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Cu^{2+}-Induced Intermolecular *Static* Excimer Formation of Pyrenealkylamine

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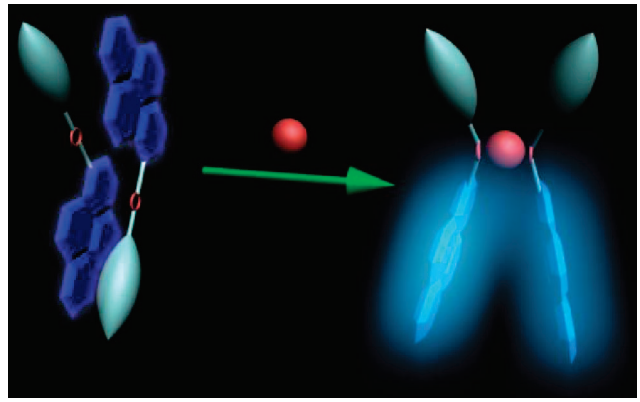
ABSTRACT



Synthesis of monopyrenylalkylamine derivative 1 and its fluorescence behavior for Cu^{2+} in H_2O/CH_3CN (1:1, v/v) were investigated. Upon Cu^{2+} binding, 1, bearing a sulfonamide group, exhibited a marked excimer emission at 455 nm along with a weak monomer emission at 375 nm. The excimer emission, driven by formation of an intermolecular pyrenyl *static* excimer upon Cu^{2+} binding to the sulfonamide group, is rationalized by experimental and theoretical DFT calculation results.

Recently, the development of fluorescent chemosensors capable of selective recognition and sensing of metal ions is one of the most challenging fields from the vantage of organic and supramolecular chemistry.[1,2] The best effective fluorescence chemosensor must convert the event of metal ion recognition by the ionophore into light signals over the fluorophore with high sensitivity and ease of monitoring.[3,4] In designing sensors, therefore, the recognition moiety linked to the fluorophore should be preliminarily considered because they are responsible for the selectivity and binding efficiency of the whole chemosensors.

Over the last few decades, considerable attention has been paid to the development of heavy metal ion sensors, because of their essential and/or deleterious roles, for one species.[1,5–7]

Over other metal ions, Cu^{2+} is an essential trace element for humans, and plays an important role in various biological

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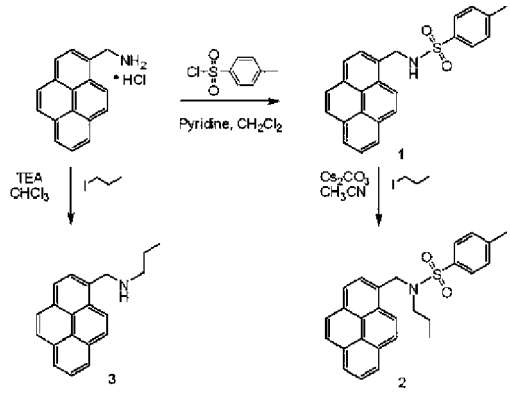
processes. However, it is toxic at higher concentration level, for example, the accumulation of Cu^{2+} in the liver and kidney may cause gastrointestinal, Wilson disease, hypoglycemia, dyslexia and infant liver damage.[8,9] Thus, a number of fluorescent sensors for the Cu(II) have been prepared and reported.[10] However, the fluorescent chemosensors that display fluorescence enhancements by the addition of the Cu(II) ion are limited.[11]

For the fluorescent copper(II) chemosensor, we previously reported that 1,3-dipyrene-appended calix[4]arene exhibited a decreased excimer emission in a function of $[Cu^{2+}]$, that is, excimer "On−Off" system.[12a] In contrast, the pyrene excimer "Off-On" system upon Cu^{2+} ion complexation has been rarely reported till now.[12b] We report herein pyrenylalkylamine derivatives that show an enhancement of the pyrenyl excimer emission by the addition of Cu^{2+} ions in an aqueous media.

Synthetic pathways of fluorogenic molecules **1**−**3** are summarized in Scheme 1. The reaction of 1-pyrenemethylamine hydrochloride with 1.1 equiv of *p*-toluenesulfonyl chloride and pyridine in CH_2Cl_2 affords the desired *N*-tosyl methylpyrene (**1**) in moderate yield. Reaction of **1** with Cs_2CO_3 in CH_3CN leads to *N*-propyl-*N*′-tosyl methylpyrene (**2**) in 63% yield. Treatment of 1-pyrenemethylamine with 1-iodopropane in the presence of Et_3N in $CHCl_3$ produced reference material **3** in 61% yield. (See detailed synthetic procedures in the Supporting Information.)

