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Ratiometric fluorescent chemosensor for fluoride ion based on inhibition of excited state intramolecular proton transfer



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HIGHLIGHTS

- Synthesis of hydroxyarylbenzimidazole based ESIPT sensor.
- Ratiometric chromofluorescent sensor for fluoride ions.
- Broad range of fluoride ion detection limit.
- Practical usability of probe **2** by dip coating method.

G R A P H I C A L A B S T R A C T



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ABSTRACT

ESIPT based benzimidazole derivative has been synthesized and investigated their photophysical behavior towards various anions. The probe **2** has been used for selective estimation of F^- ions as compared to other anions and signaled the binding event through formation of new absorption band at 360 nm and emission band at 420 nm. The probe **2** showed fluorescence behavior towards fluoride ions through hydrogen bonding interactions and restricted the ESIPT emission at 540 nm from OH to nitrogen of benzimidazole moiety to release its enol emission at 420 nm.

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Introduction

Fluoride ion, being the smallest and most electronegative anion has received much attention due to its profound effects on human

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health, thus intake of acute amount of it is beneficial to the treatment of osteoporosis and dental health [1–3]. But an overdose of fluoride ion can cause many problems such as bone disorder, collagen breakdown, thyroid activity and depression [4]. Thus, to determine the level of fluoride ions, various detection methods have been reported including highly accurate but expensive analytical instruments that use ion selective electrodes and chromogenic and fluorescent probes [5–7]. Fluoride ions can contaminate the human body and other materials in the surroundings during the manufacture of rocket fuel and fireworks [8]. Detection of these traces is a major concern in the field of analytical and forensic

Abbreviations: ESIPT, excited state intramolecular proton transfer; TMS, tetra methyl silane; ASC II, American Standard Code for Information Interchange; B3LYP, Becke, 3-Parameter, Lee–Yang–Parr; TD-DFT, Time Dependent-Density Functional Theory; Mpt., melting point; Excel TM, Microsoft Excel Trade Mark; 6-31G(d,p), basis set method-double diffuse function.

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sciences. Colorimetric sensors do not need any spectroscopic instrument since colorimetric changes can be detected by the naked eve. But use of such sensors is limited because of their low absorption. Fluorescent sensors based on excited-state intramolecular proton transfer (ESIPT), as seen from 2-(2-hydroxyphenyl) benzimidazole/thiazole/oxazole have been attracted more attention [9]. ESIPT sensors exhibit dual emissions from both the excited enol and keto tautomers [10]. Fluorescent sensing of fluoride ion could realize by prohibiting ESIPT through coordination or deprotonation induced by fluoride with ESIPT centers, resulting in detectable spectral change. Compared with widely used photoinduced electron transfer (PET) mechanism for sensing [11], the fluorescent sensors based on ESIPT can afford many advantages including dual fluorescence intensity changes and large stokes shift, thus the excited state intramolecular proton transfer (ESIPT) has attained a special importance due to vast applications as laser dves. UV-photostabilizer. scintillators. membrane and protein probes and as a potential component for photo switches and organic LEDs. ESIPT usually occur in the molecules bearing an H-bond donor group usually a phenolic/amino moiety associated with basic site (O, N, S) in the ground state through H-bond interactions. This proton which is covalently attached in the electronically excited state migrates to a neighboring hydrogenbonded atom which is less than 2 Å. The significant amount of excited state energy is dissipated in this process. The formed phototautomer emits light at a lower energy with an unusually large Stokes shift (range from 100 to 500 nm) and thermally equilibrates back to the ground state with the proton bound to its original atom. This large stokes shift is an important property for fluorophores because the self-absorption, or the inner filter effect, can be avoided and the fluorescent analysis can also be improved. They can detect metal ions with ratiometric fluorescence response, providing self calibration function and avoiding photodamage, scattering light and strong interference derived from short wavelength emission in biological media.

We have recently reported some ESIPT based cation and anion sensors based on hydroxyarylbenzimidazole moiety [12]. In the present manuscript ESIPT fluorescent probe **2** has been synthesized with different strategy other than reported scheme [13] which showed sensitivity changes towards fluoride ions. The presence of fluoride ions caused decrease in absorption intensity at 335 nm and immergence of new absorption band at 360 nm. However, in case of emission presence of fluoride ion caused quenching of keto tautomer at 540 nm and enol tautomer band is released at 420 nm.

