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Electronic Supplementary Information

L-tyrosine derived fluorescent molecular probes as solvent mediated flip-flop halide (iodide/fluoride) sensors and reversible chromogenic pH indicators

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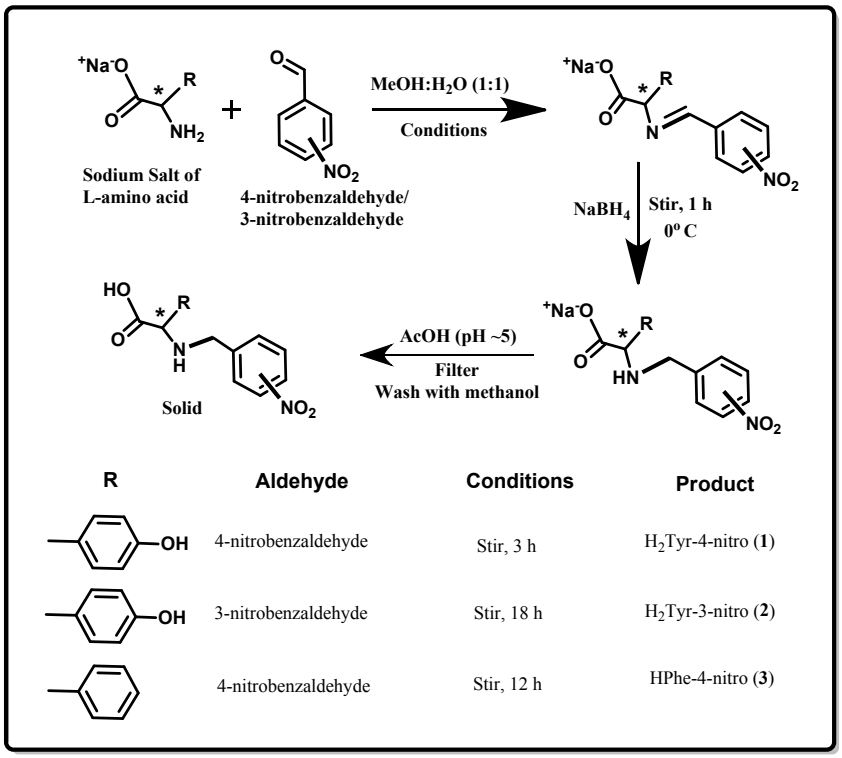
Experimental section

Materials and methods. All chemicals and solvents used for synthesis were obtained from commercial sources and were used as received, without further purification. All reactions were carried out under aerobic conditions.

Physical measurements. ^{1}H NMR spectra of the sodium salt of the probes were obtained in D_2O at 25 °C on a Bruker ARX-400 spectrometer; chemical shifts are reported relative to the residual solvent signals. FTIR spectra were measured in the 4000-400 cm^{-1} range on a Perkin-Elmer Spectrum I spectrometer with samples prepared as KBr pellets. UV-Vis spectra of the compounds in methanol (a typical concentration of 1 mM) were recorded in a Cary 60 UV-Vis spectrophotometer by Agilent Technologies using a quartz cuvette of path length 10 mm. ESI mass spectrometry was performed using either Waters HRMS instrument or Thermo Scientific LTQ XL LC-MS instrument for the 50-2000 amu range. Fluorescence spectra were recorded using Shimadzu RF5301PC Fluorescence Spectrophotometer.



Scheme S1. Synthesis of the probes **1**, **2** and **3**.

Synthesis of H_2Tyr-4-nitro (1). It is synthesized using the method reported in reference 8.

Synthesis of H_2Tyr-3-nitro (2). To a solution of 500 mg of L-tyrosine (2.8 mmol) and 220 mg of NaOH (5.6 mmol) in 14 mL of a methanol:water mixture (v/v 1:1) was added 417 mg (2.8 mmol) of 3-nitrobenzaldehyde. The resulting yellow solution was stirred for 18 h at room temperature prior to the addition of 105 mg of $NaBH_4$ (4.8 mmol) at 0 °C. The solution was stirred further until the yellow color lightens. The pH of the solution was adjusted to 5 using (~2 mL) glacial acetic acid and stirred for half an hour. An off-white precipitate was filtered off using a G4 crucible, washed with water and air dried. Yield: 0.666 g (78%). M.pt. 253 ^{o}C. ^{1}H NMR (D_2O): δ 2.62 (t, 2H, J = 6.2 Hz), 3.10 (d, 1H, J = 6.7 Hz), 3.51 (d, 1H, J = 13.6 Hz), 3.72 (d, 1H, J = 13.68 Hz), 6.31 (d, 2H, J = 2.2 Hz), 6.69 (d, 2H, J = 2 Hz), 7.20 (d, 2H, J = 8.8 Hz), 7.91 (d, 2H, J = 1.8 Hz); Selected FTIR peaks (KBr, cm^{-1}): 3419(br), 3183(s), 3016(w), 2809(m), 2691(w), 1607(w), 1587(s), 1525(s), 1439(s), 1397(s), 1378 (s), 1356(s), 1247(s), 1105(s), 841(s), 736(s), 530(s); HRMS (ESI-TOF): m/z calcd for $[(H_2Tyr\text{-}3\text{-}NO_2)H]^+$, 317.1137; found, 317.1091.

Synthesis of HPhe-4-nitro (3). It was prepared following the procedure described above for H_2Tyr-3-nitro except 500 mg (2.8 mmol) of L-phenylalanine was used instead of L-tyrosine. In this case, the resulting yellow solution was stirred for 12 h at room temperature. A white precipitate was filtered off using a G4 crucible, washed with water and air dried. Yield: 730 mg (81%). M.pt. 217 ^{o}C. ^{1}H NMR (D_2O): δ 2.50 (t, 2H, J = 5.2 Hz), 3.00 (t, 1H, J = 5.4 Hz), 3.42 (d, 1H, J = 7.2 Hz), 3.58 (d, 1H, J = 12.2 Hz), 3.68 (d, 1H, J = 12.2 Hz), 6.30 (d, 2H, J = 1.9 Hz), 6.67 (d, 2H, J = 2.4 Hz), 7.22 (d, 2H, J = 6.7 Hz), 7.82 (d, 2H, J = 2.1 Hz). Selected FTIR peaks (KBr, cm^{-1}): 3380(br), 3238(s), 3025(w), 2923(w), 1627(s), 1495(s), 1455(s), 1435(m), 1371(s), 1344(s), 1241(w), 1079(s), 975(s), 747(s), 696(s). HRMS (ESI-TOF): m/z calcd for $[(HPhe\text{-}4\text{-}NO_2)H]^+$, 301.1118; found, 301.1168.

For Sensing Experiments

Stock solutions of 0.6 mM of the sensor was prepared in methanol or DMSO whereas 0.1 M solution of each anion was prepared in solvent ratio of 1:3 water:methanol or water:DMSO. For each measurement, 12.6 μL of the analyte was added to 2 mL solution of the sensor. Stock solution of sensors: (i) Methanolic solution of monosodium salt of H_2Tyr-4-nitro (**1a**); (ii) DMSO solution of monosodium salt of H_2Tyr-4-nitro (**1b**); (iii) Methanolic solution of monosodium salt of H_2Tyr-3-nitro (**2a**); (iv) DMSO solution of monosodium salt of H_2Tyr-3-nitro (**2b**); (v) Methanolic solution of monosodium salt of HPhe-4-nitro (**3a**); (vi) DMSO solution of monosodium salt of HPhe-4-nitro (**3b**).