Scheme 1. Synthetic Pathways of **1**−**3**



In consideration of the solvent system, related to the ratiometry between monomer and excimer emissions of **1** and of its corresponding applicability in aqueous media, we used a mixed solvent of CH_3CN/H_2O (1:1). The solution of **1** displays an intensive absorption band at 342 nm, which is for the pyrene band.

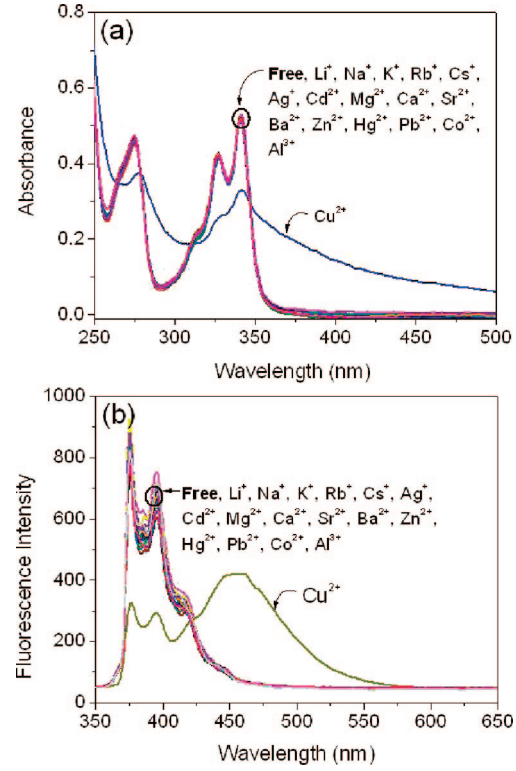


Figure 1. (a) Absorption spectra of **1** (20.0 μM) and (b) fluorescence spectra of **1** (6.0 μM) with addition of ClO_4^- salts of Li^+, Na^+, K^+, Rb^+, Cs^+, Ag^+, Cd^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Hg^{2+}, Pb^{2+}, Co^{2+}, Cu^{2+}, and Al^{3+} (100 equiv, respectively) in H_2O/CH_3CN (1:1, v/v) with an excitation at 342 nm.

UV/vis spectra of **1** over other metal cations (Figure 1). The band broadening and red-shift in the UV spectra of **1** upon the addition of Cu^{2+} ions are attributable to the favorable intermolecular $\pi-\pi$ stacking dimerization of the two pyrenes in the ground state.[13]

To this solution, various metal cations (Li^+, Na^+, K^+, Rb^+, Cs^+, Ag^+, Cd^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Hg^{2+}, Pb^{2+}, Co^{2+}, Cu^{2+}, and Al^{3+}) were added, and the complexation abilities of **1** toward the metal cations were examined from the spectral changes.

Interestingly, we have found unusual fluorescence changes in **1** that, upon addition of Cu^{2+}, gave a pyrene excimer emission at 455 nm in a solution of CH_3CN/H_2O (1:1) as shown in Figure 1b. In contrast, the pyrenyl monomer emission in **1** at 375 nm declines concomitantly to show a ratiometry. For formation of excimer emission in **1**, along with ratiometry when Cu^{2+} is added, we were

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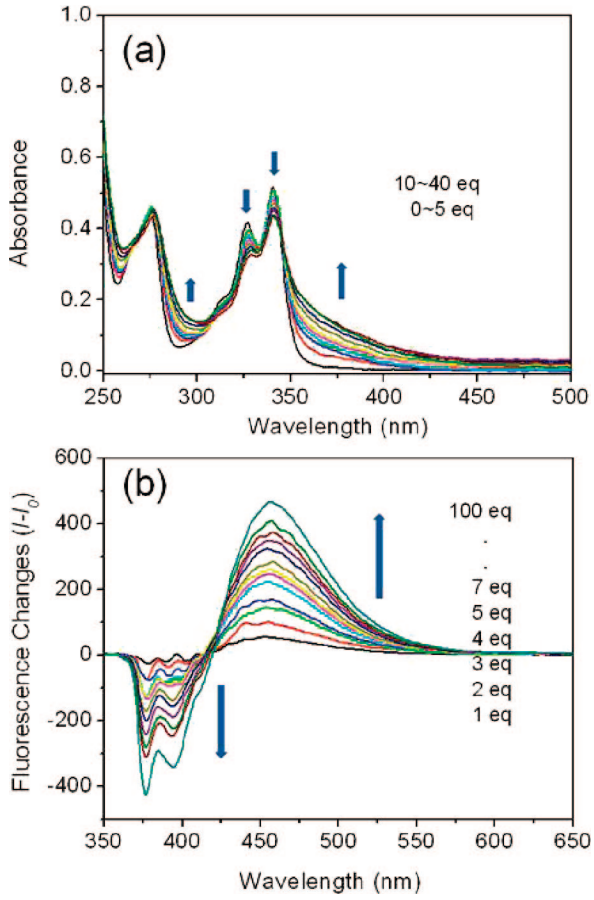

