

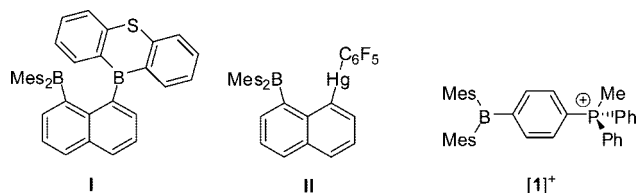
Fluoride Ion Chelation By a Bidentate Phosphonium/Borane Lewis Acid

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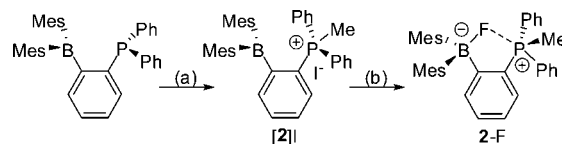
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Because of applications in dental care or in the treatment of osteoporosis, the introduction of fluoride anions (F^-) in drinking water, toothpastes, and medications has become widespread. This recent trend is raising concerns because high doses of F^- have been associated with dental and skeletal fluorosis, among other diseases.¹ For these reasons, discovering methods for the recognition of this anion has become a topical research objective.² One of the most successful strategies adopted to date relies on the use of fluorophilic boron compounds.^{3,4} Bidentate boranes⁵ such as **I**⁶ and **II**⁷ are among the best receptors thus far identified. Their high fluorophilicity results from cooperative effects involving the neighboring Lewis acidic centers which both interact with the fluoride ion to form a chelate complex. Such bifunctional boranes are however supplanted by cationic boranes such as **[1]**⁺ whose enhanced fluorophilicity arises from favorable Coulombic effects.^{8,9} In principle, boron based receptors that are bidentate and cationic should capitalize on both Coulombic and cooperative effects leading to a further enhancement of their F^- affinity.¹⁰ In this report, we provide a dramatic illustration of this principle in the F^- binding properties of **[1-Mes₂B-2-MePh₂P-(C₆H₄)]⁺ (2⁺), the ortho isomer of **1**⁺. We also demonstrate that the latent phosphorus-centered Lewis acidity¹¹ of the phosphonium moiety^{12,13} can be harnessed to enhance F^- binding via chelation.**



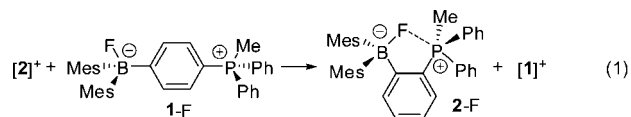
The iodide salt of **[2]**⁺ could be easily obtained by reaction of the corresponding neutral phosphinoborane **1-Mes₂B-2-Ph₂P-(C₆H₄)**¹⁴ with methyl iodide in dichloromethane (Scheme 1). This salt has been characterized by multinuclear NMR spectroscopy as well as by single crystal X-ray diffraction. The ¹H NMR of **[2]I** displays broad multiple signals for the protons on the mesityl substituents, indicative of a congested structure about the boron center. The phosphorus bound methyl group gives rise to a characteristic doublet (²J_{H-P} = 13.5 Hz) at 2.86 ppm and the ³¹P NMR resonance appears at 23.9 ppm. In CHCl₃, **[2]I** features a broad absorption band at 347 nm corresponding to the triarylborane chromophore. Observation of this band indicates that the boron center remains coordinatively unsaturated as in the case of the para isomer **[1]**.⁸ In the crystal, the boron center of **[2]**⁺ is trigonal planar ($\Sigma_{C-B-C} = 359.7^\circ$) and separated from the phosphorus atom P(1) by only 3.494(3) Å. This short separation indicates that the unsaturated boron center is sterically encumbered. This conclusion is in agreement with (i) the large B(1)–C(1)–C(2) angle (130.1(3)°

Scheme 1^a

^a Conditions: (a) MeI, CH₂Cl₂, 25 °C, 87%; (b) [S(NMe₂)₃][SiMe₃F₂], CHCl₃, 25 °C, 91%.

which substantially deviates from the ideal value of 120° and (ii) the elongated C(1)–C(2) bond of 1.462(4) Å. Distortions are also evident in the coordination geometry of the phosphorus atom with the sum of the C(2)–P(1)–C(30), C(30)–P(1)–C(41), and C(41)–P(1)–C(2) angles α equal to 335.2° rather than 328.4° which would be expected if the phosphorus atom adopted a regular tetrahedral geometry.

