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A PCT-Based, Pyrene-Armed Calix[4]crown Fluoroionophore

Jung Kyu Choi,[†] Su Ho Kim,[†] Juyoung Yoon,[‡] Keun-Hyeung Lee,[§]
Richard A. Bartsch,[⊥] and Jong Seung Kim*,[†]

Department of Chemistry, Institute of Nanosensor & Biotechnology, Dankook University, Seoul 140-714, Korea, Department of Chemistry and Division of Nano Sciences, Ewha Womans University, Seoul 120-750, Korea, Department of Chemistry, Inha University, Incheon 402-751, Korea, and Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79401

jongskim@dankook.ac.kr

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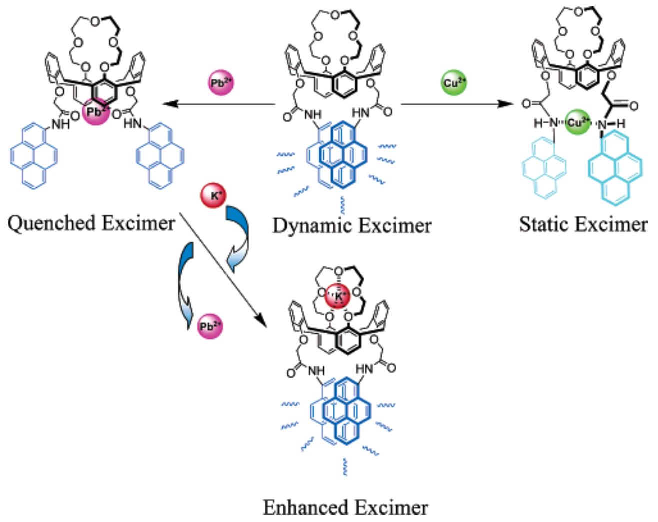

A photoinduced charge transfer (PCT)-based 1,3-alternate calix[4]crown fluoroionophore containing two cation recognition sites, a crown ether ring and two facing pyreneamide groups, is synthesized. Upon addition of K^+, Pb^{2+}, or Cu^{2+}, wavelength changes are observed in both the fluorescence and absorption spectra, but with different binding modes. With K^+, fluorescence emissions of the ligand scarcely change, while addition of Pb^{2+} or Cu^{2+} produces a remarkable change in both the excimer and monomer emissions. The observed data indicate that the metal cation is encapsulated in the crown-5 ring for K^+ and by the two facing amide groups in the latter case, which is verified by a metal ion exchange experiment. The wavelength shifts in both fluorescence and absorption spectra upon addition of Cu^{2+} show that, in contrast to Pb^{2+}, Cu^{2+} interacts with the nitrogen atoms of the amide groups, resulting in a PCT mechanism.

Introduction

On the basis of the concepts provided by host−guest chemistry, cation sensing has recently risen to a dominant position in research devoted to the detection of designated species.[1] This rapid growth is derived from the realization of the diverse roles played by cations in biological and chemical systems.[2] Fluorescent chemosensors capable of selectively recognizing cations have potential analytical applications in many different fields, including chemistry, biology, and medicine.[3,4] Most of the fluorescent chemosensors for cations are

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[†] Dankook University.
[‡] Ewha Womans University.
[§] Inha University.
[⊥] Texas Tech University.

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composed of a cation recognition unit (ionophore) together with a fluorogenic unit (fluorophore) and are called fluoroionophores.[3] An effective fluorescence chemosensor must convert the event of cation recognition by the ionophore into an easily monitored and highly sensitive light signal from the fluorophore.[5] As fluorogenic units, pyrenes (Py) are one of the most useful tools due to their relatively efficient excimer formation and emission.[6] Broan reported that a calixarene-containing pyrenyl ester groups forms an intramolecular excimer due to strong $\pi-\pi$ interaction between two pyrene units.[7]

