

Al³⁺ Selective Chemosensor: Pyrenyl Polyether Pentant Calix[4]arene

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The crucial recognition events of chemistry, biology, and materials science occur in a much smaller world than the one we are accustomed to. Information about these events can be conveniently transmitted to us *via* light signals emitted by purpose-built molecular devices.^{1,2} Besides this sensory role, such molecular devices also have potential for information processing since their emission can be switched between two distinguishable states by environmental stimuli. As a result, much attention has been paid to the fluorometric sensing of specific molecule based on the host-guest interaction.³⁻⁸

Among fluorophores for these purposes, a pyrenyl group has often been used as an excellent fluorescence probe on account of its high sensitivity for detection. In particular, host molecules containing plural pyrenyl groups show an intramolecular excimer emission due to π - π stacking of the pyrene rings in the free state and the emission intensity decreases with the increase of monomer emission intensity upon the addition of metal cations,^{9,10} which is ascribed to the structural change in the host molecules. Since the degree of the structural change is highly dependent on the kind of metal ions, these compounds show selectivity toward a specific metal ion.^{1,10-12}

Therefore, a certain device to bring about the structural change in response to a specific metal ion should be of

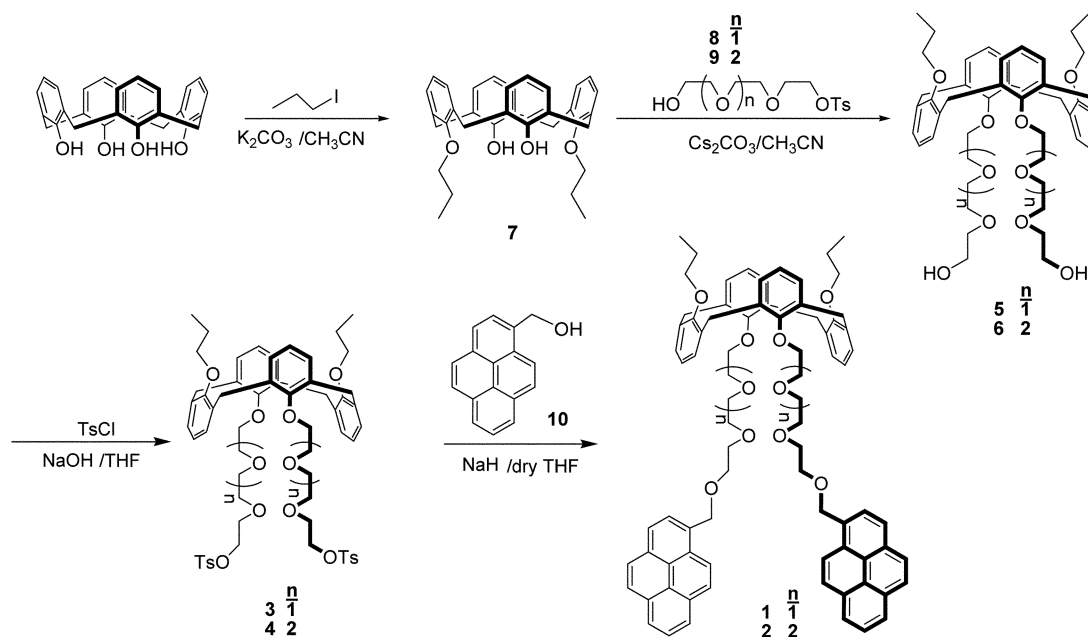
importance in the molecular design of new fluorophore. Indeed, a variety of detection systems for guest molecules and ions has been developed by use of excimer to monomer emission ratio (I_E/I_M) derived from the conformational changes of the pyrene-appended receptor.¹²

In the biochemistry centered on the toxicity of the metal,¹³ Al³⁺ ion has never been known to give a beneficial biological function, but has gained prominence through a possible link to Alzheimer's disease.¹⁴ The detection of Al³⁺ ion is of great interest because of the potential toxicity and the widespread presence of the ion. Our strategy for this purpose is to use the effective coordination of the polyether pendant¹⁵ of the calix[4]arene to Al³⁺ ion.

