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Highly selective ratiometric estimation of fluoride ion based on a BINOL imidazolium cyclophane with dual-channel

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ABSTRACT

A novel imidazolium cyclophane S-**1**, which displays a high selectivity for the recognition toward fluoride ion, has been constructed by using BINOL as scaffold. The fluoride ion induced remarkable red shift both in absorption and emission spectra, which might allow S-**1** to be employed as a ratiometric receptor with dual-channel. The chiral recognitions of S-**1** with chiral carboxylates were also examined.

Motivated in part by the essential roles played by anionic species in a range of biological, chemical, medical, and environmental processes, considerable attention continues to be shown in the design and synthesis of anion receptors possessing high affinity and selectivity.[1] In contrast to well-known N–H···anion hydrogen bonding or N^+–H···X^--type hydrogen bonding for anion binding such as that found in amide, pyrrole, urea, ammonium or guanidinium groups, the imidazolium group can interact with anions through $(C–H)^+\cdots X^-$-type ionic hydrogen bonding, therefore the recognition is dominated by charge–charge electrostatic interactions.[2,3] Recently, numerous efforts have been devoted to the imidazolium receptors, including benzene tripodal, cyclophane and caliximidazolium, fluorescent imidazolium, ferrocenyl imidazolium, cavitand and calixarene, and polymeric imidazolium systems.[4,5] Among these systems, imidazolium cyclophanes were found to show a high degree of structural rigidity, and therefore the ability to form unusually strained structures. The various binding pockets might provide different binding properties toward anions, or might encapsulate and stabilize a large number of guest molecules through non-covalent interactions.[6–8]

We have recently reported the imidazolium-functionalized BINOL as a multifunctional receptor for chromogenic and chiral anion recognition.[9] As an extension of this approach, we herein synthesized BINOL-based cyclophane containing imidazolium and OH moieties as binding sites, and compared the anion recognition properties between imidazolium cyclophane S-**1** and its acyclic analogue S-**2** (Fig. 1). The receptor S-**1** also exhibited moderate selectivity for L-Boc-phenylalanine over (D)-isomer. We chose S-**1** in our anion recognition studies for the following reasons: (1) S-**1** contains acidic tetrahydroxyl and two imidazolium groups, which are good hydrogen bond donors and acceptors. The additional charge–charge electrostatic interactions can improve the binding abilities of S-**1** with the anions; (2) the rigid structure of S-**1** may provide high selectivity for the anions due to a defined cavity; (3) the binding abilities between imidazolium cyclophane and more basic anions (such as fluoride ion) can be greatly enhanced by acidic phenolic OH. The anion complexing properties of S-**1** and S-**2** have been investigated by UV–vis, fluorescence, and ^{1}H NMR spectroscopy.

The syntheses of S-**1** and S-**2** have been achieved in moderate yields (35% for S-**1**, and 55% for S-**2**; Scheme S1-2, Supplementary data).[10,11] Both the ^{1}H NMR and ^{13}C NMR spectra of S-**1** gave two signals for the diastereotopic methylene protons. The dimer of S-**1** was also confirmed by ESI-MS and HRMS (Supplementary data).

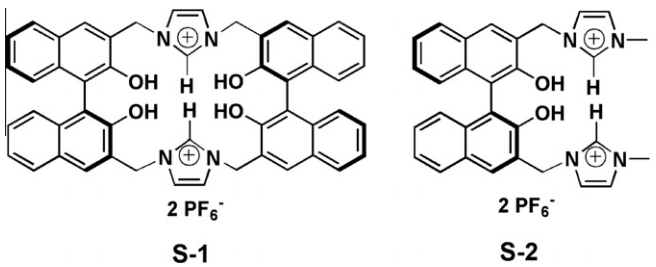

Figure 1. Imidazolium cyclophane S-**1** and its acyclic analogue S-**2**.

