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VIP **H_2 Activation**

Turning Frustration into Bond Activation: A Theoretical Mechanistic Study on Heterolytic Hydrogen Splitting by Frustrated Lewis Pairs**

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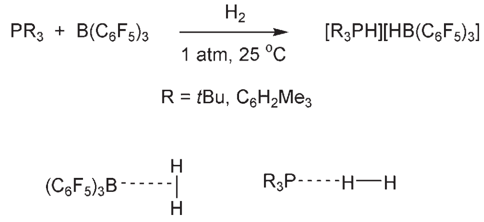
It has long been noted that the strength of the dative bond in a Lewis acid–base pair is strongly influenced by steric factors, which can even preclude the formation of a donor–acceptor adduct.[1] These systems remained only exotic textbook examples[2] until quite recently, when Stephan et al. brought into sharp focus their inherent synthetic potential.[3–8] In their landmark experiments, they demonstrated that the incapability of adduct formation in a "frustrated Lewis pair"[3] is a key element to remarkable chemical transformations. For instance, mixtures of frustrated phosphines (PR_3, R = $C_6H_2Me_3$ or *t*Bu) and boranes (BR'_3, $R' = C_6F_5$) can easily cleave molecular hydrogen (H_2) in a heterolytic manner under very mild conditions,[4,5] and they can undergo addition reactions with olefins as well.[6] Furthermore, compounds of the type $R_2P{-}C_6F_4{-}BR'_2$ have been shown to reversibly activate and liberate H_2[7] and act as effective hydrogenation catalysts for the reduction of C=N multiple bonds.[8] These unprecedented findings represent major advances in metal-free bond activation, because they may lead to novel strategies in various branches of synthetic chemistry and also to developments relevant to hydrogen economy.[9,10] Further achievements, however, require detailed knowledge of the mechanism of these reactions, which is presently not available.[11] In this paper, we report the first theoretical mechanistic study of the heterolytic cleavage of H_2 by frustrated Lewis pairs and describe a new model that accounts for the reactivity of these compounds.

As reported by Welch and Stephan,[4] experiments carried out with stoichiometric mixtures of $PR_3/B(C_6F_5)_3$ pairs (R = *t*Bu and $C_6H_2Me_3$) showed no evidence of the formation of Lewis acid–base adducts, but the exposure of their solutions to H_2 at 1 atm pressure and 25 °C resulted in the facile formation of $[R_3PH][HB(C_6F_5)_3]$ products (Scheme 1). To interpret these results, the authors outlined two possible stepwise reaction mechanisms. By analogy to transition-metal chemistry and considering previous studies on the existence of a weakly bound $H_3B{\cdots}H_2$ adduct,[12] a side-on interaction of H_2 with $B(C_6F_5)_3$ was assumed to initiate the dissociation process. However, no evidence for the formation of the $(C_6F_5)_3B{\cdots}H_2$ species was found in related experiments.[4] As an alternative scenario, the end-on approach of H_2 to PR_3 was also mentioned, but again, weak $R_3P{\cdots}H_2$ interactions have been observed only at cryogenic conditions.[13]



Scheme 1. Heterolytic cleavage of H_2 and the two proposed intermediates.

To gain further mechanistic insight into this reaction, we initiated a theoretical study. We used a combination of DFT and ab initio methods, namely B3LYP/6-31G(d) geometry optimizations followed by single-point SCS-MP2/cc-pVTZ energy calculations,[14] to characterize possible reaction pathways and intermediates. The latter computational approach has recently been shown to provide reliable energy predictions for noncovalent interactions[15] and for reactions relevant to organocatalysis.[16] First, we examined the proposed $(C_6F_5)_3B{\cdots}H_2$ and $(tBu)_3P{\cdots}H_2$ interactions by deriving potential energy curves with respect to X–H distances (X = B and P). Our calculations indicate that both side-on and end-on approaches of H_2 to $B(C_6F_5)_3$ are unfavorable owing to Pauli repulsion (see Figure 1). This is somewhat in contrast to previous theoretical and matrix-isolation studies of BH_5 that pointed toward the existence of a weakly bound $H_3B{\cdots}H_2$ complex. However, our systematic investigation of substituted boranes shows an appreciable delocalization of aryl π electrons into the *p*(B) orbital that limits stabilizing σ donation from H_2 and prevents $R'_3B{\cdots}H_2$ complexation.[17] The repulsive potential energy curves obtained in our calculations are in line with experimental observations that borane–H_2 adducts are unstable even at low temperatures.[4] The interaction between H_2 and $P(tBu)_3$ is also found to be repulsive for the chemically relevant *d*(P–H) range. These results firmly suggest that other reaction channels should be considered to provide a rationale for the reactivity of the $P(tBu)_3/B(C_6F_5)_3$ pair with hydrogen. For further discussion we note that both end-on $(C_6F_5)_3B{\cdots}H_2$ and $(tBu)_3P{\cdots}H_2$ interactions induce appreciable polarization of the H_2 molecule already at relatively large X–H distances with an opposite charge separation pattern in these two cases (see Figure 1).

