New Reactions with N-Heterocyclic Carbene Boranes and Amidine Boranes, and the Study of Initiators in the Radical Hydrostannation of Propargyl Silyl Ethers

by

Timothy R. McFadden

B. S. in Chemistry with Honors, The Pennsylvania State University, 2010

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This dissertation was presented

by

Timothy R. McFadden

It was defended on

December 22, 2017

and approved by

Jan Beumer, Associate Professor, School of Pharmacy

Kazunori Koide, Associate Professor, Department of Chemistry

Peter Wipf, Distinguished University Professor, Department of Chemistry

Committee Chair: Dennis P. Curran, Distinguished Service Professor and Bayer Professor, Department of Chemistry

New Reactions with N-Heterocyclic Carbene Boranes and Amidine Boranes, and the Study of Initiators in the Radical Hydrostannation of Propargyl Silyl Ethers

Timothy R. McFadden, Ph. D.

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The development of new reactions of *N*-heterocyclic carbene (NHC) boranes and amidine-boranes is described. Additionally, the mechanism of the AIBN- and triethylborane-initiated radical hydrostannation of propargyl silyl ethers is studied.

Chapter 1 describes the reaction of NHC-boranes with dimethyl acetylenedicarboxylate (DMAD) to form alkenylboranes and boriranes. These products arise through formal single and double *trans*-selective hydroborations. The reaction conditions were optimized and applied to produce a small library of NHC-borane derived products. Alkenylboranes were formed as the major product from the reaction of *N,N*-dialkyl NHC-boranes with DMAD, while boriranes were the major product formed from the reactions of *N,N*-diaryl NHC-boranes. Scope and limitation studies were performed to show that borirane-formation is specific to the reaction of NHC-boranes and borohydrides with DMAD. Boriranes were not formed from the reaction of NHC-boranes with any other alkynes or from the reaction of amine-borane complexes with DMAD. Control experiments showed that the products could not be interconverted. The mechanism was probed by deuterium-labeling experiments.

Chapter 2 describes the synthesis and characterization of amidine-boranes. These ligated borane complexes can be prepared in good yield from the reaction of heterocyclic amidines, such as 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) or 1,2-dimethylimidazole, with borane. These complexes are air- and water-stable solids at room temperature and do not decomplex in solution

at elevated temperature. The amidine-boranes are demonstrated to be reactive towards acids and halogens, in addition to being competent aldehyde, ketone, and imine reducing agents. Compared to other ligated boranes, DBU-borane is a more reactive hydride donor.

In Chapter 3, the azobisisobutyronitrile (AIBN)- and triethylborane (Et_3B)/oxygen (O_2)-initiated hydrostannation of propargyl silyl ethers to form alkenylstannanes is studied extensively. When Et_3B/O_2 is used to initiate the reaction, the resulting alkenylstannane is formed with high Z-selectivity, while little selectivity is observed when the reaction is initiated by AIBN. Recent publications asserted that the difference in selectivity is derived from differing reaction mechanisms of the two initiators. The role of initiator, temperature, and reaction time are probed to demonstrate that both AIBN and Et_3B/O_2 initiated the reaction by the same mechanism, but at differing efficiencies, leading to different product ratios.

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LIST OF ABBREVIATIONS

Å	Angstrom
Ac	acetyl
AIBN	azobisisobutyronitrile
Bn	benzyl
br	broad
brsm	based on recovered starting material
Bu	normal butyl
d	doublet
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublets
DFT	density functional theory
diMe	dimethyl
dipp	2,6-diisopropylphenyl
DMAD	dimethyl acetylenedicarboxylate
DMAP	*N,N*-dimethylaminopyridine

DMF	dimethylformamide
DMI	1,3-dimethyl-2-imidazolidinone
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	dimethylsulfoxide
equiv	equivalents
ESI	electrospray ionization
Et	ethyl
FLP	frustrated Lewis pair
g	grams
h	hours
pin	pinacol
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
Imd	imidazole
iPr	isopropyl
IR	infrared
KIE	kinetic isotope effect
LDBB	lithium 4,4'-di-*tert*-butylbiphenylide
M	molarity
m	multiplet
Me	methyl
Mes	mesityl

mg	milligrams
M	mega
min	minutes
mL	milliliters
mmol	millimole
mp	melting point
MWI	microwave irradiation
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
pent	pentet
Ph	phenyl
ppm	part per million
q	quartet
Q-TOF	quadrupole time of flight
R_f	retention factor
rt	room temperature
s	singlet
sept	septet
SMD	solvation model based on density
t	triplet
TBS	*tert*-butyldimethylsilyl
tBu	tertiary butyl
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl

Tf	triflate
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
Ts	tosyl
UV	ultraviolet

PREFACE

This thesis is the culmination of my graduate studies at the University of Pittsburgh. During my time here, I have had the great fortune to work with a number of high-quality individuals who contributed to my development as a chemist. I would like to thank them here.

First and foremost, I would like to thank my advisor, Professor Dennis Curran, for his mentorship over the last six years. I am appreciative of the time, patience, ideas, attention, and funding that he has provided me. He afforded me with a considerable amount of freedom to develop and guide my research projects. I am proud to have worked under his guidance and will carry his lessons and philosophies with me throughout my professional career.

I would like to express my gratitude to Professor Peter Wipf, Professor Kazunori Koide, and Professor Jan Beumer for serving on my graduate committee. Their time and contributions to my comprehensive exam, research proposal, and thesis are greatly appreciated. I would also like to thank Professor Paul Floreancig for his service as my proposal advisor. Additionally, I am grateful to my project collaborators, Professor Peng Liu, Cheng, Fang, and Professor John Walton, for their contributions to our joint work.

I would like to thank the directors of our instrument facilities, Dr. Steven Geib, director of the x-ray crystallography facility; Dr. Damodaran Krishnan Achary, director of the NMR facility; and Bhaskar Godugu, director of the mass spectrometry facility. I am grateful for their upkeep of these excellent facilities, technical support, and assistance with spectral analysis.

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I would like to thank my undergraduate advisor, Professor Ayusman Sen at the Pennsylvania State University for providing me with an opportunity to begin my research career in his lab. Additionally, I am grateful for the mentorship of Ryan Pavlick and Sam Sengupta while in the Sen lab. I would like to thank Dr. Sheryl Dykstra and Dr. Jackie Bortiatynski for their instruction and guidance during my time at Penn State. I participated in the American Chemical Society's Project SEED at Duquesne University and would like to thank the program's director, Dr. Jennifer Aitken, as well as Dr. Ellen Gawalt and Dr. Steven Firestine. Lastly, I would like to thank my high school chemistry teacher, Mr. Josh Lucas. These individuals helped to define and execute my career goals.

My friends have made my time in Pittsburgh much more enjoyable. So, I would like to thank Tyler, Halina, Dave, Mark, Robert, Nicole, Jim, Chris, Lexi, Tait, Tim, and the rest of the Avocados and Hounds; I cherish our friendship immensely. I would like to thank my parents, Richard and Yvonne, my sister, Courtney, and Aunt Cheryl for encouraging me to pursue my education and challenging me to do my best. Lastly, I would like to thank my wonderful girlfriend, Greddie, for her unfaltering support over the last two years. I must express my heartfelt gratitude to everyone mentioned here for their support, for instilling me with my positive traits, and for shaping me into the individual that I am today.

1.0 SYNTHESIS OF BORIRANES AND ALKENYLBORANES BY HYDROBORATION REACTIONS OF N-HETEROCYCLIC CARBENE BORANES AND ELECTRON-DEFICIENT ALKYNES

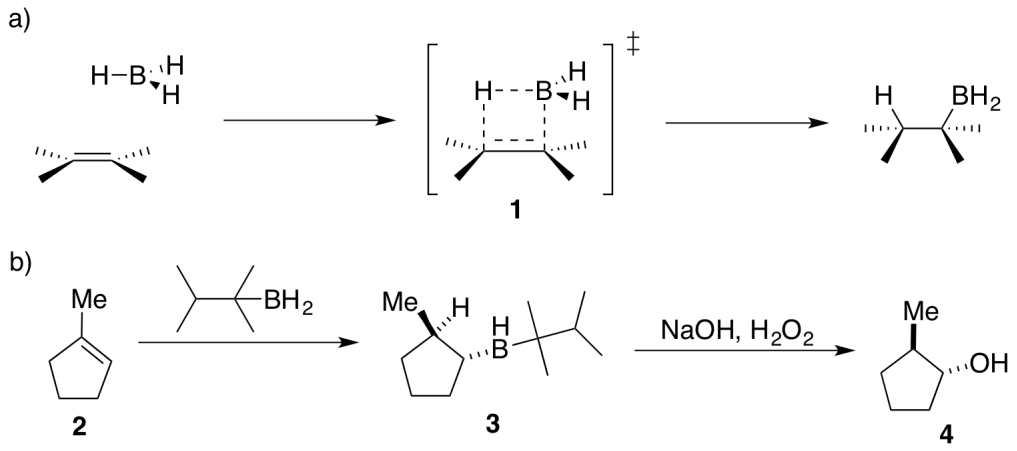
1.1 INTRODUCTION

1.1.1 Hydroboration

In 1956 and 1957, H. C. Brown published procedures for the reaction of borane with alkenes to form organoboranes.[1-2] The reaction was previously known to occur very slowly,[3-4] but Brown and coworkers showed that products formed rapidly when ether solvents were used.[2] This discovery sparked considerable interest in the formation of organoboranes,[2, 5-6] the selectivity[7-8] and stereochemistry[9] of the reaction, and downstream transformations of the products[10-11] (most notably, oxidation of organoboranes with alkaline peroxide to form alcohols[7]). For his groundbreaking work, H. C. Brown was awarded the Nobel Prize in Chemistry in 1979.[12]

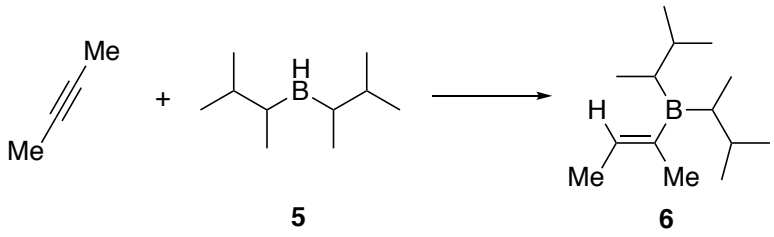
The mechanism of hydroboration is shown in **Scheme 1a**. The reaction of borane (BH_3) with an alkene results in the *syn*-addition of H_2B–H across a π bond through 4-center transition state **1**.[13] This was determined from the study of hydroborations of cyclic alkenes. For example, the reaction of methylcyclopentene **2** with thexylborane (thex-BH_2) gives organoborane **3**, which exclusively forms *trans*-2-methylcyclopentanol **4** upon oxidation with alkaline peroxide

(**Scheme 1b**).[9] Since the oxidation of **3** to **4** occurred with retention, the hydroboration of **2** to **3** must be a *syn*-addition.



Scheme 1. (a) Hydroboration transition state; (b) synthetic example of hydroboration and oxidation

Alkenylboranes can be formed through a similar mechanism from the reaction of borane with alkynes. Borane ($H–BH_2$) adds *syn* across an alkyne (here, 2-butyne) to give alkenylborane **6** (**Scheme 2**). A second hydroboration of **6** is possible (albeit quite slow in the case of internal alkenylboranes), but is blocked when bulky reagents such as disiamylborane **5** are used.[13] The hydroboration of internal alkynes results in (Z)-configured alkenylboranes, while terminal alkynes react with boranes to form (E)-alkenylboranes.

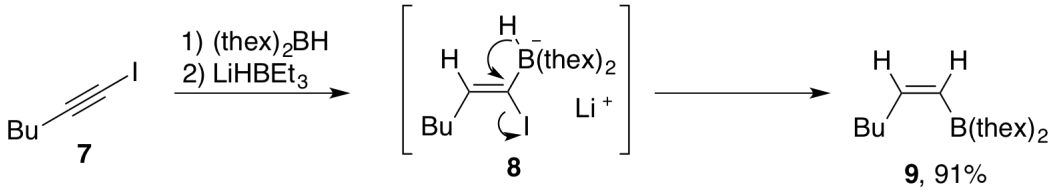


Scheme 2. The reaction of borane **5** with 2-butyne

Hydroborations are valuable reactions because they provide access to synthetically useful organoborane compounds. With careful choice of reagents and conditions, the transformation often proceeds with predictable chemo-, regio-, and stereoselectivity.

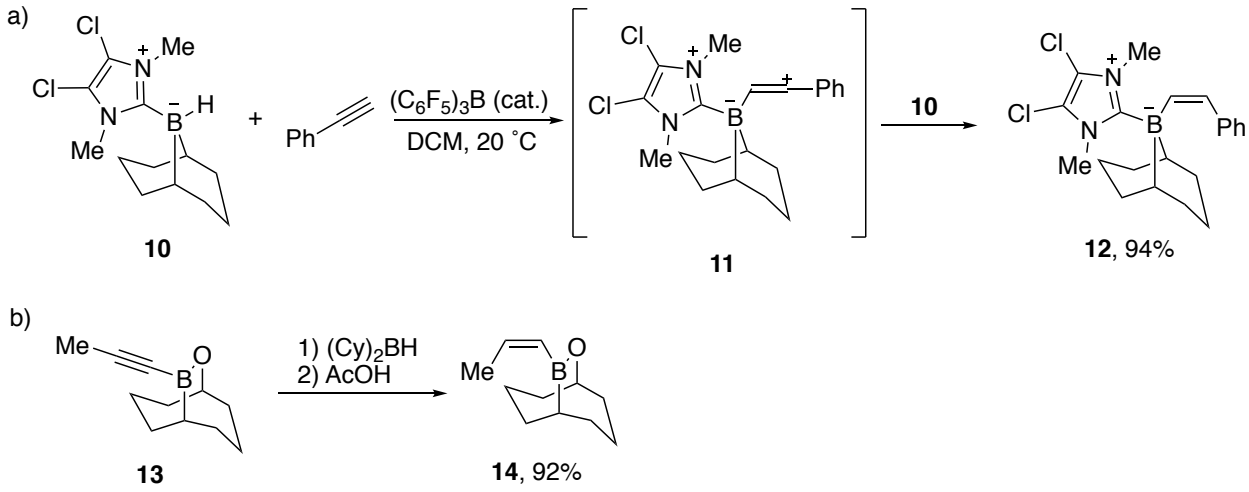
1.1.2 Trans-selective hydroboration reactions

Alkenylboronate esters have become increasingly valuable for use as Suzuki-coupling partners. Accordingly, both (E)- and (Z)-alkenylboranes must be accessible, which has placed importance on the development of *trans*-hydroboration methods. Early methods to synthesize terminal (Z)-alkenylboranes required two steps and used metal hydride reagents.[14-16] In an example from Negishi, hydroboration of iodo-alkyne **7** with thexylborane ($(thex)_2BH$) followed by reduction with lithium triethylborohydride gave organoborohydride **8** (**Scheme 3**).[14] Intramolecular hydride transfer resulted in loss of iodide to form (Z)-alkenylborane **9** in a 91% yield. Other early approaches to access *trans*-hydroboration products involve either the catalytic *cis*-hydrogenation of alkynylboranes[17] or the stepwise hydrozirconation and hydrolysis of 1-alkynyldiisopropoxyboranes.[18]



Scheme 3. Negishi's two-step method to form (Z)-alkenylboranes

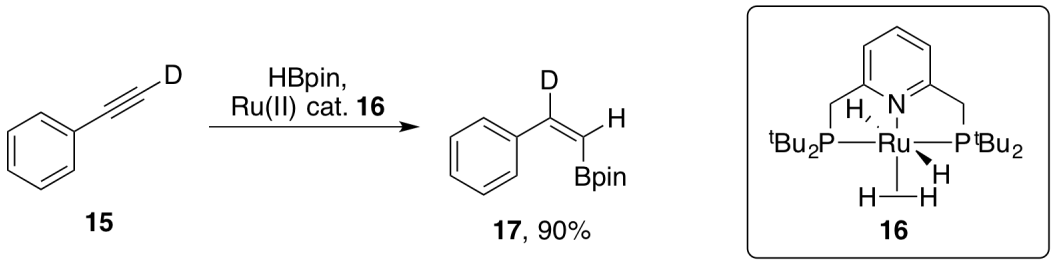
Ingleson and coworkers developed a borenium ion catalyzed hydroboration of terminal alkynes using *N*-heterocyclic carbene (NHC) borane reagents. NHC-borane **10** reacts with phenylacetylene to generate alkenyl cation **11** (**Scheme 4a**).[19] A second molecule of **10** donates hydride to **11** to give *trans*-alkenylborane **12** in a 94% yield. The reaction is catalyzed by tris(pentafluorophenyl)borane ($(C_6F_5)_3B$), which abstracts hydride from NHC-borane **10** to generate a borenium ion. Ramos showed that hydroboration of alkynyl borinate **13** with bis(cyclohexyl)borane (Cy_2BH) followed by protodeborylation with acetic acid results in (Z)-alkenylborane **14** in 92% yield (**Scheme 4b**);[20] this is an example of an uncatalyzed method to form (Z)-1-alkenylboranes.



Scheme 4. Metal free methods to access terminal (Z)-alkenylboranes

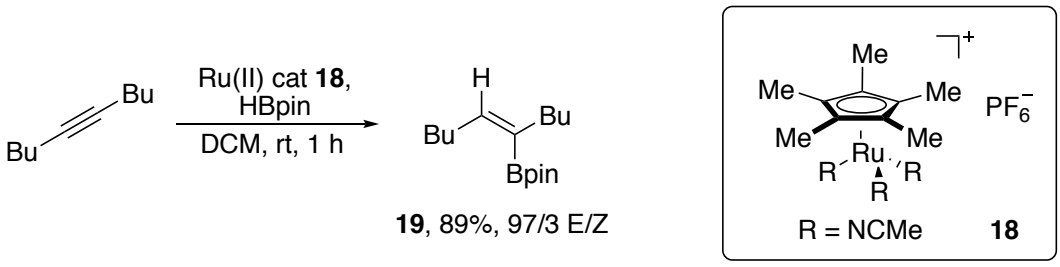
Transition metal-catalyzed *trans*-selective hydroborations have been developed by several groups.[21-23] In an example from Leitner, pinacolborane (HBpin) is added to deutero-alkyne **15** using Ru(II) catalyst **16** to give alkenylborane **17** in 90% yield (**Scheme 5**).[21] The deuterium from the alkyne, rather than the hydrogen from HBpin, is *anti* to the boron moiety in

17, suggesting a 1,2-hydrogen (deuterium) shift occurs during the formation of a metal-vinylidene complex. Labeling experiments by Miyaura and Fernandéz showed the same migration.[22, 24] This hydrogen transfer explains why these methods cannot be used for internal alkynes.



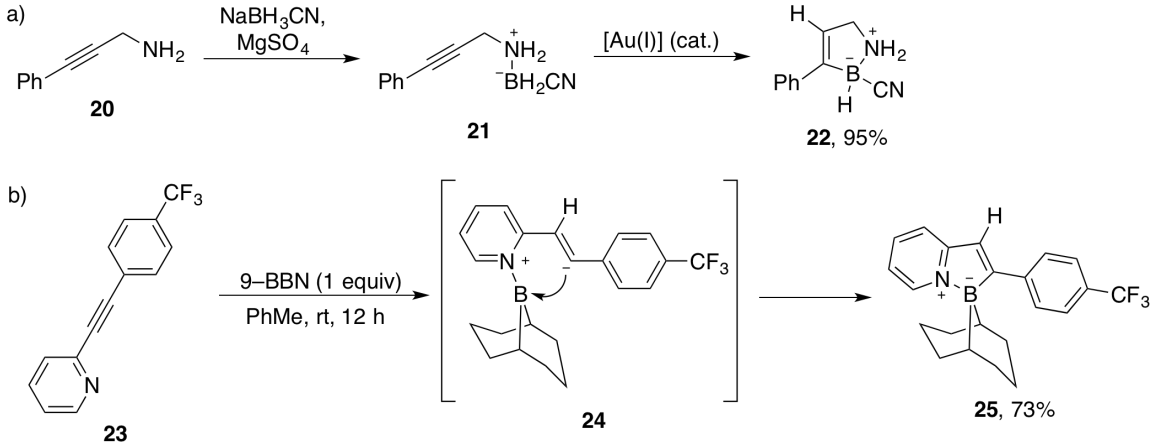
Scheme 5. Example of Ru(II)-catalyzed *trans*-hydroboration from Leitner

Fürstner and coworkers developed a *trans*-selective variant of the reaction for internal alkynes. They used Ru(II)-Cp* complexes to catalyze the formation of (E)-alkenylboranes from the hydroboration of internal alkynes with pinacolboranes.[25] In a simple example, Ru(II) catalyst **18** was used to add HBpin to 5-dodecyne to give the corresponding alkenylborane **19** in an 89% with a 97/3 E:Z selectivity (**Scheme 6**). The authors attributed the high-selectivity to the large steric influence imparted by the Cp* ligand. This method was demonstrated to have a wide scope and functional group tolerance, allowing access to a variety of internal alkenylboranes.



Scheme 6. Example of Fürstner's Ru(II)-catalyzed *trans*-hydroborations

Recently, both Shi and Wang have developed *trans*-selective hydroborations of amines and pyridines. Shi treated propargylamine **20** with sodium cyanoborohydride to form amine-borane complex **21**, which reacts with triazole-Au(I) catalyst to form BN-heterocycle **22** in 95% yield over the 2 steps (**Scheme 7a**).[26] Wang formed pyridyl-borane complex **25** from **23** and 9-borabicyclo[3.3.1]nonane (9-BBN) (**Scheme 7b**).[27] Intramolecular hydride transfer from borane to the proximal acetylene carbon gives carbanion **24** that cyclizes to BN-heterocycle **25** in 73% yield. These reactions rely on initial formation of amine- or pyridyl-borane complex that undergoes intramolecular hydride transfer and cyclization to give a net *trans*-hydroboration.



Scheme 7. Nitrogen-directed *trans*-hydroborations

Undirected or uncatalyzed hydroboration reactions almost always result in the *cis*-addition of B–H across a π bond. In spite of this mechanistic preference, several groups have developed methods to give *trans*-addition using transition metals, electrophiles, or directing groups.

1.1.3 N-Heterocyclic carbene boranes

NHC-boranes are a class of organic complexes made from Lewis basic carbenes and Lewis acidic boranes. For example, 1,3-dimethylimidazol-2-ylidene **26** complexes with borane to form NHC-borane **27a** (**Figure 1a**).[28] NHC-boranes are tetravalent, neutral (though zwitterionic) compounds with properties and reactivity distinct from both neutral, trivalent boranes and from tetravalent, anionic borohydride compounds.[28] NHC-boranes are usually high-melting solids that are stable to air, water (and other protic solvents), and chromatography.[28] Representative NHC-borane compounds **27**–**29** are shown below in **Figure 1**.

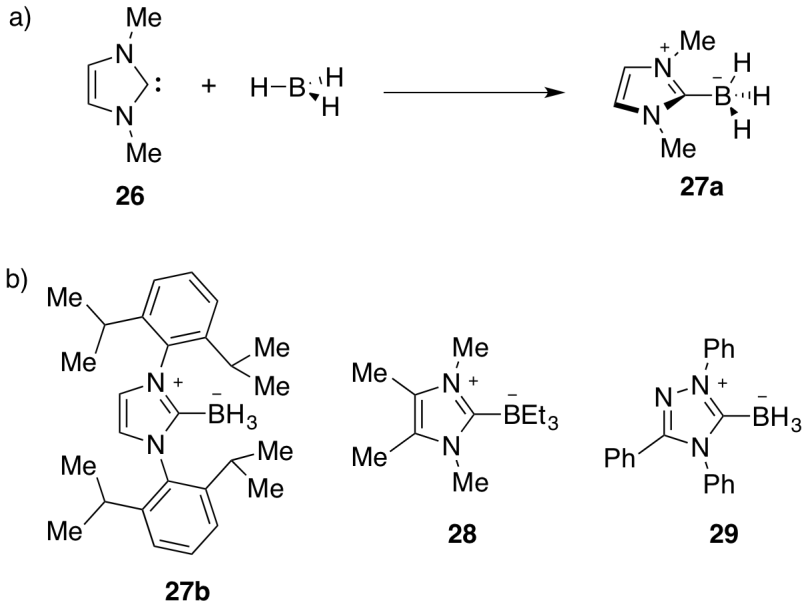
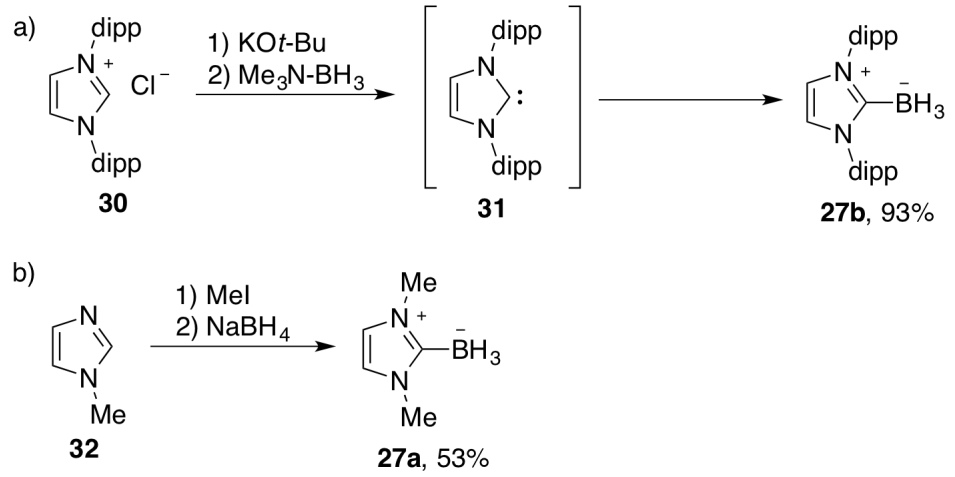


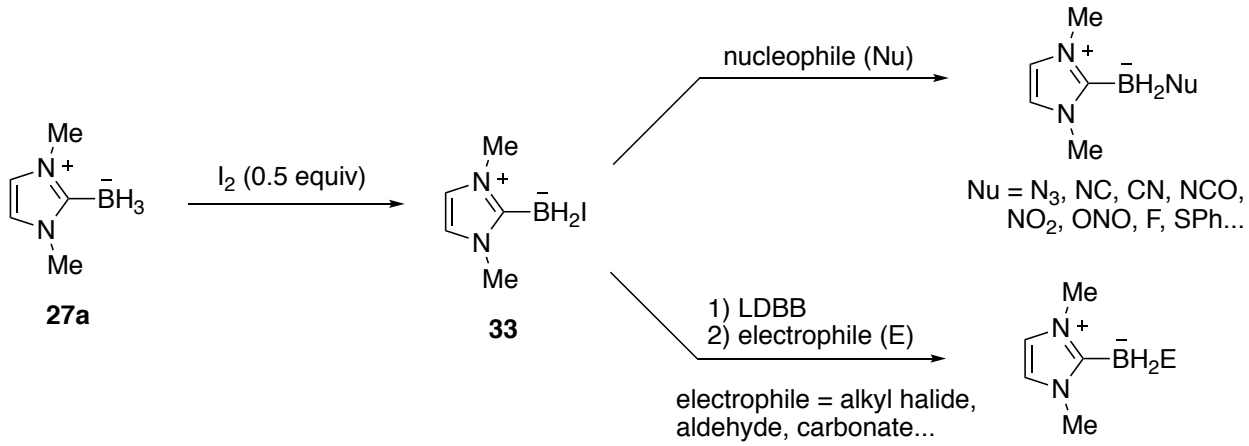
Figure 1. (a) Formation and (b) representative structures of NHC-boranes

Unsaturated imidazol-2-ylidene-derived diaminocarbenes, such as **26**, are commonly ligated with borane. This class of NHC was first prepared by Arduengo from the deprotonation of imidazolium salts.[29] This method of generating carbenes is often employed to synthesize NHC-boranes. As a representative example, deprotonation of imidazolium chloride **30** with potassium *tert*-butoxide forms stable carbene **31**; subsequent treatment with a borane source, here trimethylamine-borane, leads to the formation of NHC-borane **27b** in 93% yield (**Scheme 8a**).[30] *N,N*-Dialkyl NHC-borane **27a** can be prepared in a similar fashion, but Curran and coworkers recently developed an atom-economical, one-pot synthesis (**Scheme 8b**).[31-32] Methylation of imidazole **32** forms the corresponding imidazolium iodide salt *in situ*. Reaction of this salt with sodium borohydride in refluxing toluene (PhMe) affords NHC-borane **27a** in 53% yield; high quality crystals of **27a** are obtained by recrystallization from water.



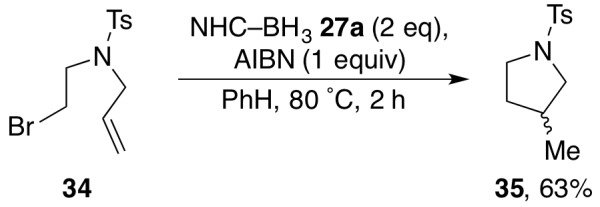
Scheme 8. Routes for the synthesis of NHC-boranes

NHC-boranes can participate in both ionic and radical reactions. In ionic reactions, they function as hydride sources in the reduction of aldehydes, ketones, imines, and alkyl halides.[33-35] NHC-boranes react instantaneously with strong acids (with pKa values at or under 1.0) or reactive halogens (e.g. Br_2 or I_2) to form substituted NHC–BH_2–X and hydrogen gas.[36] NHC-borane **27a** reacts with 0.5 equiv I_2 to form mono-iodide **33**; the iodide can be substituted with nucleophiles or electrophiles *in situ* (the latter of which first requires reduction to the corresponding boryl anion by reaction with lithium 4,4'-di-*tert*-butylbiphenylide (LDBB). **Scheme 9**).[28]



Scheme 9. Two-step substitution of NHC-borane **27a**

NHC-boranes can be used in place of tributyltin hydride in radical reductions.[37-39] For example, AIBN was used to initiate the radical debromination of **34** by **27a** to form an alkyl-centered radical that cyclized to give **35** in a 63% yield (**Scheme 10**).[37] Radical reductions of halides and xanthates have also been initiated with triethylborane/O_2 and organic peroxides.[37, 39]

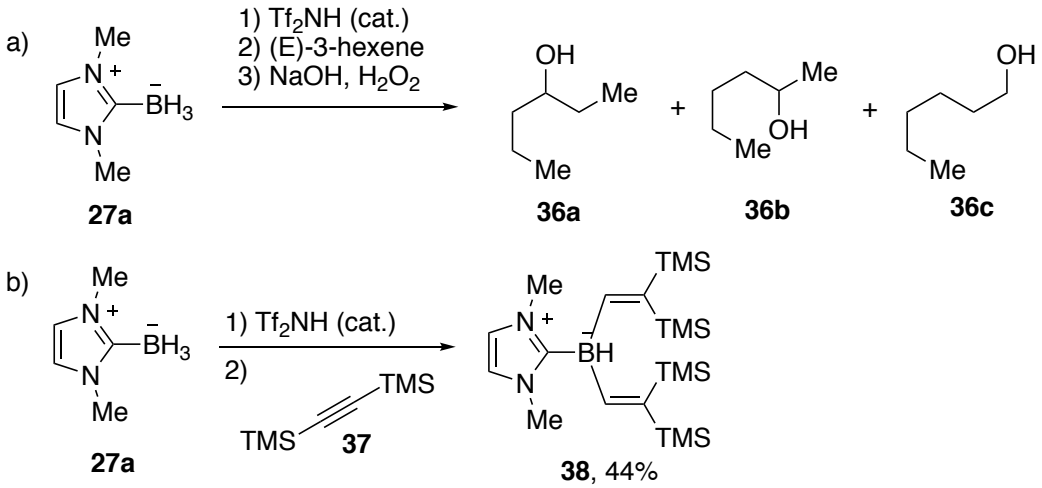


Scheme 10. Example of a radical reduction with NHC-borane **27a**

In summary, NHC-boranes are a relatively new class of reagents that can be made from simple starting materials in a few steps. They are bench-stable solids that can be used in a wide array of transformations, both ionic and radical. Their chemistry is different from loosely complexed boranes and borohydrides.

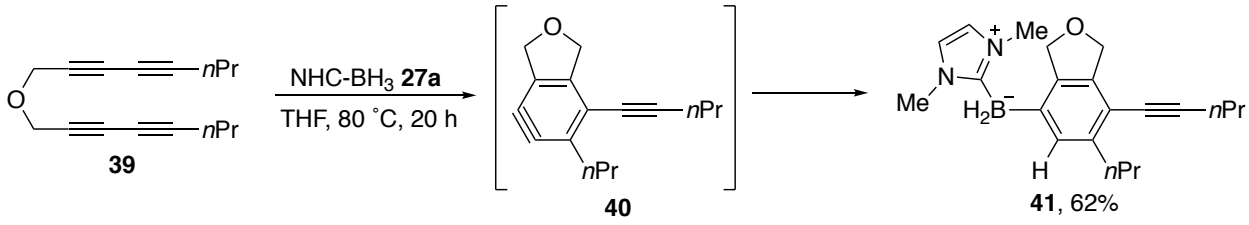
1.1.4 Hydroborations with NHC-boranes

NHC-boranes can perform hydroboration reactions provided that a suitable catalyst is present. Curran, Vedejs, and Lacôte reported the hydroboration of (E)-3-hexene by **27a** following catalytic activation by triflimide (Tf_2NH) or iodine (**Scheme 11a**).[40] After 20 min, a 91/9 mixture of 3-hexanol **36a** and 2-hexanol **36b** was isolated following oxidative workup. Interestingly, longer reaction times led to starkly different product ratios. For example, a 6/76/18 ratio of **36a**/**b**/**c** was obtained after 4 h, indicating that boryl migration occurred. Brown observed similar migrations when studying the hydroboration of internal alkenes at high temperature and long reaction times.[41-42] In a later study by Curran, the triflimide-catalyzed hydroboration of **27a** of alkynylsilane **37** gave dihydroboration product **38** in 44% yield (**Scheme 11b**).[43] Here silyl migration occurred to give a net 1,1-hydroboration product and not the expected 1,2-hydroboration product.



Scheme 11. Examples of borenium ion-catalyzed hydroborations with NHC-boranes

Direct (uncatalyzed) NHC-borane additions to arynes have also been reported. Aryne intermediates generated through hexadehydro Diels-Alder (HDDA) cyclizations[44] or elimination of aryl triflates[45] can be trapped by NHC-boranes. In an example from Curran and Taniguchi, tetra-yne **39** cyclizes on heating to give aryne **40** (**Scheme 12**).[45] Addition of **27a** gave phenyl-NHC-borane **41** as the major product in 62% yield.



Scheme 12. Hydroboration of arynes using NHC-boranes

NHC-boranes have proven to be effective hydroboration reagents. These reactions proceed following either the generation of catalytic borenium ions or aryne intermediates to give 1,2- and, in some cases, 1,1-hydroboration products.

1.1.5 Synthesis of boriranes

Boracyclopropanes or, from hereon, boriranes are three-membered heterocycles containing a boron atom. The simplest borirane, **42**, has never been isolated, but Lewis base ligated boriranes **43** are often stable compounds (**Figure 2**).

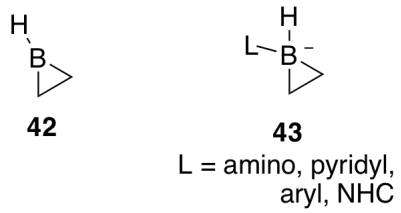
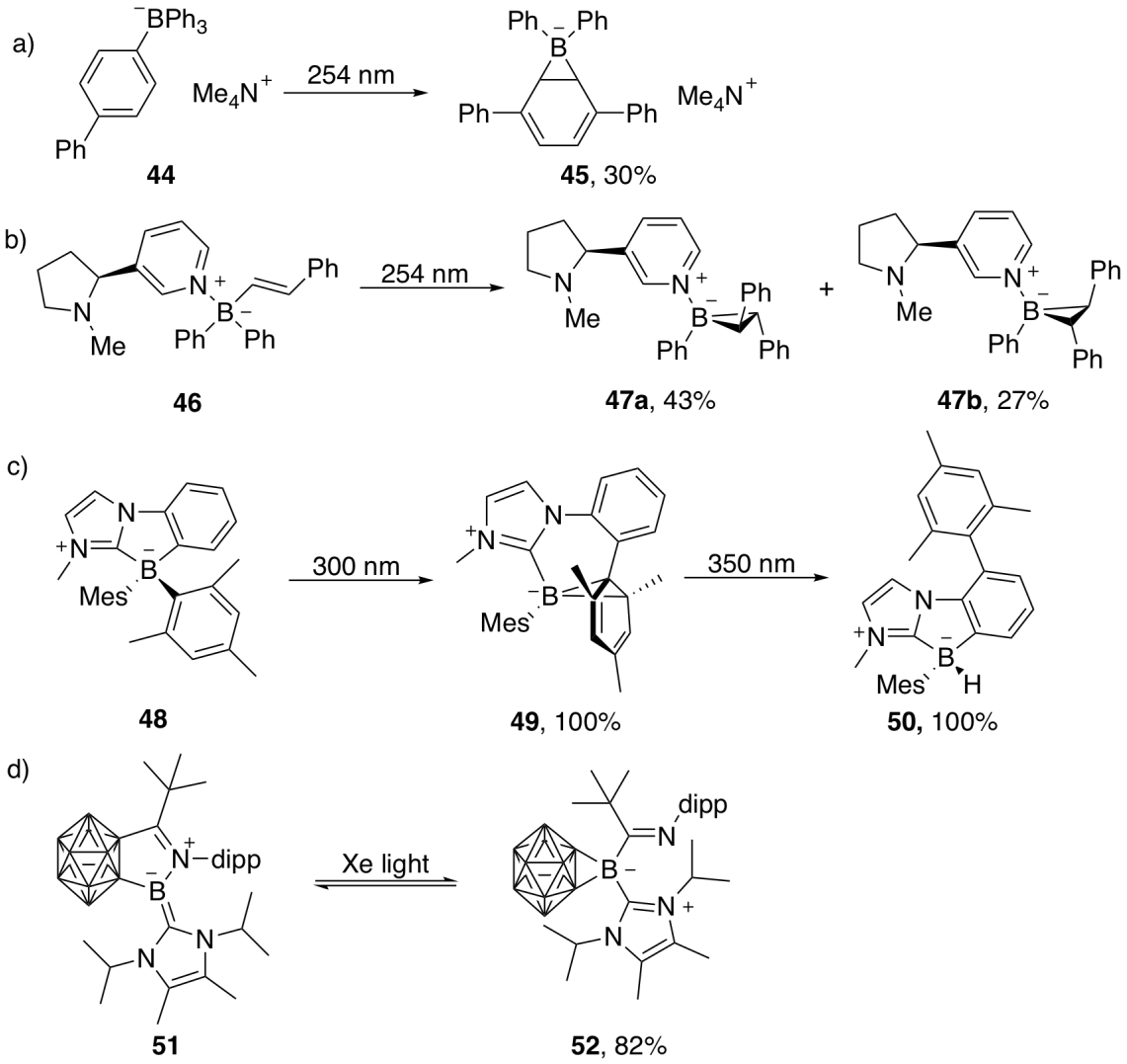


Figure 2. Structure of a neutral borirane and ligated borirane

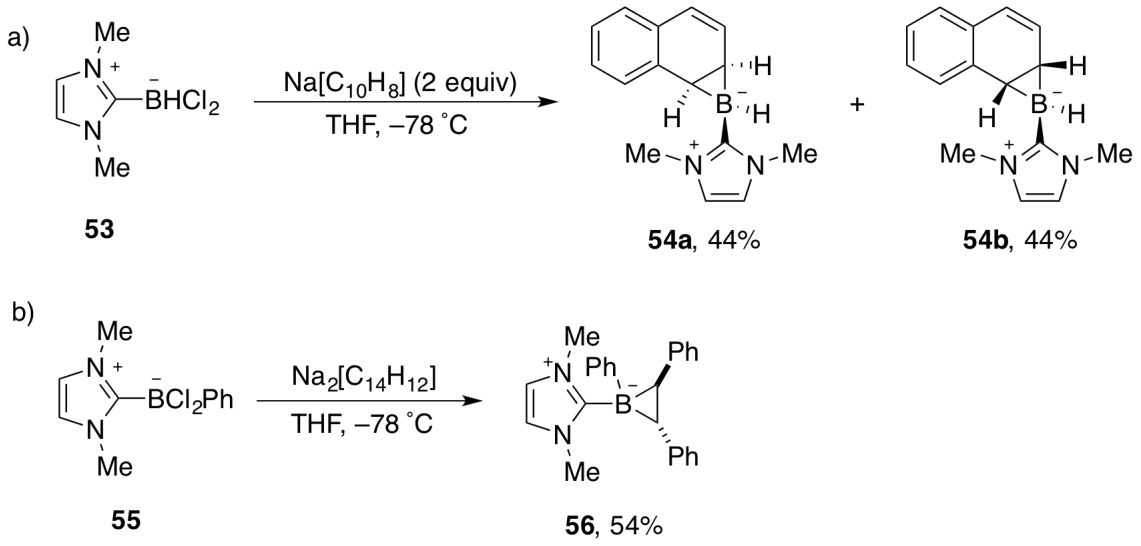
The first boriranes were prepared by Schuster in 1988 (**Scheme 13a**).[46] Irradiation of tetraphenylborate salt **44** afforded stable borirane salt **45** in a 30% yield.[46] In a later example from Denmark, treatment of alkenylborane **46** with 254 nm UV light formed borirane diastereomers **47a** and **47b** in 43% and 27% yields following a tandem radical cyclization and aryl migration (**Scheme 13b**).[47] The Wang laboratory synthesized borirane **49** quantitatively following the photoisomerization of NHC-borane **48** with 300 nm UV light.[48] Subsequent exposure of **49** to 350 nm UV-light resulted in the quantitative formation of heterocycle **50** (**Scheme 13c**).[48] More recently, Xie and coworkers converted carborane-fused azaborole **51** to a tetrahedral borirane **52** in 82% yield under photothermal conditions (**Scheme 13d**).[49]



Scheme 13. Examples of photon-driven borirane formation

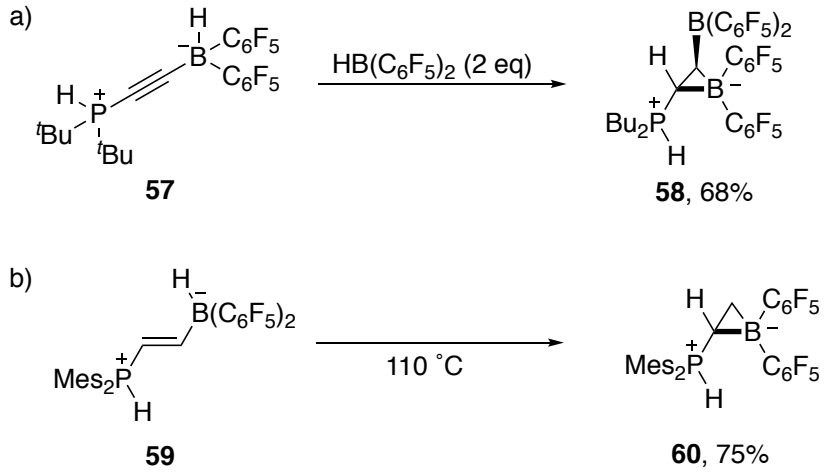
Braunschweig and coworkers drove the formation of NHC-boriranes through the use of strong reductants and good leaving groups. In their initial study, dichloro-substituted NHC-borane **53** was reacted with 2 equiv of sodium naphthalenide at –78 ˚C to form a 1:1 mixture of **54a** and **54b** in 88% yield (**Scheme 14a**).[50] Their DFT calculations supported a [2+1] cycloaddition of a borylene with a π-bond,[50] though Curran suggested a radical-radical anion coupling pathway.[51] In a later example, dichlorophenyl-NHC-borane **55** was reacted with the

dianion of *trans*-stilbene ($Na_2[C_{14}H_{12}]$) to give *trans*-borirane **56** in 54% yield (**Scheme 14b**).[52] In each example, the concomitant formation of 2 equiv of NaCl helps to drive the reaction forward.



