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Authors: Saurabh Chitnis, Felix Krischer, and Douglas Wade Stephan

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Catalytic hydrodefluorination of C-F bonds by an air-stable P(III) Lewis acid

Saurabh S. Chitnis, Felix Krischer and Douglas W. Stephan*^[a]

Dedication ((optional))

Abstract: Catalytic hydrodefluorination (HDF) of unactivated fluoroalkanes or CF₃-substituted aryl species is performed using the P(III) Lewis acids, [(bipy)PPh]²⁺ (1²⁺)and [(terpy)PPh]²⁺ (2²⁺) under mild conditions (25 °C or 50 °C). Mechanistic studies indicate that activation of C-F bond by the P(III) center is key. Particularly noteworthy is that the catalyst 2[B(C₆F₅)₄]₂ is air-stable and readily accessible from bench-stable, commercially available reagents in one-step and can be used without isolation.

The high thermodynamic and kinetic stability of C-F σ -bonds underpins the numerous applications of fluorocarbons as small molecules and materials. On the other hand, this stability limits opportunities for functionalization leading to accumulation of organofluorine compounds in the environment, posing toxicity and global warming concerns. Thus, developing new synthetic tools for C-F bond functionalization is not only fundamentally interesting but relevant to environmental remediation efforts. A number of stoichiometric and catalytic protocols have emerged for the modification of C-F bonds.^[1] Several transition metal and lanthanide complexes effect catalytic hydrodefluorination (HDF) offering an attractive strategy for reduction of C-F groups, with most examples involving C(sp²)-F bonds (aryl or vinyl fluorides).^[2]

HDF catalysis with p-block Lewis acids has emerged as a complementary strategy that selectively targets C(sp³)-F bonds. A variety of boron, silicon, aluminum, and antimony electrophiles have been reported as catalysts or precatalysts for the HDF of fluoroalkanes (Figure 1, I-V).^[1b, 3] Our group has systematically evolved electrophilic phosphonium, [XPR₃]⁺ (X = electron withdrawing group) and diphosphonium, [R₃PPR₃]²⁺, cations, as tunable catalysts for hydrosilylation, transfer hydrogenation, hydroarylation, hydrothiolation, hydrodeoxygenation and fluoroalkane HDF (Figure 1, VI and VII).^[4] The Lewis acidity of these P(V) cations is derived from an energetically accessible P-X σ^* -antibonding orbital.

P(III) compounds (e.g. phosphines) are typically recognized as Lewis bases, acting as electron donors in coordination chemistry and Lewis base catalysis.^[5] Nevertheless, a rich coordination and reaction chemistry has been described for neutral P(III) halides and phosphenium cations.^[6] Burford has systematically studied P(III) acceptors, highlighting the electrophilicity of bipyridine-stabilized P(III) polycations. Such

 [a] Dr. S. S. Chitnis, Mr. F. Krischer, and Professor Dr. D. W. Stephan Department of Chemistry, University of Toronto, 80 St. George St., Toronto, Ontario, Canada M5S3H6 E-mail: dstephan@chem.utoronto.ca

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species can stoichiometrically activate strong E-H (E = H, C, P) bonds.^[7] In a related sense, Gudat has pioneered the reactivity of the masked phosphenium cations derived from N-heterocyclic phosphines.^[8] Recently the Vidovic group showed that P(III) dications exhibit stoichiometric activation of C-F bonds at 100 °C, albeit with a limited scope of substrates (only α-phenyl C-F bonds).^[9] The same group also showed abstraction of hydrides from silanes and amine/pyridyl-boranes under ambient conditions.^[10] Despite the above Lewis acidic behavior, applications of electrophilic P(III) compounds in catalysis have been limited to N-heterocyclic phosphines (NHPs) and triaminophosphines.^[11]



Figure 1. Main group Lewis acids for catalytic HDF of fluoroalkanes.

In targeting applications of electrophilic P(III) compounds for HDF catalysis, we have explored the reactivity of P(III) dications featuring bipyridine (bipy) or terpyridine (terpy) ligands, [(bipy)PPh]²⁺, 1²⁺, and [(terpy)PPh]²⁺, 2²⁺ (Figure 1). Herein, we demonstrated that despite the formally hypervalent environment around the phosphorus atom, the air stable P(III) species, $2[B(C_6F_5)_4]_2$, is sufficiently electrophilic to realize catalytic HDF of primary, secondary, and tertiary alkyl C-F bonds.

