A BODIPY-PHENOL-BASED SENSOR FOR SELECTIVELY RECOGNIZING THREE BASIC ANIONS

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ABSTRACT

A novel BODIPY-based anion sensor **1** bearing *di-tert*-butyl phenol unit was designed and prepared. In the presence of three basic anions F⁻, AcO⁻ or H₂PO₄⁻, **1** exhibited two novel partially overlapped red-shift absorption bands at 718 nm and 757 nm, respectively. The formation of allotropic structures, after deprotonation of phenol OH, is responsible for these two emerging bands. Fluorescence quenching was also observed due to intramolecular charge transfer (ICT) from phenolate to BODIPY core. As results revealed, the anion affinity mainly depended on the acidity of binding site OH and the basicity of the target anion. Moreover, two bulky *tert*-butyl groups cannot effectively exclude the approach of large anions to phenol OH, but can facilitate the formation of allotropic resonance structures.

Keywords: BODIPY, phenol, anion sensor, deprotonation, steric effect

1. INTRODUCTION

Currently, the development of optical anion sensors is an active research area of paramount significance in supramolecular chemistry¹⁻⁶. In particular, phenol-based anion chemosensors have garnered considerable attention in the last decades, because phenol OH can act as an anion receptor through hydrogen bonding or deprotonation⁷⁻¹³. These chemosensors are generally chromogenic and/or fluorescent probes, which efficiently change their photophysical properties in the presence of anions. Among numerous fluorophores, BODIPY dyes possess excellent photophysical properties and applications in the areas of anion sensors, metal probes, and pH indicators¹⁴⁻²⁰. This versatile utility is due to the capacity to substitute the many positions of the BODIPY core in Figure 1. Recent reviews have enumerated a number of peripheral BODIPY substituents acting as various sensors based on Photoinduced electron transfer (PET) and intramolecular charge transfer (ICT) mechanisms. In general, C(8)-substituent BODIPY perform a standard green emitting PET fluorophore, while vinyl C(3)-substituent derivatives represent a longer wavelength absorbing and red emitting ICT fluorophore. In previous work, we have reported PET anion sensors **3** and **4** with phenol unit at the C(8)-position of BODIPY core in Figure 1²¹. Where **3** shows the special selectivity for F⁻ through color change and fluorescence quenching, the hindrance of *tert*-butyl groups and the fitness of Brønsted acid-base are responsible for selective F⁻ recognition over other tested anions. To our knowledge, both PET and ICT processes could lead to different optical output^{22,23}. We therefore wonder if phenol unit can be introduced at C(3)-position of BODIPY by a vinyl spacer to acquire an ICT-based anion sensor. In this report, we synthesized two BODIPY-phenol derivatives **1** and **2** according to the route illustrated in Figure 1. The large bulky *tert*-butyl groups were introduced to tune the acidity and the anion affinity of phenolic OH in compound **1**²⁴; reference **2** was prepared for control experiments.

Figure 1. i) The structure of BODIPY derivatives; ii) The synthetic route of compound **1** and **2**.

2. MATERIAL AND METHODS

All anions in the tetrabutylammonium salts were purchased from Alfa Aesar Chemical Co., stored in a desiccator under vacuum, and used without further purification. CH₃CN used in the context was chromatographic pure. Silica gel (mesh 200-300) was used for column chromatography. ¹H NMR and ¹³C NMR spectra were performed on a Varian INOVA 400 MHz spectrometer in CDCl₃. ESI-MS studies were carried out using a Waters Micromass ZQ-4000 spectrometer. UV-vis titration experiments were made on a Perkin Elmer Lambda 35 spectrometer at 298 K. Fluoremetric titrations were recorded on a Perkin Elmer LS55 spectrometer at 298 K. The affinity constant *K* was obtained by non-linear least squares calculation method for data fitting.

