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Perspective

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Frustrated Lewis Pairs

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ABSTRACT: The articulation of the notion of "frustrated Lewis pairs" (FLPs), which emerged from the discovery that H_2 can be reversibly activated by combinations of sterically encumbered Lewis acids and bases, has prompted a great deal of recent activity. Perhaps the most remarkable consequence has been the development of FLP catalysts for the hydrogenation of a range of organic substrates. In the past 9 years, the substrate scope has evolved from bulky polar species to include a wide range of unsaturated organic molecules. In addition, effective stereoselective metal-free hydrogenation catalysts have begun to emerge. The mechanism of this activation of H_2 has been explored, and the nature and range of Lewis acid/base combinations capable of effecting such activation have also expanded to include a variety of non-metal species. The reactivity of FLPs with a variety of other small molecules, including olefins, alkynes, and a range of element oxides, has also been developed. Although much of this latter chemistry has uncovered unique stoichiometric transformations, metal-free catalytic hydroamination, CO_2 reduction chemistry, and applications in polymerization have also been achieved. The concept is also beginning to find applications in bioinorganic and materials chemistry as well as heterogeneous catalysis. This Perspective highlights many of these developments and discusses the relationship between FLPs and established chemistry. Some of the directions and developments that are likely to emerge from FLP chemistry in the future are also presented.

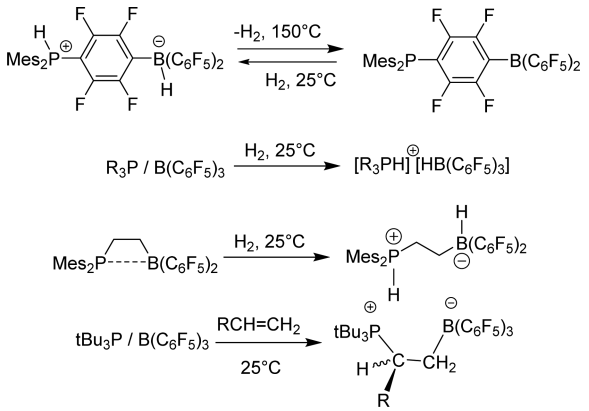
INTRODUCTION

A fundamental pillar of modern catalysis is the activation and subsequent reaction of small molecules. Over the past 50 years, studies in organometallic chemistry have provided a remarkable toolbox of homogeneous catalytic methods for the construction of new bonds and the synthesis of desirable materials. The developments are too numerous to list comprehensively, but some of the transformative advances include the discovery of hydrogenation catalysts,[1,2] the elegant design of chiral catalysts for asymmetric synthesis,[3,4] the advent of a variety of strategies for cross-coupling reactions[5] affording controlled C−C bond formation, the development of highly efficient transition metal olefin polymerization catalysts,[6] and the uncovering of metathesis catalysts[7,8] for molecular and materials synthesis.

A feature common to all of these breakthroughs has been the exploitation of the chemistry of transition metal elements. The reactivity of transition metal species is derived from their dual ability to both accept electron density from a substrate molecule and donate electron density to the anti-bonding orbitals via back-bonding. In comparison to the extensive investigation of the catalytic properties of transition metals, the analogous reactivity of the p-block elements has received far less attention. Certainly the acceptor capabilities of group III species and electron-donating nature of group V element derivatives were viewed as classic examples of the concepts of Lewis acidity and basicity, respectively. Nonetheless, the notion that these features could be exploited in a simple synergistic fashion to activate small molecules was not appreciated.

In 2006, we discovered that *p*-$(Mes_2PH)C_6F_4(BH(C_6F_5)_2)$ could be reversibly liberate H_2 to yield *p*-$(Mes_2P)C_6F_4(B(C_6F_5)_2)$ (Scheme 1).[9] In 2007, the much less esoteric

Scheme 1. First FLP Activations of H_2 and Olefins



combination of a bulky donor such as tBu_3P or Mes_3P and a bulky acceptor such as $B(C_6F_5)_3$ was found to be capable of activating the H_2 molecule (Scheme 1).[10] Subsequently, the ethylene-bridged phosphine/borane $(Mes_2P)C_2H_4(B(C_6F_5)_2)$ was also shown to activate H_2 (Scheme 1).[11] In these cases, the key feature that permitted these non-metal species to activate H_2 was the presence of sterically demanding substituents on P and B that precluded association and formation of a classical Lewis acid−base adduct. In this fashion, the unquenched Lewis acidity and basicity are available to accept and donate electron density, respectively, to the H_2 molecule, effecting the heterolytic cleavage of H_2. This finding prompted us to apply this strategy to the activation of other small molecules. Thus, in another study from 2007, combinations of Lewis acids and bases were allowed to react with olefins to generate zwitterionic 1,2-addition products (Scheme 1). It was in the paper describing these experiments that these special combinations of donor and acceptor, sterically frustrated from the formation of classic adducts, were termed "frustrated Lewis pairs" or "FLPs".[12]

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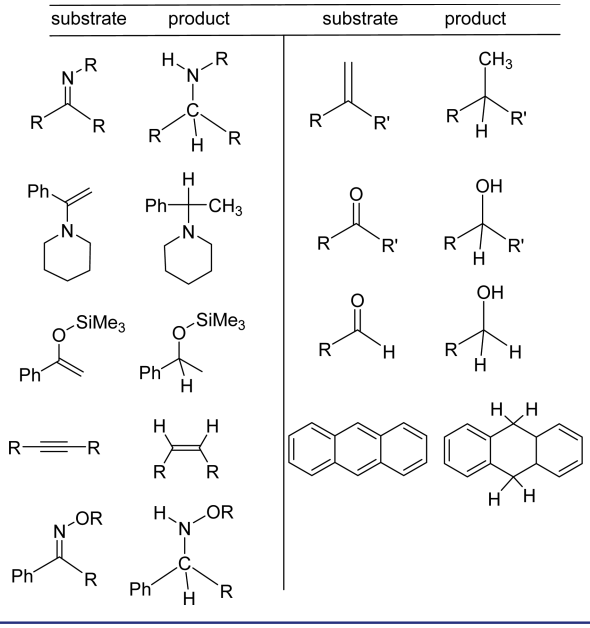
The above findings proved to be seminal, leading to a large number of studies probing the chemistry of FLPs and their applications from research groups around the world. Progress has been rapid, diverse, and exciting. Consequently, various aspects of FLP chemistry have been reviewed numerous times.[13−20] In this Perspective, we provide an overview of FLP chemistry from the past 9 years. While other sources provide detailed review of the rapidly growing body of FLP literature, the present article focuses on highlighting and discussing the major areas of advancement, our understanding of FLP reactivity, and the areas of application that hold promise for the future.

FLP HYDROGENATIONS

An unstated tenet of inorganic/organometallic catalysis held throughout the 20th century required transition metal species for the activation of H_2. The discovery of FLPs and their application in metal-free hydrogenation of organic substrates proved this dogma to be rather narrow-minded.

Polar Substrates. The heterolytic nature of H_2 cleavage achieved by FLPs prompted tests with polar substrates, with the goal of sequential proton and hydride delivery. Initial reports demonstrated metal-free reductions of imines (Table 1),

Table 1. Selected Examples of Substrate Scope for Catalytic FLP Hydrogenations



aziridines, and protected nitriles using *p*-$(Mes_2P)C_6F_4(B(C_6F_5)_2)$[21] or $B(C_6F_5)_3$[22] as the catalyst. This strategy was subsequently extended to the reduction of enamines and silyl-enol ethers (Table 1) using the related FLP catalysts $Mes_2PC_2H_4B(C_6F_5)_2$[23] and $C_{10}H_6(PPh_2)_2/B(C_6F_5)_3$,[24] respectively. More recently, Oestreich developed a clever extension of imine reduction, exploiting derivatization of oximes (Table 1) to allow for subsequent metal-free reductions using $B(C_6F_5)_3$.[25]

Reduction of imine substrates was also been achieved by FLP transfer hydrogenations. Using ammonia/borane[23] or *i*Pr_2NH[26] as surrogate hydrogen sources, a series of imines and enamines were reduced in the presence of catalytic $B(C_6F_5)_3$. Oestreich[27] has also demonstrated related reductions employing cyclohexadienes as the H_2 source.

