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Synthesis of Double-Armed Lariat Ethers with Pyrene Moieties at Each End of Two Sidearms and Their Fluorescence Properties in the Presence of Alkali Metal and Alkaline Earth Metal Cations

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Received February 3, 2004

Two types of double-armed lariat ether derivatives having pyrene moieties at each end of two sidearms, (3x + 1)-crown-x derivatives **1** (x = 5), **2** (x = 6), and **3** (x = 4) (type A) and 3y-crown-y derivatives, **6** (y = 5) and **7** (y = 6) (type B), were synthesized, and their complexation behavior toward alkali metal and alkaline earth metal cations was examined by fluorescence spectroscopy. Pyrene excimer emission decreased accompanied by an increase in monomer emission upon metal ion complexation. This finding is ascribed to the change of the spatial distance of two pyrene rings by movement suppression of both the crown ring and one of the two sidearms based on complexation with the metal cation. The selectivity for alkaline earth metal cations was highly dependent on the fitness of the host cavity and the guest size. Although most of the fluorophores did not respond to alkali metal cations, only *trans*-**7a** containing an 18-crown-6 ring showed K^+ selectivity.

Introduction

Recently, a variety of artificial optical sensors that selectively respond to a specific molecule have been developed.[1] High selectivity toward specific guest molecules should be achieved by using appropriate host molecules based on host−guest interactions. As for realizing high sensitivity, fluorometric sensing has been used. The pyrenyl group has often been used as an effective fluorescence probe because of its high detection sensitivity.[2] Host molecules containing plural pyrenyl groups show an intramolecular excimer emission due to $\pi-\pi$ stacking of the pyrene rings in the free state. Their structures change upon the addition of guest molecules as a direct result of complexation, which results in a decrease of the excimer emission intensity with an increase of monomer emission intensity. Since the degree of structural change highly depends on the kind of guest molecules, these compounds show selectivity toward specific molecules. Thus, a certain event that brings about structural changes in response to specific guest molecules is important in the molecular design of new fluorophores. Indeed, a variety of detection systems for guest molecules and ions using fluorescence changes in intramolecular excimer emission or fluorescence quenching of various pyrene functionalized ligands have been developed.[3] We recently proposed a new strategy using the coordination of the electron-donating sidearm of lariat ethers to metal cations to cause fluorescence changes.[4] Lariat ethers are known to be effective host molecules for alkali metal and alkaline earth metal cations on the basis of the cooperative coordination of the crown ring and the electron-donating sidearm to the cations.[5−8] In addition, other types of double-armed lariat

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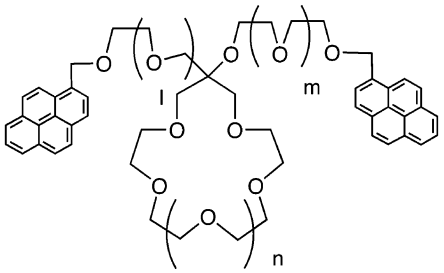
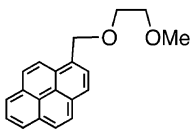
10.1021/jo0498056 CCC: $27.50
Published on Web 06/04/2004

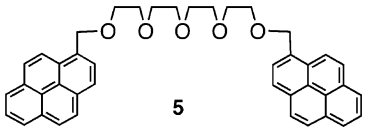
CHART 1





4

1a (l = 1, m = 0, n = 1)
1b (l = 1, m = 1, n = 1)
1c (l = 1, m = 2, n = 1)
1d (l = 0, m = 1, n = 1)
2 (l = 1, m = 1, n = 2)
3 (l = 1, m = 1, n = 0)



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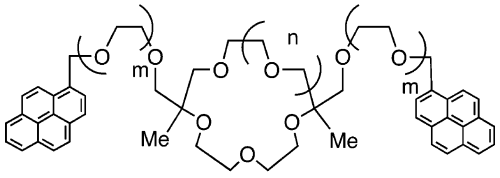

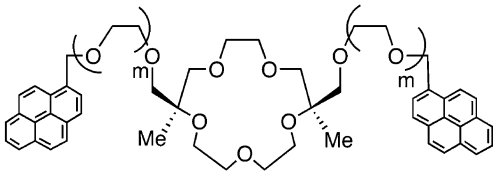

trans-**6a** (m = 0, n = 1)
trans-**6b** (m = 1, n = 1)
trans-**6c** (m = 2, n = 1)
trans-**7a** (m = 0, n = 2)
trans-**7b** (m = 1, n = 2)

cis-**6a** (m = 0)
cis-**6b** (m = 1)

ethers having two sidearms on the different carbon of the crown ring[9,10] show different complexation behaviors from lariat ethers containing two sidearms on the same carbon of the crown ring.[11] From this standpoint, we describe the synthesis of two new types of double-armed lariat ethers (types A and B): type A has two sidearms containing two pyrene rings on the same carbon atom of (3*x* + 1)-crown-*x*, (*x* = 4, 5, 6) and type B has two sidearms on the different carbon atoms of 3*y*-crown-*y*, (*y* = 5, 6) (Chart 1). Complexation properties toward alkali metal and alkaline metal cations were evaluated using fluorescence spectroscopy.

Results and Discussion

Design and Synthesis of Lariat Ethers. Two types of double-armed lariat ethers containing two pyrene rings were designed to afford systematic variations of crown ring size, sidearm type, and sidearm location on the crown ring. Pyrene moieties were introduced into the end of the sidearm of crowns as optical responding units. The general synthetic procedures[11] for compounds **1**−**3** (type A) are summarized in Scheme 1.

Starting materials 3*x*-methylene-(3*x* + 1)-crown-*x* **8a** (*x* = 5) and **8b** (*x* = 6) were prepared according to the literature.[12] Compound **8c** (*x* = 4) was prepared in a method similar to that for **8a** and **8b** with minor modifications. Compounds **9a**−**e** were obtained by bromoalkoxylation of 3*x*-methylene-(3*x* + 1)-crown-*x* (*x* = 4, 5, 6) (**8a**−**c**) using *N*-bromosuccinimide (NBS) and oligoethylene glycol. Hydroxyl groups of compounds **9** were protected by treatment with 3,4-dihydro-2*H*-pyran according to conventional methods to give corresponding tetrahydropyranyl ethers **10**, which were reacted with ethylene glycol monotetrahydropyran-2-yl ether under basic conditions, followed by deprotection under acidic