The chemistry of calixarenes, cyclic oligomers composed of phenolic and methylene moieties, has been extensively studied in recent years.¹⁶ Their pre-organized binding sites, easy derivatization and flexible three-dimensional steric structures make them perfect platforms for sensor to generate fluorescent receptors.¹⁶

From this point of view, we herein report a synthesis of new fluorescent compounds **1** and **2** bearing dipyrenyl polyether on the lower rim of the calix[4]arene, and their complexation properties for Al³⁺ ion by fluorescence spectrometry.

As shown in Scheme 1, the reaction of dipropyloxy



Scheme 1. synthetic routes for fluorescent chemosensor **1** and **2**.

Table 1. Fluorescence changes ($I - I_0$) of **1** and **2** upon the addition of various metal cations^a

ligand	λ_{em} (nm)	Fluorescence change ($I - I_0$)									
		Li ⁺	Na ⁺	K ⁺	Cs ⁺	Ag ⁺	Mg ²⁺	Ca ²⁺	Pb ²⁺	Cu ²⁺	Al ³⁺
1	398	-6	-10	-5	-7	-1	-3	150	-60	-121	621
	475	-30	-27	-22	-31	-62	-30	-5	-558	-548	-531
2	398	-6	-7	-9	-10	-9	-8	142	-73	-135	644
	475	-26	-36	-19	-26	-74	-35	-11	-563	-528	-502

^aConditions: **1** and **2**: 6.0 μ M in MeCN; excitation at 343 nm; metal ions, 500 equiv. in MeCN. I_0 : fluorescence emission intensity of free **1** and **2**; I : fluorescence emission intensity of metal ion-complexed **1** and **2**. (+) and (-) denote fluorescence intensity increase and decrease, respectively.

calix[4]arene **7**¹⁷ with **8** in the presence of Cs₂CO₃ in MeCN affords **5**, which undergoes tosylation with *para*-toluenesulfonyl chloride to provide **3**. Subsequently, the tosylated calix[4]arene is treated with pyrenemethanol and NaH in dry THF to give **1** in 76% yield. Compound **2** was prepared by the same method that used for **1**. Compounds **1-6** are in the 1,3-alternate conformation as confirmed by their NMR spectra: (a) a singlet around 3.8 ppm for methylenic protons of ArCH₂Ar in the ¹H NMR spectra and (b) singlet at about 38 ppm for the ArCH₂Ar bridge carbons in the ¹³C NMR spectra.

The fluorescence titrations of **1** and **2** with various metal ions were conducted to examine the selectivity. Addition of alkali and alkaline earth metal ions gave no change of the fluorescence of **1** and **2** (Table 1). In the case of addition of Pb²⁺ and Cu²⁺ ions, we observed a fluorescence intensity quenched in both monomer and excimer emission bands (Figure 1). This results from the cation- π interactions between the heavy metal ion and the electron-rich aromatic moiety.¹⁸ As a result, the pyrene-Cu²⁺ complex induces an

extensive charge transfer from *d*-orbital of the metal ion to δ^* -orbital of the pyrene leading to a complete quenching.¹⁹ The noticeable changes of the fluorescence are in a good agreement with many other analogous observations previously reported.¹²

On the other hand, interestingly, we observed a unique ratiometry of monomer and excimer emissions of the pyrenes in the event of the addition of Al³⁺ ion to a solution of **1** or **2** (Table 1). The Al³⁺ ion complexation revealed a markedly increasing monomer emission with concurrently decreasing excimer emission of the two pyrenes (Figure 2). This ratiometry was observed only in the case of addition of Al³⁺ ion to a solution of **1** or **2**.

