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Phosphorus Lewis Acids: Emerging Reactivity and Applications in Catalysis

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Phosphorus Lewis Acids: Emerging Reactivity and Applications in Catalysis

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Part of the renaissance in main group chemistry has been a result of the focus on reactivity. This has led to the development of applications in stoichiometric reactivity and catalysis. In this tutorial review, we focus attention on the role of phosphorus-based Lewis acids in such advances. While early literature recognizes the role of P(III) and P(V) electrophiles in coordination chemistry, it has generally been more recent studies that have focused on applications of this Lewis acidity. Applications of these novel P-based Lewis acids in stoichiometric reactivity, Lewis acid catalysis and frustrated Lewis pair (FLP) reactivity are reviewed. These advances demonstrate that P-based Lewis acids are a powerful tool for further developments in metal-free catalysis.

Key Learning Points

1. The development of main group catalysis has contributed to significant advancements in catalytic and stoichiometric transformations.
2. Although P(III) species are typical Lewis bases, phosphenium cations have demonstrated electron accepting abilities.
3. As saturated acceptors, phosphorus(V)-based Lewis acids derive their acidity from a low lying σ* orbital.
4. The Lewis acidity of P-based compounds can be modified by tuning their electron properties.

Introduction

Catalysts are critical to the production of desirable chemicals and materials that are used to manufacture goods which are the basis of our modern economy. From pharmaceuticals and polymers to agrochemicals and electronics, these advances of civilization depend on effective catalyst technologies. At the same time, manufacturing and production technologies are under increasing scrutiny with respect to their impact on the environment. While catalysis offers increased efficiencies and lower production costs, these technologies also come with some environmental concerns. Certainly, the majority of catalyst technologies presently employ precious metals in either homogeneous or heterogeneous catalysis. Concerns regarding the use of such metals in catalysis are associated with cost, toxicity and carbon footprint of obtaining these materials.

To begin to offer alternative catalyst technologies, there has been much effort in recent years within the organometallic chemistry community to uncover catalysts based on earth abundant, first row transition metals.[1] Alternative approaches that are also emerging are based on the notion of metal-free catalysis. In these latter efforts, organocatalysis[2] has emerged as active area of study. While generally less studied, the use of main group species for catalysis has begun to garner increasing attention in the last decade. One of the advances that has prompted this interest has been the articulation of the concept of "frustrated Lewis pairs" (FLPs).[3-4] The concept of FLPs has been responsible for the advent of metal-free hydrogenation technologies, prompting the reduction of a variety of organic unsaturated species. At the same time, the activation of other small molecules by FLP chemistry has, also led to the development of catalysts for the metal-free hydroamination of alkynes and the reduction of CO_2.[5] While the bulk of the advances of FLP chemistry has exploited boron-based Lewis acids, this chemistry has prompted questions about the potential reactivity and utility of other main group Lewis acids in both Lewis acid catalysis and FLP chemistry.

Phosphorus compounds are generally employed as Lewis bases. Indeed much of the homogeneous organometallic chemistry in the literature utilizes phosphines as donors to stabilize transition metal species of interest. However, there are indications in the literature that some phosphorus derivatives exhibit Lewis acidic properties that could be exploited for catalysis. Indeed, more recent attention has led to a number of developments, and these advances in phosphorus-based Lewis acid catalysis are beginning to emerge. These developments offer new avenues for both stoichiometric and catalytic transformations, and the versatility of P-based electrophiles is defining new Lewis acid-mediated transformations. This tutorial review summarizes recent progress in this area, with the intention of lighting the way to future advances.

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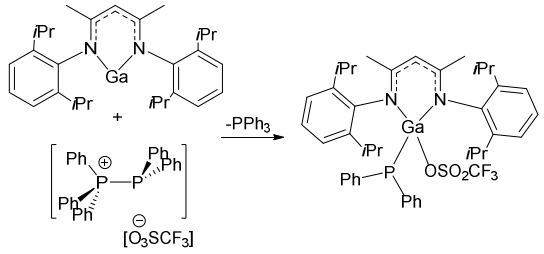
Discussion

P(III) Lewis Acids

P(III) compounds are typical Lewis bases, due to the accessible lone pair of electrons. However, after the initial discovery of phosphenium cations in 1964,[6] evidence of Lewis acidity at phosphorus began to emerge. In their 1985 review, Cowley and Kempe[7] highlighted some of the first Lewis acidic phosphenium ions. Some of the early examples included electrophilic reactions of phosphenium cations resulting in insertions into C-H bonds in Cp_2Sn, as well as reactions with 1,3- and 1,4-dienes to give cyclopentene-phosphonium derivatives.

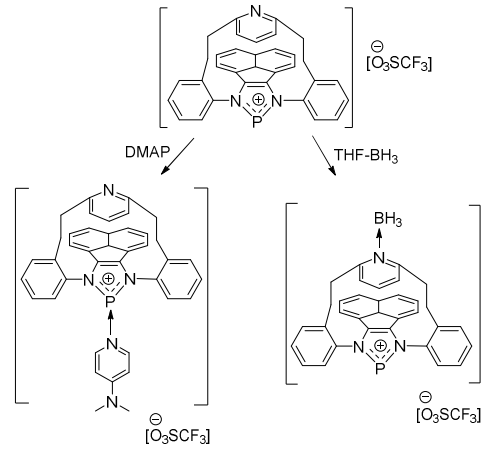
In 2000, Nieger *et al*., developed the interesting N-heterocyclic phosphenium (NHP) cation $[(C_2H_2NR)_2P]^+$. These compounds are isovalent to Arduengo's N-heterocyclic carbenes, but with inverse electronic properties- that is, being more Lewis acidic than donating.[8] Computational studies confirmed the electrophilic character at P, and these authors demonstrated that these species could form adducts with Lewis bases such as nucleophilic amidines. In a subsequent study,[9] the related NHP-phosphide adduct, $[(C_2H_2NMes)_2PPPh_2]$, was shown to react with a series of small molecules including dichloromethane, isopropanol, water, acrylonitrile and methyl acrylate to affect P-P bond cleavage.

While Burford and Ragogna reviewed further examples of the coordination chemistry of phosphenium cations,[10] Power *et al*. drew attention to the electrophilic reactivity of phosphenium cations.[11] In that report, they described the reaction of the phosphinophosphonium cation $[Ph_3PPPh_2][OSO_2CF_3]$ with a β-diketiminate Ga(I) complex, $HC(CMeN(2,6\text{-}iPr_2C_6H_3))_2Ga$. Interestingly, this led to displacement of Ph_3P generating the Ga-phosphide derivative $HC(CMeN(2,6\text{-}iPr_2C_6H_3))_2GaPPh_2(OSO_2CF_3)$ (Scheme 1). This was described as a "coordination chemistry umpolung" as this was a rare example of reactivity with a Lewis acidic P(III) species.



Scheme 1. Reaction of a triphenylphosphine-diphenylphosphenium triflate salt with a β-diketiminate Ga(I) complex.

