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Acc. Chem. Res., **2009**, 42 (2), 388-397• DOI: 10.1021/ar8001816 • Publication Date (Web): 13 January 2009

Accounts of Chemical Research is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

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Fluoride Ion Recognition by Chelating and Cationic Boranes

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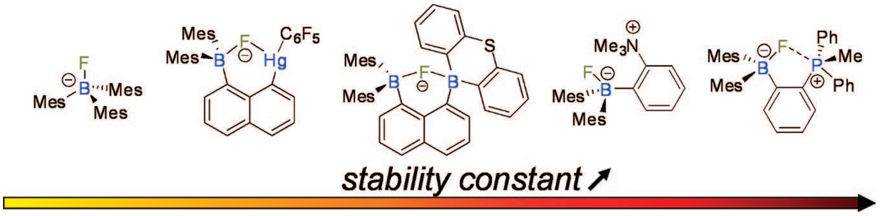
RECEIVED ON AUGUST 21, 2008

CONSPECTUS



Because of the ubiquity of fluoride ions and their potential toxicity at high doses, researchers would like to design receptors that selectively detect this anion. Fluoride is found in drinking water, toothpaste, and osteoporosis drugs. In addition, fluoride ions also can be detected as an indicator of uranium enrichment (via hydrolysis of UF_6) or of the chemical warfare agent sarin, which releases the ion upon hydrolysis. However, because of its high hydration enthalpy, the fluoride anion is one of the most challenging targets for anion recognition.

Among the various recognition strategies that are available, researchers have focused a great deal of attention on Lewis acidic boron compounds. These molecules typically interact with fluoride anions to form the corresponding fluoroborate species. In the case of simple triarylboranes, the fluoroborates are formed in organic solvents but not in water. To overcome this limitation, this Account examines various methods we have pursued to increase the fluoride-binding properties of boron-based receptors.

We first considered the use of bifunctional boranes, which chelate the fluoride anion, such as 1,8-diborylnaphthalenes or heteronuclear 1-boryl-8-mercurio-naphthalenes. In these molecules, the neighboring Lewis acidic atoms can cooperatively interact with the anionic guest. Although the fluoride binding constants of the bifunctional compounds exceed those of neutral monofunctional boranes by several orders of magnitude, the incompatibility of these systems with aqueous media limits their utility.

More recently, we have examined simple triarylboranes whose ligands are decorated by cationic ammonium or phosphonium groups. These cationic groups increase the electrophilic character of these boranes, and unlike their neutral analogs, they are able to complex fluoride in aqueous media. We have also considered cationic boranes, which form chelate complexes with fluoride anions. Our work demonstrates that Coulombic and chelate effects are additive and can be combined to boost the anion affinity of Lewis acidic hosts.

The boron compounds that we have investigated present a set of photophysical and electrochemical properties that can serve to signal the fluoride-binding event. We can also apply this approach to cyanide complexation and are continuing our investigations in that area.

Introduction and Background

Thedesign of fluoride sensors is an area of active investigation because of the possible toxicity of this anion,[1,2] which is present in drinking water, toothpaste, and osteoporosis drugs. The use of such sensors can also be envisaged for tracking UF_6 and phosphorofluoridate nerve agents, which release fluoride upon hydrolysis.

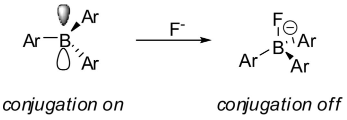
Fluoride displays a high hydration enthalpy ($\Delta H° = -504$ kJ/mol), and its recognition by abiotic hosts is a definite challenge. As a result, a great deal of effort has been devoted to the design of molecular receptors that selectively sense fluoride. In most cases, the binding sites of the sensors consist of amide, urea, thiourea, guanidinium, or pyrrole functionalities that are capable of hydrogen bonding with the anionic

10.1021/ar8001816 CCC: $71.50

guest.[3−21] Implementation of this strategy has led to the design of very selective fluoride receptors and sensors. However, as noted by Fabbrizzi, fluoride recognition by these derivatives mostly takes place in organic solvents, which greatly limits the scope of their use.[22]

In addition to receptors capable of hydrogen bonding with the anionic guest, Lewis acidic receptors that can covalently bind fluoride ions have also been reported.[23−25] Simple triarylboranes, such as trimesitylborane, readily complex fluoride anions in organic solvents (Scheme 1).[26] While this property has long been overlooked in the context of anion sensing, Tamao and Yamaguchi showed that triarylboranes can serve as fluoride sensors. In particular, this group demonstrated that derivatives featuring a tridurylborane (duryl = 2,3,5,6-Me_4C_6H) or a tri(9-anthryl)borane core readily complex fluoride anions with binding constants in the 10^5−10^6 M^{-1} range in organic solvents (Scheme 1).[27−29] Unfortunately, the resulting anionic complexes dissociate in the presence of water, which is undoubtedly driven by the high hydration energy of the small fluoride anion.

SCHEME 1[a]



[a] Ar = Aryl group.

Despite these limitations, fluoride recognition by triarlyboranes has been widely investigated.[30−37] One of the attractive aspects of this approach pertains to the photophysical changes that accompany fluoride binding. In such triarylborane derivatives, the boron empty p-orbital mediates conjugation of the unsaturated aryl substituents and contributes largely to the LUMO of the molecule. This situation is altered in the presence of fluoride, which, upon binding to the boron center, populates the formerly vacant boron p-orbital (Scheme 1). This event disrupts the frontier orbitals of the organoborane and is accompanied by drastic changes in the photophysical properties.[38] These changes directly affect the absorption and emission spectra of the receptors that can therefore be used as colorimetric or fluorescent fluoride ion sensors, respectively. These studies show that organoboranes present a set of chemical and photophysical properties especially appealing in the context of fluoride ion sensing.

