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Colorimetric and ratiometric fluorescence sensing of fluoride ions based on competitive intra- and intermolecular proton transfer

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Abstract—Receptors **1** and **4** show fluoride ion selective changes in their absorbance and emission behaviours amongst F^-, Cl^-, Br^-, I^-, NO_3^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$ and ClO_4^- anions. Fluoride ion mediated 'ON–OFF–ON' switching behaviour of **4** provides opportunities for ratiometric estimation of fluoride ions.

The development of optical molecular or polymeric systems capable of sensing various biologically and/or environmentally important anions has generated significant interest in recent years.[1,2] In this context, the detection of fluoride (F^-) is of particular interest as it plays an essential role in a broad range of biological, medical and chemical processes and applications such as dental care,[3] treatment of osteoporosis,[4] fluorination of water supplies,[5] or even in chemical and nuclear warfare agents.[6] Being small and highly electronegative, fluoride has unique chemical properties and can form strong hydrogen bonds with hydrogen-bond donors. Different signalling mechanisms, viz. photo-induced electron transfer (PET),[7] intramolecular charge transfer (ICT),[8] metal-to-ligand charge transfer (MLCT),[9] excited state proton transfer (ESPT),[10] fluorescence resonance energy transfer (FRET),[11] etc. have been used to design anion sensors. The majority of reported fluoride sensors are based on colorimetric changes[12] or fluorescent quenching,[13] few of them experience fluorescence enhancement.[14] There are only a few reports on ratiometric fluorescence[10b,15] where the fluorescent emission wavelength changes on interaction with fluoride ions. Ratiometric fluorescence measurements can increase the selectivity and sensitivity of the detection because the ratio of fluorescence intensities at two wavelengths is independent of the concentration of the sensor.

In the design of anion receptors based on proton transfer mechanisms, the proton transferring ability of the ligand controls the sensitivity and selectivity. In the case of fluorescent molecules with ESPT ability, on addition of anions, the intermolecular proton transfer from ligand to anion may restrict the intramolecular proton transfer mechanism. These two competitive events, if signalled by variation in absorption or emission wavelengths and/or their intensities, would provide highly sensitive systems for anion sensing.

Here we report that 3-(1*H*-benzimidazol-2-yl)naphthalen-2-ol[16] (**1**) and its dimeric derivative 3,3′-bis-(1*H*-benzimidazolyl-2-yl)-[1,1′]binaphthalenyl-2,2′-diol (**4**) show highly fluoride ion selective changes in absorption and emission properties. The fluoride ion based 'ON–OFF–ON' switching in receptor **4** provides highly sensitive and receptor concentration independent ratiometric fluorescence sensing of fluoride anions.

Receptor **1** was synthesized via the reported procedure[16] and new receptor **4** was synthesized[17] (Scheme 1) by 1:2 condensation of 2,2′-dihydroxy-[1,1′]binaphthalenyl-3,3′-dicarboxylic acid (**2**)[18] with 1,2-diaminobenzene (**3**) under N_2 in refluxing ethylene glycol.

In receptors **1** and **4** (10 μM, CH_3CN), the appearance of absorption bands at λ_{max} 282 (ε 26,000), 312 (ε 34,000), 330 (ε 34,000) and 360 (ε 6500) nm (for **1**) and at λ_{max} 283 (ε 50,000), 315 (ε 52,000), 333 (ε 52,000) and 368 (ε 12,000) nm (for **4**) indicates that as expected, the conjugate effects of the two naphthylene units in **4** were not observed but an additive effect on the intensities was apparent. In the case of addition of excess tetrabutylammonium salts of anions (Fig. 1), only the addition of fluoride (1000 μM) led to changes in λ_{max}

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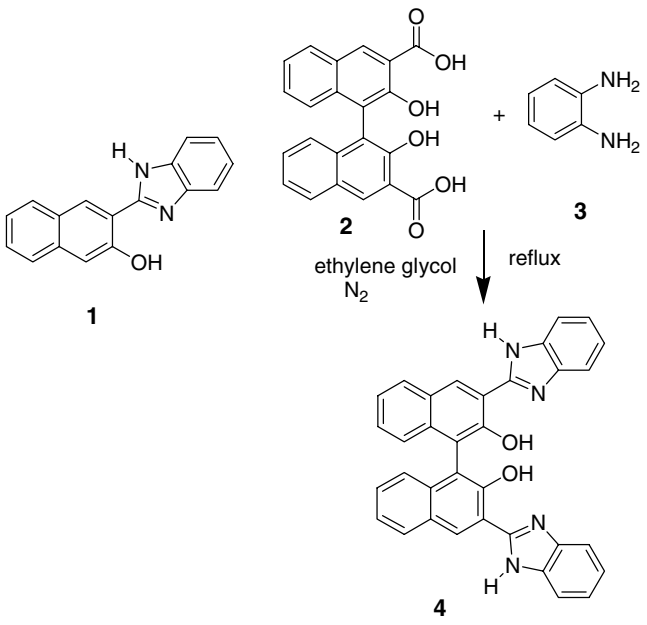


Scheme 1.