With this new cationic borane in hand, we became eager to compare its F^- binding properties to those of its para isomer **[1]**⁺. Remarkably, when equimolar amounts of **[2]I** and **1-F** were mixed in CDCl₃, ³¹P NMR spectroscopy indicated quantitative formation of **[1]**⁺ along with a new species assigned to **2-F** and characterized by a doublet at 28.3 ppm (eq 1). Encouraged by these results, we decided to compare the F^- binding constants (*K*) of **[1]**⁺ and **[2]**⁺. Since **[2]I** is not stable in neutral water, the titrations were carried out in MeOH by monitoring the absorbance of the boron-centered chromophore upon F^- addition. Fitting of the resulting isotherms to a 1:1 binding model, indicates that the F^- binding constant of **[2]**⁺ ($K > 10^6 \text{ M}^{-1}$) exceeds the measurable range and is at least 4 orders of magnitude higher than that measured for **[1]**⁺ ($K = 400 (\pm 50) \text{ M}^{-1}$). In an effort to identify the origin of this difference, we isolated **2-F** from the reaction of **[2]I** with [S(NMe₂)₃][Me₃SiF₂] (TASF) and proceeded with its characterization. The ¹¹B NMR signal of the four coordinate boron center of **2-F** appears at 5.7 ppm. The ¹⁹F NMR spectrum features a broad signal at –158 ppm which is comparable to the chemical shift observed in other triarylfluoroborate complexes.⁸ The ³¹P NMR signal at 28.3 ppm appears as a doublet because of coupling to the fluorine nucleus (*J*_{P-F} = 24.3 Hz). Although the *J*_{P-F} coupling constant is much smaller than reported for ¹*J*_{P-F} values,¹⁵ the down-field shift of the ³¹P NMR resonance in **2-F** suggests that the fluorine atom may actually be chelated by the borane and phosphonium moieties of **[2]**⁺.



This conclusion was confirmed by determination of the X-ray crystal structure of **2-F** (Figure 1). Indeed, the boron bound fluorine atom F(1) (B(1)–F(1) = 1.482(3) Å) is located only 2.666(2) Å away from the P(1) atom, which is well within the sum of the van der Waals radii of the two elements (ca. 3.45 Å).¹⁶ Another conspicuous feature

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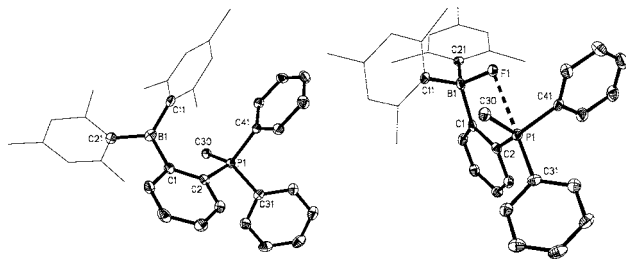


Figure 1. Crystal structure of $[2]^+$ (left) and 2-F (right) (50% ellipsoid, mesityl groups represented by thin lines, H-atoms omitted). Pertinent parameters are provided in the text.

