Chemistry SELECT

Supporting Information

Addressing Multiple Ions Using Single Optical Probe: Multi-Color Response via Mutually Independent Sensing Pathways

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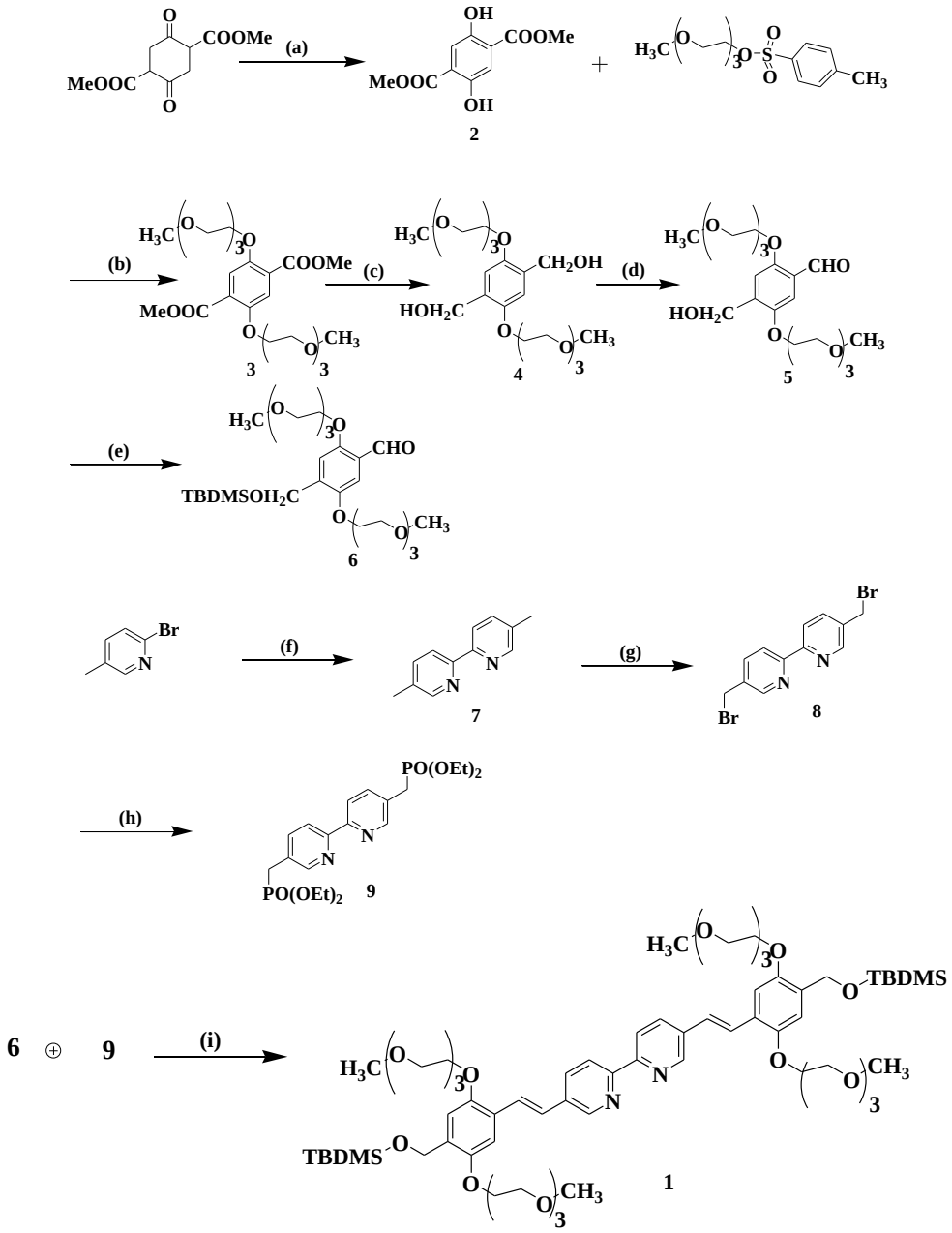
Design and Synthesis of Compound

Synthesis and characterization: Compound **2** was prepared according to a literature reported procedure using N-chlorosuccinimide as a reagent in glacial acetic acid.[S1] Compounds **3**, **4** and **5** were prepared following a reported procedure in literature.[S2] Compound **7** was synthesized by modified Ullmann coupling using palladium acetate as a catalyst.[S3] Compound **8** and **9** were synthesized according to a literature reported procedure.[S4]

Synthetic Scheme:



Reagents, conditions and yields: (a) NCS, glacial AcOH, 80 °C, 1h, 80%; **(b)** K_2CO_3, DMF, 60 °C, 2d, 68.5%; **(c)** LAH, Dry THF, reflux, 2 h, 80%; **(d)** DDQ, dry DCM, rt, 12h, 58%; **(e)** TBDMSCl, Imidazole, dry DCM, rt, 1h, 77.5%; **(f)** $Pd(OAc)_2$, TBAB, K_2CO_3, DMF/H_2O, Isopropanol, 115 °C, 45 h, 85%; (**g**) NBS, CCl_4, AIBN, 4h, reflux; (**h**) $P(OEt)_3$, 110 °C, 4h, 20%; (**i**) NaH, dry THF, rt, 10 minute, 70%.

TBDMS protected Aldehyde-Alcohol (6): To a solution of 5 (0.208 g, 0.452 mmol), Imidazole (102 mg, 0.678 mmol), DMAP (11 mg, 0.09 mmol) in Dry DCM (4 mL), TBDMSCl (102 mg, 0.676 mmol) was added at a time. The mixture was stirred for 2 hour at room temperature. The solvent was removed by rotary evaporation. The crude product was purified by column chromatography (SiO_2). The column has started with 1% MeOH/$CHCl_3$ and then polarity has increased graduliiy upto 3% MeOH/$CHCl_3$ to get the pure product (0.24 g) as a light yellow liquid: yield 92%; IR (Neat, cm^{-1}) 3421, 2928, 2880, 2860, 1678, 1612, 1450, 1423, 1364, 1259, 1110, 952, 838, 777, 674; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.13 (s, 6H), 0.97 (s, 9H), 3.38 (s, 6H), 3.54-3.64 (m, 4H), 3.66-3.75 (m, 12H), 3.82-3.3.89 (m, 4H), 4.13-4.24 (m, 4H), 4.77 (s, 2H), 7.22-7.23 (m, 2H), 10.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 25.7, 58.8, 59.9, 67.8, 68.5, 69.4, 70.2, 70.3, 70.4, 70.5, 70.6, 70.8, 71.6, 71.8, 108.2, 111.6, 123.2, 139.6, 149.0, 156.3, 189.1; HRMS: *m/z* calcd. for $C_{28}H_{50}O_{10}SiNa$ $[M+Na]^+$: 597.3071, found: 597.3070.