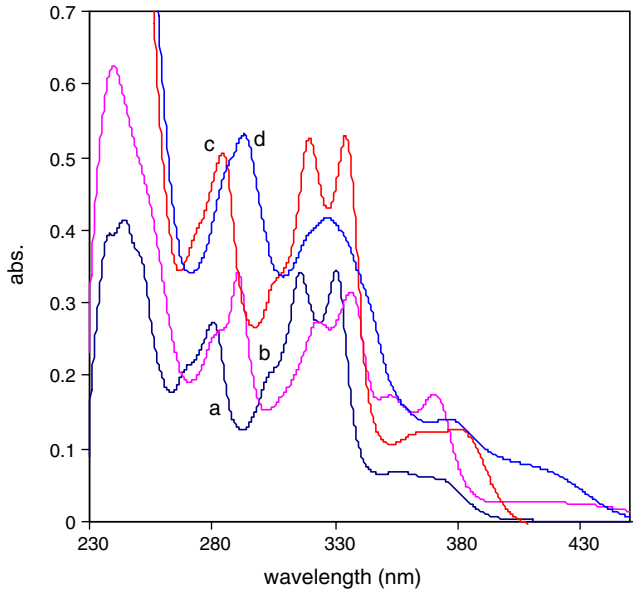


Figure 1. The effect of F^- on the absorption spectra of the receptors in CH_3CN: (a) **1** (10 μM); (b) **1** + F^- (90 μM); (c) **4** (10 μM); and (d) **4** + F^- (90 μM).

and absorption intensities in both receptors, whereas the addition of other anions, viz. Cl^-, Br^-, I^-, NO_3^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$ and ClO_4^- resulted in insignificant changes in the absorption spectra of receptors **1** and **4**. The addition of hydroxide ions (2 equiv) caused changes in the absorption and fluorescence spectra of receptors **1** and **4** similar to those observed with F^- (100 equiv).

On addition of fluoride anions, the appearance of a new absorption band between 400 and 440 nm in the case of **4** (but not in receptor **1**) results in a visible change in colour from colourless to yellow.

A solution of **1** (10 μM) on addition of F^- showed a gradual increase in absorbance at λ_{max} 290, 340 and 370 nm with an increase in the concentration of F^-. Similarly, **4** on addition of F^- showed an increase in absorbance at λ_{max} 292, 346 and 410 nm. The spectral fitting of the absorbance data shows the formation of LF_2 ($\log \beta_{LF_2} = 8.08 \pm 0.06$) in the case of **1**. Significantly, the formation of a 1:1 (LF) complex of **1** was not observed. With receptor **4**, a mixture of LF, LF_2 and LF_3 ($\log \beta_{LF} = 4.44 \pm 0.13$, $\log \beta_{LF_2} = 8.92 \pm 0.08$ and $\log \beta_{LF_3} = 11.96 \pm 0.15$) complexes was formed.

Receptor **1** (1 μM, CH_3CN) on excitation at λ_{max} 330 nm exhibits two emission bands at λ_{max} 375 nm and 575 nm. The longer wavelength emission is typical of intramolecular ESPT emission bands.[16] The solution of **1** (0.25 μM, CH_3CN) on addition of Cl^-, Br^-, I^-, NO_3^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$ and ClO_4^- anions (1000 equiv) showed insignificant changes in fluorescence, but on addition of fluoride, two new emission bands appeared at 425 and 500 nm (Fig. 2). The intensity of these emission bands increased gradually on slow addition of fluoride anions[19] and achieved a plateau above 300 equiv of fluoride. Spectral fitting of these data shows the formation of LF_2 ($\log \beta_{LF_2} = 8.49 \pm 0.02$), which is quite close to that found from absorbance titration data. Therefore, **1** can be used for the estimation of 10–75 μM fluoride ions and other anions do not interfere in its estimation.