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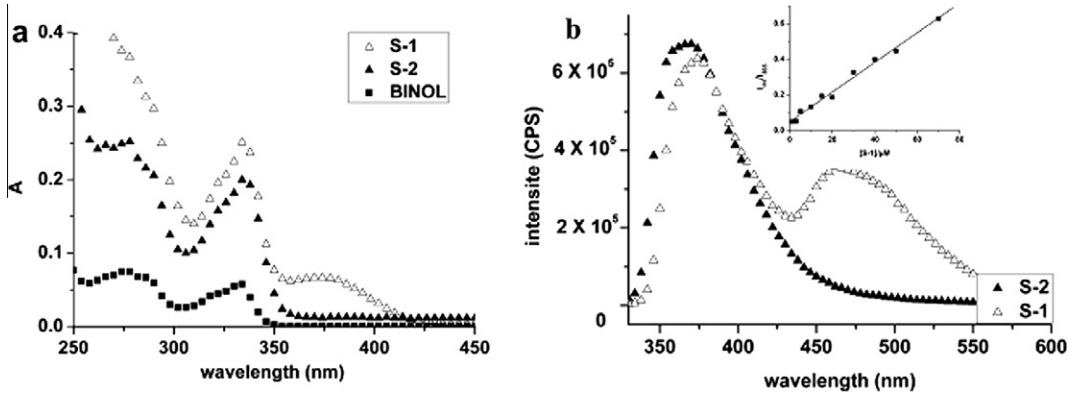


Figure 2. (a) Absorption spectra of S-**1**, S-**2**, and BINOL (2×10^{-5} M). (b) Emission spectra of S-**1** and S-**2** (5×10^{-5} M), λ_{ex} = 290 nm. The inset of (b) shows the emission spectra responses (I_{465}/I_{370}) of S-**1** in CH_3CN at different concentrations: 0–7 $\times 10^{-5}$ M.

The optical properties of S-**1** and S-**2** in acetonitrile are shown in Figure 2. Firstly, the UV spectra of S-**1** (λ_{abs} 336 nm, ε = 12100) and S-**2** (λ_{abs} 336 nm, ε = 10700) were compared with S-BINOL in acetonitrile (Fig. 2a). Although cyclophane S-**1** showed similar absorption spectrum to BINOL and S-**2** in acetonitrile, a dual emission consisting of a structured band with a λ_{max} value of 370 nm and a broad band centered at 465 nm could be found for S-**1** (Fig. 2b). The concentration had little effect on the peak positions and the shapes of absorption spectra (Fig. S1), but a large concentration dependence ratio (I_{465}/I_{370}) was observed for the fluorescence spectrum of cyclophane S-**1** (inset of Fig. 2b). These observations suggest that the long wavelength emission (465 nm) was formed due to the excimer emission of S-**1** between an excited molecule and another molecule at ground state.[12] In contrast, S-**2** showed only a monomer emission at 370 nm.

In CH_3CN–DMSO (9:1, v/v), a solution of S-**1** (20 μM) was treated with tetrabutylammonium (TBA) fluoride as the representative anion. The absorbance at 336 nm underwent gradual decrease in its intensity with concomitant increase at 378 nm with isobestic point at 340 nm (Fig. 3a). The presence of a clear isobestic point might suggest that only one new species was formed during the titration process. The 1:1 stoichiometry for host–guest system was further confirmed by job plots (Fig. S3).[13] Similar detectable changes could also be seen in the S-**1** solution with acetate (5 equiv, as TBA salt, Fig. S4). The other anions such as Cl^-, Br^-, I^-, HSO_4^- (300 equiv, as TBA salts), and $H_2PO_4^-$ (10 equiv, as TBA salt) caused no significant change in the absorption spectra of S-**1** (Fig. S5). Compared to S-**1**, S-**2** showed similar UV–vis spectral changes (Fig. S6).