Compounds **1**[X]₂ (X = OTf and B(C₆F₅)₄) were prepared according to Scheme 1a. The ³¹P NMR spectra of the cations showed singlets at δ_P = 131 ppm and 144 ppm, respectively, for the triflate and borate salts, and these values are consistent with values for other tricoordinate P(III) polycations.^[7] The structure of **1**[OTf]₂ was determined in the solid state by single-crystal diffraction confirming the pyramidal environment around the phosphorus atom (Figure 1a). The structure of the cation shows two sets of inter-ion contacts, one of which is *trans* to the P-C bond and the other *trans* to one of the P-N bonds. The compound

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1[B(C₆F₅)₄]₂ exhibits a high Lewis acidity as suggested by the Gutmann-Beckett acceptor number (AN) of 93 (Figure S1, ESI). This is notably greater than that of B(C₆F₅)₃ (AN 82) and slightly less than that of the electrophilic phosphonium cation [FP(C₆F₅)₃]⁺ (AN 102). DFT calculations revealed that the LUMO of **1**²⁺ also exhibits a prominent lobe at the phosphorus atom (Figure 1b) suggesting the potential for Lewis acid behavior at the central atom. Consistent with its exceptional Lewis acidity, **1**[B(C₆F₅)₄]₂ decomposes quantitatively and rapidly (< 1 h) to a complex mixture of products upon exposure to air.



Scheme 1. Synthesis of $1[X]_2$ and $2[X]_2$ (X = OTf, B(C₆F)₄].

Combination of terpyridine (terpy), PhPCl₂, and either KB(C₆F₅)₄ or Me₃SiOTf in DCM at room temperature (Scheme 1a) for 5 minutes yielded salts formulated as [(terpy)PPh][X]₂, 2[X]₂ (X = OTf or $B(C_6F_5)_4$), in >80 % isolated yield (Scheme 1b). The ³¹P NMR spectra of the two salts showed peaks at 34 ppm and 38 ppm for the OTf and the $B(C_6F_5)_4$ salt, respectively. These values are ca. 100 ppm upfield compared to those for salts 1[X]₂. Single crystals of 2[OTf]₂·EtCN grown from a mixture of EtCN and Et₂O were studied by X-ray diffraction (Figure 1c). The nitrile of crystallization shows no interactions with the cation. The geometry at P is best described as a seesaw geometry, typical of four coordinate P(III) centers with a stereochemically active lone pair. The two axial P-N interactions are nearly identical (2.002(3) and 1.971(2) Å) and, notably, approximately 0.2 Å longer than the equatorial P-N bond (1.820(3) Å). The three aromatic rings of the terpy ligand deviate slightly from coplanarity due to the tridentate interaction while the phenyl substituent is angled at 102.7(2)° with respect to the (N)₃P plane. Two inter-ion P-O contacts of 3.268(2) and 3.309(2) Å, are similar to the sum of the P, O van der Waals radii (3.32 Å) and occur trans to the P-C bond. To the best of our knowledge, cation 2²⁺ represents the first terpyridine complex of phosphorus.

A solid sample of $2[B(C_6F_5)_4]_2$ left in air for 3 days retained its characteristic bright yellow colour, while NMR data obtained upon redissolution were identical to those of a sample stored under nitrogen (Figure S3, ESI). Similarly, a DCM solution of





Figure 2. a) Crystallographic structure of the cation in 1[OTf]₂, b) calculated LUMO of 1^{2+} , c) crystallographic structure of the cation in 2[OTf]₂·EtCN, d) calculated LUMO of 2^{2+} . Hydrogen atoms and noninteracting triflate and solvent molecules are omitted.

DFT calculations (PBE1-D3/cc-pVTZ) were carried out to assess the hypervalent electronic structure of cation 2²⁺ in the gas phase. The optimized structure revealed very similar bond lengths and angles to those observed in 2[OTf]₂·EtCN and confirmed the asymmetry of the axial and equatorial P-N interactions. The Wiberg Bond Indices for the P-N bonds (WBIs, equatorial P-N: 0.62 axial P-N: 0.56) are consistent with the dative $N \rightarrow P$ donoracceptor interactions. The LUMO of 22+ is delocalized over the terpy ligand framework but with a prominent lobe at the phosphorus atom that is antibonding with respect to the P-N and P-C interactions (Figure 2d). Due to the mutually trans disposition of two axial P-N interactions, the sites opposite to the central P-N bond or the P-C bond are expected to interact with incoming nucleophiles. This view is supported by contact with the triflate anion trans to the P-C bond in the solid-state structure of 2[OTf]₂·EtCN, which also evidence a retention of Lewis acidity despite the hypervalent electronic structure of the cation.

The potential for catalytic HDF using $1[B(C_6F_5)_4]_2$ was probed (Figure S4-S7, ESI). Quantitative reduction of C-F bonds was observed for primary, secondary, or tertiary fluoroalkanes (Table 1, entries 1-3) in the presence of Et₃SiH as a hydride donor. The CF₃ groups in *c*-C₆H₁₁CF₃ and PhCF₃ were converted at room temperature to CH₃ groups (entries 4, 5) with no evidence of CHF₂ or CH₂F containing intermediates even when limiting amount of Et₃SiH was used. Very slow conversion was observed for PhOCF₃ even at elevated temperature (entry 6).

