Dihydrogen Activation with "Frustrated" Lewis Acid-Base Pairs

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Although transition metals have long been known to activate H_2 under ambient conditions, the discovery in 2006 of similar reactivity in main molecules surprised chemists.[1] These molecules combine Lewis acid and Lewis base moieties, both being sterically hindered so as to prevent acid-base adduct formation.[2] Stephan and coworkers term such molecules "frustrated Lewis pairs".[1] Despite the initial surprise, this discovery can be readily rationalized. In oxidative additions of H_2, the metal center acts both as a π-donor populating the σ^* orbital of H_2, and as a σ-acceptor receiving the σ electrons of the H_2 bond.[3] In heterolytic cleavage these two functions reside on the separate components of a Lewis acid-base pair.[3] Hydrogenases provide a well known example of such reactivity, in which a transition metal acts as the Lewis acid and a nearby ligand such as an amine serves as the Lewis base.[3] The discovery in 2006 demonstrated that H_2 can be activated by molecules in which both the Lewis acid and the Lewis base are main group compounds.

Stephan and coworkers initially attempted to form an adduct between $B(C_6F_5)_3$ and dimesitylphosphine, mes_2PH, where mes = 2,4,6-trimethylphenyl.[1] Instead, the phosphine attacked at the *para*-position of a perfluorophenyl substituent of the borane. Rapid migration of the fluoride to the boron center afforded compound **1** (Figure 1A). Treatment of **1** with Me_2SiHCl provided the zwitterionic phosphonium borate **2**. Heating **2** above 100 °C released H_2; most notably, exposure of the new phosphine-borane **3** to H_2 at room temperature cleaved H_2 to regenerate species **2**. The reaction was demonstrated to involve direct participation of dihydrogen by showing that exposure of **3** to D_2 generated the dideuterated species **d_2-2**. Further mechanistic studies revealed that heating **2** to produce **3** follows first order kinetics, strongly suggesting that the rate-determining step for H_2 loss is unimolecular. In contrast to this finding, heating an equimolar ratio of **2** and **d_2-2** releases a statistical distribution of H_2, HD, and D_2, demonstrating that an intermolecular scrambling occurs. Despite the kinetic data, subsequent theoretical studies of the reaction of **3** with H_2 supported a termolecular mechanism, in which two molecules of **3** form a head-to-tail encounter complex, which heterolytically cleaves H_2 via concerted electron donation from the H_2 σ bond to the vacant p orbital of B on one molecule and from the lone pair of P on a second molecule to the H_2 σ^* orbital.[4] Later studies of the system demonstrated that both **2** and **3** are active catalysts for hydrogenation of bulky imines and nitriles,[5] although the rates are slow compared with those of active transition metal catalysts.

