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Molecular Iodine Initiates Hydroborations of Alkenes with N-Heterocyclic Carbene Boranes

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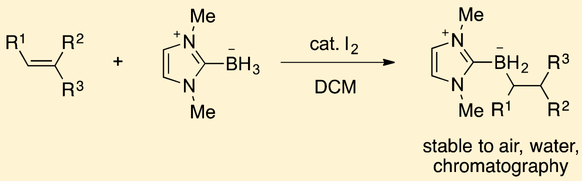
Ⓢ *Supporting Information*

ABSTRACT: The hydroboration of alkenes of diverse structural types by assorted N-heterocyclic carbene boranes can be accomplished by addition of 5−10% diiodine. For example, reaction of 1,3-dimethylimidazol-2-ylidene borane (diMe-Imd-BH_3) with 10% I_2 followed by addition of 2,3-dimethyl-2-butene provided the corresponding thexyl NHC-borane (diMe-Imd-BH_2thexyl) in 75% yield. This and related monohydroboration products are stable to chromatography and storage. The scope of the new reaction is described, and the mechanism is probed by ^{11}B NMR experiments.



INTRODUCTION

The consummate reaction of Lewis base complexes of borane (LB−BH_3) is hydroboration of alkenes.[1] Such reactions occur because most Lewis bases (ethers, sulfides) can undergo rapid exchange with alkenes. The resulting alkene−borane complexes rapidly transform to alkyl boranes by hydroboration. In contrast, complexes of borane with Lewis bases including phosphines[2] and N-heterocyclic carbenes[3] are inert to alkene hydroboration because of their stability. Amine−borane complexes are in the middle, either leading to hydroboration or not depending on the structure of the amine and the reaction temperature.[2,4] Hydroboration only occurs when the amine can decomplex from the borane.

Vedejs and co-workers have spearheaded a new mode of activation for stable Lewis base complexes of borane including amine− and phosphine−boranes.[5] Activation occurs not by decomplexation of the Lewis base but instead by formation of a borenium ion (LB−BH_2^+) or a species that reacts like a borenium ion.[6] Stabilized borenium ions have been characterized,[7] but like free borane, free borenium ions often do not exist in solution. So called "borenium ion equivalents" are present, including charged complexes of borenium ions with solvent, borane, or another Lewis base (called boronium ions[8]), or neutral, covalent LB−borane complexes with an excellent leaving group (LB−BH_2X where X is the leaving group).[6]

In collaboration with Vedejs, we recently reported the first hydroboration reactions of alkenes with stable N-heterocyclic carbene boranes (Figure 1).[9] This reaction, which otherwise does not occur even under forcing conditions, can be induced by adding 5−15% bis(trifluoromethanesulfonimide) (hereafter, triflimide or Tf_2NH). Dihydroborated products quickly form at rt or below. In a complementary activation approach, Parrain and co-workers made NHC−boracyclopentanes by rhodium-catalyzed intramolecular hydroborations.[10]

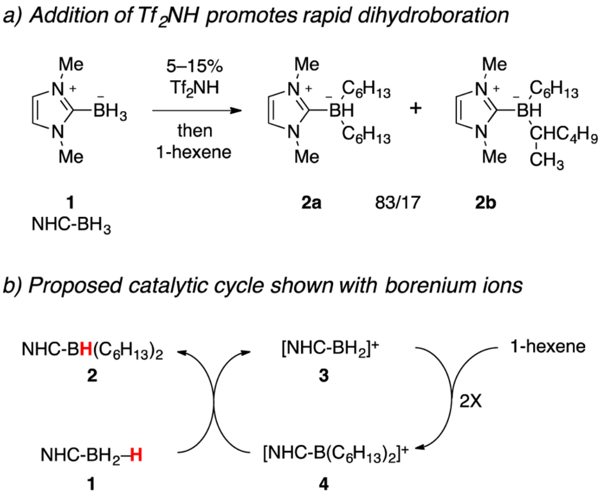


Figure 1. NHC−borane **1** hydroborate alkenes when triflimide is added: (a) a typical example and (b) a simplified catalytic cycle illustrated with free borenium ions.

