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Lithium Aminoborohydrides 16. Synthesis and Reactions of Monomeric and Dimeric Aminoboranes[§]

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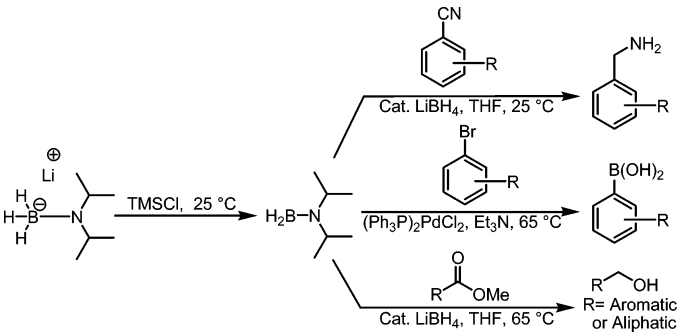

Aminoboranes are synthesized in situ from the reaction of the corresponding lithium aminoborohydrides (LABs) with methyl iodide, trimethylsilylchloride (TMS-Cl), or benzyl chloride under ambient conditions. In hexanes, the reaction using methyl iodide produces aminoborane and methane, whereas in tetrahydrofuran (THF) this reaction produces amine−boranes ($R_1R_2HN{:}BH_3$) as the major product. The reaction of *i*Pr-LAB with TMS-Cl or benzyl chloride yields exclusively diisopropylaminoborane [BH_2-N(*i*Pr)$_2$] in THF as well as in hexanes at 25 °C. Diisopropylaminoborane and dicyclohexylaminoborane exist as monomers due to the steric requirement of the alkyl group. All other aminoboranes studied are not sterically hindered enough to be monomers in solution, but instead exist as a mixture of monomers and dimers. The dimers are four-membered rings formed through boron−nitrogen coordination. In general aminoboranes are not hydroborating reagents. However, monomeric aminoboranes, such as BH_2-N(*i*Pr)$_2$, can reduce nitriles in the presence of catalytic amounts of $LiBH_4$. This BH_2-N(*i*Pr)$_2$/$LiBH_4$ reducing system also reduces ketones, aldehydes, and esters. Diisopropylaminoborane, synthesized from *i*Pr-LAB, can be converted into boronic acids by a palladium-catalyzed reaction with aryl bromides. Aminoboranes derived from heterocyclic amines, such as pyrrole, pyrazole, and imidazole, can be prepared by the direct reaction of borane/tetrahydrofuran (BH_3:THF) with these heterocyclic amines. It has been reported that pyrazole-derived aminoborane forms a six-membered dimer through boron−nitrogen coordination, where as, pyrrolylborane forms a dimer through boron−hydrogen coordination. Pyrrolylborane monohydroborates both alkenes and alkynes at ambient temperatures. Hydroboration of styrene with pyrrolylborane followed by hydrolysis gives the corresponding boronic acid, 2-phenylethylboronic acid, in 40% yield. Similarly phenylacetylene is mono-hydroborated by pyrrolylborane, to give *E*-2-phenylethenylboronic acid in 50% yield.

1. Introduction

Aminoboranes (R_1R_2N-BH_2) have been known since the discovery of the hydroboration reaction in 1956, as they are well-known in material science as precursors of BN-based ceramics.[1] The methods to synthesize aminoboranes include thermally induced dehydrogenation of secondary amine−borane adducts ($R_1R_2HN{:}BH_3$) and metal-catalyzed dehydrogenation reduction of the corresponding amine−borane adducts.[2] Ami-

[§] Dedicated in memory of Christopher Schmid, Associate Editor of Organic Process Research & Development, who passed away on December 26, 2007.

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(1) Thevenot, F.; Doche, C.; Mongeot, H.; Guilhon, F.; Miele, P.; Cornu, D.; Bonnetot, B. *J. Solid State Chem.* **1997**, *133*, 164.

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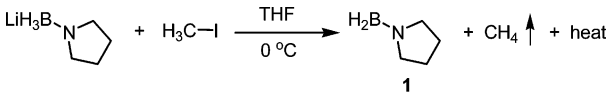
SCHEME 1. Synthesis of Pyrrolidinoborane from LAB



noboranes can also be synthesized by the reduction of the corresponding (amino)dihaloboranes.[3] Unfortunately, aminoboranes are known to form mixtures of dimers and oligomers easily, which prevents further purification.[4] Consequently, they have been scarcely studied as useful tools for synthetic organic chemistry. Recently, monomeric (dialkylamino)boranes (H_2B-NR_1R_2, with R_1 and R_2 being sterically demanding alkyl groups) have found use in the palladium-catalyzed synthesis of boronic acids from the corresponding aryl and alkenyl halides.[5] Aminoboranes can potentially serve as hydroborating agents. To date, only 1-pyrrolylborane has been studied for its hydroborating potential.[6,7] 1-Pyrrolylborane is able to hydroborate alkenes and alkynes and is also able to reduce carbon−oxygen double bonds in aldehydes and ketones.[7] The requirement for efficient and safe methods for hydrogen storage has recently renewed interest in the synthesis of aminoboranes. Several papers have appeared in the literature on the synthesis of aminoboranes (H_2BNR_2), which could potentially be used as a hydrogen source.[2d,8]

During our studies on LABs we observed that aminoboranes can be synthesized readily in situ by the reduction of methyl iodide using LAB reagents (Scheme 1).[9]

Our studies of the properties of pyrrolidinoborane **1** revealed that it was inert toward most of the functional groups encountered in organic synthesis.[9] ^{11}B NMR analysis showed that pyrrolidinoborane **1** exists as a pure dimer.[17] We have now learned to synthesize monomeric and dimeric aminoboranes from LAB reagents. In this paper, we report the synthesis and properties of various aliphatic aminoboranes. For comparison we have included the synthesis of representative heterocyclic aminoboranes.