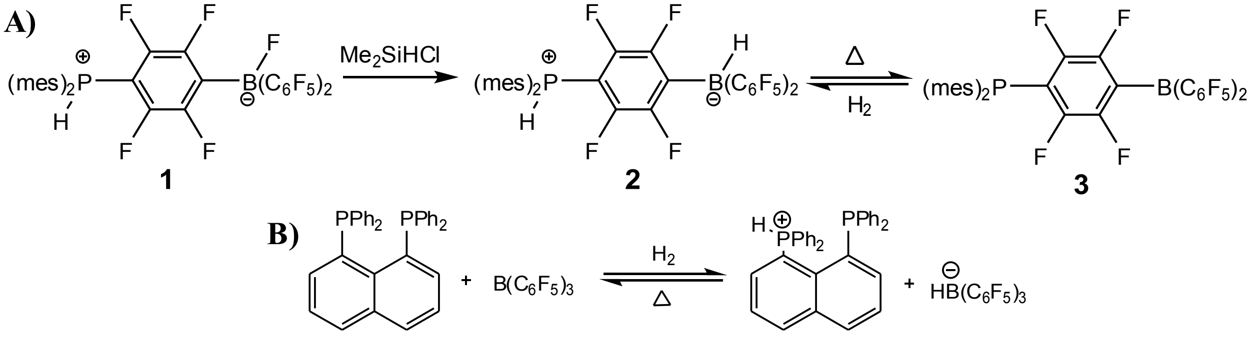

Figure 1

Subsequent investigations by Stephan and coworkers demonstrated that H_2 activation could also be achieved with phosphines and boranes not tethered to one another. A key characteristic of these two-component systems is steric frustration, in which the use of bulky tertiary phosphines such as tri-tert-butylphosphine prevents both nucleophilic attack on the borane and phosphine-borane adduct formation, but still allows activation of H_2 to form phosphonium borate salts.[6] Interestingly, the resultant phosphonium borate salts do not release H_2, even when heated to 150 °C. If triphenylborane is used in place of the more electron withdrawing tris(perfluorophenyl)borane, H_2 is still activated but the yield of the phosphonium borate salt is smaller. Lewis acid-base pairs capable of forming adducts, such as $P(Me)_3$ and $B(C_6F_5)_3$, are unable to activate H_2 when combined. Finally, sterically bulky Lewis pairs in which the substituents on the B and P are the same (either both strongly electron-donating mesityl groups, or both strongly electron-withdrawing perfluorophenyl groups) neither form an adduct nor cleave H_2. Thus, in untethered systems, both steric bulk and electronic contrast must be large to activate H_2. Theoretical studies of these two-component frustrated systems again favor a concerted mechanism for heterolytic cleavage over initial association of H_2 with either the phosphine or the borane.[7]

Several other Lewis acid-base pairs can also activate H_2, and the most interesting of these do so reversibly. 1,8-Bis(diphenylphospino)naphthalene forms a frustrated Lewis pair with $B(C_6F_5)_3$; the pair readily adds H_2, releasing it when heated to 60 °C (Figure 1B). This Lewis acid-base pair is able to catalyze the hydrogenation of silyl enol ethers.[8] The combination of bulky secondary amines and $B(C_6F_5)_3$ can also activate H_2,[9] occasionally even when an adduct is formed, presumably because the adduct and free acid-base pair are in equilibrium.[10] Bulky aldimines, ketimines, and aziridines can be hydrogenated catalytically with $B(C_6F_5)_3$ alone, as these substrates themselves form frustrated Lewis pairs with $B(C_6F_5)_3$.[11] Acting on the insight that carbenes act in other systems as Lewis bases, two research groups reported simultaneously the reaction of frustrated N-heterocyclic carbene-$B(C_6F_5)_3$ pairs to cleave H_2 and NH_3.[12,13]

Because frustrated Lewis pairs represent the analog of heterolytic cleavage of H_2 at metal centers with a nearby Lewis base, the question might arise: Does homolytic cleavage at a single metal center also have a main group analog? In striking similarity to the activation of H_2 at transition metal centers, Bertrand and coworkers have demonstrated that certain singlet (alkyl)(amino)carbenes can activate H_2 without a separate Lewis acid partner.[14] In contrast to metal centers, however, theory and experiment together suggest that the activation step is not an oxidative addition, but rather the filled σ orbital of the carbene polarizes H_2 and then the hydridic end attacks the orthogonal vacant orbital on the carbene, generating the product in a heterolytic manner. The (alkyl)(amino)carbenes can also cleave the N-H bond in NH_3, a reaction that is rare for transition metals. This finding provides further support for the heterolytic mechanism of H_2 activation, and suggests that diaminocarbenes in combination with boranes react with H_2 by a similar mechanism, albeit with the borane, rather than the carbene, serving as the Lewis acid.

Although the available data do not yet allow conclusive identification of a mechanism of H_2 activation by all frustrated Lewis pairs, several lessons are clear. First, a whole range of main group compounds, in combination or even alone, react with H_2. Second, by drawing analogy to the orbitals on transition metal centers, we can readily rationalize the observed reactivity. Third, the combined acidity and basicity must exceed a certain threshold before H_2 activation becomes favorable. Finally, several indications exist that the stronger of the Lewis acid and base determines whether the reaction begins with nucleophilic or electrophilic attack.

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