Hydrogen Activation

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Heterolytic Cleavage of Dihydrogen by “Frustrated Lewis Pairs” Comprising Bis(2,4,6-tris(trifluoromethyl)phenyl)borane and Amines: Stepwise versus Concerted Mechanism**

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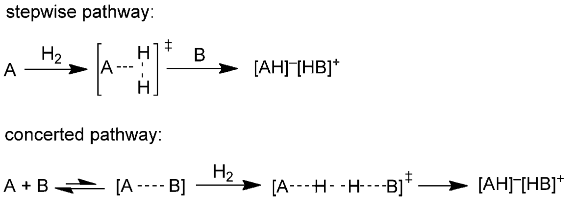
Dedicated to Professor Gerhard Erker on the occasion of his 65th birthday

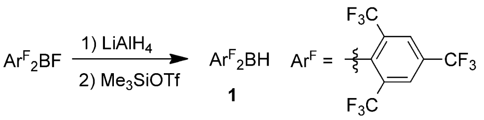
Recently, the chemistry of “frustrated Lewis pairs” (FLPs), which was introduced by the research groups of Stephan and Erker, has received considerable attention.[1,2] One of the most remarkable applications of FLPs is in the heterolytic activation of H_2 without the involvement of transition-metals. A variety of FLP systems have been shown to activate H_2 under mild conditions,[3] and have been applied as catalysts in metal-free hydrogenation reactions.[4] By analogy to the transition metal chemistry, it was originally proposed by Stephan and co-workers that the activation of H_2 is a stepwise process, in which H_2 is initially activated by the Lewis acid, followed by proton transfer to the Lewis base (Scheme 1).[1,3a]



Scheme 1. Proposed reaction pathways for FLP-mediated activation of H_2 (A: Lewis acid; B: Lewis base).

However, theoretical studies suggest that the stepwise activation pathway for $B(C_6F_5)_3$/Lewis base or other related FLP systems is unlikely, because of a prohibitively high energy barrier.[3d,5,6,7] These calculations indicated that H_2 is activated in a synergistic way when interacting with both the Lewis acid and the Lewis base. As all these studies on the mechanism of H_2 activation have been limited to fluoroarylborane-based FLPs, it is interesting to extend the Lewis acid partner in a FLP to “non-C_6F_5”-substituted boranes, which could lead to unique reaction pathways. Herein, we describe a novel FLP system formed by bis(2,4,6-tris(trifluoromethyl)-phenyl)borane (**1**) and amines. Our studies of the mechanism of the reaction show that the H_2 activation process can undergo either stepwise or concerted pathways, depending on the Lewis base partner.

To synthesize **1**, we started from the known compound $Ar^F{}_2BF$ (Ar^F = 2,4,6-tris(trifluoromethyl)phenyl).[8] Treatment of $Ar^F{}_2BF$ with excess $LiAlH_4$ in diethyl ether afforded lithium dihydridoborate $Li^+[Ar^F{}_2BH_2]^-$, which was then treated with Me_3SiOTf to give the target compound **1** in 71% yield (Scheme 2). The ^1H NMR spectrum of **1** showed a broad singlet at $\delta = 3.53$ ppm, which was assigned to the BH moiety. The *ortho*-CF_3 group of Ar^F in **1** appeared as a doublet in the ^{19}F NMR spectrum ($\delta = -56.7$ ppm, $J = 4.7$ Hz), as a result of coupling with the hydrogen atom on the boron center. The signal for the *para*-CF_3 group of Ar^F appeared as a singlet at $\delta = -63.3$ ppm. A broad singlet was detected at $\delta = 64.5$ ppm in the ^{11}B NMR spectrum of **1**, which suggests that **1** exists as a monomer in solution. This is in contrast with the closely related dimesitylborane (Mes_2BH), which exists as a mixture of dimers and monomers in solution.[9] To evaluate the Lewis acidity of **1**, we employed the Guttmann–Beckett method. This method is based on the change in the ^{31}P NMR chemical shift of Et_3PO upon coordination to Lewis acids.[10] We found the $\Delta\delta$ value for **1** was 32.7 ppm. For comparison, the $\Delta\delta$ value for $B(C_6F_5)_3$ was 30.1 ppm. These results suggest that **1** is slightly more acidic than $B(C_6F_5)_3$ in C_6D_6.



