BORENIUM CATIONS AS CATALYSTS FOR THE REDUCTION OF ORGANIC MOLECULES AND MECHANISTIC INVESTIGATIONS INTO THEIR MODE OF OPERATION

by

Adrian Mark Bailey

A thesis submitted to the Department of Chemistry

In conformity with the requirements for

the degree of Master of Science

Queen's University

Kingston, Ontario, Canada

(October, 2012)

Abstract

The generation and isolation of two novel borenium cations has been described. The observation that the reaction of the Lewis acid $B(C_6F_5)_3$ and the Lewis base diazabicyclo[2.2.2]octane (DABCO) with pinacol borane (HBpin) resulted in the activation of the B–H bond of HBpin and formation of a stable borenium cation/borohydride salt. This stable salt was used as a catalyst in the hydroboration reaction. It was shown to catalytically reduce a wide array of substrates including imines, *N*-heterocycles, nitriles, and ketones using pinacol borane as the source of hydride. Another borenium ion, synthesized from trityl tetrakis-pentafluorophenyl borate, DABCO, and HBpin did not contain a nucleophilic borohydride counterion and it was isolated in the solid state. This salt was also found to reduce the same substrates with similar yields and reaction times.

The mechanisms of both of these catalysts were investigated and were found to be proceeding by a similar borenium catalyzed process. Quantitative analysis of the initial rates of each catalyst under identical conditions yielded rate constants on the same order of magnitude which strongly suggested that both catalysts operated via similar mechanisms. Stoichiometric experiments and isotope labelling using deuterated pinacol borane demonstrated that the nucleophilic counterion was not a kinetically relevant reducing agent under the reaction conditions. Furthermore, these reactions and the use of an isolable iminium ion as a hydride acceptor indicated that the hydride delivery agent was a DABCO•HBpin adduct. The DABCO•HBpin adduct was observed spectroscopically at ambient and subzero temperatures. Lastly, the rate of reduction using pinacol borane and [d_1]-pinacol borane were significantly different and produced a high kinetic isotope effect (KIE = k_H/k_D = 6.6 ± 0.2). This high KIE strongly indicates that hydride delivery is the rate limiting step in the catalytic cycle. With this knowledge an asymmetric model is discussed and the beginnings of the development of an asymmetric borenium cation catalyzed process are described.

Co-Authorship

I hereby declare that this thesis incorporates material that is result of joint research, as follows:

This thesis incorporates the outcome of research undertaken with the assistance of a post doctoral research fellow, Patrick Eisenberger, and doctoral students, Jonathan D. Webb and Cristina Pubill. In all cases, the primary contributions, a majority of the experimental efforts, data analysis and interpretation, were performed by the author. All data contained in the experimental section were acquired by the author.

I certify that, with the above qualification, this thesis, and the research to which it refers, is the product of my own work.

Acknowledgements

During my six years at Queen's I have encountered many hurdles and shared numerous amazing experiences. Luckily, I had some fantastic people to help me climb these mountains and share these eventful times. Among these people are the members of the Crudden group and members of the Department of Chemistry, without whom my time spent in the laboratory would not have been the same. Thus I must thank each and every one of you for your friendship and kinship during this time of learning and growth. First, thank you to Dr. Patrick Eisenberger. Without your bizarre European humour, intense drum and bass music, and incredible knowledge of chemistry I would not have enjoyed my time at Queen's nearly as much. Next, I'd like to thank Dr. Matthew Kitching. It's your critique of my scientific method, your constant questioning of my every chemical choice, and your unwavering support that got me through much of my troubling times over the last two years. I'd also like to thank Dr. Thomas K. Wood. All I should say here is... should we have another Rusty Nail? But I must also say thank you for starting me off in the right direction and helping me stay the course both in and out of chemistry. I will miss you all very much and I will be forever honoured to call you my friends.

No acknowledgement section is complete without paying tribute to "the Boss", Dr. Cathleen Crudden. First, I must thank you for giving me (a confused physicist) the opportunity to learn the trade of organic chemistry and helping me grow into the chemist I have become. You have inspired me and challenged me. You've given me a thick skin and given where I'm going I must thank you for that.

Dr. Nicholas Mosey, I must thank you for always being there when I had questions. Your door was always open and you were always there to talk and ready to do whatever you could to help me get my answer. I have learned so much from you and I will be eternally grateful.

I would to thank my parents for their unending love and support. Without them I would not be where I am today. I must thank them for their friendship and their mentorship in my early

years that enabled me to accomplish what I have done so far in my life. I cannot repay you for the number of times I relied on you in my youth and I can only hope that continuing to make you proud will be payment enough.

Lastly, I would like to thank my partner Monique Kleczek. You have always been there for me. Thank you for giving me strength and inspiration when I needed it. Thank you for taking care of me physically, mentally, and, most importantly, emotionally during this challenging time in my life. You are my best friend and I love you.

Table of Contents

List of Figures

List of Schemes

List of Tables

List of Abbreviations

Name	Abbreviations
9-boracyclo[3.3.1]nonane	9-BBN
1,2-bis-2,5-diarylphospholanylbenzene	DuPhos
1,2-di(cyclohexyl(2-anisole)phosphino)ethane	DiPAMP
1,4-bis(diphenylphosphino)butane	dppb
1,4-diazabicyclo[2.2.2]octane	DABCO
1,5-cyclooctadiene	COD
1,8-diazabicycloundec-7-ene	DBU
2,2'-(2,2-diaryl-1,3-dioxolane-4,5-diyl)bis(propan-2-ol)	TADDOL
2,2,6,6-tetramethylpiperdine	TMP
2,2'-bis(diphenylphosphino)-1,1'-binaphthyl	BINAP
2,2'-oxybis(benzo[1,3,2]dioxaborole	catBOBcat
2,4,6-trimethylphenyl, mesityl-	Mes
2'-amino-[1,1'-binaphthalen]-2-ol	NOBIN
atmospheres	atm
catecholborane	HBcat
CBS	Corey-Baski-Shibata
chapter	ch
cyclohexyl(2-anisole)(methyl)phosphine	CAMP
Dative ligand	L
Deuterium	d, ^{2}H, D
diisopinocamphenylborane	Icp_2BH
diisopropylphenyl	DiPP
dimethyl sulfide	DMS
dimethylaminopyridine	DMAP
electrophile	E
enantiomeric excess	*ee*
free induction decay	FID
frustrated Lewis pair	FLP
iso	i
kinetic isotope effect	KIE
N,N-dimethylaniline	$PhNMe_2$
N-heterocyclic borane	NHC
no reaction	NR
normal	n
nuclear magnetic resonance	NMR
nucleophile	Nuc
parts per million	ppm

pinacolborane	HBpin
precipitate	ppt
room (or ambient) temperature	rt
sodium triacetoxyborohydride	STAB
tert	t
tetrahydrofuran	THF
trifluoromethylsulfonate	Tf
triphenylmethylium	trityl, Tr
α,α,α-trifluorotoluene	$PhCF_3$
σ-bound ligand	R

Chapter 1

A Introduction to Frustrated Lewis Pairs, Hydroboration, and Boron Cations

1.1 Introduction

The selective transformation of complex organic molecules can be an arduous task, involving a diverse range of challenging obstacles. In many cases, organic chemists perform numerous reactions to achieve a synthetic goal. The reactions aimed at producing these complex molecular targets often include the incorporation of heteroatom containing functional groups into a largely hydrocarbon scaffold. Once installed, functional groups may require further manipulation to yield a desirable molecule. These transformations can be tedious as regiochemistry, stereochemistry, and chemoselectivity must be controlled to form the target molecule in high yield. If the selectivity of a transformation is not controlled then the synthetic approach may quickly become obsolete. Thus, reaction protocols that have defined functional group tolerance and high regio- and stereoselectivities enable organic chemists to push material through a sequence with high yields. Alternatively, one could decrease the reactivity of specific functional groups by preserving them with protecting groups. While use of protecting groups is highly beneficial it increases the number of steps a molecule must transition through to reach the target. Furthermore, multiple protection and deprotection steps increase cost, waste, and may have affects on the overall yield of the process. In principle, a series of reactions with high yields, selectivities, and few steps would allow the synthesis of numerous sought-after targets. However, in practice, only select examples exist with ideal selectivities encouraging the development of

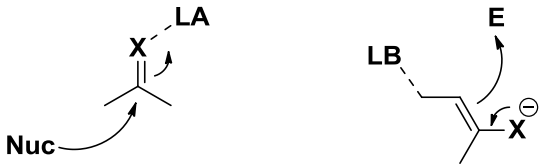
new procedures. Developing general methods and improving them by way of mechanistic investigations is a main avenue taken by chemists wishing to fulfill this goal. The improvement of organic reaction libraries through reaction development is a fundamental goal of chemistry and is especially important in the preparation of complex organic molecules.

Reduction is a process largely governed by the use of transition metals and hydrogen gas. However, other methods of reduction, such as hydrosilylation and hydroboration, have enabled the production of similar products without the use of hydrogen gas. In recent years, metal free hydrogenation and hydrosilylation of imines and ketones have been discovered but examples of catalytic metal free hydroboration reactions without the use of borane remain elusive. A novel metal free catalyst, its ability to affect the hydroboration reaction, and the mechanism of its operation will be discussed in detail in this thesis.

1.2 Lewis Acids and Bases

Catalytic asymmetric reactions provide powerful and economical methodologies for the production of novel compounds and are aptly suited for use in pharmaceutical and agrochemical industries.[1] A majority of these reactions include transition metal or main group catalysts that are combined with asymmetric molecules, such as ligands or auxiliaries, to carry out reactions that produce optically active products. These catalytic reactions often proceed with high selectivities and high turnover numbers.[1a, 2] Through efforts to develop molecules designed to increase the reactivity of carbon heteroatom double bonds, Lewis acids and bases emerged as effective reagents.[3] These reagents were proposed to increase activity based on one of the two following methodologies: 1) nucleophiles with low reactivity are combined with chiral Lewis bases to form

an activated nucleophilic complex that is capable of reacting with prochiral electrophiles[3a, 4] or 2) less-reactive electrophiles are coordinated to chiral Lewis acids which are subsequently attacked with nucleophiles to provide optically active products (Figure 1-1).[4] However, application of this approach has difficulties which are challenging to overcome, such as tuning the reactivity of the reagent. A novel method involving simultaneous activation of both the electrophile and nucleophile may provide solutions to this problem.[5] Three general strategies of *dual activation* have been formulated: 1) a molecular motif containing both Lewis acidic (electrophilic) and Lewis basic (nucleophilic) sites within the same molecular scaffold, 2) one catalytic system based on the cooperation of two separate catalysts, or 3) one catalyst that can activate the nucleophile (or electrophile) to generate a reactive species which can further activate electrophiles (or nucleophiles). Multicomponent catalytic systems are common within the chemical community and have been reviewed in detail.[6, 7]



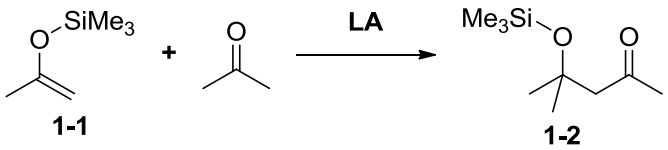
Nuc = Any nucleophile; **E** = Any electrophile; **X** = Any donor site

Figure 1-1: Examples of Lewis acid/base activation.

Central to any of these systems are Lewis acids and bases. The designation of electron pair acceptor and donor as Lewis acids and bases, respectively, was firmly laid down by Lewis in 1923.[8] Lewis acids and bases are pivotal reagents as is evident from their use in asymmetric synthesis as described below.[3]

1.2.1 Lewis Acid Catalysis

Lewis acid catalysis can be defined as a reaction between a donor site on one of the substrates and the acceptor site of the Lewis acid that increases the reactivity of the organic substrate, in turn, increasing the rate of the desired reaction.[9, 10] Additionally, the Lewis acid must not be consumed during the course of the reaction. A quintessential example of Lewis acid catalysis is the Mukaiyama aldol reaction, in which Lewis acids are added to mixtures of preformed enol silyl ketenes (**1-1**) and carbonyl compounds forming *β*-silyloxycarbonyls (**1-2**) (Scheme 1.2-1).[11] The seminal work utilized stoichiometric titanium tetrachloride as the Lewis acid[12] but a variety of Lewis acids, including $SnCl_4$, $AlCl_3$, BCl_3, BF_3•OEt_2, and $ZnCl_2$ were also shown to promote or catalyze this reaction.[13]

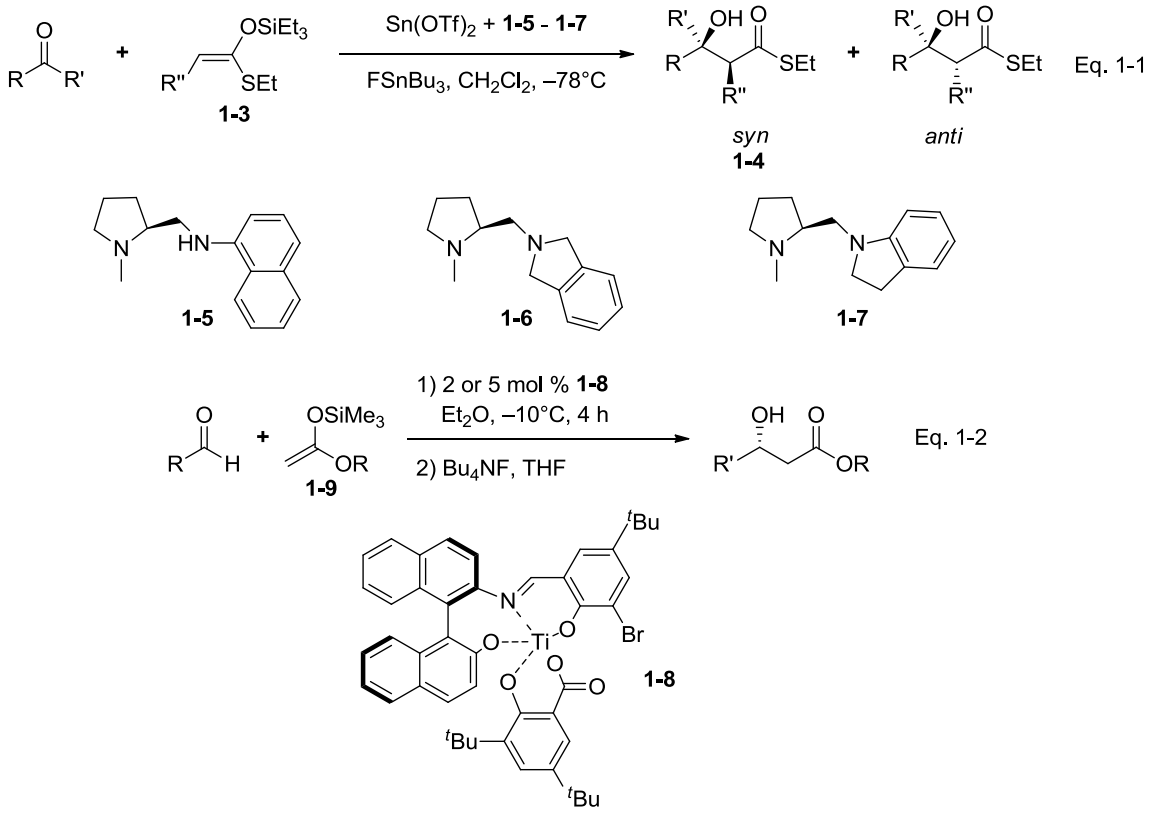


LA = $TiCl_4$, $SnCl_4$, $AlCl_3$, BCl_3, $BF_3{\cdot}Et_2O$, $ZnCl_2$

Scheme 1.2-1: General Mukaiyama aldol reaction.

Tin(II) and titanium(IV) based enantiopure Lewis acids were among the first used to control stereochemistry in Mukaiyama aldol reactions.[14,16] Mukaiyama and Kobayashi used stoichiometric amounts of the proline derived ligand **1-5** to facilitate the asymmetric aldol reactions promoted by tin Lewis acids (Scheme 1.2-2, Eq. 1-1).[14] In this study, silyl enol ethers derived from acetic acid thioesters (**1-3**) were reacted with aldehydes producing *syn β*-hydroxythioesters **1-4** in high enantiomeric excess (*ee*). Kobayashi *et al.* developed a similar reaction in which alkyl or aryl methyl esters were reacted with (*Z*)-*β*-alkoxysilyl ketene acetals.[15] Furthermore, Kobayashi and coworkers were able to select the diastereomeric configuration of the product by utilizing either proline ligand **1-6** or **1-7** (Scheme 1.2-2, Eq. 1-1).[15] Titanium complexes are often strong Lewis acids and Carreira and coworkers utilized them to affect one of

the first catalytic asymmetric Mukaiyama aldol reactions. A specialized tridentate ligand derived from (–)-2'-amino-[1,1'-binaphthalen]-2-ol (NOBIN), 3-bromo-5-*t*-butyl-salicaldehyde, and 3,5-di-*t*-butylsalic acid was used in concert with titanium (IV) tetra-*i*-propoxide (**1-8**) to accomplish a similar aldol reaction between a silyl ketene acetal (**1-9**) and an aldehyde (Scheme 1.2-2, Eq. 1-2).[16] This unique catalyst produced ee's in excess of 87% with moderate to high yields. These are two examples among the multitudes of Lewis acid catalyzed reactions. Other chiral Lewis acids have been developed to increase the stereoselectivity of these reactions and have also shown promise in dictating the selectivity in Diels-Alder, Strecker, and allylation reactions as well.[9]



Scheme 1.2-2: An example of a stoichiometric Mukaiyama aldol reaction using a chiral diamine promoter (Eq. 1-1) and an example of a catalytic asymmetric Mukaiyama aldol reaction using a chiral titanium catalyst (Eq. 1-2).

Lewis acid catalysis is a common method used when activating a carbon heteroatom double bond with low electrophilicity. These catalysts are highly useful when racemic products with high conversions are desired. Unfortunately, this type of system has numerous drawbacks preventing widespread application. High catalyst loadings and use of catalysts with high molecular weight often prohibits the use of these catalysts on large scales.[9] Increasing the loading of these systems enables the production of optically active compounds in high yields but at a significant cost. These chiral catalysts are not easily made and often require the use of enantioenriched starting materials.[17] It is important to note that the diastereo- and enantioselectivity of this process is variable and dependent on the stereochemistry of the reactant but independent of the reacting geometry of the nucleophilic enolsilane.[17, 18] Furthermore, most Lewis acid catalyzed aldol reactions are highly *syn* selective, which has been a common theme beginning with the early works of Mukaiyama. The lack of *anti* selective methods for α substituted silyl ketene acetals is a significant drawback.[16, 19] To address these deficiencies a chiral Lewis base catalyzed version of the Mukaiyama aldol reaction was developed.

1.2.2 Lewis Base Catalysis

Although significantly more recent and less general, Lewis base catalysis also plays an important role in the production of optically active molecules.[3a] The major distinction between Lewis base catalysis and Lewis acid catalysis is that the donor activates the acceptor to create a more reactive nucleophile. The youth and limited scope of Lewis base catalysis is a direct consequence of this mode of action simply because most organic molecules have few functional groups that can productively interact with Lewis bases. One main group compound aptly suited for activation by Lewis bases are organosilanes. Silicon compounds are well known to adopt hypervalent states in the presence of nucleophiles; these hypervalent silanes are also known to exhibit increased reactivity.[20] The silyl enol ether, which is the reacting nucleophile in the

Mukaiyama aldol reaction, can be activated by addition of a nucleophilic Lewis base. This nucleophile reacts with the silane creating the ate complex **1-10** which is more reactive than the tetracoordinate silicon. This newly formed complex is still Lewis acidic and complexation of the Lewis basic aldehyde results in a highly reactive silicon complex **1-11**. This intermittent intermediate effectively breaks down via a closet transition state yielding compound **1-12**. Liberation of the Lewis base concludes the catalytic cycle and releases the desired aldol product **1-13** (Figure 1-2).[21]

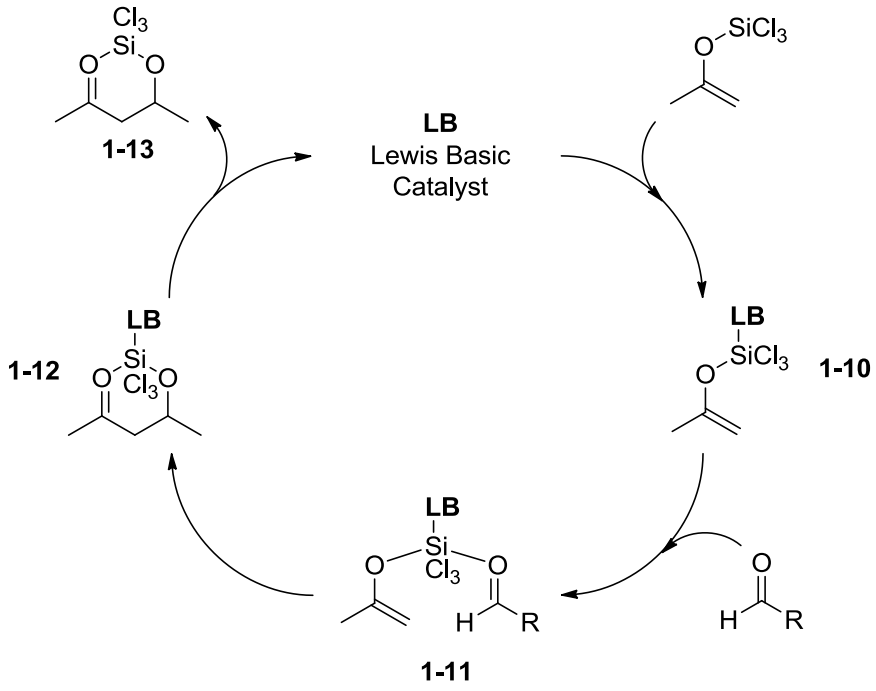
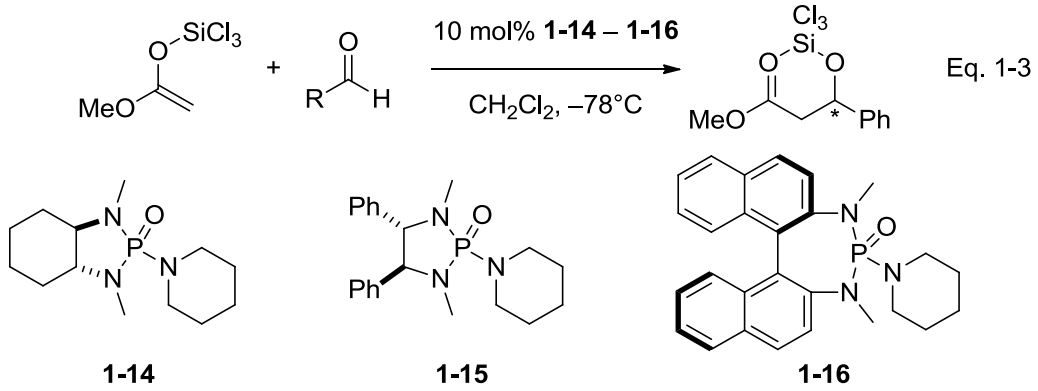


Figure 1-2: Hypothetical catalytic cycle for Lewis base catalyzed Mukaiyama aldol reactions.

This hypothetical reaction was realized by Denmark *et al*. who showed that chlorosilyl enolates could undergo Lewis base promoted Mukiayama aldol reactions.[22] Reactions of benzaldehyde or pivaldehyde with methyl trichlorosilyl acetate and use of phosphoramide promoters **1-14** – **1-16** yielded the desirable *β*-hydroxyketones with high yields but moderate *ee*s (Scheme 1.2-3). Denmark and coworkers further developed the scope of this reaction to include

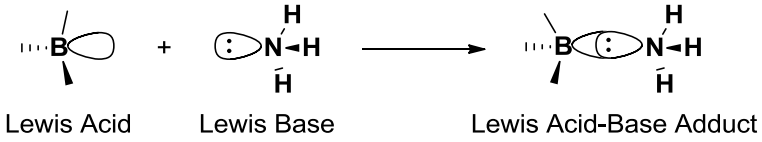
methyl ketone enolates,[23] and developed the chemistry of vinylogous aldol reactions with high selectivity.[24] A detailed mechanistic study was performed and a clear picture of the phosphoramide catalyzed reaction mechanism was presented.[25] Through continued efforts these reactions have become characterized by high yields, high enantio- and (predictable) diastereoselectivity with widespread functional group compatibility.[3a, 24, 25]



Scheme 1.2-3: Chiral p hosphoramide catalyzed Mukaiyama aldol reaction.

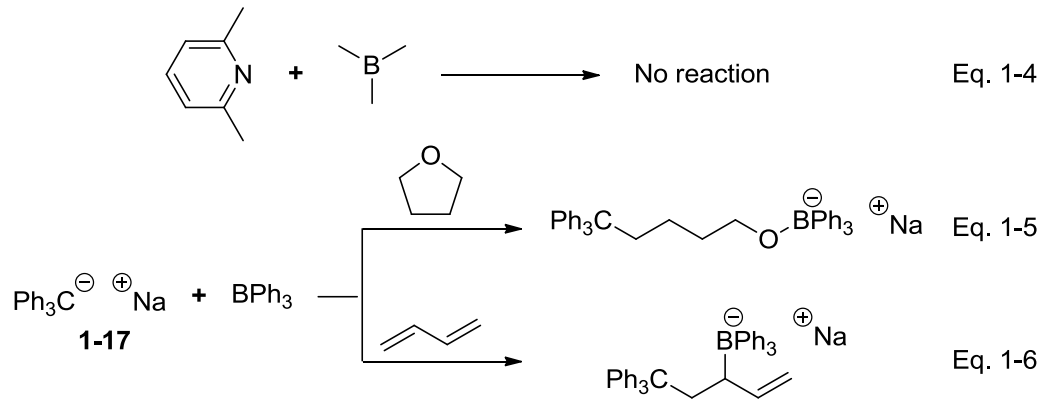
1.2.3 Lewis Pairs

Independently, Lewis acids and bases can use their electron deficiency or sufficiency to act as catalysts in reactions that create optically active commodity chemicals. However, although counterintuitive, Lewis acids and bases can be combined to lead to increased activity for certain transformations. The obvious, expected transformation is for the Lewis acid and base to interact with each other to form an inert Lewis pair (Scheme 1.2-4).[8] Since this effect results in the apparent quenching of both Lewis acidic and Lewis basic activity, little attention has been given to the concept of combined Lewis acid and base catalysis.



Scheme 1.2-4: Formation of a classical Lewis acid-base adduct.

Solutions to this problem have been noted as curiosities in the literature over the past 70 years. In 1942, Brown and coworkers noted that a stoichiometric mixture of trimethylborane and 2,6-lutidine did not form a Lewis acid/base adduct, which was contrary to the adduct formation observed for equivalent mixtures of trimethylborane and pyridine (Scheme 1.2-5, Eq. 1-4).[26] The presumed preclusion of adduct formation was attributed to the increased steric bulk around the basic nitrogen center. Eight years later, Wittig and Riickert reported that the addition of triphenylborane to sodium triphenylmethanide (**1-17**) in tetrahydrofuran (THF) resulted in the ring opening of THF and no adduct formation was observed (Scheme 1.2-5, Eq. 1-5).[27] Tochtermann further investigated these Lewis acid/base interactions by adding 1,3- butadiene to a mixture of triphenylborane and sodium triphenylmethanide and observed exclusive 1,2-addition (Scheme 1.2-5, Eq. 1-6).[28] These results remained chemical curiosities and contradictions to Lewis' axiom until recent developments from Stephan and coworkers who defined and developed the chemistry of Lewis acids and bases, which are too sterically encumbered to form a Lewis adduct.[29] The major focus of this work was to develop a metal-free system for the facile manipulation of small molecules, including such unreactive molecules as H_2.



Scheme 1.2-5: Examples of contradictions to Lewis'axiom.

1.3 Reductions in Organic Chemistry

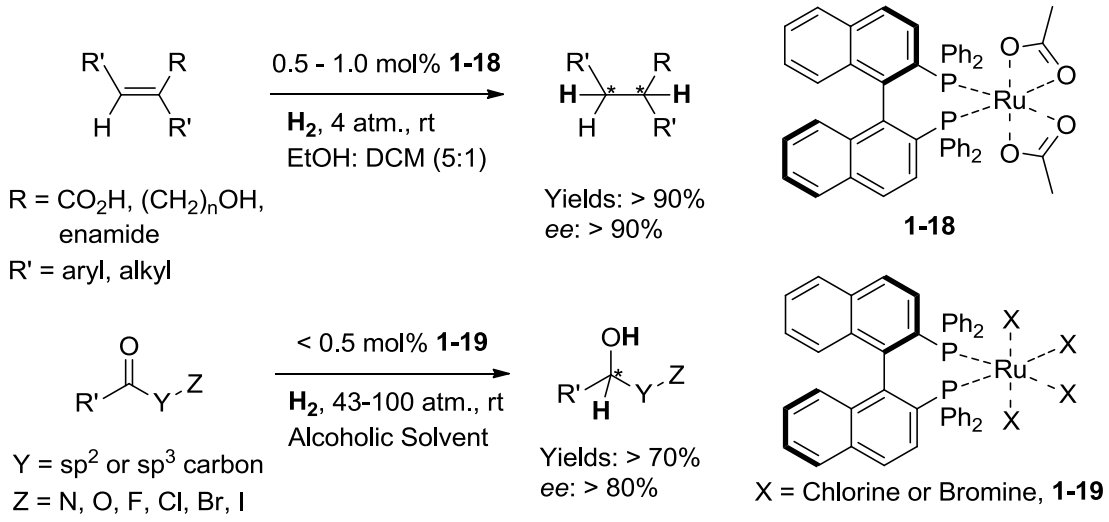
The reduction of functional groups is one of the most widely used and well developed processes in organic chemistry. Numerous reductive reactions are used throughout organic chemistry and without them, many natural, pharmaceutical, and agrochemical products could not be synthesized. Some of the methods currently used to affect these transformations involve toxic heavy metals, such as rhodium or ruthenium in combination with easily combustible hydrogen gas, or highly water sensitive, explosive alkali earth metals such as lithium or potassium.[30, 31] Despite their utility, the reactivity and rigorous techniques required for the handling of these compounds motivated synthetic organic chemists to search for safer, more facile, yet equally effective methods to reduce a wide array of chemical moieties.

No one method has alleviated all of the troubles associated with current methods of reduction and great scientific endeavors have been undertaken to remedy the issues surrounding the chemo-, regio-, and stereoselectivities of these processes. However, several methods have recently been discovered that have targeted problems and successfully developed solutions. These

systems are based on metal-free (main-group) compounds which, when used in unison, affect the hydrogenation of certain functional groups in small organic molecules.

1.4 Hydrogenation

A hydrogenation reaction consists of the addition of molecular hydrogen to further saturate an organic molecule. This is an atom economical, efficient, and synthetically appealing process. Dihydrogen has a high bond dissociation energy (104.2 kcal.mol),[30] making its uncatalyzed addition a challenging process. The appeal and difficulty of this reaction motivated the scientific community to develop catalysts capable of facilitating hydrogenation.[32] In addition to catalyst development, considerable ligand design studies have been performed with the goal of achieving an enantioselective reduction. Most notably, Noyori and coworkers reported that cationic 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) ruthenium complexes (**1-18**, **1-19**) catalyzed the hydrogenation of α-(acylamino) acrylic acids or esters yielding the corresponding amino acid derivatives in high *ee*s (Scheme 1.4-1).[33] BINAP is only one of several chiral phosphine ligands utilized in asymmetric hydrogenation, other historically significant chiral ligands include cyclohexyl(2-anisole)(methyl)phosphine (CAMP) and 1,2-di(cyclohexyl(2-anisole)phosphino)ethane (DiPAMP).[34] It was for these efforts that Knowles and Noyori shared part of the 2001 Nobel Prize in Chemistry.[35] Catalytic systems such as these have repeatedly been shown to be capable of affecting the hydrogenation of various functional groups. In an ever diversifying field, novel insight was needed to achieve a major breakthrough and this was accomplished after considerable thought was dedicated to the mechanism of hydrogen activation.

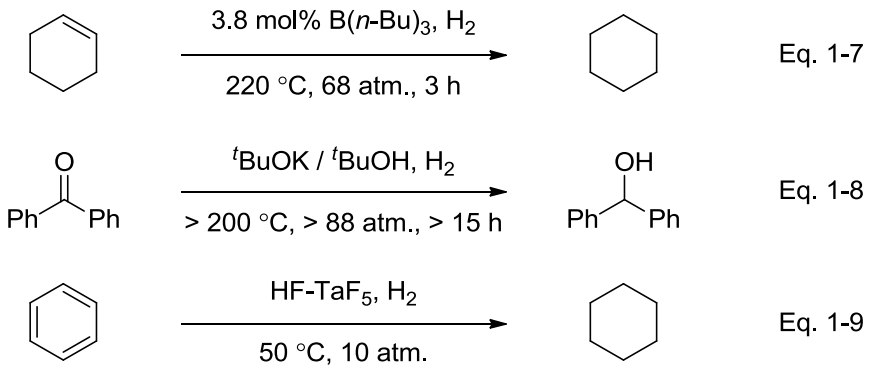


Scheme 1.4-1: Noyori's asymmetric ruthenium based hydrogenation reactions.

In both transition metal and metal-free hydrogenation, the modes of hydrogen activation are similar and can proceed via three possible mechanisms. One mechanism of activation is the heterolytic cleavage of dihydrogen resulting in a hydride (or hydrogen anion) and a proton (or hydrogen cation). The hydride moiety becomes bonded to the transition metal and the proton to an appropriate Lewis base. Another mode is homolytic cleavage of dihydrogen where both atoms end up equivalently incorporated into the catalyst via an insertion type mechanism. Third is an electron transfer process that is often associated with redox reactions and as such are less common in organic synthesis. Of these modes of activation, heterolytic bond activation of dihydrogen made metal-free hydrogenations possible,[29,30] creating another novel field of chemistry.

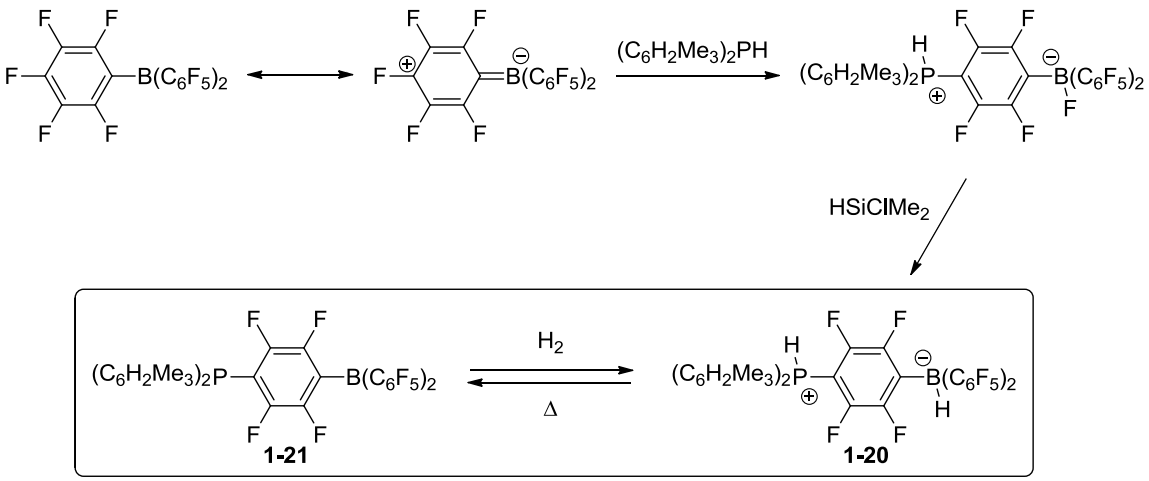
1.4.1 Transition Metal-Free Hydrogenation and Frustrated Lewis Pairs

Metal-free systems may be defined as those that do not use a transition metal to activate hydrogen or substrate. Organic catalysts have most often been used to activate carbonyl containing compounds facilitating enantioselective allylations, aldol reactions, and conjugate additions, to name a few.[36] However, transition metal-free systems that react with simple molecules such as dihydrogen are rare. Unsurprisingly, a significant amount of research has been dedicated to developing methodologies that enable the hydrogenation of organic molecules without the use of toxic transition metals. One of the first examples of metal-free hydrogenation was reported by DeWitt and coworkers.[37] The authors describe a process where neat cyclohexene or 1-octene is hydrogenated at 220 °C and 68 atm of hydrogen pressure in the presence of catalytic amounts of tri-*n*-butyl borane (Scheme 1.4-2, Eq. 1-7). Shortly thereafter, the base-catalyzed homogeneous hydrogenation of benzophenone was reported at temperatures over 200 °C and pressures ranging from 88 to 135 atm (Scheme 1.4-2, Eq. 1-8).[38] Unfortunately, the use of high temperatures and strong base restricts the substrate scope of this reaction to stable ketones with non-enolizable protons. Another early example used either of the strong Brønsted acids formed from mixtures of HF-TaF_5 or HF-SbF_5 as catalysts for the hydrogenation of benzene (Scheme 1.4-2, Eq. 1-9).[39] The authors note that this concept is limited to acids that cannot be reduced by hydrogen or those that do not react with aromatics such as sulfuric or nitric acid. These reactions are limited by their forcing conditions and limited substrate scope. It wasn't until many years later that metal-free hydrogenation systems were described in detail and with wider scope.



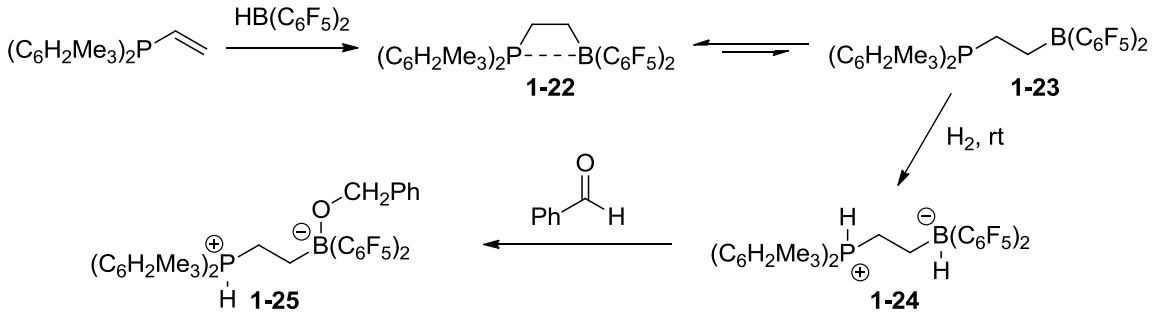
Scheme 1.4-2: Early examples of unconventional methods of hydrogenation.

In 2006, Stephan and coworkers reported the first metal-free, reversible hydrogen activation system.[40] The linked phosphonium borate species **1-20**, formed from nucleophilic aromatic substitution and subsequent treatment with dimethylchlorosilane, underwent elimination of dihydrogen upon heating to 100 °C in toluene yielding phosphine borane **1-21**. Upon cooling to ambient temperature and treatment with high purity hydrogen gas, the dihydro-phosphonium borate was reformed (Scheme 1.4-3). The Lewis acid tris-pentafluorophenyl borane ($B(C_6F_5)_3$) is well known for its use as a polymerization co-catalyst[41] and it typically behaves as a standard Lewis acid, forming Lewis adducts and coordinating to donor sites, however, in the presence of the sterically bulky Lewis base bis-(2,4,6-trimethyl)phenyl phosphine, adduct formation was precluded and the unusual reactivity was discovered. Much like Brown's system, the inhibition of adduct formation was attributed to overwhelming steric interactions, which inspired Stephan and coworkers to coin the term frustrated Lewis pairs (FLPs).[29, 42] This ground-breaking publication shifted the scope of molecules capable of affecting hydrogen activation and sparked a myriad of investigations into the applicability of metal-free systems based on FLPs as hydrogenation and small molecule activation catalysts.

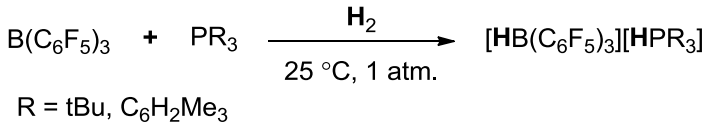


Scheme 1.4-3: Linked phosphonium borate generation and hydrogen elimination – activation.

Intramolecular FLP systems have been used to activate other small molecules in addition to dihydrogen, such as carbon dioxide,[43] but these systems require several steps to prepare and are highly air and moisture sensitive.[29, 44] One example is (2-(bis(perfluorophenyl)boryl)ethyl) dimesitylphosphine (**1-22**), which exists in an equilibrium between a closed four membered adduct and an open chain form (**1-23**) in the absence of hydrogen (Scheme 1.4-4).[45] However, upon introduction of H_2, an open zwitterionic phosphonium borate (**1-24**) was formed. This species was characterized spectroscopically; no X-ray structure was given.[45] Furthermore, it was shown to stoichiometrically reduce benzaldehyde yielding **1-25** (Scheme 1.4-4). **1-25** is presumed to be resistant towards catalytic turnover because of the strength of the oxygen boron bond formed in the final product. To date, **1-25** and the perfluorophenyl bridged complex **1-21** remain the only species in which a carbonyl functionality is activated with a non-metal FLP (Scheme 1.4-4).[45, 46, 47]

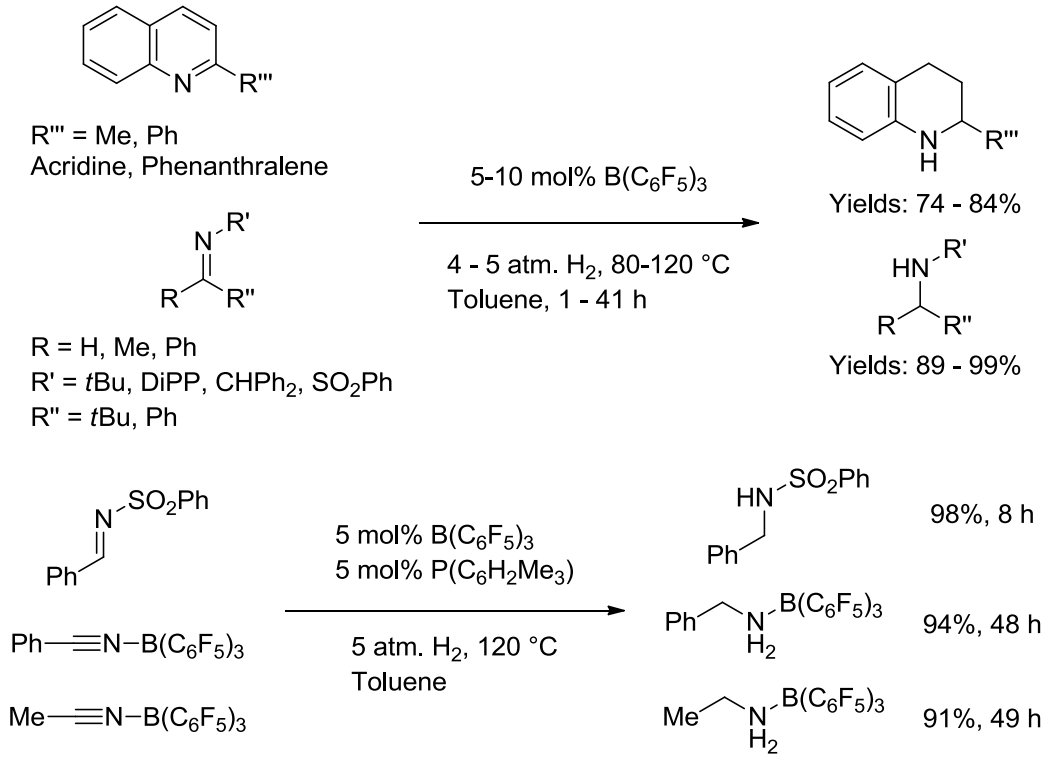


Scheme 1.4-4: Intramolecular FLP activation of dihydrogen and reaction with benzaldehyde.



Scheme 1.4-5: Hydrogen activation by an intermolecular FLP.

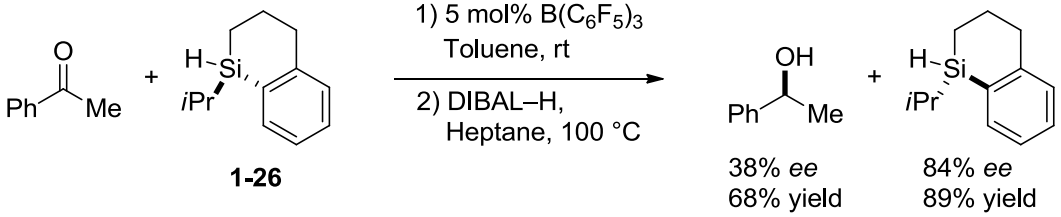
To further extend the scope of FLPs, reactions involving non-tethered Lewis acids and bases were investigated. Notably, mixtures of bulky phosphines or amines with boranes were investigated and discovered to split hydrogen gas (Scheme 1.4-5).[48] It was these systems that were further probed for catalytic activity and they were utilized in the hydrogenation of imines, nitriles, and *N*-heterocycles (Scheme 1.4-6).[49, 50] *N*-heterocycles and certain imines did not require the use of an additional Lewis base to accommodate their reduction as the basicity of the substrate was sufficient for dihydrogen activation.[49] However, the use of phosphines was necessary for the reductions of weakly basic imines and nitriles.[49] Nitriles required the use of a slight excess of $B(C_6F_5)_3$ to substrate as a robust classical Lewis adduct was formed upon mixing. Thus, the FLP hydrogenation of nitriles was conducted by first forming the Lewis adduct, then utilizing a catalytic amount of phosphine and $B(C_6F_5)_3$ to facilitate the reduction (Scheme 1.4-6).[49]



Scheme 1.4-6: Initial scope of FLP hydrogenations.

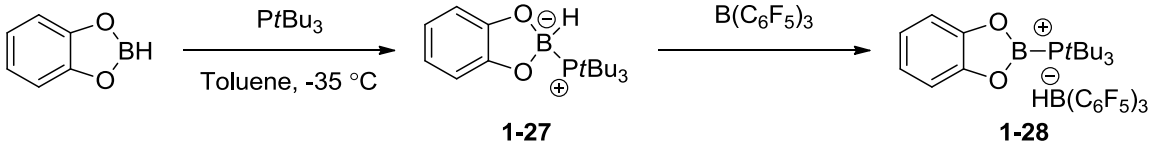
In recent years, the substrate scope of catalytic FLP hydrogenations has grown remarkably; including enamines,[51] silyl enol ethers,[52] aziridines, diimines, aniline derivatives,[53] α,β-unsaturated imines, and, in one unique case, the olefinic portion of (*S*)-carvone.[54] Stoichiometrically, FLPs have been used to activate alkenes,[55] dienes,[56] alkynes,[57] CO_2,[58] and other small molecules.[29, 59] Furthermore, $B(C_6F_5)_3$ has been used as a Lewis acid in the activation of H–Si[60, 61] and H–B[62] bonds as well as in the allylstannylation of aldehydes.[63] Silane activation catalyzed by $B(C_6F_5)_3$, developed prior to the discovery of FLP chemistry, has been successfully implemented in the catalytic hydrosilylation of ketones,[60a] imines,[60d] silyl enol ethers,[60e] and olefins.[61] Additionally, carbonyl functionalities have been asymmetrically hydrosilylated using enantio-enriched 1-isopropyl-1,2,3,4-tetrahydrobenzo[b]siline (**1-26**) as a silylating reagent with $B(C_6F_5)_3$ as a catalyst (Scheme 1.4-7).[64] On the other hand, only the demonstration of B–H bond

heterolysis by dual activation has been published; its application in organic chemistry has yet to be investigated.[62] Stephan *et. al.* observed that the B–H bond of catecholborane (HBcat) was heterolytically cleaved by stoichiometric mixtures of tris-*t*-butyl phosphine (P*t*Bu$_3$) and B(C$_6$F$_5$)$_3$ forming the corresponding boryl phosphonium hydridoborate salt, **1-28** via the Lewis adduct **1-27** (Scheme 1.4-8).[62] These systems highlight the potential for FLPs to become efficient and industrially applicable catalysts for organic reductions.



1-26

Scheme 1.4-7: Use of enantio-enriched silane **1-26** as a chiral hydrosilylating agent.



1-27 **1-28**

Scheme 1.4-8: Heterolytic cleavage of a B–H bond by FLPs.

Despite their ability to catalytically reduce *N*-containing functional groups, numerous pitfalls exist for FLP-type systems. For example, the inability to catalytically reduce the C=O bond in carbonyl functionalities is a major hindrance on their widespread applicability. Furthermore, catalyst loadings are far too high to allow industrial application of FLPs; recall that the ruthenium systems require less than 1 mol% in most cases and catalysts are easily recyclable. Also, the cost of synthesizing B(C$_6$F$_5$)$_3$ on multi kilogram scales is often not surpassed by the value of the chemicals produced from its use in FLP systems. Furthermore, B(C$_6$F$_5$)$_3$ is highly sensitive to water; trace quantities can result in the quenching of the effectiveness of this Lewis

acid.[41b] Alternatives needed to be developed and insight into their development may come from investigations into the mechanism of FLP-catalyzed hydrogenation.

1.4.2 Mechanism of FLP Hydrogenation

Although FLPs have been shown to be catalytically competent in the facile hydrogenation of *N*-containing functional groups,[29] the catalytic cycle has remained largely speculative. The first step in all FLP processes is the activation of hydrogen. Consider, for example, the activation of dihydrogen with $B(C_6F_5)_3$ and P*t*Bu_3. No evidence for adduct formation in toluene was observed at ambient or sub zero temperatures yet exposure to 1 atm of H_2 quantitatively yields the phosphonium borate salt.[48] In the absence of such an adduct, this activation step could proceed via one of two pathways: 1) end-on complexation of the Lewis basic phosphine to the antibonding σ^* orbital of a molecule of dihydrogen followed by hydride abstraction by the Lewis acidic borane (**M1-1**), or 2) side-on complexation of the σ orbital of dihydrogen to the vacant *p* orbital of the Lewis acid which would facilitate protonation of an approaching Lewis base (**M1-2**) (Figure 1-3).[48] Both of which would yield the phosphonium hydridoborate, **1-29**. Despite computational evidence supporting the existence of an $(\eta^2\text{-}H_2)BH_3$ species,[65] NMR experiments conducted by Stephan and Welch showed no complexation of H_2 to $B(C_6F_5)_3$, even at temperatures as low as –83 ℃, which suggests that, if present, the σ adduct is in a fast equilibrium or is highly unstable.[48] Van der Waals complexes of phosphines with H_2 have been observed in an argon matrix[66] and could lead to such end-on interactions aiding in dihydrogen activation.

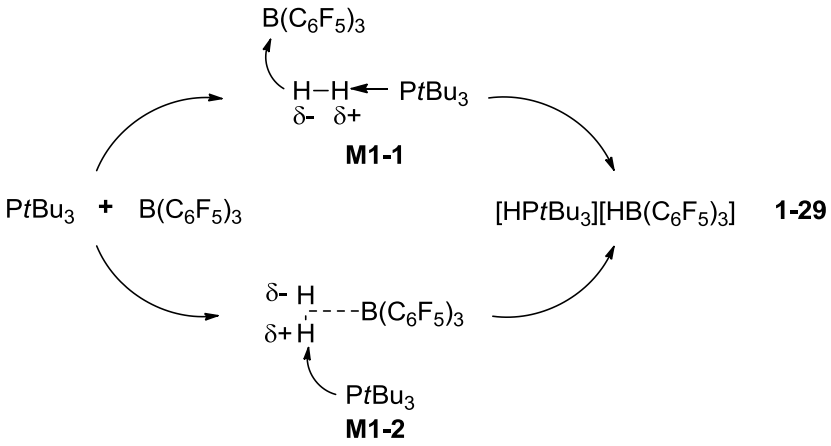


Figure 1-3: Potential mechanisms of heterolytic hydrogen activation.

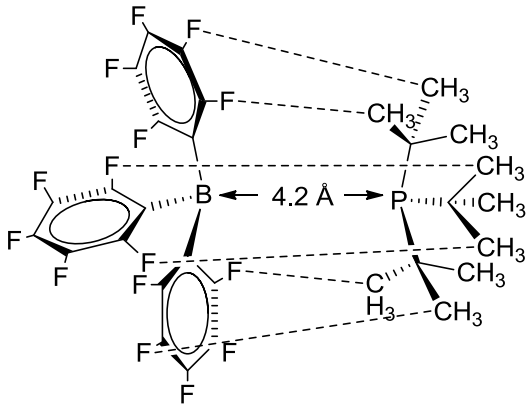


Figure 1-4: Pictorial representation of the encounter complex.

A computational study by Papai and coworkers was unable to distinguish the active mechanism based on both energetic pathways.[67] Instead they proposed that dihydrogen could undergo heterolysis through an unprecedented "encounter complex" (Figure 1-3).[67] This complex is proposed to arise from long distance hydrogen bonding and dispersion interactions between the Lewis acid and Lewis base.[67] This organization creates an intermittent electric field that polarizes dihydrogen to the extent that bond cleavage is facile. Despite the apparent energetic favourability of this encounter complex, rigorous attempts to experimentally identify this species have proven futile.[68] Furthermore, the likelihood of an encounter complex for linked

phosphonium borate species, such as **1-20**, seems particularly unlikely due to the rigidity of the backbone and other indirect mechanisms of hydrogen activation have been proposed.[68] Interestingly, a theoretical study by Li and coworkers proposed a concerted process in which both mechanisms, **M1-1** and **M1-2**, are active simultaneously.[69] The energetics presented demonstrated that double activation of dihydrogen is thermodynamically preferred to either of the deprotonation (**M1-2**) or hydride delivery (**M1-1**) mechanisms. In the concerted activation process, electron density from the Lewis basic lone pair is donated into the σ^* orbital at the same time as the Lewis acid is abstracting electron density from σ orbital of the H–H molecule. The experimental and theoretical data are growing but no general consensus on the mode of activation of hydrogen has been reached.

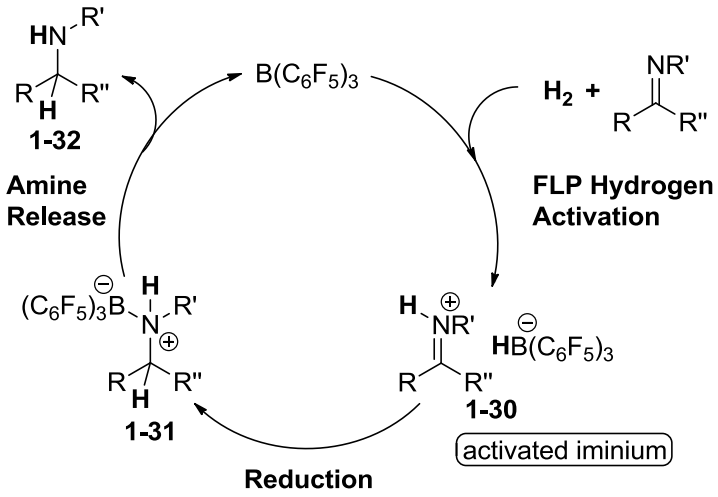


Figure 1-5: Catalytic cycle for FLP hydrogenation of imines.

Depending on the substrate, the steps following hydrogen cleavage can vary. In the FLP catalyzed hydrogenation of imines, the nitrogen center acts as the Lewis base and forms an activated iminium ion, such as **1-30**, after protonation (Figure 1-5).[49] Subsequently, the hydridoborate counterion ($HB(C_6F_5)_3^-$) may nucleophilically deliver a hydride to the electrophilic carbon of the iminium, collapsing the ion pair to an amine-borane **1-31**. Dissociation of the amine

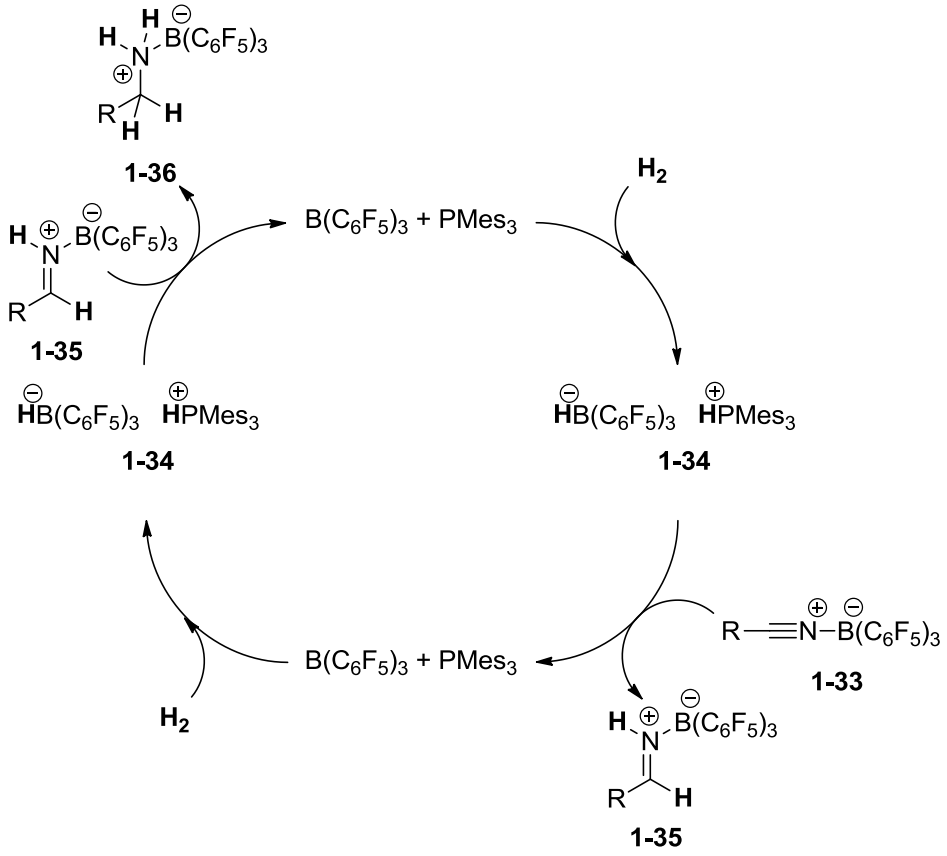


Figure 1-6: Catalytic cycle for the FLP catalyzed reduction of nitriles

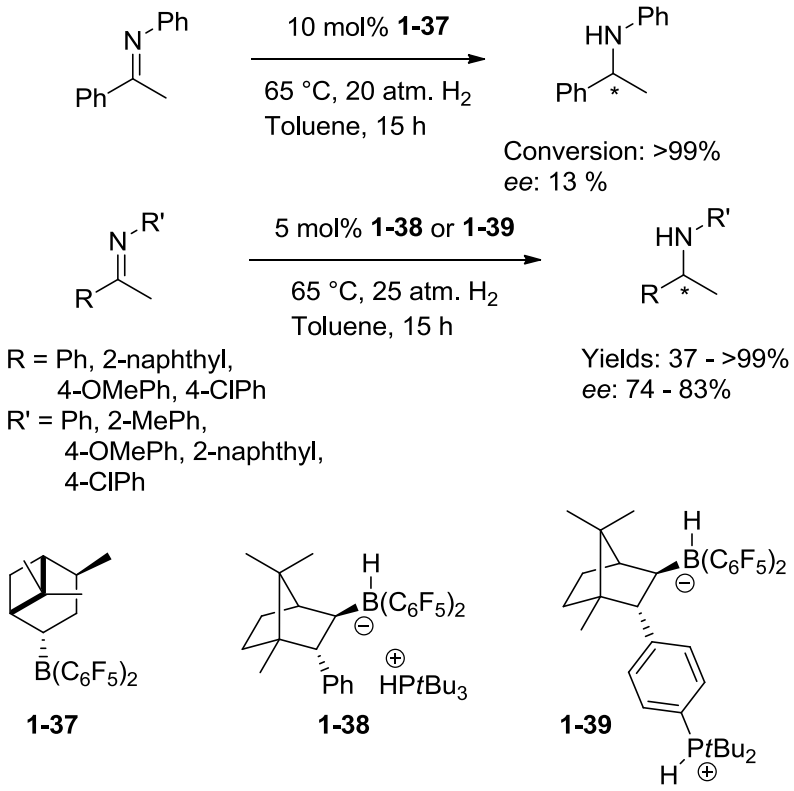
borane produces the amine product **1-32** and allows the borane catalyst to re-enter the catalytic cycle. The dissociation of the borane is believed to be the turnover limiting step as only sterically bulky imines are feasible substrates. Without significant steric bulk on the nitrogen, the amine-borane will remain intact and prevent catalyst turnover. This is a potential explanation for the requirement of elevated temperatures or pressures for unhindered substrates.[49, 70] In the reduction of nitriles and less basic imines, the addition of a stronger Lewis base, such as a phosphine, is required for catalysis. For nitriles, this is attributed to the necessity for a strongly Lewis acidic protecting group, which forms a species, such as **1-33**, which has no accessible Lewis basic site to accommodate the activation of dihydrogen. Thus, the additional Lewis base allows hydrogen activation forming **1-34**, and enabling nucleophilic attack of the hydridoborate

and subsequent proton transfer, which regenerates the catalyst and creates an activated iminium ion (**1-35**) that is reduced by **1-34** a second time to yield product **1-36**. For imines of low basicity, the additional Lewis base is required to activate hydrogen. Once this is accomplished proton transfer from Lewis base to substrate will enter an equilibrium, which drives the reaction forwards. The overall catalytic cycle for both processes can be summarized in three elementary steps: 1) activation of dihydrogen by a Lewis acid/base pair, 2) reduction of substrate by nucleophilic hydride delivery, and 3) release of the amine and regeneration of the Lewis acid catalyst. Interestingly, no detailed mechanistic studies have been performed on the catalytic activity of FLPs. Perhaps it is the elegant nature of this mechanism that has enabled it to remain largely unquestioned in the literature. In addition to its simplicity it also gives insight into transitioning FLP hydrogenation into an asymmetric process.

1.4.3 Enantioselective FLP Reductions

The prochiral iminium salt has the potential to be reduced enantioselectively if an appropriate chiral Lewis acid is employed. Klankermayer and Chen reported the first enantioselective FLP hydrogenation using the chiral borane **1-37**, derived from (+)-α-pinene (Scheme 1.4-8).[71] The borane catalyst **1-37** proved to be competent in hydrogenation reactions producing conversions >99% but only 13% *ee*.[71] The major drawback of this catalyst was its tendency to undergo retrohydroboration under the reaction conditions, which results in the generation of the less hindered achiral borane $HB(C_6F_5)_2$.[72] Despite this flaw, the induction of asymmetry implied that hydride delivery from a chiral Lewis acid was capable of creating optically active molecules and it inspired further exploration into the design of chiral boranes. In 2010, Klankermayer and coworkers produced a much more competent borane **1-38** based on a functionalized (1*R*)-(+)-camphor backbone.[73] The authors reported the successful isolation and characterization (spectroscopically and crystallographically) of two diastereomerically pure salts.

Furthermore, they demonstrated the ability to select the stereochemistry of the product by their choice of chiral salt. The Klankermayer group has continued to demonstrate the use of this family of catalysts as recyclable[74] (catalyst **1-39**) and as able to perform other types of bond activation/reduction processes, such as asymmetric hydrosilylation (catalyst **1-38**).[75]



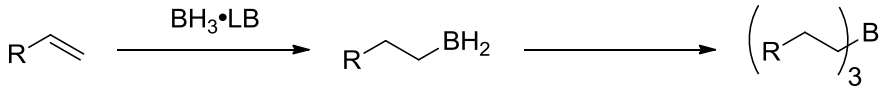
Scheme 1.4-9: Enantioselective FLP hydrogenations: Catalysts and Scope.