BiPY-Ox-OPV-TBDMS (1): To a solution of 6 (35 mg, 0.077 mmol) and 9 (88 mg, 0.15 mmol) in dry THF (4 mL), NaH (27 mg, 1.12 mmol) was added at room temperature and stirred for 10 min. Water (few drops) was then added to the reaction mixture. The solvent was removed by high vaccum. The crude product was purified by column chromatography (neutral alumina) using 80% EtOAc/$CHCl_3$. 70 mg of pure product was isolated as a light yellow oil: yield 70%; IR (Neat, cm^{-1}) 3409, 2926, 2857, 1646, 1458, 1419, 1375, 1252, 1202, 1109, 1021, 837, 776, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (s, 6H), 3.34 (s, 6H), 3.48-3.53 (m, 8H), 3.60-3.76 (m, 24H), 3.82-3.89 (m, 8H), 4.15 (s, 8H), 4.74 (s, 4H), 7.07-7.12 (m, 6H), 7.57 (d, J = 16.4 Hz, 2H), 7.96 (d, J = 8.4 Hz, 2H), 8.37 (d, J = 8.4 Hz, 2H), 8.74 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3, 25.9, 58.8, 58.9, 59.9, 68.2, 68.8, 69.7, 69.8, 70.5, 70.6, 70.7, 70.8, 71.7, 71.8, 76.7, 76.9, 77.3, 109.2, 112.2, 120.7, 124.3, 124.5, 124.7, 131.9, 133.2, 133.5, 148.0, 149.4, 150.9, 154.3; HRMS: *m/z* calcd. for $C_{68}H_{108}N_2O_{18}Si_2Na$ $[M+Na]^+$: 1319.7033, found: 1319.7031.

References:

S1. L. Hintermann, K. Suzuki, *Synthesis* **2008**, 2303-2306.

S2. G. Fabbirini, R. Riccó, E. Menna, M. Maggini, V. Amendola, M. Garbin, M. Villano, M. Meneghetti, *Phys. Chem. Chem. Phys.*, **2007**, *9*, 616-621.

S3. J. Hassan, V. Penalva, L. Lavenot, C. Gozzi, M. Lemaire, *Tetrahedron* **1998**, *54*, 13793-13804.

S4. A. E. Dennis, R. C. Smith, *Chem. Comm.* **2007,** 4641-4643.

Experimental Section

Material and methods: All reagents, starting materials, and silica gel for TLC and column chromatography were obtained from the best-known commercial sources and were used without further purification. Solvents were distilled and dried prior to use. FTIR spectra were recorded on a Perkin-Elmer FT-IR Spectrum BX system and were reported in wave numbers (cm^{-1}). ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker Advance DRX 400 spectrometer operating at 400 and 100 MHz for ^{1}H and ^{13}C NMR spectroscopy, respectively. Chemical shifts were reported in ppm downfield from the internal standard, tetramethylsilane (TMS). Mass spectra were recorded on Micro mass Q-TOF Micro TM spectrometer.

Spectroscopic studies: The UV−vis and fluorescence spectra were recorded on a Shimadzu model 2100 UV-vis spectrometer and Cary Eclipse spectrofluorimeter respectively. Compound **1** was dissolved in appropriate amount in DMSO to prepare the stock solutions (1×10^{-3} M). Nitrate salts of different metal ions and potassium salts of different anions were used for sensing studies. To monitored the effect of pH, sensing experiment were performed in buffered media of different pH (HCO_2Na/ HCl buffer for pH 2-4, CH_3CO_2Na/ HCl buffer for pH 4.5-6.5, PBS buffer for pH 7-9 and $Na_2B_4O_7 \cdot 10H_2O$/NaOH for pH 10-12).

Fluorescence decay experiment: Fluorescence lifetime values were measured by using a time-correlated single photon counting fluorimeter (Horiba Jobin Yvon). The system was excited with 390 nm nano LED of Horiba - Jobin Yvon with a pulse duration of 1.2 ns (slit width of 2/2, λ_{em} 515 nm for **1** and **1** + Cu^{2+} and 570 nm for **1** + Zn^{2+}). Average fluorescence lifetimes (ι_{av}) for the exponential iterative fitting were calculated from the decay times (ι_i) and the relative amplitudes (a_i) using the following relation

$$\iota_{av} = (a_1\iota_1^2 + a_2\iota_2^2 + a_2\iota_2^2) / (a_1\iota_1 + a_2\iota_2 + a_3\iota_3)$$

Where a_1, a_2 and a_3 are the relative amplitudes and ι_1, ι_2, and ι_3 are the lifetime values, respectively. For data fitting, a DAS6 analysis software version 6.2 was used.

Detection limit determination: The method used for the calculation of the detection limit is known as the blank variability method. In this method, the calibration curve was prepared by gradual addition of the analyte to a fixed concentration of the ligand by fluorescence titration.

From the equation obtained from the calibration plot, the added analyte concentrations were calculated. Then another calibration curve was drawn between the C_{real} (added analyte) vs. $C_{calc.}$ (calculated amount of analyte). This afforded a value of the slope (b).

The signal of the ligand in absence of the added analyte was taken as blank reading. 10 replicates of the blank were measured. The standard deviation from the blank readings was calculated by fitting the absorbance/fluorescence reading into the equation obtained from the first calibration curve (titration spectra). Using this standard deviation value, we calculated decision limit by this following equation.

$L_C = t_C \times s \times (1 + 1/N)^{1/2}$……..…….... (1)

where, N = the number of blank replicates taken; the value of t_c for 10 blank readings is 1.833; and s = the standard deviation value.

The detection limit (LD) was calculated as the double of the decision limit obtained,

$L_D = 2\ L_c$ ……. (2)

In concentration term, the detection limit appeared as,

$x_D = 2 \times C = 2\ L_C / b$ …… (3)

where, b = slope of the second calibration curve (Creal vs. Ccalc.).

Determination of Fluorescence Quantum Yield in Solution Fluorescence quantum yield was determined in spectroscopic grade in water medium using optically matching solutions of quinine sulfate (Φ_r = 0.546 in 1N H_2SO_4 at 25) as standard at an excitation wavelength of 364 nm. The quantum yield is calculated using the following equation,

$\Phi_s = \Phi_r (A_r F_s / A_s F_r)(\eta_s^2 / \eta_r^2)$

Where, A_s and A_r are the absorbance of the sample and reference solutions, respectively, at the same excitation wavelength, F_s and F_r are the corresponding relative integrated fluorescence intensities, and η is the refractive index of the solvents.