2. Results and Discussion

2.1. Syntheses of Aminoboranes. During our previous work on the hydroboration of β,β-disubstituted enamines, we were puzzled by the unexpected formation of aminoboranes as one of the reaction products (Scheme 2).[10a,b]

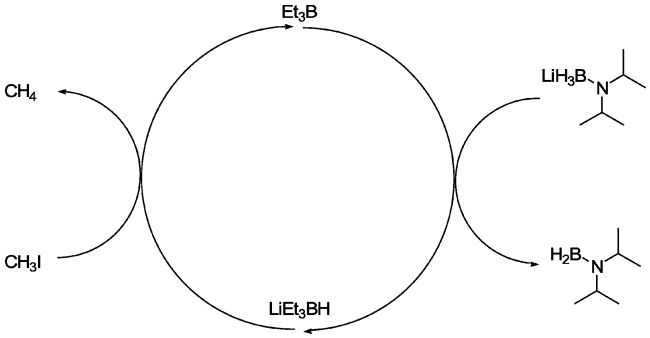
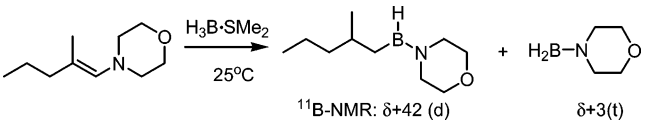


FIGURE 1. Catalytic cycle in the reaction of Et_3B with LAB and methyl iodide.

SCHEME 2. Hydroboration of β,β-Disubstituted Enamines



In order to verify this result, an authentic sample of the aminoborane was required. Reaction of morpholino-LAB **2**, prepared with 1.1 equiv of *n*-BuLi, with methyl iodide at 0 °C gave morpholinoborane (Table 1, entry 6) in high purity as determined by ^{11}B NMR spectroscopy (Scheme 3). We have now used this procedure to synthesize representative aminoboranes (Table 1).

Several of the aminoboranes presented in this table exist as mixtures of dimers and monomers (Table 1, entries 1, 2, 7). However, some of the aminoboranes can form pure dimers, and others exist as pure monomers. We believe that the sterics around the amine of aminoborane is a key factor in the formation of monomer, dimer, or monomer/dimer mixtures. The most sterically hindered aminoborane, diisopropylaminoborane, exists as a monomer (Table 1, entry 3). The least sterically demanding aminoboranes such as piperidino-, pyrrolidino-, and morpholinoboranes form pure dimers (Table 1, entries 4−6). Therefore, by changing the amine of the LAB reagent we can control the formation of monomer or dimer aminoborane.

Unfortunately, the reaction of methyl iodide with LABs is sensitive to temperature (Scheme 3). At 0 °C this reaction produces a mixture of amine−borane (BH_3:$NMeR_2$) along with the desired aminoboranes.[11] However, the reaction of LABs with methyl iodide in the presence of a catalytic amount of triethylborane produces aminoboranes exclusively (Scheme 4).[12]

It has been shown in the past that addition of a catalytic amount of triethylborane to LABs generates catalytic amounts of $LiEt_3BH$ (Super-Hydride) and aminoborane.[13,14] Super-Hydride is known to reduce methyl iodide regenerating trieth-

(2) (a) Burg, A. B.; Randolph, C. L. *J. Am. Chem. Soc*. **1949**, *71*, 3451. (b) Green, I. G.; Johnson, K. M.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1989**, *12*, 1963. (c) Jaska, C. A.; Temple, K.; Lough, A. J.; Manners, I. *Phosphorus, Sulfur Silicon Relat. Elem*. **2004**, *179*, 733. (d) Clark, T. J.; Russell, C. A.; Manners, I. *J. Am. Chem. Soc*. **2006**, *128*, 9582.

(3) Maringgele, W.; Noltemeyr, M.; Schmidt, H. G.; Meller, A. *Main Group Met. Chem.* **1999**, *22*, 715.

(4) Jaska, C. A.; Temple, K.; Lough, A. J.; Manners, I. *J. Chem Soc., Chem. Commun*. **2001**, 962.

(5) (a) Euzenat, L.; Horhant, D.; Ribourdouille, Y.; Duriez, C.; Alcaraz, G.; Vaultier, M. *Chem. Commun.* **2003**, 2280. (b) Vaultier, M.; Alcaraz, G.; Duriez, C.; Euzenat, L.; Ribourdouille, Y. U.S. Patent 7,179,940 B2, 2007.

(6) (a) Ioffe Sz. L.; Lyashenko, A. A.; Shitov, O. P.; Negrebetskii, V. V. *Khim. Geterotsil. Soedin*. **1971**, *7*, 1056. (b) Gyori, B.; Emri, J.; Szarvas, P. *Acta Chim. Acad. Sci. Hung.* **1975**, *86*, 235.

(7) (a) Anez, M.; Uribe, G.; Mendoza, L.; Contreras, R. *Synthesis* **1981**, 214. (b) Wrackmeyer, B.; Schwarze, B.; Milius, W. *Inorg. Chim. Acta* **1996**, *241*, 87. (c) Wrackmeyer, B.; Schwarze, B. *J. Organomet. Chem.* **1997**, *534*, 207.

(8) Stephens, F. H.; Baker, R. T.; Matus, M. H.; Grant, D. J.; Dixon, D. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 746.

(9) Fisher, G. B.; Harrison, J.; Fuller, J. C.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett.* **1992**, *33*, 4533.

(10) (a) Singaram, B.; Goralski, C. T.; Fisher, G. B. *J. Org. Chem.* **1991**, *56*, 5691. (b) Fisher, G. B.; Juarez-Brambila, J. J.; Goralski, C. T.; Wipke, W. T.; Singaram, B. *J. Am. Chem. Soc.* **1993**, *115*, 440. (c) Fisher, G. B.; Nicholson, L. W.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett.* **1993**, *34*, 7693.

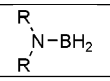
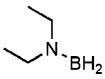
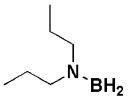
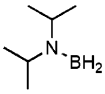
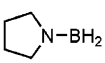
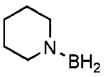
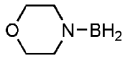
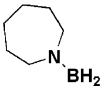
(11) Paumansky, L.; Collins, C. J.; Pratt, L. M.; Nguyen, N. V.; Ramachandran, B.; Singaram, B. *J. Org. Chem.* **2007**, *72*, 971.

(12) Harrison, J.; Alvarex, S. G.; Godjoin, G.; Singaram, B. *J. Org. Chem.* **1994**, *59*, 7193.

