

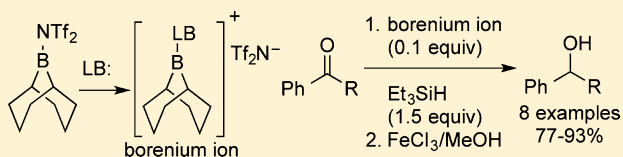
Lewis Base Activation of Lewis Acids: Group 13. In Situ Generation and Reaction of Borenium Ions

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S Supporting Information

ABSTRACT: A variety of Lewis bases were combined with 9-BBN-NTf₂ to establish the requirements for the generation of borenium cations. Five different types of behaviors were found, but the most interesting was the combination of Et₃N, DABCO, 2,6-lutidine, or Ph₃P=S, which formed borenium ions exclusively even in sub- or superstoichiometric quantities. The 9-BBN borenium ion complex of 2,6-lutidine rapidly catalyzes the hydrosilylation of a variety of ketones in the presence of Et₃SiH. Preliminary mechanistic experiments suggest that the reduction involves borenium ion activation of Et₃SiH and not the ketone.



Foregoing studies from these laboratories have provided extensive preparative and mechanistic illustration of the counterintuitive concept of Lewis base activation of Lewis acids.¹ The majority of the early investigations focused on the activation of silicon tetrachloride with chiral bisphosphoramides to generate a highly reactive, chiral trichlorosiliconium ion complex that catalyzed the diastereo- and enantioselective aldol additions of enoxysilanes derived from aldehydes, ketones, esters, amides, and nitriles.² In recent years, our attention has turned to the Lewis base activation of Lewis acidic reagents in group 16 (selenium³ and sulfur⁴) as well as group 17 (bromine⁵ and chlorine⁶) to effect enantioselective cyclofunctionalizations of unactivated alkenes. Despite the dramatic difference in the chemical transformations involved, the underlying principle of catalysis is the same: namely, the electronic redistribution in donor–acceptor complexes first articulated by Gutmann (Figure 1).⁷ To date, all of our mechanistic studies have demonstrated that the ionization of the dative complexes into highly electrophilic, cationic species is required for catalysis.

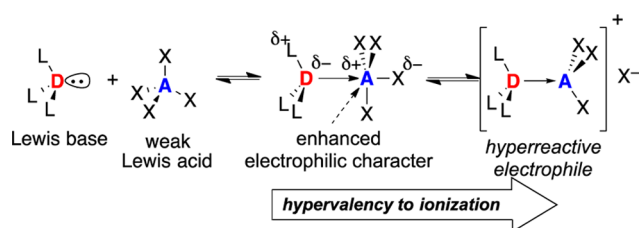


Figure 1. Gutmann formulation of Lewis base activation of Lewis acids.

In continuation of these investigations, we were drawn to the possibility of activating Lewis acids in group 13, in view of the recent interest in the chemistry of tricoordinate cationic boron species (borenium ions).⁸ Many different methods for borenium ion generation are on record,⁹ and these highly reactive species have been used as stoichiometric reagents (e.g.,

in arene and alkane borylation).¹⁰ On the other hand, the main focus in borenium cation catalysis has been the development of oxazaborolidine catalysts and other application methods are very rare.¹¹ Very recently, borenium ion catalyzed hydrogenation and hydroboration have been reported. In 2012, Crudden and co-workers reported a novel, metal-free, catalytic method for the reduction of imines using air-stable, non-hazardous boranes. The catalysts for this process are discrete, well-characterized borenium salts derived from pinacolborane.^{12a} In addition, Curran, Vedejs, and co-workers reported a borenium ion catalyzed hydroboration of alkenes with N-heterocyclic carbene–boranes,^{12b} Stephan and co-workers described hydrogenation of imines with 9-BBN–NHC borenium ion complexes,^{12c} and Jäkle recently described the preparation of chiral borenium ions that effected asymmetric hydrosilylation of a ketone.^{12d}

