

A Series of Polyamide Receptor Based PET Fluorescent Sensor Molecules: Positively Cooperative Hg²⁺ Ion Binding with High Sensitivity

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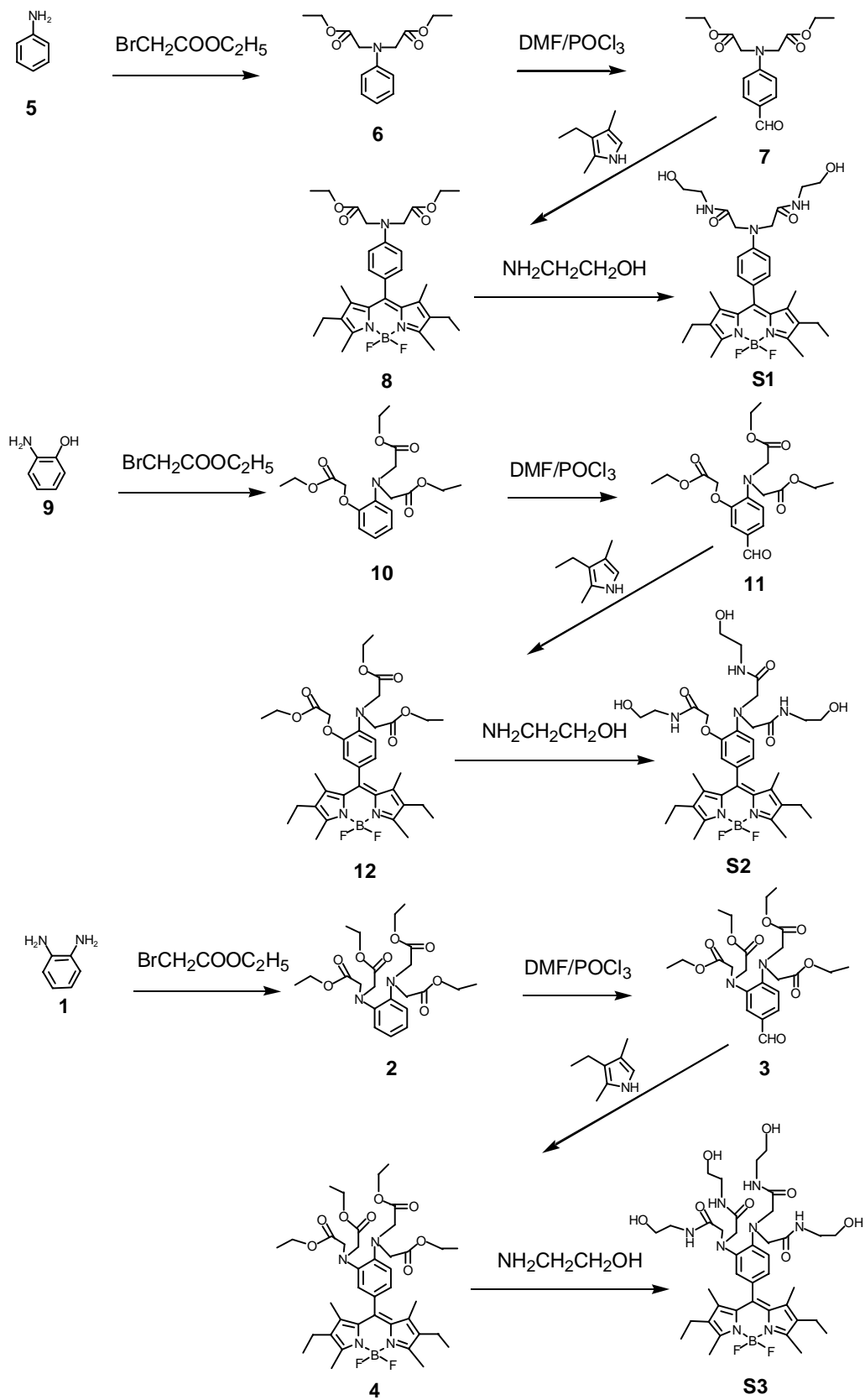
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***N,N,N',N'*-tetra{(2-hydroxyethyl)carbamoylmethyl}-*o*-phenylenediamine (2).**