1,8-Diborylnaphthalenes

In an effort to overcome the aforementioned limitation faced by borane-based fluoride receptors in water, our group decided to investigate the fluoride anion binding properties of chelating boranes. When we initiated this work, the fluoride binding constant of chelating diboranes had never been determined. However, it had been firmly established that bifunctional diboranes with rigid aromatic backbones[39−41] such as 1,8-bis(dimethylboryl)naphthalene[42,43] or 1,2-$((C_6F_5)_2B)_2C_6F_4$[44] form stable chelate complexes with small anions including fluoride. Encouraged by these reports, we chose to further investigate 1,8-bis(boryl)naphthalenes and focused on a class of derivatives incorporating at least one diarylboryl moiety. This choice was driven by our desire to increase the stability of the boranes while imparting photophysical properties that could be used to monitor anion binding.

With this in mind, we carried out the reaction of 1,8-dilithionaphthalene (**1**) with Mes_2BF (Mes = 2,4,6- $Me_3C_6H_2$), which afforded the $Li(THF)_4$ salt of dimesityl-1,8-naphthalenediylborate (**2**, Scheme 2, Figure 1) rather than the targeted diborane.[45−48] Because of the strain present in the four-membered ring, this borate is very reactive and undergoes ring-opening reactions with electrophiles including boron halide reagents. These reactions afford unsymmetrically substituted 1,8-diborylnaphthalene species such as **3**, **4**, **5**, and **6** where the boron centers are separated by 3.2−3.4 Å.[47−49] In a similar way, **2** reacts with 10-bromo-9-oxa-10-boranthracene (**7**) or 10-bromo-9-thia-10-boranthracene (**8**) to afford diboranes **9** and **10** (Scheme 2).[26,50]

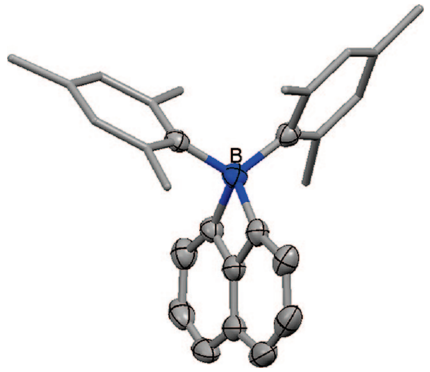
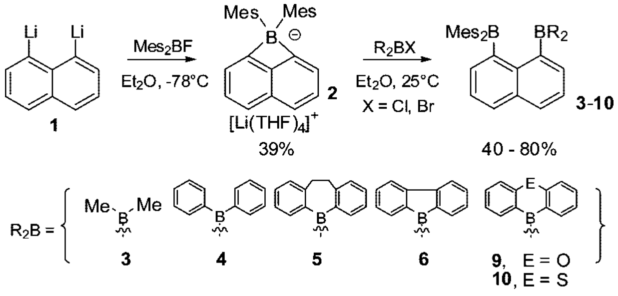
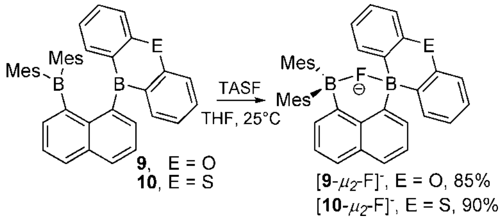


FIGURE 1. Molecular structure of the dimesityl-1,8-naphthalenediylborate anion in **2**.

SCHEME 2



SCHEME 3



The reaction of diboranes **3**, **9**, and **10** with $[S(NMe_2)_3][Me_3SiF_2]$ (TASF) has been investigated and found to afford the anionic chelate complexes [**3**-μ_2-F]$^-$, [**9**-μ_2-F]$^-$ and [**10**-μ_2-F]$^-$ (Scheme 3).[26,49,50] Complexation of larger halides or polyatomic anions such as NO_3^- and $H_2PO_4^-$ is not observed thus indicating that fluoride anion complexation is selective. As previously proposed,[43] the size of the binding pocket provided by these bidentate boranes may be responsible for this phenomenon. These reactions can be followed by monitoring the UV−vis absorption spectra of the diboranes. Indeed, fluoride complexation leads to population of the empty boron p-orbitals, which disrupts the frontier orbitals, especially the LUMO (Figure 2). As a result, anion binding is accompanied by an instantaneous quenching of any transitions involving the LUMO. In the case of **10**, which absorbs in the blue part of the visible spectrum, fluoride binding leads to a loss of the yellow color of the diborane.

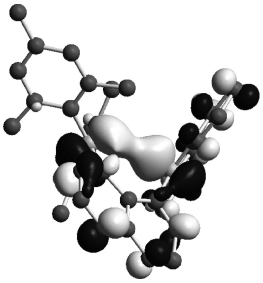


FIGURE 2. DFT orbital picture of **10** showing the LUMO (H-atoms omitted for clarity). The contribution of the boron p-orbitals is obvious from this view.

The crystal structures of the fluoride adducts [**3**-μ_2-F]$^-$, [**9**-μ_2-F]$^-$ and [**10**-μ_2-F]$^-$ have been investigated. In all cases, the fluorine atom is located between the two boron atoms with B−F bond lengths in the 1.58−1.64 Å range (Figure 3). In agreement with the bridging location of the fluorine atom, the B−F bond lengths are distinctly longer than the distance of 1.48 Å observed in typical triarylfluoroborate moieties.