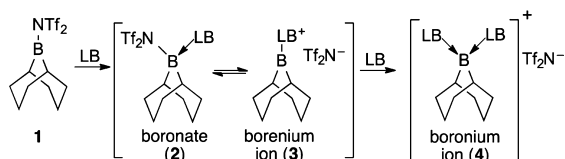
To develop a *catalytic* method for the generation of borenium ions presented far greater challenges than those encountered with group 14, 16, and 17 elements in previous endeavors, such as (1) the design features for Lewis base activation are entirely different in view of the high affinity of the Lewis acidic elements in this group, (2) the intrinsic Lewis acidity of any precursors presents a major problem for suppression of background reactions, (3) ionization of a labile ligand is essential (at least for boron) to provide the coordinative unsaturation needed for catalysis, and (4) there is a lack of an established suite of known reactions of borenium ions for which (asymmetric) catalysis would be useful. Thus, we viewed this exercise as an exploratory investigation to learn the rules for the catalytic generation of borenium ions to enable the discovery of new reaction chemistry of these novel species.

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The first phase of the study required the identification of a suitable boron precursor and its behavior in the presence of a wide range of Lewis bases. The structures of the possible adducts in Scheme 1 could be identified by ^{11}B , ^{19}F , and ^{31}P NMR spectroscopy. From the pioneering work of Vedejs, we chose 9-borabicyclo[3.3.1]nonane bis(triflimide) (9-BBN-NTf₂, **1**). Vedejs demonstrated that **1** was effective for the generation of borenium and boronium cations with amine Lewis bases owing to the excellent nucleofugality of the bis(triflimide) group.¹³

Scheme 1



Initially, ^{11}B and ^{19}F NMR spectroscopic analysis of isolated, purified **1** was performed in CH₂Cl₂ (0.1 M) at room temperature and sharp singlets were observed at 58.9 and -70.0 ppm, respectively. To assay the potential of Lewis bases to generate borenium cations from **1**, 0.5, 1.0, and 2.0 equiv of each Lewis base were titrated to the 0.1 M solution of **1** and analyzed by NMR spectroscopy (Table 1). The ^{19}F NMR resonance at ca. -80.0 ppm is characteristic of bis(triflimide) anion¹³ and thus allowed the assignment of the boron-

Table 1. Titration Experiments with **1** and Various Lewis Bases: ^{11}B NMR Data^a

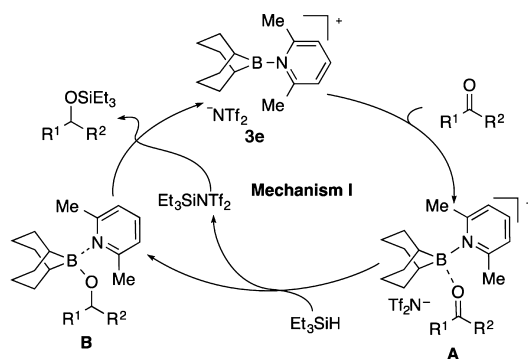
Lewis base	boronate complex (ppm) (2)	borenium ion (ppm) (3)	boronium ion (ppm) (4)
Et ₃ N (a)		84.8 (85.1) ^b	
DABCO (b)		56.9	
pyridine (c)			5.2
2,4-lutidine (d)	39.4		9.7
2,6-lutidine (e)		84.4	
DMAP (f)		(66.5) ^b	(3) ^b
proton sponge (g) ^c			(16.2) ^b
HMPA (h)		64.9	17.8
Ph ₃ P=O (i)		67.4	17.3
<i>n</i> -Bu ₃ P=O (j)		65.1	14.5
Ph ₃ P=S (k)		80.4	
(Me ₂ N) ₃ P=S (l)		80.9	46.9
pyridine- <i>N</i> -oxide (m)		64.2	14.4
DMSO (n)		66.1	15
<i>n</i> -Bu ₃ P (o)	33.1		-5.4
benzophenone (p)	35.6 ^d		

^a ^{11}B NMR spectra were recorded at 128 MHz (CH₂Cl₂) with proton decoupling. Chemical shifts are reported in ppm from BF₃·OEt₂ (0.0 ppm) as the external standard. ^bData in parentheses are from ref 13. ^c1,8-Bis(dimethylamino)naphthalene. ^d2.0 equiv of Lewis base.

