophilic fluorine sources

As discussed in section 1.6.2, the selective synthesis of NHC-difluoroboranes using electrophilic fluorine sources such as Selectfluor is not practical. Efficient synthesis of diMe-Imd-BF_2H **143** is potentially useful because substituted NHC-difluoroboranes prepared in Section 1.5 by hydroboration reactions. So we decided to use nucleophilic fluorine sources to prepare the target diMe-Imd-BF_2H **143**. Dr. Andrey Solovyev had shown earlier that the dipp NHC mono- and di-fluroborane could be synthesized by reaction of tetrabutylammonium fluoride with the dipp NHC mono or di-triflate (Section 1.2.3, Scheme 15).[27]

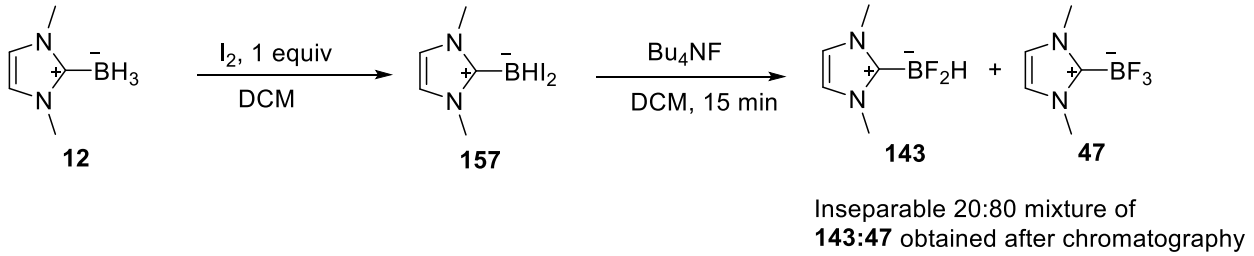
Analogously, the diMe-Imd-$BH(OTf)_2$ **156** was prepared by reaction of 2 equiv of triflic acid with diMe-Imd-BH_3 **12** (Scheme 45). The ^{11}B NMR spectrum was taken to check the formation of the ditriflate **156** (broad singlet at −6 ppm). Tetrabutylammonium fluoride was added and the reaction mixture was stirred at rt for 1 h. The ^{11}B NMR spectrum of an aliquot was recorded to check completion of the reaction and it showed the presence of diMe-Imd-BF_3 **47** (quartet at 0.2 ppm) as the only product.



Scheme 45. Attempted synthesis of NHC-difluoroborane from NHC-ditriflate

The reaction was then attempted using the diMe-Imd-BHI_2 **157** as the electrophilic substrate. The diiodide was prepared by reaction of 1 equiv of I_2 with diMe-Imd-BH_3 **12** in DCM (0.2 M) (Scheme 46). After stirring the mixture for 30 min to allow for complete conversion, TBAF

solution (1 M in THF) was added to the reaction mixture (Scheme 46). After 15 min, a ^{11}B NMR spectrum showed the presence of two products, diMe-Imd-BF_2H **143** (doublet of triplets at 2.2 ppm) and diMe-Imd-BF_3 **47** (quartet at 0.2 ppm). An aliquot was removed to check if the ratio of the diMe-Imd-BF_2H **143** to the diMe-Imd-BF_3 **47** changed over time. Then water was added to the main reaction mixture and the product was extracted 3 times with DCM. The solvent was then evaporated and the mixture was chromatographed giving an 80/20 mixture of the diMe-Imd-BF_3 **47** to diMe-Imd-BF_2H **143**. After 2 h, ^{11}B NMR spectrum of the removed aliquot showed the presence of only diMe-Imd-BF_3 **47**. This suggests that a shorter reaction time is beneficial to selectively preparing diMe-Imd-BF_2H **143**.

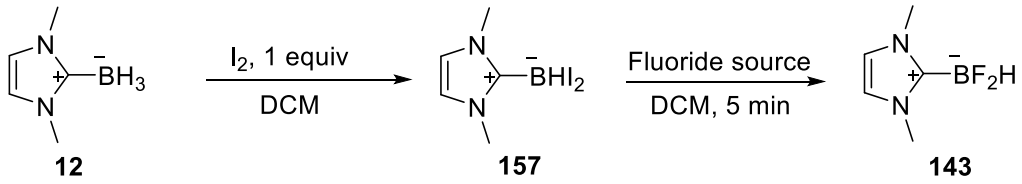


Scheme 46. Di-Me-Imd-BF_2H **143** synthesis from diMe-Imd-BHI_2 **156** and TBAF

Based on the above results, we decided quench the fluorination of diMe-Imd-BHI_2 **157** and after 5 min. TBAF (2 equiv) was added to a solution of in-situ prepared diMe-Imd-BHI_2 **157** (Scheme 47). After 5 min, saturated $NaHCO_3$ solution was added and the product was extracted with DCM. A ^{11}B NMR spectrum of the crude mixture after extraction showed the presence of diMe-Imd-BF_2H **143** as the major product (~90% by integration) and small amounts of diMe-Imd-BF_3 **47** and diMe-Imd-BH_3 **12** (~5% by integration each). The target product diMe-Imd-BF_2H **143** was isolated in 29% yield after flash chromatography (Scheme 47).

The reaction using TBAF as the nucleophilic fluorine source is very fast and needs to be quenched immediately. We used TBAT as the source of nucleophilic fluorine since it is a milder fluorinating reagent. DiMe-Imd-BF_2H **143** was isolated in 35% yield after flash chromatography

(Scheme 47). The yields of the both the reactions were similar, so TBAF was used in future reactions due to its lower cost and better atom economy. Scale up of the reaction of diMe-Imd-BHI_2 **157** with TBAF from 2 mmol to 10 mmol gave the same amounts of diMe-Imd-BF_2H **143**. The reaction was repeated on small scale multiple times to get around 400 mg of diMe-Imd-BF_2H **143**. We also tried to use NMe_4F as the source of nucleophilic fluorine but ^{11}B NMR spectrum showed no conversion to diMe-Imd-BF_2H **143** (reaction mixture was cloudy and the tetramethylammonium fluoride did not dissolve in DCM) (Scheme 47).



12 **157** **143**

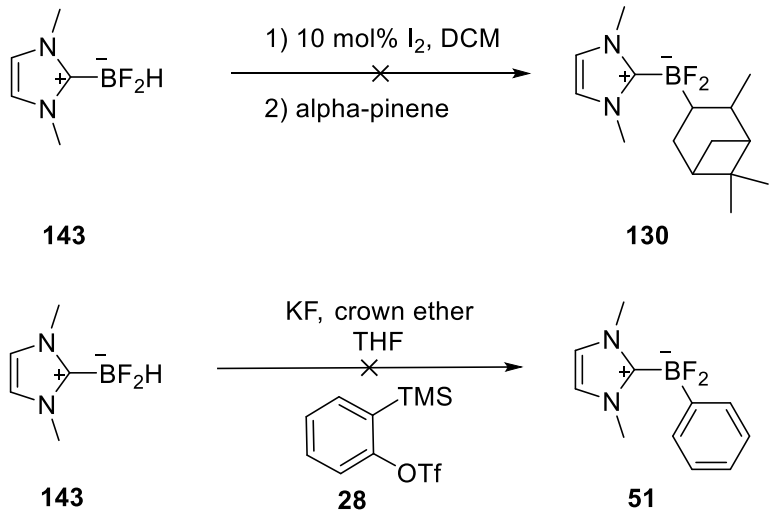
fluoride source	yield **143**
TBAF	29%
TBAT	35%
NMe_4F	N.D.

Scheme 47. Synthesis of diMe-Imd-BF_2H **143** by using different fluorine sources

1.8.2 Reactions of diMe-Imd-BF_2H 143

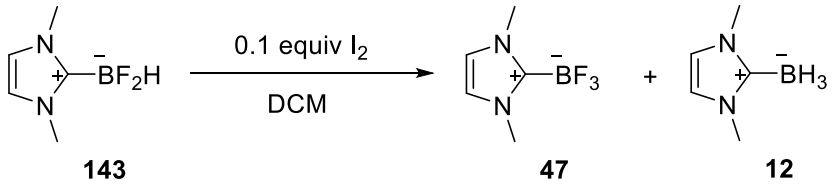
With the diMe-Imd-BF_2H **143** in hand, we checked whether we could use it directly in hydroboration reactions to give the substituted NHC-difluoroboranes directly. I_2 (0.1 equiv) was added to a solution of diMe-Imd-BF_2H **143** in DCM (1 M) followed by addition of α-pinene (Scheme 48). A ^{11}B NMR spectrum after 30 min showed the presence of two products, diMe-Imd-BF_3 **47** (quartet at 0.2 ppm) and diMe-Imd-BH_3 **12** (quartet at −36 ppm). No change was observed

in the ^{11}B NMR spectrum taken after 6 h. We also attempted the hydroboration of benzyne precursor **28** (Scheme 48). DiMe-Imd-BF_2H **143** (2 equiv) was added to a solution of KF and 18-crown-6 (2 equiv each) in THF followed by addition of the α-silyltriflate **28** (1 equiv). The ^{11}B NMR spectrum after 6 h showed no conversion to B-phenyl NHC-difluoroborane **51** (triplet at 4.5 ppm).



Scheme 48. Hydroboration reactions attempted with NHC-BF_2H **143**

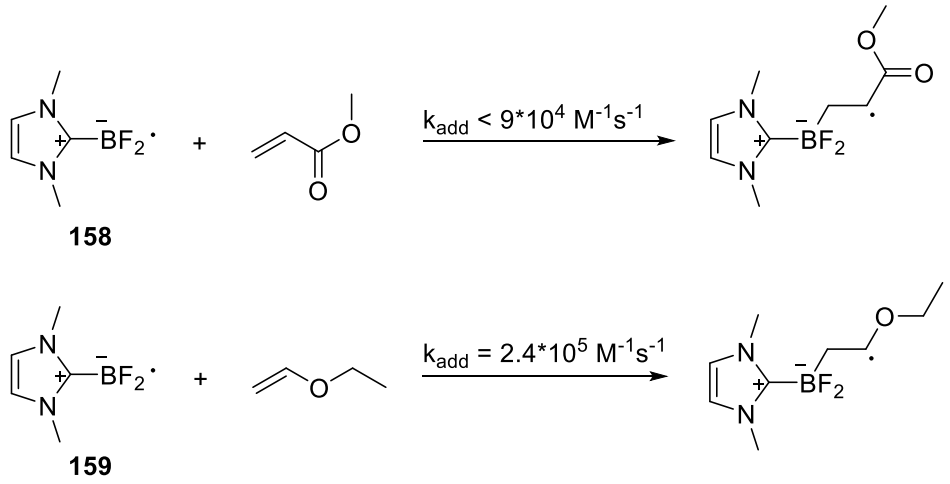
A control reaction was setup to see if addition of catalytic amounts of I_2 results in disproportionation of the diMe-Imd-BF_2H **143**. I_2 (0.1 equiv) was added to a solution of diMe-Imd-BF_2H **143** in DCM in an NMR tube (Scheme 49). After 10 min, ^{11}B NMR spectrum of the reaction mixture showed the presence of two products, diMe-Imd-BF_3 **47** (quartet at 0.2 ppm) and diMe-Imd-BH_3 **12** (quartet at −36 ppm). This result shows that the diMe-Imd-BF_2H **143** is not stable in the presence of iodine. The NMR spectra for diMe-Imd-BF_2H **143** in $CDCl_3$ shows disproportionation to diMe-Imd-BF_3 **47** and diMe-Imd-BH_3 **12**.



Scheme 49. Reaction of diMe-Imd-BF_2H **142** with catalytic I_2

Dr. Emanuel Lacôte, Dr. Jacques Lalevée and co-workers attempted generation and reactivity of diMe-Imd-$BF_2^{\cdot}$ **158** by hydrogen atom abstraction. First, they studied the hydrogen abstraction of diMe-Imd-BF_2H **143** by *t*$BuO^{\cdot}$ using EPR spectroscopy. The rate of H-abstraction was calculated to be 0.5×10^8 $M^{-1}s^{-1}$. Compared to 2.6×10^8 $M^{-1}s^{-1}$ for the diMe-Imd-BH_3 **12**.[57-58] Based on the EPR data, the bond dissociation energy (BDE) for the B-H bond in diMe-Imd-BF_2H **143** was calculated to be 80.79 kcal/mol. This value is lower than the BDE observed for the B-H bond in diMe-Imd-BH_3 **12** (81.93 kcal/mol).

Lalevée also observed that diMe-Imd-$BF_2^{\cdot}$ radical **158** reacts with oxygen to give the boryl-peroxyl radical. This reaction is not observed with diMe-Imd-$BH_2^{\cdot}$ radical **158**. The rate constant for addition of difluoro boryl radical **158** onto an electron poor alkene methylacrylate was calculated to be $< 9\times10^4$ $M^{-1}s^{-1}$ (Scheme 50). Compare to 3.8×10^7 $M^{-1}s^{-1}$ for boryl radical **159**.[58] Conversely, the rate constant for addition of the boryl radical **158** onto the electron rich alkene ethyl vinyl ether was calculated to be 2.4×10^5 $M^{-1}s^{-1}$(Scheme 49). Compare to $< 1\times10^5$ $M^{-1}s^{-1}$ for the boryl radical **159**. Based on these results, the diMe-Imd-$BF_2^{\cdot}$ radical **158** is electrophilic in nature while the diMe-Imd-$BH_2^{\cdot}$ radical **159** is nucleophilic in nature.



Scheme 50. Reactivity of boryl radicals **160** with alkenes

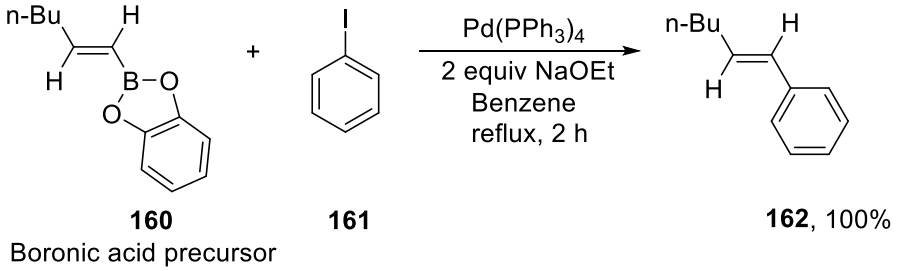
1.9 CONCLUSIONS

At this point, we have established the conversion of substituted NHC-boranes to other Suzuki coupling precursors like boronic acids, pinacol boronates and MIDA boronates. Fluorination of substituted NHC-boranes using Selectfluor to give bench stable substituted *B,B*-difluoro NHC-boranes has been established. The next stage of this study is the direct use of the halogenated NHC-boranes in Suzuki cross-coupling and other C-C bond formation reactions.

2.0 SUZUKI CROSS-COUPLING WITH HALOGENATED NHC-BORANES

2.1 SUZUKI COUPLING REACTION

The Suzuki-Miyaura reaction is the cross-coupling of a boronic acid (or a boronic acid precursor) with an aryl, alkyl or vinyl halide catalyzed by a palladium (0) complex.[52] The reaction was discovered in 1979 by Akira Suzuki when he reacted the boronate ester **160** with aryl iodide **161** in the presence of palladium catalyst and base to give compound **162** in quantitative yield (Scheme 51).[59] Suzuki shared the 2010 Nobel Prize in Chemistry for discovery and development of this reaction, which has been one of the most important modern synthetic transformations. The Suzuki reaction is popular due to mild reaction conditions and commercial availability of the boron reagents. The non-toxicity, easy handling and by-product removal of the of the diverse boranes have made them especially useful in large scale reactions.



Scheme 51. Example of the first Suzuki coupling reaction in 1979

According to Smith, the mechanism of the Suzuki reaction[60] (Figure 10) starts with oxidative addition of the aryl halide **161** to the Pd(0) complex to give Pd(II) intermediate **163** (step i). Exchange of the anion attached to the palladium for the anion of the base (metathesis) forms **164** (step ii). This is followed by transmetalation with boronate species **165** to give palladium species **166** (step iii). Reductive elimination gives the final product **167** and regenerates the Pd(0)

catalyst (step iv). Many mechanistic studies have been conducted to identify the role of the base in the reaction. Depending on the type of boron reagent used, the base is needed to form a boronate **168** (boronate pathway) which is the transmetalating species or to form an oxopalladium species **169** (Figure 11).[61-62]

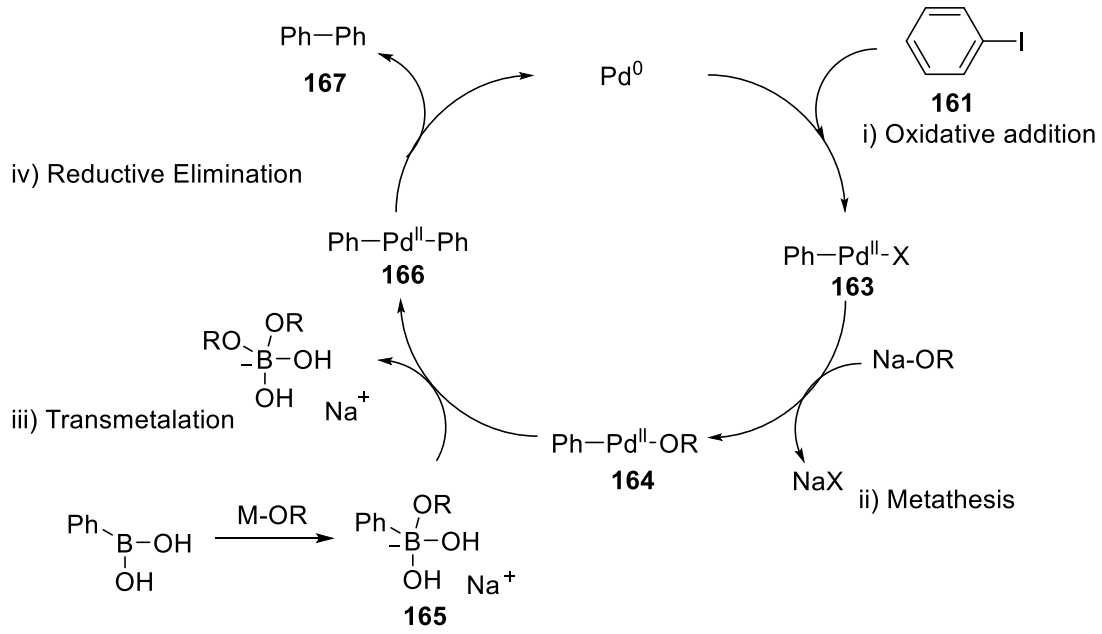


Figure 10. Mechanism of the Suzuki cross-coupling reaction

Mechanistic studies conducted into transmetalation of boronic acids assumed formation of boronate species due to low barrier for the reaction in basic medium. However, recent studies into the mechanism of Suzuki coupling with boronic acids show that the oxo-palladium pathway is kinetically favored to the boronate pathway(Figure 11).[62] It has been observed that in majority of Suzuki reactions developed, use of inorganic bases creates an aqueous biphase.[63] The quaternary boronate is generally sequestered in the aqueous phase while the remaining boronic acid remains in the organic phase and takes part in the transmetalation step.