Scheme 14. Boriranes synthesized by Braunschweig

Boriranes have also been formed from frustrated Lewis pair (FLP) compounds. In 2011, Stephan and coworkers treated FLP **57** with Piers' borane ($HB(C_6F_5)_2$) to form borirane **58** in a 68% yield (**Scheme 15a**).[53] A crystal structure confirmed the *trans*-relationship of the phosphonium and borane substituents.[53] In a related example from Erker, heating FLP **59** gave borirane **60** in 75% yield following an intramolecular hydride transfer and cyclization (**Scheme 15b**).[54]



Scheme 15. Boriranes formed from the hydroboration of FLPs

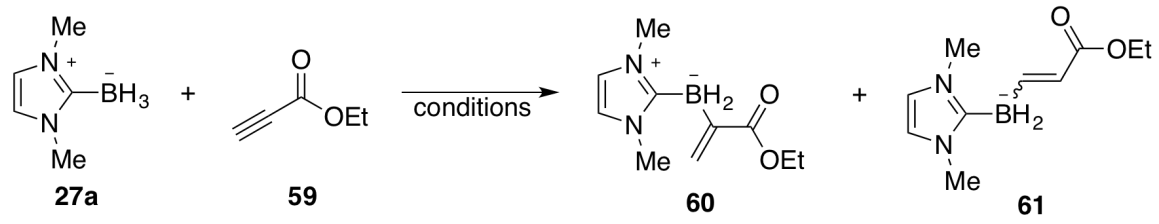
In these examples, strained boriranes are synthesized under high-energy conditions. Some systems required photons, while others proceeded through reactive intermediates, like borylenes. In the cases of Stephan and Erker, high potential FLP molecules were used as borirane precursors.

Here we report a *trans*-selective double-hydroboration of electron-deficient alkynes with NHC-boranes to form boriranes under mild conditions. The reaction conditions are optimized and the reaction scope and limitations are defined. A mechanism for the transformation is proposed based on both experimental results and DFT calculations.

1.2 RESULTS AND DISCUSSIONS

1.2.1 Hydroboration reactions of electron-poor alkynes with N-heterocyclic carbene boranes

The initial aim was to study the reaction of NHC-boranes with propiolates. Saegusa and coworkers studied the reduction of propiolates with diisobutylaluminum hydride in the presence of hexamethylphosphoric triamide to determine that 2-alkenylaluminates were the sole products.[55] Negishi showed that (E)-3-boranylacrylate was the major product of the reaction of propiolates with dialkylboranes.[56] Accordingly, α-boranylacrylate **60** and β-boranylacrylate **61** were the expected products for the reaction of **27a** and **59** (**Scheme 16**).



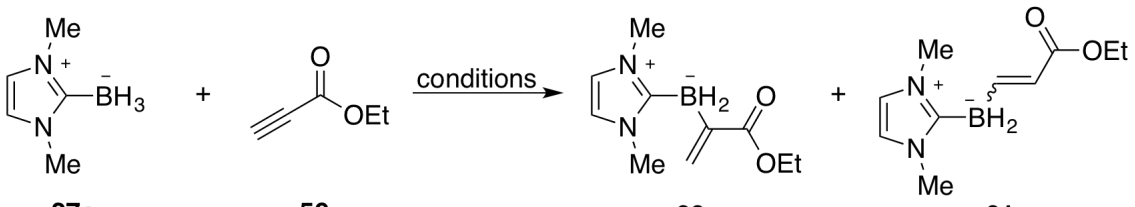
Scheme 16. Possible products arising from the hydroboration of **59** with **27a**

To start, NHC-borane **27a** was dissolved in tetrahydrofuran (THF) and propiolate **59** (0.5 equiv) was added dropwise by syringe. The resulting solution was stirred at 25 ˚C for 7 d, but no changes were observed by ^{11}B NMR spectroscopy. The solution was then heated to 100 ˚C in a pressure tube for 24 h. The initially colorless solution turned yellow, then to red, before ultimately turning dark brown over several hours. The ^{11}B NMR spectrum of the final solution showed unreacted **27a** (q, –37.5 ppm, 87%) along with two new resonances, both triplets (–26.9

ppm, J_{BH} = 87.2 Hz, 11% and –28.8 ppm, J_{BH} =82.4 Hz, 2%). Purification was attempted by flash chromatography, but only the major product, tentatively assigned as **60**, was isolated as a mixture with unreacted **27a**.

New reaction conditions were screened to improve the yields of **60** and **61**. Solutions of propiolate **59** and 2 equiv **27a** were prepared in acetonitrile (MeCN), ethanol (EtOH), and toluene (PhMe) and heated to 100 ˚C for 24 h in a pressure tube (**Table 1**). The crude products were analyzed by ^{11}B NMR spectroscopy to show a 12/88 mixture of **60**/**27a** with MeCN (entry 2), a 2/98 mixture of **60**/**27a** for EtOH (entry 3), and a 20/trace/80 mixture of **60**/**61**/**27a** when PhMe was used (entry 4). The reaction in THF was repeated with 10 mol% acetic acid (AcOH) to give a 6/2/92 mixture of **60**/**61**/**27a** (entry 5). NHC-borane **27a** and iodine (I_2, 25 mol%) were combined in THF and the solution was stirred until the brown color dissipated. An ^{11}B NMR spectrum showed the NHC-boryl iodide **33** had formed (br t, –31.1 ppm). Propiolate **59** (0.5 equiv) was added and the solution was heated to reflux for 8 h. ^{11}B NMR analysis showed a 12% conversion to **60** (entry 6). In the end, none of these conditions were deemed suitable for preparative reactions.

Table 1. ^{11}B NMR yields of **60** and **61** for solvent and additive studies



27a **59** **60** **61**

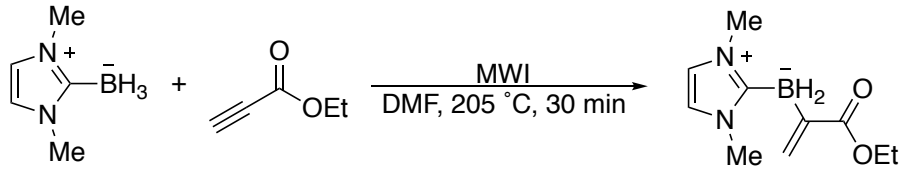
entry	conditions[a]	solvent	additive	yield **60**[b]	yield **61**[b]
1	A	THF	–	11%	2%
2	A	MeCN	–	12%	0%
3	A	EtOH	–	2%	0%
4	A	PhMe	–	20%	trace
5	A	THF	10 mol% AcOH	6%	2%
6	B	THF	25 mol% I_2	12%	0%

[a]conditions: (A) **59**, NHC-BH_3 (2 equiv), 100 ˚C, 24 h; (B) **59**, NHC-BH_3 (2 equiv), 60 ˚C, 8 h; [b]as determined by ^{11}B NMR spectroscopic analysis of the crude products

Microwave irradiation (MWI) was explored as a means of driving the reaction forward, and the results are summarized in **Table 2**. Propiolate **59** and 1 equiv NHC-borane **27a** were dissolved in *N,N*-dimethylformamide (DMF) and the solution was heated to 205 ˚C for 30 min by microwave. ^{11}B NMR analysis showed a 12/88 ratio of **60**/**27a** (entry 1). With 2 equiv of **27a**, a 10/90 ratio of **60**/**27a** was observed, or a 20% yield of **60** using **59** as the limiting reagent (entry 2). A 24% yield of **60** was obtained when 3 equiv **27a** were used (entry 3). Next, the loading of **59** was increased. With 2 and 3 equiv **59**, 36% and 69% yields of **60** were observed by ^{11}B NMR spectroscopy. Purification was attempted by flash chromatography, but pure products were not

isolated. When excess alkyne was used, the reaction mixtures turned black and became viscous, which was attributed to the formation of propiolate-derived oligomer. NHC-borane **27a** was dissolved in PhMe and heated to reflux. A solution of propiolate **59** (3 equiv) in PhMe was added to the refluxing solution over 18 h by syringe pump. ^{11}B NMR analysis showed a 4/96 ratio of **60**/**27a** indicating that the oligomerization of **59** was faster than reaction with **27a**.

Table 2. Results for the MWI reactions of propiolate **59** with NHC-borane **27a**

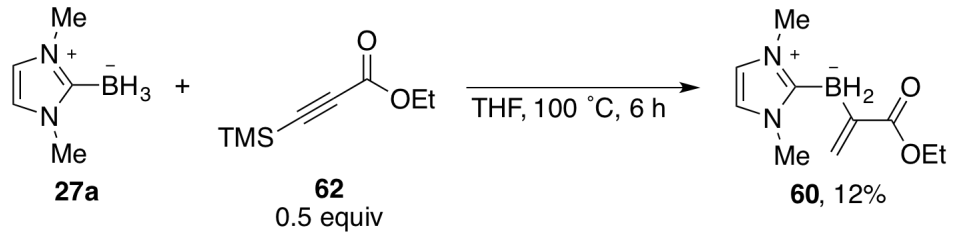


27a **59** **60**

entry	equiv **27a**	equiv **59**	**60**/**27a** ratio[a]	normalized yield **60**[b]
1	1	1	12/88	12%
2	2	1	10/90	20%
3	3	1	8/92	24%
4	1	2	36/64	36%
5	1	3	69/31	69%

[a]as determined by ^{11}B NMR analysis; [b]normalized NMR yield of **60** based on the limiting reagent

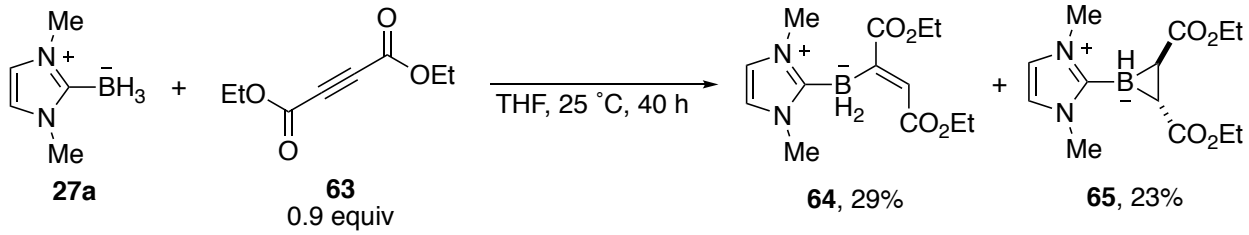
The reaction of **27a** with other propiolates was studied. Electron-rich 3-trimethylsilylpropiolate **62** was reacted with 2 equiv **27a** in THF at 100 ˚C for 6 h in a pressure tube (**Scheme 17**). ^{11}B NMR analysis showed a triplet (–26.9 ppm, J_{BH} = 85.6 Hz) along with unreacted **27a** in a 19/81 ratio. The crude ^{1}H NMR showed that desilylation had occurred to give **60** as the major product.



Scheme 17. Reaction of **27a** with electron rich alkyne **62**

1.2.2 Discovery of a new borirane-forming reaction

Next, electron-deficient diethyl acetylenedicarboxylate **63** was reacted with **27a** following a procedure from Dr. Everett Merling.[57] Diethyl acetylenedicarboxylate **63** was added dropwise to a stirring solution of **27a** (2 equiv) in THF at room temperature (**Scheme 18**). The solution immediately turned yellow to red to brown. Aliquots were periodically removed from the reaction mixture to monitor the conversion to products by ^{11}B NMR; it was determined that the reaction had stopped at 40 h. The resulting ^{11}B NMR spectrum showed 71% of **27a** was consumed to give two products in a 61/39 ratio. The major product exhibited a triplet resonance at –28.8 ppm (J_{BH} = 87.7 Hz) and the minor product exhibited a doublet at –26.6 ppm (J_{BH} = 122.9 Hz). These results were consistent with Dr. Merling's, who identified the triplet as alkenylborane **64** and the doublet as a bis(alkenyl)borane product.[57] Alkenylborane **64** was isolated with unreacted NHC-borane **27a** in 44% yield (67% purity), while the second product, identified as borirane **65**, was isolated in a 23% yield.

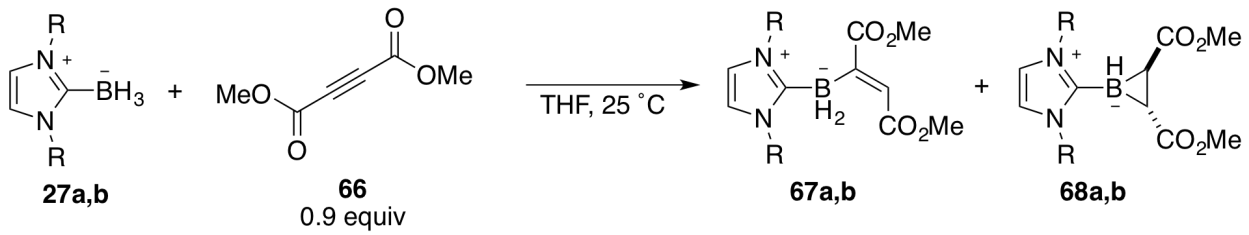


Scheme 18. Reaction of electron poor alkyne **63** with NHC-borane **27a**

The NMR spectra of **64** and **65** confirmed the identity of the products. For alkenylborane **64**, a broad singlet was observed at 6.41 ppm corresponding to the alkenyl proton and two sets of ethyl resonances were observed in the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of **65** showed two doublet of doublet resonances at 2.19 and 1.99 ppm (one appeared as a broad triplet), both integrating to one proton, corresponding to the borirane protons. The ^{13}C NMR spectrum showed two broad signals at 26.3 and 24.6 ppm corresponding to borirane carbons of **65**; this broadening is consistent with other carbons bonded to boron atoms. Since two sets of ester signals were observed in the ^{1}H and ^{13}C NMR spectra, they were determined to be *trans* to one another. High-resolution mass spectrometry (HRMS) confirmed the molecular formula of **65** as $C_{13}H_{22}BN_2O_4$, $[M+H]^+$. Boriranes, like **65**, are uncommon and their preparation merited further study.

Dimethyl acetylenedicarboxylate (DMAD) **66** was used in place of **63** to simplify the ^{1}H NMR spectra of the products. NHC-borane **27a** was reacted with **66** in THF at 25 ˚C for 18 h to give alkenylborane **67a** and borirane **68a** in 27% and 16% yields, respectively (**Scheme 19**). Next, diisopropylphenyl (dipp) NHC-borane **27b** and **66** (0.9 equiv) were stirred in THF at room temperature for 7 d. The reaction mixture turned light yellow. ^{11}B NMR analysis of the products showed 58% of **27b** was consumed to give two products, a broad triplet (–27.8 ppm) and a doublet (–26.0 ppm). Here, the selectivity of the reaction was reversed and a 12/88 ratio of **67b**/**68b** was observed. Alkenylborane **67b** was isolated in a 9% yield as a white solid with a

melting point (mp) of 180–182 ˚C, while borirane **68b** was isolated in a 39% yield as a yellow-white solid with an mp of 225–227 ˚C.



R	NHC-BH_3	time	yield **67**	yield **68**
Me	**27a**	18 h	27%	16%
dipp	**27b**	7 d	9%	39%

Scheme 19. Reaction of NHC-boranes **27a** and **27b** with **66**

The spectral data of **67b** and **68b** were consistent with **64** and **65**. The ^{1}H NMR spectrum of **67b** showed an alkenyl resonance at 6.16 ppm and two sets of methyl doublets from the isopropyl groups at 1.28 and 1.10 ppm (12 protons each, J = 6.5 Hz) suggesting slow rotation about the NHC–B bond. The ^{11}B NMR spectrum of **67b** showed a triplet at –28.2 ppm with a coupling constant of 88.0 Hz. The ^{1}H NMR spectrum of **68b** showed low-molecular symmetry: two distinct signals were observed for the isopropyl methines (integrating to 2 protons each) and four methyl doublets from the isopropyl groups were observed. Only one cyclopropyl proton was observed (an apparent triplet at 1.58 ppm) while the other was overlapped by the isopropyl methyl doublet at 1.06 ppm (which gave a total integration of 7 protons). ^{11}B NMR analysis showed a doublet at –26.1 ppm with a coupling constant of 123.2 Hz. In the ^{13}C NMR spectrum, the borirane carbon signals appeared as broad signals at 26.8 and 25.0 ppm, which was consistent

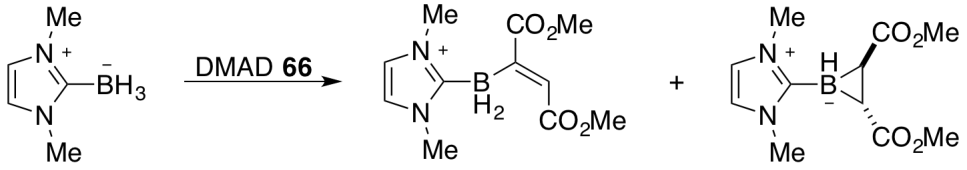
with **67a**. HRMS analysis confirmed the molecular formulae of **67a**,**b** and **68a**,**b** ($[M–H]^+$ and $[M+H]^+$, respectively).

A sample of borirane **68b** was resolved using chiral high-performance liquid chromatography (HPLC). On an (S)-Whelk column with a 1:9 isopropyl:hexanes mobile phase, two peaks with equal areas were cleanly resolved, confirming that the reaction forms borirane **68b** as a chiral racemate. This again shows that the esters are *trans*-configured because the *cis*-isomer is not chiral.

1.2.3 Optimization of the borirane-forming reaction

Conditions were optimized for the borirane-forming reaction. The results for the reaction of *N,N*-dialkyl NHC-borane **27a** and DMAD **66** are summarized in **Table 3**. The yields are reported after isolation by flash chromatography. When NHC-borane **27a** was reacted with 0.9 equiv **66** in THF at 25 ˚C, 27% of alkenylborane **67a** and 16% borirane **68a** were obtained (entry 1). However, ^{11}B NMR analysis of the crude products showed 27% unreacted **27a**. Heating the reaction mixture to reflux under otherwise identical conditions led to significant decomposition (>20%) to boric acid or ester; no products were isolated (entry 2). Increasing the loading of **66** to 2 equiv, led to full consumption of **27a** after 20 min, but significant decomposition was observed (entry 3).

Table 3. Summary of optimization studies for the reaction of **27a** with **66**



27a **67a** **68a**

entry	equiv **66**	[**27a**] (M)	solv	temp	time	yield **67a**	yield **68a**
1	0.9	0.50	THF	25 ˚C	18 h	27%	16%
2	0.9	0.50	THF	reflux	15 min	–[a]	–[a]
3	2.0	0.50	THF	25 ˚C	20 min	–[a]	–[a]
4	2.0	0.25	THF	0 ˚C	3 h	20%	12%
5	1.0	0.33	THF	–78 to 25 ˚C	18 h	26%	7%
6	1.5	0.33	THF	–78 to 25 ˚C	18 h	35%	17%
7	1.5	0.33	DCM	–78 to 25 ˚C	18 h	24%	20%
8	2.0	0.10	THF	25 ˚C	6 h	36%	23%

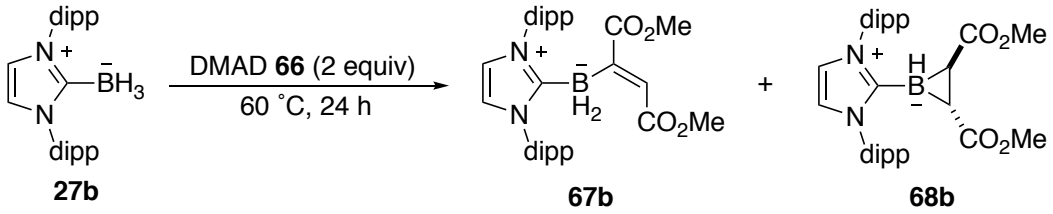
[a]products were not isolated

Better results were obtained when the reaction mixture was cooled. A solution of **27a** in THF was prepared and cooled to 0 ˚C before **66** (2 equiv) was added dropwise over several minutes. After 3 h, 20% **67a** and 12% **68a** were cleanly isolated (entry 4). Next, a solution of **27a** was prepared in THF and cooled to –78 ˚C before 1 equiv **66** was added dropwise as a solution in THF. The dry ice was allowed to evaporate, allowing the reaction mixture to warm to room temperature over 18 h to give **67a** and **68a** in 26% and 7% yields, respectively (entry 5). Increasing to 1.5 equiv **66** with the dry ice/acetone conditions led to 35% and 17% of **67a** and **68a**, respectively (entry 6). Switching the solvent to DCM led to poorer yields (entry 7). The

conditions in entry 6 were reported as the preferred conditions in our publication.[58] However, it was recently determined that comparable results are obtained by the dropwise addition of 2 equiv **66** to a dilute (0.10 M) solution of **27a** in THF (entry 8). After 6 h, a 36% yield of **67a** and 23% yield of **68a** were obtained. This avoids cryogenic conditions without compromising the yields.

It was previously observed (**Scheme 19**) that *N,N*-diaryl NHC-borane **27b** was less reactive towards **66** than **27a**. Accordingly, reactions with **27b** demanded different conditions. NHC-borane **27b** and 2 equiv **66** were combined in THF and the resulting solution was heated to reflux. After 42 h, it was determined by ^{11}B NMR spectroscopy that all of the NHC-borane **27b** was consumed. Alkenylborane **67b** was isolated in a 5% yield and borirane **68b** was isolated in a 52% yield (**Table 4**, entry 1). Several solvents were screened in an effort to increase the yield of **68b** while also decreasing the reaction time. Solutions of **27b** and **66** (2 equiv) were prepared in several solvents and heated to 60 ˚C for 24 h. ^{11}B NMR spectra were taken to measure the conversion to **67b** and **68b** by integration of each with respect to the remaining **27b**. In THF, only 1% **67b** and 41% **67b** were observed (entry 2). The reactions in PhMe and ethyl acetate (EtOAc) gave comparable results to THF, which gave combined yields of 51% and 49%, respectively (entries 3 and 4). The best results were obtained with 1,2-dichloroethane (DCE), MeCN, and dimethylsulfoxide (DMSO), which gave combined yields of 92%, 97%, and 100%, respectively (entries 5–7). Moving forward, MeCN and DCE were selected for preparative studies over DMSO for practicality.

Table 4. Summary of solvent studies for the reaction of **27b** and **66**



27b **67b** **68b**

entry	solvent	yield **67b**[a]	yield **68b**[a]	combined yield
1	THF[b]	5%	52%	57%
2	THF	1%	41%	42%
3	PhMe	4%	47%	51%
4	EtOAc	5%	44%	49%
5	DCE	9%	83%	92%
6	MeCN	11%	86%	97%
7	DMSO	10%	90%	100%

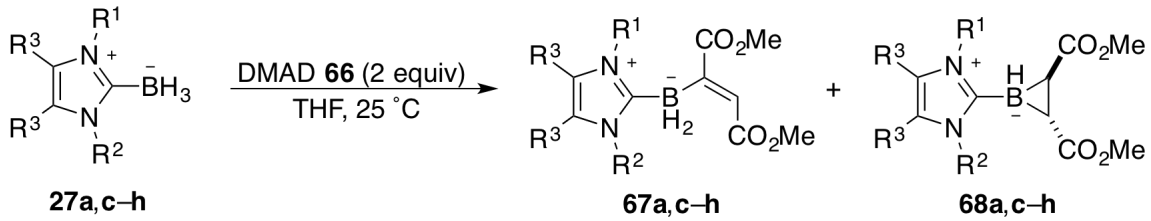
[a]as determined by ^{11}B NMR yield; [b]reaction run for 42 h

Optimized reaction conditions were developed for both *N,N*-dialkyl and *N,N*-diaryl NHC-boranes. The best results were obtained when 2 equiv DMAD **66** were added to a 0.10 M solution of **27a** in THF (**Table 3**, entry 8). These conditions will be used for the reaction of other *N,N*-dialkyl NHC-boranes with **66**. The reaction of **27b** with 2 equiv **66** in DCE and MeCN at 80 ˚C afforded **67b** and **68b** in >90% combined yields (**Table 4**, entries 5–6). The preparative reactions of *N,N*-diaryl NHC-boranes with **66** will be evaluated in these solvents.

1.2.4 Preparative synthesis of NHC-ligated boriranes

The generality of the borirane-forming reaction was determined next. Using the optimized conditions identified in **Table 3** (entry 8), six additional *N,N*-dialkyl NHC-boranes were reacted with DMAD **66**. The reaction times and yields are shown in **Table 5**.

Table 5. Alkenylboranes and boriranes obtained through variation of NHC-boranes



entry	NHC-BH_3	R^1	R^2	R^3	time (h)	yield **67**[a]	yield **68**[a]
1[b]	**27a**	Me	Me	H	6	36%	23%
2	**27c**	iPr	iPr	H	6	26%	23%
3	**27d**	Me	iPr	H	6	26%	27%
4	**27e**	Me	Bu	H	8	32%	28%
5	**27f**	Me	Bn	H	8	25%	24%
6	**27g**	Me	Me	Me	0.75	7%	16%
7	**27h**	Me	Me	$–(CH)_4–$	40	28%	24%

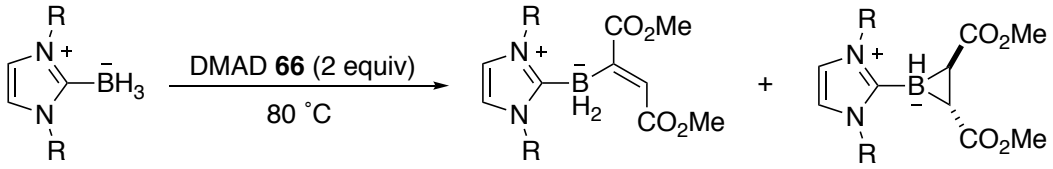
[a]isolated yield; [b]repeated from **Table 3**, entry 8 for comparison

The reaction of NHC-borane **27a** with 2 equiv **66** in THF at 25 ˚C went to completion in 6 h to give alkenylborane **67a** in 36% and borirane **68a** in 23% (entry 1). Di-isopropyl (iPr) NHC-borane **27c** reacted with **66** in 6 h to give **67c** as a red oil and **68c** as a yellow solid in 26%

and 23%, respectively (entry 2). Methyl isopropyl NHC-borane **27d**, methyl butyl (Bu) NHC-borane **27e**, and methyl benzyl (Bn) NHC-borane **27f** gave comparable yields of **67d–f** and **68d–f** (entries 3–5). Tetramethyl NHC-borane **27g** reacted with 2 equiv **66** in THF at room temperature in 45 min (entry 6). However, **67g** and **68g** were isolated in low yields, 7% and 16%. Lastly, the reaction of benzimidazole NHC-borane **27h** was sluggish at 25 ˚C and required 40 h to go to completion to give **67h** in 28% and **68h** in 24%. For all reactions, ^{11}B NMR analysis of the crude products showed that alkenylborane **67** was the major product of the reaction, formed in approximately a 55/45 ratio with borirane **68**. The optimized conditions from **Table 3** proved to be suitable for all of the *N,N*-dialkyl NHC-boranes evaluated.

Preparative reactions of *N,N*-diaryl NHC-boranes with DMAD **66** were conducted. In **Table 4**, the best results were obtained with MeCN and DCE. NHC-borane **27b** and 2 equiv **66** were dissolved in MeCN and the resulting solution was heated to 80 ˚C for 18 h (entry 1). Alkenylborane **67b** was isolated in 5% and borirane **68b** was obtained in 80%. The reaction in DCE also went to completion in 18 h; **67b** and **68b** were isolated in 6% and 59%, respectively (entry 2). Di-mesityl (2,4,6-trimethylbenzene, Mes) NHC-borane **27i** was reacted with 2 equiv **66** in MeCN at 80 ˚C. It was determined that the reaction had gone to completion after 1 h. Alkenylborane **67i** and borirane **68i** were isolated as white solids in 10% and 31% yields, respectively (entry 3). With DCE, the reaction of **27i** and **66** went to completion in 6 h, giving 4% of **67i** and 38% **68i** (entry 4). Reactions of *N,N*-diaryl NHC-borane with **66** have a strong preference for forming borirane **68** over alkenylborane **67** (about 85/15 **68**/**67**).

Table 6. Results for the preparative reactions of *N,N*-diaryl NHC-boranes with **66**

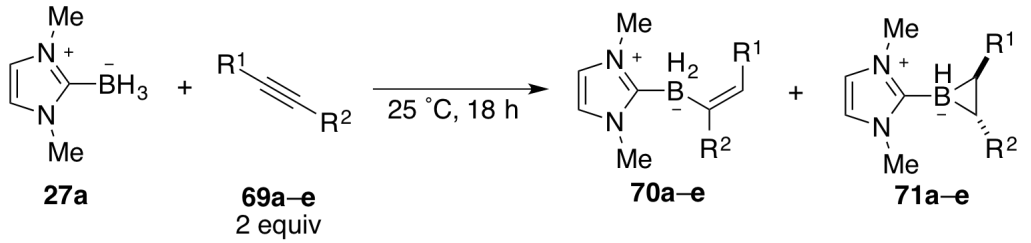


27b,**i** **67b**,**i** **68b**,**i**

entry	R	NHC-BH_3	solvent	time (h)	yield **67**	yield **68**
1	dipp	**27b**	MeCN	18	5%	80%
2	dipp	**27b**	DCE	18	6%	59%
3	Mes	**27i**	MeCN	1	10%	31%
4	Mes	**27i**	DCE	6	4%	38%

Other alkynes were screened to determine if they could react with NHC-boranes to form boriranes; the results are summarized in **Table 7**. In a typical procedure, NHC-borane **27a** was reacted with 2 equiv methyl 3-phenylpropiolate **69a** in THF at room temperature for 18 h (entry 1). ^{11}B NMR analysis of the solution showed only **27a**. Reaction of **27a** with acetylene dicarboxylic acid **69b** in MeCN resulted in the formation of a complex mixture of products (entry 2). No signals were observed between –20 and –30 ppm in the resulting ^{11}B NMR spectrum, suggesting no alkenylborane **70** or borirane **71** had formed. No reaction was observed when **27a** was reacted with 2 equiv acetylene dicarboxamide **69c**, diphenyl acetylene **69d**, or 1-heptyne **69e** (entries 3–5). These results, along with those in **Table 1** and **Scheme 17a**, indicate that the reaction was specific for di-ester substituted alkynes.

Table 7. Other alkynes screened for their reactivity with **27a**



entry	R^1	R^2	alkyne	solvent	result[a]
1	CO_2Me	Ph	**69a**	THF	no reaction
2	CO_2H	CO_2H	**69b**	MeCN	complex mixture
3	$C(O)NH_2$	$C(O)NH_2$	**69c**	DMSO	no reaction
4	Ph	Ph	**69d**	DMSO	no reaction
5	nC_5H_{11}	H	**69e**	MeCN	no reaction

[a]as determined by ^{11}B NMR spectroscopy

To determine the configurations of the alkenylborane and borirane products, crystals were grown. Using slow vapor diffusion with DCM/pentanes, both alkenylboranes **67b** and **67i** formed white, crystalline solids. X-ray analysis by Dr. Steven Geib showed that both alkenes were E-configured resulting from a net *trans*-1,2-hydroboration of **66** by **27b** and **27i**, respectively (**Figure 3**).

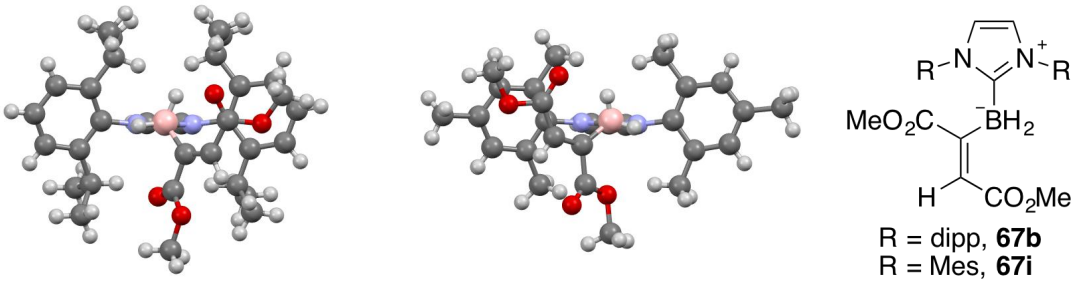


Figure 3. Crystal structures of alkenylboranes **67b** (left) and **67i** (right)

Crystals of boriranes **68b**, **68c**, and **68i** were grown using slow-vapor diffusion. All three X-rays confirmed that the products were NHC-ligated boriranes with *trans*-configured ester substituents (**Figure 4**).

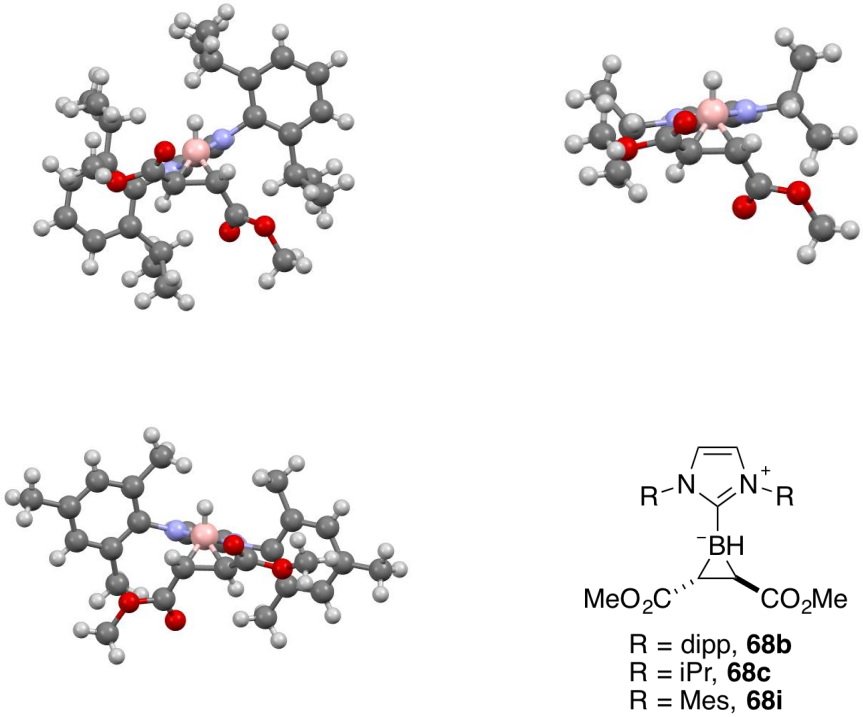
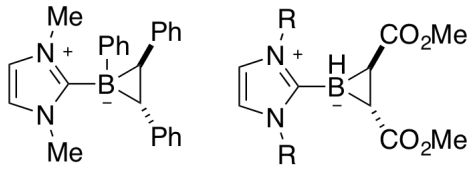


Figure 4. Crystal structures of boriranes **68b** (top left), **68c** (top right), and **68i** (bottom left)

The borirane bond lengths and internal angles for **68b**, **68c**, and **68i** are summarized below in **Table 8** along with the values for borirane **54** synthesized by Braunschweig.[52] In cases where there are two bonds or angles, the average of the two is given. The internal bond angles for the borirane ring are close to equilateral; however, the C–B–C bond angles deviate the most from 60˚. The C–H bonds are unusually short (0.95–1.00 Å); the C–H bonds in cyclopropane are estimated to be 1.08 Å.[59]

Table 8. Borirane bond lengths and internal angles



54

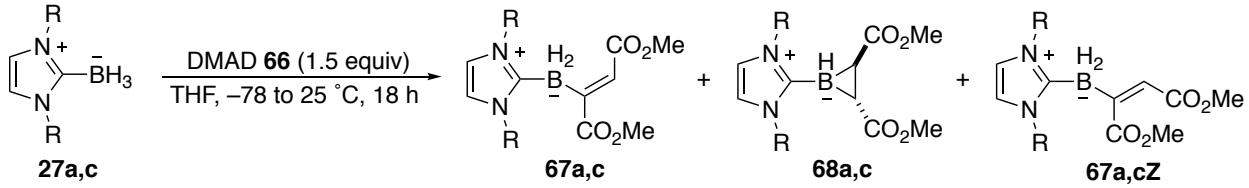
R = dipp, **68b**
R = iPr, **68c**
R = Mes, **68i**

entry	borirane	B-C-C ∠[a]	C-B-C ∠	B-H (Å)	C-H (Å)[b]	B-C (Å)[b]	C-C (Å)
1	**68b**	61.6˚	57.0˚	1.09	0.99	1.61	1.53
2	**68c**	61.9˚	56.3˚	1.13	0.95	1.62	1.52
3	**68i**	61.6˚	56.8˚	1.12	0.97	1.60	1.52
4	**54**	61.7˚	56.6˚	–[c]	1.00	1.62	1.53

[a]average value of the two bond angles; [b]average value of the two bond lengths; [c]**54** does not have a B–H bond

During the optimization of the reaction of *N,N*-dialkyl NHC-borane **27a** with **66**, a small additional signal was observed in the ^{11}B NMR spectra, typically overlapped by the borirane signal. Careful analysis of the ^{11}B NMR spectra revealed it was a triplet at –26.4 ppm (J_{BH} = 89.6 Hz). This is similar to but distinct from the signal observed for the isolated E-alkenylborane **67a** (t, –28.7 ppm, J_{BH} = 87.7 Hz); so it could be the Z-alkenylborane **67Z**. To isolate this

product, NHC-borane **27a** was reacted with alkyne **66** using the conditions described in **Table 3**, entry 6. The crude ^{11}B NMR spectrum showed three products, E-alkenylborane **67a**, borirane **68a**, and suspected Z-alkenylborane **67aZ** in a 67/30/3 ratio (**Scheme 20**). Evaporation of the volatiles followed by flash chromatography gave E-alkenylborane **67a** in 34% yield, Z-alkenylborane **67aZ** in 4% yield, and borirane **68a** in 12% yield. The alkenyl resonance was observed at 5.45 ppm for **67aZ** (compared to 6.46 ppm for the E-isomer) by ^{1}H NMR analysis. HRMS confirmed that **67aZ** was isomeric with **67a** and **68a**. Under identical conditions with NHC-borane **27c**, 24% **67c**, 27% **68c**, and 3% **67cZ** were isolated. The spectra of **67cZ** were consistent with **67aZ**.



R	NHC-borane	yield **67**	yield **68**	yield **67Z**
Me	**27a**	34%	12%	4%
iPr	**27c**	24%	27%	3%

Scheme 20. Detection and isolation of Z-alkenylboranes

These results show that the E/Z selectivities in two cases are about 90/10. *N,N*-diaryl NHC-boranes probably give similar selectivities, but the Z-isomers are difficult to identify because they are formed in such small quantities.

In summary, suitable reaction conditions were developed for both *N,N*-dialkyl and *N,N*-diaryl NHC-boranes. These conditions were applied to produce several additional examples of NHC-ligated borirane and alkenylborane compounds formed from the hydroboration of DMAD

66 by NHC-borane **27**. The hydroboration reactions are highly *trans*-selective to form E-alkenylborane **67** and *trans*-configured borirane **68**, but the Z-alkenylborane **67Z** was observed and isolated. The structures of **67** and **68** were proven by X-ray crystallography.

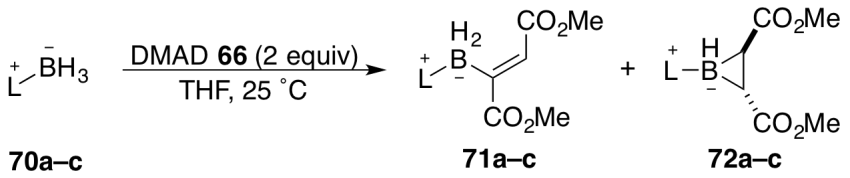
1.2.5 Determining the scope and limitations of borirane formation with other ligated boranes

It was next determined whether other ligated boranes (L-BH_3) would react with DMAD **66** to form boriranes. The results are summarized in **Table 9**.

Three ligated boranes, trimethylamine-borane (Me_3N-BH_3) **70a**, pyridine-borane (pyr-BH_3) **70b**, and dimethylaminopyridine-borane (DMAP-BH_3) **70c** were evaluated for their reactivity towards DMAD **66** under the optimized conditions from **Table 3**, entry 8. With Me_3N-BH_3 **70a**, the solution turned yellow-orange over several hours. An ^{11}B NMR spectrum showed only **70a** (q, –7.5 ppm) after 24 h, indicating that no reaction had occurred (**Table 9**, entry 1). The reaction of pyr-BH_3**70b** with DMAD **66** led to a similar color change. Three resonances were observed by ^{11}B NMR spectroscopy taken at 24 h, a quartet corresponding to **70b** (–11.3 ppm, 20%), a broad singlet possibly corresponding to **71b** or **72b** (3.1 ppm, 40%), and a broad singlet corresponding to boric acid or ester (19.7 ppm, 40%; entry 2). The solvent was removed under reduced pressure to give a yellow oil that was purified by flash chromatography. However, no boron-containing products were isolated. DMAP-BH_3 **70c** reacted rapidly with **66** at room temperature. The colorless solution turned yellow to orange to dark red over several minutes. A proton-decoupled ^{11}B NMR spectrum showed full consumption of **70c** and new resonances at –9.5 ppm (56%), –11.2 ppm (27%), and –12.9 ppm (16%). The solvent was removed under

reduced pressure to give a red oil that was purified by flash chromatography. One product was isolated, presumed to be alkenylborane **71c** in 23% yield.