(13) Thomas, S.; Huynh, T.; Enriquez-Rios, V.; Singaram, B. *Org. Lett.* **2001**, *3*, 3915.

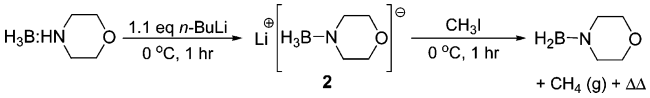
(14) Dimethylaminoborane was synthesized from the corresponding LAB, methyl iodide, and 1 equiv of triethylborane. This showed the dimethylaminoborane to be 100% dimer by ^{11}B NMR (80.25 MHz, THF). (t, $\delta = +3.3$, $J = 98$ Hz).

TABLE 1. ^{11}B NMR Spectroscopy of Aminoboranes (H_2BNR_2) Prepared in Hexanes

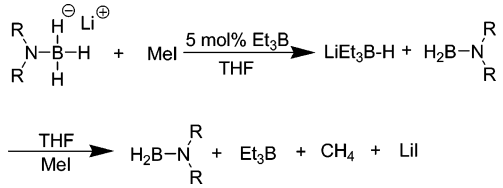
Entry		%[a]	Monomer	%[a]	Dimer
1		40	δ +36.6, (t, J=127 Hz)	60	δ +2.5, (t, J=112 Hz)
2		20	δ +37.3 (t, J=126 Hz)	80	δ +2.8 (t, unresolved)
3		100	δ +35.1 (t, J=127 Hz)	0	None formed
4		0	None formed	100	δ +3.1, (t, J=112 Hz)
5		0	None formed	100	δ +2.0 (t, J=111 Hz)
6		0	None formed	100	δ +1.9 (t, unresolved)
7		5	δ +38.0 (t, J=126 Hz)	95	δ +3.2 (t, J=111 Hz)

[a] The yield of aminoboranes were not determined, but the ratio was determined by ^{11}B NMR spectroscopy (80.25 MHz, hexanes).

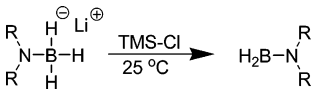
SCHEME 3. Preparation of Morpholinoborane



SCHEME 4. Synthesis of Aminoborane from LAB, CH_3I, and 5 mol % Et_3B



SCHEME 5. Synthesis of Aminoborane from LAB and TMS−Cl



ylborane, which in turn reacts with more LAB, generating Super-Hydride and aminoborane (Figure 1). While this method of generating aminoborane is interesting, it requires the use of pyrophoric triethylborane.

To explore formation of aminoboranes even further, we synthesized various aminoboranes from different LABs and other alkyl halides. Gratifyingly, we found that the reactions of LAB reagents produce exclusively the corresponding aminoboranes (BH_2-NR_2) when treated with either TMS-Cl or benzyl chloride at 25 °C (Scheme 5). These aminoboranes were characterized in solution by ^{11}B NMR spectroscopy which displayed only the signal attributable to aminoboranes, indicating essentially quantitative formation of the products. These results are summarized in Table 2.

The same trend of monomer/dimer formations of aminoboranes is observed during these syntheses, except for diethylaminoborane.[15] Sterically hindered aminoboranes exist exclusively as monomers (Table 2, entries 2 and 3), whereas less sterically demanding aminoboranes either form pure dimers (Table 2, entries 5 and 6) or monomer/dimer mixtures in different ratios (Table 2, entries 1 and 4). Hence, monomer/dimer formation is only dependent on the steric environment of aminoborane, regardless of preparation method.

In contrast to LAB reagents containing secondary amines, heterocyclic LAB reagents, such as pyrazolyl-LAB and imidazolyl-LAB,[16] did not afford the corresponding aminoboranes when reacted with TMS-Cl. Unfortunately, it is difficult to synthesize pyrrolyl-LAB from pyrrole, BH_3:THF, and *n*-BuLi. This is due to the fact that pyrrole does not form a pyrrole−borane complex.[17] Consequently, pyrrolylborane was synthesized by the direct reaction of pyrrole with BH_3:THF (Scheme 6) (Table 3, entry 2).[7]

Pyrazole and imidazole also produced the corresponding aminoboranes with BH_3:THF at 65 °C (Table 3, entries 1 and 3).

It has been reported that pyrrole and pyrazole form dimeric aminoboranes,[7,19] whereas imidazole generates polymeric aminoboranes.[18] Pyrazole-derived aminoborane has been reported to form a six-membered dimer through boron−nitrogen coordination (Figure 2 a).[19] In contrast, the pyrrole analog forms a four-membered dimer through boron−hydrogen coordination

(15) At present it is not apparent why different ratios of monomer/dimer are obtained for diethylaminoborane synthesized from methyl iodide or TMS-Cl and LAB.

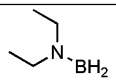
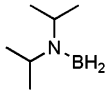
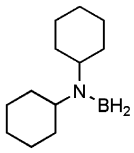
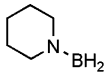
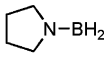
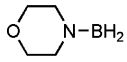
(16) These LAB reagents were prepared from corresponding heterocyclic borane complex and *n*-BuLi.

(17) Noeth, H.; Wrackmeyer, B. *Chem. Ber.* **1974**, *107*, 3070.

(18) Keller, P. C.; Knapp, K. K.; Rund, J. V. *Inorg. Chem.* **1985**, *24*, 2382.

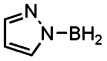
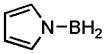
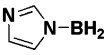
(19) (a) Trofimenko, S. *J. Am. Chem. Soc.* **1967**, *89*, 3165. (b) Weiss, A.; Barba, V.; Pritzkow, H.; Siebert, W. *J. Organomet. Chem.* **2003**, *680*, 294. (c) Weiss, A.; Pritzkow, H.; Siebert, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 547.