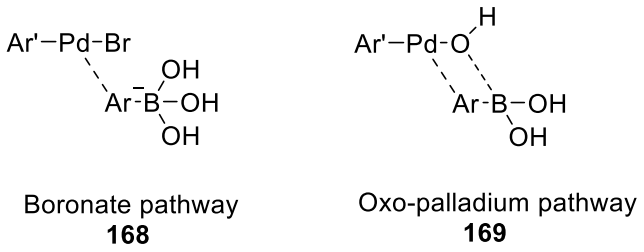
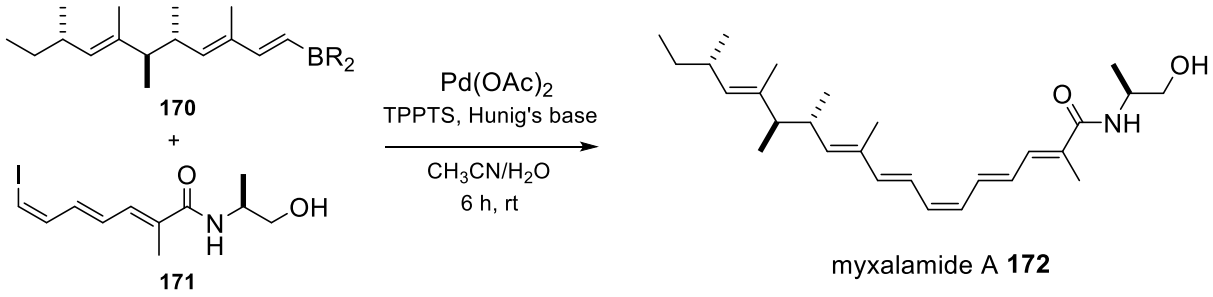


Figure 11. Two possible pathways for trasnmetalation in Suzuki coupling

The Suzuki reaction accounts for about 40 % of the carbon-carbon bond forming reactions used in drug discovery and has often been used in natural product syntheses.[64] In an example for natural product synthesis, Heathcock and co-workers employed the Suzuki cross-coupling to couple an (E)-vinylborane **170** and a (Z)-iodotriene **171** as the final step in a convergent synthesis of myxalamide A **172** (Scheme 52).[65]



Scheme 52. Synthesis of myxalamide A using Suzuki reaction

Various advances have been made in the Suzuki reaction with respect to the expansion of substrate scope[66], reaction at lower temperatures[67] and development of different catalyst/ligand systems resulting in lower catalyst loadings.[68] In addition, much work has been focused on the nature of the boron reagent partner and how different boron reagents interact differently with the catalyst and additives (base) used in the reaction.

2.2 BORON REAGENTS USED IN SUZUKI COUPLING

Figure 12 summarizes the common boron reagents used in Suzuki coupling reaction today. Use of boronic acids and pinacol esters had been established in the 1980's.[69] The last decade has seen development of various alternative boron reagents (with improved stability) for the Suzuki coupling with potassium trifluoroborate salts, MIDA boronates and diaminonaphthyl boronamides being widely used.[69]

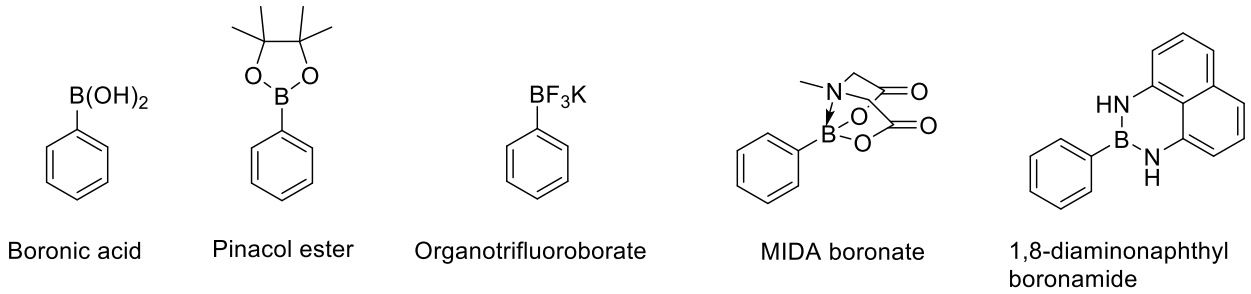
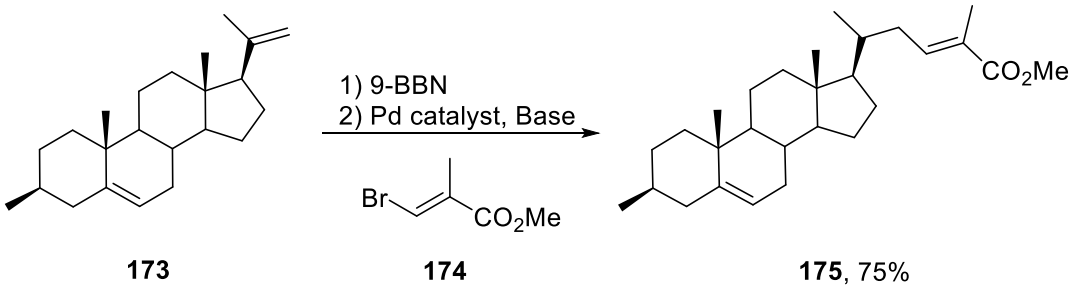


Figure 12. Common boron reagents used in Suzuki coupling

2.2.1 Organoboranes

Boron reagents used in seminal publications of the Suzuki coupling were alkenylboranes and catechol boronic esters[59], which were made by simple hydroboration of alkenes or alkynes.[70] For example, Suzuki reacted steroid **173** with 9-BBN followed by addition of the alkenyl bromide **174** and palladium catalyst to give the cross-coupled product **175** in 75 % yield (Scheme 53).[71]



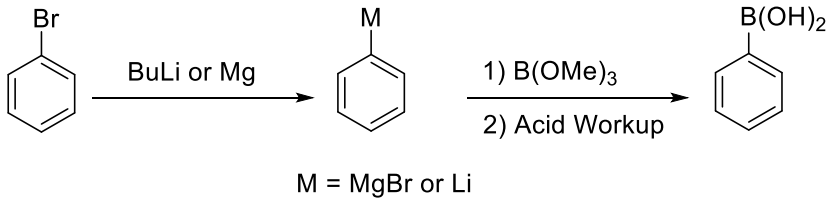
173 **174** **175**, 75%

Scheme 53. Use of organoborane in Suzuki-Miyuara coupling reaction

Secondary alkyl groups were preferred on the boron reagent to aide distinction of the R group undergoing transmetalation. The commonly used secondary groups were 9-borabicyclo[3.3.1]nonane (9-BBN), disiamylborane and dicyclohexyl boranes.[71] The main disadvantage for the use of these substrates in reactions is their propensity for oxidation unless extreme care is taken to avoid oxygen in the system. Because of this, such boranes cannot be isolated and must be prepared in-situ.

2.2.2 Boronic Acids

Boronic acids were first used for the Suzuki reaction in 1981 and are still the most widely used reagents in coupling reactions.[72] Boronic acids are commonly made by reaction of an organometallic reagent with trimethylborate followed by hydrolysis (Scheme 54).[73] Other methods include palladium catalyzed borylation using tetrahydroxydiboron.



Scheme 54. General synthesis of boronic acids from organometallic reagents

While boronic acids are popular substrates due to their ease of preparation and high atom economy, they have certain disadvantages. There is often an equilibrium between the boronic acid and its trimeric anhydride (boroxine) (Figure 13) which can make measuring the exact amounts of the reagent difficult (the boronic acid is often used in excess).

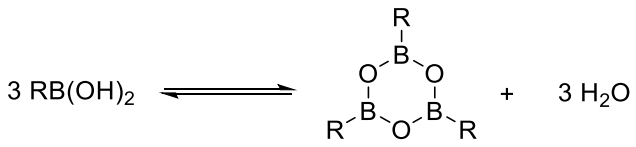


Figure 13. Equilibrium between boronic acid and boroxine

Protodeboration (Figure 14) is the major side reaction in Suzuki coupling[74] of boronic acids along with palladium catalyzed homocoupling of the boronic acids. In addition to this, boronic acids cannot be chromatographed.

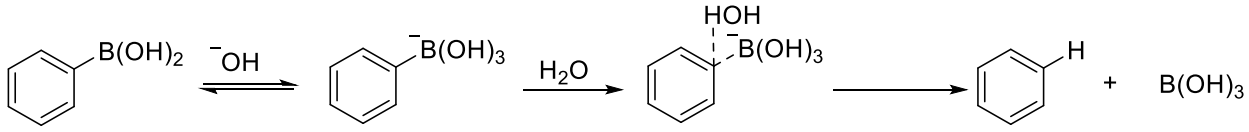


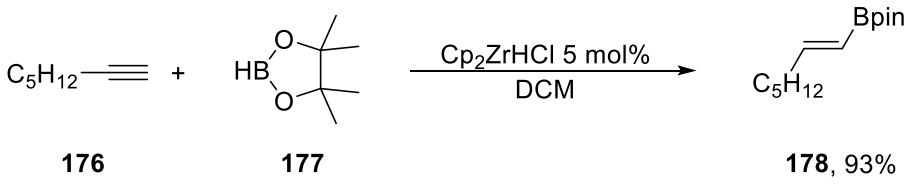
Figure 14. Mechanism of protodeboration of boronic acids

2.2.3 Boronic Esters

The most commonly used boronic esters in Suzuki coupling are pinacol, neopentyl and catechol esters. The σ donating ability of carbon results in better conjugation of the lone pair of the oxygens with the electron deficient boron center. This results in boronic esters being less reactive than the corresponding boronic acids. Hindered esters are generally stable towards chromatography or can be distilled easily if they are liquids. Due to the lack of hydrogen bond donors, they are monomeric in nature unlike the corresponding boronic acids.

Pinacol boronate esters were the reagents of choice for Miyuara boration reaction.[75] The Miyuara boration involves reaction of bis-pinacol esters with aryl or vinyl halides to give corresponding aryl and vinyl boronates.

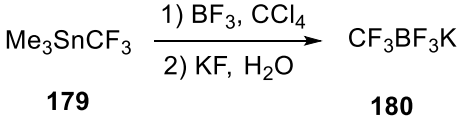
Synthesis of the boronic acid esters is generally accomplished by transition metal catalyzed hydroboration of alkynes.[76] Various rhodium and zirconium based catalysts have been developed to achieve highly stereoselective transformations.[77] For example, Srebnik reacted 1-octyne **176** with pinacol borane **177** in the presence of zirconium catalyst to give the trans alkene **178** in 93% isolated yield (Scheme 55).[77] Chiral ligands on the rhodium center have enabled enantioselective variations of this transformation.[78] Non-precious metal catalysts such as copper were also developed with electron rich ligands. The general stereochemistry for the reaction with alkynes give trans alkenes. Miyuara has developed a rhodium catalyzed system to selectively get cis alkenes via trans-hydroboration.[79]



Scheme 55. Zirconium catalyzed synthesis of alkenyl boronic esters

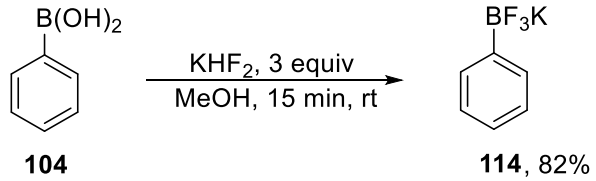
2.2.4 Organotrifluoroborate Salts

Organotrifluoroborate salts were discovered by Chambers in 1960.[80] He reacted Me_3SnCF_3 **179** with BF_3 gas. After an aqueous KF workup, trifluoroborate salt **180** was isolated (Scheme 56).



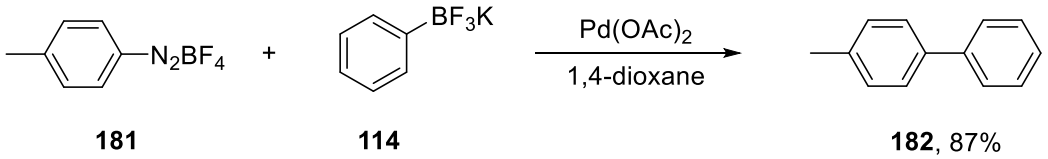
Scheme 56. Initial synthesis of organotrifluoroborates by Chambers

However, the use of gaseous boron trifluoride and toxic tin reagents was not appealing and trifluoroborates remained a curiosity. Vedejs and co-workers published a robust method of preparation.[53] They reacted phenylboronic acid **104** with KHF_2 in methanol and isolated phenyltrifluoroborate **114** via recrystallization (Scheme 57).



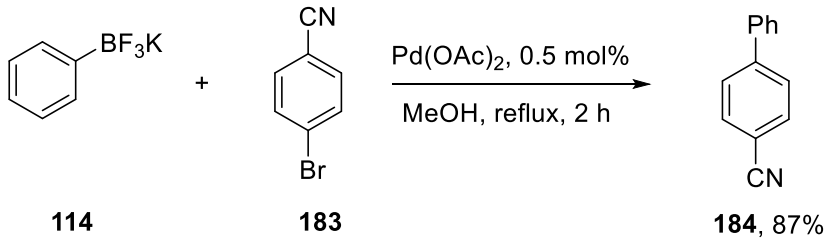
Scheme 57. Synthesis of trifluoroborate salts reported by Vedejs

Genet and coworkers first used these salts in coupling reactions with aryldiazonium salts.[81] They reacted aryl diazonium salt **181** with potassium phenyltrifluoroborate **114** with palladium acetate in 1,4-dioxane to give the cross-coupled product **182** in 87% yield (Scheme 58).



Scheme 58. Use of organotrifluoroborates in coupling reactions by Genet

Molander introduced the use of organotrifluoroborates for Suzuki coupling with aryl halides.[82] For example, potassium phenyl trifluoroborate **114** was reacted aryl halide **183** in the presence of palladium acetate in refluxing methanol to give the biaryl **184** in 87% yield (Scheme 59). Over the last decade, potassium trifluoroborate salts have become popular boron components in the Suzuki reaction due to the ease of their preparation.[83]



Scheme 59. Use of trifluoroborate salt in Suzuki Coupling

Trifluoroborate salts themselves are not competent substrates in the coupling reaction. NMR and DFT studies suggest that the mechanism of the Suzuki reaction with trifluoroborates involves in-situ slow release of the boronic acid **104** and fluoride from the salt[63, 84-85] (Figure 15) via intermediates **185A** and **185B**. This attenuates many of the side reactions that arise from direct use of the boronic acid. The intermediates **185A** and **185B** can participate in the transmetalation step of the coupling reaction.

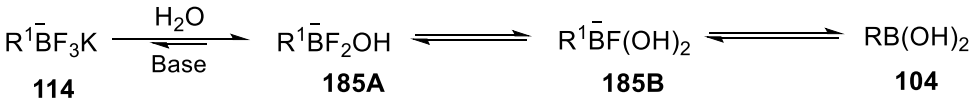


Figure 15. Hydrolysis of trifluoroborate salts

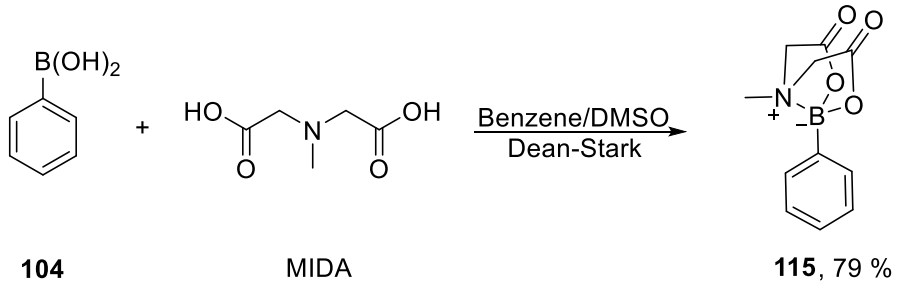
As opposed to boronic acids, tetrafluoroborate salts are tetrahedral and not lewis acidic. They are also crystalline making them easier to handle than the corresponding boronic acids or esters. Various unstable boronic acids have been converted to stable trifluoroborate salts and used for coupling. For example, potassium vinyl trifluroborate (CH_2=$CHBF_3K$) **186** is a stable compound compared to corresponding vinylboronic acid (CH_2=$CHBOH_2$) **187**.[86] A key advantage of RBF_3K compared to other boron components in the Suzuki reaction is that other reactions can be performed on the substrate in their presence. The trifluoroborate salts can tolerate conditions for Swern oxidations[87], ozonolysis, 1,3-dipolar cycloadditions[88] and Wittig reactions.[89]

Today many alkyl and aryl trifluoroborate salts are commercially available. Despite their many advantages, trifluoroborates are salts. This makes them difficult to chromatograph and use

in multistep synthesis. In addition, the synthesis of BF_3K salts is via boronic acids and they can be viewed as a boronic acid protecting group. KHF_2 is also corrosive in nature, so care must be taken in its use.