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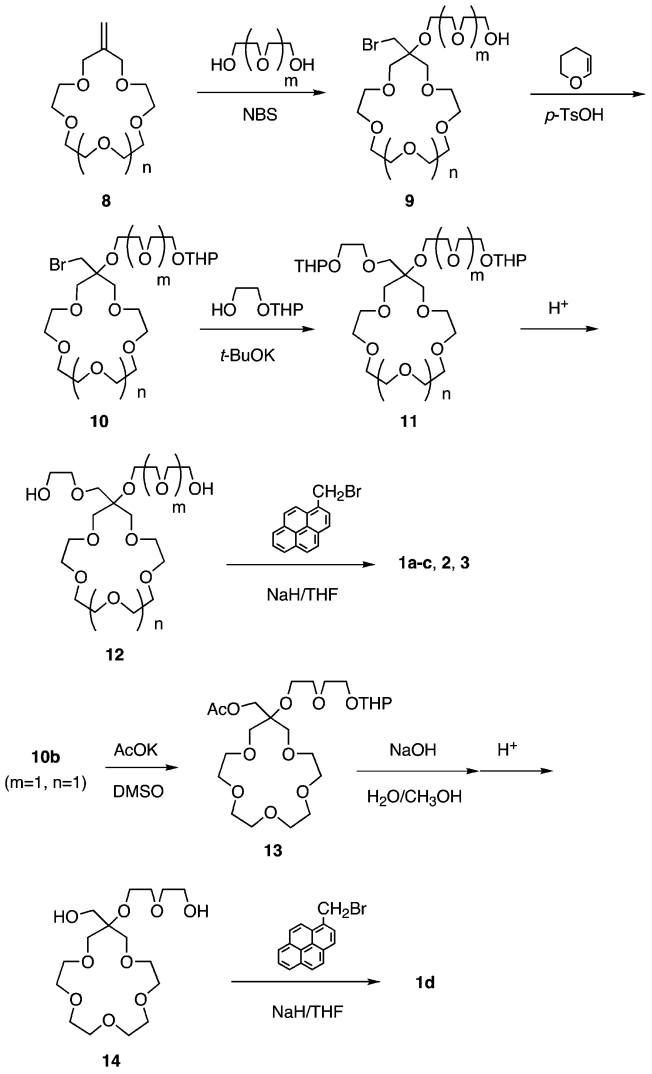
SCHEME 1

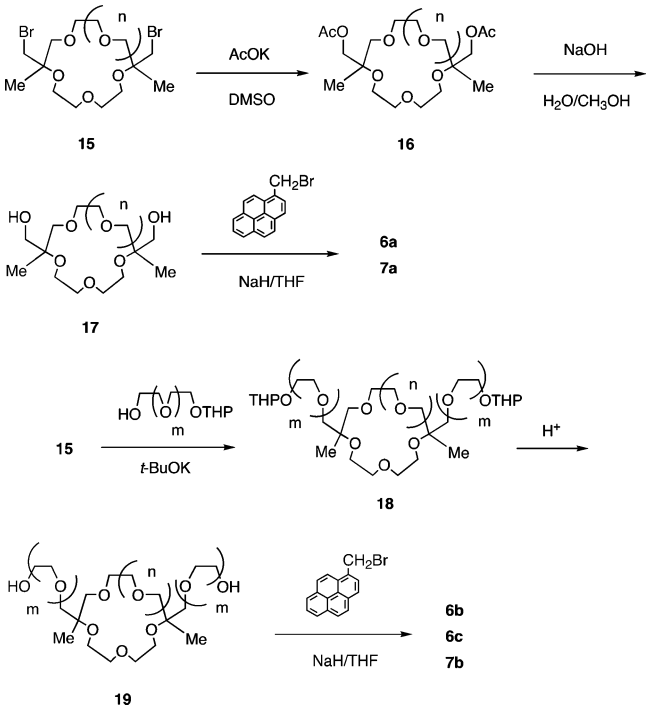


conditions to give compounds **12**. Compounds **12** were reacted with 1-bromomethylpyrene in THF in the presence of NaH at reflux temperature for 36 h to produce **1**−**3**.

Another type of fluorophores **6** and **7** (type B) was synthesized according to the procedure summarized in Scheme 2.

The presence of methyl groups at the pivot positions of compounds **6** and **7** was previously verified to play an important role in increasing their complexation ability toward alkali metal and alkaline earth metal cations by us[8] and others.[7] *trans*- and *cis*-[2,(3*y* − 6)-bis(bromomethyl)-2,(3*y* − 6)-dimethyl-3*y*-crown-*y*, (*y* = 5, 6)] **15** were treated with potassium acetate in DMSO at 100 °C for 48 h to give the corresponding diacetyl derivatives **16**. Crown diols **17** were obtained by hydrolysis of **16** in EtOH−H_2O in the presence of sodium hydroxide. Crown diols **19** having two oxyethylene chains were acquired by the reaction of **15** with ethylene glycol monotetrahydropyran-2-yl ether under basic conditions, followed by deprotection under acidic conditions. Compounds **6** and **7** were prepared from **17** and **19** by the same method as **1**−**3**. All structures were ascertained by ^{1}H NMR and IR spectroscopy, mass spectrometry, and elemental analyses.

SCHEME 2



Fluorescence Spectra of Fluorophores in the Free State. Figure 1A shows the fluorescence spectra of fluorophores **1a**−**c** and **4**.

Compound **4** containing one pyrene ring showed only monomer emission at 395 nm at a concentration of 2×10^{-6} M, whereas compounds **1a**−**c** containing two pyrene rings showed strong excimer emission at 480 nm at a concentration of 1×10^{-6} M. Judging from the concentration of fluorophore, excimer emission of **1a**−**c** is attributed to intramolecular $\pi-\pi$ stacking of two pyrene rings. In comparison with type A crowns (**1**−**3**), type B crowns (**6** and **7**) are featured by the presence of *cis* and *trans* isomers. Interestingly, the fluorescent behavior of *trans* isomers was found to be highly dependent on the combination of crown ring size and sidearm length (Figure 1B). Excimer emission of *trans* isomer **6a** is rather weak in comparison to those of *trans* isomer **6b** that has more flexible sidearms, *trans* isomer **7a** that has a larger ring size, and the corresponding *cis* isomer **6a**. The rigidity of the 15-crown-5 ring may prevent the approach of two pyrene rings of *trans*-**6a**, located in the opposite side of the crown ring plane.

Fluorescence Spectra of Fluorophores in the Presence of Metal Cations. To evaluate the complexation behavior of fluorophores, we measured fluorescence spectra as functions of the concentrations of alkali metal and alkaline earth metal cations in a mixed CH_3CN/$CHCl_3$ (99/1) solvent at room temperature. As a typical example, spectral changes of fluorophores **1a** and *trans*-**6b** upon complexation with Ca^{2+} are shown in Figure 2.