The reported hydrogen-splitting reaction proved to be rather facile, which can hardly be explained in terms of a

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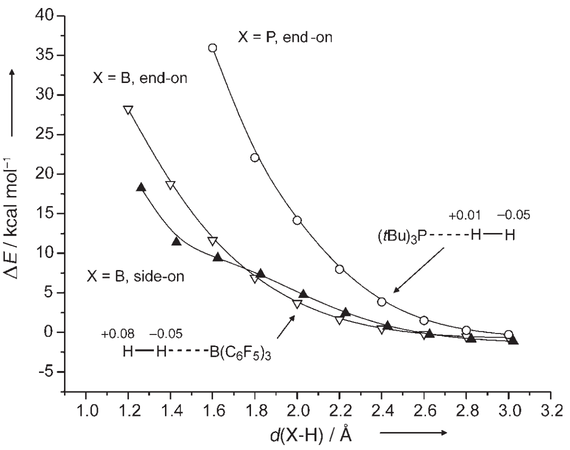

Figure 1. Interaction energy of H_2 with $B(C_6F_5)_3$ and $P(tBu)_3$ as a function of X–H distance. Net atomic charges on H atoms as obtained from natural bond orbital (NBO) analysis are shown for d(B–H) = 2.0 Å and d(P–H) = 2.4 Å.

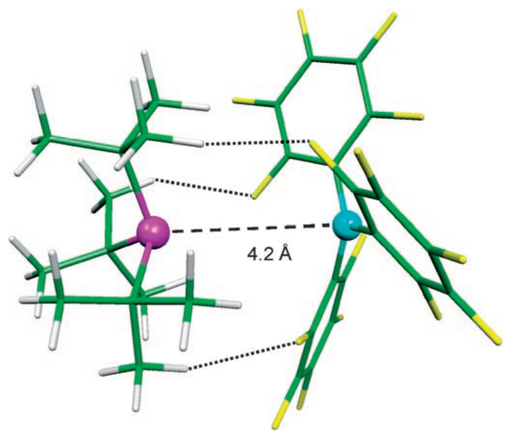

Figure 3. Structure of the $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ complex at the minimum of the SCS-MP2 curve of Figure 2. C–H···F type hydrogen bonds (with d(H–F) < 2.4 Å) are indicated with dotted lines.

termolecular collision between the reactants. Although not observed in NMR experiments,[4] we envisioned that secondary interactions may lead to weak association between the molecules of a frustrated Lewis pair. This idea is supported by recent quantum chemical calculations carried out for a series of classical phosphine–borane Lewis adducts, which revealed considerable contribution of dispersion interactions to the overall binding energy.[18] Indeed, we identified a weakly bound $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ complex as a minimum on the B3LYP potential energy surface, and a potential energy curve with respect to the P–B distance was also derived at the SCS-MP2 level[14] (see Figures 2 and 3). The bonding in this adduct can be characterized as a combination of multiple C–H···F hydrogen bonds and dispersion interactions.[19] No charge transfer occurs in this complex, which is apparent from the planarity of the central BC_3 unit in $B(C_6F_5)_3$. The association energy is predicted to be $\Delta E = -11.5\,\text{kcal mol}^{-1}$, which is about the half of the interaction energy found for classical Lewis adducts.[18] This surprisingly large stabilization energy suggests a certain degree of association even at room temperature.[20] Another characteristic feature of the $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ complex is its structural flexibility, which stems from the dominance of weak nondirectional long-range forces. For instance, the P–B distance in $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ can be varied in a quite broad range at only a small energetic cost (see Figure 2).