Figure 2. (a) Absorption titration spectra of **1** (20 μM) upon addition of various amounts of $Cu(ClO_4)_2$ (0, 1, 2, 3, 4, 5, 10, 20, 30, and 40 equiv) and (b) fluorescence titration spectra of **1** (6 μM) in H_2O/CH_3CN (1:1, v/v) upon addition of various amounts of $Cu(ClO_4)_2$ (0, 1, 2, 3, 4, 5, 7, 10, 15, 20, 30, 50, and 100 equiv) with an excitation at 342 nm.

motivated to elucidate the complexation mechanism in more detail.

Pyrene is one of the most useful fluorogenic units for fluorescent sensors because it displays not only a well-defined monomer emission but also an efficient excimer emission. Depending upon the origin of the pyrene dimer, there are two kinds of excimers: a *dynamic* excimer and a *static* excimer. The former results from a pyrene dimer formed in the excited state, whereas the latter arises from a pyrene dimer in the ground state. Formation of a *dynamic* or *static* excimer depends on the distance between the two pyrene units.[12,13] A useful method to differentiate a dynamic excimer from a *static* one is the excitation spectrum.[12]The excitation spectra of **1**•Cu^{2+} monitored at 455 nm are red-shifted ($\Delta\lambda$ = 15 nm) in comparison to that recorded at 376 nm, as well as at decreased monomer emission. This is explicit evidence for the formation of intermolecular pyrenyl *static* excimer of **1** in the event of Cu^{2+} ion binding (Figure S1, Supporting Information). Thus, the chemical species corresponding to 455 and 375 nm emissions are different.

To quantify the complexation ratio between **1** and the Cu^{2+} ion, the Job plot measurement was executed by varying concentration of both **1** and Cu^{2+} ion (Figure S2, Supporting Information). The maximum point appears at the mole fraction of 0.6, close to the typical ligand mole fraction (0.66) for 2:1 ligand-to-metal complex. Mass spectrum also confirms the formation of the 2:1 complex (Figure S3, Supporting Information) where there are two major peaks at *m*/*z* 385 and 832, corresponding to [[**1**] + Cu]$^{2+}$ and [**1** • Cu^{2+} • **1**], respectively.

Figure 2 gives detailed absorption and fluorescence changes of **1** upon gradual titration with Cu^{2+} ion. As the Cu^{2+} concentration increases, the excimer band at 455 nm garadually increases. Based on this titration data in Figure 2, the association constant of **1** for Cu^{2+} is 2.8×10^4 M^{-2}.[14] Thus, upon Cu^{2+} binding, **1** is stacked together to have a strong $\pi-\pi$ interaction between two pyrenes, inducing an enhanced excimer emission.

An important feature of **1** is its high selectivity toward Cu^{2+} over other competitive species. Fluorescence spectral changes of **1** were investigated with addition of miscellaneous cations including: Li^+, Na^+, K^+, Rb^+, Cs^+, Ag^+, Cd^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Zn^{2+}, Hg^{2+}, Pb^{2+}, Co^{2+}, Cu^{2+}, and Al^{3+} (Figure S4, Supporting Information). No changes were observed, except in the case of the Cu^{2+} ions. Moreover, in competition experiments of **1**, other miscellaneous cations did not interfere the Cu^{2+} selectivity, which is applicable for the Cu(II) sensing in the industrial field.

To gain insight into the complexation mode of **1** for Cu^{2+} to give an excimer emission, pyrene derivative **3**, bearing no sulfonyl group, was synthesized and its fluorescence studies with Cu^{2+} implemented. When the Cu^{2+} ion is added, the fluorescence of **3** rarely changes, unlike **1** (Figure S5, Supporting Information). Thus, it is notable that the sulfonamide group of **1** plays an important role in the Cu^{2+} complexation.[15]

To further elucidate the binding mechanism of **1** to Cu^{2+}, we also synthesized **2**, bearing propyl groups on the nitrogen atom. Compound **2** showed almost the same binding behavior toward metal ions as did **1**, with respect to the spectral changes (Figure S6, Supporting Information). From the titration experiment, association constants of **1** and **2** for Cu^{2+} in H_2O/CH_3CN (1:1, v/v) were calculated to be 2.4×10^4 and 2.3×10^3 M^{-2}, respectively.