The independent reaction of $1[B(C_6F_5)_4]_2$ with a ten-fold excess of fluoroadamantane proceeds quantitatively in 30

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minutes (Figure S15, ESI). Monitoring by ³¹P and ¹⁹F NMR spectroscopy revealed resonances attributable to species containing PF and PF₂ fragments as well as PhPF₂ ($\delta_P = 100$ ppm, $\delta_F = -107$ ppm, ¹*J*_{PF} = 1223 Hz).^[13] These observations indicate fluoride ion abstraction from the fluoroalkane by the P(III) dication.

Compound 1[B(C₆F₅)₄]₂ also reacts with excess Et₃SiH over 20 h to give complete conversion to a species exhibiting a resonance at δ = -97 ppm with a ¹J_{PH} of 347 Hz in the ³¹P NMR spectrum (Figure S16). This species was identified as the bissilylated cation [PhP(SiEt₃)₂H]⁺ (3⁺) by independent synthesis of $3[B(C_6F_5)_4]$ from the reaction of PhP(H)SiEt₃ and [Et₃Si(PhMe)][B(C₆F₅)₄] (Scheme 2). This implies interception of transiently formed phenylphosphinidene [PPh] by a silylium cation (generated by hydride transfer from Et₃SiH to 1²⁺), affording the phosphenium cation [Et₃SiPPh]⁺ (Scheme 2), which reacts further with silane to give [PhP(SiEt₃)₂H]⁺. Repeating the above reaction in MeCN yielded crystals of [Et₃Si(NCMe)][B(C₆F₅)₄], confirming hydride abstraction from the silane (Figure S18). Interestingly, the reaction of 1[OTf]₂ with Et₃SiH, led to the quantitative formation of the cyclic polyphosphines $(PhP)_x$ (x = 4, 5), supporting the intermediacy of a phosphinidene (Figure S16, ESI). Apparently, the in-situ formed Et₃SiOTf is not sufficiently Lewis acidic to trap phosphinidene, allowing oligomerization to proceed. The ¹H NMR spectrum (Figure S17) of the reaction between $1[B(C_6F_5)_4]_2$ and Et₃SiH also indicated significant amounts of the protonated bipyridine cation. 4⁺ suggesting abstraction of hydride from silane by 1²⁺ is followed by reductive elimination, affording protonated bipyridine. Related reductive elimination of protonated bipyridine has been observed by Burford in reactions of FLPs derived from a P(III) trication / tBu₃P with H₂.^[7] In addition, this redox process is reminiscent of elimination of C₆F₅H from the reactions of $[Sb(C_6F_5)_4]^+$ with silane described by Gabbai et al.^[3h] The reaction of 1²⁺ with fluoroadamantane suggests that 1²⁺ behaves as a catalyst. On the other hand, the reaction with silane is consistent with hydride abstraction, raising the possibility that 12+ acts as an initiator generating a silvlium cation that catalyses HDF. The present data do not enable a definitive determination of the mechanistic role of 12+.



Scheme 2. Reaction of $1[OTf]_2$ and $1[B(C_6F_5)_4]_2$ with Et₃SiH.

Compound $2[B(C_6F_5)_4]_2$ was also found to mediate the catalytic HDF of C-F bonds. Using 5-10 mol% catalyst loading, nearly quantitative conversion of unactivated primary, secondary, and tertiary fluoroalkanes was observed at ambient temperature (Table 1, entries 7-13). Runs involving CF₃-containing substrates showed no evidence of partial HDF products (R-CF₂H or R-CFH₂). Interestingly, reduction of CF₃ groups occurred selectively even in the presence of an olefin with no evidence of hydrosilylation products (entry 11). The more electron-deficient trifluoromethyl group in PhOCF₃ reacted very slowly at room temperature but excellent conversion was observed upon heating to 50 °C for 96 hours (entry 15). However, negligible conversion was observed for the most electron-deficient CF₃ group in C₆F₅CF₃ (entry 16).

Table 1. HDF Catalysis using 1²⁺ or 2²⁺ as the catalyst.