In the emission spectrum, on the addition of TBA fluoride, a steady and significant decrease in the fluorescence intensity of the monomer at 370 nm was observed, whereas the excimer emission was turned on. After addition of 5 equiv of TBA fluoride, we observed a marked increase in the I_{485}/I_{370} ratio and a bathochromic shift of 20 nm. As a result, the excimer of S-**1** exhibited enhanced emission with a maximum at 485 nm (Fig. 3b). Moreover, when S-**1** was excited at 365 nm in the presence of a fluoride ion, a bright fluorescent response was also observed (insets of Fig. 3b). By contrast, we observed negligible changes in the longest wavelength emission of acyclic compound S-**2** upon addition of TBA fluoride (Fig. S12). We speculated that it is easier for the rigid macrocycle S-**1** to achieve a stronger intermolecular interaction

Table 1
Binding constants of S-**1** and S-**2** determined by fluorescent method

Anion[b]	K_a[a] (M^{-1})	
	S-**1**	S-**2**
F^-	~2.57×10^6	2.62×10^5
Cl^-	341	6.23×10^3
Br^-	180	933
I^-	75	154
HSO_4^-	1.06×10^3	1.35×10^3
$H_2PO_4^-$	1.35×10^4	8.65×10^3
AcO^-	2.79×10^5	1.36×10^5

[a] Error <10%.
[b] As tetrabutylammonium salts.

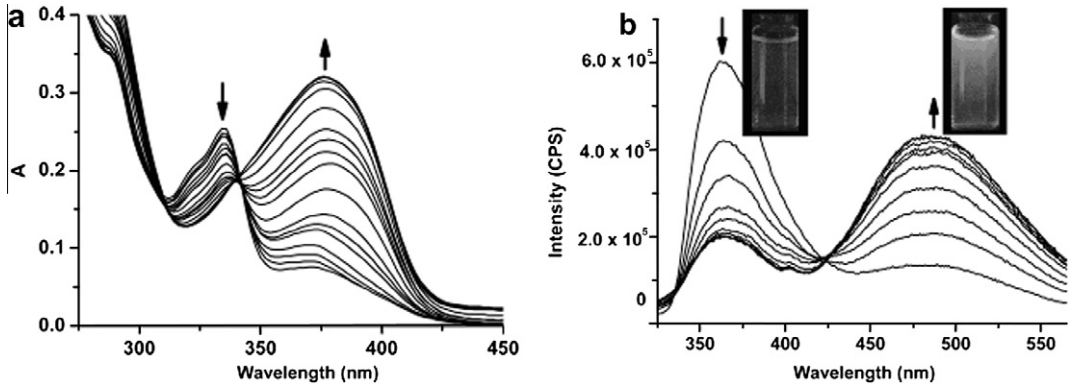


Figure 3. Effect of incremental addition of TBA fluoride on: (a) UV–vis spectrum of S-**1** (2×10^{-5} M) in CH_3CN–DMSO (9:1, v/v); (b) emission spectrum of S-**1** (5×10^{-6} M) in CH_3CN (λ_{ex} = 290 nm).

because it may be less solvated than the flexible acyclic compound S-**2**.[12]

The changes in the fluorescent spectra allowed us to calculate the values of the binding constants (as 1:1 host/guest model, Figs. S8–S17, Table 1) and a detection limit of 0.4 μM.[13] In order to further investigate the effective applications of the S-**1**, we examined the ratiometric response of S-**1** toward F^- in the presence of other potentially competing species (Cl^-, Br^-, I^-). Results showed that most of the other species only displayed minimum interference in the detection of F^-, which further supported the selective sensing of F^- even under competition from other related halide ions (Fig. S18). The high selectivity for F^- indicates that the preorganized rigid binding pocket and the acidic hydroxyls might play an important role in the binding with anions.