Titration experiments monitored by UV−vis spectroscopy show that the stability constant of [**10**-μ_2-F]$^-$ is at least equal to 5×10^9 M^{-1} in THF (Figure 4).[26] This binding constant is at least 3 orders of magnitude greater than that measured for the monofunctional boranes including Mes_3B, thereby providing a measure of the cooperative effects occurring in such compounds. Moreover, while **10** slowly hydrolyzes in water/THF mixtures, addition of water to [**10**-μ_2-F]$^-$ does not lead to decomplexation of the fluoride anion as typically observed for fluoride adducts of monofunctional boranes.[27] Similar properties are displayed by **3** and **9**, which also form very stable fluoride adducts. Theoretical calculations support these experimental findings. Indeed, the computed gas-phase fluoride ion affinity (FIA) of **3** (71.5 kcal mol^{-1}) and **9** (73.28 kcal mol^{-1}) substantially exceeds those of monofunctional model compounds such as $PhBMes_2$ (FIA = 64.18 kcal mol^{-1}).[49,50] It is important to note that fluoride binding induces a change in the coordination geometry of the boron atom from trigonal planar to distorted tetrahedral (Figure 3). As a result of these changes, the aryl substituents are able to adopt a more divergent orientation in the fluoride adducts and are therefore less sterically hindered than in the starting diboranes. Thus, steric effects may contribute favorably to the high fluoride affinity displayed by these diboranes and may significantly complement the observed chelate effects.[50]

Several of these diboranes have been investigated by cyclic voltammetry. In the case of fully arylated systems such as **4**, **5**, **6**, **9**, and **10**, the voltammogram exhibits two quasi-reversible reduction waves, which correspond to the successive reduction of the two boron centers (Figure 5).[48−50] These electrochemical properties have been used to probe fluoride complexation by **9** and **10**.[50] For both diboranes, incremental

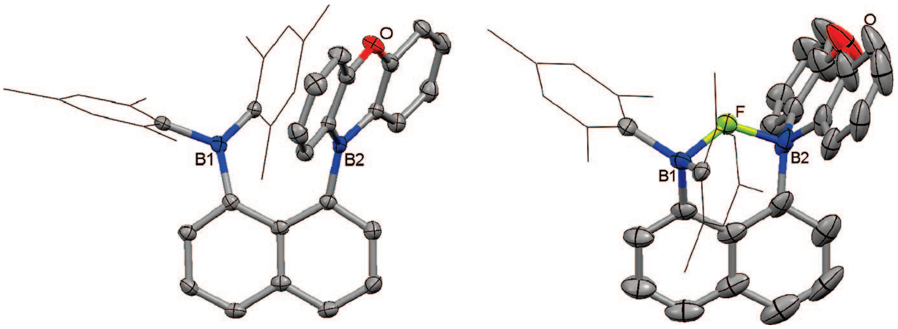


FIGURE 3. View of the crystal structure of **9** (left) and [**9**-μ_2-F]$^-$ (right) outlining the structural changes induced by fluoride complexation. The mesityl groups are represented by thin lines for clarity.

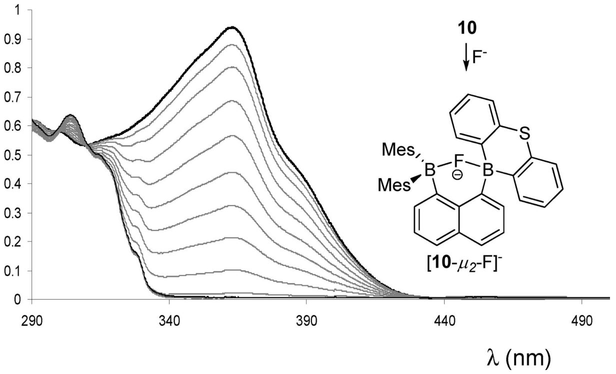


FIGURE 4. Spectral changes accompanying fluoride binding to **10**.

addition of fluoride to the electrochemical cell results in the progressive disappearance of the two reduction waves. These two waves disappear in a synchronous fashion confirming the simultaneous coordination of the fluoride ion to the neighboring boron centers.

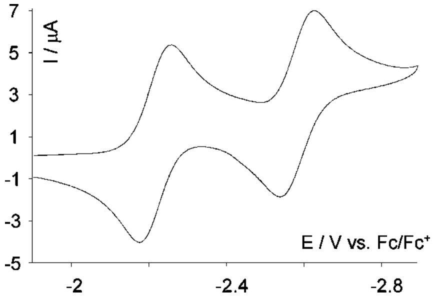


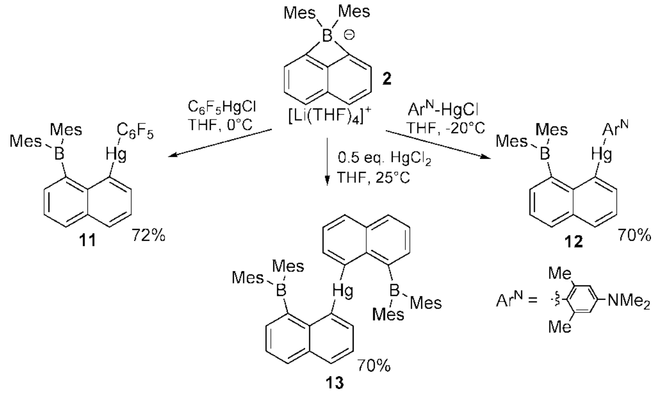
FIGURE 5. Cyclic voltammogram of **9**.

B/Hg Heteronuclear Multidentate Lewis Acids

In an extension of this research, we have investigated the synthesis of heteronuclear bidentate Lewis acids such as **11**, **12**, and **13**, which are obtained by reaction of **2** with the corresponding mercury chloride reagents for **11** and **12** or $HgCl_2$ for **13** (Scheme 4).[49,51,52] These heteronuclear bifunctional boranes have been characterized by conventional means including ^{199}Hg NMR spectroscopy. In the case of **11**, the ^{199}Hg NMR signal, which appears at 741.9 ppm, is split into a triplet of triplets as a result of coupling with fluorine nuclei of the pentafluorophenyl group ($^{3}J_{Hg-F} = 499$ Hz and $^{4}J_{Hg-F} = 165$ Hz).[51] As shown by the crystal structures of these derivatives, the boron and mercury atoms are separated by approximately 3.3–3.5 Å. This short separation indicates that these electron-deficient main-group centers are sufficiently close to cooperate in the binding of anions.