A solution of **1** (4.4 g, 40.7 mmol), ethyl bromoacetate (26.8 mL, 241 mmol), sodium iodide (5.1 g, 34 mmol) and diisopropylethylamine (33.3 mL, 200 mmol) in 40 mL acetonitrile was refluxed under nitrogen for 7 hours, then cooled and poured into 200 mL water. The resulting mixture was extracted with dichloromethane (3×150 mL). The extract was dried over sodium sulfate and was concentrated to give a brown oil, which was purified by flash chromatography using hexane/ethyl acetate (7: 3, v/v) as eluant. The product was added 45 mL ethanol and was kept in the refrigerator to give 8.3 g (45%) of **2** as a white solid: m.p. 61.3-63.7 °C; ¹H NMR (CDCl₃) δ 7.03-7.06 (m, 2 H), 6.93-6.96 (m, 2 H), 4.30 (s, 8 H), 4.11 (q, *J* = 7.2 Hz, 8 H), 1.20 (t, *J* = 7.2 Hz, 12 H); MS (APCI) Calcd for ([M+H])⁺, 453; Found, 453.

4-Formyl-*N,N,N',N'*-tetra{(2-hydroxyethyl)carbamoylmethyl}-1,2-phenylene-diamine (3). 0.452 g of **2** (1 mmol) was dissolved with stirring in 10 mL dry DMF containing 2 mL dry pyridine, the mixture was cooled in an ice bath, and 7.5 mL phosphorus oxychloride was added dropwise in ten minutes, stirred for 1 h and then warmed up to 75 °C for 40 minutes. The cooled reaction mixture was dissolved in 50 mL dichloromethane and poured onto crushed ice mixed with sodium carbonate. The aqueous layer was extracted with dichloromethane (3×100 mL), and the extract was dried over sodium sulfate and then concentrated under vacuum. The product was purified by flash chromatography using

dichloromethane/methanol (100: 2, v/v) as eluant, affording 0.288 g (60%) of **3** as a light yellow solid: m.p. 69.8-71.8 °C; ^1H NMR (CDCl_3) δ 9.83 (s, 1 H), 7.60 (s, 1 H), 7.49 (d, J = 8 Hz, 1 H), 7.10 (d, J = 8 Hz, 1 H), 4.42 (s, 4 H), 4.28 (s, 4 H), 4.09-4.16 (m, 8 H), 1.21 (t, J = 6.8 Hz, 12 H); MS (APCI) Calcd for $([\text{M}+\text{H}])^+$, 481; Found, 481.

BODIPY Compound (4). 0.24 g of **3** (0.5 mmol) and 0.123 g (1 mmol) of 2,4-dimethyl-3-ethylpyrrole were dissolved in 100 mL of absolute dichloromethane under nitrogen atmosphere, one drop of trifluoroacetic acid was added and the solution was stirred at room temperature for 5 h. A solution of dichlorodicyanobenzo- quinone (DDQ, 114 mg, 0.5 mmol) in 10 mL dichloromethane was added and stirring was continued for 15 minutes, followed by the addition of diisopropylethylamine (3 mL, 17.1 mmol) and $\text{BF}_3\text{-OEt}_2$ (3 mL, 23.7 mmol). After stirring for another 30 minutes, the reaction mixture was washed with 80 mL water, extracted with dichloromethane (5×100 mL). The extract was dried over sodium sulfate and then concentrated under vacuum. The product was purified by flash chromatography using hexane/ethyl acetate (7: 3, v/v) as eluant, and then recrystallized from ethanol to give 0.15 g (40%) of **4** as a red solid: m.p. 138.4-140.2 °C; ^1H NMR (CDCl_3) δ 7.18 (d, J = 8 Hz, 1 H), 6.92 (s, 1 H), 6.83 (d, J = 8 Hz, 1 H), 4.35 (s, 4 H), 4.29 (s, 4 H), 4.04-4.15 (m, 8 H), 2.52 (s, 6 H), 2.29 (q, J = 7.6 Hz, 4 H), 1.30 (s, 6 H), 1.17-1.23 (m, 12 H), 0.97 (t, J = 7.6 Hz, 6 H); MS (APCI) Calcd for $([\text{M}+\text{Na}])^+$, 777; Found, 777.

