

Fluorescent PET Chemosensor for Cadmium Ions in 100% Aqueous Solution

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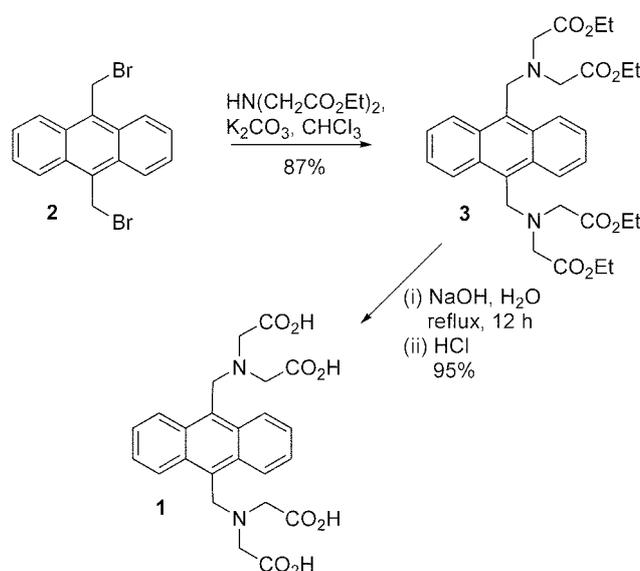
Fluoroionophores chemically communicate ion concentrations and have been the subject of substantial investigation in metal ion analysis. Particularly, photoinduced electron transfer (PET) has been widely used as a tool of choice in fluorescent sensor design for protons and metal ions by many groups.¹

Due to the adverse biological effects of cadmium, the monitoring of cadmium levels in environmental samples, industrial waste and tissue samples has been of particular interest.² There have been few reports regarding the fluorescent receptors for Cd²⁺.³ However, these compounds generally do not display sufficient selectivity for Cd²⁺ over the other transition metals. Noteworthy was a paper reported by Savage *et al.* in which 5-chloro-8-methoxyquinoline appended diaza-18-crown-6 selectively responds to Cd²⁺ in methanol.^{3h} Therefore, there is still a need for a selective fluorescent chemosensor for Cd²⁺ which works in 100% aqueous solution.

We report herein a new anthracene derivative **1** as a fluorescent PET chemosensor for Cd²⁺. Chemosensor **1** displays a selective CHEF (chelation-enhanced fluorescence) effect with Cd²⁺ among the metal ions examined at pH 10.

Our synthesis began with 9,10-bis(bromomethyl) anthracene **2**, produced using the published method.⁴ Treatment of **2** with diethyl iminodiacetate and potassium carbonate in chloroform at 40 °C for 5 hours led to the tetraester **3** in 85 % yield after purification by silica gel column chromatography using 10% MeOH/CHCl₃ as eluent (Scheme 1). The tetra acid **1** was obtained in 95% yield by hydrolysis with potassium hydroxide in water. The structures of these compounds were confirmed by ¹H NMR, ¹³C NMR, and mass spectroscopy.

Protonation of an amine group in fluorophore-amine conjugates results in the elimination of photo-induced electron transfer. Therefore, fluorescence is expected to be a function of pH, and pH measurement using anthrylamines has been described by de Silva.⁵ The fluorescence quenching behavior of compound **1** was evaluated by the examination of its pH-fluorescence profile. The fluorescence emission was monitored 428 nm after excitation at 367 nm. The pH of each aqueous solution compound **1** (6 μM) was adjusted by the addition of HCl or NaOH solution. From the pH-



Scheme 1. Synthesis of compound **1**.

fluorescence profile, pK_a of compound **1** was calculated as 8.7. Considering the pK_a's of amine moieties in the anthracene derivatives containing azacrown or polyamine ligands are reported to be around 7.0,⁶ the pK_a of amine moiety in this compound is somewhat higher than those values. Because of the adjacent carboxylic acid groups, this compound must be a zwitterion at pH 7.0, in which each side has two negative and one positive charge.