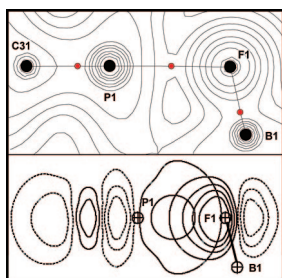


Figure 2. AIM and NBO analyses of the B-F→P interaction. (Top) AIM electron density map with relevant bond paths and bond critical points; (bottom) NBO contour plot showing the $lp(F) \rightarrow \sigma^*(P-C)$ interaction.

concerns the F(1)–P(1)–C(31) angle of $176.36(9)^\circ$ which indicates that the fluorine atom occupies an axial coordination site directly opposite to a phenyl ring. In agreement with this view, we note a slight elongation of the P(1)–C(31) bond ($1.813(3) \text{ \AA}$) when compared to the P(1)–C(41) bond ($1.796(3) \text{ \AA}$) and a notable increase in the sum of angle α on going from $[2]^+$ to 2-F ($\alpha = 340.4^\circ$ in 2-F vs 335.2° in $[2]^+$). Altogether, the structural and spectroscopic results support the presence of a B-F→P interaction, which may be the origin of the increased fluorophilicity of $[2]^+$. These results also establish that the phosphorus atom of $[2]^+$ is acting as a Lewis acid, an intrinsic property of phosphonium cations¹² that has so far never been exploited for anion sensing.¹³ In fact, the structure of 2-F is strikingly similar to that of the anionic fluoride chelate complexes of $[1-\text{Mes}_2\text{B}-2-\text{FPh}_2\text{Si}-(\text{C}_6\text{H}_4)]^4$ and $[1-\text{MePhB}-2-\text{FMe}_2\text{Sn}-\text{Fc}]^{17}$ (Fc (Fc = ferrocenediyl) which possess Lewis acidic fluorosilane and fluorostanane moieties, respectively.

The DFT optimized structure of 2-F is in excellent agreement with that experimentally determined (see Supporting Information). In particular, the P(1)–F(1) separation of 2.665 \AA is close to that observed in the crystal ($2.666(2) \text{ \AA}$). Atoms in molecules (AIM)¹⁸ calculations show the presence of a bond path between the P(1) and F(1) atoms with an electron density $\rho(r)$ of $2.05 \times 10^{-2} \text{ e bohr}^{-3}$ at the BCP (Figure 2). The presence of this interaction can be further asserted through a natural bond orbital (NBO) analysis performed at the optimized geometry. This analysis identifies a donor–acceptor interaction involving a fluorine lone-pair as a donor and the phosphorus–carbon σ^* -orbital as the acceptor (Figure 2). Moreover, a deletion calculation carried out by zeroing the Kohn–Sham matrix elements corresponding to the $lp(F) \rightarrow \sigma^*(P-C)$ interaction leads to an increase of the total energy of the molecule by 5.0 kcal/mol . Further insight into the increased fluorophilicity of $[2]^+$ was gained from a computation of the enthalpy for the reaction shown in eq 1. To this end, molecules $[1]^+$, $[2]^+$, and 1-F were optimized at the level of theory used for 2-F. Each molecule was then subjected to a single point energy calculation (6-311+g(2d,p) basis set for all atoms) using the polarizable continuum model (PCM) with methanol as a solvent. The relative enthalpies

obtained from these calculations afforded $\Delta H = -7.6 \text{ kcal/mol}$ for the reaction shown in eq 1. The exothermicity computed for this reaction is in line with experimental findings and indicates that the fluoride ion affinity (FIA) of $[2]^+$ significantly exceeds that of $[1]^+$. Furthermore, $[1]^+$ and $[2]^+$ have virtually identical LUMO energies (-2.57 eV for $[1]^+$ and -2.56 eV for $[2]^+$) thus suggesting that inductive effects in these cationic boranes¹⁹ do not play a major role in the increased FIA of $[2]^+$.

In summary, the results reported herein show that the F^- affinity of cationic boranes can be drastically enhanced via cooperative effects arising, in the present case, from the enforced proximity of a Lewis acidic phosphonium and borane moiety.

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Supporting Information Available: Experimental and computational details. Crystallographic data for $[2]^+$ and 2-F in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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