A BODIPY boronium cation for the sensing of fluoride ions†‡

Todd W. Hudnall and François P. Gabbaï*

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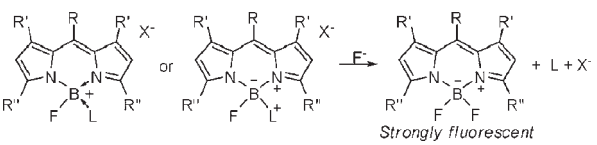
In the presence of iodide ions, the cationic *p*-dimethylaminopyridine adduct of 1,3,5,7,8-pentamethylpyrromethene-boron fluoride [1–DMAP]$^+$ reacts with fluoride ions to afford the corresponding brightly fluorescent difluoride 1–F.

The recognition of fluoride anions is attracting a great deal of interest because of the importance of this anion in dental heath and its possible toxicity when administered in high doses. Because of their inherent fluorophilicity, organoboron compounds have often been considered for the complexation of F^-.[1,2] For example, both neutral[3] and cationic triarylboranes[4] react with F^- to form the corresponding fluoroborate species. In the case of cationic boranes, the resulting boron–fluorine interaction is strengthened by favourable Coulombic attractions leading to greater binding constants. In most cases, however, F^- binding is associated to a turn-off response both in the absorption and emission spectra of the borane.[3,4] The turn-off rather than turn-on nature of the observed response inherently limits the sensitivity of such sensors. Because of this limitation, boron-based fluoride sensors which give a turn-on response upon F^- binding are now attracting attention.[2,5] As part of our contribution to this area, we have decided to investigate the use of fluorescent dipyrromethene boron (BODIPY) compounds.[6] More specifically, we contemplated a situation in which a BODIPY boronium[7] cation would react with F^- to afford a highly fluorescent difluoride derivative (Scheme 1).

The reaction of 1,3,5,7,8-pentamethylpyrromethene-boron-difluoride[8] (**1**–F) with trimethylsilyltriflate (TMSOTf) was monitored by ^{1}H NMR spectroscopy in $CDCl_3$ which allowed for the detection of **1**–OTf as the main product of the reaction

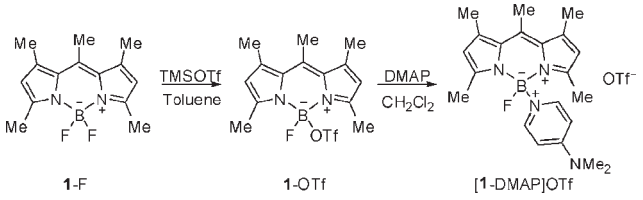


Scheme 1 Conceptual scheme describing the proposed approach (L = neutral ligand; X^- = anion; R, R′ and R″ = hydrocarbon groups). A conventional resonance formula is also provided for the starting boronium cation.

Department of Chemistry, Texas A&M University, College Station, Texas 77843, USA. E-mail: francois@tamu.edu; Fax: +1 979 845 4719; Tel: +1 979 862 2070

† This paper is dedicated to Prof Seiji Shinkai on the occasion of his 65th birthday.

‡ Electronic supplementary information (ESI) available: Spectroscopic details as well as crystallographic data. CCDC reference numbers 689181, 689182. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b808740g



Scheme 2 Formation of **1**–OTf and [**1**–DMAP]OTf from **1**–F.

(Scheme 2).§ Some of the salient NMR spectroscopic features of **1**–OTf include: a ^{11}B NMR resonance at 0.92 ppm in agreement with the existence of a four coordinate boron atom and a ^{19}F NMR signal at −148.96 (bs) ppm which can be compared to the value of −147.6 ppm (q, $^1J_{FB}$ = 33.8 Hz) measured for **1**–F. Compound **1**–OTf is moisture sensitive and was not isolated in bulk quantities. Single crystals of **1**–OTf could be obtained from toluene at −25 °C.¶ This derivative crystallizes in the monoclinic $P2_1/c$ space group (Fig. 1).¶ The B(1)–F(1) bond length of 1.370(3) Å is shorter than that measured in **1**–F (1.395 Å)[9] suggesting an increase in the positive character of the boron center. In agreement with this view, we note that the B(1)–O(1) bond of 1.568(3) Å is somewhat longer than those observed in other four coordinate boron-triflate species featuring chelating dinitrogen ligands.[10]