In a typical example of triflimide activation, addition of 15% triflimide to 1,3-dimethylimidazol-2-ylidene borane (diMe-Imd-BH_3) **1** followed by addition of 1-hexene provided dihydroborated products **2a** (with two 1-hexyl groups) and **2b** (with one 1-hexyl group and one 2-hexyl group) in a ratio of about 83/17 (Figure 1a). These NHC−dialkylboranes did not survive flash chromatography, but they were oxidized to provide the expected 91/9 mixture of 1-hexanol and 2-hexanol in high yield. A key problem with the triflimide procedure was the limited scope of alkenes that could be used.[9]

The catalytic cycle shown in Figure 1b is proposed to account for these results, with free borenium ions shown for simplicity. Reaction of Tf_2NH with **1** gives the catalyst **3**. The two-step cycle consists of hydroboration of 1-hexene with **3**

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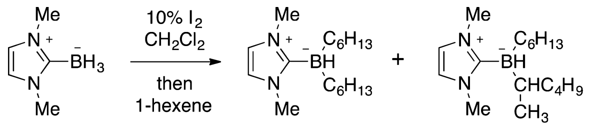
(which occurs a second time) followed by hydride transfer from **1** to **4** to regenerate the catalyst **3**. This ability of NHC−boranes and NHC−boreniums to exchange hydride closes a catalytic cycle that so far has not succeeded with other ligated boranes (1 equiv of activator is usually needed).[5b,g]

Here we expand the scope of borenium ion catalyzed hydroborations of NHC−boranes in three directions. First, we report that sensitive and expensive triflimide can be replaced with easy to handle and inexpensive diiodine (I_2) as activator. Second, we learn that with many types of alkenes monohydroboration occurs rather than dihydroboration. This is important because the monohydroborated products are typically stable to chromatography and can be directly isolated and characterized. Third, we find that the range of alkene types that participate in the hydroboration is significantly expanded. Finally, we also describe experiments that provide insight into the nature of the reactive intermediates in the catalytic cycle.

■ RESULTS AND DISCUSSION

Reaction Development. The triflimide activator is thought to serve as a precatalyst in the reactions in Scheme 1, and we tested several other activators (TfOH, Br_2, NIS) in preliminary experiments. Among these, diiodine (I_2) quickly gave promising results. In an early experiment patterned after that in Figure 1a, 10 mol % diiodine was added to 1 equiv of **1** in CH_2Cl_2 (Scheme 1).[11] After the bubbling ceased (hydrogen gas), 3 equiv of 1-hexene was added. Then 1 h later, a ^{11}B NMR spectrum was recorded. The resulting spectrum closely resembled that from the prior triflimide experiment, with the major peaks for **2a** and **2b** detected in about 83/17 ratio. Thus, a reactive borenium ion equivalent can be access by using iodine, and this equivalent undergoes both hydroboration and hydride transfer to close a catalytic cycle.

Scheme 1. Results of a Preliminary Hydroboration Experiment with Diiodide in Place of Triflimide

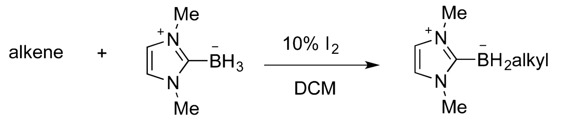


1 **2a** 83/17 **2b**

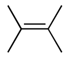
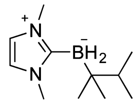
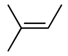
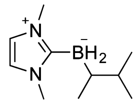
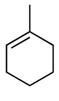
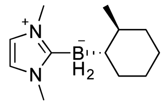
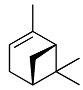
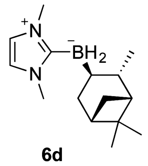
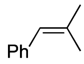
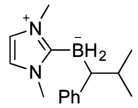
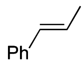
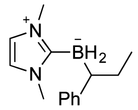
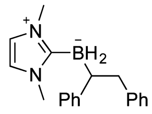
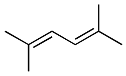
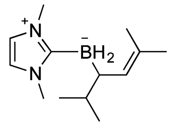
The two activators Tf_2NH and I_2 are not as similar as they look based on this product analysis. Reaction of **1** with a substoichiometric amount of triflimide in the absence of alkene provides a borenium ion complexed to a B−H bond of the starting borane ($[NHC{-}BH_2{-}H{-}BH_2{-}NHC]^+\ Tf_2N^-$).[9,12] In contrast, the reaction of **1** with substoichiometric diiodine produces the covalent boryl iodide $NHC{-}BH_2I$ that is not complexed to the remaining borane **1**.[11b] The results in Figure 1a and Scheme 1 suggest that these two different species, one ionic and one covalent, are both capable of setting off hydroborations by NHC−boranes.