As for simple triaryl boranes, the complexation of anions to the boron center can be monitored by UV–vis spectroscopy. Compounds **11** and **12** selectively complex fluoride to form the corresponding anionic chelate complexes [**11**-μ_2-F]$^-$ and [**12**-μ_2-F]$^-$.[51,52] The stability constants of these anionic complexes in THF exceed the measurable range and are at least equal to 10^7 M^{-1}. Unlike diboranes such as **9** and **10**, compounds **11** and **12** are water-stable and can also bind fluoride in a 90/10 (v/v) THF/water mixture with binding constants of $(2.3 \pm 0.2) \times 10^4$ M^{-1} for **11** and $(1.3 \pm 0.1) \times 10^2$ M^{-1} for **12**. These values are much larger than that measured for Mes_3B (1.0 ± 0.3 M^{-1}) in the same THF/water mixture, in agreement with the formation of chelate complexes. The higher fluoride binding constant of **11** can be assigned to the electron-withdrawing properties of the C_6F_5 group, which increases the Lewis acidity of the mercury center. In the case of **13**, binding of two fluoride anions can be observed by UV–vis spectroscopy or electrochemistry in THF.[49] However, fluoride binding occurs in two very distinct regimes. As expected, the first fluoride binding constant ($K_1 > 10^8$ M^{-1}) is much larger than the second one ($K_2 = (5.2 \pm 0.4) \times 10^3$ M^{-1}). This shows that formation of the dianion by capture of the second fluoride anion is electrostatically and possibly sterically less favorable.

SCHEME 4



The existence of a B–F–Hg chelate motif in [**11**-μ_2-F]$^-$ and [**12**-μ_2-F]$^-$ can be easily confirmed using NMR spectroscopy.[51,52] In particular, the ^{199}Hg nucleus is coupled to the bridging fluoride ($^{1}J_{Hg-F} = 135.2$ Hz for [**11**-μ_2-F]$^-$, $^{1}J_{Hg-F} = 109.8$ Hz for [**12**-μ_2-F]$^-$) pointing to the presence of a direct Hg–F interaction. A similar conclusion can be derived from the crystal structure of $[S(NMe_2)_3]$[**11**-μ_2-F] in which the fluorine atom F(1) forms a short bond of 1.483(4) Å with the boron atom B(1) and a longer one of 2.589(2) Å with the mercury atom Hg(1) (Figure 6). The latter is well within the sum of the van der Waals radii of the two elements and is, in fact, comparable to the distances observed in a fluoride adduct of a tetranuclear mercuracarborand (2.56 and 2.65 Å).[23]

In addition to being compatible with aqueous environments, such compounds possess unusual photophysical properties, which can be used to signal anion binding. As

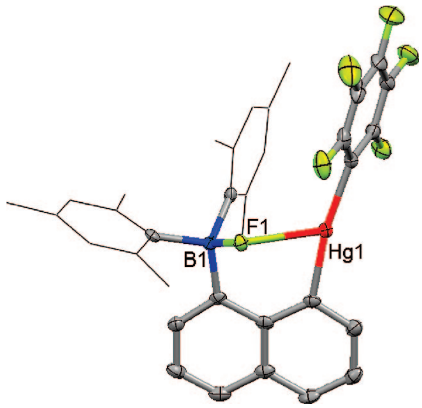
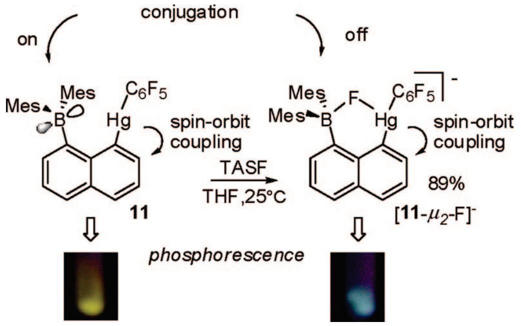


FIGURE 6. Crystal structure of [**11**-μ_2-F]$^-$. The mesityl groups are represented by thin lines for clarity.

demonstrated in the case of **11**, the unsaturated boron center mediates conjugation of the naphthalenediyl and mesityl substituents that collectively behave as a single chromophore.[51] Because of the presence of a mercury atom, which provides spin–orbit perturbation to the chromophore, excitation of solid **11** leads to phosphorescence of the dimesityl-borylnaphthalenediyl moiety and gives rise to a red emission. Since fluoride complexation leads to population of the boron empty p-orbital, conjugation of the naphthalenediyl and mesityl substituents in [**11**-μ_2-F]$^-$ is no longer operative. As a result, the naphthalene moiety of [**11**-μ_2-F]$^-$ behaves as an isolated chromophore, which readily emits a characteristic green phosphorescence (Scheme 5). Thus, the interplay of conjugative and spin–orbit coupling effects mediated by the boron and mercury atoms, respectively, results in the phosphorescent signaling of fluoride binding.

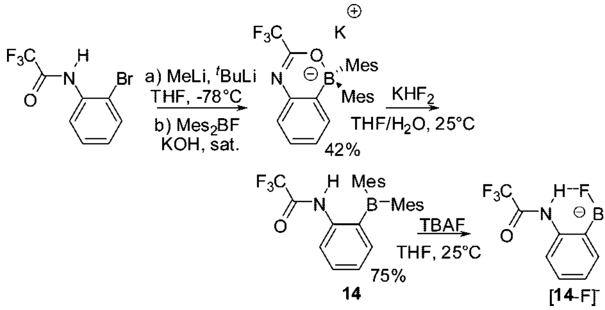
SCHEME 5. Fluoride Complexation by **11** and Emission Observed in the Solid State under UV Irradiation a Few Seconds after Immersion in Liquid Nitrogen



