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A Benzodithiophene-Based Fluorescence Probe for Rapid Detection of Fluoride Ion

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A novel and simple fluorescence probe was synthesized from benzo[1,2-*b*:4,5-*b*']dithiophene (BDT) and trimethylsilylethyne via Sonogashira reaction, and showed highly selective and sensitive fluorescence decreasing response towards F^-. The probe molecule turned to a weakly fluorescent terminal alkyne moiety because its trimethylsilyl (TMS) group was cleaved by fluoride, which was proved by ^1H NMR titration. Whereas no distinct fluorescent changes were observed with the addition of other anions, such as Cl^-, Br^-, I^-, AcO^- and $H_2PO_4^-$. Upon the addition of F^-, the maximum fluorescence emission wavelength shifted from 460 nm to 450 nm with a decrease of fluorescence intensity by 40% within 20 s. Moreover, the detection limit towards F^- was calculated to be as low as 73.5 nmol/L.

Keywords fluorescent probe, benzodithiophene, fluoride anion, trimethylsilylethynyl group

Introduction

The development of fluorescent probe to sense important ions has received considerable attention as these ions play important roles in many chemical and biological processes.[1-4] In recent years, a number of sensors for anions have been reported,[5-7] and fluoride ion is an important anion in the dental health and the treatment of osteoporosis.[8-10] Fluoride ion is easy to be absorbed by human body but difficult to be excreted. However, too much fluoride can cause acute stomach and kidney problems.[11-12] Therefore, many fluorescent probes have been synthesized to detect fluoride.[13]

So far, the major features of the reported fluoride sensors are based on three kinds of methods and listed as follows: hydrogen bonding,[14-16] Lewis acid-base interaction[17-19] and specific reactivity with silicon.[20,21] Moreover, a new method, which utilizes target anions to induce specific chemical reactions, displays high selectivity when proper fluorophores and reactive groups are introduced into the probes.[22,23] The sensors based on Si—C bond for fluoride ion detection were reported.[24,25] Rao *et al*.[26] reported a Boron-dipyrromethene based specific chemodosimeter to detect F^- and the reaction completed within 5 min duration. Buckland *et al*.[27] reported a chemodosimer based on a core-substituted naphthalene diimide for fluoride, which displayed weak fluorescent intensity and could hardly recognize the color changes under 365 nm UV-lamp.

On the other hand, benzo[1,2-*b*:4,5-*b*']dithiophene (BDT) has often been used as an electron-donating unit. Its large planar π-conjugated structure promotes facile π-π stacking and improves hole mobility.[28] At the same time, the planar and rigid fused aromatic ring of BDT would be helpful to strengthen interactions among polymer chains, which is favourable for charge-transportation.[29] However, the chemosensors based on BDT as core structure have never been reported for F^- detection via the fluoride-triggered cleavage of SiC. In this work, a fluorescent probe (**P1**) with excellent fluorescence quantum yields ($\Phi_F = 0.21$) (See Supporting Information, Table S1) for F^- detection was synthesized, in which BDT derivative was used as fluorophore and trimethylsilylethynyl was used as fluoride chelating moiety. Upon the addition of F^- into **P1** solution, the fluorescence intensity decreased with a 10 nm blue-shift. Meanwhile, the probe displayed high selective sensing, lower detection limit and fast fluorescence response towards F^- within 20 s (See Supporting Information,

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Table S2).

Experimental

Material and instruments

All the reagents were purchased from commercial suppliers and used without further purification. And all solvents and reagents, unless otherwise stated, were CP or AR level. Solvents for chemical synthesis such as THF, triethylamine were purified by dehydration and distillation with standard methods. $Pd(PPh_3)_2Cl_2$ was synthesized according to the reference and stored in dry container. ^1H NMR and ^{13}C NMR in $CDCl_3$ were obtained by a Bruker AV-400 spectrometer with tetramethylsilane (TMS) as an internal standard at room temperature. High resolution mass spectra (HRMS) were obtained by a Waters LCT Premier XE spectrometer. Absorption spectra were measured on a Varian Cary 500 spectrophotometer. Fluorescence spectra were recorded on a Varian Cary Eclipse fluorescence spectrophotometer (1 cm quartz cell).