Ca²⁺, Cd²⁺, Mg²⁺, Mn²⁺, Sr²⁺, and Zn²⁺ ions as perchlorate salts were used to evaluate metal ion binding of compound **1**. Fluorescence studies were conducted at pH 10 [0.1 M CAPS (3-cyclohexylamino-1-propanesulfonic acid)] since the CHEF effects can be maximized in this pH range. Using these metal ions (60 μM), compound **1** (6 μM) displayed a selective and large CHEF effect only with Cd²⁺ even though there was a relatively small CHEF effect with Zn²⁺ (Figure 1). Since the communicating mechanism is a PET process, the overall fluorescence emission change is over 20 fold for Cd²⁺. From the fluorescence titration experiments (Figure 2), the association constants for Cd²⁺ and Zn²⁺ are calculated as 69,100 and 3,200 M⁻¹ (errors < 10%), respectively.⁷ The selectivity for Cd²⁺ ion is more than 20 times that for Zn²⁺. We also confirmed the 1:1 binding of compound **1** with Cd²⁺ from the Job's plot using the fluorescent changes. Obviously,

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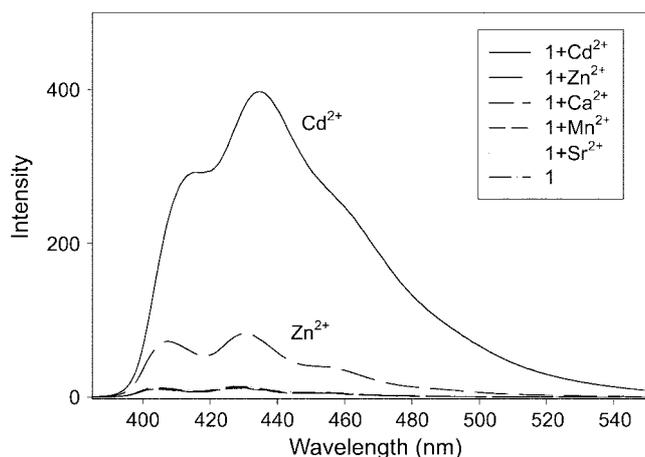


Figure 1. Fluorescence emission spectra of compound **1** (6 μM) upon the addition of metal ions (60 μM) at pH 10 (0.1 M CAPS) (excitation: 367 nm).

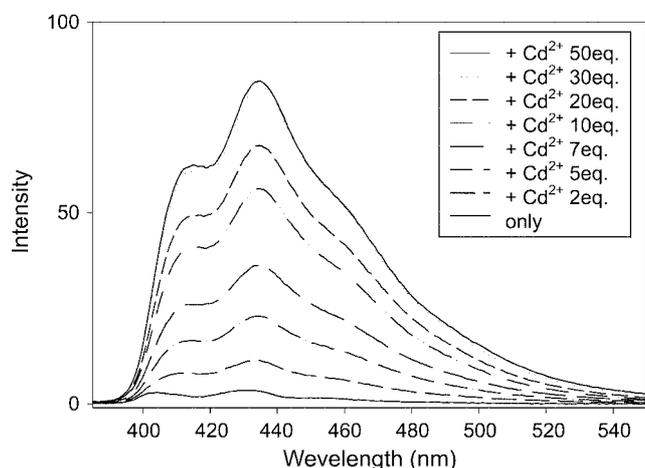


Figure 2. Fluorescent titrations of compound **1** (1 μM) with Cd^{2+} at pH 10 (0.1 M CAPS) (excitation: 367 nm).

the two binding sites at 9,10-positions of anthracene generate a cooperative binding site for metal ions.

In conclusion, compound **1** was synthesized as a new PET fluorescent chemosensor, which displayed a selective binding with environmentally important Cd^{2+} ions in 100 % aqueous solution at pH 10. The ion selectivity and a large CHEF effect with Cd^{2+} make **1** a promising candidate as a useful fluorescent chemosensor for Cd^{2+} .