S3. 60 mg of **4** (0.077 mmol) was dissolved in 10 mL acetonitrile, and 10 mL 2-aminoethanol was added. The solution was refluxed under nitrogen for 1.5 h, cooled and concentrated under vacuum to get rid of the acetonitrile, then poured into 50 mL saturated brine. The mixture was neutralized with sodium dihydrogen phosphate, and extracted with dichloromethane (5×100 mL). The extract was dried over sodium sulfate and then concentrated under vacuum. The product was purified by flash chromatography using methanol/triethylamine/dichloromethane/ (50: 3: 100, v/v/v) as eluant, and then recrystallized from ethyl ether/ ethanol to give 51 mg (80%) of **S3** as a red solid: m.p. 239.1-240.8 °C; ¹H NMR (DMSO-d₆) δ 8.00 (s, 2 H), 7.94 (s, 2 H), 7.01 (d, *J* = 8.4 Hz, 1 H), 6.81 (s, 1 H), 6.73 (d, *J* = 8.4 Hz, 1 H), 4.61-4.66 (m, 4 H), 4.08 (s, 4 H), 4.04 (s, 4 H), 3.25-3.33 (m, 8 H), 2.96-3.06 (m, 8 H), 2.41 (s, 6 H), 2.28 (q, *J* = 7.2 Hz, 4 H), 1.26 (s, 6 H), 0.94 (t, *J* = 7.2 Hz, 6 H); FTIR (ethanol, cm⁻¹) 3427, 2931, 2872, 1642, 1542, 1477, 1406, 1389, 1320, 1265, 1194, 1161, 1116, 1063, 980; HRMS (ES⁺) Calcd for ([M+H])⁺, 815.4439; Found, 815.4445.

S1 and **S2** were similarly prepared from **S3**.

***N,N*-di{(2-hydroxyethyl)carbamoylmethyl}-aniline (6)** was synthesized following the literature method.¹

***p*-formyl-*N,N*-di{(2-hydroxyethyl)carbamoylmethyl}-aniline (7).** Light yellow solid (72%); m.p. 62.5-64.3 °C; ¹H NMR (CDCl₃) δ 9.79 (s, 1 H), 7.75 (d, *J* = 8.8 Hz, 2 H), 6.66 (d, *J* = 8.8 Hz, 2 H), 4.20-4.27 (m, 8 H), 1.28 (t, *J* = 7.2, 6 H); MS (APCI) Calcd for ([M+H])⁺, 294; Found, 294.

BODIPY compound (8). Red solid (51%); m.p. 184.1-186.5 °C; ¹H NMR (DMSO-d₆) δ 7.08 (d, *J* = 8.8 Hz, 2 H), 6.72 (d, *J* = 8.8 Hz, 2 H), 4.24 (s, 4 H), 4.12 (q, *J* = 7.2, 4 H), 2.47 (s, 6 H), 2.29 (q, *J* = 7.6 Hz, 4 H), 1.33 (s, 6 H), 1.17 (t, *J* = 7.6 Hz, 6 H), 0.94 (t, *J* = 7.2 Hz, 6 H); MS (APCI) Calcd for ([M+H])⁺, 568; Found, 568.

S1. Red solid (75%); m.p. 243.3-224.8 °C; ¹H NMR (DMSO-d₆) δ 7.08 (d, *J* = 8.4 Hz, 2 H), 6.56 (d, *J* = 8.4 Hz, 2 H), 4.13 (s, 4 H), 3.35 (t, *J* = 5.6 Hz, 4 H), 3.09 (t, *J* = 5.6 Hz, 4 H), 2.41 (s, 6 H), 2.28 (q, *J* = 7.6 Hz, 4 H), 1.32 (s, 6 H), 0.94 (t, *J* = 7.6 Hz, 6 H); FTIR (KBr, cm⁻¹) 3425, 2960, 2869, 1641, 1541, 1476, 1318, 1191, 976; HRMS (ES⁺) Calcd for ([M+H])⁺, 598.3376; Found, 598.3370.

[(2-Ethoxycarbonylmethoxy-phenyl)-ethoxycarbonylmethyl-amino]-acetic acid ethyl ester (10). Light yellow oil (77%); ¹H NMR (CDCl₃) δ 6.87-6.92 (overlapped, 3 H), 6.81 (d, *J* = 7.2 Hz, 1 H), 4.66 (s, 2 H), 4.14-4.27 (m, 10 H), 1.23-1.30 (m, 9 H); MS (APCI) Calcd for ([M+H])⁺, 368; Found, 368.