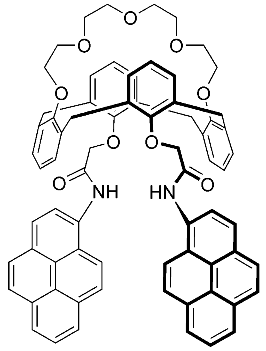
Host molecules with more than one pyrenyl group exhibit intramolecular excimer emission by two different mechanisms. One results from $\pi-\pi$ stacking of the pyrene rings in the free state, which results in a characteristic decrease of the excimer emission intensity and a concomitant increase of monomer emission intensity. The other mechanism is due to interaction of an excited pyrene (Py*) unit with a ground-state pyrene (Py) unit. Some pyrene-containing hosts exhibit excimer emission due to the former mechanism[8] and some due to the latter.[9]

Calixarenes with appropriate appended groups are good candidates as recognition moieties for cation probes because of their high selectivity toward specific cations.[1] Reported calixarene-based fluorescence sensors utilize photophysical changes produced by cation binding: photoinduced electron transfer (PET),[10] photoinduced charge transfer (PCT),[3b,11] and excimer/exciplex formation and extinction.[12] For the PET type, we have previously reported a series of "Molecular Taekwondo I and II" sensors with intramolecular metal ion exchange.[13,14]

In further research on the PCT-based chemosensors, we designed molecule **1** with a crown-5 ring on the lower rim of calix[4]arene (Figure 1). To elucidate the role of the crown ether loop in calixcrown **1**, we utilized analogue **2**.

Results and Discussion

Synthesis of **1** began with calix[4]arene diester **3** (Scheme 1). Compound **6** was obtained from cyclization of **3** with tetraethyleneglycol ditosylate and Cs_2CO_3 in MeCN, followed by basic hydrolysis and then chlorination of dicarboxylic acid **5** with $SOCl_2$.[11a,14] Subsequently, amination of **6** with 2-aminopyrene and Et_3N in THF gave **1** in 54% yield. We also prepared **2** for comparison by adaptation of a synthetic method published earlier.[14]



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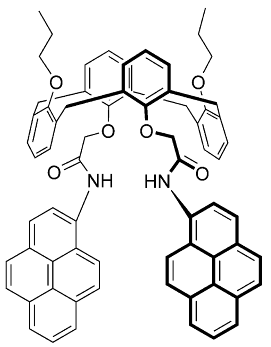

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FIGURE 1. Structures of fluorescence chemosensors **1** and **2**.

Compounds **1** and **2** display both monomer ($\lambda_{em} = 384$ nm) and excimer ($\lambda_{em} = 484$ nm) fluorescence emissions when irradiated at 343 nm in MeCN. Figure 2 shows the changes in the ratio of monomer and excimer emission intensities for **1** and **2** in the presence of large excesses of metal perchlorates. Both **1** and **2** exhibit much greater responses to Pb^{2+} and Cu^{2+} compared to the other metal ions examined. The UV and fluorescence spectral changes for the other transition metal ions were very small and irregular in the titration test.

Titration of Pb^{2+} or Cu^{2+} into MeCN solutions of **1** gave a decrease in fluorescence intensity for both the monomer and excimer bands, as shown in Figure 3. It seems most reasonable that the Pb^{2+} is bound to two facing amide oxygen atoms in conjunction with a conformational change to give quenched monomer and excimer emissions due to a heavy metal ion effect.[14,15] It is reported that Pb^{2+} is coordinated by the oxygen atoms of an amide ligand, while Cu^{2+} is coordinated by the nitrogen atoms.[16] This is verified in the present case by absorption spectroscopy. Upon addition of Pb^{2+}, no change was observed in the UV absorption band of **1**, whereas a red shift was observed upon the addition of Cu^{2+} (Figure S1). The red shift is attributed to a PCT mechanism.[3b,10c] A blue shift of the monomeric fluorescence band of **1** observed upon metal ion complexation is also due to a PCT-based mechanism (Figure 3).[3b,10c,d,16,17] Leblanc et al. previously reported PCT-based peptidyl fluorescent chemosensors for detection of Cu^{2+}, in which they observed a UV band shift of the ligand resulting from N---Cu^{2+} binding.[16a]