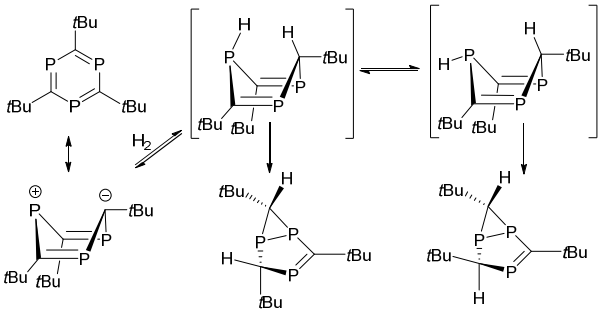
Subsequently, in 2010, the Lewis acidity of NHPs was further highlighted by Ragogna *et al*.,[12] wherein they synthesized a unique intramolecular FLP comprised of an NHP and a pendant lutidine donor. While the Lewis acidic P cation formed no adduct with PMe_3 or pyridine, the 4-*N*,*N*-dimethylaminopyridine (DMAP) adduct was observed. Similarly, the pendant lutidine was shown to form a BH_3 adduct (Scheme 2).



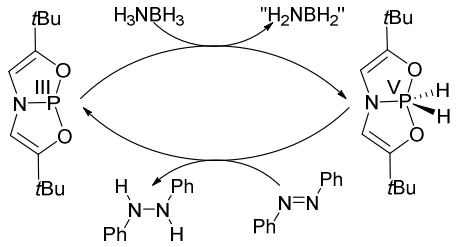
Scheme 2. Reactions of a phosphenium/lutidine FLP with DMAP and BH_3.

In 2012, Slattery and Hussein[13] probed the Lewis acidity of phosphenium cations by developing a scale of fluoride ion affinities from computationally-determined fluorophilicities. From the gas-phase calculations, they reported that some phosphenium cations are substantially more Lewis acidic than the main group Lewis acids BF_3, BCl_3, $AlCl_3$ and SbF_5.

A unique example of P-based Lewis acidic behaviour was observed in a recent report of the direct reaction of 2,4,6-tri-*t*butyl-1,3,5-triphosphabenzene with H_2.[14] Upon exposure to 4 atm of H_2, after 24 h at ambient temperature, the triphosphabenzene $(PCtBu)_3$ reacted with H_2 affording addition of one equivalent of H_2 and the formation of an isomeric mixture of the [3.1.0]bicyclic product, which was comprised of fused 5 and 3 membered rings $(PCtBu)_3H_2$ (Scheme 3). Variable temperature data in conjunction with p*ara*-hydrogen experiments were consistent with the initial generation of an intermediate formed by 1,4-addition of H_2 to the triphosphabenzene derivative. Computational data supported that this reaction with H_2 proceeds from a boat conformation of a resonance form of triphosphabenzene in which negative and positive charges are formally located on *para*- C and P atoms.



Scheme 3. Hydrogenation of 2,4,6-tri-*t*butyl-1,3,5-triphosphabenzene.



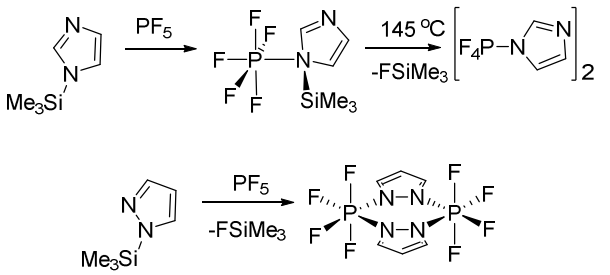
Scheme 4. Catalytic reduction of azobenzene facilitated by a Lewis acidic phosphonium intermediate.

In 2012, Radosevich *et al.*[15] reported the first redox P(III)/P(V) catalytic cycle to affect the reduction of azobenzene. This was achieved with a P(III) species in which the NO_2 tridentate ligand imposed a distorted geometry and facilitated reaction with ammonia-borane, resulting in the formation of a P(V) dihydridophosphorane (Scheme 4). It was proposed that the ammonia-borane first protonates the P(III) species generating a Lewis acidic phosphonium intermediate which then abstracts hydride from the aminoborate. The Lewis acidity of this P(V) species prompted reactions with azobenzene derivatives, triggering the reduction of the P(V) species to P(III) with concurrent transfer of H_2 to azobenzene (Scheme 4).

P(V) Lewis Acids

Unlike neutral P(III) compounds, neutral P(V) species are more easily recognized as Lewis acids. Perhaps the most notable example is the Wittig reagent.[16] These ubiquitous ylide reagents of the form R_3P=CHR' are electrophilic at P and thus are highly effective for the conversion of aldehydes and ketones to alkenes. In the 1960s, pentacoordinate phosphoranes with electron-withdrawing substituents were recognized to be Lewis acidic due to the low-lying σ* orbital.[17] Indeed these species are known to form a variety of Lewis acid-base adducts as well as a myriad of six-coordinate species derived from bi- and tridentate ligands.[18]

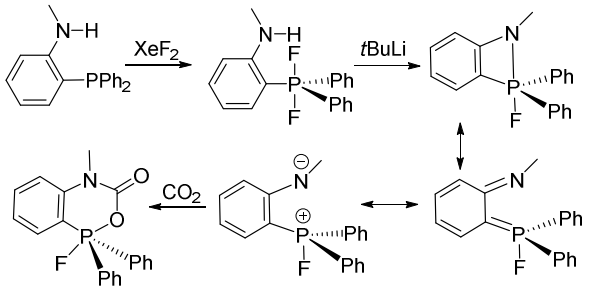
One example of such coordination chemistry and reactivity was reported by Schmutzler *et al.*[19] They highlighted the Lewis acidity of neutral P(V) species through reactivity of PF_5 with some *N*-trimethylsilyl nitrogen heterocycles. In this example, the combination of PF_5 and *N*-trimethylsilylimidazole formed a hexacoordinate P(V) Lewis acid-base adduct, which upon heating generated the corresponding pentacoordinate amidophosphorane (Scheme 5). Conversely, the addition of PF_5 to trimethylsilylpyrazole resulted in the direct formation of an amidophosphorane dimer (Scheme 5) with no observed adduct formation presumably *via* a transient phosphorane intermediate. The differing reactivity in these two cases is attributed to the formation of a stable six-membered ring in the latter reaction.



Scheme 5. Reactivity of PF_5 with two *N*-trimethylsilyl nitrogen heterocycles.

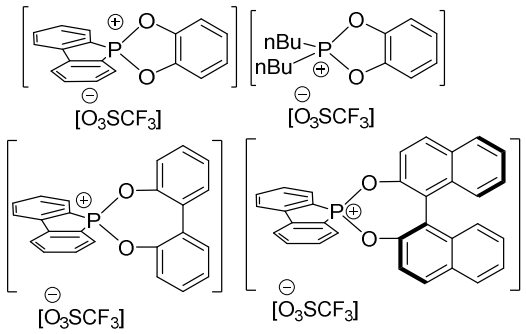
In his review, Cavell noted that beyond coordination chemistry, the reactivity of electrophilic P(V)[18] had received limited attention. While this is generally true throughout the 20th century, there are a couple of examples that foreshadow the potential utility of P(V) as a Lewis acid. For instance, in 1977, Cavell *et al.*[20] reported the first example of CO_2 insertion into a pentacoordinate amidophosphorane, demonstrating CO_2 and CS_2 capture with $CH_3(CF_3)_3P$-$N(CH_3)_2$, affording $CH_3(CF_3)_3PO_2CN(CH_3)_2$, and $CH_3(CF_3)_3PS_2CN(CH_3)_2$, respectively. While not described as such, this can be viewed as an FLP reaction in which the phosphonium centre acts as the Lewis acid binding O or S while the amido N-atom is the Lewis base.