For Detection Limit Calculations

By plotting fluorescence intensity (enhanced/quenched) with increasing concentration of analyte, slope (positive/negative) (m) of graph was observed. Standard deviation (σ) was calculated from three blank measurements of sensor. Detection limit is calculated according to the formula: Detection limit = 3σ/m

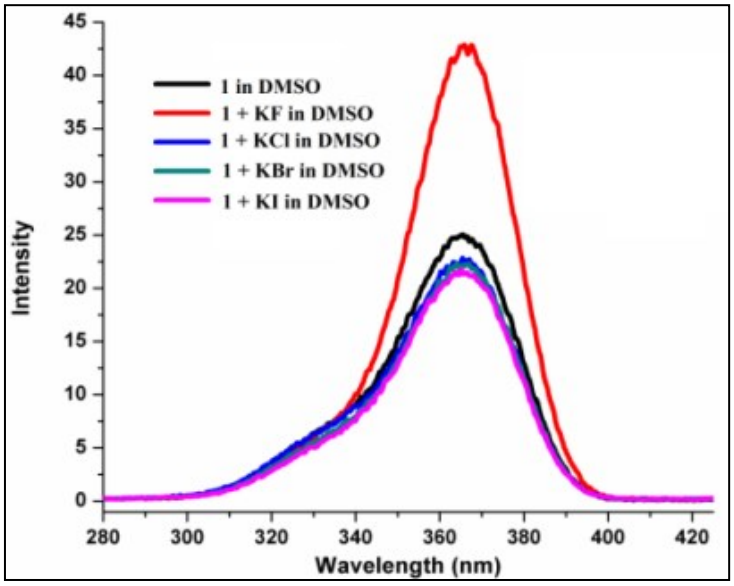


Fig. S1 Effect of various anions on fluorescence intensity of **1** in aq. DMSO.

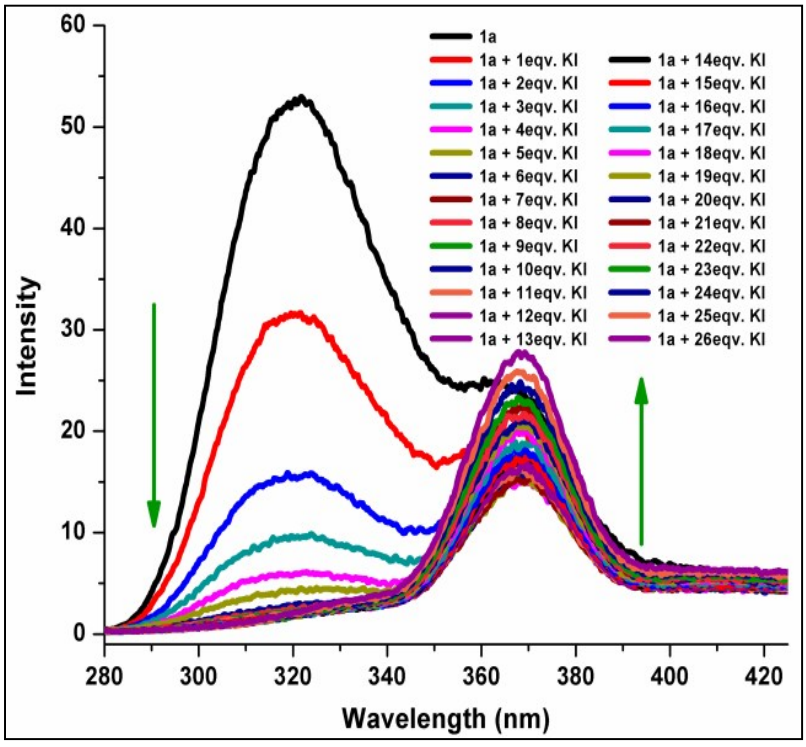


Fig. S2 Quenching of fluorescence on successive addition of iodide ions to **1a**.

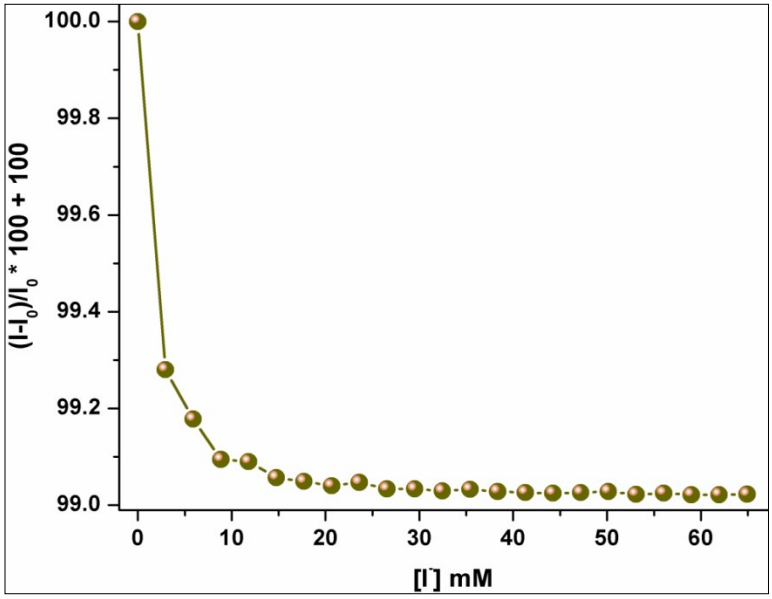


Fig. S3 Percentage decrease in fluorescence intensity upon addition of iodide ions to **1a.**

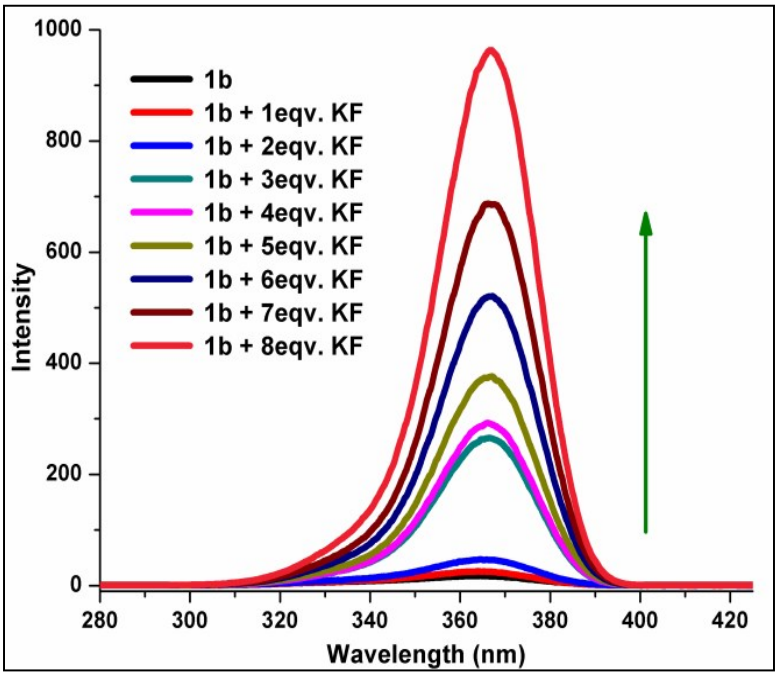


Fig. S4 Enhancement of fluorescence on successive addition of fluoride ions to **1b**.

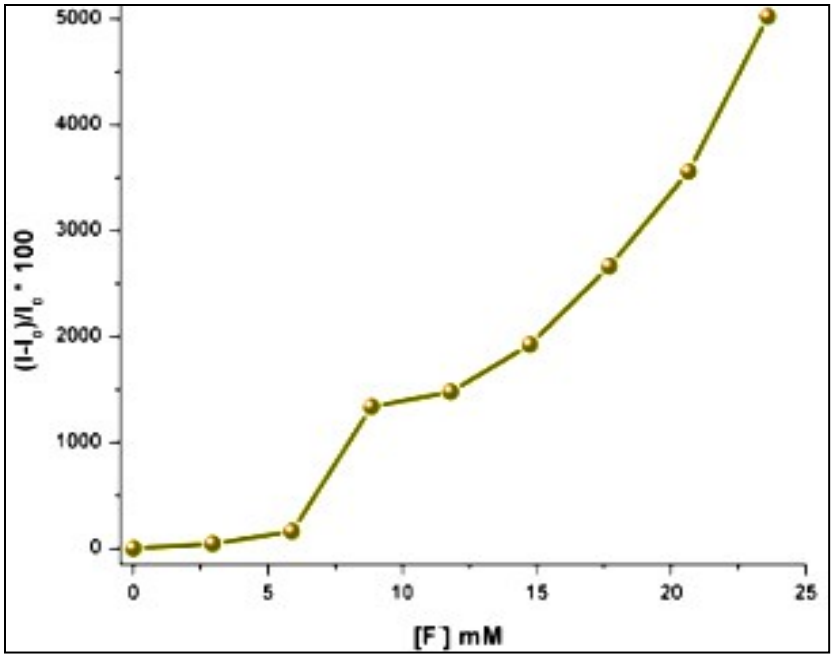


Fig. S5 Percentage increase in fluorescence intensity upon addition of fluoride ions to **1a**.