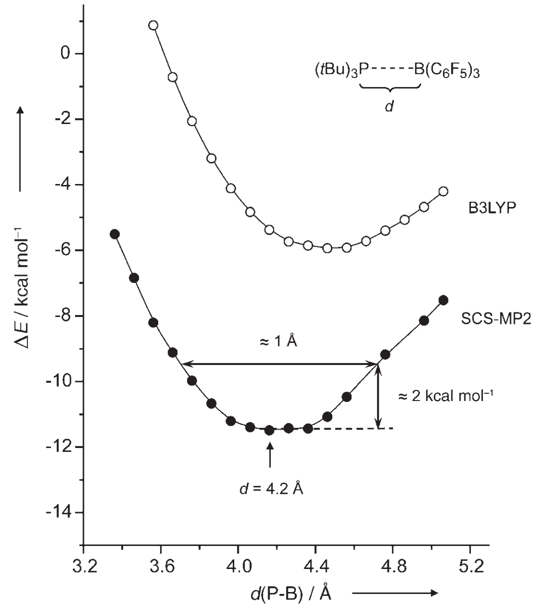

Figure 2. Potential energy curves derived at B3LYP/6-31G(d) and SCS-MP2/cc-pVTZ levels for the interaction between $P(tBu)_3$ and $B(C_6F_5)_3$.

Considering the flexible nature of the frustrated $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ complex and the small size of the H_2 molecule, one expects that H_2 can easily reach the vicinity of the P···B axis of the adduct and may interact with both active centers of the phosphine–borane pair. The potential energy surface has been explored in this region, and we have located a transition state (TS) associated with the H–H bond cleavage (see Figure 4a), which lies only $10.4\,\text{kcal mol}^{-1}$ in energy above $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ + H_2. The calculations show that this TS describes an essentially direct route from $[(tBu)_3P]\cdots[B(C_6F_5)_3]$ + H_2 to the $[(tBu)_3PH][HB(C_6F_5)_3]$ product,[21] and it represents the highest stationary point on the reaction pathway. In the transition structure, the H_2 molecule is nearly aligned with the P···B axis, and it is only slightly elongated suggesting an early TS for H–H bond cleavage.[22] It is also worth noting that the C–H···F and van der Waals contacts between the phosphine and borane molecules are maintained in the TS.

The electron density difference map and the population analysis indicate that H_2 becomes polarized in the TS and that a notable amount of electron density is shifted in the $(tBu)_3P \rightarrow B(C_6F_5)_3$ direction (see Figure 4b). The partial electron transfer is clearly borne out by the pyramidal distortion of the borane, whereas the polarization effect is apparent from the large absolute value of the computed dipole moment vector ($\mu_{\text{calc}} = 5.5$ D). The polarization effect is consistent with those observed for the binary $(C_6F_5)_3B\cdots H_2$ and $(tBu)_3P\cdots H_2$ interactions (see Figure 1), and because they act synergistically, they tend to reduce repulsion on both sides