More recently, we[21] reported the irreversible sequestration of CO_2 with a ring-strained amidofluorophosphorane. In this case, oxidation of *o*-phosphinoaniline, $Ph_2P(o\text{-}C_6H_4NHMe)$, with XeF_2 afforded the corresponding difluorophosphorane. Addition of *t*BuLi facilitated deprotonation and fluoride abstraction, generating the four-membered amidofluorophosphorane (Scheme 6). Exposure to 1 atm of CO_2 at ambient temperature resulted in insertion of CO_2 into the P-N bond giving the six-membered carbamatofluorophosphorane, $Ph_2P(o\text{-}C_6H_4NMe)(CO_2)$ (Scheme 6). Similarly, double CO_2 insertion was observed from the analogous reaction sequence with $PhP(o\text{-}C_6H_4NHMe)_2$, affording $PhP(o\text{-}C_6H_4NMe(CO_2))_2$. These products are viewed as a result of the action of P-N FLPs on CO_2. This view is supported by the resonance structure of the amido-phosphoranes, which presumably are comprised of a formally cationic P centre and anionic N centre.



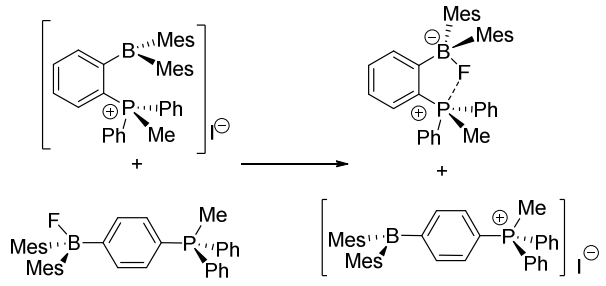
Scheme 6. CO_2 sequestration with a pentacoordinate amidophosphorane.

Phosphonium cations have also been shown to exhibit electrophilic properties. In contrast to boranes where the Lewis acidity arises from a vacant p-orbital, phosphonium cations derive their reactivity from a low-lying σ* orbital oriented opposite the electron withdrawing group.[22] In 2006, Terada and Kouchi supported this proposition with experimental evidence,[23] showing that electron deficient alkoxyphosphonium cations (Scheme 7) derived from catechols acted as Lewis acid catalysts for the Diels-Alder reactions of α,β-unsaturated amides. In contrast, structurally related biphenol derivatives were inactive. These observations were also consistent with the ability of the catechol-derivatives to coordinate dimethylformamide (DMF). In contrast, the biphenol derivatives (Scheme 7) did not bind DMF, consistent with the notion that steric congestion precluded access to the σ* orbital.



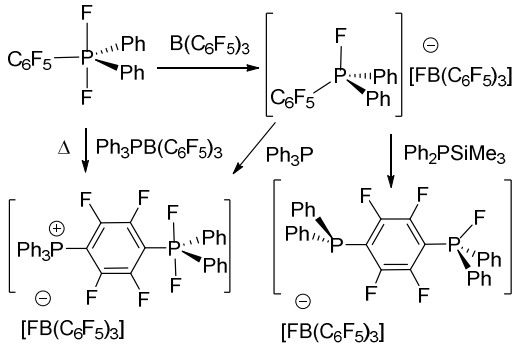
Scheme 7. Some examples of alkoxyphosphonium cations.

In 2008, Gabbaï *et al*.[24] examined the impact of a proximal P(V) Lewis acid on the Lewis acidity of boron. To this end, they prepared the species $[1\text{-}(Mes_2B)\text{-}2\text{-}(MePh_2P)(C_6H_4)]^+$ in which a phosphonium centre is *ortho*- to a borane centre. At the same time, the *para* analogue $[1\text{-}(Mes_2B)\text{-}4\text{-}(MePh_2P)(C_6H_4)]^+$ was fluorinated with $[S(NMe_2)_3][SiMe_3F_2]$, generating $[1\text{-}(Mes_2BF)\text{-}4\text{-}(MePh_2P)(C_6H_4)]$. This latter species reacts with the *ortho*-phosphonium borane, resulting in fluoride transfer to the *ortho*- substituted phosphonium cation (Scheme 8). This is consistent with cooperative enhancement of the Lewis acidity at B as a result of the proximal phosphonium centre. Interestingly, interaction between the boron-bound fluoride and the P centre was observed in the X-ray crystal structure, further corroborating the electrophilicity of the cationic P centre.



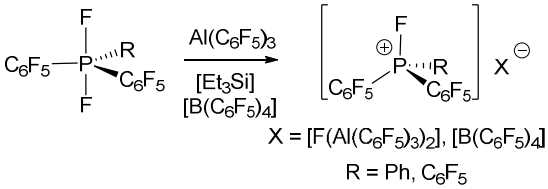
Scheme 8. Fluoride migration between two phosphorus Lewis acids bearing borane moieties.

In addition to stoichiometric transformations, phosphonium cations have been used to catalyse a wide variety of organic reactions. Some of the first examples include the addition to polar unsaturates[25] and the cyanosilylation of aldehydes[26] and ketones.[27] Moreover, in 2009, Werner[28] reviewed the use of phosphonium salts as Lewis acid catalysts for a variety of C-C, C-O and C-N bond forming reactions under homogenous conditions.



Scheme 9. Synthesis and reactivity of an electron deficient fluorophosphonium cation.

A unique approach to P-based Lewis acid catalysis targeted electrophilic phosphonium cations (EPCs).[29] Synthetically, such species were prepared by phosphine oxidation with XeF_2 followed by fluoride abstraction. Thus for example, the phosphine, $P(Ph)_2(C_6F_5)$ could be converted to $PF_2(Ph)_2(C_6F_5)$ and subsequent reaction with $B(C_6F_5)_3$ or $Me_3SiOSO_2CF_3$ was used to generate the corresponding fluorophosphonium salts $[(C_6F_5)Ph_2PF][X]$ (X = $FB(C_6F_5)_3$ or OSO_2CF_3).[29] It is important to note that the presence of the electron withdrawing substituents on this phosphonium cation lowers the energy of the σ* orbital, which results in its orientation opposite the polar P-F bond. Interestingly, upon exposure to PPh_3 $[(C_6F_5)Ph_2PF][FB(C_6F_5)_3]$ undergoes thermally induced *para*-attack, affording P-C bond formation and fluoride transfer to the electron deficient P-cation yielding $[Ph_3P(C_6F_4)Ph_2PF_2][FB(C_6F_5)_3]$ (Scheme 9). Similar reactivity was observed with Ph_2PSiMe_3.It is noteworthy that this reactivity is reminiscent of a Mes_2PH/ $B(C_6F_5)_3$ FLP, which in a similar manner formed $1\text{-}(Mes_2PH)(BF(C_6F_5)_2(C_6F_4))$; the precursor to the initial FLP system known to activate dihydrogen.[30]

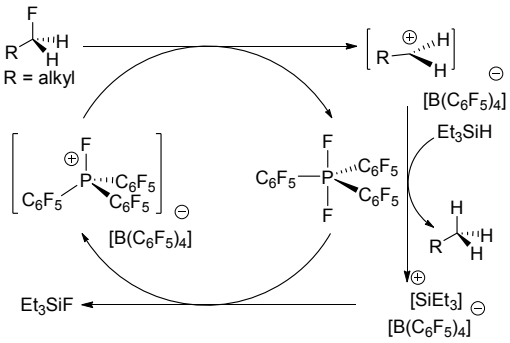


Scheme 10. Syntheses of highly electrophilic phosphonium cations.