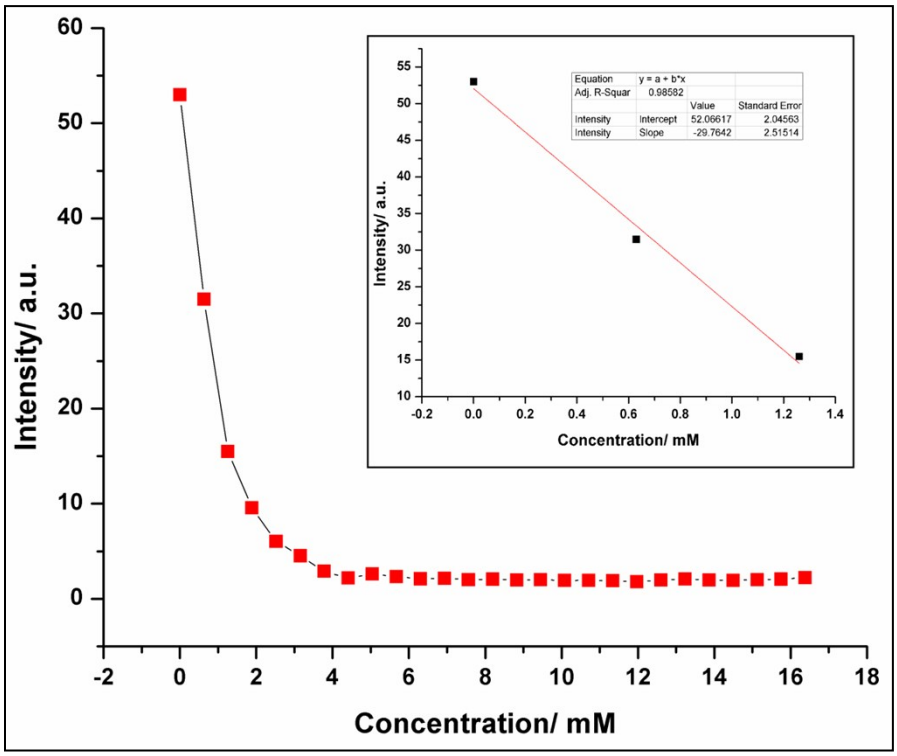


Fig. S6 Fluorescence intensity of **1a** decreases with increasing concentration of iodide, Inset: the slope (m) of graph was found to be -29.7642 (R^2 = 0.98582).

Table S1. Standard deviation for **1a**.

Blank Reading (Only **1a**)	Fluorescence intensity
Reading 1	52.42
Reading 2	51.92
Reading 3	52.16
Standard Deviation (σ)	0.250067

Table S2. Detection limit for 1**a** in case of iodide as an analyte.

Slope from graph (m)	-29.7642	mM^{-1}
Detection limit (3σ/m)	0.0259	mM
Limit of detection (LOD)	3.28	ppm

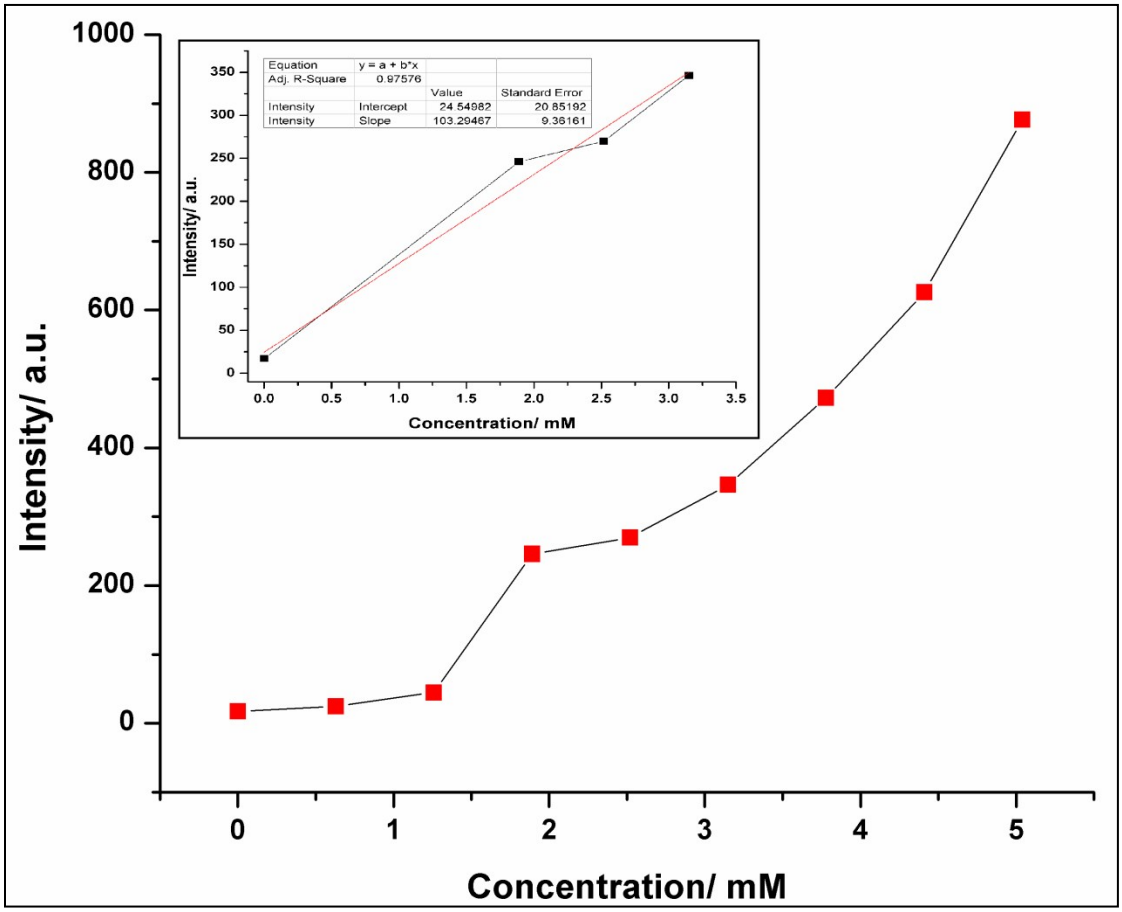


Fig. S7 Enhancement of fluorescence intensity of **1b** with increasing concentration of fluoride; Inset: the slope (m) of graph was found to be 103.29647 (R^2 = 0.97576).

Table S3. Standard deviation for **1b**.

Blank Reading (Only **1b**)	Fluorescence intensity
Reading 1	17.112
Reading 2	16.926
Reading 3	17.422
Standard Deviation (σ)	0.25057

Table S4. Detection limit for **1b** in case of fluoride as an analyte.