Scheme 2. Synthesis of borane **1**. Tf = trifluoromethanesulfonyl

Although **1** does not react with H_2 in C_6D_6, the deuterium-substituted analogue $Ar^F{}_2BD$ undergoes H/D exchange with H_2 (4 bar) at 50 °C, as indicated by the changes in the ^{19}F NMR spectra over time (Figure 1). A similar H/D

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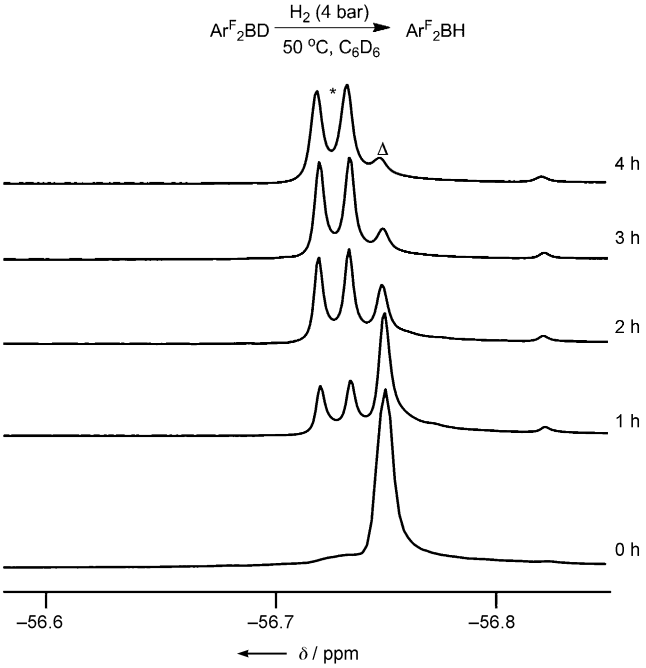


Figure 1. ^{19}F NMR spectra of the reaction of $Ar^F{}_2BD$ with H_2 (4 bar) at 50 °C in C_6D_6 over time. *: *ortho*-CF_3 of $Ar^F{}_2BH$, Δ: *ortho*-CF_3 of $Ar^F{}_2BD$.

exchange has been reported for boron compounds, such as B_2H_6[11,12] and F_2BH.[13] Nevertheless, such an observation is unprecedented for arylboron compounds. This H/D exchange reaction suggests that H_2 can coordinate to $Ar^F{}_2BD$ to form the adduct $Ar^F{}_2BD{\cdot}H_2$, which can then undergo bond-to-bond rearrangement to form $Ar^F{}_2BH$ and HD.

When we investigated the mechanism of this H/D exchange reaction by DFT (M06-2X) calculations,[14] we found the η^2-$H_2{\cdot}B(C_6F_5)_3$ adduct **2** to be an intermediate in the reaction pathway (Figure 2).[15] The intermediate **2** is 13.2 kcal mol^{-1} (ΔE_0 at 0 K with zero-point vibrational energy correction) above free **1** and H_2, which is only 0.3 kcal mol^{-1} lower than the first transition state **TS1**, and implies that **2** must be highly reactive. It is noteworthy that a similar, side-on H_2 adduct was proposed as the intermediate in the reaction between pentaarylborole and H_2.[16] In the calculated structure of **2**, the B···H(H_2) distances are 1.43 Å and 1.42 Å. Furthermore the H–H bond is elongated to 0.79 Å, which indicates significant H–H bond activation. This was also corroborated by Natural Bond Orbital analysis, which showed that the H–H bond order is only 0.55. There were two noncovalent interactions between the hydrogen atom of H_2 and a fluorine atom of the *ortho*-CF_3 group of Ar^F (2.03 Å and 2.16 Å), which implies that the Ar^F substituents might play an important role in stabilizing **2**. The second transition state **TS2** is 18.0 kcal mol^{-1} above free **1** and H_2, which is in agreement with our finding that the H/D exchange takes place at 50 °C.