Further study targeted even more electrophilic phosphonium cations. To this end, the phosphoranes $(C_6F_5)_2PhPF_2$ and $(C_6F_5)_3PF_2$ were prepared from the precursor phosphines and XeF_2. Interestingly, neither difluorophosphorane underwent fluoride abstraction with $B(C_6F_5)_3$, but $Al(C_6F_5)_3{\bullet}C_7H_{18}$ or $[Et_3Si][B(C_6F_5)_4]{\bullet}2(C_7H_8)$ did abstract fluoride, generating the salts

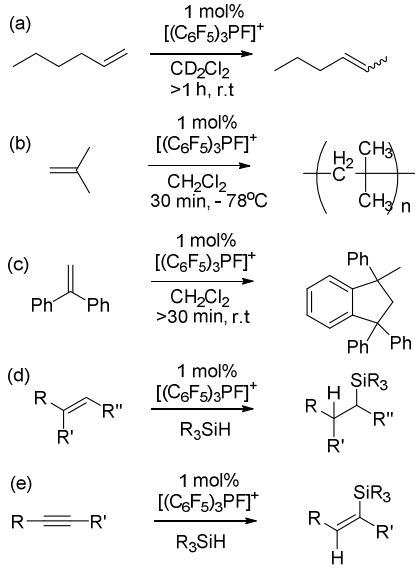
$[(C_6F_5)_2PhPF][X]$ and $[(C_6F_5)_3PF][X]$ (X = F $(Al(C_6F_5)_3)_2$ or $B(C_6F_5)_4$) respectively (Scheme 10).[29]

It is important to note that the inability of $B(C_6F_5)_3$ to abstract fluoride infers that the fluorophosphonium cations are in fact more fluorophilic than $B(C_6F_5)_3$.[31] Reflecting this Lewis acidity, the EPC $[(C_6F_5)_3PF][B(C_6F_5)_4]$ was shown to form an adduct with *N,N*-dimethylformamide (DMF), formulated as $[(Me_2NC(O)H)(C_6F_5)_3PF][B(C_6F_5)_4]$. Additionally, adduct formation with Et_3PO, in what is referred to as "the Gutmann-Beckett Lewis acidity test"[32] showed a ^{31}P NMR chemical shift that is significantly higher than that exhibited by the corresponding adduct of $B(C_6F_5)_3$ ($\Delta\delta$ 40.4 ppm vs 26.6 ppm).[31] Moreover, stoichiometric reaction of this EPC with Ph_3CF resulted in the isolation of the difluorophosphorane, $(C_6F_5)_3PF_2$. This reactivity prompted further investigation of the scope of C-F bond activation. Remarkably, in the presence of equimolar amounts of Et_3SiH and fluoroalkene/fluoroalkane, $[(C_6F_5)_3PF][B(C_6F_5)_4]$ rapidly catalysed hydrodefluorination reactions with relatively low catalyst loadings (1-10%) and mild reaction conditions. The substrate scope spanned a range of alkyl fluorides, while C(sp^2)-F groups were unreactive. While Lewis acids based upon boron,[33] silicon[34] and aluminium[35] have been shown to catalyse hydrodefluorination reactions, this was the first system to exploit the Lewis acidity of a σ*-orbital for this challenging reaction.[36]



Scheme 11. Mechanism of hydrodefluorination of fluoroalkanes.

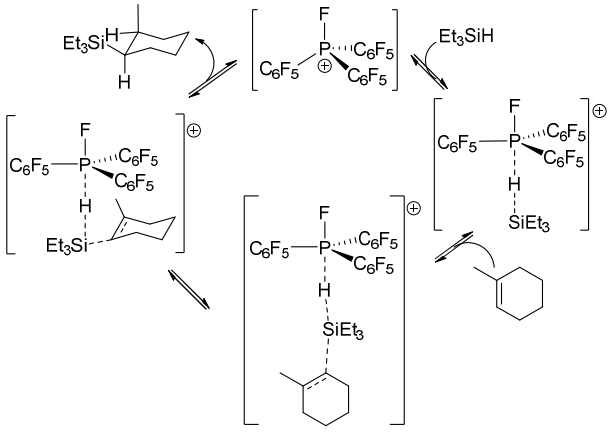
Experimental and theoretical studies of this hydrodefluorination reaction were consistent with a mechanism involving initial C-F bond cleavage, generating a difluorophosphorane and a carbocation. The latter reacts immediately with silane to form alkane while the generated silylium cation abstracts a fluoride from the difluorophosphorane to regenerate the fluorophosphonium cation catalyst (Scheme 11). It is important to note that control experiments demonstrated that octafluorotoluene was preferentially activated by $[(C_6F_5)_3PF][B(C_6F_5)_4]$ in the presence of $[Et_3Si][B(C_6F_5)_4]$ which confirms that this EPC is the Lewis acid catalyst and not the silylium cation.[36]



Scheme 12. a) Isomerisation of 1-hexene. b) Polymerization of isobutylene. c) Friedel-Crafts dimerization of 1,1-diphenylethylene. d) Hydrosilylation of alkenes. e) Hydrosilylation of alkynes.

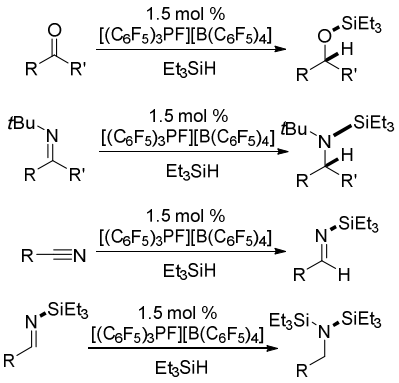
The utility of these EPCs as catalysts for other reactions was also investigated. For example, in the presence of 1-hexene, 1 mol% of $[(C_6F_5)_3PF][B(C_6F_5)_4]$ was seen to rapidly catalyse the isomerization of the olefin to 2-hexene (Scheme 12(a)).[37] This is believed to proceed *via* activation of the olefin by the electrophilic P centre generating a transient carbocation, which then facilitates a 1,3-proton migration to yield the internal olefin. The EPC was also shown to catalyse the cationic polymerization of isobutylene and the Friedel-Crafts dimerization of 1,1-diphenylethylene affording the cyclo-dimerization product (Scheme 12(b), (c)). In addition, catalytic hydrosilylation reactions of a range of olefins and alkynes was mediated by the Lewis acid catalyst $[(C_6F_5)_3PF][B(C_6F_5)_4]$ (Scheme 12(d), (e)).[37] In this case, mechanistic and computational data supported the supposition that the cationic P centre activates the Si-H bond, generating a transient hypervalent silane species. Upon addition of olefin or alkyne, SN_2 attack at the silane centre generates a transient silylated carbocation which prompts hydride delivery to the less sterically hindered face (Scheme 13).[38-39] This *anti*-1,2 addition of Si-H across the olefin regenerates the active catalyst and releases the hydrosilylated product. A similar mechanism was proposed for the hydrosilylation of imines[40] and carbonyl compounds[41] with $B(C_6F_5)_3$ as the Lewis acid catalyst.

