

Hybrid Lewis Acid/Hydrogen-Bond
Donor Receptor for Fluoride

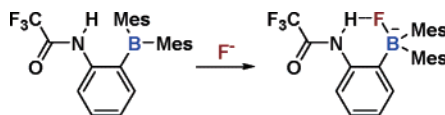
Todd W. Hudnall, Mohand Melatmi, and François P. Gabbaï*

Department of Chemistry, Texas A&M University, College Station, Texas 77843

francois@tamu.edu

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ABSTRACT



To verify if hydrogen-bond donor groups can assist fluoride binding at the boron center of triaryl boranes, *o*-(dimesitylboryl)trifluoroacetanilide has been synthesized. Reaction of this new borane with $[n\text{-Bu}_4\text{N}][\text{F}]$ in acetone affords the corresponding fluoroborate complex whose stability constant exceeds that of $[\text{Mes}_3\text{BF}]^-$ by at least 2 orders of magnitude. Presumably, the higher fluoride affinity of *o*-(dimesitylboryl)-trifluoroacetanilide results from the cooperativity of the Lewis acidic boron center and the hydrogen-bond donor trifluoroacetamide group.

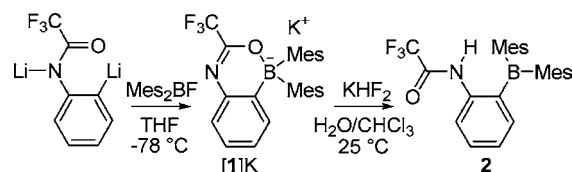
The molecular recognition of fluoride continues to attract a great deal of attention because of the importance of this anion in dental health¹ and in the treatment of osteoporosis.² In addition to receptors which interact with the anionic guest via hydrogen bonds,³ Lewis acidic triarylboranes^{4,5} which form boron–fluorine coordination bonds have also been considered. Such receptors present attractive photophysical properties and capture fluoride anions with association constants in the 10^5 – 10^6 M^{-1} range in organic solvents. To increase the binding constant of borane-based receptors, we and others have explored the use of bidentate boranes that chelate fluoride.^{6–8} We also investigated heteronuclear

bidentate Lewis acids and showed that the fluoride binding constant of 1-(dimesitylboron)-8-(pentafluorophenylmercury)naphthalenediyl, a hybrid boron/mercury derivative, exceeds 10^8 M^{-1} in THF.⁹ These results indicate that a weakly fluorophilic Lewis acidic site such as mercury may serve to assist fluoride binding at a neighboring boron center. To generalize this paradigm, we are now questioning whether hydrogen-bond donor groups can be used to assist triarylboron moieties in the binding of fluoride anions. In this letter, we report the synthesis and behavior of a hybrid derivative containing both a Lewis acidic boron center and a hydrogen-bond donor trifluoroacetamide group.

Double lithiation of *o*-bromotrifluoroacetanilide followed by reaction with dimesitylboron fluoride affords, after treatment with KOH, $\text{K}[1]$ as a pale yellow air- and water-stable salt (Scheme 1). The ¹¹B NMR signal of $[1]^-$ appears at 5 ppm which is in agreement with a tetracoordinated boron center. The structure of compound $[1]^-$ was confirmed by a

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Scheme 1. Synthesis of *o*-(Dimesitylboryl)trifluoroacetanilide (2)



single-crystal X-ray analysis of $[\text{S}(\text{NMe}_2)_3][\mathbf{1}]$ obtained from $\text{K}[\mathbf{1}]$ and $[\text{S}(\text{NMe}_2)_3][\text{SiF}_2\text{Me}_3]$. This borate anion can be easily protonated with KHF_2 to afford *o*-(dimesitylboryl)-trifluoroacetanilide (**2**) (Figure 1). The presence of an uncoor-

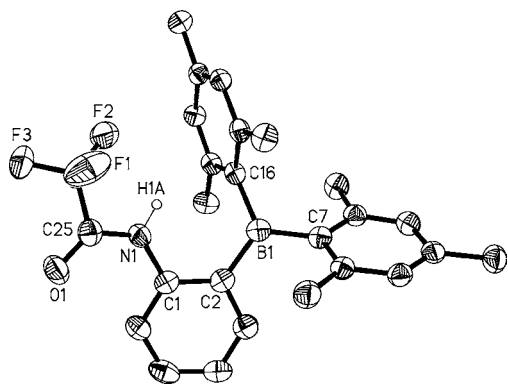


Figure 1. Ortep view of **2** (right) (50% ellipsoids). H-atoms, except H(1A), are omitted for clarity.