To gain insight into the role of the crown ether ring in this system, **2** with two propoxy groups instead of the crown-5 ring was prepared. Upon addition of Pb^{2+} and Cu^{2+}, the absorption and emission bands of **2** showed the same patterns as did those of **1** (Figure S2), revealing that the metal ion is encapsulated in the amide functional part rather than in the crown-5 ring.

Depending upon the origin of the pyrene dimer, there are two kinds of excimers: a *dynamic* excimer and a *static* excimer.[6b] The former results from a pyrene dimer formed in the excited state, whereas the latter arises from a pyrene dimer

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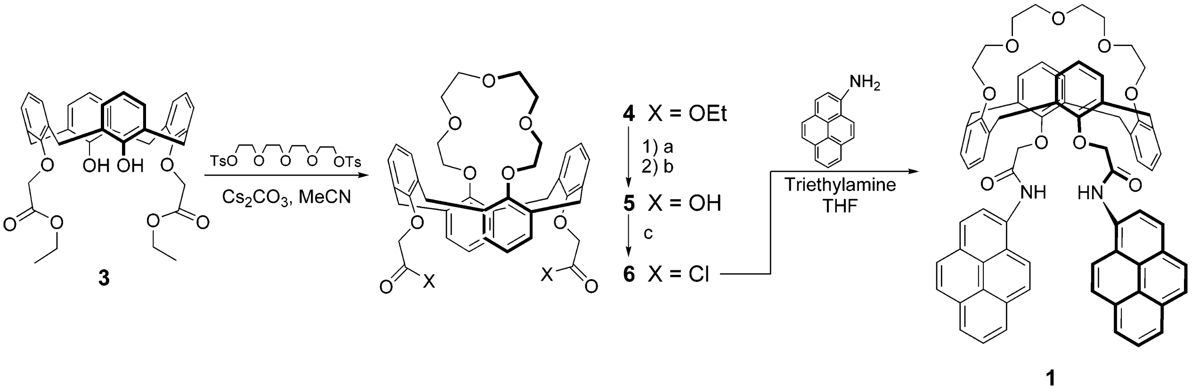
SCHEME 1. Synthetic Routes to Fluorescent Chemosensor 1[a]



[a] (a) NaOH, THF/H_2O/EtOH. (b) 10 % aqueous HCl. (c) $SOCl_2$, toluene.

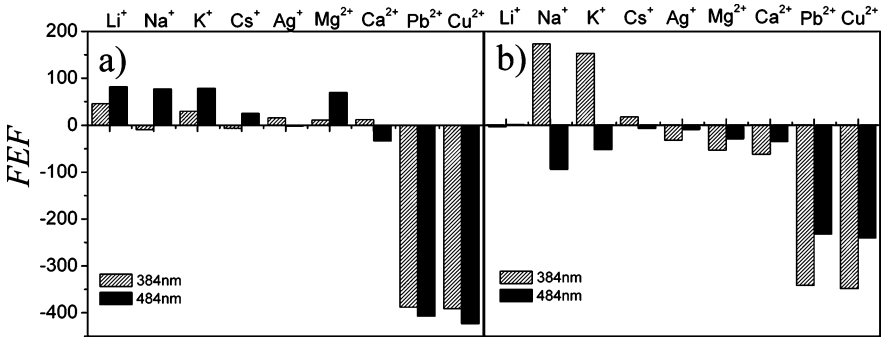


FIGURE 2. Fluorescence enhancement factors (FEF = $I_0 - I$) of (a) **1** and (b) **2** upon addition of various metal cations. Conditions of **1** and **2**: 6.0 μM in MeCN; excitation at 343 nm; metal ions, 500 equiv in MeCN. I_0 = fluorescence emission intensity of free **1** or **2**; I = fluorescence emission intensity of metal ion-complexed **1** or **2**. The two bands at 384 and 484 nm correspond to the monomer and excimer emission bands, respectively.