Synthesis of 2,6-bis(trimethylsilylethynyl)-4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*']dithiophene (P1)

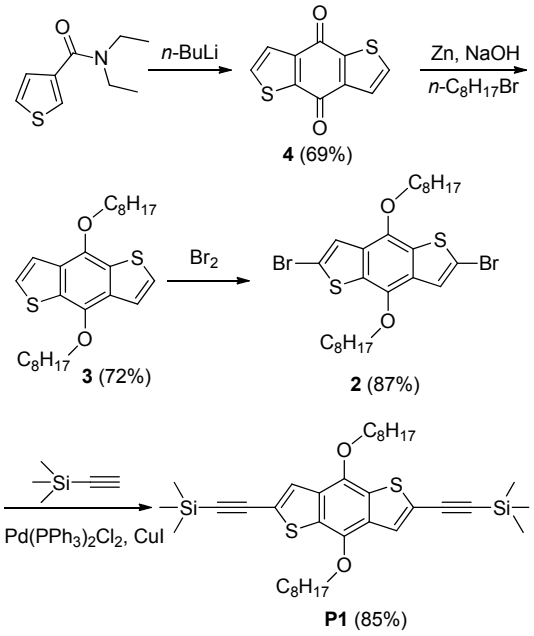
2,6-Di-bromo-4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*']dithiophene (1.2 g, 1.99 mmol) was dissolved into 25 mL THF and 25 mL triethylamine in a 100 mL three-neck flask, and degassed with Ar over 30 min. Then, $Pd(PPh_3)_2Cl_2$ (72.8 mg, 0.10 mmol) and CuI (38.1 mg, 0.20 mmol) were added into the flask under Ar atmosphere. Subsequently, trimethylsilylacetylene (1.56 g, 15.89 mmol) was added dropwise under Ar atmosphere. The mixture was stirred at room temperature for 6 h. After removing solvent, the crude product was purified by column chromatography [*V*(methylene chloride)/*V*(petroleum ether)=1∶15], **P1** (yield 85%) was obtained as yellow solid. m.p. 99−101 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.56 (s, 2H), 4.21 (t, J=6.6 Hz, 4H), 1.87−1.80 (m, 4H), 1.53 (dd, J=9.7, 5.1 Hz, 4H), 1.38−1.29 (m, 16H), 0.90 (s, 6H), 0.28 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.1, 132.0, 130.4, 126.2, 123.1, 101.9, 98.0, 74.4, 32.0, 30.7, 29.6, 29.5, 26.2, 22.9, 14.4, 0.22; HRMS (ESI) *m*/*z*: $[M+H]^+$ calcd for $C_{36}H_{55}O_2S_2Si_2$ 639.3182, found 639.3182.

Results and Discussion

Synthesis

The synthetic route of **P1** was shown in Scheme 1. 4,8-Dihydrobenzo[1,2-*b*:4,5-*b*']dithiophen-4,8-dione (**4**), 4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*'] dithiophene (**3**), and 2,6-dibromo-4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*']dithiophene (**2**) were prepared from the starting material *N*,*N*-diethylthiophene-3-carboxamide according to the literature procedures.[30] Meanwhile, 2,6-bis(trimethylsilylethynyl)-4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*'] dithiophene (**P1**) was prepared by compound **2** and trimethylsilylacetylene via Sonogashira reaction (85% yield). The synthesized target compounds were characterized by ^1H NMR, ^{13}C NMR, and HRMS (See Supporting Information, Figures S1−S9).

Scheme 1 Synthesis of 2,6-bis(trimethylsilylethynyl)-4,8-dioctyloxybenzo[1,2-*b*:4,5-*b*']-dithiophene



Response time for P1

The effect of the reaction time of **P1** towards F^- was evaluated by the fluorescence method. Fluorescence spectra were recorded within 60 s in THF after F^- was introduced to the solution. As shown in Figure 1, it can be seen that there is almost no time-dependent effect in the fluorescence sensing process, and a saturation of fluorescence intensity appeared after 20 s. It is well known that this reaction occurs more rapidly than that of Si−O bond-cleavage processes.[31-35]