The scope of these EPC-catalysed hydrosilylation reactions was subsequently expanded to ketones and imines (Scheme 14).[42] In the case of imines, *N*-tertbutyl substituted aldimines were required as smaller substituents inhibited hydrosilylation, presumably due to a donor-acceptor interaction between the nitrogen and phosphorus centres. Hydrosilylation of nitriles with one equivalent of Et_3SiH resulted in conversion to the corresponding *N*-silylimines while two equivalents of Et_3SiH generated the corresponding *N,N*-disilylamines (Scheme 14).



Scheme 13. Mechanism of the hydrosilylation of methylcyclohexene with $[(C_6F_5)_3PF][B(C_6F_5)_4]$; anions has been omitted for clarity.

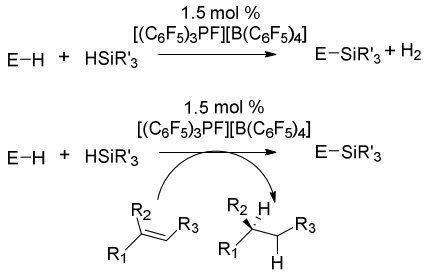
To probe the selectivity of the catalyst $[(C_6F_5)_3PF][B(C_6F_5)_4]$ in these hydrosilylation reactions, competition reactions were undertaken. Interestingly, equimolar mixtures of ketone, imine or nitrile substrates with 1-decene led to the selective hydrosilylation of the polar unsaturated bonds, leaving the olefin unaltered. Additional competition experiments involving polar unsaturates revealed the following general decreasing reactivity trend: ketones > nitriles > imines > olefins.



Scheme 14. Hydrosilylation of ketones, imines and nitriles.

The related EPCs, $[(C_6F_5)_3PCl]^+$ and $[(C_6F_5)_3PBr]^+$ were readily prepared using SO_2Cl_2 and Br_2 as the oxidants, respectively, followed by halide abstraction with $[Et_3Si][B(C_6F_5)_4]\bullet 2(C_7H_8)$. These phosphonium cations were shown to catalyse the aforementioned hydrosilylation reactions, albeit at slower rates relative to fluorophosphonium cation, usually requiring higher temperatures.[42] These catalysts exhibited the reactivity trend: $[(C_6F_5)_3PF]^+$ > $[(C_6F_5)_3PBr]^+$ > $[(C_6F_5)_3PCl]^+$. Computational studies indicated that although Cl is more electronegative than Br, $[(C_6F_5)_3PCl]^+$ has a lesser hydride affinity. It was speculated that this is due to electron back-donation into the 3d orbitals at the P centre, diminishing the Lewis acidity at P.

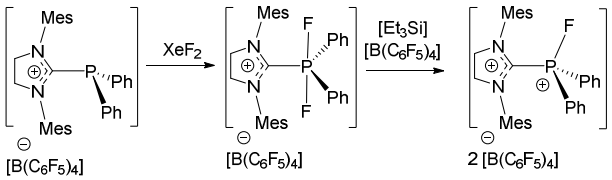
$[(C_6F_5)_3PF][B(C_6F_5)_4]$ also catalyses dehydrocoupling reactions of silanes with amines, thiols, phenols and carboxylic acids evolving H_2 and forming the corresponding N-Si, S-Si or O-Si bonds, respectively.[43] The mechanism for dehydrocoupling is believed to be similar to the olefin hydrosilylation pathway with nucleophilic attack by the base at hypervalent Si centre.[37, 42] In addition these reactions can be adapted for *in situ* transfer hydrogenation of olefins. Thus, dehydrocoupling in the presence of olefin affords concurrent formation of both the dehydrocoupled product and hydrogenated olefin (Scheme 15). These reactions are tolerant of different functionalities such as aryl-halides, ethers and esters and are chemoselective, as no hydrosilylated olefin by-products were observed.



Scheme 15. Dehydrocoupling of silanes with E-H (E = NR_2, SR, OR, OC(O)R) bonds and dehydrocoupling with concurrent hydrogenation of olefins.

In a very recent report, $[(C_6F_5)_3PF][B(C_6F_5)_4]$ was shown to catalyse the hydroarylation and Markovnikov hydrothiolation of olefins with a range of aromatic compounds and some methylstyrene derivatives, respectively.[44] The first step in this mechanism is believed to be olefin activation, which generates a transient carbocation and affects electrophilic attack on the aryl moiety with concurrent proton transfer to the olefin. This regenerates the fluorophosphonium catalyst while releasing the Friedel-Crafts product. Interestingly, addition of $B(C_6F_5)_3$ to one of the Friedel-Crafts products, *p*-$(C_8H_{17}(Me)CH)C_6H_4NHPh$, under 4 atm of H_2 resulted in the FLP reduction of both N-bound aryl groups to give dicyclohexylamine derivative, $[4\text{-}(C_8H_{17}(Me)CH)(C_6H_{10})NH_2Cy]^+$.

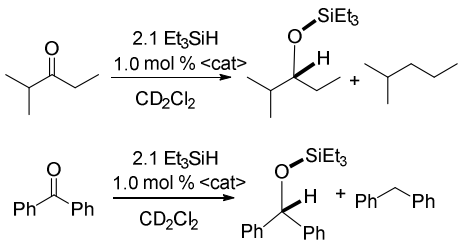
While the EPC $[(C_6F_5)_3PF][B(C_6F_5)_4]$ is clearly reactive, the requirement of such strongly electron withdrawing substituents limits the tunability. To address this issue, we developed a synthesis for a fluorophosphonium dication, $[(SIMes)PFPh_2][B(C_6F_5)_4]_2$.[45] Such species are prepared from the XeF_2 oxidation of phosphenium cations derived from the reaction of N-heterocyclic carbenes with P(III) halides. Subsequent fluoride abstraction from the difluorophosphorane affords the corresponding dication (Scheme 16).



Scheme 16. Synthesis of an electrophilic fluorophosphonium dication.