In conclusion, the introduction of FLPs as an alternative to transition metal catalysis has significant promise in the area of small molecule activation; in particular, their use as catalysts in the hydrogenation of unsaturated molecules is remarkable. The growth and applications within this field is clearly demonstrated by the number of publications on FLPs since the seminal work of Stephan in 2006.[40] Furthermore, metal-free asymmetric hydrogenation was unprecedented prior to the work of Klankermayer.[71, 73-75] Despite the surge in development of metal-free catalysts, their use in heterolytic bond activation remains largely unexplored. Specifically, no FLP system

has been utilized in the hydroboration reaction, notwithstanding the fact that FLPs have been used to demonstrate their ability to heterolytically cleave a B–H bond.[62] Before discussing our foray into this unexplored bond activation, a brief discussion on the hydroboration reaction is required.

1.5 Hydroboration

Although FLP hydrogenation is a process capable of affecting the reduction of various *N*-containing unsaturated molecules by varying the choice of Lewis pairs, problems can arise with functional group tolerance. Additionally, experimental issues arise when dealing with large quantities of hydrogen gas due to its facile combustion with oxygen at concentrations as low as 5% (by volume).[76] These issues, among others, led to the invention of numerous other reductive processes.[77] Of these, one of the most useful is the hydroboration reaction. This reaction involves the concerted *syn* addition of a boron-hydrogen bond across a degree of chemical unsaturation, such as an olefin or ketone (Scheme 1.5-1). In all cases, uncatalyzed hydroboration proceeds via a concerted asynchronous transition state and is selective for the anti-Markovnikov installation of boron. However, if the hydroboration reaction is catalyzed by a transition metal, the regio-, chemo-, and enantioselectivity of this fundamental reaction can be altered and controlled.[77, 78]

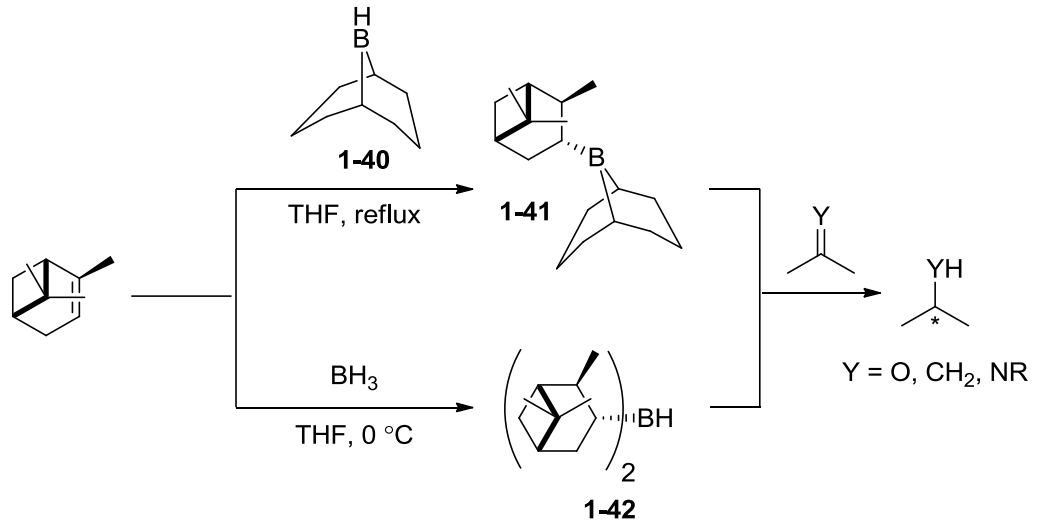


Scheme 1.5-1: A general hydroboration reaction and redistribution process.

1.5.1 Uncatalyzed Hydroboration

The pioneering work and much of the synthetic development of hydroboration chemistry was conducted within the laboratories of Brown (Nobel Prize 1979).[79] Originally, hydroboration was conducted thermally (uncatalyzed) and, in its simplest form, is conducted with the use of borane (BH_3) which exists as a toxic gas in its dimeric form, B_2H_6. Borane is an electrophilic Lewis acidic reducing agent, which affects the hydroboration of a wide array of functional groups by complexing to a Lewis basic center and delivering a hydride in a very selective and specific manner. Brown noted that ethers, such as diethyl ether or THF, and sulfides, such as dimethyl sulfide (DMS), could catalyze the reaction.[80] He suggested that this was a result of the Lewis basic oxygen (or sulfur) nucleophilically attacking diborane making weak borane adducts which is more reactive than the B_2H_6 dimer. Borane•Lewis base adducts, such as BH_3•THF and BH_3•DMS, are commercially available, paying tribute to their usefulness as reducing agents.

Unfortunately, the reactivity of borane with olefins tends to yield trialkylboranes as opposed to the target monoalkyl borane (Scheme 1.5-1). This redistribution reaction hampers the use of reagents like BH_3•THF where a 1:1 stoichiometry of reaction is desired. This motivated a search for more synthetically applicable hydroborating reagents. A major breakthrough came in the form of the cyclic dialkylborane, 9-boracyclo[3.3.1]nonane (9-BBN, **1-40**), produced by the reaction of 1,5-cyclooctadiene (COD) with BH_3.[81] Chiral versions of dialkyl boranes were developed by Brown which he summarized in a comprehensive review.[82] These chiral boranes were easily synthesized starting from enantiopure natural products.



Scheme 1.5-2: Synthesis of chiral stoichiometric hydroborating reagents.

In the late 1970s, Midland and coworkers reported the use of B-3-*α*-pinanyl-9-BBN (**1-41**) as an enantioselective hydroborating reagent for the reduction of deutero-aldehydes and ketones.[83] This chiral reagent is easily accessible from the reaction of (+)-*α*-pinene with 9-BBN in refluxing THF (Scheme 1.5-2).[84] The asymmetric induction of this process is comparable to that of similar enzymatic reductions. This reagent was commercialized by the Aldrich Chemical Co. under the name Alpine-Borane®.[85] The asymmetric reduction of an unsaturated moiety with Alpine-Borane is known as the Midland reduction. Alternatively, a chiral borane known as diisopinocamphenylborane (Icp_2BH, **1-42**) can be synthesized directly from (+)-*α*-pinene and borane (Scheme 1.5-2). Borane **1-42** was capable of hydroborating prochiral ketones and *cis*-olefins at cryogenic temperatures with unprecedented *ee*s.[86, 87]

These methodologies have left their mark on academia as is evident by the commercialization of the processes mentioned above. However, there are serious drawbacks to uncatalyzed hydroboration. Most important is the necessity for a stoichiometric amount of the chiral borane. Despite the effectiveness and ability to induce asymmetry into prochiral molecules,

the need to perform the reaction at cryogenic temperatures and the stoichiometric use of chiral borane are significant limitations to the industrial appeal of these reactions. The chiral natural product can be reclaimed from the reaction mixture and recycled,[88] however, this task further complicates an already difficult process. Second, the instability of alkyl boranes is a problem under atmospheric conditions. Lewis basic molecules, such as water, can complex to the Lewis acidic boron atom, degrading the purity and usefulness of the reagents. This directly limits the further use of the element-boron bond and also precludes isolation of the alkylborane making *in situ* oxidation to alcohols a necessary protocol (see Section 1.5.2). Lastly, functional group tolerance of the uncatalyzed process can be an issue as the most reactive unsaturated moiety is often the first to be reduced. All of these factors contributed to the development of transition metal catalyzed hydroboration reactions.

1.5.2 Metal Catalyzed Hydroboration

Several different contributions aided the development of a transition metal catalyzed hydroboration process. Seminal work on this topic came in a series of papers from Sneddon and coworkers. They reported that the hydroboration of alkynes could be accomplished with pentaborane in the presence of cobalt,[89] iridium,[90] and palladium[91] transition metal complexes. In 1985, Männig and Nöth discovered that the hydroboration of alkenes could be accomplished with catecholborane (HBcat) in the presence of Wilkinson's catalyst, $Rh(PPh_3)_3Cl$.[92] The dioxaborolane, HBcat is part of a series of compounds developed for their reduced reactivity when compared to alkylboranes. The oxygen atoms covalently linked to the boron center dramatically decrease its Lewis acidity through overlap of the oxygen lone pairs with the vacant *p* orbital situated on boron (Figure 1-7). A direct result is that the thermal activation of these species requires elevated temperatures and lengthened reaction times. The consequence of this

decreased reactivity is that the background hydroboration reaction is no longer a factor and the catalyzed process governs the reactivity and selectivity of the hydroboration.

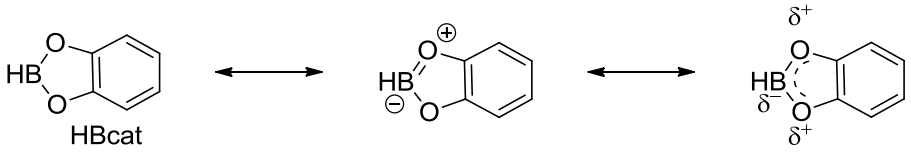
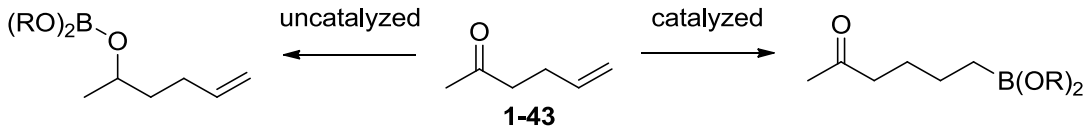


Figure 1-7: Diminished Lewis acidity of boron by electron donation from oxygen.

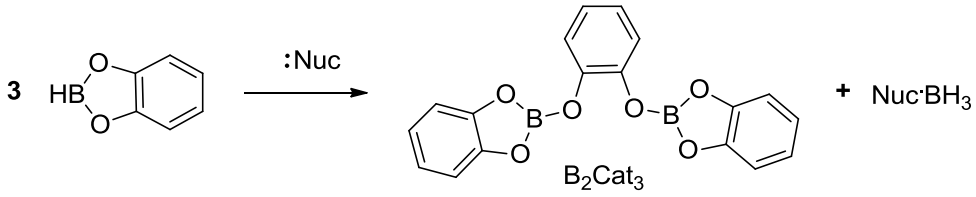
The most important feature of the rhodium catalyzed hydroboration process is the stark change in chemoselectivity from the thermal process. In Männig and Nöth's influential paper, they noted that 5-hexen-2-one (**1-43**) could be selectively hydroborated under thermal or catalytic conditions (Scheme 1.5-3). Thermal conditions result in hydroboration of the ketone moiety as the major product whereas under catalytic conditions the hydroborated olefin is the major product.[92]



Scheme 1.5-3: A comparison of chemoselectivty of Rh-catalyzed and non-catalyzed hydroboration.

Several metal–based processes flooded the literature in the years following Männig and Nöth's impacting publication. Novel catalysts for this process were developed based on late transition metals such as ruthenium,[93] palladium, nickel,[94] and iridium.[95] Early transition metals, such as zirconium,[96, 97] were also shown to be competent catalysts for this process. Interestingly, lanthanides, specifically samarium[98, 99] and lanthanum,[100] were shown to catalyze the hydroboration of olefins as well. The mechanism of the lanthanide–catalyzed systems is less well understood but coordination of the metal to an oxygen atom of the dioxaborolane is proposed to

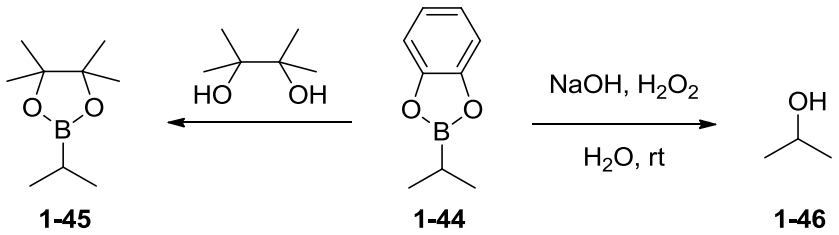
aid in its activation.[98] Of these systems, rhodium based catalysts have proven to be the most efficient and widely utilized by academia and industry.[77] In particular, cationic rhodium species, originally developed as hydrogenation catalysts, have dramatically improved the scope of transition metal catalyzed hydroboration.[101] Among others, improvements include increased yields, better selectivities, incorporation of asymmetry through the use of chiral ligands, and the ability to use less reactive boranes (see Scheme 1.5-6 for an example).



Scheme 1.5-4: Disproportionation of catecholborane.

Although, HBcat was developed to diminish its thermal reactivity, it is still quite reactive. HBcat can readily disproportionate to 1,2-bis(benzo[d][1,3,2]dioxaborol-2-yloxy)benzene (B_2Cat_3) and an equivalent of BH_3; furthermore, HBcat can also decompose to form BH_3 and 2,2'-oxybis(benzo[1,3,2]dioxaborole), also known as catBOBcat.[102] This disproportionation reaction is accelerated by nucleophiles (Nuc), such as phosphines or amines, which are common ligands in transition metal catalyzed hydroboration (Scheme 1.5-4). This often results in the use of excess HBcat to affect full conversion of starting material. Further complications may arise from the generation of BH_3 which can degrade the chemoselectivity of the reaction. Also, as mentioned in Section 1.5.2, *in situ* oxidation of hydroboration products to alcohols is performed to facilitate the isolation of final products (**1-46**; Scheme 1.5-5).[103] An alternate protocol developed by Crudden and coworkers enabled the isolation of the hydroborated product with the carbon boron bond intact.[104] In this report, pinacol was directly added to the reaction mixture after the hydroboration reaction, enabling the conversion of the catecholboronate esters (**1-44**) into pinacolboronate esters

(**1-45**) via a trans-esterification reaction (Scheme 1.5-5). The pinacolboronate ester is significantly less air- and moisture-sensitive facilitating its purification by column chromatography. Isolation of these boronate esters is particularly appealing because of their potential reactivity as nucleophiles in the Suzuki-Miyaura cross-coupling reaction.[105]



Scheme 1.5-5: Oxidation and transesterification of catecholboronate esters.

The observed reduced reactivity of dioxaborolanes initiated a vast expansion in the construction and development of novel B–H containing molecules (Figure 1-8). In addition to HBcat, Männig and Nöth also reported the use of the dioxoborolane **1-49**, and showed it to be significantly less reactive than HBcat. Other heteroatom-containing boranes developed and successfully used in rhodium catalyzed hydroboration reactions include the sulfur and nitrogen analogues of HBcat, which were applied to the hydroboration of 1-octene under thermal and rhodium catalyzed conditions.[106] The sulfur analogue, 1,3,2-benzodithioborolane, **1-47**, reacted with 1-octene under thermal conditions whereas the nitrogen analogue, 1,3,2-benzodiazaborolane, **1-48**, did not. Both reagents reacted under catalytic conditions using Wilkinson's catalyst. Furthermore, both reagents underwent triphenylphosphine catalyzed disproportionation, although at a significantly slower rate than HBcat. The nitrogen stabilized borane, 1,3-dimethyl-1,3,2-diazaborolidine, **1-51**, found use in lanthanide catalyzed hydroboration-cyclization of 1,5- and 1,6-dienes.[99, 107]

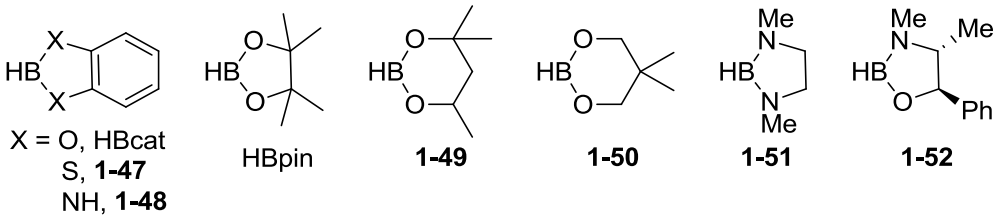
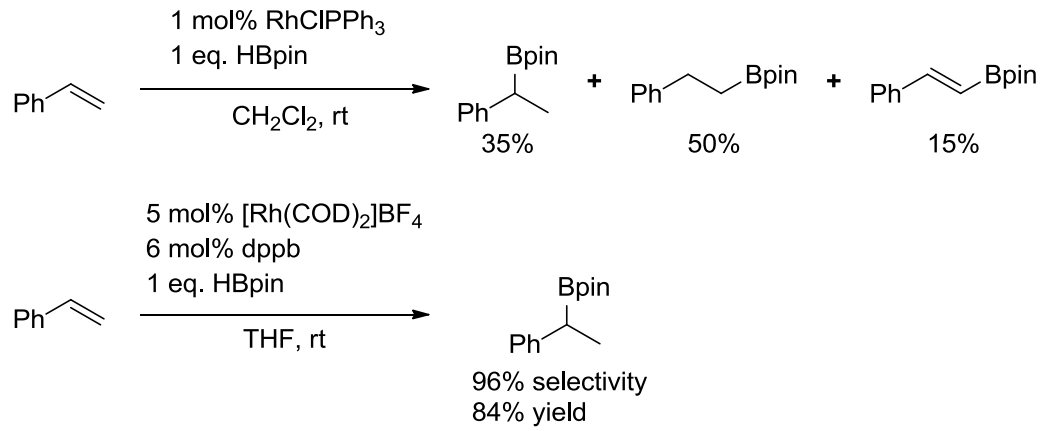


Figure 1-8: A small collection of hydroborating reagents.

Similar to uncatalyzed hydroboration, compounds were extracted from the chiral pool to aid in asymmetric incorporation in rhodium catalyzed hydroboration of olefins.[108] In this case, however, the chiral component could not be used as a recyclable auxiliary. Since the borane backbone must be able to reduce the reactivity of the borane to prevent an undesirable thermal reduction, the chiral framework is further removed from the reactive metal center. Therefore boranes, such as **1-52**, were developed but produced moderate *ee*s and did not compare with those attained in the Midland reduction.[108, 109]

Pinacolborane (HBpin) has become a significant borane that has been used in numerous types of reactions. Srebnik and coworkers first utilized it in the rhodium and zirconium catalyzed hydroboration.[96, 97, 110] Unlike HBcat, HBpin is not as efficient a hydroborating reagent for the rhodium catalyzed hydroboration of styrenes with neutral rhodium catalysts, such as Wilkinson's catalyst. As mentioned, cationic rhodium complexes are significantly more active, and this results in a much higher aptitude for utilizing this less reactive borane (Scheme 1.5-6).[111] HBpin has also been used in the palladium catalyzed[112] and magnesium catalyzed[113] borylation of aryl halides. Furthermore, the use of various chiral phosphine ligands has made this process asymmetric with high selectivities.[115, 114] HBpin has become one of the most utilized and robust hydroborating reagents because of its stability and ability to facilitate the isolation of organoborane products.



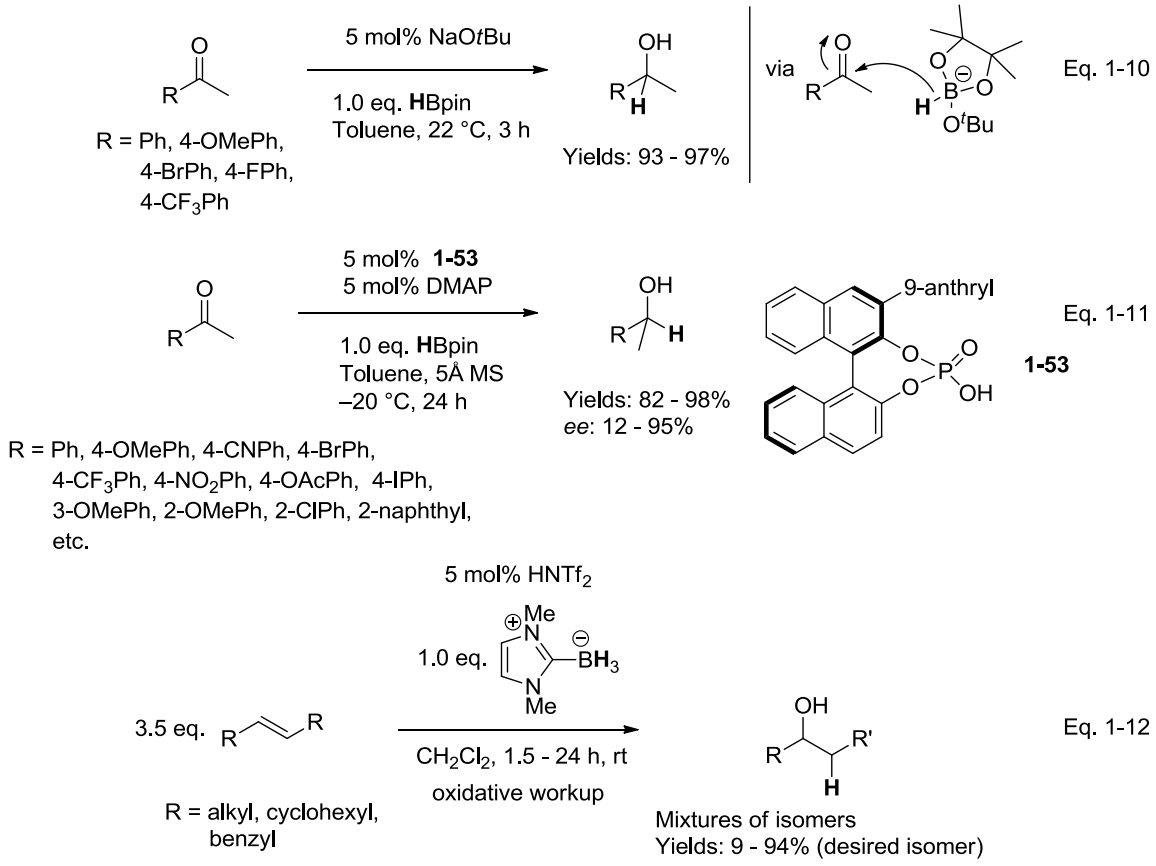
Scheme 1.5-6: A comparison between neutral and cationic rhodium catalyzed hydroboration.

Rhodium catalyzed hydroboration has become an important synthetic reaction. Significant effort has been dedicated to transforming organoboranes in other functional groups, such as carboxylic acids, amines, and alcohols.[115] The ability to control regio-, enantio- and chemoselectivity has allowed the widespread use of this reaction in the total synthesis of a non steroidal anti-inflammatory drug, Naproxen.[111] Additionally, this reaction is typically high yielding, has a broad substrate scope, and often proceeds with high selectivities. Drawbacks to this reaction include the use of toxic heavy metals and recovery of the metal can often be a tedious process. The decreased atom efficiency is overcome by the inherent chemical utility of the C–B bond. But difficulties associated with extracting and collecting the expensive, toxic metals inspired chemists to search for hydroboration catalysts without these issues.

1.5.3 Metal-Free Hydroboration

Catalytic metal-free hydroboration reactions which do not use BH_3 are quite rare with sparse examples being published over the past few years. Hydroboration using amine-boranes, such as pyridine-borane, have been reported but require the use of substoichiometric activators, such as iodine.[116] Although the scope and selectivities for this reaction is high compared to BH_3•THF, it remains a thermal process, requiring stoichiometric amounts of reagents.[117] Catalytic

metal-free hydroboration has been accomplished with Brønsted acids (Eq. 1-11)[118] and bases (Eq. 1-10),[119] and with stoichiometric *N*-heterocyclic carbene (NHC)-boranes and catalytic Brønsted acids (Scheme 1.5-7, Eq. 1-11).[120] Limited functional group diversity and, in one case, the need for expensive NHC-boranes are current drawbacks to these methods. However, the development of these reactions has provided synthetically viable alternatives to thermal and metal catalyzed hydroboration without expensive transition metals or the laborious use of chiral auxiliaries being involved.



Scheme 1.5-7: Examples of catalytic metal-free hydroboration reactions.

1.5.4 New Insight into the Mechanism of Rhodium Catalyzed Hydroboration

Rhodium catalyzed hydroboration of olefins is believed to proceed in a stepwise fashion. The foundations of this mechanism were proposed by Männig and Nöth in their original publication and their proposal remains similar to the currently accepted mechanism.[92] Several mechanistic investigations have been performed to elucidate the validity of the original mechanism.[121-123] Prior to the shaping work of Männig and Nöth, Kono and associates showed that HBcat could undergo oxidative addition into Wilkinson's catalyst with loss of one equivalent of PPh_3.[121] Westcott *et al.* isolated the P(*i*-Pr)$_3$ analogue of the oxidative addition product and determined its structure by X-ray crystallography.[122] Another detailed study carried out by the Evans group included investigations into substrate stability and deuterium labeling of products.[123] The culmination of these data supports a mechanism beginning with dissociation of one equivalent of phosphine which is promptly followed by reversible coordination of olefin to the rhodium center. Following olefin insertion, reversible oxidative addition of borane oxidizes the rhodium center from Rh(I) to Rh(III). Hydride insertion and subsequent reductive elimination yields the desired organoborane product and regenerates the active Rh(I) catalyst (Figure 1-9).

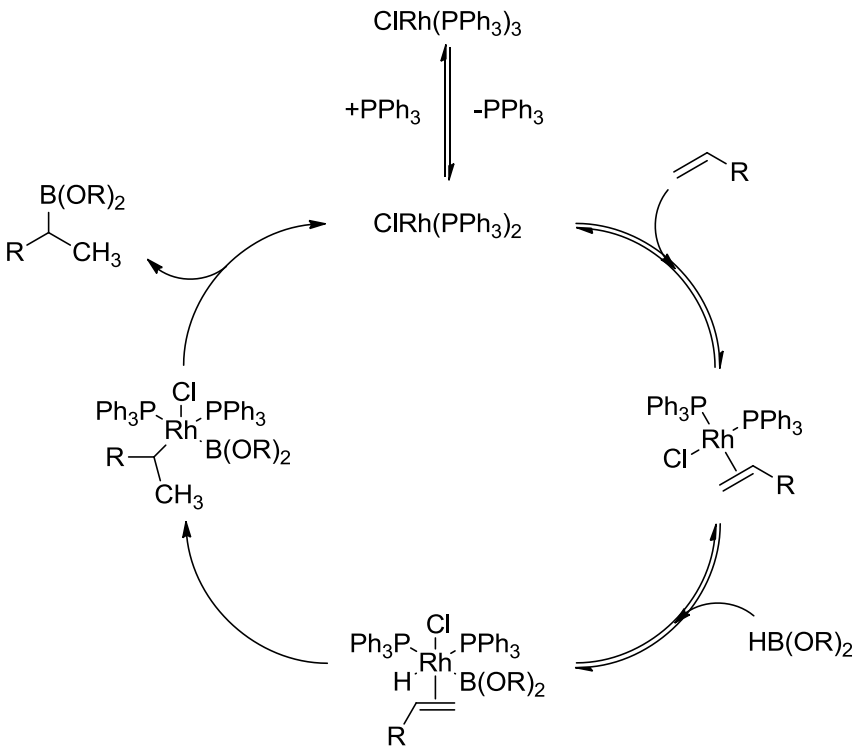
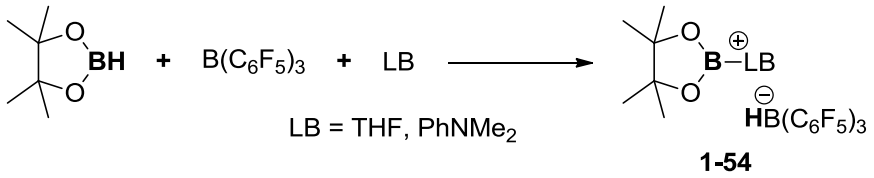


Figure 1-9: Proposed mechanism of rhodium catalyzed hydroboration.

Inspired by the uses of Lewis acids to catalyze novel reactions with pinacolboronate esters,[124] and altered regioselectivities in Lewis acid catalyzed hydroboration,[98] Crudden and Lata began a systematic investigation into effects of Lewis acids on the rhodium catalyzed hydroboration of olefins.[125] A screen of solvent, ligand, and Lewis acid additive demonstrated a remarkable shift in the regioselectivity of the reaction upon inclusion of both Lewis acid and transition metal catalysts. This, and the observation that the addition of two equivalents of $B(C_6F_5)_3$ to one equivalent cationic rhodium catalyst significantly increased the rate of the reaction encouraged Crudden and Lata to analyze the reaction mechanistically. ^{11}B NMR analysis of reaction mixtures provided insight into the reason for the dramatic change in rate. Peaks at ca. –25 ppm and +26 ppm in ^{11}B NMR indicated that two boron species (different from HBpin**)** were being formed in solution. A comparison between these shifts and those reported in FLP

hydrogenation[49] and FLP B–H bond activation[62] showed that this reaction forms the hydridoborate species, $HB(C_6F_5)_3^-$, which is the same species formed after dihydrogen heterolysis in FLP chemistry. Further investigation showed evidence supporting the idea that stoichiometric mixtures of $B(C_6F_5)_3$, HBpin, and a Lewis base, such as THF or *N*,*N*-dimethylaniline ($PhNMe_2$), could heterolytically cleave the B–H bond of HBpin and generate the boron cation/hydridoborate ion pair **1-54** (Scheme 1.5-8).



Scheme 1.5-8: Dual activation of HBpin by Lewis pairs.

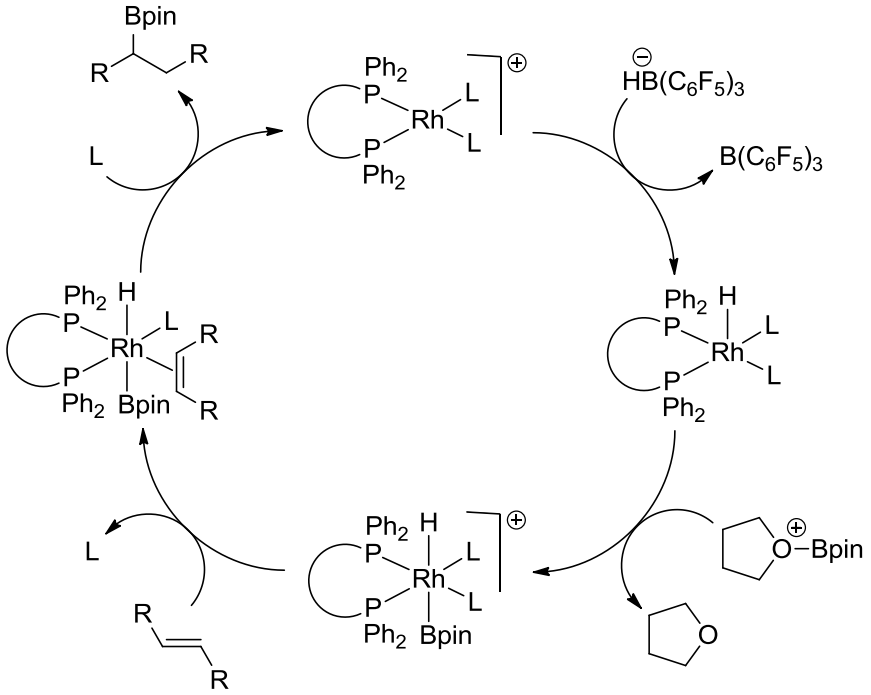


Figure 1-10: Proposed mechanism for Lewis acid assisted rhodium catalyzed hydroboration of olefins.

This dual activation of HBpin aided in explaining the rate increase in Lewis acid assisted rhodium catalyzed hydroboration. The proposed mechanism begins with hydride delivery from $HB(C_6F_5)_3^-$ to the cationic Rh catalyst yielding a neutral Rh(I) hydride, which then undergoes oxidative addition of the cationic boron•THF complex producing a cationic Rh(III) species (Figure 1-10). Departure of THF or a ligand opens a coordination site which allows coordination of an equivalent of olefin yielding a neutral Rh(III) complex. Hydride transfer and subsequent reductive elimination yields the desired organoborane and association of ligand regenerates the cationic rhodium(I) catalyst. The authors note that other potential mechanisms may be underway including mechanisms containing Rh(V) intermediates. Additionally, if present, the equilibrium of hydride transfer between $B(C_6F_5)_3$ and Rh lies towards $HB(C_6F_5)_3^-$, thus the role of $B(C_6F_5)_3$ could facilitate oxidative addition by abstracting a hydride from rhodium. The mechanism of this reaction is not fully understood and further mechanistic investigations would be highly advantageous.

The dramatic rate increase of rhodium catalyzed hydroboration through the addition of Lewis acids marked a significant achievement for these systems. Numerous questions came to light including: Could the observed boron cations been cleanly synthesized and isolated? Are they stable? What is their reactivity? Where else have boron cations been used in organic synthesis? And, most importantly, could they act as catalysts for hydroboration protocols on their own?

Boron cations are peculiar compounds; one would not expect such a Lewis acidic atom to be willing or even able to tolerate positive charge. Despite this, boron cations have been synthesized in such a way that reactivity is attenuated through the use of Lewis basic donors.[126] Furthermore, these cations have been utilized as novel, highly active reagents for hydroboration and borylation reactions.

1.6 Boron Cations

Historically, boron chemistry has been dominated by neutral and anionic complexes. These complexes have found use in many facets of synthetic organic chemistry. Anionic complexes are most commonly used as reducing agents, such as sodium borohydride. Neutral boron species have significantly different reactivity. Triethylborane, for example, can be used as an ignition source for rocket fuel[127]or as a radical initiator in organotin reactions.[128] On the other hand, boron cations have remained largely a chemical curiosity and not until recently have they started to gain attention as reagents in organic synthesis.[129]

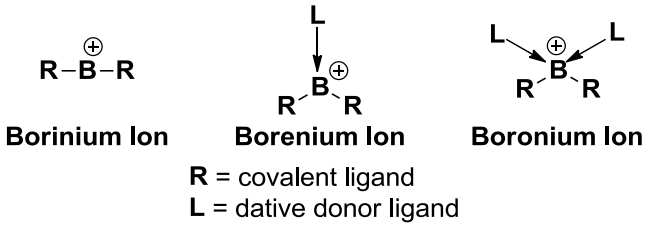


Figure 1-11: Nomenclature used to describe boron cations based on coordination number.

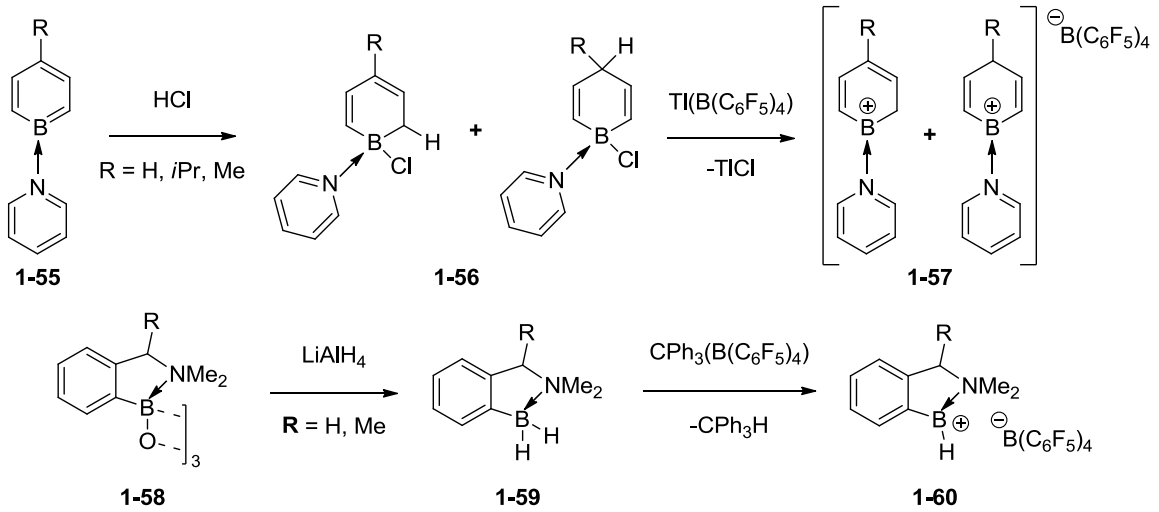
In 1985, Nöth and Kölle thoroughly summarized cationic boron chemistry and coined the nomenclature currently used in the chemical community.[130] Boron cations can be classified into three distinct categories based on the coordination number at boron (Figure 1-11). Two coordinate boron cations, known as borinium ions, are typically bound to substituents that can alleviate the electron deficiency at boron through lone pair delocalization into the vacant *p* orbitals on boron. These cations are notoriously reactive making their observation in the condensed phase quite difficult due to significant interactions with solvent and/or counterions. Through the use of low molecular weight boron species, such as trimethyl borane, two coordinate boron cations could be observed by electron impact mass spectrometry.[131] However, borinium cations with sterically bulky nitrogen donors have been isolated and characterized by X-ray

crystallography.[132] Although, the coordination number at boron is formally two, the bond order of the nitrogen-boron bond is more likely closer to two, which contributes to the increased stability of these compounds. Borenium cations are three coordinate species in which boron is bonded to two σ-bound substituents (R) and one dative donor (L) which occupies a third coordination site on boron. The added stabilization from the donor ligand renders borenium cations significantly more amenable to condensed phase study. Four coordinate boron cations, known as boronium cations, are by far the most common class of boron cations. Existing in tetrahedral geometries with two σ-bound substituents and two dative donor ligands, these species have filled the coordination sphere around boron and their stability is reflected in the number of reports on their generation and isolation.[133] For borenium and boronium ions the positive charge is often depicted as localized on the donor ligand. Considering that boron is significantly more electropositive than L and that the compounds often react as if they were cationic at boron, the positive charge will be drawn as if it lies on boron. The discussion in the remainder of this section will focus on generation and application of borenium cations.

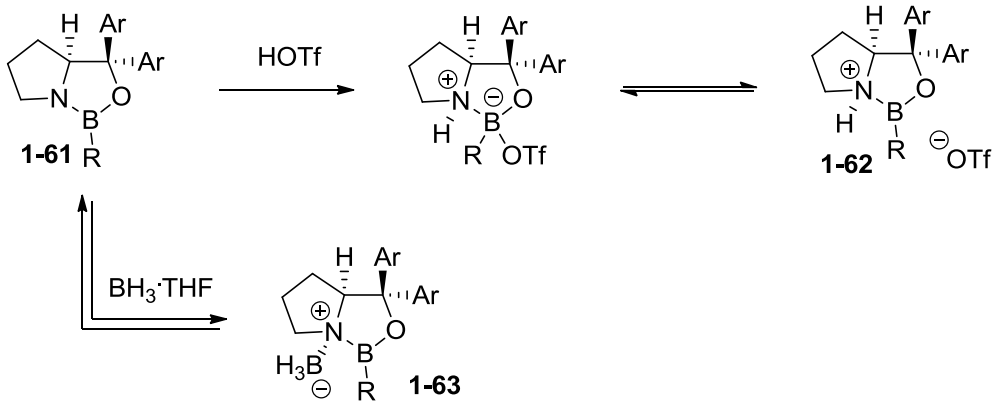
1.6.1 Synthesis of Borenium Cations

Until recently, reports of isolated borenium cations remained surprisingly rare with only three examples mentioned in Nöth's 1985 review.[130] A more recent review by Piers *et al*. clearly showed the dramatic increase in the number of reports of these cations.[134] These reviews focused on the methods of borenium synthesis. One of the two most common methods of borenium ion generation is through either halide or hydride abstraction from four coordinate neutral boron complexes. Strong Lewis acids are typically employed to facilitate the hydride/halide abstraction. Oft times, Lewis bases, such as pyridine, are added to a neutral three coordinate borane creating a Lewis base•borane adduct. The adduct is then reacted with a halide–based Brønsted acid or an appropriate hydride source which is subsequently abstracted by the Lewis acid, forming the

desired borenium cation (Scheme 1.6-1). Unsurprisingly, the survival of the borenium cation is directly related to the nucleophilicity of the newly formed counterion. An example of this approach was discussed in the FLP activation of the B–H bond (Section 1.4.1; Scheme 1.4-7). In this process, $B(C_6F_5)_3$ acts to abstract a hydride from the phosphine borane-adduct which yields stable borenium/hydridoborate salt, **1-28**. Piers and coworkers also applied this process in the synthesis of borinine derived borenium cations, **1-57**.[135] Reaction of pyridine-borinine (**1-55**) with dry HCl produced neutral Lewis base-chloroborane adducts, **1-56**. Exposure to a Lewis acidic $Tl(I)B(C_6F_5)_4$ complex facilitated hydride abstraction and produced two isomeric borenium ions **1-57**. In a similar process, Vedejs *et al*. reduced an arylboronic anhydride **1-58** with the standard reducing agent lithium aluminum hydride to the corresponding neutral borane stabilized by an intramolecular Lewis base, **1-59**.[136] Addition of a highly Lewis acidic tritylium salt abstracted a hydride from the neutral borane cleanly producing the borenium ion, **1-60** whose structure was determined by X-ray crystallography. As is evident, this methodology is typically employed when borenium formation is the desired target and examples of the utility of these borenium ions remains elusive.



Scheme 1.6-1: Examples of borenium ion generation via halide/hydride abstraction.



Scheme 1.6-2: Borenium formation through protonation or Lewis acid coordination.

A second method of borenium ion generation is by protonation or coordination of Lewis acids to aminoboranes. This method highlights the fact that borenium ion generation need not be a result of manipulations at boron but instead can result from decreasing the electron density of neighbouring Lewis basic sites. This depletion of electron density in the vicinity of a boron atom has the same effect as directly removing electrons from the boron center itself. The most significant application of this method of borenium formation is in the activation of the Corey-Itsuno catalyst **1-61** (Scheme 1.6-2).[137, 138] The oxazaborolidine commonly utilized in the asymmetric reduction of ketones (CBS reduction) is also an active catalyst in asymmetric Diels Alder reactions.[137] The catalyst can be activated through either protonation (**1-62**), as is the case in the Diels-Alder applications, or by addition of a Lewis acid (**1-63**), as is the case for the CBS reduction. The coordination of borane to nitrogen increases the electrophilicity and, in turn, the Lewis acidity of the boron atom within the oxazaborolidine. It should be noted that through the complexation of a Lewis acid no net charge is generated although the molecule now contains a borenium subunit that enables it to react in the observed fashion. This method of activation enables the metal-free asymmetric hydroboration of prochiral ketones.

1.6.2 Applications of Boron Cations

The borenium ion formed from the reaction of borane with the Corey-Itsuno catalyst is the most widely applied borenium cation in organic chemistry.[138] The increased Lewis acidity created from borane coordination allows for complexation of a prochiral ketone to **1-63**, which results in the enantioselective formation of chiral alcohols (Figure 1-12). These reactions are highly selective with a broad range of ketones being amenable to this process. Furthermore, the synthesis of this catalyst originates from proline, which enables the synthesis of both enantiomers of the Corey-Itsuno catalyst.[139] This facilitates the selection of stereochemistry in the product which is a characteristic of widely applicable enantioselective reactions. Furthermore, this reaction does not require the use of borane; for example, borohydrides and other more stable boranes are suitable hydride sources. This hydroboration reaction has few limitations with the reduction of unsymmetrical aliphatic ketones being its most substantial drawback. This hindrance notwithstanding, the catalytic asymmetric reduction of unsymmetrical ketones via the use of borenium cations has become an efficient and reliable protocol to produce optically active alcohols.

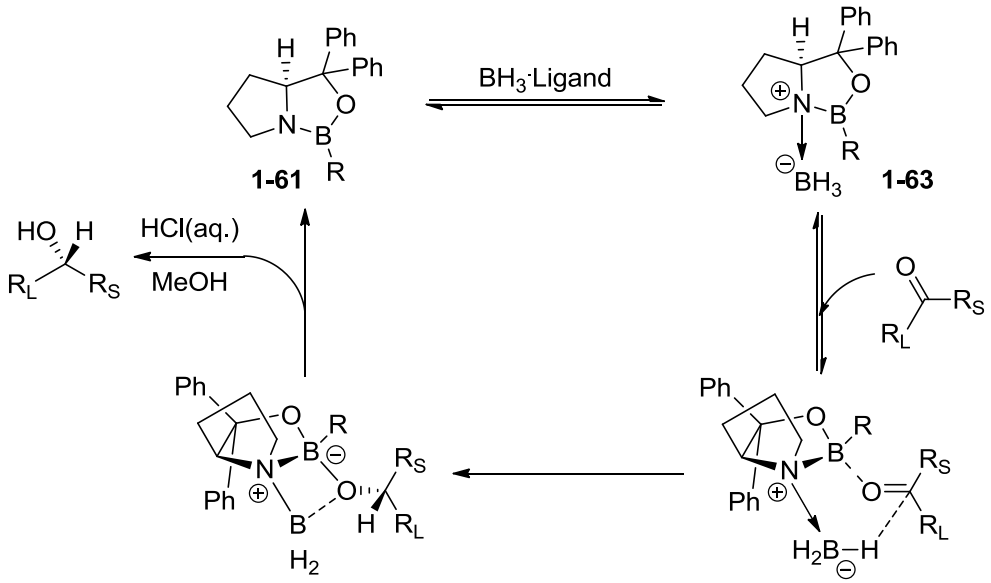
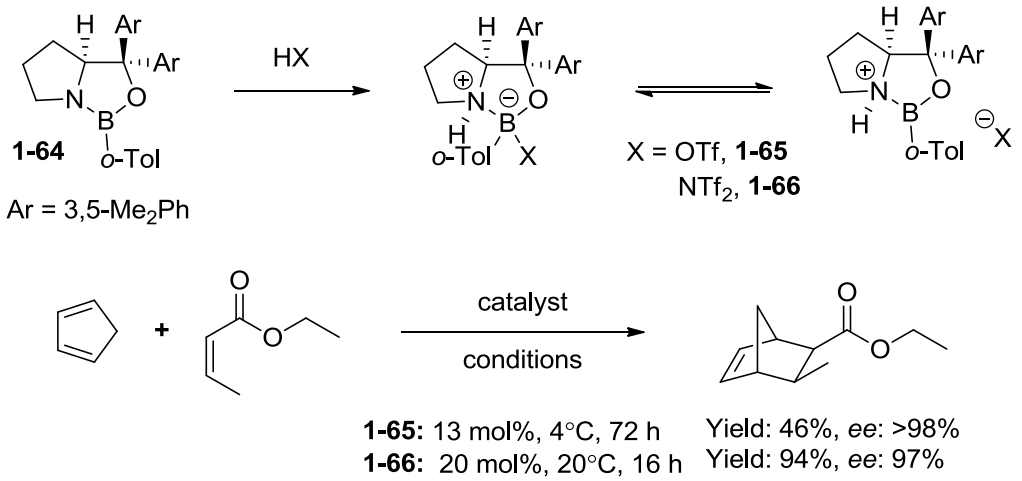


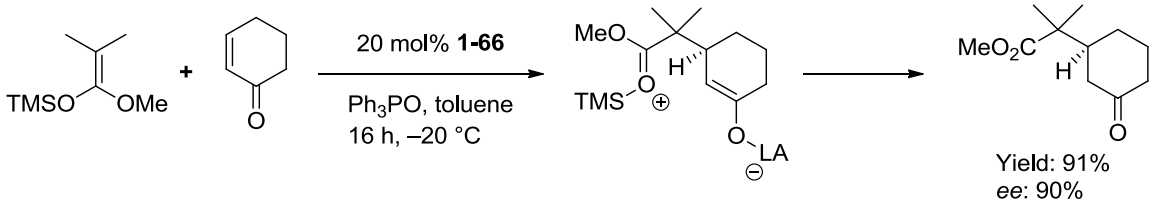
Figure 1-12: One of the proposed mechanisms of enantioselective oxazaborolidine reductions.

The applications of **1-63** are largely restricted to the carbonyl reductions but the catalytic applications of **1-62** are far broader in scope and functional group transformations. As mentioned, protonation of the α nitrogen dramatically increases the Lewis acidity of the boron center. This allows the oxazaborolidine borenium ion to act as a chiral Lewis acid, much like the chiral metal complexes discussed in Section 1.2.1. The Diels-Alder applications mentioned earlier are restricted to dienophiles containing carbonyl functionalities as their reactivity heavily relies upon complexation of the borenium to the carbonyl oxygen of the dienophile. Corey and coworkers took advantage of this Lewis acidity to facilitate Diels Alder reactions with very high endo/exo selectivities. [137, 140] Changing the Brønsted activator to triflimide ($HNTf_2$) drastically increased the reactivity of the catalyst enabling the use of less active dienes, further extending the scope of this reaction (Scheme 1.6-3).[141, 142]



Scheme 1.6-3: An example of the Diels-Alder reaction catalyzed by a borenium ion.

In these Diels-Alder reactions the borenium cation acts as an oxophilic activating agent and this phenomena has been exploited in several other Lewis acid catalyzed reactions. For example, **1-66** has been used to catalyze the Mukaiyama-Michael reaction of a ketene-silyl acetal and an enone, which resulted in the expected 1,4-product with high selectivities (Scheme 1.6-4).[143] This small collection of reactions exemplifies the breadth of highly selective, asymmetric chemistry possible when a highly Lewis acidic borenium-type Corey-Itsuno catalyst is employed.

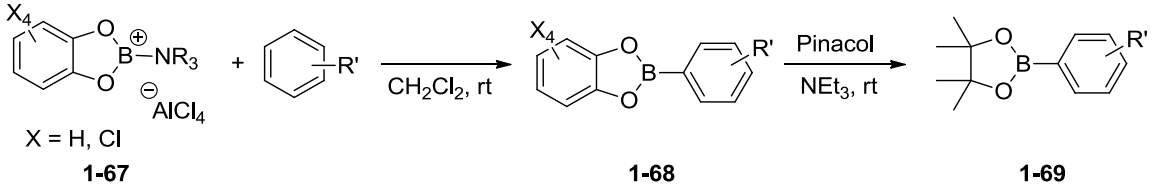


Scheme 1.6-4: An example of a Mukaiyama-Michael reaction catalyzed by borenium ion **1-66**.

Another application of borenium cations is their ability to stoichiometrically borylate arenes. Intramolecular borylation of aromatic rings has long been known and often requires harsh Friedel-Crafts conditions in excess of 100℃, including several examples that produce boron containing heterocycles.[144] However, intermolecular borylation of unactivated aromatics rings is a

much more desirable process because it is an easy, direct route to coupling partners used in the Suzuki-Miyaura cross coupling reaction. This production of aryl boranes is often accomplished with expensive iridium catalysts. However, recent work from Ingelson and colleagues further demonstrated the impact of borenium cations by showing that they could stoichiometrically borylate a large scope of unactivated aromatic rings (Scheme 1.6-5).[145, 146] Furthermore, they used transesterification of the boronates as a reaction quenching process that enabled purication of the organoborane by column chromatography.

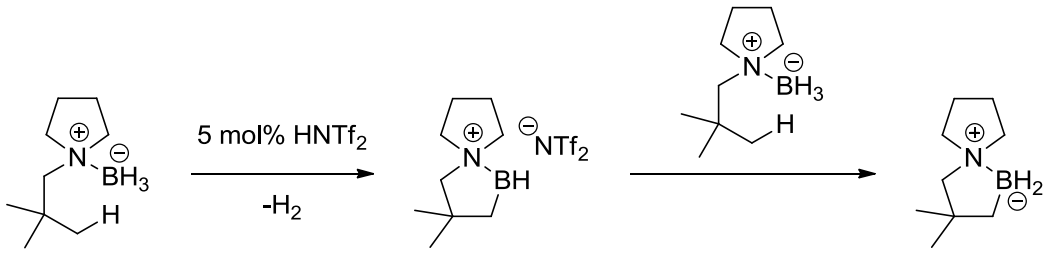
Ingelson *et al.* applied a halide abstraction method to synthesize a borenium based on a chlorinated analogue of catecholborane, **1-67**. Following formation of **1-67**, slow addition of an arene resulted in a rapid reaction between the borenium cation and the unactivated aromatic substrate producing the aryl catecholborate ester, **1-68**, which was converted to **1-69** on quench. Although the authors did not speculate on a reaction mechanism, one could envision a mechanism synonymous with classical electrophilic aromatic substitution reactions. This remarkable reaction proceeded in high yields and with excellent regioselectivity. They were also able to isolate and characterize their borenium salt by X-ray crystallography paying tribute to the stability of dioxaborolane structures.



Scheme 1.6-5: Use of borenium cations to stoichiometrically borylate arenes.

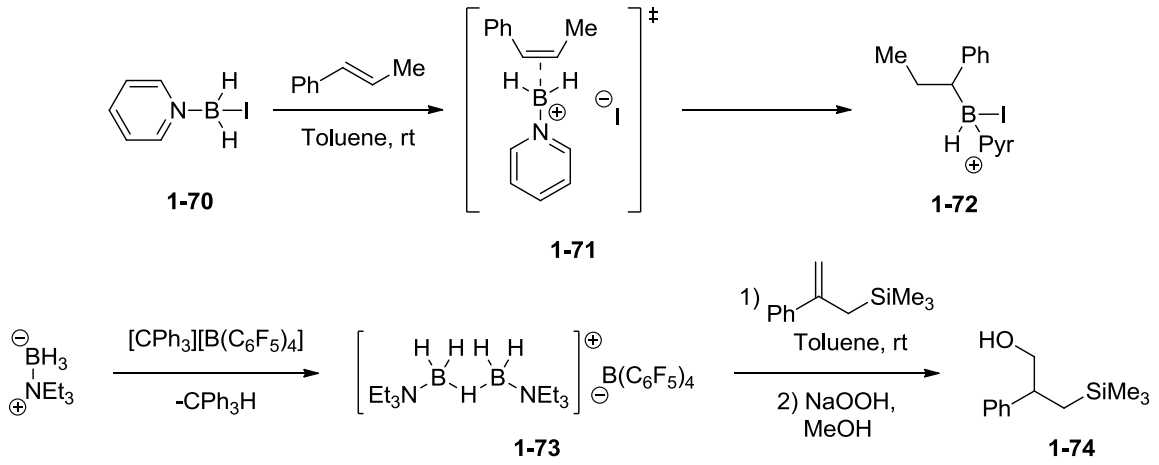
Recently, borenium cations have been proposed to be involved in the intramolecular insertion of activated amine-boranes into sp^3 hybridized C–H bonds in the presence of catalytic amounts of strong Brønsted acids (Scheme 1.6-6).[147] This report demonstrates the feasibility of

N-directed borylation via borenium cations in the presence of strong electrophiles. In addition to catalytic amounts of potent Brønsted acids and elevated temperatures, the same reaction could take place in the presence of stoichiometric amounts of strong Lewis acids, such as trityl tetrakis-2,3,4,5,6-pentafluorophenyl borate. The overall mechanism of this reaction remains purely speculative at present.



Scheme 1.6-6: Intramolecular C–H insertion by borenium ions.

Investigations into olefin hydroboration using activated amine-boranes have encountered species that might be considered borenium ion equivalents. Vedejs and coworkers showed that pyridine iodoborane (**1-70**) reacted with *β*-methylstyrene to produce the branched iodoborane adduct **1-72** which was subsequently converted into the corresponding pinacolboronate by treatment with pinacol and base (Scheme 1.6-7).[148] In this reaction, the borenium ion-olefin adduct **1-71** is not directly observed and its proposal is debatable but the authors believe it to be present based on the high branched selectivities observed. Another amine-borane, triethylamine-borane, has been utilized in hydroboration reactions.[144] The amine-borane was activated by a tritylium salt to form the hydride–bridged dimer **1-73**. Subsequent reaction of this dimer with an allylic silane followed by an oxidative workup cleanly produced the alcohol **1-74**. This experiment was conducted with the goal of observing a borylation/desilylation sequence but only hydroborated product was observed. This result indicated that the borenium ion **1-73** is an effective hydroborating reagent (Scheme 1.6-7).



Scheme 1.6-7: Borenium cations in hydroboration reactions.

Examples of the application of boron cations were sparse until the mid 1990's when significant developments were made towards their generation and isolation.[129] Their applications in synthetic organic chemistry have grown since that time.[129] With the discovery that boron cations play a role in reductions and hydroboration various questions came to light. Further exploration into the synthesis and reactivity of these complexes is required to unlock the secrets of these formally elusive now synthetically relevant borenium cations.

1.7 Conclusions and Research Objectives

The search for new reactions through mechanistic investigations and probing the nature of interesting chemical reactions has led to the discovery and development of novel chemical transformations and catalysts. The observation that pairs of Lewis acids and bases could violate Lewis' axiom led to the discovery of FLPs and in turn their application as hydrogenation catalysts. The use of FLPs to activate the B–H bond in combination with the utilization of Lewis acids to activate pinacol boronates led to the discovery that adding Lewis acids to rhodium

catalyzed hydroboration dramatically increased the rate of reaction. Through mechanistically probing this rate change, novel borenium-hydridoborate salts were observed and they do not appear to be innocent bystanders in hydroboration reactions. A literature investigation into boron cations clearly demonstrates their synthetic utility and highlights how seldom their reactivity has been exploited. This acted as inspiration to synthesize stable borenium cations, probe their reactivity, and investigate their mode of catalysis.

The main goals of the project discussed herein were to design, synthesize, and apply stable borenium cations to the catalytic hydroboration of various functional groups. We hypothesized that borenium cations could be generated through dual activation of dioxaborolanes by sterically hindered Lewis acids and bases. This borenium cation/borohydride ion pair could then be used to hydroborate moieties of chemical unsaturation. For example, we speculated that an imine could accept a positively charged boron fragment forming an iminium type species and subsequent hydride delivery from the borohydride would produce the reduced product and regenerate the FLP. Investigations began with generation of stable borenium cations and their ability to affect hydroboration was investigated. Following this, a substrate scope analysis and a detailed mechanistic discussion is presented.

1.8 References

[1] a) Collins, A.; Sheldrake, G.; Crosby, J. *Chirality in Industry II* **1997**, Wiley, West Sussex, England. b) Ojima, I. *Catalytic Asymmetric Synthesis, 3rd Ed.* **2010**, Wiley, Hoboken. c) Nugent, T.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753. d) Macdonald, S.; Cooper, T.; Campbell, I. *Angew. Chem. Int. Ed.* **2010**, *49*, 8082.

[2] Kagan, H. *Comprehensive Asymmetric Catalysis Vol. 1* **1999**, Springer, Heidelberg.

[3] For a review on Lewis base catalysis see: a) Denmark, S. E.; Beutner, G. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 1560. For a review on Lewis acid catalysis see: b) Corma, A.; Garcia, H. *Chem. Rev.* **2003**, *103*, 4307.

[4] S. Woodward, *Tetrahedron* **2002**, *58*, 1017.

[5] For reviews on dual activation see: a) Xiao, W.; Lu, L.; An, X.; Chen, J. *Syn. Lett.* **2012**, *23*, 490. b) Yamamoto, H. *Tetrahedron* **2007**, *63*, 8377. c) Ito, Y.; Sawamura, M. *Chem. Rev.* **1992**, *92*, 857. d) Steinhagen, H.; Helmchen, G. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2339. e) Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1236.

[6] Ito, K.; Kanemasa, S. *Eur. J. Org. Chem.* **2004**, 4741.

[7] Cahard, D.; Ma, J. *Angew. Chem. Int. Ed.* **2004**, *43*, 4566.

[8] Lewis, G. N. *Valence and the Structure of Atoms and Molecules* **1923**, Chemical Catalog Company, New York.

[9] Yamamoto, H.; Futatsugi, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 1924.

[10] For definitions of catalysis see: a) Noyori, T. S. R. *Asymmetric Catalysis in Organic Synthesis* **1994**, Wiley, Weinheim.

[11] Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis* **2005**, Elsevier, Philadelphia.

[12] Mukaiyama, T.; Narasaka, K.; Banno, K. *Chem. Lett.* **1973**, 1011.

[13] Mukaiyama, T.; Narasaka, K.; Banno, K. *J. Am. Chem. Soc.* **1974**, *94*, 7503.

[14] Mukiayama, T.; Kobayashi, S.; Uchiro, H.; Fujishita, Y.; Shiina, I. *J. Am. Chem. Soc.* **1991**, *113*, 4247.

[15] Kobayashi, S.; Horibe, M.; Saito Y. *Tetrahedron* **1994**, *50*, 9629. Note: This work also demonstrated the ability to switch the selectivity from *anti* to *syn*. This is clearly highlighted in the original work but is not discussed here for the sake of conciseness.

[16] Carreira, E. M.; Singer, R. A.; Lee, W. *J. Am. Chem. Soc.* **1994**, *116*, 8837.

[17] Carreira, E. M. *Mukaiyama Aldol Reaction.* In *Comprehensive Asymmetric Catalysis, Vol. III* **1999**, Jacobsen, E.; Pfaltz, A.; Yamamoto, H. Springer-Verlag, Heidelberg.

[18] Nelson, S. *Tetrahedron: Asymm.* **1998**, *9*, 357.

[19] a) Mukaiyama, T.; Inubushi, A.; Suda, S.; Hara, R.; Kobayashi, S. *Chem. Lett.* **1990**, 1015. b) Evans, D.; Murry, J.; Kozlowski, M. *J. Am. Chem. Soc.* **1996**, *118*, 5814. c) Kobayashi, S.; Furuya, M.; Ohtsubo, A.; Mukaiyama, T. *Tetrahedron: Asymmetry* **1991**, *2*, 635. d) Kobayashi, S.; Fujishita, Y.; Mukaiyama, T. *Chem Lett*. **1990**, 1455.

[20] Chuit, C.; Corriu, R.; Reye, C.; Young, J. *Chem. Rev.* **1993**, *93*, 1371.

[21] Denmark, S.; Stanvenger, R. *Acc. Chem. Res.* **2000**, *33*, 432.

[22] Denmark, S.; Winter, S.; Su, X.; Wong, K. *J. Am. Chem. Soc.* **1996**, *118*, 7404.

[23] Denmark, S.; Stavenger, R.; Wong, K. *J. Org. Chem.* **1998**, *63*, 918.

[24] Denmark, S.; Beutner, G.; Wynn, T.; Eastgate, M. *J. Am. Chem. Soc.* **2005**, *127*, 3774.

[25] Denmark, S.; Stanvenger, R. *Acc. Chem. Res.* **2000**, *33*, 432.

[26] Brown, H. C.; Schlesinger, H. I.; Cardon, S. Z. *J. Am. Chem. Soc.* **1942**, *64*, 325.

[27] Wittig, G.; Riickert, A. *Liebigs Ann. Chem.* **1950**, 101.

[28] Tochtermann, W. *Angew. Chem. Int. Ed.* **1966**, *5*, 351.

[29] Stephan, D. W.; Erker, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 46.

[30] de Vries, J. G.; Elsevier, C. J. *Handbook of Homogeneous Hydrogenation, Vol. 1-3* **2007**, Wiley, Weinheim.

[31] Andersson, P. G.; Munslow, I. J. *Modern Reduction Methods* **2008**, Wiley, Weinheim.

[32] "The Nobel Prize in Chemistry 1912". Nobelprize.org. August 9th, 2012: http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1912/

[33] a) Noyori, R.; Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T. *J. Am. Chem. Soc.* **1980**, *102*, 7932-7934. b) Noyori, R.; Ohta, M.; Hsiao, Y.; Kitamura, M.; Ohta, T.; Takaya, H. *J. Am. Chem. Soc.* **1986**, *108*, 7117. c) Noyori, R.; Ohta, T.; Takaya, H. *Tetrahedron Lett.* **1990**, *31*, 7189.

[34] Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106.

[35] "The Nobel Prize in Chemistry 2001". Nobelprize.org. July 18th, 2012: http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2001/

[36] Dalko, P.; Moisan, L. *Angew. Chem. Int. Ed.* **2001**, *40*, 3726.

[37] DeWitt, E. J.; Ramp, F. L.; Trapasso, L. E. *J. Am. Chem. Soc.* **1961**, *83*, 4672.

[38] Walling, C.; Bollyky, L. *J. Am. Chem. Soc.* **1964**, *83*, 2968-2969.

[39] Siskin, M. *J. Am. Chem. Soc.* **1974**, *95*, 3641.

[40] Stephan, D. W.; Welch, G. C.; San Juan, R. R.; Masuda, J. D. *Science* **2006**, *314*, 1124-1126.

[41] a) Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170. b) Piers, W. *Adv. Organomet. Chem.* **2005**, *52*, 1.

[42] Stephan, D. W.; Welch, G. C.; Cabrera, L.; Chase, P. A.; Hollink, E.; Masuda, J. D.; Wei, P. *Dalton Trans.* **2007**, 3407.