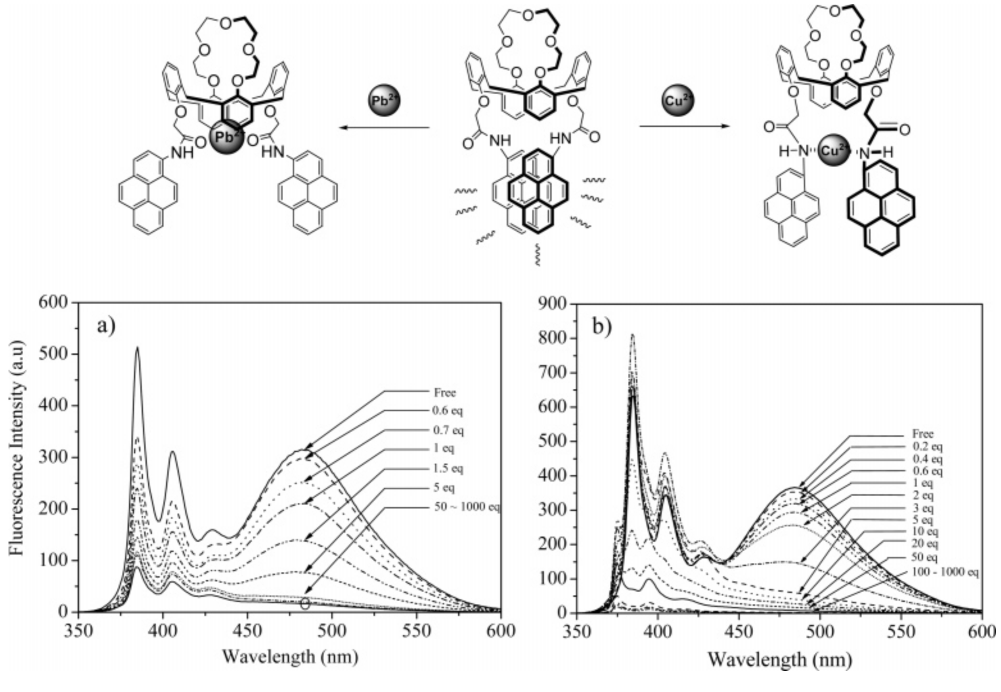


FIGURE 3. Titration profiles for fluorescence emission spectra of (a) **1**·Pb^{2+} and (b) **1**·Cu^{2+} complex in MeCN. Excitation wavelength is 343 nm. Ligand concentration is 6.0 μM.

in the ground state.[6b,11a,15a] Formation of a *dynamic* or *static* excimer depends on the distance between the two pyrene units.[6b] In this study, we found that the excitation spectra of **1** and **1**·Pb^{2+} monitored at the monomer wavelength (380 nm) are almost identical to that recorded at the excimer wavelength (470 nm). On the other hand, the excitation spectrum of **1**·Cu^{2+} monitored