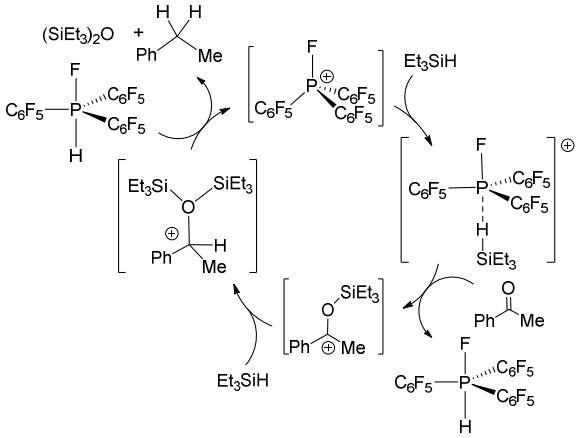
In these cases, attempts to employ the Gutmann-Beckett test proved uninformative as addition of Et_3PO to the dication $[(SIMes)PFPh_2][B(C_6F_5)_4]_2$ resulted in an oxide-fluoride exchange generating $[Et_3PF][B(C_6F_5)_4]$ and $[(SIMes)POPh_2][B(C_6F_5)_4]$. However, reaction of this phosphonium dication with $(C_6F_5)_3PF_2$ resulted in fluoride abstraction giving the difluorophosphorane $[(SIMes)PF_2Ph_2][B(C_6F_5)_4]$ and $[(C_6F_5)_3PF][B(C_6F_5)_4]$. This reactivity demonstrates that the dication is more fluorophilic than $[(C_6F_5)_3PF]^+$, inferring that the presence of the dicationic charge plays a greater role in generating Lewis acidity than electron-withdrawing substituents. Indeed the dication $[(SIMes)PFPh_2][B(C_6F_5)_4]_2$ was shown to catalyse the polymerization of tetrahydrofuran, the Friedel-Crafts dimerization of 1,1-diphenylethylene, hydrodefluorination of fluoroalkanes and the hydrosilylation of a variety of substrates under mild reaction conditions.[45]

EPCs were also shown to mediate ketone deoxygenation in the presence of excess silane.1 mol% of one of the mono- and dications $[(C_6F_5)_3PF]^+$, $[(C_6F_5)_2PFPh]^+$, $[(C_6F_5)PFPh_2]^+$, $[Ph_3PF]^+$, $[(SIMes)POPh_2]^+$, $[(SIMes)PFR_2]^{2+}$ (R = Ph, Et, Me), $[(SIMes)PClPh_2]^{2+}$ were shown, in some cases, to mediate the deoxygenation of 2-methylpentanone or benzophenone in the presence of 2.1 equivalents of Et_3SiH (Scheme 17).[46] While the dications effected deoxygenation of 2-methylpentanone and benzophenone affording 2-methylpentane and diphenylmethane respectively, the less Lewis acidic cation, $[(C_6F_5)PFPh_2]^+$ or use of the Lewis acid $B(C_6F_5)_3$ gave the silyl-ether of 2-methylpentanone and a mixture of the silyl-ether and deoxygenation products for the reaction of benzophenone. Decreasing the Lewis acidity further with $[Ph_3PF]^+$, or use of the phosphonium oxide $[(SIMes)POPh_2]^+$ showed no reactivity.



Scheme 17. Hydrosilylation/Deoxygenation of 2-methylpenanone and benzophenone.

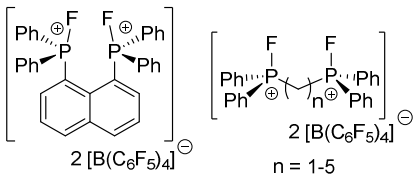
The substrate scope for such deoxygenation of ketones were broadened using the monocation $[(C_6F_5)_3PF]^+$ and the dication $[(SIMes)PFPh_2]^{2+}$. In both cases, a variety of alkyl- and aryl-substituted ketones could be fully reduced to the alkane deoxygenation products. Interestingly, in contrast to aryl ketones, dialkyl ketones could be selectively hydrosilylated in the presence of one equivalent of silane, and subsequently deoxygenated with more silane.



Scheme 18. Mechanism for deoxygenation of acetophenone with $[(C_6F_5)_3PF]^+$; anions are omitted for clarity.

Computational study of the mechanism of deoxygenation suggests that hydrosilylation attack of Lewis acid activated silane by silyl ether prompts C-O bond cleavage. Alternatively, reaction of the silyl ether cation with a second equivalent of Et_3SiH generates the siloxy-cation which is then cleaved by reaction with the hydrido-phosphorane affording the alkane, siloxane and regenerating EPC (Scheme 18). The latter pathway is operative for aryl ketones as deoxygenation proceeds even in the presence of less than two equivalents of silane, whereas dialkyl ketones proceed by the stepwise reduction.

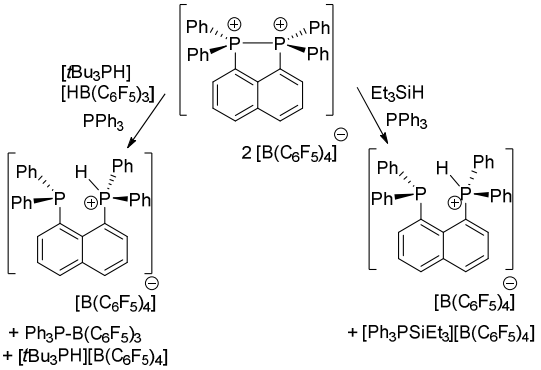
An alternative approach to phosphonium dications exploited the enhanced Lewis acidity that comes from the proximity of two Lewis acidic centers.[24] To this end, we synthesized a family of *bis*-fluorophosphonium dications derived from commercially available diphosphines.[47] For example, the naphthalene-based diphosphine, $(C_{10}H_6)(Ph_2P)_2$, was converted to the corresponding fluorophosphonium dication, $[(C_{10}H_6)(Ph_2PF)_2][B(C_6F_5)_4]_2$, using protocols described above (Scheme 19). In a similar fashion, alkyl-linked diphosphines ($(CH_2)_n(PPh_2)_2$ n = 1-5) were converted to the corresponding dication derivatives (Scheme 19). While the naphthyl-linked *bis*-phosphonium dication exhibited Lewis acidity less than $B(C_6F_5)_3$, but more than $[Ph_3PF]^+$ based on the Gutmann-beckett test, the alkyl-linked analogues could not be assessed due to deprotonation and/or slow fluoride-oxide exchange. Nonetheless, the Lewis acidity of the phosphonium dications, in particular, $[(C_{10}H_6)(Ph_2PF)_2][B(C_6F_5)_4]_2$ and $[(CH_2)(Ph_2PF)_2][B(C_6F_5)_4]_2$ was evidenced by the effectiveness in catalysing Friedel Crafts-type dimerization of olefins, hydrosilylation of olefins, dehydrocoupling of amines and silanes, deoxygenation of ketones and hydrodefluorination of alkylfluorides. It is noteworthy that these species are significantly more reactive than the analogous mono-cations ($[Ph_3PF][B(C_6F_5)_4]$ and $[MePh_2PF][B(C_6F_5)_4]$), which is consistent with enhanced Lewis acid arising from proximity.



Scheme 19. *Bis*-fluorophosphonium salts.