[43] Erker, G.; Momming, C. M.; Oten, E.; Kehr, G.; Fröhlich, R.; Grimme, S.; Stephan, D. W. *Angew. Chem. Int. Ed.* **2009**, *48*, 6643.

[44] Erker, G. *Dalton Trans.* **2011**, *40*, 7475.

[45] Stephan, D. W.; Spies, P.; Erker, G.; Kehr, G.; Bergander, K.; Fröhlich, R.; Grimme, S. *Chem. Commun.* **2007**, 5072.

[46] Erker, G.; Momming, C. M.; Frömel S.; Kehr, G.; Fröhlich, R.; Grimme, S. *J. Am. Chem. Soc.* **2009**, *131*, 12280.

[47] Stephan, D. W.; Chase, P. C.; Welch, G. C.; Jurca, T. *Angew. Chem. Int. Ed.* **2007**, *47*, 8050.

[48] Stephan, D. W.; Welch, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 1880.

[49] Stephan, D. W.; Jurca, T.; Chase, P. A. *Chem. Commun.* **2008**, 1701.

[50] Stephan, D. W.; Geier, S. J.; Chase, P. A. *Chem. Commun.* **2010**, 4884.

[51] Erker, G.; Spies, P.; Schwendemann, S.; Lange, S.; Kehr, G.; Fröhlich, R. *Angew. Chem. Int. Ed.* **2008**, *47*, 7543.

[52] Erker, G.; Wang, H.; Fröhlich, R.; Kehr, G. *Chem. Commun.* **2008**, 5966.

[53] Stephan, D. W.; Mahdi, T.; Heiden, Z. M.; Grimme, S. *J. Am. Chem. Soc.* **2012**, *134*, 4088.

[54] Soós, T.; Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 6559.

[55] Stephan, D. W.; McCahill, J. S. J.; Welch, G. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 4968.

[56] Stephan, D. W.; Ullrich, M.; Seto, K.; Lough, A. J. *Chem. Commun.* **2009**, *17*, 2335.

[57] Stephan, D. W.; Dureen, M. A. *J. Am. Chem. Soc.* **2009**, *131*, 8396.

[58] Erker, G.; Stephan, D. W.; Mömming, C. M.; Otten, E.; Kehr, G.; Fröhlich, R.; Grimme, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 6643.

[59] Stephan, D. W. *Dalton Trans.* **2009**, 3129.

[60] a) Piers, W. E.; Parks, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 9440. b) Piers, W. E.; Blackwell, J. M.; Foster, K. L; Beck, V. H. *J. Org. Chem.* **1999**, *64*, 4887. c) Piers, W. E.; Parks, D. J.; Blackwell, J. M. *J. Org. Chem.* **2000**, *65*, 3090. d) Piers, W. E.; Blackwell, J. M.; Sonmor, E. R.; Scoccitti, T. *Org. Lett.* **2000**, *2*, 3921. e) Piers, W. E.; Blackwell, J. M.; Morrison, D. J. *Tetrahedron* **2002**, *58*, 8247.

[61] Gevorgyan, V.; Rubin, M.; Schwier, T. *J. Org. Chem.* **2002**, *67*, 1936.

[62] Stephan, D. W.; Dureen, M. A.; Lough, A.; Gilbert, T. M. *Chem. Commun.* **2008**, 4303.

[63] a) Piers, W. E.; Blackwell, J. M.; Parvez, M. *Org. Lett.* **2000**, *2*, 695. b) Piers, W. E.; Blackwell, J. M.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295.

[64] Oestreich, M.; Rendler, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 5997.

[65] a) Jursic, B. S. *J. Mol. Struct.* **1999**, *492*, 97. b) Watts, J. D.; Bartlett, R. J. *J. Am. Chem. Soc.* **1995**, *117*, 825. c) Tague, T. J. J.; Andrews, L. *J. Am. Chem. Soc.* **1994**, *116*, 4970. d) Schreiner, P. R.; Schaefer, H. F.; Schleyer, P. v. R. *J. Chem. Phys.* **1994**, *101*, 7625.

[66] Sweany, R. L.;Moroz, A.; Whittenburg, S. L. *J. Phys. Chem.* **1990**, *94*, 1352.

[67] Pápai, I.; Rokob, T. A.; Hamza, A.; Stirling, A.; Soós, T. *Angew. Chem. Int. Ed.* **2008**, *47*, 2435.

[68] Piers, W. E.; Marwitz, A. J. V.; Dutton, J. L.; Mercier, L. G. *J. Am. Chem. Soc.* **2011**, *133*, 10026.

[69] Li, S.; Guo, Y. *Inorg. Chem.* **2008**, *47*, 6212.

[70] Stephan, D. W.; Heiden, Z. M. *Chem. Commun.* **2011**, *47*, 5729.

[71] Klankermayer, J.; Chen, D. *Chem. Commun.* **2008**, 2130.

[72] Piers, W. E.; Parks, D. J.; Yap, G. P. A. *Organometallics* **1998**, *17*, 5492.

[73] Klankermayer, J.; Chen, D.; Wang, Y. *Angew. Chem. Int. Ed.* **2010**, *49*, 9475.

[74] Klankermayer, J.; Ghattas, G.; Chen, D.; Pan, F. *Dalton Trans.* **2012**, *41*, 9026.

[75] Klankermayer, J.; Chen, D.; Leich, V.; Pan, F. *Chem. Eur. J.* **2012**, *18*, 5184.

[76] Patnaik, P. *A Comprehensive Guide to the Hazardous Properties of Chemical Substances*, *3rd Ed.* **2007**, Wiley, Hoboken.

[77] Andersson, P. G.; Munslow, I. J. *Modern Reduction Methods* **2008**, Wiley-VCH, Weinheim.

[78] Pelter, A.; Beletskaya, I. *Tetrahedron* **1997**, *53*, 4957.

[79] "The Nobel Prize in Chemistry 1979". Nobelprize.org. July 18th, 2012: http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1979/

[80] Matos, K. Burkhardt, E. R. *Chem. Rev.* **2006**, *106*, 2617.

[81] Dhillon, R. S. *Hydroboration and Organic Synthesis: 9-Boracyclo[3.3.1]Nonane (9-BBN)* **2007**, Springer: New York.

[82] Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, *37*, 3547.

[83] Midland, M. M.; Tramontano, A.; Zderic, Z. A. *J. Organomet. Chem.* **1977**, *134*, C17.

[84] Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1977**, *99*, 5211.

[85] Alpine-Borane is a registered trademark of the Aldrich Chemical Co.

[86] Brown, H. C.; Yoon, N. M. *Israel J. Chem.* **1977**, *15*, 12.

[87] Mandal, A. K.; Yoon, N. M. *J. Organomet. Chem.* **1978**, *156*, 183.

[88] Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4303.

[89] Wilczynski, R.; Sneddon, L.G. *J. Am. Chem. Soc.* **1980**, *103*, 2857-2858.

[90] Wilczynski, R.; Sneddon, L. G. *Inog. Chem.* **1981**, *20*, 3955-3962.

[91] Davan, T.; Corcoran, E. W.(Jr.); Sneddon, L. G. *Organometallics* **1983**, *2*, 1693-1694

[92] Männig, D. and Nöth, H. *Angew. Chem. Int. Ed.* **1985**, *24*, 878-879.

[93] Burgess, K; Jaspars, M. *Organometallics* **1993**, *12*, 4197.

[94] Suzuki, A.; Gridnev, I. D.; Miyaura, N. *J. Org.Chem.* **1993**, *58*, 5351.

[95] Sneddon, L. G.; Mirabelli, M. G. L. *J. Am. Chem. Soc.* **1988**, *110*, 449.

[96] Srebnik, M.; Pereira, S. *Organometallics* **1995**, *14*, 3127.

[97] Srebnik, M.; Pereira, S. *J. Am. Chem. Soc.* **1996**, *118*, 909.

[98] Evans, D. A.; Muci, A. R.; Stürmer, R. *J. Org. Chem.* **1993**, *58*, 5307.

[99] Molander, G. A.; Pfeiffer, D. *Org. Lett.* **2001**, *3*, 361.

[100] Marks, T. J.; Harrison, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 9220.

[101] Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*,1179.

[102] a) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *Inorg. Chem.* **1993**, *32*, 2175. b) Burgess, K.; van der Donk, W. A.; Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350.

[103] Brown, H. C.; Rao, B. C. S. *J. Org. Chem.* **1957**, *22*, 1137.

[104] Crudden, C. M.; Chen, A.; Ren, L. *J. Org. Chem.* **1999**, *64*, 9704-9710.

[105] For reviews on Suzuki- Miyaura cross couplings reactions see: a) Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6723. b) Sigmun, M. S.; Jana, R.; Pathak, T. P. *Chem. Rev.* **2011**, *111*, 1417. c) Percec, V.; Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.; Garg, N. K. *Chem. Rev.* **2011**, *111*, 1346. d) Snieckus, V.; Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062.

[106] Robinson, R.; Hadebe, S. *Eur. J. Org. Chem.* **2006**, 4898.

[107] Biedenzu, K.; Merriam, J. S. *Inorg. Synth.* **1972**, *44*, 162.

[108] Lloyd-Jones, G. C.; Brown, J. M. *Tetrahedron: Asymm.* **1990**, *12*, 869.

[109] Lloyd-Jones, G. C.; Brown, J. M. *Chem. Commun.* **1992**, 710.

[110] Srebnik, M.; Pereira, S. *Tetrahedron Lett.* **1996**, *37*, 3283.

[111] Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 9200.

[112] Lin, Z.; Lam, K. C.; Marder, T. B. *Organometallics* **2010**, *29*, 1849.

[113] Duñach, E.; Pintaric, C.; Olivero, S.; Gimbert, Y.; Chavant, P. Y. *J. Am. Chem. Soc.* **2010**, *132*, 11825.

[114] Crudden, C. M.; Glasspoole, B. W.; Lata, C. J. *Chem. Commun.* **2009**, 6704.

[115] Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695.

[116] Vedejs, E.; Clay, J. M. *J. Am. Chem. Soc.* **2005**, *127*, 5766.

[117] Vedejs, E.; Scheideman, M.; Wang, G. *J. Am. Chem. Soc.* **2008**, *130*, 8669.

[118] Antilla, J. C.; Zhang, Z.; Jain, P. *Angew. Chem. Int. Ed.* **2011**, *50*, 10961.

[119] Clark, T. B.; Query, I. P.; Squier, P. A.; Larson, E. M.; Isley, N. A. *J. Org. Chem.* **2011**, *76*, 6452.

[120] Vedejs, E.; Prokofjevs, A.; Boussonnière, A.; Li, L.; Bonin, H.; Lacôte, E.; Curran, D. P. *J. Am. Chem. Soc.* **2012**, ASAP, DOI: 10.1021/ja305061c.

[121] Kono, H.; Ito, K. *Chem. Lett.* **1975**, 1095.

[122] Westcott, S. A.; Taylor, N. J.; Marder, T. B.; Baker, R. T.; Jones, N. J.; Calabrese, J. C. *Chem. Commun.* **1991**, 304.

[123] Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679.

[124] a) Hall, D. G.; Kennedy, J. W. J. *J. Am. Chem. Soc.* **2002**, *124*, 11586. b) Miyaura, N.; Ishiyama, T.; Ahiko, T. *J. Am. Chem. Soc.* **2002**, *124*, 12414. c) Hall, D. G.; Kennedy, J. W. J. *Angew. Chem. Int. Ed.* **2003**, *42*, 4732.

[125] Lata, C. J.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *132*, 131.

[126] Piers, W. E.; Bourke, S. C.; Conroy, K. D. *Angew. Chem. Int. Ed.* **2005**, *44*, 5016.

[127] Chehroudi, B.; Talley, D.; Yang, V. *Encyclopedia of Aerospace Engineering* **2010**, Wiley, New York.

[128] Renaud, P.; Beauseigneur, A.; Brecht-Forster, A.; Becattini, B.; Darmency, V.; Kandhasamy, S. Montermini, F.; Ollivier, C.; Panchaud, P.; Pozzi, D.; Scanlan, E. M.; Schaffner, A.; Weber V. *Pure. Appl. Chem.* **2007**, *79*, 223.

[129] Vedejs, E.; De Vries, T. S.; Prokofjevs, A. *Chem Rev.* **2012**, *112*, 4246.

[130] Nöth, H.; Kölle, P. *Chem. Rev.* **1985**, *85*, 399.

[131] Beauchamp, J. L.; Murphy, M. K. *J. Am. Chem. Soc.* **1976**, *98*, 1433.

[132] Nöth, H.; Staudigl, R.; Wagner, H. *Inorg. Chem.* **1982**, *21*, 706.

[133] (a) Shitov, O. P.; Ioffe, S. L.; Tortakowskii, V. A.; Novikov, S. S. *Russ. Chem. Rev.* (Engl. *Transl.)* **1970**, *39*, 906. (b) Ryschkewitsch, G. E. in *Boron Hydride Chemistry* **1975**, Academic Press: New York.

[134] Piers, W. E.; Bourke, S. C.; Conroy, K. D. *Angew. Chem. Int. Ed.* **2005**, *44*, 5016.

[135] Piers, W. E.; Ghesner, I.; Parvez, M.; McDonald, R. *Chem. Commun.* **2005**, 2480.

[136] Vedejs, E.; Nguyen, T.; Powell, D. R.; Schrimpf, M. R. *Chem. Commun.* **1996**, 2721.

[137] Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3808.

[138] Corey, E. J.; Helal, E. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986.

[139] Cho, B. T. *Chem. Soc. Rev.* **2009**, *38*, 443.

[140] Corey, E. J.; Liu, D.; Canales, E. *J. Am. Chem. Soc.* **2007**, *129*, 1498.

[141] Corey, E. J.; Ryu, D. H. *J. Am. Chem. Soc.* **2003**, *125*, 6388.

[142] Corey, E. J.; Ryu, D. H.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 9992.

[143] Corey, E. J.; Liu, D.; Hong, S. *J. Am. Chem. Soc.* **2006**, *128*, 8160.

[144] Prokofjevs, A. Ph. D. Dissertation, University of Michigan, **2012**.

[145] Ingleson, M. J.; DelGrosso, A.; Singleton, P. J.; Muryn, C. A. *Angew. Chem. Int. Ed.* **2011**, *50*, 2102.

[146] Ingleson, M. J.; DelGrosso, A.; Helm, M. D.; Soloman, S. A.; Caras-Quintero, D. *Chem. Commun.* **2011**, *47*, 12459.

[147] Vedejs, E.; Prokofjevs, A. *J. Am. Chem. Soc.* **2011**, *133*,20056.

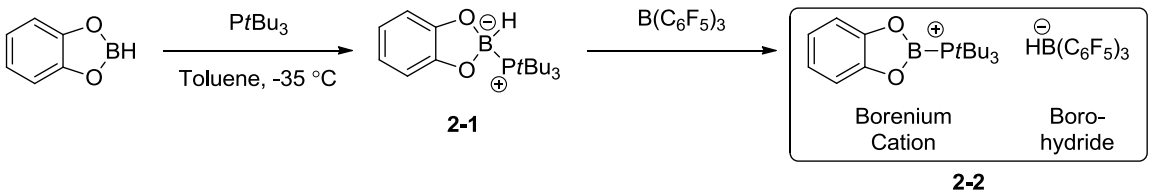
[148] Vedejs, E.; Karatjas, A. G. *J. Org. Chem.* **2008**, *73*, 9508.

Chapter 2

Synthesis and Reactivity of Borenium Cations

2.1 Introduction

The synthesis and isolation of stable borenium cations is a challenging task as sterically bulky or electron rich ligands are often required.[1] Furthermore, using these species in catalysis is often difficult due to the inability to isolate the active catalysts, which are typically activated *in situ* with strong acid at cryogenic temperatures.[2] However, new results have dramatically changed the way in which borenium cations can be manufactured. As highlighted in the previous chapter, frustrated Lewis pairs (FLPs) are able to heterolytically cleave the B–H bond of catecholborane by dual activation with the strong Lewis acid tris-pentafluorophenyl borane ($B(C_6F_5)_3$) and a sterically bulky phosphine, tris-*t*-butyl phosphine (Scheme 2.1-1).[3] This remarkable bond activation technique represents a novel way of generating a stable borenium cation and an anionic borohydride from two nonionic starting materials. This complex was stable in solid form at ambient temperature and was characterized by X-ray crystallography. This method of salt generation is facilitated by the inability of the phosphine to complex with $B(C_6F_5)_3$ enabling the hydride abstraction to proceed. The potential of employing this activation in a hydroboration process is clearly evident. Following cleavage of the B–H bond, the salt **2-2** contains a highly electrophilic borenium cation and a nucleophilic borohydride.



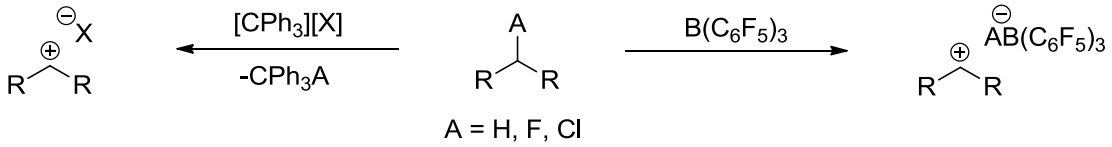
Scheme 2.1-1: Heterolytic cleavage of a B–H bond forming a borenium cation and borohydride.

One could imagine a stepwise hydroboration of C=X bonds taking place in two steps: transfer of the borenium cation to a Lewis basic ketone or imine activates it towards a subsequent nucleophilic attack of the borohydride, $HB(C_6F_5)_3^-$. Herein, the results of an exploration into B–H bond activation via FLP-type systems and their applications as hydroboration catalysts are presented. After a discussion of the dual activation of boranes by Lewis acid/base pairs, their reactivity and catalytic competence is evaluated.

2.2 Generation of Borenium Cations

An appealing method of B–H bond activation is the abstraction of a hydride or halide from dioxoborolane derivatives.[3] These borane reagents are commonly used in metal-catalyzed hydroboration and borylation reactions because of their reduced electrophilicity, which allows the catalyst to govern their reactivity.[4, 5] This diminished reactivity can be utilized as an asset when aiming to abstract the hydride after complexation of the borane to a Lewis base, as the oxygen atoms proximal to the boron atom will stabilize the cationic character at boron. Ideal reagents for this reaction are hydrido- or halophiles (compounds designed to have high affinities for hydrides or halides, respectively) depending on the nature of the starting boron species. Numerous metal salts are capable of acting as halophiles, such as silver (I) triflate or platinum dichloride.[6] However, one of the goals of this project was to perform a hydroboration reaction without the use of any transition metals as such other abstraction reagents were considered. In particular, two Lewis acids have been used as anion abstraction agents in numerous systems. The highly hydridophilic, commercially available Lewis acid $B(C_6F_5)_3$ is one of these Lewis acids. Its ability to abstract a hydride from a borane was demonstrated by Stephan an coworkers,[3] who added $B(C_6F_5)_3$ to a mixture of catecholborane and tris-*t*-butyl phosphine and generated a boryl-phosphonium cation (Scheme 2.1-1). A second set of Lewis acids aptly suited for this transformation are stabilized carbocations charge matched with weakly coordinating counterions.

One such Lewis acid is the triaryl stabilized triphenylmethylium carbocation which can be charge matched by various counterions, including BF_4^-, SbF_6^-, or $B(C_6F_5)_4^-$.[7] Both of these Lewis acids, have demonstrated their ability to abstract small anions (Scheme 2.2-1).[8, 9]



Scheme 2.2-1: Demonstration that $B(C_6F_5)_3$ and trityl salts are capable of abstracting small anions.

The Lewis acid, $B(C_6F_5)_3$, originally synthesized by Massey,[10] has a Lewis acidity strength between that of BF_3 and BCl_3 on the Child's Lewis acidity scale.[11] Its ability as an anion abstraction agent was thoroughly studied when it became clear that this Lewis acid could be used as an effective initiator for Ziegler-Natta type polymerization reactions.[12, 13] In addition, it is able to cleanly abstract hydrides, halides, and methyl groups from main group and transition metal complexes,[11, 14, 15] and hydrides from organic hydride sources such as 1,4-dihydropyridines.[16] Detailed mechanistic studies on the hydrosilylation of ketones catalyzed by $B(C_6F_5)_3$ revealed that its true role was to abstract a hydride from the silane and not to act as an activator for the carbonyl functionality (Figure 2-1).[17, 18] The range of nucleophilic hydrides amenable to abstraction by $B(C_6F_5)_3$ along with its well documented successes in element–H bond activation and FLP chemistry made it an ideal starting point for Lewis pair dual activation of boranes.

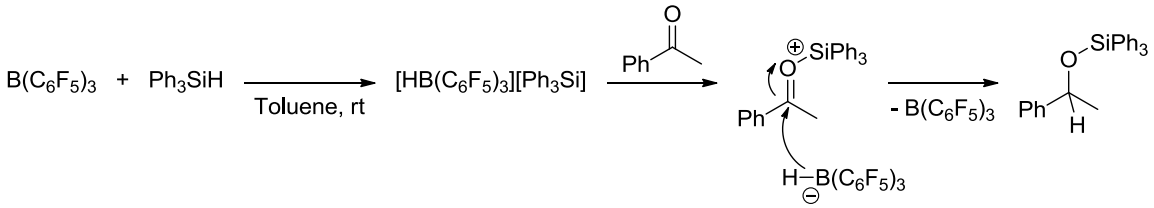
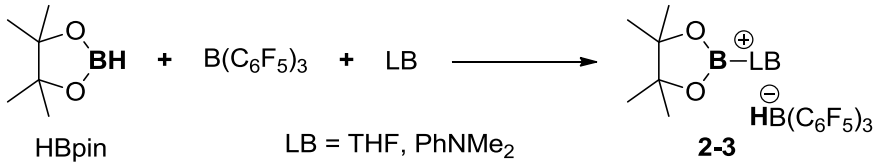


Figure 2-1: Mechanism of hydrosilylation of ketones catalyzed by $B(C_6F_5)_3$.

Much like trivalent boranes, carbocations have long been used as reagents in organic synthesis. They are widely known to mediate rearrangements, ring expansions,[19] have found use

in the synthesis of protecting groups,[20] and numerous other transformations.[21] A particular carbocation, triphenylmethylium (trityl), is a remarkably stable, yet highly Lewis acidic cation that is compatible with various counterions.[22] In particular, trityl tetrakis-pentafluorophenyl borate ($TrB(C_6F_5)_4$), has become a common trityl reagent due to the non-coordinating nature of the counterion and the salts' resistance to air and moisture induced decomposition.[23] Primary applications include use as an initiator in polymerization reactions[24] and as a catalyst in reactions such as the alkylmetallation of alkynes[25] and Mukaiyama aldol reactions.[26] However, as it pertains to this work, the most important property of trityl salts is their hydride affinity. $TrB(C_6F_5)_4$ and other trityl salts have been used to abstract hydrides to facilitate the conversion of dihydroaromatics into aromatics,[27] oxidation of acetals to ketones,[28] and abstract hydrides to create benzylic carbocations,[29] silylium cations,[30] and borenium cations.[31] The prior successes of trityl salts led us to investigate their use to abstract hydride from Lewis base activated dioxaborolanes.

Studying rhodium catalyzed hydroborations, a previous graduate student C. J. Lata observed the formation of species similar to **2-2**. Lata hypothesized that these salts could be formed independently though equimolar mixtures of HBpin, a suitable Lewis base, and the Lewis acid, $B(C_6F_5)_3$ (Scheme 2.2-2).[32, 33] After acquiring significant spectroscopic data, he proposed the formation of species **2-3** with either THF or $PhNMe_2$.[32, 33] Unfortunately, the THF stabilized borocation was unstable and tended to polymerize THF (see Table 1, entry **2-15**).[33] Similar reactivity was observed when THF was used as solvent in $B(C_6F_5)_3$ assisted rhodium catalyzed hydroboration.[33] The reactivity of these boron cations in addition to the stability of the pinacol group inspired an investigation into forming more stable borenium/borohydride salts, like **2-3** and gauge their reactivity in the hydroboration reaction.

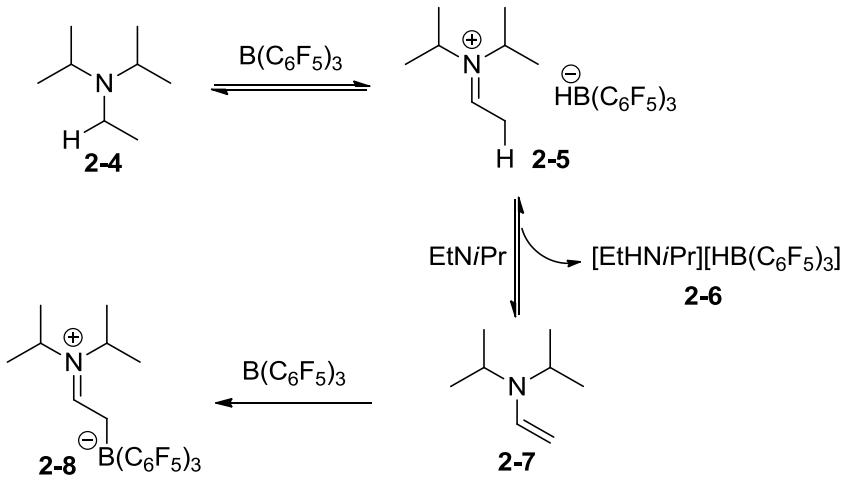


Scheme 2.2-2: Generation of borenium cations and borohydrides from HBpin.

This project was investigated in conjunction with postdoctoral fellow Dr. Patrick Eisenberger. Some of the experiments discussed in this chapter were performed by him, and acknowledgements can be found directly in the text. Compounds manufactured by Dr. Eisenberger are not included in Chapter 5.

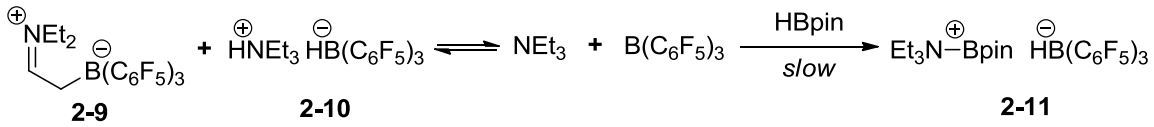
2.2.1 Activation of Boranes with $B(C_6F_5)_3$

Complexes of Lewis bases with $B(C_6F_5)_3$ are well documented in the literature.[34] As such, the selection of Lewis bases required to nucleophilcally activate a borane in the presence of $B(C_6F_5)_3$ must be strategically chosen. Furthermore, the ability of $B(C_6F_5)_3$ to abstract hydrides from sp^3 hybridized *α* carbons of certain *N*-containing Lewis bases via an iminium intermediate further limits the scope of applicable Lewis bases.[35] However, it should be noted that in certain cases this hydride abstraction has significant affects on the reactivity of the system. Consider, for example, the addition of $B(C_6F_5)_3$ to an excess of Hunig's base (**2-4**) which will result in C–H activation of an *α* hydrogen yielding salt **2-5** (Scheme 2.2-3).[36] Subsequent deprotonation by another equivalent of base results in formation of salt **2-6** and enamine **2-7**. **2-7** further reacts with another equivalent of $B(C_6F_5)_3$, which is proposed to be an irreversible step, resulting in the quenching of the reactivity of the Lewis acid through formation of zwitterion **2-8**. This reactivity prevents the use of trialkyl amines which have easily activated *α* hydrogen atoms. However, if the C–H activation step was reversible then this type of system may give rise to B–H activation.



Scheme 2.2-3: Reaction of Hunig's base with $B(C_6F_5)_3$ resulting in quenched reactivity.

Interestingly, work performed by former Crudden group member J. D. Webb demonstrated that this type of system could result in the formation of a borenium cation via B–H activation.[37] Upon mixing HBpin with triethyl amine, no complexation or disproportionation was observed. However, subsequent addition of $B(C_6F_5)_3$ resulted in hydride abstraction from the α position of NEt_3, to form complexes **2-9** and **2-10** (Scheme 2.2-4).[38, 39] Over a period of **2-7** days, the reaction mixture transformed into the borenium cation/borohydride salt, **2-11**. ^{11}B and ^{1}H NMR NMR exhibited several changes throughout the course of the reaction. A decrease in the HBpin resonance and increase in two new resonances, one corresponding to a borenium cation[40] and one corresponding to a borohydride anion strongly suggest the presence of **2-11**. This reaction can be explained in two possible ways: 1) that the C–H activation is reversible, which has been noted by other groups,[38, 39, 41] and is contrary to the observations made with Hunig's base, or 2) **2-10** is able to eliminate hydrogen and form a classical Lewis adduct which subsequently activates the dioxoborolane.



2-9 **2-10** **2-11**

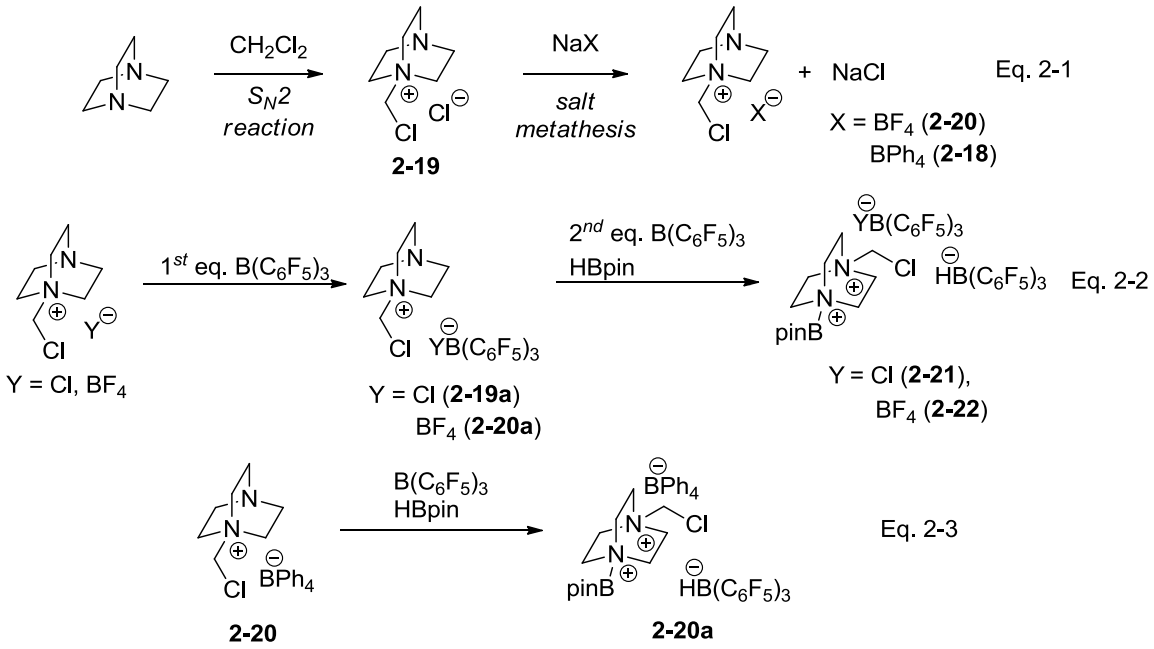
Scheme 2.2-4: Activation of HBpin through reversible reaction between a Lewis acid and Lewis base.

In our studies, focus was shifted to Lewis bases that are not susceptible to C–H bond activation, including 2,2,6,6-tetramethylpiperdine (TMP), a series of aromatic *N*-containing bases, 1,8-diazabicycloundec-7-ene (DBU), diazabicyclo[2.2.2]octane (DABCO) and several cationic DABCO derivatives (Table 1). In a stoichiometric reaction between HBpin, TMP, and $B(C_6F_5)_3$, no reaction was observed. This lack of reactivity could be attributed to the demanding steric bulk around the Lewis basic nitrogen center.[37]

Further exploration with aromatic Lewis bases such as indole, pyridine, and 2,6-lutidine under the same reaction conditions exhibited no desirable B–H bond activation. Furthermore, no B–H bond activation was observed in the case of 2,6-lutidine, despite literature precedent for reversible Lewis adduct formation.[42] Instead a mixture of unreacted HBpin, free amine, free Lewis acid, and the classical Lewis adduct **2-12** were observed. Triphenyl amine showed no complexation to $B(C_6F_5)_3$ or HBpin which is most likely a result of the combination of low basicity and high steric demand. Pyridine was observed to form complex **2-13** (Table 1), which did not react with HBpin, even over extended periods of time, indicating that adduct formation is not a reversible process. Indole reacted with $B(C_6F_5)_3$ in a predictable fashion yielding compound **2-14**, already reported by Focante and coworkers;[43] no further reaction in the presence of HBpin was observed. Former graduate student C. J. Lata observed that $PhNMe_2$ reacted to yield the borenium cation **2-17**. Despite the successful B–H activation by C. J. Lata, acquiring similar results proved to be challenging, which led to the investigation of other Lewis bases.[37, 32]

The first major successes in stoichiometric reactions came from the utilization of DABCO and its derivatives, **2-18** - **2-20** (Scheme 2.2-5, Eq. 2-1).[44] DABCO reacts in an S_N2

fashion with CH_2Cl_2 to yield the ammonium chloride salt **2-19**,[44] which can then undergo salt metathesis to yield **2-18** and **2-20** (Scheme 2.2-5, Eq. 2-1). This reaction progresses slowly at room temperature enabling the use of DABCO in methylene chloride, and refluxing conditions were required to synthesize **2-19** in high yields. Due to the high Lewis acidity of $B(C_6F_5)_3$, complexation of small anionic counterions can occur in preference to hydride abstraction from the activated borane forming species like **2-19a** and **2-20a**.[37] J. D. Webb and C. J. Lata realized this and a direct consequence was the required use of two equivalents of $B(C_6F_5)_3$ to form the desired B–H activated salts, **2-21** and **2-22** (Scheme 2.2-5, Eq. 2-2).[37] In an effort to reduce the amount of $B(C_6F_5)_3$ used to one equivalent, a salt metathesis to the non-coordinating counterion, tetraphenylborate was performed, yielding salt **2-18**. Unfortunately, the low solubility of this salt prevented its use in suitable solvents and salt **2-20a** was not observed (Scheme 2.2-5, Eq. 2-3).

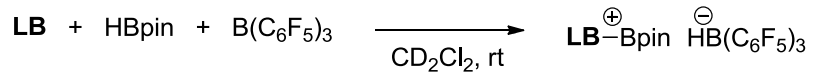


Scheme 2.2-5: Formation of DABCO derivatives (Eq. 2-1) and their use in borenium salt formation (Eq. 2-2 and 2-3).

Reactions with DBU resulted in formation of a small amount of borenium/borohydride salt, but the major product of the reaction was Lewis adduct **2-16**. Further attempts to form the

target salt with DBU failed. Luckily, using DABCO as the Lewis base resulted in clean activation of the B–H bond resulting in full conversion to the desired [DABCO-Bpin][$HB(C_6F_5)_3$] salt **2-23**. Knowing that an investigation into the catalytic activity of this species was going to commence, a solvent without an undesirable side rection was needed. Utilization of *α,α,α*-trifluorotoluene ($PhCF_3$) resulted in no change in reactivity and full conversion was observed in this solvent.

Table 1: Lewis bases screened for B–H bond activation with $B(C_6F_5)_3$.

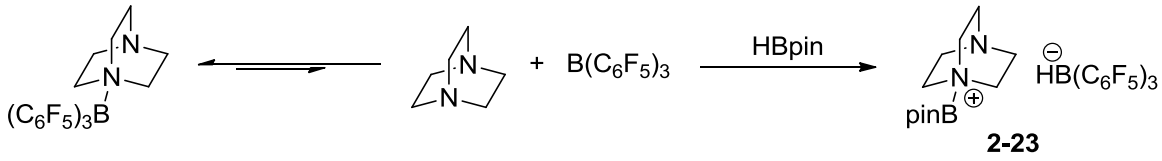


LB	Product[a]	LB	Product[a]
NPh_3	**NR**	(DBU)	**2-16**
(TMP)	**NR**		
	2-12		**2-17**[d]
	2-13	**2-18**	**NR**
	2-14	X = Cl (**2-19**)[b], BF_4 (**2-20**)[b]	X = Cl (**2-21**),[d,e] BF_4 (**2-22**)[d,e]
(THF)	**2-15**[c]	(DABCO)	**2-23**

[a] All product structures determined by ^1H and ^{11}B spectroscopy. [b] Two equivalents of BCF were used. [c] ref 32. [d] ref 33. [e] ref 37.

Full spectroscopic characterization of **2-23** was easily accomplished. However, all attempts to isolate it in solid form failed as the salt decomposed upon removal of solvent *in vacuo*. Addition of apolar solvents, such as hexanes or pentanes, also resulted in decomposition prior to precipitation of the salt. The solid residue after removal of solvent only exhibits ^{11}B resonances corresponding to B_2pin_3 and the borohydride $HB(C_6F_5)_3^-$. This indicates that the cation does not contain boron and is most likely an ammonium salt. Trace water could promote this process.

An interesting physical observation is that mixtures of $B(C_6F_5)_3$ and DABCO yielded a white precipitate which is insoluble in a wide range of organic solvents, including CH_2Cl_2, $CHCl_3$, toluene, benzene, 1,2-dichloroethane, nitromethane, dimethoxyethane, *t*-butyl methyl ether, acetone, hexanes, and pentanes; this solid is proposed to be the classical Lewis adduct. However, upon addition of one equivalent or more of HBpin homogeneity is obtained within ca. 3 minutes of shaking and reaction is complete in less than 15 minutes. Evidence for the reaction and its completeness was determined by ^{11}B and ^{1}H NMR spectroscopy. Thus the classical Lewis adduct and free $B(C_6F_5)_3$ and free DABCO are most likely in equilibrium, enabling the free Lewis base to activate HBpin prior to hydride abstraction by $B(C_6F_5)_3$ (Scheme 2.2-6). Furthermore, the order of addition in this reaction proved to be pertinent and, if not carried out in the aforementioned order, disproportionation to B_2pin_3 and BH_3 was often the major reaction pathway (see section 1.5.2).



2-23

Scheme 2.2-6: B–H activation of HBpin starting from classical Lewis adduct.

The $B(C_6F_5)_3$•DABCO Lewis adduct proved inert to spectroscopic analysis due to its insolubility in many organic solvents. However, **2-23** was verified by resonances in agreement with data previously reported in the literature.[3, 33] The ^{11}B spectra contained two major

resonances: at +25.5 ppm is a signal consistent with a three coordinate boron cation,[33] and the peak at –25.1 ppm is consistent with a four coordinate B–H containing boron anion (Figure 2-2).[55] The spectrum also contains residual HBpin, appearing as a broad doublet at +28.1 ppm, and B_2pin_3, appearing as a singlet at 21.5 ppm. The ^1H NMR contains two major resonances: at 2.79 ppm is a signal which corresponds to two inequivalent sets of six protons contained within the unsymmetrical DABCO fragment and the singlet at 1.15 ppm is the methyl groups of the pinacol backbone (Figure 2-3). Low temperature NMR experiments, conducted by Dr. Patrick Eisenberger, resolved the signal at 2.15 ppm into two separate resonances.

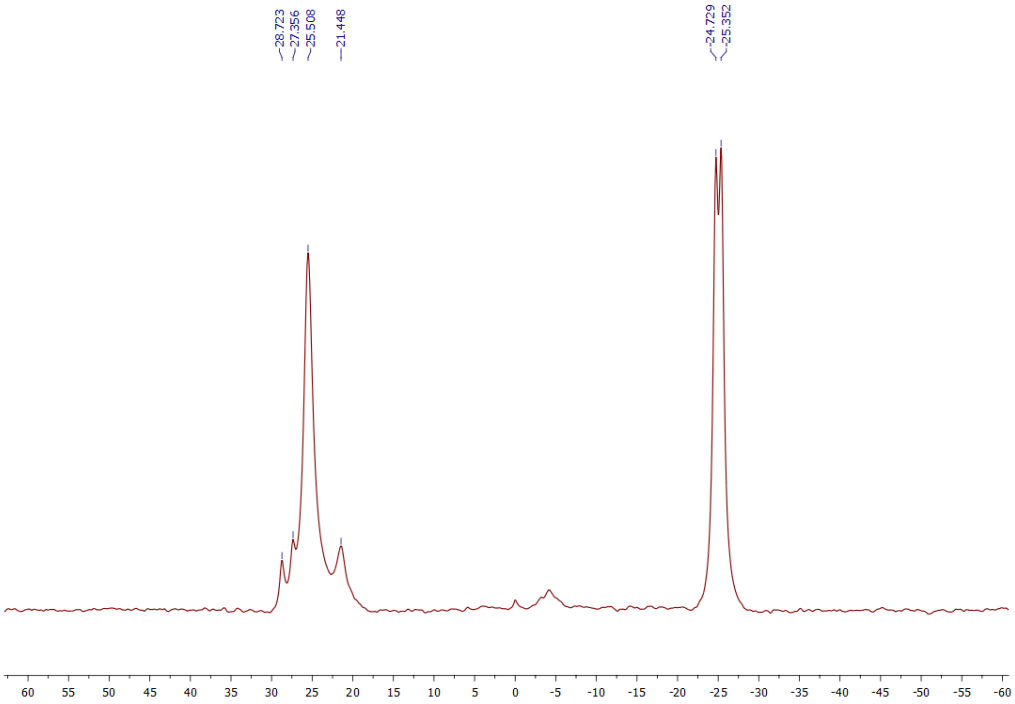


Figure 2-2: ^{11}B NMR spectrum of **2-23** in $PhCF_3$.

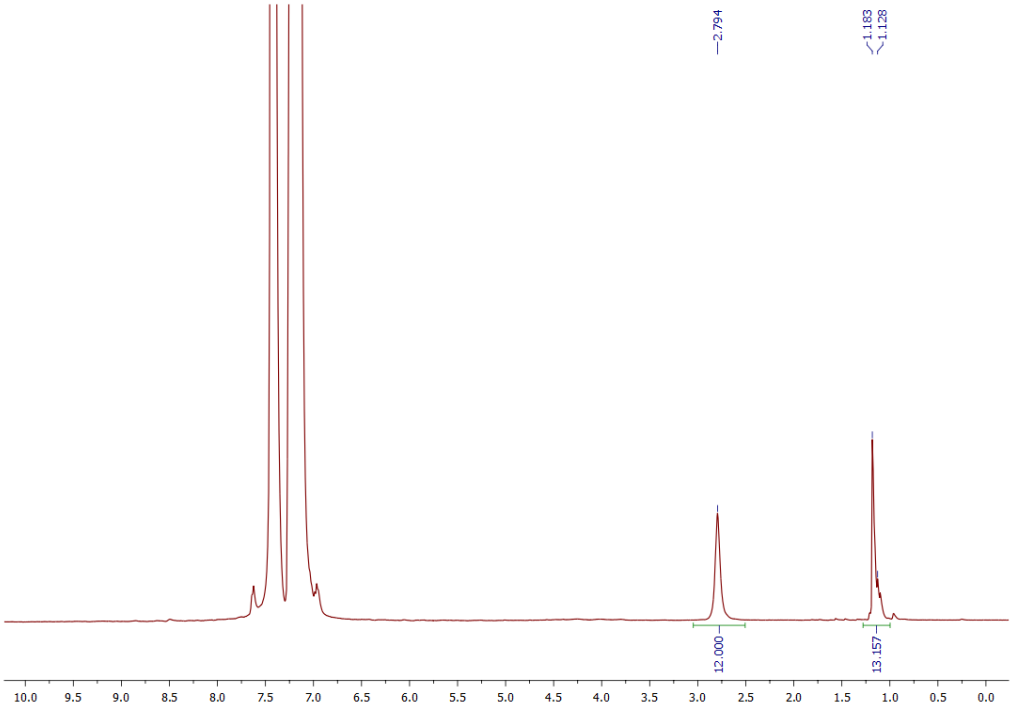


Figure 2-3: ^{1}H NMR spectrum of **2-23** in $PhCF_3$.

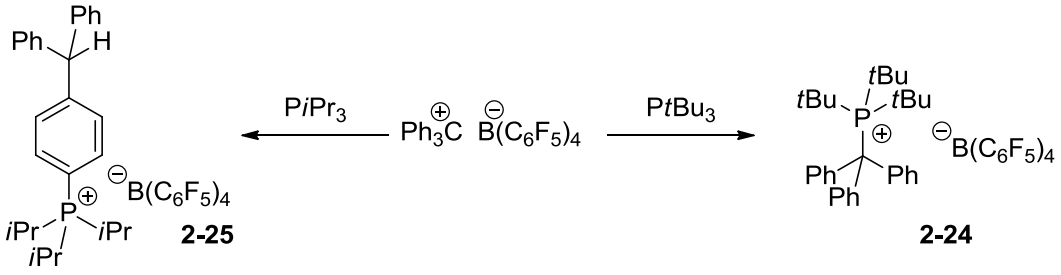
In addition to Lewis acid/base B–H bond activation with HBpin, attempts at B–H bond activation with HBcat were conducted. In these reactions, DBU only acted to disproportionate the borane and complex with $B(C_6F_5)_3$ and no salt formation was observed. Performing a stoichiometric reaction with DABCO, HBcat, and BCF in CD_2Cl_2 resulted in a white milky solution. In some attempts, the solution would slowly become homogeneous and produce signals in the ^{11}B NMR corresponding to a borenium cation/borohydride salt. However, in other attempts, the suspension persisted and increases in the borohydride signal and disproportionation products were observed. This lack of reproducibility steered us away from utilization of HBcat in further studies of the reactivity of these boron salts.

The *in situ* generation of a borenium/borohydride salt was accomplished under facile conditions via dual activation of HBpin with the Lewis acid $B(C_6F_5)_3$ and Lewis base DABCO. Thus with **2-23** in hand, attempts at using this catalyst for hydroboration reactions and reductions could begin.

2.2.2 Activation of Boranes with Trityl tetrakis-pentafluorophenyl borate

As previously noted, like $B(C_6F_5)_3$, $TrB(C_6F_5)_4$ is highly efficient in hydride abstraction. It is commonly synthesized from $LiB(C_6F_5)_4$ and triphenylmethylchloride in refluxing hexanes for 24 hours.[45] One pot procedures starting from bromopentafluorobenzene have also been developed.[46] The successes of $TrB(C_6F_5)_4$ in borenium cation formation have been summarized in a thorough review by Vedejs and coworkers.[1] On the Child's Lewis acidity scale, trityl salts are typically more acidic than trivalent boranes, which is understandable due the increased electron demand of the carbocationic center. Furthermore, during redistribution experiments with organic hydrides, J. D. Webb observed that $TrB(C_6F_5)_4$ was capable of cleanly abstracting a hydride from $HB(C_6F_5)_3^-$ pyridinium based salts.[37] The increased Lewis acidity and easy removal of stable byproducts (Ph_3CH) suggested that trityl salts might be preferable to $B(C_6F_5)_3$.

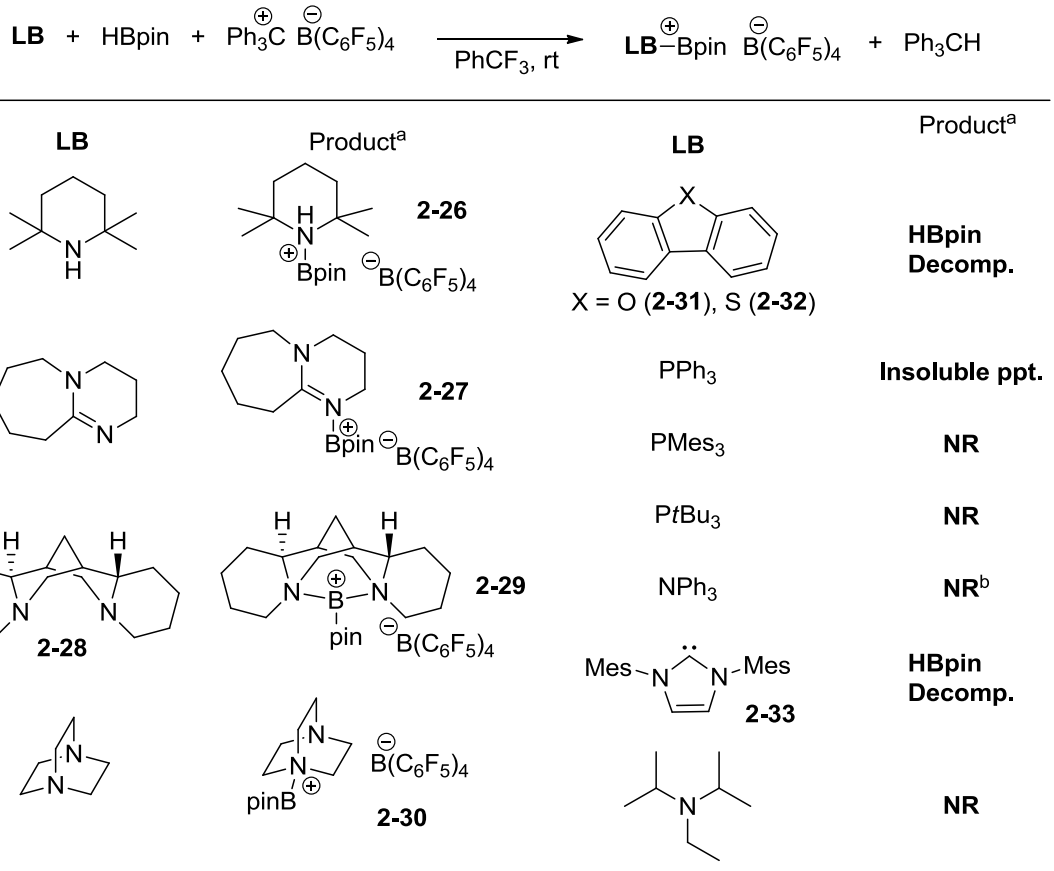
Complexes of Lewis bases with trityl salts are less common as the increased electrophilicity often results in a reaction as well as a complexation. Stephan and coworkers demonstrated that significantly sterically bulky Lewis bases, such as P*t*Bu$_3$, led to direct complexation with $TrB(C_6F_5)_4$, **2-24**.[47] However, when the *i*Pr analogue was employed, *para*-attack on a phenyl ring of the carbocation (**2-25**) was observed (Scheme 2.2-7). Performing similar reactions using pyridine and *para*-substitued pyridines all resulted in classical Lewis adducts.[47] Reactions with secondary and tertiary amines and $TrB(C_6F_5)_4$ have also been reported; the major products in all cases were the classical Lewis adducts.[48]



Scheme 2.2-7: Reactivity of $TrB(C_6F_5)_4$ with phosphines.[47]

Isolation of stable borenium cations is seldom reported in the literature and they are often made *in situ* to ensure minimal decomposition and high activity.[1, 2] The bottling of a borenium cation was one of the goals of this project and has yet to be accomplished in the literature. In order to accomplish this, postdoctoral fellow Patrick Eisenberger began a screen of Lewis bases in stoichiometric reactions with $TrB(C_6F_5)_4$ and HBpin in $PhCF_3$. Electron rich ethers (**2-31**) and thioethers (**2-32**) resulted in disproportionation of HBpin. Phosphines showed no desirable reactivity with HBpin. A reaction with PPh_3 resulted in a white precipitate that is most likely the classical Lewis adduct. Triaryl and trialkyl amines also resulted in no desirably reactivity. Surprisingly, an *N*-heterocyclic carbene (**2-33**) showed no complexation to the trityl cation and only acted to nucleophilically disproportionate HBpin.

Table 2: Lewis bases screened for B–H bond activation with $TrB(C_6F_5)_4$.



[a] All product structures determined by ^1H and ^{11}B spectroscopy. [b] A colour change from clear to green was observed. Mes = 2,4,6-trimethylphenyl-, NR = no reaction, ppt = precipitate.

Much like the $B(C_6F_5)_3$ reactions, success was achieved when alkyl *N*-containing Lewis bases were employed. TMP resulted in B–H activation yielding salt **2-26** although conversions were low and product formation was incomplete. DBU reacted similarly to TMP but with higher conversions producing salt **2-27**. (–)-Sparteine (**2-28**) produced the boronium cation **2-29** instead of a borenium cation, as one would expect due to the orientation of the nitrogen atoms within the hydrocarbon backbone. This is clearly evident from the chemical shift of the resulting species in ^{11}B NMR (+7.0 ppm as opposed to +25.5 ppm observed for **2-23**). Lastly, DABCO provided full, clean conversion to borenium cation salt, **2-30**. However, unlike the $B(C_6F_5)_3$ system, removal of $PhCF_3$ *in vacuo* resulted in a dark grey solid, washing with pentanes removed triphenylmethane leaving pure, light grey salt. Full spectroscopic analysis of **2-30** was carried out, however all attempts to crystallize **2-30** failed. Only X-ray quality crystals of the hydrolysis product were grown, indicating that this is a highly water sensitive complex. When stored in the glove box at ambient temperatures for extended periods of time, the compound showed little to no decomposition. The reaction could be scaled up to approximately one gram and yields were reproducibly greater than 90%.

The spectroscopic data acquired for borenium cation **2-30** are similar to that for salt **2-23**. The major distinction between the two salts spectroscopically is the difference in the resonances attributed to the counterions. In salt **2-30**, the ^{11}B NMR has the same resonance for the borenium cation at +25.4 ppm but contains a singlet at –16.5 ppm corresponding to the four coordinate tetraaryl counterion instead of the previously observed doublet of the borohydride at –25.1 ppm Figure 2-3). The ^{1}H NMR is identical to that of salt **2-23** (Figure 2-4).

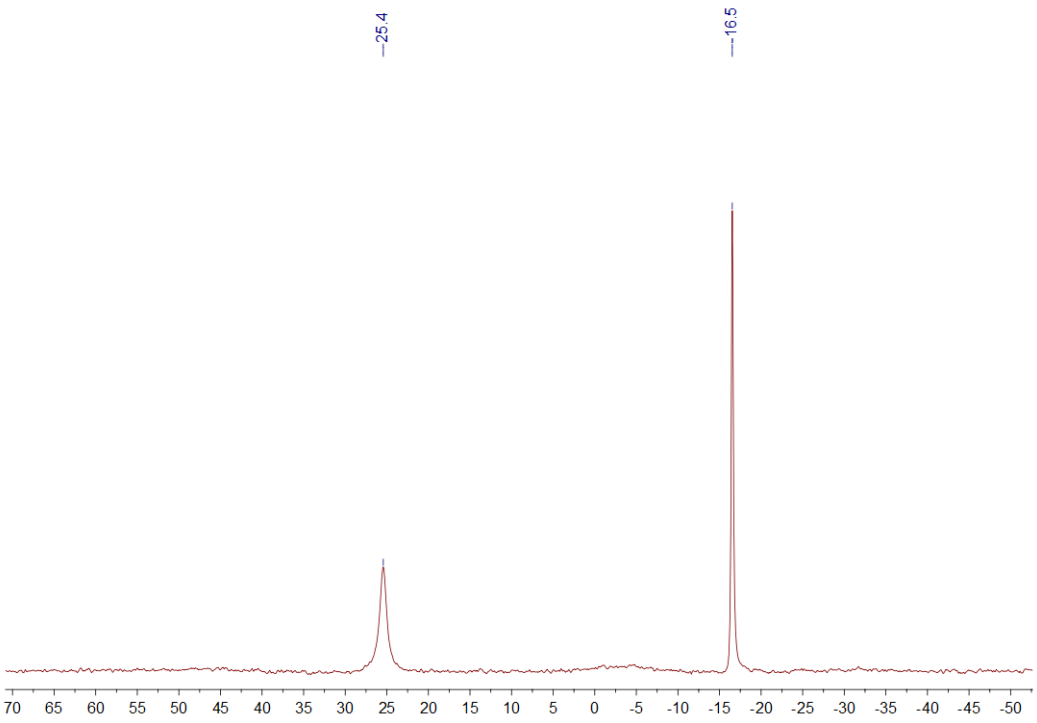


Figure 2-4: ^{11}B NMR spectrum of **2-30** in $PhCF_3$.

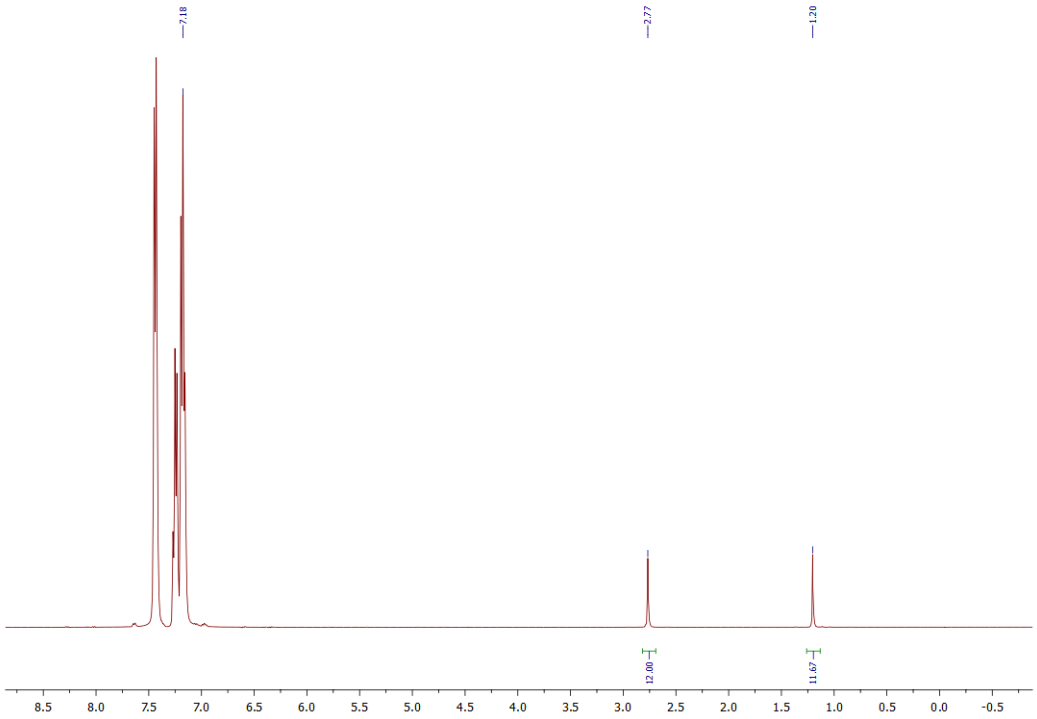


Figure 2-5: ^{1}H NMR spectrum of **2-30** in $PhCF_3$.

The activation of the B–H bond of HBpin was accomplished with a series of Lewis bases in the presence of Lewis acids $B(C_6F_5)_3$ or $TrB(C_6F_5)_4$. B–H activation with the Lewis base DABCO resulted in the formation of stable borenium cations with different counterions. The salt formed in the presence of $B(C_6F_5)_3$ is unstable in the solid form but could be cleanly generated *in situ* and remained stable in solution for several hours. On the other hand, $TrB(C_6F_5)_4$ generated a borenium salt that could be stored in solid form for extended periods of time. We hypothesized that borenium salt **2-23** could be used to cleanly hydroborate several unsaturated functional groups and that the stable, isolable borenium salt **2-30** could be applied in as a stoichiometric borylation reagent and as a potential activator in hydroboration reactions.

2.3 Reactivity of Borenium Cations

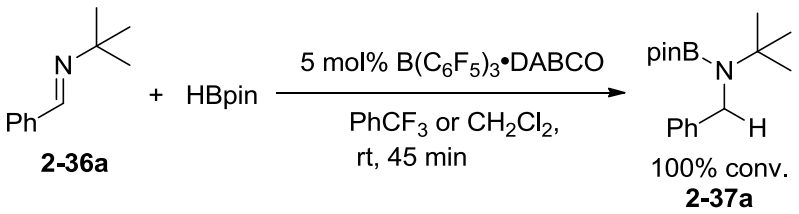
Borenium cations are notoriously reactive.[1, 49] Their high reactivity is easily demonstrated by their ability to facilitate difficult reactions at ambient or cryogenic temperatures.[2, 50] Due to their increased electrophilicity, these species react readily with nucleophiles and Lewis bases.[49] Most are highly water sensitive and readily hydrolyze or complex on exposure to trace amounts of moisture dampening their ability to facilitate the target process.[49] However, this inherent reactivity has made them desirable species for performing difficult organic reactions as well as developing new ones. For example, borenium ions have been shown to heterolytically cleave C-F bonds,[51] promote Diels-Alder reactions,[52] and borylate unactivated arenes[40, 53] at ambient or cryogenic temperatures. Since cryogenic temperatures are often difficult on scale, energy requirements often prevent industrial applications of borenium–mediated reactions. Having demonstrated the synthesis of stable borenium cations at ambient temperatures from Lewis pairs, we then moved to investigate the reactivity of these species in hydroboration reactions.

2.3.1 Catalytic Hydroboration of Imines with $B(C_6F_5)_3$•DABCO

The first examples of the catalytic activity of FLPs was in the hydrogenation of aldimines, ketimines, and aziridines using the air- and moisture-stable linked phosphonium borate species, $(R_2PH)(C_6F_4)BH(C_6F_5)_2$ (R = 2,4,6-trimethylphenyl (**2-34**) and *t*Bu (**2-35**)).[54] Stephan and coworkers noted that the substituent on nitrogen must be significantly sterically bulky to acquire a high yield of amine under the reaction conditions. This was clearly demonstrated by the differences in reactivity of *N*-benzyl vs. *N*-benzhydryl (benzhydryl = *N*$CHPh_2$) imines. The *N*-benzyl imine proceeded to 5% conversion after 48 h, whereas the *N*-benzhydryl yielded 88% product after 1 h under identical conditions.[54] Switching to an intermolecular FLP as a catalyst resulted in little to no change in yields but significant decreases in rate were observed.[54, 55] Soós *et al.* utilized DABCO•$B(C_6F_5)_3$ as the catalyst in an FLP hydrogenation[56] and showed similar results to Stephan *et al.* for imine reductions.

In order to compare the catalytic abilities of the $B(C_6F_5)_3$•DABCO/B–H bond activation system developed in Section 2.2.1 with the catalysts used in FLP hydrogenations, we chose to investigate their reactivity on a similar set of imine substrates. Initial studies of exposing *N*-benzylidene-2-methylpropan-2-amine (**2-36a**) to 1 equivalent of HBpin and 5 mol% $B(C_6F_5)_3$•DABCO (which generates **2-23** *in situ*) in $PhCF_3$ resulted in clean reduction and full conversion to the corresponding pinacolboramide **2-37a** (δ_B = 24.7 ppm) after 45 min (Scheme 2.3-1). Similar reactivity was observed in methylene chloride, despite the previously described background reaction with DABCO. This high reactivity and high rate of reduction is consistent with the conversions and rates observed for the same substrate in linked FLP hydrogenations.[54] However, immediate differences in reaction conditions demonstrate the improvement of this catalyst. First, FLP hydrogenations for this substrate take place at 80℃ and 1 atm of hydrogen gas. A similar hydrogenation reaction using the same substrate performed with 5 mol% $B(C_6F_5)_3$ as a catalyst resulted in 89% yield of reduced product.[55] In this case, the reaction was performed

at 120℃ with 5 atm H_2 with a 2 h reaction time. Obvious benefits to our protocol include the ability to perform the reaction at ambient temperatures and without the use of explosive hydrogen gas. However, a drawback is the creation of one equivalent of boron waste.



Scheme 2.3-1: Results of screen for catalytic activity using **2-23** and aldimine **2-36a**.