Characterization of Compound Involved in Present Study

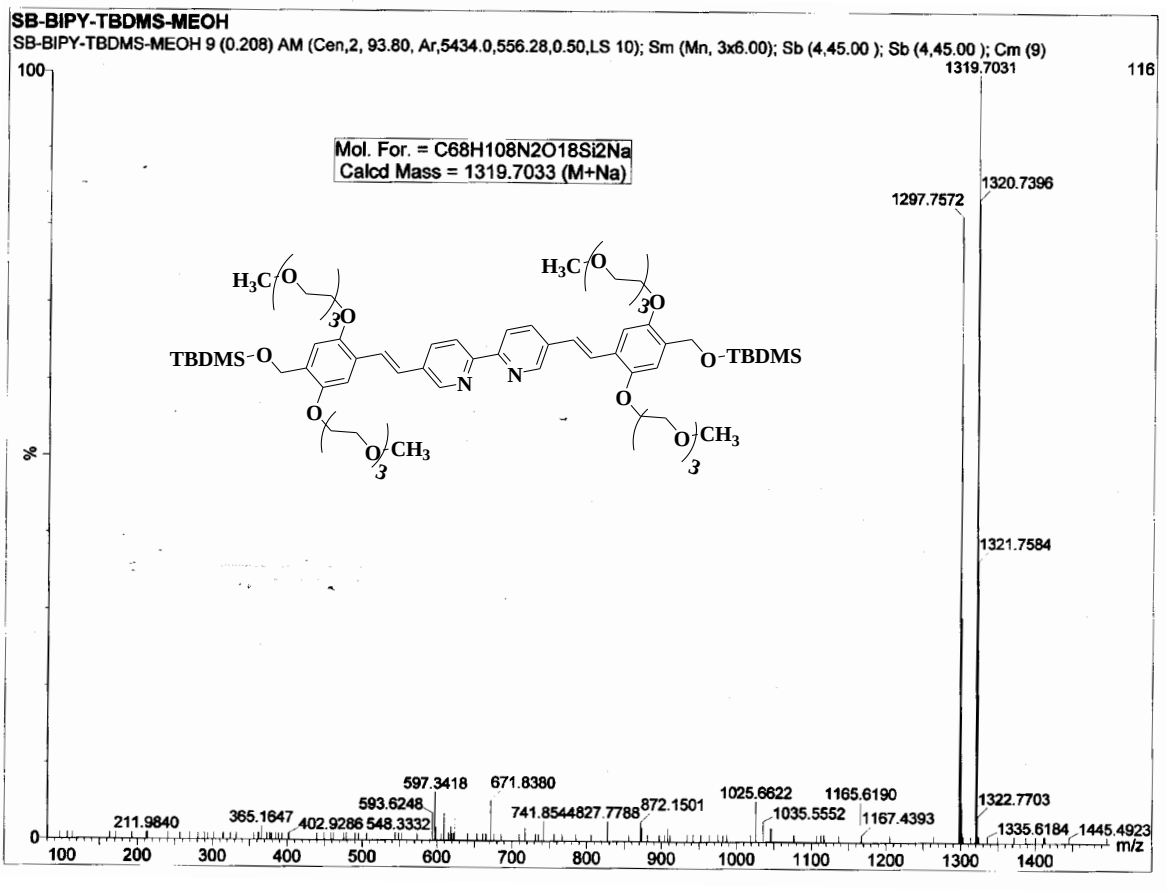


Fig S1. HRMS mass spectrum of compound **1**.

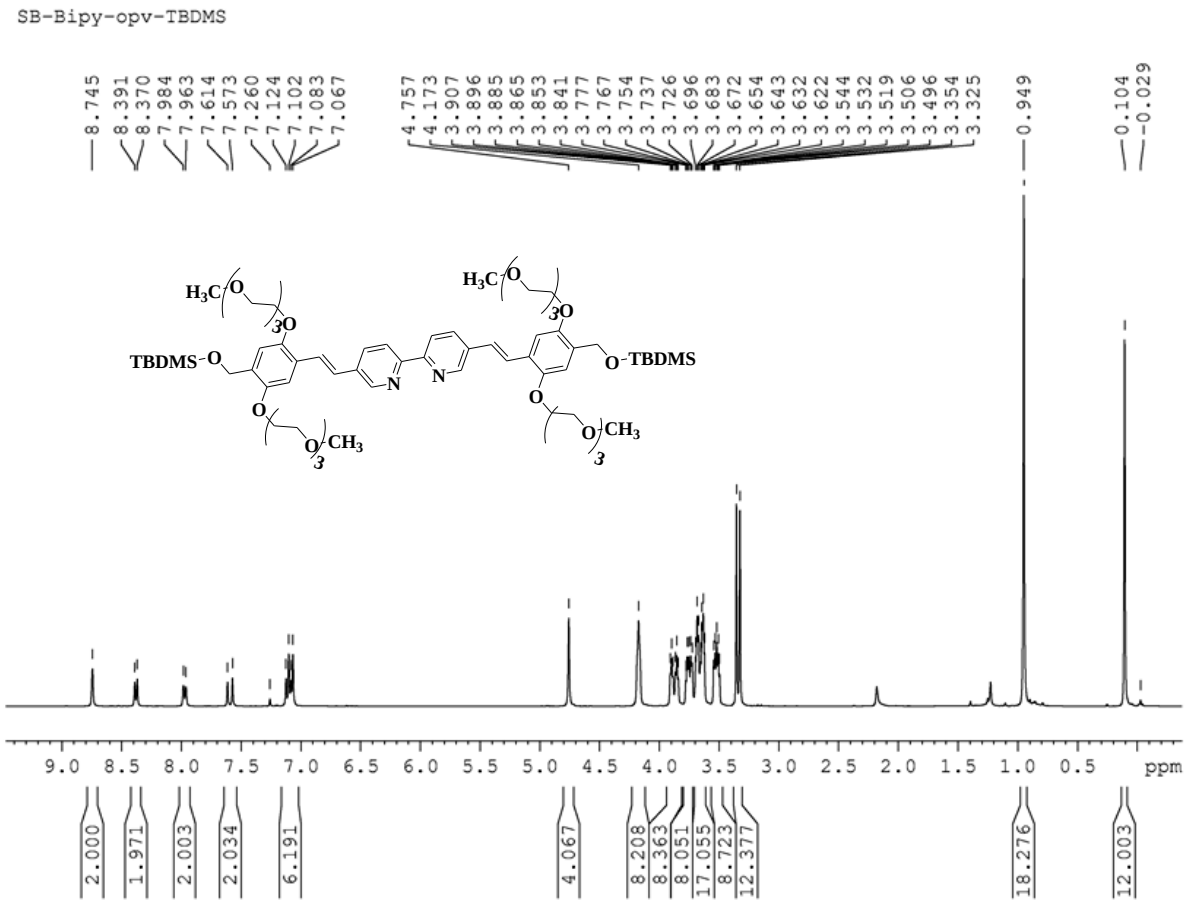


Fig S2. ^{1}H-NMR spectrum of compound **1** in $CDCl_3$ medium.

