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Fluorometric Sensing of Alkaline Earth Metal Cations by New Lariat Ethers Having Plural Pyrenylmethyl Groups on the Electron-Donating Sidearms

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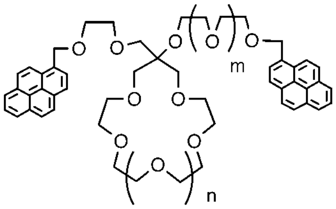
ABSTRACT



1a (m = 0, n = 1)
1b (m = 1, n = 1)

New fluorescent compounds (1), lariat ethers having plural pyrenylmethyl groups on the sidearms, were prepared, and their complexation behavior with alkaline earth metal cations was examined by fluorescence spectrometry. The pyrene excimer emission decreased accompanied with an increase in the monomer emission upon complexation with the metal ion. This finding is ascribed to the cooperative participation of one of the two sidearms in the complexation of the crown ring with the metal ion.

Recently, much attention has been paid to the fluorometric sensing of a specific molecule based on the host−guest interaction.[1] For example, a pyrenyl group has often been used as an excellent fluorescence probe on account of its high sensitivity for detection.[2] In particular, host molecules containing plural pyrenyl groups show an intramolecular excimer emission due to $\pi-\pi$ 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, 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. 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 fluorophores. Indeed, a variety of detection systems for guest molecules and ions have been developed by use of fluorescence changes in intramolecular excimer emission or fluorescence quenching of various pyrene-functionalized ligands.[3] Our strategy for this purpose is to use the effective coordination of the

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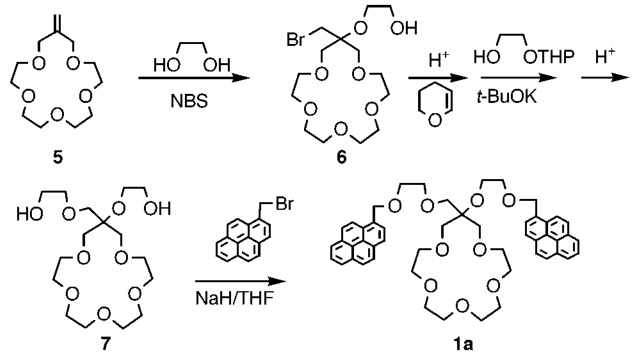
electron-donating sidearm of lariat ethers to metal ions. Lariat ethers are known to be effective as host molecules for alkali metal and alkaline earth metal cations on the basis of their cooperative coordination function of the crown ring and the electron-donating sidearms to the cations.[4−8]

From this point of view, we describe the synthesis of new fluorescent compounds, lariat ether derivatives possessing plural pyrenylmethyl groups on the sidearms, and their complexation properties with alkali metal and alkaline earth metal cations by fluorescence spectrometry.

The synthetic route to compound **1a** is summarized in Scheme 1. Compound **6** was prepared by the bromoalkoxylation reaction of 15-methylene-16-crown-5 (**5**)[9] using *N*-bromosuccinimide (NBS) and ethylene glycol. The hydroxyl group of **6** was protected by treatment with 3,4-dihydro-2*H*-pyran according to the conventional method, and then the compound was reacted with ethylene glycol monotetrahydropyran-2-yl ether under basic conditions, followed by deprotection to give **7**. The reaction of **7** and 1-bromomethylpyrene was carried out in THF in the presence of NaH at reflux temperature for 36 h to afford **1a**. Compounds **1b** and **2** were also prepared in a similar way to **1a**. All the structures (Figure 1) were ascertained by ^{1}H NMR and IR spectroscopy, mass spectrometry, and elemental analysis.

Scheme 1. Preparation of Compound **1a**



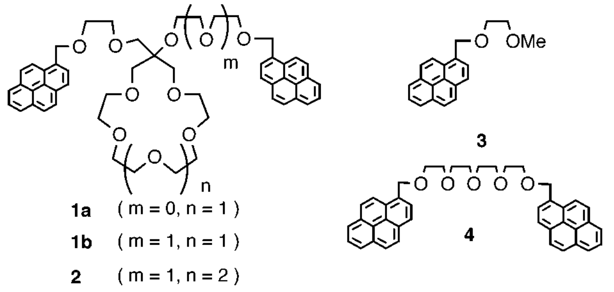


Figure 1. Structures of fluorophores

Figure 2 shows the fluorescence spectra of **1a**, **1b**, and **3**. Compound **3** containing one pyrene ring showed only a monomer emission at 395 nm at the concentration of 2 × 10^{-6} M, whereas compounds **1a** and **1b** containing two pyrene rings showed strong excimer emission at 480 nm at the concentration of 1 × 10^{-6} M. On the basis of the concentration of fluorophore, the excimer emission of **1a** and **1b** is attributed to the intramolecular $\pi-\pi$ stacking of two pyrene rings.