[(2-Ethoxycarbonylmethoxy-4-formyl-phenyl)-ethoxycarbonylmethyl-amino]-acetic acid ethyl ester (11). Light yellow solid (65%); m.p. 53.2-55.4 °C; ^1H NMR (CDCl_3) δ 9.77 (s, 1 H), 7.40 (d, $J = 8.0$ Hz, 1 H), 7.27 (s, 1 H), 6.81 (d, $J = 8.0$ Hz, 1 H), 4.66 (s, 2 H), 4.28 (s, 4 H), 4.20-4.27 (m, 6 H), 1.26-1.31 (m, 9 H); MS (APCI) Calcd for $([\text{M}+\text{H}])^+$, 396; Found, 396.

BODIPY compound (12). Red paste (55%); ^1H NMR (CDCl_3) δ 6.96 (d, $J = 8.0$ Hz, 1 H), 6.81 (d, $J = 8.0$ Hz, 1 H), 6.65 (s, 1 H), 4.62 (s, 2 H), 4.25 (s, 4 H), 4.16-4.23 (m, 6 H), 2.52 (s, 6 H), 2.29 (q, $J = 7.6$, 4 H), 1.50 (s, 6 H), 1.14-1.30 (m, 9 H), 0.97 (t, $J = 7.6$, 6 H); MS (APCI) Calcd for $([\text{M}+\text{H}])^+$, 670; Found, 670.

S2. Red solid (82%); m.p. 203.1-204.9 °C; ^1H NMR ($\text{DMSO}-d_6$) δ 8.26 (t, $J = 6.0$ Hz, 2 H), 8.07 (t, $J = 6.0$ Hz, 1 H), 6.96 (d, $J = 8.4$ Hz, 1 H), 6.86 (s, 1 H), 6.78 (d, $J = 8.4$ Hz, 1 H), 4.57 (s, 2 H), 3.93 (s, 4 H), 3.32-3.39 (overlapped, 6 H), 3.12-3.17 (m, 6 H), 2.42 (s, 6 H), 2.29 (q, $J = 7.6$, 4 H), 1.32 (s, 6 H), 0.94 (t, $J = 7.6$, 6 H); FTIR (KBr, cm^{-1}) 3405, 2926, 1655, 1542, 1477, 1318, 1190, 979; HRMS (ES^+) Calcd for $([\text{M}+\text{H}])^+$, 715.3802; Found, 715.3806.

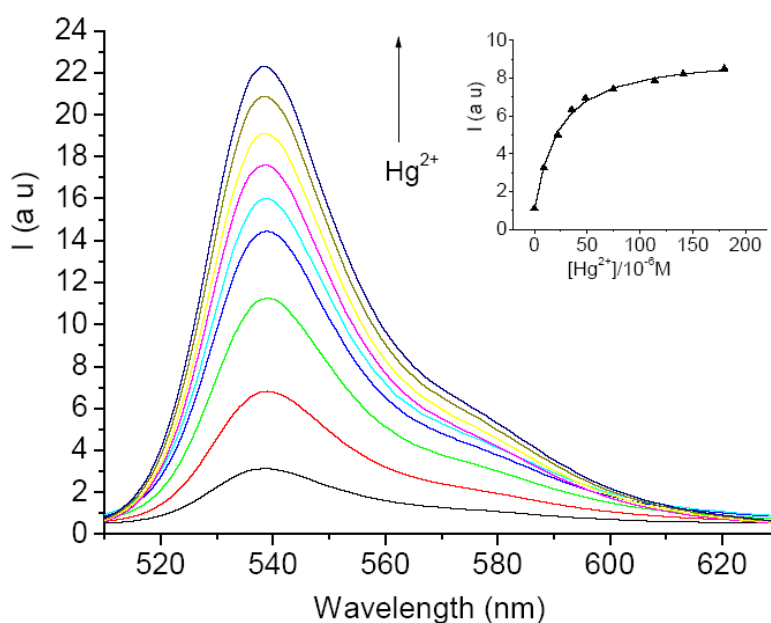


Figure S1. Emission spectra (excitation at 490 nm) of **S2** (4.4 μM) in phosphate (0.1 M) solution (pH = 7.5) in the presence of different concentrations of Hg²⁺ ions. The up-arrow indicates the increase of [Hg²⁺] from 0 to 180 μM. Inset: Integrated fluorescence intensity from 510 to 630 nm as a function of Hg²⁺ ion concentration.