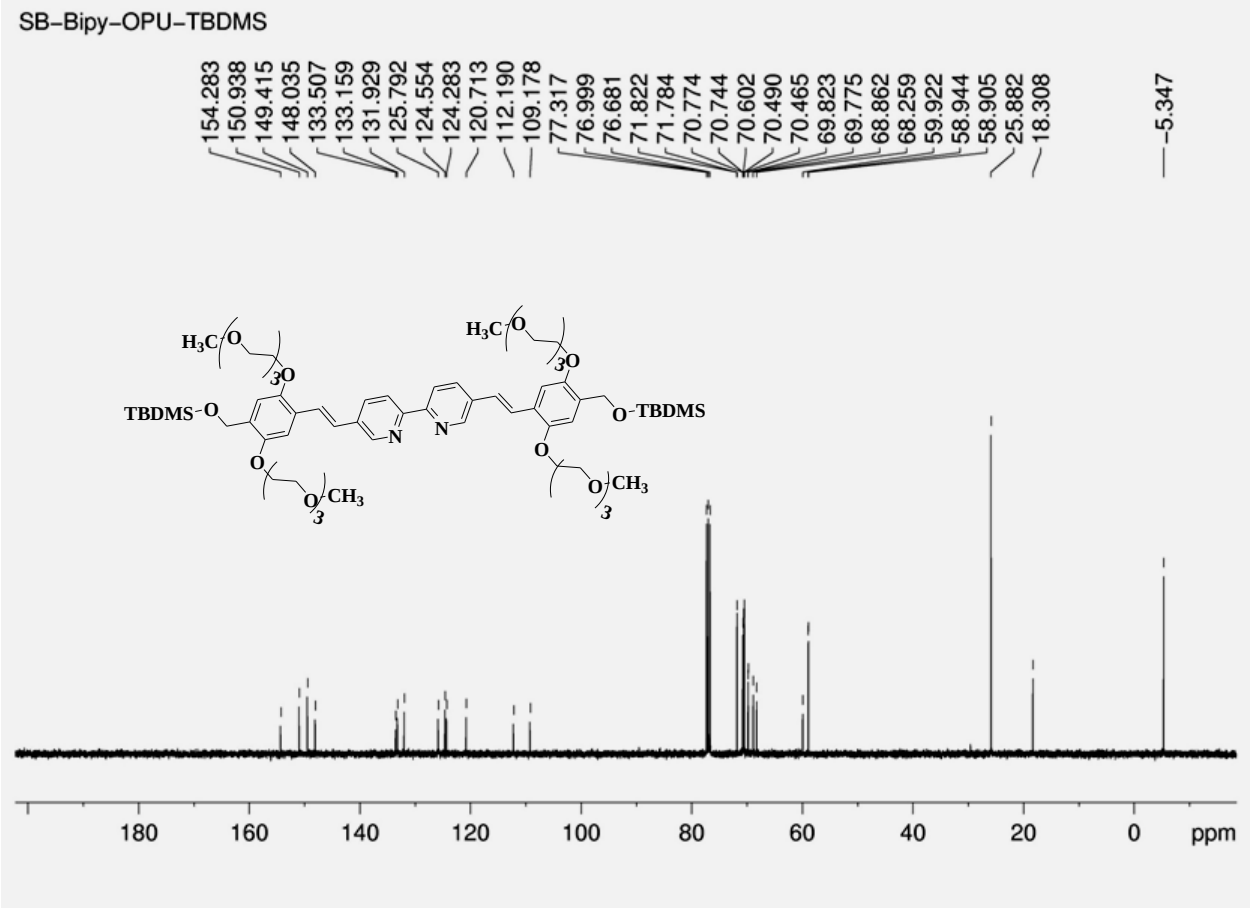


Fig S3. ^{13}C-NMR spectrum of compound **1** in $CDCl_3$ medium.

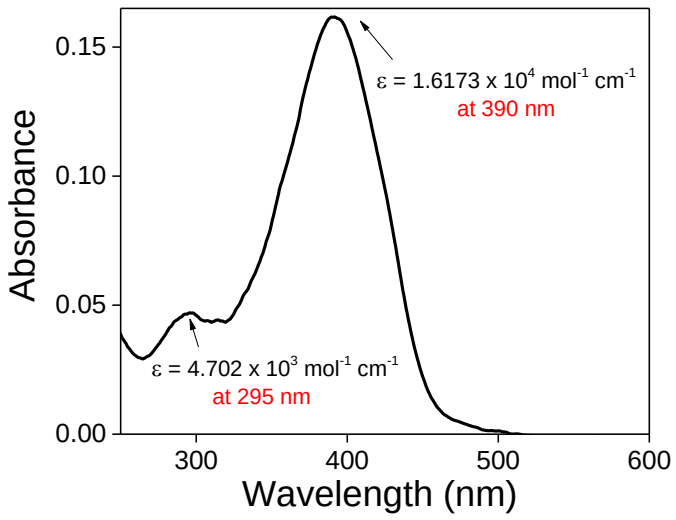


Fig S4. Calculation of absorption coefficient of **1** (10 µM) in PBS buffer medium (pH 7.4).

Additional Spectroscopic Studies

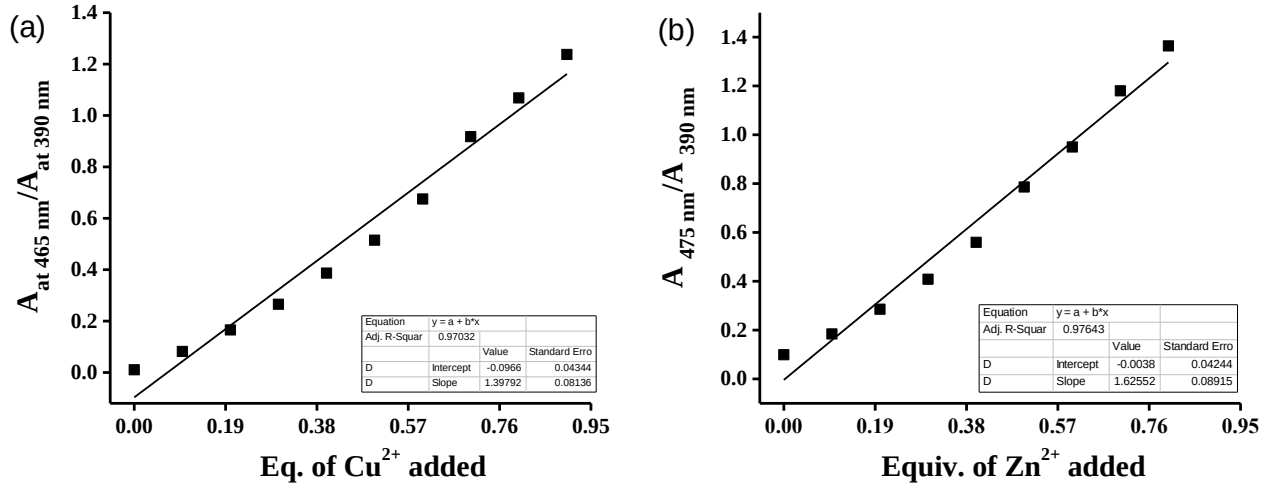


Fig S5. (a) Plot of the absorbance ratio of **1** (10 μM) at 465 and 390 nm with added Cu^{2+} in PBS buffer (pH 7.4). (b) Plot of the absorbance ratio of **1** (10 μM) at 475 and 390 nm with added Zn^{2+}.