The fluorescence intensity of the excimer emissions of **1a** and *trans*-**6b** decreases with increasing Ca^{2+} concentrations, and the fluorescence intensity of monomer emissions increases. This drastic spectral change is ascribed to conformational changes of each fluorophore caused by the cooperative coordination of the crown ring and the electron-donating sidearm to Ca^{2+}, resulting in

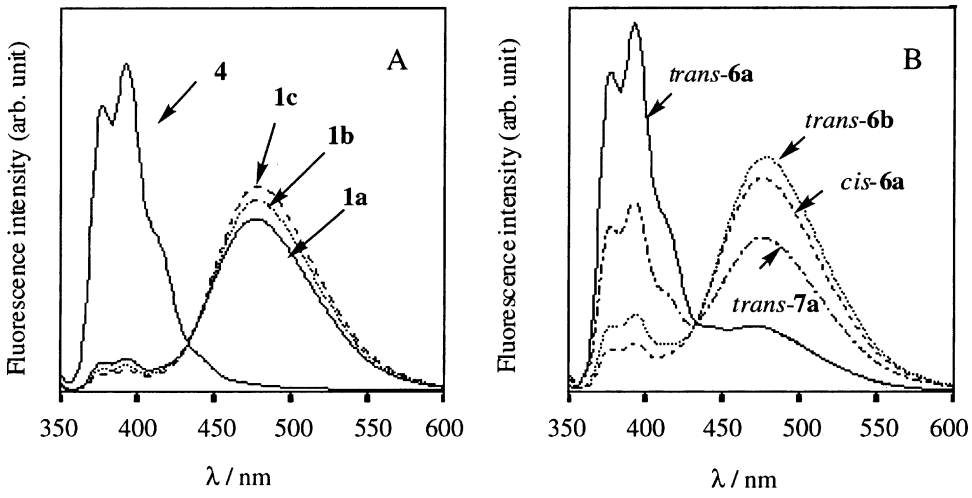


FIGURE 1. Fluorescence spectra of **1a**−**c** (1×10^{-6} M), **4** (2×10^{-6} M), *trans*-**6a** (1×10^{-6} M), *cis*-**6a** (1×10^{-6} M), *trans*-**6b** (1×10^{-6} M), and *trans*-**7a** (1×10^{-6} M) in $CH_3CN/CHCl_3$ (99:1 v/v). Excitation wavelength: 340 nm.

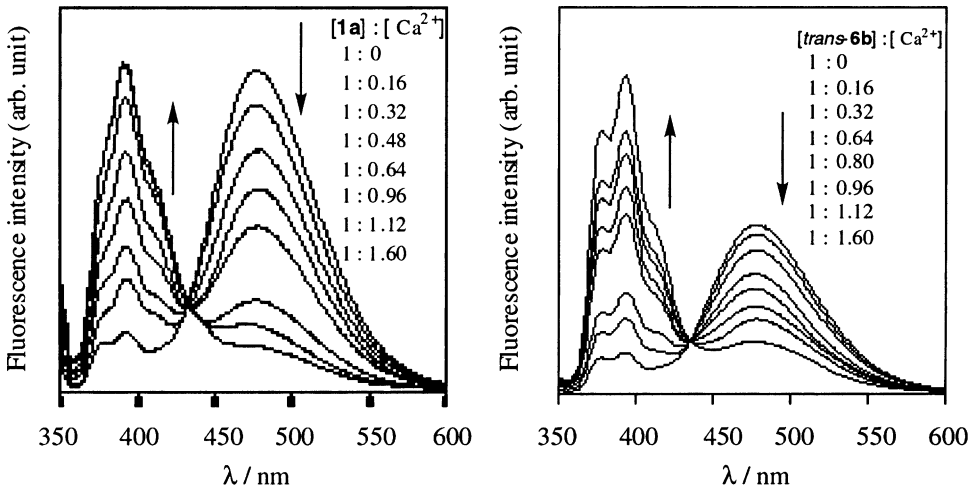


FIGURE 2. Fluorescence spectral changes in **1a** (1×10^{-6} M) and *trans*-**6b** (1×10^{-6} M) with different concentrations of $Ca(ClO_4)_2$ in $CH_3CN/CHCl_3$ (99:1 v/v). Excitation wavelength: 340 nm.

inhibition of intramolecular $\pi-\pi$ stacking of the pyrene rings. An isoemissive point at 433 nm indicates only one type of fluorophore−Ca^{2+} complex is involved. On the other hand, an acyclic fluorophore **5** as a reference hardly responds to any kinds of alkali metal and alkaline earth metal cations, indicating that higher complexing ability toward metal ions are needed for the fluorophore and that the presence of a crown ring is effective.

The stability constants (K) of the complex were evaluated from plots of excimer emission intensities vs [metal]/[ligand] by means of a nonlinear least-squares curve fitting method[14] (not shown here, see the Supporting Information). The curve showed that all the ligands formed 1:1 complexes. Binding constant (K) values for fluorophores toward alkali metal and alkaline earth metal cations are summarized in Tables 1 and 2.

The ratio of excimer fluorescence intensity to the total fluorescence intensity $I_E/(I_E + I_M)$ of **1a**−**d**, **2**, and **3** was plotted against the ratio of [metal]/[ligand] (Figure 3), where I_E and I_M are fluorescence intensities at 480 nm (excimer emission) and at 395 nm (monomer emission), respectively, and all graphs were normalized to compare $I_E/(I_E + I_M)$ changes upon metal cation additions.

As shown in Figure 3, the presence of alkaline earth metal cations except for Mg^{2+} noticeably decreased excimer emission fluorescence intensities of **1** containing a 16-crown-5 ring with an increase in corresponding monomer emission intensities. On the other hand, alkali metal cations (Li^+, Na^+, K^+) caused no changes in the fluorescence spectra (not shown here). Compounds **1a**, **1b**, and **1c** showed selectivity toward Ca^{2+}, Sr^{2+}, and Sr^{2+} or Ba^{2+}, respectively, among seven alkali metal and alkaline earth metal ions examined. In this work, "selectivity" corresponds to the largest change in $I_E/(I_E + I_M)$ and not the highest stability constant (K). Cation selectivity was clearly affected by the number of oxyethylene units in the sidearm. This finding is reasonably explained by considering the enlargement of the cavity by elongation of the oxyethylene chain. It should be noted that cation selectivity of compound **1d** is almost the same as that of

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TABLE 1. Ratio of Excimer Fluorescence Intensity to Total Fluorescence Intensity $I_E/(I_E + I_M)$ of Fluorophore 1−3 in the Presence of Alkaline Earth Metal Cations and the Stability Constants of Corresponding Complexes

probe $[I_E/(I_E + I_M)]^a$	M^{2+} ($\times 10^6$ M)	$I_E/(I_E + I_M)^b$	log K (M^{-1})
1a [0.85]	Mg^{2+} (3)	0.83	nd
	Ca^{2+} (3)	0.17	7.6
	Sr^{2+} (3)	0.45	6.8
	Ba^{2+} (3)	0.74	6.9
1b [0.89]	Mg^{2+} (3)	0.89	nd
	Ca^{2+} (3)	0.71	6.7
	Sr^{2+} (3)	0.40	8.2
	Ba^{2+} (3)	0.66	7.4
1c [0.92]	Mg^{2+} (3)	0.92	nd
	Ca^{2+} (3)	0.85	nd
	Sr^{2+} (3)	0.65	8.6
	Ba^{2+} (3)	0.71	8.7
1d [0.94]	Mg^{2+} (3)	0.94	nd
	Ca^{2+} (3)	0.54	6.3
	Sr^{2+} (3)	0.33	8.7
	Ba^{2+} (3)	0.51	8.2
2 [0.95]	Mg^{2+} (3)	0.94	nd
	Ca^{2+} (3)	0.82	5.5
	Sr^{2+} (3)	0.88	6.9
	Ba^{2+} (3)	0.88	9.0
3 [0.93]	Mg^{2+} (10)	0.88	nd
	Ca^{2+} (10)	0.15	6.5
	Sr^{2+} (10)	0.62	6.7
	Ba^{2+} (10)	0.56	7.0

[a] These values were calculated by the fluorescence intensity, I_E (480 nm) and I_M (395 nm), in the free state. [b] These values were calculated by the fluorescence intensity, I_E (480 nm) and I_M (395 nm), in the presence of metal ions.