Before determining the scope of this reaction, various potential background reactions needed to be investigated. Equimolar amounts of **2-36a** and HBpin stirred in CD_2Cl_2 at ambient temperature resulted in no reduction or disproportionation over a period of 72 h. Similarly, equimolar mixtures of DABCO, **2-36a**, and HBpin as well as equimolar mixtures of $B(C_6F_5)_3$, **2-36a**, and HBpin resulted in no reduction over the same time interval. Analogous results were obtained when $B(C_6F_5)_3$ or DABCO were used in catalytic quantities. These results indicated that both Lewis acid and Lewis base are required for the catalysis to occur. Unfortunately this reaction is not without flaw. An undesirable side reaction that occurs is the nucleophilic disproportionation of HBpin, presumably mediated by free DABCO, which results in the formation of B_2pin_3 and DABCO•BH_3. This reagent was not directly observed in the reaction mixtures and this side reaction typically results in only a small amount of HBpin decomposition, however, the potent reducing capabilities of BH_3 are well documented in the literature and it was necessary to eliminate this species as a potential reducing agent. A potential cycle for DABCO catalyzed decomposition of HBpin followed by reduction of substrate is shown in Figure 2-6.

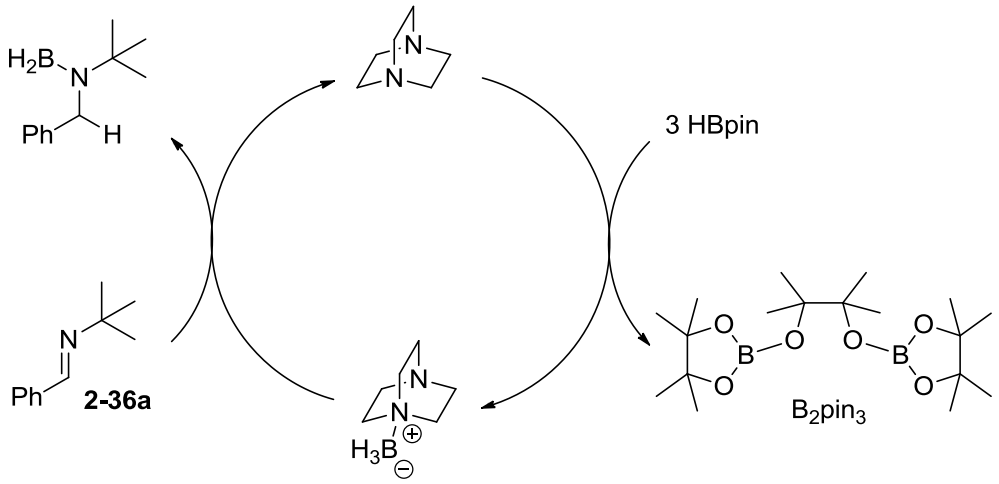
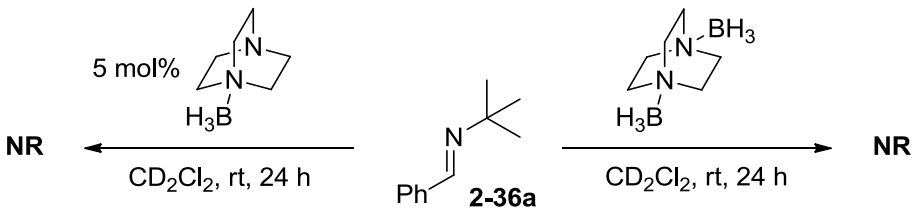


Figure 2-6: Potential catalytic cycle for DABCO mediated hydroboration of imines.

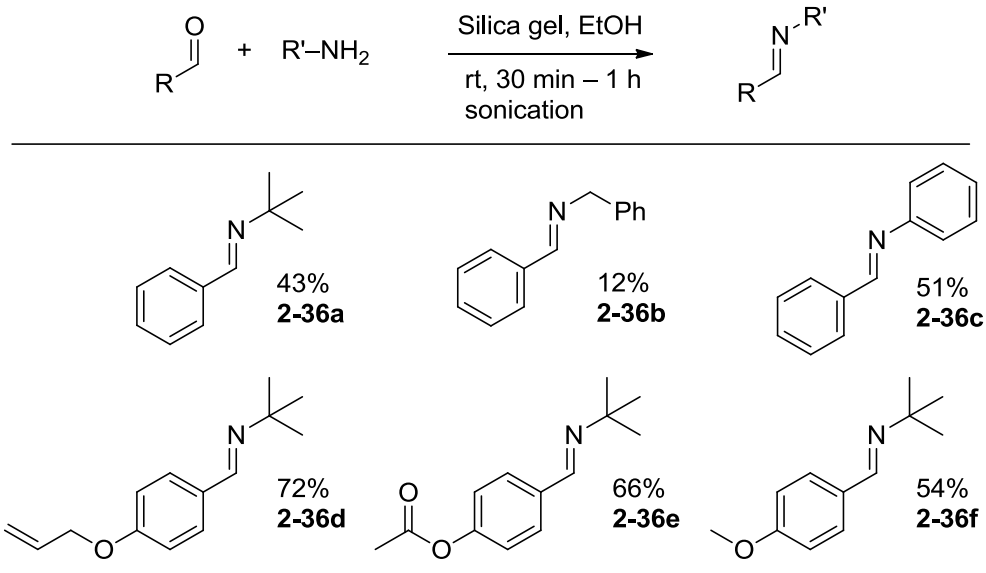
Direct synthesis of DABCO•$(BH_3)_2$ was easily accomplished by mixing DABCO and BH_3•THF in a 1:2 ratio in THF at 0℃ and allowing the solution to warm to ambient temperature while stirring overnight. The monoadduct was prepared by former visiting PhD student Cristina Pubill. Stoichiometric and catalytic reactions of the mono- and bis- DABCO•BH_3 adducts with imine **2-36a** resulted in no reduction (Scheme 2.3-2). This important result signified that DABCO•BH_3 adducts were not suitable hydride donors to unactivated imines. Lastly, control reactions utilizing catecholborane instead of HBpin, showed that HBcat was capable of reducing imine **2-36a** in less than 4 h without either catalyst present. This result is in agreement with results published by Westcott *et al.*[57] and clearly showed that unlike HBPin, HBcat has a significant background reaction with imines and was not used in further studies. With knowledge that the reaction was indeed catalytic in Lewis acid and Lewis base the scope and reactivity of this catalyst was assessed.



Scheme 2.3-2: Reactions of imine **2-36a** with DABCO•BH_3 under various conditions.

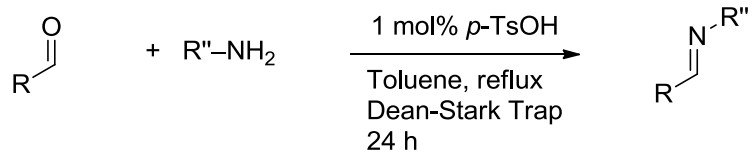
The high reactivity of this catalyst inspired a substrate scope investigation of various aldimines. In order to determine functional group tolerances, a series of aldimines were synthesized. Two separate methods were used to produce this set of substrates: 1) aldehydes could be mixed with amines and silica gel, converting them into imines with ultrasonication (Table 3; method **IM1**),[58] and 2) aldehydes mixed with high boiling amines could be converted into corresponding imines using catalytic amounts of *para*-toluene sulfonic acid and a Dean-Stark trap (Table 4; method **IM2**).[59] Most of these reactions proceeded with low to moderate yields due to product losses during purification but were easily scalable allowing the production of multiple grams of material from one reaction. In addition to the aldimines synthesized in our lab, two aldimines (*N*-benzylidenebenzenesulfonamide (**2-36i**) and N-benzylidenebenzhydrylamine (**2-36j**)) were provided by the Stephan group from at the University of Toronto as a part of an ongoing collaboration between the two groups.

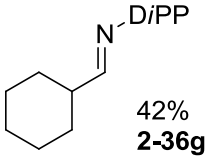
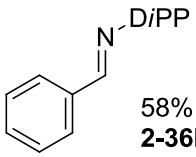
Table 3: Aldimines synthesized using method **IM1**.[a]



[a] See Chapter 5 for experimental details.

Table 4: Aldimines synthesized using method **IM2**.[a]



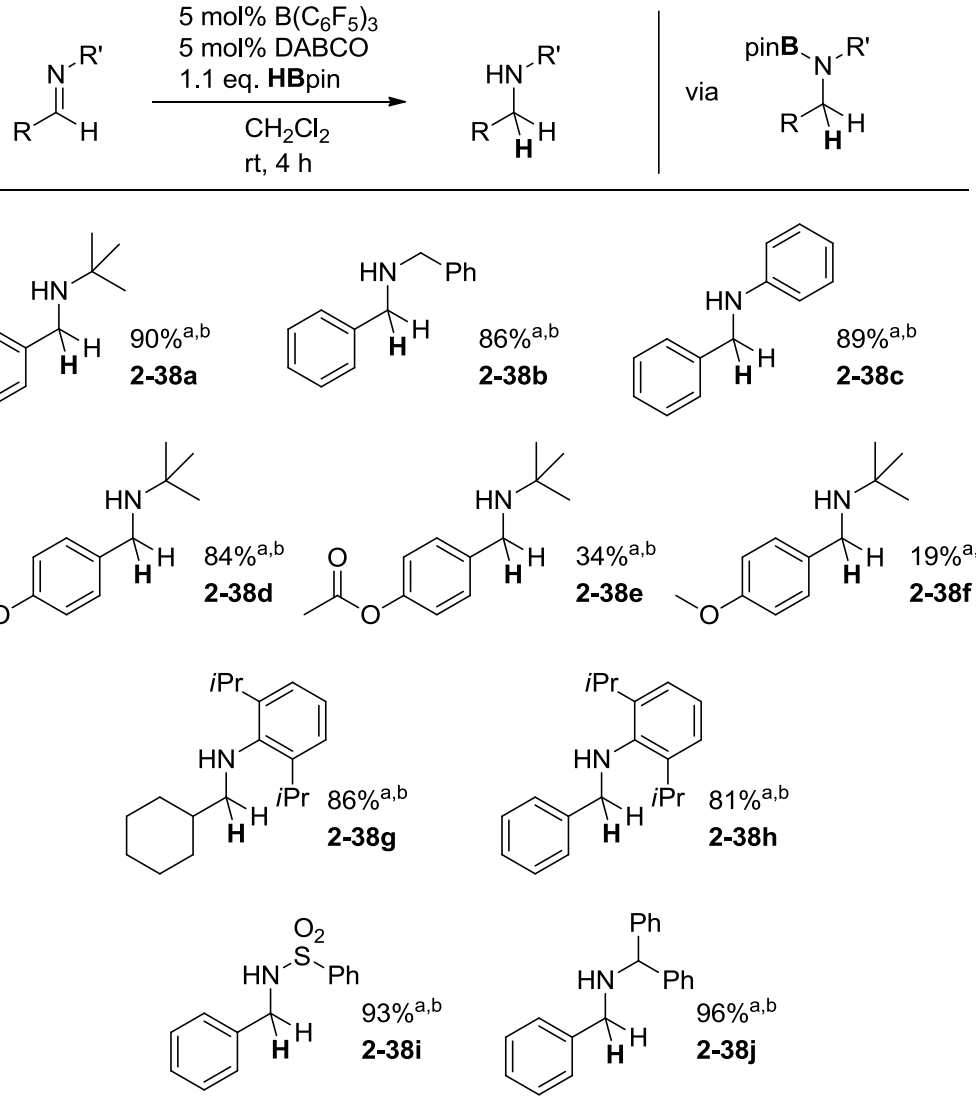
 42% **2-36g**	 58% **2-36h**

[a] See Chapter 5 for experimental details. D*i*PP = 2,6-di-*iso*-propylphenyl

With a set of aldimines in hand, numerous experiments were performed to determine the extent of substrates amenable to this hydroboration protocol. Reacting 5 mol% of **2-23**, 1.1 equivalents of HBpin, and 1 equivalent of substrate at ambient temperature in methylene chloride for 4 h under an inert N_2 atmosphere proved to be a facile and generally applicable procedure. Reactions were quenched with H_2O, which hydrolyzed the nitrogen-boron bond, and the product amines were purified by flash column chromatography. Isolated yields of amines **2-38a**, **2-38i**, and **2-38j** were very similar to those acquired with FLP-type hydrogenations.[54, 55, 56] However, a stark change is observed for substrates with *N*- substituents that are not particularly bulky. Recall that the FLP hydrogenation of **2-36b** proceeded to 5% completion with 5 mol% **2-34** and 5 mol% $B(C_6F_5)_3$ after 48 h at 120℃ with 5 atm H_2. Remarkably, the use of *in situ* generated catalyst **2-23** at 5 mol% loading in the presence of excess HBpin resulting in reduction of **2-36b** to the corresponding amine, **2-38b** in 86% yield under considerably milder conditions. Furthermore, less basic aldimines, such as **2-36c** and **2-36i**, are difficult to reduce under FLP conditions because the basic nitrogen center must be able to deprotonate the phosphonium cation or heterolytically cleave dihydrogen (depending on the catalyst used; see Section 1.4.2). This does not seem to hamper the hydroboration protocol, as is evident from the yields of **2-38c** and **2-38i**.

Inclusion of steric bulk around the Lewis basic nitrogen center in the form of *iso*-propyl groups does not seem to inhibit the reaction to a large extent (entries **2-38g** and **2-38h**). However, methyl ethers (entry **2-38f**) and acyl groups (entry **2-38e**) were not tolerated. This result may be explained by competition between the Lewis basic oxygen and nitrogen atoms for delivery of the borenium fragment. Surprisingly, this does not seem to be a problem for either the sulfonamide (entry **2-38i**) or the allyl ether (entry **2-38d**), both of which reacted with high yields.

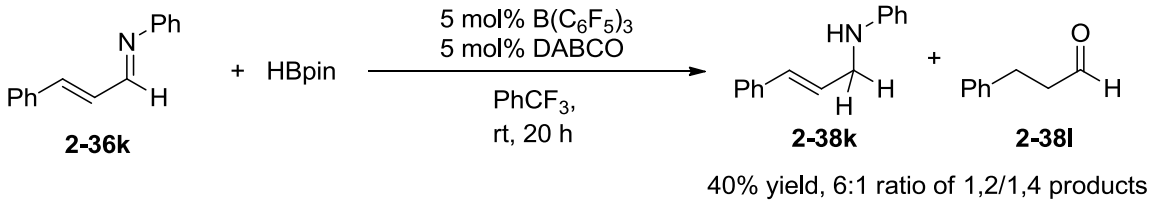
Table 5: Scope of **2-23** catalyzed aldimine hydroborations.



[a] Isolated yields. [b] Amounts of reagents: 1.5 mmol imine, 1.65 mmol HBpin, 0.075 mmol $B(C_6F_5)_3$, 0.075 mmol DABCO in 3 mL CH_2Cl_2.

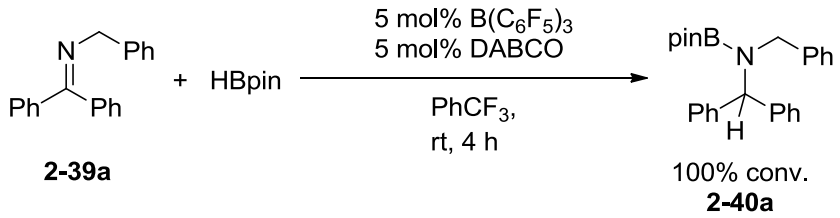
The *α,β*-unsaturated aldimine **2-36k** was also amenable to hydroboration with catalytic amounts of **2-23**. Addition of 1 equivalent of **2-36k** to 5 mol% **2-23** and 1.1 equivalents of HBpin in $PhCF_3$ yielded 40% of a mixture of products (Scheme 2.3-3). The isolated fractions contained the 1,2-reduced amine, **2-38k** and the hydrolyzed 1,4-product, hydrocinnamaldehyde, **2-38l** in a 6:1 ratio. Despite the lower yield, the tendency for 1,2-reduction of an *α,β*-unsaturated imine is a

process not yet available in FLP hydrogenations, which proceed via either complete reduction or selective 1,4-reduction.[56]



Scheme 2.3-3: Catalytic hydroboration of *α,β*-unsaturated aldimine **2-33k** with **2-23**.

With a firm grasp on the capabilities of the **2-23** catalyst in aldimine reduction, the hydroboration of ketimines was examined. The substrate chosen was *N*-(diphenylmethylene)-1-phenylmethanamine (**2-39a)**, which was synthesized by **IM2**. Surprisingly, no reaction proceeded under the conditions used in Table 5. Interestingly, switching from CH_2Cl_2 to $PhCF_3$ resulted in clean reduction to the corresponding pinacolboramide **2-40a** with full conversion in less than 4 h (Scheme 2.3-4). The nature of this solvent effect is not yet understood but it may be a consequence of the side reaction between DABCO and CH_2Cl_2 and longer reaction times.



Scheme 2.3-4: Catalytic hydroboration with **2-23** and ketimine **2-39a**.

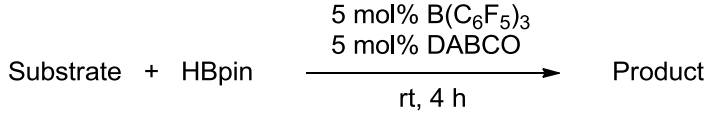
The classical Lewis adduct, $B(C_6F_5)_3$•DABCO, has proved to be a useful catalyst for the hydroboration of various aldimines and the hydroboration of a select ketimine. Producing similar yields and differing selectivities to those acquired in FLP hydrogenation reactions while avoiding the use of high temperatures, pressures (which requires special equipment such as autoclaves), and rigorously dry hydrogen gas are further advantages of our protocol. Furthermore, the substrate scope of this reaction is larger than that of typical FLP processes, without the need of

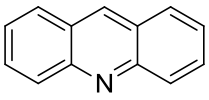
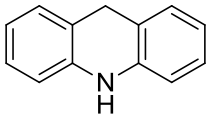
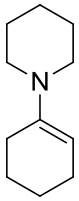
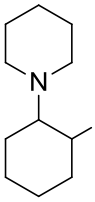
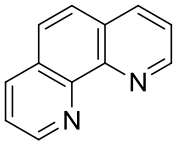
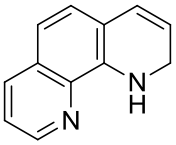
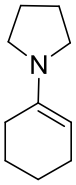
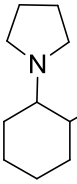
significant steric bulk on the nitrogen atom of the imine. Detailed analysis of potential background reactions revealed the requirement of both Lewis acid and Lewis base for high catalytic activity and that other potential reducing agents generated *in situ* were not able to reduce the imine substrates. Having a solid understanding of the tolerances of this catalyst system in the reduction of imines, a mechanistic proposal was discussed and a subsequent screen of other unsaturated molecules was performed in an effort to determine the breadth of reactivity of this catalyst.

2.3.2 Hydroboration of other Functional Groups with $B(C_6F_5)_3$•DABCO

Other substrates commonly used to test the diversity of FLP systems include other polar unsaturated molecules such as *N*-heterocycles,[60] nitriles,[55] and enamines.[61] Using our optimized conditions, the *N*-heterocycles acridine and 1,10-phenantroline were cleanly reduced to the 9,10- (**2-41a**) and 1,2- (**2-41b**) dihydro- products respectively under similar reaction conditions (Table 6). In FLP hydrogenations, 1,10-phenanthroline derivatives are able to incorporate two equivalents of dihydrogen resulting in the 1,2,3,4-tetrahydro products. The ability to stop at the 1,2-dihydro product in the hydroboration protocol is most likely a consequence of the steric bulk of the *N*–Bpin fragment as well as the high barrier associated with breaking the aromaticity associated with the 1,4-reductions. Furthermore, the mono reduction is also a result of the stoichiometry. With addition of one equivalent of HBpin there is no borane available for a subsequent reduction. This process is also 1,2-selective and there is no potential for isomerization, as there is in metal catalyzed hydrogenation reactions.[62] Attempts to reduce enamines, 1-(cyclohex-1-en-1-yl)piperidine, **2-42a** and 1-(cyclohex-1-en-1-yl)pyrrolidine, **2-42b**, which were provided by the Stephan lab, resulted in no reaction. The results of the reactions performed with *N*-heterocycles and enamines are summarized in Table 6.

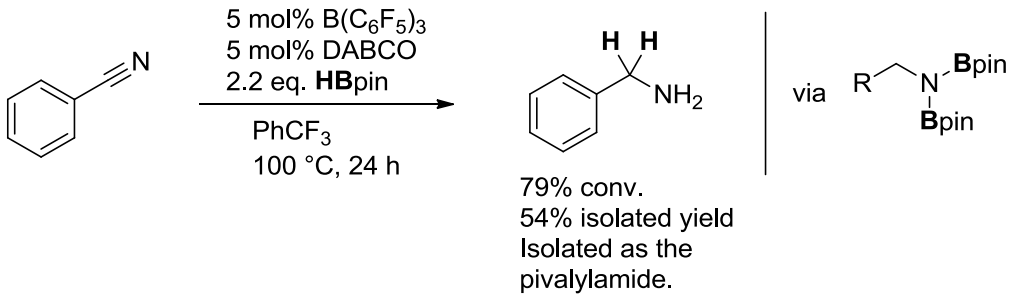
Table 6: *N*-heterocycle and enamine substrate screen.



Substrate	Product		Substrate	Product
		95%[a, b, d] **2-41a**	 **2-42a**	 NR [c] **2-42c**
		84%[a, c] **2-41b**	 **2-42b**	 NR [c] **2-42d**

[a] Isolated yield. [b] $PhCF_3$ used as solvent. [c] CH_2Cl_2 used as solvent. [d] 1 h reaction time.

Lastly, the reduction of benzonitrile was attempted using 2.2 equivalents of HBpin yielding benzylamine. Unfortunately, the reaction did not proceed at ambient temperature. However, elevating the temperature to 100℃ and allowing the reaction to run for 24 hours resulted in 79 % conversion to benzylamine (Scheme 2.3-5). The product was obtained in a 54 % yield, protected as the pivavlylamide to facilitate isolation. Examination of the background reaction between HBpin and benzonitrile showed that there was no reduction after 48 h at 100℃, which confirmed that this was a catalyzed process. Thus far, the lack of reactivity of enamines is the only major difference between classical Lewis adduct–catalyzed hydroborations and FLP hydrogenation reactions. Enamine hydroboration may take place with HBcat or elevated temperatures but these experiments have not yet been performed.



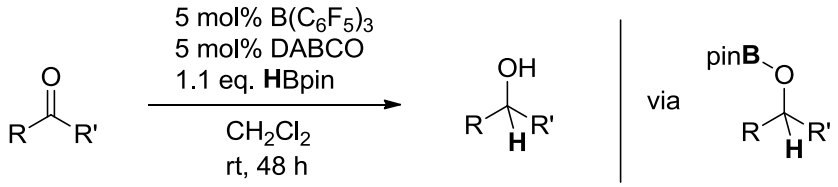
Scheme 2.3-5: Double hydroboration of benzonitrile to benzylamine.

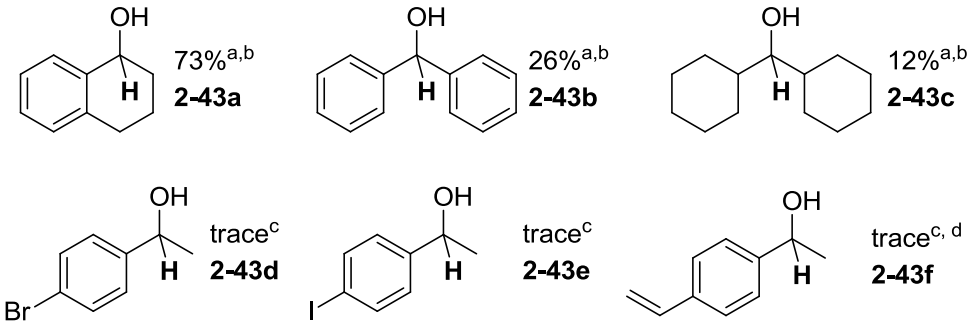
FLP hydrogenations are plagued with difficulties surrounding the catalytic reduction of carbonyls.[54, 63] FLPs have been shown to catalytically reduce carbonyl derivatives, such as silyl enol ethers[64] and the olefinic portion of enones,[56a, 65] but no direct catalytic hydrogenation of a carbonyl functional group has been accomplished to date. The proposed difficulties surrounding this reaction are a consequence of the free Lewis acid, $B(C_6F_5)_3$, irreversibly binding to the oxygen of the carbonyl immediately following hydride delivery. In other words, the borohydride created when the FLP heterolytically cleaves dihydrogen undergoes a concerted hydroboration of the carbonyl resulting in the quenching of the reactive Lewis acid component. Without the Lewis acid, the reaction stops. It should be noted that FLPs[66] and $B(C_6F_5)_3$[67] have been used extensively in the hydrosilylation of carbonyls.

Regardless of the shortcomings of FLP hydrogenation of carbonyl compounds, the hydroboration of carbonyl compounds with catalytic amounts of **2-23** was attempted. A small scale reaction carried out in an NMR tube using benzophenone as a test substrate showed trace amounts of product formation. Encouraged by this result, larger scale reactions were set up in vials equipped with magnetic stirrers. This increased conversions such that after 48 h at ambient temperature, a modest 26% isolated yield of desired alcohol **2-43b** was obtained (Table 7). This approach was applied to other ketones and isolated alcohols **2-43a** and **2-43c** were obtained in 73% and 12% yield, respectively. However, extending this methodology to *para*-bromo-, *para*-

iodo-, and *para*-vinyl acetophenone resulted in only trace amounts of alcohols, **2-43d**, **2-43e**, and **2-43f** as detected by NMR spectroscopy.

Table 7: 2-23 catalyzed hydroborations of ketones.





[a] Isolated yields after H_2O-quench and column chromatography. [b] Amounts of reagents: 1.5 mmol ketone, 1.65 mmol HBpin, 0.075 mmol $B(C_6F_5)_3$, 0.075 mmol DABCO in 3 mL CH_2Cl_2. [c] Product formation confirmed by ^1H and ^{11}B NMR analysis of an aliquot at 48 h. [d] Reaction performed in $PhCF_3$.

In spite of the decreased activity of the **2-23** catalyst for the hydroboration of ketones, the ability to turn the catalyst over is a marked improvement over previously reported FLP systems using hydrogen gas as reducing equivalents. The pinacolboronate residing on the oxygen atom may contribute to the departure of $B(C_6F_5)_3$ from the oxygen atom, allowing it to re-enter the catalytic cycle. This could be a result of the increased steric bulk of the pinacolboronate as well as a result of the decreased Lewis basicity of the oxygen atom of the reduced product.

Similar yields were obtained for the reductions of *N*-heterocycles whereas diminished reactivity was observed for enamines and nitriles. Enamine hydroboration may require the use of more forcing conditions or the addition of a more reactive borane such as HBcat or 9-BBN. Nitriles may be driven to completion by increasing the number of equivalents of HBpin used

since disproportionation products were observed in significant quantities. Although **2-23** may not be able to reduce as many different functional groups as FLP hydrogenations, marked improvements in the catalytic reductions of carbonyl compounds has been accomplished and further investigations into improving reaction conditions will most likely lead to increased activity and yields.

2.3.3 Potential Mechanism of $B(C_6F_5)_3$•DABCO Catalyzed Hydroboration

With the plausible mechanistic proposal for FLP catalyzed hydrogenations of imines in mind (see section 1.4.2), a FLP-type mechanism for the Lewis adduct catalyzed hydroboration can be formulated (Figure 2-6). In this FLP-type mechanism, the classical Lewis adduct $B(C_6F_5)_3$•DABCO heterolytically cleaves the B–H bond of HBpin producing the NMR observable salt, **2-23**. This is most likely a result of an equilibrium between the free and bound Lewis acid and base (discussed in section 2.2.1). After this point, the borenium fragment of **2-23** is transferred to the imine substrate, forming an activated iminium species, **2-44**, releasing DABCO. Following this, borohydride **2-23a** can deliver a hydride to **2-44**, producing the product pincaolboramide **2-45** and regenerating $B(C_6F_5)_3$. Free DABCO and $B(C_6F_5)_3$ may recombine to form the Lewis adduct regenerating the active catalyst and turning the cycle over.

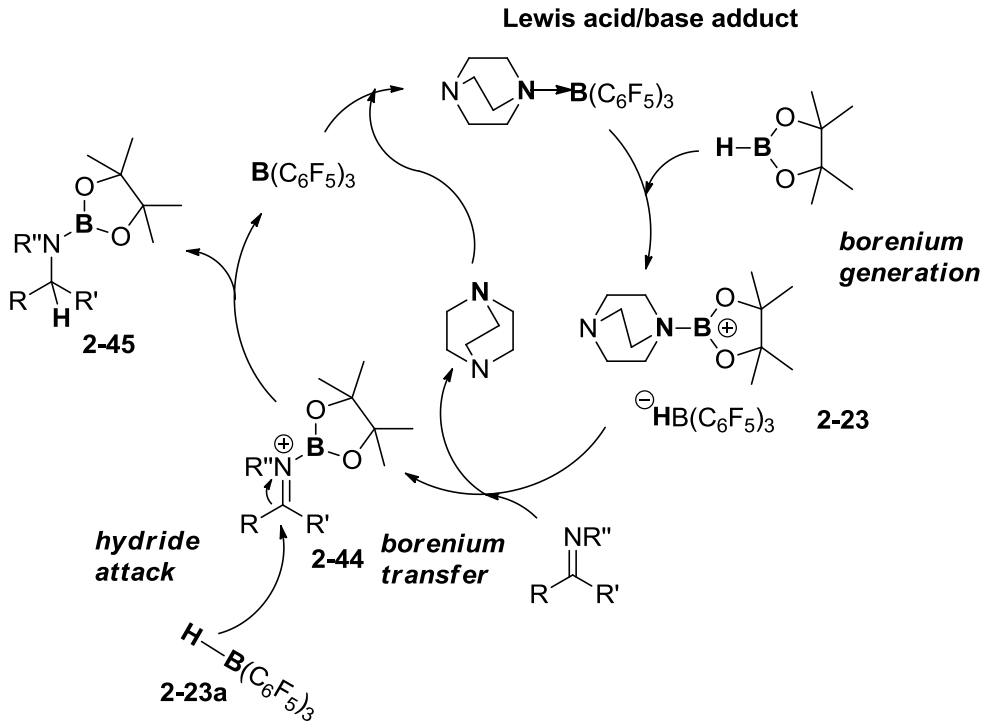
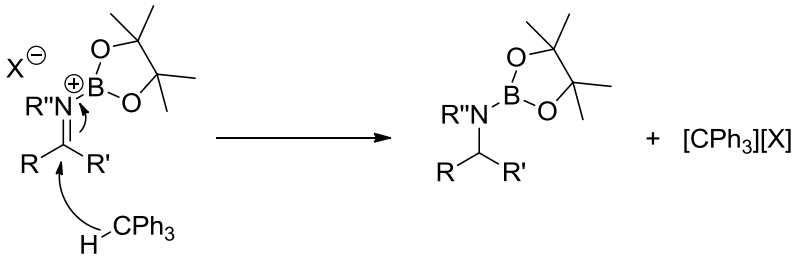


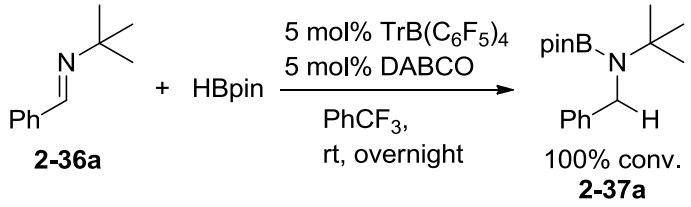
Figure 2-7: An FLP-inspired potential mechanism for the Lewis acid/base adduct catalyzed hydroboration of imines.

If this mechanism is sound, then other Lewis acids, in addition to $B(C_6F_5)_3$, should be able to catalyze this process. We formulated the hypothesis that the Lewis acid $TrB(C_6F_5)_4$, which when reacted with DABCO and HBpin forms the stable borenium ion **2-30** and an equivalent of triphenylmethane ($HCPh_3$) would *not* be able to catalyze the hydroboration of imines due to the formation of the unreactive (hydride-free) counterion. It is reasonable to assume that the carbon-hydrogen bond of triphenylmethane is not able to deliver a hydride to the activated iminium ion formed following borenium transfer (Scheme 2.3-6). In other words, the heterolytic bond dissociation energy of the sp^3 C–H bond in Ph_3CH is too high for a borenium activated electrophilic imine to act as a hydride abstraction agent. As a proof of principle experiment, catalytic amounts of $TrB(C_6F_5)_4$ and DABCO were mixed with 1 equivalent of HBpin and 1.1 equivalents of imine **2-36a** under identical conditions to the aldimine test reaction with **2-23**.

Remarkably, the imine was cleanly converted into pincaolboramide **2-37a** overnight with full conversion (Scheme 2.3-7).



Scheme 2.3-6: Hypothetical reduction step using $HCPh_3$ as the reducing agent.



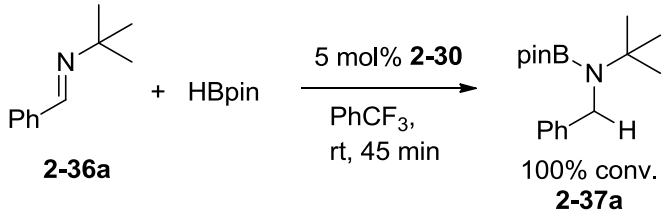
Scheme 2.3-7: Catalytic hydroboration of aldimine **2-36a** using catalytic amounts of $TrB(C_6F_5)_4$ and DABCO.

This result has several important implications. First, the nucleophilicity of the C–H bond of $HCPh_3$ or the eletrophilcity of the iminium ion might have been underestimated. Or the mechanistic proposal could be incorrect and an alternative mechanism is at play. Before examining the mechanism in depth, examinations into the catalytic activity of isolated borenium salt, **2-30** were performed. We hypothesized that if the reactivity of **2-23** and **2-30** were comparable then perhaps both catalysts affect hydroboration via a similar mechanism.

2.3.4 Catalytic Hydroboration with Isolatable [DABCO•Bpin][$B(C_6F_5)_4$] (2-30)

Isolation of **2-30** is easily accomplished by reaction of equimolar amounts of $TrB(C_6F_5)_4$, DABCO and HBpin. $HCPh_3$ could be removed by washing with pentanes. With clean, isolated borenium salt **2-30** in hand, its catalytic activity could be directly investigated. Dissolution of catalytic amounts of **2-30** in $PhCF_3$ followed by addition of 1.1 equivalents of HBpin and 1 equivalent of imine produced the same results as the $TrB(C_6F_5)_4$ initiated system except on a

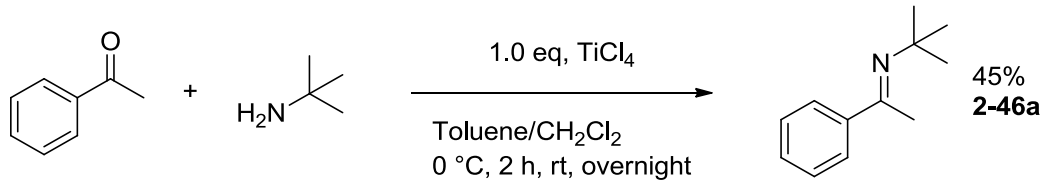
shorter timescale (Scheme 2.3-8). The hydroboration reaction was complete in ca. 45 minutes with **2-30** as opposed to overnight in reactions mediated with $TrB(C_6F_5)_4$. The speed of hydroboration with **2-30** compared with **2-23** is surprising and raises considerable mechanistic questions. Before discussing experiments probing the mechanism of these reactions (Chapter 3) a brief description of the scope of hydroboration reactions with catalyst **2-30** will be discussed.



2-36a **2-37a**

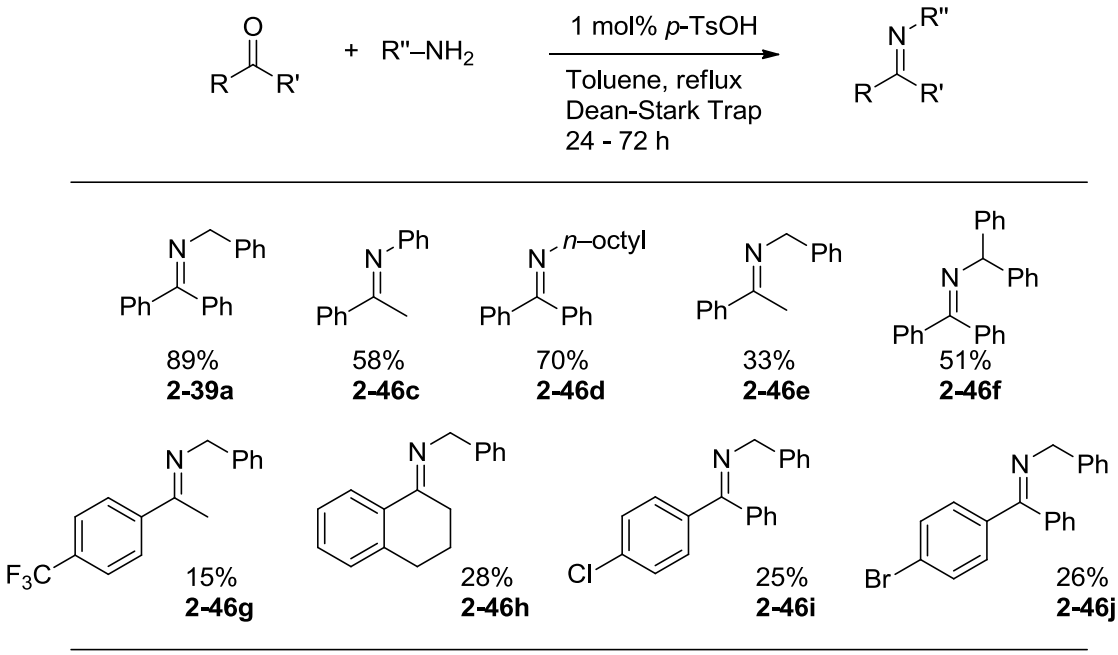
Scheme 2.3-8: Catalytic hydroboration of aldimine **2-36a** using catalytic amounts of **2-30**.

With evidence that both catalysts could easily reduce aldimines, a similar set of yields and reactivities was expected for other substrates. Due to difficulties reducing ketimines with **2-23** in CH_2Cl_2, these substrates were investigated using **2-30** as a catalyst. Several ketimines were synthesized by **IM2** (Table 8), and one ketimine was synthesized by Lewis acid mediated condensation (Scheme 2.3-9; method **IM3**).



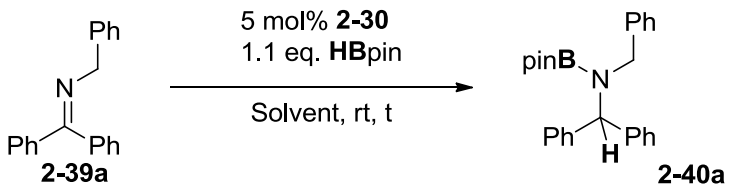
Scheme 2.3-9: Imine synthesized using method **IM3**.

Table 8: Ketimines synthesized using **IM2**.



With a wide selection of ketimines in hand, the hydroboration catalyzed by **2-30** was accomplished as described in Table 8. The use of 5 mol% **2-30** in $PhCF_3$ proved to be an effective method to affect the hydroboration of a majority of the ketimines synthesized. However, two of the ketimines were not soluble in the optimal reaction solvent, $PhCF_3$, thus, to accommodate these substrates a solvent screen was conducted (Table 9). Imine **2-39a** is soluble in $PhCF_3$ and the ability to produce it in high purity with high yields led us to choose it as a screening substrate. This screen revealed $PhCF_3$ as the optimal solvent, but mixtures with CH_2Cl_2 were also capable of affecting this transformation. 1,2-dichloroethane (DCE) was also a viable solvent to perform the reaction in although it gave products with lower conversions. The similar polarities of $PhCF_3$ and CH_2Cl_2 but a lack of nucleophilic side reactions could be a reason for the high conversions produced in this solvent. The high reactivity of **2-30** in $PhCF_3$ was exploited in a substrate scope analysis (Table 10).

Table 9: Solvent screen for hydroboration with catalyst **2-30** and imine **2-38a**.



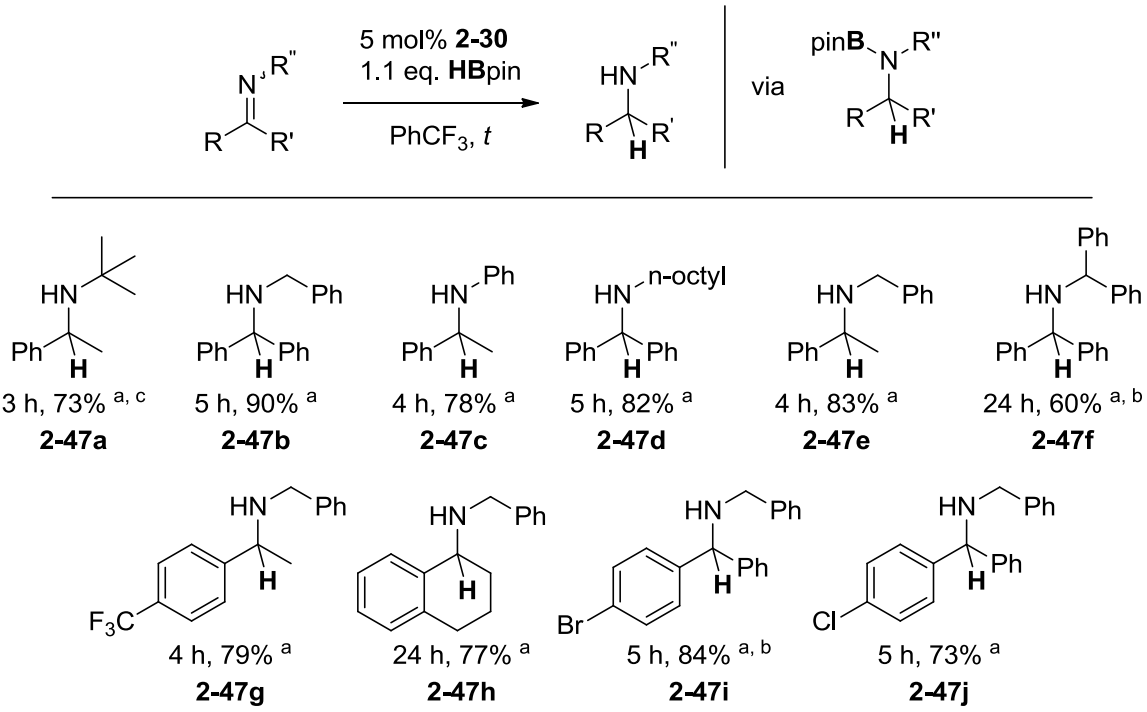
Entry	Solvent	Time(t)	Conversion (%)
1	Toluene	5 days	-
2	Benzene	5 days	-
3	$CHCl_3$	99 h	-
4	DME	48 h	-
5	TBME	99 h	-
6	CH_2Cl_2	5 days	33% [a]
7	CH_3NO_2	7 h	5%[a, b]
8	DCE	24 h	51% [c]
9	$PhCF_3$:CH_2Cl_2 (1:1)	24 h	55% [c]
10	$PhCF_3$:CH_2Cl_2 (2:1)	24 h	87% [c]
11	$PhCF_3$	4 h	100% [a]

[a] Conversion calculated relative loss of to starting material. [b] Side reactions evident by ^{1}H NMR. [c] Conversion calculated relative to internal standard (mesitylene).

The substrate scope of hydroborations catalyzed by **2-30** is similar to that of the hydroborations catalyzed by **2-23**. Slightly lower but consistent yields were obtained for all substrates. Difficulties associated with isolation of amine **2-47a**, including incomplete protection reactions and its instability to column chromatography, prevented acquisition of an isolated yield. Thus, only ^{1}H NMR conversions could be reported for that substrate. The reaction appears to proceed smoothly independent of the basicity and the steric environment of the imine substrate. Amine **2-47f** had to be protected as the trifluoroacetamide, isolated, and then deprotected to obtain pure product. With an NMR conversion of 70% the lower yield is most likely a result of added experimental steps and the steric environment around the imine. The ketimine reduction tolerated halides as well as trifluoromethyl groups, indicating that **2-30** is tolerate to organic

halides.[68] The similarities for imine reductions between the **2-23** and **2-30** led us to speculate whether the similarities existed for other substrates as well.

Table 10: Scope of **2-30** catalyzed ketimine hydroborations.



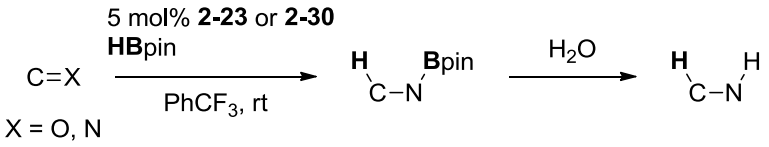
[a] Isolated yield. [b] 2:1 mixture of $PhCF_3$ / CH_2Cl_2. [c] NMR conversion. Substrate unstable to column chromatography.

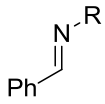
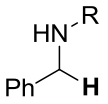
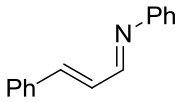
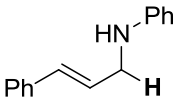
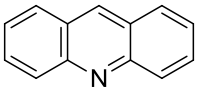
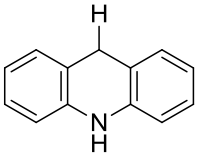
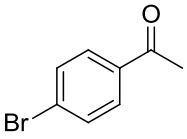
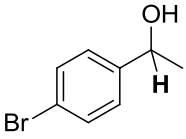
The reduction of other substrates by borenium catalyst **2-30** displayed similarities but also some peculiar differences to the observed reactivity of **2-23**. For example, the hydroborations of aldimines **2-36a**, **2-36b**, and **2-36c** with **2-30** all proceeded with very similar conversions and produced isolated yields slightly above those observed utilizing **2-23**. Furthermore, reduction of the *N*-heterocycle, acridine proceeded to completion over the same reaction time with an identical yield. However, the hydroboration of the *α,β*-unsaturated aldimine **2-36k**, with catalytic amounts of **2-30** resulted in a 39% increase in yield and almost exclusive selectivity for the 1,2-product. Conversely, reduction of benzonitrile with **2-23** provided conversions 55% greater than those produced with **2-30**. Lastly, hydroboration of ketones was also possible with catalyst **2-30** and the

reduction of *para*-bromoacetophenone was able to reach 62% conversion after 9 days of reaction time. These results are summarized in Table 11.

The surprising difference in reactivity and selectivity of the two catalysts is most likely a result of subtle differences in the mechanism of each catalyst, or a result of the culmination of more than one mechanism being active at one time. These mechanistic questions are addressed in Chapter 3. Prior to this discussion, a short comparison on the reductions presented in this section and other borane/borohydride reductions as well as a brief discussion on the differences between FLP catalyzed hydrogenations, FLP catalyzed hydrosilylations, and Lewis adduct/ borenium salt catalyzed hydroborations of ketones and imines is presented.

Table 11: A summary of the reactivity of **2-23** and **2-30**.



Entry	Substrate	Product	Time	Yield[a] 2-23	Yield[a] 2-30
1			45 min	**2-38a**, 100% (70%)[b]	100% (71%)[b]
2			3 h	**2-38b**, 89% (80%)	100% (90%)
3			1 h	**2-38c**, 91% (86%)[c]	100% (96%)
	R = *t*Bu, **2-36a**, R = Bn, **2-36b** R = Ph, **2-36c**				
4	 **2-36k**	 **2-38k**	2 h	(40%)[d]	(79%)[e]
5	PhCN	$PhCH_2CH_2$	24 h[f]	79% (54%)[g]	24% (18%)[g]
6		 **2-41a**	1 h	(95%)	(96%)
7		 **2-43d**	48 h	trace	62%[h]

[a] Conversions relative to substrate. Isolated yields in brackets. [b] Isolated as the trifluoroacetamide. [c] 8 h reaction time. [d] 20 h reaction time. Product isolated along with hydrocinnamaldehyde as a 6:1 mixture. [e] Only trace hydrocinnamaldehyde observed. [f] 100 °C. [g] Isolated as the pivalylamide. [h] 9 days reaction time.

2.4 Comparison to Other Reductive Methodologies

The most basic metal free method of turning a ketone into an amine is via reductive amination.[69] Following condensation of the ketone and the amine, a reducing agent is often added directly to the imine containing reaction mixture. This reducing agent can range from catalytic quantities of transition metals and hydrogen gas to simple inorganic reagents such as sodium borohydride. Due to the reactivity of hydrogen gas and cost of transition metals, stoichiometric amounts of inexpensive borohydride reagents are often used. A particular borohydride reagent, which is quite relevant to this discussion, is sodium triacetoxyborohydride (STAB).[71] This reagent is added to mixtures of aldehydes or ketones with ammonia or with primary or secondary amines to produce primary, secondary, or tertiary amines respectively.[71] It is especially useful when nonaqueous conditions are preferable. The three electron withdrawing acetoxy groups act to make STAB a very mild reducing agent and it is almost exclusive selective for imines or iminium ions.

Other B–H containing reducing agents can be harmful to the chemists who use them. For example, borane is toxic and sodium cyanoborohydride can release poisonous fumes during the quenching protocol.[69] Fortunately, this is not a problem for STAB which generates easy to handle byproducts.[69] Optimal conditions for STAB reductions involve mixing the carbonyl, amine, and STAB (1:1.05: 1.3-1.6 equivalents, respectively) in a variety of organic solvents and stirring at ambient temperatures.[70] There are numerous advantages to this process including low costs, scalability, and broad substrate scope, making it ideal for the industrial production of secondary and tertiary amines.[71] Disadvantages to STAB reductions are minimal but include the need for it in super stoichiometric quantities and its inability to introduce asymmetry.

At present, the technology developed within this chapter is a poor alternative to STAB reductions but it does have promise. For example, stoichiometric amounts of HBpin are used in

all cases but the catalytic nature of the reactions developed herein may enable the development of chiral catalysts capable of reducing imines enantioselectivity, thus, producing optically active amines. Optically active amines are highly desirable in the pharmaceutical industry and methods to produce them without the use of stoichiometric reducing agents, or toxic transition metal catalysts are rare. In order to develop a chiral catalyst a certain degree of mechanistic understanding is required, further motivating the upcoming investigations.

The efforts towards the development of catalytic metal–free reductions of organic molecules have increased within the chemical community over the past two decades. However, few metal free hydroboration techniques have been developed (see section 1.5.3). A comparison between catalytic FLP hydrogenations, hydrosilylations and borenium–catalyzed hydroboration produces several encouraging thoughts. First, FLP hydrogenations are, at present, unable to reduce ketones, and FLP hydrosilylations can reduce ketones, but additional steps are often required to cleave the oxygen-silicon bond. The hydroboration protocol developed in Chapter 2 is able to reduce a ketone to a secondary alcohol, albeit slowly and in low yields, without further deprotection reactions required. Furthermore, the substrate scope of imine hydroborations is significantly larger than that of FLP hydrogenations, allowing the reduction of imines with small *N*-substituents and those of low basicity. The synthetic applications of the reactions discussed and developed in this chapter are larger than that of FLP catalyzed processes but fail to surpass industrially utilized reductants. However, the improvements over current metal-free techniques, developed herein, clearly demonstrate the value of the reactions.

2.5 References

[1] Vedejs, E.; De Vries, T. S.; Prokofjevs, A. *Chem Rev.* **2012**, *112*, 4246.

[2] Corey, E. J. *Angew. Chem. Int. Ed.* **2009**, *48*, 2100.

[3] Stephan, D. W.; Dureen, M. A.; Lough, A.; Gilbert, T. M. *Chem. Commun.* **2008**, 4303.

[4] Lin, Z.; Lam, K. C.; Marder, T. B. *Organometallics* **2010**, *29*, 1849.

[5] Pelter, A.; Beletskaya, I. *Tetrahedron* **1997**, *53*, 4957.

[6] Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, *7*, 959.

[7] Beck, W.; Sünkel, K. *Chem. Rev.* **1988**, *88*, 1405.

[8] Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170.

[9] Chien, J. C. W.; Tsai, W.; Raush, M. D., *J. Am. Chem. Soc.* **1991**, *113*, 8570.

[10] Massey, A. G.; Park, A. J.; Stone, F. G. A. *Proc. Chem. Soc.* **1963**, 212.

[11] Döring, S.; Erker, G.; Fröhlich, R.; Meyer, O.; Bergander, K. *Organometallics* **1998**, *17*, 2183.

[12] Marks, T. J. *Acc. Chem. Res.* **1992**, *25*, 57.

[13] Yang, X.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10015.

[14] Erker, G. *Dalton Trans.* **2005**, 1883.

[15] Piers, W. E. *Adv. Organomet. Chem.* **2005**, *52*, 1.

[16] Crudden, C. M.; Webb, J. D.; Laberge, V. S.; Geier, S. J.; Stephan, D. W. *Chem. Eur. J.* **2010**, *16*, 4895.

[17] Piers, W. E.; Parks, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 9440.

[18] Piers, W. E.; Parks, D. J.; Blackwell, J. M. *J. Org. Chem.* **2000**, *65*, 3090.

[19] De Kimpe, N.; Leemans, E.; D'hooghe, M. *Chem. Rev.* **2011**, *111*, 3268.

[20] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, *3rd Ed.* **1999**, Wiley, New York.

[21] McLelland, R. A. *Carbocations: Organic Reaction Mechanisms* **2007**, Interscience, London.

[22] a) Harmon, K. M.; Dauben, H. J.; Honnen, L. R. *J. Org. Chem.* **1960**, *25*, 1442. b) Olah, G. A.; Svoboda, J. J.; Olah, J. A. *Synthesis* **1972**, 544.

[23] *Trityl Tetrakis(pentafluorophenyl)borate, Encyclopedia of Reagents for Organic Synthesis*. Wiley. Retrieved online: August 14th, 2012.

[24] Chien, J. C. W.; Song, W.; Raush, M. D. *Macromolecules* **1993**, *26*, 3239.

[25] a) Yamanoi, S.; Ohrui, H.; Seki, K.; Matsumoto,T.; Suzuki, K. *Tetrahedron Lett.* **1999**, *40*, 8407. b) Yamanoi, S.; Seki, K.; Matsumoto, T.; Suzuki, K. *J. Organomet. Chem.* **2001**, *624*, 143.

[26] a) Mukaiyama, T.; Yanagisawa, M.; Iida, D.; Hachiya, I. *Chem. Lett.* **2000**, 606. b)Yanagisawa, M.; Shimamura, T.; Iida, D.; Matsuo, J.; Mukaiyama, T. *Chem. Pharm. Bull.* **2000**, *48*, 1838.

[27] a) Müller, P. *Helv. Chim. Acta* **1973**, *56*, 1243. b) Giese, G.; Heesing, A. *Chem. Ber.* **1990**, *123*, 2373. c) Zimmerman, H. E.; Aasen, S. M. *J. Org. Chem.* **1978**, *43*, 1493. d) Komatsu, K.; Tomioka, I.; Okamoto, K. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 856. e) Yamamura, K.; Miyake, H.; Murata, I. *J. Org. Chem.* **1986**, *51*, 251.

[28] a) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Strecker, G.; Zurr, D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 542. b) Barton, D. H. R.; Magnus, P. D.; Smith, G.; Zurr, D. *J. Chem. Soc., Chem. Commun.* **1971**, 861.

[29] Kumar, A.; Doddi, V. R.; Vankar, Y. D. *J. Org. Chem.* **2008**, *73*, 5993.

[30] Johannsen, M.; Jorgensen, K. A.; Helmchen, G. *J. Am. Chem. Soc.* **1998**, *120*, 7637.

[31] Vedejs, E.; De Vries, T. S.; Prokofjevs, A. *Chem Rev.* **2012**, *112*, 4246.

[32] Lata, C. J. M. Sc. Dissertation, Queen's University, **2009**.

[33] Lata, C. J.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *132*, 131.

[34] Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170.

[35] Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170.

[36] Millot, N.; Santini, C. C.; Fenet, B.; Basset, J. M. *Eur. J. Inorg. Chem.* **2002**, *2002*, 3328.

[37] Webb, J. D. Ph. D. Dissertation, Queen's University, **2011**.

[38] Sironi, A.; Di Saverio, A.; Focante, F.; Camurati, I.; Resconi, L.; Beringhelli, T.; D'Alfonso, G.; Donghi, D.; Maggioni, D.; Mercandelli, P. *Inorg. Chem.* **2005**, *44*, 5030.

[39] Rieger, B.; Sumerin, V.; Schulz, F.; Nieger, M.; Leskelä, M.; Repo, T. *Angew. Chem. Int. Ed.* **2008**, *47*, 6001.

[40] Ingleson, M. J.; Del Grosso, A.; Singleton, P. J.; Muryn, C. A. *Angew. Chem. Int. Ed.* **2011**, *50*, 2102-2106.

[41] Stephan, D. W.; Farrell, J. M.; Heiden, Z. M. *Organometallics* **2011**, *30*, 4497.

[42] Stephan, D. W.; Geier, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 3476.

[43] Focante, F.; Camurati, I.; Nanni, D.; Leardini, R.; Resconi, L. *Organometallics* **2004**, *23*, 5135.

[44] Banks, R. E.; Besheesh, M. K.; Mohialdin-Khaffaf, S.; Sharif, I. *J. Fluorine Chem.* **1996**, *78*, 43.

[45] Chien, J. C. W.; Tsai, W.-M.; Raush, M. D. *J. Am. Chem. Soc.* **1991**, *113*, 8570.

[46] Germany Pat. DE 4235092 (to Doellein, G.) (1994) (Chem. Abstr. **1994**, *121*, 83618).

[47] Stephan, D. W.; Cabrera, L.; Welch, G. C.; Masuda, J. D.; Wei, P. *Inorg. Chim. Acta* **2006**, *359*, 3066.

[48] Damico, R.; Broaddus, C. D. *J. Org. Chem.* **1966**, *31*, 1607.

[49] Piers, W. E.; Bourke, S. C.; Conroy, K. D. *Angew. Chem. Int. Ed.* **2005**, *44*, 5016.

[50] Ingleson, M. J.; DelGrosso, A.; Singleton, P. J.; Muryn, C. A. *Angew. Chem. Int. Ed.* **2011**, *50*, 2102.

[51] Vedejs, E.; Nguyen, T.; Powell, D. R.; Schrimpf, M. R. *Chem. Commun.* **1996**, 2721.

[52] Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3808.

[53] Ingleson, M. J.; Del Grosso, A.; Pritchard, R. G.; Muryn, C. A. *Organometallics* **2010**, *29*, 241.

[54] Stephan, D. W.; Chase, P. C.; Welch, G. C.; Jurca, T. *Angew. Chem. Int. Ed.* **2007**, *47*, 8050.

[55] Stephan, D. W.; Jurca, T.; Chase, P. A. *Chem. Commun.* **2008**, 1701.

[56] a) Soós, T.; Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 6559. b) Soós, T.; Erős, G.; Nagy, K.; Mehdi, H.; Pápai, I.; Nagy, P.; Király, P.; Tárkányi, G. *Chem. Eur. J.* **2012**, *18*, 574.

[57] Westcott, S. A.; Baker, R. T.; Calabrese, J. C. *J. Organomet. Chem.* **1995**, *498*, 109.

[58] Stefani, H.; Guzen, K.; Guarezemini, A.; Órfão, A.; Cella, R.; Pereira, C. *Tetrahedron Lett.* **2007**, *48*, 1845.

[59] Valdés, C.; Barluenga, J.; Jiménez-Aquino, A.; Anzar, F. *J. Am. Chem. Soc.* **2009**, *131*, 4031.

[60] Stephan, D. W.; Geier, S. J.; Chase, P. A. *Chem. Commun.* **2010**, 4884.

[61] Erker, G.; Spies, P.; Schwendemann, S.; Lange, S.; Kehr, G.; Fröhlich, R. *Angew. Chem. Int. Ed.* **2008**, *47*, 7543.

[62] de Vries, J. G.; Elsevier, C. J. *Handbook of Homogeneous Hydrogenation, Vol. 1-3* **2007**, Wiley, Weinheim.

[63] Stephan, D. W.; Spies, P.; Erker, G.; Kehr, G.; Bergander, K.; Fröhlich, R.; Grimme, S. *Chem. Commun.* **2007**, 5072.

[64] Erker, G.; Wang, H.; Fröhlich, R.; Kehr, G. *Chem. Commun.* **2008**, 5966.

[65] Erker, G.; Stephan, D. W.; Reddy, J.; Xu, B.; Mahdi, T.; Frölich, R.; Kehr, G. *Organometallics* Ahead of Print, dx.doi.org/10.1021/om3006068.

[66] Klankermayer, J.; Chen, D.; Leich, V.; Pan, F. *Chem. Eur. J.* **2012**, *18*, 5184.

[67] a) Piers, W. E.; Parks, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 9440. b) Piers, W. E.; Parks, D. J.; Blackwell, J. M. *J. Org. Chem.* **2000**, *65*, 3090.

[68] Lata, C. J.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *132*, 131.

[69] a) March, J.; Smith, M. B. *March's Advanced Organic Chemistry: Reactions. Mechanisms, and Structure, 6th Ed.* **2007**, Wiley, Hoboken. b) Clayden, J.; Wothers, P.; Greeves, N.; Warren, S. *Organic Chemistry* **2001**, Oxford University Press, New York.

[70] Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849.

[71] Matos, K. Burkhardt, E. R. *Chem. Rev.* **2006**, *106*, 2617.

Chapter 3

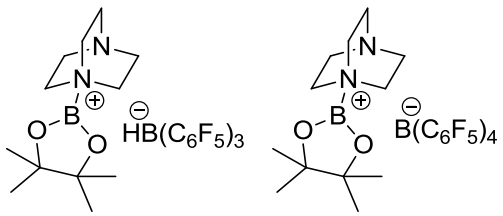
On the Mechanism of Borenium Catalyzed Hydroboration

3.1 Introduction

The mechanism of a chemical reaction is a culmination of elementary chemical processes that describe an overall change in a molecule or molecules. In most cases, the conversion of starting materials into products is easily observable through the use of modern spectroscopic techniques. However, identification of the elementary steps the reaction takes to yield the overall product is a much more challenging process. Experimental and theoretical studies into the inner workings of a chemical process can provide valuable insight into each of these elementary steps. While computational investigations typically rely on the calculation of the relative energies of a series of proposed intermediates along a given pathway, experimental insight into these intermediates can be gained in a myriad of different ways. For example, a comparison between the rates of formation of one product by two different catalysts can provide insight into whether they are going by similar or different mechanisms. Another method often used is isolation of intermediates along a reaction coordinate. While this method does not conclusively demonstrate that these isolated species are on the reaction pathway, it does provide merit for their proposition, especially if they can be shown to be kinetically competent under the reaction conditions. It should be noted that it is rare for experimental techniques to allow transition state analysis whereas this is a fundamental goal of theoretical work in mechanistic reaction analysis. Other common experimental methods include isotopic labeling and their associated effects, stoichiometric reactions, kinetic analysis, and many others.[1]

In chapter 2, two similar yet novel catalysts were developed (Scheme 3.1-1). Both containing the same borenium cationic fragment but distinct anions; species **3-1**, formed from

$B(C_6F_5)_3$•DABCO reacting with HBpin, contains an active, hydridic counterion, tris-pentafluorophenyl hydridoborate ($HB(C_6F_5)_3^-$), whereas catalyst **3-2** is charge matched by the inert, non-hydridic anion, tetrakis-pentafluorophenylborate ($B(C_6F_5)_4$). The reactivity of $HB(C_6F_5)_3^-$ has been demonstrated numerous times in the diversity of catalytic FLP hydrogenations.[2] To our knowledge, no experimental evidence for hydride delivery from $HB(C_6F_5)_3^-$ has been reported in the FLP literature, although other options are difficult to envision. However, Piers and coworkers acquired substantial experimental evidence for hydride delivery from $HB(C_6F_5)_3^-$ being the final step in $B(C_6F_5)_3$ catalyzed hydrosilylation of aldehydes and ketones.[3] Strong support came in the form of deuterium labeling studies as well as the measurement of a kinetic isotope effect, theoretical structure determination, and substrate-catalyst interactions. These $B(C_6F_5)_3$ catalyzed hydrosilylation reactions proceed at ambient temperatures but FLP hydrogenations often require temperatures in excess of 80 ℃. In the Piers system, the facile nature of hydride delivery is potentially a result of strong activation of the carbonyl by an *in situ* generated silylium cation. In the FLP catalyzed hydrogenation of imines a similar mechanism is proposed to be at play; protonation of substrate leads to iminium ion formation, in turn, initiating hydride delivery from $HB(C_6F_5)_3^-$. The requirement of elevated temperatures may be a result of differences in the electrophilicity between the iminium and oxonium cations.