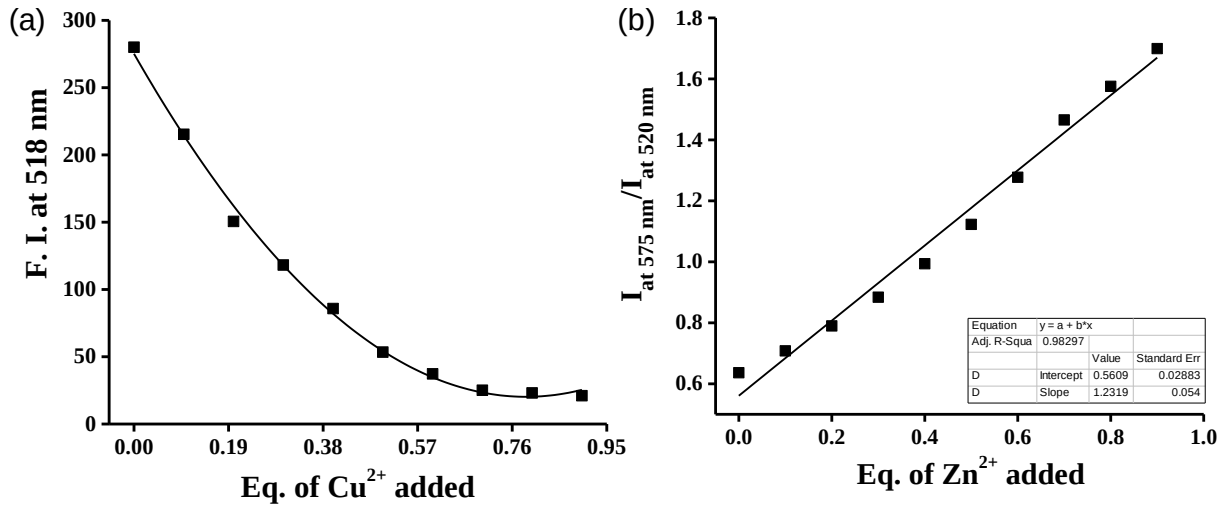


Fig. S6 (a) Plot of fluorescence intensity of **1** (5 μM) in PBS buffer (pH 7.4) (λex. = 390 nm) at 518 nm with added Cu^{2+}. (b) Plot of the fluorescence intensity ratio **1** (5 μM) in PBS buffer (pH 7.4) (λex. = 390 nm) at 575 and 520 nm with added Zn^{2+}.

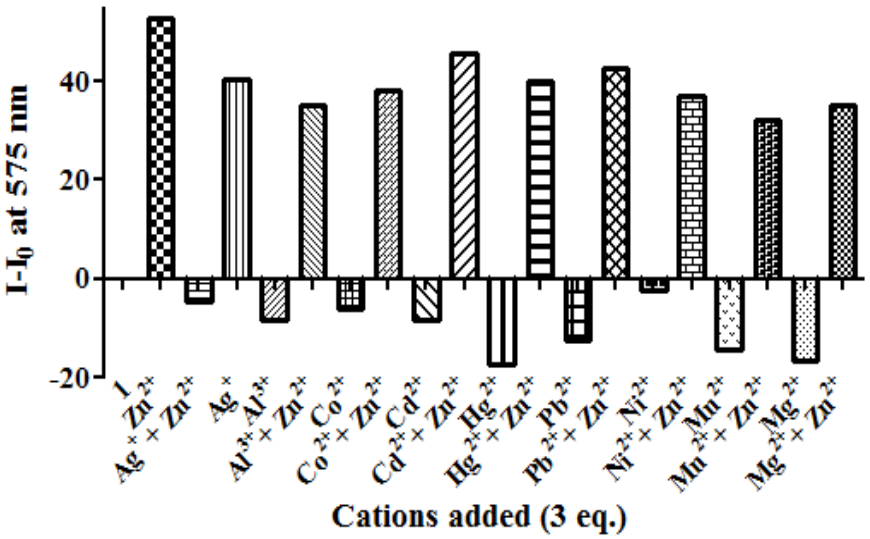


Fig. S7 Plot of change in fluorescence (at 575 nm) of the sensor **1** (10 μM) (λ_{ex} = 390 nm) with Zn^{2+} (1 equiv.) in presence of an excess of other cations (3 equiv.) in PBS buffer (pH 7.4).

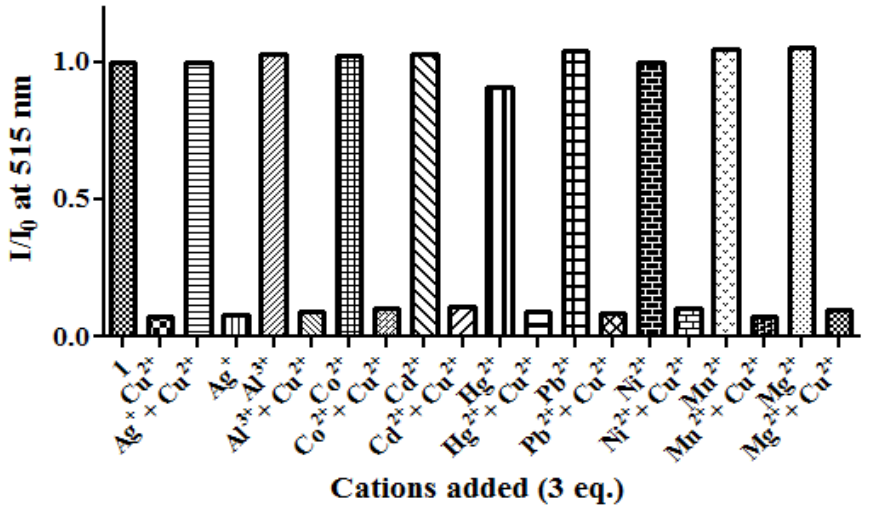


Fig. S8 Plot of change in fluorescence (at 515 nm) of the sensor **1** (10 μM) (λ_{ex} = 390 nm) with Cu^{2+} (1 equiv.) in presence of an excess of other cations (3 equiv.) in PBS buffer (pH 7.4).