ordinated trigonal planar boron center is confirmed by detection of a ^{11}B NMR signal at 74 ppm. Other spectroscopic features include: an ^{19}F NMR signal at -77 ppm corresponding to the trifluoromethyl group and a broad ^1H NMR signal at 8.79 ppm corresponding to the proton trifluoroacetamide functionality. The structure of this compound was also studied by single-crystal X-ray diffraction (Figure 1). The boron atom in **2** adopts a trigonal planar geometry ($\Sigma_{\text{C-B-C}} = 359.9^\circ$). The absence of a boron–oxygen bond indicates that the carbonyl group of the trifluoroacetamide functionality is not sufficiently basic to neutralize the Lewis acidic boron center.

To probe the Lewis acidic properties of this compound, we studied its interaction with neutral bases. We first noted that the ^{11}B NMR chemical shift of **2** is very sensitive to the solvent. In CDCl_3 , the resonance is detected at 74 ppm, indicating that the boron center remains three coordinate. In DMF, however, the ^{11}B NMR resonance of **2** undergoes a high-frequency shift and appears at 11 ppm which is close to that of $[\mathbf{1}]^-$. Although it can be argued that this observed high-frequency shift results from coordination of the carbonyl functionality of the DMF molecule to the boron center, the formation of a hydrogen-bonded complex between **2** and DMF appears to be at the origin of this observation. Indeed, slow crystallization of **2** from DMF leads to formation of the hydrogen-bonded complex **2**-DMF (Figure 2). The $\text{N}(1)\cdots\text{O}(2)$ distance of 2.730(4) Å confirms the presence of a hydrogen bond between these two atoms. Formation of this hydrogen bond is accompanied by coordination of the oxygen atom to the boron center. The resulting $\text{B}(1)\text{--}\text{O}(1)$ bond of 1.650(5) Å is distinctly longer than that observed in $[\text{S}(\text{NMe}_2)_3][\mathbf{1}]$ (1.576(5) Å). It is also longer than the boron–oxygen bond observed in related derivatives such as

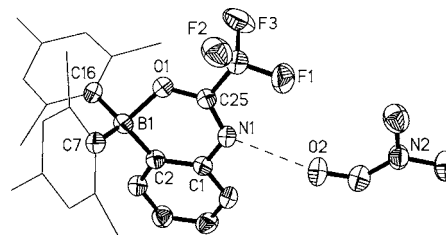


Figure 2. ORTEP view of **2**-DMF (50% ellipsoids). H-atoms are omitted for clarity. The mesityl substituents are drawn as thin lines for clarity.

1,1-difluoro-3-(methylamino)-1*H*-2,4,1-benzoxazaborine 10 (1.520(2) Å) suggesting that it is relatively weak. Despite the weakness of this linkage, coordination of the carbonyl oxygen atom to the boron center most likely polarizes the trifluoroacetamide functionality thus increasing its hydrogen-bond donor ability. Similar arguments have been used to rationalize the affinity of boronate-urea derivatives for carboxylate anions. 11

Compound **2** readily chelates fluoride anions in a variety of solvents. For example, treatment of **2** with $[\text{n-Bu}_4\text{N}][\text{F}]$ in acetone leads to formation of $[\text{n-Bu}_4\text{N}][\mathbf{2-F}]$ (Figure 3).

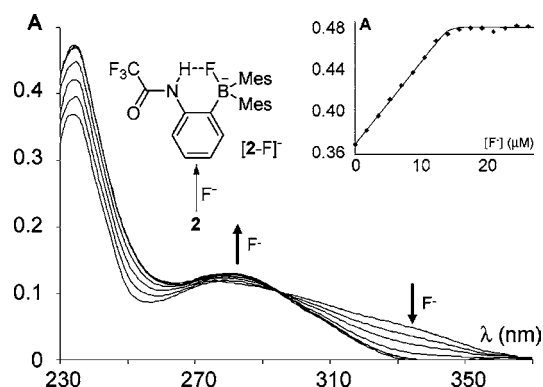


Figure 3. Spectral change accompanying the formation of $[\mathbf{2-F}]^-$ upon addition of nBu_4NF to a THF solution of **2** (1.43×10^{-5} M). The inset shows the absorbance at 236 nm as a function of $[\text{F}^-]$ (\blacklozenge). The thin line corresponds to the binding isotherm calculated with $K = 10^8 \text{ M}^{-1}$.

