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 \(\pi\)-donor populating the \(\sigma^*\) orbital of H\(_2\), and as a \(\sigma\)-acceptor receiving the \(\sigma\) electrons of the H\(_2\) bond.\(^3\) In heterolytic cleavage these two functions reside on the separate components of a Lewis acid-base pair.\(^5\) 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\(_6\)F\(_5\))\(_3\) and dimesitylphosphine, mes\(_2\)PH, where mes = 2,4,6-trimethylphenyl.\(^1\) Instead, the phosphine attacked at the \textit{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\(_2\)SiHCl provided the zwitterionic phosphonium borate 2. Heating 2 above 100 °C released H\(_2\); most notably, exposure of the new phosphate-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\(_2\) \(\sigma\) 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\(_2\) \(\sigma^*\) 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](image-url)
Subsequent investigations by Stephan and coworkers demonstrated that H₂ 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 H₂ to form phosphonium borate salts. Interestingly, the resultant phosphonium borate salts do not release H₂, even when heated to 150 °C. If triphenylborane is used in place of the more electron withdrawing tris(perfluorophenyl)borane, H₂ 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(C₆F₅)₃, are unable to activate H₂ 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 H₂. Thus, in untethered systems, both steric bulk and electronic contrast must be large to activate H₂. Theoretical studies of these two-component frustrated systems again favor a concerted mechanism for heterolytic cleavage over initial association of H₂ with either the phosphine or the borane.

Several other Lewis acid-base pairs can also activate H₂, and the most interesting of these do so reversibly. 1,8-Bis(diphenylphosphino)naphthalene forms a frustrated Lewis pair with B(C₆F₅)₃; the pair readily adds H₂, releasing it when heated to 60 °C (Figure 1B). This Lewis acid-base pair is able to catalyze the hydrogenation of silyl enol ethers. The combination of bulky secondary amines and B(C₆F₅)₃ can also activate H₂ occasionally even when an adduct is formed, presumably because the adduct and free acid-base pair are in equilibrium. Bulky aldimines, ketimines, and aziridines can be hydrogenated catalytically with B(C₆F₅)₃ alone, as these substrates themselves form frustrated Lewis pairs with B(C₆F₅)₃. 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(C₆F₅)₃ pairs to cleave H₂ and NH₃.

Because frustrated Lewis pairs represent the analog of heterolytic cleavage of H₂ 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 H₂ at transition metal centers, Bertrand and coworkers have demonstrated that certain singlet (alkyl)(amino)carbenes can activate H₂ without a separate Lewis acid partner. 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 H₂ 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 NH₃, a reaction that is rare for transition metals. This finding provides further support for the heterolytic mechanism of H₂ activation, and suggests that diaminocarbenes in combination with boranes react with H₂ 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 H₂ 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 H₂. 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 H₂ 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.


8. Wang, H.; Frölich, R.; Kehr, G.; Erker, G. "Heterolytic dihydrogen activation with the 1,8-bis(diphenylphosphino)naphthalene/B(C$_6$F$_5$)$_3$ pair and its application for metal-free catalytic hydrogenation of silyl enol ethers," *Chem. Commun.* **2008**, *5966-5968*.