3-1 **3-2**

Scheme 3.1-1: Catalysts developed in Chapter 2.

Turning to the hydroboration reactions discussed in the previous chapter, this mode of hydride delivery is possible for only one of the catalyst systems examined. In reactions catalyzed by $B(C_6F_5)_3$•DABCO, borenium transfer from DABCO to an imine may create a boryl-iminium

ion which is expected to be more electrophilic than a protonated iminium due to the electron deficient nature of the boron atom increasing the electrophilicity of the imine. This species may be more reactive than a protonated iminium ion facilitating hydride delivery from $HB(C_6F_5)_3^-$. However, this proposal as a mode of hydride delivery is not an option for hydroboration reactions catalyzed by **3-2**. The non-hydridic counterion, $B(C_6F_5)_4$, has no hydride to deliver, and therefore, some other mechanism must be at play.

Several experimental techniques were used to probe this mechanism. Initial rate experiments were used to determine whether the catalysts proceed via a similar mechanism. Deuterium labeling studies determined if indeed borenium transfer is occurring and what the source of hydride in reactions catalyzed by $B(C_6F_5)_3$•DABCO and **3-2**. Thoroughout this work, it became clear that several other experiments could shed light on the nature of this mechanism and these are discussed in detail.

3.2 Kinetic Investigations: Part I

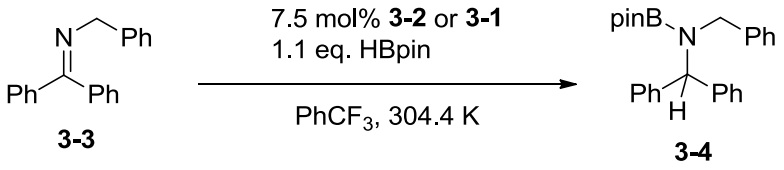
Kinetic analysis of novel multistep organic reactions is a crucial part of fundamental mechanistic studies. Such endeavors are focused on providing useful information including concentration dependencies and rate and/or equilibrium constants pertaining to the elementary steps of a chosen reaction. The measurement of reaction rates can be a difficult task and two general types of rate measurement are available: 1) integral measurements involve the quantification of a relationship between a measureable parameter and the concentration of a given substance in the reaction medium, and 2) differential measurements are those which directly measure the rate of reaction.[4] Examples of integral measurement techniques include acquisition of conversions through spectroscopy or chromatography. These techniques use the measurable

parameter percent conversion of starting material to product, and monitor it as a function of time to determine the reaction rate. This extrapolation is quite simple as the concentration of product in solution is directly proportional to the integral of the reaction rate. Differential measurements work in the opposite manner. The observed parameter is the rate of reaction from which the percent conversion can be calculated. An example of this methodology is calorimetry, which measures the instantaneous heat flow of a reaction. More specifically, the heat flow, q, is related to the rate of reaction through the thermodynamic heat of reaction, ΔH_{rxn}. These useful analytical techniques allow the determination of both rate of reaction and order of reaction parameters. We hypothesized that through the use of integral techniques we could determine the initial rates of both catalysts, thus enabling educated speculation on whether or not they operate by the same mechanism.

3.2.1 Initial Rates through NMR

Determining the initial rates for each catalyst was most easily accomplished through NMR analysis. Performing a reaction under identical conditions and monitoring the growth of product peaks in ^{1}H NMR proved most useful. A substrate was chosen that met the following criteria: the formation of product was easily observed, conversion to product occurred on a reasonable timescale, and signals were well resolved from a non interacting internal standard. *N*-(diphenylmethylene)-1-phenylmethanamine (**3-3**) was chosen as the substrate since the inclusion of hydrogen at the electrophilic carbon produced a peak in an otherwise unoccupied region and the reaction proceeded to completion with both catalysts in a few hours. Mesitylene was selected as the internal standard since addition of small amounts was found to have no observable effect on the course of the reaction. The reaction conditions used were slightly different than those optimized in chapter 2, namely, the catalyst loading was increased from 5 mol% to 7.5 mol% to increase the overall percent conversion of the reaction (Scheme 3.2-1). The percent conversion of these NMR scale reactions, which were always performed without mixing, seldom exceeded

80%. This was presumed to be a consequence of the lack of mixing, which may have led to catalyst decomposition or HBpin degradation. To perform the reactions accurately, the temperature within the spectrometer needed to be rigorously controlled and the reaction started at a definitive time. Through the use of a liquid nitrogen-cooled cold-well in a glove box, each component of the reaction was frozen in $PhCF_3$, creating as an independent layer of reagent in a J. Young tube.



Scheme 3.2-1: Reaction conditions used in NMR rate experiments.

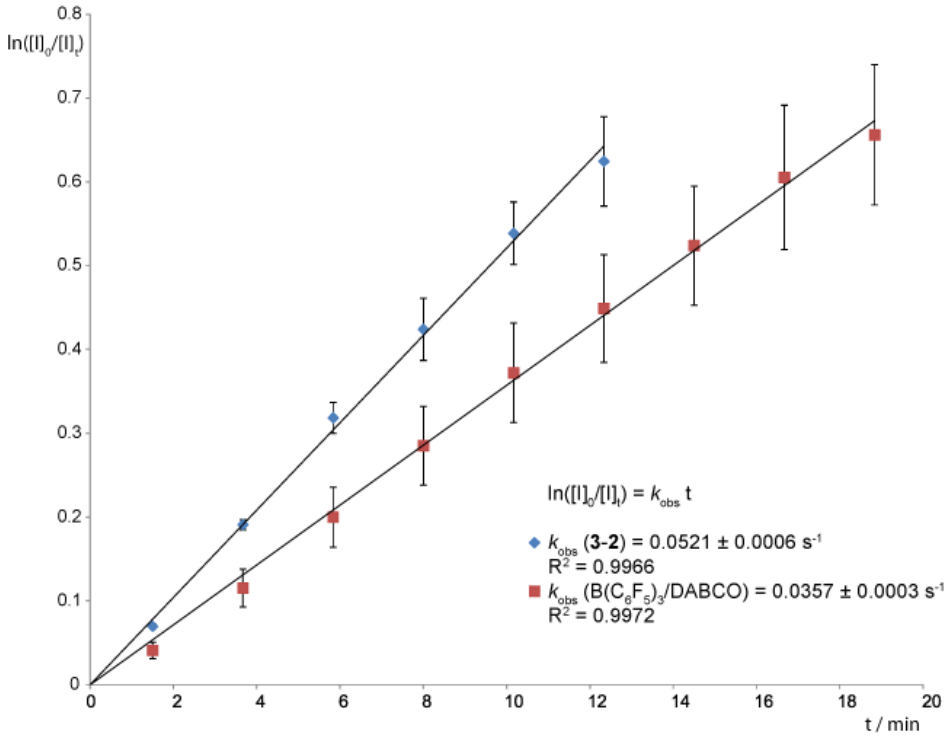


Figure 3-1: A comparison of initial rates for the reduction of **3-3** catalyzed by 7.5 mol% of $B(C_6F_5)_3$•DABCO (or **3-1**) (red) and **3-2** (blue) under identical conditions.

The frozen sample was then removed from the glove box and placed in a dry ice/acetone bath and transferred to a 500 MHz spectrometer. The internal temperature of the probe was set to 304.4 ± 0.1 K, and confirmed through the use of an external standard. A multi-acquisition experiment was set up in which a proton NMR was collected at defined intervals for the duration of the reaction. The progression of reaction was monitored by increases in the product resonances. This experiment was performed in triplicate for each catalyst and the results are shown in Figure 3-1 (derivation of rate equation and data analysis is given in Appendix B). The rates for these reactions were analyzed up to ca. 50% conversion in order to maintain a high degree of linearity in the data.

The reaction rates for both catalytic systems are on the same order of magnitude with the preformed borenium cation **3-2** reacting slightly faster than the catalyst **3-1**. This direct comparison of reaction rates demonstrates that it is reasonable to assume that the reaction mechanisms are going via similar elementary steps. This implies that hydride delivery from $HB(C_6F_5)_3^-$ may not be happening under the reaction conditions; if it were, then a larger difference in rate would be expected. A potential reason for the slightly increased rate of reaction when catalyst **3-2** was employed is that the borenium cation is added directly to the reaction, whereas in $B(C_6F_5)_3$•DABCO catalyzed reactions the active catalyst **3-1** must first formed in solution before entering into the catalytic cycle. An additional explanation is that the difference in counterions may play a role in the activity of the catalyst. The difference in anions may result in a different stabilization of the cationic character of the borenium ion through a difference in coordination strength. The counterion with a more diffuse anionic charge will be less capable of coordinating to the cation, thus facilitating the localization of positive charge. This presumably results in an increase in the activity of the destabilized charge-carrying molecule.[5] Counterion $B(C_6F_5)_4^-$ has a more diffuse negative charge and as a result is less able to stabilize the positively

charged DABCO•Bpin fragment. Meanwhile, $HB(C_6F_5)_3^-$ is less able to delocalize its negative charge and may result in a more stable ion pair. Both of these logical arguments are in agreement with the experimental evidence provided by the initial rate analysis.

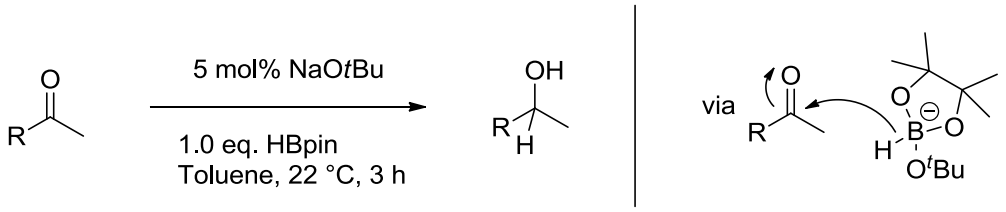
Such a close relationship between the rates suggests that a similar mechanism is under way for both catalysts. The reduction in rate for the $B(C_6F_5)_3$•DABCO system may be accounted for by the requirement of *in situ* borenium generation or differences in ion pairing energies which could be a result of the different anions but these arguments are suggestive and by no means definitive. An alternative method investigating the rate differences would be through computational analysis. Despite these results, this analysis does not explain if the source of hydride in these catalytic reductions is HBpin or $HB(C_6F_5)_3^-$. To answer this question, deuterium labelling studies and stoichiometric reactions were performed on the $B(C_6F_5)_3$•DABCO system.

3.3 Experimental Evidence for a Novel Mechanism

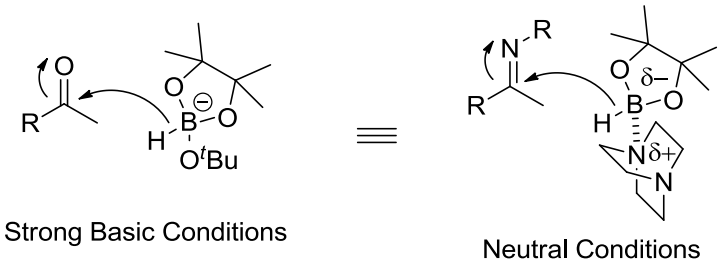
3.3.1 A New Mechanistic Proposal

The nucleophilic delivery of a hydride to an electrophilic carbon is a common feature of most reductions of polarized bonds.[6] In FLP hydrogenations and $B(C_6F_5)_3$-catalyzed hydrosilylations the presumed hydride delivery reagent is $HB(C_6F_5)_3^-$.[2, 3] However, in borenium catalyzed hydroboration reactions, the observation of reactivity in non-hydridic systems such as those with **3-2** and similar rates of reaction for hydride-containing catalyst **3-1** suggest that a different mode of hydride delivery might be occurring. An alternate mechanistic proposal was inspired by the Brønsted base initiated hydroboration of ketones in which strong basic conditions promote this reductive process.[7] The authors propose that the basic alkoxide activates HBpin by forming a borate (Scheme 3.3-1). This borate then nucleophilically delivers a hydride to the

electrophilic carbon of an unactivated ketone. A similar mechanism may be proposed for the hydroboration reactions from Ch. 2 and the similarities are highlighted in Scheme 3.3-2. With this precedent it is reasonable to propose that DABCO is capable of nucleophilically activating HBpin, which, in turn, facilitates the hydride delivery step. Another alternative is that HBpin delivers its hydride independently of DABCO activation. This path seems particularly unlikely as it would result in the generation of two-coordinate cationic pinacol borinium ion. To find evidence supporting a Lewis base catalyzed reaction and experimental support for this hydride delivery pathway several mechanistic experiments were performed.



Scheme 3.3-1: Brønsted base initiated hydroboration of ketones via nucleophilic activation of HBpin.



Scheme 3.3-2: An alternate possibility for the mechanism of hydride delivery.

Given the precedent of nucleophilic activation of boranes, a new catalytic cycle can be proposed (Figure 3-2). The first step in this new borenium catalyzed mechanism involves transfer of the Bpin fragment from DABCO to the Lewis basic center of the substrate, in this case, the Schiff base. This liberates DABCO and forms the boryl-iminium ion **3-5**. Hydride delivery from the activated DABCO•HBpin adduct **3-6** regenerates the borenium cation catalyst and forms the desired product.

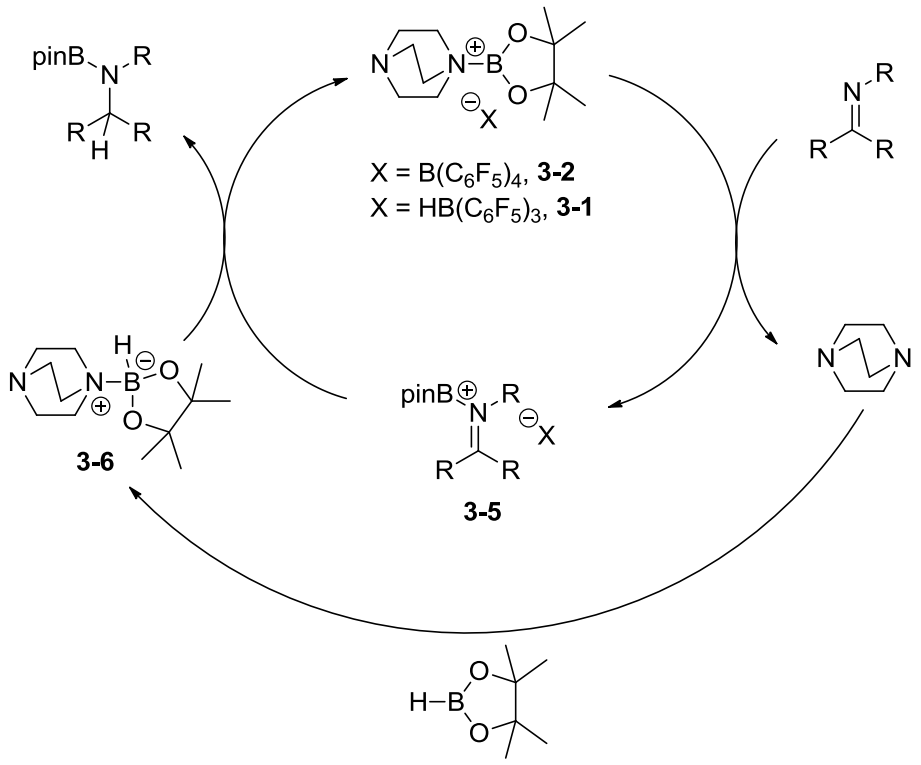


Figure 3-2: Proposed mechanism based on Lewis base activation of HBpin.

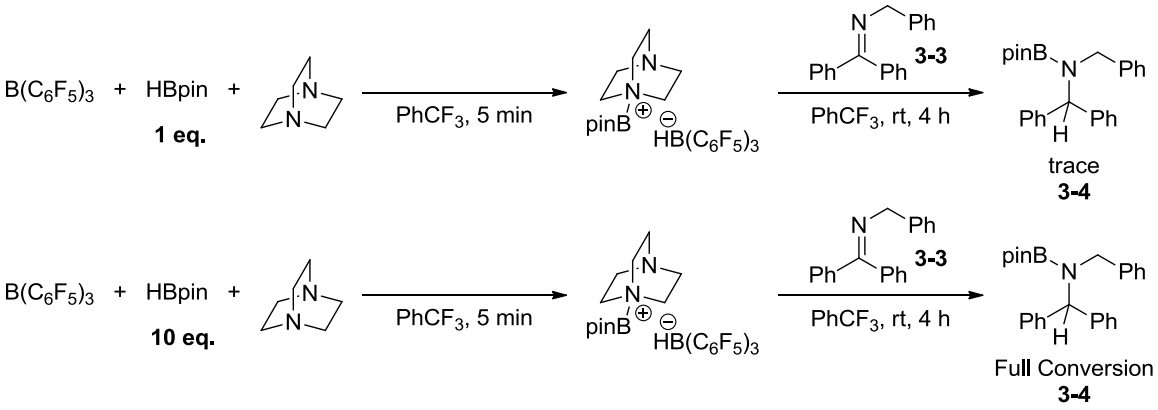
We suspected that several aspects of this mechanism could be resolved with various experimental mechanistic techniques. For example, the borenium transfer and hydride delivery steps were investigated through isotope labeling. Furthermore, if $HB(C_6F_5)_3^-$ was not the active reducing agent then we hoped the reaction would not proceed under stoichiometric hydroboration conditions. We also hypothesized that, through the use of deuterated catalysts and substrates, we could elucidate the hydride source in both reactions. Furthermore, we speculated that if HBpin was involved in the turnover limiting step of this reaction, a large kinetic isotope effect could be observed by comparing differences in rate between reactions using HBpin and its deuterated analogue.

Dr. Patrick Eisenberger aided in the mechanistic study of this reaction. He performed some of the deuterium labeling experiments, manufactured the deuterated substrate HBpin-[$\mathbf{d_{12}}$],

carried out low temperature NMR studies, and aided in the development of a model that helped describe the hydride delivery step.

3.3.2 A Stoichiometric Reaction

A useful method for investigating the transfer of chemical moieties between catalyst and substrate is to perform stoichiometric reactions. Insights into active catalytic species or isolation of intermediates are typical goals of this type of experiment. In this case, a stoichiometric reaction utilizing equimolar amounts of $B(C_6F_5)_3$, HBpin, DABCO, and imine **3-3** was performed to investigate the hydride delivering ability of $HB(C_6F_5)_3^-$ under standard reducing conditions. First, borenium borohydride salt **3-1** was generated *in situ* and its clean formation confirmed by ^{11}B and ^1H NMR. Following this, one equivalent of **3-3** was added as a solution in $PhCF_3$ (Scheme 3.3-3); a process identical to the reactions performed in Ch. 2. Over the course of 4 hours, only trace amounts of product **3-4** were observed, and after 52 hours the reaction had only reached ca. 20% conversion. This indicates that $HB(C_6F_5)_3^-$ is not capable of reducing an activated boryl-iminium on anywhere near the same time frame as is observed under catalytic conditions. This supports the argument that $HB(C_6F_5)_3^-$ is simply a counterion to the active borenium catalyst.



Scheme 3.3-3: Stoichiometric reduction of **3-3** with **3-1** and identical reaction with 10 eq. HBpin.

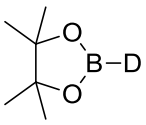
Performing an identical reaction utilizing $B(C_6F_5)_3$, DABCO, and imine **3-3** in a 1:1:1 stoichiometry but using10 eq. of HBpin exhibited a rate of reaction similar to that observed in the

catalytic reactions discussed in Ch. 2 (Scheme 3.3-3). This result not only agrees with the result of the stoichiometric experiment (which indicates that $HB(C_6F_5)_3^-$ is not a kinetically relevant reducing agent) but also indicates that the active reducing agent is HBpin. If evidence supporting a DABCO•HBpin adduct can be found then this result strongly indicates that adduct **3-6** is the active reducing agent.

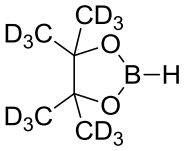
3.3.3 Deuterium Labeling Studies

Isotope labeling is commonly used to tract the path of an isotope through a reaction, metabolic pathway, or cell.[8] To monitor a chemical reaction via the use of isotopes one must first synthesize a substrate or reagent with isotopically enriched starting materials. The labeled reagent is introduced in place of a standard reagent and tracked either during the reaction, located in the final product, or both. Modern spectroscopic techniques have made this task quite simple although interpretation of results and synthesis of isotopically enriched starting materials remains a challenging task.

Two isotopically enriched reagents were used to provide support for several aspects of this mechanistic study. [$\mathbf{d_1}$]-Pinacol borane (DBpin) is aptly suited to determine the source of hydride by tracking the incorporation of deuterium into the final product. It also allowed us to determine whether $HB(C_6F_5)_3^-$ was capable of reducing the boryl-iminium ion **3-5** under standard reaction conditions, as opposed to direct HBpin reduction. Lastly, [$\mathbf{d_{12}}$]-pinacol borane (HBpin-$\mathbf{d_{12}}$) is an ideal reagent to investigate the borenium transfer step. Logical reaction procedures and observation of deuterium incorporation into products aided our understanding of the mechanism at hand and further verified the results of the reduced activity observed in the stoichiometric reaction.



[$\mathbf{d_1}$]-pinacol borane
DBpin



[$\mathbf{d_{12}}$]-pinacol borane
HBpin-**$\mathbf{d_{12}}$**

Maintaining some semblance of the proposed mechanism of FLP catalyzed hydrogenation, we speculated that the first step in the mechanism of borenium catalyzed hydroboration was transfer of the positively charged Bpin fragment from DABCO to the substrate by the stepwise process shown in Figure 3-3. Due to the unlikely formation of a two-coordinate borinium cation this transfer is unlikely to proceed via an S_N1-type mechanism. The two remaining possibilities are an S_N2-type mechanism and an associative type mechanism. No experimental or theoretical evidence has been collected and due to the lack of an observable intermediate an S_N2-type process is likely (Figure 3-3).

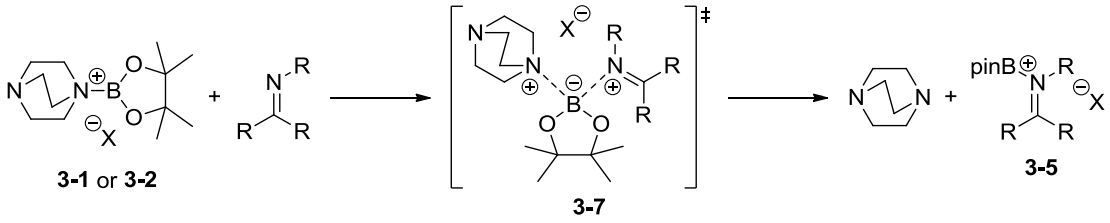
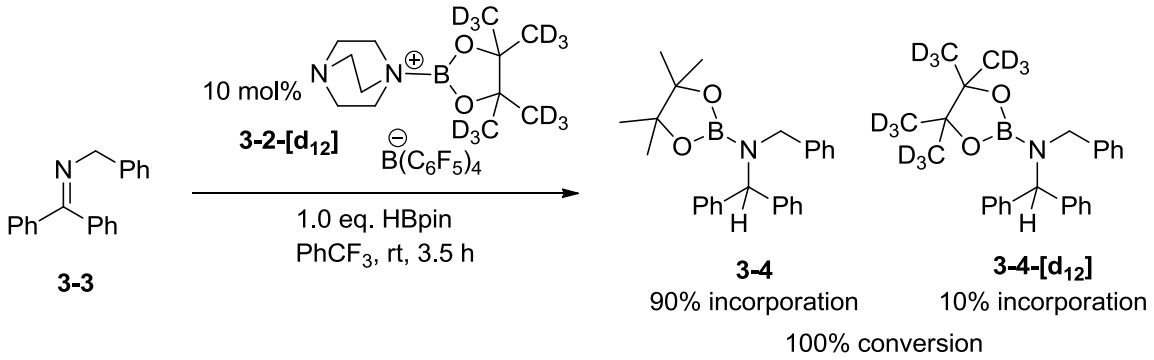


Figure 3-3: Hypothetical transition state for borenium transfer from DABCO to imine.

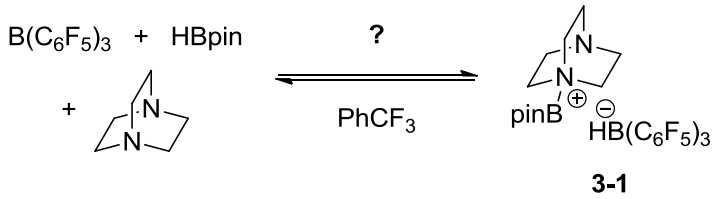
To ensure borenium transfer was underway, we hypothesized that labeling the pinacol backbone and observing the labeled product by high resolution mass spectroscopy would support a borenium transfer mechanism. Dr. Patrick Eisenberger synthesized HBpin-[$\mathbf{d_{12}}$] from a known literature procedure.[9] Using this isotopically enriched reagent, borenium ion **3-2-[$\mathbf{d_{12}}$]** was made through a reaction with $TrB(C_6F_5)_4$ and DABCO in $PhCF_3$. This deuterated borenium ion was used as a catalyst in the catalytic reduction of imine **3-3** and HBpin (Scheme 3.3-4). High resolution EI/TOF mass spectrometry was performed on an aliquot taken directly from the reaction vial after 3.5 hours. The products **3-4** and **3-4-[$\mathbf{d_{12}}$]** were observed in an approximately 9:1 ratio based on signal intensities. This result is consistent with a mechanism in which the Bpin fragment originally located on DABCO is incorporated into the product and the borenium cation is regenerated subsequent to hydride transfer from HBpin to the activated iminium ion. Due to the unlikely production of a positively charged two coordinate borinium Bpin fragment, we

speculated that DABCO was likely involved in this step as well. Investigations into the role of DABCO are discussed in section 3.3.4.



Scheme 3.3-4: Borenium transfer experiment from catalyst to substrate.

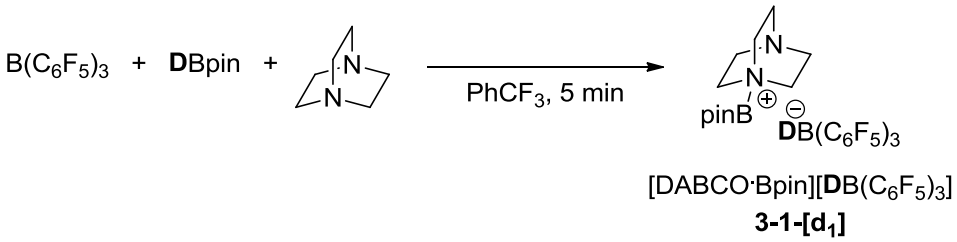
Prior to examining the hydride delivery step with valuable deuterated materials, we first needed to determine if *in situ* formation of **3-1** was a reversible process (Scheme 3.3-5). If borenium formation is reversible, then deuterium scrambling might take place and the observed label incorporation (or lack thereof) may be difficult to interpret. Changes in the multiplicities of peaks in ^{11}B NMR for mixtures of **3-1-[d$_1$]** with HBpin (or **3-1** with DBpin) may indicate the reversibility of borenium cation formation.



Scheme 3.3-5: Reversibility of the formation of **3-1**.

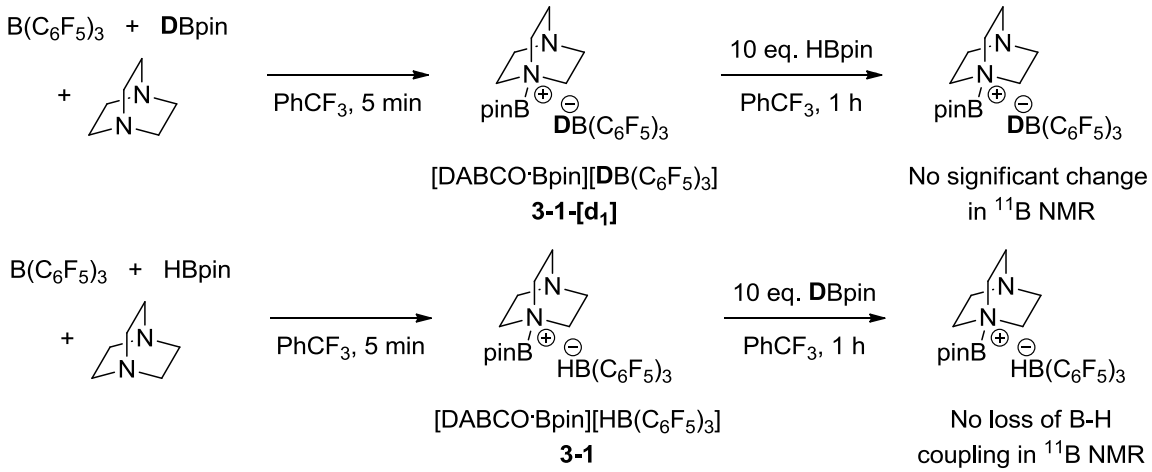
To test this hypothesis, equimolar amounts of $B(C_6F_5)_3$, DABCO, and DBpin were reacted and **3-1-[d$_1$]** was cleanly generated (Scheme 3.3-6). Deuterium incorporation was confirmed by the change in multiplicity of the borohydride peak at –25.4 ppm from a doublet to a singlet (Figure 3-4). Due to the broadness of the proton peak attributed to $HB(C_6F_5)_3^-$ in ^{1}H NMR, its disappearance caused by deuterium incorporation could not be confirmed by ^{1}H NMR. However, the appearance of a peak in the reported region for $HB(C_6F_5)_3^-$ in ^{2}H NMR led us to

conclude that clean generation of **3-1-[d_1]** had occurred (Figure 3-5). The lack of appearance of a peak for $HB(C_6F_5)_3^-$ in ^1H NMR may indicate that there is a rapid equilibrium between the two environments for this proton, one being in HBpin and the other being in $HB(C_6F_5)_3^-$. The observation of a peak corresponding to $DB(C_6F_5)_3^-$ in ^2H NMR may indicate a strong isotope effect. This potential isotope effect was examined in more detail and will be revisited shortly.



Scheme 3.3-6: Generation of **3-1-[d_1]**.

With **3-1-[d_1]** in solution, 10 eq. of HBpin were added to the reaction mixture (Scheme 3.3-7). The ^{11}B NMR spectra exhibited subtle changes indicating that this process may be reversible (Figure 3-4). The appearance of a peak at 2.5 ppm in the ^{11}B NMR and broadening of the singlet at –25.4 ppm lent support to this hypothesis. Also, rapid consumption of HBpin was observed and the peak at 2.5 ppm is potentially a previously unobserved decomposition product.



Scheme 3.3-7: Exchange experiments designed to look for borenium formation reversibility by observation of isotopic changes in ^{11}B NMR.

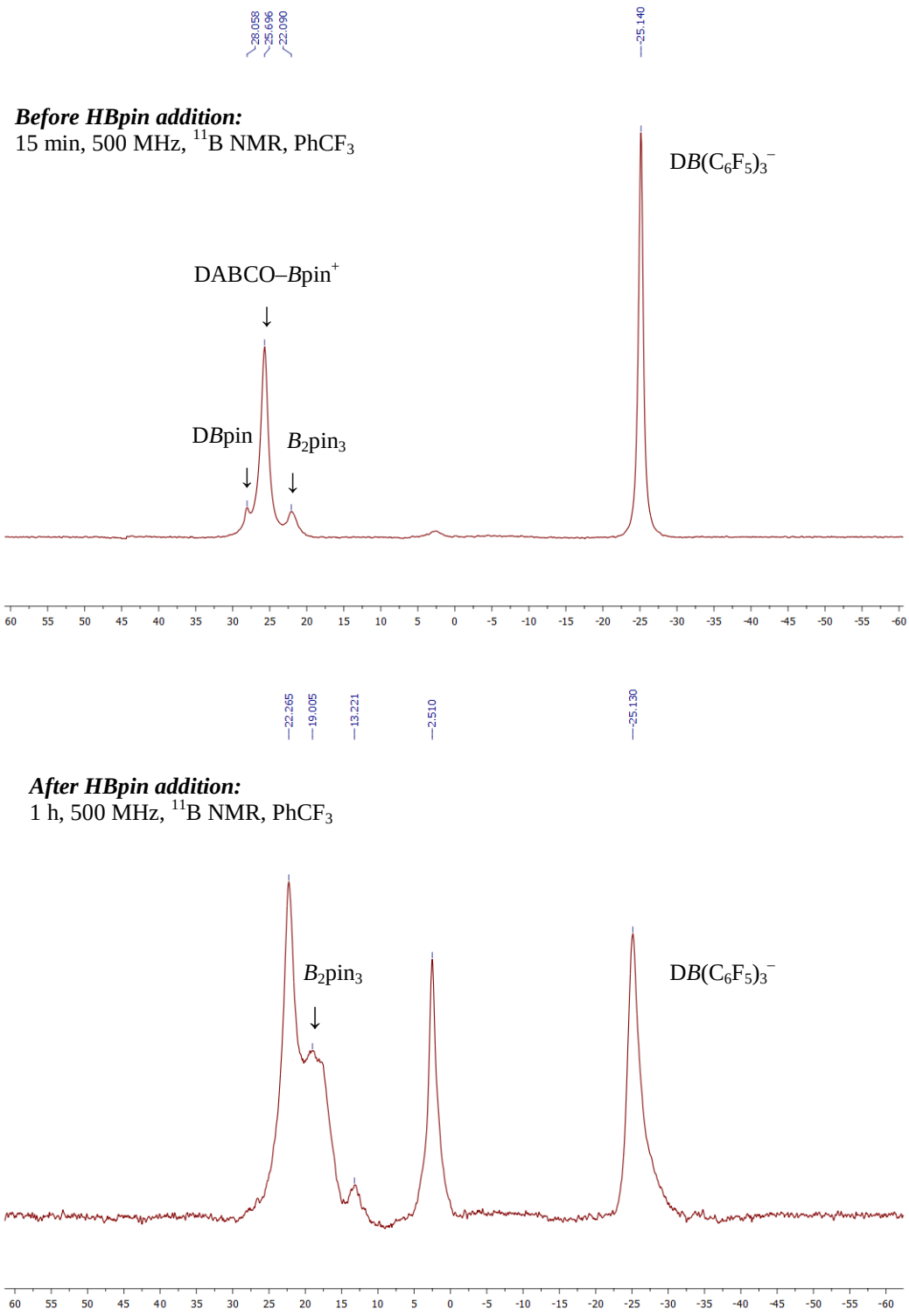


Figure 3-4: ^{11}B NMR spectrum of **3-1-[d_1]** before addition of HBpin (top) and ^{11}B NMR spectrum of **3-1-[d_1]** 1 hour after addition of HBpin (bottom).

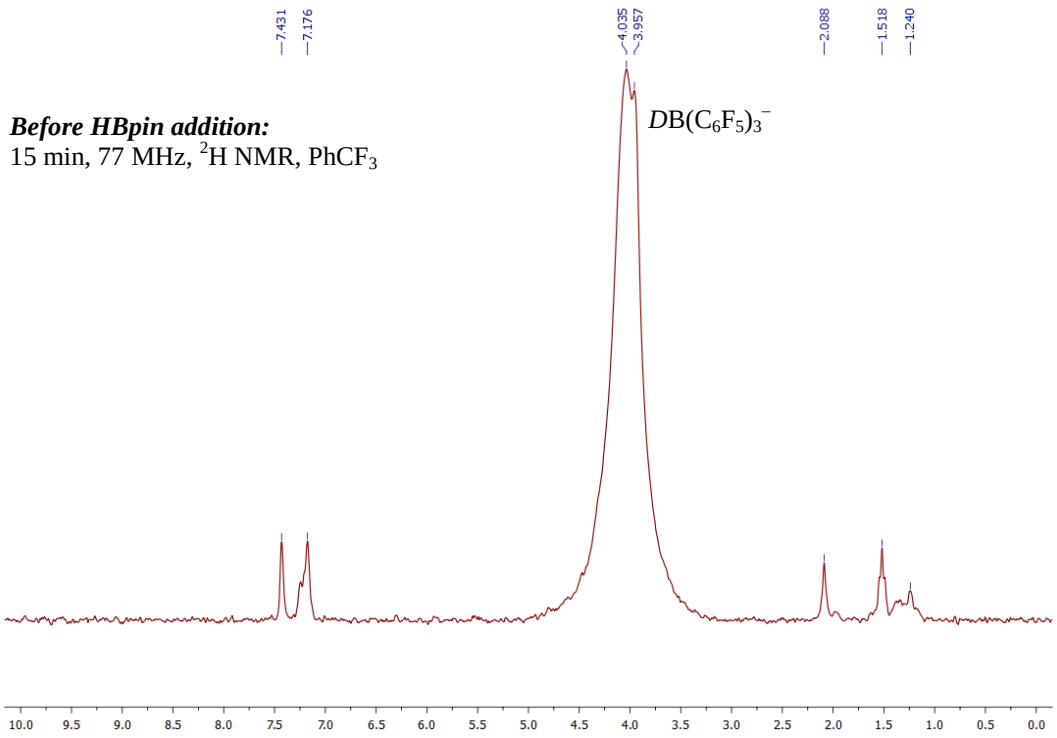


Figure 3-5: ^{2}H NMR spectrum of **3-1-[d_1]** before addition of HBpin.

Repeating this experiment using **3-1** and DBpin (Scheme 3.3-7), resulted in no change in the signals in the ^{11}B NMR spectrum and the byproduct at 2.5 ppm was not observed (Figure 3-6). The coupling constant for the borohydride doublet at –25.4 ppm remained the same within experimental error before and after DBpin addition ($^{1}J_{B–H}$ = 89.2 and 88.6 Hz respectively). These experiments are inconclusive and do not support the reversibility or irreversibility of borenium formation via the use of (H/D)Bpin, DABCO, and $B(C_6F_5)_3$. However, it was very interesting to note that the resonance attributed to (H/D)B$(C_6F_5)_3^-$ was only observable in the ^{2}H NMR spectrum. This experimental result motivated the search for differences in isotopic reactivity and a kinetic isotope effect.

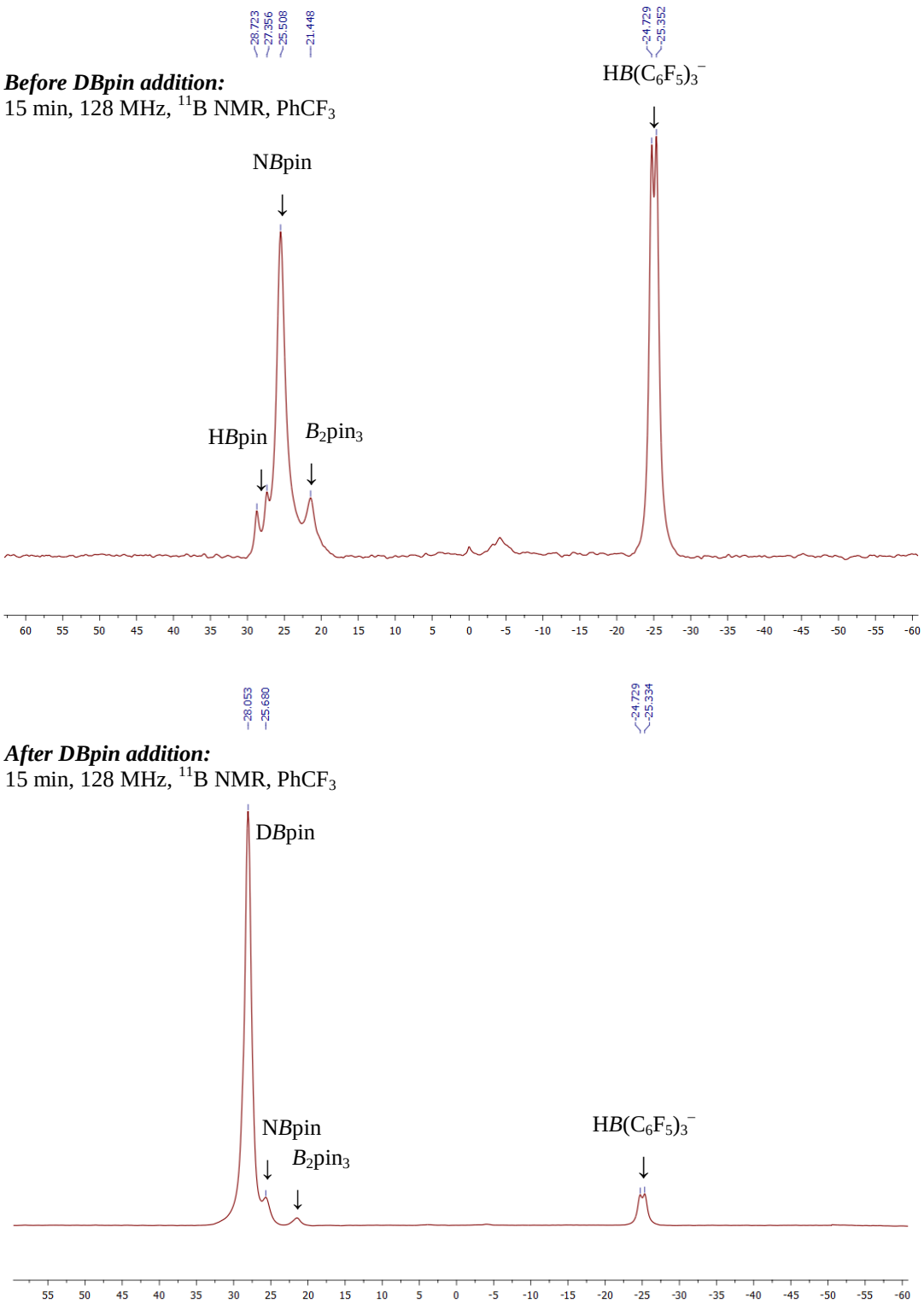
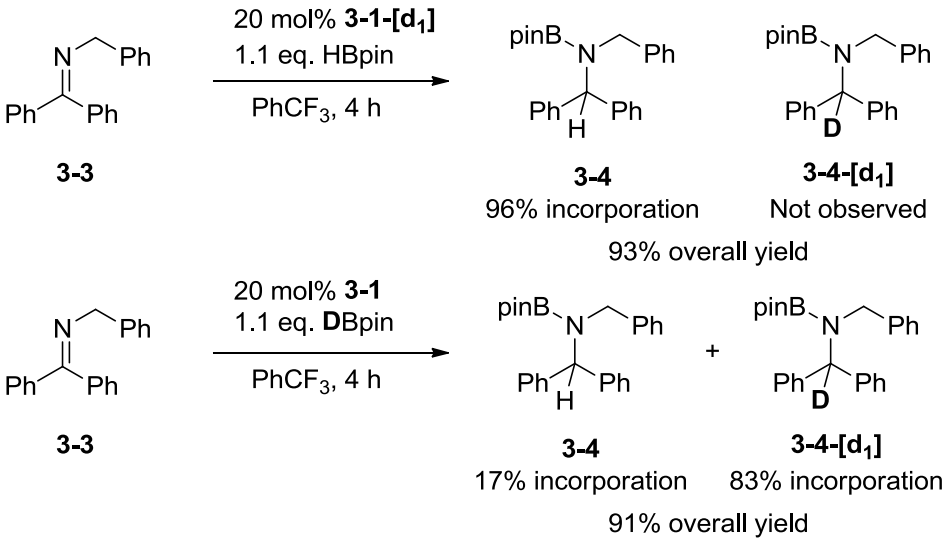


Figure 3-6: ^{11}B NMR spectrum of **3-1** before addition of DBpin (top) and ^{11}B NMR spectrum of **3-1** 15 minutes after addition of DBpin (bottom).

Following these reversibility experiments a series of deuterium labeling experiments were conducted with the goal of assessing the kinetic competence of $HB(C_6F_5)_3^-$ as a source of hydride. Hydroboration experiments using **3-1** and **3-1-[d_1]** along with stoichiometric amounts of DBpin and HBpin respectively were carried out. Imine **3-3** was added to a solution containing 20 mol% **3-1-[d_1]** and HBpin (Scheme 3.3-8). After 4 hours, the reaction was quenched with H_2O and the product was purified by column chromatography. The pure product **3-4a**, isolated with a 93% yield, contained 96% protium incorporation and the corresponding deuterium analogue **3-4a-[d_1]** was not observed. This reaction indicates that $DB(C_6F_5)_3^-$, and potentially, by analogy $HB(C_6F_5)_3^-$, is not a kinetically competent reducing agent under these conditions.



Scheme 3.3-8: Hydroboration of **3-3** with **3-1-[d_1]** and HBpin exclusively produces product **3-4** whereas hydroboration of **3-3** with **3-1** and DBpin resulted in full protio incorporation.

However, performing the isotopically inverted reaction with **3-1** and DBpin resulted in 17% protium incorporation with the remainder of the product containing the deuterium from DBpin. Thus **all of the available protium from the anionic borohydride was incorporated into the product**, and the remaining reduced product employed the deuterium from DBPin. This result is in direct contradiction with the previous deuterium labeling experiment and the

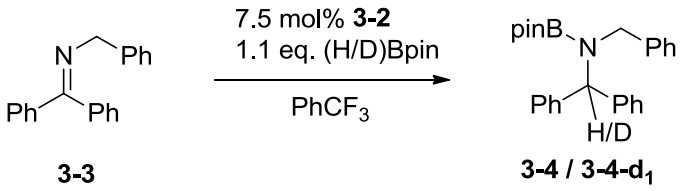
stoichiometric experiment, which both showed that the hydride of $HB(C_6F_5)_3^-$ was not kinetically competent.

One potential explanation for this observation was the presence of a high kinetic isotope effect, which would slow the reduction with DABCO•DBpin to such an extent that the hydride of $HB(C_6F_5)_3^-$ became kinetically competent. Another potential explanation is that borenium formation is reversible. This would generate HBpin in solution and form $DB(C_6F_5)_3^-$. The HBpin could then react with DABCO to form DABCO•HBpin which could reduce the activated boryl iminium species. Both processes could explain the observation of full protio incorporation. Further exploration into the reversibility of this process could provide insight into which mechanism is at play in the labeling reactions.

It should be noted that all deuterium incorporation values are corrected for trace amounts of protium present in the starting material before reaction. NMR integrations were carried out after optimizing the T_1 relaxation time prior to acquiring the free induction decay (FID) data. The baseline and region around each peak were normalized. In order to determine if there was a significant kinetic isotope effect (KIE), NMR rate experiments similar to those performed to compare the rates of catalysts **3-2** and **3-1** were conducted. The experiments were set up in an analogous manner using DBpin instead of HBpin with **3-2** as a catalyst.

The inconclusiveness of the reversibility experiments led us to choose catalyst **3-2** to catalyze the deuteroborations of substrate **3-3**. By performing the reactions as shown in Scheme 3.3-9 and analyzing the rate of product formation a direct comparison between the protio and deutero reactions could be made. The result was a significant decrease in the rate for reactions when DBpin was used as the source of reducing agent. The reaction only proceeded to 44% conversion after 24 hours as opposed to full conversion using HBpin under otherwise identical reaction conditions. Analysis of the rates for these experiments gave a large primary KIE of k_H/k_D = 6.6 ± 0.2 (Figure 3-7). This strongly suggests that the cleavage of the B–H bond is

involved in the rate limiting step. This high KIE also indicates that the B–H bond is ca. 50% cleaved in the transition state involving reduction of the boryl-iminium ion.[1]



3-3 **3-4 / 3-4-d$_1$**

Scheme 3.3-9: Conditions used for KIE rate experiments.

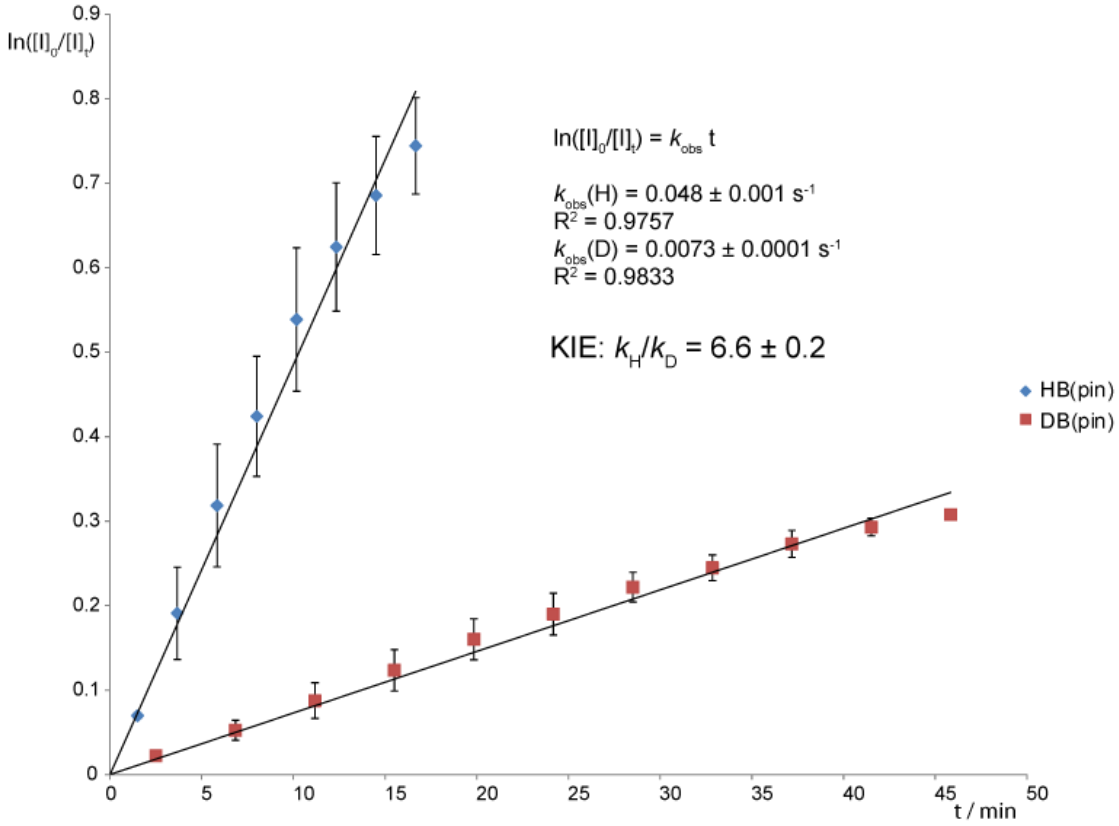


Figure 3-7: A direct comparison between the initial rates of HBpin and DBpin hydroboration of **3-3**catalyzed by **3-2**.

Because of the high KIE, the rates of the various protonated or deuterated reducing agents will be significantly different. This result may explain the observed proton incorporation for hydroboration reactions using catalyst **3-1** and DBpin (Scheme 3.3-9). The kinetic experiments and the deuteration experiment using catalyst **3-1-[d$_1$]** indicate that the proposed

active reducing agent **3-6** is the fastest reducing agent. The stoichiometric reaction indicates that $HB(C_6F_5)_3^-$ is capable of performing reduction although very slowly by comparison with HBpin/DABCO. Lastly, the deuteration experiment using catalyst **3-1** indicates that $HB(C_6F_5)_3^-$ and the deuterated proposed active reducing agent **3-6-[d_1]** affect hydride delivery with similar rates. These experiments provide a qualitative order of reactivity for the four reducing agents presented in this section (Figure 3-8).

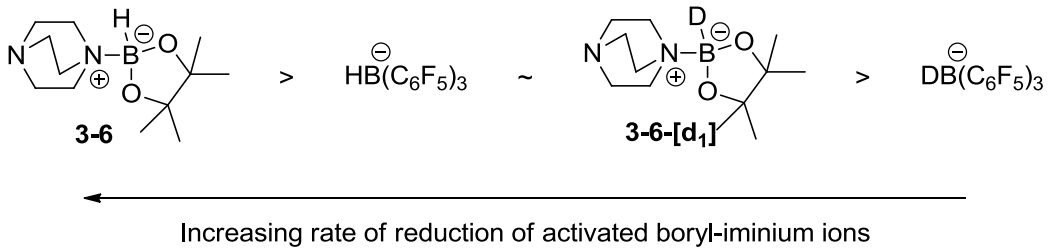


Figure 3-8: Qualitative order of reactivity for four potential active reducing agents.

3.3.4 Hydride Delivery Model

No experimental evidence has been put forward to confirm the role of DABCO in these reactions. However, it is reasonable to presume that DABCO is activating HBpin to form the active reducing agent **3-6**. This reagent is accessible by both catalytic systems and would account for the similarities in the initial rates observed by NMR. Furthermore, control experiments indicated that HBpin was unable to reduce an imine independently. Therefore, we set out to elucidate the role of DABCO in this catalytic system. Considering the similar pKa values of the imine substrates and DABCO,[10] it was uncertain which species was activating HBpin. Both imine adducts with Lewis acidic boron centers[11] and trialkyl amine boranes[12] are documented in the literature. To determine which species was activating HBpin, Dr. Patrick Eisenberger looked for evidence for the amine borane adduct of both DABCO and the imine. HBpin appears as a doublet centered around 28 ppm in ^{11}B NMR. Equimolar mixtures of imine **3-3** and HBpin in $PhCF_3$ at ambient temperatures showed no obvious change in ^{11}B NMR which likely means that adduct formation is not occuring. Cooling the sample to –25℃ also gave no change in the ^{11}B NMR,

leading to the conclusion that imine **3-3** is either not basic enough or too sterically encumbered to form a Lewis adduct with HBpin. However, ^{11}B NMR of equimolar mixtures of DABCO and HBpin showed a doublet with a chemical shift of 23.1 ppm at ambient temperature. Cooling to –2.5℃ and then to –25℃ further decreased the chemical shift to 18.5 ppm and 15.8 ppm respectively (Figure 3-9). This change in ^{11}B NMR chemical shift strongly supports the proposal of adduct formation between HBpin and DABCO. The decreasing chemical shift indicates that adduct strength increases as the temperature decreases.

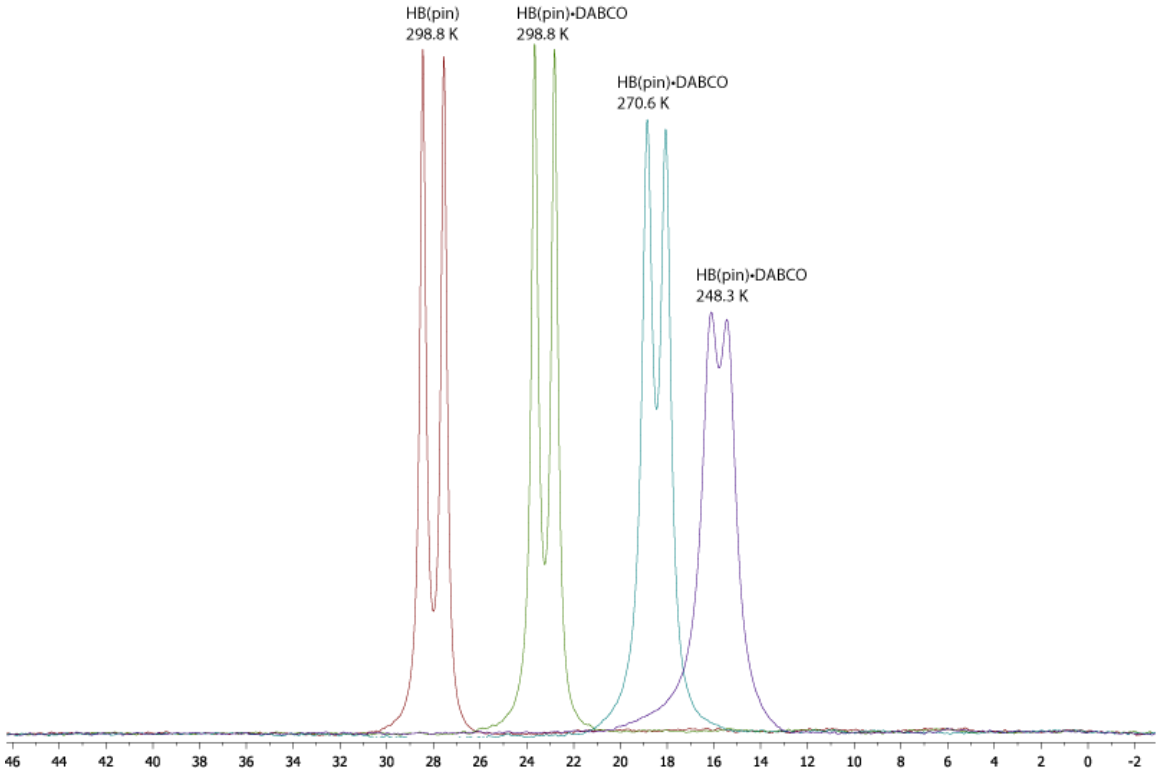
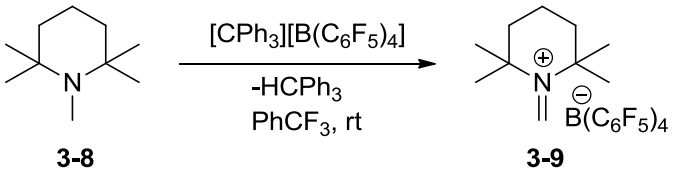


Figure 3-9: ^{11}B NMR of HBpin (red), and equimolar mixtures of HBpin and DABCO at 298.8 K (green), 270.6 K (blue), and 248.3 K (purple) in $PhCF_3$.

With spectroscopic evidence for adduct formation between HBpin and DABCO, its ability to act as a reducing agent for iminium ions needed to be determined. Attempts to make a borenium ion from 1,2,2,6,6-pentamethyl piperdine (**3-8**) and $TrB(C_6F_5)_4$ resulted in the formation of the iminium ion, 2,2,6,6-tetramethyl-1-methylenepiperidin-1-ium tetrakis-

pentafluorophenyl borate (**3-9**) as the major product (Scheme 3.3-10). This iminium ion was used as a model for hydride delivery from mixtures of Lewis bases and HBpin.



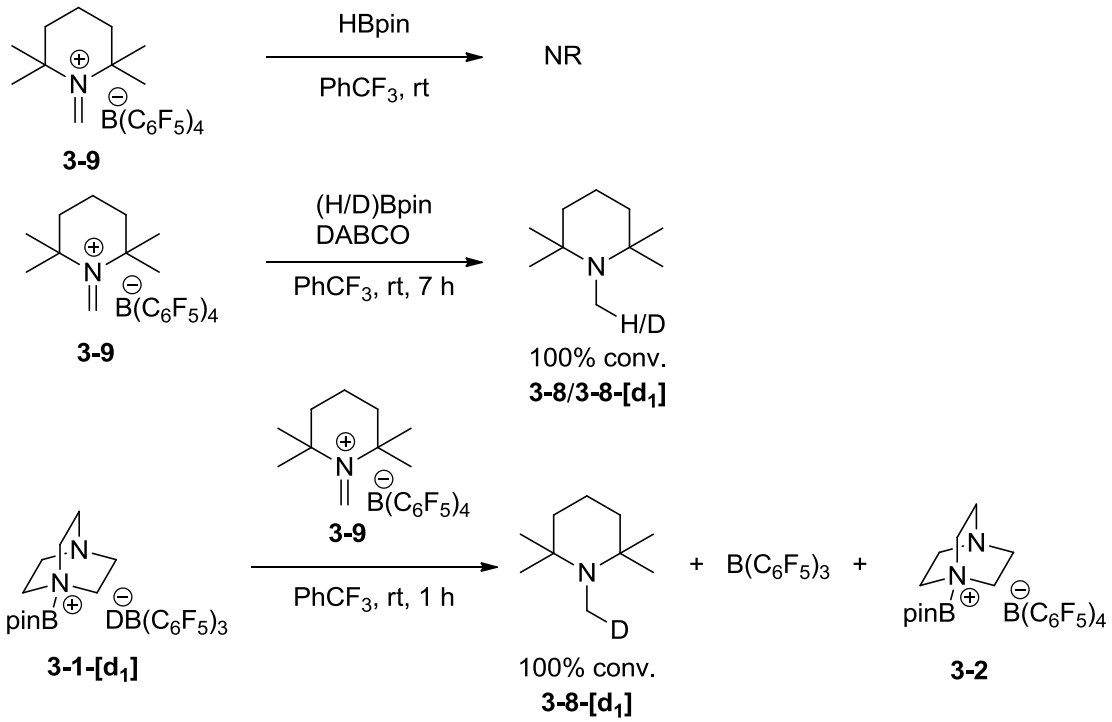
3-8 **3-9**

Scheme 3.3-10: Synthesis of iminium ion **3-9**.

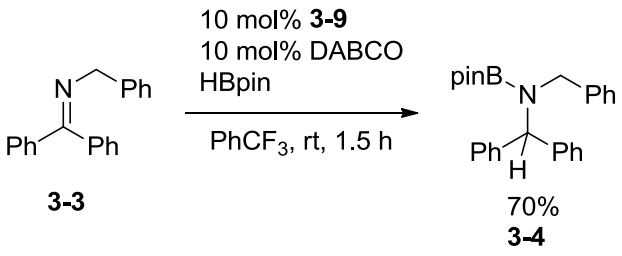
Although iminium ion **3-9** is not activated by a boron group, Dr. Patrick Eisenberger employed it as a surrogate for an electrophilic hydride acceptor. A reaction between **3-9** and HBpin showed no reduction back to **3-8**, supporting the conclusion that HBpin itself can not reduce an iminium species, and that the borinium ion $^{+}$Bpin was not being produced. We then speculated that, due to a lack of adduct formation between imine **3-3** and HBpin, no reaction would take place under equimolar or catalytic conditions. Reassuringly, no reaction was observed under these conditions. Performing a similar reaction using **3-9**, DABCO, and HBpin resulted in complete disappearance of the alkenyl CH_2 resonance of **3-9** after 7 hours. A synonymous experiment using DBpin showed deuterium incorporation and formation of **3-8-[d$_1$]**. Furthermore, addition of 1 equivalent of **3-9** to a solution of **3-1-[d$_1$]** also resulted in complete disappearance of the alkenyl CH_2 resonance, liberation of $B(C_6F_5)_3$, and formation of an equivalent of **3-2**, illustrating that in the absence of other reducing agents, the $DB(C_6F_5)_3^-$ anion is a competent reducing agent. This series of reactions is illustrated in Scheme 3.3-11.

With these data in hand, we hypothesized that **3-9** could act as an initiator for the catalytic hydroboration of imines. Since reaction of **3-6** with an equivalent of **3-9** results in the formation of **3-2**, a reaction utilizing catalytic amounts of DABCO and **3-9** with 1 equivalent of HBpin and imine should proceed similarly to reactions using **3-2** directly. Executing this procedure using 10 mol % **3-9** and 10 mol% DABCO resulted in 70% conversion of imine **3-3**

into pinacolboramide **3-4** (Scheme 3.3-12). This reaction most likely occurs at a slower rate than direct use of **3-2** because formation of the borenium ion must occur before reduction can ensue.



Scheme 3.3-11: Experiments demonstrating the hydride donor ability of reducing agents **3-6**, **3-6-[d$_1$]**, and **3-1-[d$_1$]**.



Scheme 3.3-12: Use of **3-9** as an initiator and DABCO as a catalyst in the hydroboration of imine **3-3**.