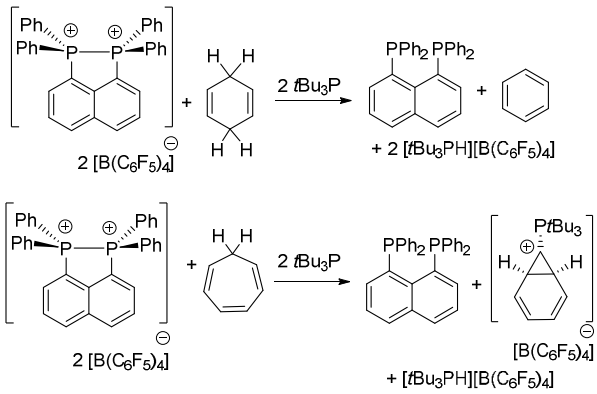
We have targeted P-Lewis acids without P-F bonds. In this regard, the napthyl-linked diphosphine $(C_{10}H_6)(Ph_2P)_2$ was first oxidized at low temperatures with one equivalent of XeF_2 to selectively give the difluorophosphorane/phosphine species $(C_{10}H_6)(Ph_2PF_2)(Ph_2P)$.[48] Addition of two equivalents of $[Et_3Si][B(C_6F_5)_4]\cdot 2(C_7H_8)$ then facilitated a double fluoride abstraction to generate the 1,2-diphosphonium dication, $[(C_{10}H_6)(Ph_2P)_2]^{2+}$ containing a P-P bond. Gutmann-Beckett tests indicated the dication is more Lewis acidic than the corresponding fluorophosphonium dication $[(C_{10}H_6)(Ph_2PF)_2][B(C_6F_5)_4]_2$.[47] It is noteworthy that the diphosphonium dication was robust and stable, showing no signs of decomposition even upon standing in air for 24 h.

The 1,2-diphosphonium dication $[(C_{10}H_6)(Ph_2P)_2]^{2+}$ reacts with $[t\text{Bu}_3\text{PH}][HB(C_6F_5)_3]$ accepting the hydride from the hydroborate to give $[(C_{10}H_6)(Ph_2P)(Ph_2PH)]^+$.[48] Performing the reaction in the presence of PPh_3 resulted in the capture of the liberated $B(C_6F_5)_3$ as PPh_3-$B(C_6F_5)_3$ (Scheme 20). The dication $[(C_{10}H_6)(Ph_2P)_2]^{2+}$ also accepts hydride from the silane Et_3SiH. Again performing the reaction in the presence of PPh_3, afforded the cation $[(C_{10}H_6)(Ph_2P)(Ph_2PH)]^+$ and $[Ph_3PSiEt_3][B(C_6F_5)_4]$ (Scheme 20). In the absence of an external base, $[(C_{10}H_6)(Ph_2P)(Ph_2PH)]^+$ is still observed, although the transient $[Et_3Si]^+$ either degrades in CD_2Cl_2 or is solvated as $[Et_3Si(CD_3CN)]^+$ in acetonitrile.



Scheme 20. Reactivity of the 1,2-diphosphonium dication with Et_3SiH and $[t\text{Bu}_3\text{PH}][HB(C_6F_5)_3]$.

In addition to reacting with B-H and Si-H bonds, $[(C_{10}H_6)(Ph_2P)_2]^{2+}$ also facilitated C-H bond activation. In reaction with 1,4-cyclohexadiene and two equivalents of $t\text{Bu}_3\text{P}$, benzene is generated *via* dehydrogenation.[48] The 1,2-diphosphonium dication is converted to $(C_{10}H_6)(Ph_2P)_2$ with formation of $[t\text{Bu}_3\text{PH}]^+$ (Scheme 21). Similarly, the corresponding reaction of 1,3,5-cycloheptatriene affords $(C_{10}H_6)(Ph_2P)_2$, $[t\text{Bu}_3\text{PH}]^+$ and the bicyclo[4.1.0]heptane species $[C_7H_7Pt\text{Bu}_3]^+$ (Scheme 21). Both reactions commence with hydride abstraction generating $[(C_{10}H_6)(Ph_2P)(Ph_2PH)]^+$. In the case of cyclohexadiene, both equivalents of $t\text{Bu}_3\text{P}$ are then protonated, to give benzene, $[t\text{Bu}_3\text{PH}][B(C_6F_5)_4]$ and $(C_{10}H_6)(Ph_2P)_2$. With cycloheptatriene, the reaction proceeds similarly with the transient tropylium cation being captured by $t\text{Bu}_3\text{P}$.



Scheme 21. C-H bond activations of 1,4-cyclohexadiene and 1,3,5-cycloheptatriene facilitated by $[(C_{10}H_6)(Ph_2P)_2]^{2+}$.

It is important to note that the phosphonium dication does not react with $t\text{Bu}_3\text{P}$ or PPh_3 on its own and thus these combinations can be described as all-phosphorus FLPs. Indeed upon exposure to 4 atm of H_2 at 100 °C, the irreversible activation of H_2 to give the diphosphine $(C_{10}H_6)(Ph_2P)_2$ and two equivalents of $[t\text{Bu}_3\text{PH}][B(C_6F_5)_4]$ was facilitated by the $[(C_{10}H_6)(Ph_2P)_2]^{2+}/t\text{Bu}_3\text{P}$ FLP.[48]

Similar to the reactions mentioned above, while the dication acts as a hydride acceptor, the intermediate product $[(C_{10}H_6)(Ph_2P)(Ph_2PH)]^+$ is deprotonated by the more basic $t\text{Bu}_3\text{P}$. The analogous reaction under D_2, gave $[t\text{Bu}_3\text{PD}][B(C_6F_5)_4]$, and reaction with HD gave a statistical mixture of $[t\text{Bu}_3\text{PH}]^+$ and $[t\text{Bu}_3\text{PD}]^+$.

In a very recent communication, we have also shown that the fluorophosphonium cation, $[(C_6F_5)_3PF][B(C_6F_5)_4]$ in combination with diarylamines acts as an FLP to form an "encounter complex" in which the N approaches P but does not form a covalent bond. Computational work suggests the closest approach of P···N is 3.52 Å. Indeed the FLP derived from the combination of $[(C_6F_5)_3PF][B(C_6F_5)_4]$ with $(p\text{-tol})_2NSiMe_3$ catalyses the hydrogenation of 1,1-diphenylethylene.[49]

Conclusions

The early literature indicated the Lewis acidity of P(III) and P(V) species in coordination chemistry. While several older studies have exploited this Lewis acidity for reactivity, it has been more recent developments that have focused attention on the potential of P-based Lewis acids in catalysis and FLP chemistry. While P(III) electrophiles have garnered less attention, the activation of H_2 by triphosphabenzene and the exploitation of P(III)-species in oxidative addition are interesting activations of small molecules that suggest new P(III) systems may provide unique applications in reduction chemistry. Also of interest are the recent advances in the

design of highly electrophilic phosphonium cations. The development of these P(V) species has opened the door to a range of Lewis acid catalysis and certainly such advancements are continuing to emerge. The examples presented in this review highlight this area as an emerging trend in the larger efforts to develop metal-free catalysis. It is also clear that P-based Lewis acid catalysis is still in its infancy; there is no doubt that this field will rapidly develop and is likely to be a fertile area for development as we go forward.