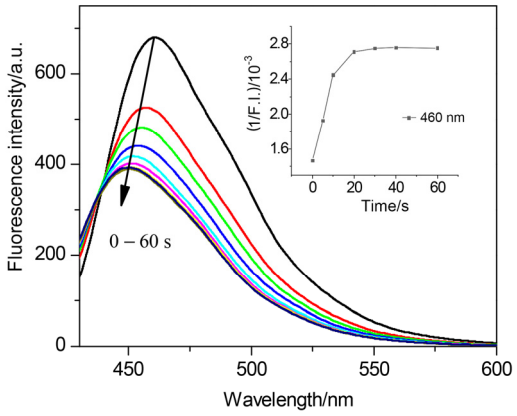
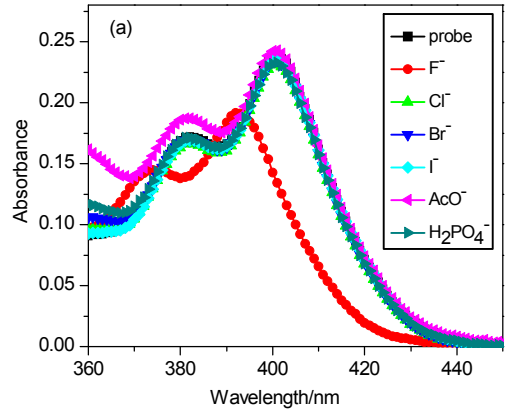


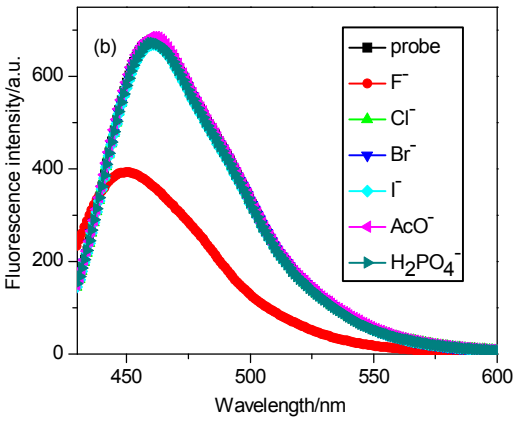
Figure 1 Time-dependent fluorescence spectra of **P1** (1×10^{-5} mol/L) in the presence of 5 equiv. fluoride.

Selectivity study

The selectivity of **P1** towards F^- was fully investi-

gated. Various anions including F^-, Cl^-, Br^-, I^-, AcO^- and $H_2PO_4^-$ were also investigated by UV-vis absorption and fluorescence spectra. As shown in Figure 2a, only upon the addition of F^- (5 equiv.), the absorbance at 401 nm decreased gradually with a blue shift ($\Delta\lambda_{abs}$ = 9 nm), and a new peak at 392 nm appeared. In comparison, only slight changes were observed in the spectra even upon the addition of 10 equiv. of other anions. These results suggest that desilylation of TMS can be caused by fluoride, rather than other anions. Based on a literature survey, it is also clear that the change is due to desilylation of the TMS moieties.[36] And **P1** exhibits strong fluorescence emission at 460 nm in the THF solution (Figure 2b). It was found that only F^- induced an obvious blue shift in the fluorescence maximum from 460 nm to 450 nm, while the other anions (10 equiv. of each) did not cause significant fluorescence spectral changes. The fluorescence color change can be observed under 365 nm UV-lamp (Figure 2c). Furthermore, as shown in Figure 3, competing experiment indicated that the detection could hardly be interfered by other anions (See Supporting Information, Figure S10).





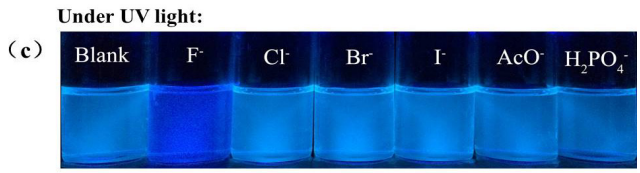


Figure 2 Absorption (a) and fluorescent spectra (b) of **P1** (1×10^{-5} mol/L) in the presence of F^- (5 equiv.), Cl^-, Br^-, I^-, AcO^-, and $H_2PO_4^-$ (10 equiv., respectively). (c) Color changes observed upon the addition of various anions (10 equiv.) to the solutions of **P1** (1×10^{-5} mol/L) under 365 nm UV-lamp.