Receptor **4** (0.5 μM, CH_3CN) on excitation at λ_{max} 330 nm mainly exhibits a 586 nm emission band and only a weak emission around 380 nm. The solution of **4** (0.5 μM, CH_3CN), on addition of Cl^-, Br^-, I^-, NO_3^-, HSO_4^-, $H_2PO_4^-$ and ClO_4^- anions (1000 equiv), showed only a small decrease (<15%) in fluorescence at 586 nm, but on addition of fluoride, the fluorescence at 586 nm gradually decreased with increasing concentrations of fluoride (up to 20 equiv) along with the appearance of a new blue shifted emission band at 515 nm. The

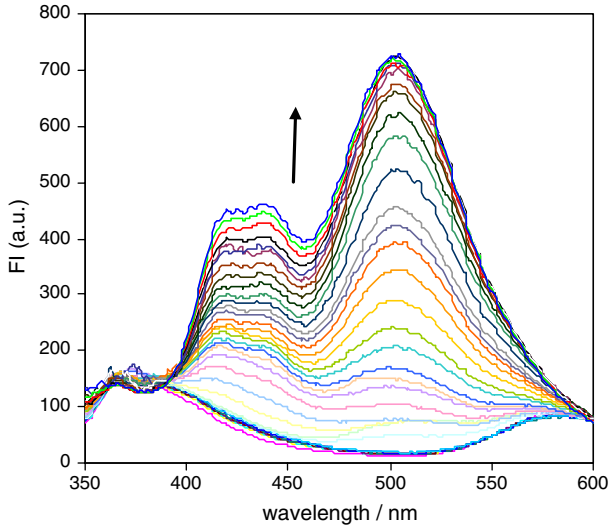


Figure 2. The effect of addition of F^- on the fluorescence spectra of receptor **1** (0.25 μM, CH_3CN).

intensity of the emission band at 515 nm gradually increased[19] with increasing concentration of fluoride (Fig. 3) and went off scale above 100 equiv of fluoride anions. The spectral fitting of the data (see Supplementary data) shows the formation of LF and LF_3 species ($\log \beta_{LF} = 4.54 \pm 0.04$, and $\log \beta_{LF_3} = 12.74 \pm 0.07$). Analysis of the distribution of the different species shows that at 60 equiv of F^-, the highest concentration of LF (48%) along with a small amount (<7%) of LF_3 was formed. On addition of 100 equiv of fluoride anions, both LF (42%) and LF_3 (40%) were nearly equally distributed (Fig. 4).

Significantly, whereas intermolecular ESPT based fluoride and other anion sensors,[10] due to increased electron density on the sensor, show bathochromic shifts of emission bands on interaction with anions; here the inhibition of intramolecular ESPT on addition of fluoride in the cases of receptors **1** and **4** causes hypsochromic shifts.

Hence, in the case of receptor **4**, the emission intensity at 586 nm is gradually 'switched off' upon incremental addition of F^- and simultaneously, the emission intensity at 515 nm is 'switched on'. This situation provides the opportunity for elaborating a ratiometric receptor which permits signal rationing and allows the estimation of analyte independent of the concentration of the receptor. Figure 5a shows a correlation between intensity ratios of emission intensity at 515 nm with those at 586 nm (FI_{515}/FI_{586}) versus fluoride ion concentration. By this approach, 5 μM F^- could be detected when **4** is employed at 0.5 μM. The ratiometric response of different anions is presented in Figure 5b.

The absorbance and emission titration data show that monomeric receptor **1** simultaneously interacts with two fluoride ions to form an LF_2 complex but the dimeric receptor **4** undergoes stepwise complexation to form LF and LF_3 complexes. Such differences in complexation behaviour of **1** and **4** are in agreement with changes in the chemical shifts of the protons in their ^1H NMR spectra, on addition of fluoride. In the ^1H NMR titration of **1**, both the benzim and binaphth signals shift simultaneously and their upfield shift is com-