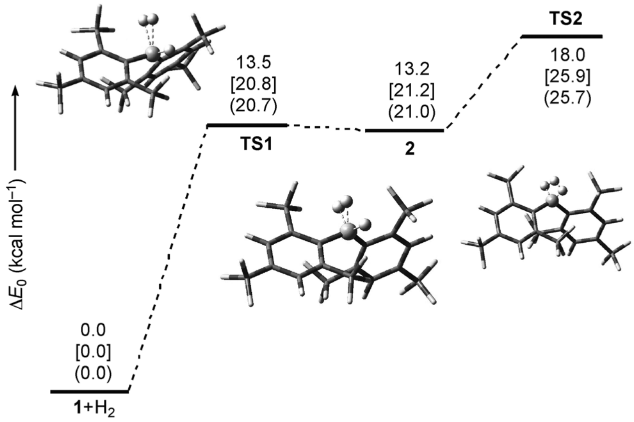
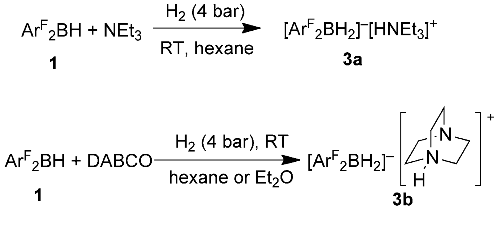


Figure 2. The energy profile for the reaction of $Ar^F{}_2BH$ with H_2. The values stated correspond to ΔE_0 (kcal mol^{-1}), ΔG in the gas phase (in square brackets, kcal mol^{-1}, 298 K), and ΔG in benzene solution (in round brackets, kcal mol^{-1}, 298 K).[17]

The ^1H NMR, ^{19}F NMR, and ^{11}B NMR spectra obtained upon mixing **1** with a stoichiometric amount of NEt_3 or 1,4-diazabicyclo[2.2.2]octane (DABCO) in C_6D_6 at room temperature, were almost the same, which suggests an FLP is formed between **1** and NEt_3 or **1** and DABCO. As $B(C_6F_5)_3$ and DABCO form a classical Lewis adduct in C_6D_6,[18] **1** appears to be more sterically hindered than $B(C_6F_5)_3$, even though it only contains two aryl substituents.

The 1:1 mixture of **1** and NEt_3 reacted smoothly with H_2 (4 bar) at room temperature in hexane. After stirring the reaction mixture for 24 h, the ammonium/dihydridoborate salt **3a** was isolated in 82 % yield (Scheme 3). In the ^1H NMR spectrum of **3a** in C_6D_6, the signal assigned to the NH moiety appeared at $\delta = 6.50$ ppm as a broad singlet, and the BH_2 signal appeared at $\delta = 3.00$ ppm as a 1:1:1:1 quartet. A triplet ($J = 72$ Hz) was detected at $\delta = -23.9$ ppm in the ^{11}B NMR spectrum, which confirmed the existence of a dihydridoborate anion. Compound **3a** was characterized by single-crystal X-ray analysis (Figure 3).[19] In the solid-state structure, the N–H···H–B interaction between the ammonium cation and the dihydridoborate anion is short. The H···H distance of 1.67 Å is among the shortest that have been reported for such a H–H bond.[20]



Scheme 3. Synthesis of **3a** and **3b**.

The reaction between **1**/DABCO and H_2 appeared to be much faster than the reaction between **1**/NEt_3 and H_2. When the 1:1 mixture of **1** and DABCO in hexane was treated with H_2 (4 bar) at room temperature both **1** and DABCO were consumed within 30 min, and the ammonium/dihydridoborate salt **3b** was isolated in 84 % yield (Scheme 3). Moreover, the reaction between **1**/DABCO and H_2 in diethyl ether gave compound **3b** in 89 % yield after 24 h. This result suggests that the Lewis acidity of **1** remains unquenched in diethyl ether, because of the bulkiness of **1**. To our knowledge, this is

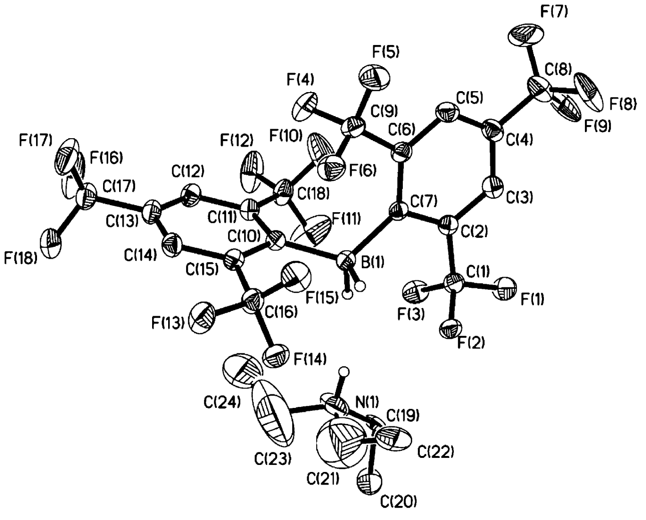


Figure 3. ORTEP plot of the molecular structure of **3a** with the thermal ellipsoids set at the 30% probability level. Hydrogen atoms (except BH_2 and NH) are omitted for clarity.