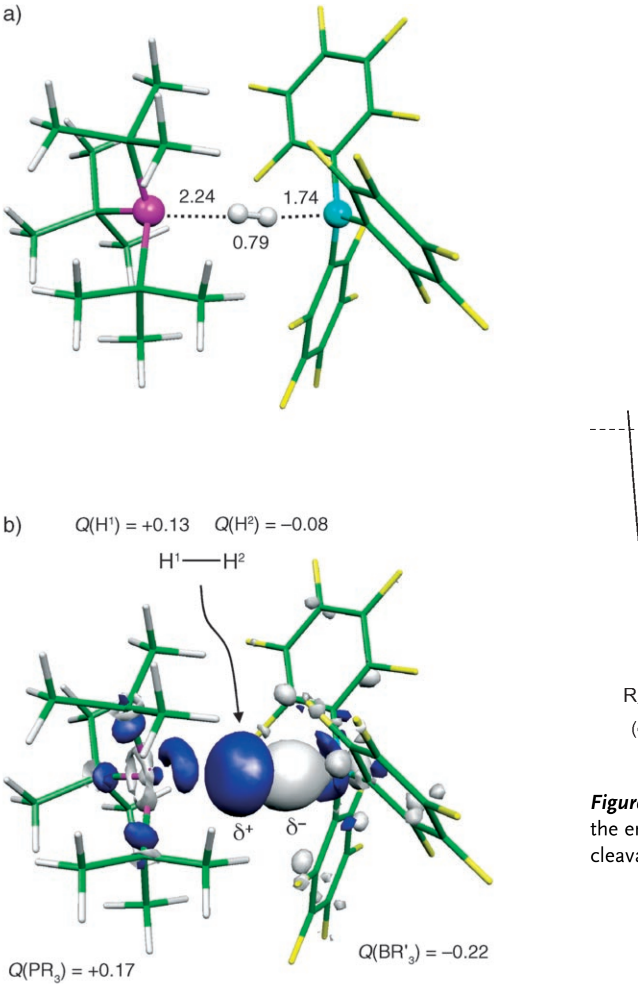

Figure 4. Structure (a) and electron density difference ($\Delta\rho$)[23] map (b) of the located TS. Distances are given in Å. Gray and blue surfaces (obtained with a cutoff parameter of ±0.0015 au) denote gain and loss of electron density. Net atomic and molecular charges (*Q*) were obtained from NBO analysis.

of the H_2 molecule. The electron transfer occurs through simultaneous $(t\mathrm{Bu})_3\mathrm{P}\rightarrow\sigma^*(\mathrm{H}_2)$ and $\sigma(\mathrm{H}_2)\rightarrow\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3$ donations in a push–pull manner and implies progressive weakening of the H–H bond along the reaction pathway. The heterolytic dissociation of H_2 is synchronized with the formation of two covalent bonds, which lead to the observed $[(t\mathrm{Bu})_3\mathrm{PH}][\mathrm{HB}(\mathrm{C}_6\mathrm{F}_5)_3]$ product. This process is predicted to be highly exothermic ($\Delta E = -26.3\ \mathrm{kcal\,mol^{-1}}$, relative to $\mathrm{P}(t\mathrm{Bu})_3 + \mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3 + \mathrm{H}_2$). The optimized structure[17] of $[(t\mathrm{Bu})_3\mathrm{PH}][\mathrm{HB}(\mathrm{C}_6\mathrm{F}_5)_3]$ is consistent with the X-ray data[4] in that the PH and BH bonds are oriented toward each other, and the P–B distance is reasonably reproduced as well. We find, however, a relatively close P–H···H–B contact in the product ion pair ($d(\mathrm{H-H}) = 1.87$ Å), which is a clear indication of the presence of a dihydrogen bond.

It might be useful at this point to expand the discussion on the nature and role of "frustration" in this hydrogen-activation process. The key element of the model emerging from our computational approach is the intermolecular association of the Lewis acidic and basic components to a "frustrated complex" in an arrangement similar to the classical Lewis donor–acceptor adduct, but having a much looser structure. The preorganized frustrated system[24] provides a range of optimal acid–base distances for bifunctional cooperativity, in our particular case, for a synergistic interaction with an incoming H_2 molecule. Moreover, in our terminology "frustration" does not only refer to steric effects, but it also implies a strain, which can be utilized for bond activation. The frustration energy (defined as ΔE_f in Figure 5) lowers the activation barrier and increases the exothermicity of the overall process by reactant-state destabilization as compared to a hypothetical classical Lewis pair having the same intrinsic acid–base properties.[25] Secondary interactions between the bulky substitutents play an important role along the entire reaction pathway. They enable the formation of frustrated complexes, and their presence provides stabilization for the TS of the activation as well as for the product. Our preliminary calculations for other sterically demanding PR_3 and BR'_3 molecules indicate that the present model may have general validity for reactions initiated by frustrated Lewis pairs.[26]

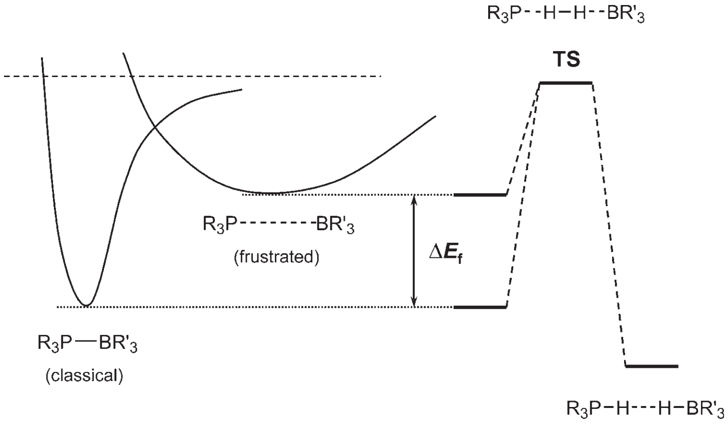

Figure 5. The role of frustration in the new mechanistic proposal. ΔE_f represents the energy of frustration that lowers the barrier to heterolytic H–H bond cleavage.

