

Supporting Information

A selective and sensitive “turn-on” fluorescent chemodosimeter for Hg²⁺ in aqueous media via Hg²⁺ promoted facile desulfurization-lactonization reaction

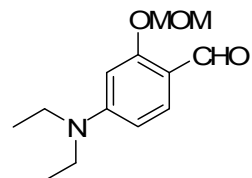
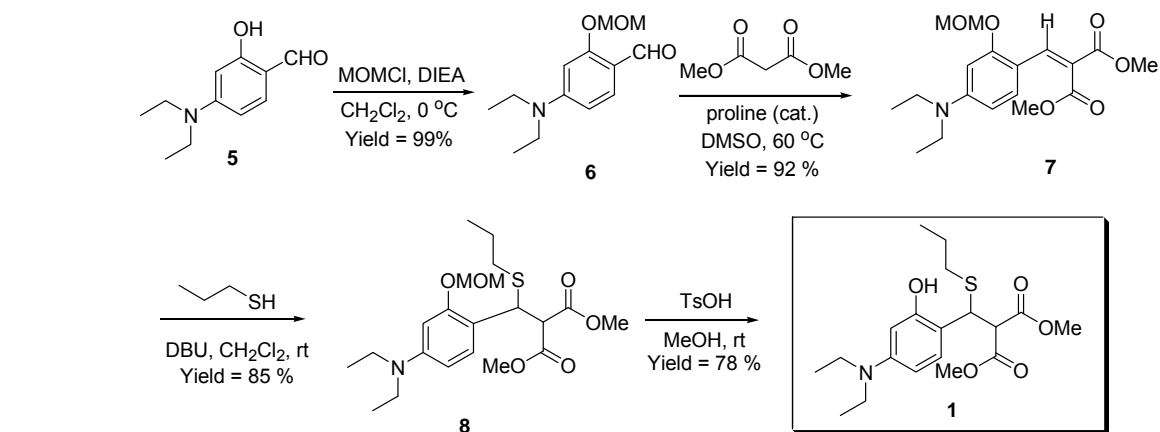
*Wei Jiang and Wei Wang**

Department of Chemistry & Chemical Biology, University of New Mexico, Albuquerque, NM 87131, USA

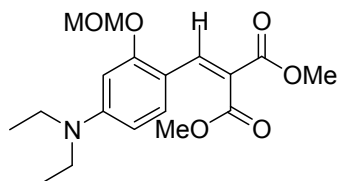
General Information: Commercial reagents were used as received, unless otherwise stated. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F₂₅₄ were used for thin-layer chromatography (TLC) analysis. ¹H and ¹³C NMR spectra were recorded on Bruker Avance 500, and tetramethylsilane (TMS) was used as a reference. Data for ¹H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Data for ¹³C NMR are reported as ppm. Mass Spectra were obtained from University of New Mexico Mass Spectral facility.

Spectroscopic materials and methods: Millipore water was used to prepare all aqueous solutions. The pH was recorded by a Beckman Φ^{TM} 240 pH meter. UV absorption spectra were recorded on a Shimadzu UV-2410PC UV-Vis spectrophotometer. Fluorescence emission spectra were obtained on a Varian Eclipse fluorescence spectrophotometer.

Scheme S1. Synthesis of probe **1**.

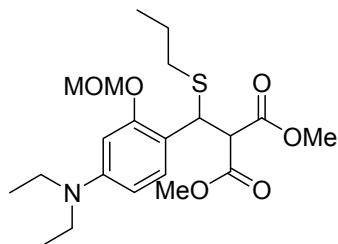


4-(Diethylamino)-2-(methoxymethoxy)benzaldehyde (6): To a solution of 4-(diethylamino)-2-hydroxybenzaldehyde (**5**) (2.03 g, 10 mmol) in 50 mL of anhydrous dichloromethane was added N,N-diisopropylethylamine (5.2 mL, 30 mmol) at room temperature under a nitrogen atmosphere. The solution was cooled to 0 °C and chloromethyl methyl ether (1.5 mL, 20 mmol) was added dropwisely. The reaction mixture was warmed up to room temperature and stirred for 24 h under a nitrogen atmosphere. The reaction solution was washed with water and extracted by dichloromethane (2 × 30 mL). The combined organic layer was dried with magnesium sulfate, filtered and evaporated *in vacuo* to afford **6** as light red solid (2.37 g, 99% yield). ¹H NMR (500 MHz, CDCl₃): δ 10.16 (s, 1H), 7.72 (d, 1H, *J* = 9.5 Hz), 6.35-6.33 (m, 2H), 5.27 (s, 2H), 3.52 (s, 3H), 3.41 (q, 4H, *J* = 7 Hz), 1.21 (t, 6H, *J* = 7 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 186.9, 162.1, 153.7, 130.2, 114.7, 105.4, 96.0, 94.8, 56.3, 44.8, 12.5.