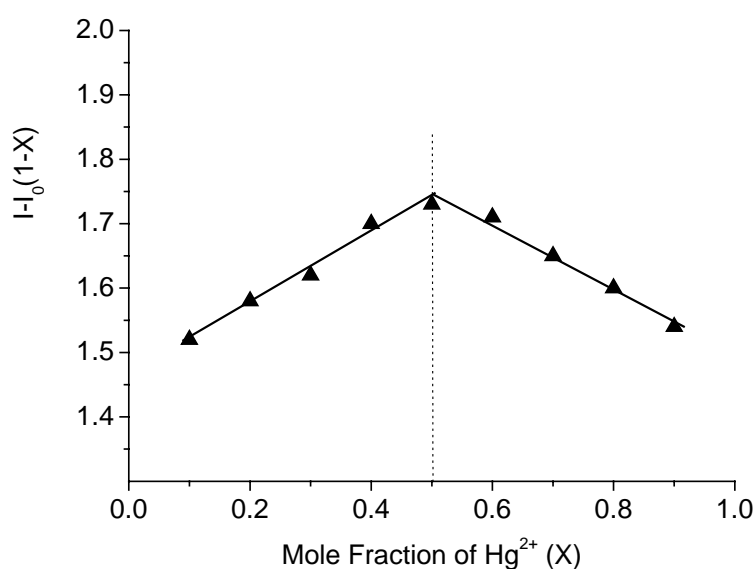


Figure S2. Job's plot of sensor **S2** in 0.1 M phosphate buffered water solution (pH = 7.5). The total concentration of sensor and Hg²⁺ ion is 4 μM.