Importantly, the ratio (S-**1**) of absorption intensities at 336 and 378 nm (A_{378}/A_{336}) displayed a continual increase from 0.29 to 1.75, and the ratios against the concentration of fluoride ion showed a straight line that attained a plateau after addition of 5 equiv of TBA fluoride (Fig. S7). On the other hand, the ratio of emission intensities (I_{485}/I_{370}) showed similar incremental trend against the increase of [F^-] (Fig. S7). Consequently, S-**1** could be used for ratiometric estimation of fluoride ion based on the dual-channel (absorption and emission spectra).

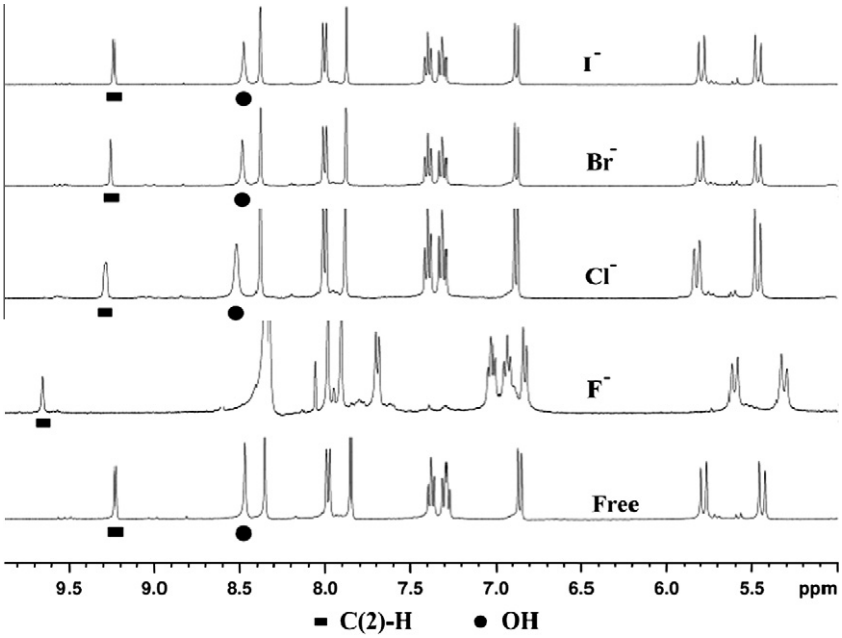
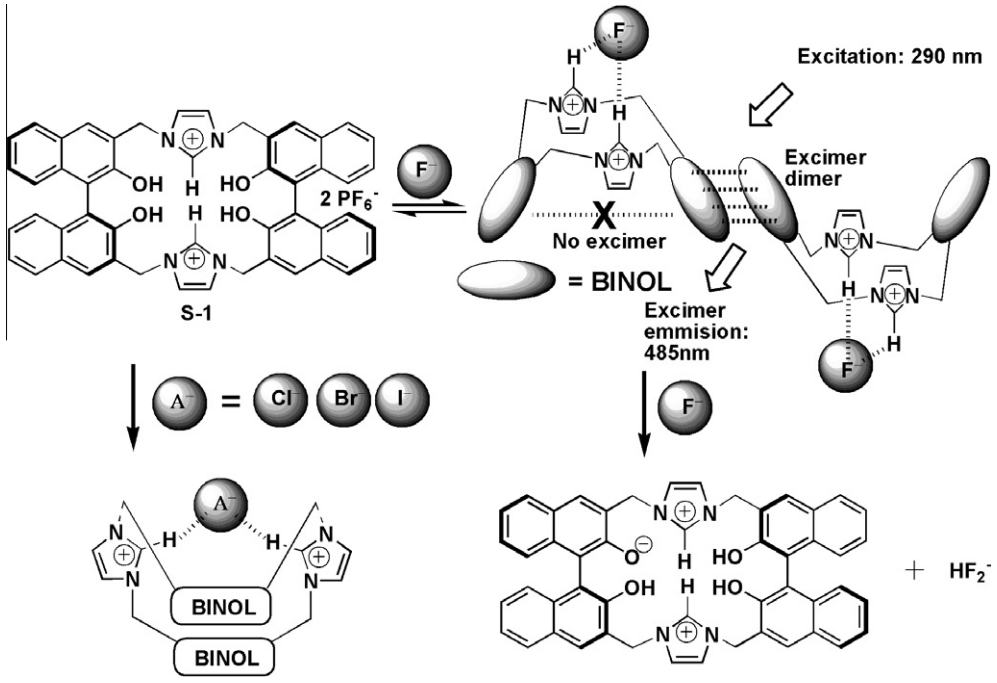