Other polar substrates of obvious interest include carbonyl derivatives. Until recently, the application of FLPs for the catalytic reduction of carbonyls was deemed unlikely as a result of the high oxophilicity of boron. Indeed, borinic esters were formed in attempts to hydrogenate ketones in toluene.[28] In contrast, use of ethereal solvents and lower temperatures enabled $B(C_6F_5)_3$-catalyzed hydrogenation of ketones and aldehydes to the corresponding alcohols (Table 1).[29,30] Mechanistic studies and intermediate model compounds affirmed that hydrogen-bonding between the transient protonated ketone and the solvent precludes borane degradation, allowing catalysis to proceed. Interestingly, use of molecular sieves and catalytic amounts of borane in toluene also precludes borane degradation, allowing efficient carbonyl reduction.[31]

Olefins and Alkynes. Efforts to broaden the substrate scope for FLP reductions have been an area of some effort. These efforts were facilitated by the finding that weakly basic donors such as $(C_6F_5)PPh_2$[32] and even Et_2O[33] in combination with $B(C_6F_5)_3$ effect HD scrambling. This result demonstrates that weak donors can participate as the base component of an FLP to activate H_2. Importantly, this interaction generates a transient but highly acidic conjugate acid that is capable of protonating 1,1-disubstituted olefins, generating a carbocation. The resulting cation is electrophilic enough to capture hydride from the borohydride anion $[HB(C_6F_5)_3]^-$, affording the corresponding alkane and regenerating the FLP (Table 1).[32] While such catalytic metal-free olefin reductions are generally slow, they are accelerated under higher pressures of H_2. Nonetheless, this strategy provides the first metal-free approach to olefin hydrogenation. Building on these initial findings, Paradies[34−36] demonstrated that the order in which the proton and hydride are delivered could be reversed in FLP reductions of a series of nitro-olefins. Alcarazo and co-workers[37] used $B(C_6F_5)_3$ and a N-base to catalytically hydrogenate allenic esters and Paradies's group used B/P FLPs to hydrogenate enones.[38] Soos showed that $B(C_6F_5)_3$ and DABCO catalytically reduce imines, enamines, and N-heterocycles. In addition, they reported one example of an reduction of an enone to the corresponding ketone.[39−42]

It was Repo et al.[43] who further broadened the substrate scope for FLP reductions to include non-functionalized internal alkynes (Table 1). Using the intramolecular FLP *o*-$C_6H_4(NMe_2)(B(C_6F_5)_2)$, the corresponding *cis*-alkenes were obtained. Mechanistic studies of these latter transformations showed that the active species was in fact *o*-$C_6H_4(NMe_2)(BH(C_6F_5))$ derived from protonation of the original FLP liberating C_6F_5H. Thus, reduction in this case proceeds via hydroboration of alkyne, subsequent H_2 activation, and then protonolysis liberating the *cis*-alkene.[43]

Aromatic Substrates. Further exploitation of the strategy of employing weakly basic donors and $B(C_6F_5)_3$ enabled the hydrogenation of several polyaromatic systems. In this fashion, dihydroanthracenes and dihydrotetracenes were obtained (Table 1).[44]

In a related sense, combinations of sterically hindered anilines and $B(C_6F_5)_3$ under H_2 at 110 °C resulted in arene ring reduction, affording the corresponding cyclohexylammonium salts (Table 2).[45] Similarly, this strategy could be applied to substituted anilines, aryl azirdines, and aryl-imines to give the related *N*-cyclohexyl derivatives. While these reductions require stoichiometric combination of amine and borane, multiple activations of H_2 were facilitated prior to the sequestration of

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Table 2. Selected Examples of FLP Aromatic Reductions

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	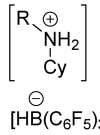	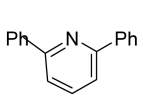	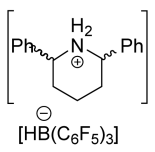
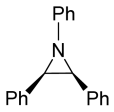	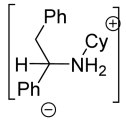	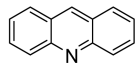	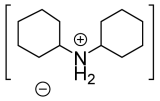
	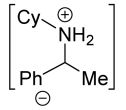	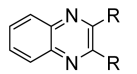	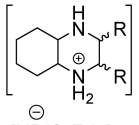

the borane in the counteranion of the isolated ammonium salt. In an interesting perturbation of this chemistry, hydrogenation of methoxy-substituted anilines led to transannular ring closure, affording unique bicyclic amine products.[46]

In similar fashion, pyridines, quinolones, and quinoxalines[47] are hydrogenated to give the corresponding saturated heterocyclic products (Table 2). It is interesting to note that both pyridine- and aniline-type rings are reduced.[48,49] However, for substrates bearing a more distal arene ring, it remains unaltered, thus providing some degree of selectivity.

FLP Catalysts. Although the originally reported *p*-(Mes_2P)-$C_6F_4(B(C_6F_5)_2)$ was nominally an intramolecular FLP,[9] it is thought that this system activates H_2 in a bimolecular fashion. In contrast, the Erker intramolecular FLP $Mes_2PCH_2CH_2B(C_6F_5)_2$ activates H_2 via the concerted action of the Lewis acid and base on H_2 and has proved to be an effective catalyst for a variety of hydrogenation reactions.[11] Similarly, "the molecular tweezers" designed by Rieger and Repo,[50] which combined tetramethylpiperidine and electrophilic borane fragments in $C_5H_6Me_4NHCH_2C_6H_4(BH(C_6F_5)_2)$ (Figure 1), is also an effective hydrogenation catalyst. Other studies have focused on the activation of H_2 by various donors in combination with $B(C_6F_5)_3$, and indeed a variety of closely related intermolecular systems involving substituted P and N donors in combinations with electrophilic boranes have been explored in the FLP activation of H_2 and catalysis. Such systematic studies have been limited, but they demonstrate the impact of the degree of fluorination of boranes on the efficacy of resulting FLP catalysts and are beginning to shed light on the key catalyst design issues.

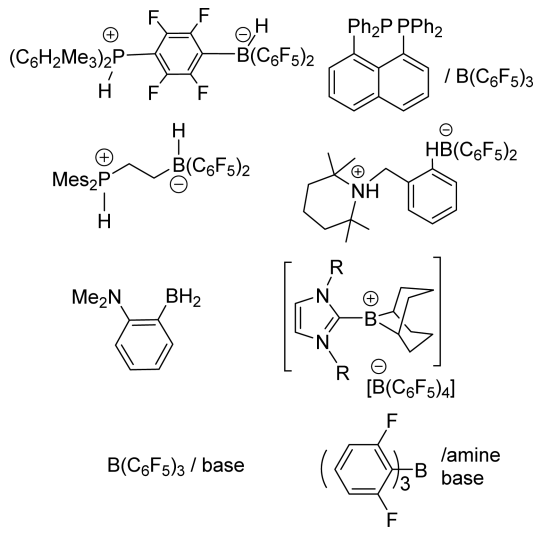

Figure 1. Selected examples of FLP hydrogenation catalysts.

One alternative strategy that provides an effective FLP catalyst exploits the use of carbene stabilized borenium cations (Figure 1).[51] Despite the absence of strongly electron withdrawing substituents, the cationic charge nominally located at B imparts sufficient electrophilicity to activate H_2 in the presence of a donor that is sufficiently bulky so as not to quench the Lewis acidity of the borenium center. Indeed such borenium cations are effective catalysts for the hydrogenation of imines and enamines at room temperatures under 100 atm of H_2. Crudden[52] demonstrated that analogous triazole-stabilized borenium cations were also viable as catalysts for the hydrogenation catalysts of imines. Detailed catalyst optimizations studied a variety of N-heterocyclic carbene (NHC) donors to obtain an optimized borenium catalyst which exhibits TONs of ~1000 h^{-1}.[53]

While the above catalyst is the best FLP system reported to date, it does not achieve the activity of metal-based catalysts. Nonetheless, it is important to note that engineering can play a major role in enhancing catalyst performance. Anecdotally, we have observed that simply moving from an NMR-scale reaction to a Schlenk flask resulted in dramatic increases in reaction rate. That being said, it is hard to see FLP catalysts as a direct replacement of a metal-based catalysts. Rather, FLP hydrogenation catalysts should be viewed as a complementary reduction technology that may find applications where trace metals are to be avoided, catalysts costs are high or where metal-toxicity is a critical issue. Thus, pharmaceuticals or electronic materials are obvious products where commercial applications may develop.