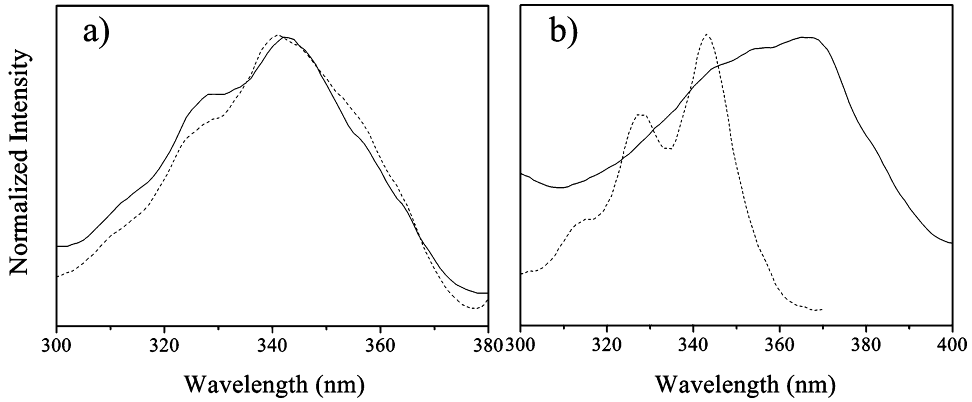


FIGURE 4. Excitation spectra (normalized) of (a) **1**·Pb^{2+} and (b) **1**·Cu^{2+} complex monitored at 380 nm (dashed line) and 470 nm (solid line).

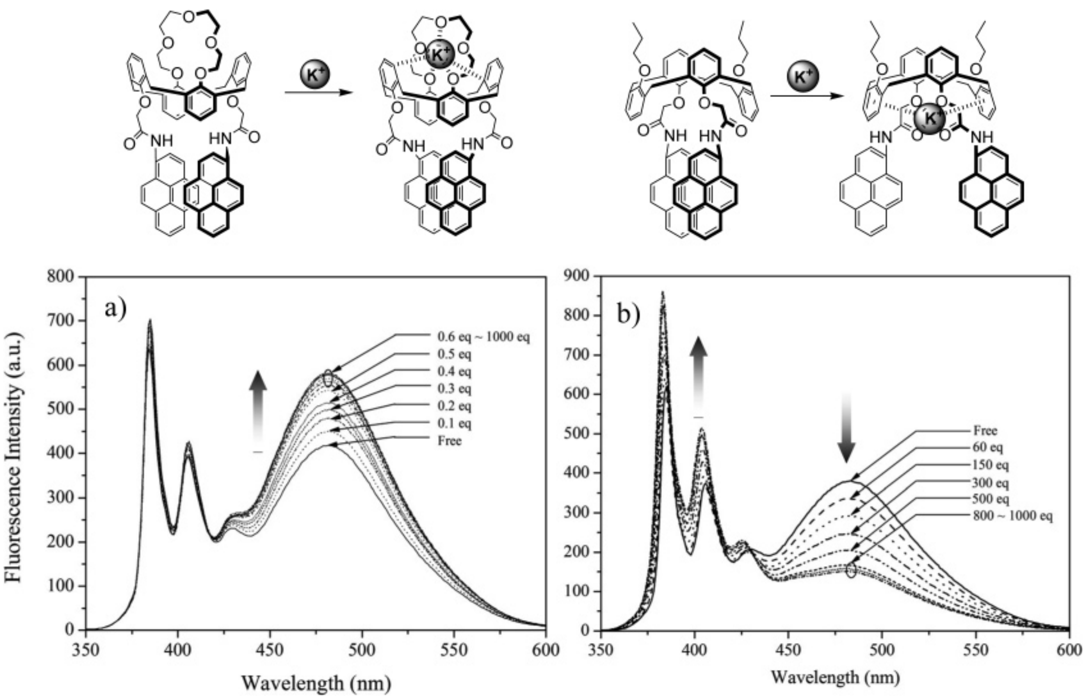


FIGURE 5. Titration profiles for the fluorescence emission spectra of (a) **1**·K^+ and (b) **2**·K^+ in MeCN. Excitation wavelength is 343 nm. Ligand concentration is 6.0 μM.

at 470 nm is remarkably red-shifted in comparison with that measured at 380 nm (Figure 4), indicating that in the **1**·Cu^{2+} complex the two pyrene groups form the *static* excimer. Apparently upon addition of Cu^{2+}, the distance between the two pyrenes becomes shorter due to the formation of HN···Cu^{2+}···NH binding. In the case of Pb^{2+}, the distance between the two pyrenes is lengthened because of C═O···Pb^{2+}···O═C binding.[14] Although the excimer emission is quenched by the heavy Cu^{2+}, the origin of the pyrene excimer emission is thought to be the *static* dimer.