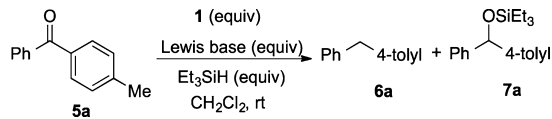
containing fragment as a cation. With this information in hand, DABCO, pyridine, 2,4-lutidine, 2,6-lutidine, HMPA, Ph₃P=O, *n*-Bu₃P=O, Ph₃P=S, (Me₂N)₃P=S, pyridine *N*-oxide, DMSO, *n*-Bu₃P, and benzophenone were used as Lewis bases and the structures of the 9-BBN–Lewis base complexes were assigned by ^{11}B and ^{19}F NMR spectroscopy titration experiments. Analysis of the results revealed that these Lewis bases could be broadly classified into five different groups: (1) type I, in which weak coordination formed a boronate complex only at all loadings of Lewis base (benzophenone), (2) type II, in which strong coordination formed a boronate complex which spontaneously ionized and bound a second Lewis base to form a boronium ion at all loadings of Lewis base (2,4-lutidine, *n*-Bu₃P), (3) type III, in which strong coordination led to ionization to form borenium ions at all loadings of Lewis base (Et₃N, DABCO, 2,6-lutidine, Ph₃P=S), (4) type IV, in which strong coordination led to ionization to form borenium ions with 1.0 equiv and then boronium ions with 2.0 equiv of Lewis base (HMPA, Ph₃P=O, *n*-Bu₃P=O, (Me₂N)₃P=S, pyridine *N*-oxide, DMSO), and (5) type V, in which strong coordination led to ionization to form only boronium ions at all loadings of Lewis base (pyridine, Proton Sponge). Notably, for type III Lewis bases, boronium cations were not formed even with 2.0 equiv of Lewis base. Furthermore, with 1.0 equiv of type IV Lewis bases, a borenium cation was formed predominantly together with a small amount of the boronium cation.

With a reliable method for the efficient, in situ generation of borenium–Lewis base complexes, the next phase involved the identification of a reaction to evaluate the catalytic potential of these species. The hydrosilylation reaction of ketones was selected as a model reaction, inspired by the imine hydrosilylation.^{12a} By analogy to the proposed catalytic cycle, ketones would be activated by the borenium complex to give the corresponding boronium complex **A**. Subsequent hydride transfer from triethylsilane would afford borinate complex **B**, which could be exchanged by Et₃SiNTf₂ to regenerate the borenium–Lewis base complex catalyst (Mechanism I) (Scheme 2).

Scheme 2



Initial experiments to probe this hypothesis were conducted by treating 4-methylbenzophenone (**5a**) with Et₃SiH (1.5 equiv) in the presence of various boron reagents. It was first established that Et₃SiH does not reduce **5a** at room temperature after 6 h (Table 2, entry 1). However, in the presence of 9-BBN-NTf₂ (**1**; 0.1 equiv) only over-reduced product **6a** was obtained in 69% yield in 10 min (entry 2). Whereas no reaction took place in the presence of 0.1 equiv of complex **3b** (entry 3), 0.1 equiv of complex **3e** afforded the

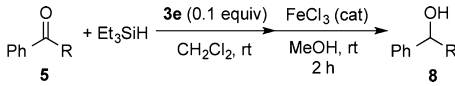
Table 2. Hydrosilylation of Ketones Catalyzed by Various Boron Reagents^a


entry	amt of 1 (equiv)	Lewis base (amt (equiv))	amt of Et ₃ SiH (equiv)	time	yield ^b of 6a (%)	yield ^b of 7a (%)
1	0		1.5	6 h	0	0
2	0.1		1.5	10 min	69	0
3	0.1	DABCO (0.1)	1.0	12 h	0	0
4	0.1	2,6-lutidine (0.1)	1.5	30 min	<5	95
5	0.05	2,6-lutidine (0.05)	1.5	20 h	<5	69

^aReactions were performed at room temperature in an NMR tube (see the Supporting Information for details). ^bYields determined by integration of product signals versus Cl₃CCH₂Cl as an internal standard.

expected reduction product **7a** in 95% yield (entry 4). Remarkably, lowering the loading of 2,6-lutidine to 0.05 equiv in the presence of 0.05 equiv of **1** still afforded exclusively **7a**, albeit much more slowly, such that after 20 h only a 69% yield was obtained (entry 5). Clearly, two different mechanisms are operative for the different catalysts, **1** and **3e**.