Acknowledgements

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Notes and references

1. R. M. Bullock, ed., *Catalysis without Precious Metals*, Wiley-VCH Verlag GmbH & Co, 2010.
2. B. List, *Chem. Rev.*, 2007, **107**, 5413-5415 and subsequent papers.
3. D. W. Stephan and G. Erker, *Angew. Chem. Int. Ed.*, 2010, **49**, 46-76.
4. D. W. Stephan and G. Erker, *Angew. Chem. Int. Ed.*, 2015, **54** 6400-6441
5. D. W. Stephan, *Accts Chem. Res.*, 2015, **48**, 306-316.
6. K. Dimroth and P. Hoffmann, *Angew. Chem. Int. Ed.* , 1964, **3**, 384.
7. A. H. Cowley and R. A. Kemp, *Chem Rev*, 1985, **85**, 367-382.
8. D. Gudat, A. Haghverdi, H. Hupfer and M. Nieger, *Chem. Eur. J.*, 2000, **6**, 3414.
9. S. Burck, D. Gudat and M. Nieger, *Angew. Chem. Int. Ed.*, 2004, **43**, 4801.
10. N. Burford and P. J. Ragogna, *Dalton Trans*., 2002, 4307-4315.
11. N. Burford, P. J. Ragogna, K. N. Robertson, T. S. Cameron, N. J. Hardman and P. P. Power, *J. Am. Chem. Soc.*, 2002, **124**, 382-383.
12. A. L. Brazeau, C. A. Caputo, C. D. Martin, N. D. Jones and P. J. Ragogna, *Dalton Trans.*, 2010, **39**, 11069-11073.
13. J. M. Slattery and S. Hussein, *Dalton Trans.*, 2012, **41**, 1808-1815.
14. L. E. Longobardi, C. A. Russell, M. Green, N. S. Townsend, K. Wang, A. J. Holmes, S. B. Duckett, J. E. McGrady and D. W. Stephan, *J. Am. Chem. Soc.*, 2014, **136**, 13453-13457.
15. N. Dunn, M. Ha and A. Radosevich, *J. Am. Chem. Soc.*, 2012, **134**, 11330-11333.
16. G. Wittig and U. Schöllkopf, *Chem. Ber.*, 1954, **87**, 1318-1330.
17. E. L. Muetterties, W. Mahler and R. Schmutzler, *Inorg. Chem.* , 1963, **2**, 613.
18. C. Y. Wong, D. K. Kennepohl and R. G. Cavell, *Chem. Rev.*, 1996, **96**, 1917-1951.
19. M. Well, P. G. Jones and R. Schmutzler, *J. Fluorine Chem.*, 1991, **53**, 261.
20. K. I. The, L. Vande Griend, W. A. Whitla and R. G. Cavell, *J. Am. Chem. Soc.*, 1977, **99**, 7379-7380.
21. L. J. Hounjet, C. B. Caputo and D. W. Stephan, *Angew. Chem. Int. Ed.*, 2012, **51**, 4714-4717.
22. K. C. K. Swamy and N. S. Kumar, *Acc. Chem. Res.*, 2006, **39**, 324-333.
23. M. Terada and M. Kouchi, *Tetrahedron*, 2006, **62**, 401-409.
24. T. W. Hudnall, Y. M. Kim, M. W. P. Bebbington, D. Bourissou and F. P. Gabbaï, *J. Am. Chem. Soc.*, 2008, **130**, 10890-10891.
25. O. Sereda, S. Tabassum and R. Wilhelm, in *Top Curr. Chem.*, 2010, pp. 349-393.
26. R. Cordoba and J. Plumet, *Tetrahedron Lett.*, 2003, **44**, 6157.
27. X. Wang and S.-K. Tian, *Tetrahedron Lett.* , 2007, **48**, 6010-6013.
28. T. Werner, *Adv. Synth. & Catal.*, 2009, **351**, 1469-1481.
29. L. J. Hounjet, C. B. Caputo and D. W. Stephan, *Dalton Trans.*, 2013, **42**, 2629-2635.
30. G. C. Welch, R. R. S. Juan, J. D. Masuda and D. W. Stephan, *Science*, 2006, **314**, 1124-1126.
31. C. B. Caputo, D. Winkelhaus, R. Dobrovetsky, L. J. Hounjet and D. W. Stephan, *Dalton Trans.*, 2015, **44**, DOI: 10.1039/C1035DT00217F.
32. M. A. Beckett, D. S. Brassington, S. J. Coles and M. B. Hursthouse, *Inorganic Chemistry Communications*, 2000, **3**, 530-533.
33. C. B. Caputo and D. W. Stephan, *Organometallics*, 2012, **31**, 27-30.
34. C. Douvris and O. V. Ozerov, *Science*, 2008, **321**, 1188-1190.
35. W. Gu, M. R. Haneline, C. Douvris and O. V. Ozerov, *J. Am. Chem. Soc.*, 2009, **131**, 11203-11212.
36. C. B. Caputo, L. J. Hounjet, R. Dobrovetsky and D. W. Stephan, *Science*, 2013, **341**, 1374-1377.
37. M. Perez, L. J. Hounjet, C. B. Caputo, R. Dobrovetsky and D. W. Stephan, *J. Am. Chem. Soc.*, 2013, **135**, 18308-18310.
38. D. J. Parks, J. M. Blackwell and W. E. Piers, *J. Org. Chem.*, 2000, **65**, 3090-3098.
39. M. Rubin, T. Schwier and V. Gevorgyan, *J. Org. Chem.* ,, 2002, **67**, 1936-1940.
40. J. Hermeke, M. Mewald and M. Oestreich, *J. Am. Chem. Soc.*, 2013, **135**, 17537-17546.
41. S. Rendler and M. Oestreich, *Angew. Chem., Int. Ed.*, 2008, **47**, 5997-6000.
42. M. Perez, Z. W. Qu, C. B. Caputo, V. Podgorny, L. J. Hounjet, A. Hansen, R. Dobrovetsky, S. Grimme and D. W. Stephan, *Chem. Eur. J.*, 2015, **21**, 6491-6500.
43. M. Perez, C. B. Caputo, R. Dobrovetsky and D. W. Stephan, *Proc. Nat. Acad. Sci.*, 2014, **111**, 10917-10921.
44. M. Pérez, T. Mahdi, L. J. Hounjet and D. W. Stephan, *Chem. Commun.*, 2015, DOI: 10.1039/c1035cc03572d.
45. M. H. Holthausen, M. Mehta and D. W. Stephan, *Angew. Chem. Int. Ed.*, 2014, **53**, 6538-6541.
46. M. Mehta, M. H. Holthausen, I. Mallov, M. Pérez, Z.-W. Qu, S. Grimme and D. W. Stephan, *Angew. Chem. Int. Ed.*, 2015, DOI: 10.1002/anie.201502579.
47. M. H. Holthausen, R. R. Hiranandani and D. W. Stephan, *Chem. Sci.*, 2015, **6**, 2016-2021.
48. M. H. Holthausen, J. M. Bayne, I. Mallov and D. W. Stephan, *J. Am. Chem. Soc.*, 2015, **137**, 7298-7301.
49. T. v. Stein, M. Peréz, R. Dobrovetsky, D. Winkelhaus, C. B. Caputo and D. W. Stephan, *Angew. Chem. Int. Ed.*, 2015, DOI: 10.1002/anie.201504109.

TOC GRAPHIC

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