Angewandte
Chemie

H_2 Activation

DOI: 10.1002/anie.200800935

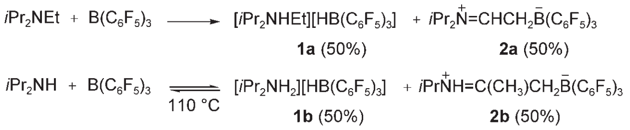
Facile Heterolytic H_2 Activation by Amines and $B(C_6F_5)_3$**

Victor Sumerin, Felix Schulz, Martin Nieger, Markku Leskelä, Timo Repo,* and Bernhard Rieger*

In industrially important reactions, such as hydroformylation and hydrogenation, H_2 gas serves as a reducing agent and/or a hydrogen-atom source.[1] Even small improvements in the efficiency of these reactions translate into large monetary savings. The key step in these transformations is the activation of H_2 at a transition metal. The nodal character of the energetically accessible d orbitals allows a transition-metal center to react directly with H_2 in a concerted reaction with a low activation barrier.[2] However, not only are transition-metal complexes expensive, but the complete removal of metal impurities from the reaction product is generally required in the production of pharmaceutical intermediates owing to toxicity concerns.[3]

Although countless synthetic complexes and enzymes with transition metals at their reactive core are well known, there are significantly fewer examples of H–H bond activation facilitated solely by a nonmetal.[4] Several reactions of H_2 with compounds containing main-group elements in low-temperature matrices have been reported;[5] however, H_2 activation at nonmetals under mild conditions had only been observed by Power and co-workers in product mixtures of digermenes, digermanes, and primary germanes,[6] until recently, when Stephan and co-workers reported the thermal liberation of H_2 from a phosphonium borate salt. The resulting product, $(C_6H_2Me_3)_2P(C_6F_4)B(C_6F_5)_2$, undergoes the addition of H_2 at 25 °C to reform the original salt.[7] In an analogous fashion, mixtures of sterically demanding phosphanes and boranes ("frustrated Lewis pairs")[8] can also cleave H_2 heterolytically to form phosphonium borates $[R_3PH][HBR'_3]$.[9] More recently, Bertrand and co-workers reported that selected organic carbenes are just nucleophilic enough to cleave H_2 and NH_3.[10] Herein we extend the family of "frustrated Lewis pairs" and demonstrate that not only bulky phosphanes and boranes or organic carbenes can cleave H_2, but also inexpensive, stable amines in combination with $B(C_6F_5)_3$.

Solutions of stoichiometric mixtures of diisopropylethylamine, diisopropylamine, or 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ in toluene were investigated by ^1H, ^{11}B, and ^{19}F NMR spectroscopy. The reactions of diisopropylethylamine and diisopropylamine with $B(C_6F_5)_3$ gave mixtures of the salt **1a** or **1b** and the zwitterion **2a** or **2b** as expected (Scheme 1);[11] however, no reaction was observed for 2,2,6,6-tetramethylpiperidine, a bulky secondary amine with no α hydrogen atoms. Whereas the reaction between diisopropylamine and $B(C_6F_5)_3$ is reversible at elevated temperature, the mixture of **1a** and **2a** from the reaction with diisopropylethylamine is thermally stable (Scheme 1).

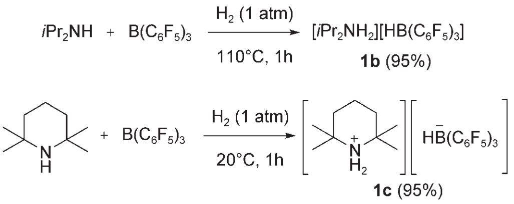


$$i\mathrm{Pr_2NEt} + \mathrm{B(C_6F_5)_3} \longrightarrow \underset{\mathbf{1a}\ (50\%)}{[i\mathrm{Pr_2NHEt}][\mathrm{HB(C_6F_5)_3}]} + \underset{\mathbf{2a}\ (50\%)}{i\mathrm{Pr_2\overset{+}{N}{=}CHCH_2\overset{-}{B}(C_6F_5)_3}}$$