TABLE 2. Aminoboranes Synthesized from LAB and TMS-Cl

Entry	R, N–BH_2, R	%[a]	Monomer	%[a]	Dimer
1		10[b]	δ +36.9 (t, *J*=125 Hz)	90[b]	δ +2.2 (t, *J*=110 Hz)
2		100	δ +35.2, t, *J*=125 Hz	0	None formed
3		100	δ +35.4 (t, *J*=113 Hz)	0	None formed
4[c]		1	δ +35.9 (t, *J*=113 Hz)	99	δ +1.9 (t, *J*=113 Hz)
5[c]		0	None formed	100	δ +3.1 (t, *J*=113 Hz)
6[c]		0	None formed	100	δ +1.8 (t, *J*=107 Hz)

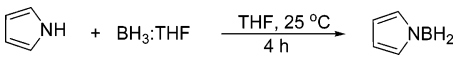
[a] The yield and ratio of aminoboranes were determined by ^{11}B NMR spectroscopy (80.25 MHz, hexanes). The spectra displayed only the signal attributable to aminoboranes indicating essentially quantitative formation of the product. [b] See ref 15. [c] Minor amounts of *N*-TMS amineborane is formed as byproduct.

TABLE 3. Aminoboranes Synthesized from Heterocyclic Amines and BH_3:THF

Entry	R, N–BH_2, R	%[a]	Monomer	%[a]	Dimer
1		0	None formed	100	δ -8.5 (t, *J*=107 Hz)
2		0	None formed	100	δ +4.7 (t, *J*=113 Hz)
3[b]		0	None formed	100	δ -9.1 (broad singlet)

[a] As determined by ^{11}B NMR spectroscopy (80.25 MHz, THF). [b] Less than 10% formed.

SCHEME 6. Synthesis of Pyrrolylborane



(Figure 2 b).[7] Although the multiplicity of the ^{11}B NMR signal shows a $-BH_2$ moiety, it is difficult to assign the degree of aggregation from the ^{11}B NMR chemical shifts alone.

Thus far, we have described several mild and convenient methods to synthesize a variety of aminoboranes in situ. Different alkyl halides have been shown to react with LABs to produce aminoboranes. Both heterocyclic and secondary amines can be used for the synthesis of aminoboranes. Depending on the steric hindrance around the amine, aminoboranes exist as monomers, dimers, or monomer/dimer mixtures. We then studied the reactivity of these aminoboranes.

2.2. Properties and Use of Aminoboranes. 2.2.1. Synthesis of Aryl Boronic Acids. During our investigation of properties of aminoboranes, we found that aminoborane dimers are inert as hydride donors both in hydroboration and reduction reactions. Consequently, we focused our study on the reactions of monomeric aminoboranes, such as diisopropylaminoborane (BH_2-N(*i*Pr)$_2$). First, we sought to examine this aminoborane prepared in situ as a potential boron source for the synthesis of boronic acids.[5] Thus, the palladium-catalyzed borylation of aryl

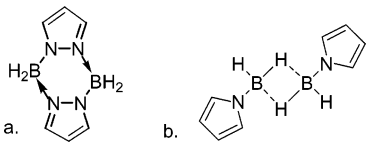
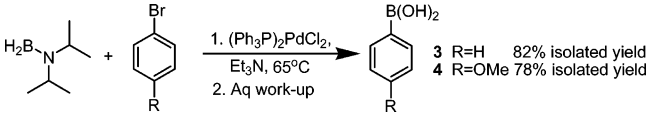


FIGURE 2. Dimers of (a) pyrazolylborane[19] and (b) pyrrolylborane.[7]

SCHEME 7. Synthesis of Boronic Acids from Aryl Bromides and $H_2BN(iPr)_2$



bromides with BH_2-N(*i*Pr)$_2$, synthesized in situ from *i*Pr-LAB, was attempted. Utilizing the reported reaction conditions we were able to successfully synthesize several different boronic acids from the corresponding aryl bromides (Scheme 7).[5]

This reaction is compatible with various functionalities, such as esters, fluorides, methoxy groups, and amines.[5,20] However,

(20) We are actively exploring the generality of this aryl boronic acid synthesis, and the results will be published elsewhere.

SCHEME 8. Reduction of Nitriles with Diisopropylaminoborane

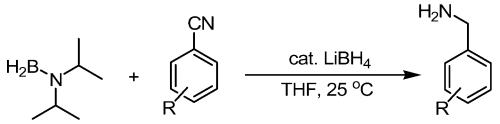
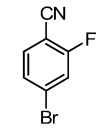
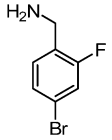
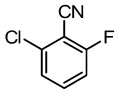
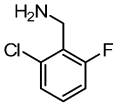
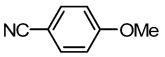
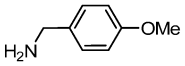


TABLE 4. Nitriles Reduced by Diisopropylaminoborane/cat. $LiBH_4$ System

Entry	Nitriles	Benzyl amine	Isolated Yield
1			90 %
2			70 %
3			80 %

nitrile-containing aryl bromides behaved differently and led us to discover new reactions of aminoboranes.

2.2.2. Reduction of Nitriles. During the synthesis of boronic acids, we discovered that BH_2-N(iPr)$_2$ reduces nitriles at room temperature in the presence of catalytic amounts of $LiBH_4$. This reaction does not require the use of any transition metal catalyst. Known methods of nitrile reduction to the corresponding amines utilize a variety of hydride-reducing agents and often require transition metal salts as catalysts.[21−23] Utilizing the BH_2-N(iPr)$_2$/cat. $LiBH_4$ reducing system we were able to successfully synthesize several different benzylamines from the corresponding benzonitriles in good to excellent yields (Scheme 8) (Table 4). It can be seen from these substrates that electron-withdrawing groups significantly raise the yield (Table 4, entry 1), whereas steric crowding of the nitrile reduces the yield (Table 4, entry 2). A catalytic amount of $LiBH_4$ is essential for this reduction to occur. It should be pointed out that $LiBH_4$ alone does not reduce nitriles even at 65 °C. There is no complex formation between $LiBH_4$ and BH_2-N(iPr)$_2$ as evidenced by ^{11}B NMR spectroscopy. In the absence of $LiBH_4$, BH_2-N(iPr)$_2$ is inert toward the reduction of nitriles, aldehydes, and ketones. It is most likely that the Li^+ ion is coordinating to the nitrogen atom and activates the nitrile group for reduction by BH_2-N(iPr)$_2$.[24]

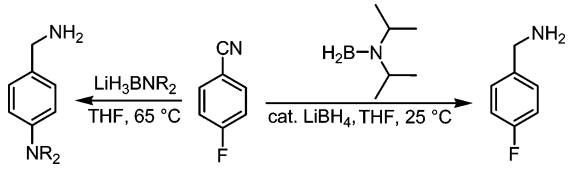
(21) (a) Wade, R. C. *J. Mol. Catal.* **1983**, *18*, 273. (b) Satoh, S. *Tetrahedron Lett.* **1969**, 4555. (c) Egli, R. A. *Helv. Chim. Acta* **1970**, *53*, 47. (d) Khurana, J. M.; Kukreja, G. *Synth. Commun.* **2002**, *32*, 1265.