In a recent development, Repo[54] also described the activation of H_2 by the species o-$C_6H_6Me_4NC_6H_4(BH_2)$ (Figure 1). This important example, unlike the initial FLPs, exploits a weak Lewis acid with a strong base. This development points to a large range of FLPs with potential utility that could also offer broader functional group tolerance due to the diminished Lewis acidity. Similarly, the recent demonstration of highly electrophilic phosphonium cations as the Lewis acid component of an FLP activation of H_2 suggests another new avenue of inquiry from which new families of FLP catalysts could emerge.[55]

Asymmetric Reductions. As an initial step toward stereoselective FLP reductions, we probed diastereoselective reactions[56] demonstrating that imines containing chiral moieties either at nitrogen or at the carbon atom were reduced using H_2 and $B(C_6F_5)_3$. Consistent with the proximity of the chiral substituent to the prochiral C center, chiral substituents on N gave poor diastereoselectivities whereas such groups on C led to high inductions. It also noteworthy that $B(C_6F_5)_3$ has been shown to epimerize benzylic chiral amines, while such chiral centers are stable in the presence of weaker Lewis acids of the form $RB(C_6F_5)_2$ suggesting that chiral boranes of this form could be effective asymmetric hydrogenation catalysts.[26]

While the above results suggests the potential of stereoselective FLP reductions, it was the work of Klankermeyer[57] that first demonstrated that the concept could be extended

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explicitly to asymmetric hydrogenation. Although the camphor-derived borane $(C_6H_8(CMe_2)Me)B(C_6F_5)_2$ (Figure 2) showed

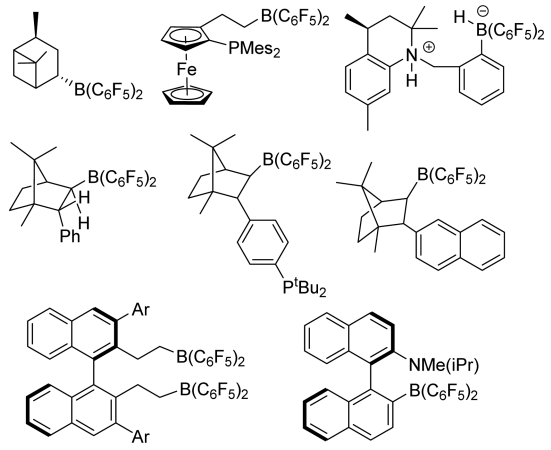


Figure 2. Selected examples of chiral FLP hydrogenation catalysts.

only a 13% enantiomeric excess (ee) in an initial report, this work was the first to demonstrate the principle of metal-free asymmetric hydrogenations, foreshadowing a number of subsequent advances. Indeed, Klankermayer's group[58] subsequently developed more effective chiral bicyclic borane catalysts derived from α-pinene (Figure 2) for the asymmetric reduction of ketimines which achieved ee's of >80%, while a related chiral P/B derivative catalyst[59] gave ca. 70% enantiomeric enrichment.

Erker et al. briefly probed the use of a chiral ferrocene derived FLPs (Figure 2) for the hydrogenation of prochiral bulky imines, achieving moderate enantioselectivities (max ee: 26%).[60] Similarly, Repo et al.[61] reported the use of a chiral N-heterocyclic N/B FLP to reduce ketimines, achieving up to 37% ee.

In related reductions of imines, Liu and Du[62] used a chiral bis-borane derived from hydroboration of a chiral divinylbinaphthyl species with bulky ortho substituents (Figure 2). Such reductions led to asymmetric inductions between 74 and 88% ee. Interestingly, related hydrogenation of pyridines using borane catalysts derived from the analogous hydroboration of alkenes with $HB(C_6F_5)_2$ gave a range of piperidines with high cis stereoselectivities.[49] It is noteworthy that chiral borane catalysts have also been used to effect stereoselective hydrosilylation reactions with ee's as high as 85%.[63,64]

Finally, in a very recent development, Repo and co-workers[65] achieved up to 99% ee in the asymmetric hydrogenation of imines and enamines using a N/B FLP with a binaphthyl backbone (Figure 2).

Mechanism. The reactions of intermolecular FLPs with H_2 presented a conceptual quandary as these reactions involve three components, yet any two components of these mixtures do not react. Of course, the implication of a trimolecular reaction mechanism is contrary to entropic considerations.

The observed reactivity rapidly prompted computational studies.[66−73] While differing methods and models were employed, these studies have converged on an understanding with common features. Intramolecular FLPs are thought to act via a concerted pathway of H−H cleavage, yielding the phosphonium and hydridoborate fragments as the internal Lewis acid−Lewis base interactions are computed to be weak. On the other hand, intermolecular FLPs which evade dative bond formation as a result of steric demands are thought to associate in an "encounter complex". This species is transiently stabilized by van der Waals interactions and reacts in a bimolecular fashion with H_2, again affording a pathway to heterolytic cleavage of H_2 and formation of the resulting phosphonium hydridoborate.

More recently, experimental studies by Autrey et al. accessed thermodynamic and kinetic parameters for FLP hydrogen activation by reaction calorimetry. The enthalpy of the H_2-splitting reaction for $(Mes_2P)C_2H_4(B(C_6F_5)_2)$ was determined to be $\Delta H_r = -7.5 \pm 1.0$ kcal mol^{-1}.[74] Moreover, Autrry reported the rate-determining step in the hydrogenation of imines is hydrogen activation, with the second-order rate constant found to be $k_r = 0.9$ M^{-1} s^{-1} at 295 K.

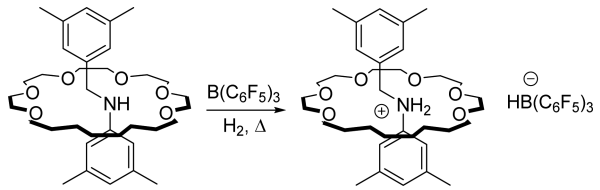
BROADENING FLPs FOR H_2 ACTIVATION

Early studies explored the range of acid base combinations that showed FLP-type reactivity. The combination of lutidine and $B(C_6F_5)_3$ was an informative case,[75] demonstrating that even in cases where the classical Lewis acid−base adduct was isolable, the existence of an equilibrium governing the formation of the adduct provided access to the corresponding FLP. Indeed, addition of H_2 to the combination of lutidine/$B(C_6F_5)_3$ resulted in the formation of lutidinium hydridoborate salt. This finding suggested that the reactivity of a great many classical Lewis acid−base adducts may have been overlooked.

Further studies demonstrated extension of the reactivity to FLPs comprised of borane and other strong donors such as bidentate phosphines and amines. Interestingly, as mentioned above, the ability to activate H_2 could also be extended to weak donor/$B(C_6F_5)_3$ combinations. Electron-deficient phosphines[32] and ethers[33] were shown to effect the isotopic scrambling of HD, affording H_2 and D_2 in a statistical mixture, demonstrating the activation of the H−D bond. In a systematic study, Paradies and co-workers studied the impact of variations of the phosphine,[76] demonstrating the breadth of tunability of the Lewis basicity for reactivity with H_2.

A unique approach to the generation of sterically FLPs was demonstrated in the reaction of an amine encircled by a crown ether with $B(C_6F_5)_3$ and H_2 (Scheme 2).[77] The rotaxane/borane activates H_2 whereas the amine/borane does not. This illustrates that non-covalent strategies can be exploited to induce FLP reactivity.[77]

Scheme 2. Activation of H_2 by a Rotaxane-Based FLP



Carbon-Based Lewis Bases. FLP reactivity has also been expanded to include a variety of C-based Lewis acids and bases. The early demonstration by Bertrand and co-workers[78] that cyclic alkyl amino carbenes react with H_2 can be regarded as a unique FLP where the donor and acceptor are located on the same atom. On the other hand, NHCs were shown to participate in more conventional FLP chemistry, activating H_2 in combination with $B(C_6F_5)_3$.[79,80] While these examples are conceptually important, the formation of these C−H bonds are

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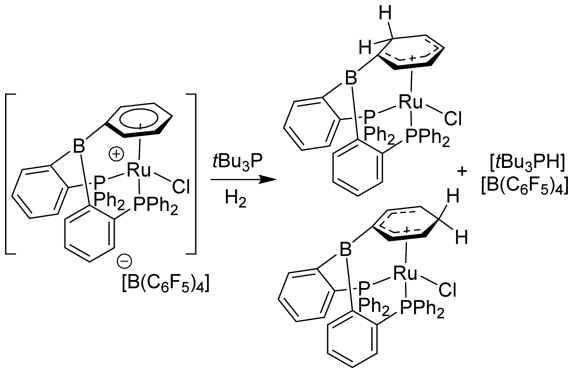
not readily reversible and thus not useful in catalytic applications.

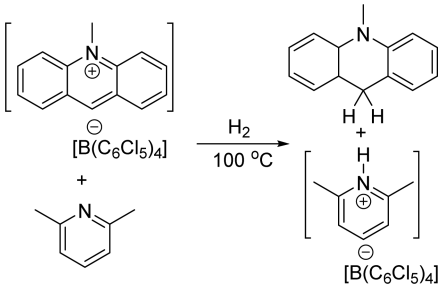
Carbon-Based Lewis Acids. In a similar fashion, Arduengo and co-workers[81] demonstrated the combination of an NHC and trityl cation could act as an FLP to irreversibly cleave H_2. In a recent effort, we developed an alternative carbon-based Lewis acid,[82,83] demonstrating that the ancillary metal center in $[((Ph_2PC_6H_4)_2B(\eta^6\text{-Ph}))RuCl][B(C_6F_5)_4]$ (Scheme 3) enhances the Lewis acidity of the aromatic carbon. In this case, the η^6 bound aromatic ring is Lewis acidic and, in combination with a sterically demanding phosphine, generates an FLP capable of heterolytically cleaving H_2. This Lewis acid can also be employed as a hydrogenation catalyst for imine reductions, with catalyst loadings as low as 1 mol%.