2.2.5 MIDA boronates

N-Methyliminodiacetic acid (MIDA) esters of boronic acids have two formal B-O bonds and a dative bond from the lewis basic nitrogen and lewis acidic boron atom. Quaternization of the boron atom makes the MIDA boronates monomeric unlike parent boronic acids. They were first synthesized by the Contreras in 1986.[90] He reacted phenyl boronic acid **104** with N-methyliminodiacetic acid (MIDA) in refluxing benzene/DMSO using a Dean-Stark apparatus (Scheme 60). The boronate ester **115** was isolated via recrystallization in 79% yield.

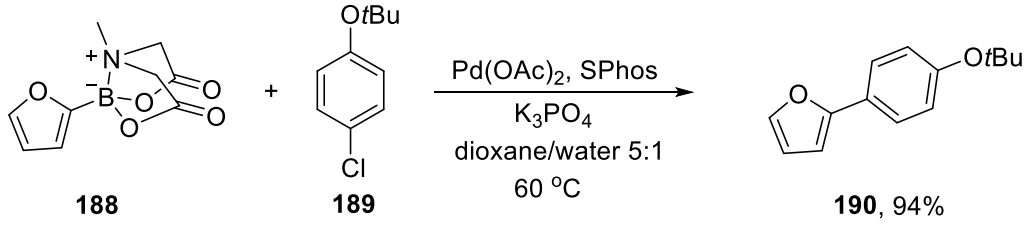


Scheme 60. Synthesis of MIDA boronates reported by Contreras

The MIDA boronate does not take part in transmetalation step in the Suzuki reaction. It needs to be hydrolyzed to give boronic acid to participate in cross-coupling. Stability of the MIDA functionality to anhydrous Suzuki coupling reaction conditions has made these substrates useful in iterative cross-coupling strategies.[91]

An important application of these N-coordinated boronates is in the cross-coupling of substrates such as the 2-pyridyl or 2-furyl substrates.[92] The 2-pyridyl or 2-furyl boronic acids

undergo rapid protodeborylation under the Suzuki coupling conditions to give reduced yields of the cross-coupled products. The N-coordination makes the MIDA boronates more stable to protodeboration. Burke optimized the Suzuki cross-coupling conditions which result in slow hydrolysis of the boronates. This generates the boronic acids in-situ in low concentrations. For example, he reacted 2-furyl MIDA boronate **188** with aryl halide **189** using $Pd(OAc)_2$ as the catalyst and K_3PO_4 as the base to give the cross-coupled product **190** in 94% isolated yield (Scheme 61). The yield with **188** was greater than the reaction in which 2-furyl boronic acid was used as the substrate (59%).



188 **189** **190**, 94%

Scheme 61. Suzuki coupling with MIDA boronates of unstable boronic acids

2.2.6 Boronamides

This class of boranes has been developed extensively over the last 15 years by the Suginome group.[93] The boron atom in the boronamides is bonded to two nitrogen atoms and is sp^2 hybridized. The diaminonaphthyl ligand (DAN) is most commonly used ligand as the boronamide complex formed shows superior stability in comparison to the other boronamide complexes with ligands such as anthranilamide (AAM) and 2-(pyrazol-5-yl)aniline (PZA) (Figure 16).[94]

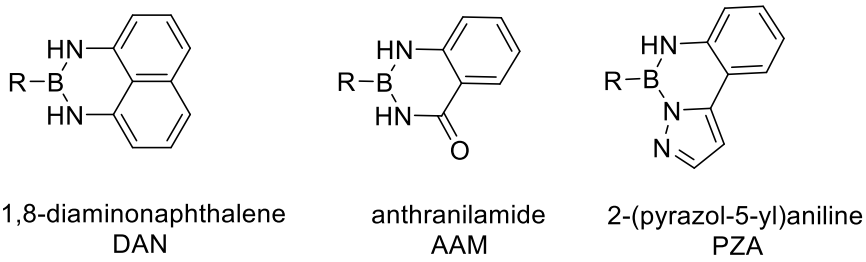
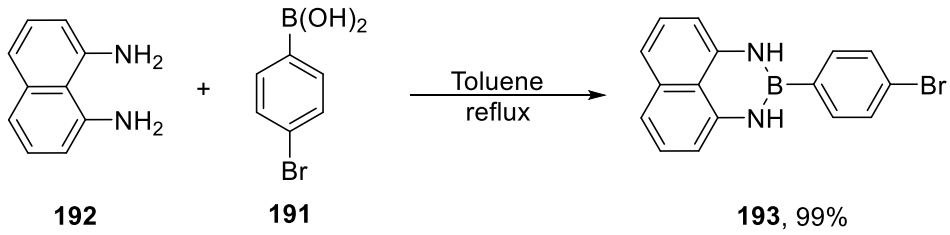


Figure 16. Common ligands used in boronamides

The diaminonaphtyl boronamides are generally prepared via a condensation reaction of the boronic acid and 1,8-diaminonaphthalene with azeotropic removal of water (Scheme 62).[93] Suginome reacted 4-bromoboronic acid **192** with diaminonaphthalene **191** in refluxing toluene to give the bromo BDAN borane **193** in 99% yield.



Scheme 62. Preparation of DAN boronamides from boronic acids

The boron center with the DAN protecting group is stable to most basic Suzuki cross-coupling conditions but is readily deprotected under acidic conditions to give the corresponding boronic acids.[95] This gives an opportunity to develop iterative cross-coupling protocols and a protecting group which is distinct from the MIDA boronates (deprotection by base).

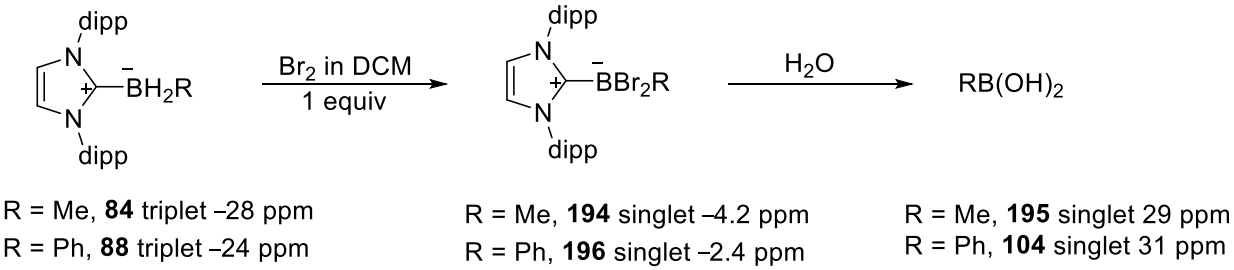
We hypothesize that halo substituted NHC-boranes could potentially be a new class of boranes used in the Suzuki coupling reaction.

2.3 RESULTS AND DISCUSSION

2.3.1 Stability of dibromo- and dichloro- substituted NHC-boranes

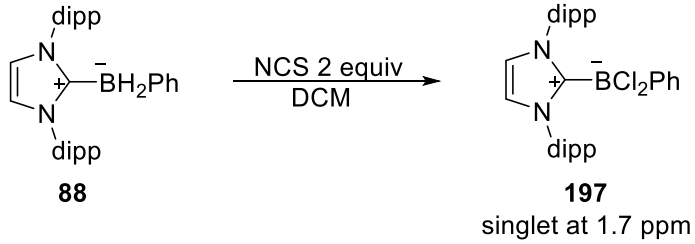
To determine the suitability of NHC-boranes as substrates in Suzuki coupling, halo-substituted B-Ph NHC-boranes were prepared. We tested bromination, chlorination and fluorination.

To prepare B-methyl NHC-dibromo borane **194** (Scheme 62), a solution of Br_2 (1 M in DCM, 1 equiv) was added to the NHC-borane **84** in DCM. Evolution of hydrogen gas was observed and the ^{11}B NMR spectrum showed the formation of brominated product **194** (singlet around –5.5 ppm). To test the stability of the **194** to ambient lab conditions, the septum was removed and the solution was exposed to air for 15 min. The ^{11}B NMR spectrum then showed two peaks (singlet at 32 ppm attributed to methylboronic acid **195** and a singlet – 5.5 ppm which is the starting dibromoborane **194**). After 15 mins, water (0.1 ml) was added to the mixture and the resulting ^{11}B NMR spectrum showed complete conversion to the methyl boronic acid **195**. The B-phenyl NHC-dibromoborane **196** was prepared via an analogous procedure (Scheme 62). After the reaction was complete (singlet at –4.2 ppm seen in the ^{11}B NMR spectrum), water was added to the reaction mixture. The ^{11}B NMR spectrum showed complete conversion to boronic acid **104** (singlet at 29 ppm). Flash chromatography of the dibromides was not attempted based on these observations.



Scheme 63. Preparation of di-bromo substituted NHC-boranes

To prepare the dichloro borane **197**, HCl (4 M in dioxane, 5 equiv) was added to B-phenyl NHC-borane **88**. A ^{11}B NMR spectrum showed that only mono-substitution had taken place (broad peak at –9 ppm). Attempts to prepare the dichloro borane **197** by a radical reaction with CCl_4 as the solvent resulted in formation of target product but the reaction was not reproducible on a larger scale. However, reaction of B-phenyl NHC-borane **88** with 2 equiv of *N*-chlorosuccinimide (Scheme 63) gave the dichloro borane **197** cleanly (singlet at 1.7 ppm in the ^{11}B NMR spectrum). The product **197** was initially exposed to air by removing the septum of the flask. After 1 h, a ^{11}B NMR spectrum showed no decomposition. The product was then stirred with water for 1 h, with the ^{11}B NMR spectrum showing formation of phenylboronic acid **104**. Attempts to isolate the product **197** by flash chromatography gave only phenylboronic acid **104**.



88 **197**
singlet at 1.7 ppm

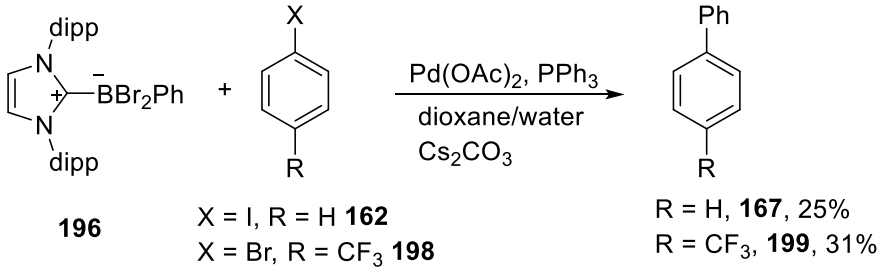
Scheme 64. Preparation of di-chloro substituted NHC-borane **197**

To summarize, bromide **196** and chloride **197** can be formed but both quickly convert to phenylboronic acid on exposure to water. Although these compounds could be made and subjected to Suzuki reaction conditions in-situ, their rapid reaction with water would result in high concentration of the boronic acid, which is undesirable for the Suzuki reaction.

2.3.2 Suzuki coupling with bromo- and chloro- substituted NHC-boranes

Experiments studying the stability of halogenated NHC-boranes showed potential for the use of these compounds in Suzuki coupling. To test this, dibromo NHC borane **196** generated in-situ and

iodobenzene **162** were dissolved in dioxane/water and palladium acetate (5 mol%), PPh_3 (10 mol%) and cesium carbonate (3 equiv) were added (Scheme 64). Based on prior results, we expect that **196** will quickly convert to phenylboronic acid **104**. TLC analysis showed formation of biphenyl **167** after 2 h and the starting material was absent after 12 h. The product biphenyl **167** was purified by prep TLC and isolated in 25% yield. When 4-bromobenzotrifluoride **198** was used as the substrate in reaction with dibromo NHC-borane **196**, 4-phenylbenzotrifluoride **199** was obtained in 31% yield after flash chromatography (Scheme 64). Next, Suzuki coupling was attempted using the dichloro NHC-borane **197** with **162** using the same procedure used for dibromo NHC-borane **196**. TLC analysis of reaction showed the formation of target product **167** along with presence of the SM spot of the halide **162**. Because the conversion was not 100 % after 16 h, the product was not chromatographed.



Scheme 65. Suzuki Coupling with NHC-borane **196**

2.3.3 Stability of *B,B*-difluoro substituted NHC-boranes

We hypothesize that di-fluoro substituted NHC-boranes like compound **51** could be analogous to trifluoroborates. Like a fluoride substituent, NHC groups are electron withdrawing in nature. Formal replacement of an F^- by NHC results in the formation of a neutral complex (Figure 19),

rather than a salt. This could be an advantage in certain systems. For example, salts often cannot be chromatographed and may not be soluble in some organic solvents.

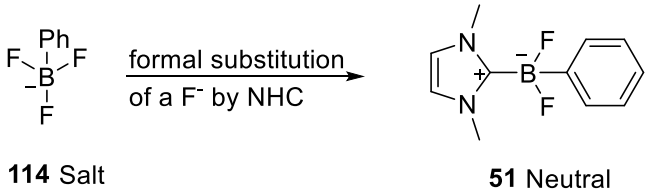


Figure 17. NHC-BF_2Ph as potential analog of $PhBF_3K$

To study if di-fluoro NHC-boranes can give the corresponding boronic acids in situ, *B,B*-difluoro NHC-borane **51** was stirred with 3 equiv of Cs_2CO_3 in THF/water for 12 h. This is similar to Molander's procedure for RBF_3K, but no catalyst or halide was added.[82] A ^{11}B NMR spectrum showed a new broad peak around 5 ppm. This peak does not belong to phenylboronic acid **104** (29 ppm). ^{19}F NMR spectrum showed the presence of a sharp singlet at –127 ppm along with a quartet at –153 ppm (attributed to *B,B*-difluoro NHC-borane **51**) . This indicates the formation of a new species in which the fluorine is not bonded to boron (Figure 18) because a boron fluorine bond would show up as a quartet in the ^{19}F NMR (^{11}B boron has a spin 3/2).

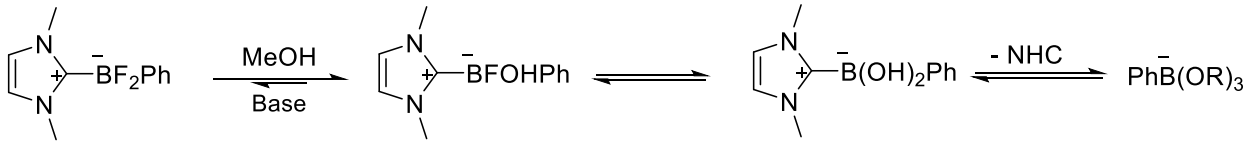


Figure 18. Possible conversion of *B,B*-difluoro NHC-borane to phenyl boronate

Molander had studied the reaction of phenyl trifluoroborate **114** with a base in methanol.[83] A new species was observed in ^{11}B NMR spectra (broad singlet at 5.47 ppm). ^{19}F NMR spectrum showed a sharp singlet at –149 ppm indicating the absence of a B-F bond.[53] We imagined that compound **51** (Figure 18) is converted to an intermediate capable of reacting in the Suzuki coupling conditions similar to the behavior of **114** (Figure 15).

A control reaction was performed with *B,B*-difluoro NHC-borane **51** being heated in methanol without base. The ^{11}B NMR spectrum showed the presence of triplet at 4.5 ppm (no broadening, attributed to the *B,B*-difluoro NHC-borane **51**) and the ^{19}F NMR spectrum showed no singlets (only quartet at –157 ppm was observed). This suggests that the base plays an important part in the formation of species which participates in the cross-coupling reaction.

2.3.4 Suzuki Coupling with *B,B*-difluoro substituted NHC-boranes

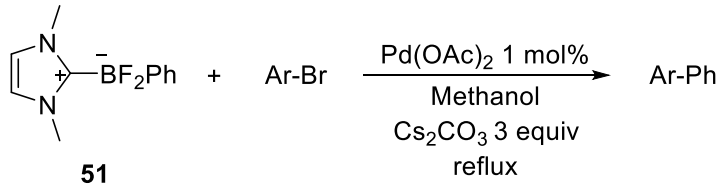
We next decided to study the use of *B,B*-difluoro NHC-borane **51** in the coupling reaction. For initial experiments, the ligand-free procedure used by Molander[82] was followed. In a typical experiment, di-fluoro NHC-borane **51** (1 equiv) and 4-bromobenzonitrile **183** (1 equiv) were mixed in methanol. Palladium acetate (1 mol%) was added along with 3 equiv of cesium carbonate. The reaction was complete by TLC analysis after 3 h at reflux. After cooling, water was added and the product was extracted with ether 3 times. The solvent was evaporated and flash chromatography of the residue gave the product **184** in 87% yield (Table 12, entry 1).