Interestingly, the presence of K^+ gave rise to a fluorescence change different from that of Pb^{2+} or Cu^{2+}. We observed an increase in excimer emission from **1** upon addition of K^+, presumably because the polyether ring of calix[4]crown-5 is more suitable for complexation of K^+ (Figure 5a).[18] In contrast, the excimer emission from **2** which has no crown-5 unit decreased as the concentration of K^+ was enhanced (Figure 5b). From titration with K^+, we obtained the association constants for **1** and **2** of 5.77×10^5 ($\pm$0.1) and 2.03×10^2 M^{-1} ($\pm$0.06), respectively.[19] Regarding this reversal of florescence behavior, one can assume that the **1**·K^+ complex results from that when the first binding event influences other binding or catalytic sites by some conformational change, inhibiting or promoting the binding of other species.[20] We propose that complexation of K^+ provides a more favorable HOMO−LUMO interaction between two pyrenylamide groups in the excited state than those in the ground state. In the case of **2**, the excimer emissions gradually decreased, presumably because K^+ is entrapped by the two facing amide groups of **2** with the aid of aromatic π−K^+

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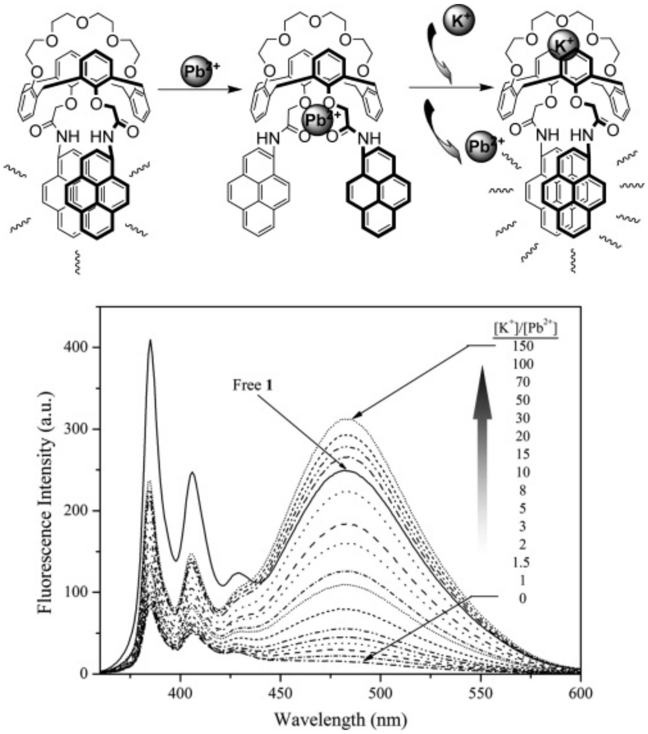

FIGURE 6. Fluorescence changes of the **1**·Pb^{2+} (6.0 μM) complex in MeCN upon addition of K^+. Excitation wavelength is 343 nm.

complexation, giving rise to a less efficient HOMO−LUMO interaction of the two pyrene units in the excited state. For complexation of **1** or **2** with K^+, no change in the UV−vis absorption band was observed, which implies that the PCT effect is no longer present.

