H_2 Activation

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Heterolytic H_2 Activation by Nonmetals

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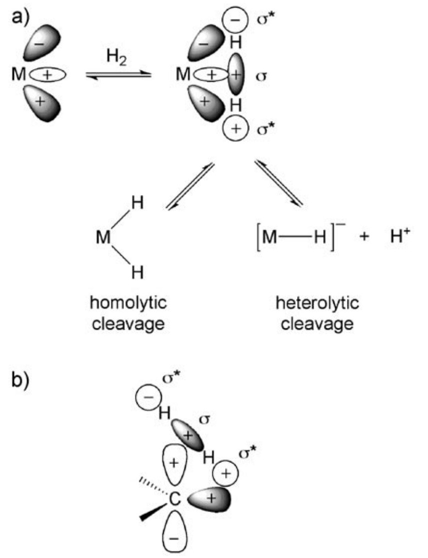
Chemical processes for the homogeneous activation of small molecules and enthalpically strong bonds are dominated by those mediated at transition-metal centers. Countless synthetic and enzymatic complexes containing transition metals at their reactive core are known for life-sustaining or industrially essential reaction classes, such as hydrogenations, oxidations, reductions, and polymerizations.[1] The versatility of transition metals in this regard has its root in the availability of d orbitals that, owing to the tuneability in electron configuration and oxidation state, provide a wide variety of filled/vacant orbital combinations for synergic activation of chemical bonds.

For example, in the well-studied example of metal-mediated oxidative addition of molecular hydrogen (H_2), bond activation is facilitated by interaction of the σ-bonding orbital of H_2 with a vacant d orbital on the metal (Scheme 1 a). Additionally, back donation from filled metal d orbitals into the σ*-antibonding orbital of H_2 further weakens the H−H bond.[2] These (η^2)(H_2)–metal σ complexes are precursors to bond cleavage, which can occur either homolytically to form a new dihydride species or heterolytically by proton transfer to a proximal base.

While bond activation by transition-metal complexes has enormous utility, there are nonetheless instances where they are either inefficient at or incapable of producing desired bond-cleavage reactions. Notably, Lewis bases will often bind strongly to empty orbitals on electrophilic metals, making bond activation difficult.[3] Furthermore, many transition-metal complexes are difficult to synthesize, economically prohibitive, or undesirable because of environmental concerns.

Bond activations by more benign main-group compounds are therefore of considerable interest. While nonmetallic main-group compounds are ubiquitous as reaction substrates, ligands, cocatalysts, and materials, there are significantly fewer examples of bond activations facilitated solely by a nonmetal. In particular, H_2 activation at nonmetals under ambient conditions has, until recently, only been observed by a stable germyne complex, as reported by Power and coworkers.[4,5] However, recent reports from the groups of Bertrand and Stephan signal a new epoch in the application of simple nonmetallic complexes in strong-bond activation.



Scheme 1. Orbital representation of H_2 activation by a) transition metals, and b) singlet carbenes (adapted from Ref. [6]).

Recognizing that carbenes are isolobal to many bond-activating transition-metal fragments, Bertrand and co-workers have demonstrated that H_2 can be activated by stable singlet carbenes.[6] While diamino carbenes **1** (N-heterocyclic carbene, NHC) and **2** do not react with H_2,[7] both cyclic and acyclic alkyl amino carbenes **3**[8] and **4**[9] cleave H_2, forming alkane products **5** and **6** (Scheme 2).

Singlet carbenes have a vacant orbital and an electron lone pair in a nonbonding orbital[10] which are oriented such that an incoming H_2 molecule can be synergically activated in a manner similar to transition-metal complexes (Scheme 1 b). The H_2 σ-bonding orbital donates into the vacant orbital of the carbene and there remains sufficient overlap so that the carbene lone pair can populate the H_2 antibonding σ* orbital, consequently weakening the bond so that cleavage occurs. A key insight, bolstered by computational investigations, was that the higher-lying highest-occupied molecular orbital (HOMO) and the smaller singlet/triplet energy gap in the amino alkyl carbenes compared to that of the NHC renders the amino alkyl carbene subclass more reactive towards the H−H bond than NHCs.