Experimental section

Materials and equipments

All chemicals were purchased from Loba and Sigma Aldrich Chemical Co and used without further purification. Column chromatography was performed using silica gel (60–120 mesh). All reactions were monitored by thin layer chromatography. Chloroform: Methanol was the adopted solvent system. Melting points were carried out by the open capillary tube method [14] and uncorrected. ¹H NMR and ¹³C NMR spectra were carried out using a JEOL ECS-400 MHz spectrometer in SAI Labs, Thapar University, Patiala with TMS as an internal reference. Mass Spectra of the synthesized compounds were recorded at MAT 120 in SAIF, Punjab University. All chemical shifts are reported in ppm relative to the TMS as an internal reference. UV–Vis studies were carried out on a Specord PC machines using slit width of 1.0 nm and matched quartz cells. Fluorescence spectra were determined on a Varian Cary Eclipse fluorescence spectrometer. Stock solution of probes **1** and **2** was prepared at 10^{-3} M in distilled CH₃CN. Tetrabutylammonium salts were used for the anions. All absorption and fluorescence scans were saved as ASC II files and further processed in ExcelTM to produce all graphs shown. Solutions of **1** and **2** were typically 20 μ M for UV–Vis studies. Stability constants were determined using Benesi–Hildebrand Equation [15] (Eq. (1))

$$\frac{1}{(A - A_0)} = \frac{1}{(A_{max} - A_0)} + \frac{1}{K[F^-]^n (A_{max} - A_0)}$$
(1)

where A_0 , A, A_{max} are the absorption considered in the absence of ion, at an intermediate, and at a concentration of saturation. K is binding constant, $[F^-]$ is concentration of ion. n is the stoichiometric ratio.

Computational methods

The ground state (S_o) geometry of probe **2** was optimized using Density Functional Theory (DFT) [16]. The functional used was B3LYP and basis set used for all atoms were 6-31G(d,p). The vertical excitation energy and oscillator strengths at the ground state equilibrium geometries were calculated using with the same hybrid functional and basis set. The low-lying first singlet excited state (S₁) of the probe **2** was relaxed using to obtain its minimum energy geometry. Frequency computations were also carried out on the optimized geometry of the low-lying vibronically relaxed first excited state of the probe **2** and probe **2.F**⁻.

Synthesis of probes 1 and 2

Probe **1** – 3,4 Diaminobenzophenone (500 mg, 2.3 mmol) and benzaldehyde (374 mg, 3.5 mmol) were dissolved in 10 mL nitrobenzene. The reaction mixture was refluxed for about 24 h, and then cooled to room temperature. The solid separated was filtered by using sintered crucible with the help of vacuum filtration method and washed with diethyl ether to obtain colorless solid of probe **1** (225 mg, 89% yield); Mpt. 220–221 °C; ¹H NMR (CDCl₃ + - DMSO-d₆, 400 MHz): δ 8.26–8.25 (m, 2H, Ar), 8.17 (s, 1H, Ar), 7.85–7.76 (m, 4H, Ar), 7.66–7.48 (m, 7H, Ar), 4.97 (bs, NH); ¹³C NMR (CDCl₃ + DMSO-d₆, 100 MHz): δ 195.52 (C=O), 137.50, 130.94, 128.72, 127.90, 127,17, 123.08, 120.82, 117.33, 113.28, 110.96 (Ar H); (Figs. S1 and S2). MS (ESI) *m/z* 299 (M⁺+H) (Fig. S3).

Probe 2 - 3,4 Diaminobenzophenone (1 g, 4.7 mmol) and salicylaldehyde (630 mg, 5.1 mmol) were dissolved in 30 mL nitrobenzene. The reaction mixture was refluxed for about 24 h, and then cooled to room temperature. The solid separated was filtered and washed with diethyl ether to obtain yellow colored solid which was further purified by column chromatography to get pure probe **2** (528 mg, 92% yield); Mpt. 240–241 °C; ¹H NMR (CDCl₃ + DMSOd₆, 400 MHz): δ 12.57 (bs, 1H, NH), 9.63 (bs, 1H, OH), 8.35 (s, 1H, ArH), 7.96 (s, 1H, ArH), 7.88 (d, 1H, J = 8.28 Hz, ArH), 7.61-7.57 (m, 4H, ArH), 7.29–7.24 (t, 1H, J = 9.16 Hz, ArH), 7.14–7.10 (t, 1H, *J* = 11.0 Hz, ArH), 7.00–6.96 (t, 1H, *J* = 7.36 Hz, ArH), 6.86–6.79 (m, 1H, ArH), 5.77 (s, 1H, ArH); ¹³C NMR (CDCl₃ + DMSO*d*₆,100 MHz): δ 195.56 (C=O), 158.29, 137.86, 131.68, 129.31, 127.90, 126.06, 124.82, 124.29, 120.72, 118.71, 117.09, 113.75, 112.06, 110.97 (ArH); (Figs. S4 and S5). MS (ESI) m/z 314.11 (M^++H) (Fig. S6) (see Scheme 1).