Scope Study. Results of a study of the scope of the iodine-activation method are summarized in Table 1. We focused on substrates that were problematic in the original triflimide procedure.[9] This procedure works well for simple mono- and disubstituted alkenes like 1-, 2-, and 3-hexene, always producing dialkylboranes (no matter whether the alkene is present in excess or deficient). However, tri- and tetra-substituted alkenes and phenyl-substituted alkenes often gave complex mixtures.

Table 1. Synthesis of NHC−Alkylborane Complexes Using Iodine-Catalyzed Hydroboration



5a-h **1** **6a-h**

entry	alkene	product	yield
1	 **5a**	 **6a**	75%
2	 **5b**	 **6b**	59% (75%[a])
3	 **5c**	 **6c**[b]	68%
4	 (+)-**5d**	 **6d**	61%
5	(−)-**5d**	ent-**6d**	61%
6	 **5e**	 **6e**	50%
7	 **5f**	 **6f**	59% (80%[d])
8	 *Z*-**5g**	 **6g**	66% (73%[d])
9	*E*-**5g**	**6g**	64%
10	 **5h**	 **6h**	37%

[a] 5 mol % iodine was used in a 2 mmol scale reaction. [b] Oxidation of this product provided racemic *trans*-2-methylcyclohexanol. [c] About 10% of the regioisomer was detected in the ^{11}B NMR spectrum of the crude product. [d] 1 equiv of alkene and 1.4 equiv of **1** were used.

In contrast, addition of 10% I_2 to **1** followed by addition of 1 equiv of 2,3-dimethylbutene **5a** (tetramethylethylene) provided NHC−thexylborane adduct **6a** as assessed by ^{11}B NMR spectroscopy (triplet, −24 ppm). No dialkylborane was detected (doublet expected at about −20 ppm). Direct solvent evaporation and flash chromatography provided **6a** in 75% yield (entry 1). We have previously made **6a** by complexation of thexylborane with 1,2-dimethylimidazol-2-ylidene,[13] but this new route is more convenient because **1** is readily available.

Results of catalyzed monohydroborations of an assortment of other alkenes are summarized in entries 2−10 in Table 1. The scales were 1 mmol of starting NHC−borane and 10% I_2 unless otherwise indicated. In all cases, the monohydroboration products were stable, and the reported yields are after purification by flash chromatography. Hydroboration of 2-methylbutene (trimethylethylene) **5b** provides **6b** as a single regioisomer with the boron atom on the secondary carbon atom in 59% yield (entry 2). Likewise, hydroboration of 1-methylcyclohexene **5c** by **1** gives a single regio- and stereoisomer **6c** in 68% yield (entry 3).

Individual hydroboration of the two enantiomers of α-pinene (+)-**5d** and (−)-**5d** provided enantiomeric pinenyl boranes **6d** and ent-**6d** as single regio- and stereoisomers in 61% yield (entries 4 and 5). The results in entries 3−5 show for the first time that NHC−borenium hydroboration reactions occur with *syn* stereochemistry, like borane hydroborations.[1]

Reactions with 2-methyl-1-phenylpropene **5e** and (*E*)-1-phenyl-1-propene **5f** provided products **6e** and **6f** in 50% and 59% yield, respectively (entries 6 and 7). In both cases, the boron atom ended up bonded to the benzylic carbon. The high regioselectivity with the trisubstituted alkene **5e** is perhaps expected based on substitution, and indeed the only resonance in the ^{11}B NMR spectrum of the crude product from **5e** was that of **6e**. There were two resonances in the spectrum of the crude product from disubstituted alkene **5f** in a ratio of about 90/10. The major resonance at −23.5 ppm belongs to **6f**. This overlaps a small resonance at −23.8 ppm that we suspect belongs to the regioisomer of **6f** (which could not be isolated in pure form). If so, then the regioselectivity in the hydroboration of **5e** with **1** is considerably higher than free borane (~3/1) and on par with pyridine-iodoborane.[5b]

Hydroborations of (*E*)- and (*Z*)-1,2-diphenylethene (stilbene) *Z*-**5g** and *E*-**5g** gave the same product **6g** in about the same yield (66% and 64%, entries 8 and 9). Hydroboration of 2,5-dimethylhexa-2,4-diene **5h** gave substituted allyl borane **6h** in 37% yield (entry 10).