Hybrid Borane/Hydrogen-Bond Donor Derivatives

The high fluoride binding affinity of heteronuclear bidentate Lewis acids such as **11** and **12** suggests that a weakly fluorophilic Lewis acidic site such as mercury may serve to assist anion binding at a neighboring boron center. To generalize this paradigm, we sought to determine whether hydrogen-bond donor groups can be used to assist triarylboryl moieties in the binding of anions. With this in mind, we synthesized *o*-(dimesitylboryl)trifluoroacetanilide (**14**) by the sequence of steps outlined in Scheme 6.[53] The crystal structure of this new borane was determined, allowing us to confirm that the carbonyl group of the trifluoroacetamide functionality is not sufficiently basic to neutralize the Lewis acidic boron center. Reaction of this new borane with [(*n*-Bu)$_4$N]F (TBAF) in THF affords the corresponding fluoroborate complex, [**14**-F]$^-$ (Scheme 6), whose stability constant exceeds that of [Mes$_3$BF]$^-$ by at least 2 orders of magnitude. While salts of [**14**-F]$^-$ could not be crystallized, valuable structural information was obtained from NMR spectroscopy. In particular, the amide proton of [**14**-F]$^-$ is coupled to the bridging fluoride and gives rise to a doublet ($^1J_{H-F}$ = 36 Hz) at 11.43 ppm (vs 8.79 ppm in **14**) indicating the presence of a NH···FB hydrogen bond (Figure 7). The DFT optimized structure of [**14**-F]$^-$ features a NH···FB hydrogen bond of 1.72 Å, thus corroborating the experimental findings. Altogether, these results indicate that the higher fluoride affinity of **14** results from the cooperativity of the Lewis acidic boron center and the hydrogen-bond donor trifluoroacetamide group.

SCHEME 6



Ammonium Boranes

The results presented above indicate that the fluoride binding constants of bidentate boranes exceed those of monofunctional analogs by 3 or 4 orders of magnitude. However, their use in protic environments remains problematic. For example, chelating diboranes such as **10**[26] will undergo a slow hydrolysis in the presence of water or methanol. The heteronuclear B/Hg derivative **11** captures fluoride in 90/10 (v/v) THF/water[51] but not in pure water. In an effort to overcome these challenges, we have recently considered an alternative approach that relies on the use of cationic boranes whose anion affinity is enhanced by favorable Coulombic effects.

The first compound that we investigated is the cationic borane [**15**]$^+$, which could be obtained by reaction of **2** with the Eschenmoser salt followed by reaction with MeOTf. This cationic borane reacts with aqueous fluoride ions under biphasic conditions (H_2O/$CHCl_3$) to form the corresponding zwitterion **15-**F.[54] Neutral boranes such as Mes_3B, **10**, and **11** fail to capture fluoride under these biphasic conditions, attesting to the favorable influence of the ammonium group on the anion affinity of [**15**]$^+$. Titration experiments carried out in THF show that [**15**]$^+$ is selective for fluoride. Indeed, while the fluoride binding constant exceeds 10^8 M^{-1}, the only other anion thus far found to interact with [**15**]$^+$ is cyanide.[55] The cyanide binding constant of $(8.0 \pm 0.5) \times 10^5$ M^{-1} is, however, smaller than the fluoride binding constant, which is surprising given the higher basicity of cyanide ($pK_a = 9.3$) when compared with fluoride ($pK_a = 3.18$). As suggested by the severely distorted structure of **15**-CN, this selectivity most likely arises from the steric effects, which impede binding of the larger cyanide anion. Interestingly, structural, spectroscopic, and computational analysis of **15**-F point to the existence of a CH···FB hydrogen bond, which may significantly contribute to the stability of this zwitterion (Scheme 7). This hydrogen bond involves one of the methylene hydrogen nuclei, which is coupled to the fluorine nucleus by 9.2 Hz and shifted downfield at 6.50 ppm (Figure 7). These results presented an important step forward in the recognition of aqueous fluoride ions and served as an inspiration for the study of additional ammonium boranes.

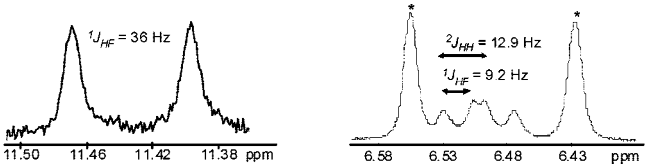
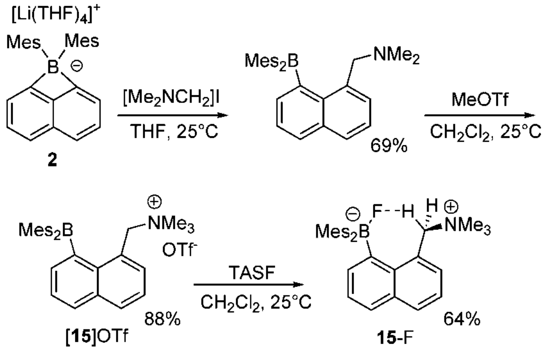


FIGURE 7. Portion of the ^1H NMR spectra of [**14**-F]$^-$ (left) and **15**-F (right) showing the resonance of the hydrogen nucleus hydrogen bonded to the fluorine atom.

SCHEME 7



In this vein, the cations [*o*-**16**]$^+$ and [*p*-**16**]$^+$ were synthesized as their triflate salt by reaction of the known aminoborane precursors with MeOTf.[56] Both of these salts have been characterized by X-ray analysis. The B(1)−C(1)−C(2) angle of 135.8(4)° in the structure of the ortho isomer indicates a great deal of steric congestion caused by the enforced proximity of the boryl and ammonium moieties (Figure 8). In organic solvents such as $CHCl_3$, both salts react with fluoride and cyanide ions to afford the corresponding fluoroborate− or cyanoborate−ammonium zwitterions *o*-**16**-F, *o*-**16**-CN, *p*-**16**-F, and *p*-**16**-CN. Both *o*-**16**-F and *p*-**16**-CN have been structurally characterized (Scheme 8). Despite pyramidalization of the boron center, the zwitterion *o*-**16-**F remains sterically encumbered as indicated by the B(1)−C(1)−C(2) angle of 132.4(2)° (Figure 9).

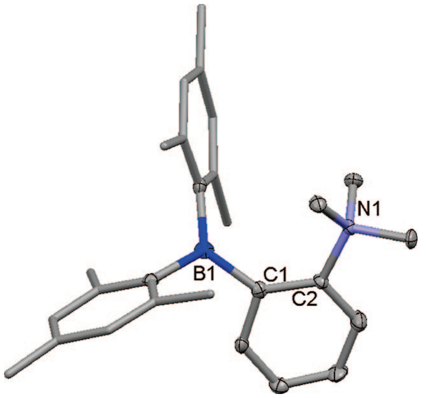


FIGURE 8. Crystal structure of [*o*-**16**]$^+$ in the triflate salt.

