

Azetidine-based Anthracenyl Chemosensor for Cu(II) Ion in Aqueous Media

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Environmental poisoning by heavy metals, such as Hg²⁺, Pb²⁺, and Cu²⁺, has been increased in the last three decades due to extensive use of them in agricultural, chemical and industrial processes, which are becoming threats to living organisms.¹ Particularly, Cu(II) is an essential element playing a fundamental role in the biochemistry of the human nervous system, but its high concentration is toxic.² Thus, its accumulation in the human body affects a wide variety of disease, such as Menkes disease³, Wilson's disease³ and Alzheimer's disease.⁴ Therefore, in recent years, many efforts have been made to develop various chemosensors specifically for the Cu²⁺ ion detection. Chang *et al.* reported BODIPY (borondipyrromethene) having thioether receptor for selective and stable binding towards Cu²⁺ in water.^{5a} Kraemer *et al.* developed fluorescein-Cu²⁺ quencher pairs in molecular beacon oligonucleotide.^{5b} Czarnik *et al.* exploited rhodamine B hydrazide based on hydrolysis in the presence of Cu²⁺ ion.^{5c}

N-Functionalized azetidine can be also expected to serve as a good binding unit due to its relatively strong electron-donor function of tertiary-*N* for specific metal ions. Of particular interest is the stability of the azetidine ring of **2** under various conditions in preparing metal complex though it can certainly be opened when the ligand is free.⁶

In this context, we report the synthesis and X-ray crystal structure of fluorescent anthracenyl complex, Cu(**1**)²⁻. In addition, we herein explore its photochemical behavior towards Cu²⁺ ion in aqueous media (CH₃CN:H₂O = 1:9, v/v).

As shown in Scheme 1, the reaction of **2**⁷ with 9-anthracenecarboxaldehyde gave a yellowish-brown oil **1**. The complex [Cu(**1**)(CH₃CO₂)(H₂O)]⁺ was prepared by the addition of Cu(CH₃CO₂)₂·H₂O to a methanol solution of **1**.

To investigate spectroscopic properties of **1** towards metal ion complexation, the perchlorate salts of Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, Cd²⁺, Co²⁺, Ca²⁺, Zn²⁺, Pb²⁺, Hg²⁺, Mg²⁺, Ba²⁺, Sr²⁺, Cu²⁺ and Ag⁺ ions were used in aqueous media (CH₃CN:H₂O = 1:9, v/v). Figure 1 shows that **1** exhibits characteristic absorption bands at 350, 367, and 385 nm (absorption coefficients, ε = 5.1 × 10³, 6.1 × 10³, and 5.3 × 10³ M⁻¹·cm⁻¹, respectively). Addition of excess metal cations gave no notable spectral changes of **1**.

Upon excitation at 367 nm, fluorescence emissions of **1** in CH₃CN:H₂O (1:9, v/v) were observed at 339, 416, and 440 nm as seen in Figure 2. Fluorescence changes are also indicated upon addition of 10 equiv. of various metal ions. With respect to this fluorescence quenching, **1** reveals Cu²⁺ selectivity over other metal cations for which only a little or

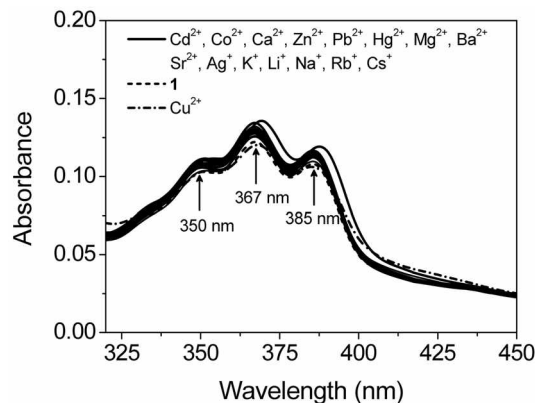
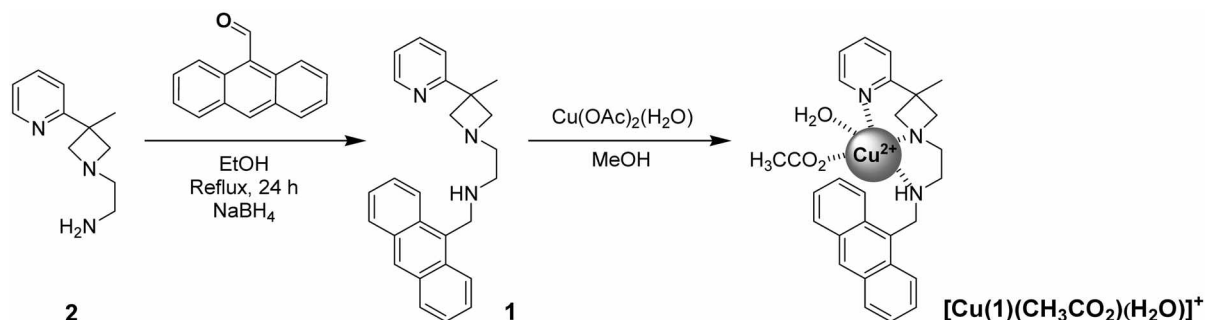