Figure 4. Partial ^1H NMR (400 MHz) spectra of S-**1** (5 mM) in the presence of anions (5 equiv) in DMSO-d_6.



Scheme 1. Two strategies for halide ion recognition by S-**1**.

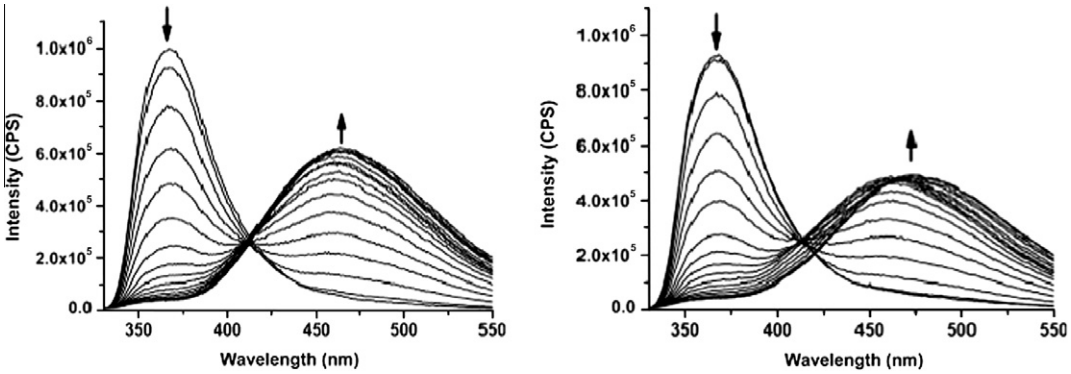


Figure 5. Fluorescent titrations of S-**1** (5×10^{-5} M) with tetrabutylammonium salts of *t*-Boc-L-phenylalaine (left) and *t*-Boc-D-phenylalaine (right) in CH_3CN.

In order to pinpoint the anion receptor sites and to fully explore the interaction modes between the anions and probe molecules, the ^{1}H NMR titration experiments in DMSO-d_6 solution were carried out. A series of anions such as F^-, Cl^-, Br^-, I^-, HSO_4^-, $H_2PO_4^-$ and AcO^- (as TBA salts) were treated with S-**1** as shown in Figure 4 (Fig. S23a for all anions). The most obvious spectral changes were observed by the treatment of F^- (Fig. S24). The hydroxyl peak at δ 8.42 ppm became broad, and the imidazolium C(2)–H moved to downfield position (from δ 9.17 to 9.65 ppm) with concomitant upfield shifts of several aromatic peaks between δ 6.5 and 8.5 ppm upon the addition of F^- up to 5 equiv, a typical phenomenon for hydrogen bonding interaction with incoming F–.[14] Moreover, an obvious triplet peak at δ 16.1 was found when excess Fwas added, indicating the most acidic hydroxyl O–H to form the HF_2^- anion.[15] Similar spectra changes were observed when S-**1** was treated with AcO^-. However, no noticeable changes were observed with Cl^-, Br^-, I^-, HSO_4^-, and $H_2PO_4^-$. When F^- was treated with S-**2** (Fig. S23b), the imidazolium C(2)–H showed similar downfield trend against the addition of F^- compared with S-**1**, however, S-**2** displayed a much smaller downfield shift (from δ 9.21 to 9.29 ppm), which supports the fluorescent data. The overall process can be expressed in Scheme 1. Several similar [2+2] type supramolecular complexes have also been reported.[14,16,17]