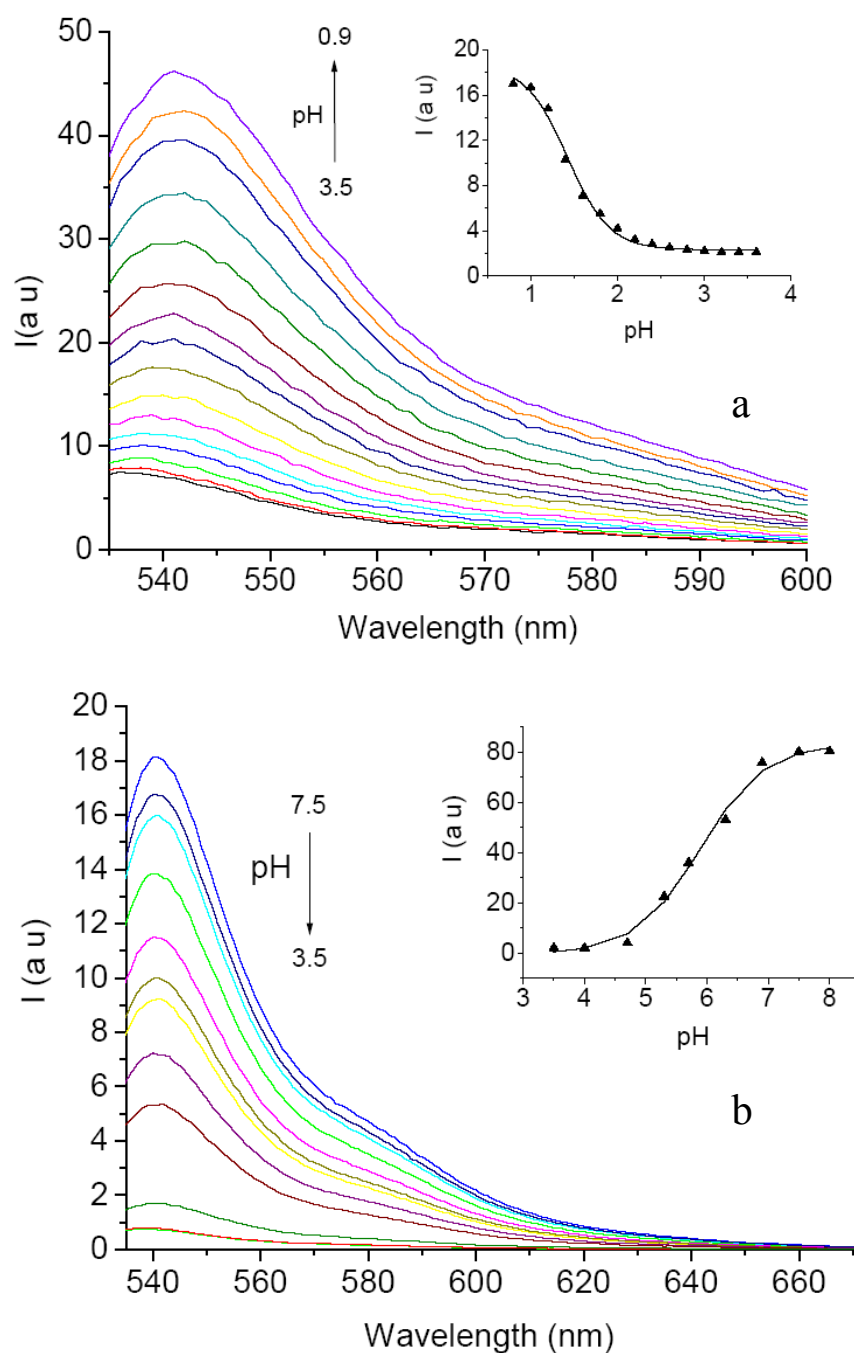


Figure S3. Dependence of the fluorescence intensity of **S3** (2 μM) (a) and **S3-Hg²⁺** complex (b) on pH in water solution (pH is adjusted by 75% HClO₄ and NaOH. Note: in Figure S3a inset, when pH is above 3.5, the curve keeps straight; in Figure S3b inset, when pH is below 3.5, the curve is identical to Figure S3a.

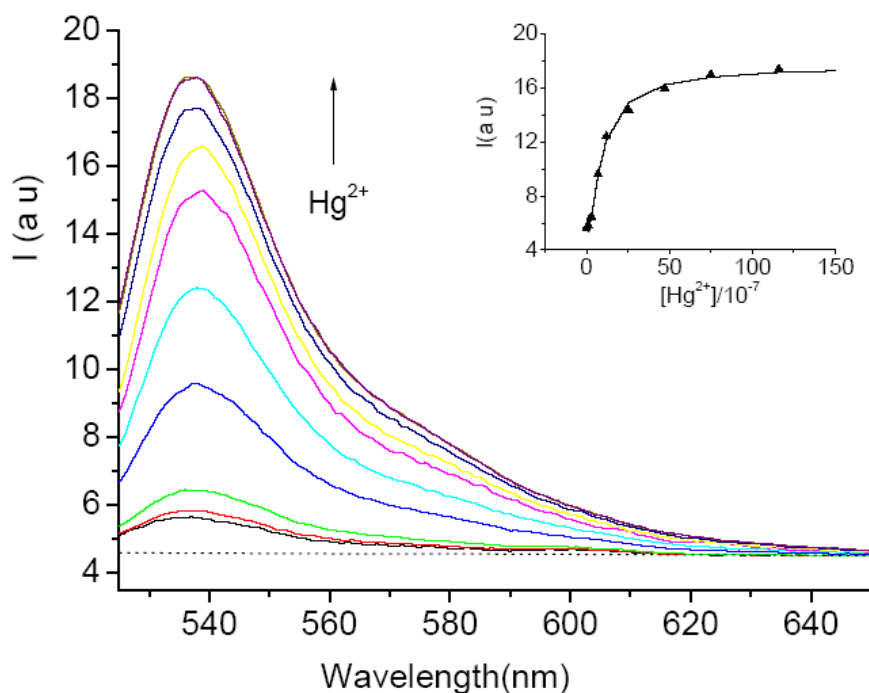


Figure S4. Emission spectra (excitation at 527 nm) of **S3** (0.1 μM) in phosphate (0.01 M) solution (pH = 7.5) in the presence of different concentrations of Hg^{2+} ions. The up-arrow indicates the increase of $[\text{Hg}^{2+}]$ from 0 to 19 μM . Inset: Integrated fluorescence intensity from 525 to 650 nm as a function of Hg^{2+} ion concentration.

K_s was determined by a nonlinear least-squares analysis of I versus c_M using the following equation:²

$$I = \frac{I_0 + c_M \Phi K_{11}[M] + I_{\text{lim}} K_s[M]^2}{1 + K_{11}[M] + K_s[M]^2}$$

Where $K_s = K_{11}K_{21}$, $[M] \approx c_M$ is Hg^{2+} ion concentration, I_0 or I is integrated emission in the absence or presence of Hg^{2+} ions, Φ is approximately substituted by 0.19, the quantum yield of the 1:1 **S2**- Hg^{2+} complex, since the quantum yield of the 1:1 **S3**- Hg^{2+} complex could not be precisely determined.