Table 9. Summary of reactions of ligated borane complexes **70a–c** with **66**

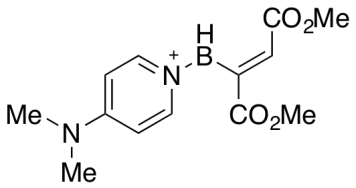


70a–c **71a–c** **72a–c**

entry	L	L-BH_3	time	result[a]
1	Me_3N	**70a**	24 h	no reaction, 24 h
2	pyr	**70b**	24 h	3.1 ppm (40%) and 19.7 ppm (40%)
3	DMAP	**70c**	15 min	–9.5 ppm (56%), –11.2 ppm (27%), –12.9 ppm (17%)

[a]as determined by ^{11}B NMR analysis of the crude products

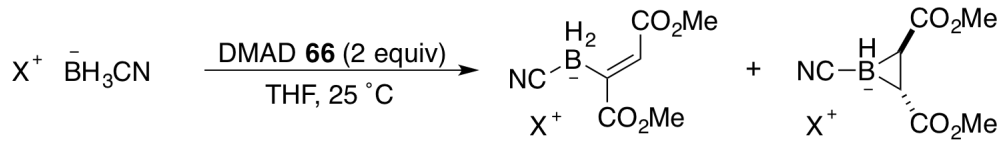
Alkenylborane **71c**, shown in **Figure 5**, was isolated as a brown oil. Its ^{1}H NMR spectrum showed a sharp singlet at 6.61 ppm corresponding to the alkenyl proton and two singlets at 3.70 and 3.61 ppm each integrating to three protons, corresponding to the ester methyl singlets. The ester groups were presumed to be *trans*-configured because the alkenyl proton had a shift similar to those observed for **67a** and **67c** (6.46 and 6.41 ppm, respectively; compared to 5.45 and 5.29 ppm for **67aZ** and **67cZ**). A broad triplet at –10.3 ppm was observed by ^{11}B NMR spectroscopy. HRMS confirmed the molecular formula as $C_{13}H_{18}BN_2O_4$ $[M–H]^+$.



71c

Figure 5. Structure of alkenylborane **71c**

Inorganic borohydride compounds were investigated for their ability to form boriranes upon reaction with alkynes. Sodium borohydride **73a** did not dissolve in THF, thus no reaction was observed when DMAD **66** was added to a suspension of **73a** in THF. Sodium borohydride **73a** and DMAD **66** reacted rapidly in dimethoxyethane (DME), leading to a color change to dark red. Only decomposition products were observed by ^{11}B NMR spectroscopy. With sodium cyanoborohydride **73b**, a gradual color change to red was observed. After 75 min, ^{11}B NMR spectroscopy showed 95% consumption of **73b** and two new resonances, a triplet (–32.3 ppm, J_{BH} = 89.3 Hz, 29%) and a doublet (–31.0, J_{BH} = 125.0 Hz, 66%), likely corresponding to **74b** and **75b**, respectively (**Scheme 21**). The reaction of tetrabutylammonium cyanoborohydride **73c** with 2 equiv **66** in THF at room temperature afforded **74c** and **75c** in 42% and 53% yields after 1 h. Evaporation of the solvent afforded a dark red oil. ^{13}C NMR spectroscopic analysis of the crude mixture of **74c** and **75c** revealed two broad resonances at 24.5 and 24.1 ppm. These signals likely correspond to the borirane carbons, as they have similar shifts and shapes to those observed for the isolated boriranes. None of the products (**74b,c** or **75b,c**) from these reactions were isolated by flash chromatography, probably because they are salts. Similarly, pure products were not isolated by aqueous extraction.



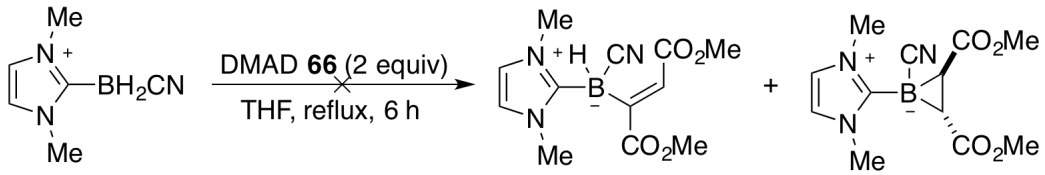
73b,c **74b,c** **75b,c**

X	borohydride	time (h)	yield **74**[a]	yield **75**[a]
Na	**73b**	1.25	29%	66%
Bu_4N	**73c**	1	42%	53%

[a]as determined by ^{11}B NMR spectroscopy

Scheme 21. Reactions of inorganic cyanoborohydrides **73** with DMAD **66**

The effect of cyano-substitution at boron was further evaluated by reacting mono-cyano NHC-borane **76** with DMAD **66** (**Scheme 22**). NHC-borane **76** was dissolved in THF and 2 equiv **66** were added dropwise. No reaction was observed at 25 °C after 2 h, so the reaction mixture was heated to reflux. Only starting material resonances were observed by ^{11}B NMR spectroscopy after 6 h, thus no alkenylborane **77** or borirane **78** were formed.

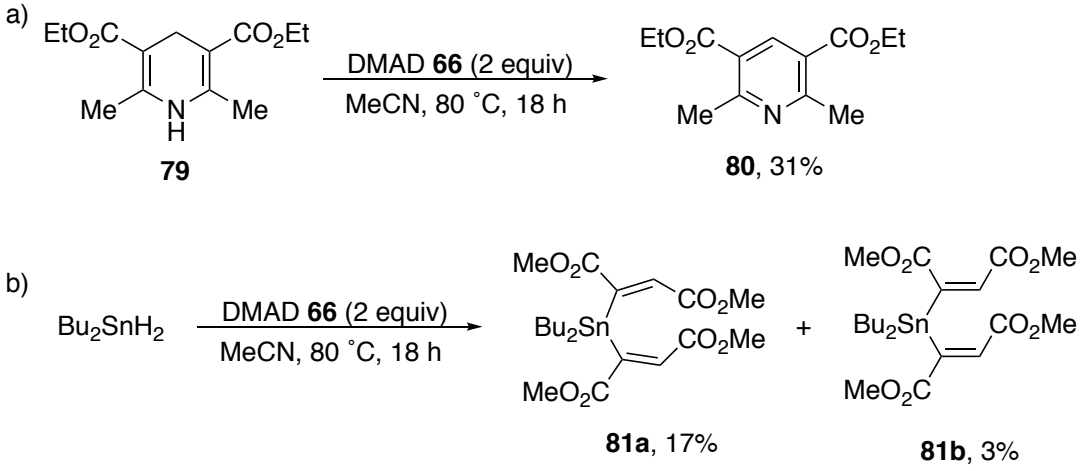


76 **77** **78**

Scheme 22. Unsuccessful reaction of **76** with DMAD **66**

Studies were performed to determine whether the cyclization reaction was unique for NHC-boranes and borohydrides. A hydrocarbation reaction was attempted using a Hantzsch ester. Reaction of **79** with 2 equiv of **66** in MeCN at 80 °C for 18 h did not result in the formation

of any cyclopropyl or alkenyl products. Instead, 31% of aromatized Hantzsch ester **80** and 70% of **66** were recovered by flash chromatography (**Scheme 23a**). It is believed that **80** formed following the reduction of **66** to give dimethyl maleate or dimethyl fumarate, but those products were not isolated. Dibutyltin dihydride (Bu_2SnH_2) was reacted with 2 equiv **66** in MeCN at 80 ˚C for 18 h (**Scheme 23b**). The reaction mixture turned dark brown over 18 h. Removal of the solvent gave a dark brown oil that was purified by flash chromatography to give the Z,Z-dialkenylstannane **81a** as a clear oil in 17%, followed by 3% of the E,Z-dialkenylstannane **81b** as a clear oil. No cyclic products were isolated.

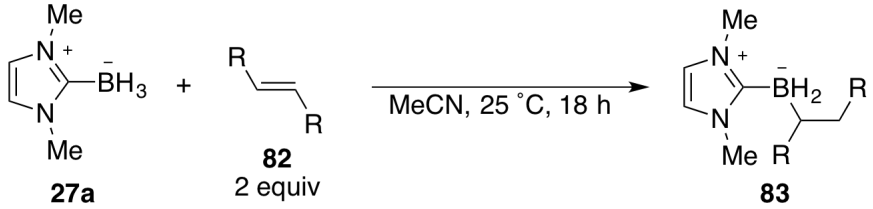


Scheme 23. Attempted cyclopropanations using carbon and tin hydride reagents

The reaction of NHC-boranes and electron-deficient alkenes was briefly studied. The results are summarized in **Table 10**. In a typical procedure, NHC-borane **27a** was dissolved in MeCN and 2 equiv alkene **82a** was added. The resulting solution was stirred for 18 h at room temperature to show a 12/88 ratio of **83a**/**27a** in the resulting ^{11}B NMR spectrum (entry 1). Product **83a** was not isolated. No reaction was observed between **27a** and fumaric acid **82b** or fumaronitrile **82c** under the same conditions (entries 2 and 3). Similarly, no reactions were

observed between NHC-borane **27b** and **82a–c** under identical conditions. Dr. Everett Merling demonstrated that the hydroboration of alkylidene malononitriles by NHC-BH_3 **27a** occurred at room temperature[57] but it appears that these alkenes are not electron-deficient enough to afford the corresponding hydroboration products.

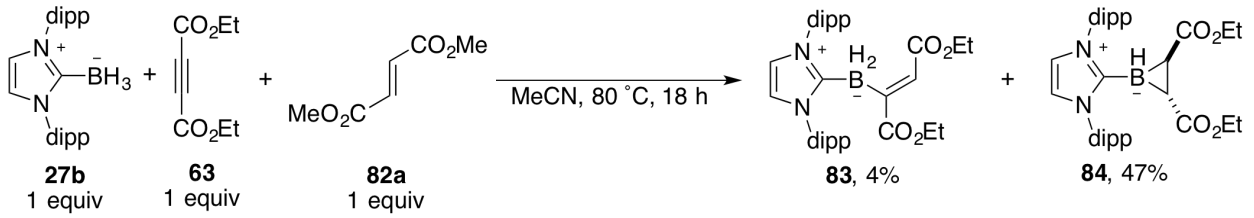
Table 10. Results of the reaction of **27a** with electron-poor alkenes



entry	R	alkene	result[a]
1	CO_2Me	**82a**	12% **83a**
2	CO_2H	**82b**	no reaction
3	CN	**82c**	no reaction

[a]as determined by ^{11}B NMR spectroscopy

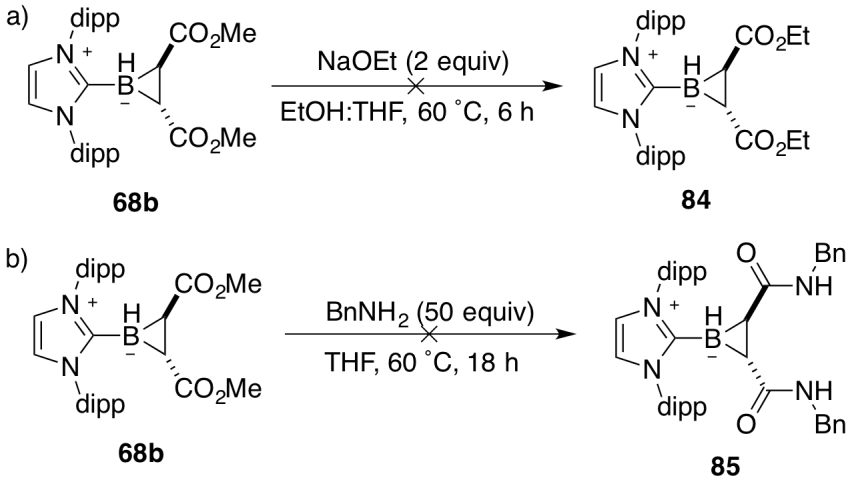
A competition experiment was performed to determine the relative reactivities between alkynes and alkenes with NHC-boranes. NHC-borane **27b** was reacted with 1 equiv diethyl acetylenedicarboxylate **63** and 1 equiv dimethyl fumarate **82a** in MeCN at 80 ˚C for 18 h (**Scheme 24**). Ethyl substituted alkenylborane **83** and borirane **84** were the only products isolated by flash chromatography, isolated in 4% and 47% yields, respectively. These results show that electron-deficient alkynes are more reactive towards NHC-boranes than similarly-substituted alkenes.



27b 1 equiv + **63** 1 equiv + **82a** 1 equiv → **83**, 4% + **84**, 47%

Scheme 24. Competition experiment with **63** and **82a**

Downstream reactions of borirane **68b** were briefly explored. This borirane was chosen because large quantities of **68b** were previously isolated and, unlike most *N,N*-dialkyl NHC-boriranes, it was solid. The transesterification of borirane **68b** was attempted using 2 equiv sodium ethoxide in an EtOH:THF co-solvent (1:1) to form diethyl ester **84**. No new products were observed by TLC or ^{11}B NMR spectroscopy after 6 h at 60 ˚C; only **68b** was recovered following flash chromatography (**Scheme 25a**). Transamidation was also attempted using 50 equiv benzylamine. The reaction was heated to 60 ˚C for 18 h in THF, but **85** was not observed by TLC or ^{11}B NMR spectroscopy (**Scheme 25b**). Subsequent attempts with secondary amines, diisopropylamine and piperidine, also proved to be unsuccessful. The ester functionalities were unreactive, likely due to a combination of deactivation from the electron-rich α-carbon and the steric congestion provided by the *N*-aryl substituents.



Scheme 25. Attempted (a) transesterification and (b) transamidation reactions of borirane **68b**

Reactions at boron were also attempted. Reaction of borirane **68b** with 1 equiv triflic acid led to rapid decomposition of the starting material (^{11}B NMR: br s, +20 ppm). With 0.50 equiv I_2, no changes to the ^{11}B NMR spectrum were observed after several hours. These results again show the high stability of borirane **68b**.

1.2.6 Investigating the mechanism of borirane formation

After investigating the scope and limitations of the reaction, the mechanism of borirane formation was studied. Three mechanisms were initially considered and are shown in **Figure 6**.

In **Figure 6a**, hydride transfer from **27a** to **66** results in ion pair **85** that could either collapse to form alkenylborane **67a** or undergo a proton transfer to give borylene **86** and dimethyl fumarate **82a** that would subsequently undergo a [1+2] cycloaddition to give borirane **68a**. This mechanism is problematic because it involves both hydride and proton transfer from the same molecule. It was also considered that **67a** arose following a 1,2-hydroboration (HB) of **66** by **27a** (**Figure 6b**). Intramolecular 1,1-hydride transfer forms carbanion **87** that collapses to

form borirane **68a**. Lastly, it was considered that 1,1-hydroboration of **66** could form carbene **88** that could either undergo an intramolecular hydride transfer to form **67a** or BH-insertion to give **68a** (**Figure 6c**). This mechanism is problematic both because there are few examples of direct 1,1-hydroboration[60-61] and carbene formation is unlikely.

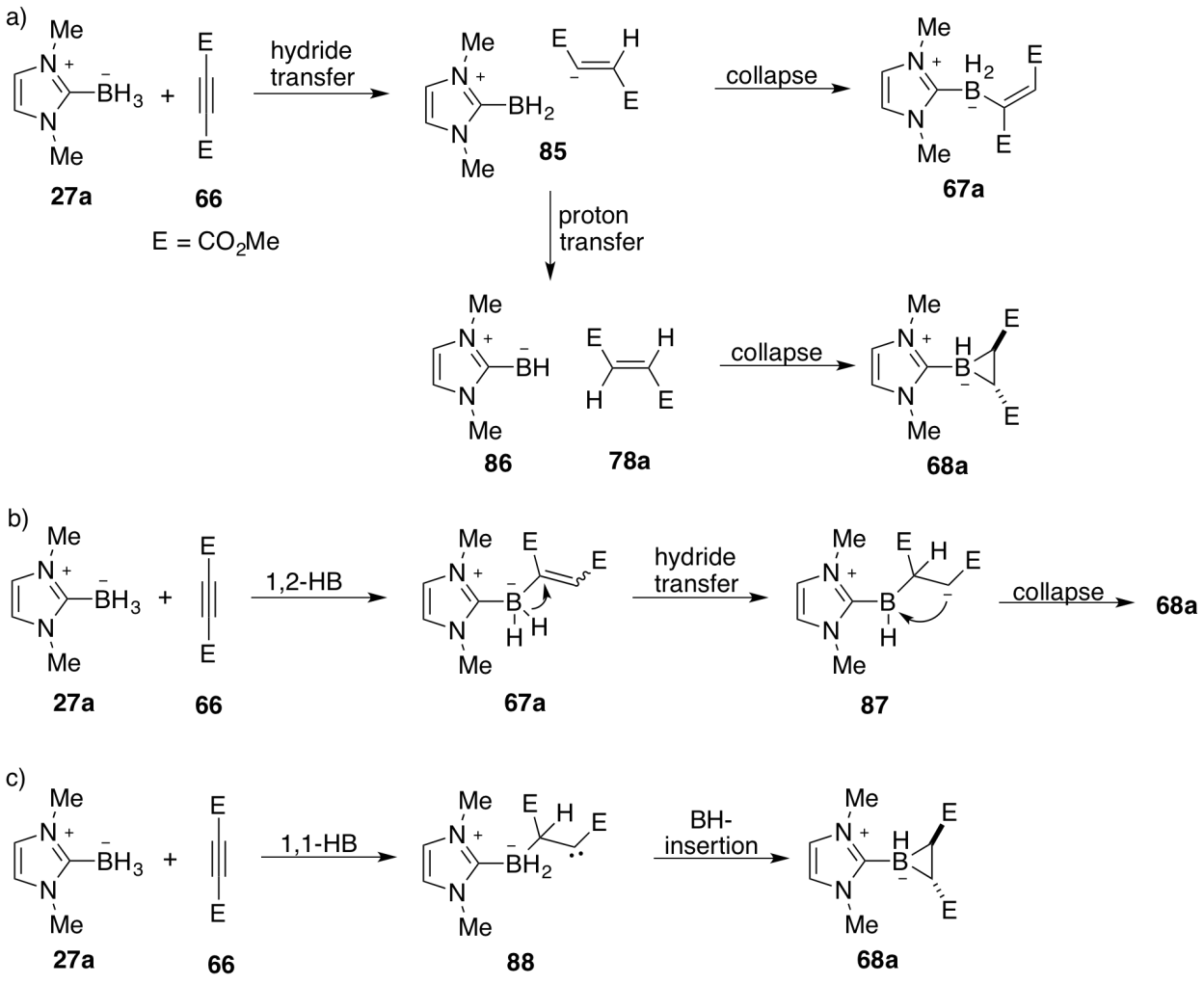
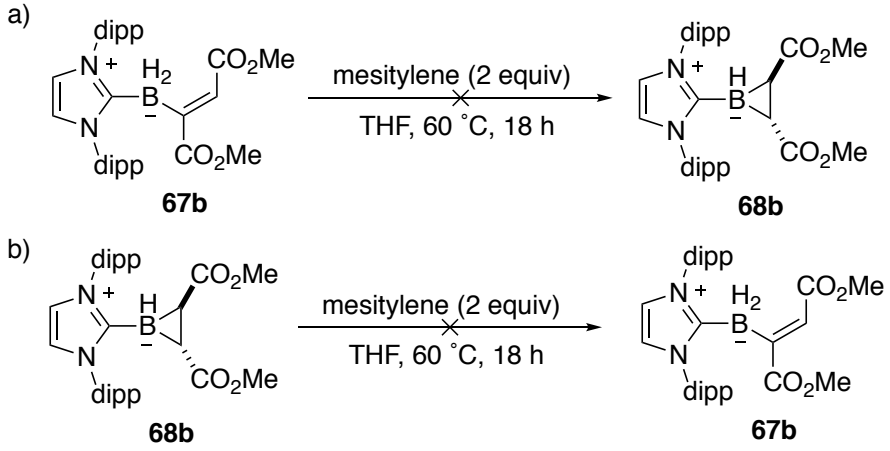


Figure 6. Possible reaction mechanisms for the formation of borirane **68a**

We first assessed whether the alkenylborane and borirane products were in equilibrium. Two control reactions were run in parallel. Pure samples of alkenylborane **67b** and borirane **68b**

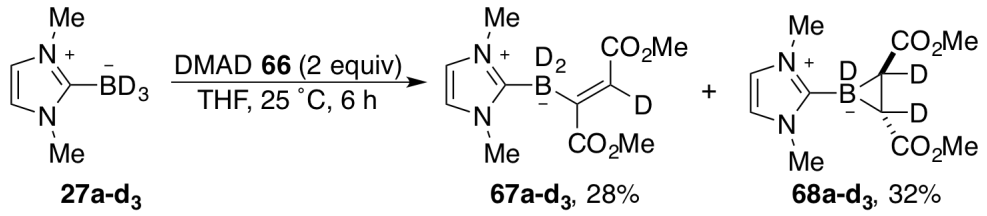
were heated in THF for 18 h (**Scheme 26**). Following heating, the samples were analyzed by ^{1}H and ^{11}B NMR spectroscopy to show that both samples were unchanged and resisted either interconversion with one another or decomposition (as determined by comparison to the internal standard, mesitylene). This indicates that alkenylborane **67b** is not a precursor to borirane **68b**, and therefore rules out the mechanism shown in **Figure 6b**.



Scheme 26. Attempted thermal equilibration reactions

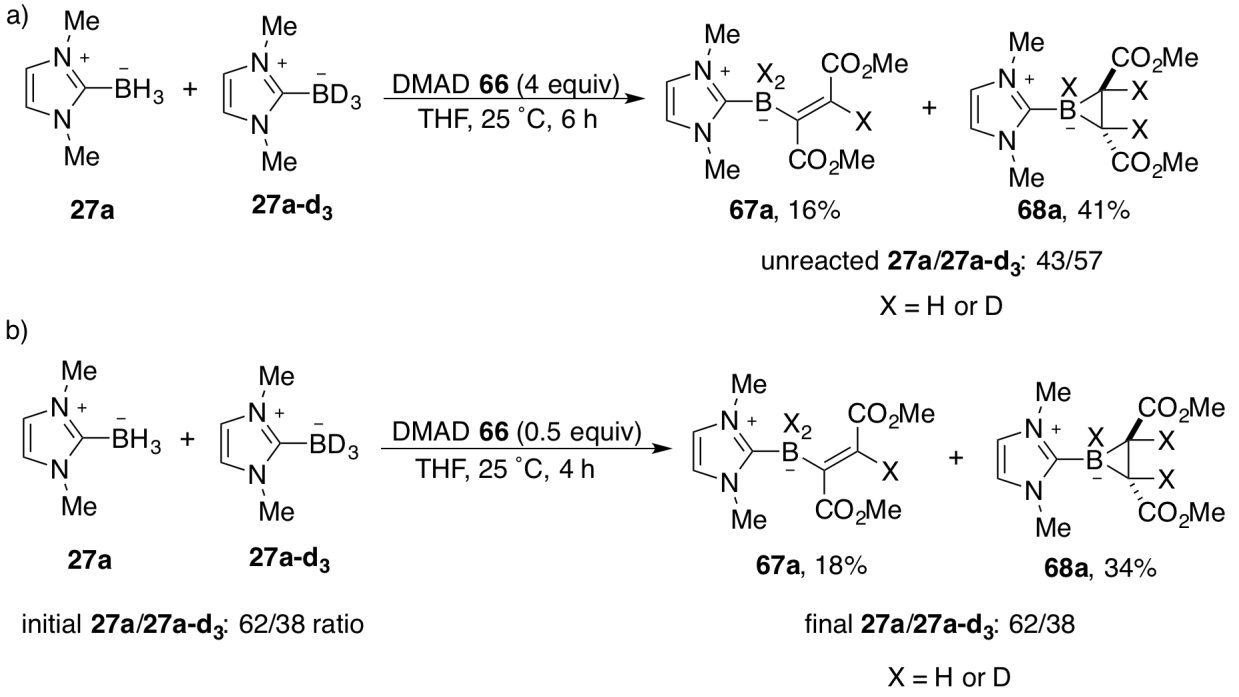
Deuterium-labeling studies were performed. As a preliminary experiment, deuterium-labeled NHC-borane **27a-d$_3$** was reacted with 2 equiv **66** under the optimized conditions shown in **Table 3**, entry 8 (**Scheme 27**). ^{11}B NMR analysis of the crude reaction mixture showed 99% of NHC-borane **27a-d$_3$** was consumed to form two products, alkenylborane **67a-d$_3$** (br pent, –29.0 ppm) and borirane **68a-d$_3$** (br t, –26.6 ppm) in a 65/35 ratio. After flash chromatography, deuterium-labeled alkenylborane **67a-d$_3$** was isolated in a 28% yield as a red oil while a 32% yield of borirane **68a-d$_3$** was obtained. HRMS data indicated that **27a-d$_3$** was approximately 93% pure with 7% diMe-NHC-BD_2H and trace amounts of diMe-NHC-BDH_2 and diMe-NHC-BH_3.

Accordingly, HRMS analysis of **67a-d$_3$** and **68a-d$_3$** showed 9% di-deuteration, attributed to di-deuterated **27a-d$_2$**.



Scheme 27. Synthesis of deuterium-labeled alkenylborane **67a-d$_3$** and borirane **68a-d$_3$**

Competition experiments were conducted to measure the kinetic isotope effect (KIE) for the reaction of **27a** with DMAD **66**. NHC-borane **27a** (1 equiv), NHC-borane **27a-d$_3$** (1 equiv), and DMAD **66** (4 equiv) were dissolved in THF at 25 °C. After 6 h, an ^{11}B NMR spectrum showed 96% of the combined **27a** and **27a-d$_3$** were consumed to give alkenylborane **67a** and borirane **68a** in a 63/37 ratio (**Scheme 28a**). Further analysis of the ^{11}B NMR spectrum showed an approximate 43/57 ratio of unreacted **27a**/**27a-d$_3$**, a 54/46 ratio of alkenylboranes **67a**/**67a-d$_3$**, and a 57/43 ratio of boriranes **68a**/**68a-d$_3$**. After flash chromatography, a 16% combined yield of alkenylboranes **67a** and **67a-d$_3$** and 41% yield of boriranes **68a** and **68a-d$_3$**. Next, NHC-boranes **27a** and **27a-d$_3$** (initial 62/38 ratio) and 0.5 equiv DMAD **66** were combined in THF at room temperature (**Scheme 28b**). The resulting ^{11}B NMR spectrum showed alkenylboranes **67a** and **67a-d$_3$** had formed in 34% (in approximately a 68/32 ratio) and boriranes **68a** and **68a-d$_3$** were formed in 18% (in about a 70/30 ratio). A 62/38 ratio of unreacted **27a**/**27a-d$_3$** was also observed.



Scheme 28. Deuterium-labeling experiments to estimate a KIE value

In both experiments in **Scheme 28**, it appears that minimal crossover had occurred. That is to say, the labeled products, **67a-d$_3$** and **68a-d$_3$**, were mostly trideuterated and little or no deuterium incorporation was observed in the unlabeled products, **67a** and **68a**. HRMS data indicated that mono- and di-deuterated products were formed in minimal amounts (6–10%) and resulted from reaction of the mono- and di-deuterated products with **66**. The ^{11}B NMR resonances of **27a-d$_3$** and **67a-d$_3$** appear as a septet and pentet, respectively. Partial D-incorporation would result in a doublet of pentets (for NHC–BHD$_2$) or triplet of triplets (for NHC–BH$_2$D) for **27a** or a doublet of triplets (for NHC–BHD–R) for **67a**;[57] these patterns were not observed in any of the spectra of these products. The ^{1}H NMR spectrum of the isolated mixture of **68a** and **68a-d$_3$** showed two dd resonances corresponding to the borirane protons (both under-integrating to approximately 0.54 H); these protons had the same chemical shifts and coupling constants as pure **27a**, further suggesting that no crossover had occurred.

The ^{11}B NMR spectra of **27a**, **27a-d$_3$** (**Scheme 27**), and the mixture of the two (**Scheme 28a**) are shown in **Figure 7**. The ^{11}B NMR spectrum of NHC-borane **27a** shows a quartet at –37.5 ppm, while **27a-d$_3$** gives a septet resonance at –37.9 ppm.

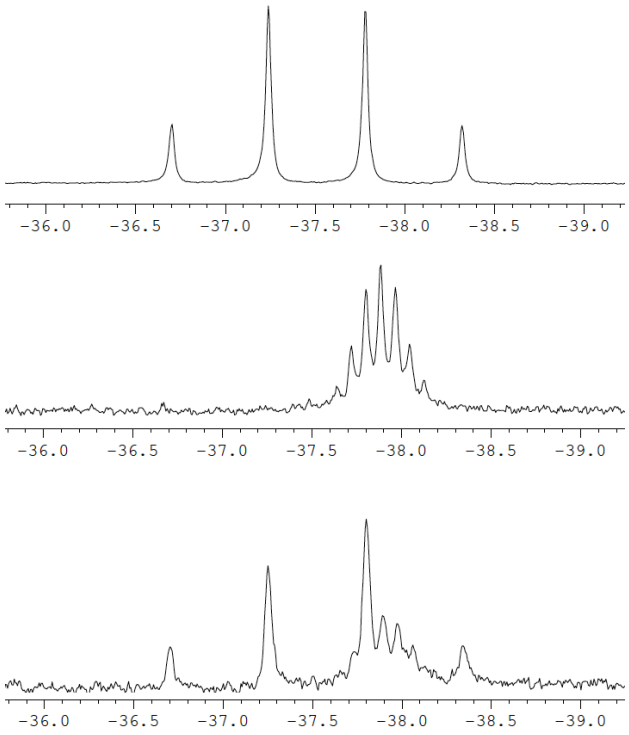


Figure 7. ^{11}B NMR spectra of **27a** (top), **27a-d$_3$** (middle), and **27a** and **27a-d$_3$** (bottom)

The ^{11}B NMR spectra of **67a** and **68a**, **67a-d$_3$** and **68a-d$_3$** (**Scheme 27**), and the mixture of the two sets of products (**Scheme 28a**) are shown in **Figure 8**. The ^{11}B NMR spectrum of alkenylborane **67a** shows a triplet at –28.7 ppm, while **27a-d$_3$** appears as a broad pentet at –29.0 ppm. While borirane **68a** gives a doublet at –26.4 ppm and **68a-d$_3$** is a broad triplet at –26.6 ppm. All deuterated NHC-boranes (**27a-d$_3$**, **67a-d$_3$, 68a-d$_3$**) have shifts more upfield than the unlabeled analogs.

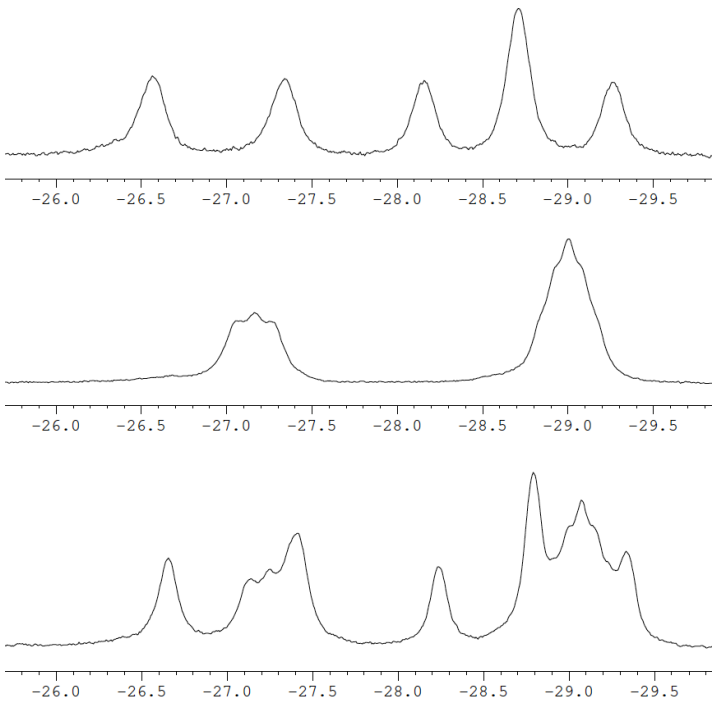


Figure 8. 11B NMR spectra of **67a** and **68a** (top), **67a-d$_3$** and **68a-d$_3$** (middle), and the mixture of the two sets of products (bottom)

The ratio of unreacted **27a** and **27a-d$_3$** can be used to determine a KIE value. At high conversion (**Scheme 28a**), the ratio of unreacted **27a**/**27a-d$_3$** give a KIE of approximately 1.3. The low conversion experiment (**Scheme 28b**) gives a KIE of approximately 1.0. Together, they give a range of 1.0–1.3, suggesting a normal, secondary kinetic isotope effect.

Density functional theory (DFT) calculations of the borirane-forming reaction were performed by Mr. Cheng Fang and Professor Peng Liu at the University of Pittsburgh. The calculations were performed at the M06-2X/6-311++G(d,p)//M06-2X/6-31G(d) level of theory and the solvation model based on density (SMD) model in THF. The most favorable pathways involved an initial, *trans*-selective hydride transfer from NHC-borane **27a** to alkyne **66** to form an ion pair of THF-stabilized borenium ion **90** and alkenyl anion **91** through transition state **89**

(**Figure 9**).[58] Subsequent hydroboration of alkenyl anion **91** by **90** forms 3-membered transition state **92** which can either immediately collapse to form the major product, alkenylborane **67a**, or undergo a [2+1] cyclization to give borirane **68a**. This mechanism is different from the three mechanisms considered in **Figure 6**. This observation that both products emerge from the same late transition state is consistent with the results shown in **Scheme 26** that demonstrated that alkenylborane **67b** and borirane **68b** did not interconvert. The KIE for the *trans*-selective hydride transfer step was calculated to be 1.35, similar to the experimental range. This value suggests that hydride transfer is the rate-determining step in the reaction mechanism.

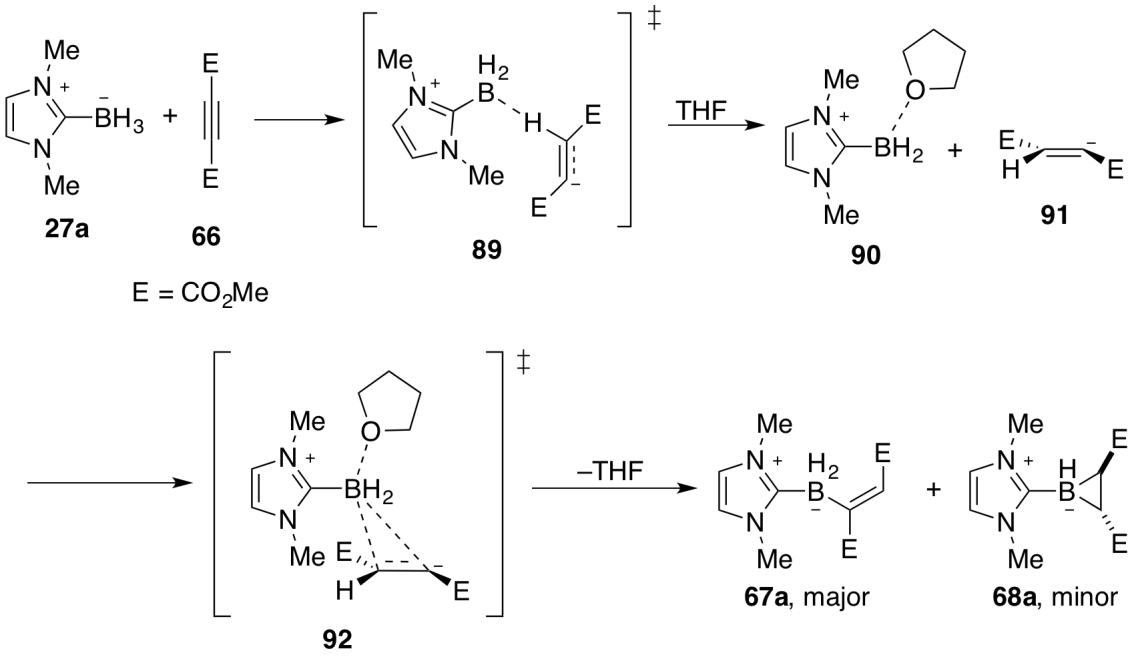


Figure 9. Mechanism of the formation of borirane and alkenylborane products

1.3 CONCLUSIONS

In this section, a new mode of reactivity of NHC-boranes has been described. It was previously known that NHC-borane reagents could be used in the hydroboration of alkynes (and alkenes), but required the generation of reactive borenium ions. Similarly, several syntheses of boriranes have been previously described, but under high-energy conditions. The borirane-forming reaction described here occurs through sequential hydroborations of an electron-deficient alkyne by NHC-borane. With *N,N*-dialkyl NHC-boranes, the reaction occurs at or below room temperature, while *N,N*-diaryl NHC-boranes require heating to drive the reaction. The reaction is highly *trans*-selective, which is rare for uncatalyzed hydroborations. While borirane formation is currently limited to the reaction of NHC-boranes or borohydrides with acetylenedicarboxylate, the ease of synthesis of these new compounds will allow for future studies in this area.

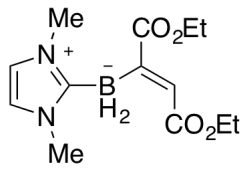
1.4 EXPERIMENTAL

General Information: All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry dichloromethane (DCM) and acetonitrile (MeCN) were obtained by passing the solvents through activated alumina. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under an argon atmosphere. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Thin layer chromatography (TLC) was performed on EMD 60 F254 silica gel and flash column chromatography was performed with 230–400 mesh silica gel purchased from Sorbent Technologies as the stationary phase. Visualization of TLC achieved

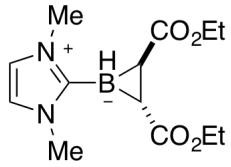
using ultraviolet light (254 nm). Melting points (mp) were measured with a Mel-Temp II apparatus and were uncorrected. IR spectra were obtained as neat samples with a Thermo-Nicolet IR 200 ATR-FTIR. Nuclear magnetic resonance spectra (NMR) were obtained on a Bruker Avance III 400 MHz and 500 MHz instruments. Chloroform (δ 7.26 ppm) was used as an internal standard for ^{1}H NMR spectra and $CDCl_3$ (δ 77.00 ppm) was used as an internal standard for ^{13}C NMR spectra. ^{11}B chemical shifts are relative to Et_2O-BF_3. The spectral data of single molecules were reported in the following order: chemical shift (δ), multiplicity, coupling constant (Hz), number of nuclei. The following abbreviations were used to describe coupling: s=singlet, d=doublet, t=triplet, q=quartet, sep=septet, m=multiplet, br=broad, dd=doublet of doublets. Due to quadrupole broadening, resonances of hydrogen or carbon atoms bonded to the boron atom are difficult to observe in ^{1}H or ^{13}C NMR spectra, respectively. HRMS were obtained with a Q-Tof analyzer. All spectra were acquired at room temperature.

N-heterocyclic carbene borane complexes **27a**–**i**,[31-32, 38, 62] **27a-d$_3$**,[57] ligated boranes **70a**–**e**,[63] and dibutyltin dihydride **76**[64] were prepared according to literature procedures. Their spectroscopic data were consistent with reported data.

Preparative hydroborations of dimethyl acetylenedicarboxylate with NHC-boranes

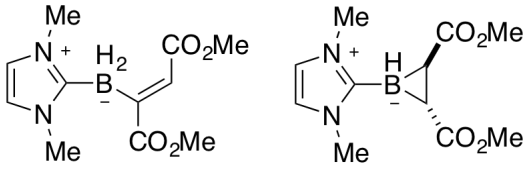


64



65

(*E*)-(1,4-Diethoxy-1,4-dioxobut-2-en-2-yl)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl) dihydroborate (64) and 1-(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis (ethoxycarbonyl)boriran-1-uide (65): NHC-borane **27a** (121 mg, 1.1 mmol, 1.1 equiv) and diethyl acetylenedicarboxylate **63** (0.16 mL, 1.0 mmol, 1.0 equiv) were dissolved in THF (4 mL) and stirred at 25 ˚C for 18 h. A 62/38 ratio of **64**/**65** was observed by ^{11}B NMR spectroscopy after 18 h. E-alkenylborane **64** was isolated as a red oil (84 mg, 30%) and borirane **65** was isolated as a brown oil (24 mg, 9%). *E*-alkenylborane **64**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (s, 2H), 6.48 (s, 1H), 4.09 (q, 2H, J = 7.0 Hz), 4.08 (q, 2H, J = 7.2 Hz), 3.73 (s, 6H), 2.05 (br q, 2H, J_{BH} = 87.3 Hz), 1.23 (t, 3H, J = 7.2 Hz), 1.21 (t, 3H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.7, 168.4, 127.8, 120.1, 60.0, 59.6, 36.1, 14.3; ^{11}B NMR (128 MHz, $CDCl_3$) δ –28.7 (t, J_{BH} = 87.7 Hz). Borirane **65**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 2H), 4.06 (q, 2H, J = 7.1 Hz), 3.84 (q, 2H, J = 8.0 Hz), 3.78 (s, 6H), 2.19 (dd, 1H, J = 8.0, 5.6 Hz), 1.99 (br t, 1H, J = 4.8 Hz), 1.20 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 177.6, 177.3, 120.7, 59.0, 58.7, 36.0, 26.3, 24.6, 14.6, 14.5; ^{11}B NMR (128 MHz, $CDCl_3$) δ –26.5 (d, J_{BH} = 122.9 Hz).



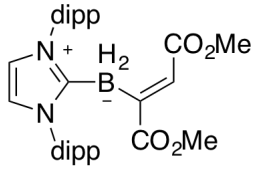
67a

68a

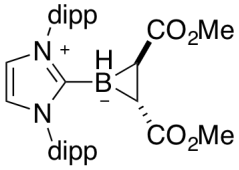
1-(1,3-Dimethyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide (68a) and (*E*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)dihydroborate (67a):

Typical Procedure 1 (TP1) for the formation of borirane and alkenylborane compounds: NHC-borane **27a** (110 mg, 1.0 mmol, 1.0 equiv) was dissolved in THF (9.0 mL). A solution of dimethyl acetylenedicarboxylate **66** (0.24 mL, 2.0 mL, 2.0 equiv) in THF (1.0 mL) was added dropwise over several minutes. The resulting solution was stirred at room temperature for 6 h. A 57/43 ratio of **67a/68a** was observed by ^{11}B NMR spectroscopy after 6 h. The volatiles were removed by evaporation and the crude residue was purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give alkenylborane **67a** as a red oil (94 mg, 36%) and borirane **68a** as a yellow oil (60 mg, 23%). *E*-alkenyl-borane **67a:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (s, 2 H), 6.46 (s, 1 H), 3.71 (s, 6 H), 3.64 (s, 3 H), 3.58 (s, 3 H), 2.28–1.76 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.97, 168.59, 162.79, 127.75, 120.11, 51.50, 50.92, 36.01; ^{11}B NMR (160 MHz, $CDCl_3$) δ –28.7 (J_{BH} = 88 Hz); IR (neat) 2950, 2340, 1703, 1599, 1484, 1432, 1225, 1192, 1172, 1015, 874, 729 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{11}H_{16}N_2O_4B$ 251.1198, found 251.1120; R_f = 0.46 (80/20 hexanes:EtOAc). Borirane **68a:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (s, 2 H), 3.79 (s, 6 H), 3.62 (s, 3 H), 3.44 (s, 3 H), 2.23 (dd, 1 H, *J* = 7.5, 5.5 Hz), 1.98 (br t, 1 H, *J* = 4.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.97, 177.74, 120.77, 50.77, 50.47, 35.95, 26.14, 24.36; ^{11}B NMR (160 MHz, $CDCl_3$) δ –26.4 (J_{BH} = 123 Hz); IR (neat) 3124, 2948, 2444, 1677,

1433, 1293, 1259, 1235, 1132, 1035, 812, 750, 707 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{11}H_{18}N_2O_4B$ 253.1354, found 253.1358; R_f = 0.52 (97/3 DCM:MeOH).