TABLE 2. Ratio of Excimer Fluorescence Intensity to Total Fluorescence Intensity $I_E/(I_E + I_M)$ of Fluorophores 6 and 7 in the Presence of Alkali Metal Cations and Alkaline Earth Metal Cations and Stability Constants of Corresponding Complexes

probe $[I_E/(I_E + I_M)]^a$	M^{n+} ($\times 10^6$ M)	$I_E/(I_E + I_M)^b$	log K (M^{-1})
trans-**6b** [0.78]	Mg^{2+} (3)	0.24	6.3
	Ca^{2+} (3)	0.07	6.2
	Sr^{2+} (3)	0.34	6.8
	Ba^{2+} (3)	0.42	6.3
trans-**6c** [0.91]	Mg^{2+} (3)	0.84	nd
	Ca^{2+} (3)	0.66	5.2
	Sr^{2+} (3)	0.35	5.5
	Ba^{2+} (3)	0.86	nd
trans-**7a** [0.45]	Li^{+} (10)	0.42	nd
	Na^{+} (10)	0.43	nd
	K^{+} (10)	0.22	6.1
	Mg^{2+} (3)	0.38	6.6
	Ca^{2+} (3)	0.11	7.0
	Sr^{2+} (3)	0.14	8.5
	Ba^{2+} (3)	0.19	8.2
trans-**7b** [0.61]	Mg^{2+} (3)	0.58	nd
	Ca^{2+} (3)	0.15	8.1
	Sr^{2+} (3)	0.24	8.0
	Ba^{2+} (3)	0.46	8.7
cis-**6a** [0.80]	Mg^{2+} (10)	0.18	7.4
	Ca^{2+} (10)	0.40	7.0
	Sr^{2+} (10)	0.43	6.7
	Ba^{2+} (10)	0.49	7.5
cis-**6b** [0.87]	Mg^{2+} (10)	0.80	nd
	Ca^{2+} (10)	0.68	nd
	Sr^{2+} (10)	0.67	6.1
	Ba^{2+} (10)	0.81	7.1

[a] These values were calculated by the fluorescence intensity, I_E (480 nm) and I_M (395 nm), in the free state. [b] These values were calculated by the fluorescence intensity, I_E (480 nm) and I_M (395 nm), in the presence of metal ions.

1b. This result clearly indicates that only the sidearm constituting the glycerol structure at the pivot position is responsible for metal cation complexation as expected from our previous work.[11] Changes in fluorescence spectra of **2** containing a 19-crown-6 ring upon addition of alkaline earth metal cations were much smaller compared to those of the 16-crown-5 derivative **1b** bearing equivalent sidearms; however, the log K values of **2** are almost comparable to those of **1b**. In the case of **1b** this result suggests that the cooperative participation of the electron-donating sidearm during complexation of the crown ring with the metal ion effectively inhibits the $\pi-\pi$ stacking of the pyrene rings. On the other hand, in the case of **2** only crown ring oxygen atoms coordinate the metal ion; in other words, the electron-donating sidearm of **2** hardly participates in metal cation coordination. Compound **3** containing a 13-crown-4 ring also responded to alkaline earth metal cations but needed the addition of a larger amount of metal salts to bring about complete conformational changes because of a low metal cation complexation ability. Accordingly, a proper combination of crown ring size and electron-donating sidearms is important in the molecular design of new fluorophores.

Figure 4 shows fluorescent properties of fluorophores **6** and **7** (type B) upon complexation with alkaline earth metal cations.

A few characteristic trends in cation selectivity were observed in these fluorophore types, when compared to type A fluorophores (**1**). For example, both *trans*-**6b** containing a 15-crown-5 ring with one oxyethylene unit per each sidearm and the corresponding 18-crown-6 derivative, *trans*-**7b**, showed the same cation selectivity (Ca^{2+}) regardless of crown ring size. However, the fitness of the cavity size of the host molecule and the metal cation size seems to be still important in this series of fluorophores, judging from the fact that *trans*-**6b** and *trans*-**7b** also showed high affinity toward Mg^{2+} and Sr^{2+}, respectively. In addition, *trans*-**6c** containing a 15-crown-5 ring with two oxyethylene units per each sidearm showed Sr^{2+} selectivity. As for stability constants (K), the 18-crown-6 derivative *trans*-**7b** possesses much higher values than the 15-crown-5 derivatives *trans*-**6b** and *trans*-**6c** (Table 2). Another important finding in this fluorophore series (type B) is that the *cis* isomer **6a** containing a 15-crown-5 ring showed Mg^{2+} selectivity by considering that even 13-crown-4 derivative **3** did not show Mg^{2+} selectivity in a series of type A. Although Mg^{2+} is one of several important divalent cations relevant to living organisms, there are few studies on Mg^{2+} sensors.[15] Therefore, *cis*-**6a** is expected to be a promising Mg^{2+}-specific indicator. Interestingly, when Ba^{2+} was added to the *cis*-**6a** solution, monomer emission did not increase in response to the excimer emission decrease. To our regret, at the present stage we have no explanation for this phenomenon. In contrast to *cis*-**6a**, the *cis* isomer

(15) (a) London, R. E. *Annu. Rev. Physiol.* **1991**, *53*, 241−258. (b) Murphy, E.; Freudenrich, C. C.; Lieberman, M. *Annu. Rev. Physiol.* **1991**, *53*, 273−287. (c) Jung, D. W.; Chapman, C. J.; Baysal, K.; Pfeiffer, D. R.; Brierley, G. P. *Arch. Biochem. Biophys.* **1996**, *332*, 19−29. (d) van der Wolk, J. P. W.; Klose, M.; de Wit, J. G.; den Blaauwen, T.; Freudl, R.; Driessen, A. J. M. *J. Biol. Chem.* **1995**, *270*, 18975−18982. (e) Brunet, E.; Garcia-Losada, P.; Rodriguez-Ubis, J.-C.; Juanes, O. *Can. J. Chem.* **2002**, *80*, 169−174. (f) Suzuki, Y.; Komatsu, H.; Ikeda, T.; Saito, N.; Araki, S.; Citterio, D.; Hisamoto, H.; Kitamura, Y.; Kubota, T. Nakagawa, J.; Oka, K.; Suzuki, K. *Anal. Chem.* **2002**, *74*, 1423−1428.