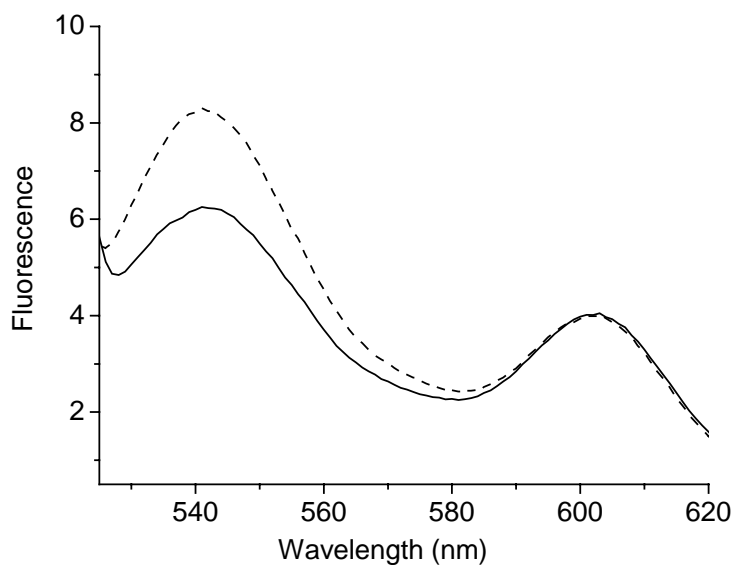


Figure S5. Fluorescence response of sensor **S3** (0.01 μM) in the presence of 2 ppb of Hg^{2+} ions. The water solution is buffered with 10 mM phosphate (pH 7.5). Solid line, free **S3**; dash line, **S3** + 2ppb Hg^{2+} ions.