Results of Suzuki reactions of *B,B*-difluoro NHC-borane **51** with other substrates are summarized in Table 9. Reaction with 4-bromo benzotrifluoride **198** (entry 2) was completed in 2 h and the cross-coupling product **199** was obtained in 72% yield. When 4-bromo nitrobenzene **200** was reacted (entry 3), reaction was complete in 1 h and the target product **201** is obtained in 84% yield. 4-Bromoanisole **202** (entry 4) was reacted with 1 equiv of the di-fluoro compound **51** to give the target product **203** in 77% yield. Reaction with compound methyl 4-bromobenzoate **204** (entry 5) gave the corresponding cross-coupling product **205** in 79% yield. Reaction of 4-bromobenzaldehyde **206** (entry 6) gave the cross-coupled product **207** in 68% yield. Small

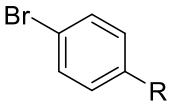
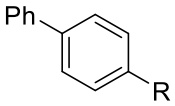
amounts of Cannizzaro reaction prodcuts (methyl esters) were observed resulting in lower yield of the target product **207**.

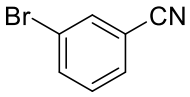
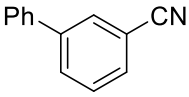
Reaction with 3-bromo substituted benzonitrile **208** gave the cross-coupling product **209** in 81% yield in 3 h (entry 7). Two control reactions were performed where the cross-coupling was attempted in the absence of palladium acetate and in the absence of base. The reactions showed no formation of the biaryl product (analyzed by TLC).

Table 9. Suzuki Coupling with *B,B*-difluoro NHC borane **51**



51

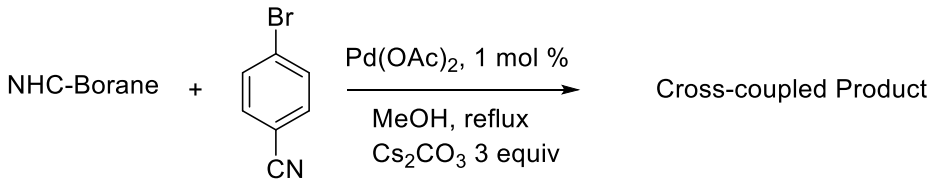
entry	R	time	product	yield[a]
				
1	**183**, R = CN	3 h	**184**, R = CN	87%
2	**198**, R = CF_3	2 h	**199**, R = CF_3	72%
3	**200**, R = NO_2	1 h	**201**, R = NO_2	84%
4	**202**, R = OMe	4 h	**203**, R = OMe	77%
5	**204**, R = CO_2Me	2 h	**205**, R = CO_2Me	79%

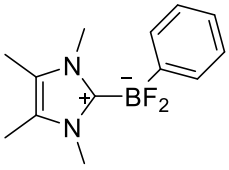
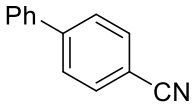
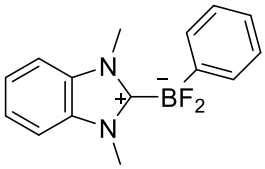
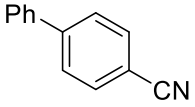
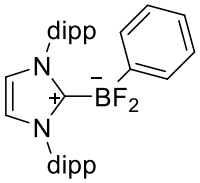
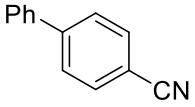
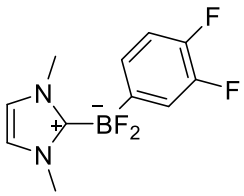
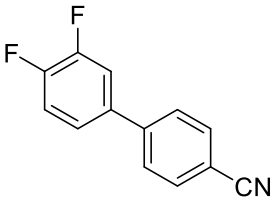
6	**206**, R = CHO	2 h	**207**, R = CHO	68%
7	 **208**	3 h	 **209**	81%

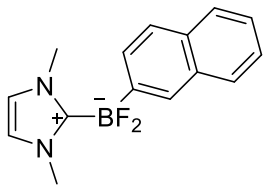
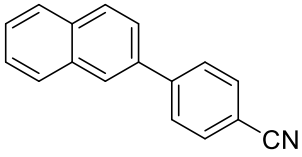
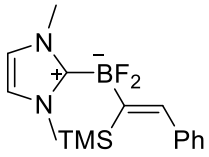
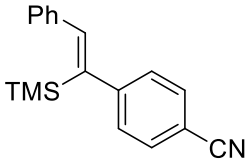
[a] after flash chromatography [b]two control reactions were run with no base and no Pd catalyst which gave no cross-coupling product.

We then attempted to use different *B,B*-difluoro NHC-boranes (both with different NHC partners and different substituents on the phenyl ring) (Table 10), all with 4-bromobenzonitrile **183** as the coupling partner. Standard reaction conditions used for *B,B*-difluoro NHC-borane **51** were followed and the reactions were monitored by TLC. The *B,B*-difluoro NHC-borane **122** and *B,B*-difluoro NHC-borane **125** (entry 1-2) gave the cross-coupling product **184** in 84% and 83% isolated yields respectively in 3 h. *B,B*-difluoro NHC-borane **123** required longer reaction time (entry 3, 6 h) for completion and gave the cross-coupled product **184** in 72% yield. Entries 4-5 show the reactions of *B,B*-difluoro NHC-boranes with different substituents on the phenyl ring. The 4,5-difluorophenyl *B,B*-difluoro NHC-borane **119** gave the corresponding cross-coupled product **210** in 68% yield (entry 4) while the reaction of 2-naphthyl *B,B*-difluoro NHC-borane **118** (entry 5) gave the cross-coupled product **211** in 72% yield. Suzuki coupling reaction of alkenyl *B,B*-difluoro NHC-borane **131** (Table 10, entry 5) was performed by Mr. Daniel Bolt to give the cross-coupling product **212** in approximately 41% yield.

Table 10. Suzuki reactions of different NHC-Boranes with 4-bromobenzonitrile

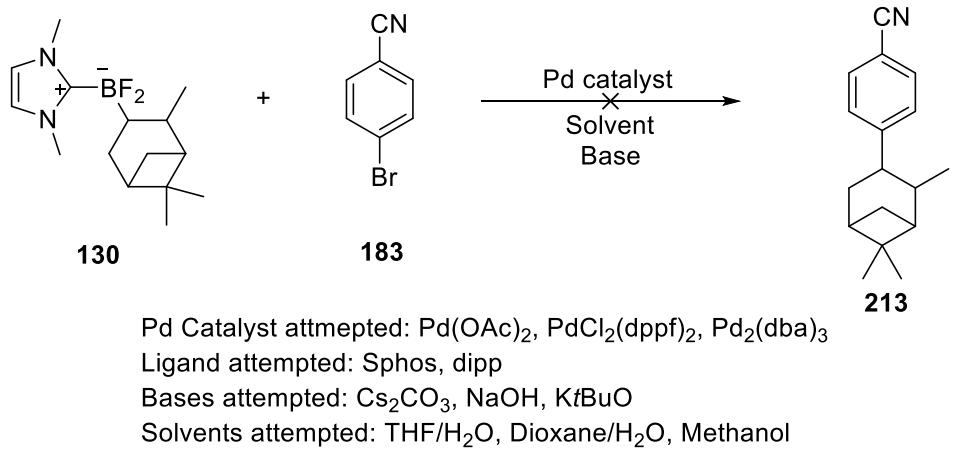


entry	NHC-borane	cross-coupled product	time	yield[a]
1	 **123**	 **184**	3 h	84%
2	 **126**	 **184**	3 h	83%
3	 **124**	 **184**	6 h	72%
4	 **119**	 **210**	4 h	68%

5	 **118**	 **211**	4 h	70%
6	 **132**	 **212**	6 h	41%

[a]after flash chromatography

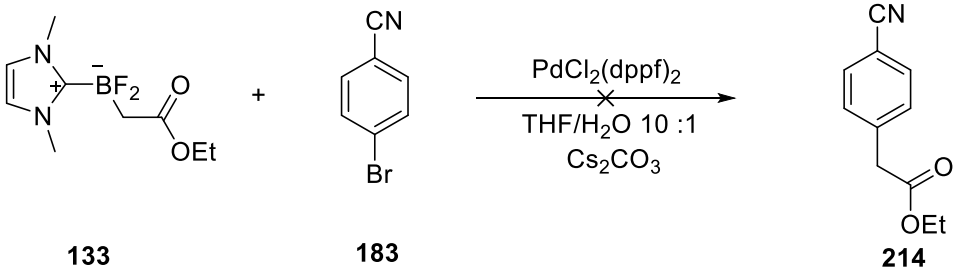
We then decided to attempt the Suzuki coupling of the alkyl-substituted *B,B*-difluoro NHC-boranes. The pinyl and thexyl substituted *B,B*-difluoro NHC-boranes **130** and **131** were chosen as attempted as substrates. Initial conditions were chosen from the report from Molander[96] in which he coupled alkyl trifluoroborates with aryl chlorides. The pinyl *B,B*-difluoro NHC-borane **130** was mixed with 3 equiv of cesium carbonate, 1 equiv of 4-bromobenzonitrile **183** as the coupling partner in THF/H_2O and $PdCl_2(dppf)_2$ was the catalyst and Sphos as the ligand (Scheme 66). The reaction mixture was heated to reflux and progress was monitored by TLC analysis. After 16 h, TLC showed starting material still present along with a small amount of the homocoupling product of the aryl bromide and no other spot. The reaction was stopped and a crude ^{1}H NMR spectrum after solvent evaporation showed no presence of the target cross-coupling product **213**. Reaction was repeated with the thexyl *B,B*-difluoro NHC-borane **131** under identical conditions and no cross-coupling product was observed. Various other catalyst systems and ligands were attempted to obtain conversion (Scheme 66) without success.



Scheme 66. Conditions attempted for Suzuki reaction of difluoro-NHC-pinene borane

A control reaction was run with just the pinyl *B,B*-difluoro NHC-borane **130** and base to check if corresponding boronic acid/boronate species is observed. A ^{11}B NMR spectrum after 3 hours showed a broad peak around −7 ppm and the ^{19}F NMR spectrum showed a singlet at −149 ppm (indicating dissociation of fluoride from the NHC-borane). However, the catalyst systems employed did not give any of the target product **213**.

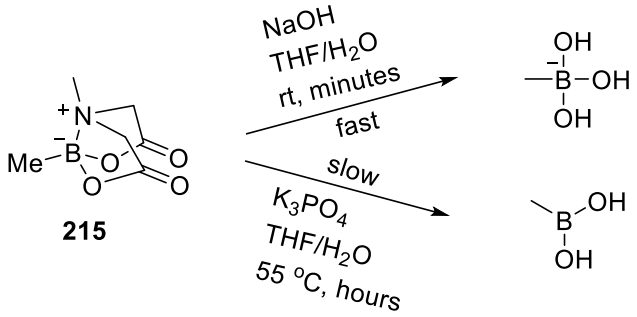
A reaction of *B,B*-difluoro NHC-borane **133** was attempted under the same reaction conditions (Scheme 67). The ^{11}B NMR after 3 h showed the presence of peak at 22 ppm (indicating possible formation of boronate species and dissociation of the NHC) but no cross-coupling product **214** peaks were observed in the crude the ^{1}H NMR spectrum.



Scheme 67. Attempted Suzuki coupling reaction of NHC-α-boryl ester **133**

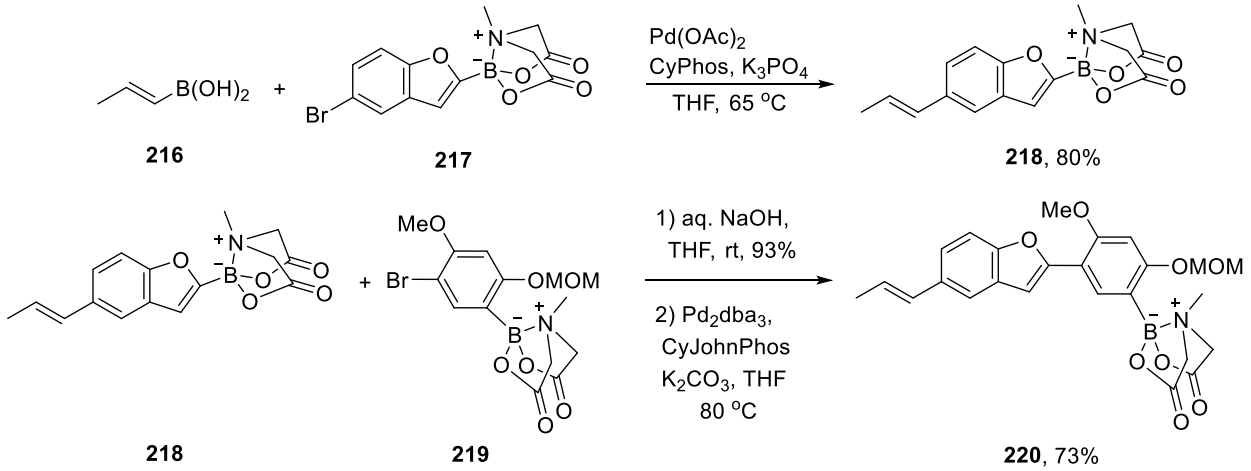
2.3.5 Iterative Suzuki coupling with *B,B*-difluoro NHC-boranes

Iterative Suzuki cross-coupling protocols are possible when one of the two boron moieties present in the reaction can be selectively coupled.[97] This method would allow for better synthesis of polyarene derivatives which have widespread applications in material technology. Use of efficient boronyl masking partners is necessary to achieve this transformation. Recently, Burke has studied the mechanism and rate of hydrolysis of the MIDA boronate esters to give the corresponding boronic acids.[98] He reported that the MIDA boronate **215** undergoes fast hydrolysis (within a few minutes) in the presence of a strong base such as NaOH but the rate is about 3 orders of magnitude slower in the presence of a weaker base like anhydrous K_3PO_4 (Scheme 68). Since K_3PO_4 is capable of being used in Suzuki cross-couplings reactions with boronic acids, development of an iterative coupling strategy is possible.



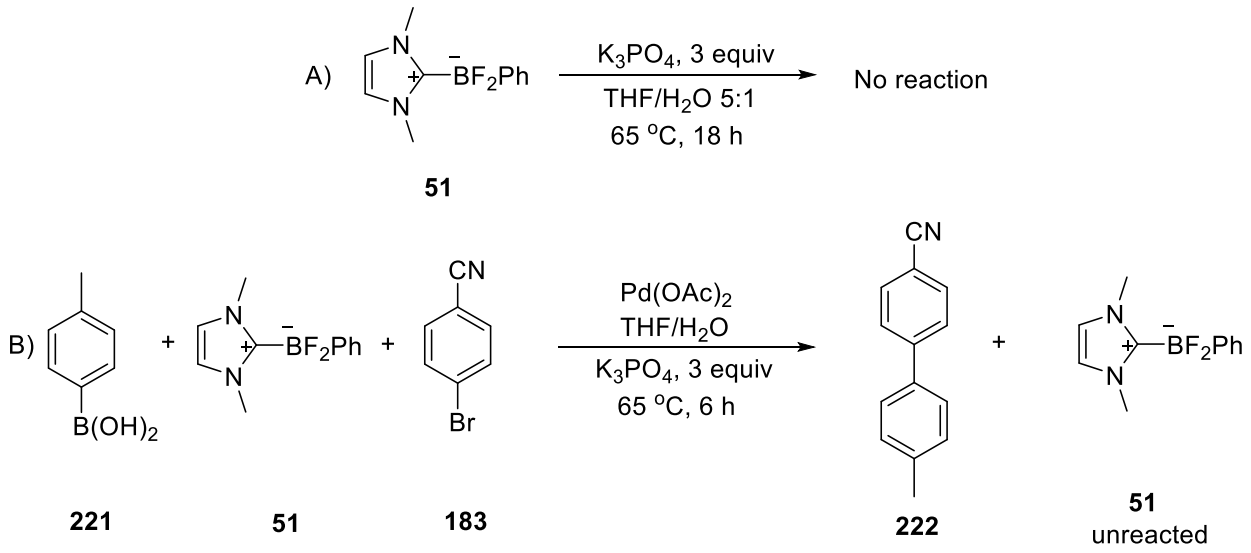
Scheme 68. Decomposition rates of MIDA boronate with different bases

In an example for iterative cross-coupling in the synthesis of natural product ratanhine, Burke reacted vinyl boronic acid **216** with MIDA boronate **217** in the presence of K_3PO_4 as the base and $Pd(OAc)_2$ to give the intermediate **218** with the MIDA boronate ester intact (Scheme 68). The MIDA boronate ester was then hydrolyzed using aq. NaOH followed by coupling with arene **219** to give **220** in 73% yield (Scheme 68).