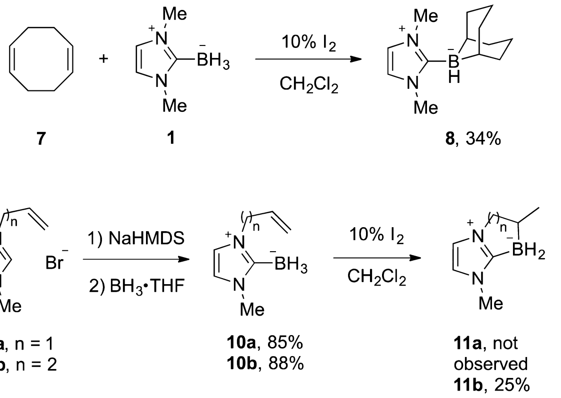
A couple of highly conjugated alkenes did not give clean hydroboration products with this procedure. Specifically, triphenylethene ($Ph_2C{=}CHPh$) and (*E,E*)-1,4-diphenylbuta-1,3-diene ($PhCH{=}CH{-}CH{=}CHPh$) did not appear to react under the standard conditions. Instead, gradual decomposition of the starting NHC−borane was observed over two days.

We also looked briefly at two modifications of the standard procedure. Reasoning that formation of the NHC−BH_2I catalyst would leave the amount of **1** deficient for product formation with a 1/1 stoichiometry of **1** and alkene, we increased the amount of **1** to 1.4 equiv in two experiments. In entry 7, the yield of **6f** increased significantly from 59% to 80%, while in entry 8 the yield of **6g** increased modestly from 66% to 73%. More practical of course is to simply decrease the amount of iodine added. We probed this on a larger scale (2 mmol) by adding only 5% iodine to **1** and **5b**. This time, the yield of **6b** increased from 59% to 75%.

Recently, NHC−9-BBN complexes (9-BBN is 9-borabicyclo[3.3.1]nonane) have attracted attention in several respects. Lindsay and co-workers made a stable borenium by reaction of 1,3-dimesitylimidazol-2-ylidene-9-BBN with triflic acid,[14] while Stephan and co-workers used the borenium ion from 1,3-(2,6-diisopropyl-phenyl)imidazol-2-ylidene-9-BBN to activate dihydrogen at room temperature.[15] In both cases, the starting complexes were made by addition of the appropriate NHC to 9-BBN.

We made the related 9-BBN complex **8** by direct hydroboration as shown in Scheme 2. Complex **1** was treated with 10% I_2 as usual, followed by addition of 1,5-cyclooctadiene. A slow reaction occurred, and after 2 days, the ^{11}B NMR spectrum of the mixture showed a large doublet at −16.2 ppm (J_{BH} = 85 Hz). These are values expected for product **8**. The 9-BBN complexes seem to be somewhat more robust than dialkylborane complexes like **2**, and **8** was isolated as a white solid in 34% yield by flash chromatography. Thus, it is now possible to make NHC−9-BBN complexes by either hydroboration of cyclooctadiene followed by complexation with the NHC or the reverse.

Scheme 2. Synthesis of Cyclic NHC−Boranes by Hydroboration



Next, we looked at two intramolecular hydroborations[10] of complexes **10a** and **10b**. Such complexes are made by deprotonation of the corresponding salt **9a,b** to generate the NHC, then addition of $BH_3 \cdot THF$.[10,16] The terminal alkene is no competition for the carbene, and alkenyl NHC−boranes **10a,b** are formed in good yield. Both compounds are stable and show no tendency to hydroborate themselves on storage.