Slope from graph (m)	103.29647	mM^{-1}
Detection limit (3σ/m)	0.007277	mM
Limit of detection (LOD)	0.14	ppm

a)

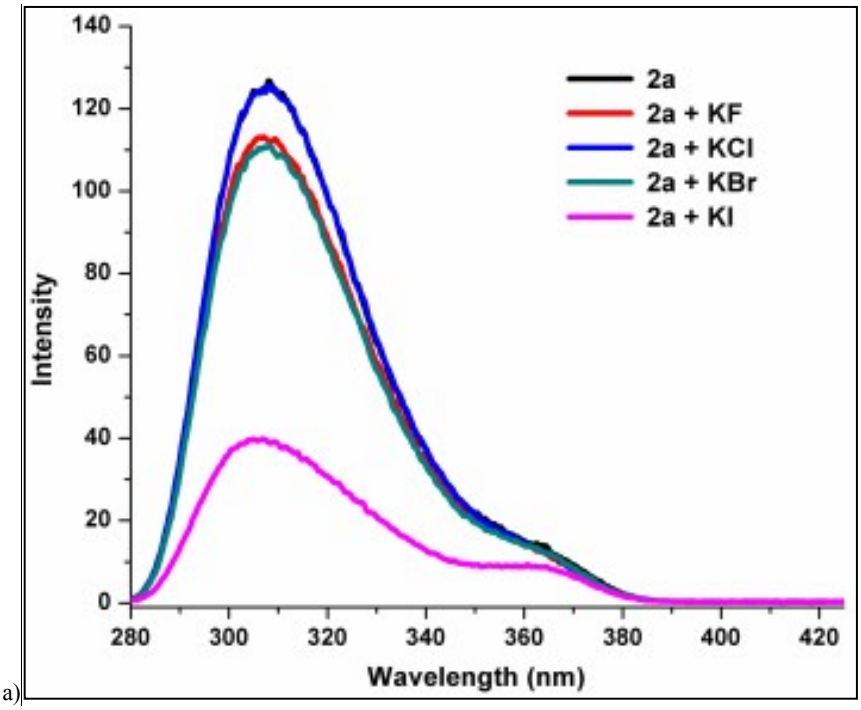


Fig. S8 Change in fluorescence intensity on addition of various anions to aqueous methanol solution of probe **2a.**

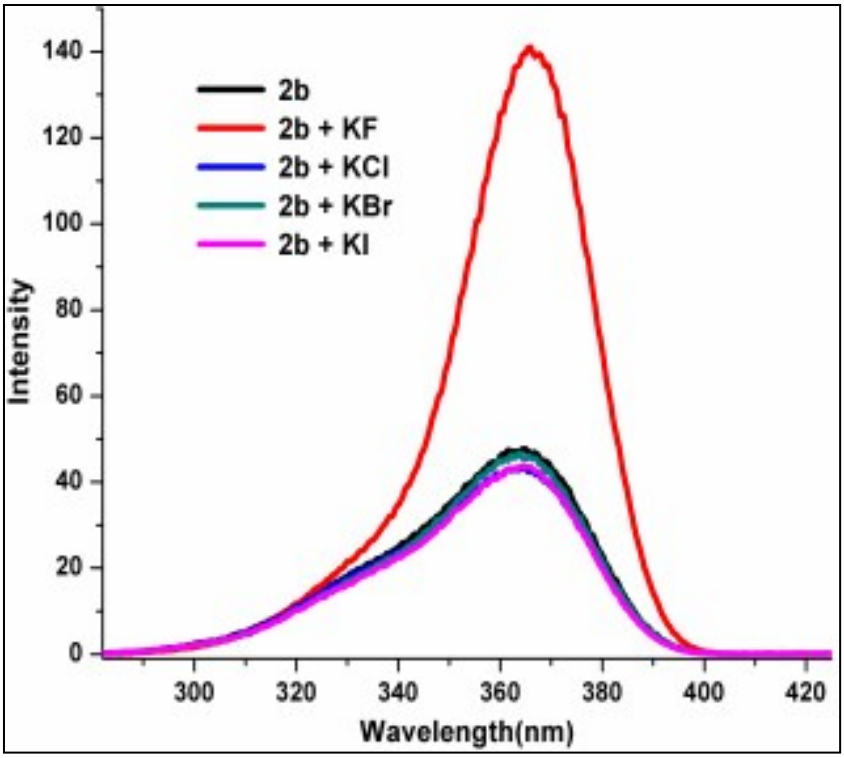


Fig. S9 Change in fluorescence intensity on addition of various anions to aqueous DMSO solution of probe **2b.**

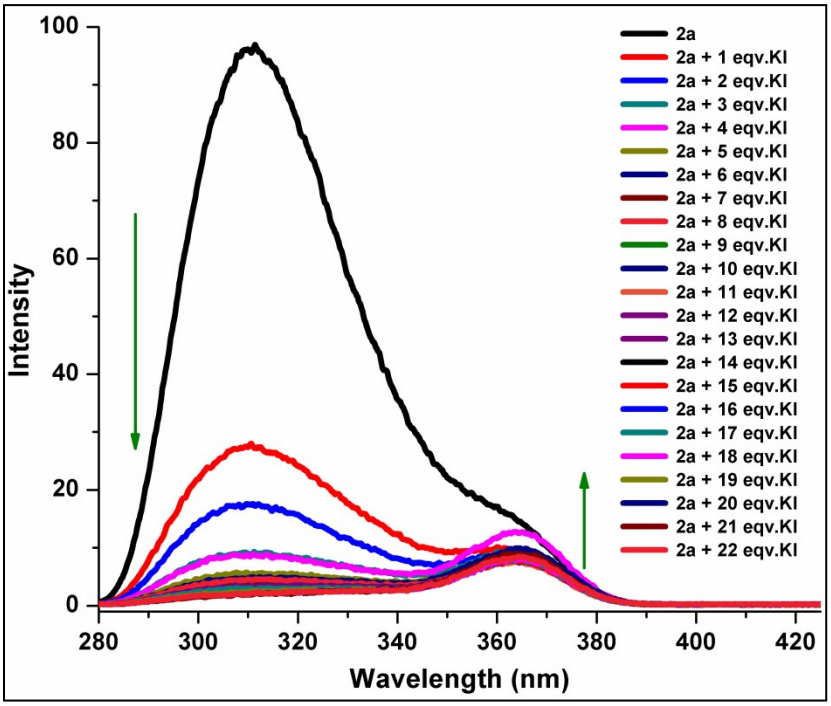


Fig. S10 Quenching of fluorescence on successive addition of iodide ions to **2a**.

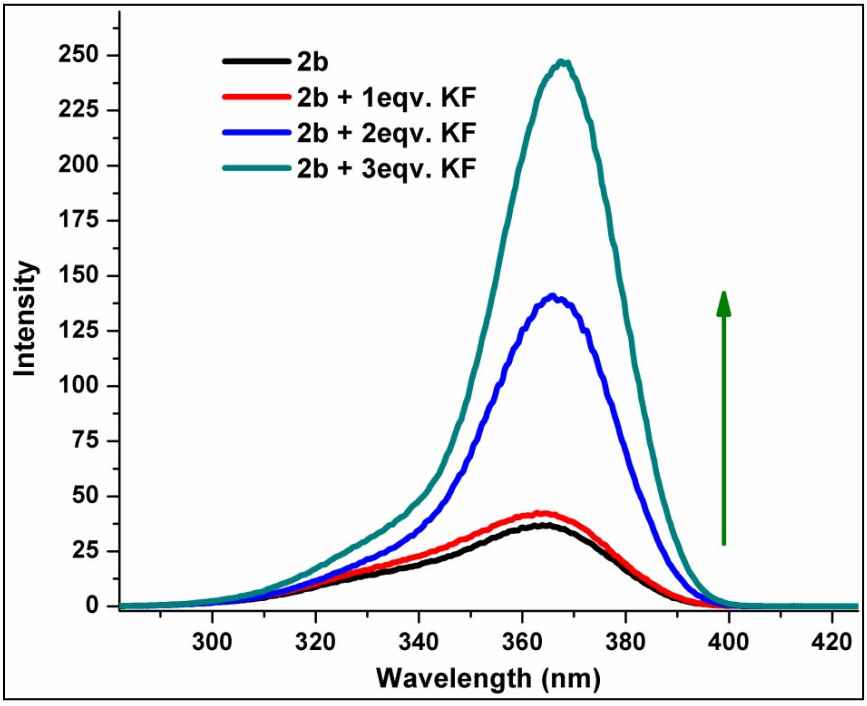


Fig. S11 Enhancement of fluorescence on successive addition of fluoride ions to **2b**