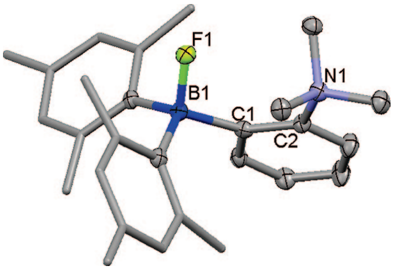
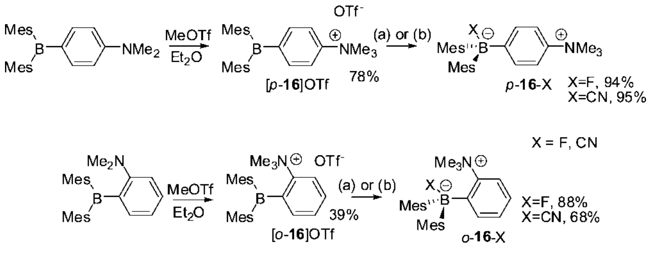


FIGURE 9. Crystal structure of *o*-**16**-F.

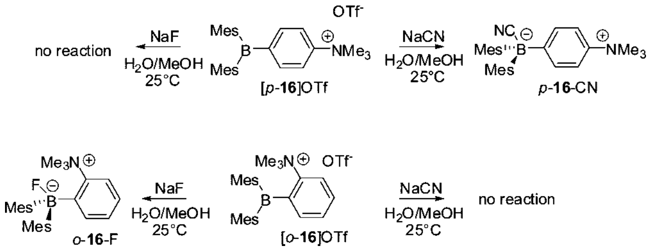
SCHEME 8



(a): TBAF, $CHCl_3$, 25°C for X = F
(b): NaCN, MeOH, 25°C for X = CN

Remarkably, anion complexation also occurs in aqueous methanolic solution (Scheme 9). However, under these conditions, anion binding is selective. Indeed, [*p*-**16**]$^+$ only complexes cyanide ions, whereas [*o*-**16**]$^+$ only complexes fluoride ions. In H_2O/DMSO 60:40 vol. (HEPES, 6 mM, pH 7), the cyanide binding constant of [*p*-**16**]$^+$ and the fluoride binding constant of [*o*-**16**]$^+$ are, respectively, equal to $(3.9 \pm 0.1) \times 10^8$ M^{-1} and 910 ± 50 M^{-1}. It is worth noting that the resulting zwitterions, namely, *p*-**16**-CN and *o*-**16**-F, tend to precipitate upon formation when the water content of the H_2O/DMSO mixture is increased. These results demonstrate that cationic boranes such as [*p*-**16**]$^+$ and [*o*-**16**]$^+$ serve as selective receptors for cyanide or fluoride in water at neutral pH. The unusual cyanide binding properties of [*p*-**16**]$^+$ can be assigned to favorable Coulombic effects, which increase the Lewis acidity of the boron atom and strengthen the receptor–cyanide interaction. Another important aspect of this research concerns the anion binding selectivity of these cationic boranes, which can be tuned using both steric and electronic effects. Indeed, when the trimethylammonium functionality is positioned ortho to the boron center as in [*o*-**16**]$^+$, the Lewis acidity of the ammonium borane is increased, making fluoride binding possible. However, in this case, the increased steric crowding of the boron center prevents coordination of the larger cyanide anion.

SCHEME 9



The ability of such cationic boranes to capture small solvated anions in water results from Coulombic effects. Conceptually, these effects can be viewed as increasing the attraction of the boranes for the anion. DFT calculations also show that the cationic character of the boranes results in a lowering of the energy of the LUMO. Since the LUMO bears an important contribution from the boron empty p-orbital, these Coulombic effects increase the Lewis acidity of the boron center. In fact, the LUMO of [*o*-**16**]$^+$ (−2.12 eV) is lower than that of [*p*-**16**]$^+$ (−2.02 eV) thus corroborating the increased fluoride affinity of the ortho isomer (Figure 10).

Both [*p*-**16**]$^+$ and [*o*-**16**]$^+$ feature a UV absorption band near 320 nm, which, as indicated by DFT calculations, bears a large HOMO to LUMO component. Since the LUMO bears an important contribution from the boron empty p-orbital, while the highest occupied molecular orbital (HOMO) is localized on the mesityl rings (Figure 10), this absorption can be regarded in a "ligand-to-element" charge-transfer transition. Both [*p*-**16**]$^+$ and [*o*-**16**]$^+$ are brightly fluorescent. In water, the emission band is centered at 458 nm for [*p*-**16**]$^+$ and 433 nm for [*o*-**16**]$^+$ (Figure 10) giving rise to a distinct blue color, which can be detected with the naked eye at micromolar concentrations. In the case of [*p*-**16**]$^+$, the blue emission is readily quenched upon addition of 1 equiv of cyanide, which binds to the boron center thereby disrupting the frontier orbitals (Figure 11).

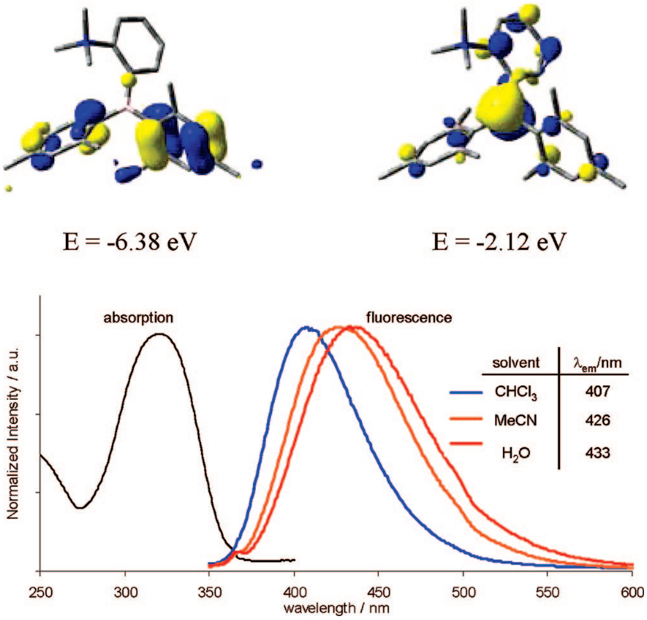


FIGURE 10. HOMO (top left) and LUMO (top right) and absorption and emission spectra (bottom) of [*o*-**16**]$^+$.