This triflate derivative reacts quickly with DMAP to afford the boronium triflate salt [**1**–DMAP]OTf (Scheme 2).[11]§ This salt can also be obtained in 82% yield by the one-pot reaction of **1**–F with TMSOTf and DMAP in toluene.§ When dissolved in chloroform, this salt can be washed with water without decomposing. As a solid, it is air-stable which facilitated its characterization. The ^{1}H NMR spectrum confirms the presence of a single DMAP ligand coordinated to the boron centre. The ^{11}B NMR resonance at 0.91 ppm appears as a doublet as a result of coupling to the fluorine nucleus ($^1J_{B-F}$ = 37 Hz). Likewise, the ^{19}F NMR resonance is split into a quartet because of coupling to the ^{11}B nucleus (I = 3/2).

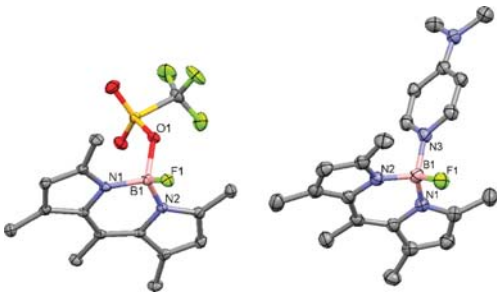


Fig. 1 Crystal structure of **1**–OTf (left) and [**1**–DMAP]$^+$ (right) in [**1**–DMAP]OTf (50% ellipsoid, H-atom omitted for clarity).

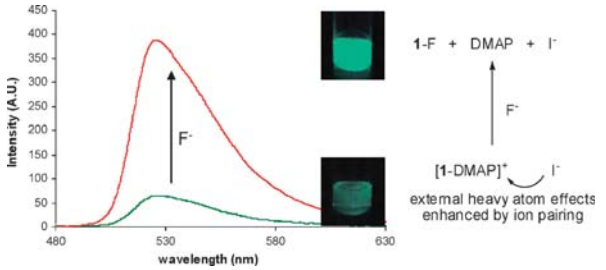


Fig. 2 Left: spectral changes in the emission spectrum of a $CHCl_3$ solution containing [**1**–DMAP]OTf (5.1×10^{-5} M) and TBAI (10 eq.) upon addition of 1 eq. of TBAF. Right: pictures of the solution under a hand held UV lamp before and after fluoride addition.

The observed coupling constant is comparable to that in **1**–F. This salt crystallizes in the monoclinic $P2_1/n$ space group (Fig. 1).¶ The structure of this derivative confirms the presence of a DMAP ligand coordinated to the boron centre. The B(1)–N(3) bond of 1.593(5) Å, which can be compared to that observed in DMAP–BF_3 (1.589 Å),[12] is short thus indicating the tight coordination of the DMAP ligand. The B(1)–F(1) bond length of 1.385(5) Å is somewhat longer than in **1**–OTf indicating a less electron deficient boron centre.

As indicated by ^{1}H NMR spectroscopy, the salt [**1**–DMAP]-OTf reacts with tetrabutylammonium fluoride (TBAF) in $CDCl_3$ to afford **1**–F. No reaction is observed in the presence of Cl^-, Br^- or I^- salts. Since the reaction with F^- is fast and quantitative, we questioned whether it could be used for the development of a fluoride assay. With this in mind, we first studied the fluorescence of [**1**–DMAP]$^+$ in $CHCl_3$ in the presence of I^- ions. Addition of 10 eq. of tetrabutyl-ammonium iodide (TBAI) to a solution of [**1**–DMAP]OTf (5.1×10^{-5} M) in $CHCl_3$ results in a drastic quenching of the fluorescence of [**1**–DMAP]$^+$ (see ESI‡). This quenching most probably results from an external heavy atom effect[13] whose effectiveness is increased by the formation of [**1**–DMAP]$^+$/I^- ion pairs (Scheme 2). Remarkably, when 1 eq. of TBAF is added, the fluorescence intensity increases by a factor f = 500%, giving a response than can be easily detected with the naked eye (Fig. 2). We propose that this increase results from the formation of **1**–F, which as a neutral compound, is not as sensitive as [**1**–DMAP]$^+$ to the external spin orbit coupling effect imparted by I^-. A much weaker response is observed upon addition of 1 eq. of Cl^- (f = 48%) or Br^- (f = 6%) ions which compete with the iodide ions in pairing with the [**1**–DMAP]$^+$ cation.