The scope of the borenium cation catalyzed hydrosilylation was explored with various ketones **5**, and the results are summarized in Table 3. Generally, the use of 0.1 equiv of **3e**

Table 3. Substrate Scope^a


entry	R	ketone	time (min)	yield ^b (%)	alcohol
1	4-Me-C ₆ H ₄	5a	30	92	8a
2	3-Me-C ₆ H ₄	5b	10	90	8b
3	4-MeO-C ₆ H ₄	5c	180	91	8c
4	4-Br-C ₆ H ₄	5d	10	93	8d
5	1-naphthyl	5e	60	86	8e
6	2-furyl	5f	10	82	8f
7	2-thiophene	5g	60	83	8g
8 ^c	isopropyl	5h	60	77	8h

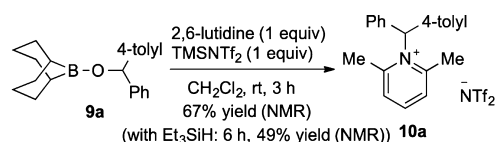
^aUnless otherwise noted, reactions were performed on a 0.1 mmol scale with 1.5 equiv of Et₃SiH in dichloromethane (1.0 mL). ^bYield of isolated, purified product. ^c0.2 equiv of **3e** was used as catalyst.

and 1.5 equiv of triethylsilane was sufficient for a smooth reaction and, after treatment of the mixture with catalytic amounts of FeCl₃ in methanol to remove the silyl protecting group, alcohols **8** were obtained in high yield. Both electron-deficient and electron-rich aryl ketones were compatible with the reduction conditions (entries 1–4). In addition, fused aromatic and heteroaromatic substituents had no negative influence (entries 5 and 7). A secondary alkyl group was also nicely accommodated (entry 8).

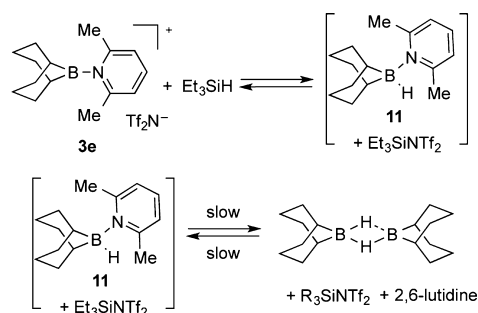
Although **3e** functioned as a catalyst for the hydrosilylation of ketones as described above, the reaction mechanism remained unclear. Several control experiments were carried out to provide mechanistic insight. First, the operation of Mechanism I (Scheme 2) was probed by the attempted

generation of intermediates **A** and **B** and subjecting them to the reaction conditions. However, the combination of **3e** and benzophenone in CH₂Cl₂ revealed no interaction by ¹¹B NMR spectroscopic analysis of the mixture.

The preparation of intermediate **B** was attempted by treatment of boronate **9a**¹⁴ with *N*-(trimethylsilyl)bis-(trifluoromethylsulfonyl)imide (TMSNTf₂) and 2,6-lutidine. However, **9a** was not converted to either silyl ether **7a** or over-reduced product **6a**; instead, it slowly converted to the corresponding lutidinium salt **10a**. In addition, **10a** was also observed in the presence of Et₃SiH (Scheme 3). These experiments suggest that the hydrosilylation reaction catalyzed by **3e** does not proceed via Mechanism I.¹⁵