Regarding the opposite fluorescence patterns produced by the different binding modes, we examined the metal ion exchange of K^+ and Pb^{2+}. It is known that the K^+ ion is encapsulated in the calixcrown-5-ether ring because of the size complementarity along with the π-metal complexation concept.[18] On the other hand, in our experiments for the binding ability of the two facing amides of **1**, Na^+ ion is better than K^+ ion. To reduce this effect on the metal ion exchange process in combination with two amides, we selected K^+ not Na^+ for investigation. We then observed that when K^+ was titrated into a solution of **1**·Pb^{2+} complex, both the excimer and monomer bands gradually reformed and then became saturated with about 150 equiv of K^+ (Figure 6). The metal ion exchange process takes place predominantly by electrostatic repulsion between the two metal ions. However, when K^+ is added to a solution of **2**·Pb^{2+} complex, the fluorescence intensity scarcely changes (Figure S4), implying that no cation exchange occurs for **2**. This is because the two propyloxy groups are unable to function as a K^+ recognition site. From this metal ion exchange experiment, it appears that the binding ability of the two pyrenylamide groups for Pb^{2+} is greater than that for K^+. In the case of addition of K^+ ion to a solution of **1**·Cu^{2+}, we could not observe the fluorescence changes as shown in Figure S5 probably because the binding ability of two facing nitrogen atoms for copper ion is much larger than that of crown-5.

To elucidate the conformational changes of the calix[4]arene framework related to the metal ion complexation, repeated attempts on the NMR study were carried out, but they were unsuccessful because of their peak broadening. Additionally, crystal growing was not successful.

In conclusion, we report the behavior of PCT-based calix[4]crown fluorescent chemosensors toward transition metal ions (Pb^{2+} and Cu^{2+}) and an alkali metal cation (K^+). For the transition metal ions, both monomer and excimer emissions from **1** and **2** are quenched due to reverse PET and conformational changes. Consistent with the PCT mechanism, wavelength shifts in both absorption and emission spectra for **1** are observed upon Cu^{2+} binding. With **1**, K^+ is encapsulated in the crown-5 ring, which induces a more favorable interaction between the HOMO and LUMO, resulting in stronger excimer formation. In contrast, complexation of **2** with K^+ gives a diminished excimer emission with a concomitant increase in the monomer emission due to the conformational change. Metal ion exchange experiments support the contention for different binding abilities of each binding site for the target metal ions. For further study to apply the compound to the aqueous media, all fluorescence experiments in a DMSO−water system are now in progress.

Experimental Section

Synthesis. Compounds **2**−**6**[11a,14] were prepared by adaptation of procedures reported earlier.

25,27-Bis[*N*-(1-pyrenyl)aminocarbonylmethoxy]calix[4]-crown-5 in the 1,3-Alternate Conformation (1). A solution of **6** (0.30 g, 0.45 mmol), 1-aminopyrene (0.14 g, 0.91 mmol), and Et_3N (1.5 mL, 2.07 mmol) in dry THF (20 mL) was refluxed with stirring for 2 days and then evaporated in vacuo. The resulting solid was dissolved in CH_2Cl_2 (100 mL), and the organic layer was washed three times with water, dried over $MgSO_4$, and evaporated in vacuo. The crude product was chromatographed on silica gel with EtOAc as eluent to give 0.25 g (54%) of **1** as a brownish solid. Mp: 179−180 °C. IR (KBr pellet): 3334, 1720 cm^{-1}. FAB MS m/z (M^+) calcd 1097.3, found 1097.0. Anal. Calcd for $C_{72}H_{60}N_2O_9$: C, 78.81; H, 5.51. Found: C, 78.89; H, 5.56.

General Procedure for Fluorescence Studies. Fluorescence spectra were recorded with an RF-5301PC spectrofluorophotometer. Stock solutions (1.00 mM) of the metal perchlorate salts were prepared in MeCN. Stock solutions of **1** and **2** (0.060 mM) were prepared in MeCN. For all measurements, excitation was at 343 nm with excitation and emission slit widths of 3.0 nm. Fluorescence titration experiments were performed using 6.0 μM solutions of **1** and **2** in MeCN and various concentrations of metal perchlorate in MeCN. After calculating the concentrations of the free ligands and complexed forms of **1** and **2** from the fluorescence titration experiments, we obtained the association constants using the computer program ENZFITTER.[19]

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Supporting Information Available: Additional fluorescence and absorption spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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