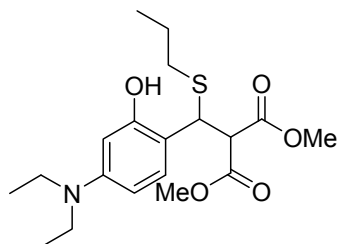


Dimethyl 2-[4-(diethylamino)-2-(methoxymethoxy)benzylidene]malonate (7): A solution of **6** (2 mmol, 475 mg), dimethyl malonate (350 μ L, 3 mmol) and proline (46 mg, 0.4 mmol) in 20 mL of DMSO

was heated to 60 °C until TLC showed that **6** was completely consumed. Solvents was removed in *vacuo*, the residue was poured into 20 mL of water and extracted by dichloromethane (3 × 20 mL). The combined organic layer was dried with magnesium sulfate, filtered and evaporated in *vacuo*. The crude product was purified by silica gel chromatography to afford **7** as yellow oil (646 mg, 92% yield). ¹H NMR (500 MHz, CDCl₃): δ 8.13 (s, 1H), 7.23 (d, 1H, *J* = 9 Hz), 6.40 (s, 1H), 6.27 (d, 1H, *J* = 9 Hz), 5.21 (s, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.49 (s, 3H), 3.36 (q, 4H, *J* = 7 Hz), 1.17 (t, 3H, *J* = 7 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 168.8, 165.9, 158.9, 151.5, 138.3, 130.4, 118.2, 109.9, 105.7, 97.2, 95.0, 56.3, 52.3, 52.1, 44.7, 12.7.



Dimethyl 2-[[4-(diethylamino)-2-(methoxymethoxy)phenyl](propylthio)methyl]malonate (8): To a solution of **7** (40mg, 0.114 mmol), 1-propanethiol (52 μL, 0.57 mmol) in 10 mL of dichloromethane was added 1,8-diazabicyclo[5.4.0]undec-7-ene (3.5 μL, 0.02 mmol) and stirred 6 h at rt. Solvents were removed under reduced pressure and the crude product was purified directly by silica gel chromatography. (41mg, 85% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.04 (d, 1H, *J* = 8.5 Hz), 6.43 (s 1H), 6.24 (d, 1H, *J* = 8.5 Hz), 5.20 (s, 2H), 4.67 (d, 1H, *J* = 11.5 Hz), 4.17 (d, 1H, *J* = 11.5 Hz), 3.79 (s, 3H), 3.53 (s, 3H), 3.50 (s, 3H), 3.31 (q, 4H, *J* = 7 Hz), 2.45-2.42 (tm, 2H), 1.58-1.50 (m, 2H), 1.14 (t, 6H, *J* = 7 Hz), 0.90 (t, 3H, *J* = 7 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 168.5, 167.7, 156.4, 148.8, 129.6, 115.3, 105.4, 98.8, 95.0, 57.8, 56.2, 52.8, 52.6, 44.6, 43.8, 34.4, 22.9, 13.7, 12.9.



Dimethyl 2-[[4-(diethylamino)-2-hydroxyphenyl](propylthio)methyl]malonate (1): A solution of **6** (30 mg, 0.07 mmol) and *p*-toluenesulfonic acid 68 mg, 0.35 mmol) in 3 mL of MeOH was stirred for 2 days at room temperature. Evaporated solvents, the residue was dissolved in 10 mL dichloromethane, washed with 10 mL of aqueous solution of sodium bicarbonate and extracted by dichloromethane (2 × 10 mL). The combined organic layer was dried over magnesium sulfate, filtered and evaporated in *vacuo* and purified by silica gel chromatography (21 mg, 78% yield). ¹H NMR (500 MHz, CDCl₃): δ 6.97-6.95 (m, 2H), 6.19-6.17 (m, 2H), 4.56 (d, 1H, *J* = 11 Hz), 3.97 (d, 1H, *J* = 11 Hz), 3.80 (s, 3H), 3.53 (s, 3H), 3.30 (q, 4H, *J* = 7 Hz), 2.44-2.38 (m, 1H), 2.34-2.28 (m, 1H), 1.60-1.48 (m, 2H), 1.14 (t, 6H, *J* = 7 Hz), 0.90 (t, 3H, *J* = 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 168.0, 156.4, 149.4, 131.3, 110.0, 104.8, 101.1, 57.1, 53.0, 52.9, 45.3, 44.5, 33.6, 22.4, 13.5, 12.9; HRMS (ESI): calcd for [M+H⁺] 384.1845, found 384.1851.

Competition Assays: A pH 6.0 phosphate buffer solution of probe **1** (5 μM) with a metal ion (10 μM) was mixed for 5 min, then the solution was taken for fluorescence measurement ($\lambda_{\text{ex}} = 430$ nm) and the fluorescence intensity was collected at 480 nm) of the emission spectrum. The metal containing solution was added Hg²⁺ (2.5 μM) and then again the solution was taken for fluorescence measurement ($\lambda_{\text{ex}} = 430$ nm) and the fluorescence intensity was collected at 480 nm) of the emission spectrum after 30 sec.