In contrast to metal-based oxidative addition, carbene-mediated H_2 activation is heterolytic in character; asymmetric

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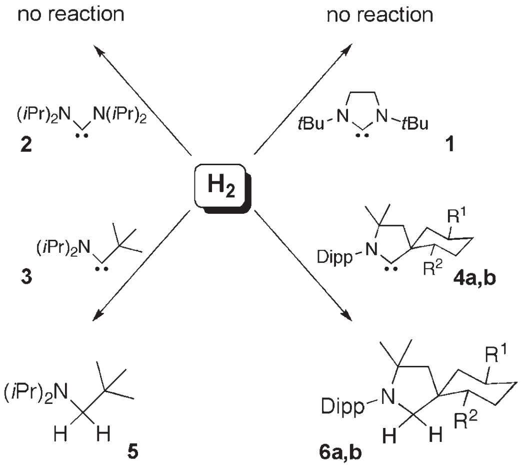
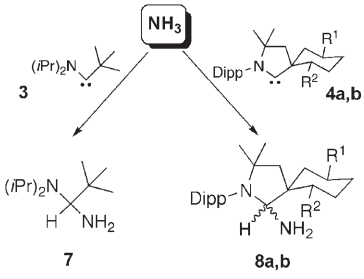


Scheme 2. H_2 activation by alkyl amino carbenes at 35 °C (ca. 30% yield for **5** and **6**). Dipp: 2,6-$i\mathrm{Pr}_2C_6H_3$; **4a**, **6a**: $R^1 = R^2 = H$; **4b**, **6b**: $R^1 = Me$, $R^2 = i\mathrm{Pr}$.

donation into the σ* orbital generates a hydridic hydrogen that accordingly nucleophilically attacks the positively polarized carbon center. Computations corroborated this method of H_2 activation, as the H–H bond in the transition state was elongated[11] and the hydrogen atoms were found at unequal distances from the carbene carbon atom, demonstrating polarization in the H_2 bond. The more distant and hydridic hydrogen atom in the transition state finally attacks at the carbene with stereochemical inversion at the carbon atom.

Even more impressively, Bertrand confirmed that carbenes **3** and **4** react rapidly with liquid ammonia forming the N–H activation products **7** and **8** (Scheme 3).[6] In these examples, it is believed that bond polarization in the transition state generates a hydrogen atom bearing a positive charge, which is bonded to the carbon atom, and an amide nitrogen atom that nucleophilically attacks the carbon atom. An advantage in using carbenes for small-molecule activation is thus exemplified; traditional transition-metal complexes will, with few exceptions,[12] bind NH_3 by the nitrogen lone-pair of electrons in Werner-type complexes and are thus unable to suitably align the NH unit for synergic bond cleavage.[3]



Scheme 3. Facile activation of liquid ammonia by alkyl amino carbenes at −78 °C (>90% yield for **7** and **8**). **4a**, **8a**: $R^1 = R^2 = H$; **4b**, **8b**: $R^1 = Me$, $R^2 = i\mathrm{Pr}$.

While the donor/acceptor character necessary to activate σ bonds is centered on the carbene carbon atom in the Bertand examples, Stephan and co-workers have demonstrated H_2 activation by nonmetals, under ambient conditions, using a Lewis acid–base strategy with what they term "frustrated Lewis pairs". It is well-known that the Lewis acid $B(C_6F_5)_3$ interacts with donor molecules, such as phosphines, to form Lewis acid–base adducts,[13] but when employing large-cone-angle phosphines, front strain destabilizes the putative adduct, opening up other reaction channels. For example, upon addition of $P(t\mathrm{Bu})_3$ or $P(C_6H_2Me_3)_3$ to a solution of $B(C_6F_5)_3$, only free phosphine and borane are detected spectroscopically; steric bulk prevents any Lewis acid–base interactions, even at −25 °C.[14] However, exposure of these "frustrated Lewis pairs" to one atmosphere of H_2 at room temperature cleanly generates the phosphonium hydridoborates **9** and **10** (Scheme 4a). It could be seen from crystallographic data that the PH and BH units are oriented towards one another, with a PH···HB separation of about 2.75 Å. Analogous reactions of PR_3 and $B(C_6F_5)_3$ with D_2 result in the isolation of $[R_3PD][DB(C_6F_5)_3]$, which confirms the hydrogen source is indeed H_2. As in the Bertrand chemistry, H_2 activation leading to phosphonium hydridoborates **9**–**11** is irreversible; even with heating to 150 °C, no loss of H_2 is detected.

a)

$$B(C_6F_5)_3 + PR_3 \xrightarrow[\text{1 atm, 25°C}]{H_2} [R_3PH][HB(C_6F_5)_3]$$

9: R = *t*Bu; **10:** R = $C_6H_2Me_3$

b)

$$BPh_3 + P(t\mathrm{Bu})_3 \xrightarrow[\text{1 atm, 25°C}]{H_2} \underset{\mathbf{11}}{[(t\mathrm{Bu})_3PH][HBPh_3]}$$

Scheme 4. Heterolytic cleavage of H_2 by "frustrated Lewis pair" phosphino boranes: a) with perfluorotriphenylborane, b) with triphenylborane.