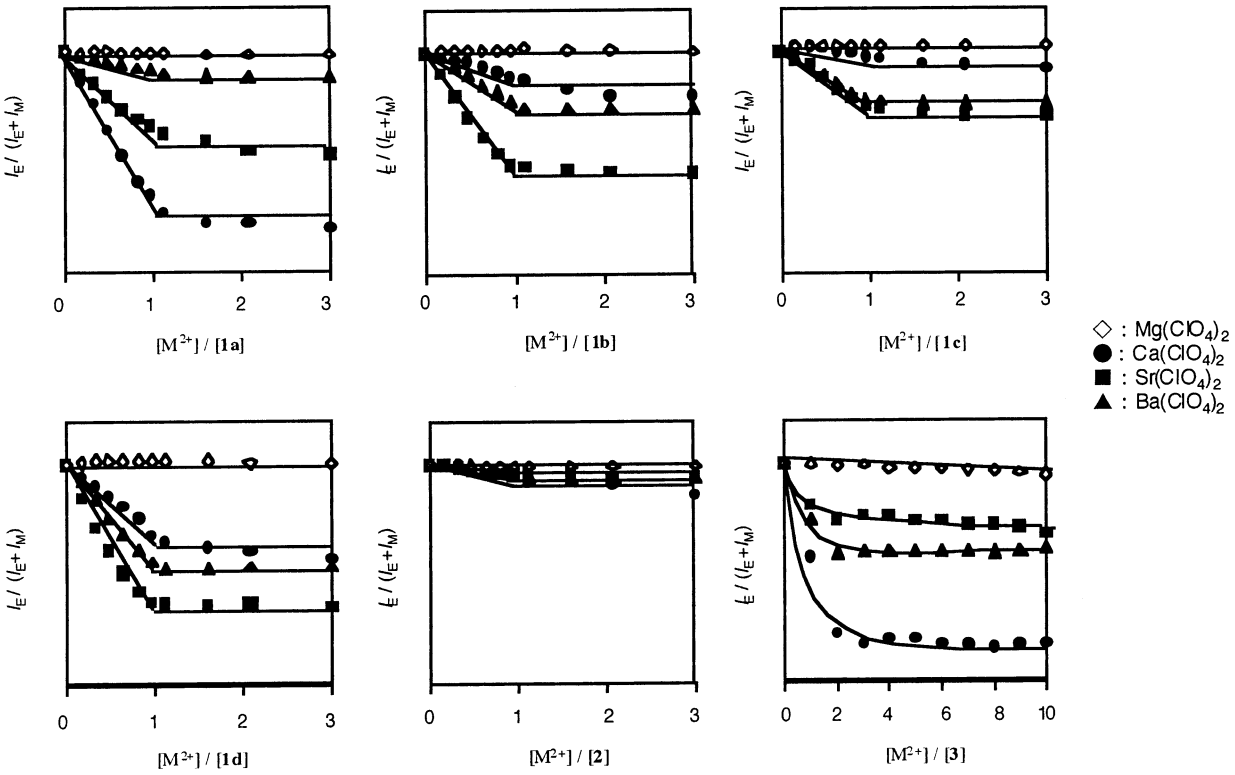

FIGURE 3. Changes of $I_E/(I_E + I_M)$ of **1a**−**c** (1×10^{-6} M), **2** (1×10^{-6} M), and **3** (1×10^{-6} M) upon addition of alkaline earth metal cations in $CH_3CN/CHCl_3$ (99:1 v/v). Excitation wavelength: 340 nm.

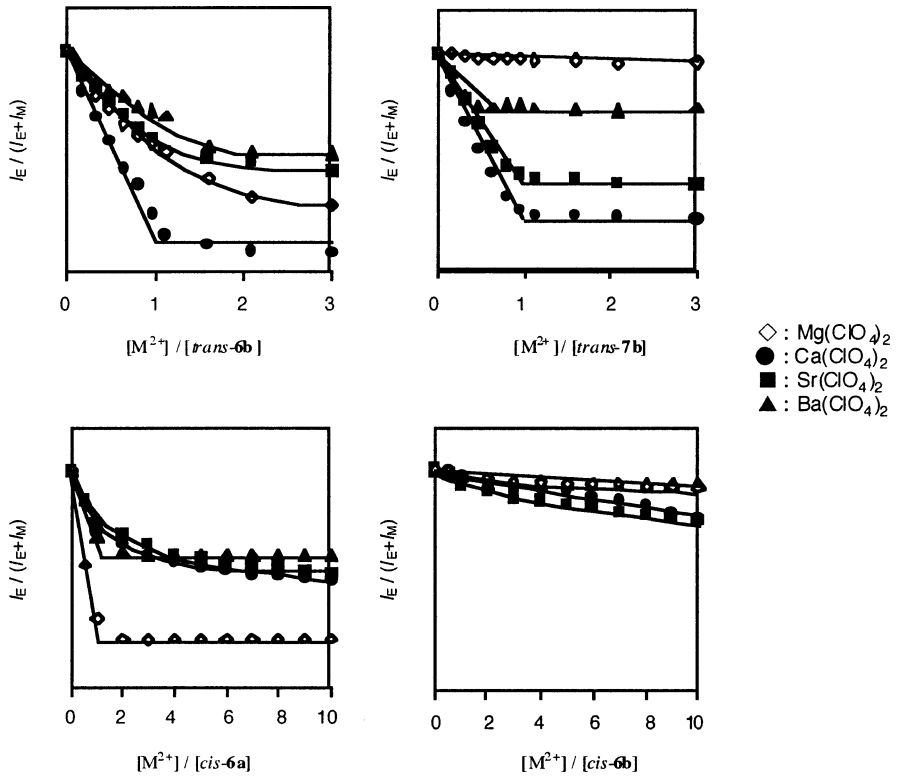

FIGURE 4. Changes of $I_E/(I_E + I_M)$ of *trans*-**6b** (1×10^{-6} M), *trans*-**7b** (1×10^{-6} M), *cis*-**6a** (1×10^{-6} M), and *cis*-**6b** (1×10^{-6} M) upon addition of alkaline earth metal cations in $CH_3CN/CHCl_3$ (99:1 v/v). Excitation wavelength: 340 nm.

6b containing a 15-crown-5 ring with one oxyethylene unit per one sidearm showed little fluorescence spectral change. This indicates that the spatial distance of two pyrenes of *cis*-**6b** is not largely changed upon metal cation complexation because of the presence of flexible oxyethylene units.