In summary, we have explored various reaction pathways for the heterolytic cleavage of H_2 by the $\mathrm{P}(t\mathrm{Bu})_3/\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3$ Lewis pair. We found no theoretical evidence in support of previously suggested mechanisms;[4] however, we arrived at a novel mechanistic proposal. The new model involves the preorganization of donor–acceptor sites into a loosely bound but energetically strained complex, which acts as a highly reactive species for bond activation. Our findings provide additional insight to the notion of frustrated Lewis pairs and broaden the applicability of this concept in catalyst design.

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[19] Our calculations carried out for the $[(t\mathrm{Bu})_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{H}_5)_3]$ adduct underline the importance of C–H···F interactions to the bonding in $[(t\mathrm{Bu})_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3]$, but our results also indicate that their presence is not a prerequisite in the formation of frustrated complexes (for details, see the Supporting Information).

[20] The exothermicity of association is likely overcompensated by entropy loss. Therefore the association is expected to be slightly endergonic at room temperature, and spectroscopic observation of weakly bound $[\mathrm{R}_3\mathrm{P}]\cdots[\mathrm{BR'}_3]$ adducts may not be obvious.

[21] Geometry optimization following initial IRC calculation leads to a very shallow energy minimum corresponding to a structure wherein H_2 is weakly bound to an open form of the $[(t\mathrm{Bu})_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3]$ adduct; in the other direction, the $[(t\mathrm{Bu})_3\mathrm{PH}][\mathrm{HB}(\mathrm{C}_6\mathrm{F}_5)_3]$ product is obtained (see the Supporting Information).

[22] The TS we located bears common structural features with that identified by Chan and Radom for base-catalyzed hydrogenation of ketones. For detailed kinetic and computational studies, see: a) A. Berkessel, T. J. S. Schubert, T. N. Müller, *J. Am. Chem. Soc.* **2002**, *124*, 8693; b) B. Chan, L. Radom, *J. Am. Chem. Soc.* **2005**, *127*, 2443.

[23] $\Delta\rho$ is defined as $\Delta\rho = \rho(\mathrm{TS})\text{-}\rho([(t\mathrm{Bu})_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3]^*) - \rho(\mathrm{H}_2^*)$, where the atomic positions of $[(t\mathrm{Bu})_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3]^*$ and H_2^* are identical to those in the TS.

[24] The importance of the preorganization of active sites for an analogous near-linear four-centered TS has already been demonstrated in Rh-assisted homolytic H_2 activation, albeit involving the intramolecular use of two metalloradical centers. See: W. Cui, B. B. Wayland, *J. Am. Chem. Soc.* **2004**, *126*, 8266.

[25] The frustration energy can be quantified, for instance, by carrying out activation–strain analysis as proposed by Bickelhaupt and co-workers. See: G. T. de Jong, F. M. Bickelhaupt, *ChemPhysChem* **2007**, *8*, 1170.

[26] Frustrated complexes $[(\mathrm{C}_6\mathrm{H}_2\mathrm{Me}_3)_3\mathrm{P}]\cdots[\mathrm{B}(\mathrm{C}_6\mathrm{F}_5)_3]$ and $[(\mathrm{C}_6\mathrm{F}_5)_2\mathrm{B}\text{–}\mathrm{C}_6\mathrm{F}_4\text{–}\mathrm{P}(t\mathrm{Bu})_2]\cdots[(\mathrm{C}_6\mathrm{F}_5)_2\mathrm{B}\text{–}\mathrm{C}_6\mathrm{F}_4\text{–}\mathrm{P}(t\mathrm{Bu})_2]$ have also been identified in our calculations (see the Supporting Information).