The usual reaction of *N*-allyl analogue **10a** did not give a clean product **11a**; however, treatment of *N*-butenyl analogue **10b** with 10% I_2 in dichloromethane provided the interesting fused bicyclic NHC−borane **11b**. This was isolated as a white solid in 25% yield by flash chromatography and characterized by the usual means. Once isolated, solid **11b** is stable. However, we suspect that material loss occurs during chromatography because the ^{11}B NMR spectrum of the reaction mixture showed formation of considerably more than 25% of **11b**. These results are complementary to those of Parrain,[10] who reported that rhodium catalysts promote intramolecular hydroborations to make boracyclopentanes (including **11a**) but not boracyclohexanes (like **11b**).

To close the scope study, we surveyed the reactions of six typical NHC−boranes with 2-methyl-2-butene **5b**. The standard procedure was used (10% I_2, CH_2Cl_2, rt), and the structures and isolated yields of the hydroboration products are shown in Figure 2. Reaction of triazol-2-ylidene and benzimidazol-2-ylidene NHC−boranes bearing (*N,N*)-dimethyl groups provided hydroboration products **12** and **13** in 70% and 71% yield.

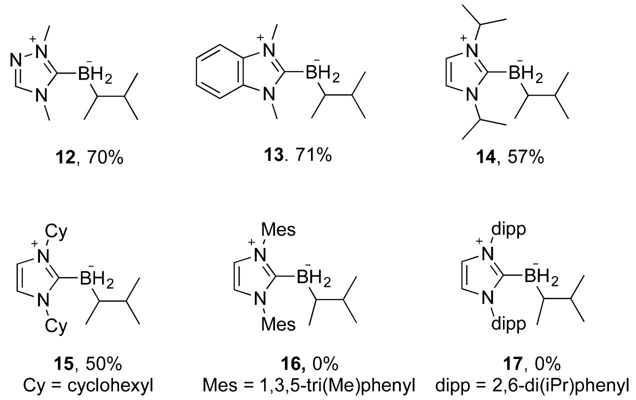


Figure 2. Structures of products and yields in a scope study of NHC−boranes with 2-methyl-2-butene.

Imidazol-2-ylidene NHC−boranes bearing medium-sized *N*-alkyl groups (isopropyl or cyclohexyl) also reacted smoothly to provide **14** and **15** in 57% and 50% yield. However, products **16** and **17** were not isolated from reactions of imidazol-2-ylidene NHC−boranes bearing large *N*-aryl groups (mesityl and 2,6-diisopropylphenyl). We know by ^{11}B NMR spectroscopy that iodine reacts with the starting boranes NHC−BH$_3$ to give the expected NHC−BH$_2$I. In the last case, the intermediate dipp-Imd-BH$_2$I is not consumed when the alkene is added, so apparently the hydroboration step fails due to the large *N*-aryl substituents.

Mechanistic Experiments. Several ^{11}B NMR experiments also probed what intermediates might be formed and how they are consumed in these reactions. Figure 3 shows plausible steps of a catalytic cycle that is more sophisticated than the cycle in Figure 1. In the catalyst generation step (1), reaction of 2 equiv of **1** with I$_2$ provides 2 equiv of covalent boryl iodide **18**.[11b] Left alone, this boryl iodide is stable for long periods in solution. However, it is sensitive to neutral nucleophiles like water, methanol, and presumably alkenes.