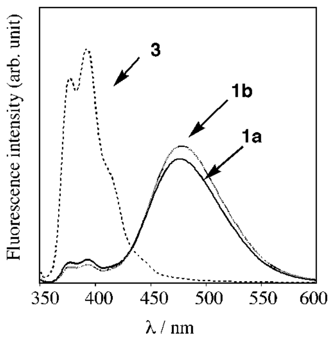


Figure 2. Fluorescence spectra of **1a** (1 × 10^{-6} M), **1b** (1 × 10^{-6} M), and **3** (2 × 10^{-6} M) in 99:1 v/v $CH_3CN/CHCl_3$. Excitation wavelength: 340 nm.

To evaluate the complexation behavior of fluorophore **1a**, we measured the fluorescence spectra of **1a** as functions of concentrations of Ca^{2+} perchlorate in a mixed solvent of 99:1 v/v $CH_3CN/CHCl_3$ at room temperature (Figure 3).

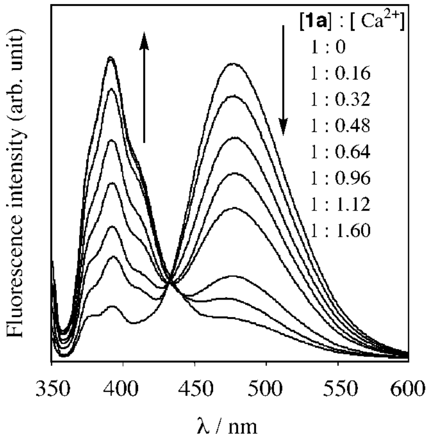


Figure 3. Fluorescence spectral changes in **1a** (1 × 10^{-6} M) with different concentrations of $Ca(ClO_4)_2$ in 99:1 v/v $CH_3CN/CHCl_3$. Excitation wavelength: 340 nm.

Figure 3 shows that the fluorescence intensity of the excimer emission of **1a** decreases with the increase of the

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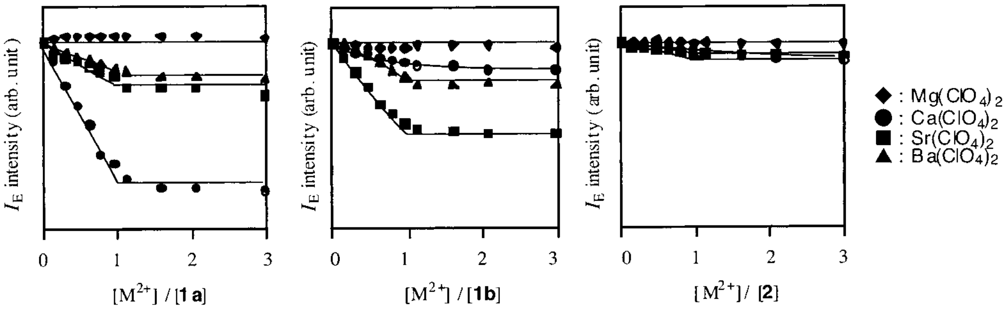

Figure 4. Changes of I_E of **1a** (left), **1b** (center), and **2** (right) upon addition of alkaline earth metal cations in 99:1 v/v $CH_3CN/CHCl_3$. [**1a**] = [**1b**] = [**2**] = 1 × 10^{-6} M. Excitation wavelength: 340 nm.

Ca^{2+} concentration, while the fluorescence intensity of the monomer emission increases. This dramatic spectral change is ascribed to the conformational change in **1a**, which inhibits the intramolecular $\pi-\pi$ stacking of the pyrene rings, caused by the cooperative coordination of the crown ring and the sidearm to Ca^{2+}. An isoemissive point at 433 nm indicates the presence of only one type of complex (**1a**·Ca^{2+}) involved. On the other hand, fluorophore **4** (a tetraethylene glycol derivative) as a reference hardly responded to any kind of alkali metal and alkaline earth metal cations. This result clearly demonstrates that higher complexing ability toward metal ions is needed for the fluorescence ionophore and the presence of a crown ring is effective.