3.4 Summary of Mechanistic Data and Mechanistic Proposal

The use of reaction kinetics and deuterium labeling studies proved highly effective in determining the mechanism of borenium catalyzed hydroboration of imines. Integral rate measurement techniques enabled quantitative determination of the rates of hydroboration of imines using $B(C_6F_5)_3$•DABCO, which generates [DABCO•Bpin][$HB(C_6F_5)_3$] (**3-1**) *in situ.* As a comparison, [DABCO•Bpin][$B(C_6F_5)_4$] (**3-2**) was also employed for the same reduction. The similarity in initial rates supports the conclusion that both catalysts react via complementary mechanisms. Deuterium-labeled **3-2-[d_{12}]** demonstrated that the borenium fragment originally in the catalyst was incorporated into the hydroborated product indicating that borenium transfer was underway. A stoichiometric reaction showed that the counterion $HB(C_6F_5)_3^-$ was not a kinetically relevant hydride delivery reagent at rates comparable to those observed with HBpin and DABCO. Deuterium labeled pinacol borane was used to manufacture **3-1-[d_1]** which was subsequently used to support the conclusions of the stoichiometric reaction. However, use of **3-1** with DBpin resulted in full protio incorporation from the catalyst. This result can be explained by the presence of a significant kinetic isotope in this reaction or by a reversible borenium formation process. Direct comparison of the rates of reactions utilizing HBpin and DBpin resulted in a KIE of k_H/k_D = 6.6 ± 0.2. These results may explain the observed incorporation of labeled material through the significant difference in rates between protio- and deutero- delivery. Experimental support for hydride delivery was first found with spectroscopic evidence for a DABCO•HBpin Lewis adduct. Subsequent application of this adduct in the hydride delivery to an iminium surrogate supported the proposition of this as a hydride delivery source to a boryl-iminium intermediate. This culmination of mechanistic data strongly suggests that the mechanistic proposal shown in Figure 3-10 is an accurate depiction of the mechanism of borenium catalyzed hydroboration of imines.

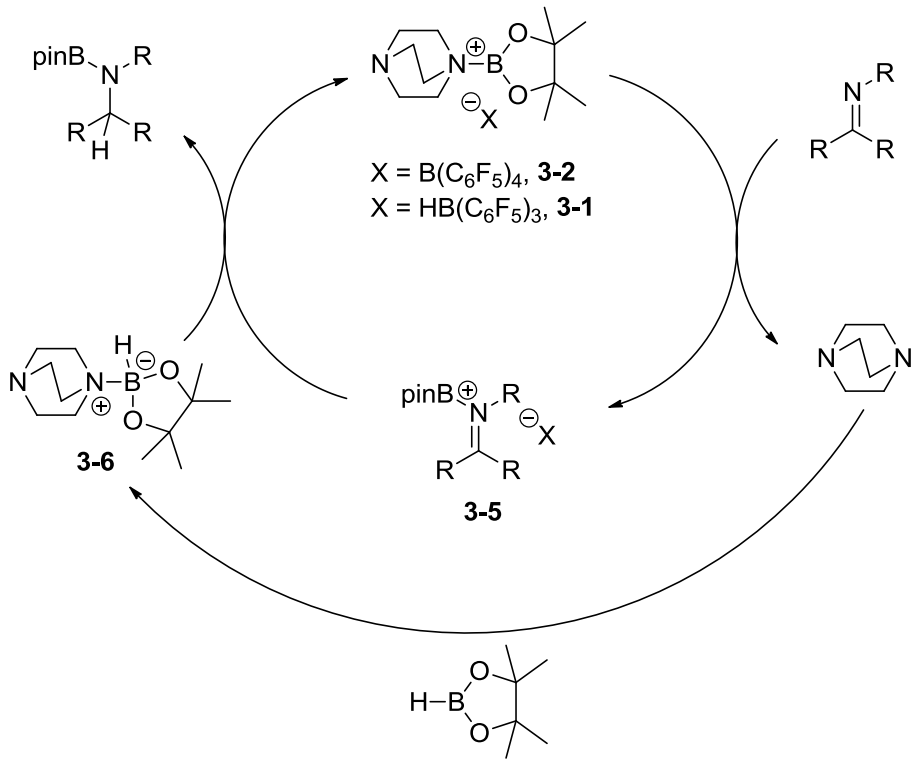


Figure 3-10: Experimentally supported borenium catalyzed hydroboration of imines.

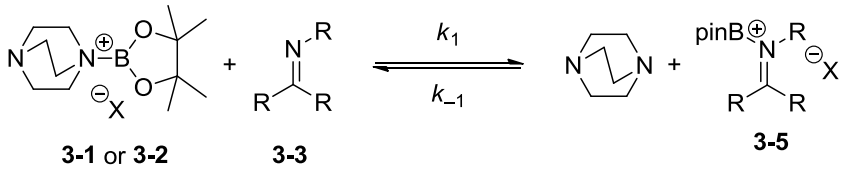
3.5 Kinetic Analysis: Part II

Integral techniques enabled a quantitative analysis of the initial rates of reaction for catalysts **3-1** and **3-2**. This analysis demonstrated that both catalysts were proceeding through similar elementary steps. We hypothesized that a more detailed analysis of these steps could be produced from a differential kinetic technique. This study is currently underway and the data presented here are not yet complete but several qualitative inferences about the rate constants and mechanism can be inferred. The technique chosen to perform this study was calorimetry due to the ease of data interpretation and connection to thermodynamic parameters.

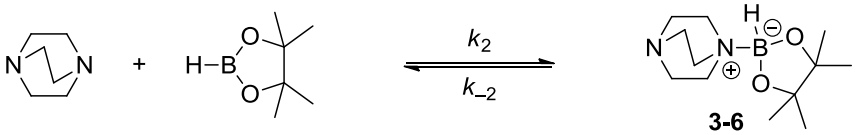
After significant thought, the elementary steps and intermediates of this reaction were proposed and are based on the mechanism proposed in the previous section. The overall reaction

can be systematically broken down into three independent steps: 1) borenium transfer from DABCO•Bpin to imine substrate to produce **3-5**, 2) Lewis adduct complexation DABCO and HBpin to form **3-6**, and 3) reaction of **3-5** and **3-6** to produce the amine product and regenerate the catalyst (Scheme 3.5-1). Investigations into these elementary steps can be gained through isolation of proposed reaction intermediates and through the thermodynamics of the reaction.

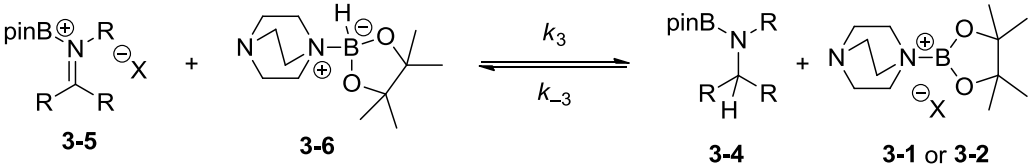
Attempts to isolate a species similar to **3-5** were conducted using equimolar amounts of imine **3-3**, HBpin, and either of the Lewis acids, $TrB(C_6F_5)_4$ or $B(C_6F_5)_3$. Both reactions produced a null result which can be attributed to a lack of significant formation of a Lewis adduct with HBpin due to diminished Lewis basicity or sterics, or the equilibrium nature of the borenium transfer. However the stability of borenium ions **3-1** and **3-2** imply that the thermodynamic stability lies heavily on the left hand side of Eq. 3-1. This implies that $k_{-1}>>k_1$ and thus the effective concentration of **3-5** in solution is an important factor for the overall rate of reaction. The observation of intermediate **3-6** was discussed in section 3.3.4 and was shown to be the only compound present in mixtures of equimolar amounts of HBpin and DABCO.



Eq. 3-1



Eq. 3-2



Eq. 3-3

Scheme 3.5-1: Elementary steps of borenium catalyzed hydroboration.

A calorimetric experiment on a standard reaction using imine **3-3**, 1.1 equivalents of HBpin, and 5 mol% **3-2** produced a heat of reaction (ΔH_{rxn}) equal to –33.2 kcal/mol. This

indicates that the overall reaction is exothermic and is consistent with a reaction that proceeds easily at room temperature. Carrying out similar calorimetric experiments but varying the concentration of borenium catalyst **3-2** and plotting the data as initial rate versus catalyst loading produces a linearly dependent graph (Figure 3-11). This linear relationship informs us that the rate of reaction is linearly dependent on the catalyst loading and that the rate of borenium transfer is dependent on the catalyst loading.

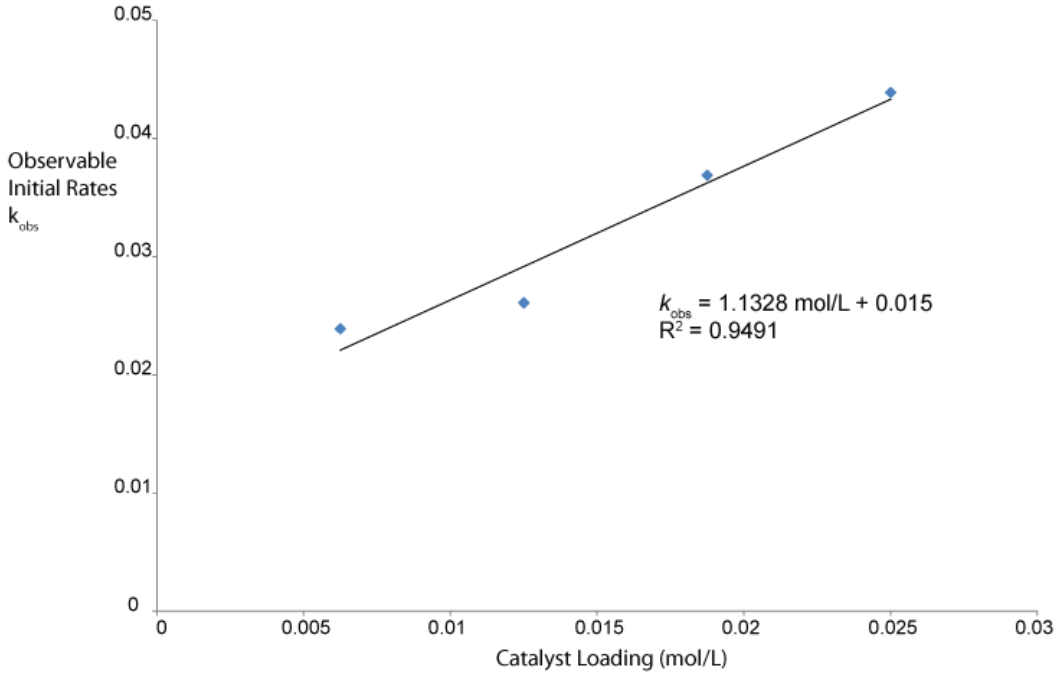


Figure 3-11: Kinetic order of borenium catalyst.

An analysis of the same relationship for HBpin produced a plot that was independent of HBpin concentration (Figure 3-12). This lack of a relationship between rate and HBpin means that the rate of reaction is independent of the concentration of HBpin in solution. This is a particular interesting result as the elementary step 2 (Scheme3.5-1, Eq. 3-2) is directly related to both the concentration of free DABCO and HBpin. This null result could imply that as soon as any DABCO is liberated then it immediately complexes with HBpin. This has two mechanistic

implications: 1) the concentration of free DABCO in solution is in the steady-state and thus subject to steady state kinetics and 2) the forward rate k_2 is significantly faster than k_{-2} (k_2>>k_{-2}).

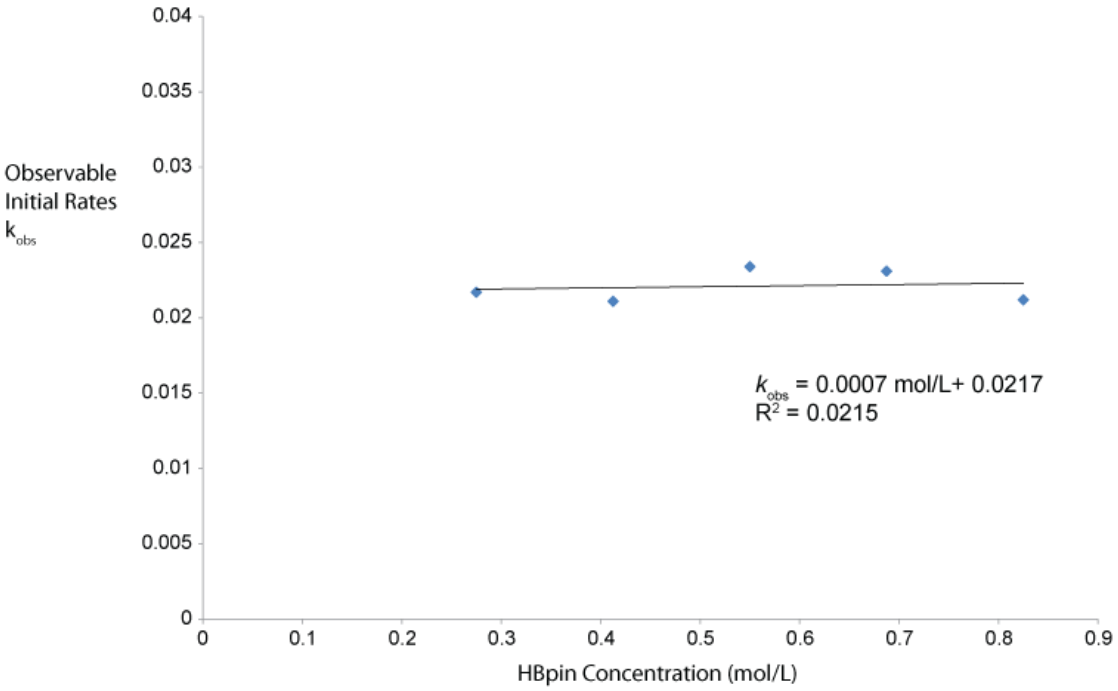


Figure 3-5: Kinetic order of HBpin at 5 mol% catalyst loading.

The third elementary step is the combination of **3-5** and **3-6** which forms the desired product and regenerates the active catalyst **3-2**. The KIE experiments, presented in section 3.3.3, led to the conclusion that 3 (Scheme 3.5-1, Eq. 3-3) was the rate limiting step of this catalytic process and, therefore, it is reasonable to assume that this is an irreversible step, thus k_3 >>k_{-3}. These results indicate that the active concentration of **3-6** in solution is significantly larger than the active concentration of **3-5**. This led to the hypothesis that addition of excess DABCO should shut down the reaction by decreasing the active concentration of **3-5** in solution. This theory is based on the assumption that the borenium transfer step exists as an equilibrium. DABCO and the Schiff base presumably shuttle the cationic Bpin fragment back and forth until an equivalent of **3-6** reduces the boryl-iminium species. Excess DABCO should inhibit borenium transfer to the Schiff base as DABCO is more Lewis basic and thus more capable of stabilizing the positively

charged Bpin fragment. Addition of 5 mol% DABCO to a reaction containing imine **3-3**, 1.1 equivalents of HBpin, and 5 mol% **3-2** resulted in a notable decrease in the rate of reaction (Figure 3-13). Furthermore, the reaction could be completely shut down by addition of 10 mol% DABCO (2:1 DABCO/**3-2**). No conversion to product was observed by calorimetry or by NMR. Kinetically, this evidence supports the hypothesis that the effective concentration of **3-5** is critical for the reaction to progress. Quenching the formation of this species by saturating the system with additional Lewis base stopped the reaction from occurring. In terms of rate constants, addition of DABCO to the reaction mixture increases the value of rate constant k_{-1} which directly affects the rate constant k_3.

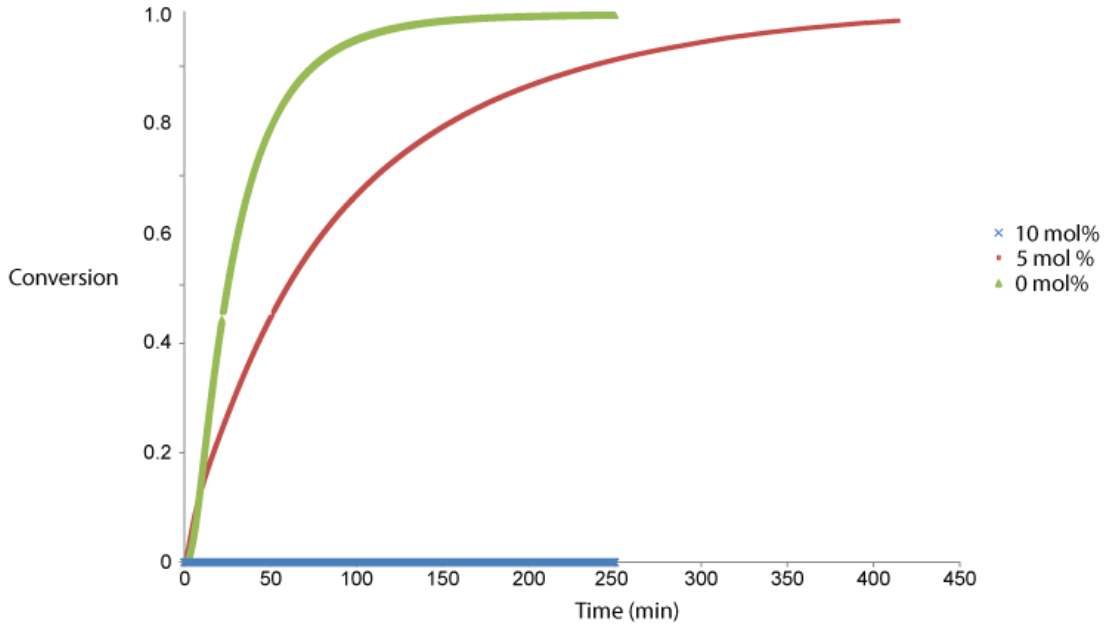


Figure 3-6: Changes of the rate of reaction through addition of excess DABCO.

In conclusion, attempts to isolate reaction intermediates and analyzing the effect of concentration of reagents had on the rate of this reaction enabled a deeper level of insight into the mechanism than was accessible from NMR rate analysis and deuterium labeling studies. The observation that addition of excess Lewis base shuts down the reaction is counterintuitive due to

the nature of the hydride delivery reagent **3-6**. Further calorimetric studies to accurately determine the inhibition constant for DABCO addition and investigating the concentration of HBpin required to reinitiate the reaction would further demonstrate the peculiarity of this novel reaction mechanism.

3.6 Conclusions

The mechanistic proposal for borenium catalyzed hydroboration is supported by deuterium labeling experiments, stoichiometric experiments, and kinetic analysis. The reaction exhibits a high KIE (k_H/k_D = 6.6 ± 0.2) which indicates that hydride delivery is the rate determining step. The synthesis of the stable iminium ion **3-9** and its use as a hydride acceptor supported the conclusion that DABCO•HBpin is the hydride delivery reagent in these hydroboration reactions. Calorimetric analysis indicated that the reaction is exothermic with a heat of reaction (ΔH_{rxn}) equal to –33.2 kcal/mol. Further calorimetric experiments indicated that the addition of excess Lewis base significantly decreased the rate of the desired reaction. A clear mechanistic picture of this reaction has been presented and with a firm understanding of the hydride delivery step an asymmetric process can begin to be developed.

3.7 References

[1] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry, 3rd Ed.* **1987**, Harper Collins, New York.

[2] Stephan, D. W.; Erker, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 46.

[3] Piers, W. E.; Parks, D. J.; Blackwell, J. M. *J. Org. Chem.* **2000**, *65*, 3090.

[4] Blackmond, D. G. *Angew. Chem. Int. Ed.* **2005**, *44*, 4302.

[5] Beck, W.; Sünkel, K. *Chem. Rev.* **1988**, *88*, 1405.

[6] Andersson, P. G.; Munslow, I. J. *Modern Reduction Methods*, **2008**, Wiley, Weinheim.

[7] Clark, T. B.; Query, I. P.; Squier, P. A.; Larson, E. M.; Isley, N. A. *J. Org. Chem.* **2011**, *76*, 6452.

[8] Hanson, J. *The Organic Chemistry of Isotopic Labeling, 1st Ed.* **2011**, Royal Society of Chemistry, London.

[9] Hartwig, F.; Boller, T.; Murphy, J.; Hapke, M.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2005**, *127*, 14263.

[10] a) Crampton, M. R.; Robotham, I. A. *J. Chem. Res. (S)* **1997**, 22. b) Benoit, R. L.; Lefebvre, D.; Fréchette, M. *Can. J. Chem.* **1987**, *65*, 996.

[11] Piers, W. E.; Blackwell, J. M.; Parvez, M.; McDonald, R. *Organometallics*, **2002**, *21*, 1400.

[12] a) Mayr, H.; Funke, M. A. *Chem. Eur. J.* **1997**, 3, 1214. b) Shioiri, T.; Izawa, K.; Konoike. T. *Pharmaceutical Process Chemsitry*, **2011**, Wiley, Weiheim.

Chapter 4

Conclusions and Future Work

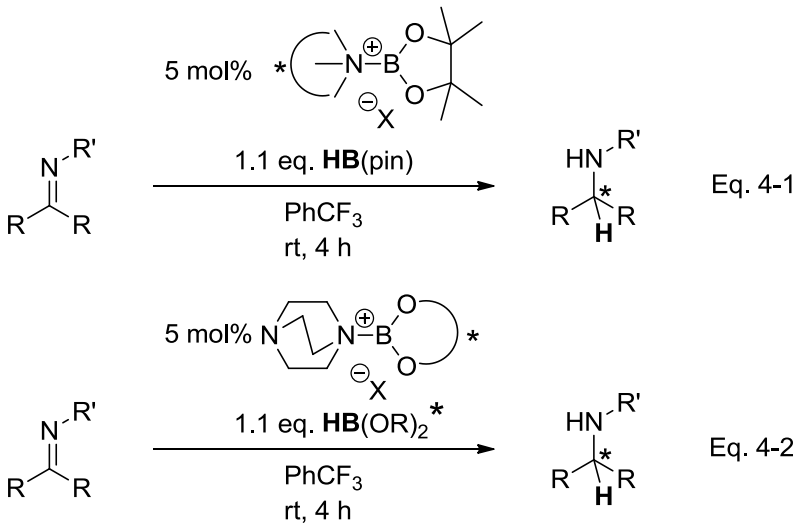
4.1 Towards the Development of an Enantioselective Reduction

There are two great veins in organic chemistry research, total synthesis and methodology. Methodological research often contains four separate aspects: 1) the discovery of a novel chemical process, such as a new element–element forming reaction or unprecedented annulation, often sparks interest and encourages further method development. Following discovery and reaction optimization one often pursues, 2) the substrate scope and functional group tolerance of the newly discovered reaction. With scope and conditions firmly understood two different avenues can be taken. Either 3) mechanistic elucidation, or, if the reaction is a part of a process involving prochiral substrates, 4) asymmetric induction is attempted.

The experimental work presented in this thesis demonstrates the discovery of a novel borenium catalyzed hydroboration reaction. The ability of this system to reduce imines, *N*-heterocycles, nitriles with moderate to high yields has been demonstrated. The metal free reduction of ketones was also described with this system albeit with lower conversions. Functional group tolerance of this reaction included sulfoxides, allyl ethers, acyl groups, halides, trifluoromethyl groups, and methyl ethers. Exploration into the mechanism of this reaction was conducted with the assistance of Dr. Patrick Eisenberger. Kinetics, deuterium labeling, and a hydride delivery surrogate supported a mechanism involving nucleophilic activation of HBpin. Calorimetric analysis enabled the determination of the heat of reaction and the observation that the reaction was inhibited by additional Lewis base.

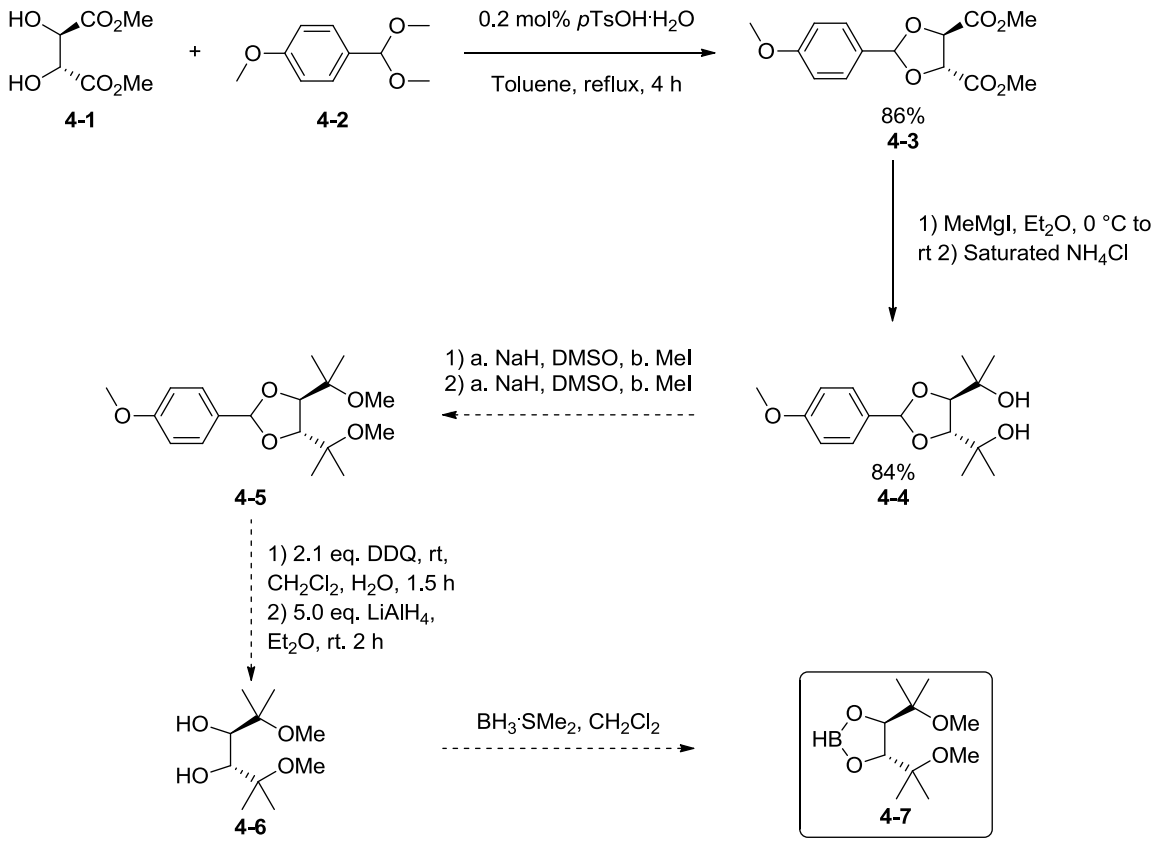
Knowledge that the turnover or rate limiting step is hydride delivery from a Lewis base•HBpin adduct enables the construction of an asymmetric model. Two potential avenues can be taken to produce a catalytic system that yields optically active amines. One, the achiral pinacol backbone of HBpin can be replaced by a chiral diol. This will increase the steric environment around hydride and facilitate an enantioselective reduction step (Scheme 4.1-1, Eq. 4-2). Although this method has the ability to induce chirality through either the borenium fragment or the Lewis base•borane adduct, it requires stoichiometric amounts of the chiral component. Chiral diols are also often difficult to reacquire after reaction making this an undesirable route. However, an advantage this method has is that chiral boranes can be of low molecular weight which allows for the preparation of large molar quantities.

Another method of facilitating an enantioselective reduction is through the use of a chiral Lewis base. The major advantage of this method is that this reaction is catalytic in Lewis base allowing for asymmetric induction without the use of a stoichiometric chiral source. A drawback to this method is that to create a highly selective organocatalytic reaction, high molecular weight species are often required.[1, 2] This weight typically comes in the form of steric bulk which is necessary to ensure that substrate and catalyst interact with the appropriate configuration. Another potential drawback to this method is the difficulty associated with synthesizing high molecular weight chiral tertiary amines with sufficient basicity. Preliminary investigations into both methods are underway.



Scheme 4.1-1: Use of a chiral Lewis base in catalytic amounts (Eq. 4-1) or use of stoichiometric amounts of a chiral borane (Eq. 4-2) to facilitate an asymmetric reduction.

Chiral diols react with BH_3 to form chiral boranes. Such chiral boranes have been successfully employed in metal catalyzed hydroboration reactions and one such reaction was discussed in the introductory chapter.[3, 4] The synthesis of the chiral diols is the challenge of this approach and certain "privileged" chiral ligands including [1,1'-binaphthalene]-2,2'-diol (BINOL), 1,2-bis-2,5-diarylphospholanylbenzene (DuPhos), or 2,2'-(2,2-diaryl-1,3-dioxolane-4,5-diyl)bis(propan-2-ol) (TADDOL) may have use in borenium catalyzed hydroboration.[5] A synthesis of a TADDOL derivative has begun and is underway at the time of this writing (Scheme 4.1-2).[6, 7] Starting from dimethyl-L-tartarate (**4-1**) acid catalyzed transacylation with anisaldehyde dimethyl acetal (**4-2**) produced acetal **4-3** in an 86% yield. Reaction with excess methyl magnesium iodide yielded diol **4-4** (84%). To finish the synthesis methylation and deprotection should yield diol **4-6**.[6] Once synthesized, diol **4-6** can be easily converted into the borane through reaction with BH_3•SMe_2.[6] This privileged chiral diol may facilitate chirality transfer through asymmetric delivery of hydride to the activated boryl-iminium cation.



Scheme 4.1-2: Partially completed synthesis of chiral borane **4-7**.

Alternatively, chiral tertiary amines can be synthesized[8] but are also found in natural products.[9] One possible starting point is cinchona alkaloids or their derivatives which contain an internal quinuclidine fragment (Figure 4-1). Quinuclidine derivatives have been used in FLP catalyzed hydrogenations[10] providing precedent for these natural products acting to promote borenium catalyzed hydroboration. Derivatives of chincona alkaloids have shown promise in Morita-Baylis-Hillman reactions demonstrating their reactivity as Lewis bases.[11] Chiral quinuclidine derivatives can also be manufactured via a multi step synthesis developed by Corey and coworkers.[12] The synthesis of these molecules and applications in borenium catalyzed hydroboration may aid in the development of an enantioselective process.

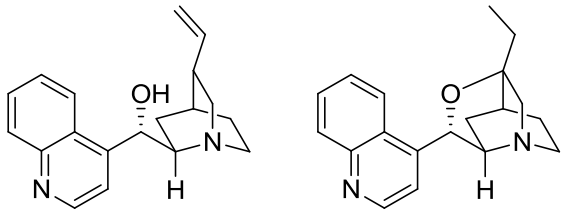


Figure 4-1: Cinchona alkaloids that may promote enantioselective reduction in borenium catalyzed hydroboration.

In conclusion, the novel borenium catalyzed hydroboration reactions developed in this thesis are a new method for affecting the reduction of imines with high yields. Studying the mechanism of this reaction enabled the determination of the rate limiting step. This important piece of information allows the intelligent selection of methods that may turn this reaction into an enantioselective process. Establishing an enantioselective process is underway and will dramatically increase the synthetic utility of this borenium catalyzed hydroboration reaction.

4.2 References

[1] Dalko, P.; Moisan, L. *Angew. Chem. Int. Ed.* **2001**, *40*, 3726.

[2] Yamamoto, H.; Futatsugi, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 1924.

[3] Lloyd-Jones, G. C.; Brown, J. M. *Tetrahedron: Asymm.* **1990**, *12*, 869.

[4] Lloyd-Jones, G. C.; Brown, J. M. *Chem. Commun.* **1992**, 710.

[5] Drury, W. J.; Pfaltz, A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5723.

[6] Pietruszka, J.; Luithle, J. E. A. *J. Org. Chem.* **1999**, *64*, 8287.

[7] Mash, E. A.; Hemperly, S. B.; Nelson, K.; Heidt, P.; Van Deusen, S. *J. Org. Chem.* **1990**, *55*, 2045.

[8] Wang, S.; Sakamuri, S.; Enyedy, I. J.; Kozikowski, A. P. *Tetrahedron Lett.* **2000**, *41*, 9949.

[9] a) Kaufmann, T.S.; Rúveda, E.A. *Angew. Chem. Int. Ed.* **2005**, *44*, 854. b) Weinreb, S.M. *Nature* **2001**, *411*, 429. c) Nicolaou, K.C.; Sorensen, E.J. *Classics in Total Synthesis: Targets, Strategies, Methods* **1996**, Wiley-VCH, Weinheim.

[10] Soós, T.; Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 6559.

[11] Hatakeyama, S.; Iwabuchi, Y.; Nakatani, M.; Yokoyama, N. *J. Am. Chem. Soc.* **1999**, *121*, 10219.

[12] Corey, E. J.; Yuen, P. *Tetrahedron Lett.* **1989**, *30*, 5825.

Chapter 5

Experimental Work

5.1 Experimental

5.1.1 Techniques

All preparative scale reactions were conducted in oven dried (160 °C) glassware with magnetic stirring using Schlenk-line techniques or in a glove box under an atmosphere of dry dinitrogen if not mentioned otherwise. Experiments on NMR tube scale were carried out in Teflon cap sealed or J. Young NMR tubes (ø 5 mm). Toluene, benzene, hexanes and pentanes were purified by passage over an activated aluminum oxide column, followed by distillation from Na-benzophenone ketal and degassed prior to use. THF and diethylether were distilled from Na-benzophenone ketal. Dichloromethane, chloroform, 1,2-dichloroethane, nitromethane, dimethoxyethane, *tert*-butyl ether, acetone and α,α,α-trifluorotoluene were distilled from CaH_2 (followed by 3 freeze-pump-thaw cycles and stored over a mixture of 4 Å molecular sieves and dry basic alumina for usage in a glove box). [D_2]-dichloromethane was vacuum transferred from CaH_2 followed by 3 freeze-pump-thaw cycles and stored over a mixture of 4 Å molecular sieves and dry basic alumina for usage in a glove box. Solvents for chromatography were used as received from commercial sources and were at least of ACS reagent grade. Silica gel 60 (particle size 0.040 – 0.063 mm) was purchased from EMD Chemicals, Inc. TLCs were run on silica gel coated aluminum plates with UV indicator (F_{254}) obtained by EMD Chemicals, Inc. and analyzed by UV/VIS and stained using a cerium ammonium molybdate or a potassium permanganate solution.

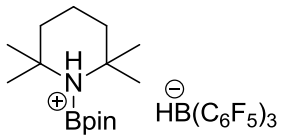
5.1.2 Analytics

Melting points were measured on an Electrothermal Mel-temp® melting point apparatus connected to a Fluke 51II thermometer. Temperatures are given in degree Celsius (°C) and are uncorrected. ***NMR*** spectra were recorded on Bruker Avance 300 (^{1}H: 300.13 ^{13}C: 75.47; QXI probe), Bruker Avance 400 (^{1}H: 400.13, ^{11}B: 128.38, ^{13}C: 100.62, ^{19}F: 376.50: BBI, BBFO and QNP probes), Bruker Avance 500 (^{1}H: 500.19, ^{11}B: 160.27, ^{13}C: 125.62; BBI and BBFO probes), or Bruker Avance 600 (^{1}H: 600.17, ^{11}B: 192.56, ^{13}C: 150.93; TBI probe) instruments operating at the denoted spectrometer frequency given in mega Hertz (MHz) for the specified nucleus. The samples were measured as solutions in the stated solvent at ambient temperature in non-spinning mode if not mentioned otherwise. To specify the signal multiplicity, the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, sept = septet, oct = octet, and m = multiplet; br. indicates a broad resonance. Shifts δ are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as an external standard for ^{1}H- and ^{13}C NMR spectra and calibrated against the solvent residual peak or in case of protio-solvents against known solvent resonances.[1] ^{2}H signals are calibrated against D_{12}-tetramethylsilane, ^{11}B against external BF_3•OEt_2, ^{19}F against $CFCl_3$. Coupling constants J are given in Hertz (Hz). Temperature calibrations were performed with 100% MeOH (T < 298 K) and 100% ethyleneglycol (T > 298 K).[2] ***Infrared spectra*** were recorded on a Varian FTIR 640 spectrometer as thin films prepared by evaporating solutions of the respective compound in CH_2Cl_2 on a NaCl window (neat). Relative intensities are abbreviated as w = weak, m = medium, s = strong, and br. indicates a broad resonance. IR-bands $\tilde{\nu}$ are given in reciprocal wave numbers (cm^{-1}). High resolution mass-spectra (***HRMS***) were measured by the Queen's Mass Spectrometry and Proteomics Unit (MSPU) at Queen`s University, Kingston, Ontario, Canada. Mass spectra were measured on Applied Biosystems/MDS Sciex QStar XL QqTOF or Waters ZQ Single Quad. Fragment signals are given in mass per charge number (m/z).

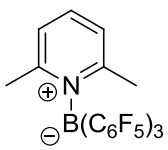
5.1.3 Reagents and Materials

Reagents for substrate synthesis were used as received without further purification unless noted otherwise. Imines were synthesized from the corresponding commercial carbonyl compounds and amines following published procedures and purified by Kugelrohr distillation or recrystallization. Pinacol borane (HBpin) and catechol borane (HBcat) were purchased from Alfa Aesar or Sigma-Aldrich and distilled at ambient temperature under high vacuum (1 mTorr), followed by 3 freeze-pump-thaw cycles and stored in the freezer (–35 °C) of a glove box. Acridine, 1,10-phenanthroline, *para*-bromoacetophenone, benzophenone, DABCO, and $B(C_6F_5)_3$ (Strem Chemicals) were sublimed prior to use. DABCO was sublimed at ambient temperature and under high vacuum. $B(C_6F_5)_3$ was sublimed at 80 ℃ and under high vacuum (1 mTorr). DBU, 2,2,6,6-tetramethylpiperidine, 2,6-lutidine, *N*,*N*,*N*-triphenylamine, *N*,*N*-dimethylaniline, pyridine, indole, α-tetralone, dicyclohexyl ketone, and benzonitrile were distilled from CaH_2 followed by 3 freeze-pump-thaw cycles. Benzonitrile distilled from CaH_2 and subjected to 3 freeze-pump-thaw cycles.

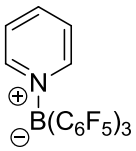
5.1.4 Synthesis of Borenium Salts



Attempt to synthesize 1-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-2,2,6,6-tetramethylpiperidine tris(pentafluorophenyl) hydridoborate . To a solution of tris-pentafluorophenyl borane (12.9 mg, 25.2 μmol) and 2,2,6,6-tetramethylpiperdine (3.7 mg, 26.2 μmol) in CD_2Cl_2 (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (3.3 mg, 25.8 μmol) in CD_2Cl_2 (0.5 mL). No B–H bond activation or adduct formation was detected by ^{11}B NMR spectroscopy. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ 23.0 (s, B_2Pin_3), 28.0 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin), 59.8 (br. s, $B(C_6F_5)_3$).

Attempt to Synthesize 1-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-2,6-lutidine tris(pentafluorophenyl)hydridoborate resulting in the synthesis of 2,6-dimethylpyridinium, 2-12.  To a solution of tris-pentafluorophenyl borane (13.0 mg, 25.4 μmol) and 2,6-lutidine (3.0 mg, 28.0 μmol) in CD_2Cl_2 (0.5 mL)in a J. Young NMR tube was added a solution of HBpin (3.3 mg, 25.8 μmol) in CD_2Cl_2 (0.5 mL).No B–H bond activation was observed. Trace amounts of adduct formation was detected by ^{11}B NMR spectroscopy. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –3.9 (s, $NB(C_6F_5)_3^-$), 28.0 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin), 59.9 (br. s, $B(C_6F_5)_3$).

Attempt to Synthesize *N*-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-*N*,*N*,*N*-triphenylammonium tris(pentafluorophenyl)hydridoborate.  To a solution of tris-pentafluorophenyl borane (51.4 mg, 0.10 mmol) and *N*,*N*,*N*-triphenylamine (25.2 mg, 0.10 mmol) in CD_2Cl_2 (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (14.1 mg, 0.11 mmol) in CD_2Cl_2 (0.5 mL). No B–H bond activation or adduct formation was detected by ^{11}B NMR spectroscopy. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ 23.0 (s, B_2Pin_3), 27.9 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin), 59.8 (br. s, $B(C_6F_5)_3$).

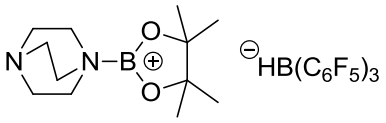
Attempt to synthesize *N*-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-pyridinium tris(pentafluorophenyl)hydridoborate resulting in the synthesis of pyridinium tris(pentafluorophenyl)borate, 2-13.  To a solution of tris-pentafluorophenyl borane (13.1 mg, 25.6 μmol) and pyridine (2.0 mg, 28.5 μmol) in CD_2Cl_2 (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (3.2 mg, 25 μmol) in CD_2Cl_2 (0.5 mL). No B–H bond activation was detected and only the classical Lewis adduct formation was observed. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –4.4 (s, $NB(C_6F_5)_3^-$), 28.0 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin).

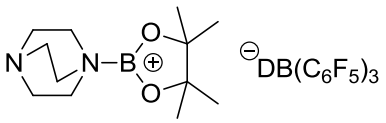
Attempt to synthesize *N*-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-indolium tris(pentafluorophenyl)hydridoborate resulting in the synthesis of *3*H-indolium tris(pentafluorophenyl)borate, 2-14.[3] To a solution of tris-pentafluorophenyl borane (38.3 mg, 74.8 μmol) and indole (8.8 mg, 75.1 μmol) in CD_2Cl_2 (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (11 μL, 75.8 μmol) in CD_2Cl_2 (0.5 mL). No B–H bond activation was detected and the rearranged classical Lewis adduct was observed. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –4.4 (s, $NB(C_6F_5)_3^-$), 28.0 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin); ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.41 (s, 12H, $C(CH_3)_2$ of HBpin), 4.3 (m, 2H), 7.37-7.62 (m, 3H), 7.72 (d, $^3J_{H,H}$ = 7.5 Hz, 1H), 8.80 (m, 1H).

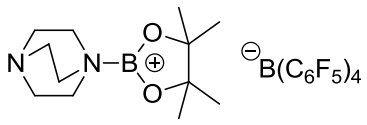
Attempt to synthesize -(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-2,3,4,6,7,8,9,10-octahydropyrimido[1,2-a]azepin-1-ium tris(pentafluorophenyl)hydridoborate resulting in the synthesis of 1-tris(pentafluorophenyl)borate-2,3,4,6,7,8,9,10-octahydropyrimido[1,2-*a*]azepinium, 2-16. To a solution of tris-pentafluorophenyl borane (37.6 mg, 73.4 μmol) and 1,8-diazabicycloundec-7-ene (11.4 mg, 75 μmol) in $PhCF_3$ (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (11.0 μL, 75.8 μmol) in $PhCF_3$ (0.5 mL). No B–H bond activation was detected and the classical Lewis adduct was observed. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –7.0 (s, $NB(C_6F_5)_3^-$), 27.9 (d, $^1J_{B,H}$ = 173.47 Hz).

Attempt to synthesize 1-(chloromethyl)-4-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-1,4- diazabicyclo[2.2.2]octan-1-ium tris-(pentafluorophenyl)hydridoborate. To a solution of tris-pentafluorophenyl borane (30.7 mg, 60.0 μmol) and 1-(chloromethyl)-1,4-diazabicyclo[2.2.2]octan-1-ium tetraphenyl borate (28.9mg, 60.0 μmol) in

CD_2Cl_2 (0.5 mL) in a J. Young NMR tube was added a solution of HBpin (7.7 mg, 60.2 μmol) in CD_2Cl_2 (0.5 mL). No B–H bond activation or adduct formation was detected by ^{11}B NMR due to the insolubility of the Lewis base. ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –5.7 (s, BPh_4^-), 23.0 (s, B_2Pin_3), 27.9 (d, $^1J_{B,H}$ = 173.5 Hz, HBpin), 59.9 (br. s, $B(C_6F_5)_3$).

Synthesis of 1-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-1,4-diazabicyclo[2.2.2]octane tris(pentafluorophenyl) hydridoborate, 2-23 (3-1).  Mixing tris-(pentafluorophenyl)-borane (21.9 mg, 42.78 μmol) and DABCO (4.8 mg, 42.79 μmol) in CD_2Cl_2 (0.5 mL) in a J. Young NMR tube resulted in a white precipitate. Upon addition of HBpin (6.3 mg, 49.22 μmol) in CD_2Cl_2 (0.5 mL) the mixture went homogeneous after shaking. Full conversion to B–H activated salt **2-23** (**3-1**) was observed after 15 min. ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.41 (s, 12H, CH_3), 3.26 (br. s, 12H, NCH_2); ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –25.4 (d, $^1J_{B,H}$ = 89.3 Hz, $HB(C_6F_5)_3^-$), 26.1 ($NB(pin)^+$); $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 100 MHz) δ 24.4 (CH_3), 44.4, 48.8 (CH_2), 90.6 ($C(CH_3)_2$), 125.3 ($C_{arom.}B$), 136.8 (d, $^1J_{C,F}$ = 246.0 Hz, $C_{arom.}F$), 138.2 (d, $^1J_{C,F}$ = 245.4 Hz, $C_{arom.}F$), 148.5 (d, $^1J_{C,F}$ = 240.4 Hz, $C_{arom.}F$); ^{19}F NMR (CD_2Cl_2, 469 MHz) δ –132.1 (d, $^3J_{F,F}$ = 22 Hz, 6F, *o*-C$F_{arom.}$), –161.0 (t, $^3J_{F,F}$ = 22 Hz, 3F, *p*-C$F_{arom.}$), –164.2 (m, 6F, *m*-C$F_{arom.}$).

Synthesis of 1-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-1,4-diazabicyclo[2.2.2]octane tris(pentafluorophenyl) deuterooborate, 3-1-[d_1].  This compound was synthesized analogous to **2-23** (**3-1**) using $B(C_6F_5)_3$ (77.0 mg, 0.15 mmol), DABCO (17.1 mg, 0.15 mmol), and DBpin (20.0 mg, 0.16 mmol) in $PhCF_3$ (1.0 mL) in a J. Young NMR tube. ^1H, ^{11}B, $^{13}C\{^1H\}$, and ^{19}F NMR are identical to **2-23 (3-1)**. ^2H NMR ($PhCF_3$, 77 MHz) δ 4.0 (br. s); ^{11}B NMR ($PhCF_3$, 160 MHz) δ –25.0 (s, $DB(C_6F_5)_3^-$), 25.8 ($NB(pin)^+$).

Synthesis of 1-(4,4,5,5-Tetramethyl-1,3,2-dioxaboronia-2-yl)-1,4-diazabicyclo[2.2.2]octane tetrakis(pentafluorophenyl)borate, 2-30 (3-2). 

To a solution of trityltetra(pentafluorophenyl)borate (463.0 mg, 0.501 mmol) in $PhCF_3$ (3 mL) was added HBpin (80 µL, 0.551 mmol) followed by a solution of DABCO (56.9 mg, 0.507 mmol) in $PhCF_3$ (3 mL). After stirring at ambient temperature for 30 min all volatiles were removed *in vacuo* and the remaining solid was extrated with pentanes (3 x 3 mL). The product **2-30** (**3-2**), in form of a white crystalline solid was dried *in vacuo*. Yield: 0.454 g (0.494 mmol, 98%). ^{1}H NMR ($PhCF_3$, 400 MHz) δ 1.20 (s, 12H, C(C*H*$_3$)$_2$), 2.77 (br. s, 12H, C*H*$_2$); ^{11}B NMR ($PhCF_3$, 128 MHz) δ –16.5 ($B(C_6F_5)_4^-$), 25.4 ($NB(pin)^+$); ^{13}C{^{1}H} NMR ($PhCF_3$, 100 MHz) δ 24.2 (*C*H$_3$), 44.6, 49.2 (*C*H$_2$), 91.2 (*C*(CH$_3$)$_2$), signals of $B(C_6F_5)_4^-$ anion omitted.

5.1.5 Imines

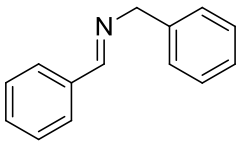
*General procedure for the synthesis of aldimines **IM1**:*[4] A 100 mL flask was charged with a magnetic stir bar, silica gel (0.3 g / mmol aldehyde), anhydrous ethanol (1 mL / mmol aldehyde), aldehyde, and amine. The reaction mixture was placed in a sonication bath for the indicated time and then filtered, the silica gel was washed with ethyl acetate, and all volatiles removed *in vacuo* to leave the crude aldimine. Pure aldimine was obtained after Kugelrohr distillation or recrystallization.

*General procedure for the synthesis of ketimines **IM2**:* A 250 mL round bottom flask equipped with a magnetic stir bar, Dean-Stark trap, and reflux condenser was removed from the oven, cooled under vacuum, and back-filled with Ar. Toluene (100 mL), ketone (30 mmol), amine (30 mmol), and *p*-toluenesulfonic acid monohydrate (0.2 - 2 mol%) were introduced into the reaction flask under a stream of Ar. The mixture was stirred at reflux until a calculated amount of water (1 mmol per mmol ketone) was collected at the base of the Dean-Stark trap. The

reaction mixture was filtered through Celite, volatile organics were evaporated and the desired compound was purified by Kugelrohr distillation or recrystallization. If E/Z isomers were observed by ^{1}H NMR, the isomeric ratio is given and the NMR data given is that of the major isomer.

*General Procedure for the synthesis of ketimines **IM3**:* A 250 mL 2-neck round bottom flask equipped with a stir bar was removed from the oven. A rubber stopper was placed in one of the openings and the flask was cooled under vacuum and back-filled with Ar. Freshly distilled diethyl ether (30 mL), ketone (30 mmol), and amine (150 mmol) were added via syringe to the flask. The reaction was cooled to 0℃ with an ice/water bath. Titanium tetrachloride in toluene (1.0M, 20 mmol) was added to an oven dried, vacuum cooled, Ar back-filled Schlenk flask via syringe and cooled to 0℃ with an ice bath. The titanium tetrachloride solution was added via cannula to the ketone/amine mixture over a period of 30 minutes. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with dilute aqueous sodium hydroxide (0.5M, 100 mL). The organics were extracted with diethyl ether (3 x 40 mL), dried with Na_2SO_4, and volatile organics were evaporated leaving behind a brown oil. In certain cases, the reaction mixture was washed through an Amberlite IR-120 solid acidic support to remove unreacted amine. The desired compound was isolated by Kuglrohr distillation or recrystallization.

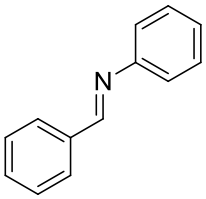
Synthesis of *N*-Benzylidene-1-phenylmethanamine, 2-36b.[5] The reaction was carried out following **IM1** from benzaldehyde (3.0 mL, 29.5 mmol), benzylamine (3.3 mL, 30.2 mmol), and silica gel (9.0 g) in EtOH (30 mL).



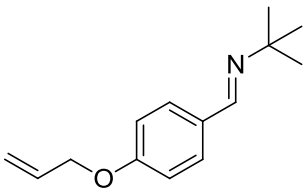
The reaction was subjected to ultrasonication at ambient temperature for 15 min. The desired product was purified by Kugelrohr distillation (1 mTorr @ 155 °C with CO_2(s)/acetone-cooling) and isolated in a 12% (0.72 g, 3.68 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.87 (s, 2H), 7.31 (m,

1H), 7.39 (d, $^{3}J_{H,H}$ = 4.4 Hz, 4H), 7.46 (m, 3H), 7.83 (dd, $^{3}J_{H,H}$ = 4.1 Hz, $^{4}J_{H,H}$ = 2.0 Hz, 2H), 8.44 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 65.1, 127.0, 128.0, 128.3, 128.5, 128.6, 130.8, 136.2, 139.4, 162.0; HRMS(TOF MS EI$^+$) Calcd. for $C_{14}H_{13}N$: m/z 195.1048 (M^+); Found: m/z 195.1041 (M^+); CAS 780-25-6.

Synthesis of *N*-Benzylideneaniline, 2-36c.[6] The reaction was carried out following **IM1** from benzaldehyde (3.0 mL, 29.5 mmol), aniline (2.8 mL, 30.7 mmol), and silica gel (9.1 g) in EtOH (30 mL). The reaction was subjected to ultrasonication at ambient temperature for 15 min. The desired product was purified by Kugelrohr distillation (1 mTorr @ 150 °C with CO_2(s)/acetone-cooling) yielding the product as a white crystalline solid in 51% yield (2.75 g, 15.17 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.23 - 7.28 (m, 3H), 7.43 (t, $^{3}J_{H,H}$ = 7.8 Hz, 2H), 7.49 - 7.53 (m, 3H), 7.94 (dd, $^{3}J_{H,H}$ = 7.1 Hz, $^{4}J_{H,H}$ = 2.5 Hz, 2H), 8.49 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz) δ 109.9, 120.8, 125.9, 128.8, 129.1, 131.3, 136.1, 152.0, 160.5; HRMS(TOF MS EI$^+$) Calcd. for $C_{13}H_{11}N$: m/z 181.0891 (M^+); Found: m/z 181.0885 (M^+); CAS 538-51-2.

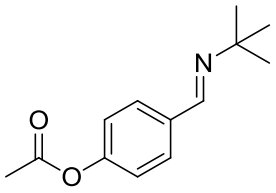


Synthesis of *N*-(4-(allyloxy)benzylidene)-2-methylpropan-2-amine, 2-33d.[7] To a solution of 4-hydroxybenzaldehyde (3.21g, 26.3 mmol) in acetone (125 mL) was added potassium carbonate (11.1 g, 80.3 mmol) followed by allyl bromide (2.6 mL, 30.1 mmol). The mixture was refluxed at 65℃ overnight. The reaction was filtered and the filtrate was reduced to an oil by removal of volatiles *in vacuo*. The product was purified by column chromatography (hexanes: EtOAc 7/1) affording the yellow oil 4-allyloxybenzaldehyde in 90 % yield (3.85 g, 23.7 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.63 - 4.67 (m, 2H), 5.33 - 5.49 (m, 2H), 6.00 - 6.13 (m, 1H), 7.01 - 7.07 (m, 2H), 7.83 - 7.87 (m, 2H), 9.91 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 70.0, 114.9, 118.3, 130.0,

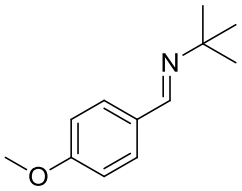


131.8, 132.1, 163.4, 190.5; CAS 40663-68-1. The subsequent reaction was carried out using **IM1** from 4-allyloxybenzaldehyde (1.62 g, 10 mmol), *tert*-butylamine (1.3 mL, 12.5 mmol), and silica gel (3.5 g) in EtOH (30 mL). The reaction mixture was subjected to ultrasonication at ambient temperature for 30 min. Recrystallization from diethyl ether/pentanes producing a white crystalline solid in 72% yield (1.56 g, 7.2 mmol). MP: 44.1 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (s, 9H), 4.52 (m, 2H), 5.31 (dd, $^{3}J_{H,H}$ = 10.5 Hz, $^{2}J_{H,H}$ = 1.4 Hz, 1H), 5.44 (dd, $^{3}J_{H,H}$ = 17.3 Hz, $^{2}J_{H,H}$ = 1.5 Hz, 1H), 6.01 - 6.13 (m, 1H), 6.95 (d, $^{3}J_{H,H}$ = 8.7 Hz, 2H), 7.70 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H), 8.23 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 28.2, 55.3, 67.2, 113.0, 116.2, 127.7, 128.7, 131.4, 152.8, 158.6; IR (NaCl) $\tilde{\nu}$ (cm^{-1}) = 2967 (m), 1641 (m), 1606 (s), 1510 (s), 1460 (w), 1421 (w), 1359 (w), 1305 (w), 1246 (s), 1166 (s), 1022 (w), 924 (w), 831 (w). HRMS(TOF MS EI^{+}) Calcd. for $C_{14}H_{19}NO$: m/z 217.1467 (M^{+}); found: m/z 217.1461 (M^{+}).

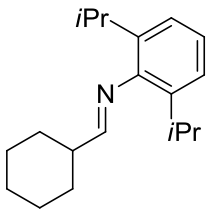
Synthesis of 4-((*tert*-butylimino)methyl)phenyl acetate, 2-36e. The reaction was carried out following **IM1** from 4-formylphenyl acetate (3.4 g, 20.7 mmol), *tert*-butylamine (2.6 mL, 25.0 mmol), and silica gel (7.0 g) in EtOH (30 mL). The mixture was subjected to ultrasonication at ambient temperature for 60 min. Recrystallization from hot hexanes yielded a white solid in 66% yield (2.90 g, 13.23 mmol). MP: 55.1 ℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.33 (s, 9H), 3.95 (s, 3H), 7.83 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 8.09 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 8.33 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 29.6, 52.2, 57.7, 127.7, 129.8, 131.4, 141.0, 154.2, 166.8; IR (NaCl) $\tilde{\nu}$ (cm^{-1}) = 2960 (m), 2904 (w), 1714 (s), 1639 (m),1435 (w), 1371 (w), 1284 (s), 1200 (m), 1112 (m). HRMS(TOF MS EI^{+}) Calcd. for $C_{13}H_{17}NO_2$: m/z 219.1259 (M^{+}); Found: m/z 219.1263 (M^{+}).



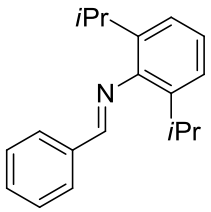
***N*-(4-methoxybenzylidene)-2-methylpropan-2-amine, 2-36f.**[8] The reaction was carried out following **IM1** from 4-methoxybenzaldehyde (2.73 g, 20.1 mmol), *tert*-butylamine (2.6 mL, 25.0 mmol), and silica gel (7.0 g) in EtOH (30 mL). The mixture was subjected to ultrasonication at ambient temperature for 60 min. The desired product was isolated by Kugelrohr distillation (1 mTorr @ 170 °C with CO_2(s)/acetone-cooling) as a white solid in 54% yield (2.07 g, 10.82 mmol). MP: 28.6℃. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (s, 9H) 3.83 (s, 3H), 6.94 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 7.70 (d, $^3J_{H,H}$ = 8.6 Hz, 2H), 8.21 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 29.7, 55.4, 27.0, 114.0, 129.5, 130.3, 154.5, 162.4; IR (NaCl) $\tilde{\nu}$ (cm^{-1}) = 2967 (m), 1655 (s), 1562 (m), 1498 (m), 1341 (w), 1277 (w), 1169 (m). HRMS(TOF MS EI$^+$) Calcd. for $C_{12}H_{17}NO$: m/z 191.1310 (M^+); Found: m/z 191.1308 (M^+); CAS 15875-74-8.



***N*-(cyclohexylmethylene)-2,6-diisopropylaniline, 2-36g.** The reaction was carried out following **IM2** from cyclohexanecarbaldehyde (3.6 mL, 29.7 mmol), 2,6-diisopropylaniline (4.4 mL, 29.8 mmol), and *p*-toluenesulfonic acid monohydrate (61 mg, 0.32 mmol, 1.1 mol%) in toluene (120 mL). Recrystallization from diethyl ether and petroleum ether yielded a yellow crystalline solid in 42% yield (3.42 g, 12.60 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.17 (d, $^3J_{H,H}$ = 6.9 Hz, 12H), 1.34 - 1.50 (m, 5H), 1.63 (s, 1H), 1.86 (m, 2H), 2.00 (m, 2H), 2.48 (br. s, 1H), 2.94 (septet, $^3J_{H,H}$ = 6.9 Hz, 2H), 7.04 - 7.15 (m, 3H), 7.51 (d, $^3J_{H,H}$ = 4.9 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 23.4, 25.5, 26.0, 27.6, 29.4, 44.2, 122.8, 123.7, 137.5, 171.1; CAS 869085-71-2.

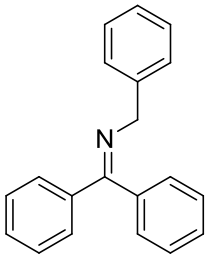


***N*-(benzylidene)-2,6-diisopropylaniline, 2-36h.**[9] The reaction was carried out following **IM2** from benzaldehyde (3.1 mL, 30.3 mmol), 2,6-diisopropylaniline (4.4 mL, 29.8 mmol), and *p*-toluenesulfonic acid

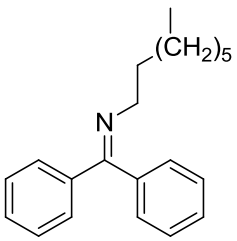


monohydrate (61 mg, 0.32 mmol, 1.1 mol%) in toluene (120 mL). Recrystallization from hexanes at ca. –12 ℃ yielded a pale yellow crystalline solid in 58% yield (4.62 g, 17.41 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, $^{3}J_{H,H}$ = 7.1 Hz, 12H), 2.81 (septet, d, $^{3}J_{H,H}$ = 7.0 Hz, 2H), 7.08 - 7.21 (m, 3H), 7.48 - 7.57 (m, 3H), 8.04 - 8.10 (m, 2H), 8.24 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 18.1, 23.0, 23.2, 122.9, 123.3, 127.1, 128.4, 130.4, 136.1, 139.1, 146.7, 169.8; HRMS(TOF MS EI^{+}) Calcd. for $C_{19}H_{23}N$: m/z 265.1830 (M^{+}); Found: m/z 265.1824 (M^{+}); CAS 117696-79-4.

***N*-(diphenylmethylene)-1-phenylmethanamine, 2-39a.**[10] The imine was prepared according to general procedure **IM2** from benzophenone (3.60 g, 30 mmol), benzylamine (3.3 mL, 30 mmol), and *p*-toluenesulfonic acid monohydrate (62 mg, 0.33 mmol, 1.0 mol%) in toluene (120 mL). The desired product crystallized from the reaction mixture. The crude white solid was dissolved in hot diethyl ether and layered with hexanes. Storing overnight at ca. –12 °C yielded the title compound as white needles 89% yield (7.24 g, 26.70 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.67 (s, 2H), 7.23-7.31 (m, 3H), 7.35 - 7.45 (m, 7H), 7.48-7.55 (m, 3H), 7.73-7.78 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 57.5, 126.5, 127.7, 127.8, 128.1, 128.4, 128.5, 128.5(9), 128.6(1), 130.1, 136.7, 139.8, 140.7, 168.8. HRMS (TOF MS EI^{+}): m/z: calcd for $C_{20}H_{17}N$: 271.1361 (M^{+}); found: 271.1367 (M^{+}); CAS 14428-98-9.

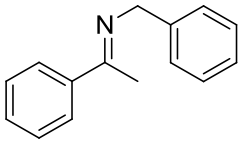


***N*-(diphenylmethylene)octan-1-amine, 2-46d**. The imine was prepared according to general procedure **IM2** from benzophenone (3.60 g, 30 mmol), *n*-octylamine (5.0 mL, 30 mmol), and *p*-toluenesulfonic acid monohydrate (62 mg, 0.33 mmol, 1.0 mol%) in toluene (120 mL). The desired product was Kugelrohr distilled from the reaction mixture (1 mTorr @ 175 °C mTorr). Trace impurities of benzophenone were remaining in the final product. Attempts to acquire

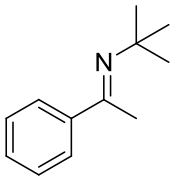


analytically clean material by distillation resulted in thermal decomposition of the desired imine. Greater than 90% pure imine was acquired and used in the subsequent reaction. The isolated material was a yellow oil and isolated in 70% yield (6.1 g, 21.0 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 (t, $^{3}J_{H,H}$ = 6.9 Hz, 3H), 1.25 - 1.45 (br. m, 10H), 1.72 (quintet, $^{3}J_{H,H}$ = 7.3 Hz, 2H), 3.41 (t, $^{3}J_{H,H}$ = 7.1 Hz, 2H), 7.16 - 7.20 (dd, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 2H), 7.31 – 7.38 (m, 3H), 7.43 – 7.52 (m, 3H), 7.63 – 7.66 (dd, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 14.6, 22.7, 27.6, 29.3, 29.5, 31.3, 31.9, 54.0, 127.9, 128.0, 128.2, 140.2, 167.6. HRMS (TOF MS EI^{+}): m/z: calcd for $C_{21}H_{27}N$: 293.2144 (M^{+}); found: 293.2149 (M^{+}); CAS 51411-33-7.