Figure 1. UV/Vis spectra of **1** (20.0 μM) upon addition of ClO₄⁻ salts of Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, Cd²⁺, Co²⁺, Ca²⁺, Zn²⁺, Pb²⁺, Hg²⁺, Mg²⁺, Ba²⁺, Sr²⁺, Cu²⁺ and Ag⁺ (10 equiv.) in aqueous system (CH₃CN:H₂O = 1:9, v/v).



Scheme 1. Synthesis of anthracene derivatives **1** and [Cu(**1**)(CH₃CO₂)(H₂O)]⁺.

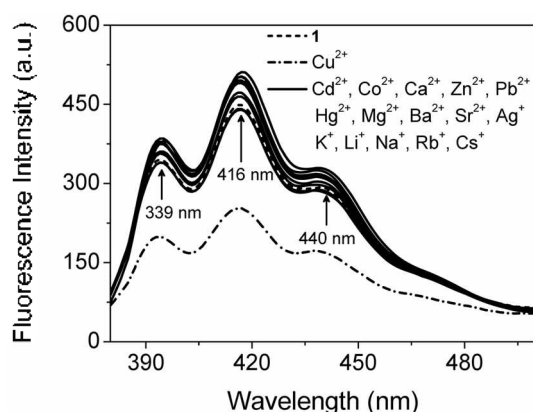


Figure 2. Fluorescence spectra of **1** (4.0 μM) upon addition of ClO_4^- salts of Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Cd^{2+} , Co^{2+} , Ca^{2+} , Zn^{2+} , Pb^{2+} , Hg^{2+} , Mg^{2+} , Ba^{2+} , Sr^{2+} , Cu^{2+} and Ag^+ (10 equiv.) in aqueous solution ($\text{CH}_3\text{CN}:\text{H}_2\text{O} = 1:9$, v/v) with an excitation at 367 nm.

no spectral change was noticed. With 10 equiv. of Cu^{2+} ions, quantum yield of **1** is found to decline from 0.59 to 0.47.⁸ The fluorescence quenching induced by the Cu^{2+} ion can be explained by an electron transfer (ET) from the excited state of the anthracene unit to the Cu^{2+} ion, that is, a heavy metal ion effect.⁹

We obviously found that the fluorescence emission intensities of **1** at 339, 416, and 440 nm (λ_{max}) decreased in a function of $[\text{Cu}^{2+}]$. As seen in Figure 3, the Cu^{2+} titration profile of **1** gives 1:1 stoichiometry, thus the association

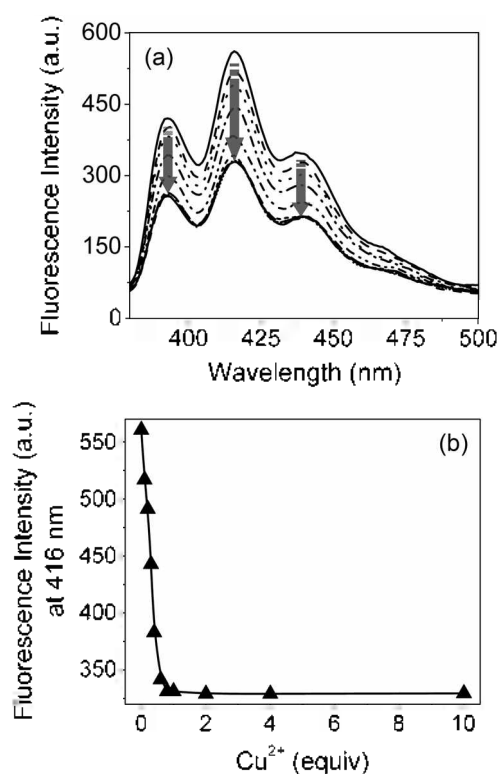


Figure 3. Fluorescence titration spectra (a) of **1** (4.0 μM) and titration profile (b) upon addition of various amounts of $\text{Cu}(\text{ClO}_4)_2$ (0, 0.1, 0.2, 0.3, 0.4, 0.6, 0.8, 1.0, 2.0, 4.0, and 10.0 equiv.) in aqueous system ($\text{CH}_3\text{CN}:\text{H}_2\text{O} = 1:9$, v/v) with an excitation at 367 nm.