67b

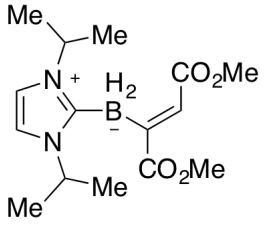


68b

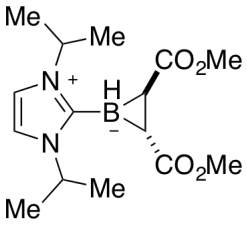
1-(1,3-Bis(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl) boriran-1-uide (68b) and (*E*)-(1,3-bis(2,6-diisopropyl-phenyl)-1*H*-imidazol-3-ium-2-yl)(1-methoxy-4-(methylperoxy)-1-oxo-4λ^2-but-2-en-2-yl)dihydroborate (67b):

Typical Procedure 2 (TP2) for the formation of borirane and alkenylborane compounds: NHC-borane **27b** (400 mg, 1.0 mmol, 1.0 equiv) and dimethyl acetylenedicarboxylate **66** (0.24 mL, 2.0 equiv, 2.0 equiv) were dissolved in MeCN (2.0 mL). The resulting solution was heated to 80 ˚C for 18 h. An 14/86 ratio of **67b**/**68b** was observed by ^{11}B NMR spectroscopy. The volatiles were removed by evaporation and the crude residue was purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give *E*-alkenyl borane **67b** (25 mg, 5%) as a white solid and borirane **68b** (432 mg, 80%) as a white solid. Crystals of **67b** and **68b** were grown for X-ray analysis by slow crystal growth using DCM/pentanes. *E*-alkenylborane **67a:** ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, 2 H, *J*=7.8 Hz), 7.24 (d, 4 H, *J*=7.6 Hz), 6.98 (s, 2 H), 6.16 (s, 1H), 3.45 (s, 3 H), 3.44 (s, 3 H), 2.81 (sep, 4 H, *J*=6.8 Hz), 1.28 (d, 2 H, *J*=6.8 Hz), 1.10 (d, 2 H, *J*=6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.50, 167.66, 145.97, 134.06, 129.85, 129.79, 123.86, 122.16, 50.89, 50.46, 28.18, 25.98, 22.46; ^{11}B NMR (160 MHz, $CDCl_3$) δ –28.1 (J_{BH} = 86.6 Hz); IR (neat) 3024, 2970, 2365, 2338, 1963, 1738, 1456, 1365, 1228, 1216, 1049, 802, 758 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{33}H_{44}N_2O_4B$ 543.3389, found 543.3368; mp 180–

182 ˚C; R_f = 0.82 (60/40 hexanes:ethyl acetate). Borirane **68b:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (t, 2 H, *J* = 7.8 Hz), 7.34 (d, 2 H, *J* = 7.5 Hz), 7.30 (d, 2 H, *J* = 7.5 Hz), 7.07 (s, 2 H), 3.39 (s, 3 H), 3.28 (s, 3 H), 2.77 (sep, 2 H, *J* = 6.8 Hz), 2.69 (sep, 2 H, *J* = 6.8 Hz), 1.58 (br t, 1 H, *J* = 7.0 Hz), 1.34 (d, 6 H, *J* = 6.5 Hz), 1.24 (d, 6 H, *J* = 7.0 Hz), 1.16 (d, 6 H, *J* = 7.0 Hz), 1.05 (d, 6 H overlapped with 1 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.02, 177.65, 167.50, 145.65, 145.42, 133.72, 130.30, 124.49 124.08, 123.12, 50.17, 49.95, 28.46, 28.44, 26.81, 26.14, 25.97, 24.98, 22.80, 21.80; ^{11}B NMR (160 MHz, $CDCl_3$) δ –26.1 (J_{BH} = 123 Hz); IR (neat) 3154, 3122, 2968, 2934, 2869, 2465, 1714, 1680, 1461, 1433, 1255, 1143, 1045, 752 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{33}H_{46}N_2O_4B$ 545.3545, found 545.3555; mp 225–227 ˚C (decomposed); R_f = 0.61 (60/40 hexanes:ethyl acetate).



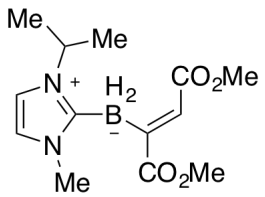
67c



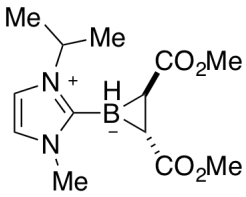
68c

1-(1,3-Diisopropyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl) boriran-1-uide (68c) and (*E*)-(1,3-diisopropyl-1*H*-imidazol-3-ium-2-yl) (1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67c): Following TP1 with NHC-borane **27c** (140 mg, 0.81 mmol, 1.0 equiv), THF (7.0 mL), and a solution of dimethyl acetylenedicarboxylate **66** (0.20 mL, 1.6 mmol, 2.0 equiv) in THF (1.0 mL), a crude ratio of 61/39 **67c**/**68c** was observed by ^{11}B NMR spectroscopy after 6 h. *E*-alkenylborane **67c** was isolated as a yellow oil (64 mg, 26%) and borirane **68c** was isolated as a white solid (58 mg, 23%). Crystals of borirane **73c** were grown for X-ray analysis by slow crystal growth using DCM/pentanes. *E*-alkenyl borane **67c:** ^{1}H NMR (400 MHz, $CDCl_3$)

δ 6.93 (s, 2 H), 6.41 (s, 1 H), 5.05 (sep, 2 H, *J*=8.5 Hz), 3.59 (s, 3 H), 3.57 (s, 3 H), 1.32 (d, 2 H, *J*=8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.81, 168.45, 126.85, 115.40, 51.33, 50.80, 49.09, 22.70; ^{11}B NMR (160 MHz, $CDCl_3$) δ –28.6 (J_{BH} = 88 Hz); IR (neat,) 3162, 3130, 2980, 2949, 2317, 1724, 1692, 1432, 1396, 1015, 883, 766, 651 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{15}H_{24}N_2O_4B$ 307.1824, found 307.1817; R_f = 0.79 (80/20 hexanes:ethyl acetate). Borirane **68c:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (s, 2 H), 5.22 (sep, 2 H, *J*=8.4 Hz), 3.61 (s, 3 H), 3.42 (s, 3 H), 2.22 (dd, 1 H, *J* = 10, 7.0 Hz), 2.05 (br t, 1 H, *J* = 5.8 Hz), 1.43 (d, 6 H, *J*=8.5 Hz), 1.38 (d, 6 H, *J*=8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.11, 177.53, 118.69, 115.98, 50.80, 50.46, 49.87, 23.35, 22.77; ^{11}B NMR (160 MHz, $CDCl_3$) δ –26.2 (J_{BH} = 122 Hz); IR (neat) 3157, 3122, 2983, 2945, 2442, 2360, 2340, 1680, 1432, 1295, 1142, 1027, 780, 715, 658 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{15}H_{26}N_2O_4B$ 309.1980; found 309.1989; mp 189–192 ˚C (decomposed); R_f = 0.39 (80/20 hexanes:ethyl acetate).



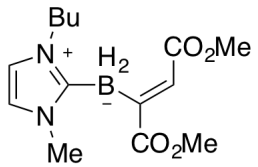
67d



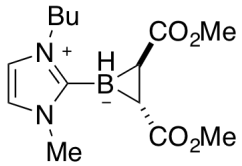
68d

1-(3-Isopropyl-1-methyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl) boriran-1-uide (68d) and (*E*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)(3-isopropyl-1-methyl-1*H*-imidazol-3-ium-2-yl)dihydroborate (67d): Following TP1 with NHC-borane **27d** (140 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (0.25 mL, 2.0 mmol, 2.0 equiv), and THF (10 mL), a 56/44 ratio of **67d/68d** was observed by ^{11}B NMR spectroscopy after 6 h. *E*-alkenylborane **67d** was isolated as a yellow oil (72 mg, 26%) and borirane **68d** was isolated as a brown oil (76 mg,

27%). *E*-alkenylborane **67d:** ^{1}H (400 MHz, $CDCl_3$) δ 6.88 (d, 1H, *J* = 2.0 Hz), 6.82 (d, 1H, *J*=2.0 Hz), 6.43 (s, 1H), 5.00 (sep, 1H, *J*=6.8 Hz), 3.70 (s, 3H), 3.60 (s, 3H), 3.57 (s, 3H), 1.31 (d, 6H, *J* = 6.8 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 175.1, 168.7, 127.3, 120.9, 114.7, 51.6, 51.0, 49.6, 36.0, 22.9; ^{11}B (128 MHz, $CDCl_3$) δ –28.7 (J_{BH} = 87.7 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{13}H_{20}BN_2O_4$ 279.1511, found 279.1520; R_f=0.54 (40:60 hexanes:ethyl acetate). Borirane **68d:** ^{1}H (400 MHz, $CDCl_3$) δ 6.92 (d, 1H, *J*=2.0 Hz), 6.86 (d, 1H, *J*=2.0 Hz), 5.13 (sep, 1H, *J*=6.9 Hz), 3.81 (s, 3H), 3.61 (s, 3H), 3.42 (s, 3H), 2.21 (dd, 1H, *J*=7.8, 5.4 Hz), 2.01 (br t, 1H, *J*=4.6 Hz), 1.41 (d, 3H, *J*=6.8 Hz), 1.36 (d, 3H, *J*=6.8 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 178.0, 177.6, 161.4, 121.4, 115.4, 50.7, 50.4, 50.1, 35.9, 26.2, 24.5, 23.1, 22.6; ^{11}B (160 MHz, $CDCl_3$) δ –26.3 (J_{BH} = 122.6 Hz); IR (neat) 3161, 3120, 2983, 2944, 2447, 1702, 1678, 1576, 1467, 1434, 1395, 1295, 1238, 1187, 1139, 1065, 1037, 952 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{13}H_{22}BN_2O_4$ 281.1677, found 281.1678; mp 123–125 ˚C; R_f = 0.41 (100% ethyl acetate).



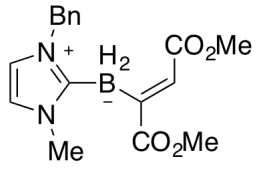
67e



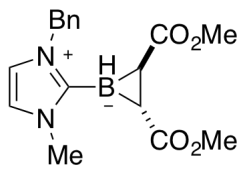
68e

1-(3-Butyl-1-methyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide (68e) and (*E*)-(3-butyl-1-methyl-1*H*-imidazol-3-ium-2-yl) (1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67e): Following TP1 with NHC-borane **27e** (150 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (0.25 mL, 2.0 mmol, 2.0 equiv), and THF (10 mL), a 56/44 ratio of **67e/68e** was observed by ^{11}B NMR spectroscopy after 8 h. *E*-alkenylborane **67e** was isolated as a yellow oil (93 mg, 32%) and borirane **68e** was isolated as a brown oil (83 mg, 28%). *E*-alkenylborane **67e:** ^{1}H (400 MHz, CDCl3) δ 6.80 (d, 1H, *J*=1.6 Hz), 6.79 (d, 1H, *J*=1.6 Hz),

6.42 (s, 1H), 4.05 (t, 2H, *J*=7.6 Hz), 3.67 (s, 3H), 3.59 (s, 3H), 3.56 (s, 3H), 2.33–1.89 (br q, 2H, J_{BH} = 86.8 Hz, 2H), 1.69–1.62 (m, 2 H), 1.33–1.24 (m, 2H), 0.87 (t, 3 H, *J*=7.4 Hz); ^{13}C (125 MHz, CDCl3) δ175.0, 168.7, 167.8, 162.8, 127.4, 120.4, 118.8, 51.5, 51.0, 48.5, 36.0, 32.3, 19.7, 13.6; ^{11}B (160 MHz, CDCl3) δ –28.7 (t, $J_{B\,H}$=87.5 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{14}H_{22}BN_2O_4$ 293.1667, found 293.1676; R_f = 0.72 (20/80 hexanes: ethyl acetate). Borirane **68e:** ^{1}H (500 MHz, $CDCl_3$) δ 6.80 (d, 1H, *J* = 2.0 Hz), 6.78 (d, 1H, *J* = 2.0 Hz), 6.42 (s, 1H), 4.05 (t, 2H, *J* = 7.6 Hz), 3.67 (s, 3H), 3.59 (s, 3H), 3.56 (s, 3H), 2.00 (br q, 2H, J_{BH} = 84.8 Hz), 1.66 (p, 2H, *J* = 7.2 Hz), 1.33–1.26 (m, 2H), 0.87 (t, 3H, *J* = 7.6 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 178.0, 177.8, 120.9, 119.3, 50.8, 50.4, 48.6, 36.0, 32.1, 26.2, 24.5, 19.7, 13.5; ^{11}B (160 MHz, $CDCl_3$) δ –28.9 (d, J_{BH}=123.4 Hz); IR (neat) 3124, 2950, 2875, 2445, 2360, 1675, 1574, 1481, 1433, 1387, 1292, 1258, 1186, 1132, 1030, 951, 886 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{14}H_{24}BN_2O_4$ 295.1824, found 295.1838; R_f = 0.21 (20/80 hexanes:ethyl acetate).



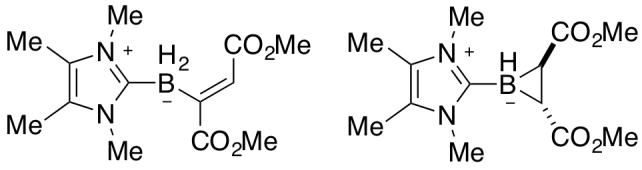
67f



68f

1-(3-Benzyl-1-methyl-1*H*-imidazol-3-ium-2-yl) -2,3-bis(methoxycarbonyl) boriran-1-uide (68f) and (*E*)-(3-benzyl-1-methyl-1*H*-imidazol-3-ium-2-yl)(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67f): Following TP1 with NHC-borane **27f** (190 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate (0.25 mL, 2.0 mmol, 2.0 equiv), and THF (10 mL), a 56/44 ratio of **67f/68f** was observed by ^{11}B NMR spectroscopy after 8 h. *E*-alkenylborane **67f** was isolated as a yellow oil (81 mg, 25%) and borirane **68f** was isolated as a brown oil (80 mg, 24%). *E*-alkenylborane **67f:** ^{1}H (500 MHz, $CDCl_3$) δ 7.36–7.24 (m, 5H), 6.83 (d, 1H, *J* = 1.5

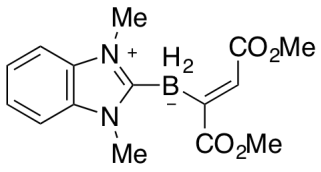
Hz), 6.71 (d, 1H, J = 2.0 Hz), 6.51 (s, 1H), 5.35 (s, 2H), 3.78 (s, 3H), 3.66 (s, 3H), 3.62 (s, 3H), 2.46–1.94 (br q, 2H, J_{BH} = 86.0 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 174.9, 168.7, 162.5, 135.9, 128.8, 128.3, 128.2, 127.8, 120.8, 118.8, 52.1, 51.6, 51.0, 36.2; ^{11}B (160 MHz, $CDCl_3$) δ –28.5 (J_{BH} = 87.0 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{17}H_{20}BN_2O_4$ 327.1511, found 327.1525; R_f = 0.58 (40/60 hexanes:ethyl acetate). Borirane **68f:** ^{1}H (500 MHz, $CDCl_3$) δ 7.30–7.19 (m, 5H), 6.78 (d, 1H, J = 2.0 Hz), 6.66 (d, 1H, J = 2.0 Hz), 5.35 (d, 1H, J = 15 Hz), 5.21 (d, 1H, J = 15 Hz), 3.75 (s, 3H), 3.53 (s, 3H), 3.38 (s, 3H), 2.20 (dd, 1H, J = 7.8, 5.8 Hz), 1.99 (br t, 1H, J=5.0 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 178.0, 177.8, 162.8, 135.0, 129.1, 128.6, 128.4, 121.3, 119.4, 52.3, 50.8, 50.6, 36.1, 26.5, 24.6, 21.1, 14.2; ^{11}B (160 MHz, $CDCl_3$) δ –26.3 (J=123.0 Hz); IR (neat) 3123, 2948, 2445, 1675, 1476, 1433, 1293, 1136, 1028, 951 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{17}H_{20}BN_2O_4$ 327.1511, found 327.1526; R_f = 0.49 (100% ethyl acetate).



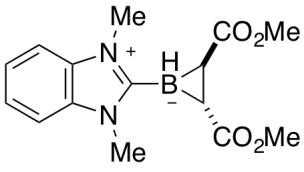
67g **68g**

2,3-Bis(methoxycarbonyl)-1-(1,3,4,5-tetramethyl-1*H*-imidazol-3-ium-2-yl)boriran-1-uide (68g) and (*E*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)(1,3,4,5-tetramethyl-1*H*-imidazol-3-ium-2-yl)dihydroborate (67g): Following TP1 with NHC-borane **27g** (140 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate (0.25 mL, 2.0 mmol, 2.0 equiv), and THF (10 mL), a 69/31 ratio of **67g/68g** was observed by ^{11}B NMR spectroscopy after 45 min. *E*-alkenyl borane **67g** was isolated as a yellow oil (20 mg, 7%) and borirane **68g** was isolated as a brown oil (46 mg, 16%). *E*-alkenylborane **67g:** ^{1}H (500 MHz, $CDCl_3$) δ 6.48 (s, 1H), 3.64 (s, 3H), 3.61 (s, 3H), 3.60 (s, 6H), 2.10 (s, 6H); ^{13}C (100 MHz, $CDCl_3$) δ 175.1, 168.9, 127.6, 123.3, 51.5, 51.0. 32.6,

8.8; ^{11}B (128 MHz, $CDCl_3$) δ –28.3 (t, J_{BH} = 87.0 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{13}H_{20}BN_2O_4$ 279.1511, found 279.1519; R_f = 0.50 (40:60 hexanes:ethyl acetate). Borirane **68g:** ^{1}H (500 MHz, CDCl3) δ 3.64 (s, 6H), 3.61 (s, 3H), 3.45 (s, 3H), 2.22 (dd, 1H, *J*=7.8, 5.8 Hz), 2.09 (s, 6H), 1.91 (br t, 1H, *J* = 4.5 Hz); ^{13}C (125 MHz, CDCl3) δ 178.2, 177.9, 124.1, 50.8, 50.5, 32.6, 26.9, 24.7, 8.8, 8.3; ^{11}B (160 MHz, CDCl3) δ –25.9 (d, J_{BH} = 122.6 Hz); IR (neat) 2923, 2852, 2388, 2163, 2010, 1705, 1578, 1434, 1397, 1296, 1255, 1203, 1145, 1095, 917 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{13}H_{22}BN_2O_4$ 281.1668, found 281.1678; R_f = 0.29 (100% ethyl acetate).



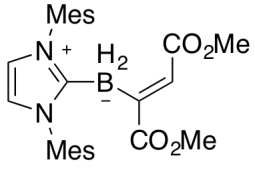
67h



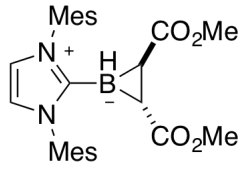
68h

1-(1,3-Dimethyl-1*H*-benzo[*d*]imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide (68h) and (*E*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)(1,3-dimethyl-1*H*-benzo[*d*]imidazol-3-ium-2-yl)dihydroborate (67h): Following TP1 with NHC-borane **27h** (160 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (0.25 mL, 2.0 mmol, 2.0 equiv), and THF (10 mL), a 44/56 ratio of **67h/68h** was observed by ^{11}B NMR spectroscopy after 40 h. *E*-alkenylborane **67h** was isolated as a yellow oil (85 mg, 28%) and borirane **68h** was isolated as a brown oil (71 mg, 24%). *E*-alkenylborane **67h:** ^{1}H (500 MHz, $CDCl_3$) δ 7.44–7.42 (m, 2H), 7.39–7.37 (m, 2H), 6.56 (s, 1H), 3.93 (s, 6H), 3.64 (s, 3H), 3.49 (s, 3H), 2.24 (br q, 2H, J_{BH} = 87.5 Hz); ^{11}B (160 MHz, $CDCl_3$) δ –28.2 (t, J_{BH} = 87.9 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{15}H_{18}BN_2O_4$ 301.1354, found 301.1366; R_f = 0.69 (40:60 hexanes:ethyl acetate). Borirane **68h:** ^{1}H (500 MHz, $CDCl_3$) δ 7.48–7.42 (m, 4H), 4.00 (s, 6H), 3.66 (s, 3H), 3.41 (s, 3H), 2.36 (dd, 1H, *J* = 5.5, 8.0

Hz), 2.09 (t, 1H, J = 4.8 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 177.8, 177.6, 170.1, 132.7, 124.8, 111.1, 50.8, 50.5, 32.3, 26.5, 24.5; ^{11}B (160 MHz, $CDCl_3$) δ –26.2 (d, J_{BH} = 123.0 Hz); IR (neat) 2949, 2450, 2031, 1680, 1469, 1432, 1395, 1290, 1255, 1187, 1134, 1057, 1025, 948, 885 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{15}H_{20}BN_2O_4$ 303.1511, found 303.1525; mp 142–145 ˚C; R_f = 0.31 (40:60 hexanes:ethyl acetate).



67i

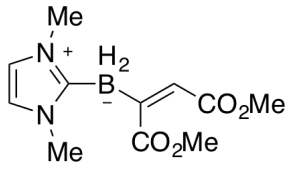


68i

1-(1,3-Dimesityl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide (68i) and (*E*)-(1,3-dimesityl-1*H*-imidazol-3-ium-2-yl)(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67i): Following TP2 with NHC-borane **27i** (320 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (0.25 mL, 2.0 mmol, 2.0 equiv), and MeCN (2.0 mL), a 19/81 ratio of **67i/68i** was observed by ^{11}B NMR spectroscopy. *E*-alkenylborane **67i** (46 mg, 10%) was isolated as a white solid and borirane **68i** (142 mg, 31%) as a white solid. Crystals of **67i** and **68i** were grown for X-ray analysis by slow crystal growth using DCM/pentanes. *E*-alkenylborane **67i:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (s, 6 H), 6.27 (s, 1 H), 3.54 (s, 3 H), 3.44 (s, 3 H), 2.32 (s, 6 H), 2.12 (s, 12 H), 1.54–1.89 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.99, 168.26, 139.08, 135.35, 134.06, 131.02, 128.91, 121.04, 51.01, 50.54, 21.09, 17.87; ^{11}B NMR (160 MHz, $CDCl_3$) δ –28.3 (t, J_{BH} = 92 Hz); IR (neat) 3133, 2943, 2922, 2854, 2333, 2291, 1729, 1696, 1600, 1487, 1432, 1218, 1165, 1031, 730 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{27}H_{32}N_2O_4B$ 459.2450; found 459.2458; mp 115–117 ˚C; R_f = 0.61 (60/40 hexanes:ethyl acetate). Borirane **68i:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (s, 4 H), 6.99 (s, 2 H),

3.37 (s, 3 H), 3.31 (s, 3 H), 2.37 (s, 6 H), 2.22 (s, 6 H), 2.03 (s, 6 H), 1.63 (br t, 1 H, J = 7.3 Hz), 1.20 (br t, 1 H, J = 5.0 Hz), 0.50–0.98 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.35, 177.86, 164.29, 139.42, 134.83, 133.54, 129.68, 129.47, 129.22, 122.10, 50.20, 50.08, 24.77, 24.23, 21.13, 18.06, 17.75; ^{11}B NMR (160 MHz, $CDCl_3$) δ: –25.6 (d, J=122 Hz); IR (neat) 3151, 3119, 2946, 2450, 2364, 1677, 1490, 1428, 1291, 1140, 1036, 870, 730 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calculated for $C_{27}H_{34}N_2O_4B$ 461.2606, found 461.2587; mp 233–235 ˚C (decomposed); R_f = 0.32 (60/40 hexanes:ethyl acetate).

Isolation and characterization of Z-alkenylboranes

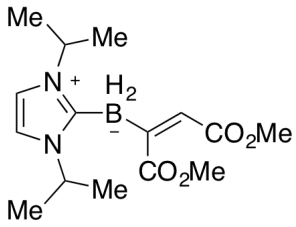


67aZ

1-(1,3-Dimethyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide (68a), (*E*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl) (1,3-dimethyl-1*H*-imidazol-3-ium-2-yl) dihydroborate (67a), and (*Z*)-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)dihydroborate (67aZ):

Typical Procedure 3 (TP3) for the formation of borirane and alkenylborane compounds: NHC-borane **27a** (110 mg, 1.0 mmol, 1.0 equiv) was added to a flask containing THF (4 mL). The flask was cooled to –78 ˚C. A solution of dimethyl acetylenedicarboxylate **66** (0.18 mL, 1.5 mmol, 1.5 equiv) in THF (1.0 mL) was added dropwise to the stirring solution. The reaction mixture was allowed to warm to room temperature over 18 h. The solution turned dark red over the course of the reaction. ^{11}B NMR spectroscopy was used to analyze an aliquot from the

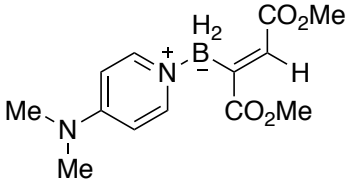
reaction mixture to show 99% conversion to products (67/30/3 **67a**/**68a**/**67aZ** ratio). The solvent was removed under reduced pressure to give a red oil. The crude residue was purified by flash chromatography (hexanes:ethyl acetate) to give *E*-alkenylborane **67a** (86 mg, 34%) as a yellow oil, the *Z*-alkenylborane **67aZ** as a yellow oil (11 mg, 4%), and borirane **68a** (31 mg, 12%) as a red oil. *Z*-alkenylborane **67aZ**: ^{1}H (500 MHz, CDCl3) δ 6.87 (s, 2H), 5.45 (s, 1H), 3.75 (s, 6H), 3.73 (s, 3H), 3.64 (s, 3H), 2.04 (br q, 2H, J_{BH}=89.3 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 176.2, 165.8, 120.8, 118.8, 51.5, 51.2, 36.2; ^{11}B (160 MHz, $CDCl_3$) δ –26.4 (J_{BH}=89.6 Hz); HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{11}H_{18}BN_2O_4$ 253.1354, found 253.1364; R_f=0.26 (80:20 ethyl acetate:hexanes).



67cZ

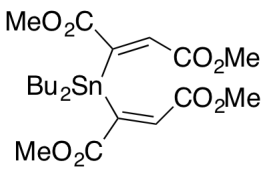
1-(1,3-Diisopropyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl) boriran-1-uide (68c), (*E*)-(1,3-diisopropyl-1*H*-imidazol-3-ium-2-yl)(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67c), and (*Z*)-(1,3-diisopropyl-1*H*-imidazol-3-ium-2-yl)(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)dihydroborate (67cZ): Following TP3 with NHC-borane **27c** (170 mg, 1.0 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (0.18 mL, 1.5 mmol, 1.5 equiv), and THF (5.0 mL), a 35/62/3 ratio of **73c/72c/72cZ** was observed after 18 h by ^{11}B NMR spectroscopy. Purification by flash chromatography (hexanes:ethyl acetate) gave *E*-alkenylborane **67c** (74 mg, 24%) as a yellow oil, *Z*-alkenylborane **67cZ** as a yellow oil (9 mg, 3%), and borirane **68c** (83 mg, 27%) as a white solid. *Z*-alkenylborane **67cZ**: ^{1}H (500 MHz,

CDCl3) δ 7.02 (s, 2H), 5.29 (s, 1H), 5.01 (sept, 2H, *J*=6.7 Hz), 3.75 (s, 3H), 3.63 (s, 3H), 1.39 (d, 12H, *J*=6.5 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 176.0, 166.0, 117.9, 116.1, 51.4, 51.2, 49.8, 23.1; ^{11}B (160 MHz, $CDCl_3$) δ –26.3 ppm (J_{BH}=88.6 Hz); HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{15}H_{26}BN_2O_4$ 309.1980, found 309.1988; R_f=0.28 (80:20 ethyl acetate:hexanes).

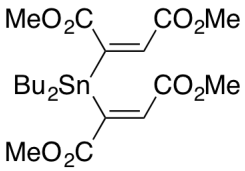


71c

4-Dimethylaminopyridine-(E)-alkenylborane (71c): Following TP1 with ligated-borane **70c** (34 mg, 0.25 mmol, 1.0 equiv), dimethyl acetylenedicarboxylate **66** (61 μL, 0.50 mL, 2.0 equiv), and THF (2.5 mL), *E*-alkenylborane **71c** was isolated as a brown oil (16 mg, 23%). *E*-alkenylborane **71c**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.20 (d, 2H, *J* = 7.0 Hz), 6.61 (s, 1H), 6.48 (d, 2H, *J* = 7.5 Hz), 3.70 (s, 3H), 3.61 (s, 3H), 3.08 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ174.3, 168.9, 155.0, 147.3, 130.4, 106.1, 51.4, 51.2, 39.5; ^{11}B NMR ($CDCl_3$, 160 MHz) δ –10.3 (br t); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{13}H_{18}BN_2O_4$ 277.1354, found 277.1364.



81a

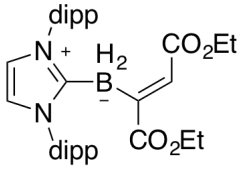


81b

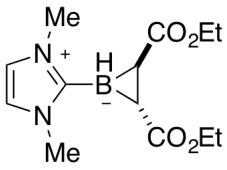
Tetramethyl 2,2'-(dibutylstannanediyl)difumarate (81a) and dimethyl 2-(dibutyl ((*E*)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)stannyl) fumarate (81b): Dibutyltin hydride **76** (120 mg, 0.51 mmol, 1.0 equiv) was dissolved in MeCN (2.0 mL) in a pressure tube. Dimethyl

acetylenedicarboxylate **66** (120 μL, 1.02 mmol, 2.0 equiv) was added dropwise and the tube was sealed and heated to 80 ˚C over 18 h. The reaction mixture turned dark brown over the course of the reaction. The solvent was removed under reduced pressure to give a brown oil that was purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give **81a** as a clear oil (71 mg, 17%) and **81b** as a clear oil (11 mg, 3%). Dialkenylstannane **81a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 2H), 3.73 (s, 6H), 3.66 (s, 6H), 1.43–1.35 (m, 4H), 1.31–1.19 (m, 8H), 0.81 (t, 6H, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 168.4, 164.7, 134.0, 51.5, 51.2, 28.9, 27.1, 16.3, 13.6; HRMS (ESI) *m/z* $[M+Na]^+$ calculated for $C_{20}H_{32}O_8SnNa$ 543.1011, found 543.1001. Dialkenylstannane **81b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.06 (s, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.728 (s, 3H), 3.725 (s, 3H), 1.57–1.46 (m, 4H), 1.35–1.25 (m, 8H), 0.88 (t, 6H, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 170.6, 169.0, 163.7, 161.2, 160.2, 134.5, 130.0, 51.9, 51.6, 51.0, 50.9, 28.5, 26.9, 14.2, 13.4.

Alkyne, alkene competition experiment



83

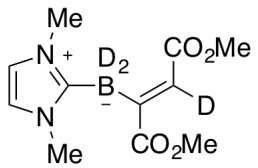


84

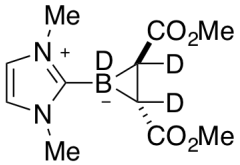
1-(1,3-Bis(2,6-diisopropylphenyl)-1*H*-imidazol-3-ium-2-yl)-2,3-bis(ethoxy-carbonyl) boriran-1-uide (84) and (*E*)-(1,3-bis(2,6-diisopropyl-phenyl)-1*H*-imidazol-3-ium-2-yl)(1-ethoxy-4-(ethylperoxy)-1-oxo-4λ^2-but-2-en-2-yl)dihydroborate (83): Following TP2 with NHC-borane **27b** (100 mg, 0.25 mmol, 1.0 equiv), diethyl acetylenedicarboxylate (36 μL, 0.25 mmol, 1.0 equiv), dimethyl fumarate **78a** (36 mg, 0.25 mmol, 1.0 equiv), and MeCN (1.0 mL), a

13/87 ratio of **80/81** was observed by ^{11}B NMR spectroscopy after 18 h. The solvent was removed under reduced pressure to give a brown oil that was purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give **83** as a white solid (6 mg, 4%) and **84** as a white solid (67 mg, 47%). *E*-alkenylborane **83**: ^1H NMR (500 MHz, C_6D_6) δ 7.42 (t, 2H, J = 7.8 Hz), 7.23 (d, 4H, J = 8.0 Hz), 6.97 (s, 2H), 6.16 (s, 1H), 3.91 (q, 2H, J = 7.0 Hz), 3.87 (q, 2H, J = 7.0 Hz), 2.83 (p, 4H, J = 6.8 Hz), 1.27 (d, 12H, J = 7.5 Hz), 1.14 (t, 3H, J = 7.0 Hz), 1.09 (d, 12H, J = 7.0 Hz). ^{11}B (160 MHz, $CDCl_3$) δ –28.2 (br t). Borirane **84**: ^1H NMR (500 MHz, C_6D_6) δ 7.48 (t, 2H, J = 7.8 Hz), 7.33 (dd, 2H, J = 8.0, 1.0 Hz), 7.30 (dd, 2H, J = 7.5, 1.0 Hz), 7.06 (s, 2H), 3.98–3.91 (m, 1H), 3.81–3.65 (m, 3H), 2.82 (p, 2H, J = 6.8 Hz), 2.70 (p, 2H, J = 6.8 Hz), 1.56 (dd, 1H, J = 7.3, 6.3 Hz), 1.33 (d, 6H, J = 6.5 Hz), 1.25 (d, 6H, J = 7.0 Hz), 1.15 (d, 6H, J = 7.0 Hz), 1.09–1.05 (m, 9H), 1.02 (t, 3H, J = 7.0 Hz); ^{11}B (160 MHz, $CDCl_3$) δ –26.2 (d, J_{BH} = 118.4 Hz).

Deuterium-labeling studies



67a-d$_3$



68a-d$_3$

(*E*)-(1,4-Dimethoxy-1,4-dioxobut-2-en-2-yl-3-*d*)(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)borate-d_2 (67a-d$_3$) and 1-(1,3-dimethyl-1*H*-imidazol-3-ium-2-yl)-2,3-bis(methoxycarbonyl)boriran-1-uide-1,2,3-d_3 (68a-d$_3$): Following TP1 with NHC-borane **27a-d$_3$** (25 mg, 0.22 mmol, 1.0 equiv), THF (2.0 mL), dimethyl acetylenedicarboxylate **66** solution (54 μL, 0.44 mmol, 2.0 equiv) in THF (0.5 mL), a 65/35 crude ratio of **67a-d$_3$/68a-d$_3$** was observed by ^{11}B NMR spectroscopy. *E*-alkenylborane **67a-d$_3$** was isolated as a red oil (16 mg,

28%) and borirane **68a-d$_3$** was isolated as a clear oil (18 mg, 32%). *E*-alkenylborane **67a-d$_3$:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (s, 2 H), 3.74 (s, 6 H), 3.66 (s, 3 H), 3.61 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1, 168.7, 120.1, 51.6, 51.0, 36.01; ^{11}B NMR (160 MHz, $CDCl_3$) δ –29.0 (br pent); HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{11}H_{14}D_2N_2O_4B$ 253.1323, found 253.1340. Borirane **68a-d$_3$:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 2H), 3.79 (s, 6H), 3.62 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 177.8, 120.8, 50.8, 50.5, 36.0; ^{11}B NMR (160 MHz, $CDCl_3$) δ –26.6 (br t); HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{11}H_{14}D_3N_2O_4B$ 256.1542, found 256.1558.

NHC-BH3, NHC-BD3 competition experiments

Scheme 28a: Following TP1 with NHC-borane **27a-d$_3$** (25 mg, 0.22 mmol, 1.0 equiv), NHC-borane **27a** (24 mg, 0.22 mmol, 1.0 equiv), THF (4.0 mL), dimethyl acetylenedicarboxylate **66** solution (0.11 mL, 0.89 mmol, 4.0 equiv) in THF (1.0 mL), a 65/35 crude ratio of **67a-d$_3$/68a-d$_3$** was observed by ^{11}B NMR spectroscopy. The mixture of *E*-alkenylboranes **67a** and **67a-d$_3$** was isolated as a red oil (16 mg, 28%) and the mixture of borirane **68a** and **68a-d$_3$** was isolated as a clear oil (18 mg, 32%).

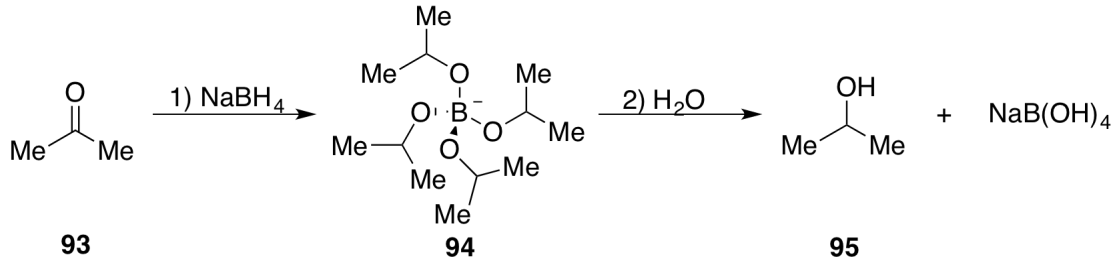
Scheme 28b: Following TP1 with NHC-borane **27a-d$_3$** (1 mg, 0.009 mmol, 1.0 equiv), NHC-borane **27a** (1 mg, 0.009 mmol, 1.0 equiv), THF (0.4 mL), dimethyl acetylenedicarboxylate **66** solution (1 μL, 0.89 mmol, 1.0 equiv) in THF (1.0 mL), a 52% conversion to give a 65/35 crude ratio of **67a/68a** was observed by ^{11}B NMR spectroscopy.

2.0 SYNTHESIS AND STUDY OF AMIDINE-BORANE COMPLEXES

2.1 INTRODUCTION

2.1.1 Borohydride

Borohydride is a tetrahedral anion with the formula BH_4^-. Borohydride salts, typically formed with alkali metals (e.g. sodium borohydride **73a**), are common reagents in organic chemistry laboratories. Sodium borohydride ($NaBH_4$) is a mild, chemoselective reagent that is used to reduce aldehydes and ketones to the corresponding primary and secondary alcohols.[65] One equivalent of $NaBH_4$ **73a** is able to donate four hydrides, thereby reducing four carbonyl compounds.[66] For example, the reduction of acetone **93** by $NaBH_4$ results in the formation of isopropoxyborate **94** that forms 2-isopropanol **95** and $NaB(OH)_4$ upon hydrolysis (**Scheme 29**).[67] Sodium cyanoborohydride ($NaBH_3CN$) **73b**, another commonly-employed borohydride reagent, is a milder reducing agent than **73a**. It is used in one-pot reductive aminations to reduce iminium ion intermediates to amines.[67]



Scheme 29. Reduction of acetone with $NaBH_4$

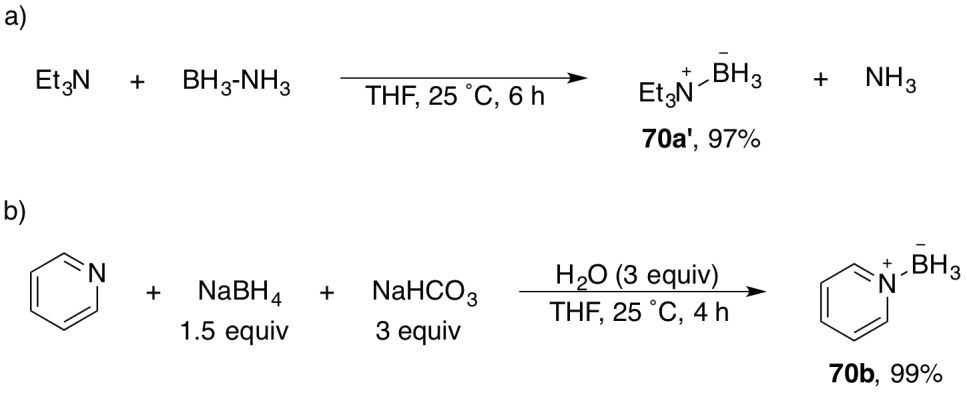
In spite of their common use, inorganic borohydrides have noted drawbacks. Both **73a** and **73b** are soluble in alcohol solvents, but are only partially soluble or insoluble in most other organic solvents.[65, 67] Tetrabutylammonium borohydride reagents (e.g. Bu_4NBH_3CN **73c**) have improved solubilities in organic solvents, but at the expense of atom economy. Sodium borohydride **73a** reacts rapidly and exothermically with acidic aqueous solutions to form diborane and hydrogen gas, posing toxicity and flammability hazards.[65] Additionally, cyano substitution makes sodium cyanoborohydride **73b** highly toxic.[67] For these reasons, ligated boranes are sometimes used in place of inorganic hydrides.

2.1.2 Ligated boranes

Ligated boranes ($L–BH_3$), the products of Lewis basic ligands and Lewic acidic boranes, are another class of borane reagent, which includes NHC-boranes (discussed in sections 1.1.3 and 1.1.4) and amine-boranes. These complexes are organic zwitterions, not salts, thus are soluble in an array of organic solvents.[68-69] Additionally, they are usually less sensitive to hydrolysis and react less violently with acids than inorganic borohydrides.[68-69]

Amine-boranes, like triethylamine-borane (Et_3N-BH_3) **70a'**, can be synthesized by direct reaction of an amine base with either BH_3-THF or BH_3-SMe_2.[70] This procedure is not commonly

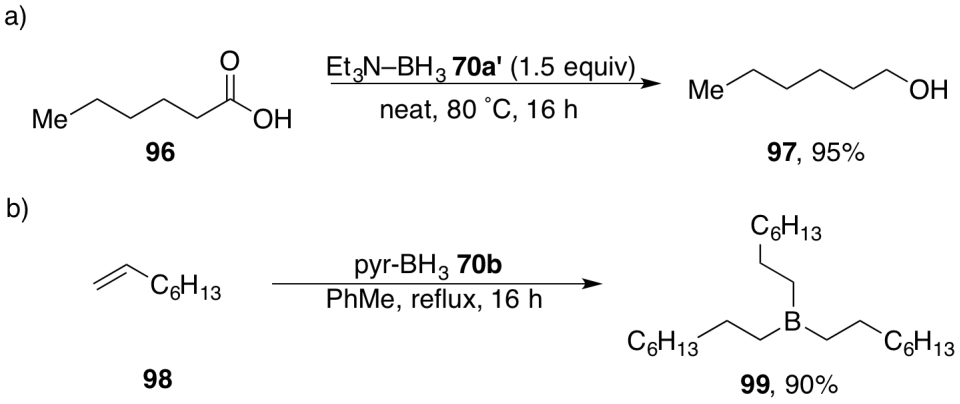
used in large-scale productions because of the low long-term stability of BH_3-THF and safety concerns arising from the release of dimethyl sulfide (Me_2S).[70] Ramachandran and coworkers developed a trans-amination procedure to synthesize amine-borane complexes from ammonia-borane (H_3N-BH_3).[63] In one example, reaction of triethylamine with ammonia-borane in THF for 6 h affords Et_3N-BH_3 **70a'** in 97% (**Scheme 30a**).[63] As an alternative, amine-boranes can be prepared through salt metathesis reactions of ammonium salts and sodium borohydride.[70] In a recent procedure from Ramachandran, amine-boranes are prepared from the reaction of primary, secondary, tertiary, and heteroaromatic amines with sodium bicarbonate ($NaHCO_3$), $NaBH_4$ **73a**, and water.[71] For instance, the reaction with pyridine afforded pyr-BH_3 complex **70b** in 99% yield after flash chromatography (**Scheme 30b**).[71] This procedure is an inexpensive and scalable alternative method to synthesizing amine-borane complexes.