This drastic spectral ratiometry is ascribed to the conformational change of **1** and **2** driven by the cooperative coordination of the pentant polyether to Al³⁺ ion, which inhibits an efficient intramolecular HOMO(π)-LUMO(π^*) interaction of two pyrenes. It is noteworthy that one isoemissive point at 433 nm in the spectra, supporting that the complex stoichiometry for ligand with Al³⁺ ion is 1 : 1. Despite a different

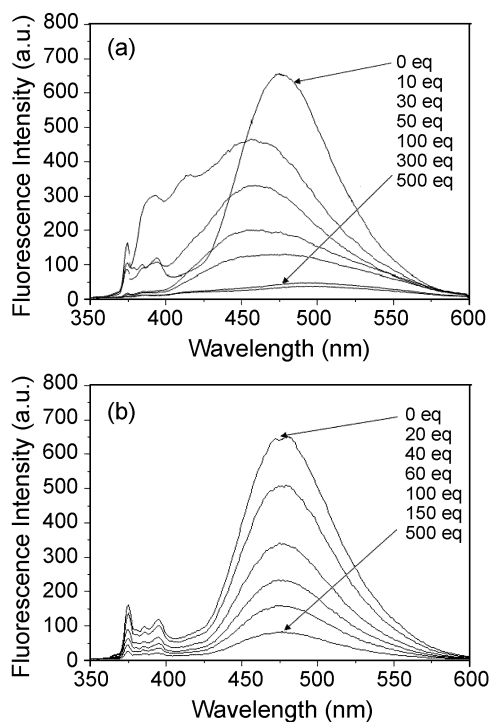


Figure 1. Fluorescence emission spectra of **1** (6.0 μ M) upon titration (a) with Cu²⁺ and (b) with Pb²⁺ in MeCN. The excitation wavelength was 343 nm.

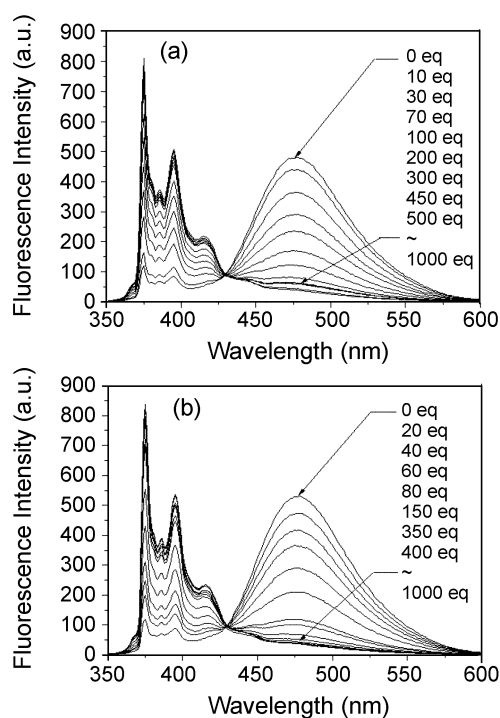


Figure 2. Fluorescence emission spectra of (a) **1** and (b) **2** (6.0 μ M) upon the addition of various amounts of Al³⁺ in MeCN. The excitation wavelength was 343 nm.

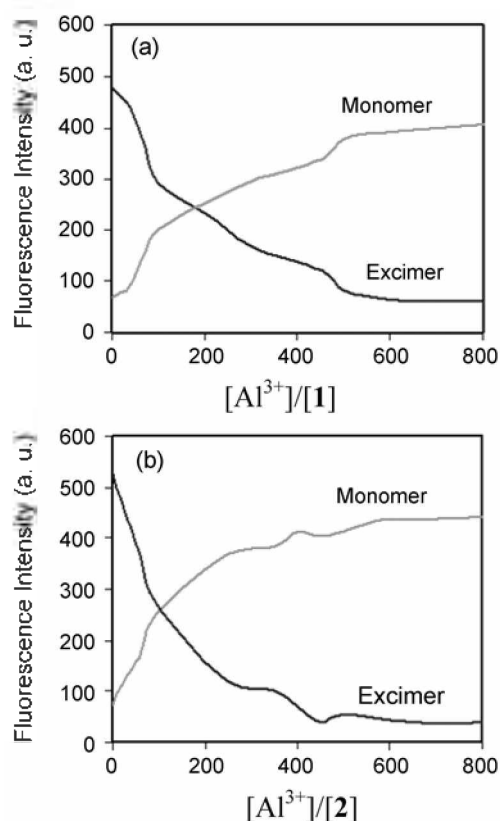


Figure 3. Changes of I_m and I_E of **1** and **2** (6.0 μ M) upon addition of Al^{3+} in MeCN. Excitation wavelength: 343 nm.