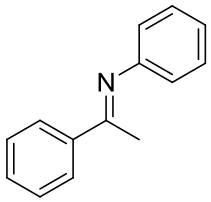
1-phenyl-*N*-(1-phenylethylidene)methanamine, 2-46e.[11] The imine was prepared according to general procedure **IM2** from acetophenone (3.5 mL, 30 mmol), benzylamine (3.3 mL, 30 mmol), and *p*-toluenesulfonic acid monohydrate (62 mg, 0.33 mmol, 1.0 mol%) in toluene (120 mL). The desired product was isolated by Kugelrohr distillation (1 mTorr @ 105 ℃) as a yellow oil in 33% yield (2.03 g, 9.70 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.38 (s, 3H), 4.80 (s, 2H), 7.30 (t, $^{3}J_{H,H}$ = 7.0 Hz, 1H), 7.36 - 7.55 (m, 7H), 7.93 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 15.9, 55.7, 126.6, 126.8, 127.7, 128.3, 128.4, 129.7, 140.6, 141.1, 166.3. HRMS (TOF MS EI^{+}): m/z: calcd for $C_{15}H_{15}N$: 209.1204 (M^{+}); found: 209.1211 (M^{+}); CAS 14428-98-9.



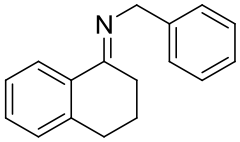
2-methyl-*N*-(1-phenylethylidene)propan-2-amine, 2-46a. The imine was prepared according to **IM3** from *tert*-butylamine (15.8 mL, 150 mmol), acetophenone (3.5 mL, 28.3 mmol), and titanium tetrachloride (1.0 M in toluene, 20.0 mL, 20 mmol). The desired product was Kuglrohr distilled from the reaction mixture (1 mTorr @ 90℃) and isolated as a yellow oil in 45% yield (2.23g, 12.7 mmol). ^{1}H NMR ($CDCl_3$,



400 MHz) δ 1.42 (s, 9H, 3 x C(2′)H_3), 2.37 (s, 3H, C(8)H_3), 7.31-7.37 (m, 3H, C(3,4,5)-$H_{arom.}$), 7.75 (m, 2H, C(2,6)-$H_{arom.}$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 30.55 (3 x *C(2′)*H_3), 55.2 (*C(1′)*), 126.6 (*C(2,6)*H), 128.1 (*C(3,5)*H), 128.9 (*C(4)*H), 143.3 (*C(1)*H), 162.1 (*C(7)*H). HRMS (TOF-EI): m/z: calcd for $C_{12}H_{17}N$: 175.1361 ($[M]^+$); found: 175.1365 ($[M]^+$); CAS: 40475-58-9.



***N*-(1-phenylethylidene)aniline, 2-46c.**[12] The imine was prepared according to general procedure **IM2** from acetophenone (3.5 mL, 30 mmol), aniline (2.7 mL, 30 mmol), and *p*-toluenesulfonic acid monohydrate (60 mg, 0.33 mmol, 1.0 mol%) in toluene (120 mL). Following removal of volatiles *in vacuo*, pentanes was added to the crude product facilitating crystallization of a white solid. The solid was filtered and recrystallized from hot diethyl ether; storing overnight at ca. –12 °C yielded pale yellow crystals in 58% yield (3.4 g, 17.4 mmol). ^1H NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H), 6.81 (d, $^3J_{H,H}$ = 6.8 Hz, 2H), 7.11 (t, $^3J_{H,H}$ = 7.1 Hz, 1H), 7.37 (t, $^3J_{H,H}$ = 7.4 Hz, 2H), 7.47 (m, 3H), 8.00 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 17.4, 119.4, 123.2, 127.2, 128.4, 129.0, 130.5, 139.5, 151.7, 165.5. HRMS (TOF MS EI^+): m/z: calcd for $C_{14}H_{13}N$: 195.1048 (M^+); found: 195.1043 (M^+); CAS 1749-19-5.



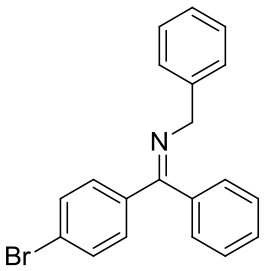
***N*-(3,4-Dihydronaphthalen-1(2*H*)-ylidene)-1-phenylmethanamine, 2-46h.** Prepared according to general procedure **IM2** from α-tetralone (4.0 mL, 30.07 mmol), benzylamine (3.3 mL, 30.20 mmol), and *p*-toluenesulfonic acid monohydrate (165 mg, 0.34 mmol, 1.1 mol%) in toluene (120 mL). The product was obtained as a clear, slightly yellow oil after two kugelrohr distillations (150 °C @ 1 mTorr torr) in 28% yield (2.0 g, 8.49 mmo). ^1H NMR (d_6-benzene, 600 MHz) δ 1.56 (m, 2H), 2.14 (t, $^3J_{H,H}$ = 6.3 Hz, 2H), 2.51 (t, $^3J_{H,H}$ = 6.0 Hz, 2H), 4.57 (s, 2H) 7.01 (d, $^3J_{H,H}$ = 7.2 Hz, 1H), 7.19 - 7.27 (m, 3H), 7.39 (t, $^3J_{H,H}$ = 7.5 Hz, 2H), 7.64 (d, $^3J_{H,H}$ = 7.2 Hz, 2H), 8.81 (d, $^3J_{H,H}$ =

7.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (d_6-benzene, 150 MHz) δ 22.5, 27.9, 29.7, 54.5, 126.4, 126.4, 126.5, 127.9, 128.2, 128.4, 129.6, 135.2, 140.3, 141.6, 164.2; HRMS(TOF EI^+) Calcd. for $C_{17}H_{17}N$: m/z 235.1361 (M^+); Found: m/z 235.1369 (M^+); CAS 32851-51-7.

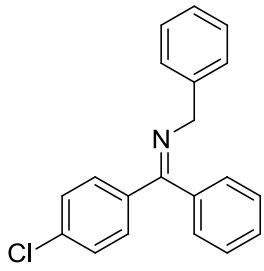
1-phenyl-*N*-(1-(4-(trifluoromethyl)phenyl)ethylidene) methanamine, 2-46g.[13] The imine was prepared according to general procedure **IM2** from 4-trifluoromethyl acetophenone (2.5 g, 13.3 mmol), benzylamine (1.5 mL, 13.3 mmol), and *p*-toluenesulfonic acid monohydrate (25 mg, 0.13 mmol, 1 mol%) in toluene (120 mL). The desired product was Kugelrohr distilled from the reaction mixture (1 mTorr @ 135 °C) and isolated as a yellow oil in 15% yield (0.524 g, 1.9 mmol). The compound was isolated as a 20:1 mixture of E/Z isomers. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3H), 4.80 (s, 2H), 7.32 (t, $^{3}J_{H,H}$ = 7.5 Hz, 1H), 7.42 (t, $^{3}J_{H,H}$ = 7.3 Hz, 2H), 7.48 (d, $^{3}J_{H,H}$ = 7.6 Hz, 2H), 7.69 (d, $^{3}J_{H,H}$ = 8.2 Hz, 2H), 8.02 (d, $^{3}J_{H,H}$ = 8.1 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 15.8, 55.9, 124.1 (q, $^{1}J_{C,F}$ = 272.1 Hz), 125.1 (q, $^{3}J_{C,F}$ = 3.7 Hz), 126.7, 127.1, 127.7, 128.4, 131.3 (q, $^{2}J_{C,F}$ = 32.4 Hz), 140.1, 144.1, 164.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –63.6; HRMS (TOF MS EI^+): m/z: calcd for $C_{16}H_{14}F_3N$: 277.1078 (M^+); found: 277.1085 (M^+); CAS 321338-01-6.

***N*-(diphenylmethylene)-1,1-diphenylmethanamine, 2-46f.**[14] The imine was prepared according to general procedure **IM2** from benzophenone (3.60 g, 30 mmol), benzhydrylamine (5.5 g, 30 mmol), and *p*-toluenesulfonic acid monohydrate (60 mg, 0.33 mmol, 1.0 mol%) in toluene (120 mL). The desired product crystallized from the reaction mixture and was recrystallized from diethyl ether/pentanes yielding white crystals in 51% yield (5.33 g, 15.3 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.61 (s, 1H), 7.09 (m, 2H), 7.19 - 7.23 (m, 2H), 7.28 - 7.32 (m, 4H), 7.34 - 7.39 (m, 7H), 7.42 - 7.45 (m,

3H), 7.75 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 70.0, 126.9, 127.7, 127.9, 128.2, 128.5, 128.57, 128.62, 128.9, 130.2, 136.9, 140.0, 145.0, 167.0. HRMS (TOF MS EI^+): m/z: calcd for $C_{26}H_{21}N$: 347.1674 (M^+); found: 347.1669 (M^+); CAS 5350-59-4.



***N*-((4-bromophenyl)(phenyl)methylene)-1-phenylmethanamine, 2-46j.** The imine was prepared according to general procedure **IM2** from 4-bromobenzophenone (7.8 g, 30 mmol), benzylamine (3.3 mL, 30 mmol), and *p*-toluenesulfonic acid (57 mg, 0.3 mmol, 1.0 mol%). Following removal of volatiles the desired product crystallized from the crude reaction mixture. The solid was filtered and recrystallized from diethyl ether/pentanes; storing overnight at ca. –12 °C yielded white crystals in 26% yield (2.7 g, 7.80 mmol). Mp.: 104 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.64 (s, 2H), 7.12 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 7.27 (m, 1H), 7.35 - 7.49 (m, 7H), 7.65 (d, $^{3}J_{H,H}$ = 8.3 Hz, 2H), 7.70 (d, $^{3}J_{H,H}$ = 6.7 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 57.4, 122.8, 126.6, 127.5, 128.1, 128.4, 128.5, 129.5, 130.3, 131.8, 135.4, 139.3, 140.3, 167.6. HRMS (TOF MS EI^+): m/z: calcd for $C_{20}H_{16}BrN$: 349.0466 (M^+); found: 349.0475 (M^+).



***N*-((4-chlorophenyl)(phenyl)methylene)-1-phenylmethanamine, 2-46i.** The imine was prepared according to general procedure **IM2** from 4-chlorobenzophenone (6.5 g, 30 mmol), benzylamine (3.3 mL, 30 mmol), and *p*-toluenesulfonic acid monohydrate (57 mg, 0.3 mmol, 1.0 mol%). Pentanes were added to the crude reaction mixture and a white solid crystallized. The solid was filtered and recrystallized from diethyl ether/pentanes; storing overnight at ca. –12 °C yielded white crystals in 25% yield (2.2 g, 7.21 mmol). Mp.: 93 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.64 (s, 2H), 7.18 (d, $^{3}J_{H,H}$ = 6.9 Hz, 2H), 7.27 (m, 1H), 7.36 –

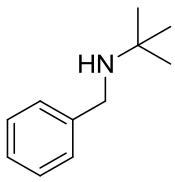
7.45 (m, 7H), 7.49 (d, $^{3}J_{H,H}$ = 6.9 Hz, 2H), 7.69 (d, $^{3}J_{H,H}$ = 8.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 57.5, 126.6, 127.6, 128.2, 128.4, 128.5, 128.9, 129.3, 134.6, 134.9. 139.4, 140.3, 167.6. HRMS (TOF MS EI^+): m/z: calcd for $C_{20}H_{16}ClN$: 305.0971 (M^+); found: 305.0982 (M^+); CAS 54220-17-6.

5.1.6 Reduced Products

General procedure for catalyzed reductions ***GPC1:*** In a nitrogen-filled glove box, at ambient temperature a J. Young NMR tube was charged with a solution of catalyst (either **2-27**, or $B(C_6F_5)_3$ followed by DABCO) in $PhCF_3$ or CH_2Cl_2. To this was added HBpin by means of an μL-Eppendorf pipette, followed by substrate (by means of an μL-Eppendorf pipette if liquid or as a solution in $PhCF_3$ in case of solids) and, if applicable, internal standard (mesitylene, added by means of an μL-Eppendorf pipette). The tube was capped, shaken and removed from the glove box and kept at the indicated temperature for the noted time. Reaction progress was monitored by ^{1}H and ^{11}B NMR spectroscopy. The product was isolated as indicated below.

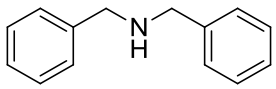
General procedure for catalyzed reductions ***GPC2:*** Identical to **GPC1** with the exception of using a vial equipped with a magnetic stir bar, and subsequent stirring for the indicated time in the glove box (temperature 28 °C). The product is then isolated as stated below after removal of the vial from the glove box.

***N*-Benzyl-2-methylpropan-2-amine, 2-38a.**[15] $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-benzylidene-2-methylpropan-2-amine (**2-36a**, 246 mg, 1.53 mmol), $B(C_6F_5)_3$ (38.4 mg, 75 μmol), DABCO (8.4 mg, 75 μmol), CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were



dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear colourless oil in 90% yield (221 mg, 1.35 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.19 (s, 9H), 1.91 (br. s, 1H, N*H*), 3.74 (s, 2H), 7.19 - 7.40 (m, 5H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 29.0, 47.5, 51.0, 127.1, 128.5, 128.7, 141.6; HRMS(TOF MS EI+) Calcd. for $C_{11}H_{17}N$: m/z 163.1361 (M^+); Found: m/z 163.1356 (M^+). CAS 3378-72-1.

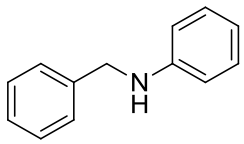
Dibenzylamine, 2-38b.[16] Borenium catalyzed: The reaction was carried out using **GPC1** from *N*-benzylidene-1-phenylmethanamine (**2-36b**, 47.8 mg, 0.25 mmol), HBpin (40 μL, 0.275 mmol), and **2-30** (11.5 mg, 12.5 μmol) in $PhCF_3$ (1 mL). Full conversion to product was observed at 3 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear oil in 90% yield (44.0 mg, 0.22 mmol).



$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out using **GPC1** from *N*-benzylidene-1-phenylmethanamine (**2-36b**, 47.8 mg, 0.25 mmol), HBpin (40 μL, 0.275 mmol), $B(C_6F_5)_3$ (6.2 mg, 12.1 μmol), and DABCO (1.2 mg, 10.7 μmol). 89% conversion to product was observed at 3 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness and subjected to column chromatography (silica gel,

pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear oil in 80% yield (39.4 mg, 0.199 mmol). Performing an analogous reaction using **GPC2** from *N*-benzylidene-1-phenylmethanamine (**2-36b**, 298.9 mg, 1.53 mmol), HBpin (0.24 mL, 1.65 mmol), $B(C_6F_5)_3$ (38.5 mg, 75.2 μmol), and DABCO (8.3 mg, 74.0 μmol) in CH_2Cl_2 (3 mL) produced the same product after 4 h in 86% yield (254 mg, 1.29 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.83 (s, 1H, NH), 3.86 (s, 4H), 7.31 (m, 2H), 7.33 - 7.42 (m, 8H); $^{13}C\{^1H\}$ NMR δ 53.2, 127.0, 128.2, 128.4, 140.3. HRMS (TOF MS EI$^+$): m/z: calcd for $C_{14}H_{15}N$: 197.1204 (M^+); found: 197.1211 (M^+); CAS 103-49-1.

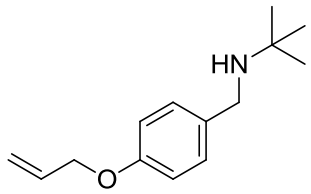
***N*-benzyl-1,1-diphenylmethanamine, 2-38c.**[16] Borenium catalyzed: The reaction was carried out using **GPC1** from *N*-benzylideneaniline (**2-36c**, 46.5 mg, 0.256 mmol), HBpin (40 μL, 0.275 mmol), and **2-30** (11.6 mg, 12.6 μmol) in $PhCF_3$ (1 mL). Full conversion to product was observed at 3 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear oil in 96% yield (45.0 mg, 0.25 mmol).



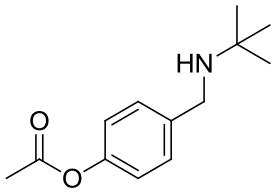
$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out using **GPC1** from *N*-benzylideneaniline (**2-36c**, 47.0 mg, 0.259 mmol), HBpin (40 μL, 0.275 mmol), $B(C_6F_5)_3$ (6.6 mg, 12.9 μmol), and DABCO (1.5 mg, 13.4 μmol). 91% conversion to product was observed at 8 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the

aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear oil in 86% yield (40.9 mg, 0.22 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.08 (br. s, 1H, NH), 4.39 (s, 2H), 6.70 (d, $^3J_{H,H}$ = 6.7 Hz, 2H), 6.79 (t, $^3J_{H,H}$ = 6.8 Hz, 1H), 7.24 (t, $^3J_{H,H}$ = 7.2 Hz, 2H), 7.34 (m, 1H), 7.43 (m, 4H); ^{13}C{^{1}H} NMR δ 48.3, 112.8, 117.5, 127.2, 127.5, 128.6, 129.2, 139.4, 148.1. HRMS (TOF MS EI$^+$): m/z: calcd for $C_{13}H_{13}N$: 183.1048 (M^+); found: 183.1052 (M^+); CAS 103-32-2.

Synthesis of *N*-(4-(allyloxy)benzyl)-2-methylpropan-2-amine, 2-38d. $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-(4-(allyloxy)benzylidene)-2-methylpropan-2-amine (**2-36d**, 302.2 mg, 1.49 mmol), $B(C_6F_5)_3$ (38.4 mg, 75 μmol), DABCO (8.4 mg, 75 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear colourless oil in 84% yield (260 mg, 1.19 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 9H), 3.69 (s, 2H), 4.52 (m, 2H), 5.31 (dd, $^3J_{H,H}$ = 10.5 Hz, $^2J_{H,H}$ = 1.4 Hz, 1H), 5.44 (dd, $^3J_{H,H}$ = 17.3 Hz, $^2J_{H,H}$ = 1.5 Hz, 1H), 6.01 - 6.13 (m, 1H), 6.95 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 7.70 (d, $^3J_{H,H}$ = 8.6 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 29.2, 46.6, 50.6, 68.9, 114.7, 117.5, 129.4, 133.4, 133.8, 157.5; HRMS(TOF MS EI$^+$) Calcd. for $C_{14}H_{21}NO$: m/z 219.1623 (M^+); found: m/z 219.1631 (M^+).

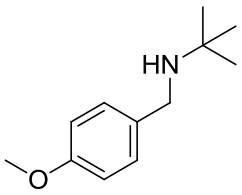


Synthesis of 4-((tert-butylamino)methyl)phenyl acetate, 2-38e.



$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), 4-((*tert*-butylimino)methyl)phenyl acetate (**2-36e**, 327.8 mg, 1.49 mmol), $B(C_6F_5)_3$ (38.5 mg, 75 μmol), DABCO (8.3 mg, 75 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 10:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear colourless oil in 34% yield (114 mg, 0.52 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18 (s, 9H), 3.79 (s, 2H), 3.90 (s, 3H), 7.42 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 7.98 (d, $^3J_{H,H}$ = 8.1 Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 29.1, 46.9, 50.8, 52.0, 128.1, 128.6, 129.7, 147.0, 167.0; HRMS(TOF MS EI$^+$) Calcd. for $C_{13}H_{19}NO_2$: m/z 221.1416 (M^+); found: m/z 221.1411 (M^+).

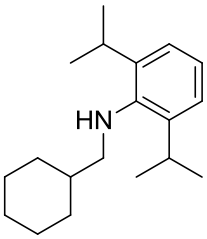
Synthesis of *N*-(4-methoxybenzyl)-2-methylpropan-2-amine, 2-38f.[17]



$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-(4-methoxybenzylidene)-2-methylpropan-2-amine (**2-36f**, 288.8 mg, 1.51 mmol), $B(C_6F_5)_3$ (38.4 mg, 75 μmol), DABCO (8.4 mg, 75 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$,

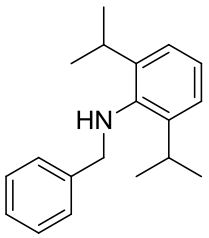
filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a clear colourless oil in 19% yield (54 mg, 0.28 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 9H), 3.70 (s, 2H), 3.80 (s, 3H), 6.90 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H), 7.28 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 29.6, 46.7, 50.7, 55.5, 113.9, 129.6, 133.8, 158.4; HRMS(TOF MS EI^{+}) Calcd. for $C_{12}H_{19}NO$: m/z 193.1467 (M^{+}); Found: m/z 193.1473 (M^{+}); CAS 22675-83-8.

Synthesis of *N*-(cyclohexylmethyl)-2,6-diisopropylaniline, 2-38g.

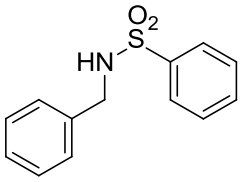


$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-(cyclohexylmethylene)-2,6-diisopropylaniline (**2-36g**, 408.4 mg, 1.50 mmol), $B(C_6F_5)_3$ (38.4 mg, 75 μmol), DABCO (8.4 mg, 75 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a white crystalline solid in 86% yield (354 mg, 1.29 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, $^{3}J_{H,H}$ = 6.8 Hz, 12H), 1.29 (m, 2H), 1.34 - 1.57 (m, 8H), 1.71 (t, 1H), 2.87 (septet, $^{3}J_{H,H}$ = 6.8 Hz, 2H), 3.12 (d, , $^{3}J_{H,H}$ = 6.3 Hz, 2H) 4.02 (br. s, 1H, N*H*), 6.93 – 7.08 (m, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 23.3, 25.5, 26.0, 28.6, 29.4, 37.1, 58.4, 127.2, 128.6, 134.5, 143.1.

Synthesis of *N*-benzyl-2,6-diisopropylaniline, 2-38h. $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.12 mL, 0.825 mmol), *N*-(benzylidene)-2,6-diisopropylaniline (**2-36h**, 200.6 mg, 0.75 mmol), $B(C_6F_5)_3$ (19.2 mg, 37.5 μmol), DABCO (4.4 mg, 39.2 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, evaporated to dryness and the mixture was subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a white crystalline solid in 81 % yield (162 mg, 0.61 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, $^3J_{H,H}$ = 7.1 Hz, 12H), 3.14 (septet, d, $^3J_{H,H}$ = 7.0 Hz, 2H), 3.98 (br. s, 1H, N*H*), 4.12 (s, 2H), 7.01 - 7.13 (m, 3H), 7.24 - 7.38 (m, 5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 18.1, 23.0, 23.2, 67.8, 127.0, 127.3, 128.2, 128.4, 139.1, 140.4, 146.7.

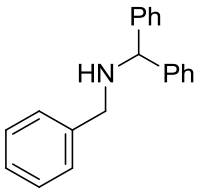


Synthesis of *N*-benzylbenzenesulfonamide, 2-38i.[18] $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-benzylidenebenzenesulfonamide (371.3 mg, 1.51 mmol), $B(C_6F_5)_3$ (38.8 mg, 75.6 μmol), DABCO (8.4 mg, 75 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 5:1 hexanes/ethyl acetate). The product was isolated as a white crystalline solid in 93% yield



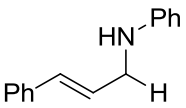
(346 mg, 1.40 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15 (d, $^{3}J_{H,H}$ = 4.3 Hz, 2H), 4.71 (br. s, 1H, N*H*), 7.20 - 7.30 (m, 5H), 7.51 - 7.62 (m, 3H), 7.88 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 49.4, 127.0, 127.9, 128.8, 129.2, 132.7, 136.2, 139.9; HRMS(TOF MS EI^{+}) Calcd. for $C_{13}H_{11}NO_2S$: m/z 247.0667 (M^{+}); Found: m/z 247.0662 (M^{+}); CAS 837-18-3.

Synthesis of *N*-benzyl-1,1-diphenylmethanamine, 2-38j.[19]



$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC2** in a 4 dram vial from HBpin (0.24 mL, 1.65 mmol), *N*-benzylidene-1,1-diphenylmethanamine (410.0 mg, 1.51 mmol), $B(C_6F_5)_3$ (38.8 mg, 75 μmol), DABCO (8.1 mg, 72.2 μmol) in CH_2Cl_2 (3 mL). After reacting at ambient temperature for 4 h the vial was opened to air and 10 mL of H_2O was added and stirred for ca. 1 h. The reaction mixture was diluted with CH_2Cl_2, poured into a separation funnel and the aqueous phase was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a white crystalline solid in 96% yield (392 mg, 1.43 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.01 (br. s, 1H), 3.77 (s, 2H), 5.69 (s, 1H), 7.09 - 7.41 (m, 15H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 45.8, 64.7, 126.5, 127.1, 127.3, 128.4, 140.6, 143.7; HRMS(TOF MS EI^{+}) Calcd. for $C_{20}H_{19}N$: m/z 273.1517 (M^{+}); Found: m/z 273.1511 (M^{+}); CAS 5669-43-2.

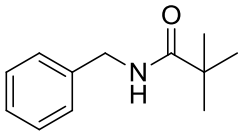
Synthesis of *N*-Cinnamylaniline, 2-38k.[20]



Borenium catalyzed: The reaction was carried out following **GPC2** from HBpin (0.120 mL, 82.5 mmol), *N*-(-3-phenylallylidene)aniline (**2-36k**, 155.1 mg, 75.8 mmol), **2-30** (33.9 mg, 36.8 μmol) in $PhCF_3$ (1 mL). After reacting at ambient temperature for 4 h, H_2O (10 mL) was added to quench the reaction. The mixture was transferred to a separation funnel and

the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, evaporated to dryness, and subjected to column chromatography (silica gel, pretreatment with 10:1 hexanes/triethylamine, eluted with 100:1:1 hexanes/ethyl acetate/triethylamine). The product was isolated as a white solid in 73% yield (116 mg, 55.4 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.87 (br. s, 1H, N*H*), 4.01 (dd, $^2J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.5 Hz, 2H), 6.41 (dt, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 15.9 Hz, 1H), 6.69 (d, $^3J_{H,H}$ = 15.9 Hz, 1H), 6.77 (m, 2H), 6.84 (t, $^3J_{H,H}$ = 7.3 Hz, 1H), 7.23 - 7.35 (m, 3H), 7.41 (m, 2H), 7.47(d, $^3J_{H,H}$ = 7.3 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 46.3, 113.2, 117.7, 126.4, 127.1, 127.6, 128.7, 129.4, 131.6, 137.0, 148.1; CAS 1142-24-1.

Synthesis of Benzylamine and isolation as *N*-benzylpivalamide.[21]

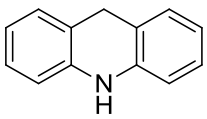


Borenium catalyzed: The reaction was carried out using **GPC1** from benzonitrile (25.8 mg, 0.25 mmol), HBpin (80 μL, 0.55 mmol), and **2-30** (11.6 mg, 12.6 μmol) in $PhCF_3$ (1 mL). 24% conversion to product was observed after 24 h at 100 °C by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. After dilution with CH_2Cl_2 (2 mL), NEt_3 (52.3 μL, 0.375 mmol) and pivalyl chloride (45.2 mg, 0.375 mmol) were added and the reaction was stirred at ambient temperature overnight. The mixture was transferred to a separation funnel to which H_2O was added (20 mL). After extraction with CH_2Cl_2 (3x), the organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The crude product was subjected to column chromatography (silica gel, 70:30 hexanes/CH_2Cl_2) producing a clear oil in 18% yield (9.0 mg, 0.047 mmol).

$B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out using **GPC1** from benzonitrile

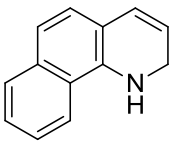
(25.8 mg, 0.25 mmol), HBpin (80 μL, 0.55 mmol), $B(C_6F_5)_3$ (6.2 mg, 12.1 μmol), and DABCO (1.2 mg, 10.7 μmol) in $PhCF_3$ (1 mL). 89% conversion to product was observed after 4 h at 100 °C by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. After dilution with CH_2Cl_2 (2 mL), NEt_3 (52.3 μL, 0.375 mmol) and pivalyl chloride (45.2 mg, 0.375 mmol) were added and the reaction was stirred at room temperature overnight. The mixture was transferred to a separation funnel to which H_2O was added (20 mL). After extraction with CH_2Cl_2 (3x), the organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The crude product was subjected to column chromatography (silica gel, 70:30 hexanes/CH_2Cl_2) producing a clear oil in 54% yield (27.0 mg (0.141 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.26 (s, 9H), 4.44 (d, $^3J_{H,H}$ = 5.6 Hz, 2H), 5.93 (br. s, 1H, N*H*), 7.29 (m, 3H), 7.36 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 128 MHz) δ 27.5, 38.7, 43.5, 127.4, 127.6, 128.7, 138.7, 178.2. HRMS (TOF MS EI$^+$): m/z: calcd for $C_{12}H_{17}NO$: 191.1310 (M^+); found: 191.1303 (M^+); CAS 26209-45-0.

Synthesis of 9,10-Dihydroacridine, 2-41a.[22] $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC1** from HBpin (36.6 mg, 0.286 mmol), acridine (52.6 mg, 0.293 mmol), $B(C_6F_5)_3$ (7.3 mg, 14.3 μmol), and DABCO (1.5 mg, 13.4 μmol) in CD_2Cl_2 (1 mL). Full conversion to product was observed after 1 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Desired product was isolated by column chromatography (silica gel, hexanes/EtOAc 20:1) as a colorless, crystalline solid in 95% yield (51.0 mg,

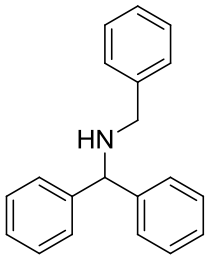


0.281 mmol). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 4.08 (s, 2H), 5.97 (s, 1H, N*H*), 6.68 (d, $^{3}J_{H,H}$ = 7.8 Hz, 2H), 6.89 (t, $^{3}J_{H,H}$ = 7.4 Hz, 2H), 7.14 (m, 4H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 150 MHz) δ 31.5, 113.7, 120.1, 120.7, 127.1, 128.7, 140.2; CAS 92-81-9.

Synthesis of 1,2-dihydro-1,10-phenanthroline, 2-41b.[23] $B(C_6F_5)_3$/DABCO catalyzed: The reaction was carried out following **GPC1** from HBpin (27.5 mg, 0.215 mmol), 1,10-phenantroline (35.1 mg, 0.195 mmol), $B(C_6F_5)_3$ (5.0 mg, 9.77 μmol), and DABCO (1.2 mg, 10.7 μmol) in CD_2Cl_2 (1 mL). 91% conversion to product was observed after 1 h by ^{1}H NMR spectroscopy. The reaction was diluted with CH_2Cl_2 and transferred to a 4 dram vial. After addition of H_2O (10 mL), the mixture was transferred to a separation funnel and the aqueous was extracted with CH_2Cl_2 (3x). The combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Desired product was isolated by column chromatography (silica gel, hexanes/EtOAc 20:1) as a yellow crystalline solid in 95% yield (51.0 mg, 0.281 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.77 (m, 2H), 4.55 (m, 1H), 6.49 (m, 1H), 7.17 (m, 1H), 7.31 (m, 1H), 7.44 (m, 1H), 8.15 (m, 1H), 8.72 (m, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz) δ 28.3, 96.0, 117.4, 120.8, 127.3, 128.4, 135.8, 147.8.

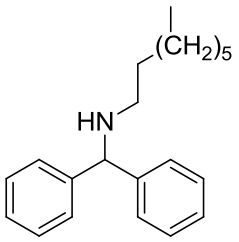


Synthesis of *N*-benzyl-1,1-diphenylmethanamine, 2-47b.[24] The reaction was carried out according to **GPC2** from *N*-(diphenylmethylene)-1-phenylmethanamine (**2-38a**, 203.4 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.8 mg, 37.7 μmol) in $PhCF_3$ (3 mL). After 5 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3X), crude ^{1}H NMR showed H_2O quench was not sufficient to hydrolyze the N-B bond. The crude reaction mixture was diluted in CH_2Cl_2, added to a separation funnel followed by 1 M HCl(aq.) (3 mL), 1 M $NaHCO_3$(aq.) (4 mL), then extracted with CH_2Cl_2

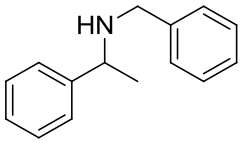


(3x). Organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. Crude ^{11}B NMR analysis showed that the acid/base treatment was able to fully cleave the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound gradient eluted with 300:1:1 then 100:1:1 hexanes/ethyl acetate/triethylamine) as a white crystalline solid with an average yield of 90% (177 mg, 0.647 mmol, 86%; 192 mg, 0.702 mmol, 93%). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.87 (br. s, 1H, N*H*), 3.78 (s, 2H), 4.89 (s, 1H), 7.22 - 7.26 (m, 2H), 7.27 - 7.30 (m, 1H), 7.31 (s, 1H), 7.33 (s, 2H), 7.34 - 7.38 (m, 5H), 7.44 - 7.47 (m, 4 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 51.9, 66.5, 127.0, 127.1, 127.4, 128.2, 128.4, 128.5, 140.5, 144.0; HRMS (TOF MS EI^+): m/z: calcd for $C_{20}H_{19}N$: 273.1517 (M^+); found: 273.1527 (M^+); CAS 5669-43-2.

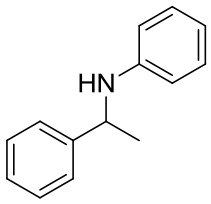
Synthesis of *N*-benzhydryloctan-1-amine, 2-47d.[25] The reaction was carried out according to **GPC2** from *N*-(diphenylmethylene)octan-1-amine (**2-46d**, 220.5 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.4 mg, 37.5 μmol) in $PhCF_3$ (3 mL). After 5 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 500:1:1 → 300:1:1 → 100:1:1 hexanes/ethyl acetate/triethylamine) as a clear oil in 82% yield (182 mg, 0.616 mmol). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.92 (s, 3H), 1.24 - 1.40 (br. m, 10H), 1.51 - 1.61 (b. m, 3H, N*H* and CH_2), 2.61 (t, $^3J_{H,H}$ = 7.1 Hz, 2H), 4.85 (s, 1H), 7.24 (tt, $^3J_{H,H}$ = 7.3 Hz, $^4J_{H,H}$ = 1.2 Hz, 2H), 7.33 (t, $^3J_{H,H}$ = 7.8 Hz, 4H), 7.44 (dd, $^3J_{H,H}$ = 7.7 Hz, $^4J_{H,H}$ = 1.3 Hz, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 14.1, 22.7, 27.4, 29.3, 29.6, 30.3, 31.9, 48.4, 67.7, 126.9, 127.3, 128.4, 144.4; HRMS



(TOF MS EI$^+$): m/z: calcd for $C_{21}H_{29}N$: 295.2300 (M^+); found: 295.2311 (M^+); CAS 128297-93-8.



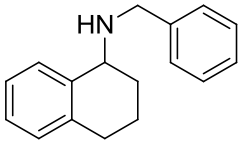
Synthesis of *N*-benzyl-1-phenylethanamine, 2-47b.[26] The reaction was carried out according to **GPC2** from 1-phenyl-*N*-(1-phenylethylidene)methanamine (**2-46e**, 157.2 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.5 mg, 37.5 μmol) in $PhCF_3$ (3 mL). After 4 h The vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 300:1:1 hexanes/ethyl acetate/triethylamine) as a yellow oil in 83% yield (131.5 mg, 0.622 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.42 (d, $^3J_{H,H}$ = 6.6 Hz, 3H), 1.74 (br. s, 1H, N*H*), 3.64 (d, $^2J_{H,H}$ = 13.1 Hz, 1H), 3.72 (d, $^2J_{H,H}$ = 13.1 Hz, 1H), 3.87 (q, $^3J_{H,H}$ = 6.6 Hz, 1H), 7.25 - 7.44 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.6, 51.7, 57.5, 126.7, 126.9, 127.0, 128.2, 128.4, 128.5, 140.7, 145.6; HRMS (TOF MS EI$^+$): m/z: calcd for $C_{15}H_{17}N$: 211.1361 (M^+); found: 211.1356 (M^+); CAS 3193-62-2.



Synthesis of *N*-(1-phenylethyl)aniline, 2-47c.[27] The reaction was carried out according to **GPC2** from *N*-(1-phenylethylidene)aniline (**2-46c**, 146.5 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (33.9 mg, 36.8 μmol) in $PhCF_3$ (3 mL). After 4 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. The desired compound was

isolated by column chromatography (pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 300:1:1 hexanes/ethyl acetate/triethylamine) as a yellow oil in 78% yield (115 mg, 0.582 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.57 (d, $^{3}J_{H,H}$ = 6.7 Hz, 3H), 4.11 (br. s, 1H, N*H*), 4.54 (q, $^{3}J_{H,H}$ = 6.7 Hz, 1H), 6.58 (br. d, $^{3}J_{H,H}$ = 7.7 Hz, 2H), 6.71 (br. t, $^{3}J_{H,H}$ = 7.3 Hz, 1H), 7.15 (br. t, $^{3}J_{H,H}$ = 7.4 Hz, 2H), 7.28 (t, $^{3}J_{H,H}$ = 7.3 Hz, 1H), 7.37 (t, $^{3}J_{H,H}$ = 7.8 Hz, 2H), 7.42 (d, $^{3}J_{H,H}$ = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 128 MHz) δ 25.0, 53.4, 113.3, 117.2, 125.8, 126.8, 128.6, 129.1, 145.2, 147.2; HRMS (TOF MS EI^{+}): m/z: calcd for $C_{14}H_{15}N$: 197.1204 (M^{+}); found: 197.1201 (M^{+}); CAS 779-54-4.

Synthesis of *N*-benzyl-1,2,3,4-tetrahydronaphthalen-1-amine, 2-47h.[28]



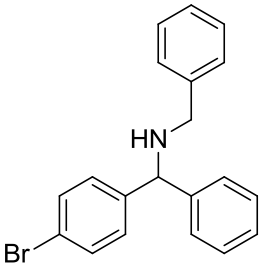
The reaction was carried out according to **GPC2** from *N*-(3,4-dihydronaphthalen-1(2*H*)-ylidene)-1-phenylmethanamine (**2-46h** 176.5 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.8 mg, 37.7 μmol) in $PhCF_3$ (3 mL). The mixture was allowed to stir for 24 h to drive the reaction to completion. The vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 100:1:1 hexanes/ethyl acetate/triethylamine) as a yellow oil in 77% yield (137 mg, 0.577 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.58 (br. s, 1H, N*H*), 1.86 - 1.94 (m, 1H), 2.05 - 2.11 (m, 2H), 2.16 - 2.24 (m, 1H), 2.86 - 2.94 (m, 1H), 2.96 - 3.04 (m, 1H), 3.98 (t, $^{3}J_{H,H}$ = 5.0 Hz, 1H), 4.01 (d, $^{2}J_{H,H}$ = 13.3 Hz, 1H), 4.11 (d, $^{2}J_{H,H}$ = 13.3 Hz, 1H), 7.25 (m, 1H), 7.29 - 7.35 (m, 2H), 7.42 (t, $^{3}J_{H,H}$ = 7.3 Hz, 1H), 7.50 (t, $^{3}J_{H,H}$ = 7.7 Hz, 2H), 7.54 (m, 1H), 7.58 (d, $^{3}J_{H,H}$ = 7.4 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 128 MHz) δ 19.3, 28.4, 29.6, 51.4, 54.9, 125.9, 126.8, 127.0, 128.3, 128.5, 129.0, 129.2, 137.6,

139.5, 141.2; HRMS (TOF MS EI$^+$): m/z: calcd for $C_{17}H_{19}N$: 237.1517 (M^+); found: 237.1522 (M^+); CAS 212250-85-6.

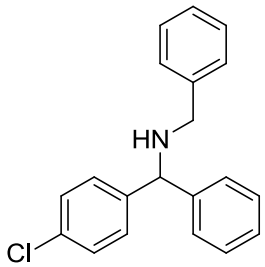
Synthesis of *N*-benzyl-1-(4-(trifluoromethyl)phenyl)ethanamine, 2-47g.[13] The reaction was carried out according to **GPC2** from 1-phenyl-*N*-(1-(4-(trifluoromethyl)phenyl)ethylidene) methanamine (**2-46g**, 208.0 mg, 0.75 mmol), HBpin (120 µL, 0.825 mmol), and **2-30** (34.0 mg, 36.9 µmol) in $PhCF_3$ (3 mL). After 4 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{1}H NMR showed H_2O quench was not sufficient to hydrolyze the N-B bond. The crude reaction mixture was diluted in CH_2Cl_2, added to a separation funnel followed by 1 M HCl(aq.) (3 mL), 1 M $NaHCO_3$(aq.) (4 mL), then extracted with CH_2Cl_2 (3x) and volatiles removed *in vacuo*. Crude ^{11}B NMR analysis showed that the acid/base treatment was able to fully cleave the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 300:1:1 → 100:1:1 hexanes/ethyl acetate/triethylamine) as a yellow oil in 79% yield (165.5 mg, 0.592 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (d, $^3J_{H,H}$ = 6.6 Hz, 3H), 1.67 (br. s, 1H, N*H*), 3.63 (d, $^2J_{H,H}$ = 13.2 Hz, 1H), 3.69 (d, $^2J_{H,H}$ = 13.2 Hz, 1H), 3.92 (q, $^3J_{H,H}$ = 6.6 Hz, 1H), 7.26 - 7.40 (br. m, 5H), 7.53 (d, $^3J_{H,H}$ = 8.1 Hz, 2H), 7.64 (d, $^3J_{H,H}$ = 8.1 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 24.8, 52.0, 57.5, 124.6 (q, $^1J_{C,F}$ = 271.8 Hz, *C*F_3), 125.7 (q, $^3J_{C,F}$ = 3.8 Hz), 127.3, 127.4, 128.3, 128.7, 129.5 (q, $^2J_{C,F}$ = 32.2 Hz), 140.6, 150.1; HRMS (TOF MS EI$^+$): m/z: calcd for $C_{16}H_{16}F_3N$: 279.1235 (M^+); found: 279.1242 (M^+); CAS 1019559-22-8.

Synthesis of Dibenzhydrylamine, 2-47f.[29] The reaction was carried out according to **GPC2** from *N*-(diphenylmethylene)-1,1-diphenylmethanamine (**2-46f**, 345.5 mg, 0.99 mmol), HBpin (142.1 mg, 1.1 mmol), and **2-30** (43.3 mg, 46.9 μmol) in a mixture of $PhCF_3$ (2.25 mL) and CH_2Cl_2 (1.5 mL). After 24 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. All attempts to purify the amine by column chromatography yielded mixtures of amine and imine. Thus, the amine was isolated as after *N*-trifluoroacetamide protection: The mixed column chromatography fractions containing amine **2-47f** and imine **2-46f** were combined and volatiles were removed *in vacuo*; the mixture was diluted in CH_2Cl_2 (2 mL) and transferred in a 4 dram vial charged with a magnetic stirbar, trifluoroacetic anhydride (0.23 mL, 1.65 mmol), and pyridine (0.18 mL, 2.25 mmol) were added to the solution via syringe. The reaction was allowed to stir at ambient temperature for 3 h then quenched with H_2O (10 mL). After an aqeous extraction with CH_2Cl_2 (3x), the mixture was subjected to column chromatography (silica gel, 300:1:1 hexanes/EtOAc/NEt_3). Refluxing in methanolic NaOH (5%, 15 mL) for 6 h deprotected the trifluoroacetamide. Following dilution in H_2O (15 mL), organics were extracted with EtOAc (3x) and volatiles were removed *in vacuo*. The solid product **2-47f** was washed with pentanes yielded a white solid in 60% yield (209 mg, 0.60 mmol). ^1H NMR ($CDCl_3$, 400 MHz) δ 2.27 (br. s, 1H, N*H*), 4.76 (s, 2H), 7.23 (t, $^3J_{H,H}$ = 6.9 Hz, 4H), 7.29 - 7.36 (m, 16H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 63.5, 127.0, 127.6, 128.4, 143.8. HRMS (TOF MS EI^+): m/z: calcd for $C_{26}H_{23}N$: 349.1830 (M^+); found: 349.1835 (M^+); CAS 5350-71-0.

Synthesis of *N*-benzyl-1-(4-bromophenyl)-1-phenylmethanamine, 2-47i. The reaction was carried out according to **GPC2** from *N*-((4-bromophenyl)(phenyl)methylene)-1-phenylmethanamine (**2-46j**, 264.5 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.5 mg, 37.5 μmol) in $PhCF_3$ (3 mL). After 5 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{1}H NMR showed H_2O quench was not sufficient to hydrolyze the N-B bond. The crude reaction mixture was diluted in CH_2Cl_2, added to a separation funnel followed by 1 M HCl(aq.) (3 mL), 1 M $NaHCO_3$(aq.) (4 mL), then extracted with CH_2Cl_2 (3x) and volatiles removed *in vacuo*. Crude ^{11}B NMR analysis showed that the acid/base treatment was able to fully cleave the N-B bond. The desired compound was isolated by column chromatography (pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 300:1:1 hexanes/ethyl acetate/triethylamine) as a pale yellow solid in 84% yield (221.9 mg, 0.629 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.86 (br. s, 1H, N*H*), 3.76 (s, 2H), 4.85 (s, 1H), 7.22 - 7.50 (br. m, 14H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 51.8, 65.8, 120.8, 127.0, 127.2, 127.3, 128.1, 128.4, 128.6, 129.1, 131.6, 140.2, 143.0, 143.5; HRMS (TOF MS EI$^+$): m/z: calcd for $C_{20}H_{20}BrN$: 351.0623 (M^+); found: 351.0629 (M^+).

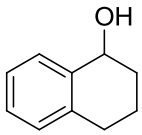


Synthesis of *N*-benzyl-1-(4-chlorophenyl)-1-phenylmethanamine, 2-47j. The reaction was carried out according to **GPC2** from *N*-((4-chlorophenyl)(phenyl)methylene)-1-phenylmethanamine (**2-46i**, 228.8 mg, 0.75 mmol), HBpin (120 μL, 0.825 mmol), and **2-30** (34.5 mg, 37.5 μmol) in $PhCF_3$ (3 mL). After 5 h the vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2

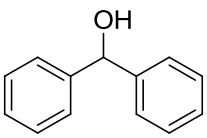


(3x), the combined organic phases were dried with $MgSO_4$, filtered, and evaporated to dryness. Crude ^{11}B NMR showed H_2O quench was sufficient to hydrolyze the N-B bond. The desired compound was isolated by column chromatography (packed and pretreated silica with 10:1 hexanes/triethylamine; compound eluted with 300:1:1 hexanes/ethyl acetate/triethylamine) as a clear oil in 73% yield (168 mg, 0.545 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.91 (br. s, 1H, N*H*), 3.79 (s, 2H), 4.89 (s, 1H), 7.23 - 7.50 (br. m, 14H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 51.8, 65.8, 127.1, 127.3, 127.3, 128.2, 128.5, 128.7, 128.8, 132.7, 140.3, 142.5, 143.6; HRMS (TOF MS EI^+): m/z: calcd for $C_{20}H_{18}ClN$: 307.1128 (M^+); found: 307.1123 (M^+); CAS 88906-20-1.

Synthesis of 1,2,3,4-tetrahydronaphthalen-1-ol, 2-43a.[30] The reaction was carried out according to **GPC2** from α-tetralone (219.3 mg, 1.50 mmol), HBpin (240 μL, 1.65 mmol), $B(C_6F_5)_3$ (38.8 mg, 75.8 μmol), DABCO (9.0 mg, 80.2 μmol) in CH_2Cl_2 (3 mL). After 48 h an aliquot was taken from the reaction, product formation was observed by ^1H NMR spectroscopy in isolatable quantities. The vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The desired compound was isolated by column chromatography (silica gel 8:1 hexanes/ethyl acetate) as a clear oil in 73% yield (162 mg, 1.09 mmol). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.76 - 2.10 (m, 4H), 2.13 (br. s, 1H, O*H*), 2.75 - 2.88 (m, 2H), 4.82 (t, $^3J_{H,H}$ = 5.0 Hz, 1H), 7.15 (m, 1H), 7.22 - 7.29 (m, 2H), 7.48 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 19.0, 29.1, 32.7, 68.1, 126.3, 127.5, 128.4, 128.9, 137.1, 138.7; CAS 529-33-9.

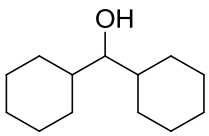


Synthesis of Diphenylmethanol, 2-43b.[31] The reaction was carried out according to **GPC2** from benzophenone (274.7 mg, 1.51 mmol), HBpin (240 μL, 1.65 mmol), $B(C_6F_5)_3$ (38.3 mg, 74.8 μmol), DABCO (8.5 mg,

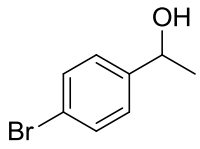


75.8 μmol) in CH_2Cl_2 (3 mL). After 48 h an aliquot was taken from the reaction, product formation was observed by ^{1}H NMR spectroscopy in isolatable quantities. The vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The desired compound was isolated by column chromatography (silica gel, 8:1 hexanes/ethyl acetate) as a white solid in 26% yield (71 mg, 0.385 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.24 (br. d, $^3J_{H,H}$ = 3.7 Hz, 1H, O*H*), 5.75 (d, $^3J_{H,H}$ = 3.7 Hz, 1H), 7.18 - 7.31 (m, 10H); ^{13}C{^{1}H} NMR ($CDCl_3$, 128 MHz) δ 77.1, 126.8, 127.8, 128.6, 143.8; CAS 91-01-0.

Synthesis of Dicyclohexylmethanol, 2-43c.[32] The reaction was carried out according to **GPC2** from dicyclohexylketone (291.1 mg, 1.50 mmol), HBpin (240 μL, 1.65 mmol), $B(C_6F_5)_3$ (38.2 mg, 74.6 μmol), DABCO (8.5 mg, 75.8 μmol) in CH_2Cl_2 (3 mL). After 48 h an aliquot was taken from the reaction, product formation was observed by ^{1}H NMR spectroscopy in isolatable quantities. The vial was removed from the glove box and H_2O (10 mL) was added to the reaction. After an aqeous extraction with CH_2Cl_2 (3x), the combined organics were dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The desired compound was isolated by column chromatography (silica gel, 8:1 hexanes/ethyl acetate) as a colourless oil in 12% yield (35.3mg, 0.180 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 - 1.31 (m, 2H), 1.41 - 1.63 (m, 20H), 3.18 (t, $^3J_{H,H}$ = 4.8 Hz, 1H), 3.62 (br. s, 1H, O*H*); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 26.4, 26.5, 30.4, 42.5, 82.4; CAS 4453-82-1.

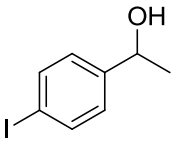


Attempt to synthesize of 1-(4-bromophenyl)ethanol, 2-43d. The reaction was carried out according to **GPC2** from *para*-bromoacetophenone (153.2 mg, 0.770 mmol), HBpin (120 μL, 0.825 mmol), $B(C_6F_5)_3$ (19.2 mg, 37.5 μmol), DABCO (4.3 mg, 38.3 μmol) in CH_2Cl_2 (1.5 mL). After 48 h an aliquot was taken from the

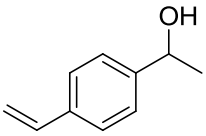


reaction, product formation was observed in trace quantities by ^{1}H NMR spectroscopy. Product formation confirmed by ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (d, 3H), 4.84 (q, 1H). Due to high signal to noise ratios percent conversions could not be reliably determined.

Attempt to synthesize of 1-(4-iodophenyl)ethanol, 2-43e. The reaction was carried out according to **GPC2** from *para*-iodoacetophenone (186.5 mg, 0.746 mmol), HBpin (120 μL, 0.825 mmol), $B(C_6F_5)_3$ (19.6 mg, 38.3 μmol), DABCO (4.3 mg, 38.3 μmol) in CH_2Cl_2 (1.5 mL). After 48 h an aliquot was taken from the reaction, product formation was observed in trace quantities by ^{1}H NMR spectroscopy. Product formation confirmed by ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.42 (d, $^{3}J_{H,H}$ = 6.4 Hz, 3H), 4.81 (q, $^{3}J_{H,H}$ = 6.3 Hz, 1H). Due to high signal to noise ratios percent conversions could not be reliably determined.

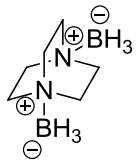


Attempt to synthesize of 1-(4-vinylphenyl)ethanol, 2-43f. The reaction was carried out according to **GPC2** from 1-(4-vinylphenyl)ethanone (109.8 mg, 0.751 mmol), HBpin (120 μL, 0.825 mmol), $B(C_6F_5)_3$ (19.8 mg, 38.7 μmol), DABCO (4.6 mg, 41.0 μmol) in $PhCF_3$ (1.5 mL). After 48 h an aliquot was taken from the reaction, product formation was observed in trace quantities by ^{1}H NMR spectroscopy. Product formation confirmed by ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.49 (d, $^{3}J_{H,H}$ = 6.6 Hz, 3H), 4.72 (q, $^{3}J_{H,H}$ = 6.5 Hz, 1H). Due to high signal to noise ratios percent conversions could not be reliably determined.



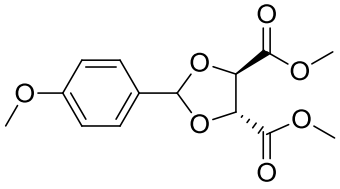
5.1.7 Miscellaneous Compounds

Synthesis of 1,4-diazabicyclo[2.2.2]octane-1,4-diium-1,4-diylditrihydroborate.



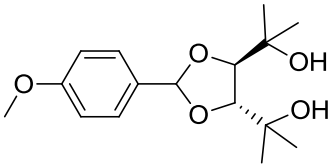
To a solution of DABCO (280 mg, 2.5 mmol) in THF (5 mL) in a Schlenk flask equipped with a magnetic stir bar which was cooled to 0℃ with an ice bath was added BH_3•THF (1.0M, 5 mL, 5 mmol). The mixture was allowed to warm to ambient temperature and stir overnight. Organic volatiles were removed *in vacuo* and filtration produced a white crystalline solid in 95% yield (332 mg, 2.37 mmol). ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 2.84 (s, 12H); ^{11}B NMR (CD_2Cl_2, 128 MHz) δ –11.4 (q, $^1J_{B,H}$ = 94.4 Hz).

Synthesis of (4R,5R)-dimethyl 2-(4-methoxyphenyl)-1,3-dioxolane-4,5-dicarboxylate, 4-3.[33]



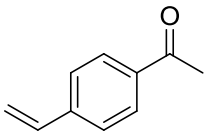
A 500 mL round bottom flask equipped with a magnetic stir bar, Dean-Stark trap, and reflux condenser was removed from the oven, cooled under vacuum, and back-filled with Ar. Toluene (100 mL), dimethyl-L-tartarate (9.98 g, 56 mmol), anisaldehyde dimethyl acetal (10.2 mL, 60 mmol), and *p*-toluenesulfonic acid monohydrate (0.2 mol%, 21 mg, 0.112 mmol) were introduced into the reaction flask under a stream of Ar. The mixture was stirred at reflux for 4 h. The reaction mixture was filtered through celite, volatile organics were evaporated to a white solid. Recrystallization from petroleum ether and diethyl ether yielded a white solid in 86% yield (14.2 g, 47.9 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 3H), 3.84 (s, 3H), 3.87 (s, 3H), 4.85 (d, $^3J_{H,H}$ = 4.0 Hz, 1H), 4.97 (d, $^3J_{H,H}$ = 4.0 Hz, 1H), 6.11 (s, 1H), 6.93 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 7.52 (d, $^3J_{H,H}$ = 8.7 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 52.8, 55.2, 76.9, 77.3, 106.7, 113.7, 127.3, 128.7, 160.9, 169.5, 170.1; CAS 130874-90-7.

Synthesis of 2,2'-((4R,5R)-2-(4-methoxyphenyl)-1,3-dioxolane-4,5-diyl)bis(propan-2-ol), 4-4.[34] A 500 mL 2-neck round bottom flask equipped with a magnetic stir bar and reflux condenser was



removed from the oven, cooled under vacuum, and back-filled with Ar. Magnesium turnings (2.35 g, 96.6 mmol) were removed from the oven and added to the round bottom flask. To the magnesium turnings was added diethyl ether (100 mL) and methyl iodide (4.00 mL, 64.4 mmol) via syringe. Gentle heating initiated Grignard formation and the reaction was stirred for 45 min. To an ice cooled solution of **4-3** (4.15 g, 14 mmol) in diethyl ether (50 mL) at 0℃ was slowly added the freshly manufactured Grignard reagent via cannula. The reaction was slowly warmed to ambient temperature and allowed to stir for 6 h. Aqueous NH_4Cl (150 mL) was added to quench the reaction. Organics extracted with diethyl ether (3x), washed with $NaHCO_3$, dried with $MgSO_4$. Removal of volatiles *in vacuo* resulted in a white solid. Purification by flash chromatography (4:1 Hexanes/ EtOAc) yielded a white solid in 84% yield (3.49 g, 11.8 mmol). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32 (app. s, 6H), 1.35 (s, 3H), 1.38 (s, 3H), 2.47 (br. s, 1H), 2.61 (br. s, 1H), 3.83 (s, 3H), 4.02 (d, $^3J_{H,H}$ = 5.5 Hz, 1H), 4.11 (d, $^3J_{H,H}$ = 5.5 Hz, 1H), 6.02 (s, 1H), 6.93 (d, $^3J_{H,H}$ = 8.7 Hz, 2H), 7.44 (d, $^3J_{H,H}$ = 8.7 Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 25.4, 25.6, 27.3, 28.1, 55.3, 71.0, 72.5, 83.4, 83.7, 104.4, 113.9, 128.1, 129.9, 160.5.

Synthesis of 1-(4-vinylphenyl)ethanone.[35] To an oven dried, vacuum cooled 125 mL Schlenk bomb equipped with a magnetic stir bar was added



palladium dichloride bis-(*tri-o*-tolyl)phosphine (1 mol%, 20 mg, 25.4 μmol), *tri-o*-tolylphosphine (4 mol%, 31 mg, 0.102 mmol), tetrabutylammonium bromide (20 mol%, 162 mg, 0.503 mol), and *para*-bromoacetophenone (500 mg, 2.54 mmol) under a stream of Ar. Dissolution of these compounds of DMF (12.5 mL) was followed by injection of 500 ppm H_2O (6.25 μL) and triethyl amine (1.5 eq., 0.525 mL, 3.76 mmol). The reaction mixture was subjected

to three freeze-pump-thaw cycles followed by addition of trimethyl vinyl silane (1.5 eq., 0.515 mL, 3.51 mmol). The reaction was heated to 120℃ for 48 h. The reaction was cooled to ambient temperature and diluted in aqueous $NaHCO_3$ (15 mL). Organics extracted with ethyl acetate (3x), dried with $MgSO_4$, filtered, and volatiles removed *in vacuo*. ^{1}H NMR spectroscopy indicated that protodesilylation was incomplete after workup. Thus, the reaction was stirred in tetrabutylammonium fluoride hydrate (1.05g, 4 mmol) in wet THF (50 mL) overnight. After addition of H_2O (25 mL), the reaction mixture was transferred to a separation funnel. Organics extracted with ethyl acetate (3x), dried with $MgSO_4$, filtered, and volatiles were removed *in vacuo*. The desired product was isolated by column chromatography (silica gel, 10:1 hexanes/ethyl acetate) as a colourless oil in 82% yield (304 mg, 2.08 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.60 (s, 3H), 5.40 (d, $^3J_{H,H}$ = 10.9 Hz, 1H), 5.91 (d, $^3J_{H,H}$ = 17.6 Hz, 1H), 6.77 (dd, $^3J_{H,H}$ = 17.6 Hz, 10.9 Hz, 1H), 7.50 (d, $^3J_{H,H}$ = 8.6 Hz, 2H), 7.91 (d, $^3J_{H,H}$ = 8.6 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 26.8, 116.9, 126.4, 128.6, 128.8, 136.0, 136.5, 142.4, 197.8; CAS 10537-63-0.

5.1.8 Procedures for Mechanistic Experiments

General comments: All NMR rate experiments were performed on a Bruker Avance 500 (^{1}H: 400.19, ^{11}B: 160.27, ^{13}C: 125.62; BBFO). Prior to commencing and following each experiment the internal sample temperature was externally verified with a pure sample of ethylene glycol. In all experiments, mesitylene was used as an internal standard. Data from HBpin experiments are shown to approximately 50% conversion and are shown to approximately 30% for DBpin experiments. Data analysis was performed using Microsoft Excel 2007; linear regression error analysis was performed using the Data Analysis Tool pack.

Deuterium incorporation values from deuterium labeling experiments were corrected for HBpin impurities in DBPin. All relevant spectra can be found in Appendix A.

Sample calculations for NMR conversions and calorimetric experimental data manipulation can be found in Appendix B.

*General procedure for **3-1** catalyzed, NMR monitored rate experiments:* A clean, oven dried J. Young tube was taken into an inert N_2 filled, dry glove box. $B(C_6F_5)_3$ (9.6 mg, 18.75 μmol, 7.5 mol%), DABCO (2.1 mg, 18.75 μmol, 7.5 mol%), and **3-3** (67.8 mg, 0.25 mmol) were weighed out in clean, new GC vials. $B(C_6F_5)_3$ and DABCO were dissolved in $PhCF_3$ and transferred to the J. Young tube in that order. A white precipitate was immediately observed. The tube was then submerged in a liquid nitrogen cooled cold well until the catalyst layer was frozen. HBpin (40.0 μL, 0.275 mmol) and mesitylene (14.0 μL, 0.1 mmol) were added to the J. Young tube via Eppendorf pipette and allowed to freeze in the cold well. Lastly, **3-3** was dissolved in $PhCF_3$ and transferred to the J. Young tube. Once the final layer was frozen the NMR tube was quickly removed from the glove box and immediately placed in a dry ice acetone bath. The reaction tube and bath were carried to a 500 MHz spectrometer and the spectrometer was heated to a controlled temperature (ca. 304 K) and spectra were collected at rigorously controlled intervals and the amount of formed product was calculated.

*General procedure for **3-2** catalyzed, NMR monitored rate experiments:* A clean, oven dried, J. Young tube was taken into an inert N_2 filled, dry glove box. **3-2** (17.2 mg, 18.75 μmol, 7.5 mol%,) and **3-3** (67.8 mg, 0.25 mmol) were weighed out in clean, new GC vials. **3-2** was dissolved in $PhCF_3$ and transferred to the J. Young tube. The tube was then submerged in a liquid nitrogen cooled cold well until the catalyst layer was frozen. HBpin (40.0 μL, 0.275 mmol) and mesitylene (14.0 μL, 0.1 mmol) were added to the J. Young tube via Eppendorf pipette and allowed to freeze in the cold well. Lastly, **3-2** was dissolved in $PhCF_3$ and transferred to the J. Young tube. Once the final layer was frozen the NMR tube was quickly removed from the glove

box and immediately placed in a dry ice acetone bath. The reaction tube and bath were carried to a 500 MHz spectrometer and the spectrometer was heated to a controlled temperature (ca. 304 K) and spectra were collected at rigorously controlled intervals and the amount of formed product was calculated.

*General procedure for **3-2** catalyzed, NMR monitored rate experiments with **D_1**-pinacol borane:* A clean, oven dried, J. Young tube was taken into an inert N_2 filled, dry glovebox. **3-2** (17.3 mg, 18.75 μmol, 7.5 mol%), DBpin (35.5 mg, 0.275 mmol), and **3-3** (67.8 mg, 0.25 mmol) were weighed out in clean, new GC vials. **3-2** was dissolved in $PhCF_3$ and transferred to the J. Young tube. The tube was then submerged in a liquid nitrogen cooled cold well until the catalyst layer was frozen. DBpin was diluted in a minimal amount of $PhCF_3$ and transferred to the J. Young tube. Subsequently, mesitylene (14.0 μL, 0.1 mmol) was added to the J. Young tube via Eppendorf pipette and allowed to freeze in the cold well. Lastly, **3-3** was dissolved in $PhCF_3$ and transferred to the J. Young tube. Once the final layer was frozen the NMR tube was quickly removed from the glove box and immediately placed in a dry ice acetone bath. The reaction tube and bath were carried to a 500 MHz spectrometer and the spectrometer was heated to a controlled temperature (ca. 304 K) and spectra were collected at rigorously controlled intervals.