Stephan and co-workers have tentatively proposed a mechanism of activation, wherein H_2 initially binds side-on to $B(C_6F_5)_3$, in a similar fashion to the initiation of H_2 oxidative addition by many transition-metal σ complexes. While no interactions were observed when $B(C_6F_5)_3$ was treated with four atmospheres of H_2, even at reduced temperatures of −80 °C, previous computations suggest that this mechanism is viable,[15] and silanes are proposed to interact with $B(C_6F_5)_3$ in a similar fashion.[16] While another plausible mechanism involves H_2 bond polarization by phosphine lone-pair attack into the σ* orbital, it is clear that further investigations are needed to elucidate the mechanism.

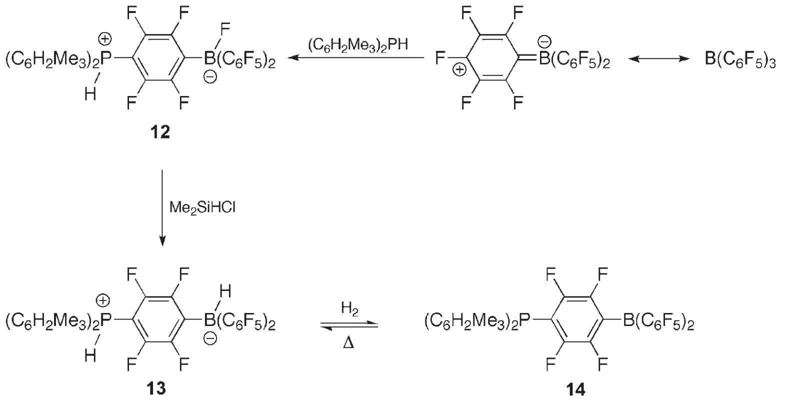
Interestingly, when BPh_3 is treated with $P(t\mathrm{Bu})_3$ and H_2, phosphonium hydridoborate **11** is produced (Scheme 4b), albeit slowly and in a reduced yield.[14] On the other hand, when less-bulky phosphines PPh_3 and PMe_3 are treated with $B(C_6F_5)_3$ in the presence of H_2, no cleavage occurs and in this case standard Lewis acid–base adducts are formed. These findings show the importance of the balance between steric and electronic features that consequently influence the ability of phosphine–borane pairs to heterolytically cleave H_2. Sufficient steric bulk is clearly necessary to ensure that adduct formation does not occur, or is at least reversible, and sufficient Lewis acidity in the borane is necessary to affect bond cleavage.

Perhaps most exciting is Stephan and co-workers' recent report of a phosphonium borate complex that exhibits a seemingly perfect balance of these qualities to afford reversible stoichiometric H_2 activation. In this study, when a secondary phosphine of moderate steric bulk, $(C_6H_2Me_3)_2PH$, is treated with $B(C_6F_5)_3$, *para*-nucleophilic aromatic substitution occurs to form zwitterion **12**, as shown in Scheme 5.[17] Further treatment of **12** with Me_2SiHCl promotes hydride–fluoride exchange at the borate center, producing phosphonium borate **13**, which is a unimolecular analogue of **9**–**11**. Zwitterion **13** has been fully characterized spectroscopically and crystographically and, unlike ion pairs **9**–**11**, it is both air- and moisture stable.

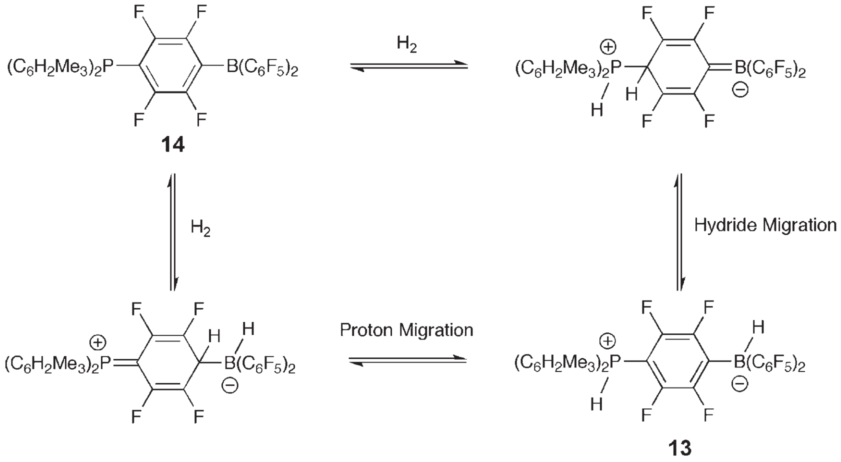
Phosphonium borate **13** is further distinguished from the aforementioned complexes in that it remarkably undergoes stoichiometric loss of H_2 when warmed to 100 °C in toluene. The resultant phosphino borane **14** can be isolated, and when subsequently exposed to one atmosphere of H_2 at room temperature, the parent phosphonium borate is cleanly regenerated, thus being the first example of reversible H_2 activation by a nonmetallic species.