the first time that an ethereal solvent has been applied in a metal-free activation of H_2. In a preliminary study, the FLP system of **1**/DABCO was employed as a metal-free catalyst for enamine hydrogenation. At 50°C with H_2 (4 bar) and 20 mol% **1**/DABCO in C_6D_6, 1-cyclohex-1-enylpiperidine was quantitatively reduced to 1-cyclohexylpiperidine in 24 h (the yield of this reaction as assessed by NMR spectroscopy was greater than 95%).

To obtain deeper insight into the mechanism of H_2 activation with **1** and NEt_3 or DABCO, we explored the possible pathways for the reaction by DFT (M06-2X) calculations. Our calculations on the reaction between H_2 and **1**/NEt_3 indicate that H_2 coordinates to **1** to form the intermediate **4a**, which is then deprotonated by the Lewis base NEt_3 to yield **3a** (Figure 4). The coordination of H_2 to **1** is the rate-determining step, and the transition state is higher in energy than the **1**/NEt_3/H_2 adduct by 11.5 kcal mol^{-1}. In the transition state **TS1**, the H–H bond is slightly elongated to 0.75 Å and the B···H(H_2) distances are 1.81 Å and 1.77 Å, which reveals there is an interaction between **1** and H_2 (the B···H bond orders are 0.19 and 0.18). In contrast, the N···H(H_2) distances are 3.71 Å and 4.35 Å. These distances are larger than the sum of the van der Waals radii of hydrogen (1.20 Å) and nitrogen atoms (1.55 Å), which indicates that NEt_3 mainly behaves as a bystander in **TS1**.[21] This is in sharp contrast to the transition state of a synergistic H_2 activation process, in which both the Lewis acid and Lewis base interact with H_2.[5–7] The calculated structure of **4a** is similar to that of **2**. The H–H distance is elongated to 0.79 Å, and the B···H(H_2) distances are 1.39 Å and 1.50 Å (the bond orders for B···H are 0.41 and 0.33, respectively). We also noted a noncovalent interaction between the nitrogen atom of NEt_3 and a hydrogen atom of H_2 (the N···H distance is 2.22 Å and the bond order is 0.04). Such an interaction stabilizes the intermediate **4a** substantially, which is 3.0 kcal mol^{-1} above the free reactants. The subsequent deprotonation process was found to occur with a very low energy barrier ($\Delta E_0 = 0.2$ kcal mol^{-1}), which implies that the proton-transfer step is very fast, and that the intermediate **4a** can only exist under steady-state conditions.[22] The calculated structure of **3a** agrees relatively well with the experimental data, and it is lower in energy by 21.5 kcal mol^{-1} (ΔE_0) than the free reactants. This calculation suggests the reaction is exothermic. To our knowledge, **1**/NEt_3 represents the first FLP that can activate H_2 in a stepwise mechanism, which closely resembles the mechanisms of heterolytic activation of H_2 by transition metals.[23]

For the reaction between H_2 and **1**/DABCO, H_2 is not activated in a stepwise manner, but in an unsymmetrical and concerted way. Through only one transition state, the H–H bond is cleaved directly by **1** and DABCO (Figure 5). The calculated barrier is 9.7 kcal mol^{-1}, which is 1.8 kcal mol^{-1} lower than the **1**/NEt_3 system. This value agrees with the experimental finding that H_2 reacts faster with **1**/DABCO than with **1**/NEt_3. In the transition state, the H–H bond length