In conclusion, we describe a novel approach for the fluorescent turn-on sensing of F^- ions. This approach is based on: (i) the use of a BODIPY boronium cation ([**1**–DMAP]$^+$) which is converted into a neutral BODIPY dye (**1**–F) in the presence of F^- ions; (ii) the greater sensitivity of cationic [**1**–DMAP]$^+$ (when compared to neutral (**1**–F) to the external heavy atom effects imparted by I^-.

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Notes and references

§ **1**–OTf: **1**–F (50 mg, 0.191 mmol) was dissolved in $CDCl_3$ (0.5 mL) and treated with TMSOTf (0.069 mL, 0.382 mmol). Formation of **1**–OTf was quantitative by NMR. ^{1}H NMR (399.57 MHz, $CDCl_3$) δ 2.42 (s, 6H, CH_3-dipyrrin), 2.49 (s, 6H, CH_3-dipyrrin), 2.60 (s, 3H, CH_3-dipyrrin), 6.11 (s, 2H, C*H*-dipyrrin). ^{19}F NMR (375.97 MHz, $CDCl_3$) δ −78.05 (s, OTf), −148.96 (bs, B–*F*). ^{11}B NMR (128.20 MHz, $CDCl_3$) δ 0.92 (bs). [**1**–DMAP]OTf: A mixture of **1**–F (100 mg, 0.382 mmol), TMSOTf (0.138 mL, 0.763 mmol) and DMAP (93.1 mg, 0.763 mmol) in toluene (5 mL) was stirred at 80 °C for 12 h. The solvent was then removed *in vacuo* and the residue dissolved in CH_2Cl_2 and washed with distilled water. After drying over $MgSO_4$, reduction of the volume followed by addition of hexanes resulted in the precipitation of an orange solid. This solid was washed with hexanes and dried *in vacuo* to afford [**1**–DMAP]OTf (161 mg, 82% yield). ^{1}H NMR (499.91 MHz, $CDCl_3$) δ 2.12 (s, 6H, CH_3-dipyrrin), 2.47 (s, 6H, CH_3-dipyrrin), 2.73 (s, 3H, CH_3-dipyrrin), 3.19 (s, 6H, N(CH_3)$_2$), 6.07 (s, 2H, C*H*-dipyrrin), 6.86 (d, ^3J = 7.5 Hz, 2H, C*H*-DMAP), 7.89 (d, ^3J = 7.5 Hz, 2H, C*H*-DMAP). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 14.63, 16.86, 17.54, 107.55, 122.98, 132.51, 141.64, 143.98, 153.70, 156.60. ^{19}F NMR (375.99 MHz, $CDCl_3$) δ −78.09 (OTf), −167.71 (q, $^1J_{B-F}$ = 37 Hz). ^{11}B NMR (128.20 MHz, $CDCl_3$) δ 0.91 (d, $^1J_{B-F}$ = 37 Hz). [**1**–DMAP]OTf is hygroscopic and water could not be completely removed for elemental analysis. (Found: C, 49.87; H, 5.13. $C_{22}H_{29}BF_4N_4SO_4$ ([**1**–DMAP]OTf·H_2O) requires C, 49.63; H, 5.49%).

¶ *Crystal data* for **1**–OTf: $C_{15}H_{17}BF_4N_2SO_3$, M_r = 392.18, monoclinic, $P2_1/c$, a = 10.715(4), b = 11.143(4), c = 14.078(5) Å, β = 91.037(7)°, V = 1680.7(10) Å^3, Z = 4, T = 110(2) K, μ = 0.253 mm^{-1}, 10 057 reflections collected, 4022 unique (R_{int} = 0.0842), R_1 = 0.0517 [$I > 2\sigma(I)$], wR_2 = 0.1710 (all data). CCDC 689181. *Crystal data* for [**1**–DMAP]OTf: $C_{22}H_{27}BF_4N_4SO_3$, M_r = 514.35, monoclinic, $P2_1/n$, a = 11.166(2), b = 17.342(3), c = 12.365(2) Å, β = 101.252(4)°, V = 2348.4(8) Å^3, Z = 4, T = 110(2) K, μ = 0.203 mm^{-1}, 10 736 reflections collected, 3684 unique (R_{int} = 0.0317), R_1 = 0.0636 [$I > 2\sigma(I)$], wR_2 = 0.1319 (all data). CCDC 689182. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b808740g

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