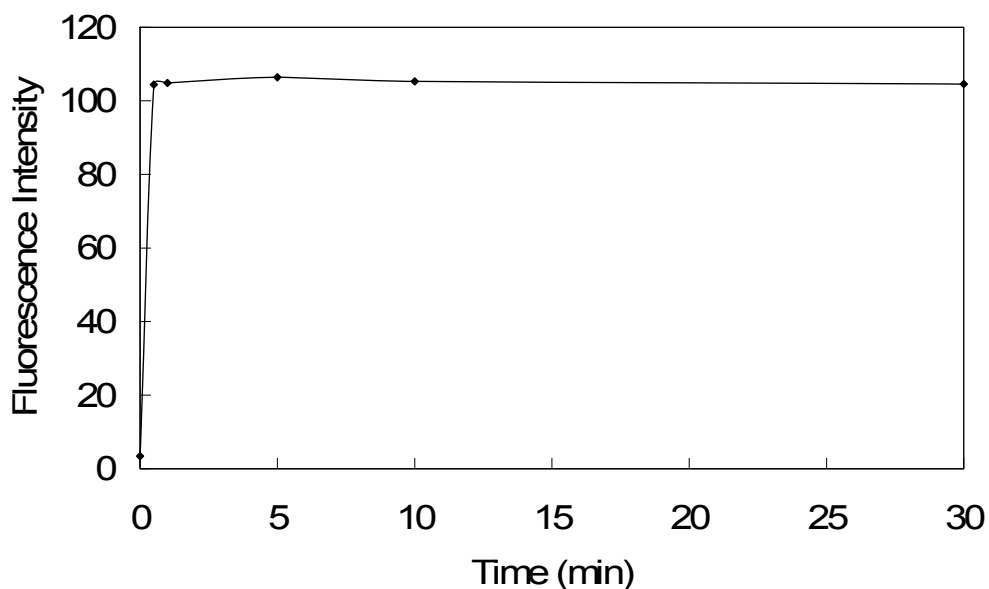


Fig. S1. Reaction time profile of probe **1** ($5 \mu\text{M}$, excited at 430 nm) towards Hg^{2+} ($2.5 \mu\text{M}$) in aqueous solution. Spectra shown are for reaction time of 0, 0.5, 1.0, 5.0, 10.0 and 30.0 minutes. Fluorescence spectra data were acquired at 480 nm in pH 6.0 phosphate buffer ($I = 0.05 \text{ M}$) at rt.

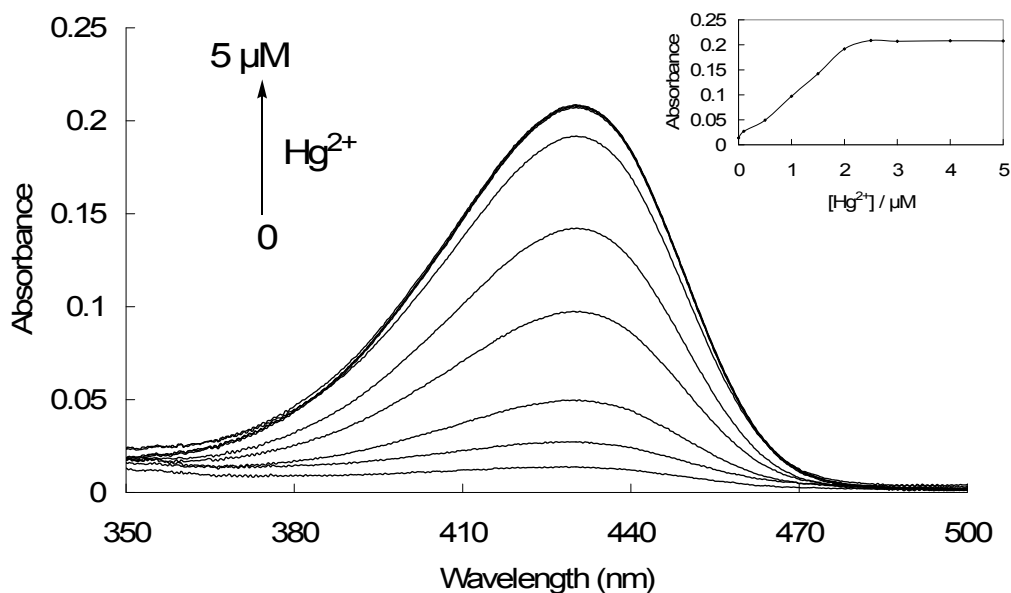


Fig. S2. UV response and plot (collected at 430 nm) of the $5 \mu\text{M}$ probe **1** to Hg^{2+} in aqueous solution. Spectra shown are for Hg^{2+} concentrations of 0, 0.1, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0 and $5.0 \mu\text{M}$. These data were measured at 30 sec in pH 6.0 phosphate buffer ($I = 0.05 \text{ M}$) at rt.