Host S-**1** was then examined for chiral recognition with various amino acid derivatives.[18] From the fluorescent titrations of S-**1** (Figs. S19–S22), the association constants for the tetrabutylammonium salts of *t*-Boc-L-phenylalanine and of *t*-Boc-D-phenylalanine (Fig. 5) were calculated to be 64,200 and 43,000 M^{-1} (errors <10%), respectively (Table S1). Although only a moderate selectivity (1.5 times) was observed, we noticed that the fluorescence spectra show a distinct change at long wavelength. Upon the addition of the D-Boc-Phe, the intensity of the excimer band at 460 nm continual, increased with the concomitant remarkable red shift, about 15 nm, but there was no bathochromic shift induced by (L)-isomer. The moderate enantioselectivity of S-**1** for the amino acid derivatives was also clearly supported by ^{1}H NMR titration experiments in DMSO-d_6 (Fig. S25). The different downfield shifts of the imidazolium C(2)–H peak are summarized in Table S2.

In conclusion, imidazolium cyclophane S-**1**, which provides a preorganized rigid binding pocket for anions, has been developed as a novel fluorescent probe for ratiometric estimation of the fluoride ion. Importantly, upon introduction of the fluoride ion, the probe displayed a remarkable red shift (120 nm) in emission due to the formed intermolecular excimer. This dual fluorescence band might allow S-**1** to be employed for quantitativedetection of the fluoride ion. Furthermore, the two axially chiral binaphthyl units of the imidazolium cyclophane might provide a good asymmetric environment, the receptor S-**1** also exhibited moderate enantioselectivity for L-Boc-phenylalanine over (D)-isomer.

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Supplementary data

Supplementary data (experimental procedures, synthetic and spectroscopic data for various compounds)) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.062.

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11. *Preparation and characterization of dimer [S-**1**]*: to a solution of *S*-3,3′-bis(imidazoylmethyl)-2,2′-dimethoxymethoxy-1,1′-dinaphthyl (350 mg, 0.65 mmol) in acetonitrile (200 mL), S-3,3′-bis(bromomethyl)-2,2′-bis(methoxymethyl)-1,1′-dinaphthyl (370 mg, 0.65 mmol) in acetonitrile (100 mL) was added dropwise over a period of 3 h. The reaction mixture was then warmed and maintained at 80 °C for 48 h. After cooling to room temperature, the solvent was evaporated to dryness under reduced pressure. Under nitrogen, the residue was dissolved in methanol (30 mL) to which 6 N HCl (15 mL) was added. After the mixture was stirred at room temperature for 24 h, the solvent was removed under reduced pressure. Acetone (30 mL) was added to the residue, after stirring for 20 min at room temperature, KPF_6 (368 mg, 2 mmol) was added to the reaction mixture. After another 36 h stirring at room temperature, the solvent was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel eluting with CH_2Cl_2/CH_3OH to give S-**1** (238 mg, 35%) as a pale yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 2H), 8.42 (s, 2H), 8.30 (s, 2H), 7.92 (d, 2H, J = 8.4 Hz), 7.80 (s, 2H), 7.33 (t, 2H, J = 14.8 Hz), 7.24 (t, 2H, J = 14.8 Hz), 6.80 (d, 2H, J = 8.4 Hz), 5.71 (d, 2H, J = 13.6 Hz), 5.37 (d, 2H, J = 13.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.9, 137.0, 135.0, 133.2, 129.0, 128.5, 127.6, 124.5, 123.9, 123.7, 122.9, 114.4, 49.8, 49.0; ESI-MS: *m/z* 757.3 $[M-2PF_6^- - H]^+$ (calcd 757.3); HRMS calcd for $C_{50}H_{37}N_4O_4$ $[M-2PF_6^- - H]^+$ 757.2804, found 757.2803.

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