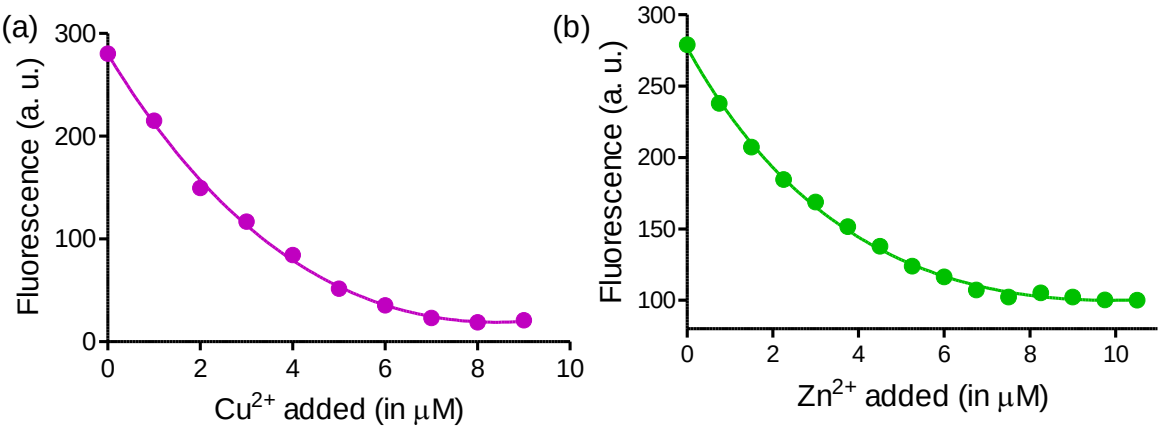


Fig. S9 (a) Calculation of binding constant of **1** with Cu^{2+} using non-linear regressive analysis (total one site nonspecific binding). (b) Calculation of binding constant of **1** with Zn^{2+} using non-linear regressive analysis (total one site nonspecific binding).

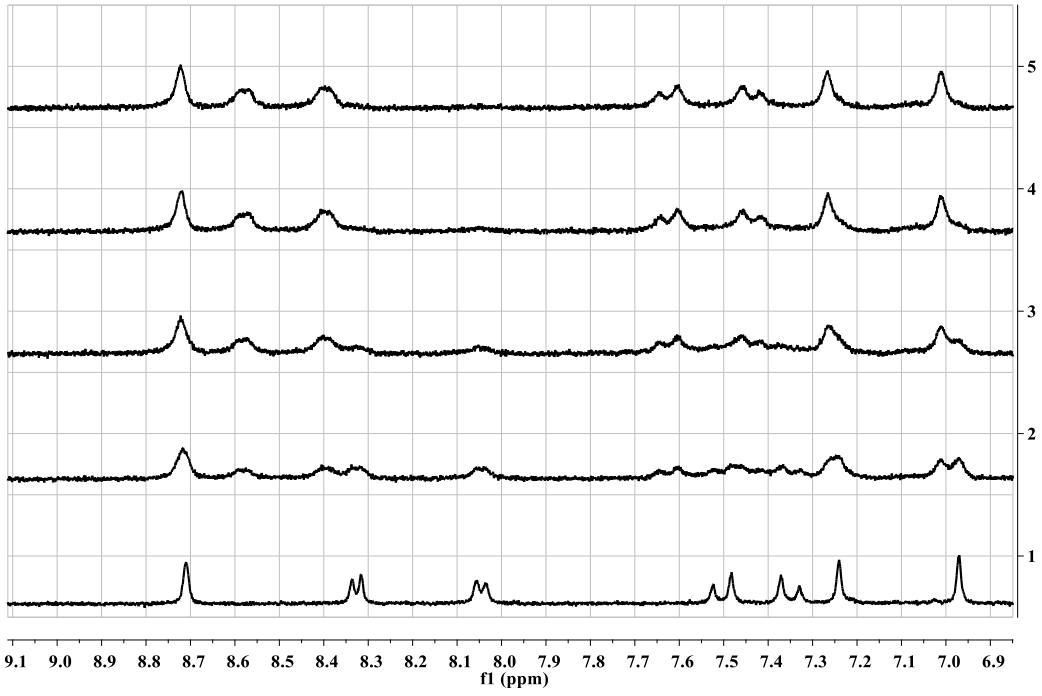


Fig. S10 Partial^{1}H-NMR (400 MHz) spectra of **1** (10 mM) in DMSO-d_6- D_2O (7:3) in the presence of [0, 0.25, 0.5, 0.75, 1.0 equiv. (1-5)] of Zn^{2+} (in D_2O).

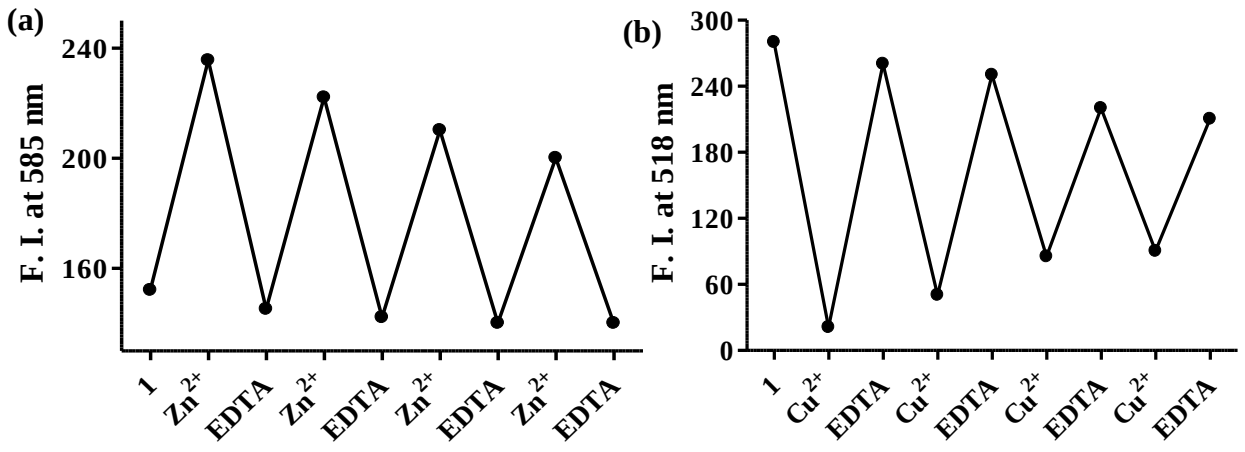


Fig. S11 (a) Recovery of the molecular absorbance at 585 nm after addition of EDTA (1 equiv.) after each addition of 1 equiv. of Zn^{2+} to the sensor **1** (5 µM). (b) Recovery of the molecular absorbance at 515 nm after addition of EDTA (1 equiv.) after each addition of 1 equiv. of Cu^{2+} to the sensor **1** (5 µM).