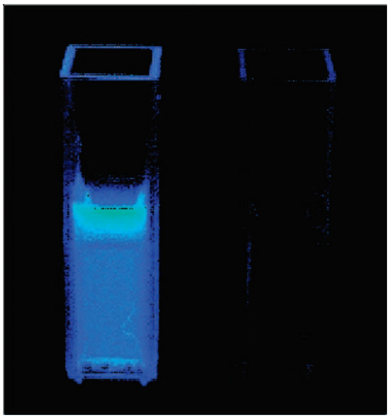
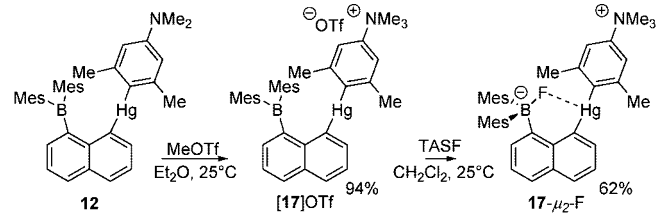


FIGURE 11. Pictures showing how the blue fluorescence of [*p*-**16**]$^+$ (left) is quenched after addition of 1 equiv of cyanide ions (right).

To verify whether the Coulombic effects could be used to increase the anion affinity of chelating bifunctional boranes, the heteronuclear B/Hg compound **12** was converted into the corresponding ammonium triflate salt [**17**]OTf by reaction with MeOTf (Scheme 10).[52] As shown by DFT calculations, conversion of the amino group into an ammonium group on going from **12** to [**17**]$^+$ results in a lowering of the mercury vacant orbitals, allowing them to mix more efficiently with the boron orbital. These changes reflect an increase in the Lewis acidity of the mercury center, which should impact the anion affinity of the entire molecule. Indeed, fluoride titration experiments carried out in THF/water (9/1, v/v) mixture afford a fluoride binding con-

SCHEME 10



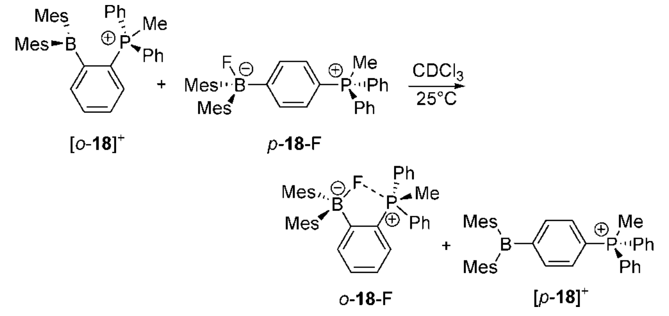
stant of (6.2 ± 0.2) × 10^4 M^{-1} for [**17**]$^+$ as opposed to (1.3 ± 0.1) × 10^2 M^{-1} for its neutral precursor **12**.

Phosphonium Boranes

To broaden the scope of our investigation and understand how simple variation in the structure and composition of the boranes impacts their anion properties, we have also investigated phosphonium boranes such as [*p*-**18**]$^+$ and [*o*-**18**]$^+$, which could be easily prepared by reaction of the corresponding diphenylphosphino boranes with MeI.[57,58] Unlike [*p*-**18**]$^+$, which is stable in water up to pH 6–7, [*o*-**18**]$^+$ quickly decomposes above pH 3 to afford a product that has not been currently identified. In water/methanol (9/1, v/v), [*p*-**18**]$^+$ captures fluoride with a binding constant in the range of 10^3 M^{-1}.[57] This observation is surprising since [*p*-**16**]$^+$ fails to capture fluoride under the same conditions.[56] The origin of this dichotomy is not entirely clear; however, we postulate that the increased hydrophobicity of [*p*-**18**]$^+$ may result in a lower solvation of the cationic borane thereby favoring the formation of neutral *p*-**18**-F.

Although [*o*-**18**]$^+$ cannot be evaluated in water, we have studied its fluoride affinity in organic solvents.[58] Remarkably, the reaction of equimolar amounts of [*o*-**18**]$^+$ (as the iodide salt) and *p*-**18**-F in $CDCl_3$ leads to [*p*-**18**]$^+$ and *o*-**18**-F in a quantitative yield, indicating that the fluoride affinity of [*o*-**18**]$^+$ is far superior to that of [*p*-**18**]$^+$ (Scheme 11). More quantitative information could be gained from fluoride titration experiments carried out in MeOH. In this solvent, the fluoride binding constant of [*o*-**18**]$^+$ ($K > 10^6$ M^{-1}) exceeds the measurable range and is at least 4 orders of magnitude higher than that measured for [*p*-**18**]$^+$ ($K = 400 \pm 50$ M^{-1}). Clues to the higher fluoride affinity of [*o*-**18**]$^+$ were derived from both spectroscopic and crystallographic measurements, which pointed to the presence of a bonding interaction between the fluorine and phosphorus atoms of *o*-**18**-F. The ^{31}P NMR signal of *o*-**18**-F at 28.3 ppm (J_{P-F} = 24.3 Hz) is shifted downfield compared with that of [*o*-**18**]$^+$ (23.9 ppm) in agreement with an increase in the coordination number of the phosphorus atom. The crystal structure of this derivative confirmed this proposal. Specifically, 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) (Figure 12). Another conspicuous feature concerns the F(1)–P(1)–C(31) angle of 176.36(9)°, which indicates that the fluorine atom occupies an axial coordination site directly opposite to a phenyl ring, a conclusion supported by the distorted trigonal bipyramidal geometry of the phosphorus atom.