length of the spacer between pyrene and calixarene, they show same propensity of the fluorescence ratiometry towards the Al^{3+} ion. On the other hand, addition of alkali metal cations (Li^+ , Na^+ , K^+ , Cs^+) and alkaline earth metal cations (Mg^{2+} , Ca^{2+}) caused no change in the fluorescence emission of **1** and **2** contrary to our expectation.

Plausible complexation mechanism of compound **1** or **2** with Al^{3+} ion is depicted in Figure 3. The two pyrenes of the ligand in solution are in strong Py-Py* interaction when they are irradiated. When the Al^{3+} ion is entrapped by a pair of polyethylene glycol unit with aid of calix[4]arene, the two pyrenes cross each other over the polyethylene group. As a result, the intramolecular π - π interaction of the two pyrenes is declined to give a decreasing excimer emission of the pyrene and the monomer emission of the pyrene increases. This fact is consistent with a result previously reported by Bartsch group.²⁰

In conclusion, we synthesized a series of pyrenyl polyether-appended fluorescence calix[4]arene chemsensor in moderate yield. Excited at 343 nm, free ligand forms a strong excimer due to an interaction of the excited Py* with the ground-stated Py. Enhancement in monomer emission with a quenched excimer emission of compounds **1** and **2** induced by Al^{3+} indicates that they show a high selectivity for Al^{3+} over other metal cations. This is presumably because the Al^{3+} binding induces a conformational change of the ligand to inhibit an efficient HOMO-LUMO interaction between two pyrenes (Py-Py*). It is believed that **1** and **2**

can be used as an innovative sensor for Al^{3+} ion in fluorescence indication.

Experimental Section

25,27-Dipropoxy-26,28-bis[(1-pyrenylmethyl)triethylene glycoloxy]calix[4]arene, 1,3-alternate (1). Under nitrogen, a mixture of 2.0 g (1.85 mmol) of **3** and 0.90 g (3.88 mmol) of 1-pyrenemethanol (**10**) in 100 mL of dry THF, anhydrous NaH 0.38 g (15.8 mmol) was added under nitrogen atmosphere. The reaction mixture was refluxed for 24 hours. After removal of the solvent *in vacuo*, HCl solution (100 mL) and CH_2Cl_2 (100 mL) were added and organic layer was separated and then washed two times with 50 mL of water. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated *in vacuo* to give a yellowish oil which was purified by column chromatography on silica gel with ethyl acetate : hexane (1 : 2) to provide 1.7 g (76%) of **1** as a yellow oil. 1H NMR (200 MHz; $CDCl_3$): δ 8.34-7.98 (m, 18H, Ar-H in pyrene), 7.14 (d, 4H, Ar- H_m , $J = 7.9$ Hz), 6.96 (d, 4H, Ar- H_m , $J = 6.1$ Hz), 6.65 (t, 4H, Ar- H_p , $J = 7.0$ Hz), 5.24 (s, 4H, Ar- CH_2 -O), 3.77-3.48 (m, 8H, Ar- CH_2 -Ar, 24H, OCH_2CH_2 O: 4H, OCH_2CH_2), 1.69-1.61 (m, 4H, CH_2 - CH_2CH_3), 0.92 (t, 6H, $CH_2CH_2CH_3$, $J = 7.04$ Hz). ^{13}C NMR ($CDCl_3$): 156.3, 155.1, 133.5, 133.3, 131.3, 131.1, 129.8, 129.7, 127.5, 127.3, 127.0, 125.8, 125.1, 124.1, 123.5, 121.6, 121.4, 73.9, 71.7, 70.7, 70.5, 70.2, 69.4, 35.5, 23.6, 10.5 ppm. FAB MS m/z (m^+): Calcd, 1201.49. Found, 1200.21.