Scheme 69. Iterative cross-coupling example with MIDA boronate ester

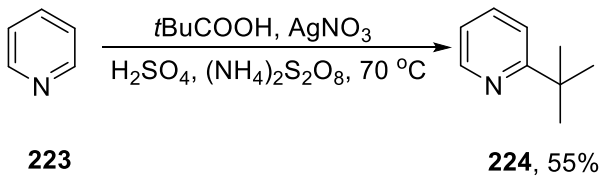
In iterative Suzuki cross-coupling reactions, the MIDA boronate functions as a protecting group for the boronic acid under mild basic conditions. Similar to the MIDA boronates, we hypothesized that the *B,B*-difluoro NHC-boranes would be stable to mildly basic conditions. To test this, we first treated 1 equiv of *B,B*-difluoro NHC-borane **51** with 3 equiv of K_3PO_4 with THF as the solvent (0.5 M) (Scheme 70a). After 6 h, the ^{11}B NMR and ^{19}F NMR spectra were unchanged showing that NHC-borane **51** is stable in these conditions. Further, we reacted *p*-tolylboronic acid **221** with 4-bromobenzonitrile **183** using $Pd(OAc)_2$ as the catalyst and K_3PO_4 as the base and added 1 equiv of NHC-borane **51** to the reaction mixture (Scheme 70b). After 6 h, TLC analysis showed that aryl halide **183** was consumed. The ^{11}B NMR and ^{19}F NMR of the crude reaction mixture showed that the *B,B*-difluoro NHC-borane **51** remained intact while the boronic acid participated in cross-coupling to give aryl compound **222**. These results set the stage for the use of difluoro-NHC-boranes as the cross-coupling reagents in iterative cross-couplings.



Scheme 70. A) Reaction of difluoro NHC-borane with K_3PO_4 B) Parallel Suzuki reaction with boronic acid

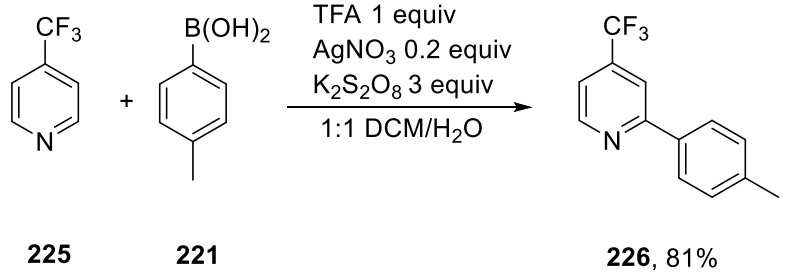
2.3.6 Use of *B,B*-difluoro substituted NHC-boranes in the Minisci reaction

N-Heteroarenes are common moieties in natural products and drug molecules. Selective C-H functionalization of heteroarenes is one of the most common strategies to make the target compounds. The Minisci reaction, which involves the addition of carbon centered radicals to electron deficient heteroarenes, is a powerful method to prepare alkyl substituted heteroaryls.[99] In a typical example, pyridine **223** was reacted with t-butyl carboxylic acid in the presence of a strong acid, silver nitrate and ammonium persulfate to give the alkyl substituted pyridine **224** in 55% yield (Scheme 71).



Scheme 71. Example of a typical Minisci reaction

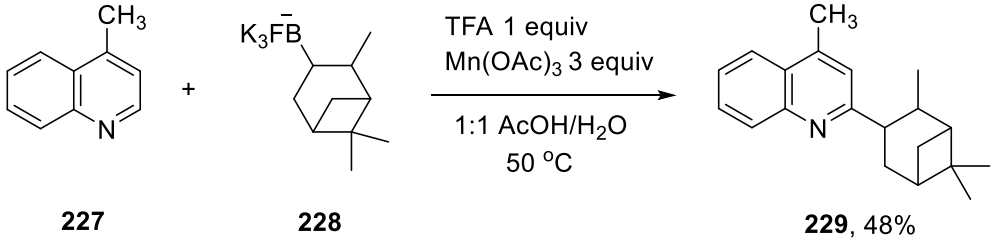
Baran first established the use of aryl boronic acids in the Minisci reaction to give the aryl substituted pyridines using catalytic silver nitrate and potassium persulfate as the oxidant.[100] For example, 4-trifluoromethyl pyridine **225** was reacted with 4-methylphenyl boronic acid **221** in a 1:1 mixture of DCM/H_2O as the solvent. TFA was used as the acid to protonate the pyridine and the substituted pyridine **226** was isolated in 81 % yield (Scheme 72).



225 **221** **226**, 81%

Scheme 72. Example of Minisci reaction using arylboronic acids by Baran

Molander showed the use of alkyl potassium trifluoroborates (particularly secondary alkyl trifluoroborates) as substrates in the Minisci reaction to give the corresponding alkyl-substituted heteroaryls.[101] Lepidine **227** was reacted with trifluoroborate salt **228** along with TFA as the acid and Manganese (III) acetate as the oxidant in AcOH/H_2O as the solvent to give the substituted quinoline **229** in 48% yield (Scheme 73).

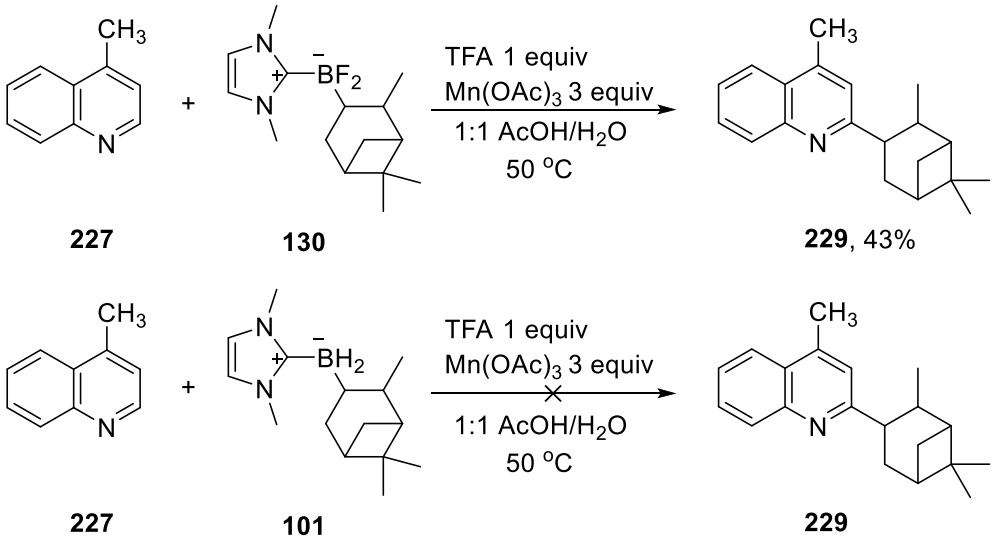


227 **228** **229**, 48%

Scheme 73. Minisci reaction of trifluroborate salts established by Molander

Based on this precedent, we attempted to use the pinyl-substituted *B,B*-difluoro NHC-borane **130** in Minisci reaction analogous to trifluoroborate salt **228**. Following Molander's

procedure, lepidine **227** was reacted with NHC-borane **130** (1 equiv), TFA (1 equiv), Manganese (III) acetate (3 equiv as the oxidant) in a 1:1 mixture of acetic acid and water as the solvent at 50 ^{o}C (Scheme 74). After 18 h, TLC analysis of the reaction mixture showed the presence of a new non-polar spot. The solvent was evaporated and target product **229** was isolated in 43% yield after flash chromatography. We also attempted a similar reaction with NHC-borane **101** but no target spot was observed in the TLC after 18 h (Scheme 74). These experiments show that alkyl-substituted *B,B*-difluoro NHC-boranes could potentially be developed as substitutes for potassium trifluoroborate salts in the Minisci reaction.



Scheme 74. Minisci reaction using alkyl substituted difluoro NHC-borane **130**

3.0 SUMMARY AND OUTLOOK

By using organolithium reagents, synthesis methyl- and phenyl-substituted NHC-boranes has been demonstrated. Other alkyl- and aryl- substituted NHC-boranes were prepared by hydroboration of the alkenes and arynes respectively. The chemistry of these substituted NHC-boranes has been linked to already established Suzuki coupling precursors. Alkyl- and aryl-substituted NHC-boranes have been converted to boronic acids, pinacol boronate esters, trifluoroborate salts and MIDA boronates.

Selectfluor was used as an electrophilic fluorinating agent to prepare NHC-(difluoro)alkyl- and aryl-boranes have been synthesized. The NHC-(difluoro)arylboranes have been used directly in the Suzuki coupling reaction and their potential as a boronyl masking partner has been established. With synthesis of NHC-(difluoro)arylboranes with either halogen or other boron group handles, the compounds can be used in iterative cross-coupling procedures. NHC-(difluoro)alkylboranes have also been used in the Minisci reaction showing their utility as substitutes for the trifluoroborate salts. Further applications especially for reactions with water sensitive substrates where low solubility of the trifluoroborates in organic solvents is a limitation would be very useful. These reactions have expanded the chemistry of NHC-boranes and provided a foundation for their development as a new class of boranes to be utilized in C-C coupling toolbox. Synthesis of diMe-Imd-BF_2H has been developed. The corresponding boryl radical has been generated by H-atom abstraction and has been compared to the boryl radical generated from diMe-Imd-BH_3.

4.0 EXPERIMENTAL

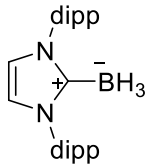
4.1.1 General methods

Chemicals were purchased from suppliers and used as received unless otherwise noted. Et_2O, CH_2Cl_2, and THF were dried by passing through an activated alumina column. Reactions were monitored by TLC analysis or ^{11}B NMR spectroscopy. TLC visualization was accomplished with a 254 nm UV lamp, or by staining with vanillin solution. Separations were performed using a Combiflash R_f automated flash chromatography from Teledyne ISCO with normal phase RediSep R_f columns containing 230-400 mesh silica gel. Unless otherwise noted the experiments were performed under argon in oven dried glassware.

Proton (^1H), carbon (^{13}C), boron (^{11}B), and fluorine (^{19}F) nuclear magnetic resonance spectra (NMR) were performed on either a Bruker Advance III 300, 400, or 500. Chloroform (δ 7.26 ppm) or TMS (δ 0.00 ppm) was used as an internal standard for ^1H NMR spectra and $CDCl_3$ (δ 77.00 ppm) was used as an internal standard for ^{13}C NMR spectra. ^{11}B chemical shifts are relative to $Et_2O{\bullet}BF_3$ and ^{19}F chemical shifts are relative to $CFCl_3$. The following abbreviations are used to describe coupling: s, d, t, q, quint, sept, m, and br represent singlet, doublet, triplet, quartet, quintet, septet, multiplet, and broad signal respectively. The resonances of hydrogen atoms connected to boron were often difficult to observe in ^1H NMR spectra due to quadrupole broadening. For the same reason, no resonances of carbon atoms bonded to the boron atom could be observed by ^{13}C NMR spectroscopy.

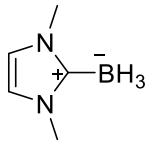
Low resolution mass spectra (LRMS) were measured by a Shimadzu LCMS and high resolution mass spectra (HRMS) were measured on a Micromass Inc. Autospec instrument with E-B-E geometry.

4.1.2 Synthesis of NHC-boranes



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene borane 11:[7]

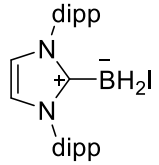
Carbene borane **11** was synthesized in 3 steps from literature procedures.



1,3-Dimethylimidazol-2-ylidene borane 12:[10]

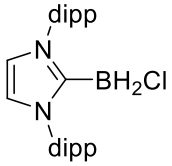
Methyl iodide (1.2 equiv, 60 mmol) was added to a solution of 1-methylimidazole **20** (4.1 g, 50 mmol) in DCM (10 mL) over 30 min. After stirring the reaction at rt for 1 h, the DCM was evaporated and the salt **21** was dried over vaccum. Toluene (50 mL) was added to the salt followed by addition of $NaBH_4$ (1.2 equiv, 60 mmol). The reaction mixture was heated at 120 ^oC for 18 h. After completion of the reaction, the toluene was decanted and fresh toluene (50 mL) was added. The mixture was heated at reflux for 30 min and decanted while it was hot. The combined toluene solutions were evaporated and the residue was purified by recrystallization from water. After

filtration and drying NHC-borane **12** (2.5 g) was isolated as white crystals in 46% yield. The spectra of the sample were identical to the one reported in literature.



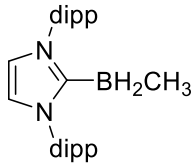
1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene boryl iodide 39:

Iodine (1 M in benzene, 0.25 mL) was added dropwise to a solution of NHC-borane **11** (0.2 g, 0.5 mmol) in benzene (5 mL) under argon at room temperature. After completion of addition, ^{11}B NMR shows the presence of a broad triplet at –32 ppm assigned to product **39** and the starting material peak is absent. The crude product is used directly for the next alkylation reaction without isolation.



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene chloroborane 43:

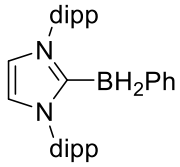
HCl solution (4 M in dioxane, 1.2 mL) was added to NHC-borane **11** (0.78 g, 1.94 mmol) in chloroform (50 mL) at 0 ^{o}C under argon. Intense bubbling was immediately observed. After 30 min, then the solvent was evaporated. The product was purified by flash chromatography (hexane: ethyl acetate, 8:1 to 3:1) yielding a white solid (0.73 g, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (t, J = 7.9 Hz, 2H, H arom.), 7.29 (d, J = 7.6 Hz, 4H, arom.), 7.1 (s, 2H, =CH(N)), 2.56 (sept, J = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.31 (d, *J* = 6.8 Hz, 12H, Me), 1.16 (d, *J* = 7 Hz, 12H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 133.1, 130.2, 123.8, 122.8, 28.8 , 25.2, 22.7; ^{11}B NMR (BF_3•Et_2O, 133 MHz, CDCl3) δ −18.6 (br s).



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene methylborane 83:

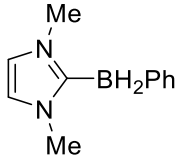
A. From $AlMe_3$: Trimethylaluminum solution (1 M in toluene, 0.21 mL) was added to a solution of carbene borane iodide **39** (0.11 g, 0.21 mmol) in toluene (2 mL) under argon at room temperature. White precipitate was formed during addition. After 15 min, water was added to quench the reaction. The layers were separated and the aqueous layer was extracted thrice with DCM. The combined organic layers were evaporated and the residue was purified by flash chromatography (hexane: ethyl acetate, 10:1 to 3:1) yielding a white solid (10 mg, 11%) with 80% purity (calculated by ^{1}H NMR spectrum).

B. From methyllithium: Methyllithium (1.6 M in ether, 1.523 mL) was added to a solution of the carbene borane chloride **43** (0.18 g, 0.41 mmol) in ether (10 mL) at 15 ^{o}C. White precipitate (presumably lithium chloride) was observed after 10 min. After 20 min, the reaction was quenched by slowly adding water. The aqueous layer was separated and extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by flash chromatography (hexane: ethyl acetate, 10:1 to 3:1) to yield 0.17 g (88%) of a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (t, *J* = 7.6 Hz, 2H, H arom.), 7.27 (d, *J* = 7.8 Hz, 4H, arom.), 6.97 (s, 2H, =CH(N)), 2.61 (sept, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.31 (d, *J* = 6.8 Hz, 12H, CH*Me*Me), 1.16 (d, *J* = 6.8 Hz, 12H, CHMe*Me*), − 0.75 (t, *J* = 6.2 Hz, 3H, B-CH3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 134.1, 130, 123.2, 121.7, 28.4 , 25.1, 22.5; ^{11}B NMR (BF_3•Et_2O, 133 MHz, $CDCl_3$) δ −28.4 (t, $J_{B\text{-}H}$ = 85.6 Hz).



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene phenylborane 87:

A solution of NHC-borane chloride **43** (0.214 g, 0.49 mmol) in ether (5 mL) was added to a phenyllithium (1.8 M in dibutyl ether, 1.37 mL) in ether (5 mL) under argon at room temperature by syringe pump over 1 h. After addition was complete, the mixture was stirred for 15 minutes and then water was added to quench the reaction. The aqueous layer was separated and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by flash chromatography (hexane: ethyl acetate, 10:1 to 3:1) to yield 0.16 g (68%) of a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.5 Hz, 2H, H arom.), 7.2 (d, *J* = 7.8 Hz, 4H, arom.), 6.94 (s, 2H, =CH(N)), 6.72-6.7 (m, 3H, arom.), 6.63-6.61 (m, 2H, arom.), 2.54 (sept, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.14 (d, *J* =7 Hz, 12H, CH*Me*Me), 1.09 (d, *J* = 7 Hz, 12H, CHMe*Me*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4, 136.1, 134.3, 126, 123.4, 122.6, 28.4 , 25.3, 22.1; ^{11}B NMR (BF_3•Et_2O, 160 MHz, $CDCl_3$) δ −23.55 (t, $J_{B\text{-}H}$ = 85.6 Hz).



1,3-Dimethylimidazol-2-ylidene phenylborane 29:

A. Procedure with phenyllithium: HCl (4 M in dioxane, 0.125 mL) was added to a solution of the carbene borane **12** (55 mg, 0.5 mmol) in benzotrifluoride (5 mL) at 0 °C under argon. The mixture was stirred for 30 min at 0 °C. A white precipitate was observed after 15 min. Additional

benzotrifluoride was added to dissolve the precipitate (15 mL, the solution remained slightly cloudy). Separately, phenyllithium (1.8 M in dibutyl ether, 1.4 mL) was added to benzotrifluoride under argon at room temperature. The NHC-borane chloride solution was added to phenyllithium by syringe pump over 1 h. After 15 min of additional stirring, water was added to quench the reaction. The aqueous layer was separated and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The compound was purified by flash chromatography (hexane: ethyl acetate, 100:0 to 50:50) to give a white solid (43 mg, 47%). See below for spectral data.