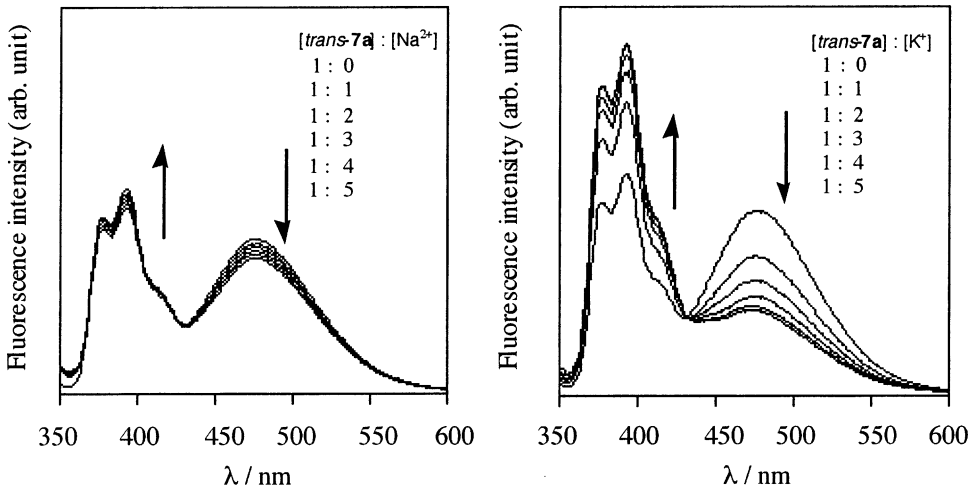

FIGURE 5. Fluorescence spectral changes in *trans*-**7a** (1×10^{-6} M) with different concentrations of NaSCN and KSCN in $CH_3CN/CHCl_3$ (99:1 v/v). Excitation wavelength: 340 nm.

Fluorescence characteristics in the presence of alkali metal cations were also examined in type B series fluorophores. Although fluorescence spectra of most fluorophores were not changed by adding alkali metal cations, only *trans*-**7a** containing an 18-crown-6 ring responded to K^+. On the other hand, Na^+ affected little change in the fluorescence spectra (Figure 5).

This demonstrates that *trans*-**7a** is potentially useful as a selective fluorescent detection device for K^+ over Na^+.

Conclusions

In this paper, we described the synthesis and complexation properties of two types of fluorophores based on double-armed lariat ethers. The difference in crown ring size and oxyethylene sidearm length affected metal ion selectivity, and as a result, selectivity for a variety of metal cations was achieved. It is noteworthy that among fluorophores examined in this study only *trans*-**7a** containing an 18-crown-6 ring responded to K^+ with very high selectivity versus Li^+ and Na^+. This is significant because there are few examples of selective fluorescence detection for alkali metal cations by monomer−excimer emission systems.[3a,b,e,16] We hope that a range of fluorophores will be designed in the future based on information obtained from this work.

Experimental Section

General Procedure for Bromoalkoxylation of 8a−c Using *N*-Bromosuccinimide (NBS) and Oligoethylene Glycol To Give Compounds 9a−e. To a stirred suspension of NBS (20 mmol) in oligoethylene glycol (0.200 mol) was added **8** (20 mmol) under cooling in an ice bath for 1 h. The resulting mixture was further stirred at 50 °C for 1 h. After the mixture was cooled to room temperature, 10% sodium carbonate aqueous solution (200 mL) was added to the mixture, and the product was extracted with dichloromethane (200 mL × 3). The solvent was evaporated to give a slightly yellowish liquid. The crude product was used for the next step without further purification.

General Procedure for the Synthesis of the Protected Compounds 10a−e. After crude compound **9** (20 mmol) and *p*-toluenesulfonic acid (1.2 mmol) were dissolved in 1,2-dichloroethane (3 mL), 3,4-dihydro-*2H*-pyrane (30 mmol) was added dropwise to the mixture under cooling in an ice bath for 10 min. The resulting mixture was further stirred at room temperature for 3 h. Sodium carbonate aqueous solution (10%, 200 mL) was added to the mixture, and the product was extracted with dichloromethane (200 mL × 3). After evaporation, the residue was purified by silica gel chromatography (dichloromethane/acetone = 95:5).

General Procedure for the Synthesis of 11a−e. After potassium *tert*-butoxide (40 mmol) was dissolved in ethylene glycol monotetrahydropyranyl ether (80 mmol), **10** (10 mmol) was added to the mixture, followed by stirring at 120 °C for 36 h. After being cooled to room temperature, the mixture was filtered and evaporated. Water (200 mL) was added to the mixture, and the product was extracted with dichloromethane (200 mL × 3). The solvent was evaporated to give a yellowish liquid. The crude product was used for the next step without further purification.

General Procedure for the Deprotection of 11a−e To Give 12a−e. After crude compound **11** was dissolved in methanol (150 mL), concentrated H_2SO_4 (5 drops) was added to the solution, followed by stirring at room temperature for 24 h. After neutralization with sodium hydroxide, methanol was evaporated in vacuo. The residue was purified by alumina chromatography (chloroform/methanol = 95:5).

General Procedure for the Synthesis of 1−3. To a suspension of NaH (7.86−11.4 mmol) and **12** (1.31−1.90 mmol) in THF (15 mL) was added dropwise a solution of 1-bromomethylpyrene (5.24−7.60 mmol) in THF (30 mL), and the resulting mixture was stirred for 36 h at refluxing temperature. After the mixture was cooled to room temperature, a small portion of ethanol was added in order to deactivate the excess NaH, and the mixture was filtered and concentrated in vacuo. Water (200 mL) was added to the residue and then extracted with dichloromethane (200 mL × 3). The combined organic layer was dried over $MgSO_4$, and the dichloromethane was evaporated off. The residue was purified by alumina chromatography (benzene/ethyl acetate = 95:5−70:30).

15-[2-(1-Pyrenylmethoxy)ethoxy]-15-[[2-(1-pyrenylmethoxy)ethoxy]methyl]-1,4,7,10,13-pentaoxacyclohexadecane (1a). By following the general procedure, **1a** was obtained from **12a** as a slightly yellowish viscous liquid in 29% yield. ^{1}H NMR ($CDCl_3$): δ 3.45−3.92 (m, 30H), 5.15 (s, 2H), 5.18 (s, 2H), 7.89−8.34 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1730, 1590, 1450, 1350, 1300, 1120, 850, 710. MS (FAB): *m*/*z* 796

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(M^+). Anal. Calcd for $C_{50}H_{52}O_9$: C, 75.36; H, 6.58. Found: C, 75.63; H, 6.30.

15-[2-[2-(1-Pyrenylmethoxy)ethoxy]ethoxy]-15-[[2-(1-pyrenylmethoxy)ethoxy]methyl]-1,4,7,10,13-pentaoxacyclohexadecane (1b). By following the general procedure, **1b** was obtained from **12b** as a slightly yellowish viscous liquid in 30% yield. ^{1}H NMR ($CDCl_3$): δ 3.38−3.82 (m, 34H), 5.19 (s, 4H), 7.88−8.35 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2870, 1730, 1600, 1460, 1350, 1300, 1120, 850, 710. MS (FAB): *m*/*z* 840 (M^+). Anal. Calcd for $C_{52}H_{56}O_{10}$: C, 74.26; H, 6.71. Found: C, 73.92; H, 6.52.