Results and discussion

Photophysical properties of probes 1 and 2

The UV–Vis spectroscopic properties of probe 1-2 were investigated in CH₃CN at 20 μ M. Probe 1 and 2 displayed an absorption band centered at 320 nm and 335 nm respectively. Addition of



Scheme 1. Synthesis of probes 1-2.

different tetrabutylammonium anions viz. CN⁻, F⁻, Cl⁻, Br⁻, AcO⁻, I⁻, HSO₄⁻, OH⁻, H₂PO₄⁻, etc. caused no significant change except presence of fluoride ions in case of probe 1 (Fig. S7). Incremental addition of fluoride ions to probe 1 caused the decrease in absorption intensity at 320 nm and formation of new absorption band at 360 nm with two isobestic points at 275 and 335 nm on addition of 1000 µM solution of fluoride ions (Fig. S10). Addition of different tetrabutylammonium anions viz. CN⁻, F⁻, Cl⁻, Br⁻, AcO⁻, I⁻, HSO₄, OH⁻, H₂PO₄, etc. caused no significant change except presence of fluoride and acetate ions in case of probe 2 (Fig. 1(a)). Upon incremental addition of fluoride ions, absorption intensity at λ_{max} 335 nm decreased gradually with simultaneous increase in new absorption band at 360 nm with well defined isobestic point at 340 nm and 270 nm (Fig. 2(a)). The presence of isobestic points showed that different species are in equilibrium and there is no stepwise formation of complexed species. The binding constant was calculated to be $6.6 \times 10^3 \, \text{M}^{-1}$ with detection limit of 2 μ M. The gradual addition of fluoride ions caused decrease in absorption intensity at 335 nm and increase at 360 nm provided the opportunity to determine fluoride ions ratiometrically. The absorption ratio at these two wavelengths varied from 0.1356 to 1.383, indicating 10.19 fold absorption ratio change. Thus, probe **2** can be used to estimate a wide range of fluoride ions between 2 and 2400 μ M through ratiometric approach (Fig. 2(b)). But in case of acetate ions new band at 272 and 350 nm appeared with addition of higher equivalents of acetate ions i.e. 1000 μ M (Fig. S8).

UV-Vis absorption changes of probe **1** in the presence of fluoride ions were similar as that of probe **2**, which clearly indicated that both molecules in the ground state caused NH deprotonation which was also supported through theoretical calculations.

The probe **2** (20 μ M, CH₃CN) on excitation at 340 nm displayed keto emission band at 540 nm. On addition of various anions like CN⁻, F⁻, Cl⁻, Br⁻, AcO⁻, I⁻, HSO₄, OH⁻, H₂PO₄, etc., no significant change was observed except fluoride and acetate ions (Fig. 1(b)). Upon incremental addition of fluoride ions keto emission band at 540 nm was quenched and new emission band at 420 nm was formed. The new emission band at 420 nm was typically due to enol emission because presence of fluoride caused deprotonation at -OH group which restrict the ESIPT phenomenon and thus released the enol emission at 420 nm (Fig. 3(a)). The binding constant was calculated to be 1.148 × 10⁴ M⁻¹ with lowest detection limit of 2 μ M. But in case of acetate ions new band at 420 nm appeared with addition of higher equivalents of acetate ions i.e. 1000 μ M (Fig. S9).

The gradual addition of fluoride ions caused decrease in emission intensity of keto tautomer at 540 nm and increase in emission intensity of enol tautomer at 420 nm and thus provided the opportunity to determine fluoride ions ratiometrically. The emission



Fig. 1. Effect of various anions on (a) absorption spectra and (b) emission spectra of probe 2 (20 μM, CH₃CN).



Fig. 2. (a) Effect of addition of fluoride ions on absorption spectrum of probe **2**; (b) plot of absorption intensity ratio between 360 and 335 nm (*A*₃₆₀/*A*₃₃₅) vs [F⁻] ions of probe **2** at 20 μM in CH₃CN.



Fig. 3. (a) Fluorescence spectra of probe 2 (20 μ M, λ_{ex} = 340 nm) CH₃CN upon complexation with increasing concentration of F⁻ ions. (b) Plot of emission intensity ratio between 420 and 540 nm (I_{420}/I_{540}) vs [F⁻] ions of probe 2 at 20 μ M in CH₃CN.