The ^{11}B NMR signal of $[\mathbf{2-F}]^-$ appears at 3 ppm as expected for a tetrahedral boron atom. The ^{19}F NMR spectrum features a characteristic broad signal at -164.4 ppm whose width and chemical shift is comparable to those observed in other triarylflyborates. 4c,8,9,12 Remarkably, the amide proton is coupled to the bridging fluoride and gives rise to a doublet

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($^1J_{\text{H-F}} = 36$ Hz) at 11.43 ppm indicating the presence of a $\text{NH}\cdots\text{F}$ hydrogen bond. This situation is reminiscent of that observed in the zwitterionic ammonium fluoroborate $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}\{\eta^5\text{-C}_5\text{H}_3(\text{BF}_3)(\text{CH}_2\text{NMe}_2\text{H})\}]$ which features a weak $\text{NH}\cdots\text{FB}$ hydrogen bond.¹³ To confirm our assignment, we carried out a heteronuclear decoupling NMR experiment and observed that the amide proton signal collapses to a singlet upon irradiation of the ^{19}F resonance of $[\mathbf{2}\text{-F}]^-$ at -164.4 ppm. $^1\text{H}\text{-}^{19}\text{F}$ coupling in fluoride complexes of hydrogen-bond donor receptors is not unprecedented and has been observed in complexes involving indole- or amide-based receptors¹⁴ among others.

Incremental addition of fluoride to a solution of **2** in THF leads to an increase in the intensity of the broad absorption bands below 296 nm and quenching of the broad absorption feature spanning the 300–350 nm range (Figure 3). This observation suggests that the spectral changes accompanying fluoride addition reflect the formation of $[\mathbf{2}\text{-F}]^-$. To get a more quantitative measure of the thermodynamic stability of $[\mathbf{2}\text{-F}]^-$, we monitored the absorbance at 236 nm and found that it reaches a plateau after addition of exactly one equivalent of fluoride. These observations reflect the formation of a 1:1 complex whose stability constant K is at least equal to 10^7 M^{-1} in THF (Figure 3) and exceeds that reported for Mes_3B ($3.3(0.4) \times 10^5\text{ M}^{-1}$).⁸ Although the inductive electron-withdrawing properties of the trifluoroacetamide functionality may be invoked, we propose that the high fluoride affinity of **2** results from the cooperativity of the Lewis acidic borane and the hydrogen-bond donor trifluoroacetamide functionality. To support this hypothesis, we have computed the gas-phase fluoride affinity of **2** and compared it to that of Mes_2BPh that does contain a hydrogen-bond donor.¹⁵ The fluoride ion affinity of **2** (75.15 kcal/mol) exceeds that of Mes_2BPh (61.53 kcal/mol) thus corroborating

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the conclusions of the solution binding studies. As part of these calculations, we also optimized the geometry of $[\mathbf{2}\text{-F}]^-$ and $[\text{Mes}_2\text{BPhF}]^-$. The computed structure of $[\mathbf{2}\text{-F}]^-$ (Figure 4) shows a $\text{NH}\cdots\text{FB}$ hydrogen bond of 1.72 Å which is much

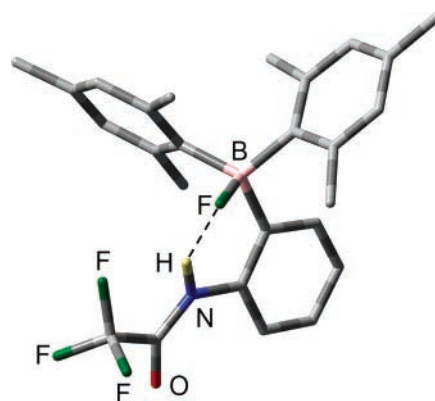


Figure 4. Tube representation of the optimized geometry of $[\mathbf{2}\text{-F}]^-$. H-atoms, except NH , are omitted for clarity.

shorter than that measured in $[(\eta^5\text{-C}_5\text{H}_5)\text{Fe}\{\eta^5\text{-C}_5\text{H}_3(\text{BF}_3)(\text{CH}_2\text{NMe}_2\text{H})\}]$.¹³ The presence of this short hydrogen bond, which also results in a lengthening of the B–F bond (1.52 Å in $[\mathbf{2}\text{-F}]^-$ vs 1.49 Å in $[\text{Mes}_2\text{BPhF}]^-$), is most likely responsible for the high fluoride binding constant displayed by **2**.

We are currently evaluating the use of **2** for fluoride complexation in partially aqueous environments.

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Supporting Information Available: Experimental procedures, analytical data, computational details, and X-ray structure data in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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