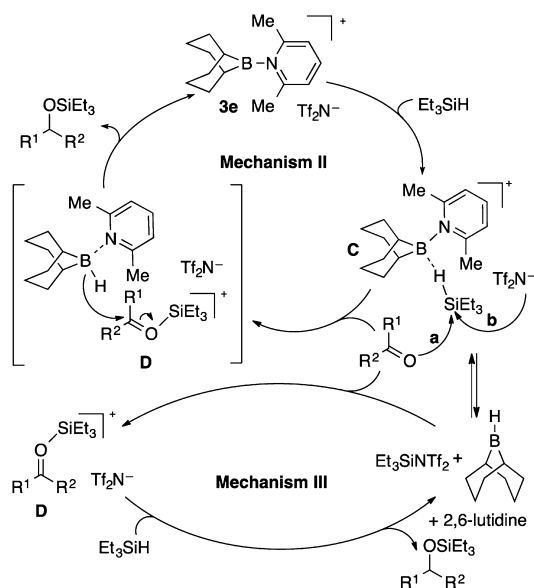
Scheme 3

In a different mechanism for the borenium ion catalyzed ketone hydrosilylation reaction, hydride abstraction from Et₃SiH by the borenium cation could generate 9-BBN-hydride-2,6-lutidine complex **11** as the active reducing reagent (Scheme 4). To investigate this possibility required the independent preparation of **11**. However, **11** did not form from 9-BBN-dimer and 2,6-lutidine.¹⁶ Instead, the existence of **11** was probed indirectly by a ¹¹B NMR experiment between **3e** and Et₃SiH. Although **11** was not detected via ¹¹B NMR spectroscopy, **3e** was slowly converted to 9-BBN-H dimer. Furthermore, on mixing 9-BBN-H dimer with TMSNTf₂ in the presence of 2,6-lutidine, 9-BBN-H dimer was also slowly converted to **3e**. Thus, the equilibrium between **3e** and 9-BBN-H dimer and the ability of **3e** to activate triethylsilane toward hydrogen transfer were confirmed (Scheme 4).

Scheme 4

With this information in hand, two plausible catalytic cycles can be constructed; one catalyzed by borenium ion **3e** (Mechanism II) and one catalyzed by Et₃SiNTf₂ (Mechanism III) (Scheme 5). Mechanism II (borenium ion activation of Et₃SiH followed by carbonyl activation via silyl transfer (path a) to form silyloxycarbenium ion **D** and consummated by hydride transfer to regenerate **3e**) finds excellent precedent in the Piers mechanism for (C₆F₅)₃B-catalyzed hydrosilylation of ketones.¹⁷ Mechanism III involves the Tf₂N[−]-assisted activation of Et₃SiH to form Et₃SiNTf₂ (path b) that in turn forms ion **D**, which is reduced by Et₃SiH.

Scheme 5



To differentiate between these two catalytic cycles, control experiments were conducted. Mechanism III posits that the reduction involves $\text{Et}_3\text{SiNTf}_2$ as the activator and Et_3SiH as the reducing agent but does not require 9-BBN-H. Accordingly, **5a**, Et_3SiH , and 0.1 equiv each of TMSNTf_2 and 2,6-lutidine were combined in CH_2Cl_2 at rt. The reaction required 6 h to reach full conversion and afforded **7a** in 92% yield. In contrast, an identical reaction containing 0.1 equiv of 9-BBN-H dimer was complete within 10 min to afford **7a** in 96% yield. Thus, although Mechanism III is viable, it does not compete with Mechanism II under the established reaction conditions.

In a final set of experiments, the stability of silyl ether **7a** in the presence of Et_3SiH and both catalysts was tested. Treatment of **7a** with **1** resulted in the formation of **6a** in 99% yield after 10 min. However, **7a** did not react with borenium cation **3e** even after 24 h. These results further support the operation of Mechanism II and also explain the formation of the reduced product **6a** in the reaction without 2,6-lutidine.

In conclusion, the interaction of various Lewis bases with 9-BBN- NTf_2 has been investigated. The stable borenium cation complex **3e** catalyzed the hydrosilylation of ketones. Mechanistic studies revealed that this reaction takes place via a hydride abstraction pathway similar to that for $(\text{C}_6\text{F}_5)_3\text{B}$ -catalyzed hydrosilylation of ketones. Further studies on this concept, including the development of other activation modes and asymmetric reactions, will be reported in due course.

■ ASSOCIATED CONTENT

● Supporting Information

Text, figures, and tables giving experimental procedures and characterization data. 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 interests.

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