R - F

#	Cat	%	R-F	t (h)	Т	%Yield	%Conv.
		cat			(°C)	(Si-F)	(C-F)
1	1 ²⁺	10	<i>n</i> -C₅H ₁₁ F	8	25	95	>99
2	1 ²⁺	10	$c-C_6H_{11}F$	5	25	93	>99
3	1 ²⁺	10	Fluoroadamantane	0.25	25	97	>99
4	1 ²⁺	5	$c-C_6H_{11}CF_3$	16	25	76	>99
5	1 ²⁺	5	$C_6H_5CF_3$	36	25	50	90
6	1 ²⁺	5	$C_6H_5OCF_3$	48	50	4	9
7	2 ²⁺	10	<i>n</i> -C₅H ₁₁ F	1.5	25	97	>99
8	2 ²⁺	10	<i>с</i> -С ₆ Н₁1F	4	25	95	97
9	2 ²⁺	5	Fluoroadamantane	4	25	80	93
10	2 ²⁺	5	$c-C_6H_{11}CF_3$	4	25	74	>99
11	2 ²⁺	5	4-isopropenyl-				
			$C_6H_4CF_3$	24	25	95	95
12	2 ²⁺	5	$C_6H_5CF_3$	20	25	73	>99
13	2 ²⁺	5	$4-Br-C_6H_4CF_3$	20	25	70	>99
14	2 ²⁺	5	$C_6H_5OCF_3$	36	25	9	10
15	2 ²⁺	5	$C_6H_5OCF_3$	96	50	80	94
16	2 ²⁺	5	$C_6F_5CF_3$	20	25	1	2
17	"[Et₃Si]+"	5	$C_6F_5CF_3$	20	25	55	75

Conditions: DCM solutions, 0.10 M fluoroalkane, 1.2 eq silane per C-F bond. Conversion and yield determined by ¹⁹F NMR integration using fluorobenzene or 1,2-difluorobenzene as internal standards.

The reaction of $2[B(C_6F_5)_4]_2$ with a ten-fold excess of fluoroadamantane was examined by ³¹P and ¹⁹F NMR spectroscopy, indicating fluoride transfer from the alkane to the P(III) dication. This afforded species containing PF and PF₂ fragments as well as PhPF₂ (Figure S15). The corresponding reaction of 2[B(C₆F₅)₄]₂ with a ten-fold excess of Et₃SiH showed no reaction after 20 h (Figure S16). The ability of 2[B(C₆F₅)₄]₂ to directly activate C-F bonds and the absence of its reactivity towards Et₃SiH support its role as a catalyst, rather than an activator and suggest a mechanism involving fluoride abstraction by 2²⁺ to give 2-F⁺ as an elementary step during catalysis (Scheme 3). Moreover, the combination of $2[B(C_6F_5)_4]_2$ and Et₃SiH is inactive in the catalytic HDF of C₆F₅CF₃ (Table 1, entry 16), whereas use of in-situ generated of [Et₃Si][B(C₆F₅)₄] effected HDF catalysis of C₆F₅CF₃ (entry 17), indicating that C-F activation by silvlium species makes a negligible contribution to catalysis involving $2[B(C_6F_5)_4]_2$. Efforts to intercept the product of fluoride

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abstraction, **2-F**⁺, from reaction of **2**[B(C₆F₅)₄]₂ with CsF or NBu₄F were unsuccessful, showing only PhPF₂ and a broadened peak in the same region as **2**²⁺ (Figure S19). Despite this inability to isolate **2-F**⁺, computations reveal that it would adopt a pseudo square-based pyramidal geometry with 12-valence electrons about the P(III) center (Figure S20) and that subsequent reaction with a silylium ion to regenerate **2**²⁺ is thermodynamically downhill by 6.8 kcal/mol.



Scheme 3. Proposed mechanisms for HDF catalyzed by 2^{2+} with R = Me. Numbers indicate calculated (PBE1-D3/cc-pVTZ) values of ΔG_{rxn} for each step (kcal/mol).

The use of $2[B(C_6F_5)_4]_2$ in HDF catalysis offers practical advantages over known electron-deficient (e.g. borane, silylium and alumenium cations) or electron-precise species (e.g. silane, stibonium or phosphonium cations).^[3-4] In contrast to such previous systems, this salt is air-stable and easily synthesized from commercially-available, bench-stable reagents within minutes with no need for purification. Indeed, catalytic HDF was also achieved by the generation of 10 mol% $2[B(C_6F_5)_4]_2$ in-situ from terpy, PhPCl₂, and K[B(C_6F_5)_4] and subsequent addition to a mixture of 1-fluoropentane and Et₃SiH in dry DCM. In addition, 2^{2+} is also unique in featuring an electron-rich (hypervalent) environment and a lone pair at the reactive electrophilic site.

In summary, we have exploited C-F bond activation by a readily accessible and air-stable salt $2[B(C_6F_5)_4]_2$ to achieve the first example of catalytic HDF by P(III) Lewis acids. The use of terpy as a stabilizing, yet potentially hemilabile ligand (Figure S20), suggests new strategies for designing more robust versions of other p-block Lewis acid catalysts. These findings bode well for wider adoption of main-group catalyzed C-F bond reduction methodologies by eliminating the challenging synthetic protocols and requirements for strictly anhydrous conditions and highly reactive intermediates that currently characterize this field.

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