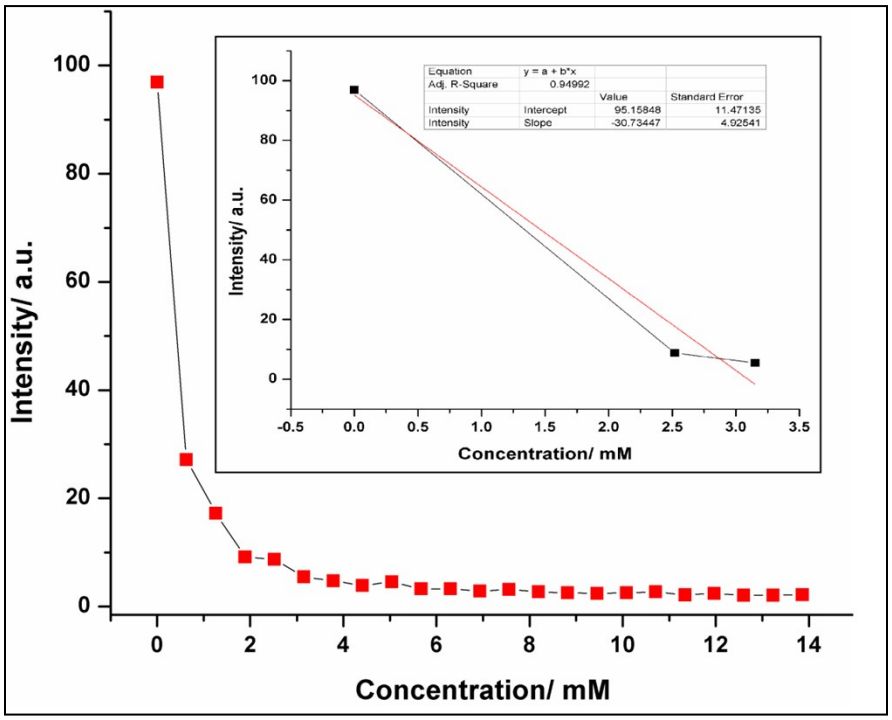


Fig. S12 Fluorescence intensity of **2a** decreases with increasing concentration of iodide, Inset: the slope (m) of graph was found to be -30.73447 (R^2 = 0.94992).

Table S5. Standard deviation for **2a.**

Blank Reading (Only **2a**)	Fluorescence intensity
Reading 1	83.411
Reading 2	83.210
Reading 3	82.683
Standard Deviation (σ)	0.375969

Table S6. Detection limit for **2a** in case of iodide as an analyte.

Slope from graph (m)	-30.73447	mM^{-1}
Detection limit (3σ/m)	0.0367	mM
Limit of detection (LOD)	4.66	ppm

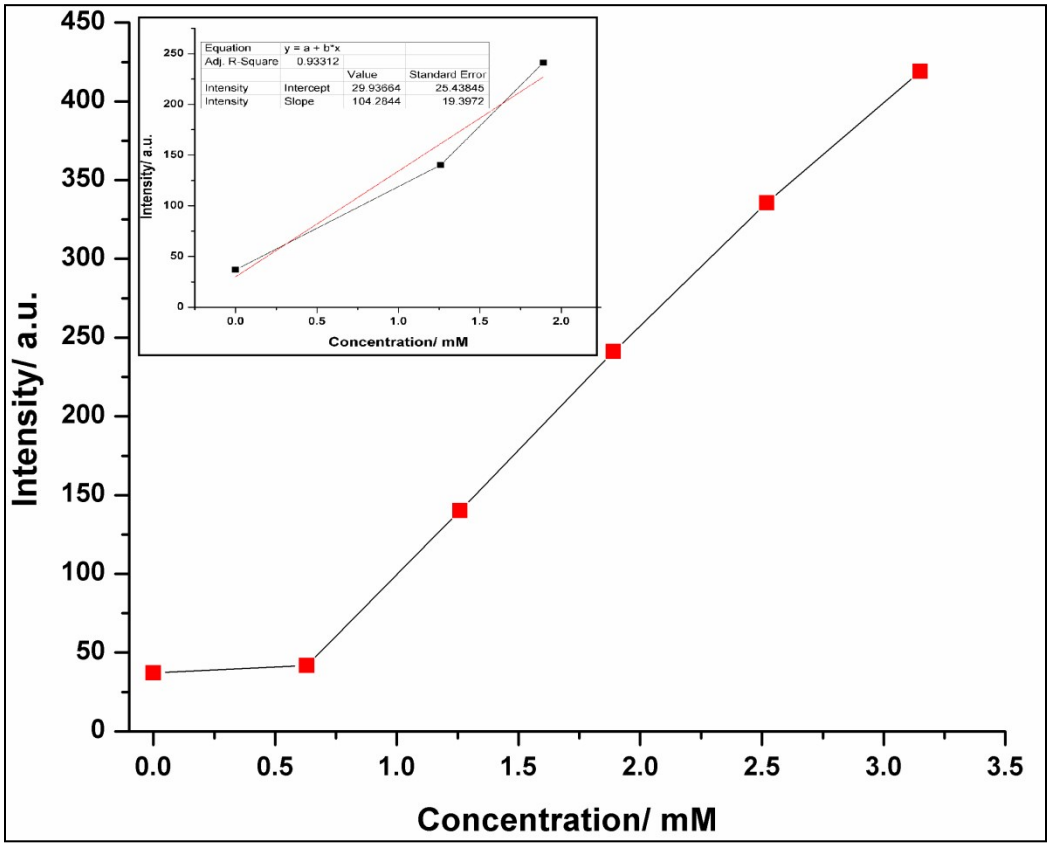


Fig. S13 Enhancement of fluorescence intensity of **2b** with increasing concentration of fluoride; Inset: the slope (m) of graph was found 104.2844 (R^2 = 0.93312).

Table S7. Standard deviation for **2b**.

Blank Reading (Only **2b**)	Fluorescence intensity
Reading 1	19.21
Reading 2	18.82
Reading 3	19.52
Standard Deviation (σ)	0.350761

Table S8. Detection limit for **2b** in case of fluoride as an analyte.

Slope from graph (m)	104.2844	mM^{-1}
Detection limit (3σ/m)	0.0101	mM
Limit of detection (LOD)	0.19	ppm

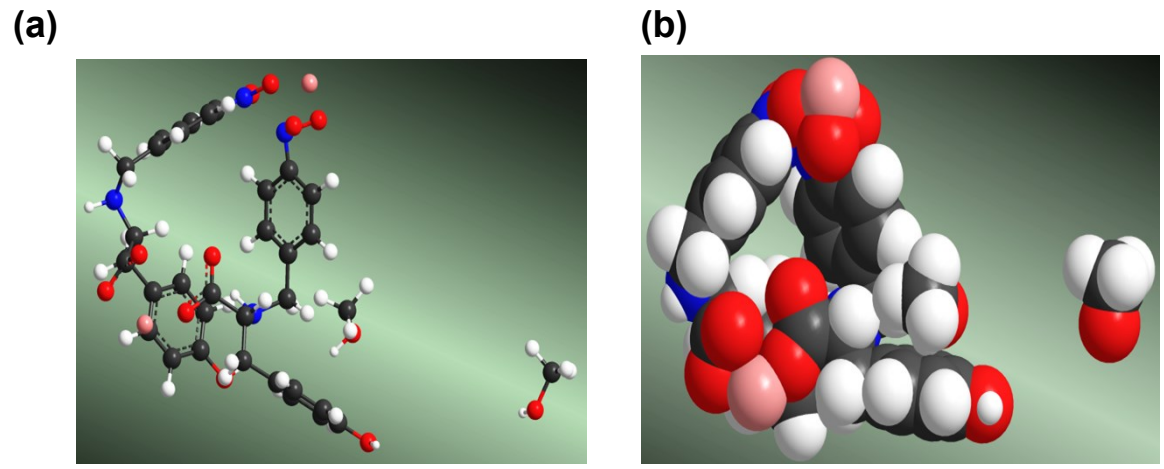


Fig. S14 Energy minimized structure of NaHTyr-4-nitro in methanol (**1a**) using MM2 calculation (Chem3D) a) ball and stick model b) spacefill model.