While the mechanism of this reversible activation is as yet unknown, Stephan and co-workers speculate that H_2 uptake by phosphino borane **14** occurs heterolytically with initial H_2 activation at boron and the adjacent carbon, followed by proton migration to phosphorus (Scheme 6), analogous to the mechanism hypothesized for H_2 activation by bulky PR_3 and $B(C_6F_5)_3$. Alternatively, initial coordination could be at phosphorus with successive hydride migration to boron.

The ability of **13** to reversibly eliminate H_2 suggests that these types of compounds might be applicable as hydrogen-storage materials. While H_2 offers considerable potential as one piece of the solution to our increasing societal energy and environmental challenge, there remains a deficiency in the ability to efficiently and affordably store H_2 on a large, transportable scale. Baker and co-workers have investigated the use of H_3NBH_3 as a H_2 source;[18] with a storage capacity of 19.6 wt% H_2, ammonia–borane is viewed as a promising material for hydrogen storage. Unfortunately, attempts to inspire reversible elimination of H_2 from H_3NBH_3 have been largely unsuccessful. On the other hand, while Stephan's



Scheme 5. Synthesis of phosphonium borate **13**, capable of reversible loss of H_2.



Scheme 6. Possible mechanisms of reversible H_2 activation by phosphino boranes **14**.

phosphonium borate **13** binds less than 0.25 wt% H_2, the reversible nature of this activation suggests that greater understanding of these Lewis pairs could lead to practical hydrogen storage materials with a greater storage capacity.

Additionally, this reversible stoichiometric H_2 cleavage and the concept of "frustrated Lewis pairs" exemplifies the potential of nonmetallic species for more generalized small-molecule activation. For example, Stephan et al. have applied their phosphonium borates to the activation of olefins.[19] While this reaction is again stoichiometric, it is nonetheless surprising considering that neither free tertiary phosphines nor free tertiary boranes alone activate olefins. More recent work has impressively demonstrated the use of these "frustrated Lewis pairs" in catalytic applications. Phosphonium borate **13** catalytically reduces imines, nitriles and aziridines in the presence of H_2 to primary and secondary amines.[20] For example, the sterically encumbered imine *t*BuN=CHPh undergoes hydrogenation in one hour under one atmosphere of H_2 at 80°C in 79% yield. More hindered and electron deficient imines, such as $PhSO_2N{=}CHPh$, require more forcing conditions, and the reduction of this imine occurs at an elevated temperature of 120°C over 10.5 h. Preliminary mechanistic studies suggest that the imine is initially protonated by **13** to afford an iminium salt; subsequent nucleophilic attack by the resultant borohydride anion produces free amine and neutral phosphino borane **14** which can then react with H_2 to regenerate **13**.

In addition to their application in bond-activation reactions, "frustrated Lewis pairs" also offer an avenue to electronically tune perfluoroaryl boranes that are commonly used as Lewis acid catalysts in organic transformations. When phosphonium borate **13** is treated with $[CPh_3][B(C_6F_5)_4]$, hydride abstraction from the borate yields cationic borane, $[(C_6H_2Me_3)_2HP(C_6F_4)B(C_6F_5)_2][B(C_6F_5)_4]$ **15**.[21] Not surprisingly, these cationic boranes are markedly more Lewis acidic than the parent $B(C_6F_5)_3$, while neutral phosphine–borane **14** exhibits decreased Lewis acidity. The ability to perturb the Lewis acidity of perfluoroaryl boranes without dramatically affecting the sterics at boron is of immediate interest to the study of Lewis acid catalyzed reactions and it likely won't be long before we see the application of these results to organic transformations.

The reactions reported in these studies represent significant advances in metal-free bond activation by the implementation of novel strategies for breaking strong bonds. Furthermore, the reversibility of the H_2 activations observed by Stephan and co-workers coupled with recent reports of application of these "frustrated Lewis pairs" in the catalytic reduction of imines is extremely encouraging for more widespread applications of these complexes in catalysis. Extension of this hydrogenation work to olefins, carbonyl functions, and a wider array of imines would be extremely valuable in pharmaceutical synthesis and the potential for asymmetric versions of such reactions is high given the wide array of chiral phosphines and (increasingly) carbenes available today.

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