Scheme 30. Synthesis of amine boranes by (a) ligand exchange and (b) salt metathesis

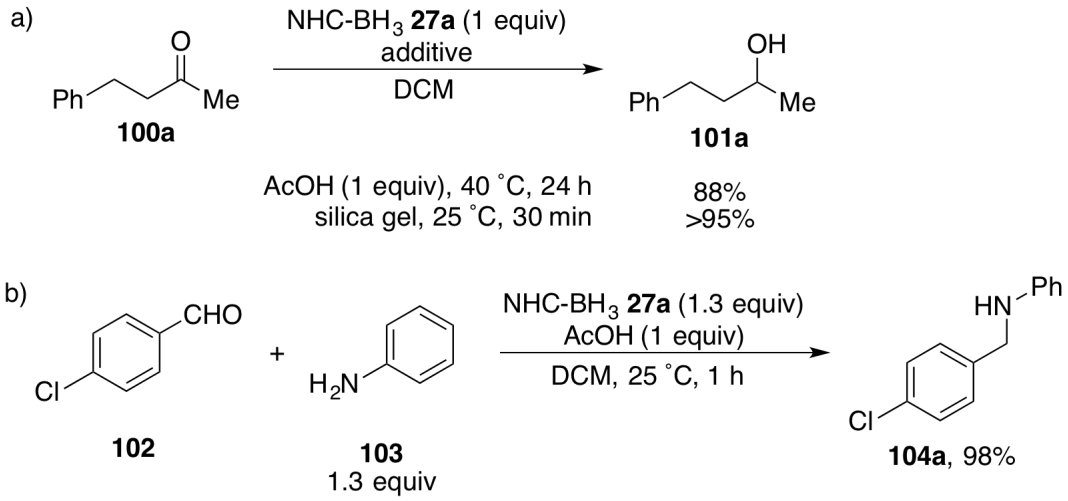
Amine-boranes can be used as both ionic reductants and hydroborating agents.[68-69] These complexes are weaker ionic reducing agents than inorganic borohydrides, but can reduce aldehydes and ketones when protic or Lewis acids are added.[68-69] Heating amine-borane complexes results in the liberation of BH_3.[68-69] Accordingly, amine-boranes, unlike sodium

borohydride **73a**, can be used to reduce carboxylic acids. In one example, the neat reaction of hexanoic acid with 1.5 equiv **70a'** at 80 ˚C for 16 h affords 1-hexanol **97** in 95% (**Scheme 31a**).[72] Amine-boranes can also function as BH_3 carriers for hydroboration reactions. The hydroboration of 1-octene with pyr-BH_3 **70b** in refluxing PhMe affords the hydroboration product **99** in 90% yield (**Scheme 31b**).[73]



Scheme 31. Examples of the reactions of ligated boranes

In addition to their previously described radical chemistry (section 1.1.3), NHC-boranes are ionic reductants. Curran and coworkers have developed procedures for the reduction of aldehydes, ketones, and iminium ions using NHC-boranes.[33-34, 74] For instance, ketone **100a** can be reduced by **27a** in the presence of either 1 equiv acetic acid or silica gel to give alcohol **101a** in excellent yield (**Scheme 32a**).[34, 74] In another report, Curran showed that NHC-BH_3 **27a** can be used for reductive aminations (**Scheme 32b**).[33] In one example, reaction of 4-chlorobenzaldehyde **102** with 1.3 equiv aniline **103**, 1.3 equiv NHC-BH_3 **27a**, and 1 equiv AcOH afforded amine **104a** in 98% yield.[33] These reductions can be performed in DCM and with NHC-borane in place of toxic sodium cyanoborohydride **73b**.



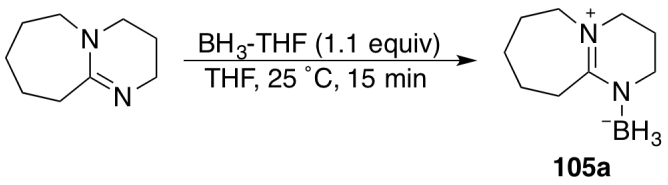
Scheme 32. Example of ionic reductions with NHC-boranes

In the following section, new amidine-borane complexes are synthesized and characterized. Their reactivity towards protic solvents, acids, and halogens is evaluated. Additionally, these complexes are used to reduce aldehydes, ketones, and imines at room temperature without additives. Their reactivity is compared to other amine- and NHC-boranes.

2.2 RESULTS AND DISCUSSIONS

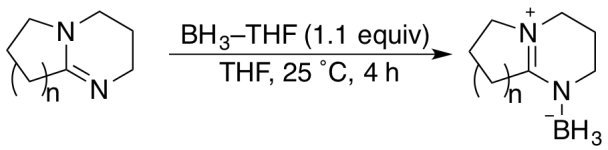
2.2.1 Preparation of amidine-borane complexes

The preparation of amidine-boranes was envisioned to occur by the one-step reaction of an amidine base with BH_3. In an NMR tube, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was dissolved in THF and 1.1 equiv BH_3–THF solution was slowly added by syringe. ^{11}B NMR analysis of the resulting solution showed BH_3–THF (s, +2.1 ppm) and a quartet at –17.4 ppm as the major signal presumed to be amidine-borane **105a** (**Scheme 33**).



Scheme 33. Reaction of DBU with BH_3-THF to give amidine-borane **105a**

The reaction was conducted on a preparative scale. DBU (1.0 g) was dissolved in THF and the mixture was cooled to 0 ˚C before 1.1 equiv BH_3–THF was added slowly by syringe. The clear solution was allowed to warm to room temperature over 1 h. ^{11}B NMR analysis of the crude mixture showed the product signal (q, –17.4 ppm, J = 93.3 Hz). The solvent was evaporated and the crude material was purified by flash chromatography to give **105a** as a white solid in 42% yield. Upon scaling up the procedure to 5.0 g of DBU, a 74% yield of **105a** was obtained after chromatography (**Scheme 34**). DBU-BH_3 **105a** has a low melting point of 54–56 ˚C. To give a second example of a bicyclic amidine-borane, the reaction of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) with borane was studied. DBN was stirred with 1.1 equiv BH_3-THF at 0 ˚C for 4 h to give complex **105b** as a clear, viscous oil in a 63% yield after chromatography (**Scheme 34**). These complexes were not previously reported in the literature.

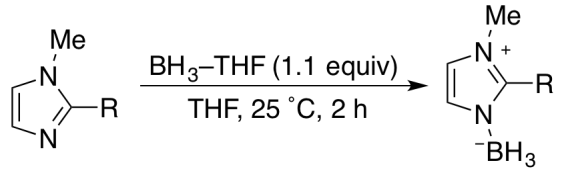


105a,b

n	amidine	amidine-borane	yield
3	DBU	**105a**	74%
1	DBN	**105b**	63%

Scheme 34. One-step preparation of amidine-borane complexes **105a** and **105b**

Imidazole (Imd) is another heterocyclic member of the amidine family. Amidine-borane complexes derived from both 1,2-dimethylimidazole and 1-methylimidazole were prepared through their reaction with 1.1 equiv BH_3–THF (**Scheme 35**). 1,2-DiMe-Imd-BH_3 **105c**, a constitutional isomer of **27a**, was isolated as a white solid in 95% after flash chromatography. When repeated on a 2.0 g scale, **105c** was isolated as a crystalline solid in 68% after recrystallization from water. 1,2-DiMe-Imd-BH_3 **105c** melted at 117–119 ˚C, a lower range than **27a** (138–139 ˚C). Amidine-borane **105d** was isolated as a clear oil in 78% yield after flash chromatography. Complexes **105c** and **105d** were previously prepared by Wrackmeyer and Nöth, and characterized by ^{11}B and ^{13}N NMR.[75-76]



105c,d

R	amidine-borane	yield
Me	**105c**	95%
H	**105d**	78%

Scheme 35. Preparation of amidine-borane complexes **105c** and **105d**

To prove the bonding pattern of the amidine-boranes, crystals were grown of **105a** and **105c** using slow vapor diffusion from DCM and pentanes. The crystal structures were solved by Dr. Steven Geib and are shown in **Figure 10**. In both cases, the borane is bonded to N1. The B–N bond in **105a** is 1.58 Å and the B–H bonds are an average of 1.13 Å; the average H–B–H angle is 108.7˚, close to the ideal angle. The bicyclic ring system gives distinct concave and convex faces for **105a**. For **105c**, the B–N bond is 1.58 Å while the average B–H bond is 1.11 Å. The H–B–H bonds are 109.0˚. The imidazole ring for borane **105c** is planar.

105a **105c**

bond	**105a** length (Å)	**105c** length (Å)
B–N	1.58	1.58
B–H[a]	1.12	1.11

[a]average length of the three B–H bonds

Figure 10. Crystal structures of amidine-boranes **105a** (left) and **105c** (right)

The ^{11}B NMR spectra of amidine-boranes **105a**–**d** showed quartets ranging from –17.4 to –20.2 ppm (**Table 11**, entries 1–4). These shifts are more upfield than other amino- and pyridyl-borane complexes **70a**–**c** (about –12 to –14 ppm, entries 5–7) and downfield of NHC-BH_3 complexes **27a** and **27b** (about –37 ppm, entries 8 and 9). Amidine-boranes **105a**–**d** have coupling constants ranging from 92.1–96.5 Hz. These values are smaller than the other amino- and pyridyl values (about 95–98 Hz, entries 5–7) and larger than NHC-BH_3 values (about 85–86 Hz, entries 8 and 9). Thus, amidine-boranes are readily differentiated from other ligated boranes by their ^{11}B NMR spectra.

Table 11. Comparison of ^{11}B NMR data for representative ligated borane complexes

entry	ligated borane	L–BH_3	^{11}B NMR shift (ppm)[a]	coupling constant (Hz)
1	DBU-BH_3	**105a**	–17.4	93.3
2	DBN-BH_3	**105b**	–18.3	92.1
3	1,2-diMe-Imd-BH_3	**105c**	–19.4	95.5
4	1-Me-Imd-BH_3	**105d**	–20.2	96.5
5	Et_3N-BH_3[71]	**70a'**	–14.0	97.0
6	pyr-BH_3[71]	**70b**	–12.6	97.6
7	DMAP-BH_3[71]	**70c**	–14.3	95.0
8	diMe-NHC-BH_3[77]	**27a**	–37.5	86.0
9	dipp-NHC-BH_3[28]	**27b**	–36.5	85.0

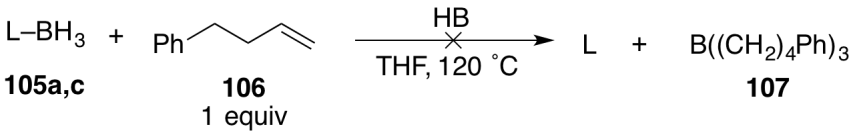
[a]all shifts measured in $CDCl_3$, all resonances observed as quartets

2.2.2 Substitution reactions of amidine-boranes

Since amidine-boranes **105a** and **105c** are solids at room temperature, they were selected over **105b** and **105d** for further studies. Boranes **105a** and **105c** are stable at room temperature in open air over several weeks. To further study their stability and reactivity, a series of NMR experiments was conducted. Amidine-boranes **105a** and **105c** were dissolved in THF and the resulting solutions were heated to 100 ˚C in pressure tubes for 48 h. The solutions remained clear and no precipitate formed in either case. The resulting ^{11}B NMR spectra showed only the starting material. Next, **105a** and **105c** were dissolved in THF:H_2O (1:1) and THF:MeOH (1:1) and heated to 50 ˚C overnight. Again, the solutions remained clear and ^{11}B NMR analysis showed only starting material and slight decomposition to boric ester or boric acid (br s, 20 ppm, <10%

by integration with respect to the starting materials for both reactions). This indicates that **105a** and **105c** are stable in solution at high temperatures and minimally reactive towards protic solvents.

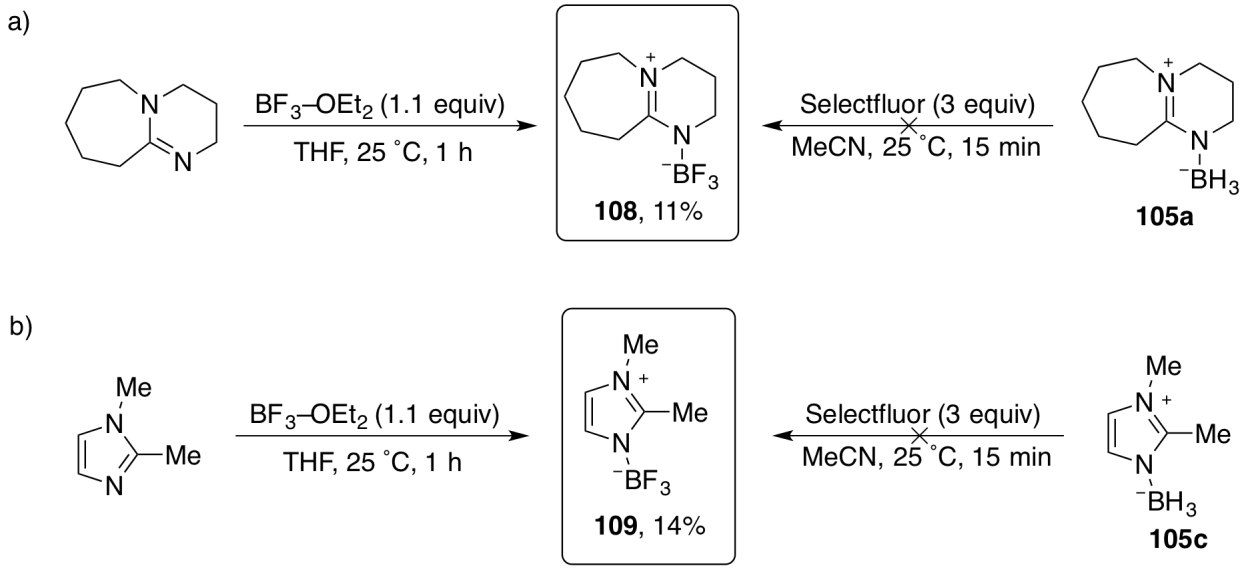
To determine whether BH_3 could be released from the corresponding amidine-borane at elevated temperatures, hydroborations were attempted. Complexes **105a** and **105c** were dissolved in THF in a pressure tube and 1 equiv of 4-phenyl-butene **106** was added. If BH_3 was liberated, then hydroboration product **107** would be expected to form (**Scheme 36**). The sealed tubes were heated to 60, 80, 100, and 120 ˚C for 30 min each. The solutions were analyzed by ^{11}B NMR analysis after each time point, but only starting materials were observed each time, indicating that neither decomplexation nor hydroboration to give **107** had occurred.



Scheme 36. Attempted hydroboration of 4-phenyl-butene **106**

To further probe the reactivity of amidine-boranes **105a** and **105c**, substitutions at boron were studied. Curran and Nerkar showed that NHC-borane compounds could be fluorinated using Selectfluor, an electrophilic fluorine source.[78] Fluorinated analogs of **105a** and **105c** were initially prepared to use as standards for the Selectflour reactions. DBU was reacted with 1.1 equiv of boron trifluoride diethyl etherate (BF_3-OEt_2) at room temperature (**Scheme 37a**). The resulting complex was unstable to silica gel, but 11% of pure **108** was isolated after evaporation of volatiles and extraction with 5% HCl solution to remove the excess DBU. The ^{11}B NMR spectrum of **108** showed a quartet at 0.00 ppm (J_{BF} = 17.1 Hz) and the ^{19}F NMR spectrum a

quartet at –144.0 (J_{BF} = 16.5 Hz). 1,2-Dimethylimidazole was reacted with 1.1 equiv BF_3-OEt_2 under identical conditions (**Scheme 37b**). Compound **109** precipitated from the reaction mixture and the white solid was isolated in 14% yield by vacuum filtration. ^{11}B NMR analysis showed a quartet at 1.1 ppm (J_{BF} = 17.5 Hz) and a quartet at –145.1 ppm (J_{BF} = 17.5 Hz) was observed by ^{19}F NMR spectroscopy.

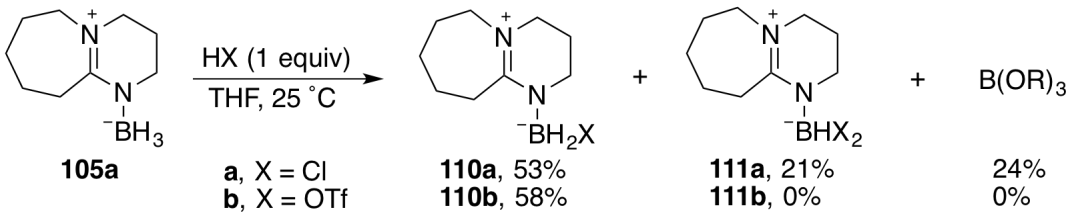


Scheme 37. Formation of fluorinated amidine-boranes

Using the procedure developed by Curran and Nerkar, fluorinations of **105a** and **105c** were attempted. DBU-BH_3 **105a** was dissolved in MeCN and 3 equiv Selectfluor were added to the stirring solution. An ^{11}B NMR taken after 15 min showed full consumption of the starting material and a singlet at –0.4 ppm and the ^{19}F NMR spectrum showed a signal at –150.3 ppm. Neither resonance matched the spectra for DBU-BF_3 **108**. With **105c**, the Selectfluor reaction was slower. Full consumption of the starting material was observed after 4 h, but the ^{11}B and ^{19}F

NMR spectra of the crude products did not match 1,2-diMe-Imd-BF_3 **109**. Unlike NHC-boranes, these new amidine-boranes are not cleanly fluorinated by Selectfluor.

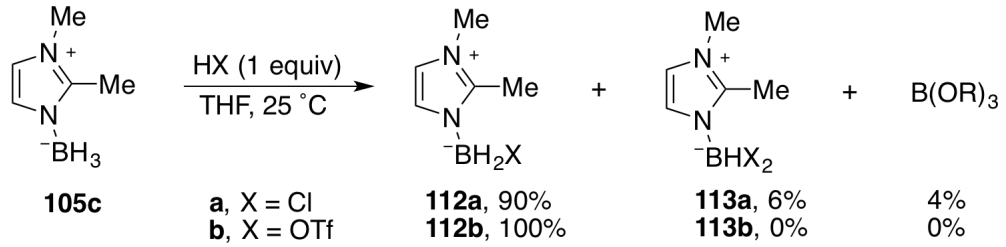
Ligated boranes typically react quickly with strong acids,[28, 68-69] so the reactivity of amidine-boranes **105a** and **105c** towards hydrochloric (HCl) and triflic (TfOH) acids was studied next. The slow addition of HCl-dioxane (1 equiv) to a solution of **105a** in THF at 25 ˚C resulted in vigorous bubbling, indicating that hydrogen gas had evolved. An ^{11}B NMR spectrum showed full consumption of **105a** to give 53% mono-chloride **110a** (t, –7.2 ppm), 21% di-chloride **111a** (d, 0.0 ppm), 2% of an unknown product (d, +7.4 ppm), and 24% boric ester or acid (br s, +19.5 ppm, **Scheme 38**). The reaction of DBU-BH_3 **105a** with 1 equiv triflic acid in THF at room temperature was also rapid. Vigorous bubbling was again observed upon addition of acid. An ^{11}B NMR spectrum showed 58% mono-triflate **110b** (br s +4.2 ppm), 29% BH_3-THF (q, –0.4 ppm), and 13% unreacted **105a**. Additionally, a spongy white precipitate formed that was insoluble in both chloroform and DMSO. This is probably DBU-H^+ OTf^-, and its formation explains why BH_3-THF was observed.



Scheme 38. Reaction of **105a** with strong acids

Next, 1,2-diMe-Imd-BH_3 **105c** was treated with HCl and TfOH. Reaction of **105c** with 1 equiv HCl-dioxane gave 90% mono-chloride **112a** (t, –7.9 ppm), 6% di-chloride **113a** (d, –0.7 ppm), and 4% boric ester or acid (**Scheme 39**). With TfOH, **105c** reacted rapidly to give

quantitative conversion to mono-triflate **112b** (br s, +0.8 ppm). Triflate **112b** was stable in solution at 2 h, but the solution turned into a gel or polymer after 4 h, possibly from the polymerization of THF. Products **110–113** were unstable to flash chromatography. In contrast, some NHC-borane chloride species can be chromatographed.[51]

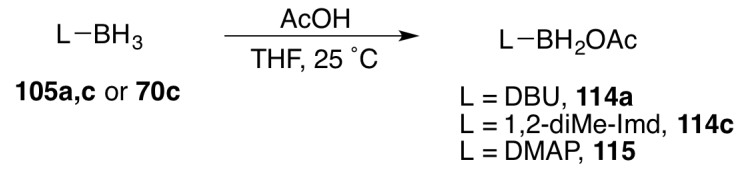


Scheme 39. Reaction of **105c** with strong acids

Since **105a** and **105c** reacted quickly with strong acids, weak acids were studied next. Acetic acid was chosen as a representative weak acid. The reaction of ligated boranes with acetic acid is summarized in **Table 12**. DBU-BH_3 **105a** was dissolved in THF and acetic acid (1 equiv) was added dropwise at 25 ˚C. No bubbling was observed, but the ^{11}B NMR spectrum taken after 1 h showed 85% **105a** with 10% of a mono-acetate **114a** (t, –2.64, J_{BH} = 101.6 Hz), and 5% decomposition to boric ester (entry 1). Reaction of **105a** with 10 equiv AcOH caused bubbling to occur upon addition. ^{11}B NMR analysis after 1 h showed 9% **105a**, 65% **114a**, 16% boric ester, and 10% of possible DBU-$B(OAc)_3$ (s, +1.77, entry 2). Only starting material was observed by ^{11}B NMR when 1,2-diMe-Imd-BH_3 **105c** was reacted with 1 equiv AcOH (entry 3), but 12% mono-acetate **114c** (t, –5.52, J_{BH} = 109.6 Hz) formed after 24 h when 10 equiv AcOH were used (entry 4). For comparison, solutions of NHC-boranes **27a** and **27b**, and DMAP-BH_3 **70c** were prepared in THF and reacted with 10 equiv AcOH. No bubbling was observed in any case. No reaction was observed for either NHC-BH_3 **27a** or **27b**, but 16% mono-acetate **115** (br t, –0.60)

was observed for the reaction of **70c** with AcOH. None of the mono-acetate products were stable to flash chromatography. Isolation was attempted by evaporation and extraction, but the products could not be separated from the unreacted ligated boranes. Although **105a** reacts only slowly with AcOH, it is significantly more reactive than other ligated boranes under these conditions.

Table 12. Summary of reactions of borane complexes with acetic acid



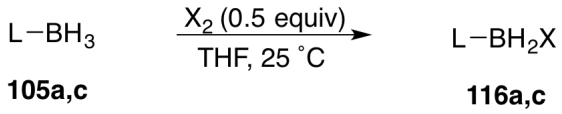
entry	amidine-borane	#	equiv AcOH	time (h)	yield[a]
1	DBU-BH_3	**105a**	1	1	10% **114a**
2	DBU-BH_3	**105a**	10	1	65% **114a**
3	1,2-diMe-Imd-BH_3	**105c**	1	24	–[b]
4	1,2-diMe-Imd-BH_3	**105c**	10	24	12% **114c**
5	diMe-NHC-BH_3	**27a**	10	24	–[b]
6	dipp-NHC-BH_3	**27b**	10	24	–[b]
7	DMAP	**70c**	10	24	16% **115**

[a]as determined by ^{11}B NMR analysis; [b]"–" means that no bubbling was observed and only starting material was observed by ^{11}B NMR analysis

Ligated boranes also react quickly with halogens.[28, 57] Accordingly, brominations and iodinations of **105a** and **105c** were attempted. DBU-BH_3 **105a** was dissolved in THF and a solution of Br_2 (1.0 M in THF, 0.5 equiv) was added dropwise at 25 ˚C (**Table 13**, entry 1). The solution bubbled and the resulting ^{11}B NMR spectrum showed full consumption of **105a** with

resonances at +19.5, +27.2, and +28.2 ppm. The signal at +19.5 ppm likely corresponds to boric acid or ester, but the other signals could not be assigned. It is likely that the rapid bromination leads to hydrolysis by trace water and decomplexation of boron from DBU. Addition of I_2 (0.5 equiv) to a solution of **105a** in THF caused vigorous bubbling. An ^{11}B NMR spectrum of the products showed signals at +19.5, +21.3, +27.2, and +28.2 ppm, suggesting similar decomposition pathways as the reaction with Br_2. A solution of **105c** was prepared in THF and a solution of Br_2 (1.0 M in THF, 0.5 equiv) was added slowly. The solution bubbled rapidly and turned yellow. The resulting ^{11}B NMR spectrum showed mono-bromide **116c** as the major product (t, –11.1 ppm, J = 123.2 Hz, 29%) with unreacted starting material **105c** (q, –20.1 ppm, 36%), boric ester or acid (br s, +18.8 ppm, 23%), and trace signals at +26.6 and +27.7 ppm (entry 3). When **105c** was reacted with 0.5 equiv I_2, no mono-iodide product was detected, only boric acid or ester (br s, +18.5 ppm) and unreacted **105c** were observed (entry 4). Amidine-boranes **105a** and **105c** react with halogens, but do not give the same products as NHC-boranes in most cases.

Table 13. Reaction of amidine-boranes with bromine and iodine



105a,c **116a,c**

entry	amidine-borane	#	X_2	result[a]
1	DBU-BH_3	**105a**	Br_2	decomposition
2	DBU-BH_3	**105a**	I_2	decomposition
3	1,2-diMe-Imd-BH_3	**105c**	Br_2	29% **116c**
4	1,2-diMe-Imd-BH_3	**105c**	I_2	decomposition

[a]as determined by ^{11}B NMR spectroscopy

In summary, amidine-boranes **105a** and **105c** were shown to react with a variety of reagents. Both compounds were shown to be resistant to decomposition and decomplexation at high temperatures. Complexes **105a** and **105c** reacted rapidly with strong acids, like HCl and TfOH, to give mono- and di-substituted boranes; while reactions with weak acetic acid were slower. Electrophilic halogen sources (Selectfluor and elemental bromine and iodine) reacted with **105a** and **105c**, but the expected mono-, di-, and tri-halogenated boranes were not observed in most cases.

2.2.3 Ligand exchange reactions with DBU and DBU-borane

Amine- and NHC-boranes can be prepared by ligand exchange of an amine or carbene with a weakly complexed borane.[30, 63] These exchanges are equilibrium processes that are thermodynamically-driven to form the most stable complex.[30, 63]

To study the stability of the DBU-borane complex **105a**, it was determined whether borane could be exchanged from **105a** to other amine bases. As a general procedure, one equivalent of amine base (L) was added to a solution of **105a** in THF in a pressure tube. The resulting solution was heated to 100 ˚C for 48 h (**Table 14**, reaction A). ^{11}B NMR analysis of the resulting solution was used to determine the relative ratio of **105a** to any formed borane complex **70a–c**. When **105a** was added to triethylamine, **70a'** was not detected after 48 h (entry 1) and only traces of **70b** were observed when pyr was used (entry 2). In both cases, **105a** was completely unchanged. The reaction with DMAP gave a 72/28 ratio of **105a**/**70c** (entry 3).

These potential equilibrium reactions were approached from the other direction. Complexes of **70a–c** and **27a** were reacted with 1 equiv DBU in THF at 100 ˚C for 48 h (**Table 14**, reaction B) and the resulting solutions were analyzed by ^{11}B NMR spectroscopy to determine the relative ratio of products by integration. With Me_3N-BH_3 **70a** and pyr-BH_3 **70b**, almost full conversion to **105a** was observed after heating to 100 ˚C for 48 h (entries 1 and 2). The reaction of DBU with **70c** resulted in a 79/21 ratio of **105a**/**70c** (entry 3). No conversion to **105a** was observed by ^{11}B NMR spectroscopy when DBU was reacted with NHC-BH_3 **27a** (entry 4).

Table 14. Summary of ligand exchange reactions with DBU and DBU-BH_3 **105a**

a) DBU-BH_3 **105a** + L (1 equiv) $\underset{\text{THF, 100 °C, 48 h}}{\overset{\text{RXN A}}{\rightleftharpoons}}$ L-BH_3 **70a–c** + DBU

b) L-BH_3 **70a–c**, or **27a** + DBU (1 equiv) $\underset{\text{THF, 100 °C, 48 h}}{\overset{\text{RXN B}}{\rightleftharpoons}}$ DBU-BH_3 **105a** + L

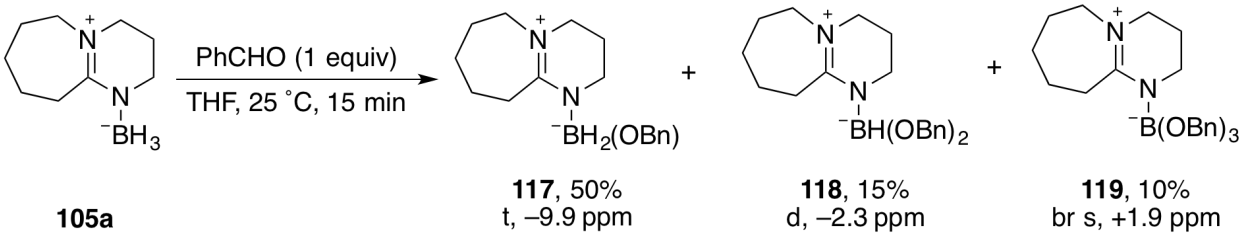
entry	ligand (L)	L-BH_3	reaction	**105a**/**70a-c** or **27a** ratio[a,b]
1	Et_3N	**70a'**	A	>99/1
2	pyr	**70b**	A	99/1
3	DMAP	**70c**	A	72/28
4	Me_3N	**70a**	B	95/5
5	pyr	**70b**	B	>99/1
6	DMAP	**70c**	B	79/21
7	diMe-NHC	**27a**	B	<1/99

[a]as determined by ^{11}B NMR spectroscopy; [b] ">99/1" or "<1/99" means that none of the minor product was observed in the ^{11}B NMR spectrum

In these experiments, BH_3 was exchanged between amines under forcing conditions. High temperature alone could not promote the decomplexation or exchange of BH_3 from **105a** (**Scheme 36**), but exchange can occur in the presence of DMAP. Collectively, the equilibrium between **105a** and **70a**–**c** was approached from both directions in these experiments. DBU-BH_3 **105a** is strongly favored over complexes **70a** and **70b**, but only slighly favored over **70c**. In the case of **27a**, it is likely that no equilibrium was reached with **105a** because **27a** is so strongly kinetically-favored.

2.2.4 Reductions with amidine-boranes

Ligated boranes are commonly used as reducing agents, so it was next determined whether amidine-boranes could reduce carbonyl compounds. As a preliminary experiment, benzaldehyde was dissolved in THF and DBU-BH_3 **105a** (1 equiv) was added. The solution was stirred at 25 ˚C for 15 min and then analyzed by ^{11}B NMR spectroscopy. The resulting spectrum showed four resonances: DBU–borane **105a** (q, –16.4, 25%), mono-substituted borane **117** (t, –9.9, 50%), di-substituted borane **118** (d, –2.3, 14%), and tri-substituted borane **119** (br s, +1.9, 9%; **Scheme 40**). This demonstrated that **105a** was a competent reducing agent and capable of donating one, two, or three hydrides. Comparatively, **27a** typically requires an acid or promoter to donate multiple hydrides.[33-34, 74]

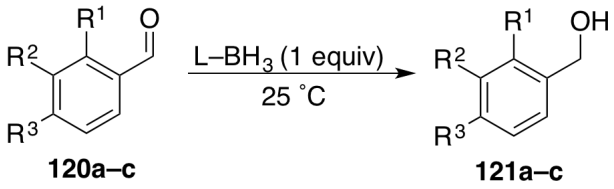


Scheme 40. Reaction of **105a** with benzaldehyde

Preparative reductions of aldehydes were performed next. As a standard procedure, ligated borane **105a** or **105c** (1 equiv) was dissolved in THF or MeOH and aldehyde (1 equiv) was added to the stirring solution at 25 ˚C. The resulting solutions were stirred until the aldehyde was fully consumed, as determined by TLC, the volatiles were removed under reduced pressure, and the crude residue was purified by flash chromatography (**Table 15**). 1-Naphthaldehyde **120a** was reduced by **105a** in 10 min to give a 94% yield of **121a** in THF, while the reaction in MeOH

gave an 80% yield over the same time (entry 1). 1,2-DiMe-Imd-BH_3 **105c** reduced **120a** in 90% in THF after 20 min and 65% in MeOH after 30 min (entry 2). DBU-BH_3 **105a** reduced 4-bromobenzaldehyde **120b** to give an 85% yield of **121b** after 5 min in THF, while an 88% yield was observed after 45 min in MeOH (entry 3). With **105c**, the reaction times were longer, but good yields of **121b** were still obtained in THF (72% in 3 h) and MeOH (80% in 90 min, entry 4). Electron-rich *N,N*-dimethylamino-benzaldehyde **120c** was reduced by **105a** after 15 min in both solvents to give **121c** in near-quantitative yields in both cases (entry 5). The reactions with **105c** were much slower, requiring 42 h in THF and 66 h in MeOH to obtain 80% and 70% yields, respectively (entry 6).

Table 15. Yields and reaction times for the reduction of aldehydes by amidine-boranes

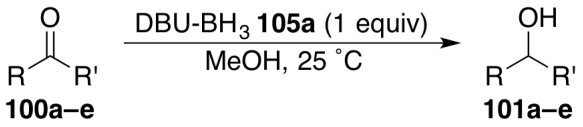


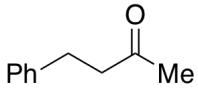
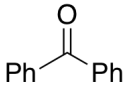
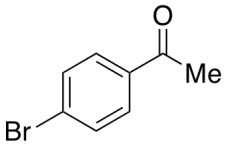
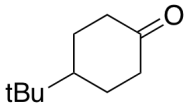
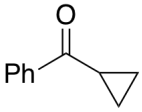
120a–c **121a–c**

entry	R^1	R^2	R^3	aldehydes	L-BH_3	THF yield, time	MeOH yield, time
1	-$(CH)_4$-	R^1	H	**120a**	**105a**	94%, 10 min	80%, 10 min
2	-$(CH)_4$-	R^1	H	**120a**	**105c**	90%, 20 min	65%, 30 min
3	H	H	Br	**120b**	**105a**	85%, 5 min	88%, 45 min
4	H	H	Br	**120b**	**105c**	72%, 3 h	80%, 1.5 h
5	H	H	NMe_2	**120c**	**105a**	97%, 15 min	95%, 15 min
6	H	H	NMe_2	**120c**	**105c**	80%, 42 h	70%, 66 h

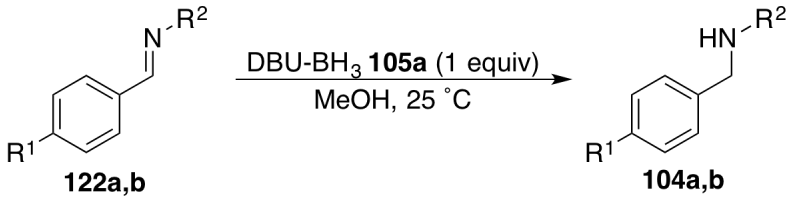
Since amidine-boranes **105a** and **105c** were able to reduce aldehydes effectively, test reductions of ketones and imines were performed next. Preliminary experiments showed that reductions with **105a** were sluggish in THF and little formation of product was observed in either solvent when **105c** was the reducing agent. Accordingly, the following reductions of ketones and imines were performed using only **105a** with MeOH as the solvent at room temperature (**Table 16**). Reaction of **105a** with 4-phenylbutanone **100a** gave **101a** in a quantitative yield after 2 h (entry 1). Both benzophenone **100b** and 4-bromoacetophenone **100c** were reduced by **105a** after 1 h to give **101b** in a 94% yield and **101c** in an 84% yield, respectively (entries 2 and 3). Reduction of 4-(*tert*-butyl)cyclohexane-1-one **100d** with **105a** gave an 85/15 *trans*/*cis* ratio of **101d** in 92% after 4 h (entry 4). This product ratio indicates that axial hydride delivery predominates and DBU-BH_3 behaves as a "small" hydride donor, like $NaBH_4$ **70a** (which gives a 60/40 ratio of axial/equatorial hydride delivery).[65] The reaction of **105a** with cyclopropyl(phenyl)methanone **100e** appeared to stop before either starting material was consumed. Secondary alcohol **101e** was isolated in 76% yield, but an 85% yield based on recovered **100e** (entry 5).

Table 16. Yields and reaction times for the reductions of ketones by **105a**



entry	ketone	#	time (h)	yield alcohol **101a–e**
1		**100a**	2	100%
2		**100b**	1	94%
3		**100c**	1	84%
4		**100d**	4	92% (84/16 *trans*/*cis*)
5		**100e**	48	76% (85% brsm)

Next, preparative reductions of imines were performed with **105a**. As a general procedure, imine was dissolved in MeOH and 1 equiv DBU-BH_3 **105a** was added. The reaction of imine **122a** with DBU-BH_3 **105a** in MeOH at rt went to completion after 24 h to afford secondary amine **104a** in 83% yield (**Scheme 41**). The reduction of tosyl imine **122b** required 48 h to give amine **104b** in 96% yield.



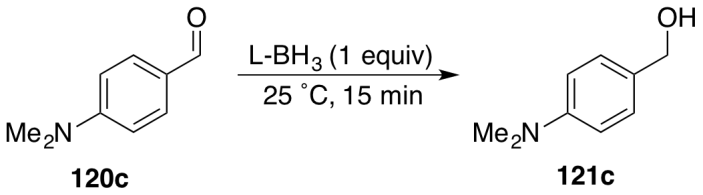
122a,b **104a,b**

R^1	R^2	imine	time (h)	yield amine **104**
Cl	Ph	**122a**	24	83%
H	Ts	**122b**	48	96%

Scheme 41. Reduction of secondary aldimines with **105a**

To compare the reactivity of **105a** with other ligated boranes, reductions of representative aldehydes, ketones, and imines were repeated using diMe-NHC-BH_3 **27a** and DMAP-BH_3 **70c**. The reduction of aldehyde **120c** was performed with either 1 equiv **27a** or **70c** in THF or MeOH at room temperature (**Table 17**). With DBU-BH_3, both the reaction in THF and MeOH went to completion after 15 min, giving **121c** in 97% and 95%, respectively (entry 1). Accordingly, the reductions with **27a** and **70c** were stopped after 15 min and purified. With NHC-BH_3 **27a**, a 38% yield of **121c** was afforded in THF and a 55% yield was afforded in MeOH. DMAP-BH_3 **70c** gave the alcohol **121c** in 74% and 72% yields in THF and MeOH after 15 min.

Table 17. Reduction of **120c** with ligated boranes



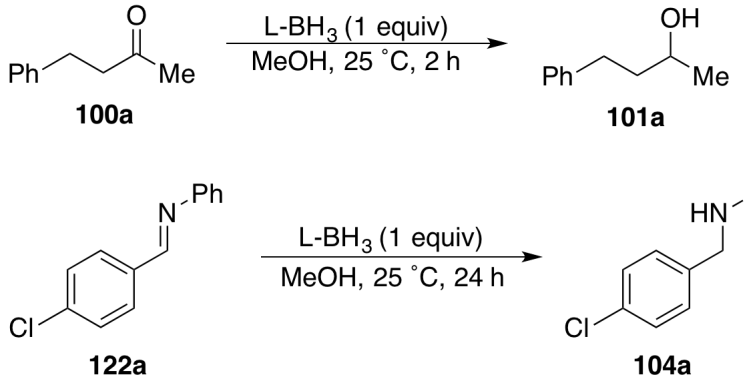
120c **121c**

entry	L-BH_3	#	yield **121c**, THF	yield **121c**, MeOH
1	DBU-BH_3	**105a**	97%[a]	95%[a]
2	diMe-NHC-BH_3	**27a**	38%	55%
3	DMAP-BH_3	**70c**	74%	72%

[a]repeated result from **Table 16**, entry 5

The reductions of ketone **100a** and imine **122a** with NHC-BH_3 **27a** and DMAP-BH_3 **70c** were performed under identical conditions as the corresponding reactions with **105a**. The reduction of ketone **100a** by **105a** in MeOH at 25 ˚C had gone to completion after 2 h to give **101a** in 100% yield (**Table 18**, entry 1). Over the same reaction times, NHC-BH_3 **27a** and DMAP-BH_3 gave alcohol **101a** in 21% and 77% yields, respectively (entries 2 and 3). The reaction of imine **122a** with **105a** in MeOH at 25 ˚C afforded amine **104a** in 83% yield after 24 h (entry 4). After 24 h, the reaction of NHC-BH_3 **27a** with **122a** afforded **104a** in 46% yield while DMAP-BH_3 gave **122a** in 73% (entries 5 and 6). In each case, DBU-BH_3 **105a** gave a higher isolated yield of the alcohol or amine product than **27a** or **70c**, demonstrating that it is a better reducing agent under these conditions.

Table 18. Reductions of **100a** and **122a** with ligated boranes



100a **101a** **122a** **104a**

entry	L–BH3	L–BH_3	carbonyl	Product	yield
1[a]	DBU-BH_3	**105a**	**100a**	**101a**	100%
2	diMe-NHC-BH_3	**27a**	**100a**	**101a**	21%
3	DMAP-BH_3	**70c**	**100a**	**101a**	77%
4[b]	DBU-BH_3	**105a**	**122a**	**104a**	83%
5	diMe-NHC-BH_3	**27a**	**122a**	**104a**	46%
6	DMAP-BH_3	**70c**	**122a**	**104a**	73%

[a]repeated from **Table 17**, entry 1; [b]repeated from **Scheme 41**

To further study **105a**, the reduction of esters, nitriles, and halides was studied. Ester **123**, nitrile **124**, and bromide **125** were reacted with 1 equiv **105a** in MeOH at 25 ˚C. The reactions were followed by TLC, but no products were observed after 48 h (**Figure 11**). While **105a** effectively reduces aldehydes, ketones, and imines, it does not react with esters, nitriles, or alkyl halides at room temperature.