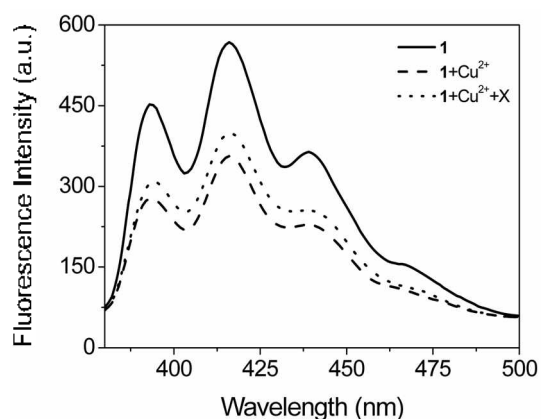


Figure 4. Fluorescence spectra of **1** (4.0 μM) in aqueous solution ($\text{CH}_3\text{CN}:\text{H}_2\text{O} = 1:9$, v/v) in the presence of the Cu^{2+} ion (10 equiv.) and miscellaneous cations (X) including Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Cd^{2+} , Co^{2+} , Ca^{2+} , Zn^{2+} , Pb^{2+} , Hg^{2+} , Mg^{2+} , Ba^{2+} , Sr^{2+} , and Ag^+ (10 equiv., respectively) with an excitation at 367 nm.

constant (K_a) of **1** could be calculated to be $8.9 \times 10^5 \text{ M}^{-1}$.¹⁰

Figure 4 is for competitive experiments performed using 4.0 μM of **1** and Cu^{2+} in the presence of miscellaneous other cations such as Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Cd^{2+} , Co^{2+} , Ca^{2+} , Zn^{2+} , Pb^{2+} , Hg^{2+} , Mg^{2+} , Ba^{2+} , Sr^{2+} , and Ag^+ (10 equiv., respectively). It is well known that Hg^{2+} or Pb^{2+} ion interferes the Cu^{2+} ion selectivity to cause a serious problem in sensory application.^{9a,11} However, the Cu^{2+} selectivity of **1** is partially disturbed in the presence of other various cations including even Hg^{2+} or Pb^{2+} ion.

To gain insight into the complexation mode of $\text{Cu}(\text{1})^{2+}$, we report here the crystal structure of $\text{Cu}(\text{II})$ complex. Green crystals of $[\text{Cu}(\text{1})(\text{CH}_3\text{CO}_2)(\text{H}_2\text{O})](\text{ClO}_4)_{0.33}(\text{PF}_6)_{1.33}$ suitable for a structure determination were obtained by adding NH_4PF_6 and LiClO_4 to a methanol solution of copper acetate. X-ray crystal structure of **1**- Cu^{2+} complex suggests that the coordination geometry of the Cu^{2+} complex gives square pyramidal and indicates 1:1 stoichiometry between **1** and Cu^{2+} . The Cu^{2+} center is tightly coordinated to the azetidine-*N* (1.995 Å), pyridine-*N* (2.075 Å), amino-*N* (2.054 Å), acetato-*O* (1.946 Å) and aqua-*O* (2.237 Å). Among three different *N*-donor centers, the azetidine-*N* forms the strongest binding with Cu^{2+} ion (Figure 5). Then, the electron transfer from excited state of anthracene to Cu^{2+} ion is

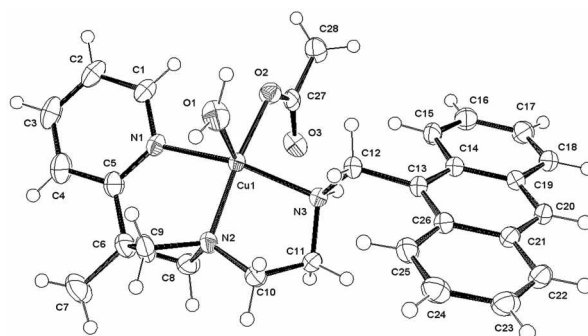


Figure 5. X-ray crystal structure of $[\text{Cu}(\text{1})(\text{CH}_3\text{CO}_2)(\text{H}_2\text{O})]^{2+}$.