15-[2-[2-[2-(1-Pyrenylmethoxy)ethoxy]ethoxy]ethoxy]-15-[[2-(1-pyrenylmethoxy)ethoxy]methyl]-1,4,7,10,13-pentaoxacyclohexadecane (1c). By following the general procedure, **1c** was obtained from **12c** as a slightly yellowish viscous liquid in 21% yield. ^{1}H NMR ($CDCl_3$): δ 3.42−3.78 (m, 38H), 5.21 (s, 4H), 7.93−8.36 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1730, 1590, 1460, 1350, 1290, 1090, 850, 710. MS (FAB): *m*/*z* 884 (M^+). Anal. Calcd for $C_{54}H_{60}O_{11}$: C, 73.28; H, 6.83. Found: C, 73.46; H, 6.72.

15-[2-[2-(1-Pyrenylmethoxy)ethoxy]ethoxy]-15-[(1-pyrenylmethoxy)methyl]-1,4,7,10,13-pentaoxacyclohexadecane (1d). By following the general procedure, **1d** was obtained from **14** as a slightly yellowish viscous liquid in 40% yield. The synthetic procedure was almost the same as that used for **1**. ^{1}H NMR ($CDCl_3$): δ 3.34−3.83 (m, 30H), 5.17 (s, 4H), 7.90−8.36 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2850, 1730, 1590, 1460, 1350, 1300, 1130, 850, 710. MS (FAB): *m*/*z* 796 (M^+). Anal. Calcd for $C_{50}H_{52}O_9$: C, 75.36; H, 6.58. Found: C, 75.57; H, 6.38.

18-[2-[2-(1-Pyrenylmethoxy)ethoxy]ethoxy]-18-[[2-(1-pyrenylmethoxy)ethoxy]methyl]-1,4,7,10,13,16-hexaoxacyclohexadecane (2). By following the general procedure, **2** was obtained from **12d** as a slightly yellowish liquid in 29% yield. ^{1}H NMR ($CDCl_3$): δ 3.45−3.79 (m, 38H), 5.18 (s, 4H), 7.92−8.37 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1730, 1600, 1460, 1350, 1300, 1100, 850, 710. MS (FAB): *m*/*z* 884 (M^+). Anal. Calcd for $C_{54}H_{60}O_{11}$: C, 73.28; H, 6.83. Found: C, 73.63; H, 6.46.

12-[2-[2-(1-Pyrenylmethoxy)ethoxy]ethoxy]-12-[[2-(1-pyrenylmethoxy)ethoxy]methyl]-1,4,7,10-tetraoxacyclotridecane (3). By following the general procedure, **3** was obtained from **12e** as a slightly yellowish liquid in 31% yield. ^{1}H NMR ($CDCl_3$): δ 3.42−3.78 (m, 30H), 5.16 (s, 2H), 5.17 (s, 2H), 7.90−8.34 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1740, 1590, 1460, 1350, 1300, 1080, 850, 710. MS (FAB): *m*/*z* 796 (M^+). Anal. Calcd for $C_{50}H_{52}O_9$: C, 75.36; H, 6.58. Found: C, 75.56; H, 6.31.

1-Methoxy-2-(1-pyrenylmethoxy)ethane (4). The synthetic procedure was almost the same as that used for compounds **1**. The crude product was purified by chromatography over alumina (benzene/ethyl acetate = 98:2) to give **4** as a slightly yellowish liquid in 65% yield. ^{1}H NMR ($CDCl_3$): δ 3.39 (s, 3H), 3.58 (t, 2H, J = 4.8 Hz), 3.72 (t, 2H, J = 4.8 Hz), 5.29 (s, 2H), 7.97−8.43 (m, 9H). IR (neat, cm^{-1}) ν: 3040, 2860, 1790, 1590, 1460, 1350, 1240, 1090, 820, 710. MS (FAB): *m*/*z* 290 (M^+). Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.47; H, 6.11.

Tetraethylene Glycol Bis(1-pyrenylmethyl) Ether (5). The synthetic procedure was almost the same as that used for compounds **1**. The crude product was purified by chromatography over alumina (benzene/ethyl acetate = 95:5) to give **5** as a slightly yellowish liquid in 22% yield. ^{1}H NMR ($CDCl_3$): δ 3.57−3.71 (m, 16H), 5.21 (s, 4H), 7.94−8.37 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1720, 1600, 1460, 1350, 1240, 1090, 850, 710. MS (FAB): *m*/*z* 622 (M^+). Anal. Calcd for $C_{42}H_{38}O_5$: C, 81.00; H, 6.15. Found: C, 80.73; H, 6.13.

General Procedure for the Synthesis of 16a and 16b. After potassium acetate (96 mmol) was dissolved in DMSO (20 mL), **15** (8 mmol) was added to the mixture followed by stirring at 100 °C for 48 h. After being cooled to room temperature, the mixture was filtered and evaporated to give a yellowish liquid. The crude compound was purified by silica gel chromatography (ethyl acetate) to give a slightly yellowish liquid.

General Procedure for the Synthesis of 17a and 17b. After sodium hydroxide (5 mmol) was dissolved in a mixed solvent of 2:1 v/v water/ethanol (30 mL), **16** (2.5 mmol) was added to the mixture followed by stirring at room temperature for 24 h. The mixture was filtered and evaporated. The residue was purified by alumina chromatography (chloroform/methanol = 95:5).

General Procedure for the Synthesis of 18a−c. After potassium *tert*-butoxide (32 mmol) was dissolved in ethylene glycol monotetrahydropyranyl ether (80 mmol), **15** (4 mmol) was added to the mixture followed by stirring at 120 °C for 36 h. After being cooled to room temperature, the mixture was filtered and evaporated. Water (200 mL) was added to the mixture, and the product was extracted with dichloromethane (200 mL × 3). The solvent was evaporated to give a yellowish liquid. The crude product was used for the next step without further purification.

General Procedure for the Deprotection of 18a−c To Give 19a−c. After crude compound **18** was dissolved in methanol (150 mL), concentrated H_2SO_4 (5 drops) was added to the solution, followed by stirring at room temperature for 24 h. After neutralization with sodium hydroxide, methanol was evaporated in vacuo. The residue was purified by alumina chromatography (chloroform/methanol = 95:5).

General Procedure for the Synthesis of 6 and 7. The synthetic procedure was almost the same as that used for **1**. The crude compound was purified was purified by alumina chromatography (benzene/ethyl acetate = 85:15−70:30).