B. Procedure with 2-(trimethylsilyl) phenyl trifluoromethanesulfonate 28:[21]

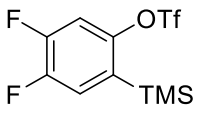
i) With CsF as the fluoride source: Cesium fluoride (2.22 g, 14.63 mmol) and NHC-borane **12** (1.6 g, 14.63 mmol) were added to a dry flask. Dry acetonitrile was added to the flask and it was purged with argon. Benzyne precursor **28** (2.18 g, 7.31 mmol) was added to the mixture at room temperature. After 6 h at room temperature, the solvent was evaporated. The crude product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:1) to give a white solid (0.78 g, 58%) plus 50% of recovered starting material **12**. See below for spectral data.

ii) With TBAF: TBAF (1 M in THF, 8 mL) was added to a solution of NHC-borane **12** (0.885 g, 8 mmol) in THF under argon. Benzyne precursor **28** (1.2 g, 4 mmol) was added at room temperature. After 2 h, the solvent was evaporated. The crude product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:1) to give a white solid (0.41 g, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (br s, 2H, H arom.), 7.16-7.13 (t, J = 7.2 Hz, 2H, arom.), 7.03 (t, J = 7.2 Hz, 1H, H arom.), 6.84 (s, 2H,=CH(N)), 3.76 (s, 6H, Me), 2.42 (br q, J = 84.8 Hz, 2H, BH2); ^{13}C NMR (125 MHz, $CDCl_3$) 171.22, 152.18, 134.2, 127, 123.5, 120.3, 36.1; ^{11}B NMR (BF_3•Et_2O, 133 MHz, $CDCl_3$) δ −25.26 (t, $J_{B\text{-}H}$ = 87.8 Hz).

iii) With KF: KF (0.29 g, 5 mmol) was added to an oven dried flask and was flame dried again under vacuum. After cooling under argon, 18-crown-6 (1.33 g, 5 mmol) was added followed by addition of NHC-borane **12** (0.55 g, 5 mmol) and dry THF (10 mL). Benzyne precursor **28** (0.75 g, 2.5 mmol) was added at room temperature. After 6 h, the solvent was evaporated. The crude product was evaporated by flash chromatography (hexane: ethyl acetate, 4:1 to 1:1) to give a white solid (0.28 g, 60%). See above for spectral data.

C) Procedure with chlorobenzene as the benzyne precursor:

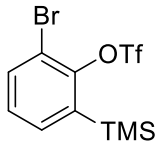
Chlorobenzene (2 g, 17.6 mmol) was added to a solution of NHC-borane **12** (3.9 g, 35 mmol) in toluene (35 mL) in a pressure tube. Potassium tert-butoxide (5.98 g, 53 mmol) was to the reaction mixture and it was heated to 130 ^{o}C for 7 h. Water (10 mL) was then added to the mixture and the product was extracted with DCM (20 mL) 3 times. The solvent was evaporated and the residue was purified by flash chromatography to the give a white solid (1.3 g, 40%). See above for spectral data.



4,5-Difluoro-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 93:[51]

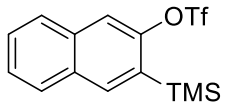
4,5-difluoro-2-bromo phenol (0.5 g, 2.4 mmol) and HMDS (0.43 g, 2.6 mmol) were mixed in dry THF (3 mL) in a dry rbf and refluxed for 1.5 h. The solvent was evaporated and the remaining HMDS was pumped off. Crude NMR was taken to confirm removal of HMDS. The product was used as is in the next reaction. To a solution of the 4,5-difluoro-2-bromo phenol TMS ether (0.68 g, 2.4 mmol) in THF was added n-BuLi (0.97 mL, 2.4 mmol) at −100 ^{o}C under argon. The temperature (outer bath) was slowly allowed to rise to − 80 ^{o}C and then cooled again to − 100 ^{o}C. Triflic anhydride (0.83 g, 2.9 mmol) was added dropwise maintaining the temperature. After

addition was complete temperature was allowed to rise to − 70 °C and the reaction was quenched with sat $NaHCO_3$. The crude mixture was extracted 3 times with ether and the organic layer was washed with brine. The solvent was evaporated and the product was purified by flash chromatography (hex/EA: 100/0 to 80/20) to give a colorless oil (0.41 g, 52%). The spectra of the compound matched with those reported in literature.[51]



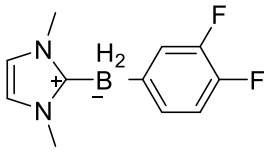
3-Bromo-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 94:[51]

The 2,6 dibromo phenol (0.5 g, 1.98 mmol) and HMDS (0.35 g, 2.18 mmol) were mixed in dry THF (5 mL) in a dry rbf and refluxed for 1.5 h. The solvent was evaporated and the remaining HMDS was pumped off. Crude NMR was taken to confirm removal of HMDS. The product was used as is in the next reaction. To a solution of the di-bromo TMS ether (0.64 g, 1.98 mmol) in THF was added n-BuLi (1.23 mL, 1.98 mmol) at −100 °C under argon. The temperature (outer bath) was slowly allowed to rise to − 80 °C and then cooled again to −100 °C. Triflic anhydride (0.61 g, 2.17 mmol) was added dropwise maintaining the temperature. After addition was complete temperature was allowed to rise to −70 °C and the reaction was quenched with sat $NaHCO_3$. The crude mixture was extracted 3 times with ether and the organic layer was washed with brine. The solvent was evaporated and the product was purified by flash chromatography (hex/EA: 100/0 to 80/20) to give a colorless oil (0.21 g, 29%). The spectra of the compound matched with those reported in literature.[51]



3-(Trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate 95:[51]

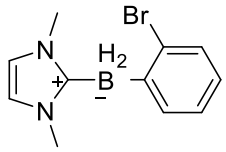
The bromo naphthol (1 g, 4.48 mmol) and HMDS (0.79 g, 4.9 mmol) were mixed in dry THF (10 mL) in a dry rbf and refluxed for 1.5 h. The solvent was evaporated and the remaining HMDS was pumped off. Crude NMR was taken to confirm removal of HMDS. The product was used as is in the next reaction. To a solution of the bromo naphthol TMS ether (1.2 g, 4.42 mmol) in THF was added n-BuLi (3.1 mL, 4.94 mmol) at −100 ^{o}C under argon. The temperature (outer bath) was slowly allowed to rise to −80 ^{o}C and then cooled again to − 100 ^{o}C. Triflic anhydride (1.52 g, 5.39 mmol) was added dropwise maintaining the temperature. After addition was complete temperature was allowed to rise to − 70 ^{o}C and the reaction was quenched with sat $NaHCO_3$. The crude mixture was extracted 3 times with ether and the organic layer was washed with brine. The solvent was evaporated and the product was purified by flash chromatography (hex/EA: 100/0 to 80/20) to give a colorless oil (1.36 g, 86%). The spectra of the compound matched with those reported in literature.[51]



(3,4-Difluorophenyl)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)dihydroborate 98:[21]

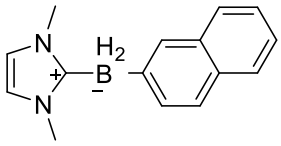
KF (37 mg, 0.64 mmol) was added to an oven dried flask and was flame dried again under vacuum. After cooling under argon, 18-crown-6 (0.17 g, 0.64 mmol) was added followed by addition of NHC-borane **12** (71 mg, 0.64 mmol) and dry THF (3 mL). Benzyne precursor **93** (0.1 g, 0.32 mmol) was added at room temperature. After 6 h, the solvent was evaporated. The crude product

was evaporated by flash chromatography (hexane: ethyl acetate, 4:1 to 1:1) to give a white solid (37 mg, 52%). The spectra of the compound matched with those reported in literature.[21]



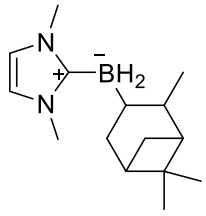
(2-Bromophenyl)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)dihydroborate 99:[21]

KF (64 mg, 1.1 mmol) was added to an oven dried flask and was flame dried again under vacuum. After cooling under argon, 18-crown-6 (0.29 g, 1.1 mmol) was added followed by addition of NHC-borane **12** (0.12 g, 1.1 mmol) and dry THF (10 mL). Benzyne precursor **94** (0.21 g, 0.55 mmol) was added at room temperature. After 24 h, the solvent was evaporated. The crude product was evaporated by flash chromatography (hexane: ethyl acetate, 3:1 to 1:1) to give a white solid (61 mg, 42%). The spectra of the compound matched with those reported in literature.[21]



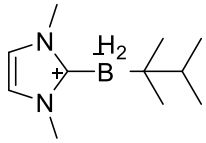
(1,3-Dimethyl-1*H*-imidazol-3-ium-2-yl)(naphthalen-2-yl)dihydroborate 100:[21]

KF (0.16 g, 2.9 mmol) was added to an oven dried flask and was flame dried again under vacuum. After cooling under argon, 18-crown-6 (0.76 g, 2.9 mmol) was added followed by addition of NHC-borane **12** (0.31 g, 2.9 mmol) and dry THF (10 mL). Benzyne precursor **95** (0.5 g, 1.43 mmol) was added at room temperature. After 6 h, the solvent was evaporated. The crude product was evaporated by flash chromatography (hexane: ethyl acetate, 3:1 to 1:1) to give a white solid (0.19 g, 55%). The spectra of the compound matched with those reported in literature.[21]



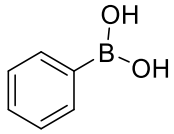
(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)(2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl) dihydroborate 101:[17]

Iodine (50 mg, 0.2 mmol) was added to a solution of NHC-borane **12** (0.22 g, 2 mmol) in DCM (2 mL). Immediate bubbling was observed and the mixture was stirred for 10 min before α-pinene (0.3 g, 2.2 mmol) was added. After stirring the reaction mixture for 16 h at room temperature, the solvent was evaporated and the crude product was purified by flash chromatography to give a white solid (0.49 g, 61%). The spectra of the compound matched with those reported in literature.[17]



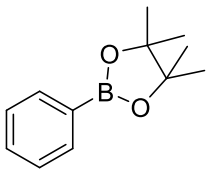
(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)(2,3-dimethylbutan-2-yl)dihydroborate 102:[17]

Iodine (25 mg, 0.1 mmol) was added to a solution of NHC-borane **12** (0.11 g, 1 mmol) in DCM (1 mL). Immediate bubbling was observed and the mixture was stirred for 10 min before 2,3-dimethyl-but-2-ene (84 mg, 1.1 mmol) was added. After stirring the reaction mixture for 24 h at room temperature, the solvent was evaporated and the crude product was purified by flash chromatography to give a white solid (0.12 g, 61%). The spectra of the compound matched with those reported in literature.[17]



Synthesis of phenyl boronic acid 104 from NHC-borane 29:

Br_2 (80 mg, 0.5 mmol) was added to a solution of NHC-borane **29** (93 mg, 0.5 mmol) in DCM (0.5 mL). Immediate bubbling was observed and water (0.1 mL) was added to the reaction mixture. After 30 min, ^{11}B NMR spectrum was taken which showed the presence of 1 peak (singlet at 29 ppm) which indicates complete conversion to phenyl boronic acid **104**.



4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane 105:

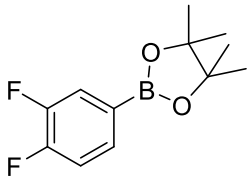
A) Using NBS and pinacol:

NBS (0.18 g, 1 mmol) was added to a solution of NHC-borane **29** (93 mg, 0.5 mmol) in DCM (0.5 mL). Immediate bubbling was observed and water (0.1 mL) was added to the reaction mixture. After 30 min, ^{11}B NMR spectrum was taken which showed the presence of 1 peak (singlet at 29 ppm) which indicates complete conversion to phenyl boronic acid **104**. The solvent was then evaporated and toluene (1 mL) was added to the residue along with molecular sieves and pinacol (60 mg, 0.5 mmol). The mixture was heated to reflux for 12 h and the solvent was evaporated. The residue was purified by flash chromatography to give a colorless oil (54 mg, 53%). The spectra of the compound matched with those reported in literature.

B) Using HCl and pinacol:

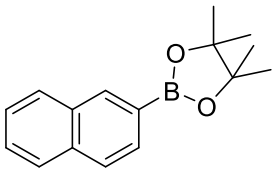
2 M HCl (aq) (0.65 mL, 1.3 mmol) was added to a solution of NHC-borane **29** (93 mg, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room

temperature for 3 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:1) to give a colorless oil **105** (76 mg, 75%).



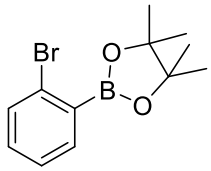
2-(3,4-Difluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 106:

Compound **106** was prepared using the same procedure as **105** using NHC-borane **98** (0.11 g, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 6 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:1) to give a colorless oil **106** (83 mg, 69%). The spectra of the compound matched with those reported in literature.[102]



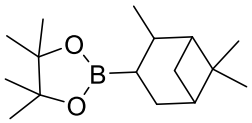
4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane 107:

Compound **107** was prepared using the same procedure as **105** using NHC-borane **100** (0.12 g, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 6 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:1) to give a colorless oil **107** (91 mg, 72%). The spectra of the compound matched with those reported in literature.[103]



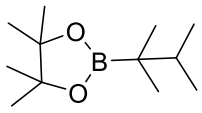
2-(2-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 110:

Compound **110** was prepared using the same procedure as **105** using NHC-borane **99** (0.13 g, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 6 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:1) to give a colorless oil **110** (0.11 g, 78%). The spectra of the compound matched with those reported in literature.[104]



4,4,5,5-Tetramethyl-2-(2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)-1,3,2-dioxaborolane 111:

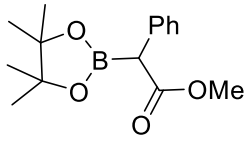
Compound **111** was prepared using the same procedure as **105** using NHC-borane **101** (0.12 g, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 8 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:2) to give a colorless oil **111** (0.1 g, 78%). The spectra of the compound matched with those reported in literature.[105]



2-(2,3-Dimethylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 112:

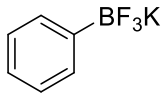
Compound **111** was prepared using the same procedure as **105** using NHC-borane **102** (97 mg, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 8 h and then evaporated. The crude material was purified by flash column

chromatography (hexane: ethyl acetate, 95:5 to 1:2) to give a colorless oil **112** (86 mg, 81%). The spectra of the compound matched with those reported in literature.[106]



Methyl 2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acetate 113:

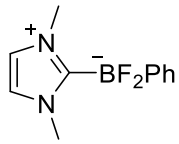
2 M HCl (aq) (0.65 mL, 1.3 mmol) was added to a solution of NHC-borane **27** (93 mg, 0.5 mmol) and pinacol (0.236 g, 1 mmol) in CH_3CN (6 mL). The reaction mixture was stirred at room temperature for 3 h and then evaporated. The crude material was purified by flash column chromatography (hexane: ethyl acetate, 95:5 to 1:2) but the target product **113** was not observed in the ^1H or ^{11}B NMR spectrum. The spectra of the compound matched with those reported in literature.



Synthesis of phenyltrifluoroborate salt 114 from NHC-borane 29:

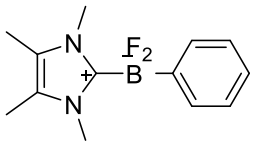
Br_2 (80 mg, 0.5 mmol) was added to a solution of NHC-borane **29** (93 mg, 0.5 mmol) in DCM (0.5 mL). Immediate bubbling was observed and water (0.1 mL) was added to the reaction mixture. After 30 min, ^{11}B NMR spectrum was taken which showed the presence of 1 peak (singlet at 29 ppm) which indicates complete conversion to phenyl boronic acid **104**. The solvent was evaporated and acetone (1 mL) was added as the fresh solvent followed by KHF_2 (0.12 g, 1.5 mmol). The reaction mixture was stirred for 1.5 h. Crude ^{11}B NMR spectrum showed a quartet at 3.4 ppm indicating complete conversion to the target product. The solvent was evaporated and the product was attempted to be purified by recrystallization from acetone. ^1H NMR spectrum showed the presence of imidazolium salt as well as target product.

4.1.3 Fluorination of NHC-boranes



1,3-Dimethylimidazol-2-ylidene difluoro(phenyl)borane 51:

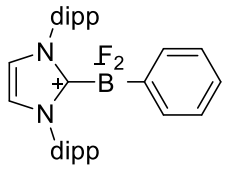
Selectfluor (1.066 g, 3 mmol) was added to a solution of the NHC-borane **29** (0.28 g, 1.5 mmol) in acetonitrile (30 mL) under argon at room temperature. After 2 h, the solvent was evaporated. The crude product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:2) to give a white solid (0.28 g, 83%): M.P 80-83 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ7.45 (d, J = 7 Hz, 2H arom.), 7.28-7.20 (m, 3H, H arom.) 6.8 (s, 2H, =CH(N)), 3.82 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 130.9 (t, $J_{C\text{-}F}$ = 3.8 Hz), 127.5, 126.8, 121.7, 36.6 ; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 4.6 (t, $J_{B\text{-}F}$ = 62.4 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –156.9 (bq, $J_{F–B}$ = 65.8 Hz); HRMS calcd for $C_{11}H_{13}{}^{11}BN_2F_2Na$ 245.1032, found 245.1034.