(22) (a) Nystrom, F.; Brown, W. G. *J. Am. Chem. Soc.* **1948**, *70*, 3738. (b) Amundsen, L. H.; Nelson, L. S. *J. Am. Chem. Soc.* **1951**, *73*, 242. (c) Brown, H. C.; Weissman, P. M.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1458.

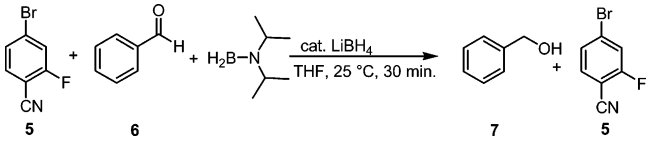
(23) (a) Hudlicky, M. *Reductions in Organic Chemistry*, 2nd ed.; ACS Monograph 188; American Chemical Society: Washington, DC, 1996. (b) Yoon, N. M.; Brown, H. C *J. Am. Chem. Soc.* **1968**, *90*, 2927. (c) Brown, H. C.; Subba Rao, B. C *J. Am. Chem. Soc.* **1960**, *82*, 681. (d) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1464.

(24) (a) Thomas, S.; Collins, C. J.; Cuzens, J. R.; Spiciarich, D.; Goralski, C. T.; Singaram, B. *J. Org. Chem.* **2001**, *66*, 1999−2004. (b) Thomas, S.; Collins, C. J.; Goralski, C. T.; Singaram, B. *Chem. Innovation* **2000**, *30* (8), 31.

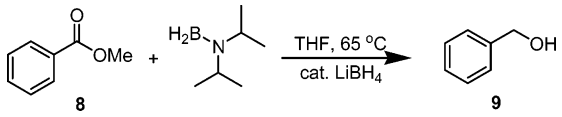
SCHEME 9. Reduction or Tandem Amination/Reduction of 4-Fluorobenzonitrile



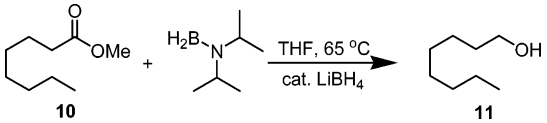
SCHEME 10. Competitive Reduction of 4-Bromo-2-fluorobenzonitrile and Benzaldehyde



SCHEME 11. Reduction of Methyl Benzoate with BH_2-N(iPr)$_2$/$LiBH_4$



SCHEME 12. Reduction of Methyl Octanoate with BH_2-N(iPr)$_2$/$LiBH_4$



We are actively investigating the mechanism and the catalytic cycle connected to this reaction.

We should point out that in the case of the ortho-fluorine-substituted benzonitriles the corresponding benzylamine is obtained with aminoboranes, while with LAB reagents the tandem displacement/reduction reaction occurs to give predominantly the corresponding 2-(dialkylamino)benzylamine.[24] Thus, the aminoborane reduction methodology complements the LAB tandem reaction methodology (Scheme 9).

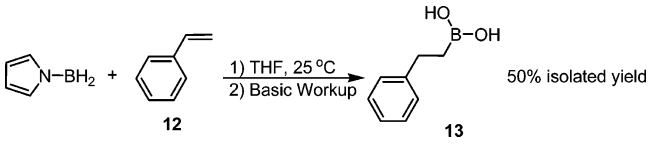
Aldehydes and ketones are reduced selectively by BH_2-N(iPr)$_2$/cat. $LiBH_4$ reducing system. In a competitive reduction of 4-bromo-2-fluorobenzonitrile **5** and benzaldehyde **6**, it was found that the very reactive benzaldehyde was reduced to benzyl alcohol **7** in 30 min, leaving 4-bromo-2-fluorobenzonitrile **5** intact (Scheme 10).

2.2.3. Ester Reductions. It was of interest to see if the BH_2-N(iPr)$_2$/$LiBH_4$ system was a general reducing agent that could reduce other functional groups. During our study on the reduction of nitriles this system was already found to reduce aldehydes and ketones at 25 °C. In order to extend the generality of the BH_2-N(iPr)$_2$/cat. $LiBH_4$ system, the reduction of methyl benzoate **8** was tested. It was found that methyl benzoate **8** was reduced to benzyl alcohol **9** in 95% isolated yield after only 2 h of heating at 65 °C (Scheme 11). In order to extend this reducing system to aliphatic esters, the reduction of methyl octanoate **10** was tested. The BH_2-N(iPr)$_2$/cat. $LiBH_4$ system reduced methyl octanoate **10** to octanol **11** in 98% isolated yield after 2 h of heating at 65 °C (Scheme 12).[25]

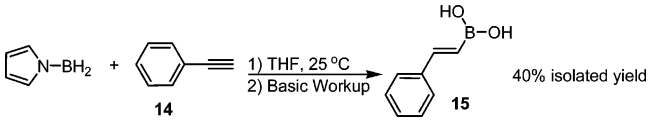
2.2.4. Hydroboration of Alkenes and Alkynes. To explore the properties of aminoboranes even further, we investigated

(25) These alcohols are contaminated with a small amount of butylboronic esters.

SCHEME 13. Hydroboration of Styrene with Pyrrolylborane



SCHEME 14. Hydroboration of Phenylacetylene with Pyrrolylborane



aminoboranes as possible hydroborating agents for alkenes and alkynes. A series of hydroboration reactions were attempted, utilizing different aminoboranes and either 1-hexene or 1-hexyne. To our disappointment, with the exception of pyrrolylborane, none of the aminoboranes exhibited hydroboration properties. However, this reveals the potential of aminoboranes as selective reducing agents for various functional groups in the presence of multiple bonds.