***trans*-2,9-bis[(1-Pyrenylmethoxy)methyl]-2,9-dimethyl-1,4,7,10,13-pentaoxacyclopentadecane (*trans*-6a)**. By following the general procedure, *trans*-**6a** was obtained from *trans*-**17a** as a slightly yellowish liquid in 20% yield. ^{1}H NMR ($CDCl_3$): δ 1.08 (s, 6H), 3.17−3.65 (m, 20H), 5.14 (d, 2H, J = 12.1 Hz), 5.25 (d, 2H, J = 12.1 Hz), 7.93−8.39 (m, 18H). IR (neat, cm^{-1}) ν: 3050, 2860, 1710, 1590, 1460, 1360, 1290, 1090, 890, 750. MS (FAB): *m*/*z* 736 (M^+). Anal. Calcd for $C_{48}H_{48}O_7$: C, 78.24; H, 6.57. Found: C, 78.00; H, 6.43.

***cis*-2,9-bis[(1-Pyrenylmethoxy)methyl]-2,9-dimethyl-1,4,7,10,13-pentaoxacyclopentadecane (*cis*-6a)**. By following the general procedure, *cis*-**6a** was obtained from *cis*-**17a** as a slightly yellowish liquid in 23% yield. ^{1}H NMR ($CDCl_3$): δ 1.14 (s, 6H), 3.29−3.68 (m, 20H), 5.15 (d, 2H, J = 12.1 Hz), 5.22 (d, 2H, J = 12.1 Hz), 7.84−8.40 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2870, 1720, 1600, 1450, 1360, 1290, 1090, 850, 730. MS (FAB): *m*/*z* 736 (M^+) Anal. Calcd for $C_{48}H_{48}O_7$: C, 78.24; H, 6.57. Found: C, 78.08; H, 6.44.

***trans*-2,12-Bis[(1-pyrenylmethoxy)methyl]-2,12-dimethyl-1,4,7,10,13,16-hexaoxacyclooctadecane (*trans*-7a)**. By following the general procedure, *trans*-**7a** was obtained from *trans*-**17a** as a slightly yellowish liquid in 50% yield. ^{1}H NMR ($CDCl_3$): δ 1.11 (s, 6H), 3.38−3.63 (m, 24H), 5.18 (s, 2H, J = 11.7 Hz), 5.23 (d, 2H, J = 11.7 Hz), 7.93−8.39 (m, 18H). IR (neat, cm^{-1}) ν: 3050, 2850, 1710, 1630, 1450, 1360, 1240, 1100, 840, 710. MS (FAB): *m*/*z* 780 (M^+). Anal. Calcd for $C_{50}H_{52}O_8$: C, 76.90; H, 6.71. Found: C, 77.17; H, 6.44.

***trans*-2,9-bis[[2-(1-Pyrenylmethoxy)ethoxy]methyl]-2,9-dimethyl-1,4,7,10,13-pentaoxacyclopentadecane (*trans*-6b)**. By following the general procedure, *trans*-**6b** was obtained from *trans*-**19a** as a slightly yellowish liquid in 32% yield. ^{1}H NMR ($CDCl_3$): δ 1.12 (s, 6H), 3.35−3.77 (m, 28H). 5.25 (s, 4H), 7.95−8.39 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2940, 1730, 1600, 1460, 1350, 1290, 1100, 850, 710. MS (FAB): *m*/*z* 824 (M^+). Anal. Calcd for $C_{52}H_{56}O_9$: C, 75.70; H, 6.84. Found: C, 75.69; H, 6.70.

***cis*-2,9-Bis[[2-(1-pyrenylmethoxy)ethoxy]methyl]-2,9-dimethyl-1,4,7,10,13-pentaoxacyclopentadecane (*cis*-6b)**. By following the general procedure, *cis*-**6b** was obtained from *cis*-**19b** as a slightly yellowish liquid in 19% yield. ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 6H), 3.37−3.74 (m, 28H). 5.23 (s, 4H), 7.94−

8.37 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2870, 1730, 1610, 1460, 1350, 1290, 1090, 850, 710. MS (FAB): *m*/*z* 824 (M^+). Anal. Calcd for $C_{52}H_{56}O_9$: C, 75.70; H, 6.84. Found: C, 75.65; H, 6.80.

***trans*-2,9-Bis[[2-[2-(1-pyrenylmethoxy)ethoxy]ethoxy]-methyl]-2,9-dimethyl-1,4,7,10,13-pentaoxacyclopentadecane (*trans*-6c)**. By following the general procedure, *trans*-**6c** was obtained from *trans*-**19b** as a slightly yellowish liquid in 48% yield. ^{1}H NMR ($CDCl_3$): δ 1.08 (s, 6H), 3.30−3.76 (m, 36H). 5.26 (s, 4H), 7.95−8.40 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2870, 1730, 1600, 1460, 1350, 1290, 1090, 850, 710. MS (FAB): *m*/*z* 912 (M^+). Anal. Calcd for $C_{56}H_{64}O_{11}$: C, 73.66; H, 7.06. Found: C, 73.84; H, 6.83.

***trans*-2,12-Bis[[2-(1-pyrenylmethoxy)ethoxy]methyl]-2,12-dimethyl-1,4,7,10,13,16-hexaoxacyclooctadecane (*trans*-7b).** By following the general procedure, *trans*-**7b** was obtained from *trans*-**19c** as a slightly yellowish liquid in 17% yield. ^{1}H NMR ($CDCl_3$): δ 1.14 (s, 6H), 3.32−3.75 (m, 32H). 5.25 (s, 4H), 7.95−8.40 (m, 18H). IR (neat, cm^{-1}) ν: 3040, 2860, 1730, 1590, 1450, 1350, 1290, 1090, 850, 710. MS (FAB): *m*/*z* 868 (M^+). Anal. Calcd for $C_{54}H_{60}O_{10}\cdot H_2O$: C, 73.12; H, 7.04. Found: C, 73.22; H, 6.72.

Measurement of Fluorescence Spectra. Fluorescence spectra were measured at room temperature. The concentration of fluorescent reagents was 1×10^{-6} M in a mixed solvent of $CH_3CN/CHCl_3$ (99:1). Alkali metal cations and alkaline earth metal cations were added into the solution of fluorescent reagent as perchlorate salts (Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}) and thiocyanate salts (Li^+, Na^+, K^+). To prevent nonlinearity of the fluorescence intensities, the excitation wavelength was set to 340 nm, which was an isosbestic point in the absorption spectra. Before each experiment, nitrogen was bubbled through the samples for 15 min.

Measurement of Stability Constants. All of the stability constants herein reported were determined from the curve by means of a nonlinear least-squares curve fitting method. The curve showed that all the ligands formed 1:1 complexes. Typically, the concentration of the host compound was fixed to be 1×10^{-6} M and the molar ratios of the guest to host were changed in the range from 0 to 10 by changing the concentrations of the guest salt. Eight data were collected for each host−guest system, and the stability constant (*K*) was calculated using an iterative nonlinear least-squares curve-fitting program.

Acknowledgment. This work was partly supported by a Grant-in-Aid for Scientific Research (Grant No. 15550118) from the Japan Society of the Promotion of Science.

Supporting Information Available: Experimental procedures, characterization data (^{1}H NMR, IR, MS, and elemental analysis) for newly prepared compounds, and the curve plots of the excimer emission intensity for stability constants (*K*) determination. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0498056