$$i\mathrm{Pr_2NH} + \mathrm{B(C_6F_5)_3} \underset{110\ ^\circ\mathrm{C}}{\rightleftharpoons} \underset{\mathbf{1b}\ (50\%)}{[i\mathrm{Pr_2NH_2}][\mathrm{HB(C_6F_5)_3}]} + \underset{\mathbf{2b}\ (50\%)}{i\mathrm{Pr\overset{+}{N}H{=}C(CH_3)CH_2\overset{-}{B}(C_6F_5)_3}}$$

Scheme 1. Interactions between bulky amines and $B(C_6F_5)_3$.

Interestingly, the exposure of these amine–borane solutions to an atmosphere of H_2 (1 atm) at 20 °C resulted in quantitative formation of the product **1** (after evaporation of the solvent) only for 2,2,6,6-tetramethylpiperidine (Scheme 2).[12] Nonetheless, product **1b** was obtained in 95 % yield at the same H_2 pressure (1 atm) at 110 °C; the concentrations of the free amine and the borane are presumably too low at room temperature. In contrast, the reactions of various bulky amines with $B(C_6H_5)_3$ resulted in no product formation at either 20 or 110 °C under H_2 (1 atm). These results support the view that the reaction with H_2 occurs only under favorable steric and electronic conditions. Not only must steric influences be sufficient to preclude the formation of the amine–borane adducts, but the Lewis acidity



Scheme 2. Heterolytic cleavage of H_2 by bulky amines and $B(C_6F_5)_3$.

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[*] V. Sumerin, Dr. M. Nieger, Prof. Dr. M. Leskelä, Prof. Dr. T. Repo
Department of Chemistry
University of Helsinki
P.O. Box 55, 00014 Helsinki (Finland)
Fax: (+358) 9-191-50198
E-mail: timo.repo@helsinki.fi
F. Schulz, Prof. Dr. B. Rieger
Wacker-Lehrstuhl für Makromolekulare Chemie
Technische Universität München
Lichtenbergstrasse 4, 85747 Garching bei München (Germany)
Fax: (+49) 892-891-3562
E-mail: rieger@tum.de

[**] The authors are very grateful to Dr. S. Heikkinen for help with the interpretation of NMR spectra and thank the DAAD (D/05/51658) and the Academy of Finland (123248) for financial support.

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and basicity must be matched correctly in terms of cumulative strength for the successful heterolytic cleavage of H_2.

The NMR spectroscopic data for products **1b** and **1c** were consistent with the structural formula $[R_2NH_2][HB(C_6F_5)_3]$. The cations exhibit broad ^{1}H NMR resonances at 4.37 and 4.32 ppm (br, 2H, NH_2) for **1b** and **1c**, respectively. Furthermore, the anion exhibits an ^{1}H NMR resonance at 3.6 ppm (br q, BH) and a resonance in the ^{11}B NMR spectrum at −24 ppm with a B–H coupling of 80 Hz. Moreover, the difference in the chemical shifts $\Delta\delta_{p,m}$ of the F atoms in the *para* and *meta* positions of the C_6F_5 fragments is consistent with the presence of a four-coordinate anionic boron center.[13] An X-ray crystallographic study of **1c** (Figure 1)[14] confirmed the proposed structure and showed that the ions were connected only by a network of N–H···F and C–H···F hydrogen bonds. In the case of **1b**, X-ray structural analysis confirmed the structural formula, but poor crystal quality precluded a fully acceptable refinement. (As a result of nonmerohedral twinning, the hydrogen atoms could not be localized.)