Experimental Section

NMR spectra were recorded at 250 MHz (for ^1H -NMR) and at 62.5 MHz (for ^{13}C -NMR) using a Bruker 250 Spectrometer. Mass spectra and elemental analysis were obtained using the JEOL-JMS-HX 110A/110A High Resolution Tandem Mass Spectrometry and Vario EL of Elemental Analyzer in the Korea Basic Science Institute in Taejeon, Korea. Melting points were determined in open capillaries, and are uncorrected. UV absorption spectra were obtained on UVIKON 933 Double Beam UV/VIS Spectrometer.

Fluorescence emission spectra were obtained using RF-5301/PC Spectrofluorophotometer (Shimadzu). Flash chromatography was carried out using Merck silica gel 60 (230 to 400 mesh). Thin layer chromatography was carried out using Merck 60 F_{254} plates with a 0.25-mm thickness.

1,8-Bis[(bisdiethylimino)methyl]anthryl tetraacetate (3). 9,10-Bis(bromomethyl)anthracene **2** (789 mg, 2.17 mmol) was added to a stirred solution of diethyl iminodiacetate (1.52 mL, 8.68 mmol) and K_2CO_3 in CHCl_3 (25 mL). After the reaction mixture was stirred at 50 $^\circ\text{C}$ for 5 hours, the reaction mixture was passed through a celite washing with CHCl_3 . The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography (CHCl_3 :MeOH = 9:1) to give **3** as a yellow solid in 87% yield (1.09 g): m.p. 120–123 $^\circ\text{C}$; ^1H -NMR (CDCl_3 , 250 MHz) δ 8.67 (m, 4H), 7.69 (m, 4H), 4.95 (s, 4H), 4.10 (q, J = 7.2 Hz, 8H), 3.57 (s, 8H), 1.19 (t, J = 7.2 Hz, 12H); ^{13}C -NMR (CDCl_3 , 62.5 MHz) δ 172.21, 132.10, 130.38, 126.38, 61.27, 54.19, 50.24, 14.88; HRMS (FAB) m/z = 581.2863 ($\text{M}+\text{H}$) $^+$, calc. for $\text{C}_{32}\text{H}_{40}\text{N}_2\text{O}_8$ = 581.2863 ($\text{M}+\text{H}$) $^+$.

9,10-Bis[(bisimino)methyl]anthryl tetracarboxylic acid (1). KOH was added to a stirred solution of **3** (500 mg, 0.86 mmol) in distilled water (50 mL). The reaction mixture was then refluxed for 12 h. After the reaction mixture was cooled to room temperature, 1 M HCl solution was added to make pH 2–3. The resulting precipitate was filtered and washed with small amount of cold distilled water. After drying at 90 $^\circ\text{C}$ *in vacuo*, compound **1** was obtained as a yellow solid in an analytically pure form (402 mg, 95%). m.p. 242 $^\circ\text{C}$ dec.; ^1H -NMR (D_2O (+ NaOD), 250 MHz) δ 8.45 (m, 4H), 7.49 (m, 4H), 4.17 (s, 4H), 3.03 (s, 8H); ^{13}C -NMR (D_2O (+ NaOD), 62.5 MHz) δ 184.89, 130.84, 130.37, 125.89, 58.68, 49.74; HRMS (FAB) m/z = 491.1429 ($\text{M}+\text{Na}$) $^+$, calc. for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_8$ = 491.1430 ($\text{M}+\text{Na}$) $^+$.

General fluorescence solution preparation. For metal titrations, stock solutions of the metal perchlorates (1 mM) and stock solution of **1** (0.06 mM) were prepared in doubly distilled demineralized water. The solutions were used on the day of preparation. Test solutions were prepared by placing 100 μL of the probe solution into a test tube, adding an appropriate aliquot of each metal stock, and diluting the solution to 4 mL with pH 10 CAPS (0.1 M) buffer.

For all measurements, excitation was at 367 nm; Both excitation and emission slit widths were 5 nm.

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