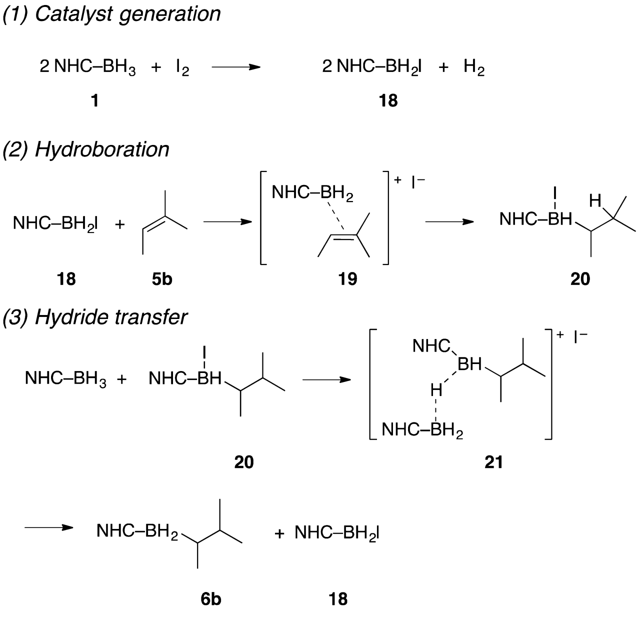


Figure 3. Plausible steps in a catalytic cycle for hydroboration illustrated with **1** (NHC is 1,3-dimethylimidazol-2-ylidene) and 2-methyl-2-butene **5b**.

The catalytic cycle has steps of hydroboration (2) and hydride transfer (3). Hydroboration with **18** could occur by displacement of the iodide by the alkene **5b** to give a species like **19** (either an intermediate or a transition state), which would rapidly hydroborate itself, then collapse by readdition of iodide to **20**. The formation of **19** can be considered a Lewis base exchange or a nucleophilic substitution at boron. Nucleophilic substitutions with anionic nucleophiles and NHC−boryl halides and triflates are well precedented.[11a]

In the hydride transfer step (3), the boryl iodide **20** again reacts by Lewis base exchange (or substitution at B) of the iodide with a BH bond of the precursor **1** to provide a bridging species **21**,[9,12] which then completes the hydride transfer to give product **6b** and return the catalyst **18**. The bridging species **21** could be a transient intermediate rather than a transition state. Related species have been observed in the absence of good nucleophiles,[9,12] though we did not observe **21** during reactions.

Several ^{11}B NMR spectroscopic experiments supported key aspects of this catalytic cycle. A stoichiometric reaction between NHC−BH$_2$I **18** and 2-methyl-2-butene **5b** provided a single major product with a broad resonance at −12 ppm. This is a reasonable chemical shift for the intermediate boryl iodide **20**. In addition, the same resonance was generated by adding a stoichiometric amount of diiodine (50 mol %) to the product **6b**.[17] As expected for a boryl iodide, intermediate **20** did not survive flash chromatography. To simulate the catalytic conditions for the hydride transfer step (3), we generated **20** in situ by adding iodine to **6b**, then adding 10 equiv of starting NHC−borane **1**. The major new resonances in the ^{11}B NMR spectrum belonged to hydride transfer products **6b** and **18**. This hydride transfer reaction might be reversible, but further hydroboration of boryl iodide **18** drives the process forward.

■ CONCLUSIONS

The new procedure for activation of NHC−boranes toward hydroboration by diiodine is both more convenient and less expensive than the original triflimide activation procedure. Most importantly, the scope of the hydroboration has been dramatically expanded. Indeed, with the exception of 1-hexene (Scheme 1), all of the hydroboration substrates used in this paper either did fail or would be expected to fail with the original triflimide method. Monohydroboration occurs with di- and tri- and tetra-substituted alkenes, and these products can be isolated by flash chromatography and are stable on storage.

^{11}B NMR experiments have also provided helpful information about the likely intermediates and the mechanism. Reactions of NHC−BH$_3$ with triflimide and diiodine provided two structurally different intermediates. Even though the first was ionic and the second was covalent, both reacted like a borenium ion in the subsequent steps of the catalytic cycle. These steps are hydroboration and hydride transfer. This and the prior results of Vedejs[5] with amine- and phosphine-boranes suggest that it is possible to evince borenium ion chemistry of N-heterocyclic carbene boranes from several different kinds of intermediates. On the basis of the results of the scope studies, the intermediates in the triflimide procedure seem more aggressive, while those in the iodine procedure seem gentler. All this bodes well for expansion of the chemistry of N-heterocyclic carbene boranes through the use of borenium ions of their reactive equivalents.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete details of experiments and compound characterization and copies of ^{1}H, ^{11}B, and ^{13}C NMR spectra of all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(17) Alkyl-subsituted boryl iodides like **20** are less stable than boryl iodide **18**. Gradual decomposition generates a resonance at 33.7 ppm in the ^{11}B NMR spectrum. This shift is consistent with a borinic acid, $RB(OH)_2$.