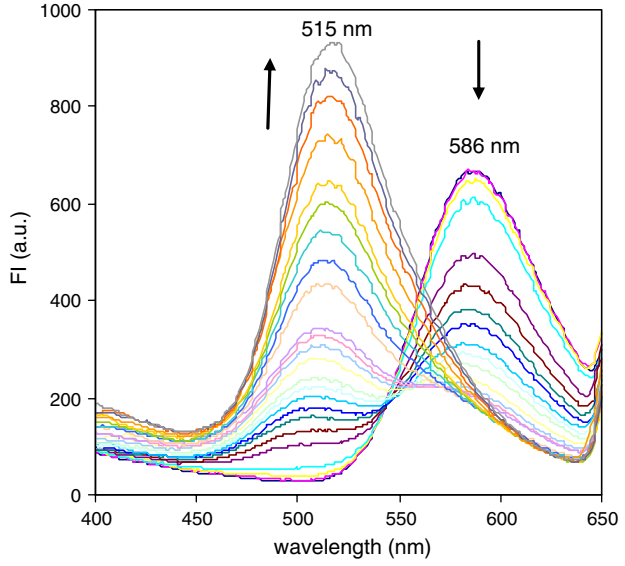


Figure 3. The effect of concentration of F^- on the fluorescence spectrum of receptor **4** (0.5 μM, CH_3CN).

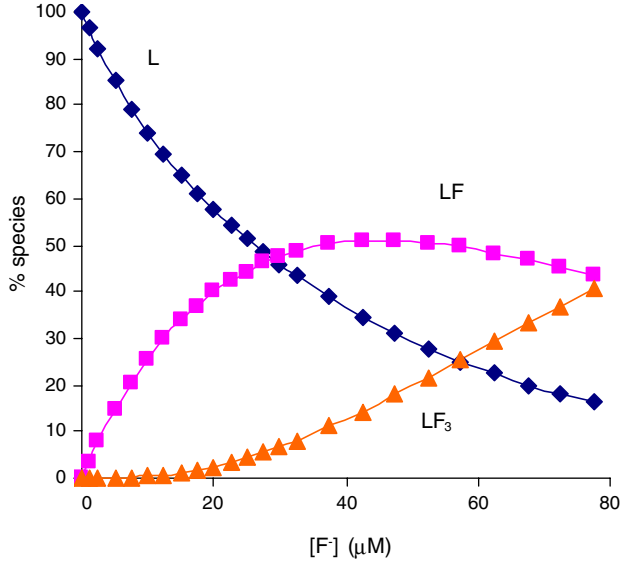


Figure 4. Distribution of various species on addition of F^- to a solution of **4** (0.5 mM, CH_3CN). L is receptor **4** and LF and LF_3 are 1:1 and 1:3 complexes of **4** with F^-.

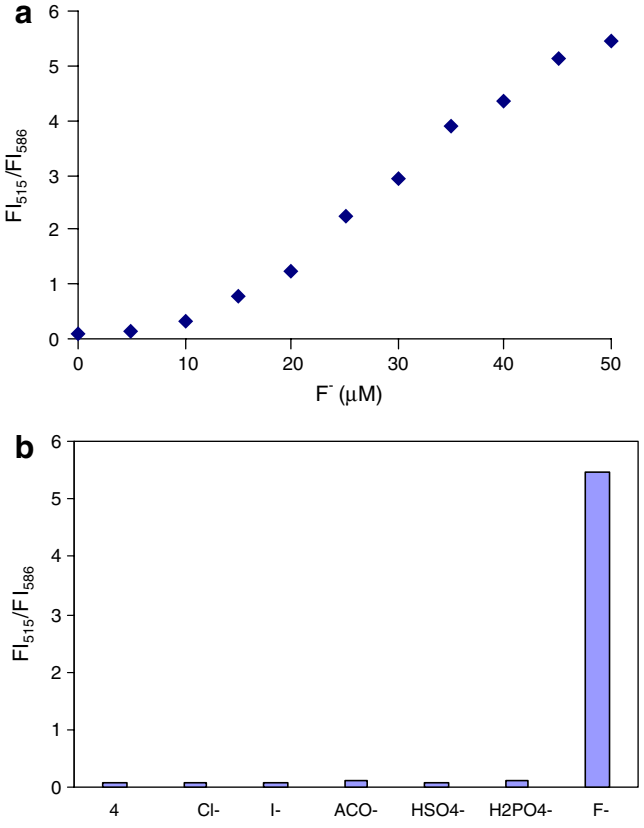
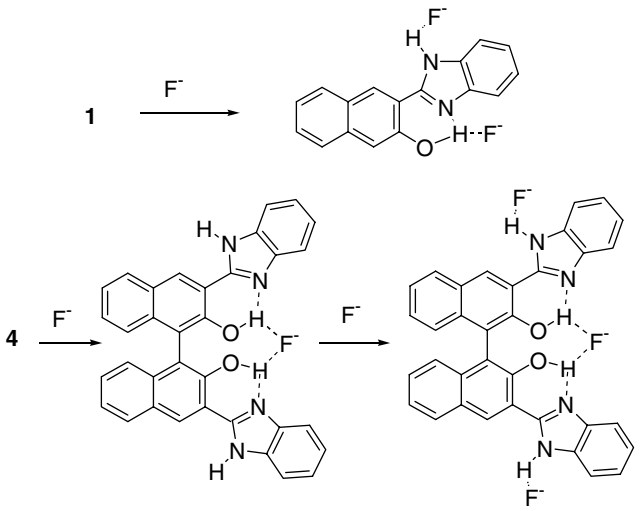