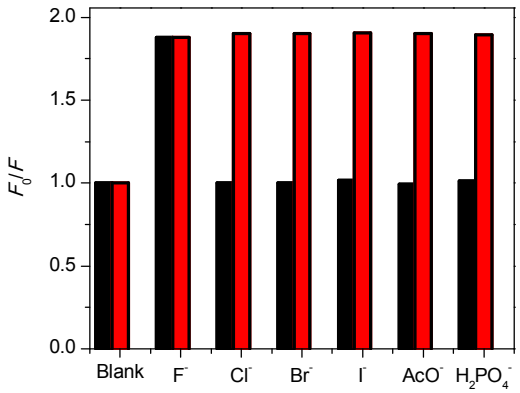


Figure 3 The selectivity of **P1** (1×10^{-5} mol/L). The black bars represent the emission intensity of **P1** in the presence of various anions (10 equiv.). The red bars represent the emission intensity that occurs upon the subsequent addition of F^- (5 equiv.) to the above solution with excitation at 401 nm.

Titration experiment

The absorption and fluorescence titration experiments of **P1** at different F^- concentrations were performed in THF at room temperature (Figure 4). In absorption titration spectra (Figure 4a), the absorption peak of 401 nm faded away with the appearance of new blue-shifted peak of 392 nm. There was a linearity of the absorption ratio (A_{392nm}/A_{401nm}) versus the F^- concentration (See Supporting Information, Figure S11). The results of the fluorescence titrations for **P1** towards various amount of F^- at room temperature are shown in Figure 4b. Upon the addition of F^- to the solution, the fluorescence intensity at 460 nm gradually decreased, and 40% of the fluorescence intensity was quenched. And there was also a good linearity of the fluorescence intensity at 460 nm versus the F^- concentration (See Supporting Information, Figure S12). At the same time, the fluorescence color also changed, which maybe stem from the deprotection of electron-donating TMS group by F^-.[37,38] Moreover, the Si—C and Si—F bond dissociation energies were different (69 and 141 kcal/mol,[1] respectively), it is likely that the Si—C bond was splited and the short wavelength fluorescent product was released with the reaction between compound **1** and F^-, which is responsible for the fluorescence decreasing and blue shifting. In addition, the near-linear correlation curves of **P1** at 460 nm demonstrated the potential utility of **P1** for quantitative determination of F^-. The detection limit of **P1** for F^- was about 73.5 nmol/L (calculated from Figure 5).

^{1}H NMR titration experiment

To further describe the mechanism of detection, the

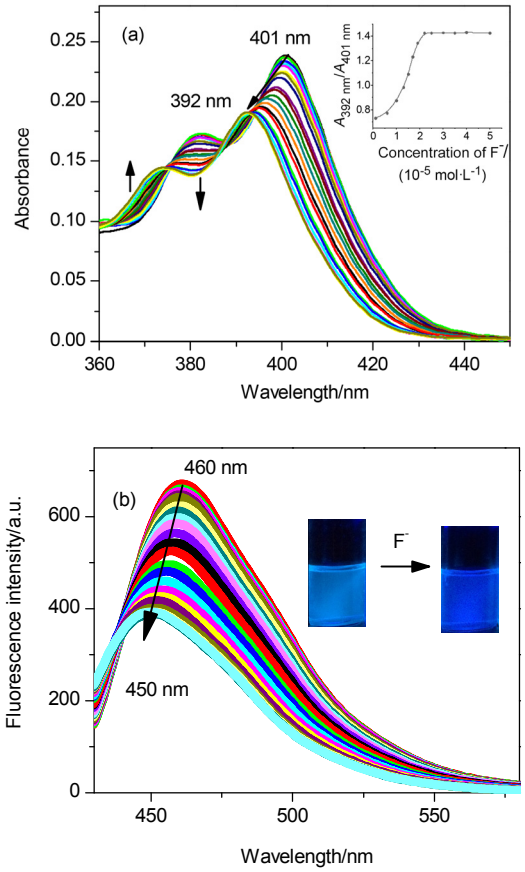


Figure 4 Spectra properties of **P1** (1×10^{-5} mol/L) upon the addition of F^- (0—2 equiv.) in THF: (a) absorption spectra, (b) fluorescence spectra.