3-(3,5-di-tert-butyl-4-hydroxyphenyl)ethenyl-4,4-difluoro-8-(4-bromophenyl)-1,5,7-trimethyl-3a,4a-diaza-4-bora-s-indacene (1)

Compound **5** (1.00 g, 2.19 mmol)²⁵ and 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (0.51 g, 2.19 mmol) were refluxed in a mixture of toluene (70 mL), piperidine (0.5 mL) and glacial acetic acid (0.5 mL). Any water formed was removed by heating in a Dean-Stark apparatus overnight. After completion monitored by TLC, the pink solutions were concentrated to evaporate solvents under reduced pressure. The crude product was purified by column chromatography (CH₂Cl₂/Hexane, 1:1) to obtain purple solid **1**. Yield 45%. ¹H NMR (400 MHz, CDCl₃) δ: 1.35 (s, 18H, 6CH₃), 1.40 (s, 6H, 2CH₃), 2.57 (s, 3H, CH₃), 5.49 (s, 1H, OH), 5.97 (s, 1H, CH), 6.60 (s, 1H, CH), 7.20 (d, *J* = 6.8 Hz, 2H, 2ArH), 7.39 (s, 2H, 2ArH), 7.49 (d, *J* = 16.4 Hz, 2H, Vinyl CH), 7.62 (d, *J* = 6.8 Hz, 2H, 2ArH). ¹³C NMR (100 MHz, CDCl₃) δ: 14.1, 14.6, 30.2, 34.3, 108.2, 116.2, 117.9, 121.0, 124.9, 127.9, 131.2, 132.7, 134.3, 136.3, 137.9, 138.4, 141.4, 142.4, 154.4, 154.5, 155.3. ESI-MS: (*m/z*): 619.1.

3-(4-hydroxyphenyl)ethenyl-4,4-difluoro-8-(4-bromophenyl)-1,5,7-trimethyl-3a,4a-diaza-4-bora-s-indacene (2)

It was synthesized according to above procedure with compound **5** (1.00 g, 2.19 mmol) and 4-hydroxybenzaldehyde (0.27 g, 2.19 mmol). Yield 30 %. ¹H NMR (400 MHz, CDCl₃) δ: 1.41 (s, 3H, CH₃), 1.45 (s, 3H, CH₃), 2.57 (s, 3H, CH₃), 5.19 (s, 1H, OH), 6.00 (s, 1H, CH), 6.58 (s, 1H, CH), 6.82 (d, *J* = 8 Hz, 2H, 2ArH), 7.18 (s, 3H, 2ArH, Vinyl CH), 7.45 (m, 3H, 2ArH, Vinyl CH), 7.63 (d, *J* = 8.4 Hz, 2H, 2ArH). ¹³C NMR (100 MHz, CDCl₃) δ: 14.6, 116.1, 121.1, 127.1, 129.3, 131.8, 141.7, 143.2, 155.3, 156.3. ESI-MS: (*m/z*): 508.9.

3. RESULTS AND DISCUSSION

3.1 Spectroscopic characteristics

Spectroscopic data for sensors **1** and **2** were gathered in Table 1. Both sensors showed a typical narrow absorption band centered at approximately 570 nm having about a 70 nm red shift in relation to the parent BODIPY **5** (λ_{Abs} = 499 nm) in tested solvents. This can be ascribed to the expanded π -system conjugation by the attachment of phenol fragment to BODIPY. Their high molar absorption coefficients indicated that the long-wavelength absorption spectra were ICT (from phenol to BODIPY) bands. Rhodamine B (Φ_f = 0.49) in EtOH was used as a standard to estimate their fluorescence quantum yields Φ_f ²⁶. **1** showed a relatively high Φ_f with respect to **2**, which can be attributed to the large bulky *tert*-butyl groups hindering π - π stacking

of the fluorophore^{27, 28}. Both **1** and **2** displayed a strong emission band at about 590 nm with small Stokes shift. In a short, both sensors exhibited desirable absorption and fluorescence properties without obvious solvent-dependent effect. The introduction of two steric *tert*-butyl groups substantially affected the fluorescence feature of BODIPY derivatives.

Table 1. Spectroscopic properties of compound **1** and **2** in various solvents.

Compound	Solvent	λ_{Abs} (nm)	λ_{em} (nm)	Φ_f	$\varepsilon \times 10^4$ (L·mol ⁻¹ ·cm ⁻¹)
1	CH ₃ CN	571	592	0.658	9.20
	EtOH	576	594	0.568	9.02
	THF	577	593	0.613	10.1
	CH ₂ Cl ₂	578	595	0.733	11.1
	Cyclohexane	577	594	0.668	7.95
2	CH ₃ CN	567	585	0.526	5.21
	EtOH	573	592	0.454	5.28
	THF	574	592	0.490	3.96
	CH ₂ Cl ₂	571	586	0.586	5.15
	Cyclohexane	570	582	0.534	3.76