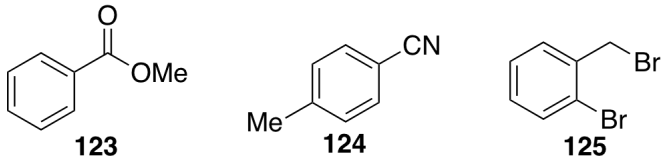
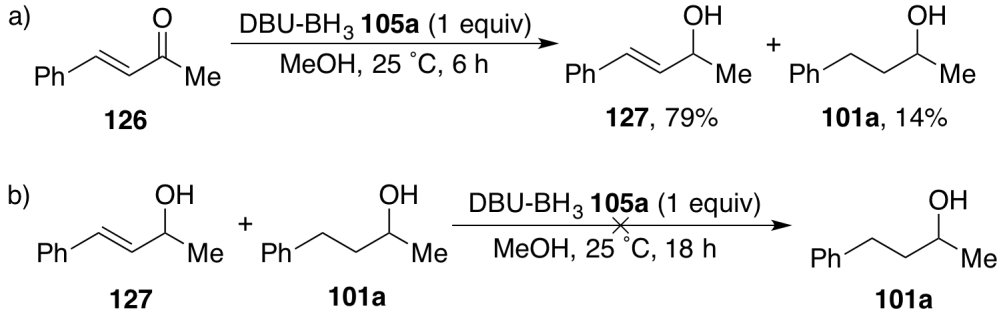


Figure 11. Functional groups that were not reduced by DBU-borane **105a**

It was next determined whether **105a** could perform 1,4-reductions of α,β-unsaturated ketones in addition to 1,2-reductions. Enone **126** was reacted with 1 equiv **105a** in MeOH at 25 ˚C. After 6 h, TLC showed full consumption of the starting material. Two products, allylic alcohol **127** and saturated alcohol **101a**, were isolated as a mixture (85/15 **127**/**101a**) in a 93% yield (**Scheme 42a**). Allylic alcohol is the product of 1,2-reduction, while **101a** probably arises after successive 1,4- and 1,2-reductions of **126**. The reaction was repeated and **126** was treated with 2 equiv **105a**, but the products formed in a lower yield (80% combined) and in nearly the same ratio (86/14). A mixture of alcohols **127** and **101a** (85/15 ratio) was resubjected to the reaction conditions (1 equiv **105a**, MeOH, rt) for 18 h, but the same ratio of products was isolated after flash chromatography (**Scheme 42b**).

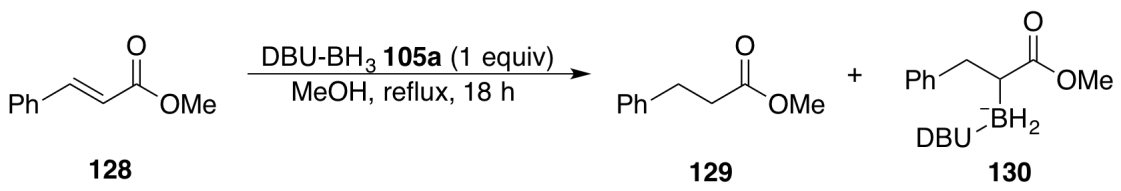


Scheme 42. Reduction of enone **126** with DBU-borane **105a**

It was previously shown that **105a** could not reduce or hydroborate a terminal alkene

even at elevated temparatures (**Scheme 36**). Together, the results in **Schemes 36** and **42b** demonstrate that **105a** is capable of reducing carbon-carbon double bonds, but only when they are in conjugation with an electron-withdrawing group. In this system, 1,2-reduction is faster than 1,4-reduction.

To further study the scope of **105a** in carbon-carbon bond reductions, methyl cinnamate **128** was reacted with **105a** (1 equiv) in MeOH (**Scheme 43**). Only trace conversion to products was observed by TLC and ^{11}B NMR spectroscopy after 24 h at room temperature, so the solution was heated to reflux overnight. ^{11}B NMR analysis showed a singlet at +4.2 ppm and a broad triplet at –8.1 ppm, indicating that new boron-containing products had formed. Purification by flash chromatography gave 32% of the saturated ester **129** (isolated as a mixture with recovered **128**) and the hydroboration product, α-boryl ester **130**, in a 13% yield. The ^{11}B NMR spectrum of **130** showed a br t at –8.35 ppm with a *J*-value of 88.3 Hz, matching the resonance observed in the crude NMR. It is assumed that **105a** donates a hydride to the β-position and the resulting anion is either protonated by the medium to form **129** or attacks the borenium ion to form **130**. Accordingly, it was hypothesized that more **130** would form when an aprotic solvent, like THF, was used. Instead, reaction of **105a** with **128** in THF afforded **129** and **130** in 4% and 3% yields, respectively.

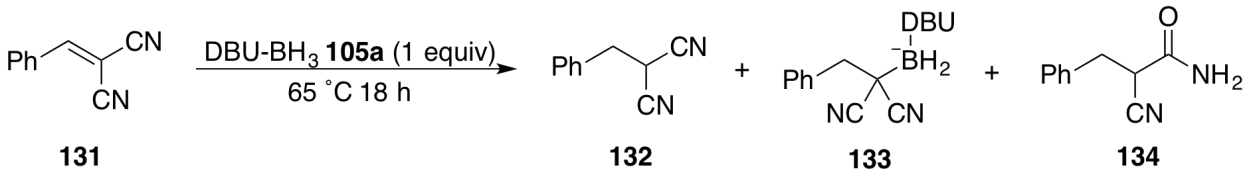


128 129 130

solvent	yield **129**	yield **130**
MeOH	32%	13%
THF	4%	3%

Scheme 43. Reduction of methyl cinnamate **128** to give reduced and hydroboration products

The reaction of **105a** with 2-benzilidenemalononitrile **131** was studied next. When Dr. Everett Merling reacted **131** with **27a** in DCM at rt for 15 min, a 57% yield of the hydroboration product and a 13% yield of the reduced product were obtained.[57] In MeOH, 1 equiv malononitrile **131** was reacted with 1 equiv **105a** at room temperature. No reaction was observed at room temperature, so the mixture was heated to reflux for 18 h. To our surprise, neither saturated malononitrile **132** nor hydroboration product **133** were formed, but instead α-cyano amide **134** was isolated in a 30% yield (**Scheme 44**). This is the product of the hydrolysis of **132**. Switching the reaction solvent to THF led to the formation of expected products. Malononitrile **132** and hydroboration product **133** were isolated in 21% and 41% yields, respectively. The ^{11}B NMR spectrum of **133** showed an apparent triplet at –8.1 ppm, but the coupling constant could not be measured due to the broadness of the signal.

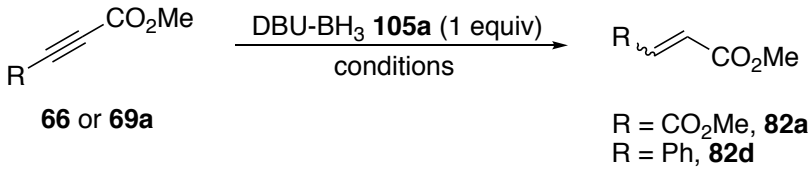


131 **132** **133** **134**

solvent	yield **132**	yield **133**	yield **134**
MeOH	0%	0%	30%
THF	21%	41%	0%

Scheme 44. Reduction of malononitrile **131** by DBU-borane

Lastly, it was determined if DBU-BH_3 **105a** could react with electron-deficient alkynes to form boriranes. Following a procedure for formation of borirane with **27a** (**Table 3**, entry 6), DBU-BH_3 was reacted with 1.5 equiv DMAD **66** at –78 ˚C in THF. The solution gradually turned red as it warmed to rt overnight. (**Scheme 45**). The resulting ^{11}B NMR spectrum showed full consumption of **105a** and several broad resonances were observed. Following purification by flash chromatography, dimethyl fumarate **82aE** and dimethyl maleate **82aZ** were isolated as clear oils in 13% and 3% yields, respectively. No boron-containing products, borirane or alkenylborane, were isolated. Methyl 3-phenylpropiolate **69a** reacted slowly with 1 equiv DBU-BH_3 **105a** at room temperature in MeOH. After 24 h, the solvent was removed under reduced pressure and the crude residue was purified by flash chromatography. Methyl (E)- and (Z)-phenylacrylates **82d** were isolated in 22% yield as a 75/25 mixture. A crude mixture of boron-containing products was also isolated. The ^{11}B NMR spectrum showed two br t resonances, –9.8 ppm (J_{BH} = 91.8 Hz) and –13.0 ppm (J_{BH} = 93.7 Hz), in a 63/37 ratio. These products likely correspond to the E- and Z-isomers of the hydroboration product of **69a** with **105a**, but ^{1}H NMR spectrum could not be confidently assigned.



R	alkyne	eq alkyne	conditions	yield alkene **82**
CO_2Me	**66**	1.5	THF, –78 to ˚C	16% (72/28 E/Z)
Ph	**69a**	1.0	MeOH, 25 ˚C	22% (75/25 E/Z)[a]

[a]products isolated as a mixture of isomers

Scheme 45. Reaction of **105a** with electron-deficient alkynes

2.3 CONCLUSIONS

Amidine-borane complexes **105a–d** were prepared in one step from their corresponding amidine bases and borane. Boranes **105a** and **105c** are bench-stable, white solids, while **105b** and **105d** are viscous oils that are stable to water, protic solvents, and silica gel. Additionally, **105a** and **105c** resisted decomplexation or decomposition at high temperatures.

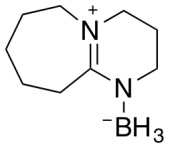
Amidine-borane **105a** is reactive towards strong (HCl) and weak acids (AcOH), as well elemental bromine and iodine. Additionally, DBU forms a stronger complex with borane than amine and pyridyl bases. DBU-BH_3 **105a** is a competent hydride donor in the reductions of aldehydes, ketones, and imines, but was incapable of reducing esters, nitriles, and alkyl halides. When reacted with an enone, both 1,2- and 1,4-reduction products were isolated. Additionally, **105a** was shown to insert into carbon-carbon double bonds when reacted with conjugated ester and malononitrile systems to give formal hydroboration products. Compared directly to **27a** and **70c**, DBU-borane **105a** was a more reactive reducing agent.

These studies show that amidine boranes are potentially useful reagents for organic synthesis given their ease of synthesis from cheap starting materials, stability to air and water, and reactivity profile.

2.4 EXPERIMENTAL

General Information: All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry dichloromethane (DCM) was obtained by passing the solvents through activated alumina. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under an argon atmosphere. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Thin layer chromatography (TLC) was performed on EMD 60 F254 silica gel and flash column chromatography was performed with 230–400 mesh silica gel purchased from Sorbent Technologies as the stationary phase. Visualization of TLC achieved using ultraviolet light (254 nm). Melting points (mp) were measured with a Mel-Temp II apparatus and were uncorrected. IR spectra were obtained as neat samples with a Thermo-Nicolet IR 200 ATR-FTIR. Nuclear magnetic resonance spectra (NMR) were obtained on a Bruker Avance III 400 MHz and 500 MHz instruments. Chloroform (δ 7.26 ppm) was used as an internal standard for ^{1}H NMR spectra and $CDCl_3$ (δ 77.00 ppm) was used as an internal standard for ^{13}C NMR spectra. ^{11}B chemical shifts are relative to Et_2O-BF_3. The spectral data of single molecules were reported in the following order: chemical shift (δ), multiplicity, coupling constant (Hz), number of nuclei. The following abbreviations were used to describe coupling: s=singlet, d=doublet, t=triplet, q=quartet, sep=septet, m=multiplet, br=broad, dd=doublet of doublets. Due to quadrupole

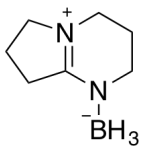
broadening, resonances of hydrogen or carbon atoms bonded to the boron atom are difficult to observe in ^{1}H or ^{13}C NMR spectra, respectively. HRMS were obtained with a Q-Tof analyzer. All spectra were acquired at room temperature.



105a

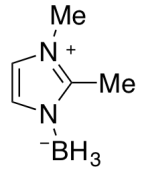
(2,3,4,6,7,8,9,10-Octahydro-1*H*-Pyrimido[1,2-*a*]azepin-5-ium-1-yl)trihydroborate (105a):

Typical Procedure 1 (TP1) or the formation of amidine-borane compounds: DBU (5.0 g, 33. mmol, 1.0 equiv) was dissolved in THF (60 mL) and the resulting solution was cooled to 0 ˚C. A solution of BH_3-THF (40 mL, 40 mmoL, 1.0 M, 1.2 equiv) was added slowly by syringe. The solution was allowed to warm to room temperature over 4 h. The solvent and volatiles were removed under reduced pressure and the residue was purified by flash chromatography (silica gel; hexanes:ethyl acetate). DBU–BH_3 **105a** was isolated as a white solid (4.0 g, 74%). Crystals for X-ray analysis were grown using slow vapor diffusion at room temperature (DCM/pentanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.40 (br t, 2H, J = 5.5 Hz), 3.37–3.35 (m, 2H), 3.29 (br t, 2H, J = 6.0), 3.01 (br s, 2H), 1.91 (BH, br q, 3H, J = 91.3), 1.90 (d pent, 2H, J = 6.1, 2.0), 1.70 (br t, 2H, J = 2.5), 1.62 (br t, 2H);^{13}C NMR (125 MHz, $CDCl_3$): 165.0, 53.8, 48.9, 48.7, 30.4, 29.2, 27.7, 23.5, 21.5; ^{11}B NMR (160 MHz, $CDCl_3$) δ –17.4 (q, J_{BH} = 93.3 Hz); IR (neat) 2930, 2852, 2231, 1603, 1502, 1440, 1314, 1154, 1103, 1076, 1019, 931, 844, 689 cm^{-1}; HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_9H_{18}N_2B$ 165.1558, found 165.1554; mp 54–56 ˚C.



105b

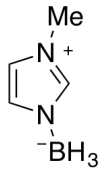
(2,3,4,6,7,8-Hexahydro-1*H*-pyrrolo[1,2-*a*]pyrimidin-5-ium-1-yl)trihydroborate (105b): Following the TP1 with DBN (1.0 g, 8.1 mmol, 1.0 equiv), THF (20 mL) and BH_3–THF solution (9.7 mL, 9.7 mmol, 1.2 equiv), **105b** was isolated as a clear oil (760 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.43 (t, 2H, J = 7.0 Hz), 3.32 (t, 2H, J = 5.8 Hz), 3.21 (t, 2H, J = 6.0 Hz), 2.91 (t, 2H, J = 8.0 Hz), 1.99 (pent, 2H, J = 7.5 Hz), 1.92 (pent, 2H, J = 5.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ163.0, 52.7, 46.9, 42.4, 31.1, 19.9, 18.8; ^{11}B NMR (160 MHz, $CDCl_3$) δ –18.3 (q, J_{BH} = 92.11 Hz). HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_7H_{14}N_2B$ 137.1245, found 137.1242.



105c

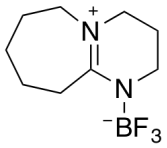
(2,3-Dimethyl-1*H*-imidazol-3-ium-1-yl)trihydroborate (105c): Following the TP1 with 1,2-dimethylimidazole (100 mg, 1.0 mmol, 1.0 equiv), THF (2.0 mL) and BH_3–THF solution (1.1 mL, 1.0 M, 1.1 mmol, 1.1 equiv), **105c** was isolated as a white solid (98 mg, 95%). Crystals for X-ray analysis were grown using slow vapor diffusion at room temperature (DCM/pentanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.75 (d, 1H, J = 1.5 Hz), 3.62 (s, 3H), 2.51 (s, 3H), 2.14 (br q, 3H, J_{BH} = 92.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 126.7, 118.9, 33.8, 10.2; ^{11}B NMR (160 MHz, $CDCl_3$) δ –20.2 (J_{BH} = 93.9 Hz); IR (neat) 3130, 2952, 2258, 2030, 1504, 1407, 1306, 1160, 1041, 945, 751, 662, 451 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_5H_{10}N_2B$ 109.0964, found 109.0932; mp 117–119 ˚C.

Purification by recrystallization (105c): 1,2-Dimethylimidazole (2.0 g, 21 mmol, 1.0 equiv) was dissolved in THF (40 mL) at 0 ˚C. BH_3–THF solution (25 mL, 1.0 M, 25 mmol, 1.2 equiv) was added by syringe. The solution was allowed to warm to 25 ˚C over 2 h. The solvent was removed under reduced pressure to give a crude white solid (3.2 g) that was recyrstallized from water (50 mL) to give **105c** as a white, crystalline solid (1.6 g, 68%).



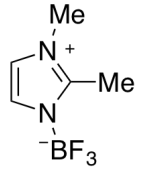
105d

(3-Methyl-1*H*-imidazol-3-ium-1-yl)trihydroborate (105d): Following the TP1 with 1-methylimidazole (0.49 mL, 6.1 mmol, 1.0 equiv), THF (10 mL) and BH_3–THF solution (6.1 mL, 1.0 M, 6.1 mmol, 1.0 equiv), **105d** was isolated as a clear oil (460 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.05 (br s, 1H), 6.87 (s, 1H), 3.74 (s, 3H), 2.21 (br q, 3H, J_{BH} = 91.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.9, 127.9, 121.0, 34.8; ^{11}B NMR (160 MHz, $CDCl_3$) δ –19.5 (J_{BH} = 93.9 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_4H_8N_2B$ 95.0775, found 95.0804.



108

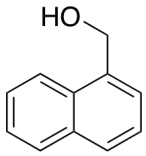
Trifluoro(2,3,4,6,7,8,9,10-octahydro-1*H*-pyrimido[1,2-*a*]azepin-5-ium-1-yl)borate (108): DBU (1.0 g, 6.6 mmol, 1.0 equiv) was dissolved in THF (10 mL). BF_3–ether (0.71 mL, 7.2 mmol, 1.1 equiv) was added dropwise by syringe to the stirring solution at 25 ˚C causing the solution to turn yellow. After 1 h, the solvent was removed under reduced pressure to give a crude yellow solid (220 mg). The solid was dissolved in DCM (10 mL) and extracted with HCl (5% aq, 3x 10 mL), water (1 x 10 mL), brine (1 x 10 mL), and then dried over sodium sulfate. Removal of the solvent under reduced pressure afforded **108** as a white solid (160 mg, 11%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.48–3.45 (m, 4H), 3.36 (t, 2H, J = 6.0 Hz), 2.93–2.90 (m, 2H), 1.94 (pent, 2H, J = 5.9 Hz), 1.76–1.68 (m, 4H), 1.66 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): 168.2, 54.0, 49.3, 41.1, 30.6, 28.8, 26.8, 23.8, 20.8; ^{11}B NMR (160 MHz, $CDCl_3$) δ 0.0 (q, J = 17.1 Hz); ^{19}F NMR (500 MHz, $CDCl_3$) δ –144.0 (q, J = 16.5 Hz); HRMS (ESI) *m/z* $[M–F]^+$ calculated for $C_9H_{16}N_2BF_2$ 201.1362, found 201.1369; mp 87–89 ˚C.



109

(2,3-Dimethyl-1*H*-imidazol-3-ium-1-yl)trifluoroborate (109): 1,2-Dimethylimidazole (96 mg, 1.0 mmol, 1.0 equiv) was dissolved in THF (2.0 mL). BF_3-etherate (0.14 mL, 1.1 mmol, 1.1 equiv) was added by syringe. The resulting solution was stirred for 1 h. A white precipitate formed and was isolated by vacuum filtration. The crude solid was washed with ethyl ether (5

mL) to afford **109** as a shiny white solid (23 mg, 14%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.28 (s, 1H), 7.20 (s, 1H), 3.74 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 146.2, 123.6, 121.0, 34.0, 10.9**;** ^{11}B NMR (160 MHz, CD_3OD) δ –11.2 (q, J_{BF} = 11.2 Hz); ^{19}F NMR (500 MHz, CD_3OD) δ –154.8 (q, J_{BF} = 11.2 Hz); HRMS (ESI) *m/z* $[M–F]^+$ calculated for $C_5H_8N_2BF_2$ 145.0749, found 145.0747; mp 128–130 ˚C.



121a

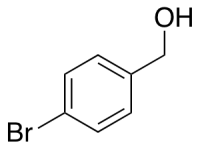
Naphthalen-1-ylmethanol (121a):

Typical Procedure 2 (TP2) for the reduction of carbonyl compounds: 1-Naphthaldehyde **120a** (68 μL, 0.50 mmol, 1.0 equiv) was dissolved in THF (2.0 mL). DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added. The resulting solution was stirred at room temperature until the starting material was consumed as determined by TLC (silica gel; hexanes:ethyl acetate). The solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel; hexanes:ethyl acetate). Alcohol **121a** was isolated as a clear oil after 10 min (74 mg, 94%).

1) Reduction with DBU–BH_3 and MeOH: Following the TP2 with 1-naphthaldehyde **120a** (68 μL, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv), **121a** was isolated as a clear oil after 10 min (63 mg, 80%).

2) Reduction with 1,2-diMe-Imd-BH_3 and THF: Following the TP2 with 1-naphthaldehyde **120a** (68 μL, 0.50 mmol, 1.0 equiv), THF (2.0 mL), and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1.0 equiv), **121a** was isolated as a clear oil after 20 min (71 mg, 90%).

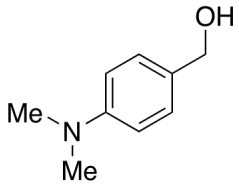
3) Reduction with 1,2-diMe-Imd-BH_3 and MeOH: Following the TP2 with 1-naphthaldehyde **120a** (68 μL, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1.0 equiv), **121a** was isolated as a clear oil after 30 min (51 mg, 65%).



121b

(4-Bromophenyl)methanol (121b):

1) Reduction with DBU–BH_3 and THF: Following the TP2 with 4-bromobenzaldehyde **120b** (93 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), **121b** was isolated as a white solid after 5 min (80 mg, 85%).
2) Reduction with DBU–BH_3 and MeOH: Following the TP2 with 4-bromobenzaldehyde **120b** (93 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), **121b** was isolated as a white solid after 45 min (83 mg, 88%).
3) Reduction with 1,2-diMe-Imd-BH_3 and THF: Following the TP2 with 4-bromobenzaldehyde **120b** (93 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1 equiv), **121b** was isolated as a white solid after 3 h (68 mg, 72%).
4) Reduction with 1,2-diMe-Imd-BH_3 and MeOH: Following the TP2 with 4-bromobenzaldehyde **120b** (93 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1 equiv), **121b** was isolated as a white solid after 90 min (75 mg, 80%).



121c

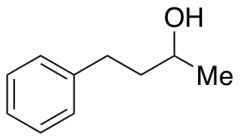
(4-(Dimethylamino)phenyl)methanol (121c):

1) Reduction with DBU–BH_3 and THF: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (74 mg, 97%).
2) Reduction with DBU–BH_3 and MeOH: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (72 mg, 95%).
3) Reduction with 1,2-diMe-Imd-BH_3 and THF: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 42 h (61 mg, 80%).
4) Reduction with 1,2-diMe-Imd-BH_3 and MeOH: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and 1,2-diMe-Imd-BH_3 **105c** (55 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 66 h (53 mg, 70%).
5) Reduction with DMAP-BH_3 and THF: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and DMAP-BH_3 **70c** (68 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (56 mg, 74%).

6) Reduction with DMAP–BH_3 and MeOH: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and DMAP-BH_3 **70c** (68 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (55 mg, 72%).

7) Reduction with diMe-NHC–BH_3 and THF: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), THF (2.0 mL) and diMe-NHC–BH_3 **27a** (55 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (29 mg, 38%).

8) Reduction with diMe-NHC–BH_3 and MeOH: Following TP2 with 4-(dimethylamino)benzaldehyde **120c** (75 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and **27a** (55 mg, 0.50 mmol, 1.0 equiv), **121c** was isolated as a clear oil after 15 min (42 mg, 55%).



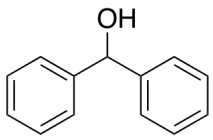
101a

4-Phenylbutan-2-ol (101a):

1) Reduction with DBU–BH_3: Following TP2 with 4-phenylbutan-2-one **100a** (74 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), the **101a** was isolated as a clear oil after 2 h (75 mg, 100%).

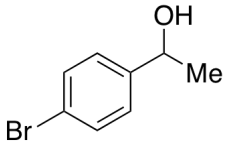
2) Reduction with DMAP-BH_3: Following TP2 with 4-phenylbutan-2-one **100a** (74 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DMAP–BH_3 **70c** (68 mg, 0.50 mmol, 1 equiv), the **101a** was isolated as a clear oil after 2 h (58 mg, 77%).

3) Reduction with diMe-NHC-BH_3: Following TP2 with 4-phenylbutan-2-one **100a** (74 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and diMe-NHC–BH_3 **27a** (55 mg, 0.50 mmol, 1 equiv), the **101a** was isolated as a clear oil after 2 h (16 mg, 21%).



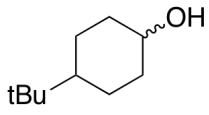
101b

Diphenylmethanol (101b): Following TP2 with benzophenone **100b** (91 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), **101b** was isolated as a white solid after 1 h (86 mg, 94%).



101c

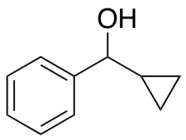
1-(4-Bromophenyl)ethan-1-ol (101c): Following TP2 with 4-bromoacetophenone **100c** (100 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), **101c** was isolated as a clear oil after 1 h (85 mg, 84%).



101d

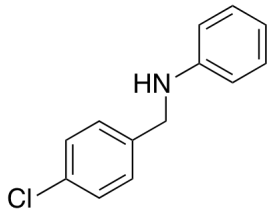
4-(*tert*-Butyl)cyclohexane-1-ol (101d): Following TP2 4-(*tert*-butyl)cyclohexane-1-one **100d** (75 mg, 0.49 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (81 mg, 0.49 mmol, 1.0

equiv), ***cis*-101d** was isolated as a white solid (11 mg, 15%) followed by ***trans*-101d** as a white solid (59 mg, 79%) after 4 h.



101e

Cyclopropyl(phenyl)methanol (101e): Following TP2 with cyclopropyl(phenyl)methanone **100e** (73 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (83 mg, 0.5 mmol, 1 equiv), unreacted starting material **100e** was recovered as a clear oil (8 mg) followed by **101e** isolated as a clear oil after 48 h (56 mg, 76%; 85% BRSM).

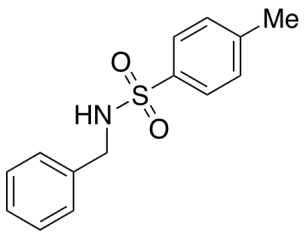


104a

***N*-(4-Chlorobenzyl)aniline (104a):**

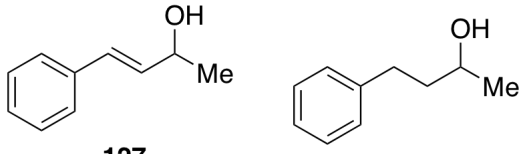
1) Reduction with DBU–BH_3: Following TP2 with (*E*)-1-(4-chlorophenyl)-*N*-phenylmethanimine **122a** (110 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1 equiv), **104a** was isolated as a clear oil after 24 h (90 mg, 83%). *2) Reduction with DMAP-BH_3:* Following TP2 with (*E*)-1-(4-chlorophenyl)-*N*-phenylmethanimine **122a** (110 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and DMAP-BH_3 **70c** (68 mg, 0.50 mmol, 1 equiv), **104a** was isolated as a clear oil after 24 h (80 mg, 73%). *3) Reduction with diMe-NHC-BH_3:* Following TP2 with (*E*)-1-(4-chlorophenyl)-*N*-

phenylmethanimine **122a** (110 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL) and diMe-NHC-BH_3 **27a** (55 mg, 0.50 mmol, 1 equiv), **104a** was isolated as a clear oil after 24 h (50 mg, 46%).



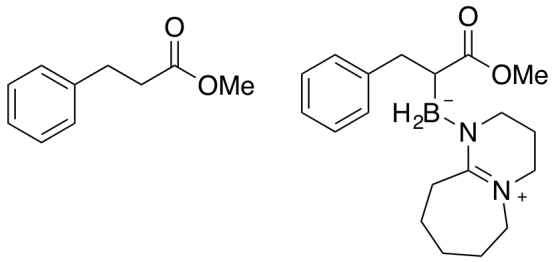
104b

***N*-Benzyl-4-methylbenzenesulfonamide (104b):** Following TP2 with (*E*)-*N*-benzylidene-4-methylbenzenesulfonamide **122b** (130 mg, 0.50 mmol, 1.0 equiv), MeOH (2.0 mL), and DBU–BH_3 **105a** (83 mg, 0.5 mmol, 1 equiv), **104b** was isolated as a white solid after 48 h (126 mg, 96%).



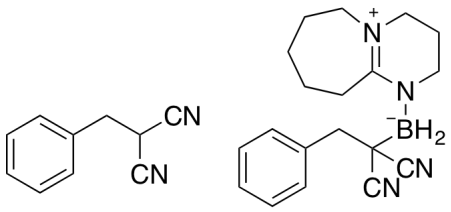
127 **101a**

(*E*)-4-Phenylbut-3-en-2-ol (127) and 4-phenylbutan-2-ol (101a): 4-Phenyl-but-3-ene-2-one (73 mg, 0.50 mmol, 1.0 equiv) was dissolved in MeOH (2.0 mL). DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added and the resulting solution was stirred at 25 ˚C for 6 h. The solvent was removed under reduced pressure to give a crude oil that was purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give a mixture of **127** and **101a** (85:15, 69 mg, 93%) as a clear oil.



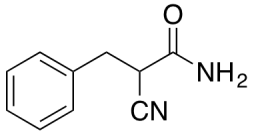
129 **130**

Methyl 3-phenylpropanoate (129) and (1-methoxy-1-oxo-3-phenylpropan-2-yl)(2,3,4,6,7,8,9,10-octahydro-1*H*-pyrimido[1,2-*a*]azepin-5-ium-1-yl)dihydroborate (130): Methyl cinnamate (81 mg, 0.50 mmol, 1.0 equiv) was dissolved in MeOH (2.0 mL). DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added and the resulting solution was heated to 65 ˚C for 18 h. The solvent was removed under reduced pressure to give a crude solid that was purified by flash chromatography (silica gel; hexanes:ethyl acetate). Methyl 3-phenylpropanoate **129** and methyl cinnamate **128** were isolated as a clear oil (51:49, 53 mg, 32% yield of alkane). α-Boryl ester **130** was isolated as a clear oil (19 mg, 13%). α-Boryl ester **130**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21–7.17 (m, 4H), 7.11–7.07 (m, 1H), 3.50 (s, 3H), 3.33–3.27 (m, 4H), 3.04–2.98 (m, 2H), 2.84–2.82 (m, 1H), 2.63–2.58 (m, 1H), 2.17–2.14 (m, 1H), 1.92–1.87 (m, 2H), 1.73–1.62 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.5, 165.9, 145.0, 128.4, 127.8, 124.9, 53.7, 50.3, 49.1, 47.9, 36.7, 29.9, 29.0, 27.3, 23.9, 21.2; ^{11}B NMR (160 MHz, $CDCl_3$) δ –8.4 (br t, J_{BH} = 88.3 Hz); HRMS (ESI) *m/z* $[M–H]^+$ calculated for $C_{19}H_{28}N_2O_2B$ 327.2238, found 327.2246.



132 133

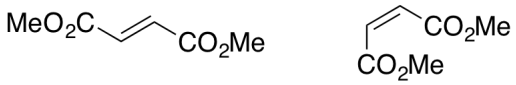
2-Benzylmalononitrile (132) and (1,1-dicyano-2-phenylethyl)(2,3,4,6,7,8,9,10-octahydro-1*H*-pyrimido[1,2-*a*]azepin-5-ium-1-yl)dihydroborate (133): 2-Benzilidenemalononitrile (77 mg, 0.50 mmmol, 1.0 equiv) was dissolved in THF (1.0 mL) in a pressure tube. DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added. The tube was sealed and heated to reflux for 18 h. The solvent was removed under reduced pressure to give a crude solid that was purified by flash chromatography. Dinitrile **132** was isolated as a white, crystalline solid (16 mg, 21%) and hydroboration product **133** was isolated as a white solid (65 mg, 41%). Hydroboration product **133**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, 2H, J = 7.0 Hz), 7.24 (d, 2H, J = 7.5 Hz), 7.14 (t, 1H, J = 7.5 Hz), 3.57 (s, 2H), 3.43–3.41 (m, 2h), 3.39–3.35 (m, 4H), 2.79–2.77 (m, 2H), 1.97–1.93 (m, 2H), 1.71 (br s, 4H), 1.66–1.65 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 137.3, 129.6, 128.4, 127.3, 121.6, 54.1, 49.5, 48.9, 41.1, 30.9, 28.8, 26.8, 24.0, 21.2; ^{11}B NMR (160 MHz, $CDCl_3$) δ –8.1 (br t); HRMS (ESI) *m/z* $[M+H]^+$ calculated for $C_{19}H_{26}N_4B$ 321.2245, found 321.2260.



134

2-Cyano-3-phenylpropanamide (134): 2-Benzilidenemalononitrile (77 mg, 0.50 mmmol, 1.0 equiv) was dissolved in MeOH (1.0 mL) in a pressure tube. DBU–BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added causing the solution bubbled and turned yellow. The tube was sealed and

heated to 65 ˚C for 18 h. The solvent was removed under reduced pressure to give a crude solid that was purified by flash chromatography. The **134** was isolated as a white solid (26 mg, 30%).



82aE **82aZ**

Dimethyl fumarate (82aE) and dimethyl maleate (82aZ): DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was dissolved in THF (8.0 mL) and cooled to –78 ˚C. A solution of DMAD **66** (0.09 mL, 0.75 mmol, 1.5 equiv) in THF (2 mL) was prepared and added dropwise over several minutes to the stirring solution. The reaction mixture gradually turned red as the solution was allowed to warm to room temperature overnight. After 18 h, the solvent as removed under reduced pressure to give a red oil that was purified by flash chromatography (silica gel; hexanes:EtOAc). Dimethyl fumarate **82aE** was isolated as a white solid (7 mg, 13%) and dimethyl maleate **82aZ** was isolated as a clear oil (2 mg, 3%).

82dE **82dZ**

Methyl (*Z*)-3-phenylacrylate (82dE) and methyl cinnamate (82dZ): Methyl 3-phenylpropiolate **69a** (80 mg, 0.50 mmol, 1.0 equiv) was dissolved in MeOH (2.0 mL) and DBU-BH_3 **105a** (83 mg, 0.50 mmol, 1.0 equiv) was added causing some bubbling to occur. The resulting solution was stirred at 25 ˚C for 24 h. Removal of the solvent gave a yellow residue that was purified by flash chromatography (silica gel; hexanes:EtOAc) to afford the mixture of alkenes **82dE** and **82dZ** as a clear oil (18 mg, 22%, 75/25 E/Z).

3.0 STUDY OF THE AIBN- AND TRIETHYLBORANE-INITIATED HYDROSTANNATION OF PROPARGYL SILYL ETHERS

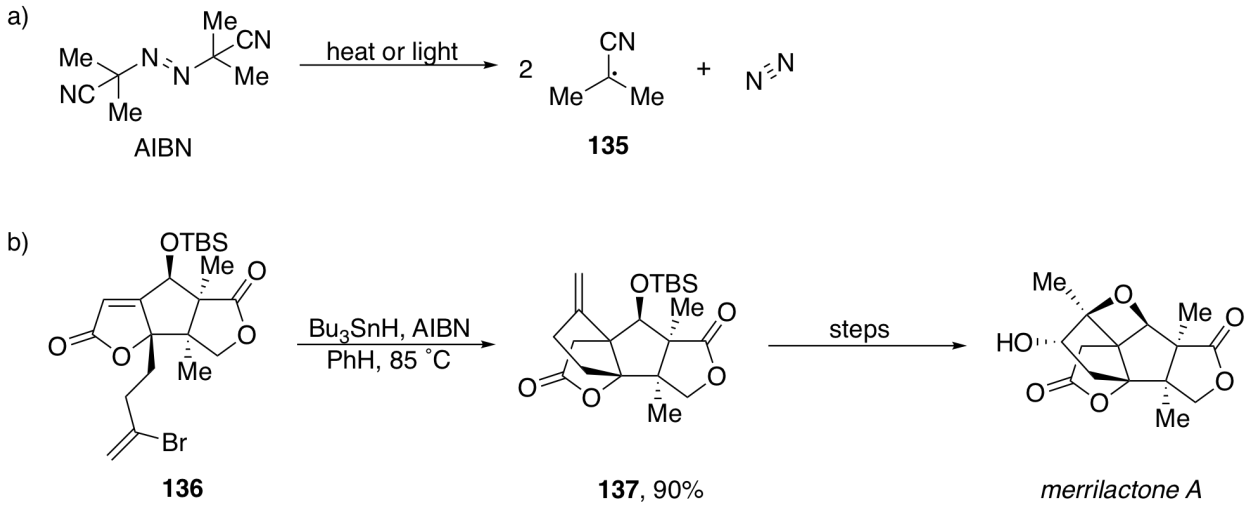
3.1 INTRODUCTION

3.1.1 Radical initiators

Radical chain reactions are often initiated by the homolytic cleavage of a covalent bond. The conditions required to achieve homolysis can be harsh. For example, the uncatalyzed, thermal cracking of petroleum, a process that results in the homolytic cleavage of alkyl C–C bonds, is performed at temperatures exceeding 400 ˚C.[79] Accordingly, radical initiators—compounds that are susceptible to homolytic cleavage at lower temperatures—are valued in modern synthesis. Radical initiators contain relatively weak covalent bonds that are usually cleaved through thermolysis or photolysis.[80] Such compounds can be used to initiate radical chain processes under mild conditions. There is a wide array of radical initiators, thus choosing the one most suitable is often key for obtaining optimal results.

3.1.2 Azo initiators

Azo compounds are a class of radical initiator consisting of R–N=N–R functional groups. The R–N bond (usually a C–N bond) can be cleaved with either heat or light as an initiation step.[80] Two of the most commonly used azo initiators are 2,2'-azobis(2-methylpropionitrile) (AIBN) and 2,2'-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70). The choice of azo initiator is often dictated by the temperature of the reaction. For example, AIBN has a half-life of 10 h in toluene at 65 ˚C, whereas V-70 has a half-life of 10 h in toluene at 30 ˚C.[81] Thermolysis or photolysis of AIBN causes homolysis of the C–N bonds to generate two 2-cyanoprop-2-yl radicals **135** and dinitrogen (**Scheme 46a**).[81] The thermolysis of AIBN in solution is less efficient than the corresponding gas-phase reaction.[80] Typically, 40% of the newly-formed cyanopropyl radicals **135** recombine before escaping the surrounding solvent cage.[80] First observed by Frank and Rabinowitch, the cage effect is strongly dependent on temperature and solvent viscosity.[80, 82-83]



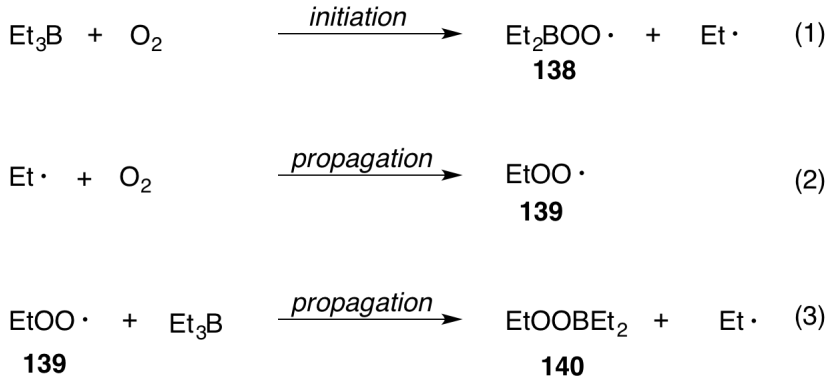
Scheme 46. (a) Decomposition of AIBN by heat or light; (b) AIBN-initiated radical dehalogenation and cyclization in the synthesis of merrilactone A

Azo initiators are commonly used in the synthesis of natural products. For example, Danishefsky and Birman used AIBN to initiate the tin hydride-mediated cyclization of alkenylbromide **136** at 85 °C to give tetracycle **137** in a 90% yield as a late-stage transformation in the total synthesis of merrilactone A (**Scheme 46b**).[84]

3.1.3 Triethylborane and O_2

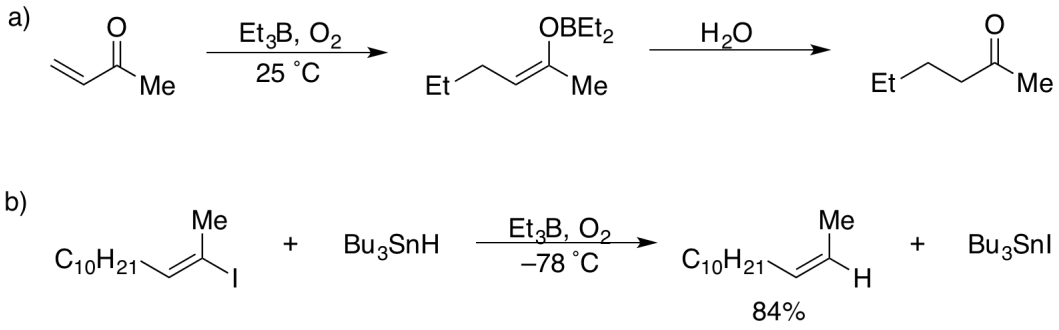
Another common radical initiator is the combination of triethylborane (Et_3B) and oxygen (O_2).[80] The oxidation of Et_3B by O_2 leads to the formation of ethyl radicals (**Scheme 47**).[80] This process was studied extensively by Brown,[85-91] Davies and Roberts,[92-94] and others.[95] They showed that the autoxidation reaction is initiated by the reaction of Et_3B with O_2 to give an ethyl radical (Et•) and diethylborylperoxy radical **138** (Et_2OO•, equation 1). Reaction of Et• with O_2 gives ethylperoxy radical **139** (EtOO•, equation 2). Radical **139** can

react with Et_3B to form ethyl diethyl(ethylperoxy)borane **140** (equation 3). With high concentrations of O_2, **140** can be further oxidized to diethyl ethylboronate ($EtB(OEt)_2$) and then to triethyl borate ($B(OEt)_3$, not shown).[87, 91, 96-98] In addition to propagating autoxidation, ethyl radicals are able to initiate radical chain processes. This combination is often used because it can generate radicals at or below room temperature (at temperatures as low as –78 ˚C).[81]



Scheme 47. Key reactions in the autoxidation of triethylborane

Triethylborane has been used as both a radical initiator and radical alkylating reagent. Brown and Midland used Et_3B to alkylate methyl vinyl ketone and other small, conjugated molecules (**Scheme 48a**).[85] Contreras used the combination of Et_3B and hydrogen peroxide to initiate the polymerization of methyl methacrylate.[99] Later, Oshima and coworkers showed that Et_3B was useful for initiating radical chains for preparative reactions (**Scheme 48b**).[100-103] In their early examples, Et_3B was used to initiate the radical dehalogenation of several different alkenyl halides. Since then, Et_3B has become widely used as a radical initiator.