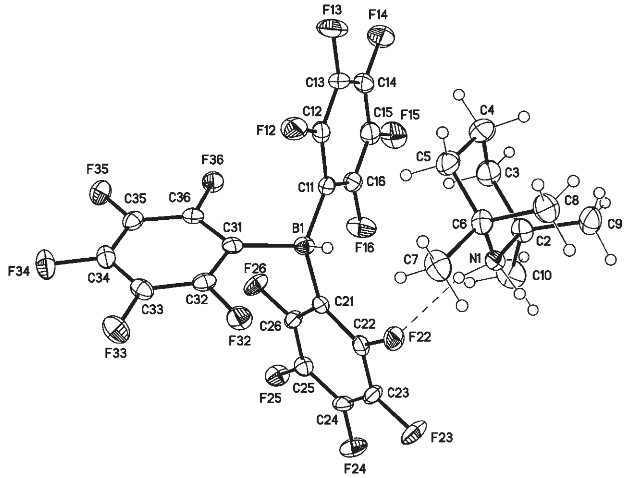
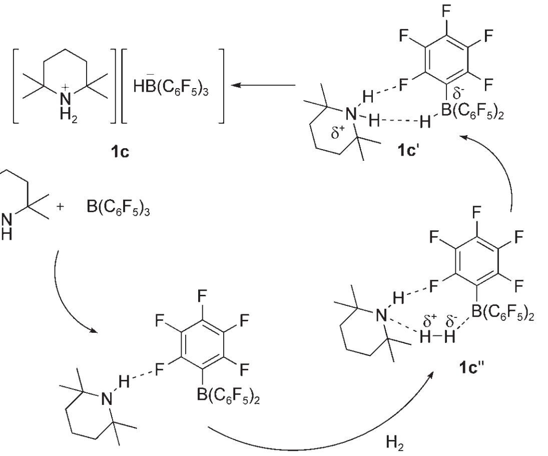


Figure 1. Molecular structure of **1c**. Thermal ellipsoids are drawn at the 50% probability level.

In an effort to garner mechanistic insight, equimolar mixtures of 2,2,6,6-tetramethylpiperidine and $B(C_6F_5)_3$ in $[D_6]$benzene under an atmosphere of H_2 were studied by ^{1}H, ^{11}B, and ^{19}F NMR spectroscopy. Solutions of the individual starting materials are colorless, whereas the mixtures are pale yellow in color. The yellow color is thought to be a result of an intermolecular N–H···F hydrogen-bonding interaction between the amine and the *ortho* F atoms of the arene rings.[15] The exposure of these amine–borane solutions to an atmosphere of H_2 (1 atm) at 20 °C resulted in the formation of the intermediate **1c′** (Scheme 3), which can be converted into the final product **1c** by evaporation of the solvent, by storing the solution at room temperature for one day, or by heating. NMR spectroscopic data for the intermediate **1c′** indicate a strong N–H···H–B hydrogen bond between the cation and the anion.[16,17]

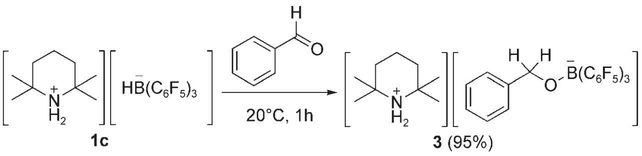
Lewis bases, including various amines, form van der Waals complexes with molecular hydrogen in argon matrices.[18]



Scheme 3. Possible mechanism for the heterolytic cleavage of H_2 by amines and $B(C_6F_5)_3$.

Such interactions are thought to lead to polarization of H_2 through an end-on base–H_2 interaction involving donation of the lone pair of electrons on the base into the σ* orbital of H_2. Furthermore, it is well known that $B(C_6F_5)_3$ is a strong enough Lewis acid to abstract a hydride ion from R_3SiH to afford $[R_3Si][HB(C_6F_5)_3]$.[19] By analogy with these phenomena, amines and $B(C_6F_5)_3$ could cleave H_2 by a concerted pathway (Scheme 3).[20] Further experimental and computational investigations should clarify this mechanism.