Scheme 3. H_2 Activation by an FLP Derived from Phosphine and an η^6-Bound Aromatic Ring Carbon



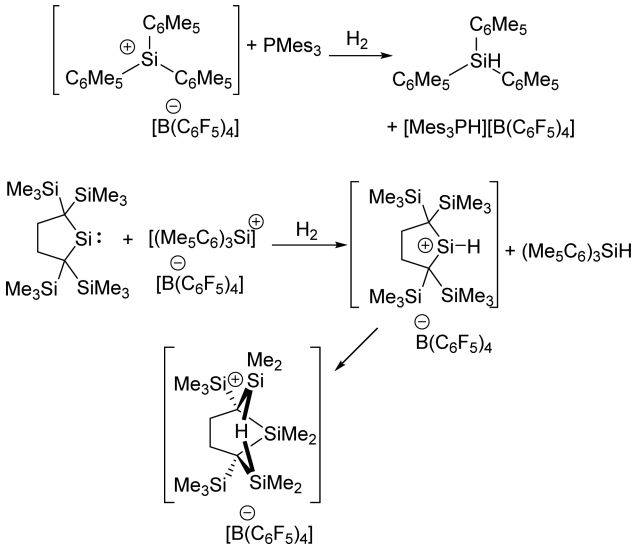
In a very interesting and insightful sequence of findings, Ingleson and co-workers[84] showed that the borenium species $[(acridine)BCl_2]^+$ acts both as a boron- and a carbon-based Lewis acid. Subsequently, the combination of methylated acridinium in combination with lutidine (Scheme 4) acted as organic FLP to activate H_2 at 100 °C.[85]

Scheme 4. H_2 Activation with a Methylated Acridinium/Lutidine FLP



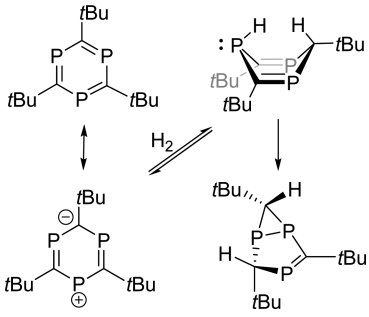
Silicon-Based FLPs. The Müller group showed that $[(C_6Me_5)_3Si]^+$ and Mes_3P, among other phosphines, acted as an FLP capable of reacting with H_2 to give the corresponding silane and phosphonium borate salt (Scheme 5).[86,87] In related work, Ashley et al.[88] showed that silylium–phosphine adducts activate H_2 under elevated temperatures, presumably via the thermal generation of an FLP. Müller and co-workers[89] also developed a silylene/silylium FLP (Scheme 5), demonstrating that it too activates H_2 although the protonated silylene rearranges to a hydrogen-bridged disilyl cation.

Scheme 5. Silicon-Based FLP Activation of H_2



Phosphorus-Based Lewis Acids. Phosphenium cations are known to exhibit Lewis acidity,[90] although they have not yet been used in FLP chemistry. However, in related reactivity, we recently reported that a triphosphabenzene derivative reacts directly with H_2.[91] Para-hydrogen experiments and computational studies support a mechanism for H_2 activation involving the resonance structure of triphosphabenzene in which a positive charge at phosphorus and a negative charge on carbon act as an intramolecular FLP to cleave the H_2 molecule. Subsequent rearrangement affords the observed [3.1.0]bicyclic product (Scheme 6).

Scheme 6. H_2 Activation with a Triphosphabenzene



Building on the notion of phosphorus as a Lewis acid, electrophilic phosphonium cations such as $[(C_6F_5)_3PF][B(C_6F_5)_4]$ was shown to be a strong Lewis acid in which the acidity is derived from a low-lying σ^* orbital.[92] Such Lewis acids mediate C–F dehydrofluorination, olefin isomerization, hydrosilylation of olefins[93] and dehydrocoupling of silanes with alcohols, acids, amines, and thiols.[94] In addition, such dehydrocoupling reactions can be performed in tandem with olefin hydrogenation.[94] Most recently, the Lewis acid $[(C_6F_5)_3PF][B(C_6F_5)_4]$ in combination with diarylamines have been shown to form an "encounter complex" which activates H_2 (Scheme 7). Further, such combinations can effect catalytic olefin hydrogenation.[55]

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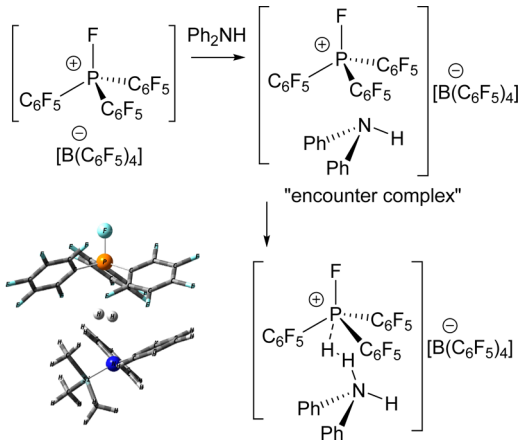
Scheme 7. H_2 Activation by a Phosphonium−Diphenylamine FLP (Computed H_2−"Encounter Complex" Interaction Shown on Lower Right)

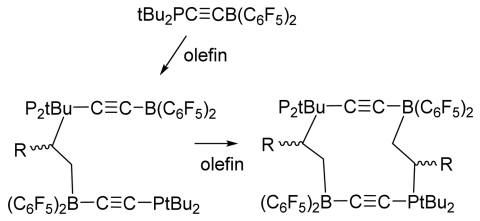


REACTIONS OF FLPs WITH OLEFINS AND ALKYNES

Given that it is the ability of a metal to act as both an acceptor and a donor that allows organometallic species to activate a range of small molecules, the reactions of FLPs with diverse small molecules became an obvious pathway for further inquiry.

Olefins. As described above, an early study described the reactions of FLPs with simple olefins. In these cases, combinations of phosphine/borane with olefin led to the addition of the FLP across the olefin bond, affording zwitterion phosphonium borate products (Scheme 8). Analogous

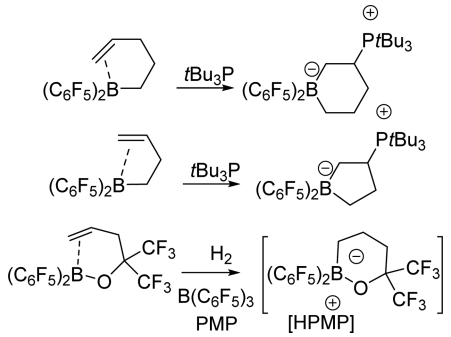
Scheme 8. Reactions of Alkynyl-Linked Phosphine/Borane with Hexane



chemistry employing the alkyne-linked P/B species tBu$_2$PCCB-$(C_6F_5)_2$ showed it reacts with hexene to generate the linear and macrocyclic species $(t\text{Bu}_2\text{PCCB}(C_6F_5)_2)_2(\text{BuCH}_2\text{CH}_2)_n$ (n = 1, 2) (Scheme 8).[95]

To probe the nature of these addition reactions, we prepared $B(C_6F_5)_2(CH_2)_nCH{=}CH_2$ (n = 2, 3) and observed an intramolecular van der Waals interaction between olefins and the Lewis acidic B center, as evidenced by NMR data in solution.[96] While calculations showed no pyramidalization of the B center, treatment with a variety of donors resulted in addition of the borane and donor across the olefin to give cyclic zwitterionic products (Scheme 9). In a similar fashion, the species $B(C_6F_5)_2(OC(CF_3)_2CH_2CH{=}CH_2)$[97] also forms an olefin−borane van der Waals complex and reacts with phosphines and bulky nitrogen-based or carbon-based nucleophiles to give analogous cyclic zwitterionic salts. Interestingly, reaction of the alkoxy-borane with 1,2,2,6,6-pentamethylpiperidine (PMP) and H_2 in the presence of a catalytic amount of $B(C_6F_5)_3$ effected the addition of hydride to

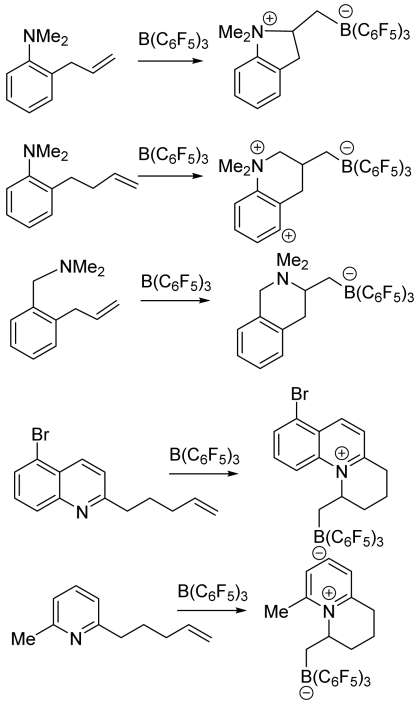
Scheme 9. Internal Alkene−Borane Interaction



the van der Waals complex to give the salt [HPMP][$B(C_6F_5)_2(OC(CF_3)_2CH_2CH_2CH_2)$] (Scheme 9).[97]

Reaction of the amine−borane adduct $PhCH_2NMe_2B(C_6F_5)_3$ with ethylene gave the zwitterionic addition product, $PhCH_2NMe_2CH_2CH_2B(C_6F_5)_3$.[98] In a similar manner, analogous reactivity of aniline derivatives with pendant olefins can be used to effect cyclizations affording zwitterionic N-heterocycles (Scheme 10).[99] This strategy has been further extended to prepare polycyclic quinoline and pyridine derivatives (Scheme 10).[100]

Scheme 10. Intramolecular Additions of N/B FLPs to Olefins



Alkynes. Shortly after the initial report of olefin−FLP reactivity, the analogous reactions of FLPs with alkynes was shown to afford similar zwitterionic addition products in which the Lewis acid and base add across the alkyne.[101] In cases where more basic donors were employed, deprotonation of terminal alkynes generated phosphonium alkynylborate salts (Scheme 11).