implemented to give a quenched emission of **1**.¹²

In summary, we developed a novel anthracene chemosensor (**1**) bearing *N*-functionalized azetidine and pyridine groups. Aqueous solution of **1** shows selectivity toward Cu²⁺ ion over other competitive ions in the aspect of fluorescence quenching. The fluorescence quenching is due to an electron transfer from excited state of the anthracene to Cu²⁺ metal ion. We elucidated from X-ray crystal structure analysis that three nitrogen atoms of **1** are coordinated to Cu²⁺ ion with 1:1 stoichiometry.

Experimental Section

Fluorescence and absorption measurements. Stock solutions (0.01 M) of the hydrated metal perchlorate salts were prepared in CH₃CN. Stock solution of **1** was prepared in CH₃CN. For all fluorescent tests, excitation wavelength was 367 nm with excitation and emission slit widths 3 nm, respectively. Fluorescence titration experiments were performed with 4 μM solutions of **1** and various concentrations of Cu²⁺ perchlorate in mixed-solvent solution (CH₃CN:H₂O = 1:9, v/v). After calculating the concentrations of the free ligand and complex form of **1** from the fluorescence titration experiments, the association constant was obtained using the computer program ENZFITTER.¹⁰

Synthesis

Synthesis of 1: 1-(2-Aminoethyl)-3-methyl-3-(2-pyridyl)azetidine (**2**) (1.0 g) and 9-anthracenecarboxaldehyde (1.0 g) were dissolved in absolute ethanol (50 mL) and stirred for 1 h before being heated at 70 °C for 24 h. After cooling to room temperature, the yellowish-brown solution was taken to dryness under reduced pressure, and the residue dissolved in methanol (100 mL) and cooled to 5 °C. Under continuous stirring, NaBH₄ (0.8 g) was slowly added and the mixture then stirred overnight at room temperature. Excess NaBH₄ was decomposed by addition of 2 M HCl (10 mL) and the solution then made basic by the addition of 1 M NaOH (30 mL) before extraction of the desired ligand with CH₂Cl₂ in water (3 × 50 mL). The combined extracts were washed with water, dried with anhydrous sodium sulfate and evaporated under reduced pressure to give a yellowish-brown oil **1** (1.9 g). ¹H NMR (CDCl₃, 200 MHz): δ 8.54 (d, 1H, *J* = 3.40 Hz), 8.40 (d, 3H, *J* = 11.20 Hz), 7.99 (d, 2H, *J* = 7.80 Hz), 7.49 (m, 6H), 7.12 (d, 1H, *J* = 7.80 Hz), 4.76 (s, 2H), 3.48 (d, 2H, *J* = 7.20 Hz), 3.41 (d, 2H, *J* = 7.20 Hz), 2.90 (t, 2H, *J*₁ = 6.00 Hz, *J*₂ = 5.80 Hz), 2.74 (t, 2H, *J*₁ = 5.80 Hz, *J*₂ = 6.40 Hz), 1.61 (s, 3H).

Synthesis of [Cu(1)(CH₃CO₂)(H₂O)](CH₃COO): Ligand **1** (1.9 g) was dissolved in methanol (50 mL) and Cu(CH₃CO₂)₂·H₂O (1.0 g in 20 mL methanol) added. After stirring for 1 hour, the green solution was taken to dryness under reduced pressure and the residue dissolved in CH₂Cl₂ (50 mL). This solution was washed with water (3 × 50 mL), then dried with anhydrous sodium sulfate, filtered and evaporated under reduced pressure to give a green powder, [Cu(1)(CH₃CO₂)(H₂O)](CH₃COO) (2.5 g). This was used to grow crystal without further characterization and analysis.

Green crystal of [Cu(1)(CH₃CO₂)(H₂O)](ClO₄)_{0.33}-(PF₆)_{1.33}: Above green powder, [Cu(1)(CH₃CO₂)(H₂O)]-(CH₃COO), was dissolved in methanol (50 mL) and an excess of both NH₄PF₆ and LiClO₄ were added. Green crystals suitable for diffraction measurements slowly deposited as the solution was allowed to evaporate at room temperature. Crystallographic data (excluding structure factors) has been deposited in the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 686205. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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