As reported previously,[7] pyrrolylborane successfully hydroborates both alkenes and alkynes. Additionally, in the earlier study,[7] it was found that 1-pyrrolylborane−tetrahydrofuran complex behaves as a monoalkylborane and reacts with two equivalents of alkenes to afford *B*-pyrrolyldialkylborane. Similarly, 1-pyrrolylborane was reported to hydroborate two equivalents of alkynes to give *B*-pyrrolyldialkenylborane. In our study, we found that alkenes and alkynes undergo stepwise hydroboration and the reaction can be stopped at the monohydroboration stage. For example, hydroboration of one equivalent of styrene **12** with pyrrolylborane at 25 °C gives 2-phenylethylboronic acid **13** as the major product after basic hydrolysis (Scheme 13). Similarly, hydroboration of one equivalent of phenylacetylene **14** at 25 °C gives *E*-2-phenylethenylboronic acid **15** as the major product after basic hydrolysis (Scheme 14).

The success of this hydroboration reaction can be attributed to the aromaticity of pyrrolylborane.[17] Subsequently, imidazolylborane and pyrazolylborane were tested in the hydroboration of both 1-hexene and 1-hexyne. Unfortunately, neither imidazolylborane nor pyrazolylborane showed any hydroborating properties. This could be due to the dimeric and oligiomeric/polymeric boron−nitrogen bonds in pyrazolylborane and imidazolylborane, respectively (Figure 2).[18,19] We are actively exploring the generality of this stepwise hydroboration reaction of 1-pyrrolylborane.

3. Conclusion

In conclusion, several mild and convenient methods for the in situ synthesis of aminoboranes in solution have been developed. Diisopropylaminoborane can be synthesized from *i*Pr-LAB and methyl iodide in the presence of 5 mol % triethylborane. Aminoboranes can also be prepared from LAB reagents by reaction with either TMS-Cl or benzyl chloride. Both heterocyclic and secondary amines can be used for the synthesis of aminoboranes. Depending on the steric hindrance around the amine, aminoboranes exist as monomers, dimers or monomer/dimer mixtures. Aminoboranes derived from heterocyclic amines, such as pyrrole, pyrazole, and imidazole, can be prepared by the direct reaction of borane−tetrahydrofuran (BH_3:THF). Pyrrole and pyrazole form dimeric aminoboranes, whereas imidazole forms polymeric aminoboranes. Pyrazole-derived aminoborane forms a six-membered dimer through boron−nitrogen coordination. Ordinarily, aminoboranes are not hydroborating reagents. However, pyrrolylborane monohydroborates both styrene and alkynes at ambient temperatures. In addition, monomeric aminoboranes, such as BH_2-N(*i*Pr)$_2$, can reduce aldehydes, ketones, esters, and nitriles in the presence of catalytic amounts of $LiBH_4$. Also, we found that BH_2-N(*i*Pr)$_2$ synthesized from *i*Pr-LAB, can be converted into boronic acids by a palladium-catalyzed reaction with aryl bromides.

4. Experimental Section

4.1. General Procedure for the Preparation of LAB Reagent 1 M Solution in THF. The following procedure for the preparation of $LiH_3BN(iPr)_2$ is representative. Diisopropylamine (5.00 g, 7 mL, 50 mmol, 1 equiv) was mixed with anhydrous THF (18 mL) in a 100-mL, round-bottom flask. The solution was cooled to 0 °C (ice bath), and borane dimethylsulfide (5 mL, 10 M, 50 mmol, 1 equiv) was added dropwise via syringe; the mixture stirred for 1 h at 0 °C and was analyzed by ^{11}B NMR. The analysis showed the solution to be diisopropylamine borane complex (δ −21.1, q, J = 95.3 Hz). Then, *n*-butyl lithium in hexanes (20 mL, 2.5 M, 50 mmol, 1 equiv) was measured in an oven-dried graduated cylinder and was added dropwise via cannula needle to the solution of amine borane at 0 °C (***CAUTION:*** *Hydrogen evolution*). After stirring at 0 °C for 1 h, an aliquot was taken and analyzed by ^{11}B NMR (80.25 MHz, THF) which showed the solution to be lithium diisopropylaminoborohydride (δ −23.6, q, J = 83.4 Hz). LAB reagent was transferred to an oven-dried, nitrogen-cooled, ampule via a cannula needle.

Note that, although the chemical shift of the corresponding amine−borane complex is virtually identical to that of the LAB, the J values of the amine−borane complex are different and range from 95 to 98 Hz. LAB reagents can be stored in an ampule under nitrogen without decomposition for at least 6 months.

4.2. General Synthesis of Aminoborane from LAB and Methyl Iodide. The following procedure for the preparation of diisopropylaminoborane is representative. To a 50-mL, round-bottom flask with a side arm was added lithium diisopropylaminoborohydride (prepared from 1.1 equiv of *n*-BuLi) (5.0 mL, 1 M in THF, 5.0 mmol, 1 equiv) and 3 mL of anhydrous THF. The reaction was cooled to 0 °C (ice bath), and methyl iodide (0.31 mL, 5.0 mmol, 1 equiv) was added dropwise (***CAUTION:*** *very exothermic reaction*). After all the methyl iodide was added, the ice bath was removed, and the reaction was stirred at room temperature for 1 h. After 1 h, the ^{11}B NMR spectrum showed formation of diisopropylaminoborane complex (δ +35, t, J = 125 Hz). For other aminoboranes prepared by this method see Table 1.

4.3. Synthesis of Diisopropylaminoborane from LAB in THF, Methyl Iodide, and Catalytic Amount of Et_3B. To a 50-mL, round-bottom flask with a side arm was added lithium diisopropylaminoborohydride (prepared from 1.0 equiv of *n*-BuLi) (5 mL, 1 M in THF, 5 mmol, 1 equiv), 3 mL of anhydrous THF, Et_3B (0.25 mL, 1 M, 5.0 mol %). The reaction was cooled to 0 °C (ice bath) and methyl iodide (0.31 mL, 5.0 mmol, 1 equiv) was added slowly dropwise (***CAUTION:*** *very exothermic reaction*). After all methyl iodide was added, the ice bath was removed, and the reaction mixture was stirred at room temperature for 1 h. After 1 h, the ^{11}B NMR spectrum showed formation of diisopropylaminoborane complex (δ +35, t, J = 125 Hz).