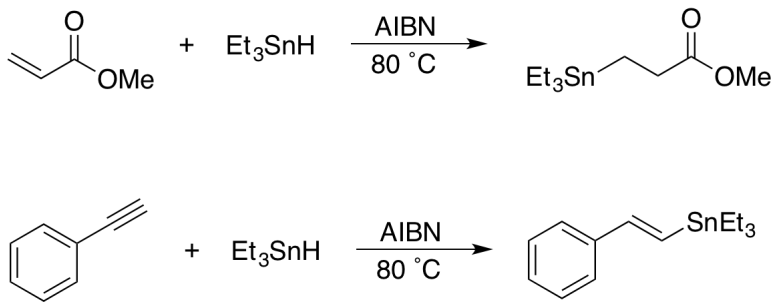


Scheme 48. (a) The oxygen-initiated addition of triethylborane to methyl vinyl ketone; (b) example of triethylborane-initiated reduction of an alkenyl halide

3.1.4 Hydrostannation reactions

Alkenylstannanes are of great synthetic utility in organic chemistry. They can be used in transmetallation processes with lithium[104] and copper[105] or the tin groups can be exchanged with iodine to afford alkenylhalides.[106] Perhaps most importantly, alkenylstannanes are precursors in palladium(0)-catalyzed cross-coupling reactions known as Stille couplings.[107-109]

Alkenylstannanes are commonly obtained through hydrostannation reactions, the addition of a tin hydride across a triple bond. The radical hydrostannation reacation was first discovered by Neumann and Sommers in 1964.[110] They showed that triethyltin hydride (Bu_3SnH) could be added to unsaturated esters, like methyl acrylate or phenylacetylene, under radical conditions (**Scheme 49**).[110-113]



Scheme 49. Earliest examples of hydrostannations from Neumann and Sommers

Since the pioneering work of Neumann and Sommers, hydrostannation methodology has expanded into two main classes, transition metal-catalyzed hydrostannations and radical hydrostannations. In the former case, metal complexes (often palladium(0) catalysts) are employed to mediate the addition of tin hydride to an alkene or alkyne.[114] The latter class is typified by the use radical initiators, like AIBN or Et_3B.[114]

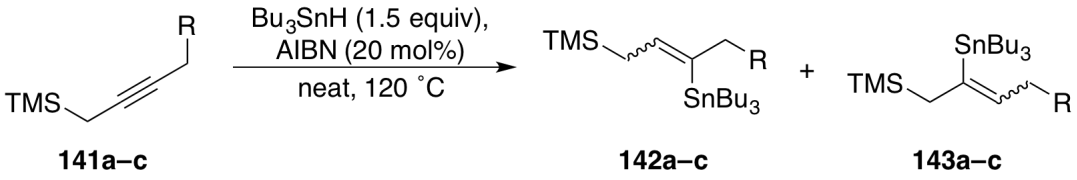
In general, the hydrostannation of alkynes with tributyltin hydride leads to the formation of alkenylstannanes with varying degrees of regio- and stereoselectivity. High regioselectivity is usually only obtained with terminal alkynes (when the tin group preferentially adds to the terminus)[114] or with directing groups (see below).[115] Generally, the undirected hydrostannation of internal alkynes gives a mixture of both regioisomers.[114] High stereoselectivity is often elusive in complicated systems.[114]

3.1.5 Hydrostannations of propargyl silyl ethers

The hydrostannations of propargyl silyl ethers often proceed with high stereoselectivity. Nativi and Taddei first studied the selectivity of the radical hydrostannation of propargylic

alcohol derivatives. Reaction of propargyl alcohol **141a** with 1.5 equiv Bu_3SnH and 20 mol% AIBN at 120 ˚C exclusively afforded alkenylstannane **142a** in a 71% yield and a 50/50 *Z/E* ratio (**Table 19**, entry 1).[115] With the TBS-protected silyl ether **141b**, an 80% yield was obtained to give **142b** in a 75/25 Z/E ratio (entry 2). The undirected hydrostannation of **141c** gave a complex mixture of the Z- and E-isomers of alkenylstannanes **142c** and **143c** (entry 3). From these experiments, Nativi and Taddei concluded that the propargyl alcohol directed the regioselective hydrostannation.[115]

Table 19. Hydrostannation of propargylic alcohol **141a–c** studied by Nativi and Taddei[115]



141a–c **142a–c** **143a–c**

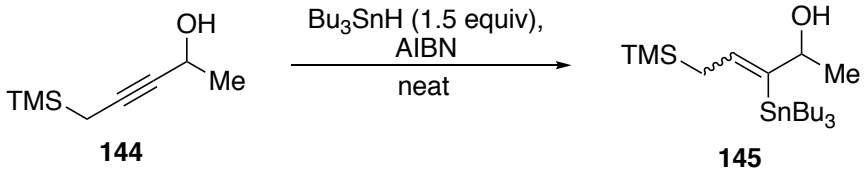
entry	R	precursor	yield **142,** Z/E	yield **143**, Z/E
1	OH	**141a**	71%, 50/50	0%
2	OTBS	**141b**	80%, 75/25	0%
3	H	**141c**	34%, 50/50	34%, 50/50

[a]determined by ^1H NMR analysis of the crude products

Nativi and Taddei also studied the effects of reaction conditions, including temperature, time, and initiator. Selected results from this study are summarized in **Table 20**. Propargylic alcohol **144** was reacted with 1.5 equiv Bu_3SnH 20 mol% and AIBN at 120 ˚C for 1 h to give alkenylstannane **145** in an 80% yield with an 80/20 Z/E ratio (entry 1). Increasing the reaction time to 8 h resulted in the full consumption of **144**, but led to a

decrease in Z-selectivity (entry 2). With a 36 h reaction time, a 50/50 mixture of Z- and E-isomers was observed (entry 3). Decreasing the temperature to 60 ˚C gave an 89/11 Z/E ratio of **145** after 8 h, while increasing the temperature to 200 ˚C led to no selectivity (50/50 Z/E) under the same conditions (entries 4 and 5). Control reactions conducted without AIBN at 120 ˚C led to 60% consumption of **144** after 8 h to give a 95/5 Z/E ratio (entry 6); continuing the reaction for 24 h led 90% consumption of **144** but a decreased 80/20 Z/E ratio (entry 7).

Table 20. Selected examples of hydrostannation reaction conditions studied by Nativi and Taddei[115]



144 **145**

entry	time (h)	temp (˚C)	mol % AIBN	% unreacted **144**	Z/E ratio[a]
1	1	120	20	20	80/20
2	8	120	20	0	67/33
3	36	120	20	0	50/50
4	8	60	20	10	89/11
5	8	200	20	5	50/50
6	8	120	0	40	95/5
7	24	120	0	10	80/20

[a]determined by ^{1}H NMR analysis of the crude products

From these results, Nativi and Taddei concluded that the Z-isomer is kinetically preferred, but the subsequent isomerization gave a mixture of the Z- and E-isomers approaching the thermodynamic ratio (50/50 Z/E, **Figure 12**). Regioselective addition of tributyltin radical (Bu_3Sn•) to C2 of alkyne **141a** gives alkenyl radical **146,** which abstracts hydrogen from a Bu_3SnH to form **142aZ** and Bu_3Sn• (**Figure 12a**). Reversible addition of Bu_3Sn• to C2 of **142aZ** gives alkyl-centered radical **147** (**Figure 12b**). Rotation about the C2–C3 bond followed by elimination of Bu_3Sn• gives **142aE**. Longer reaction times (compare entries 1–3) and higher temperatures (compare entries 2, 4, and 5) promoted this isomerization process. Additionally, they showed that the reaction could be run in the absence of an initiator, albeit at a lower rate.[115] Together, these results show that tin radicals react more quickly with disubstituted alkynes than trisubstituted alkenes, thus the isomerization of alkenylstannane **142a** only becomes competitive with the initial hydrostannation of alkyne **141a** once most of the alkyne is consumed.

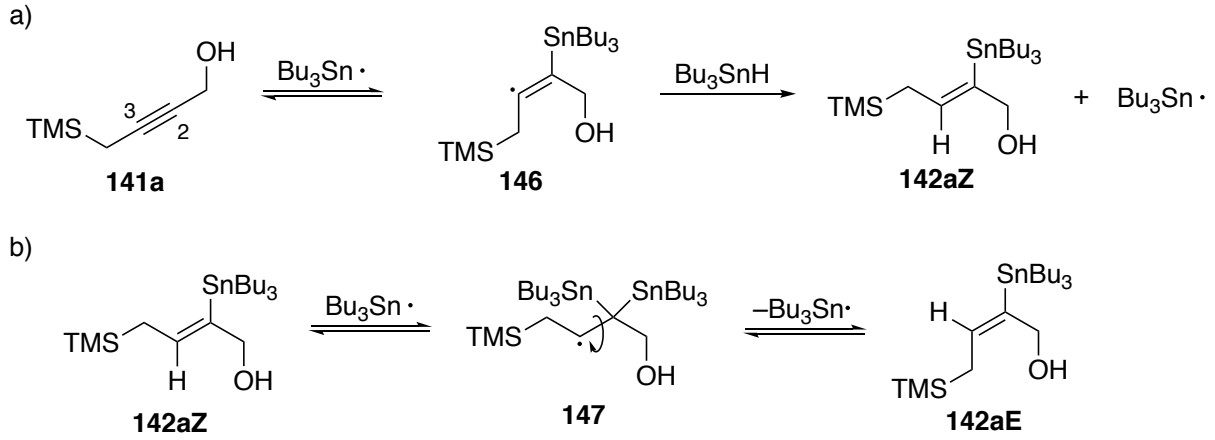
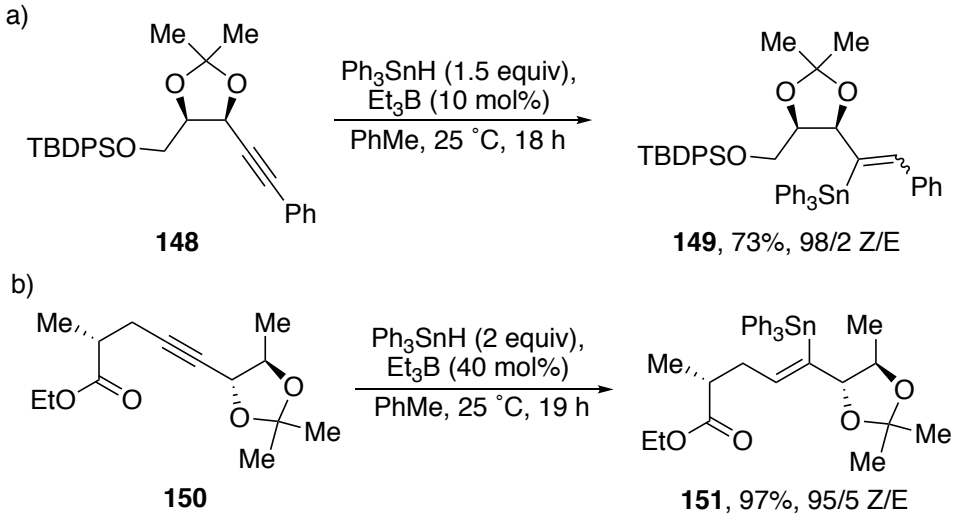


Figure 12. Proposed mechanisms for the (a) hydrostannation of propargyl alcohol **141a** and (b) the tin-mediated isomerization of **142a**

Propargylic alcohol derivatives are important precursors for radical hydrostannations because of the predictable regiochemistry of the products. Hale and coworkers extensively studied the Et_3B/O_2-initated hydrostannations of propargyl silyl ethers to give the corresponding alkenylstannanes in high regio- and stereo-selectivity.[116-119] For example, the triphenyltin hydride (Ph_3SnH) hydrostannation of propargyl dioxolane **148** afforded alkenylstannane **149** as the only regioisomer in 73% yield and a 98/2 Z/E ratio (**Scheme 50a**).[117] Hale later applied this methodology in the formal synthesis of (+)-pumiliotoxin B; reaction of alkyne **150** with 2 equiv triphenyltin hydride and 40 mol% Et_3B gave alkenylstannane **151** in 97% yield (95/5 Z/E, **Scheme 50b**).[119] Hale and coworkers were able to achieve better stereoselectivity than Nativi and Taddei at lower reaction temperatures, making the Et_3B/O_2 hydrostannation conditions desirable for modern synthesis.



Scheme 50. Examples of Et_3B/O_2-initiated hydrostannations of propargyl dioxolones

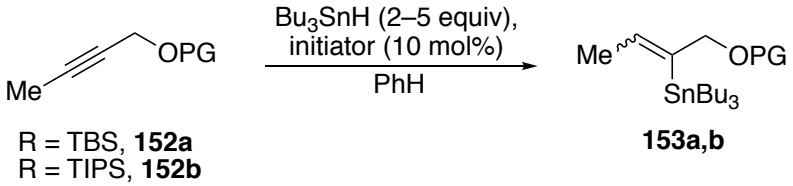
3.1.6 New results concerning the radical hydrostannation of propargyl silyl ethers

Recently, Organ and coworkers published a series of papers challenging the accepted understanding of the mechanisms of AIBN- and Et_3B/O_2-initiated hydrostannation of internal alkynes with tributyltin hydride.[120-123]

First, they studied the stereoselectivity of the hydrostannation of several propargylic silyl ethers.[120] The reaction of *tert*-butyldimethylsilyl (TBS) ether **152a** with Bu_3SnH (2–5 equiv) and 10 mol% initiator, either AIBN or Et_3B, in PhH was studied (**Table 21**). The AIBN-initiated reaction was performed at 80 ˚C, whereas the Et_3B-initiated reactions were run at both 25 and 80 ˚C. For all reactions, the reagents were combined in open air before sealing the flasks. Using AIBN, a 98% yield of alkenylstannane **153a** was obtained after 3 h, but with little stereoselectivity (55/45 Z/E, entry 1). With Et_3B/O_2, high yields of alkenylstannane **153a** were achieved with 5 equiv Bu_3SnH at room temperature after 48 h or with shorter times and lower tin loadings at 80 ˚C (compare entries 2 and 3). In all cases, the Et_3B/O_2-initiated reactions exclusively gave the Z-isomer (>99/1 Z/E). When both initiators were used together at 80 ˚C, little stereoselectivity was observed, matching the AIBN result (compare entries 1 and 4). With triisopropylsilyl (TIPS) ether **152b**, no reaction was observed when AIBN was used as the initiator at 80 ˚C (entry 5), but the Et_3B/O_2-initiated reaction gave a 96% yield with >99/1 Z/E selectivity comparable to the result obtained with **152a** under identical conditions (compare entries 5 and 6). The result in entry 5 was unusual because Nativi and Taddei demonstrated that the

hydrostannation of propargyl alkynes still proceeded, albeit at a slower rate, in the absence of initiator (see **Table 20**, entries 6 and 7).[115]

Table 21. Results from Organ's stereoselectivity studies



R = TBS, **152a**
R = TIPS, **152b**

153a,b

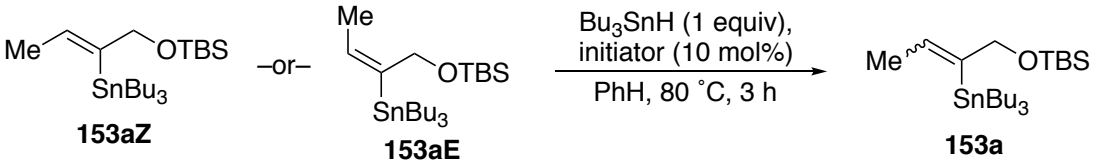
entry	prec.	equiv Bu_3SnH	initiator	T (˚C)	t (h)	yield **153**	Z/E[a]
1	**152a**	2	AIBN	80	3	98%	55/45
2	**152a**	5	Et_3B/O_2	23	48	95%	>99/1
3	**152a**	2	Et_3B/O_2	80	3	95%	>99/1
4	**152a**	2	AIBN, Et_3B/O_2	80	3	n. d.	55/45
5	**152b**	2	AIBN	80	3	0%	–
6	**152b**	2	Et_3B/O_2	80	48	96%	>99/1

[a]determined by ^1H NMR analysis of the crude products; [b] n. d. is "not determined"

To study the isomerization of the alkenylstannanes, pure samples of **153aZ** and **153aE** were reacted with either AIBN or Et_3B/O_2 (10 mol %) and tributyltin hydride (1 equiv) in PhH at 80 ˚C for 3 h (**Table 22**). With AIBN, **153aZ** gave a 55/45 Z/E mixture, while **153aE** did not react (<1/99 Z/E, entries 1 and 2). Organ and coworkers explained that **153aZ** gave the thermodynamic product ratio while the E-isomer was a "thermodynamic sink" and could not isomerize.[120] Using Et_3B/O_2, neither **153aZ** nor

153aE isomerized and isomerically-pure samples were observed after the reaction (entries 3 and 4).

Table 22. Results from Organ's isomerization of **153aZ**



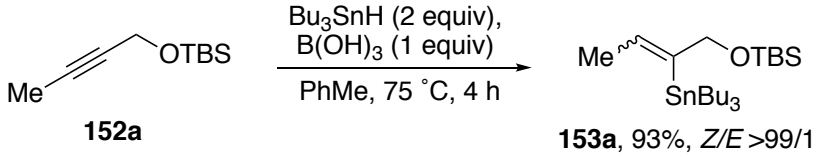
entry	initiator	initial Z/E[a]	final Z/E[a]
1	AIBN	>99/1	55/45
2	AIBN	<1/99	<1/99
3	Et_3B/O_2	>99/1	>99/1
4	Et_3B/O_2	<1/99	<1/99

[a]as determined by ^1H NMR spectroscopy

Finally, the hydrostannation and isomerization of **152a** were followed by ^1H NMR spectroscopy. Solutions of **152a**, tributyltin hydride (2 equiv), and either AIBN or Et_3B (10 mol %) in PhMe were heated to 80 ˚C. With AIBN, a 90% yield of **153a** with a 95/5 Z/E ratio was observed after 20 min. The reaction proceeded at a slower rate with Et_3B/O_2. A 35% yield of **153aZ** was observed after 20 min. From these results, Organ and coworkers concluded that the AIBN- and Et_3B/O_2-initiated hydrostannations proceeded through different mechanisms and the latter operated under strict kinetic control.[120]

In a second paper, Organ and coworkers screened several borinate, boronate, and borate species for their ability to initiate the hydrostannation of internal alkynes.[121] Different boron species were used as additives in the hydrostannation of **152a**. The

starting materials were combined in open air before the reaction vessels were sealed. In the most striking example, a 93% yield of **153a** was obtained when 1 equiv of boric acid ($B(OH)_3$) was added to the reaction (**Scheme 51**). By varying solvents, it was observed that the reaction was faster in THF than PhMe, which Organ and coworkers identified as a polar accelerating effect and suggested that the reaction pathway could include polar intermediates.[121] This observation was counter to the radical mechanism proposed by Nativi and Taddei.[115]



Scheme 51. Boric acid-initated hydrostannation of propargyl alcohol derivative **152a**

In a follow-up study, the solvent effect on the hydrostannation of propargylic alcohol derivatives was further probed. Organ and coworkers screened several polar solvents for their ability to accelerate the reaction rate.[122] Solutions of TIPS ether **152b**, Bu_3SnH (1.5–2 equiv), and Et_3B (20–50 mol %) were prepared in various solvents in open air before the reaction vessels were sealed and stirred at 25 ˚C for 90 min. The reactions were halted and the yields of **153b** were determined. Several polar solvents were screened, including THF, THF/water, acetone, DMF, 1,3-dimethyl-2-imidazolidinone (DMI), 1,3-dimethyl-3,4,5,6-tetrahydro2(1*H*)-pyrimidinone (DMPU), and isobutyronitrile. Compared to PhH, which gave a 5% yield of **152b** under their standard reaction conditions, all of the other solvents led to significantly higher yields of **153b**, with THF, DMI, and DMPU giving comparably-high yields of 82%, 86%, and 87%, respectively. They also reported that no

product was formed when the reactions were run under high oxygen conditions (using an oxygen-filled balloon) regardless of which solvent was used, concluding that the autoxidation of Et_3B was too rapid under these conditions to initiate the hydrostannation reaction. Organ and coworkers stated that these results corroborated their claim that the rate of the Et_3B/O_2-initiated hydrostannation reaction can be influenced by solvent polarity.[122]

These conclusions from Organ and coworkers run counter to accepted mechanistic understanding of Et_3B autoxidation and the radical hydrostannation of alkynes. Here, the AIBN- and Et_3/O_2-initiated hydrostannations of propargyl alcohol derivatives were studied extensively to show that new mechanistic understandings of AIBN- and Et_3B/O_2-initiatior were not required. Instead, both initiators operate under the same mechanism.

3.2 RESULTS AND DISCUSSIONS

3.2.1 Mechanistic hypotheses

The results from Organ do not require new mechanistic explanations for the radical hydrostannation of propargyl silyl ethers. Instead, Organ's results can be explained by the following mechanistic hypotheses:

(1) Both AIBN and Et_3B/O_2 function as radical initiators.

(2) The reaction of Bu_3SnH with propargyl silyl ethers occurs through the mechanism shown in **Figure 13**. (a) Hydrostannation occurs through the addition of $Bu_3Sn•$ to an alkynyl carbon to form an alkenyl radical **154** that abstracts hydrogen from Bu_3SnH to form an alkenylstannane. (b) Isomerization occurs through the addition of $Bu_3Sn•$ to an alkenylstannane, forming alkyl radical **155**. Free rotation about the C2–C3 σ bond, followed by elimination of $Bu_3Sn•$ affords the alkenylstannane. (c) The hydrostannation of alkynes is much faster than the isomerization of the corresponding alkenylstannane. The latter reaction only becomes competitive when the concentration of alkyne is low.

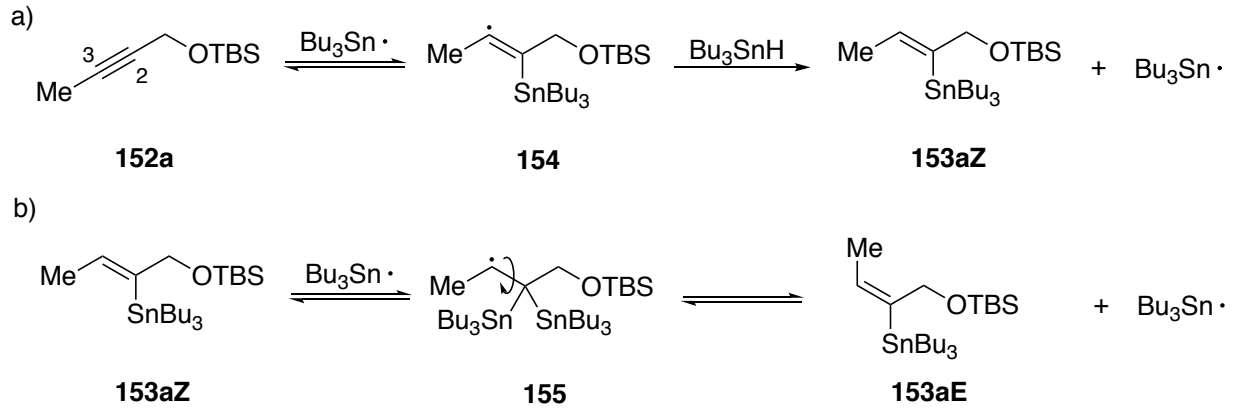


Figure 13. Proposed mechanism for the (a) hydrostannnation of **151a** and (b) isomerization of **152aZ**

(3) The AIBN-initiated hydrostannation of propargyl alcohol derivatives **152a** and **152b** with excess Bu_3SnH provides the thermodynamic ratio of **153a** and **153b**.

(4) The Et_3B/O_2-initiated hydrostannation of propargyl alcohol derivatives **152a** and **152b** provides the kinetic ratio of the alkenylstannanes **153a** and **153b** under most reaction conditions.

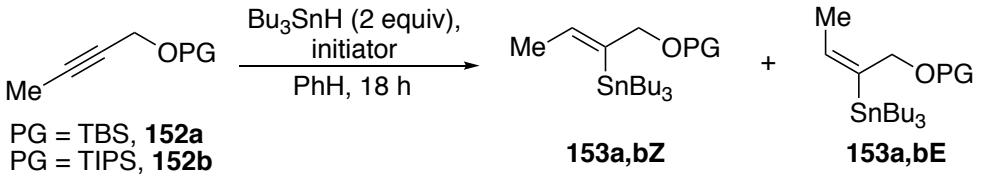
3.2.2 Preparative hydrostannations of propargyl alcohol derivatives

To acquire isomerically-pure or enriched samples of **153a,bZ** and **153a,bE**, 1 mmol preparative hydrostannations were performed. These samples would be used as NMR standards and for later experiments.

As a general procedure for the AIBN-initiated reactions, AIBN (10 mol%) was added to a flask, the air was purged, and the flask was filled with argon. Alkyne **152a** or **152b**, PhH, and 2 equiv Bu_3SnH were added by syringe and the resulting solution was heated to 80 ˚C. Propargyl silyl ether **152a,b** was reacted with 2 equiv Bu_3SnH and 10 mol% AIBN in PhH at 80 ˚C for 18 h (**Table 23**). With **152a**, a 36% yield of **153aZ** (88/12 Z/E) and 19% **153aE** (5/95 Z/E) were isolated following flash chromatography (entry 1). The AIBN-initiated hydrostannation of **152b** yielded 35% of **153bZ** (>99/1 Z/E) and 19% of pure **153bE** (<1/99 Z/E; entry 2).

For the Et_3B/O_2-initiated reactions, alkyne **152a** or **152b**, PhH, 2 equiv Bu_3SnH, and 50 mol% Et_3B were added sequentially to an argon-filled flask. Oxygen was introduced by piercing the rubber septa atop the reaction flask with a needle to allow free exchange of the argon with air. With **152a**, a 68% yield of **153aZ** (96/4 Z/E) and 2% yield **153aE** (6/94 Z/E) were obtained after flash chromatography (entry 3), while 62% **153bZ** (98/2 Z/E) and 6% **153bE** (24/76 Z/E) were afforded from the hydrostannation of **152b** (entry 4). These isomerically-pure or isomerically-enriched samples of **153a,bZ** and **153a,bE** were used as standards for the kinetics experiments.

Table 23 Examples of preparative hydrostannations of **152a** and **152b**



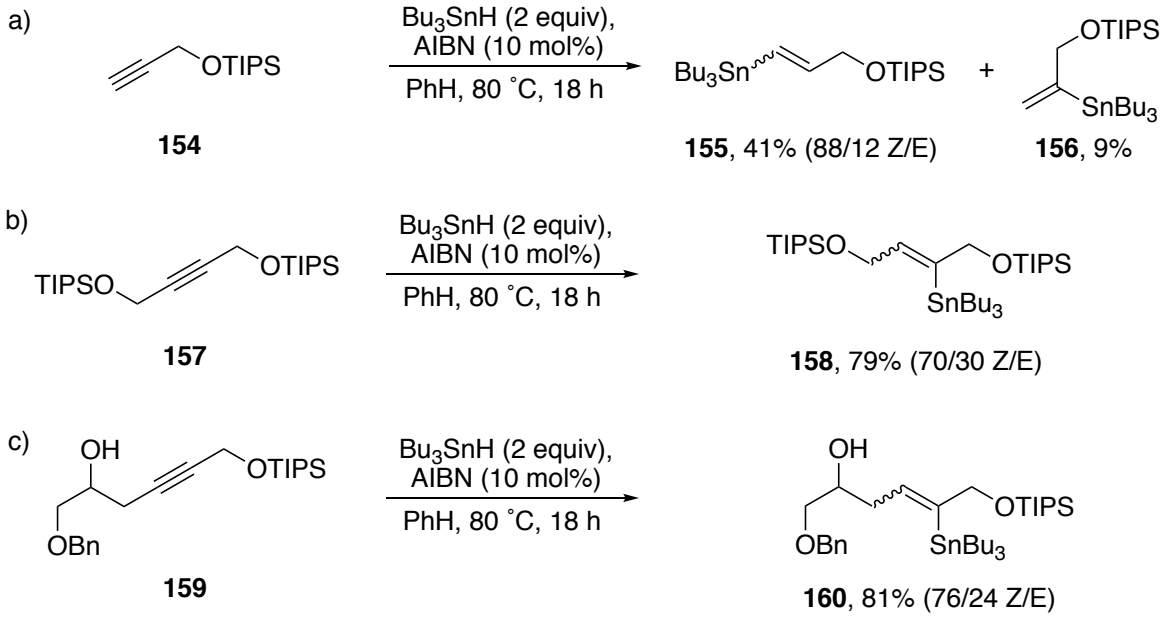
entry	prec	init	mol% init	T (˚C)	yield **153Z** (Z/E)[a]	yield **153E** (Z/E)[a]
1	**152a**	AIBN	0.1	80	36% (88/12)	19% (5/95)
2	**152b**	AIBN	0.1	80	35% (>99/1)	19% (<1/99)
3	**152a**	Et_3B/O_2	0.5	25	68% (96/4)	2% (6/94)
4	**152b**	Et_3B/O_2	0.5	25	62% (98/2)	6% (24/76)

[a]isolated yields after flash chromatography

Isolation of pure samples of **153a,bZ** and **153a,bE** proved to be difficult for three reasons. First, low yields of the alkenylstannane products **153a,b** were observed after flash chromatography when hexanes/ether were used as the mobile phase and silica gel was used as the stationary phase. It is believed that decomposition due to protodestannylation was occurring. Better results yields were obtained when Et_3N (1%) was added to the mobile phase. Second, the products were very non-polar. For example, alkenylstannanes **152aZ** and **152aE** had retention factors (R_f) of 0.91 and 0.73 on silica gel thin-layer chromatography (TLC) when a 97/2/1 hexanes/ether/Et_3N mobile phase was used. Third, unreacted Bu_3SnH often co-eluted with the alkenylstannane products. Despite these problems, it was possible with peak-shaving to obtain fractions with high isomeric enrichment from preparative experiments.

Organ reported that the AIBN-initiated hydrostannation of TIPS-protected propargyl alcohols led to no reaction, while the corresponding Et_3B-initated reactions were high-yielding.[120] In our case, the AIBN-initiated reaction of **152b** with Bu_3SnH gave a 54% isolated

yield of **153b** (compare **Table 21**, entry 5 with **Table 23**, entry 2). To test the generality of this observation, the hydrostannation of additional TIPS-protected propargyl alcohol derivatives was attempted using the AIBN conditions described in **Table 23** (entries 1 and 2). With terminal alkyne **154**, a 41% yield of terminal alkenylstannane **155** (88/12 Z/E) and 9% of internal alkenylstannane **156** were obtained after flash chromatography (**Scheme 52a**). Symmetric TIPS alkyne **157** afforded a 79% yield of **158** with a 70/30 ratio of Z- and E-isomers (**Scheme 52b**). Reaction of alkyne **159** with Bu_3SnH gave alkenylstannane **160** in an 81% with a 76/24 Z/E ratio (**Scheme 52c**).



Scheme 52. Preparative hydrostannations of TIPS-protected propargyl silyl ethers

The results in **Tables 23** and **Scheme 52** show that the AIBN-initiated hydrostannation of TIPS-protected propargyl alcohols afford the corresponding alkenylstannanes in high yield. This stands in contrast to Organ's report that the AIBN-initiated hydrostannation of TIPS-alkynes **152b** and **159** led to no reaction.

3.2.3 The effects of initiator, temperature, and time on the resulting Z/E ratio of alkenylstannanes

Following the isolation of authentic samples of alkenylstannanes **153a**,**b**, NMR experiments were conducted to better study the effects of initiator, temperature, and time on the resulting Z/E ratio of alkenylstannane products. As a general procedure for the azo-initiated reactions, AIBN or V-70 (10 mol%) was added to a flask and the air was purged and replaced with argon. Alkyne **152a** or **152b**, PhH, and 2 equiv Bu_3SnH were added by syringe to the flask and the resulting solution was heated to 80 ˚C. Aliquots were removed at regular intervals and analyzed by ^1H NMR spectroscopy to determine the conversion to **153a,b** and corresponding Z/E ratios. The starting alkynes **152a,b** were discernible from the resulting alkenylstannane products **153a,b** by ^1H NMR spectroscopy. For example, the α-protons of **152a** have a chemical shift of 4.23 ppm in C_6D_6 (**Figure 14**, top). The α- and alkenyl protons of **153aZ** have chemical shifts of 4.31 and 6.32 ppm, while the corresponding resonances of **153aE** have shifts of 4.47 and 5.72 ppm, respectively (**Figure 14**, bottom).

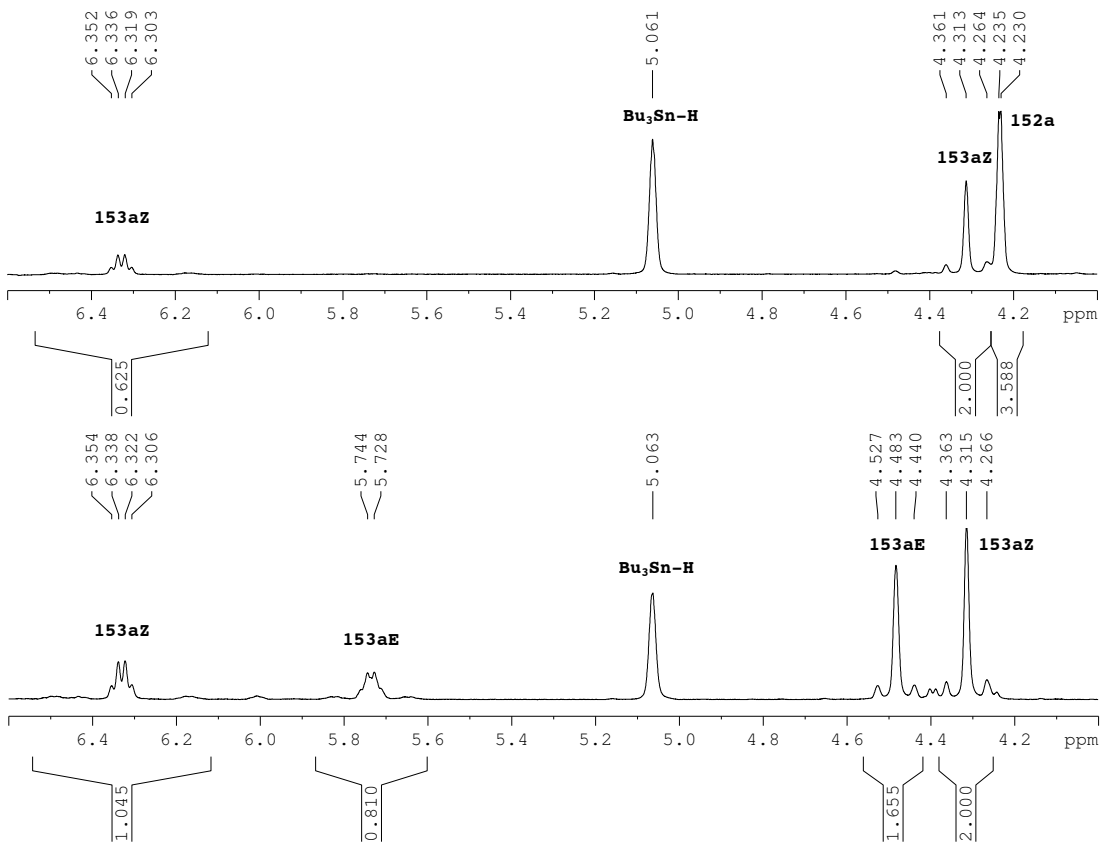


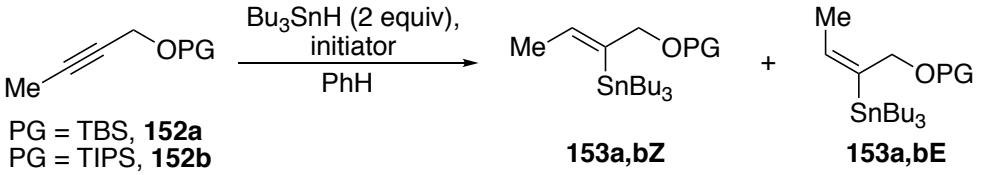
Figure 14. ^{1}H NMR spectrum of **152a** and **153aZ** (top); ^{1}H NMR spectrum of **153aZ** and **153aE** (bottom)

Propargyl silyl ether **152a**, 2 equiv Bu_3SnH, and 10 mol% AIBN were combined in PhH and the resulting solution was heated to 80 ˚C for 1 h (**Table 24**, entry 1). After solvent evaporation, a ^{1}H NMR spectrum of the crude products showed full consumption of **152a** to afford **153aZ** and **153aE** in an 80/20 ratio. Under the same conditions, **152b** was fully converted to **153b** to give an 82/18 Z/E ratio after 1 h (entry 2). Reaction of **152a** with 2 equiv Bu_3SnH at 80 ˚C for 3 h led to a 55/45 Z/E ratio (entry 3) and that ratio was also observed when the reaction was run for 48 h under the same conditions (entry 4). When 10 mol% V-70 was used to initiate the reaction of **152a** with Bu_3SnH at 40 ˚C, all of **152a** was consumed to give a 54/46 ratio of

152aZ and **152aE** (entry 5). Clearly longer reaction times lead to diminished Z-selectivity regardless of the reaction temperature.

For the Et_3B/O_2-initiated reactions, alkyne **152a** or **152b**, PhH, 2 equiv Bu_3SnH, and 10 mol% Et_3B were added sequentially to an argon-filled flask. Oxygen was introduced by piercing the rubber septa atop the reaction flask with a needle to allow free exchange of the argon with air. Aliquots were removed at regular intervals and analyzed by ^1H NMR spectroscopy to determine the conversion to **153a,b** and corresponding Z/E ratios using the method described above (**Figure 14**). Reaction of **152a** with 5 equiv Bu_3SnH and 10 mol% Et_3B at 25 ˚C for 24 h resulted in a 76% conversion to **153a** with a 97/3 Z/E ratio (entry 5). Heating **152a** with 2 equiv Bu_3SnH and 10 mol% Et_3B at 80 ˚C led to full conversion (>99% conversion) to **153a** with an 80/20 Z/E ratio (entry 6). For entries 5 and 6, 10 mol% was added at the outset, but Et_3B was periodically until the conversions were about 90% **153a,b**. Reaction of **152a** with 2 equiv Bu_3SnH and a total of 30 mol% Et_3B in PhH at 25 ˚C resulted in a 91% conversion to **153a** (95/5 Z/E) after 3 h (entry 7). Under the same conditions with **152b**, 40 mol% of Et_3B was required to afford **152b** in 90% yield (97/3 Z/E; entry 8).

Table 24. Conversions and Z/E ratios in representative hydrostannation experiments



entry	prec	equiv Bu_3SnH	init. (mol%)	T (˚C)	t (h)	yield **153**, Z/E[a]
1	**152a**	2	AIBN (10 mol%)	80	1	>99%, 80/20
2[c]	**152b**	2	AIBN (10 mol%)	80	1	>99%, 82/18
3[b]	**152a**	2	AIBN (10 mol%)	80	3	>99%, 55/45
4	**152a**	2	AIBN (10 mol%)	80	48	>99%, 55/45
5	**152a**	2	V-70 (10 mol%)	40	3	>99%, 54/46
6[d]	**152a**	5	Et_3B (10 mol%)	25	24	76%, 97/3
7[e]	**152a**	2	Et_3B (10 mol%)	80	8	>99%, 80/20
8	**152a**	2	Et_3B (30 mol%)	25	3	91%, 95/5
9	**152b**	2	Et_3B (40 mol%)	25	3	90%, 97/3

[a]as determined by integration of the ^1H NMR spectrum of products; [b]compare to Table 21, entry 1; [c]compare to Table 21, entry 5; [d]compare to Table 21, entry 2; [e]compare to Table 21, entry 3

Several key differences were observed between our results in **Table 24** and those obtained by Organ (**Table 21**). Organ observed a 98% yield and 55/45 Z/E ratio of **153a** when AIBN was used to initiate the reaction at 80 ˚C (**Table 21**, entry 1). We observed full consumption of **152a** (>99% yield) and an 80/20 Z/E ratio after 1 h (**Table 24**, entry 1) and >99% yield and a 55/45 Z/E ratio after 3 h (entry 3). Organ reported no reaction when **152b** was reacted with AIBN and Bu_3SnH at 80 ˚C for 3 h (**Table 21**, entry 5), while we observed full conversion to afford **152b** in >99% after 1 h (**Table 24**, entry 2). For the Et_3B/O_2-initiated

hydrostannations of **152a**,**b**, Organ obtained a ≥95% yield of **153a,b** either with 5 equiv Bu_3SnH at rt in 24 h or with 2 equiv Bu_3SnH at 80 ˚C in 3 h (**Table 21**, entries 2 and 3). Regardless of the loading of Bu_3SnH, temperature, or time, Organ observed a >99/1 Z/E ratio of **153a,b**. In our hands, a >90% yield of **153a,b** was obtained at 25 ˚C in 3 h provided that the reaction was re-initiated with additional Et_3B at regular intervals (**Table 24**, entries 8 and 9). We did not observe complete Z-selectivity in these experiments, rather 95–97% Z-selectivity (**Table 24**, entries 6, 8, 9), however that selectivity diminished to 80/20 Z/E at 80 ˚C for 8 h (entry 7).

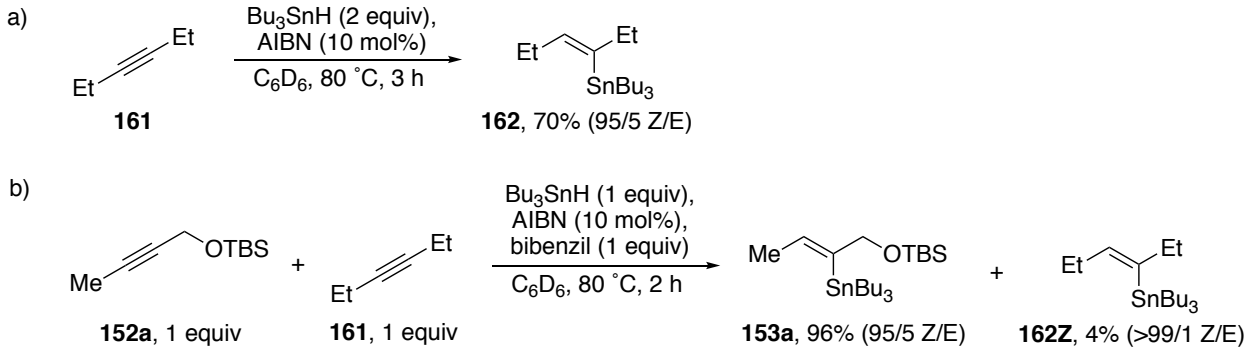
The results in **Table 24** support mechanistic hypotheses 2–4. When alkyne **152a** was reacted with 2 equiv Bu_3SnH at 80 ˚C for 1 h, >99% conversion to **153aZ** and **153aE** (80/20 ratio) was observed, but the Z-selectivity diminished at 3 h to 55/45 (entries 1 and 3). This observation supports mechanistic hypothesis 2, because the hydrostannation reaction was complete before the isomerization. Additionally, the thermodynamic ratio of **153a,b** (approximately 55/45 Z/E in the temperature range of 40–80 ˚C) was obtained when the reaction was run for 3 h or more, supporting mechanistic hypothesis 3. The Et_3B/O_2-initiated reactions provided the kinetic ratio (97/3 Z/E) of **153a,b** when the reaction was performed at rt (entries 6, 8, and 9; mechanistic hypothesis 4).