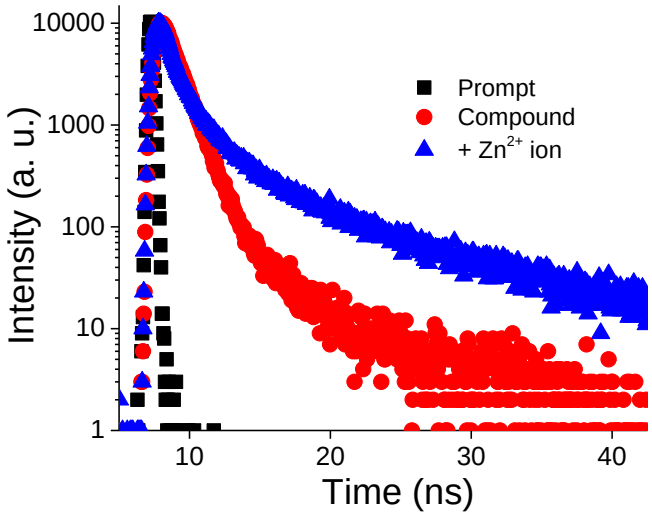


Fig. S12 Fluorescence lifetime of **1** (5 µM, λ_{ex} = 390 nm) in presence of Zn^{2+} (5 µM) at pH 7.4 in PBS buffer.

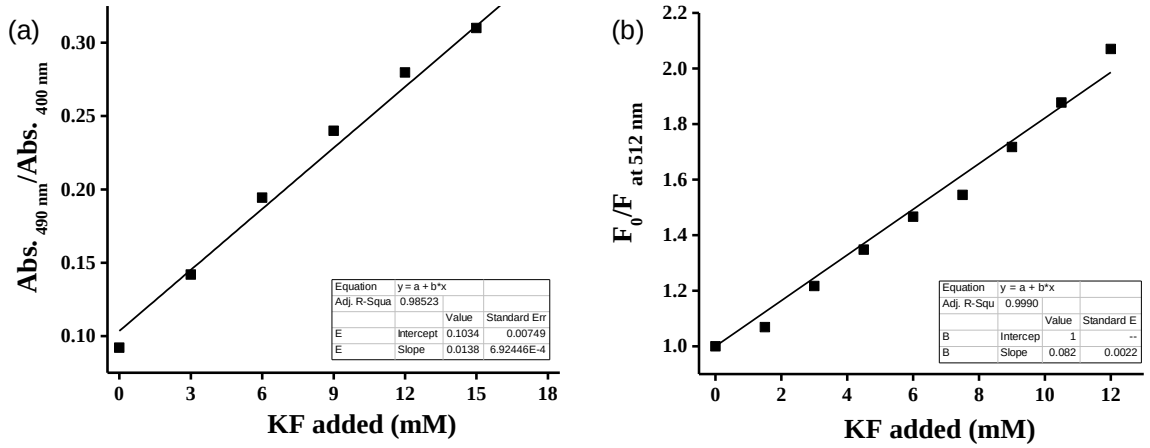


Fig. S13 (a) Calculation of binding constant with histamine using Benesi-Hildebrand method for 1:2 binding. (b) Stern-Volmer plot of **1** in presence KF. [**1**] = 10 μM in PBS buffer (pH 7.4). (λ_{ex} =390 nm).

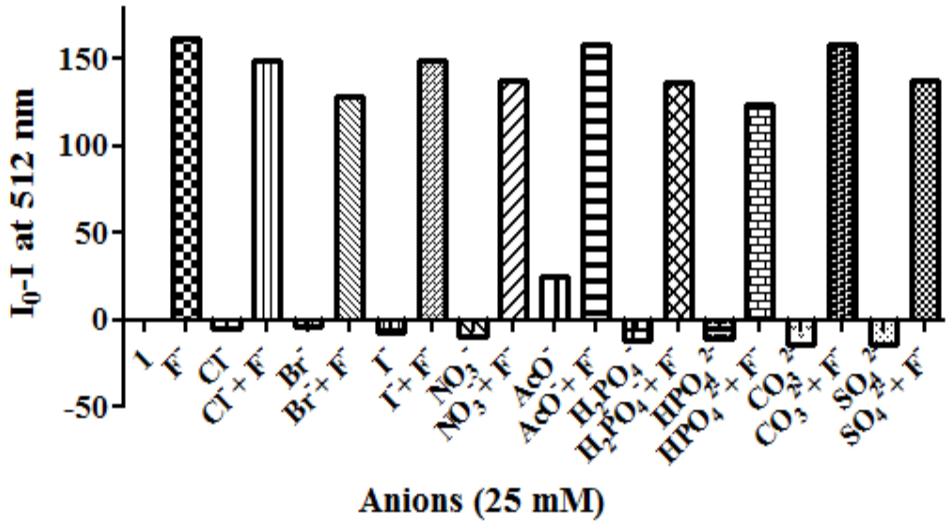


Fig. S14 Plot of change in fluorescence (at 512 nm) of the sensor **1** (5 μM) (λ_{ex} = 390 nm) with KF (15 mM) in presence of an excess of other anions (25 mM) in PBS buffer (pH 7.4).

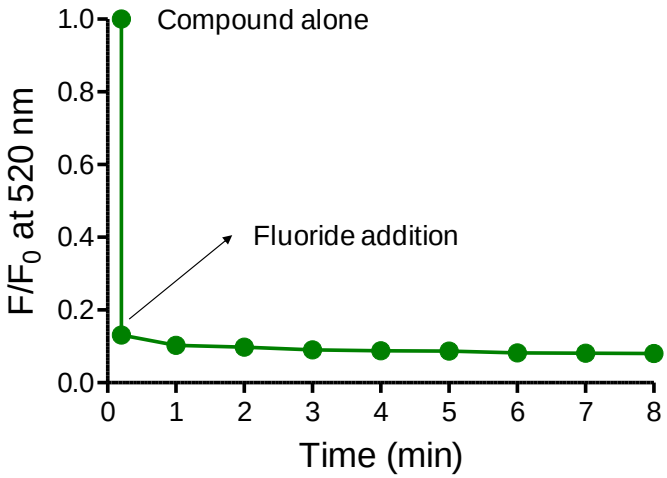


Fig. S15 Time-Course Study of interaction of **1** with KF. [**1**] = 10 μM in PBS buffer (pH 7.4). (λ_{ex} =390 nm, monitored at 520 nm).