4.4. General Synthesis of Aminoboranes from LAB and TMS-Cl. The following procedure for the preparation of diisopropylaminoborane is representative. A 100-mL, round-bottom flask equipped with a magnetic stir bar and fitted with rubber septum was charged with lithium diisopropylaminoborohydride (prepared from 1.0 equiv

of *n*-BuLi) (25 mL, 1 M solution in THF 25 mmol, 1 equiv). Trimethylsilylchloride (3.20 mL, 25 mmol, 1 equiv) was added dropwise over 5 min via syringe while stirring at 25 °C. After 1 h of stirring at 25 °C, a 0.5 mL aliquot was taken and analyzed via ^{11}B NMR, which showed the solution to be monomeric diisopropylaminoborane (δ +35.2, t, J = 125 Hz). For other aminoboranes prepared by this method see Table 2.

4.5. General Synthesis of Aminoborane from the Direct Reaction of Heterocyclic Amines with BH_3:THF. To a 50-mL flask was added BH_3:THF (30 mL, 10 M solution in THF, 30 mmol, 1 equiv). To this flask was added pyrrole (2.1 mL, 30 mmol, 1 equiv) dropwise over 3 min. After the mixture stirred at 25 °C for 1 h, an aliquot was withdrawn for ^{11}B NMR analysis, and the spectra showed significant amounts of unreacted BH_3:THF (δ −1.5, t, J = 104 Hz). After 4 h, ^{11}B NMR spectroscopy analysis showed the completion of the reaction and exclusive formation of pyrrolylborane (δ +4.0, t, J = 113 Hz). For other heterocyclic aminoboranes prepared by this method see Table 3.

4.6. Synthesis of Aryl Boronic Acids. A Representative Procedure. A 100-mL, round-bottom flask with side arm was charged with triethylamine (3.47 mL, 25 mmol, 5 equiv), 4-bromoanisole (0.61 mL, 5 mmol, 1 equiv), and THF (3 mL). The septum was replaced with a reflux condenser while adding palladium (0.175 g, 0.5 mmol, 5 mol %). Finally, diisopropylaminoborane (15 mL, 1 M solution in THF, 15 mmol, 3 equiv) was added to the reaction mixture via syringe. The reaction mixture was subsequently heated to reflux at 65 °C. After 19 h of refluxing the solution was cooled to 25 °C, and methanol (8 mL) was added slowly (***CAUTION:*** *exothermic reaction*). The solvent was evaporated in vacuo (25 Torr), and the residue was dissolved with sodium hydroxide (3 M, 8 mL). The aqueous layer was washed with hexanes (3 × 10 mL) and then acidified with 3 M HCl (pH = 1). In most cases, the boronic acid precipitated out of the solution. The slurry was extracted with diethyl ether (4 × 15 mL). The organic portions were combined, dried with anhydrous $MgSO_4$, and filtered. Solvents were evaporated in vacuo to produce 4-methoxyphenylboronic acid as a white solid.

4.6.1. Phenylboronic acid (3): white solid; 82% yield (0.501 g); mp = 215−218 °C [lit.[26] mp 216 °C]. ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.31 (m, 3H), 7.56 (d, J = 6.5 Hz, 1H), 7.71 (d, J = 7 Hz, 1H); ^{13}C NMR (125 MHz, MeOH-d_4) δ 128.6, 128.7, 130.8, 131.3, 134.6, 135.0; ^{11}B NMR (80.25 MHz, MeOH-d_4) δ +18 (s).

4.6.2. 4-Methoxyphenylboronic acid (4): white solid; 78% yield (0.598 g); mp = 203−207 °C [lit.[26] mp 209−210 °C]; ^{1}H NMR (500 MHz, MeOH-d_4) δ 3.74 (s, 3H), 6.85 (d, J = 8 Hz, 2H), 7.55 (s, 2H), 7.7 (d, J = 8 Hz, 2H; ^{13}C NMR (125 MHz, MeOH-d_4) δ 55.5, 114.1, 136.7, 163.9; ^{11}B NMR (80.25 MHz, MeOH-d_4) δ +30.0 (s).

4.7. General Procedure for Nitrile Reduction. To a 50-mL round-bottom flask equipped with a magnetic stir bar and fitted with a rubber septum was added 4-bromo-2-fluorobenzonitrile (1.0 g, 5 mmol, 1 equiv). The round-bottom flask was charged with diisopropylaminoborane (20.0 mL, 0.5 M in THF, 10 mmol, 2 equiv). Lithium borohydride (0.25 mL, 2 M in THF, 0.5 mmol, 10 mol %) was then added, and the solution turned deep red in color. The reaction went to completion in 3 h at 25 °C, as evidenced by TLC (Hex/EtOAc, 2:1) analysis. The reaction mixture was cooled to 0 °C (ice bath), and unreacted BH_2-N(iPr)$_2$ was quenched with 3 M HCl (7 mL). (**CAUTION**: *hydrogen evolution!*) The acidic solution was stirred for 30 min and then washed with Et_2O (3 × 10 mL). The acidic solution was than made basic with NaOH pellets to pH ≈ 10. 4-Bromo-2-fluorobenzyl amine was extracted with 1:1 Et_2O/THF (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford 4-bromo-2-fluorobenzylamine as a light-yellow oil.

4.7.1. 4-Bromo-2-fluorobenzylamine (Table 4, entry 1): yellowish oil; 90% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80 (brd s, 2H), 3.83 (s, 2H), 7.18−7.25 (mult, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.1, 119.2, 120.8, 127.5, 129.3, 130.4, 160.8; FTIR (neat, cm^{-1}) 876, 1223, 1365, 1439, 1662, 1704, 2975, 2947, 2954, 3292, 3360; HRMS (70 eV) m/z (M^+ + 1) calcd 202.97459, found 202.97558.