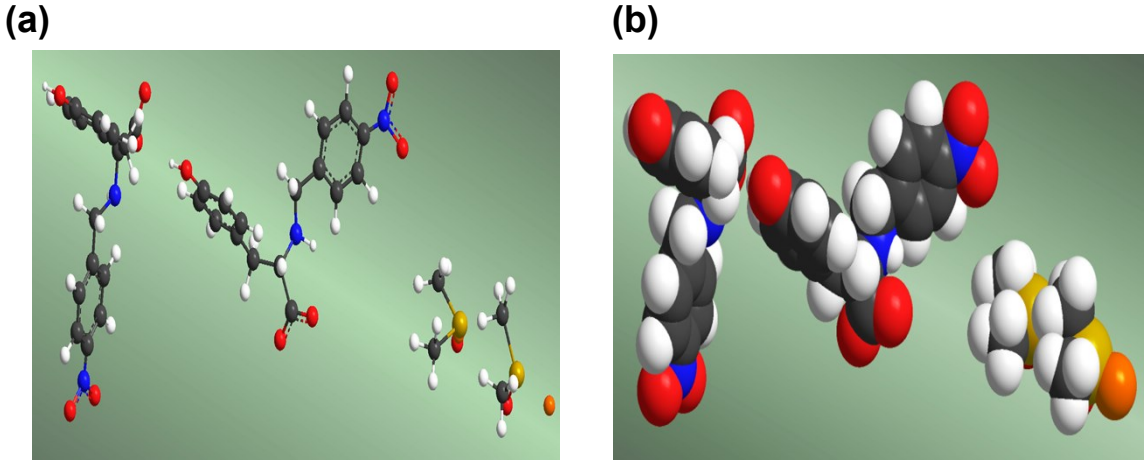
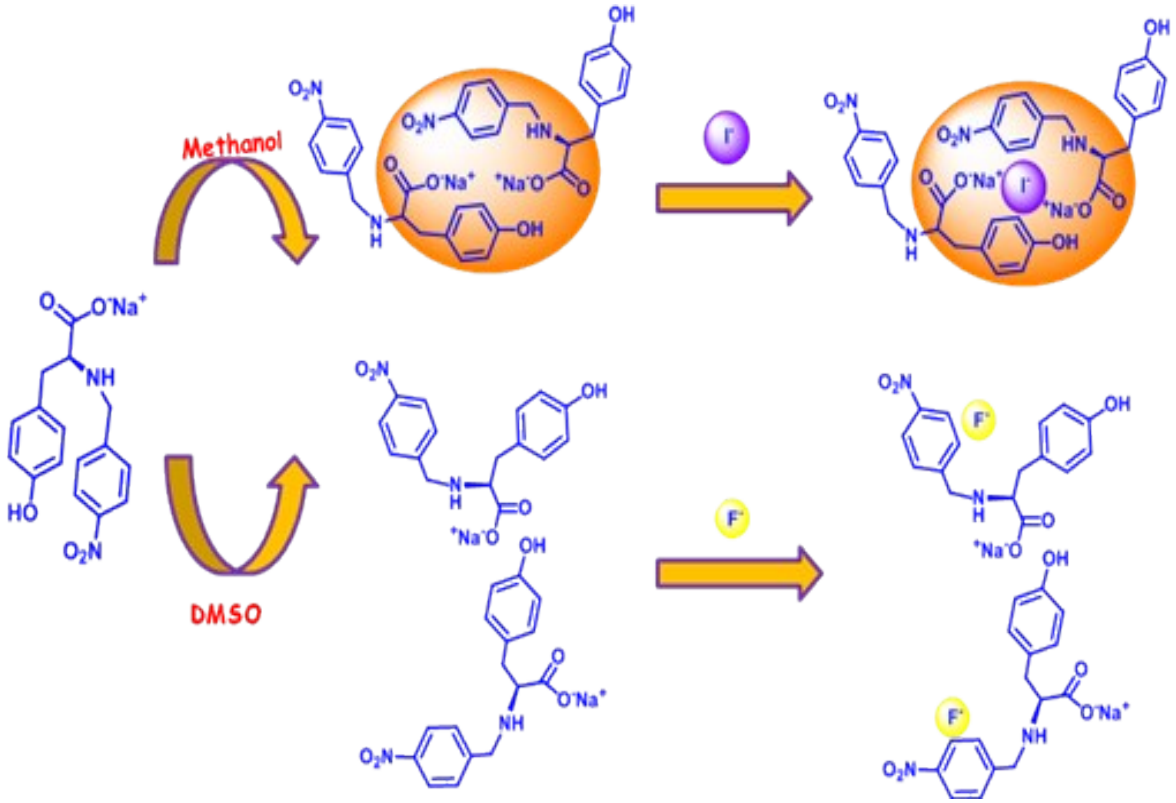


Fig. S15 Energy minimized structure of NaHTyr-4-nitro in DMSO (**1b**) using MM2 calculation (chem3D) a) ball and stick model b) spacefill model.



Scheme S2. Mechanism of flip-flop differential halide sensing depending on the solvent.

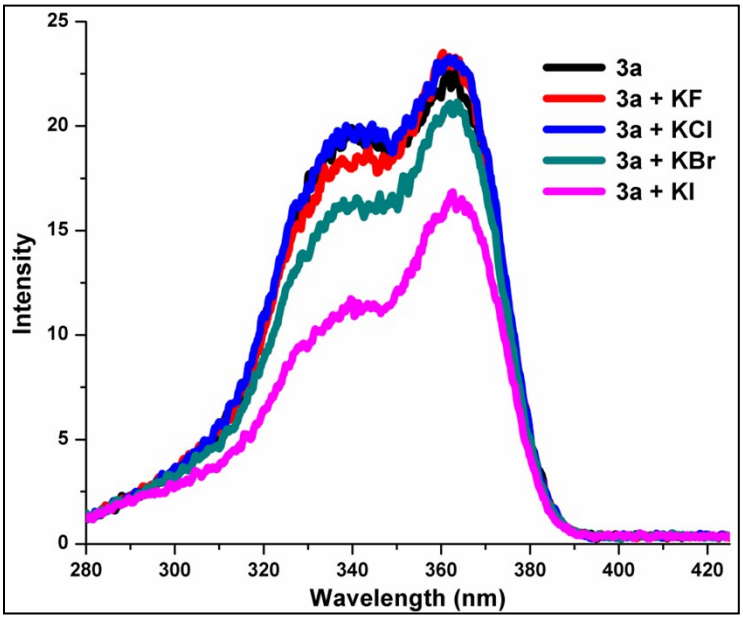


Fig. S16 Change in fluorescence intensity on addition of various anions to aqueous methanolic solution of probe **3a.**

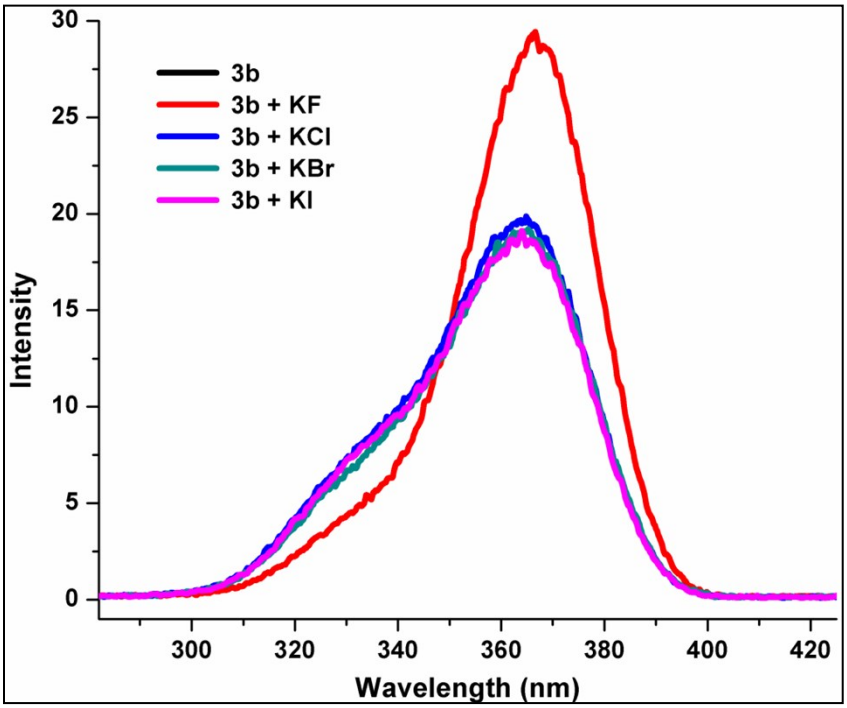


Fig. S17 Change in fluorescence intensity on addition of various anions to aqueous DMSO solution of probe **3b.**