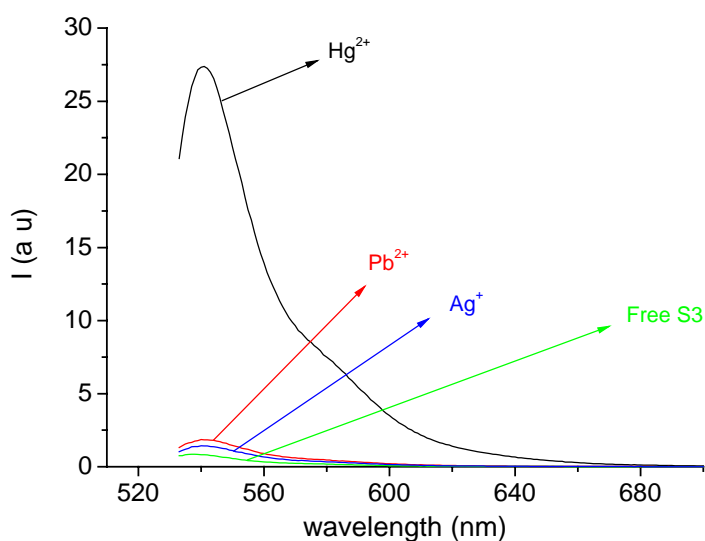
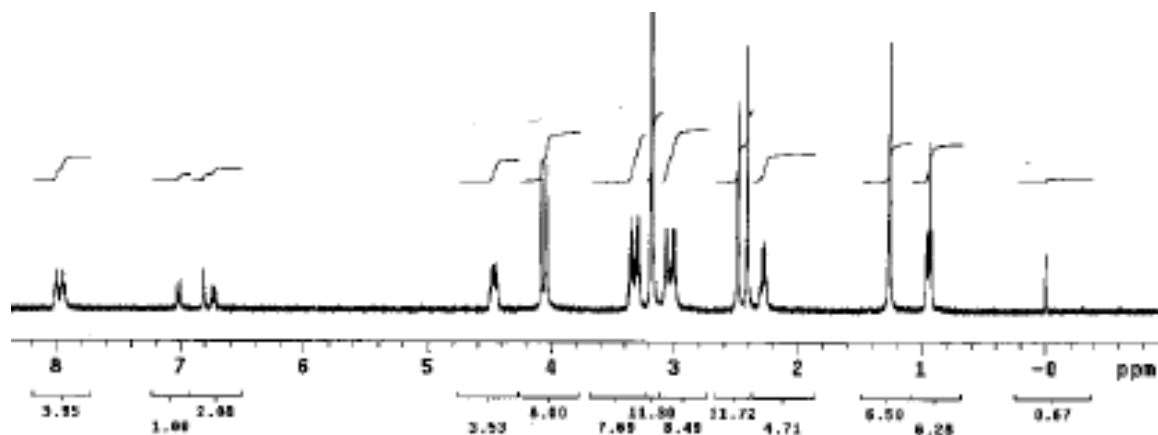
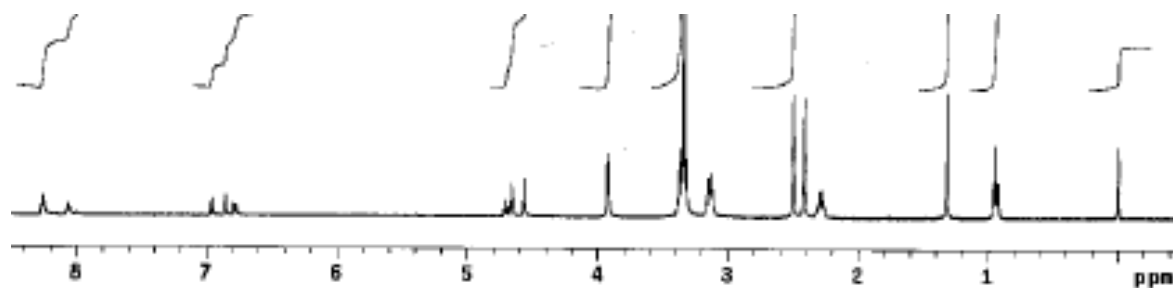
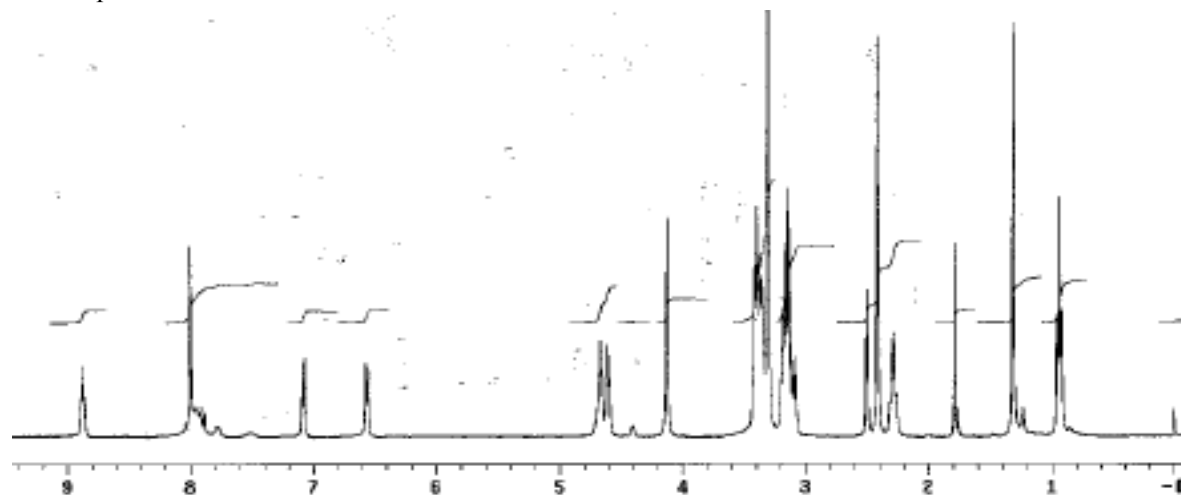


Figure S6. Fluorescence response of sensor **S3** (2 μM) to different detected metal ions (4 μM) in neat water solution. The spectra for other detected cations are just similar to free **S3** and are not listed for clarity.

¹H-NMR spectrum of S3¹H-NMR spectrum of S2¹H-NMR spectrum of S1

Reference:

- (1) Gunnlaugsson, T.; Lee, T. C.; Parkesh, R. *Org. lett.* **2003**, 5, 4065.
- (2) Valeur, B. *Molecular Fluorescence: Principles and Applications*; Wiley-VCH, Weinheim, Germany, 2002.