4.7.2. 2-Chloro-5-fluorobenzylamine (Table 4, entry 2); yellowish oil; 70% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80 (brd s, 2H), 3.99 (s, 2H), 6.99 (m, 1H), 7.17 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.5, 37.7, 114.4, 114.5, 125.6, 128.9, 128.9, 160.4, 162.4, 163.5; FTIR (neat, cm^{-1}) 782, 1055, 1244, 1361, 1454, 1579, 1606, 2873, 2931, 3085, 3365; HRMS (70 eV) m/z (M^+ + 1) calcd 159.02511, found 159.02601.

4.7.3. 4-Methoxybenzylamine (Table 4, entry 3): yellowish oil; 80% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 2H), 3.87 (s, 2H), 6.92 (t, 1H, J = 9 Hz), 7.33 (m, 1H), 7.49 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 132.5, 129.7, 129.6, 128.4, 114.1, 55.4, 52.5; FTIR (neat, cm^{-1}) 812, 1033, 1513, 1611, 2869, 2929, 2954, 3294, 3366; HRMS (70 eV) m/z (M^+ + 1) calcd 137.08406, found 137.08511.

4.8. General Procedure for Competitive Reduction of Aldehyde in the Presence of Nitrile. A 50-mL, round-bottom flask, equipped with a magnetic stir bar and fitted with a rubber septum, was charged with 4-bromo-2-fluorobenzonitrile (0.20 g, 1 mmol, 1 equiv), mesitylene (0.08 g, 1 mmol, 1 equiv), benzaldehyde (0.106 g, 1 mmol, 1 equiv), and THF (10 mL). An aliquot (0.1 mL) was withdrawn from the reaction mixture before the addition of diisopropyl aminoborane to serve as a reference (t_0). Diisopropylaminoborane (2.4 mL, 1.2 mmol, 1.2 equiv) was then added to the flask via syringe. Finally, $LiBH_4$ (0.05 mL, 2 M solution in THF, 0.1 mmol, 10 mol %) was added to the flask via syringe. The reaction was monitored by analyzing aliquots via GC. Aliquots (0.1 mL) were diluted with pentane (1 mL) to precipitate diisopropylaminoborane to avoid contamination of the GC column by boron compounds. The percentage of unreacted 4-bromo-2-fluorobenzonitrile and benzaldehyde was determined from the peak areas using mesitylene as the internal standard.

4.9. General Procedure for the Reduction of Esters. A 50-mL, round-bottom flask with a side arm, condenser, and stir bar was charged with diisopropylaminoborane (10 mL, 1 M solution in THF, 10 mmol, 2 equiv) and lithium borohydride (0.5 mL, 2 M solution in THF, 1 mmol, 10 mol %). Methyl octanoate (0.90 mL, 5 mmol, 1 equiv) was added to this solution via syringe. The reaction mixture was subsequently heated to 65 °C. The reaction went to completion after 2 h of heating as evidenced by the disappearance of methyl octanoate on TLC (Hex/EtOAc, 2:1) analysis. The reaction mixture was cooled to 0 °C (ice bath), and unreacted BH_2-N(iPr)$_2$ was quenched with 1 M HCl (5 mL). (**CAUTION**: hydrogen evolution!) The reaction mixture was than extracted with pentane (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford octanol as colorless oil.

4.9.1. Benzyl alcohol (9): colorless oil; 96% yield (0.518 g).

4.9.2. Octanol (11): colorless oil; 98% yield (0.637 g).

4.10. General Procedure for Hydroboration and Boronic Acid Synthesis. To a 50-mL, round-bottom flask equipped with a magnetic stir bar and fitted with a rubber septum was added pyrrolylborane (5.3 mL, 1 M solution in THF, 5 mmol, 1 equiv). The reaction flask was cooled to 0 °C (ice bath), and styrene (0.573 mL, 5 mmol, 1 equiv) was added. The reaction was then allowed to warm to 25 °C. After 19 h the reaction mixture was mixed with pentane (25 mL) and NaOH (10 mL, 3 M). (**CAUTION**: *hydrogen evolution!*) After 1 h of stirring the reaction mixture the aqueous layer was removed. The pentane layer was then extracted with NaOH (2 × 5 mL, 3 M) collecting all the aqueous layers together. The aqueous layers were then acidified with HCl (8 mL, 12 M solution in H_2O, 96 mmol) while at 0 °C, forming a white precipitate. Sodium chloride (2 g) was added to aid precipitation.

(26) Lappert, M. F. *Chem. Rev.* **1956**, *56*, 959.

The precipitate was collected by filtration while under Ar. The precipitate was then washed with water (3 × 5 mL), yielding a purplish solid. This purplish solid was then further purified by redissolving it in NaOH (10 mL, 3 M) and reprecipitating with HCl (8 mL, 12 M) and salt (1 g). The newly formed precipitate was then filtered and washed with water (3 × 5 mL), yielding a white solid.

4.10.1. 2-Phenylethylboronic acid (13): white solid; 51% yield (0.388 g); ^{1}H NMR (600 MHz, $CDCl_3/D_2O$ (99:1)) δ 1.21 (t, J = 8 Hz, 2H), 1.70 (brd s, 2H), 2.77 (t, J = 7.8 Hz, 2H), 7.20−7.7.32 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3/D_2O$ (99:1)) δ 30.2, 125.9, 127.9, 128.6, 143.8; ^{11}B NMR (80.25 MHz, $CDCl_3/D_2O$ (99:1)) δ +32.5 (s).

4.10.2. *E*-2-Phenylethenylboronic acid (15): white solid; 42% yield (0.61 g); ^{1}H NMR (600 MHz, $CDCl_3/D_2O$ (99:1)) δ 1.63 (brd s, 2H), 6.16 (d, J = 22 Hz, 2H), 7.28−7.52 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3/D_2O$ (99:1)) δ 127.2, 127.7, 128.8, 129.2, 148.4; ^{11}B NMR (80.25 MHz, $CDCl_3/D_2O$ (99:1)) δ +28.7 (s).

Supporting Information Available: The preparation of lithium aminoborohydrides and spectroscopy data for all compounds characterized. This material is available free of charge via the Internet at http://pubs.acs.org.

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