For the latter case, the decrease in the association constant is primarily due to two factors: (a) perturbation of electron density over the donor *N*-atom by the additional propyl group and (b) steric hindrance imposed by the propyl group.[16] Therefore, it should be noteworthy that formation of the excimer emission of **1** upon Cu(II) complexation is quite dependent on the presence of the sulfonyl unit to bind Cu(II), and the presence of an H atom on the nitrogen is a secondary factor to form the dymeric pyrenes (*vide infra*).

For the investigation of fluorescence spectral changes upon Cu^{2+} ion binding to **1**, the density functional theory (DFT)

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calculations were employed using the Gaussian 03 package.[17] Due to the 2:1 ligand-to-metal complexation behavior determined by both mass spectrum and job plot measurements, the dimers of **1** with and without Cu^{2+} ion were subjected to the energy optimization at the B3LYP hydrid functional with 3−21G* basis set.[18] Several different starting geometries were used for the geometry optimization to ensure that the optimized structures corresponded to a global minima. The optimized geometry for the monomer of **1** is represented in Figure S7 (see Supporting Information) and the energy minimized structures for the dimer of **1** both with (**1**-Cu^{2+}) and without the Cu^{2+} ion are shown in Figure 3.

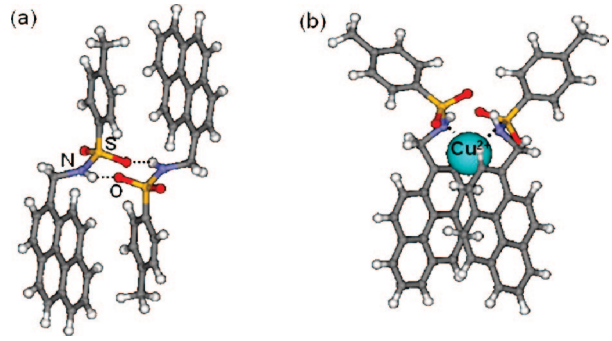

Figure 3. B3LYP/3−21G* optimized geometries for the dimer of **1** (a) and the dimer of **1** with Cu^{2+}ion (b).

Without the Cu^{2+} ion, as shown in Figure 3a, two pyrene groups interact with two benzene groups independently employed by the $\pi-\pi$ interaction.

The resulting dipole moment is to be 0 due to the symmetry. Two, tight NH---OS hydrogen contacts (1.81 Å) are present, contributing to the stability of the dimer of **1**, as shown by the dashed line in Figure 3a.

Converseley, the lowest energy conformation for **1**-Cu^{2+} is located with two pyrene groups facing each other, where the Cu^{2+} ion is recognized by two nitrogen atoms with a distance of 1.97 and 1.99Å, respectively (Figure 3b). Four sulfonamide oxygen atoms also exhibit minor interactions with the Cu^{2+} ion (3.31 Å in average).

It is observed that the distance between two nitrogens in **1**-Cu^{2+} ion is 2.88 Å, whereas that in the dimer of **1** without Cu^{2+} ion is 4.23 Å. Two nitrogen atoms in proximity of the sulfonamide groups might be the dominant factor for Cu^{2+} ion recognition. Overall, the major binding mode in **1**-Cu^{2+} is the electrostatic interaction between Cu^{2+} and the electronegative nitrogen atoms in **1**, and the van der Waals interactions between the stacked pyrenes also stabilize the complex. It is noted that the **1**-Cu^{2+} complex is also stabilized by two NH---OS hydrogen bonds with an average distance of 1.85 Å.

In addition, a time-dependent density functional theory (TDDFT) calculation[19] was executed to characterize the nature of the fluorescence behavior of **1** upon Cu^{2+} ion complexation. The molecular orbital energies and the assocaited electronic transitions were calculated from the optimized geometry of the S_0 state by TDDFT/B3LYP/3-21G* level. Several studies,[20] including our recent reports,[21] have shown that hybrid functionals give the best performance for evaluating electronic transitions in organic molecules. On the basis of the TD-B3LYP/B3LYP/3-21G* calculations, the efficient HOMO-1 to LUMO+1 excitation from one pyrene and to the other pyrene (Py-Py* interaction) presumably contribute to the strong fluorecence excimer bands for **1**-Cu^{2+}, whereas no excimer transitions were found in the dimer of **1** without Cu^{2+} ion, as shown in Figures S1 and S2. In this regard, the experimental observation is in excellent agreement with the theoretical DFT calculation result that the excimer emission corresponding to the Cu^{2+} ion complexation for **1** requires a preorganized cavity with two proximate nitrogen atoms of the sulfonamide groups to recognize the metal ion as well as hydrogen bonds to stabilize the complex.

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Supporting Information Available: Additional figures of UV/vis, fluorescence emission spectra, and optimized geometry for the monomer of **1** (Figure S1−S10). This material is available free of charge via the Internet at http://pubs.acs.org.

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