SCHEME 11



These results indicate the presence of a B–F→P interaction, which contributes to the increased fluorophilicity of [*o*-**18**]$^+$. While the F→P interaction must bear a large electrostatic component, an AIM analysis carried out at the DFT optimized geometry indicates the presence of a bond path connecting the two

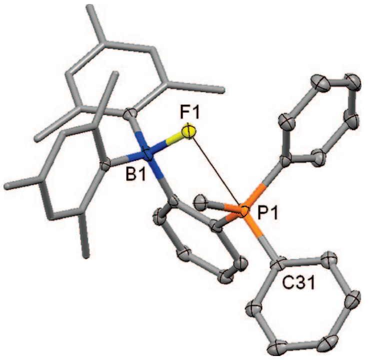


FIGURE 12. Crystal structure of *o*-**18**-F.

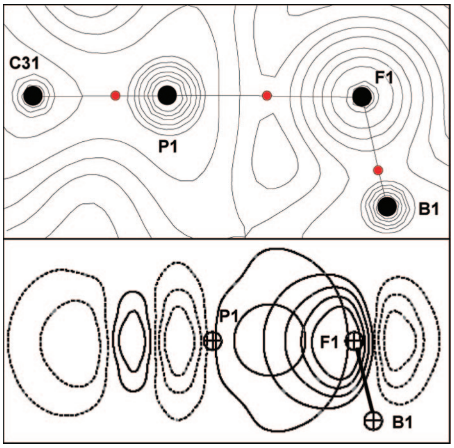


FIGURE 13. AIM and NBO analyses of the B–F→P interaction in *o*-**18**-F: (top) AIM electron density map with relevant bond paths and bond critical points; (bottom) NBO contour plot showing the $lp_{(F)} \rightarrow \sigma^*_{(P-C)}$ interaction.

atoms (Figure 13). The presence of this interaction can be further asserted through a natural bond orbital (NBO) analysis. This analysis identifies a donor–acceptor interaction involving a fluorine lone-pair as a donor and the phosphorus–carbon σ^*-orbital as the acceptor. 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. Thus, [*o*-**18**]$^+$ can be regarded as a cationic bidentate Lewis acid, whose high fluoride affinity arises from both fluoride ion chelation and Coulombic attractions. In turn, these results further demonstrate that Coulombic and chelate effects are additive and can be combined to boost the anion affinity of Lewis acidic hosts. A key aspect of this result pertains to the nature of the Lewis acidic sites involved in fluoride ion chelation. Indeed, in *o*-**18**-F, the boron bound fluoride anion interacts with the phosphorus atom of the phosphonium unit. While it has been previously shown that phosphonium ions are Lewis acidic, this property had never been exploited for the recognition of small anions.

Conclusion and Outlook

Our work demonstrates that the fluoride anion affinity of boron-based receptors can be drastically enhanced through both cooperative and Coulombic effects. We have also demonstrated that these effects are in fact additive as in derivatives [**17**]$^+$ and [*o*-**18**]$^+$. While much weaker than Lewis acids such as $B(C_6F_5)_3$, many of the boron-based fluoride receptors investigated in our group can be used in water without undergoing neutralization at neutral pH. In turn, some of the boranes described in this Account may find applications for the recognition of fluoride ions in aqueous environments.

We have obtained some promising results that indicate that cationic boranes may be very well suited for the recognition of cyanide anions. Taking into account the toxicity of this anion, we plan to further investigate this possibility. Finally, much remains to be done in order to understand how simple structural variations impact the anion affinity of such boranes. For this reason, we will remain engaged in a fundamental synthetic effort aimed at fine-tuning the Lewis acidic properties of this type of derivative.

This work was supported by the National Science Foundation (CHE-0646916), the Welch Foundation (A-1423), the Petroleum Research Funds (44832-AC4) and the US Army Medical Research Institute of Chemical Defense.

BIOGRAPHICAL INFORMATION

Todd W. Hudnall was born in 1979 in Corpus Christi, Texas. After receiving a B.S. degree from Texas State University–San Marcos in 2004, he joined the group of F. P. Gabbaï at Texas A&M University where he studied Lewis acidic boron compounds. Upon completion of his Ph.D. in the fall of 2008, he moved to the University of Texas at Austin to work with C. W. Bielawski as a postdoctoral fellow.

Ching-Wen Chiu was born in 1977 in Taiwan. After completing her undergraduate studies at National Chiao-Tung University (Taiwan), she joined the group of H. T. Chiu at the same institution to work on various aspects of nanomaterials synthesis and was awarded a M.S. degree in 2001. From 2001 until 2003, she studied light-emitting materials under T. J. Chow at the Institute of Chemistry, Academia Sinica, in Taipei (Taiwan). In 2003, she joined the group of F. P. Gabbaï at Texas A&M University to work on the synthesis, electrochemistry and anion affinity of cationic main group compounds. She obtained a Ph.D. in May 2008 and moved to the Julius-Maximillians Universität Würzburg where she is currently working as a postdoctoral fellow under the guidance of H. Braunschweig.

François Gabbaï was born in 1968 in Montpellier (France). Before joining the research group of A. H. Cowley at the University of Texas at Austin, he studied chemistry at the Université de Bordeaux (France). In 1992 and 1993, he fulfilled his French National Duties by taking part in a Franco-American cooperation under the supervision of G. Bertrand and A. H. Cowley. After completing his Ph.D. degree in 1994, he was awarded an Alexander von Humboldt Fellowship as well as Marie Curie Fellowship from the European Commission, which allowed him to work with H. Schmidbaur at the Technische Universität München (Germany) as a postdoctoral fellow and later as a "Habilitand". Upon completion of his habilitation work in 1998, he joined Texas A&M University where he is now a professor of chemistry. His research is concerned with various aspects of main-group element chemistry.

FOOTNOTES

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