1,3-tetramethylimidazol-2-ylidene difluoro(phenyl)borane 123:

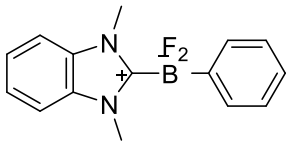
Compound **123** was prepared using the same procedure as NHC-difluoro borane **51** by using Tetramethyl-NHC phenylborane **122** (0.11 g, 0.5 mmol) and Selectfluor (0.35 g, 1 mmol) in acetonitrile. After 1 h, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:2) to give a white solid (0.11 g, 87%); MP 87-90 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.46 (d, J = 6.8 Hz, 2H arom.), 7.28-7.24 (t, 2H arom.), 7.20 (t, J = 7.2 Hz), 3.82 (s, 6H, *N*-Me), 2.12 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 130.9 (t, $J_{C\text{-}F}$ = 3.14 Hz), 127.4, 126.5, 124.7, 32.6 (t, $J_{C\text{-}F}$ = 5.65 Hz), 8.5; ^{11}B NMR (BF_3•OEt_2, 128 MHz) δ 4.7

(t, $J_{B\text{-}F}$ = 62.7 Hz); ^{19}F NMR ($CFCl_3$, 376 MHz) δ –156 (bq); HRMS calcd for $C_{13}H_{17}{}^{11}BN_2F_2Na$ 273.1345 found 273.1348.



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene difluoro(phenyl)borane 124:

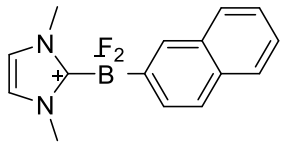
Compound **124** was prepared using the same procedure as **51** by using dipp-NHC phenylborane **88** (0.24 g, 0.5 mmol) and Selectfluor (0.35 g, 1 mmol) in acetonitrile. After 3 h, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 10:1 to 2:1) to give a white solid (0.186 g, 72%); M.P 222-225 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.8 Hz, 2H, H arom.), 7.26 (d, *J* = 8 Hz, 4H, arom.), 7 (s, 2H, =CH(N)), 6.93 (t, *J* = 7 Hz, 1H, arom.), 6.88 (t, *J* = 7.2 Hz, 2H, arom.), 6.77 (d, *J* = 6.8 Hz, 1H, arom.), 2.57 (sept, *J* = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.19 (d, *J* = 6.8 Hz, 12H, Me), 1.09 (d, *J* = 6.8 Hz, 12H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.3, 134.1, 131.6, 130.2, 126.4, 123.7, 123.5, 28.8, 25.7, 22.1; ^{11}B NMR (BF_3•Et_2O, 128 MHz, $CDCl_3$) δ 3.5 (br s) ^{19}F NMR ($CFCl_3$, 376 MHz) δ –153.4 (br q); HRMS calcd for $C_{33}H_{41}{}^{11}BN_2F_2Na$ 537.3223, found 537.3224.



1,3-Dimethylbenzimidazol-2-ylidene difluoro(phenyl)borane 126:

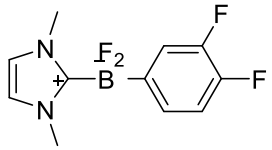
Compound **126** was prepared using the same procedure as NHC-difluoro borane **51** by using Benzimidazole-NHC phenylborane **125** (0.13 g, 0.5 mmol) and Selectfluor (0.35 g, 1 mmol) in acetonitrile. After 90 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 5:1 to 1:1) to give a white solid (0.12 g, 90%); MP 100-

102 °C ; ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.54-7.47 (m, 6H arom.), 7.28 (t, *J* = 7.6 Hz, 2H, H arom.) 7.21 (t, *J* = 7.2 Hz, 1H, H arom.), 4.1 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.2 , 130.9 (t, $J_{C\text{-}F}$ = 3 Hz), 127.6, 127 (t, $J_{C\text{-}F}$ = 9 Hz), 125.2, 112.6, 111.5, 32.6 (t, $J_{C\text{-}F}$ = 4.5 Hz); ^{11}B NMR (BF_3•OEt_2, 128 MHz) δ 4.9 (t, $J_{B\text{-}F}$ = 57 Hz); ^{19}F NMR ($CFCl_3$, 376 MHz) δ –156.4 (bq); HRMS calcd for $C_{11}H_{13}{}^{11}BN_2F_2Na$ 295.1189, found 295.1192.



1,3-Dimethylimidazol-2-ylidene difluoro(naphthyl)borane 118:

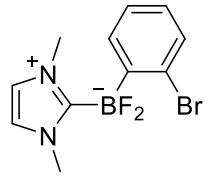
Compound **118** was prepared using the same procedure as NHC-difluoro borane **51** by using the corresponding NHC-borane **100** (0.19 g, 0.79 mmol) and Selectfluor (0.56 g, 1.58 mmol) in acetonitrile. After 1 h, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 6:1 to 1:2) to give an off-white solid (0.15 g, 70%); MP 94-96 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.9 (s, 1H arom.), 7.8-7.74 (m, 3H arom.), 7.59 (d, *J* = 8 Hz, 1H arom.), 7.41-7.38 (m, 2H arom.) 6.83 (s, 2H, =CH(N)), 3.91 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 133.4 , 133, 130 (t, $J_{C\text{-}F}$ = 3.8 Hz), 129.3 (t, $J_{C\text{-}F}$ = 3.8 Hz), 127.9, 127.5, 126.6, 125.1, 124.9, 121.7, 36.7 (t, $J_{C\text{-}F}$ = 5 Hz); ^{11}B NMR (BF_3•OEt_2, 128 MHz) δ 4.75 (br s); ^{19}F NMR ($CFCl_3$, 376 MHz) δ –156.8 (bq); HRMS calcd for $C_{11}H_{13}{}^{11}BN_2F_2Na$ 295.1189, found 295.1192.



1,3-Dimethylimidazol-2-ylidene difluoro(3,4-difluorophenyl)borane 119:

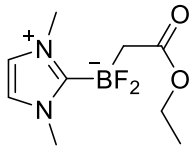
Compound **119** was prepared using the same procedure as NHC-difluoro borane **51** by using corresponding NHC-borane **98** (0.13 g, 0.6 mmol) and Selectfluor (0.43 g, 1.2 mmol) in

acetonitrile. After 15 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:2) to give a colorless oil (0.13 g, 81.2%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.19 (br t, J = 10 Hz, 1H arom.), 7.11-7 (m, 2H, H arom.) 6.87 (s, 2H, =CH(N)), 3.85 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 150.2 (dd, $J_{C\text{-}F}$ = 13.8 Hz, $J_{C\text{-}F}$ = 248.8 Hz), 149.6 (dd, $J_{C\text{-}F}$ = 9 Hz, $J_{C\text{-}F}$ = 245 Hz), 126.6 (br dt), 121.9, 119.2 (dt, $J_{C\text{-}F}$ = 3.8 Hz, $J_{C\text{-}F}$ = 12.5 Hz), 116.3 (d, $J_{C\text{-}F}$ = 15 Hz), 36.6 (t, $J_{C\text{-}F}$ = 3.8 Hz) ; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 3.96 (t, $J_{B\text{-}F}$ = 58.9 Hz); ^{19}F NMR ($CFCl_3$, 376 MHz) δ –140.9 to –141 (ddd, $J_{H\text{-}F}$ = 7.5 Hz, $J_{H\text{-}F}$ = 11.3 Hz, $J_{F\text{-}F}$ = 18.8 Hz), –141.9 to –142.1 (ddt, $J_{H\text{-}F}$ = 3.8 Hz, $J_{H\text{-}F}$ = 7.5 Hz, $J_{F\text{-}F}$ = 18.8 Hz), –156.4 (bq); HRMS calcd for $C_{11}H_{11}{}^{11}BN_2F_4Na$ 281.0484 found 281.0847.



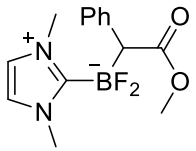
1,3-Dimethylimidazol-2-ylidene difluoro(2-bromophenyl)borane 120:

Compound **120** was prepared using the same procedure as NHC-difluoro borane **51** by using corresponding NHC-borane **99** (0.13 g, 0.5 mmol) and Selectfluor (0.35 g, 1 mmol) in acetonitrile (5 mL). After 15 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:3) to give a white solid (0.13 g, 83%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ7.82 (d, J = 7 Hz, 1H arom.), 7.38 (d, J = 7 Hz, 1H, H arom.) 7.28 (t, J = 7 Hz, 1H, H arom.), 7.07 (t, J = 7 Hz, 1H, H arom.), 6.83 (s, 2H, =CH(N)), 3.74 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 134.25 (t, $J_{C\text{-}F}$ = 3.75 Hz), 132.1, 128.8, 127.9, 126.5, 121.7, 36.6 (t, $J_{C\text{-}F}$ = 3.75 Hz) ; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 3.82 (t, $J_{B\text{-}F}$ = 59 Hz); ^{19}F NMR ($CFCl_3$, 376 MHz) δ –157.7 (q, $J_{B\text{-}F}$ = 54 Hz).



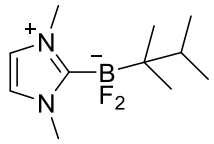
1,3-Dimethylimidazol-2-ylidene difluoro(2-methoxy-2-oxoethyl)borane 133:

Compound **133** was prepared using the same procedure as NHC-difluoro borane **51** by using substituted NHC-borane **128** (0.16 g, 0.85 mmol) and Selectfluor (0.63 g, 1.7 mmol) in acetonitrile. After 5 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 2:1 to 1:10) to give a colorless oil (0.11 g, 56%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ6.89 (s, 2H, =CH(N)), 3.95 (q, J = 7 Hz, CH_2), 3.87 (s, 6H, *N*-Me), 1.79 (t, *J* = 8.5 Hz, 2H, CH_2-B), 1.14 (t, *J* = 7 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.1, 121.8, 59.6, 36.3, 31.8, 14.3; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 4.45 (t, $J_{B\text{-}F}$ = 64.2 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –152.4 (q, $J_{B\text{-}F}$ = 65.8 Hz).



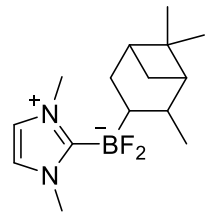
1,3-Dimethylimidazol-2-ylidene difluoro(2-methoxy-2-oxo-1-phenylethyl)borane 134:

Compound **134** was prepared using the same procedure as NHC-difluoro borane **51** by using substituted NHC-borane **27** (0.26 g, 1 mmol) and Selectfluor (0.74 g, 2 mmol) in acetonitrile. After 5 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 2:1 to 1:10) to give a white solid (0.17 g, 57%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ7.24-7.20 (m, 2H arom.), 7.17-7.14 (m, 2H arom.) 7.1-7.04 (m, 1H arom.),6.76 (s, 2H, =CH(N)) 3.66 (s, 3H, Me), 3.46 (s, 6H, *N*Me), 3.36 (br s, 1H, CH-B); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.4, 139.9, 128.1, 127.7, 124.8, 121.8, 51.1, 36.2; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 4.41 (t, $J_{B\text{-}F}$ = 65.6 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –153 (m), –155 (m).



1,3-Dimethylimidazol-2-ylidene difluoro(2,3-dimethylbutan-2-yl)borane 131:

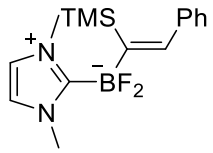
Compound **131** was prepared using the same procedure as **51** by using dipp-NHC phenylborane **102** (97 mg, 0.5 mmol) and Selectfluor (0.35 g, 1 mmol) in acetonitrile. After 1 h, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 2:1 to 1:3) to give a white solid (0.1 g, 89%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 2H, =CH(N)), 3.92 (s, 3H, *N*Me), 1.68 (sept, *J* = 6.8 Hz, 1H, $CH(CH_3)_2$), 0.87 (d, *J* = 6.8 Hz, 6H, Me), 0.65 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 121.8, 37.1, 33.5, 21.8, 18.8; ^{11}B NMR (BF_3•Et_2O, 128 MHz, $CDCl_3$) δ 7.73 (t, $J_{B\text{-}F}$ = 71.7 Hz) ^{19}F NMR ($CFCl_3$, 376 MHz) δ –156 (br q).



1,3-Dimethylimidazol-2-ylidenedifluoro(2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)borane 130:

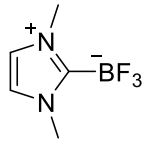
Compound **130** was prepared using the same procedure as NHC-difluoro borane **51** by using the corresponding NHC-borane **101** (0.19 g, 0.79 mmol) and Selectfluor (0.56 g, 1.58 mmol) in acetonitrile. After 2 h, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 6:1 to 1:3) to give an off-white solid (0.15 g, 70%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.87 (s, 2H =CH(N)), 3.93 (s, 6H, Me), 2.2 (m, 1H), 1.95 (m, 1H), 1.84 (m, 1H), 1.78 (m, 2H), 1.66 (m, 1H), 1.15 (s, 3H), 1.04 (s, 3H), 0.96 (d, J = 9 Hz, 1H), 0.8 (m, 1H), 0.66 (d, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 121.5, 48.7, 41.8, 38.9, 37.6, 37.5,

36.5 (t, $J_{C\text{-}F}$ = 5 Hz), 28.3, 23.1, 22.9 ;^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 6.28 (br s); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –161.6 (bq), –164 (bq).



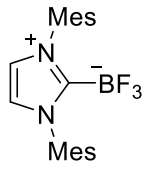
1,3-Dimethylimidazol-2-ylidene difluoro(2-phenyl-1-(trimethylsilyl)vinyl)borane 132:

Compound **132** was prepared using the same procedure as NHC-difluoro borane **51** by using the corresponding alkenyl NHC-borane **127** (0.28 g, 1 mmol) and Selectfluor (0.74 g, 2 mmol) in acetonitrile. After 5 min, the solvent was evaporated and product was purified by flash chromatography (hexane: ethyl acetate, 4:1 to 1:2) to give a white solid (85 mg, 26%); ^{1}H NMR (C_6D_6, 500 MHz) δ 7.31 (m, 2H arom.), 7.16 (m, 1H arom.), 7.07 (m, 1H arom.), 7. 03(m, 1H arom.), 5.54 (s, 1H), 3.28 (s, 6H, Me), 0.42 (s, 9H, *Si*Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 145.7 (t, J = 8.75 Hz), 144.3, 128.5, 126.5, 122.4, 120.7, 36 (t, $J_{C\text{-}F}$ = 4 Hz); ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 6.42 (br s); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –146.6 (bq).



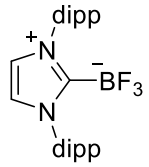
1,3-Dimethylimidazol-2-ylidene trifluoroborane 47:

Selectfluor **59** (0.21 g, 0.6 mmol) was added to a solution of NHC-borane **12** (22 mg, 0.2 mmol) in acetonitrile (2 mL). After 3 h, the solvent was evaporated. The crude product was purified by flash chromatography to (hexane: ethyl acetate, 3:1 to 1:5) to give a white solid (24 mg, 73%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.91 (s, 2H, =CH(N)), 3.93 (s, 6H, Me); ^{13}CNMR ($CDCl_3$, 125 MHz) δ 122, 36.5; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ –0.24 (q, $J_{B\text{-}H}$ = 35.2 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –140.1 (q, $J_{F\text{–}B}$ = 37.6 Hz).



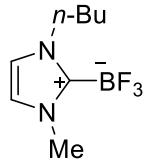
1,3-Dimesitylimidazol-2-ylidene trifluoroborane 137:

Selectfluor (0.21 g, 0.6 mmol) was added to a solution of NHC-borane **136** (64 mg, 0.2 mmol) in acetonitrile (2 mL). After 12 h, the solvent was evaporated. The crude product was purified by flash chromatography to (hexane: ethyl acetate, 8:1 to 1:1) to give a white solid (54 mg, 72%).^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 (s, 2H, =CH(N)), 7.0 (s, 4H, arom.), 2.34 (s, 6H, Me), 2.11 (s, 12H, Me); ^{13}CNMR ($CDCl_3$, 125 MHz) δ 139.7, 134.6, 129, 122.4, 21.1, 17.2 ; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ –0.88 (q, $J_{B\text{-}F}$ = 33.6 Hz).



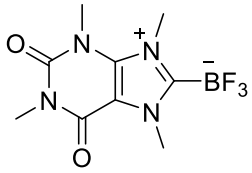
1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene trifluoroborane 54:

Selectfluor (0.21 g, 0.6 mmol) was added to a solution of NHC-borane **11** (84 mg, 0.2 mmol) in acetonitrile. After 12 h, solvent was evaporated. The crude product was purified by flash chromatography to (hexane: ethyl acetate, 3:1 to 1:4) to give a white solid (48 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, J = 7.6 Hz, 2H, H arom.), 7.29 (d, J = 7.6 Hz, 4H, arom.), 7.1 (s, 2H, =CH(N)), 2.53 (sept, J = 6.8 Hz, 4H, $CH(CH_3)_2$), 1.31 (d, J = 6.8 Hz, 12H, Me), 1.18 (d, J = 6.8 Hz, 12H, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 133.1, 130.5, 123.8, 123.3, 29.9 , 23.1, 22.8; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ –0.84 (q, $J_{B\text{-}F}$ = 33.6 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –140.3 (q, $J_{F\text{–}B}$ = 33 Hz).



(1-Butyl-3-methyl-1H-imidazol-3-ium-2-yl)trihydroborate 139:

Selectfluor (0.53 g, 1.5 mmol) was added to a solution of NHC-borane **138** (76 mg, 0.5 mmol) in acetonitrile. After 4 h, solvent was evaporated. The crude product was purified by flash chromatography to (hexane: ethyl acetate, 3:1 to 1:4) to give a white solid (48 mg, 73%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ6.96 (d, *J* = 2 Hz, 1H, =CH(N)), 6.94 (d, *J* = 2 Hz, 1H, =CH(N)), 4.26 (t, J = 7.5 Hz, 2H, *N*CH_2), 3.93 (s, 6H, Me), 1.81 (m, 2H, CH_2), 1.38 (m, 2H, CH_2), 0.96 (t, J = 7.5 Hz, CH_3) ; ^{13}C NMR ($CDCl_3$, 125 MHz): δ122, 120.5, 49.3, 36.4, 33.1, 19.6, 13.5; ^{11}B NMR (BF_3•OEt_2, 160 MHz):δ − 0.22 (q, J_{B-F} = 36.9 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz):δ –139.8 (q, $J_{F–B}$ = 37.6 Hz).