Further extension of this addition chemistry has led to analogous reactivity employing a variety of different FLPs. Secondary and even bulky primary phosphines as well as

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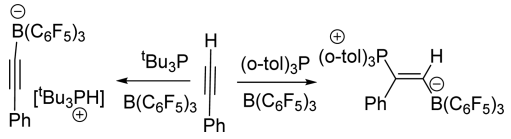
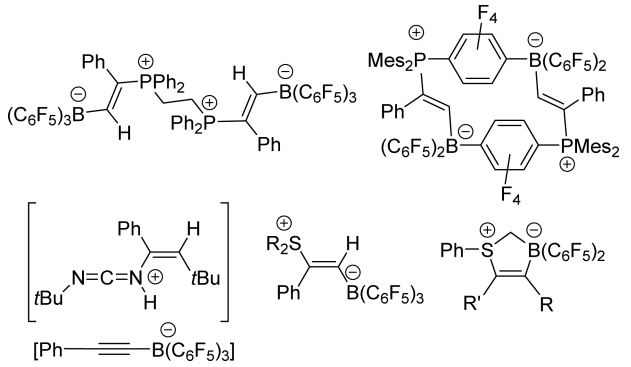
Scheme 11. Divergent Reaction Pathways of FLPs with Alkynes



polyphosphines were shown to participate in additions to alkynes. Examples include addition reactions with species such as $(PhP)_5C(Ph)=CH(B(C_6F_5)_3)$,[102] in which the chain-like species *trans*-$(CH_2PPh_2(Ph)C=C(H)B(C_6F_5)_3)_2$ (Scheme 12)

Scheme 12. Examples of Products of FLP Addition to Alkynes



and the macrocyclic $[(H)C=C(Ph)Mes_2PC_6F_4B(C_6F_5)_2]_2$ were produced.[103] In contrast, $PhCH_2NMe_2$ in FLP reactions with alkyne gave mixtures of protonation and addition products, while imines led exclusively to iminium alkynylborate.[103] Reaction of the carbodiimide *t*BuNCN*t*Bu, $B(C_6F_5)_3$, and 2 equiv of PhCCH led to concurrent addition/deprotonation reactions affording the species [*t*BuNCN(H)C(Ph)=C(H)*t*Bu][$PhCCB(C_6F_5)_3$] (Scheme 12).[103]

Analogous reactions of alkynes with FLPs derived from borane and either imine or carbene as the base gave deprotonation products,[103,104] whereas thioethers yielded the *trans*-addition products *E*-$R_2SC(Ph)=C(H)B(C_6F_5)_3$ (R = Me, $PhCH_2$) (Scheme 12). In contrast, the dimeric intramolecular FLP $(PhSCH_2B(C_6F_5)_2)_2$ reacts with alkynes to give *cis*-addition species of the form $(PhSCH_2B(C_6F_5)_2)(R'C=CR)$ (Scheme 12).[105] While basic amines lead predominantly to deprotonation products in reactions of terminal alkynes, lutidine was shown to give the addition product $(C_5H_3Me_2N)C(Ph)=CH)(B(C_6F_5)_3)_2$.[106]

Recently, we reported the analogous reaction of the Te/B FLP $PhCH_2TeC(Ph)=C(C_6F_5)B(C_6F_5)_2$ to give the zwitterionic $PhCH_2TeC(Ph)=C(C_6F_5)B(C_6F_5)_2(PhC=CH)$.[107] In related chemistry, reaction of $Te(CCR)_2$ with borane has been shown to give the double carboboration heterocyclic product $Te(C(Ph)=C(C_6F_5))_2B(C_6F_5)$. However, in some cases the kinetic product derived from the FLP addition of Te and B to the alkyne moiety of the mono-carboborated intermediate afforded $[Te(C(Ph)=C(C_6F_5))B(C_6F_5)_2(PhC=CH)]_2$ (Figure 3).[108]

Exploiting C-based nucleophiles provides an avenue to C−C bond formation. Using enamines as the base in such reactions gave a mixture of both deprotonation and addition products. However, FLPs based on pyrrole derivatives and $B(C_6F_5)_3$ react with alkynes to generate solely the addition products. In the

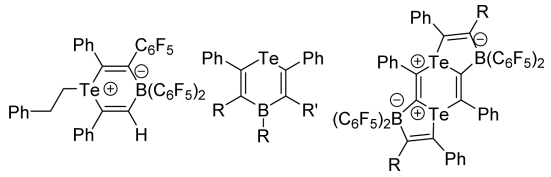
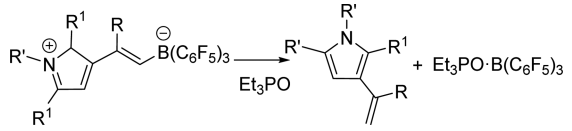


Figure 3. Te/B FLP alkyne addition products.

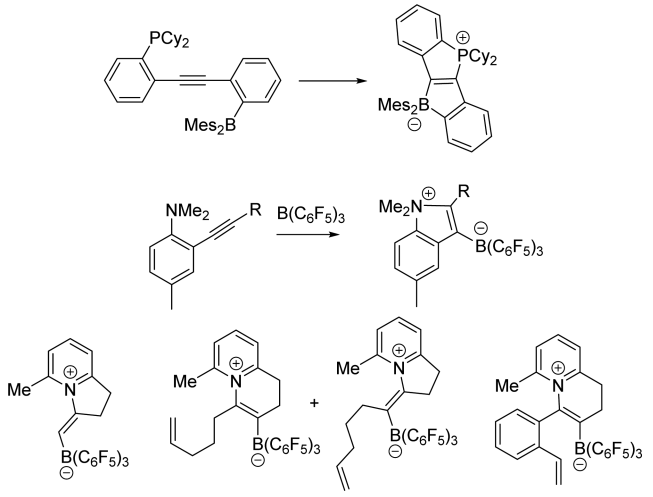
case of the less hindered *N*-methylpyrrole, a mixture of the 2- and 3-substituted pyrrole derivatives were obtained,[104] while the bulky *N*-*t*Bu-pyrrole gave exclusively the 3-substituted product. Subsequent reactivity provided routes to a series of vinyl pyrroles (Scheme 13).

Scheme 13. Conversion of Pyrrole−Borane Alkyne Addition Product to Vinyl Pyrroles



FLP−alkyne addition reactions can also be exploited in an intramolecular fashion. Yamaguchi and co-workers[109] exploited intramolecular addition of phosphines and boranes to make the zwitterionic species $C_6H_4(PCy_2)C_2B(Mes)_2C_6H_4$ (Scheme 14).

Scheme 14. Intramolecular FLP Additions to Alkynes and Sample Products



In a similar fashion, pendant alkyne fragments on aniline or pyridine rings react with borane to effect intramolecular cyclizations[99] yielding zwitterionic bicyclic ammonium salts (Scheme 14).[100]

More recently, these addition reactions have been shown to provide synthetic routes to novel heterocycles. For example, reaction of propargyl amides with $B(C_6F_5)_3$ was shown to effect a stoichiometric intramolecular cyclization reaction, affording 5-alkylidene-4,5-dihydrooxazolium borate species (Scheme 15).[110] Using secondary propargyl amides and $B(C_6F_5)_3$ as a catalyst, the corresponding oxazoles were obtained catalytically. Similarly, $B(C_6F_5)_3$ and propargyl carboxylates reacted via initial cyclization followed by ring opening and concurrent R-group migration (Scheme 15).[111] Further reactivity was found to depend on the substitution pattern of the precursor.