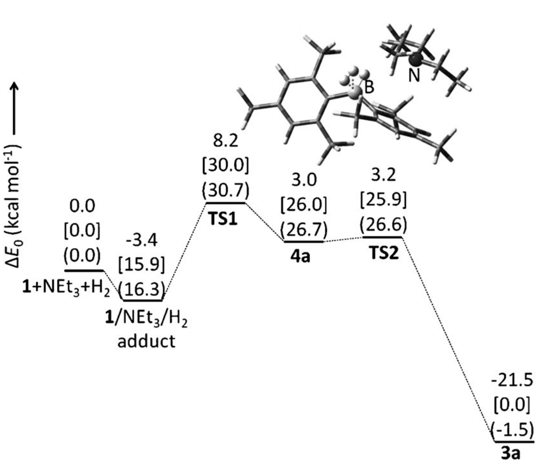


Figure 4. The calculated structure of **TS1** and the energy profile for the reaction between **1**/NEt_3 and H_2. The values correspond to ΔE_0 (kcal mol^{-1}), ΔG in gas phase (in square brackets, 298 K, kcal mol^{-1}), and ΔG in hexane solution (in round brackets, 298 K, kcal mol^{-1}).

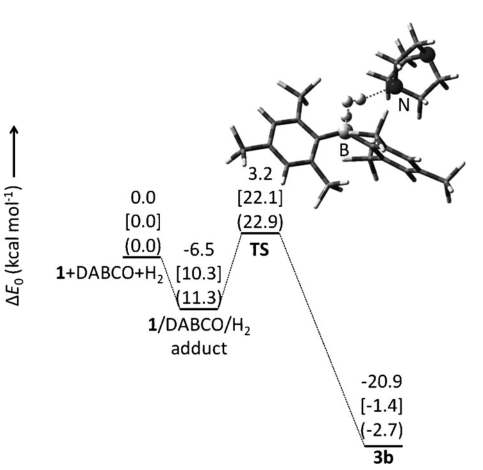


Figure 5. The calculated structure of **TS** and the energy profile for the reaction between **1**/DABCO and H_2. The values correspond to ΔE_0 (kcal mol^{-1}), ΔG in gas phase (in square brackets, 298 K, kcal mol^{-1}), and ΔG in hexane solution (in round brackets, 298 K, kcal mol^{-1}).

is 0.75 Å, and the B···H and N···H distances are 1.99 Å and 2.10 Å, respectively. These distances indicate that both of **1** and DABCO interact with H_2 (the bond orders of B···H and N···H are 0.12 and 0.03, respectively). The H_2 molecule does not lie in the boron–nitrogen axis, as indicated by the B−H−H angle of 85°.

The difference in the H_2 activation processes could be due to the different steric demand of the Lewis bases in the reaction. In the case of **1**/NEt_3, the steric repulsion between the ethyl group of NEt_3 and CF_3 group of Ar^F in **1** may prohibit the interaction between NEt_3 and H_2 in the transition state, thus resulting in a stepwise pathway of activation. In contrast, for the "less frustrated" **1**/DABCO, the smaller steric bulk around the nitrogen center allows a comparably short interaction between DABCO and H_2 in the transition state, which leads to a concerted mechanism of activation. To further support our hypothesis, we carried out a calculation for the reaction pathway of the **1**/NMe_3/H_2 system.[18] As predicted, the activation process for this FLP with a small Lewis base appears to be concerted, as suggested by the distances of N···H (2.10 Å) and B···H (1.99 Å) in the transition state.

In summary, bis(2,4,6-tris(trifluoromethyl)phenyl)borane was successfully synthesized and the combination of this borane with NEt_3 or DABCO activated H_2 at ambient temperature. Our mechanistic studies suggested that **1**/NEt_3 activates H_2 in a stepwise manner. On the other hand, we found that H_2 is activated in a concerted way with the **1**/DABCO system. The dramatic change in the reaction mechanism can be attributed to the different steric demand of the Lewis bases. Our results could provide important new insight into the mechanism of FLP-mediated activation of H_2. Further exploration of the chemistry of FLPs containing "non-C_6F_5" substituents is currently underway.

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[18] See the Supporting Information.

[19] Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center: CCDC 832936 (**3a**) and 832937 (**3b**) contain the

supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

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[21] The only noticeable interaction between **1** and NEt_3 in **TS1** is the contact between the CF_3 of Ar^F and the CH_3 moiety of the Et groups. The shortest F⋯H distance is 2.52 Å, slightly smaller than the sum of the van der Waals radii of hydrogen (1.20 Å) and fluorine atoms (1.47 Å).

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