25,27-Dipropoxy-26,28-bis[(1-pyrenylmethyl)tetraethylene glycoloxy]calix[4]arene, 1,3-alternate (2). Compound **2** was prepared by almost the same method that used for **1**. 1H NMR (200 MHz; $CDCl_3$): δ 8.41-7.98 (m, 18H, Ar-H in pyrene), 7.02 (d, 4H, Ar- H_m , $J = 7.9$ Hz), 6.96 (d, 4H, Ar- H_m , $J = 7.9$ Hz), 6.72 (t, 4H, Ar- H_p , $J = 8.0$ Hz), 5.24 (s, 4H, Ar- CH_2 -O), 3.74-3.53 (m, 8H, Ar- CH_2 -Ar, 32H, OCH_2CH_2 O: 4H, OCH_2CH_2), 1.72-1.65 (m, 4H, $CH_2CH_2CH_3$), 0.96 (t, 6H, $CH_2CH_2CH_3$, $J = 7.1$ Hz). ^{13}C NMR ($CDCl_3$): 156.3, 155.7, 133.5, 133.4, 131.3, 131.1, 130.7, 129.8, 129.7, 129.3, 128.1, 127.5, 127.3, 126.9, 125.8, 125.1, 124.8, 124.6, 124.4, 123.4, 121.6, 121.4, 73.8, 71.7, 70.7, 70.5, 70.2, 69.5, 35.6, 23.6, 10.4 ppm. FAB MS m/z (m^+): Calcd, 1311.50. Found, 1312.32.

25,27-Dipropoxy-26,28-bis[(triethylene glycoloxy)calix[4]arene ditosylated, 1,3-alternate (3). To a solution of **5** (1.46 g, 1.9 mmol) and *p*-toluenesulfonyl chloride (1.85 g, 9.7 mmol) in 100 mL of THF was added dropwise a solution of NaOH (0.3 g, 9.7 mmol) in 5 mL of water at 0 $^\circ$ C. The solution was warmed to room temperature and stirred for additional 24 h. After removal of THF *in vacuo*, the crude product was dissolved in CH_2Cl_2 (100 mL) and the organic layer was washed three times with water. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated *in vacuo* to give a yellowish oil which was further purified by column chromatography on silica gel with ethyl acetate : hexane (1 : 2) to provide 1.54 g (74%) of **3**. 1H NMR (200 MHz; $CDCl_3$): δ 7.81-7.77 (d, 2H, ArH, tosyl, $J = 7.9$ Hz), 7.34-7.30 (d, 2H, ArH, tosyl, $J = 7.9$ Hz).

7.06-6.97 (t, 8H, Ar- H_m , $J = 4.4$ Hz), 6.70-6.61 (m, 4H, Ar- H_p), 3.79-3.53 (m, 8H, ArCH₂Ar; 24H, OCH₂CH₂O; 4H, OCH₂CH₂), 2.43 (s, 6H, ArCH₃, tosyl), 1.72-1.65 (m, 4H, OCH₂CH₃), 0.99-0.92 (t, 6H, OCH₂CH₃, $J = 7.2$ Hz) ¹³C NMR (CDCl₃): 156.3, 155.7, 133.5, 129.8, 128.16, 121.7, 74.9, 70.4, 70.2, 69.23, 68.7, 35.6, 28.1, 21.6, 10.5 ppm. FAB MS m/z (m^+): Calcd, 1081.34. Found, 1080.01.

25,27-Dipropoxy-26,28-bis[tetraethylene glycoloxy]-calix[4]arene ditosylated, 1,3-alternate (4). Compound 4 was prepared by almost the same method that used for 3. ¹H NMR (200 MHz, CDCl₃): δ 7.81-7.77 (d, 2H, ArH, tosyl, $J = 7.9$ Hz), 7.34-7.30 (d, 2H, ArH, tosyl, $J = 7.9$ Hz), 7.05-6.97 (t, 8H, Ar- H_p , $J = 7.9$ Hz), 6.66-6.58 (m, 4H, Ar- H_p), 3.78-3.57 (m, 8H, ArCH₂Ar; 32H, OCH₂CH₂O; 4H, OCH₂-CH₂), 2.42 (s, 6H, ArCH₃), 1.74-1.67 (m, 4H, OCH₂CH₃), 1.00-0.98 (t, 6H, OCH₂CH₃). ¹³C NMR (CDCl₃): 156.3, 155.7, 133.4, 129.7, 128.0, 121.6, 73.9, 70.6, 70.2, 69.2, 68.6, 35.54, 28.6, 23.6, 10.5 ppm. FAB MS m/z (m^+): Calcd, 1191.53. Found, 1191.0. Anal. FAB MS m/z (m^+): Calcd, 1191.53. Found, 1191.00.