3.2 UV-vis spectra

The sensing ability of sensor **1** with various anions was investigated in CH₃CN by UV-vis spectroscopy. The titration results of **1** (1.5×10^{-5} mol·L⁻¹) with F⁻ were shown in Figure 2. The absorption spectrum of free **1** displayed a standard absorption band centered at 571 nm, accompanied by a weak shoulder at 540 nm. With the stepwise addition of F⁻, the absorption band at 571 nm decreased and disappeared eventually and two partially overlapped bands emerged at 718 nm and 757 nm ($\Delta\lambda=186$ nm), respectively. Simultaneously the color of solution changed from pink to light green. A clear isosbestic point at 600 nm was observed, indicating the formation of F⁻-sensor complex. Interestingly, the addition of a strong base [Me₄N]OH to the solution of **1** induced similar changes, which revealed that the interaction between **1** and F⁻ was the Brønsted acid-base reaction (deprotonation) in essence. According to the Job plot, sensor **1** interacted with F⁻ in a 1:1 ratio in Figure 2 insert. Consequently, the affinity constant *K* for F⁻ was determined using the method of non-linear least squares calculation²⁹. UV-vis titration experiments of other tested anions were also conducted. In particular, AcO⁻ and H₂PO₄⁻ caused similar changes, while the absorption band at 571 nm would not disappear even upon the excessive addition (Figure S1-S2). Their affinity constants were listed in Table 2 with the order: F⁻ > AcO⁻ > H₂PO₄⁻. Such trend may be mainly attributed to the basic properties of three anions. F⁻ itself is a less strong base than AcO⁻ and H₂PO₄⁻, though two F⁻ can form a great basic complex HF₂⁻ which is second only to OH⁻³⁰. Besides, two *tert*-butyl groups might tentatively prevent the affinity of AcO⁻ and H₂PO₄⁻ to phenol OH in varying degrees. Adding Cl⁻, Br⁻, I⁻, HSO₄⁻ and ClO₄⁻ induced negligible responses in Figure 3, owing to their slight or no basic properties.

Table 2. Affinity constants for compound **1** and **2** with putative anions as determined from UV-vis at 571 nm and 567 nm in CH₃CN, respectively.

Anion	<i>K</i> (1)	<i>K</i> (2)
F ⁻	2.72×10^4	2.17×10^4
AcO ⁻	8.13×10^3	3.42×10^3
H ₂ PO ₄ ⁻	3.79×10^3	1.11×10^3

Interestingly, in our previous work, sensor **3** can selectively recognize F⁻ over AcO⁻ and H₂PO₄⁻ owing to the fitness in the acidity of OH group with strong basic F⁻. To account for such different sensing behaviors, their molecular configurations had to be considered. C(8)-phenol ring and BODIPY plane adopted a perpendicular configuration in **3**, but in **1** both fragments might fix a coplanar arrangement in favor of the p-system conjugation in overall molecule. Furthermore, BODIPY core could serve as an electron-withdrawing group, which increased the acidity of phenolic OH proton in **1**. This acidity enhancement can be also reflected by their chemical shifts of OH proton in ¹H NMR. Under the same experimental condition, the OH proton signal of

1 appeared at 5.49 ppm in the more downfield than that of **3** at 5.37 ppm. On this basis, **1** is relatively more acidic than **3** and undergoes deprotonation in the presence of two less basic anions AcO⁻ and H₂PO₄⁻ except F⁻. Apart from the structural influence, we wonder if the steric hindrance of two *tert*-butyl groups makes substantial contributions to coordinating tested anions. Control experiments were resultantly carried out using compound **2** without *tert*-butyl groups.

Figure 2. UV-vis titration of compound **1** (1.5×10^{-5} mol·L⁻¹) upon the addition of F⁻ ($0 \sim 2.7 \times 10^{-5}$ mol·L⁻¹) in CH₃CN. Insert: A job plot of **1** with F⁻.

Figure 3. UV-vis spectra of compound **1** (1.5×10^{-5} mol·L⁻¹) upon the addition of respective anions (1.6×10^{-4} mol·L⁻¹) in CH₃CN.