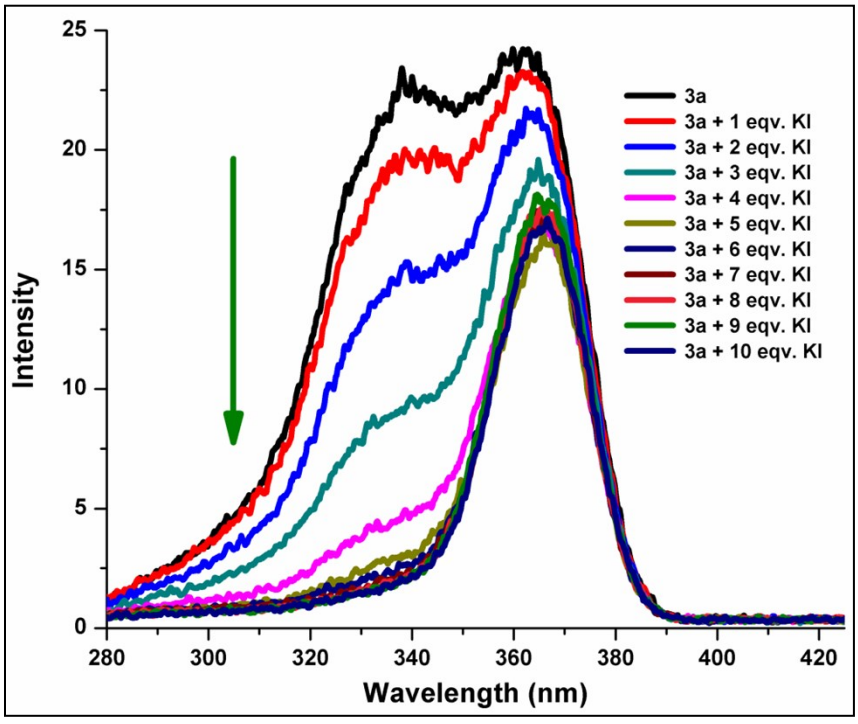


Fig. S18 Quenching of fluorescence on successive addition of iodide ions to **3a**.

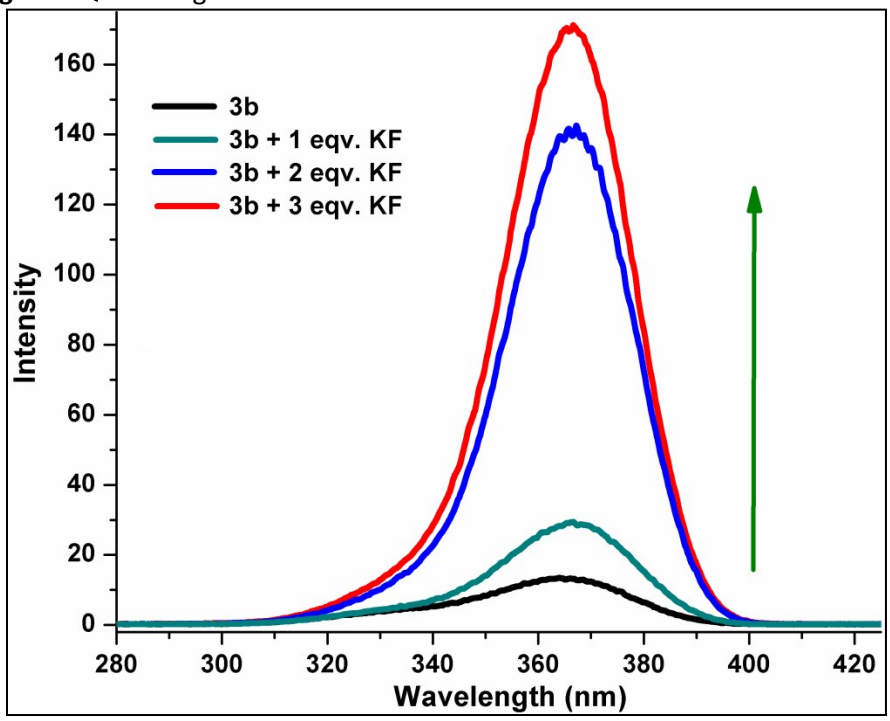


Fig. S19 Enhancement of fluorescence on successive addition of fluoride ions to **3b**.

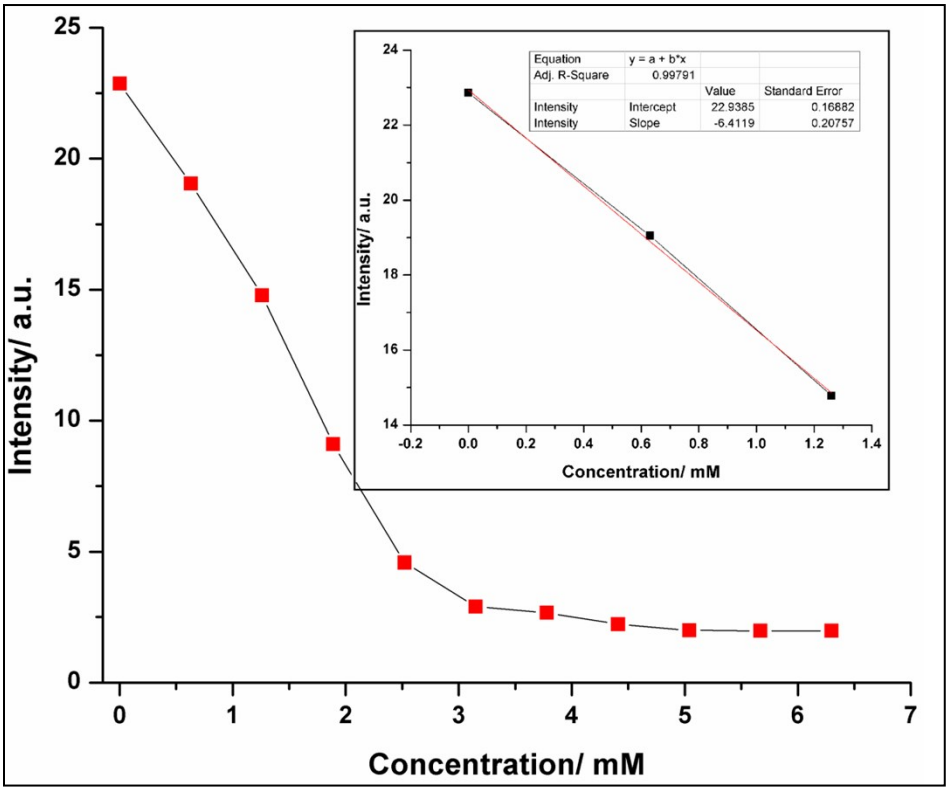


Fig. S20 Fluorescence intensity of **3a** decreases with increasing concentration of iodide, Inset: the slope (m) of graph was found to be -6.4119 (R^2 = 0.9971).

Table S9. Standard deviation for **3a.**

Blank Reading (Only **3a**)	Fluorescence intensity
Reading 1	24.012
Reading 2	23.826
Reading 3	24.222
Standard Deviation (σ)	0.198121

Table S10. Detection limit for **3a** in case of iodide as an analyte.