1,3,7,9-Tetramethyl-8-(trifluoro-l4-boranyl)-3,7,8,9-tetrahydro-1H-purine-2,6-dione 141:

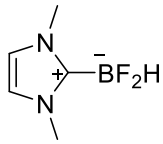
Selectfluor (0.106, 0.3 mmol) was added to a solution of caffeine-borane **140** in acetonitrile. After 12 h, the solvent was evaporated. The crude product was purified by flash chromatography to (hexane: ethyl acetate, 3:1 to 1:4) to give a white solid (18 mg, 66%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.29 (s, 3H, N*Me*), 4.23 (s, 3H, N*Me*), 3.85 (s, 3H, N*Me*), 3.43 (s, 3H, N*Me*); ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ –0.43 (q, J_{B-F} = 33.6 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz) δ –138.1 (q, $J_{F–B}$ = 33 Hz).

Reaction of NHC-borane 12 with 1 equiv of Selectfluor:

Selectfluor (0.35 g, 1 mmol) was added to a solution of the NHC-borane **12** (0.19 g, 1 mmol) in acetonitrile (10 mL) under argon at room temperature. ^{11}B NMR spectrum of the reaction mixture was recorded after 10 min. The spectrum showed presence of NHC-difluoro borane **145** (doublet of triplets at 2.2 ppm), mono-fluorination product **144** (doublet of triplets at −6 ppm), NHC-trifluoroborane **47** and unreacted NHC-borane **12**. After 30 min, the peak for the mono-fluorination product disappears. The solvent was evaporated and the product was purified by flash chromatography (hexane : ethyl acetate, 3:1 to 100%). The difluoro NHC-borane **145** and NHC-trifluoroborane **47** were isolated as an inseparable mixture.

Reaction of NHC-borane 12 with 2 equiv of Selectfluor:

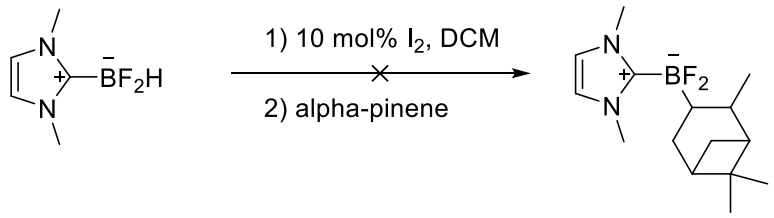
Selectfluor (0.7 g, 2 mmol) was added to a solution of the NHC-borane **12** (0.19 g, 1 mmol) in acetonitrile (10 mL) under argon at room temperature. ^{11}B NMR spectrum of the reaction mixture after 30 min showed the presence of NHC-difluoro borane **145** (doublet of triplets at 4.61 ppm) as the minor product (19%) and NHC-trifluoroborane **47** as the major product (80%). Almost no mono-fluorination product **144** peak was observed.



(1,3-Dimethyl-1*H*-imidazol-3-ium-2-yl)difluorohydroborate 143:

I_2 (0.51 g, 2 mmol) was added to a solution of diMe-Imd-BH_3 **12** (0.11 g, 1 mmol) in DCM (5 mL). Bubbling was observed and the reaction mixture was stirred at rt for 15 min. TBAF (2 mL, 1 M in THF, 2 mmol) was added to the solution and the reaction was quenched immediately by adding sat.$NaHCO_3$ (5 mL). The product was extracted with DCM 3 times and the solvent was evaporated and the crude product was purified ;by flash chromatography (hexane : ethyl acetate,

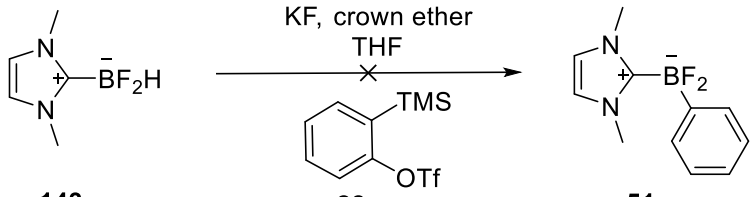
1:1 to 100 %) to give a white solid (40 mg, 29%): M.P 110-115 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.9 (s, 2H arom.), 3.89 (s, 6H, Me); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 121.5, 35.6; ^{11}B NMR (BF_3•OEt_2, 160 MHz) δ 2.1 (dt, $J_{B\text{-}F}$ = 72 Hz, $J_{B\text{-}H}$ = 120 Hz); ^{19}F NMR ($CFCl_3$, 470 MHz): δ–165.8 (dq, $J_{F–B}$ = 70 Hz, $J_{F\text{-}H}$ = 14.1 Hz); HRMS calcd for $C_5H_8N_2BF_2$ 145.07431 found 145.07355.



143 **130**

Iodine catalyzed hydroboration of α-pinene with diMe-Imd-BF_2H 143:

Iodine (5.1 mg, 0.02 mmol) was added to a solution of diMe-Imd-BF_2H **143** (30 mg, 0.2 mmol). Bubbling was observed indicating evolution of H_2 gas. α-pinene (30 mg, 0.22 mmol) was added immediately. An ^{11}B NMR spectrum was taken after 15 min. Only two peaks were observed in the 11B NMR spectrum, quartet at 0.24 ppm (corresponding to diMe-Imd-BF_3 **47**) and a quartet at −36 ppm (corresponding to diMe-Imd-BH_3 **12**). No change was seen in the crude ^{11}B NMR spectrum after 3 h, so the reaction was discontinued.



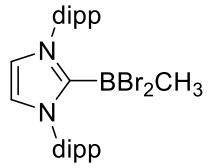
143 **28** **51**

Hydroboration of benzyne precursor 28 with diMe-Imd-BF_2H 143:

KF (11 mg, 0.2 mmol) was added to an oven dried flask and was flame dried again under vacuum. After cooling under argon, 18-crown-6 (53 mg, 0.2 mmol) was added followed by addition of diMe-Imd-BF_2H **143** (30 mg, 0.2 mmol) and dry THF (0.5 mL). Benzyne precursor **28** (29 mg,

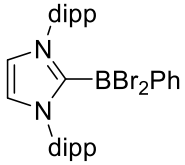
0.1 mmol) was added at room temperature. After 6 h, crude 11B NMR spectrum was taken which showed no conversion to target product. The reaction was discontinued after no change was observed in the ^{11}B NMR spectrum after 24 h.

4.1.4 Suzuki coupling



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene dibromo methylborane 194:

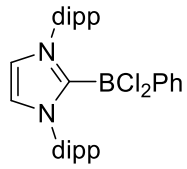
Bromine (1 M in DCM, 0.05 mL) was added a solution of NHC-borane **83** (20 mg, 0.048 mmol) in DCM in a flask under argon. Intense bubbling was observed. An ^{11}B NMR spectrum after 10 min showed that the peak at –28 ppm (starting material **83**) disappeared and there was a new peak at –4.26 ppm assigned to target product **194**. The septum of the flask was removed. After 15 min, ^{11}B NMR spectrum showed the presence of decomposition peaks along with the product peak. Flash chromatography was not attempted.



1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene dibromo phenylborane 195:

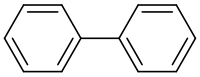
Bromine (1 M in DCM, 0.1 mL) was added a solution of NHC-borane **87** (47.8 mg, 0.1 mmol) in DCM in a flask under argon. Intense bubbling was observed. An ^{11}B NMR spectrum after 10 min showed that the peak at –24 ppm (starting material **87**) disappeared and there was a new peak at –

2.4 ppm assigned to target product **195**. Flash chromatography was not attempted and the product was used directly for the next reaction.



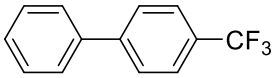
1,3-Bis-(2,6-diisopropylphenyl)imidazol-2-ylidene dichloro phenylborane 196:

N-Chlorosuccinimide (18 mg, 0.13 mmol) was added to a solution of NHC-borane **87** (30 mg, 0.063 mmol) in DCM under argon. An ^{11}B NMR spectrum after 15 min showed the disappearance of starting material peak (triplet at –24 ppm) and appearance of a new peak at 1.7 ppm assigned to target product **196**. The solvent was evaporated and purification of the crude product was attempted via flash chromatography. ^{1}H NMR and ^{11}B NMR spectrum showed that the product recovered from the column was phenylboronic acid **104**.



Biphenyl 167 from di-bromo NHC-borane 196:

Iodobenzene **165** (3.2 mg, 0.016 mmol) was added to freshly prepared di-bromo NHC-borane **196** (10 mg, 0.016 mmol) in dioxane. Palladium catalyst $Pd(OAc)_2$ (10 mol %, 0.0016 mmol), PPh_3 (10 mol %, 0.0016 mmol), cesium carbonate (20 mg, 0.063 mmol) and water were added to the reaction under argon. The mixture was refluxed for 6 h till completion of the reaction. The solvent was evaporated and the residue was purified by prep TLC (hexane) yielding a white solid (1 mg, 25%).



4-Phenylbenzotrifluoride 199 from di-bromo NHC-borane 196:

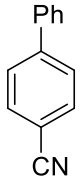
4-bromo benzotrifluoride **198** (22.5 mg, 0.1 mmol) was added to freshly prepared di-bromo NHC-borane **196** (63.5 mg, 0.1 mmol) in dioxane. Palladium catalyst $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.01 mmol), cesium carbonate (0.13 g, 0.4 mmol) and water were added to the reaction under argon. After 4 h, the solvent was evaporated and the residue was purified by flash chromatography (hexane) yielding a white solid **196** (7 mg, 31%).

Control reaction (No palladium or aryl bromide):

NHC-difluoro borane 8 (22.2 mg, 0.1 mmol) was added to a solution of cesium carbonate (97.7 mg, 0.3 mmol) in methanol-d_4 and the mixture was refluxed. The reaction was monitored by ^{11}B and ^{19}F NMR spectroscopy. After 3 h, new singlet (−147 ppm) is seen in the ^{19}F NMR spectrum. The sharp triplet around 5 ppm in the ^{11}B NMR spectrum seems to broaden and is indicative of an $ArB(OR)_3$ species.

Control reaction (No base):

4-Bromobenzonitrile (90 mg, 0.5 mmol) was added to a solution of NHC-di-fluoro borane 8 (0.11 g, 0.5 mmol) in methanol (3 mL). Solution of palladium acetate in methanol (2 mM, 2.5 mL, 10 μmol) was added to the mixture. After refluxing for 16 h, TLC analysis shows negligible presence of the cross-coupled product.



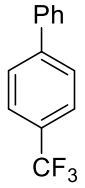
4-Phenylbenzonitrle 184 [Cas No. # 2920-38-9]:

With cesium carbonate:

4-bromobenzonitrile **183** (90 mg, 0.5 mmol) and cesium carbonate (0.98 g, 1.5 mmol) were added to a solution of NHC-difluoro borane **51** (0.11 g, 0.5 mmol) in methanol (3 mL). A solution of palladium acetate in methanol (2 mM, 2.5 mL, 10 μmol) was added to the mixture. After refluxing for 3 h, water (10 mL) was added to precipitate the product. The precipitate was filtered, thoroughly washed with water, then dissolved in diethyl ether and filtered again to eliminate the palladium black. The ether layer was dried over Na_2SO_4 and evaporated. The crude product was purified by flash chromatography (hexane: ethyl acetate, 100:0 to 8:1) giving a white solid (0.16 g, 87%). The spectra of the compound match with those reported in literature.[107]

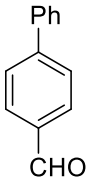
With potassium carbonate:

4-Bromobenzonitrile **183** (90 mg, 0.5 mmol) and cesium carbonate (0.98 g, 1.5 mmol) were added to a solution of NHC-difluoro borane **51** (0.11 g, 0.5 mmol) in methanol (3 mL). A solution of palladium acetate in methanol (2 mM, 2.5 mL, 10 μmol) was added to the mixture. After refluxing for 3 h, the estimated conversion was less than 50%. Following this result, future experiments were done with Cs_2CO_3.



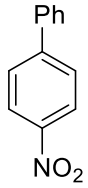
4-Phenylbenzotrifluoride 199 [Cas No. # 398-36-7]:

Compound **199** was prepared following same procedure as **183** by using 4-Bromobenzotrifluoride **198** (0.11 g, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and cesium carbonate in methanol (3 mL). After refluxing for 2 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane) gave the product as a white solid (0.16 g, 72%). The spectra of the compound match with those reported in literature.[107]



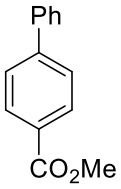
4-Phenylbenzaldehyde 207 [Cas No. # 3218-36-8]:

Compound **207** was prepared following same procedure as **184** by using 4-Bromobenzaldehyde **206** (93 mg, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and potassium carbonate in methanol (3 mL). After refluxing for 2 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane) gave the product as a white solid (0.124 g, 68%). The spectra of the compound match with those reported in literature.[107]



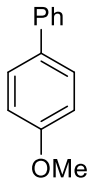
4-Nitro 1,1'-biphenyl 201 [Cas No. # 92-93-3]:

Compound **201** was prepared following the same procedure as **184** by using 4-Bromonitrobenzene **200** (0.1 g, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and cesium carbonate in methanol (1 mL). After refluxing for 1 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane: ethyl acetate, 100:0 to 10:1) gave the product as a yellow solid (0.17 g, 84%). The spectra of the compound match with those reported in literature.[107]



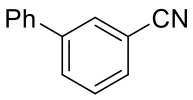
Methyl [1,1'-biphenyl]-4-carboxylate 205 [Cas No. # 72-75-2]:

Compound **205** was prepared following the same procedure as **184** by using Methyl 4-bromobenzoate **204** (0.11 g, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and cesium carbonate in methanol (3 mL). After refluxing for 2 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane: ethyl acetate, 10:1 to 3:1) gave the product as a white solid (0.17 g, 81%). The spectra of the compound match with those reported in literature.[107]



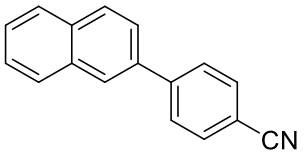
4-Methoxy 1,1'-biphenyl 203 [Cas No. # 613-37-6]:

Compound **203** was prepared following the same procedure as **184** by using 4-Bromoanisole **202** (94 mg, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and cesium carbonate in methanol (3 mL). After refluxing for 4 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane: ethyl acetate, 10:1 to 4:1) gave the product as a white solid (0.15 g, 82%). The spectra of the compound match with those reported in literature.[107]



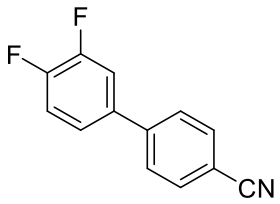
3-Phenylbenzonitrile 209 [Cas No. # 24973-50-0]:

Compound **209** was prepared following same procedure as **184** by using 3-Bromobenzonitrile **208** (90 mg, 0.5 mmol), NHC-difluoro borane **51** (0.11 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and cesium carbonate in methanol (3 mL). After refluxing for 3 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane) gave the product as a white solid (0.145 g, 81%). The spectra of the compound match with those reported in literature.[107]



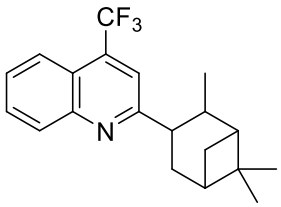
4-(2-Naphthyl)benzonitrile 211 [Cas No. # 93328-79-1]:

Compound **211** was prepared following same procedure as **184** by using 4-Bromobenzonitrile **183** (90 mg, 0.5 mmol), NHC-difluoro borane **119** (0.13 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and potassium carbonate in methanol (3 mL). After refluxing for 4 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane) gave the product as a white solid (0.16 g, 70%). The spectra of the compound match with those reported in literature.



4-(3-4-Difluoro)phenylbenzonitrile 210 [Cas No. # 151559-21-6]:

Compound **210** was prepared following same procedure as **184** by using 4-Bromobenzonitrile **183** (90 mg, 0.5 mmol), NHC-difluoro borane **120** (0.136 g, 0.5 mmol), palladium acetate (2 mM, 2.5 mL, 10 μmol) and potassium carbonate in methanol (3 mL). After refluxing for 4 h, water (10 mL) was added to precipitate the product. Workup and flash chromatography (hexane) gave the product as a white solid (0.15 g, 68%). The spectra of the compound match with those reported in literature.



4-(Trifluoromethyl)-2-(2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)quinoline 229:

NHC-difluoroborane **130** (0.27 g, 1 mmol) and lepidine (0.14 g, 1 mmol) were dissolved in a 1:1 mixture of AcOH:H_2O (13 mL). The mixture was stirred at room temperature till the compounds dissolved. Manganese (III) acetate (0.58 g, 2.5 mmol) was added to the reaction mixture and the mixture was stirred at 50 ^oC for 18 h. The reaction mixture was allowed to cool to room temperature and slowly to a sat.$NaHCO_3$ solution. The product was extracted with ethyl acetate and the organic layer was washed with water and dried with $MgSO_4$. The solvent was evaporated after filtration and the residue was purified by flash chromatography (hexane : ethyl acetate 5:1 to 1:2) to give a colorless oil (0.12 g, 43%). The spectra was identical to the one reported in literature.[101]

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