3.2.4 The kinetic ratio of alkenylstannanes is afforded when tributyltin hydride is the limiting reagent

To study the mechanism of the hydrostannation of alkynes, the competitive hydrostannation of 3-hexyne **161** and TBS-protected alkyne **152a** was studied. First, the hydrostannation of **161** was performed using the AIBN conditions described in **Table 24**, entry 3. Hexyne **161** was combined with deuterated benzene (C_6D_6), 2 equiv Bu_3SnH, and 10 mol% AIBN and the resulting solution

was heated to 80 ˚C for 3 h (**Scheme 53**). Analysis of the ^{1}H NMR of crude products showed 70% consumption of 3-hexyne **161** to afford alkenylstannane **162** in a 95/5 Z/E ratio. The yield was determined by comparison of the integral of the propargyl protons of 3-hexyne **161** (q, 2.28 ppm) with the alkenyl protons of the **162Z** (t, 6.06 ppm) and **162E** (t, 5.74 ppm). While the hydrostannation of **152a**,**b** goes to completion and reaches the thermodynamic product ratio of **153a**,**b** in 3 h, unreacted **161** is still present under the same conditions. Thus, that 3-hexyne **161** is much less reactive under the same conditions than propargyl alcohol derivatives **152a,b**.

Propargyl alcohol derivative **152a** (1 equiv), 3-hexyne **161** (1 equiv), Bu_3SnH (1 equiv) AIBN (10 mol%), and bibenzil (1 equiv, internal standard) were dissolved in deuterated benzene (C_6D_6) and the resulting solution was heated to 80 ˚C (**Scheme 53b**). After 2 h, an aliquot was removed and analyzed by ^{1}H NMR spectroscopy to show full consumption of Bu_3SnH. A 96% yield of **153a** (95/5 Z/E ratio) and 4% yield of **162Z** (>99/1 Z/E ratio) were observed, indicating that propargyl alcohol derivative **152a** is about twenty times more reactive towards Bu_3SnH than 3-hexyne **161**. Additionally, both alkenylstannanes **153a** and **162** were formed with high Z-selectivity.



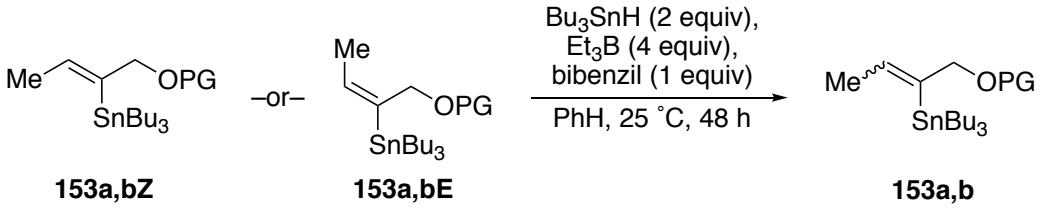
Scheme 53. Mixed hydrostannation reaction of **152a** and 3-hexyne **161**

Since Bu_3SnH was used as the limiting reagent, it was consumed by the initial hydrostannation reaction before much isomerization could occur. This supports mechanistic hypothesis 2. The 95/5 Z/E ratio of **152a** is close to the kinetic ratio of 97/3 observed for the Et_3B/O_2-initiated reactions (**Table 24**, entries 6, 8, and 9). In this reaction, the isomerization of **153a** was inhibited by the hydrostannation of **161**.

3.2.5 Triethylborane can initiate the isomerization under forcing conditions

To determine whether Et_3B/O_2 could initiate the tin hydride-mediated isomerization of alkenylstannes, forcing reaction conditions were explored. Isomerically-enriched samples of **153a,bZ** or **153a,bE** (>75% isomeric purity) were reacted with 2 equiv Bu_3SnH and 4 equiv of Et_3B in PhH at 25 ˚C for 48 h. Bibenzil was added as an internal integration standard. The starting materials were combined in open air before the reaction vessels were sealed. ^1H NMR spectroscopy was used to analyze the crude products to determine the resulting Z/E ratio of products with respect to the internal standard. With Z-enriched **153a**, the initial 99/1 isomeric ratio was isomerized to an 80/20 Z/E (**Table 25**, entry 1). Starting with 88/12 ratio of **153b**, a final Z/E ratio of 69/31 was obtained (entry 2). While the E-enriched samples (20/80, 21/79 Z/E ratios for **153a** and **153b**, respectively) both gave 37/63 Z/E ratios after 48 h (entries 3 and 4). As a control, a Z-enriched sample of **153b** (97/3 Z/E) was stirred in PhH with 2 equiv Bu_3SnH and 1 equiv bibenzil at 25 ˚C for 48 h in the absence of Et_3B (entry 5). Analysis of the resulting ^1H NMR spectrum showed an identical 97/3 Z/E isomeric ratio, indicating that Et_3B/O_2 is needed for the isomerization.

Table 25. Et_3B/O_2-initiated isomerizations of **153a,b**



153a,bZ **153a,bE** **153a,b**

entry	PG	precursor	initial Z/E[a]	final Z/E[a]
1	TBS	**153a**	99/1	80/20
2	TIPS	**153b**	88/12	69/31
3	TBS	**153a**	20/80	37/63
4	TIPS	**153b**	21/79	37/63
5	TIPS	**153b**	97/3	97/3[b]

[a]as determined by ^{1}H NMR spectroscopy; [b] with 0 equiv Et_3B

These experiments demonstrate that Et_3B/O_2 can initiate the partial isomerization of **153a,b**, but only under forcing conditions and much less efficiently than AIBN. These results provide support for mechanistic hypothesis 2, because they demonstrate that the Et_3B-initiated isomerization reaction can occur when the concentration of alkyne is low.

3.2.6 Tin exchange reactions of alkenylstannanes to probe the mechanism of isomerization

Two possible isomerization mechanisms of **153a** by Bu_3SnH are shown in **Figure 15**. As proposed by Nativi and Taddei (**Figure 12b**), addition of tributylstannyl radical ($Bu_3Sn\bullet$) to C2 of alkenylstannane **153a** results in the formation of alkyl-centered radical **163** (**Figure 15a**). Rotation about the resulting C2–C3 σ bond followed by radical elimination of $Bu_3Sn\bullet$ gives

153aE.[115] Alternatively, $Bu_3Sn\bullet$ could add to C3 to form alkyl radical **164** followed by bond rotation and subsequent elimination of $Bu_3Sn\bullet$ to afford **153aE** (**Figure 15b**).

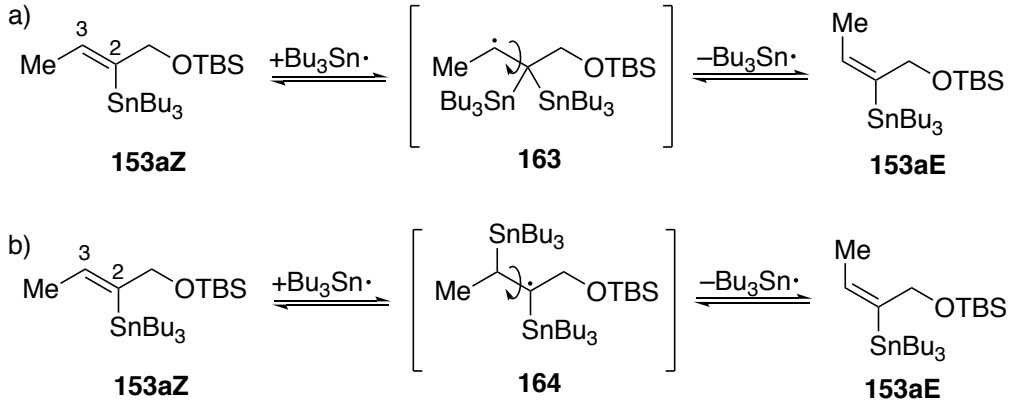
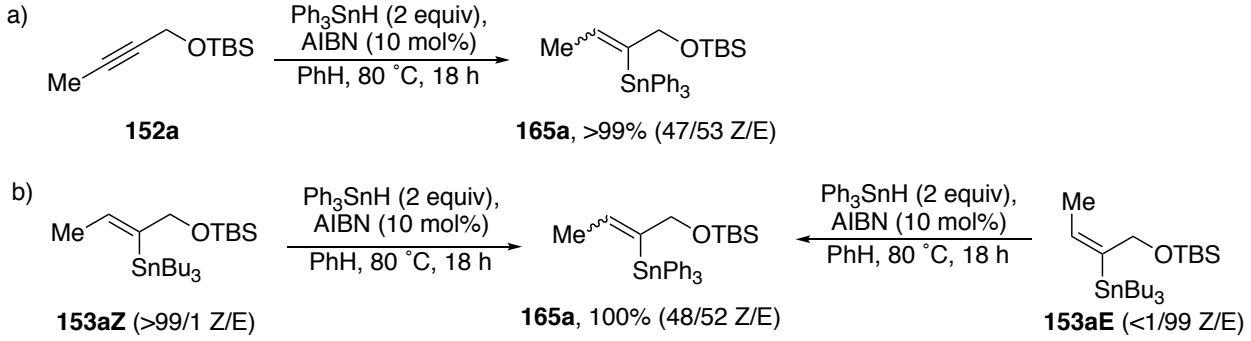


Figure 15. Possible isomerization mechanisms of **153a** by addition of tin radicals to (a) C2 or (b) C3

To probe the isomerization mechanism, the tin exchange reactions with Ph_3SnH shown in **Scheme 54b** were performed. If isomerization occurs through tin addition to C2 (**Figure 15a**), then a mixture of Bu_3Sn-substituted alkenylstannane **152a** and Ph_3Sn-substituted alkenylstannane **165a** should be observed. If isomerization occurs through tin addition to C3 (**Figure 15b**), then **152a** should be the only product.

To acquire NMR standards of alkenylstannane **165a**, alkyne **152a** was reacted with 2 equiv triphenyltin hydride (Ph_3SnH) and AIBN in PhH at 80 ˚C for 18 h (**Scheme 54a**). Full consumption of **152a** was observed to afford alkenylstannane **165a** in a 47/53 Z/E ratio. The α-protons and alkenyl proton resonances for **165aZ** were observed at 4.41 and 6.52 ppm in C_6D_6, respectively. The corresponding signals for **165aE** were observed at 4.62 and 5.90 ppm in C_6D_6. These diagnostic signals were discernible from the corresponding resonances for alkenylstannanes **153aZ** and **153aE** (see **Table 27** at the end of section 3.4).

Isomerically-enriched samples of **153a** (>99/1 or <1/99 Z/E) were reacted with Ph_3SnH (2 equiv), AIBN (10 mol%), and 1,2-dimethoxybenzene (1 equiv, internal standard) in PhH at 80 ˚C for 18 h. ^1H NMR analysis of the resulting products for both reactions showed full consumption of **153a** to give **165a** in a 48/52 Z/E ratio. In both reactions, the internal standard evaporated or decomposed, as >100% yields of **165a** were observed.

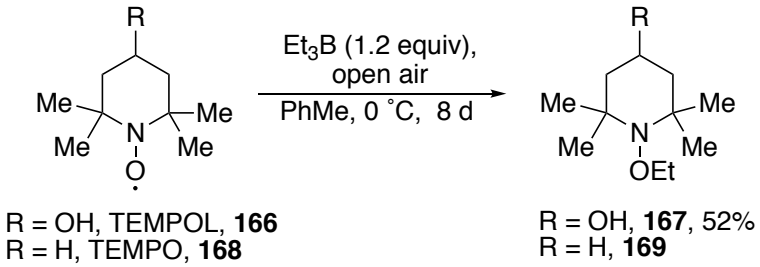


Scheme 54. Tin exchange of **153a** with Ph_3SnH to give **165a**

For both reactions, tin exchange was accompanied by E/Z isomerization to afford a thermodynamic ratio of **165a** (48/52 Z/E). These results indicate that the C2 isomerization mechanism shown in **Figure 15a** occurs since **165a** was formed as the only product. However, the results do not rule out the possibility that the C3 isomerization mechanism (**Figure 15b**) also occurs. The results in **Scheme 54** provide additional support for mechanistic hypothesis 3. The AIBN-initiated hydrostannation conducted with excess Bu_3SnH at 80 ˚C afforded a 48/52 ratio of alkenylstannanes **165aZ** and **165aE**, the thermodynamic ratio.

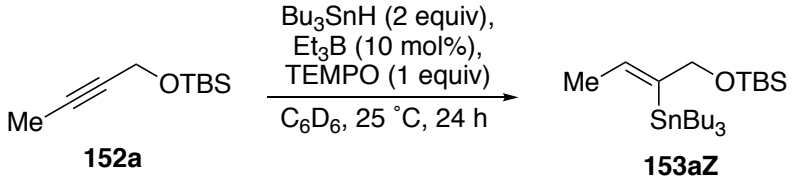
3.2.7 TEMPO inhibits the Et_3B/O_2-initiated hydrostannation of alkynes

To support the accepted radical chain mechanism for the Et_3B/O_2-initiated hydrostannation, a radical inhibition experiment was conducted. Braslau demonstrated that 4-hydroxy-2,2,6,6-tetramethylpiperidin-1-yl-oxy (TEMPOL, **166**), a persistent radical species, reacted with Et_3B in PhMe at 0 ˚C over 8 d to form **167** in 52% yield (**Scheme 55**).[124] Based on these results, a persistent radical would be able to compete with tin hydride in the reaction with ethyl radicals. If the Et_3B/O_2-initiated hydrostannation occurs by a radical chain, then the reaction of TEMPO **168** with ethyl radicals to form **169** should inhibit it.



Scheme 55. Reaction of TEMPOL with Et_3B to form **167**

TBS silyl ether **152a**, 2 equiv Bu_3SnH, 1 equiv TEMPO **168**, and C_6D_6 were combined by syringe in an argon-filled flask and stirred at room temperature for several minutes until the TEMPO had completely dissolved. Triethylborane was added by syringe to the stirring solution and the rubber septum was pierced with a needle to allow the free exchange of air. A ^1H NMR spectrum of the crude products showed approximately 1% of **153aZ** had formed, while the corresponding control reaction, run in the absence of TEMPO, showed an 80% yield (97/3 Z/E) of **153aZ** (**Scheme 56**).



equiv TEMPO **168**	yield **153a**, Z/E[a]
1	1%, >99/1
0	80%, 97/3

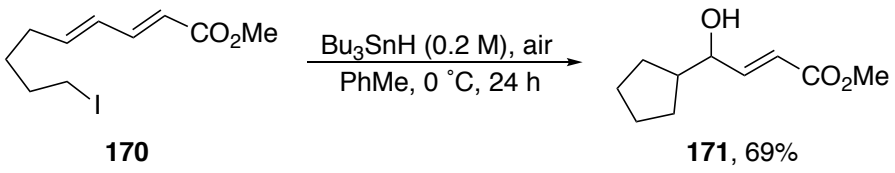
[a]as determined by ^{1}H NMR spectroscopy

Scheme 56. Et_3B/O_2-initiated hydrostannation of **152a** with TEMPO **168**

It was clear that TEMPO was able to compete with tributyltin radicals in the reaction with ethyl radicals, leading to a greatly decreased yield of **153a**. This shows that Et_3B/O_2 initiates the hydrostannation reaction through a radical pathway, supporting mechanistic hypothesis 1.

3.2.8 Air-initiated hydrostannation of propargyl silyl ethers

Nakamura observed that tin-mediated radical dehalogenations and cyclizations could be initiated by bubbling dry air into the reaction mixture.[125] For example, the reaction of iodide **170** with tributyltin hydride and dry air afforded **171** in 69% yield (**Scheme 57**).



170 **171**, 69%

Scheme 57. Nakamura's air-initiated radical dehalogenation and cyclization reactions

One possible mechanism for the initiation of Bu_3SnH by O_2 is shown in **Figure 16**. Oxygen can abstract a hydrogen atom from tributyltin hydride to form a tin-centered radical and peroxy radical (equation 1). The resulting peroxy radical can react with a second equivalent of tributyltin hydride to form another tin radical and hydrogen peroxide (equation 2).

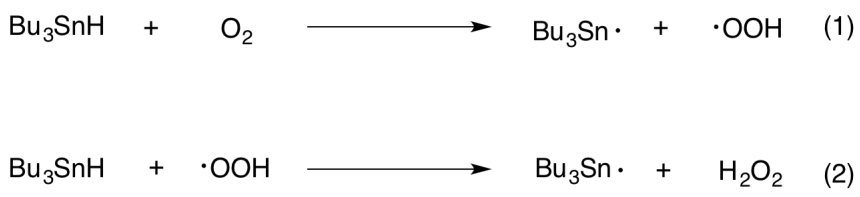
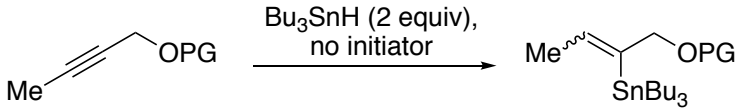


Figure 16. Possible initiation steps for the reaction of Bu_3SnH and O_2

To determine whether O_2 could initiate the hydrostannation of **152a,b**, initiator-free reactions were conducted. For these experiments, the reagents were combined in open air, but no additional efforts were made to feed air into the reactions unless otherwise specified. No reaction was observed when **152a** or **152b** was stirred with 2 equiv Bu_3SnH in PhH at 25 ˚C for 7 d (**Table 26**, entries 1 and 2). Dry air was bubbled into the stirring solution of **152b** and Bu_3SnH in PhH for 24 h at room temperature, but no conversion to products was observed (entry 3). Heating solutions of **152a** or **152b** with 2 equiv tin hydride to 80 ˚C for 24 h led to the formation of 36% **153aZ** (95/5 Z/E) and 16% **153bZ**, respectively (entries 4 and 5). The neat reaction of **152b** with 1.05 equiv Bu_3SnH at 75 ˚C for 4 h gave **153bZ** in 65% yield (99/1 Z/E; entry 6). Increasing the tin hydride loading to 2 equiv under otherwise identical conditions afforded **153b** in 95% yield with a 93/7 Z/E ratio after 4 h (entry 7).

Table 26. Initiator-free hydrostannations of **152a,b**



PG = TBS, **152a**
PG = TIPS, **152b**

153a,b

entry	PG	prec	equiv Bu_3SnH	solv	T (˚C)	t	yield **153**[a]	Z/E[a]
1	TBS	**152a**	2	PhH	25	7 d	0%	–
2	TIPS	**152b**	2	PhH	25	7 d	0%	–
3[b]	TIPS	**152b**	2	PhH	25	24 h	0%	–
4	TBS	**152a**	2	PhH	80	24 h	36%	95/5
5	TIPS	**152b**	2	PhH	80	24 h	16%	>99/1
6	TIPS	**152b**	1.05	none	75	4 h	65%	99/1
7	TIPS	**152b**	2	none	75	4 h	95%	93/7

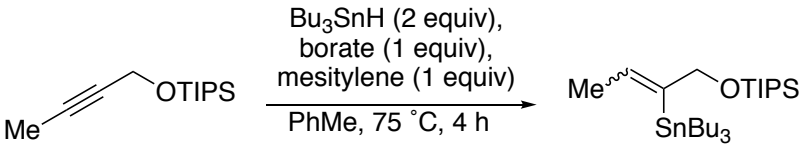
[a]as determined by ^{1}H NMR spectroscopic analysis of the crude products; [b]dry air was slowly bubbled into the stirring solution over the course of the reaction

Oxygen can initiate the radical hydrostannation of alkynes **152a** and **152b** at elevated temperatures, but it does not initiate the subsequent isomerization reaction. Thus, even when high yields of **153a** and **153b** are obtained, the Z/E ratio of products is approximately the kinetic ratio of 97/3 (**Table 26**, entries 6 and 7). Mechanistic hypothesis 2 is supported by these results since the hydrostannation reaction went to completion to afford alkenylstannane **153a** and **153b** in approximately the kinetic ratio, but no isomerization occurred. Also, these results suggest that a better way to obtain high Z-stereoselectivity might be to conduct neat reactions in the presence of O_2 (or air), but without an initiator.

3.2.9 Boric acid does not initiate the hydrostannation of propargyl alcohol derivatives

Organ and coworkers observed that fully oxidized borate species (e.g. boric acid, $B(OH)_3$) could initiate or promote the hydrostannation of propargyl alcohol derivatives.[121] In a typical reaction, alkyne **152b** was combined with 2 equiv Bu_3SnH, 1 equiv $B(OH)_3$, and PhMe in open air before heating the resulting mixture to 75 ˚C to obtain the corresponding alkenylstannane in high yield and Z-selectivity.[121] There is no obvious way for borates to initiate radical chains, so these results from Organ seem to support an ionic pathway. However, our results from **Table 26** demonstrate that O_2 can initiate the hydrostannation of **152a** and **153b**.

Boric acid and trimethyl borate were tested as possible initiators for the hydrostannation reaction shown in **Scheme 58**. TIPS alkyne **152b** was combined with 2 equiv Bu_3SnH, 1 equiv $B(OH)_3$, and PhMe in a pressure tube. Mesitylene (1 equiv) was added as an internal standard and the resulting mixture was heated to 75 ˚C for 4 h. Boric acid remained insoluble in PhMe throughout the reaction. The resulting ^1H NMR spectrum showed 47% of alkenylstannane **153bZ** (>99/1 Z/E ratio) with respect to the internal standard. With trimethyl borate ($B(OMe)_3$), a 33% yield of **153bZ** was observed after 4 h. When alkyne **152b** was reacted with 2 equiv Bu_3SnH in the absence of a borate additive, a 45% yield of **153bZ** was observed.



152b **153b**

borate	yield **153b**, Z/E[a]
$B(OH)_3$	47%, >99/1
$B(OMe)_3$	33%, >99/1
none	45%, >99/1

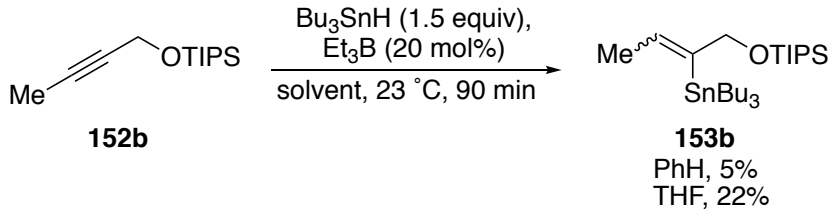
[a]as determined by ^{1}H NMR spectroscopy

Scheme 58. Borate-initiated hydrostannation of **152b**

The borate additives did not promote the hydrostannation reaction since comparable yields were obtained with and without borate additives. Instead, the reactions in **Scheme 58** and those performed by Organ were likely initiated by O_2.

3.2.10 Benzene inhibits the radical hydrostannation of alkynes

Organ studied the effect of solvent on the Et_3B/O_2-initiated hydrostannation of propargyl alcohol derivatives by screening solvents under similar reaction conditions. The reaction of alkyne **152b** with 1.5 equiv Bu_3SnH and 20 mol% Et_3B afforded a 5% yield of **153bZ** in PhH, while a 22% yield was observed in THF under otherwise identical conditions (**Scheme 59**).[122] Higher yields of **153b** were obtained when more polar acetone, DMI, and DMPU were used (with 50 mol% Et_3B and 2 equiv Bu_3SnH), leading Organ to conclude that more polar solvents accelerate the rate of hydrostannation.[122]

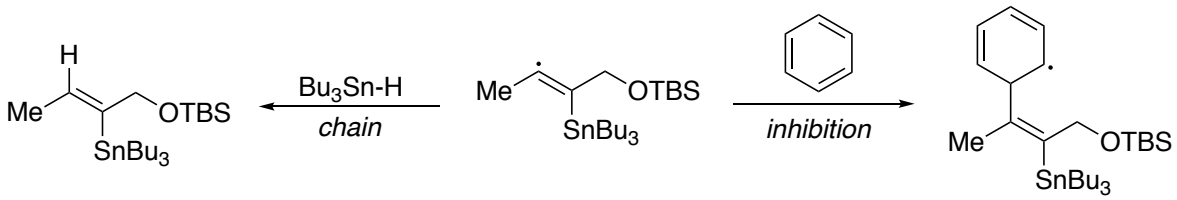


Scheme 59. Selected results from Organ's solvent study

As an alternative explanation for these observations, it is proposed that PhH acts as a partial inhibitor in the hydrostannation of **152a**. The AIBN-initiated radical dehalogenation of 1-bromoheptane by tin hydride was measured to be approximately 50-fold slower in aromatic solvents (e.g. PhH, PhMe) than in cyclohexane, *n*-hexane, ethyl acetate, and THF.[126] This can be explained by Szwarc's observation that methyl radicals rapidly add to PhH to form cyclohexadienyl radicals.[127-128] The addition of alkenyl-centered radicals to PhH is about 50 times faster than the addition of primary and secondary alkyl-centered radicals.[126] Beckwith, Curran, and Crich all observed that cyclohexadienyl radicals are virtually incapable of abstracting hydrogen atoms from Bu_3SnH[129-131] as the reaction is slightly endothermic, whereas alkyl-centered radicals rapidly abstract H-atoms from Bu_3SnH.[132]

In this context, the addition of alkenyl-centered radicals (e.g. **154**) to aromatic solvents, like PhH, is a chain-terminating step (**Scheme 60**). The corresponding reactions run in THF, DMI, and DMPU do not face this problem. Following the formation of alkenyl-centered radical **154**, hydrogen abstraction from Bu_3SnH results in the formation of **153a** and a new tin radical to continue the chain. However, the reaction of **154** with an aromatic solvent, like PhH, results in the formation of cyclohexadienyl radical **172**, which would not be expected to abstract hydrogen from Bu_3SnH. While Organ concluded that polar solvents, like THF, are *good* solvents for

radical hydrostannation reactions, it is more accurate that PhH is a *bad* solvent for these radical reactions.



153aZ **154** **172**

Scheme 60. Possible chain-terminating reaction of **154** with benzene

3.3 CONCLUSIONS

The AIBN- and Et_3B/O_2-initiated hydrostannations of propargylic silyl ethers by tin hydride were studied extensively. These experiments provided extensive support for the mechanistic hypotheses outlined in section 3.2.1.

The hydrostannation of propargyl silyl ethers with Bu_3SnH affords the corresponding alkenylstannanes with a kinetic ratio of approximately 97/3 Z/E and the subsequent isomerization can diminish the Z-selectivity to the thermodynamic ratio, approximately 55/45 Z/E. As stated in mechanistic hypothesis 2, the hydrostannation of alkynes **152a** and **152b** was faster than the isomerization of **153a** and **153b**. This was evident because high yields of alkenylstannanes **152a** and **152b** were obtained with high Z-selectivity, while the opposite (<90% yield **153a,b** with >10% E-isomer) was never observed in any experiment.

The azo initiators, AIBN and V-70, are better radical initiators than Et_3B/O_2 at 40–80 ˚C. They are able to initiate both the hydrostannation and isomerization reactions to afford the thermodynamic ratio of alkenylstannanes in quantitative yields after 3 h.

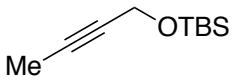
Triethylborane is only able to initiate the faster hydrostannation reaction and is a poor initiator of the slower isomerization reaction, because the latter reaction competes with its autoxidation. Thus, only the kinetic ratio of alkenylstannanes is obtained when Et_3B/O_2 initiates the hydrostannation under most reaction conditions. Partial Et_3B/O_2-initiated isomerization of isomerically-enriched samples of **153a** and **153b** was observed, but only when high loadings of Et_3B were used (4 equiv) and when no alkyne was present.

No new mechanistic explanations for these observations by us or Organ are required. Both AIBN and Et_3B/O_2 initiate the hydrostannation of propargyl alcohol derivatives with Bu_3SnH through radical pathways. The differences in product ratios are derived from differences in initiator efficiency, rather than them operating by different mechanistic pathways.

3.4 EXPERIMENTAL

General Experimental: All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry dichloromethane (DCM) was obtained by passing the solvents through activated alumina. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under an argon atmosphere. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Thin-layer chromatography (TLC) was performed on EMD 60 F254 silica gel and flash column chromatography was performed with 230–400 mesh silica gel purchased from Sorbent

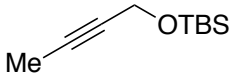
Technologies as the stationary phase. Visualization of TLC achieved using ultraviolet light (254 nm) or iodine chambers. Melting points (mp) were measured with a Mel-Temp II apparatus and were uncorrected. IR spectra were obtained as neat samples with a Thermo-Nicolet IR 200 ATR-FTIR. Nuclear magnetic resonance spectra (NMR) were obtained on a Bruker Avance III 400 MHz and 500 MHz instruments. Chloroform (δ 7.26 ppm) and benzene (δ 7.16) were used as internal standards for ^{1}H NMR spectra and $CDCl_3$ (δ 77.00 ppm) was used as an internal standard for ^{13}C NMR spectra. ^{11}B chemical shifts are relative to Et_2O-BF_3. The spectral data of single molecules were reported in the following order: chemical shift (δ), multiplicity, coupling constant (Hz), number of nuclei. The following abbreviations were used to describe coupling: s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet, br = broad, dd = doublet of doublets. HRMS were obtained with a Q-Tof analyzer. All spectra were acquired at room temperature. Tributyltin hydride (Bu_3SnH) was prepared according to literature procedure.[133] Its spectra was consistent with literature values.



152a

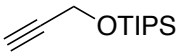
(But-2-yn-1-yloxy)(*tert*-butyl)dimethylsilane (152a): A solution of 2-butyn-1-ol (2.0 g, 28 mmol, 1 equiv), imidazole (4.0 g, 58 mmol, 2.1 equiv), and *tert*-butyldimethylsilyl chloride (3.6 g, 23 mmol, 0.83 equiv) in DCM (50 mL) was stirred at room temperature for 18 h. The resulting solution was diluted with DCM (50 mL) and the reaction was quenched with water (25 mL). The aqueous layer was separated and extracted with DCM (2 x 25 mL). The organic layers were combined and washed with water (2 x 25 mL) and brine (1 x 25 mL) before being dried over sodium sulfate. The solvent was removed under reduced pressure to give a yellow oil that was

purified by column chromatography (4% Et_2O in hexanes) to give **152a** as a clear oil (3.9 g, 88%).



152b

(But-2-yn-1-yloxy)triisopropylsilane (152b): A solution of 2-butyl-1-ol (3.0 g, 43 mmol, 1 equiv), imidazole (6.2 g, 90 mmol, 2.1 equiv), and triisopropylsilyl chloride (7.7 mL, 36 mmol, 0.83 equiv) in DCM (75 mL) was stirred at room temperature for 18 h. The resulting solution was diluted with DCM (25 mL) and the reaction was quenched with water (50 mL). The aqueous layer was separated and extracted with DCM (2 x 25 mL). The organic layers were combined and extracted with water (2 x 50 mL) and brine (1 x 50 mL) before being dried over sodium sulfate. The solvent was removed under reduced pressure to give a yellow oil that was purified by column chromatography (4% Et_2O in hexanes) to give **152b** as a clear oil (7.6 g, 93%).

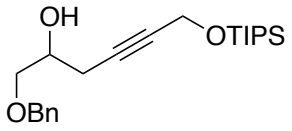


154

Triisopropyl(prop-2-yn-1-yloxy)silane (154): Prop-2-yn-1-ol (0.51 mL, 8.9 mmol, 1.0 equiv) and imidazole (1.5 g, 22 mmol, 2.5 equiv) were dissolved in DCM (60 mL). The resulting solution was stirred at room temperature for several minutes before TIPS-chloride (2.3 mL, 11 mmol, 1.2 equiv) was added by syringe. The reaction was stirred at room temperature for 24 h. Solvent was removed under reduced pressure to give a yellow oil that was purified by flash chromatography (silica gel; 4% ether in hexanes) to give silyl ether **154** as a clear oil (1.4 g, 73%).

157

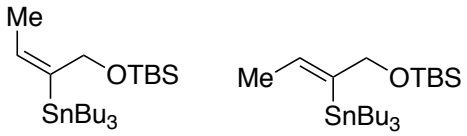
3,3,10,10-Tetraisopropyl-2,11-dimethyl-4,9-dioxa-3,10-disiladodec-6-yne (157): 2-Butyn-1,4-diol (500 mg, 5.8 mmol, 1.0 equiv) and imidazole (0.99 g, 15 mmol, 2.5 equiv) were dissolved in DCM (40 mL). The resulting solution was stirred at room temperature for several minutes before TIPS-chloride (2.7 mL, 13 mmol, 2.2 equiv) was added by syringe. The reaction was stirred at room temperature for 24 h. Solvent was removed under reduced pressure to give a yellow oil that was purified by flash chromatography (silica gel; 4% ether in hexanes) to give silyl ether **157** as a clear oil (1.7 g, 71%).



159

1-(Benzyloxy)-6-((triisopropylsilyl)oxy)hex-4-yn-2-ol (159): Silyl ether **154** (500 mg, 2.4 mmol, 2 equiv) was dissolved in THF (2.0 mL). The resulting solution was cooled to –78 ˚C. *n*-Butyllithium (1.2 mL, 2.5 M, 2.9 mmol, 2.5 equiv) was added dropwise over several minutes and the resulting solution was stirred for 15 min. BF_3–Et_2O (0.17 mL, 1.4 mmol, 1.2 equiv) was added dropwise over 5 min followed by 2-((benzloxy)methyl)oxirane (0.18 mL, 1.2 mmol, 1.0 equiv). The reaction mixture was allowed to warm to rt overnight. The reaction mixture was diluted with ether (10 mL) and extracted with aqueous NH_4Cl (1 x 10 mL). Upon separation, the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were dried over sodium sulfate. Removal of the solvent under reduced pressure gave a yellow oil that was

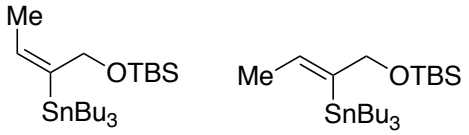
purified by flash chromatography (silica gel; hexanes:ethyl acetate) to give silyl ether **159** as a clear oil (340 mg, 77%).



153aE **153aZ**

(*E*)-*tert*-Butyldimethyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153aE) (*Z*)-*tert*-butyldimethyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153a*Z*):

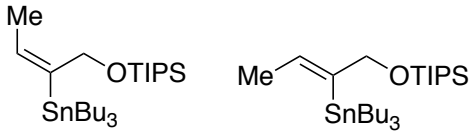
Typical Procedure 1 (TP1) for the AIBN-initiated hydrostannation of alkynes: Alkyne **152a** (200 mg, 1.1 mmol, 1.0 equiv), tributyltin hydride (630 mg, 2.2 mmol, 2.0 equiv), and AIBN (18 mg, 0.1 mmol, 0.1 equiv) were added to a flask containing benzene (2.2 mL). The reaction mixture was heated to 80 ^{o}C for 18 h. The solvent was removed under reduced pressure to give a clear yellow oil. A ^{1}H NMR spectrum of the crude products showed full consumption of **152a** to give **153a** in a 52/48 Z/E ratio. The crude residue was purified by flash chromatography (97:2:1 hexanes:diethyl ether:triethylamine) to give alkenylstannanes **153aE** (110 mg, 21%, 5/95 Z/E) and **153aZ** (190 mg, 36%, 88/12 Z/E) as clear oils.



153aE **153aZ**

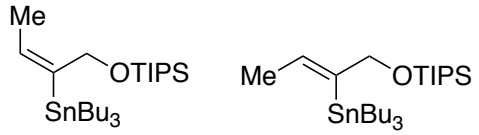
(*E*)-*tert*-Butyldimethyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153aE) (*Z*)-*tert*-butyldimethyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153aZ):

Typical Procedure 2 (TP2) for the Et_3B/O_2-initiated hydrostannation of alkynes: Alkyne **152a** (200 mg, 1.1 mmol, 1.0 equiv), tributyltin hydride (630 mg, 2.2 mmol, 2.0 equiv), and Et_3B (0.54 mL, 0.5 mmol, 0.5 equiv, 1.0 M solution in hexanes) were added to a flask containing benzene (2.0 mL). The reaction mixture was stirred at 25 ^oC for 18 h. The solvent was removed under reduced pressure to give a clear yellow oil. A ^1H NMR spectrum of the crude products showed full consumption of **152a** to give **153a** in a 90/10 Z/E ratio. The crude residue was purified by flash chromatography (97:2:1 hexanes:diethyl ether:triethylamine) to give alkenylstannanes **153aE** (7 mg, 2%, 6/94 Z/E) and **153aZ** (350 mg, 68%, 96/4 Z/E) as clear oils.



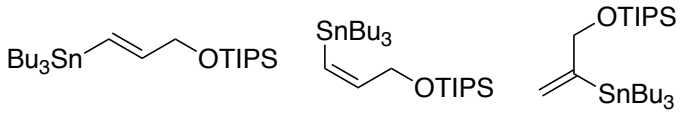
153bE **153bZ**

(*E*)-Triisopropyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153bE) and (*Z*)-triisopropyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153bZ): Following TP1 with silyl ether **152b** (200 mg, 0.9 mmol, 1.0 equiv), AIBN (15 mg, 0.10 mmol, 0.10 equiv), tributyltin hydride (510 mg, 1.8 mmol, 2.0 equiv), and benzene (2.0 mL), alkenylstannane **153bE** (86 mg, 19%, <1/99 Z/E) and alkenylstannane **153bZ** (160 mg, 35%, >99/1 Z/E) were isolated as clear oils.



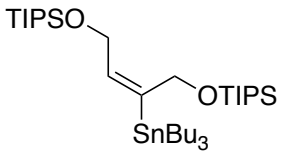
153bE **153bZ**

(*E*)-Triisopropyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153bE) and (*Z*)-triisopropyl((2-(tributylstannyl)but-2-en-1-yl)oxy)silane (153bZ): Following TP2 with silyl ether **152b** (200 mg, 0.9 mmol, 1.0 equiv), Et_3B (48 mL, 0.50 mmol, 0.50 equiv, 1.0 M solution in hexanes), tributyltin hydride (510 mg, 1.8 mmol, 2.0 equiv), and benzene (2.0 mL), alkenylstannane **153bE** (30 mg, 6%, 24/76 Z/E) and alkenylstannane **153bZ** (282 mg, 62%, 98/2 Z/E) were isolated as clear oils.

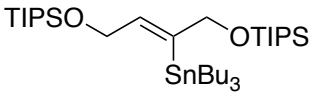


155E **155Z** **156**

(*E*)-Triisopropyl((3-(tributylstannyl)allyl)oxy)silane (155E), (*Z*)-triisopropyl((3-(tributylstannyl)allyl)oxy)silane (155Z), and triisopropyl((2-(tributylstannyl)allyl)oxy)silane (156): Following TP1 with silyl ether **154** (210 mg, 1.0 mmol, 1.0 equiv), AIBN (16 mg, 0.10 mmol, 0.10 equiv), tributyltin hydride (580 mg, 2.0 mmol, 2.0 equiv), and benzene (2.0 mL), full consumption of **154** to give **155** and **156** in a 90/10 ratio was observed by ^{1}H NMR spectroscopy after 18 h. Alkenylstannane **156** (36 mg, 7%), a mixture of **155** and **156** (28 mg, 6%, 23/77 **1156/155**), and alkenylstannane **155** (184 mg, 37%, 88/12 Z/E) were isolated as a clear oil.

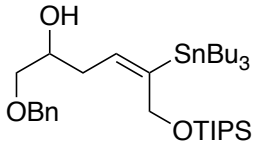


158E

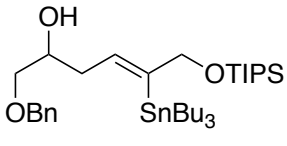


158Z

(*E*)-3,3,10,10-Tetraisopropyl-2,11-dimethyl-6-(tributylstannyl)-4,9-dioxa-3,10-disiladodec-6-ene (158E) and (*Z*)-3,3,10,10-tetraisopropyl-2,11-dimethyl-6-(tributylstannyl)-4,9-dioxa-3,10-disiladodec-6-ene (158Z): Following TP1 with silyl ether **157** (400 mg, 1.0 mmol, 1.0 equiv), AIBN (16 mg, 0.10 mmol, 0.10 equiv), tributyltin hydride (580 mg, 2.0 mmol, 2.0 equiv), and benzene (2.0 mL), full consumption of **157** to give **158** in a 63/37 Z/E ratio was observed by ^{1}H NMR spectroscopy after 18 h. Alkenylstannane **158E** (160 mg, 23%) and alkenylstannane **158Z** (390 mg, 56%) were isolated as a clear oil.



160E



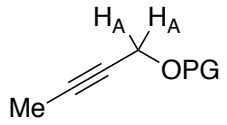
160Z

(*E*)-1-(Benzyloxy)-5-(tributylstannyl)-6-((triisopropylsilyl)oxy)hex-4-en-2-ol (160E) and (*Z*)-1-(benzyloxy)-5-(tributylstannyl)-6-((triisopropylsilyl)oxy)hex-4-en-2-ol (160Z): Following TP1 with silyl ether **159** (380 mg, 1.0 mmol, 1.0 equiv), AIBN (16 mg, 0.10 mmol, 0.10 equiv), tributyltin hydride (580 mg, 2.0 mmol, 2.0 equiv), and benzene (2.0 mL), full consumption of **159** to give **160** in a 76/24 Z/E ratio was observed by ^{1}H NMR spectroscopy after 18 h. Alkenylstannane **160Z** (290 mg, 43%, 93/7 Z/E), a mixture of **160Z** and **160E** (200 mg, 30%, 58/42 Z/E), and alkenylstannane **160E** (56 mg, 8%, 30/70 Z/E) were isolated as clear oils.

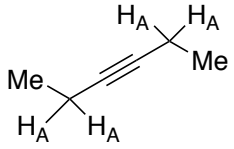
Summary of NMR shifts for key compounds

All ^{1}H NMR shifts are reported in C_6D_6 relative to the solvent signal (7.16 ppm):

Alkynes



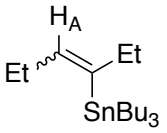
PG = TBS, **152a**, H_A = 4.23 ppm
PG = TIPS, **152b**, H_A = 4.31 ppm



161, H_A = 2.28 ppm

Figure 17. Summary of diagnostic ^{1}H NMR shifts for key alkyne starting materials

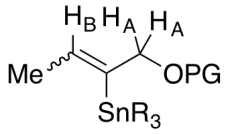
Alkenylstannanes



162Z, H_A = 6.06 ppm
162E, H_A = 5.90 ppm

Figure 18. Diagnostic alkenyl proton ^{1}H NMR signals for alkenylstannanes **162E** and **162Z**

Table 27. Summary of diagnostic ^{1}H NMR shifts for key alkenylstannanes products



entry	PG	R	Z/E	#	H_A (ppm)	H_B (ppm)
1	TBS	Bu	Z	**153aZ**	4.31	6.32
2	TBS	Bu	E	**153aE**	4.47	5.72
3	TIPS	Bu	Z	**153bZ**	4.42	6.45
4	TIPS	Bu	E	**153bE**	4.56	5.76
5	TBS	Ph	Z	**165aZ**	4.41	6.52
6	TBS	Ph	E	**165aE**	4.62	5.90

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