Slope from graph (m)	-6.4119	mM^{-1}
Detection limit (3σ/m)	0.0927	mM
Limit of detection (LOD)	11.77	ppm

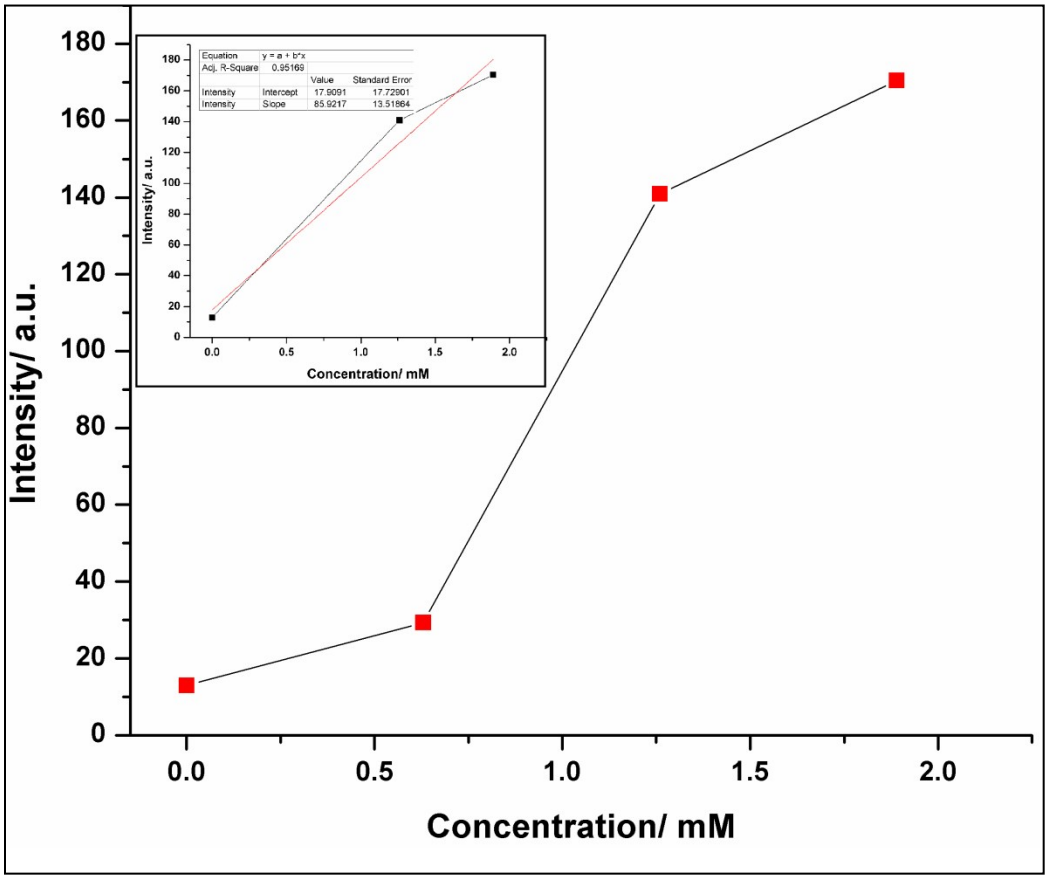


Fig. S21 Enhancement of fluorescence intensity of **3b** with increasing concentration of fluoride; Inset: the slope (m) of graph was found to be 29.7642 (R^2 = 0.95169).

Table S11. Standard deviation for **3b**.

Blank Reading (Only **3b**)	Fluorescence intensity
Reading 1	12.906
Reading 2	12.312
Reading 3	12.516
Standard Deviation (σ)	0.301815

Table S12. Detection limit for **3b** in case of fluoride as an analyte.

Slope from graph (m)	29.7642	mM^{-1}
Detection limit (3σ/m)	0.0304	mM
Limit of detection (LOD)	0.577	ppm

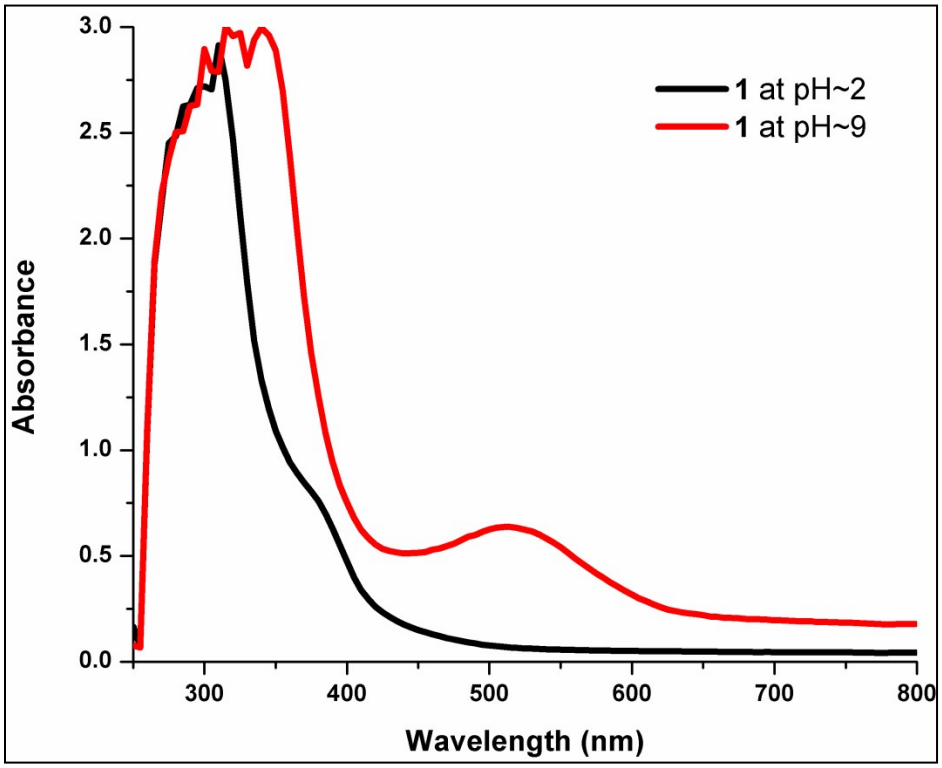


Fig. S22 Absorption spectrum of **1** (in DMSO) at pH~2 and pH~9.

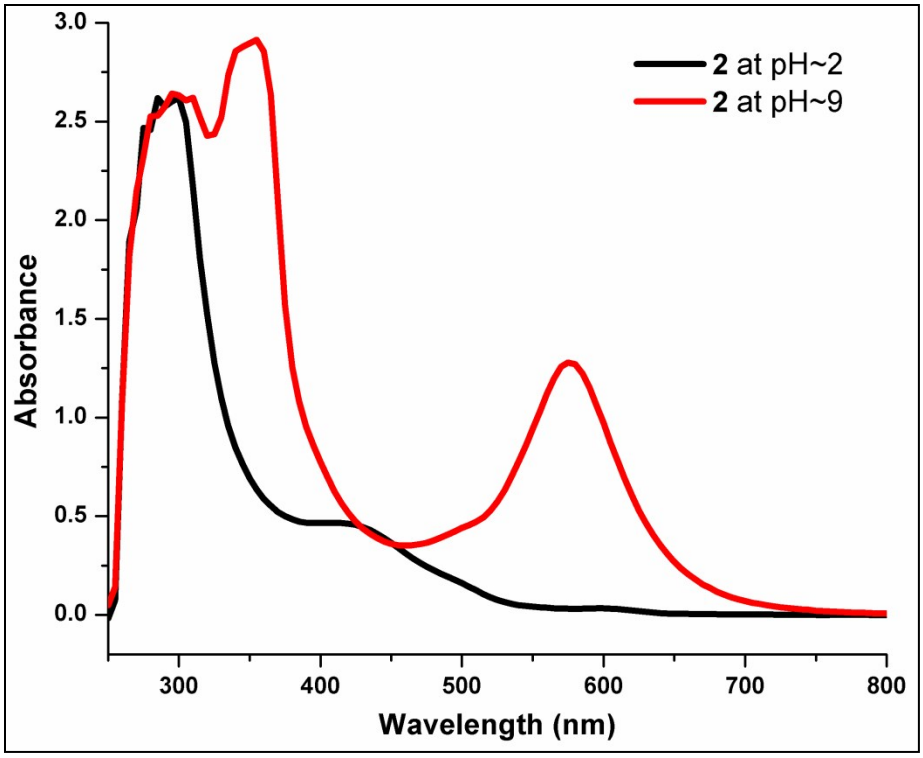


Fig. S23 Absorption spectrum of **2** (in DMSO) at pH~2 and pH~9.