General Procedure for stoichiometric [DABCO/$B(C_6F_5)_3$] experiments: At ambient temperature in a N_2 filled glove box a clean, **3-1** was oven dried J. Young tube was charged with a solution of $B(C_6F_5)_3$ (126.9 mg, 0.25 mmol) in $PhCF_3$. DABCO (27.0 mg, 0.25 mmol) was weighed into a clean, new GC vial and added to the J. Young tube as a solution in $PhCF_3$. A white precipitate was immediately observed. Addition of HBpin (36.5 μL, 0.25 mmol) via Eppendorf pipette facilitated homogenization of the reaction mixture after ca. 3 min of shaking. **3-3** (67.8 mg, 0.25 mmol) was weighed out in a clean, new GC vial and added to the *in situ*

generated borenium hydridoborate salt **3-1** as a solution in $PhCF_3$. ^{11}B, ^{1}H, and ^{13}C data was collected periodically over a period of 4 h. Only trace amounts of **3-4** is formed over the course of 4 h indicating **3-1** to be a slow reducing agent compared to the catalytic systems **3-1** or **3-2** with HBpin.

Procedure for borenium formation reversibility experiments: At ambient temperature in a N_2 filled glove box a clean, oven dried J. Young tube was charged with a solution of $B(C_6F_5)_3$ (51.2 mg, 0.10 mmol) in $PhCF_3$. DABCO (11.2 mg, 0.10 mmol) was weighed into a clean, new GC vial and added to the J. Young tube as a solution in $PhCF_3$. A white precipitate was immediately observed. Addition of d_1-pinacol borane (DBpin, 12.3 mg, 0.10 mmol) via pipette facilitated homogenization of the reaction mixture after ca. 3 min of shaking. ^{11}B and ^{2}H NMR data indicated clean formation of **3-1-[d_1]**. Subsequent addition of 10 eq. of HBpin (128.0 mg, 1.0 mmol) followed by ^{11}B NMR monitoring indicated no appreciable formation of **3-1**. After 1 h complete decomposition of the borenium (DABCO-$B(pin)^+$) and HBpin are observed.

Following the same procedure **3-1** was synthesized using $B(C_6F_5)_3$ (12.7 mg, 0.025 mmol), DABCO (2.8 mg, 0.025 mmol), and HBpin (3.5 mg, 0.027 mmol) in $PhCF_3$. ^{11}B and ^{1}H NMR data indicated clean formation of **3-1**. Subsequent addition of 10 eq. of DBpin (32.2 mg, 0.25 mmol) followed by ^{11}B and ^{1}H NMR monitoring indicated no appreciable formation of **3-1-[d_1]**.

Procedure for deuterium labeling experiments: At ambient temperature in a N_2 filled glove box a clean, oven dried 20 mL vial was charged with a stirbar and a solution of $B(C_6F_5)_3$ (77.0 mg, 0.15 mmol) in $PhCF_3$. DABCO (17.1 mg, 0.15 mmol) was weighed into a clean, new GC vial, dissolved in $PhCF_3$ and added to the solution of $B(C_6F_5)_3$ via pipette. A white precipitate was immediately observed. Addition of DBpin (20.0 mg, 0.15 mmol) via pipette facilitated

homogenization of the reaction mixture after ca. 3 min of stirring. The reaction was stirred for an additional 10 min before a solution of **3-3** (204.1 mg, 0.75 mmol) and HBpin (105.6 mg, 0.825 mmol) in $PhCF_3$ was added via pipette to the solution of **3-1-[d_1]**. After 4 h, ^1H and ^{11}B NMR analysis indicated the reaction had gone to completion. The reaction was worked up and purified as described for the synthesis of compound **2-47b** and was isolated in 93% yield (190.8 mg, 0.70 mmol). Spectroscopic data matched that of compound **2-47b**. D1 relaxation time was optimized to 10.65 s for optimal integrations and less than 5% deuterium incorporation was observed.

Following the same deuterium labeling procedure, **3-1** was synthesized using $B(C_6F_5)_3$ (76.6 mg, 0.15 mmol), DABCO (16.7 mg, 0.15 mmol), and HBpin (19.0 mg, 0.15 mmol). The reaction was shaken for ca. 3 min before a solution of **3-3** (203.5 mg, 0.75 mmol) and DBpin (106.4 mg, 0.825 mmol) in $PhCF_3$ was added via pipette to the solution of **3-1**. After 4 h, the reaction was worked up and purified as described for the synthesis of compound **2-47b** and isolated as a clear oil in 91% yield (186 mg, 0.68 mmol). D1 relaxation time was optimized to 10.65 s for optimal integrations. A mixture of deuterated and protonated products were isolated. The amount of protonated product acquired corresponds to full protio incorporation (from residual HBpin in DBpin and $HB(C_6F_5)_3^-$).

General Procedure for Calorimetry experiments: At ambient temperature in a N_2 filled glove box a clean, oven dried 20 mL vial was charged with a stir bar and a solution of **3-3** in $PhCF_3$ (2.2 mL). HBpin was added via Eppendorf pipette and the vial was capped with a penetrable Teflon lid. **3-1** was weighed out in a clean GC vial and dissolved in $PhCF_3$ (0.8 mL). The solution was taken up into a syringe which was capped. A blank vial containing a stir bar and $PhCF_3$ (3 mL) was also prepared. Both vials and the syringe were removed from the glove box and positioned within the calorimeter. Data collection was started and the instrument was allowed

to equilibrate. At this time the catalyst was injected into the mixture of imine and HBpin and the heat flow was monitored as a function of time. Several unique experiments were performed. In each experiment the amount of HBpin, catalyst, and additional Lewis base was varied but the total volume remained constant.

5.2 References

[1] H. E. Gottlieb, V. Kotlyar, A. Nudelman *J. Org. Chem.* **1997**, *62*, 7512.

[2] Bruker Instruments, VT calibration manual.

[3] Guidotti, S.; Camurati, I.; Focante, F.; Angellini, L.; Moscardi, G.; Resconi, L.; Leardini, R.; Nani, D.; Mercandelli, P.; Sironi, A.; Beringhelli, T.; Maggoni, D. *J. Org. Chem.* **2003**, *68*, 5445.

[4] A modification of a literature procedure was used: K. P. Guzen, A. S. Guarezemini, A. T. G. Órfão, R. Cella, C. M. P. Pereira, H. A. Stefani *Tetrahedron Letters* **2007**, *48*, 1845.

[5] A. M. Seayad, B. Ramalingam, K. Yoshinaga, T. Nagata, C. L. L. Chai *Org. Lett.* **2010**, *12*, 264.

[6] O. R. Luca, T. Wang, S. J. Konezny, V. S. Batista, R. H. Crabtree *New J. Chem.*, **2011**, *35*, 998.

[7] Gu, W.; Silverman, R. B. *Org. Lett.* **2003**, *5*, 415.

[8] Troisi, L.; Fabio, M.; Ronzini, L. *Tetrahedron*, **2008**, *64*, 4979.

[9] Chang, X.; Jiang, Y.; Guo, Y.; Zhu, X.; Song, D.; Wang, Y.; Song, X.; Verpoort, F. *Inorg. Chim. Acta* **2011**, *376*, 144.

[10] D. Armesto, M. Ortiz, R. Perez-Ossorio *J. Chem. Soc., Perkin Trans 1* **1986**, *12*, 2021.

[11] H. Naeimi, H. Sharghi, F. Salimi, K. Rabiei *Heteroat. Chem.* **2008**, *19*, 43.

[12] J. Barluenga, A. Jimenez-Aquino, F. Aznar, C. Valdez *J. Am. Chem. Soc.* **2009**, *131*, 4031.

[13] S. Shirai, H. Nara, Y. Kayaki, T. Ikariya *Organometallics* **2009**, *28*, 802.

[14] L. Liu, S. Zhang, X. Fu, C. Yan *Chem. Commun.* **2011**, *47*, 10148.

[15] P. Frøyen, P. Juvvik *Tetrahedron Letters* **1995**, *36*, 9555.

[16] S. Liu, Y. Yang, X. Zhen, J. Li, H. He, J. Feng, A. Whiting *Org. Biomol. Chem.* **2012**, *10*, 663.

[17] Soós, T.; Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G. *Angew. Chem. Int. Ed.* **2010**, *49*, 6559.

[18] Pattarawarapan, M. Rattanaburi, P.; Khumraksa, B. *Tetrahedron Lett.* **2012**, *53*, 2689.

[19] Lam, Y.; Che, J. *Adv. Synth. Catal.* **2010**, *352*, 1752.

[20] V. Kumar, U. Sharma, P. K. Verma, N. Kumar, B. Singh *Adv. Synth. Catal.* **2012**, *354*, 870.

[21] F. Beaumard, G. Molander *Org. Lett.* **2011**, *13*, 1242.

[22] G. Erős, K. Nagy, H. Mehdi, I. Pápai, P. Nagy, P. Király, G. Tárkányi, T. Soós *Chem. Eur. J.* **2012**, *18*, 574.

[23] Van der Kerk, G. J. M.; de Koning, A. J.; Budzelaar, P. H. M.; Boersma, J. *J. Organomet. Chem.* **1980**, *199*, 153.

[24] X. Yang, L. Zhao, T. Fox, Z. Wang, H. Berke *Angew. Chem. Int. Ed.* **2010**, *49*, 2058.

[25] A. R. Katritzky *J. Chem. Soc., Perkin Trans. 1* **1990**, *3*, 667.

[26] P. M. Wehn, J. Du Bois *Org. Lett.* **2005**, *7*, 4685.

[27] H. Kato, I. Shibata, Y. Yasaka, S. Tsunoi, M. Yasuda, A. Baba *Chem. Commun.* **2006**, *40*, 4189.

[28] C. Wang, A. Pettman, J. Bacsa, J. Xiao *Angew. Chem. Int. Ed.* **2010**, *49*, 7548.

[29] R. Shintani, S. Hayashi, M. Murakami, M. Takeda, T. Hayashi *Org. Lett.* **2009**, *11*, 3754.

[30] Shaikh, N. S.; Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem. Int. Ed.*, **2008**, *47*, 2497.

[31] Cheng, C.; Karthikeyan, J.; Jeganmohan, M. *Chem. Eur. J.* **2010**, *16*, 8989.

[32] Magin, R. W.; House, H. O. *J. Org. Chem.* **1963**, *28*, 647.

[33] Pietruszka, J.; Luithle, J. E. A. *J. Org. Chem.* **1999**, *64*, 8287.

[34] Mash, E. A.; Hemperly, S. B.; Nelson, K.; Heidt, P.; Van Deusen, S. *J. Org. Chem.* **1990**, *55*, 2045.

[35] Jesús, E.; Gordillo, A.; Forigua, J.; López-Mardomingo, C. *Organometallics*, **2011**, *30*, 352.

Appendix A

Spectroscopic Data

Spectroscopic Data For Borenium Cations

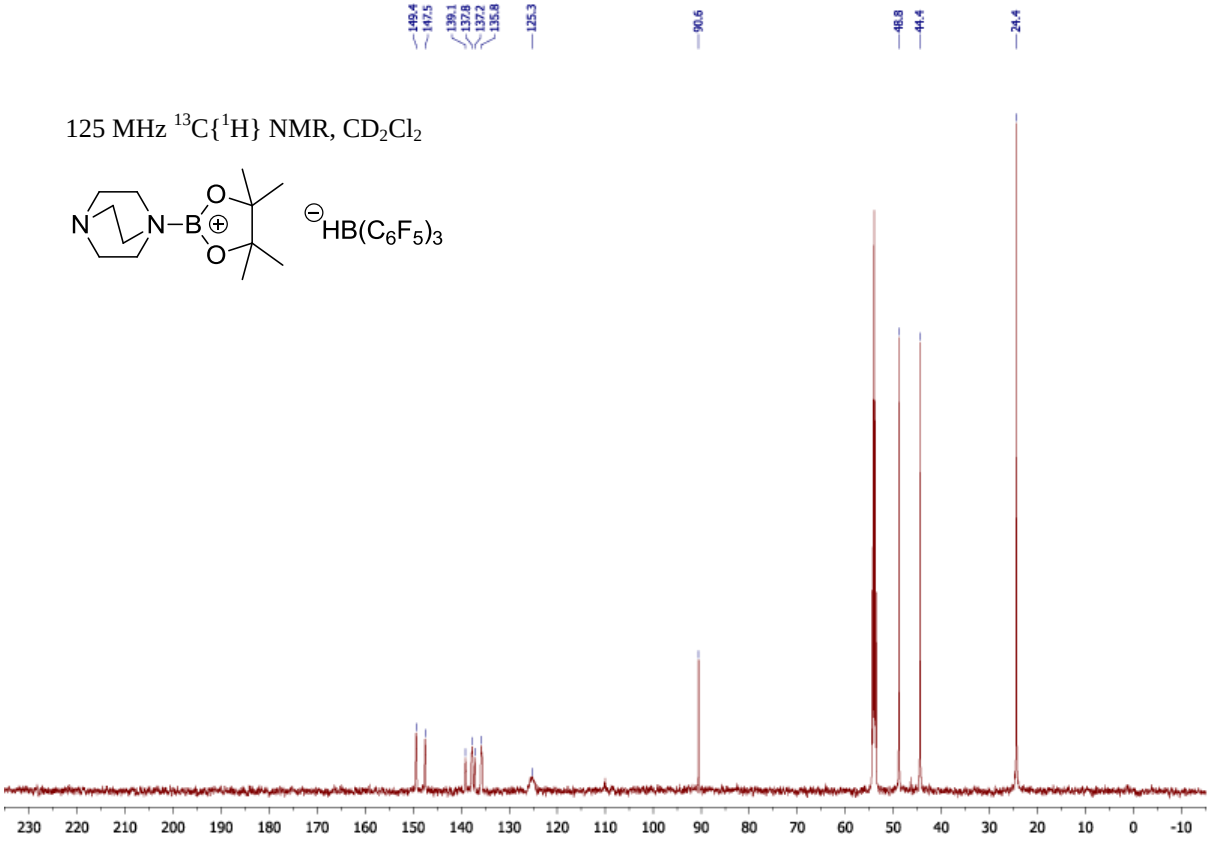


Figure A1-1: ^{13}C NMR spectrum of **2-23** (**3-1**).

469 MHz ^{19}F NMR, CD_2Cl_2

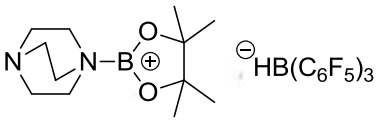
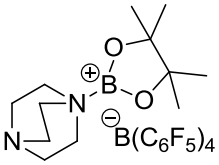


Figure A1-2: ^{19}F NMR spectrum of **2-23** (**3-1**).

100 MHz $^{13}C\{^1H\}$ NMR, $PhCF_3$



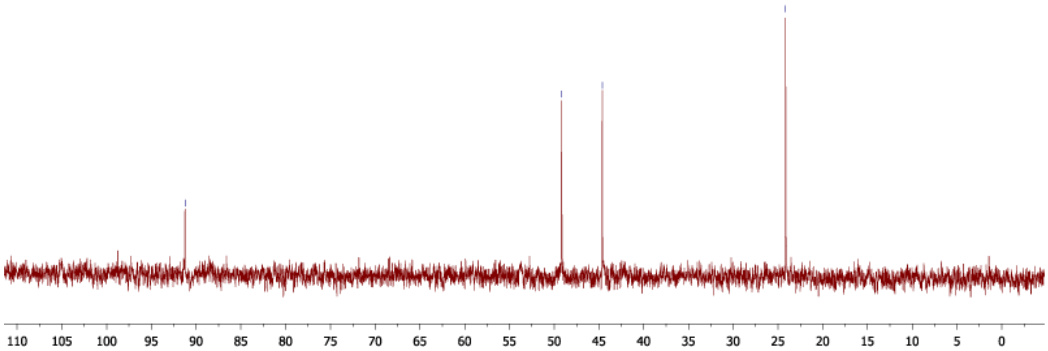
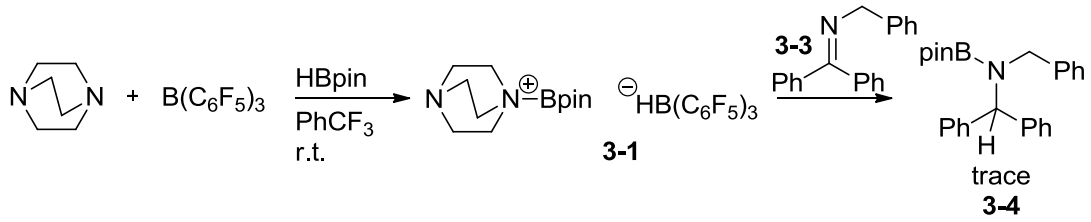


Figure A1-3: $^{13}C\{^1H\}$ NMR spectrum of **2-30** (**3-2**).

Additional Spectroscopic Data for Mechanistic Experiments

Spectroscopic data for the stoichiometric experiment:



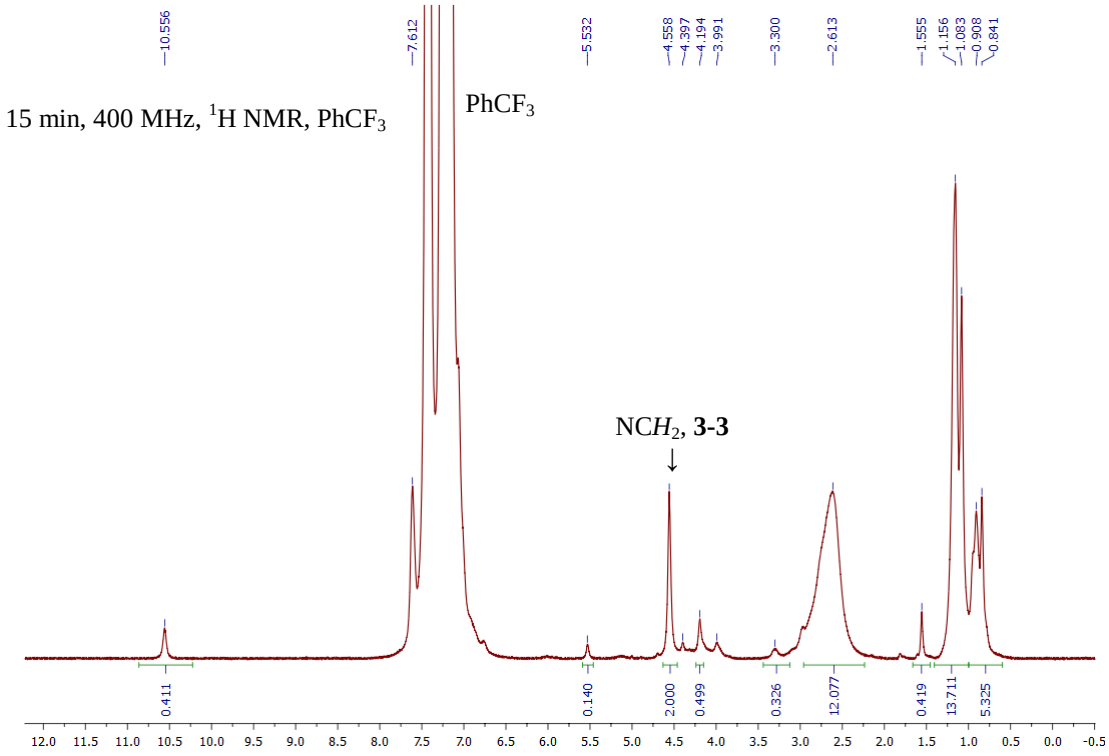


Figure A1-4: ^{1}H NMR spectrum of stoichiometric experiment in $PhCF_3$ using **3-1** at 15 minutes.

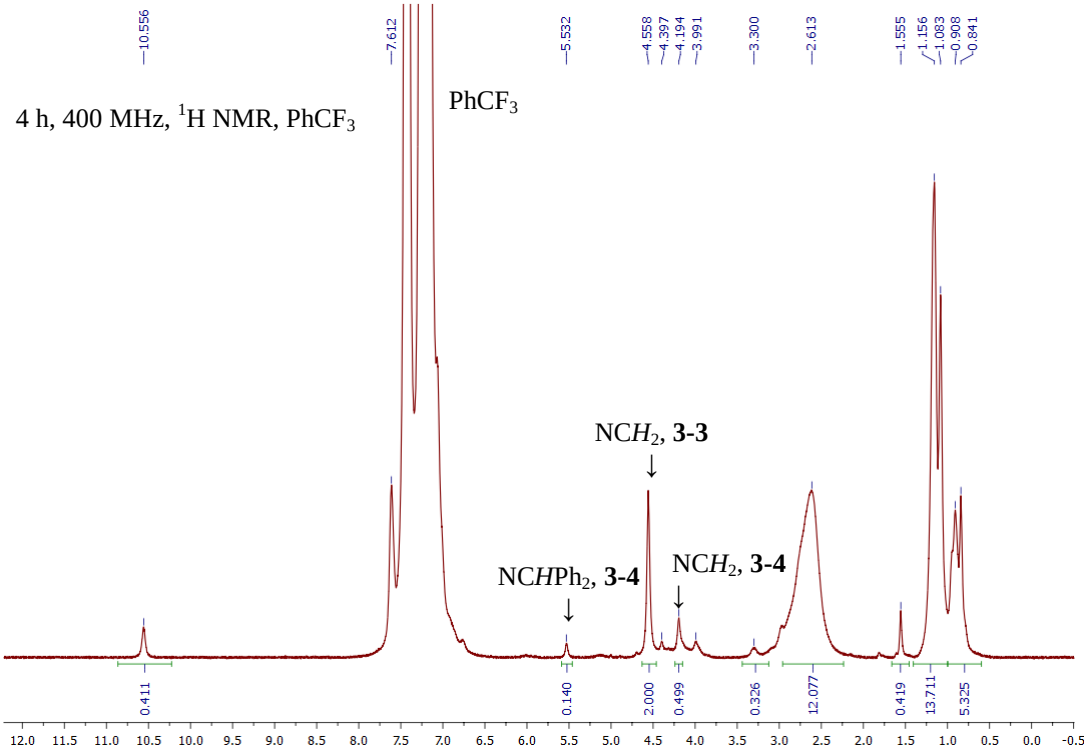


Figure A1-5: ^{1}H NMR of stoichiometric experiment using **3-1** at 4 hours in PhCF$_3$.

Additional spectroscopic data for borenium reversibility experiments

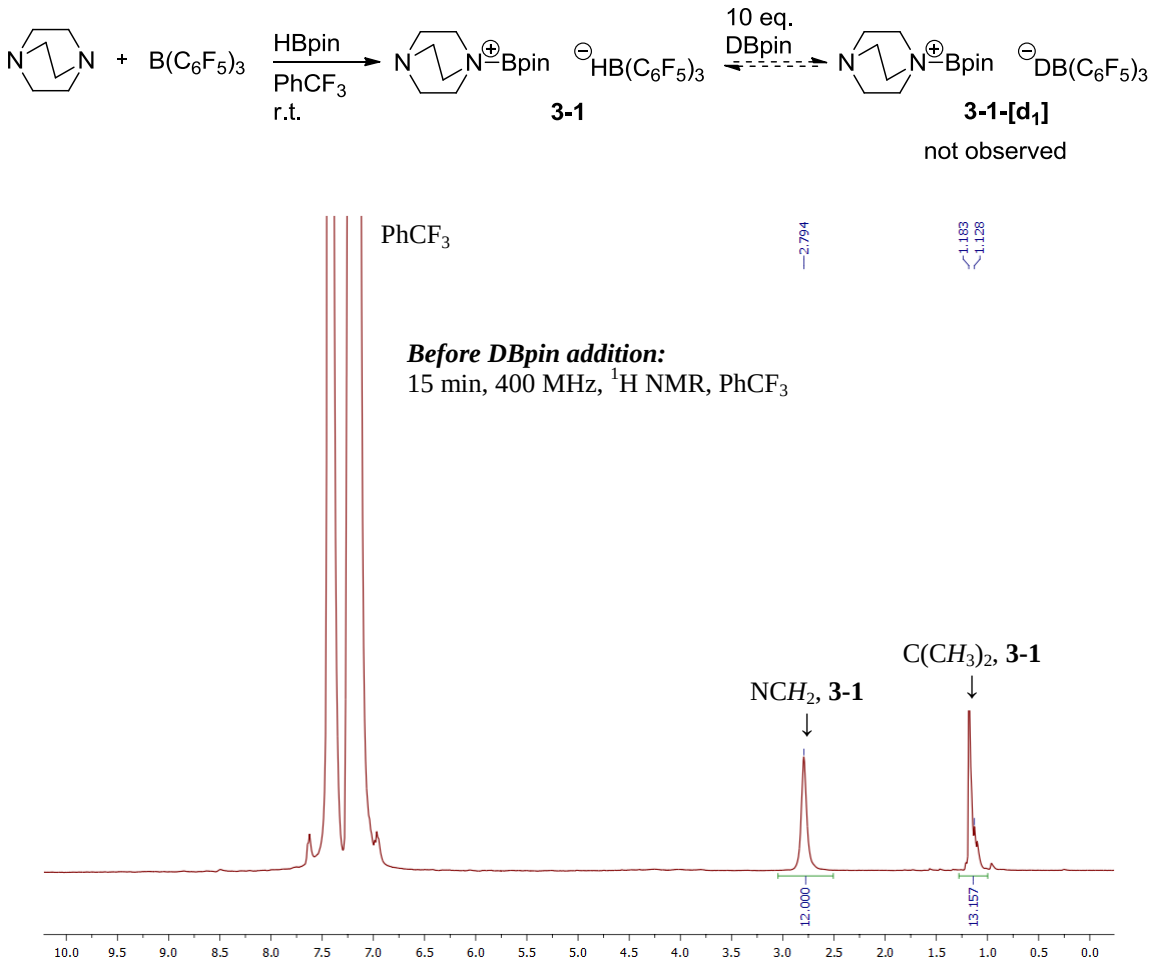


Figure A1-6: ^{1}H NMR spectrum of **3-1-[d$_1$]** before addition of DBpin in $PhCF_3$.

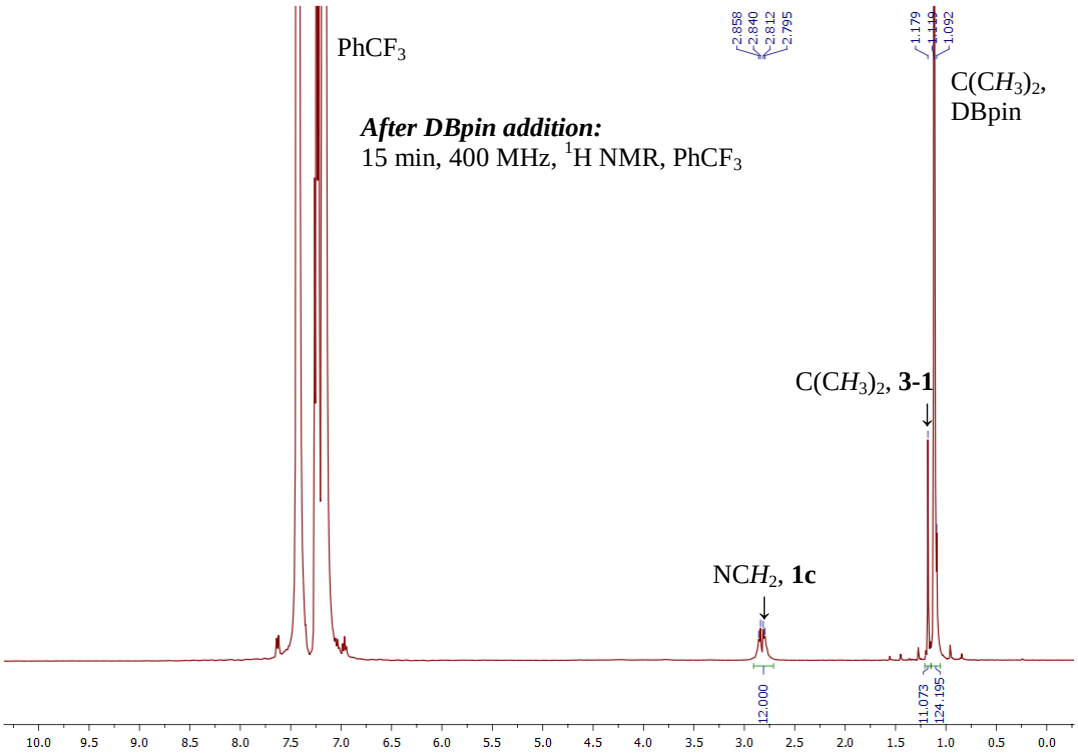
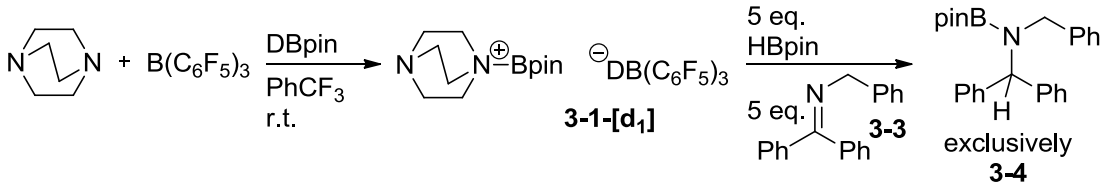


Figure A1-7: ^{1}H NMR spectrum of **3-1-[d$_1$]** 15 minutes after addition of DBpin in $PhCF_3$.

Spectroscopic data for deuterium labeling experiments:



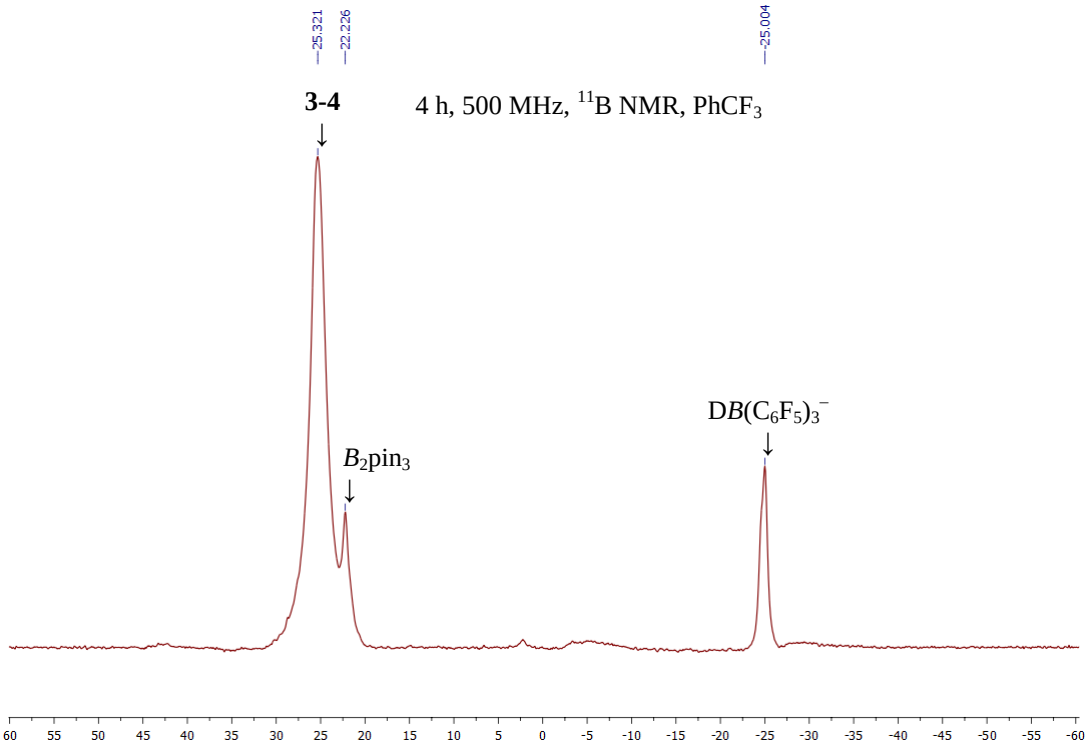


Figure A1-8: ^{11}B NMR of a deuterium labeling experiment after 4 hours.

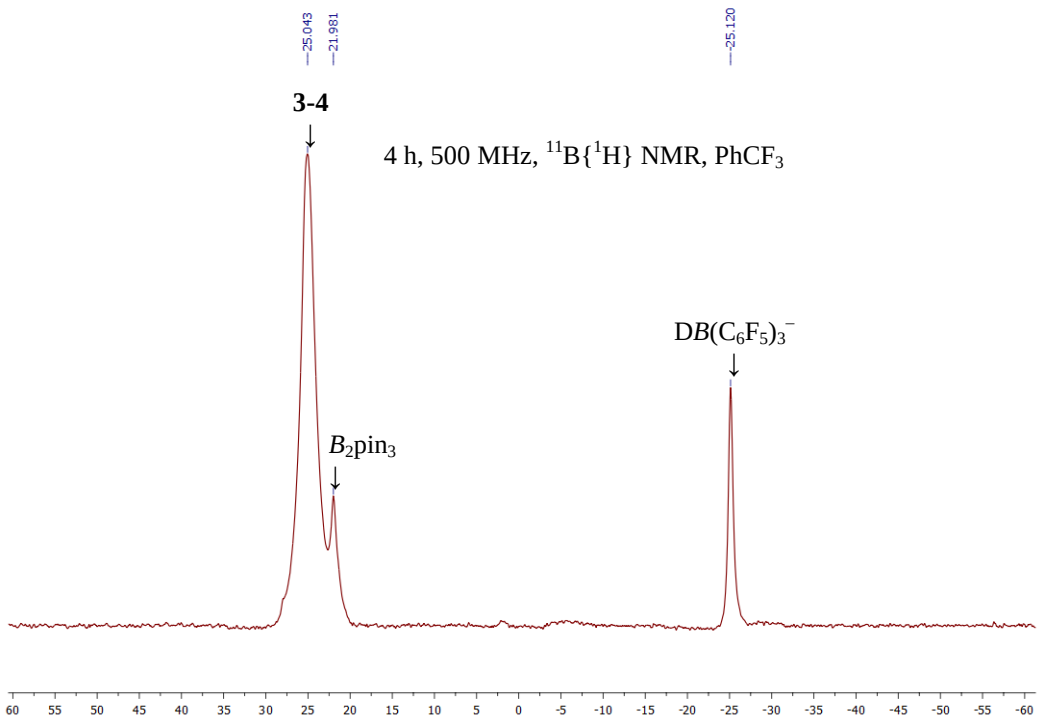


Figure A1-9: $^{11}B\{H\}$ NMR of a deuterium labeling experiment after 4 hours.

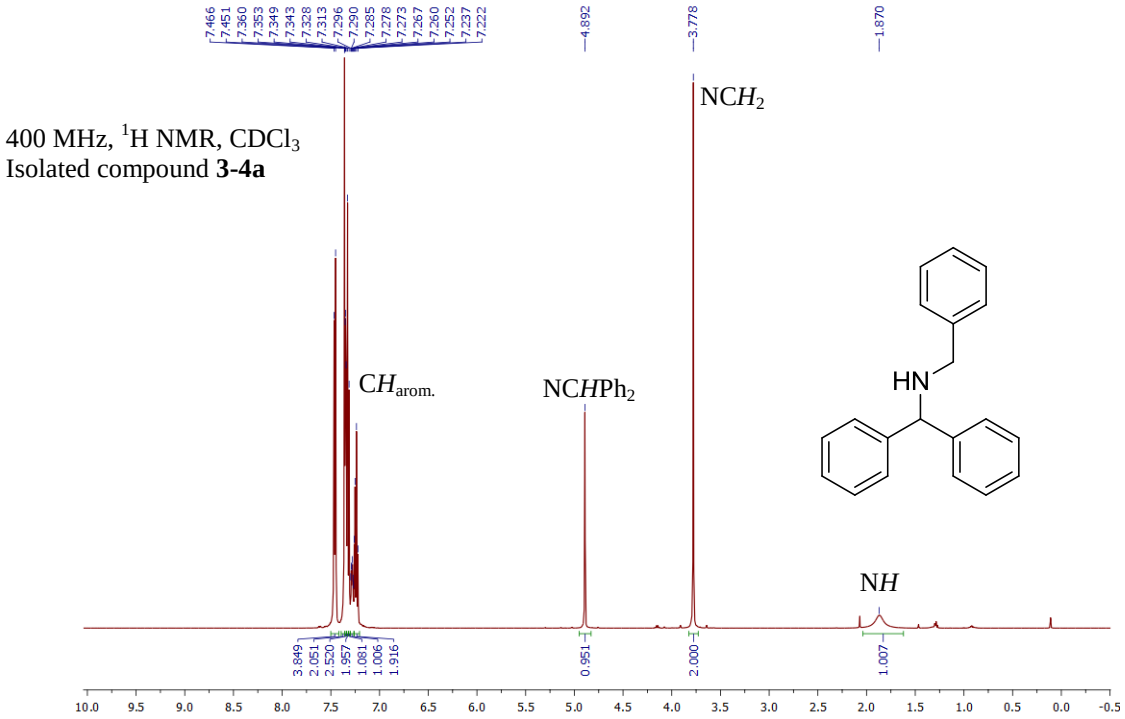


Figure A1-6: ^{1}H NMR spectrum of **3-4a** after purification by column chromatography. T_1 relaxation time was optimized to 10.65 s.

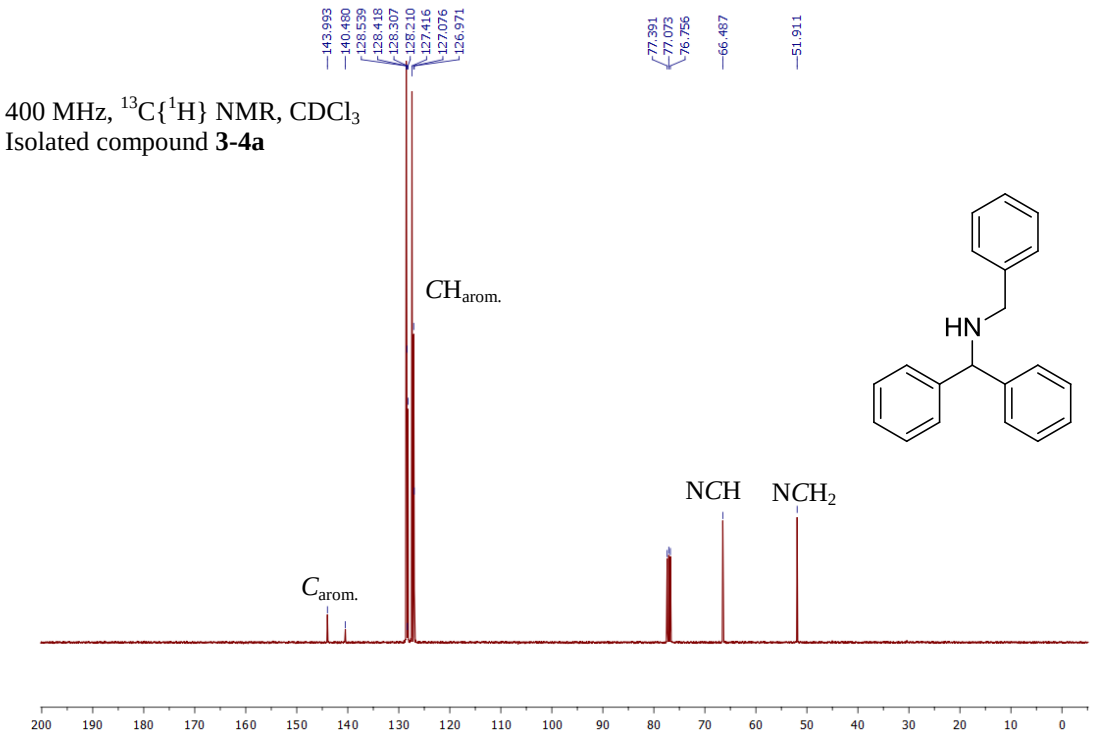
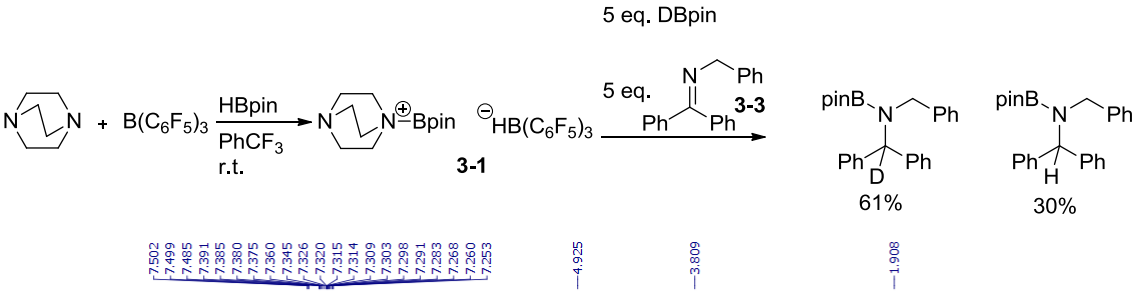


Figure A1-7: $^{13}C\{^{1}H\}$ NMR spectrum of **3-4a** after purification by column chromatography.



500 MHz, ^{1}H NMR, $CDCl_3$
Isolated compound **3-4a** and **3-4a-[d$_1$]**

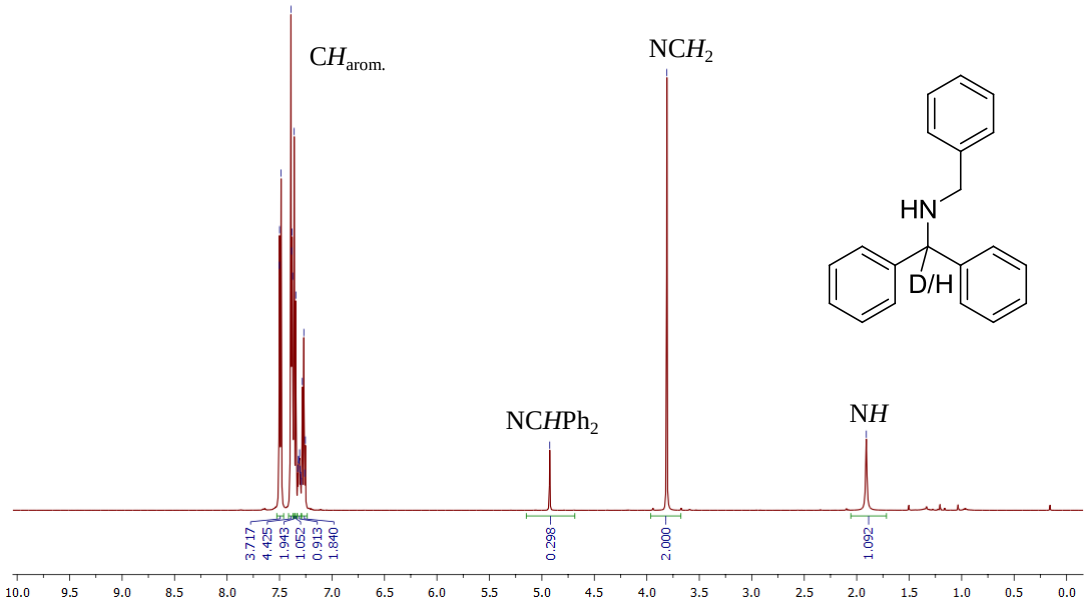


Figure A1-8: ^{1}H NMR spectrum of a mixture of **3-4a** and **3-4a-[d$_1$]** after purification by column chromatography. T relaxation time was optimized to 10.65 s.

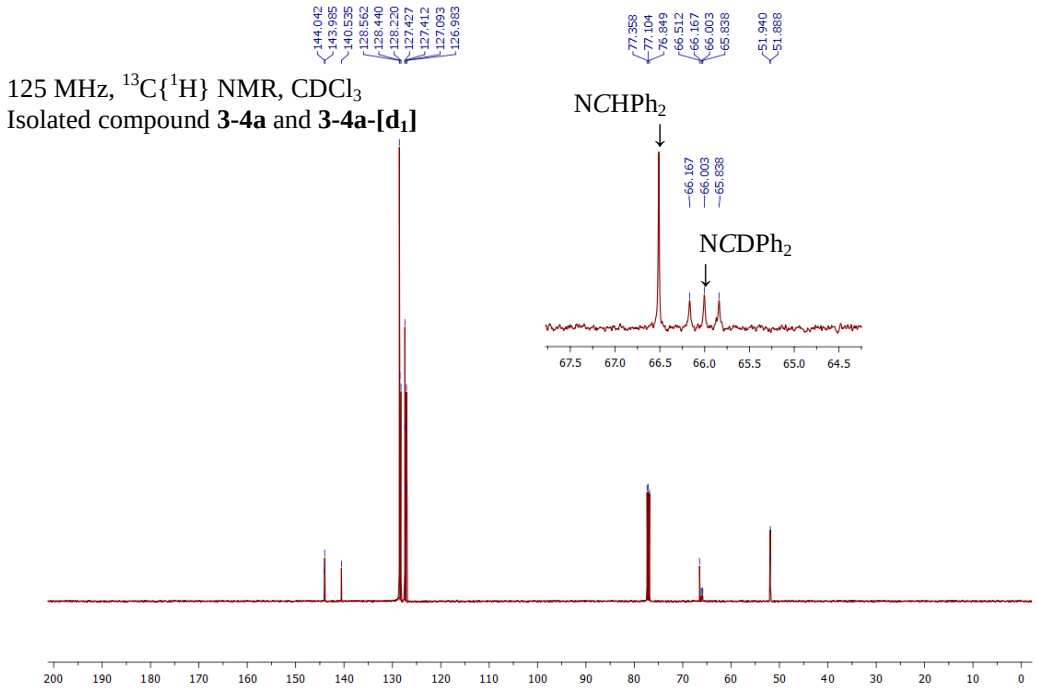


Figure A1-9: $^{13}C\{^{1}H\}$ NMR spectrum of a mixture of **3-4a** and **3-4a-[d$_1$]** after purification by column chromatography.

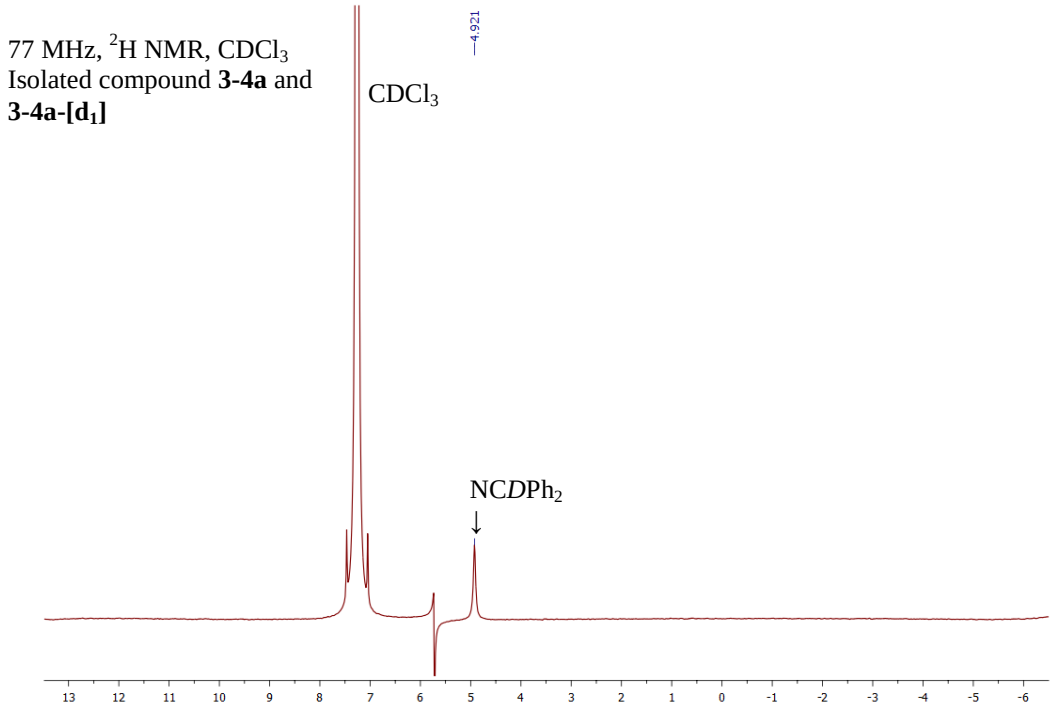
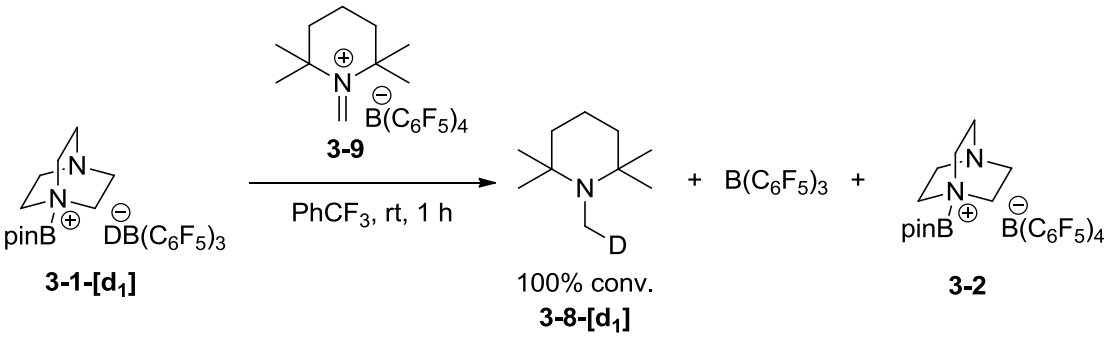


Figure A1-14: ^{2}H NMR spectrum of a mixture of **3-4a** and **3-4a-[d$_1$]** after purification by column chromatography.



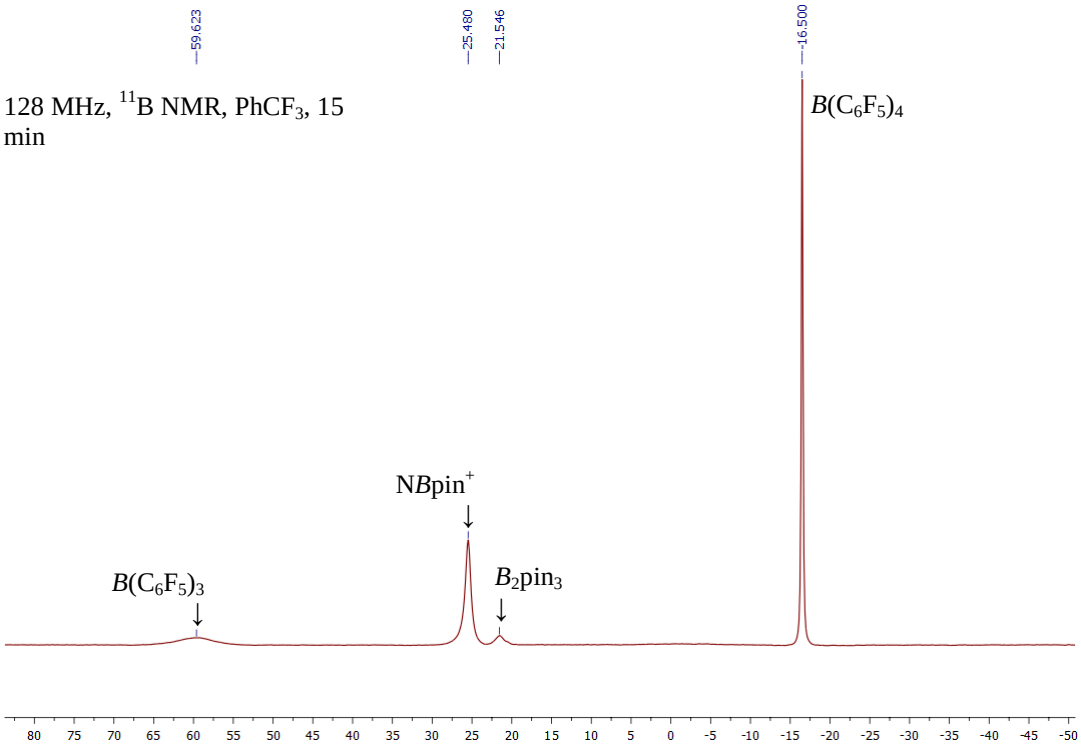


Figure A1-15: ^{11}B NMR spectrum of the reaction of **3-9** with **3-1-[d$_1$]**.

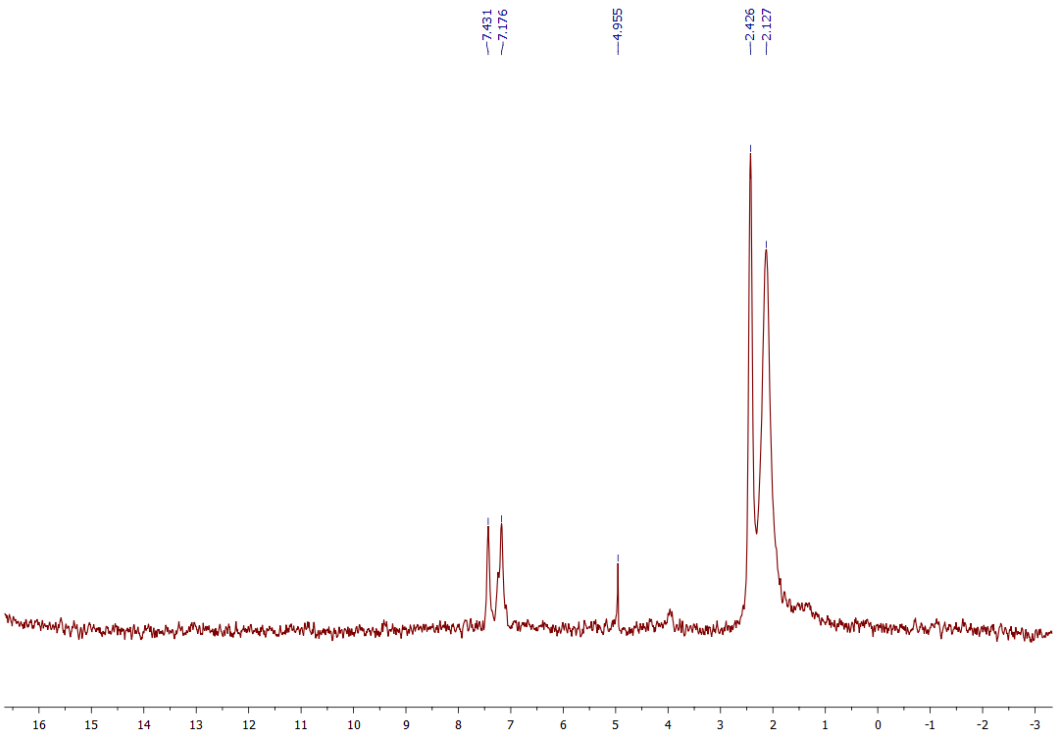


Figure A1-16: ^{2}H NMR spectrum of the reaction of **3-9** with **3-1-[d$_1$]**.

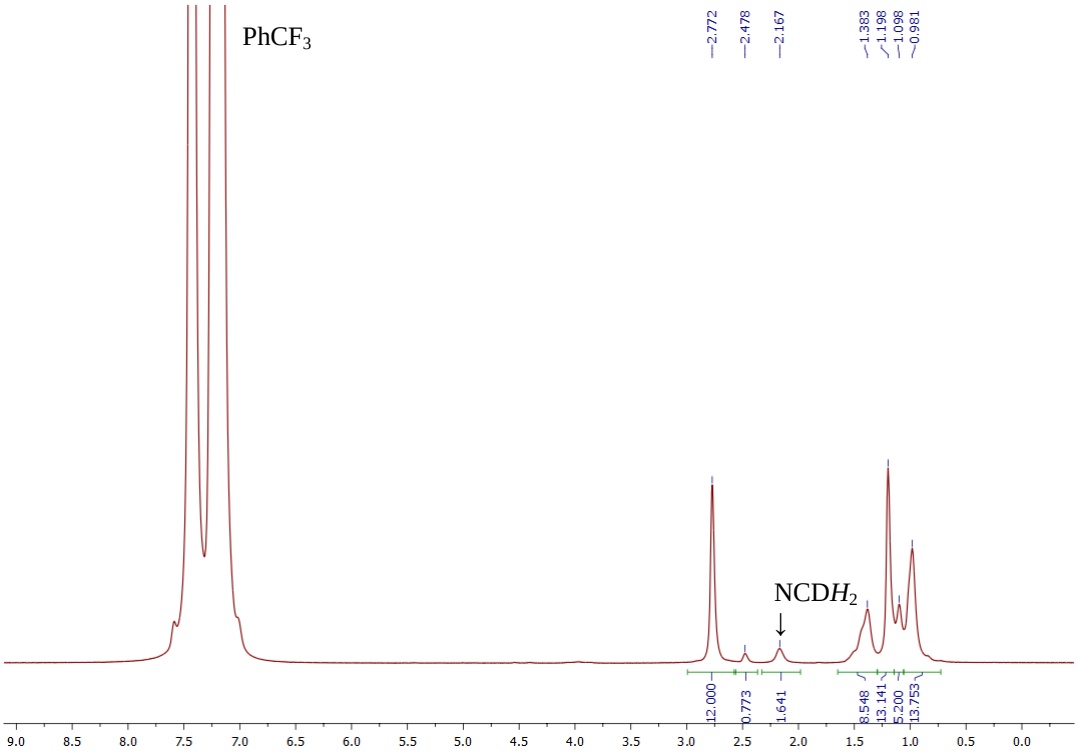


Figure A1-17: ^{1}H NMR spectrum of the reaction of **3-9** with **3-1-[d$_1$]** in $PhCF_3$.

Appendix B

Sample Calculations

NMR Kinetic Analysis

The rate of a chemical reaction can be dependent upon the concentration of each component of a reaction. However, making simple assumptions simplifies the overall rate equation into manageable terms. In order to evaluate the initial rate of reaction for borenium cation catalyzed hydroboration reactions the rate of formation of product was monitored by ^{1}H NMR spectroscopy.

Assuming a first order rate of reaction dependent upon the concentration of imine allows writing a rate equation in the form of Eq. B1-1, where k_{obs} is the observed rate constant, $[I]_0$ is the initial concentration of imine starting material, and $[I]_t$ is the concentration of imine starting material at time *t*.

$$\partial[I]_t/\partial t = -k_{obs}[I]_t \qquad \text{(Eq. B1-1)}$$

Solving the first order homogeneous differential equation for *t* yields the first order integral rate law (Eq. B1-2),

$$\ln[I]_t = -k_{obs}t + \ln[I]_0 \qquad \text{(Eq. B1-2)}$$

Which can be rewritten in the form of Eq. B1-3.

$$\ln [I]_0/[I]_t = k_{obs}t \qquad \text{(Eq. B1-3)}$$

The concentration of imine at time *t* is equal to $[I]_0 - [P]_t$. Therefore, this equation may be rewritten as,

$$\ln {[I]_0}/{[I]_0 - [P]_t} = k_{obs}t \qquad \text{(Eq. B1-4)}$$

By collecting a ^{1}H NMR spectrum at regular intervals and monitoring the formation of product (in terms of its concentration). One can create a plot which will be linear for initial conversions and become asymptotic at high conversions. Performing a linear regression on the early regime of this plot and by setting the intercept equal to zero, a quantitative observed rate constant can be calculated.

The concentration of product at any time *t* may be written as Eq. B1-5, where $[P]_t$ is the concentration of product at time *t*, I_p is the integral of the product peak, I_s is the concentration of the internal standard, P_s is the number of protons in the standard peak, and P_p is the number of protons in the product peak.

$$[P]_t = I_p * [I]_s * {P_s}/{P_p} \qquad \text{(Eq. B1-5)}$$

Therefore to calculate the rate at any time *t* one must know the initial concentration of imine, the concentration of internal standard, the integral of the product peak, and the ratio of product to standard. The initial concentration of imine was 0.25 M for all reactions. The time was monitored by stopwatch and NMR spectra were collected at defined margins. The concentration of internal standard was 0.1 M for all reactions. Thus, calculating $[I]_t$ as outlined and plotting $\ln [I]_0/[I]_t$ vs. *t* for low conversions yielded the figures shown in Chapter 3. The errors given are standard errors of the mean (the standard deviation divided by the number of trials).

Calorimetric Analysis

The heat of reaction (ΔH_{rxn}) is related to the integral of the heat flow out of a system (q) as a function of time (t) (Eq. B1-6). The calorimeter software (WinCRC Turbo) integrates the area under the heat curve (Figure B1-1) and yields an integrated heat of reaction in joules, which can be converted into kcal/mol by a standard SI conversion and knowledge that 0.75 mmol of substrate was used in the reaction.

$$\Delta H_{rxn} = \int_{t_0}^{t_f} q\, dt \qquad \text{(Eq. B1-6)}$$

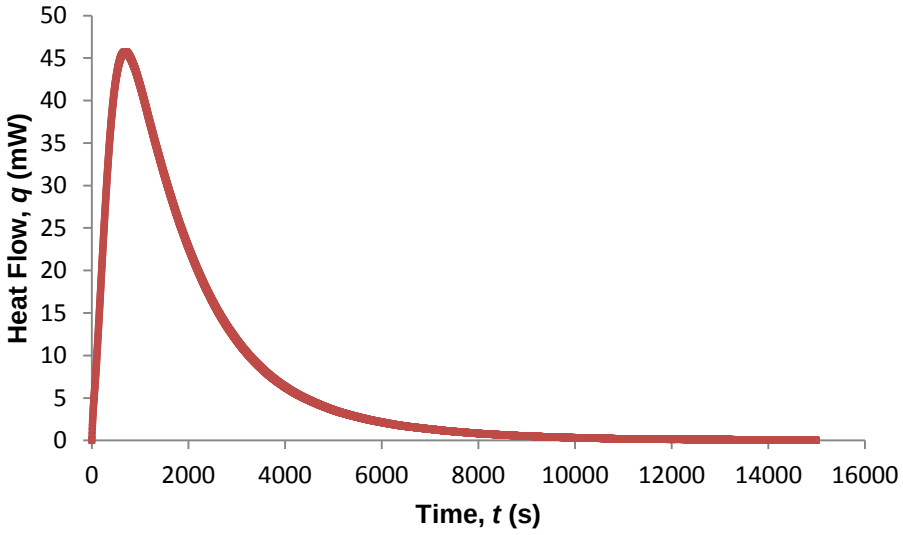


Figure B1-1: A general heat flow curve for a borenium catatlyzed hydroboration reaction.

The order of catalyst and HBpin were determined by performing a linear analysis on the linear regime of this heat flow curve to generate an initial rate of reaction. The first 5 % conversion was not included due to a sensory delay which is a systematic error caused by the apparatus. Performing the reaction with varying concentrations of borenium catalyst and HBpin and determining the initial rates in the same way enabled the qualitative analysis discussed in Chapter 3.

Determining the percent conversion of a reaction based on the heat flow curve is not a trivial task. In its simplest form, the relationship between heat flow and rate of a reaction can be written as Eq. B1-7, where *V* is the total volume of the reaction and *k* is the rate of reaction.

$$\partial q/_{\partial t} = \Delta H_{rxn} * V * k \qquad \text{(Eq. B1-7)}$$

The first principles derivation of this equation is beyond the scope of this report but it can be found in most intermediate physical chemistry textbooks (Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry, 3rd Ed.* **1987**, Harper Collins, New York.). From this equation the percent conversion at time *t* can be found through a ratio between the heat flow at time *t* and the total heat flow. This is shown mathematically in Eq. B1-8, where t_f is the time at the end of the reaction.

$$\%\ \text{conversion} = \int_{t=0}^{t=t} q(t)\mathrm{d}(t) \Big/ \int_{t=0}^{t=t_f} q(t)\mathrm{d}(t) \qquad \text{(Eq. B1-8)}$$

This approach was used to determine the percent conversion for the Lewis base dependancies.