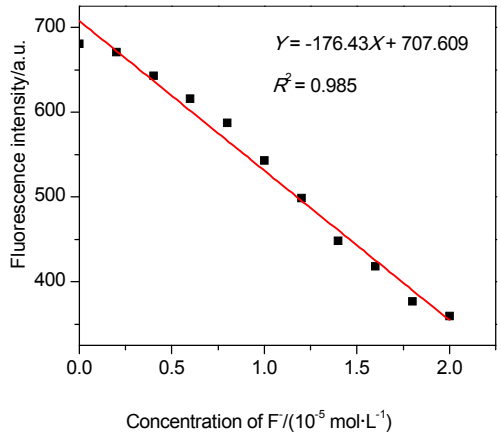


Figure 5 Linear region of fluorescence intensity of **P1** (1×10^{-5} mol/L) in THF upon the addition of F^- (0—2 equiv.) in THF. The fluorescence intensities of five blank measurements for **P1** were 258.012, 258.201, 258.782, 258.946, and 259.143, respectively. σ=0.432302 μmol/L; S=176.43. The detection limit was calculated to be 73.5 nmol/L ($3\sigma/S$).

detection process of **P1** was studied by ^{1}H NMR titration in $CDCl_3$. As shown in Figure 6, it depicts the changes in the chemical shifts of **P1** in the absence and presence of F^-. Upon the addition of 1 equiv. of fluoride ion, a new peak at δ=3.30 appeared, and a saturated height was observed when 2 equiv. of fluoride were added into the solution. This may be due to the formation of terminal acetylene, which was originated from the cleaved reaction of TMS group in the presence of fluoride. In addition, the $SiCH_3$ signal shifted upfield from δ 0.28 to δ 0.0, which suggested that the free TMS moieties were generated. Moreover, no significant changes in the ^{1}H NMR signals or chemical shift were observed for other anions.

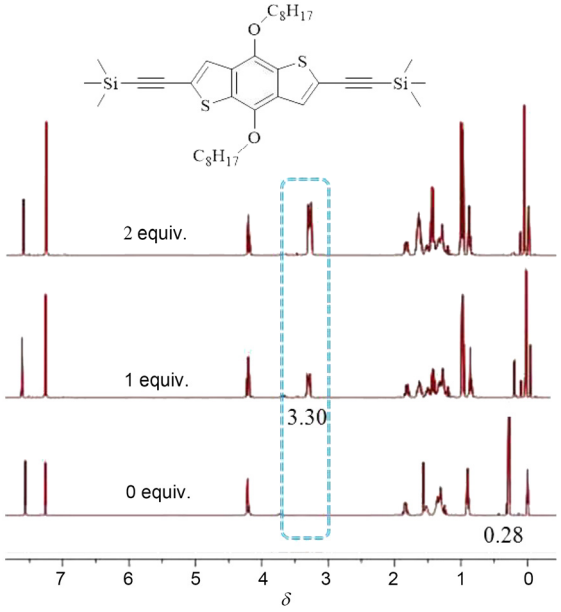


Figure 6 ^{1}H NMR titration spectra of **P1** in $CDCl_3$ in the presence of various equivalents of TBAF.

Conclusions

In summary, a novel and simple fluorescent probe for F^- based on benzodithiophene derivative was synthesized. The fluorescent probe performs high selectivity, short response time and excellent sensitivity toward F^- over other anions (Cl^-, Br^-, I^-, AcO^-, $H_2PO_4^-$) in the THF solution with small Stokes shift and excellent fluorescence quantum yield. Upon the addition of fluoride anions, the color change was observed under 365 nm UV-lamp, which is attributed to the elimination of the TMS substituents through a strong interaction between the fluoride anion and the silicon atoms. All these experimental results indicate that **P1** could be used to detect F^- as an excellent fluorescent probe. In addition, the detection limit is calculated to be as low as 73.5 nmol/L.

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