As shown in Figure 4, adding F⁻, AcO⁻ or H₂PO₄⁻ to the solution of **2** led to a 133 nm red-shift absorption band at 700 nm. This large red shifts are attributable to the removal of phenol OH proton, which can be also identified by the addition of [Me₄N]OH. Their affinity constants *K* were calculated using UV-vis titrations (Figure S3-S5) and listed in Table 2. Compared with **1**, **2** suggested only one absorption peak and the same order of magnitude in affinity constants yet slight smaller values. First, this new emerging band corresponds to one peak at 718 nm for **1**-anion complex, which results from ICT process from phenolate to BODIPY core. After deprotonation, an increase of the electron density on oxygen would cause delocalization with the electron-withdrawing BODIPY unit. Thus, the electrons are rearranged and the p-electron delocalization extends in the whole molecule leading to an obvious red shift³¹. In the process of delocalization, two electron-rich *tert*-butyl groups would help delocalize and form allotropic **1b** in Figure 5³²⁻³⁴. It can be

speculated that the other novel band at 757 nm can be assigned to the formation **1b**. On the contrary, **2** cannot effectively develop an allotropic structure due to lack of *tert*-butyl groups. Second, the anion binding capacity of **1** and **2** suggests only slight difference, which indicates two *tert*-butyl groups could not reveal the significant steric effect for AcO^- and H_2PO_4^- . Without hindrance, K values of **2** also followed the trend: $\text{F}^- > \text{AcO}^- > \text{H}_2\text{PO}_4^-$, owing to the basic properties of anions³⁰. For special anion, $K(\mathbf{1})$ is a little bigger than $K(\mathbf{2})$ which indicates that the acidity of OH in **1** is slight greater than in **2**. This can be confirmed by the OH proton signal of **1** and **2**, refer to as 5.49 ppm and 5.19 ppm, in ^1H NMR. Namely, interaction of anions with BODIPY-phenol sensors primarily rely on not the hindrance of *tert*-butyl groups, but the acidity of phenol OH and the basicity of anions.

Figure 4. UV-vis spectra of compound **2** ($1.5 \times 10^{-5} \text{ mol} \cdot \text{L}^{-1}$) upon the addition of 10 equiv of respective anions in CH_3CN .

Figure 5. Proposed sensing mechanism of compound **1** with anions.

3.3 Fluorescence spectra

The responses of **1** toward tested anions were also investigated by fluorescence technology in CH_3CN . Just as Figure 6 showed, the fluorescence intensity at 592 nm diminished in pace with the addition of F^- without any obvious changes in the emission wavelength. Similar changes was also observed upon the stepwise addition of AcO^- and H_2PO_4^- (Figure S6 and S7), respectively. Such quenching can be attributable to the occurrence of ICT quenching the excited state of BODIPY moiety by the phenolate salt²². It was found that **1** demonstrated fluorescence quench in varying degrees, which was 97-fold for F^- , 10-fold for AcO^- and 5-fold for H_2PO_4^- in Figure 7. This trend is in agreement with those affinity constants obtained using UV-vis analyses. Besides, compared with **2**, **1** revealed significant quenching for F^- and insufficient quenching for AcO^- and H_2PO_4^- (Figure S8-S10), because of their different acidity of phenol OH and their stability of allotropic structures. Nevertheless there was no significant quenching of both sensors for other anions.

Figure 6. Fluorescence spectra of compound **1** ($1.5 \times 10^{-6} \text{ mol} \cdot \text{L}^{-1}$) upon the addition of F^- ($0-4.8 \times 10^{-6} \text{ mol} \cdot \text{L}^{-1}$) in CH_3CN . Excitation was at 570 nm.

Figure 7. Changes intensity of the emission band at 592 nm in compound **1** ($1.5 \times 10^{-6} \text{ mol} \cdot \text{L}^{-1}$) and at 585 nm in compound **2** ($1.5 \times 10^{-6} \text{ mol} \cdot \text{L}^{-1}$) in presence of 10 equiv of anions tested in CH_3CN .

4. CONCLUSION

In conclusion, an optical anion sensor **1** incorporating *di-tert*-butyl phenol unit at 3-position of BODIPY was successfully prepared, which can selectively recognize three basic anions based on the deprotonation mechanism. Addition of F^- , AcO^- or H_2PO_4^- elicited two novel partially overlapped bands in UV-vis spectra and fluorescence quenching in varying degrees, owing to ICT process from phenolate salt to BODIPY core. These behaviors are closely related to the acidic tendencies of the sensor **1** and to the basic properties of the anion. Although two bulky *tert*-butyl groups could not impede the contiguity of large anions with phenol OH, they can facilitate the formation of allotropic structure after deprotonation. Hence, the acidity of anion binding site should be delicately tuned by introducing multifunctional groups in order to fit the targeted basic anion.

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