25,27-Dipropoxy-26,28-bis[triethylene glycoloxy]-calix[4]arene, 1,3-alternate (5). Under nitrogen, a mixture of 7 (3 g, 5.8 mmol), triethyleneglycol monotosylate (8) (3.59 g, 12 mmol), and Cs₂CO₃ (5.76 g, 12.8 mmol) in MeCN (250 mL) was refluxed for 24 h, and the solvent was removed *in vacuo*. To the resulting yellowish, it was dissolved in CH₂Cl₂ (250 mL) and the organic layer was washed three times with water. The organic layer was dried over anhydrous MgSO₄, and the solvent was evaporated *in vacuo* to give a yellowish oil which was purified by column chromatography on silica gel with ethyl acetate : hexane (1 : 2) to provide 1.7 g (35%). ¹H NMR (200 MHz, CDCl₃): δ 7.09-7.05 (d, 4H, Ar- H_m , $J = 7.9$ Hz), 7.01-6.98 (d, 4H, Ar- H_m , $J = 6.1$ Hz), 6.72-6.64 (t, 4H, Ar- H_m , $J = 7.0$ Hz), 3.80-3.50 (m, 8H, ArCH₂Ar; 24H, OCH₂CH₂O; 4H, OCH₂CH₂), 1.69-1.61 (m, 4H, CH₂CH₂CH₃), 0.95-0.88 (t, 6H, CH₂CH₂-CH₃, $J = 7.04$ Hz). ¹³C NMR (CDCl₃): 156.53, 155.8, 133.6, 129.7, 128.2, 121.5, 73.6, 72.6, 70.5, 61.8, 36.0, 28.7, 23.5, 10.4 ppm. FAB MS m/z (m^+): Calcd, 772.96. Found, 773.21.

25,27-Dipropoxy-26,28-bis[tetraethylene glycoloxy]-calix[4]arene, 1,3-alternate (6). Compound 6 was prepared by almost the same method that used for 5. ¹H NMR (200 MHz, CDCl₃): δ 7.09-7.05 (d, 4H, Ar- H_m , $J = 7.9$ Hz), 7.00-6.97 (d, 4H, Ar- H_m , $J = 6.1$ Hz), 6.74-6.62 (t, 4H, Ar- H_m , $J = 7.1$ Hz), 3.80-3.50 (m, 8H, ArCH₂Ar; 32H, OCH₂CH₂O; 4 H, OCH₂CH₂), 1.68-1.60 (m, 4H, CH₂CH₂CH₃), 0.93-0.85 (t, 6H, CH₂CH₂CH₃, $J = 7.03$ Hz). ¹³C NMR (CDCl₃): 156.3, 155.5, 133.1, 129.4, 128.0, 121.2, 73.3, 72.3, 70.2, 61.3, 35.6, 28.4, 23.2, 10.1 ppm. FAB MS m/z (m^+): Calcd, 861.07. Found, 861.00.

General Procedure for Fluorescence Studies. Fluorescence spectra were recorded with a RF-5301PC spectrofluorophotometer. Stock solutions (1.00 mM) of the metal perchlorate salts were prepared in MeCN. Stock solutions of 1 and 2 (0.06 mM) were prepared in MeCN. For all measurements, excitation was made at 343 nm with excitation slit widths at 1.5 nm and emission slit widths at 3 nm.

Fluorescence titration experiments were performed using 6.0 μ M solutions of 1 and 2.

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