Fig. 4. Red bars represent selectivity of probe **2** (20 μ M, λ_{ex} = 340 nm) upon addition of different metal ions in CH₃CN and blue bars shows the competitive selectivity of probe **2** in the presence of interfering metal ions. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

ratio at these two wavelengths varied from 0.376 to 4.058, indicating 10.86 fold emission ratio change. Thus, probe **2** can be used to estimate a wide range of fluoride ions between 2 and 75 μ M through ratiometric approach (Fig. 3(b)).

In case of probe **1**, absence of hydroxyl group led to exhibition of very weak enol emission at 420 nm with lesser stokes shift of \sim 90 nm than probe **2** of \sim 200 nm at higher concentration. These studies clearly predicted that –OH participates in ESIPT phenomenon.

Interference studies of probe 2

Addition of other anions (100 equiv.) such as Cl^- , Br^- , AcO^- , I^- , HSO_4^- , OH^- , $H_2PO_4^-$, no significant change in fluorescence intensity was observed by comparison with and without other anions. To determine the practical applicability of probe **2**, we carried out competitive experiments in the presence of 10 equiv. of F^- ions

mixed with 50 equiv. of each of the various metal ions. The complex formed in the presence of acetate ions is very week as compared to fluoride complex. Whereas, no significant variation in the fluorescence intensity was found when comparing the results with or without the other anions (Fig. 4).

Practical application of probe 2 by dip coating technique

In order to check the practical applicability of probe **2**, TLC strips were prepared by dip-coating a solution of probe **2**, followed by drying them in a vacuum in order to check for residual contamination in contact mode. We prepared several samples of solution-coated TLC strips and studied the response of their fluorescence towards fluoride ions in contact mode and solution phase. Solution of fluoride ions were placed over coated TLC strips for 5 s. Upon illumination with a UV lamp, blue spots were observed in the contact area (Fig. 5). The minimum amount of fluoride ions detectable by the naked eye was as low as, thereby registering a detection limit at the 10^{-6} M.

Theoretical studies

To explore the origin of each induced absorption band, theoretical calculation were employed to optimize the structure through DFT and TD calculation with B3LYP-631G methods. The probe **2** was optimized using DFT calculations. It was found that O-H bond acquires partial double bond character and hydrogen of O-H orient itself to the closer vicinity to imine Nitrogen of benzimidazole moiety (Fig. 6). The presence of fluoride ion caused deprotonation at hydroxyl group and acquired keto form.

The Theoretical calculation of probe **2**, showed that band at 330 nm was due to HOMO to LUMO+1, which has oscillating strength 0.2424 and excitation energy 4.0026 eV. The HOMO of probe **2** locates mainly on benzimidazole ring and LUMO mainly on benzophenone moiety but for LUMO+1 it exhibit an expanding π -nature orbital covering both benzimidazole and benzophenone moiety. The other bands at 260 and 280 nm were due to HOMO-1



Fig. 5. Photographs of probe 2 coated TLC strips under different experimental conditions.



Fig. 6. Optimized structures and HOMO and LUMO of probe 2.

 Table 1

 Excitations for probe 2 that contribute to the transitions in the 250–700 nm and their expansion coefficients in gaseous phase.

	λ_{max} (nm) Experimental	λ_{max} (nm) Theoretical	$E_{\rm exc}~({\rm eV})$	Oscillator strength	Excited state	Expansion coefficient
Probe 2	335	330	4.0026	0.2424	HOMO to LUMO+1	0.63898
	262	280	4.3661	0.3049	HOMO–3 to LUMO	0.52184
Probe 2+F ⁻	360	360	3.1007	0.2974	HOMO to LUMO+2	0.65909
	280	280	4.5082	0.1449	HOMO-2 to LUMO+2	0.60937

to LUMO+1 and HOMO-3 to LUMO respectively (Table 1). In case of probe **2.F**⁻ band at 360 nm was due to HOMO to LUMO+2 transitions, which has oscillating strength 0.2974 and excitation energy 3.1007 eV. The HOMO of probe **2+F**⁻ locates mainly on benzimid-azole ring and LUMO mainly on benzophenone moiety but for LUMO+2, it exhibit an expanding π -nature orbital covering both benzimidazole and benzophenone moiety. The other bands at 280 and 305 nm were due to HOMO-2 to LUMO+2 and HOMO-3 to LUMO respectively (Table 1).

Conclusion

Hydroxyaryl benzimidazole derivative has been synthesized for selective sensing of fluoride ions. Probe **2** showed ratiometric absorption and emission behavior towards fluoride ions to sense fluoride ion between a broad ranges of 2–2400 μ M. The presence of fluoride ion caused inhibition of keto tautomer and release of

enol emission. The probe **2** showed practical applicability to sense fluoride ions at micromolar level through dip coating method.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2014.11.026.

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