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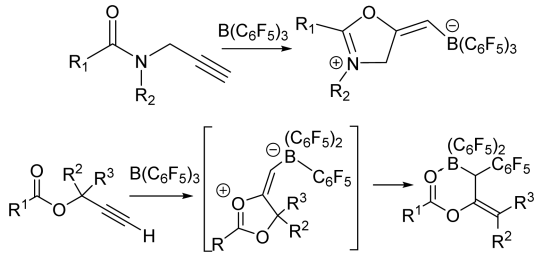
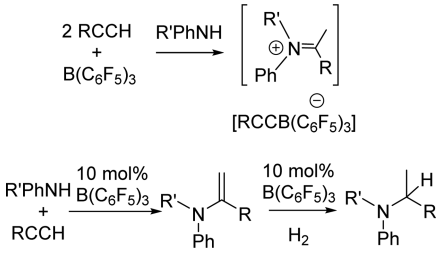
Scheme 15. Cyclization of Propargyl Amides and Esters in Reactions with $B(C_6F_5)_3$



Hydroamination. Stoichiometric reactions of alkynes with aryl amine/borane-based FLPs consumed 2 equiv of alkyne, affording iminium salts of the form $[RCH{=}NHR][RCCB(C_6F_5)_3]$ (Scheme 16).[112] Alternatively with slow addition of

Scheme 16. Stoichiometric and Consecutive Catalytic Hydroamination and Hydrogenation of Alkynes



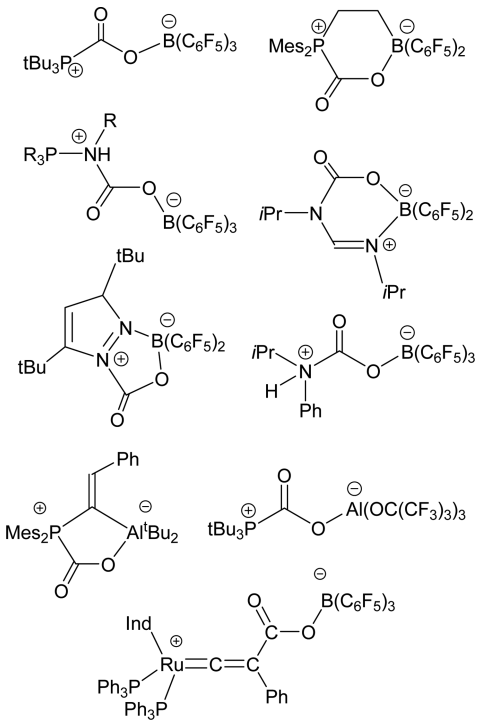
alkyne to the amine/borane catalyst mixture the catalytic generation of the corresponding enamines was achieved (Scheme 16). These reactions proceed via initial addition of the N/B FLP across the alkyne followed by proton migration, liberating the enamine and borane for further reaction.[112] The requirement of proton migrations limits the scope of bases to aryl amines. Nonetheless, the reactivity provides the first metal-free hydroamination catalysis. Interestingly, this catalysis can be performed in tandem with a subsequent catalytic hydrogenation, affording the corresponding saturated amine product (Scheme 16).[112]

FLP CHEMISTRY OF SMALL MOLECULE OXIDES

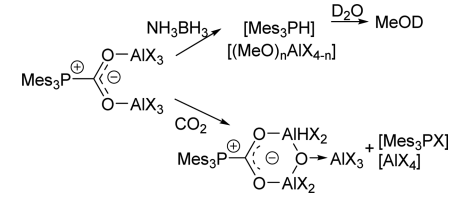
CO_2 Capture. The initial report of thermally reversible CO_2 capture by P/B FLPs was described for $R_3PCO_2B(C_6F_5)_3$ and $Mes_2PCH_2CH_2B(C_6F_5)_2(CO_2)$ (Scheme 17).[113] The thermodynamics of the capture of CO_2 by $tBu_3P/B(C_6F_5)_2Cl$ were recently determined via an ingenious microfluidic method developed by Kumacheva and co-workers.[114] A number of reports have shown that a broad range of FLPs are capable of capturing CO_2. Both inter- and intramolecular FLPs variants have been explored, including those derived from B,[115−118] Al,[119−125] Ti,[117] Zr,[126−129] Hf,[130] and Si[131] electrophiles and donors including NHCs,[132−135] amines,[98,136−138] phosphinimines,[139] pyrazoles,[140] or even the β-carbon of a Ru-acetylide species (Scheme 17).[141] While a broad range of systems have been described, they are similar in that the base binds to C while one of the oxygen atoms interacts with the Lewis acid.

It is also possible to bind both oxygen atoms of CO_2 to Lewis acidic centers employing bis-borane/phosphine FLPs such as $Me_2C{=}C(BCl_2)_2O_2CPtBu_3$ and $Me_2C{=}C(B(C_6F_5)_2)_2O_2$-$CPtBu_3$ (Scheme 18).[142] In contrast, the bis-borane $C_6H_4(BCl_2)_2/tBu_3P$ captures CO_2, affording $C_6H_4[BCl_2(Cl)$-

Scheme 17. Examples of CO_2 Capture by FLPs



Scheme 18. Stoichiometric Reductions of CO_2 with P/Al FLPs



$BCl(O_2CPtBu_3)$,[143] where CO_2 binds to a single boron atom with a bridging Cl atom between the B centers (Figure 4).

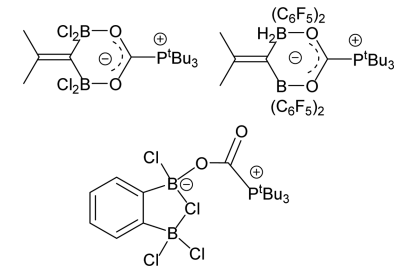


Figure 4. Phosphine/bis-borane FLP products with CO_2.

Seemingly quenched donors and acceptors have also been shown to react with CO_2. For example, CO_2 inserts into the four-membered B-amidinate $HC(iPrN)_2B(C_6F_5)_2$,[144] affording $HC(iPrN)_2(CO_2)B(C_6F_5)_2$ (Scheme 19), presumably a result of the transient availability of the open-form of this N/B FLP. Similarly, CO_2 reacts with $C_6H_4(NMe)PFPh_2$ and $[C_6H_4(NMe)]_2PPh$ to give $C_6H_4(NMe)(CO_2)PFPh_2$ and $[C_6H_4NMe(CO_2)]_2PPh$, respectively (Figure 5). Interestingly in these latter cases, the FLP is comprised of the Lewis acidic P(V) center and the Lewis basic amido-N atom.[145]

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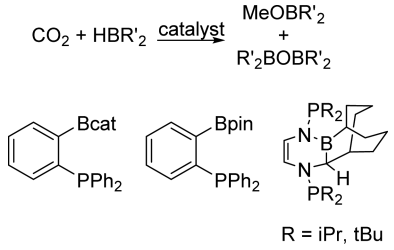
Scheme 19. Catalytic Hydroboration of CO_2 by B/P FLPs



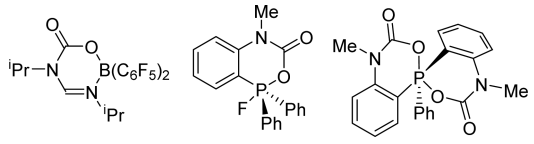


Figure 5. Products of CO_2 into four-membered ring precursors.

Stoichiometric Reduction of CO_2. Beyond capture, Al/P FLP $PMes_3/AlX_3$ can be exploited for stoichiometric reductions. Initial exposure of this FLP to CO_2 generates the species $Mes_3P(CO_2)(AlX_3)_2$.[119] This species is stable to 80 °C but reacts rapidly with H_3NBH_3 to give Al-methoxy species which generates MeOH upon workup (Scheme 18). Interestingly, upon prolonged exposure of CO_2 to $Mes_3PC(OAlI_3)_2$ stoichiometrically reduces CO_2, affording $Mes_3PC(OAlI_2)_2OAlI_3$, $[Mes_3PI][AlI_4]$, and CO (Scheme 18).[120,121] Detailed studies of the latter transformation was studied in detail showing the mechanism involves dissociative equilibria and associative insertion of CO_2 into an Al−X bonds, leading to CO_2 reduction and oxidation of the phosphine to the iodophosphonium cation.[121]

In efforts to reduce CO_2 with a hydrogen equivalent, reaction of $[tBu_3PH][RBH(C_6F_5)_2]$ with CO_2 was shown to give the formate derivative $[tBu_3PH][((C_6F_5)_2BR)_2(\mu\text{-}HCO_2)]$ while $[tBu_3PH][(C_6F_5)_2BR(O_2CH)]$ (Figure 6) were derived from

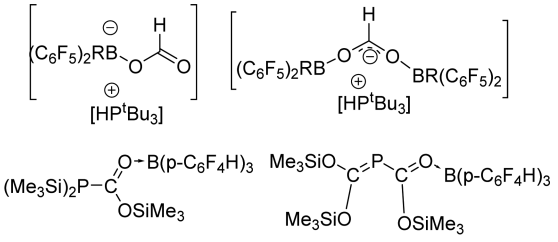


Figure 6. Products of stoichiometric FLP reduction of CO_2.

the reaction of the FLP with formic acid.[146] In related chemistry, the FLP $(Me_3Si)_3P/B(p\text{-}C_6F_4H)_3$ reacts with CO_2 to yield $((Me_3Si)_2PC(OSiMe_3)O)B(p\text{-}C_6F_4H)_3$[147] and $((Me_3SiO)_2C{=}P{-}C(OSiMe_3){=}O)B(p\text{-}C_6F_4H)_3$, depending on the solvent. These products are derived from initial FLP capture of CO_2 followed by silyl group migration.