In preliminary experiments, benzaldehyde was reduced under mild conditions by **1c** as a stoichiometric reductant (Scheme 4). The NMR spectra of the product are consistent with the structural formula $[R_2NH_2][PhCH_2OB(C_6F_5)_3]$. Efforts towards the catalytic hydrogenation of carbonyl and related compounds and the design of catalysts with fine-tuned Lewis acidity at the boron center are in progress.



Scheme 4. Stoichiometric reduction of benzaldehyde with **1c**.

The facile heterolytic cleavage of H_2 under mild conditions was made possible by the cooperative action of Lewis acidic $B(C_6F_5)_3$ and Lewis basic amines. The successful reduction of benzaldehyde is encouraging for the development of amine–$B(C_6F_5)_3$ systems for catalytic hydrogenation. The reactivity and utility of this remarkably simple system for the activation of small molecules are the focus of ongoing studies.

Experimental Section

All experiments were performed on double-manifold H_2(Ar)/vacuum lines or in a glove box filled with argon (MBraun Labmaster 130). Solvents were dried by a solvent-purification system (MB SPS-800, MBraun). Hydrogen gas was purchased from AGA Ab and passed through a drying unit prior to use. Organic reagents were purchased from Acros Organics, Sigma-Aldrich, or Strem and purified by conventional methods.[21] NMR spectroscopic experiments were performed on a Bruker ARX-300 (^{1}H, ^{13}C, ^{19}F) or Bruker DPX-400 spectrometer (^{11}B). ^{1}H and ^{13}C NMR spectra are referenced to $SiMe_4$ on the basis of the residual solvent peak. ^{11}B and ^{19}F NMR spectra were referenced to the external standards $BF_3{\cdot}Et_2O$ (0 ppm) and CF_3CO_2H (−78.5 ppm relative to $CFCl_3$ at 0 ppm), respectively.

General procedure: $B(C_6F_5)_3$ (0.2 mmol, 102.4 mg), dry toluene (1 mL), and an amine (0.2 mmol) were placed in a 25 mL flame-dried Schlenk tube equipped with a stir bar, a teflon stopcock, and a glass stopper in a glove box (Glindemann sealing rings were used for conical joints instead of grease). The reaction mixture was degassed by freezing, evacuation, and thawing, and the Schlenk tube was refilled with H_2 (1 atm). The reaction mixture was stirred at 1000 rpm at a suitable temperature for 1 h. All volatiles were removed in vacuo to give the product as a white solid. Crystals suitable for X-ray diffraction were grown by covering a solution of the product in toluene with a layer of pentane at 20 °C.

The single-crystal X-ray diffraction study of **1c** was carried out on a Bruker-Nonius Kappa-CCD diffractometer at 123(2) K with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å).[14] The structure was solved by direct methods (SHELXS-97)[22] and full-matrix least-squares refinement on F^2 (SHELXL-97).[22] Hydrogen atoms were localized by difference Fourier synthesis and refined by using a riding model. The H atoms bonded to the B and N atoms were refined freely. The absolute structure could not be determined reliably (Flack parameter: $x = 0.1(4)$).[23] CCDC 678875 (**1c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: February 26, 2008
Published online: July 4, 2008

Keywords: amines · boranes · hydrogen · Lewis acids · Lewis bases

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[16] NMR spectroscopic data for **1c′** showed that the proton resonance shift of the NH_2 group was shifted to higher field (from 4.32 to 3.76 ppm), whereas that for BH was shifted downfield (from 3.74 to 4.24 ppm). The boron resonance was shifted downfield, and the ^{19}F signal for C_6F_5 was shifted upfield (*para* position: from −162.12 to −163.13 ppm; *meta* position: from −165.95 to −166.58 ppm). The coupling constants in the ^{19}F spectrum are identical for **1c′** and **1c**. a) E. W. Randall, C. A. Mitsopoulou in *Amino, Nitroso, Nitro and Related Groups* (Ed.: Z. Rappoport), Wiley-VCH, Weinheim, **1996**, pp. 295–335; b) T. E. Cole, "^{11}B NMR Chemical Shifts", **2008**; see: http://www.chemistry.sdsu.edu/research/BNMR/.

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