Figure 5. (a) Plot of fluorescence intensity ratio between 515 nm and 586 nm (FI_{515}/FI_{586}) versus concentration of F^- in CH_3CN; (b) ratiometric emission response of **4** to different anions.



Scheme 2.

plete upon addition of 2 equiv of fluoride ions. However, in the case of receptor **4**, on addition of up to 2 equiv of fluoride ions, both the naphth and benzim signals are shifted upfield and on further addition of fluoride (up to 5 equiv), only the benzim signals are further shifted upfield (see Supplementary data). These results clearly show that for **1** both the OH and NH protons H-bond with fluoride simultaneously. However, in the case of **4**, at lower concentrations of fluoride ions the OH protons preferentially hydrogen bond with fluoride and at higher concentrations of fluoride, stronger H-bonds between the benzim NH and fluoride ions take place (Scheme 2).

Therefore, receptors **1** and **4**, which demonstrate highly efficient intramolecular ESPT, can be used for highly selective estimation of fluoride ions through inhibition of this phenomenon. Receptor **4**, due to its 'ON–OFF–ON' behaviour, provides an opportunity for ratiometric estimation of fluoride ions. The effect of substituents and the acidity of protons on the sensitivity and selectivity of such receptors are under investigation.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.02.095.

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17. 3-(1*H*-Benzimidazol-2-yl)naphthalen-2-ol (**1**): yellow solid, 60%; mp 273–275 °C (lit.[16] 268–272 °C); ^{1}H NMR (300 MHz) ($CDCl_3$–DMSO-d_6): δ 7.27–7.36 (m, 4H, ArH), 7.46 (t, $J = 6.9$ Hz, 1H, ArH), 7.62 (d, $J = 7.2$ Hz, 1H, ArH), 7.72 (d, $J = 8.1$ Hz, 2H, ArH), 7.86 (d, $J = 8.1$ Hz, 1H, ArH), 8.65 (s, 1H, ArH); elemental analysis: Found: C, 78.55; H, 4.55; N, 10.60. $C_{17}H_{12}N_2O$ requires C, 78.44; H, 4.65; N, 10.76. 3,3′-Bis-(1*H*-benzimidazolyl-2-yl)-[1,1′]binaphthenyl-2,2′-diol (**4**). A solution of 2,2′-dihydroxy-[1,1′]binaphthalenyl-3,3′-dicarboxylic acid (**2**) (375 mg, 1 mmol) and 1,2-diaminobenzene (**3**) (216 mg, 2 mmol) in ethylene glycol (15 ml) was refluxed under N_2 for 36 h. On cooling the reaction mixture, a yellow solid was obtained which was recrystallized from ethanol to give pure **4** (240 mg, 46%); mp 300 °C (decomp.); FAB mass 518 (M^+); ^{1}H NMR (300 MHz) (DMSO-d_6–CD_3CN): δ 7.15 (d, $J = 7.8$ Hz, 2H, benzim H), 7.28–7.41 (m, 8H, ArH), 7.68 (d, $J = 7.8$ Hz, 4H, benzim H), 8.02 (d, $J = 7.2$ Hz, 2H, ArH), 8.89 (s, 2H, ArH); ^{13}C NMR (75 MHz) ($CDCl_3$ + TFA): δ 110.1 (C), 113.6 (CH), 113.8 (C), 124.0 (CH), 126.7 (CH), 127.7 (CH), 128.6 (C), 130.1 (CH), 130.3 (C), 131.8 (CH), 133.3 (CH), 136.0 (C), 146.6 (C), 149.9 (C). Elemental analysis: Found: C, 78.65; H, 4.25; N, 10.99. $C_{34}H_{22}N_4O_2$ requires C, 78.75; H, 4.28; N, 10.80.
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19. Log β values were determined using curve fitting specfit 3.0.36 software.