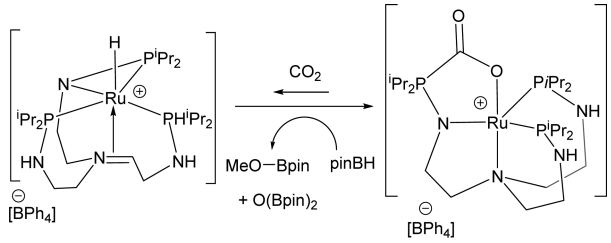
Catalytic CO_2 Reduction. O'Hare and Ashley[148] described the first evidence of FLP-catalyzed reduction of CO_2 when they combined CO_2 and H_2 in the presence of tetramethylpiperidine (TMP)/$B(C_6F_5)_3$. This gave $CH_3OB(C_6F_5)_2$ after 6 days at 160 °C. In a related study, Piers and co-workers[146] used Et_3SiH to effect catalytic reduction of CO_2, yielding CH_4 and $(Et_3Si)_2O$.[146]

Fontaine and co-workers[149] described reduction of CO_2 using borane as the reductant and the intramolecular FLP $Ph_2PC_6H_4B(O_2C_6H_4)$ (Scheme 19), generating $MeOBR_2$ and $O(BR_2)_2$.[150] In closely related work, we reported the use of $C_3H_2(NPR_2)_2BC_8H_{14}$ (Scheme 19) as a catalyst which was derived from the insertion of $C_3H_2(NPR_2)_2$ into 9-BBN.[151] In a further study, we[152] showed that hydroboration of CO_2 by 9-BBN is catalyzed by phosphine, affording a mixture of $MeOB(C_8H_{14})$ and $O(B(C_8H_{14}))_2$ in 98% yield with as little as 0.02% phosphine as the catalyst.

In a recent collaborative effort with the Fontaine group[153] we explored B/N FLPs of the form 1-BR_2-2-NMe_2-C_6H_4 for the hydrogenation of CO_2, with initial reactions with H_2 resulting in protodeborylation, affording $(1\text{-}BH_2\text{-}2\text{-}NMe_2\text{-}C_6H_4)_2$. Subsequent reaction with H_2/CO_2 gave formyl, acetal, and methoxy derivatives, suggesting that judicious FLP design may permit catalytic hydrogenation of CO_2.

Targeting alternative strategies to catalytic CO_2 reduction, we developed the metal-based FLP derived from the Ru complex $[(N((CH_2)_2NHPiPr_2)((CH_2)_2NPiPr_2)(CHCH_2\text{-}NHPiPr_2))RuH][BPh_4]$ (Scheme 20).[154,155] In this species

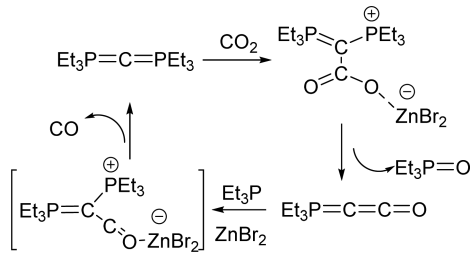
Scheme 20. Catalytic Hydroboration of CO_2 by Ru/P FLP



the metal center and the pendant phosphine act as the acid and base, respectively. This FLP captures CO_2, catalyzes the hydroboration of CO_2 in the presence of excess HBpin, HBcat, or 9-BBN, and generates MeOB and BOB species as the reduction products.[154,155]

A further alternative exploited the combination of Et_3P and CO_2 in the presence of a catalytic amount of CH_2I_2 and $ZnBr_2$ to effect the catalytic reduction of CO_2. This afforded the oxidation of phosphine and concurrent liberation of CO.[156] Mechanistic and computational studies suggest that the action of phosphine/ZnX_2 as an FLP on transient ketene intermediates prompts loss of CO and regeneration of a bis-ylide catalyst (Scheme 21).[156]

Scheme 21. Catalytic Reduction of CO_2 by P/Zn FLPs



N_2O Capture and Chemistry. In a fashion similar to the capture of CO_2, FLPs have been shown to capture N_2O, affording the species $tBu_3P(N_2O)B(C_6F_5)_3$[157] in which phosphine is bound to the terminal N and boron to O, yielding a PN_2OB linkage. While smaller or less basic phosphines are readily oxidized in the presence of N_2O, related FLP−N_2O complexes could be prepared using a variety of

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FLPs derived from strong donor phosphines and B- and Al-based Lewis acids (Figure 7).[158,159] Alternatively, such species

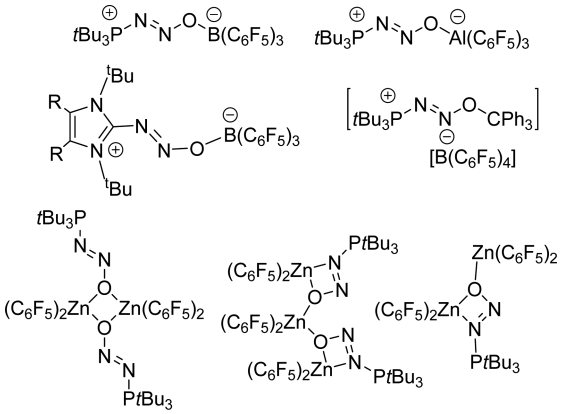
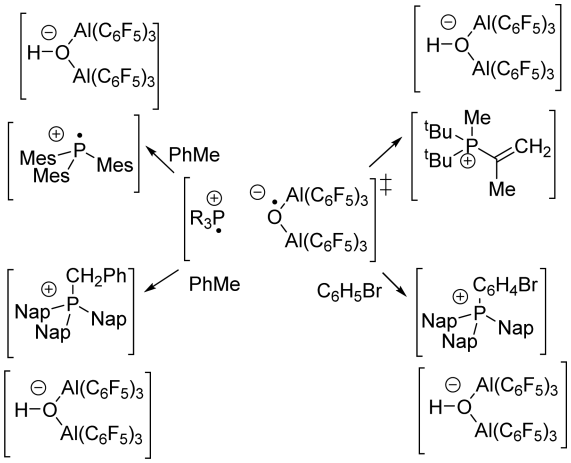


Figure 7. Examples of FLP–N_2O adducts and PN_2O exchange products.

can be accessed by Lewis acid exchange reactions. For example, the PN_2O fragment could be transferred to Zn (Scheme 21), generating several new metal N_2O derivatives. Severin prepared related complexes employing carbene-based FLPs (Figure 7).[160,161]

Further reaction of the species $tBu_3P(N_2O)Al(C_6F_5)_3$[158] with a second equivalent of Lewis acid was shown to generate the transient "frustrated radical pair" (FRP) $[R_3P^{\bullet}]^{+}[(\mu\text{-}O^{\bullet})(Al(C_6F_5)_3)_2]^{-\bullet}$ (Scheme 22). This species effects C–H bond

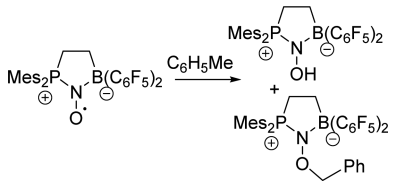
Scheme 22. C–H Activation by Transient FRPs



activations. In the case where R = *t*Bu the species $[tBu_2PMe(C(CH_2)Me)][(\mu\text{-}OH)(Al(C_6F_5)_3)_2]$ (Scheme 22) was formed[158] resulting from the activation of a C–H bond of one of the *t*-butyl groups. For R = Mes, activation of solvent C–H bonds afforded the isolation of the deep purple radical cation salt $[Mes_3P^{\bullet}][(\mu\text{-}HO)(Al(C_6F_5)_3)_2]$. Where R = naphthyl, the species $[(Nap)_3PCH_2Ph][(\mu\text{-}OH)(Al(C_6F_5)_3)_2]$ is derived from C–H activation of the solvent toluene, while the species $[(Nap)_3PC_6H_4Br][(\mu\text{-}HO)(Al(C_6F_5)_3)_2]$ (Scheme 22) is formed in bromobenzene.[158]

NO Capture and Chemistry. The ethylene-bridged P/B FLP system has been shown to react with NO yielding the five-membered heterocyclic $Mes_2P(CH_2)_2B(C_6F_5)_2(NO)$ persistent radical.[162] This species behaves as an oxygen-centered radical, reacting with toluene to effect H-atom abstraction to give the products, $Mes_2P(CH_2)_2B(C_6F_5)_2(NOR)$ (R = H, CH_2Ph) (Scheme 23). While this reactivity was extended to other

Scheme 23. Reaction of an FLP–NO Radical



intramolecular P/B FLPs[162,163] for detailed kinetic and mechanistic studies,[164] such species could also be used in the radical polymerization of styrene.[162]