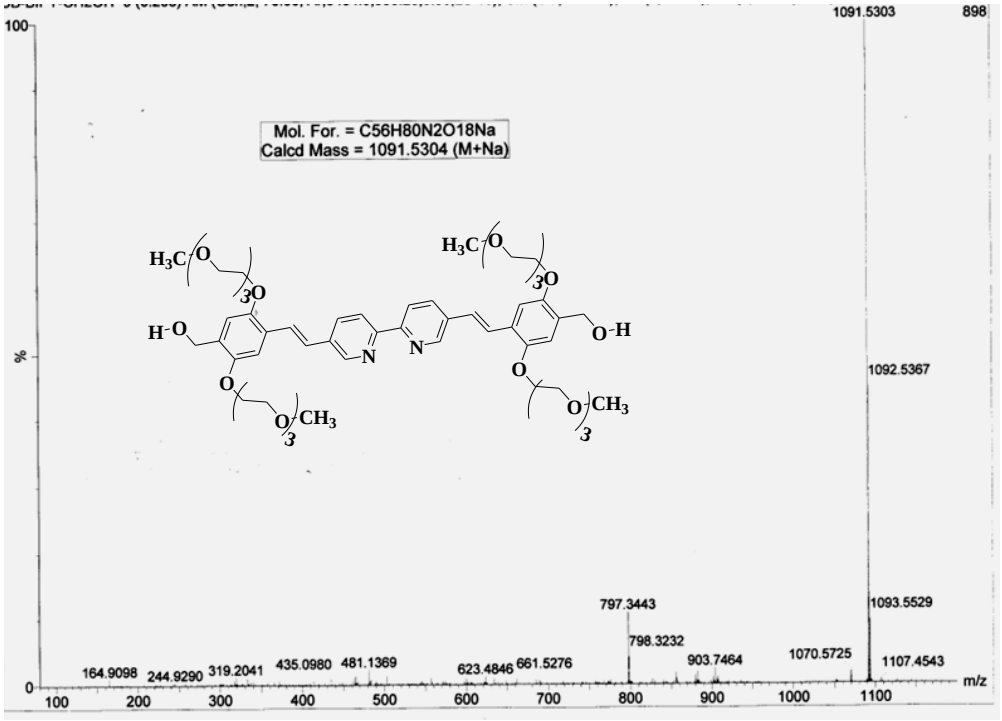


Fig. S16 ESI-MS mass spectrum of compound in presence of fluoride ion shows desilylated adduct.

	Zn^{2+} (in ppm) (present method)	Zn^{2+} (in ppm) (AAS method)	Av. Recovery values (%)	RSD (%)
In Tap water	0.53 ± 0.01	0.5	106.0	2.71
	1.05 ± 0.05	1	105.0	1.16
	1.48 ± 0.02	1.5	98.7	1.80
In Pond water	0.51 ± 0.03	0.5	102.0	2.03
	1.03 ± 0.02	1	103.0	3.51
	1.52 ± 0.02	1.5	101.3	3.02
In Sea water	0.48 ± 0.01	0.5	96.0	2.16
	0.98 ± 0.04	1	98.0	2.38
	1.47 ± 0.03	1.5	98.0	1.82

Table S1. Estimation of Zn^{2+} (using emission change at 570 nm) in different natural water samples

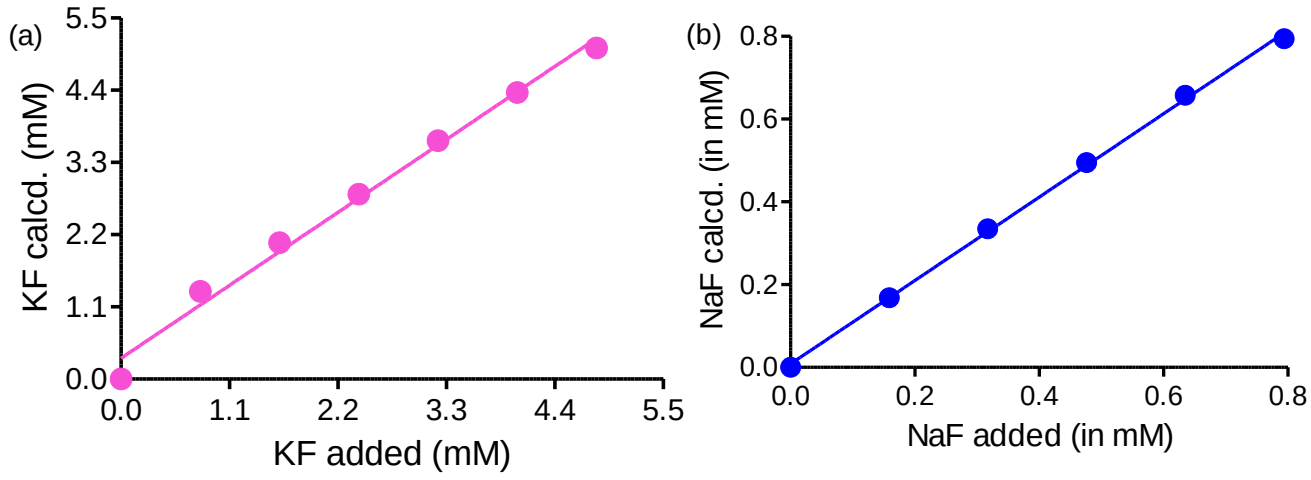


Fig. S17 (a) Recovery plot shows quantitative estimation of NaF in mouth wash sample (based on fluorescence change at 510 nm band). (b) Recovery plot shows quantitative estimation of NaF in toothpaste sample (based on fluorescence change at 510 nm band).

Protocol for estimating fluoride ion in real-life samples. The mouth wash samples were diluted with pH 7.4 HEPES buffer and directly used for analysis. On the other hand, the toothpaste sample was dried overnight in oven (Temperature ~ 90 ºC). to remove the water. Subsequently, the powdered sample was weighed different amounts (5 samples; 20, 40, 60, 80 and 100 mg) in small vials and mixed with 3 mL of water in each case. After that, the solutions were sonicated at 50 ºC for 15 minute and equilibrated for 2 hours at room temperature. Then they were centrifuged at 1000 rpm and filtered to get clear solution. After that, the solutions were treated with the probe solution and corresponding emission changes were recorded at 510 nm band.

Conc of NaF (mM)	Conc of NaF (mM) estimated by present method			Average value	Recovery (%)	% RSD
0	0	0	0	0	0	0
0.8	0.92	0.85	0.87	0.88	110	4.10
1.6	1.54	1.52	1.50	1.52	95.0	1.32
2.4	2.32	2.35	2.42	2.36	98.5	2.17
3.2	3.33	3.27	3.31	3.30	103.2	0.93
4.0	3.94	4.02	4.10	4.02	100.5	1.99
4.8	4.85	4.94	4.92	4.90	102.1	0.96

Table S2. Estimation of NaF (using emission change at 510 nm) in a mouth wash sample.

Conc of NaF (mM)	Conc of NaF (mM) estimated by present method			Average value	Recovery (%)	% RSD
0.000	0.0000	0.000	0.00	0	0	0
0.159	0.1620	0.175	0.170	0.166	104.4	2.44
0.317	0.3250	0.345	0.336	0.332	104.7	1.83
0.476	0.4870	0.503	0.492	0.494	103.8	1.66
0.635	0.6430	0.672	0.658	0.651	102.5	1.16
0.794	0.8060	0.783	0.814	0.801	100.8	2.01

Table S3. Estimation of NaF (using emission change at 510 nm) in a mouth wash sample.