The existence of the **1a**·Ca^{2+} complex in solution was evidenced by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of **1a** showed two signals at 4.82 and 4.84 ppm based on the methylene protons adjacent to two pyrene rings in 2:1 v/v $CD_3CN/CDCl_3$. Upon addition of an equimolar amount of $Ca(ClO_4)_2$, the methylene protons were shifted downfield to 4.87 and 5.04 ppm. This downfield shift clearly indicates the effective coordination of the electron-donating sidearm to the calcium ion.[8a] The difference in the extent of the peak shifts between the two kinds of methylene protons by the addition of calcium ion suggests that only one of the two sidearms participates in complexation with the cation. The sidearm constituting the glycerol structure at the pivot carbon should be responsible for the complexation, according to our previous work.[8d]

Next, the fluorescence intensity of excimer emission (I_E) of **1a**, **1b**, and **2** at 480 nm was plotted against the ratio of [metal]/[ligand] (Figure 4).

The stability constant (K) of the complex was evaluated from the curve by means of a nonlinear least-squares curve-fitting method. The curve showed that all the ligands formed 1:1 complexes. The K values of **1a**, **1b**, and **2** toward alkaline earth metal cations are summarized in Table 1.

Table 1. Stability Constant (log K) of **1a**, **1b**, and **2** for Alkaline Earth Metal Cations in 99:1 v/v $CH_3CN/CHCl_3$

	log K (M^{-1})			
	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
1a	nd	7.6	6.8	6.9
1b	nd	6.7	8.2	7.4
2	nd	5.5	6.9	9.0

As shown in Figure 4, alkaline earth metal cations except for Mg^{2+} noticeably decreased the fluorescence intensity of excimer emission of **1a** and **1b** with an increase in the intensity of the corresponding monomer. On the other hand, alkali metal cations (Li^+, Na^+, K^+) caused no change in the fluorescence spectra of **1a** and **1b** contrary to our expectations. Compounds **1a** and **1b** showed selectivity toward Ca^{2+} and Sr^{2+}, respectively, among seven alkali metal and alkaline earth metal ions examined in this work. The stability constants of **1a** and **1b** for alkaline earth metal cations also afforded the same cation selectivity (Table 1). The increase in the stability constant toward Sr^{2+} of **1b** in comparison with that of **1a** should be ascribed to the participation of the electron-donating sidearm in the complexation of the cation. This observed change in the cation selectivity is reasonably explained by considering the enlargement of the cavity size by elongation of the oxyethylene chain in the latter case.

Furthermore, the effect of crown ring size on the fluorescence behavior was evaluated by comparing **1b** and **2**.

The change in the fluorescence spectra of **2** upon addition of alkaline earth metal cations was much smaller compared to that of **1b** bearing the same sidearms, although the log K values of **2** are almost comparable to those of **1b** as shown

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in Table 1. This result suggests that the cooperative participation of the electron-donating sidearm in the complexation of the crown ring with the metal ion effectively inhibits the $\pi-\pi$ stacking of the pyrene rings in the case of **1b**. On the other hand, in the case of **2**, only the oxygen atoms of the crown ring coordinate to the metal ion; in other words, the electron-donating sidearms of **2** hardly participate in the coordination with the metal cation. Accordingly, a proper combination of the crown ring size and the electron-donating sidearms is important in the molecular design of new fluorescence ionophores.

In conclusion, we have designed a new type of crown ether derivative with unique recognition and sensing properties. These fluorophores have a well-defined structure for efficient and selective complexation with alkaline earth metal cations in a 1:1 binding stoichiometry. This fluorescence change could possibly be utilized in fluorescence sensors for alkaline earth metal cations, even in the presence of alkali metal cations. Indeed, our preliminary experiment indicates that the response of fluorophore **1a** toward Ca^{2+} was hardly affected even in the presence of a large excess of Na^{+}(100 equiv). Further study is in progress in our laboratory.

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Supporting Information Available: Experimental procedures and characterization data for newly prepared compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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