SO_2 and RNSO Capture and Chemistry. FLPs have also been used to capture SO_2, affording inter- and intramolecular FLP adducts. $tBu_3PSO_2B(C_6F_5)_3$ and $Mes_2P(CH_2)_2B(C_6F_5)_2(SO_2)$ (Figure 8).[165] Binding of the phosphine to S

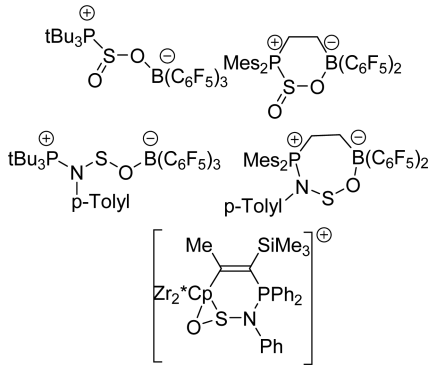
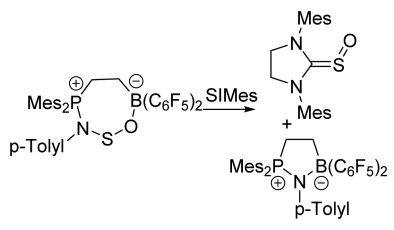


Figure 8. FLP–SO_2 and FLP–RNSO adducts.

yields species reminiscent of FLP–CO_2 adducts, although the S exhibits a pseudo-pyramidal geometry. Analogs derived from chiral intramolecular FLPs have been obtained as mixtures of diastereomers resulting from the chirality at S.[166]

In closely related chemistry, Erker described the reaction of a Zr^{+}/P FLP system with N-sulfinylamines. However, in this case, formation of a P–N bond is seen with the S–O fragment binding to the Zr^{+} in a side-on fashion (Figure 8).[167] The analogous reaction of RNSO with P/B FLPs leads to its capture as well in this case; however, a 1,3-addition was observed, with P bound to N and O to B.[168] The intramolecular FLP adduct $Mes_2P(CH_2)_2B(C_6F_5)_2(RNSO)$ (Scheme 24) exhibits an unusual seven-membered heterocycle. These RNSO adducts can be described as phosphinimine/borane FLP adducts of SO. Indeed, this heterocyclic species was subsequently shown to act as a source of SO, reacting with phosphine to give

Scheme 24. Reaction of FLP–NSO Adduct with NHC



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phosphineoxide and phosphinesulfide with concurrent formation of the five-membered ring $Mes_2P(CH_2)_2B(C_6F_5)_2(NR)$. Similarly, delivery of intact SO to carbene and Rh afforded (SIMes)SO (Figure 8) and $[RhCl(\mu\text{-}\eta^1\eta^2\text{-}SO)(PPh_3)_2]_2$, respectively, again with concurrent formation of $Mes_2P(CH_2)_2B(C_6F_5)_2(NR)$.

FLP CHEMISTRY: IN CONTEXT

It is true that the articulation of the notion of FLPs in 2006−2007 seemingly unleashed a flurry of activity; however, it is important to note that previous investigators had made observations that foreshadowed this concept. Brown[169] certainly observed that steric bulky could preclude classical adduct formation. Wittig[170−172] and Tochtermann[173] reported unexpected reactivity of such combinations with benzyne and butadienes. Erker[174] reported unexpected reactivity of a phosphorus-ylide and $B(C_6F_5)_3$ which affords *para*-substitution; however, it was the work of Piers that best illustrated the principle of FLP chemistry without describing it as such.[175] In this work, carried out more than a decade before the term FLP was used, Piers and co-workers foreshadowed the field with their description of the mechanism of borane-mediated hydrosilylation of ketones. Their careful mechanistic studies demonstrated that dissociation of the ketone/borane adduct allows for the interaction of the silane Si−H bond with the borane, prompting nucleophilic attack by the ketone. Further confirmation of the details of this mechanism were subsequently provided by the work of Oestreich,[176,177] who employed a chiral silane to confirm the inversion of stereochemistry at silicon, consistent with Piers's proposal. Most recently, the interaction of electrophilic boron centers with silane was unambiguously confirmed when Piers isolated an adduct of silane with a highly electrophilic borole.[178]

The relation of the notion of FLPs to established organometallic chemistry is also worthy of comment. Perhaps most relevant is the heterolytic cleavage of H_2 achieved by bifunctional catalysts.[4] In such cases, a donor and an adjacent metal center act in concert to heterolytically activate H_2, reminiscent of the process seen for FLPs. One distinction between these systems is the presence of the covalent interaction between the donor and metal center in bifunctional metal catalysts. However, it should be pointed out that the covalently bound phosphine and boron centers in $R_2PB(C_6F_5)_2$ act in concert to effect H_2 activation. It is the energetic mismatch of the highest occupied molecular orbital on phosphorus with the lowest unoccupied molecular orbital on boron, described as "electronic frustration", that presumably accounts for this reactivity.[179] This situation is highly reminiscent of bifunctional transition metal catalysts. In this regard it is also important to draw attention to transition metal-based FLPs in which metal centers with pendant donors activate a range of small molecule substrates, which has been explored by the groups of Wass[126,127,180−183] and Erker[128,129,184−188] among others.[130]

The concept of FLPs has also been exploited to describe a variety of systems that activate small molecules. For example, several papers[189−192] describing hydrogenase models in which H_2 is heterolytically split between a metal center and a remote N donor have described the analogy of the mechanism of action to FLPs. Similarly, Peters[193] developed the chemistry of a Ni species with a pendant borane center which activates H_2 in a heterolyic fashion, drawing attention to the analogy with FLP reactivity. Similarly, given the role of gold species as Lewis acids in catalysis,[110,194,195] the analogy to FLP chemistry has been made. At the same time, the concept of FLPs has recently been employed to describe the heterogeneous hydrogenation of imines and nitriles by a gold surface−phosphine solution interface[196] and the heterogeneous reduction of CO_2 on the surface of InO.[197]

FUTURE PROSPECTS

The concept of FLPs has contributed significantly to the renaissance of main group chemistry. While the scope of substrates for FLP hydrogenation has broadened considerably in the past 9 years, the majority of studies have focused on B/P FLPs. Only recently has the variety of donors and acceptors capable of H_2 activation begun to be explored. With the emergence of a broadening variability in the range of donor−acceptor combinations capable of splitting H_2, a broadening scope of substrates, improved functional tolerance, and enhanced catalyst activity are expected to emerge. Such developments are expected to be rapid, benefiting from the broad knowledge base derived from the design of organometallic catalysts. In this regard, given that stereoselective FLP hydrogenation is still in its infancy, we expect significant advances to continue to emerge for chiral metal-free FLP catalysts. Indeed, the terrific progress seen to date augurs well for future developments. The potential of such advances to find commercial application will of course depend on catalyst efficacy and functional group tolerance. Nonetheless, the promise of lower catalyst costs, lower catalyst toxicity, and thus reduced purification costs are prospects that will be of much interest.

The application of FLP chemistry in organic synthetic chemistry is another area in its infancy. Certainly FLP chemistry offers routes to the reduction of a number of functional groups, and we also see potential in the synthetic utility of metal-free FLP aromatic reductions. As such reactions offer an interesting and unconventional approach to polycyclic amines, this suggests the prospect of combining conventional methods of aromatic substitution with stereoselective aromatic reduction as a synthetic strategy to polycyclic amine natural products.

The activation of small molecules by FLPs is an area that continues to grow and is ripe for future development of applications. Certainly it is reasonable to query the potential of FLPs in C−H activation, dehydrogenation catalysis or perhaps even O_2 or N_2 chemistry. FLP chemistry of judiciously substituted alkenes and alkynes may find applications in organic synthesis. It is perhaps obvious that efforts to reduce CO_2 will continue as this is a subject of broad interest and high potential impact. At the same time, developments in materials chemistry are also anticipated. While FLP chemistry may offer new synthons for unique materials, the use of FLP−NO radical[198] catalysts in polymerizations as well as the ability of FLPs to mediate the polymerization catalysis of acrylates and vinyl monomers developed by Chen[199−203] foreshadows further applications in materials chemistry.

While all chemistry involves the action of electron-donating and electron-accepting centers, FLP chemistry is conceptually interesting as it focuses attention on three component reactions in which nucleophilic and electrophilic centers act on a third component. Initial reports suggested the requirement of non-interacting Lewis acid and bases; however, it is now clear that this is but one extreme. Indeed, systems in which equilibria govern adduct formation can clearly exhibit FLP reactivity.

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From fundamental theoretical and physical perspectives, this focuses attention on the role of van der Waals interactions and molecular dynamics. Synthetically, while initially opening a new avenue to main group reactivity, the implications extend well beyond as such three component reactions offer opportunities to impact on catalysis, organic synthesis, and materials chemistry. Moreover, there are now signs that the notion of FLPs can be conceptually exploited in other areas, including transition metal and bioinorganic chemistry as well as surface science. Thus, while FLP chemistry has been focused on applications of main group species in synthetic chemistry, the concept is primed for broader impact. It will be exciting to see how the creativity of the chemical community exploits this concept.

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Notes

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