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SYNTHESIS AND COMPLEXATION BEHAVIOR OF 4,10-*BIS*(1-PYRENYLMETHYL)-1,7-DIOXA-4,10-DIAZACYCLODODECANE†

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Abstract – Fluorescent photoinduced electron transfer (PET) fluoroionophore (**2c**) that consists of diaza-12-crown-4 and two 1-pyrenylmethyl pendants shows fluorescent enhancement with various metal cations. The sensor (**2c**) exhibited Zn^{2+} selectivity and in the presence of this cation the host fluorescence was increased by a factor of 38.

Photoresponsive supramolecular systems are of great significance particularly for their potential application to nanoscale devices for cation sensor and switch.[1-6] There are extensive investigations toward the characterization of fluoroionophores including crown ether, calixarene, and cyclodextrin derivatives with naphthalene, umbelliferone, anthracene, or pyrene fluorophore. Recently, a number of fluoroionophores has been designed for metal ions. Most of them operate by a photoinduced electron transfer (PET) mechanism. In a classic example from the de Silva group,[7,8] the binding component of the sensor is *N*-(9-anthrylmethyl)-18-azacrown-6. The uncomplexed fluoroionophore is weak fluorescent, as the photoexcited fluorophore is quenched by the electron transfer from amine group. Following metal incorporation (Na^+ and K^+), the metal-ligand interaction decreases the amine oxidation potential drastically and prevents the electron transfer. As a consequence, the intense and characteristic anthracene

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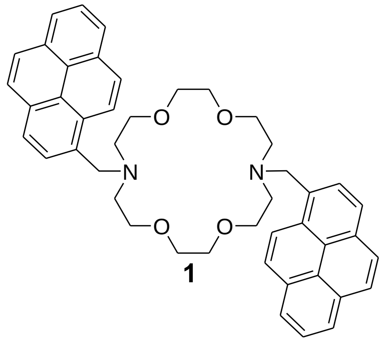
†Dedicated to Professor Dr. Albert Eschenmoser on the occasion of his 85th birthday.

fluorescence is largely restored. We have also reported that multi-donor-spacer-multi-acceptor systems such as diazacrown ethers carrying two fluorophores which have higher fluorescent switch-on ability for guest cation complexation than the corresponding monoazacrown derivatives,[9-12] while the cation binding such as alkali metal cation exerted a strong effect on the ratio of the monomer/excimer fluorescence intensity of 7,16-bis(1-pyrenylmethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**1**).[12,13] As an approach to the manipulation of PET fluoroionophores, we now report the complexation and fluorescence behavior of the diaza-12-crown-4 ether (**2c**) with two 1-pyrenylmethy pendants in the presence of guest salts.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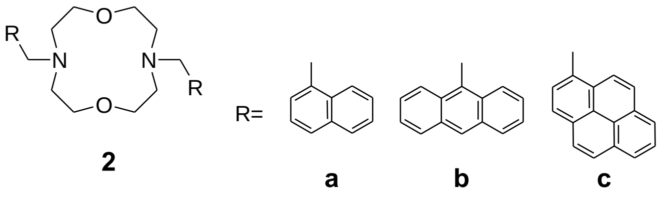
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The pyrene-functionalized diaza-12-crown-4 ether (**2c**) was prepared by the *N*-alkylation of 1,7-diaza-12-crown-4 with 1-chloromethylpyrene in triethylamine-toluene-tetrahydrofuran solution. The structure of **2c** was ascertained by NMR spectroscopy and HR FAB MS.

Figure 1 illustrates the fluorescence spectral behavior of **2c** (1.0 x 10^{-6} M) and 1-methylpyrene (**1-MP**, 2.0 x 10^{-6} M) in MeOH-CHCl$_3$ (9:1 *v/v*). Fluoroionophore **2c** (when excited at 342 nm) gave a broad

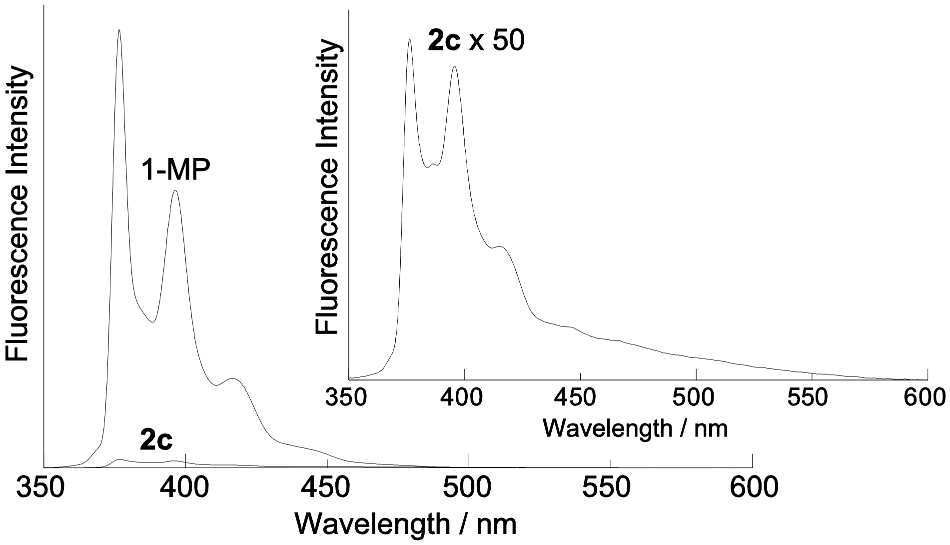

Figure 1. Fluorescence spectra of **2c** (1.0 x 10^{-6} M) and 1-methylpyrene (**1-MP**, 2.0 x 10^{-6} M) in MeOH-CHCl$_3$ (9:1 *v/v*) at room temperature.

fluorescence band in a range from 450 to 580nm in addition to monomer fluorescence (376, 396, and 416 nm). The formation of an intramolecular exciplex should be responsible for the appearance of the former fluorescence band. The latter fluorescence-band intensity of **2c** was reduced to approximately one-52nd that of standard substance (**1-MP**). This indicates that the quenching of the excited pyrene chromophore by the azacrown unit proceeds in a mechanism similar to that for the classical pyrene-dialkylamine system.[14,15] The quenching efficiency ($I_{2c}/I_{1\text{-}MP}$: 1.9 x 10^{-2}) of **2c** is lower than that ($I_1/I_{1\text{-}MP}$: 3.7 x 10^{-3})[12,13] of **1**. This means that the smaller macrocycle ring inhibits the PET occurring from the nitrogen atoms in the crown to excited fluorescent moieties.

In Figure 2 is illustrated the relative fluorescence spectral behavior of guest cation complexes **2c** (1.0 x 10^{-6} M) in MeOH-CHCl$_3$ (9:1 *v/v*) at room temperature. A dramatic change in the fluorescence intensity of **2c** (I_{2c}) was observed upon the addition of various amounts of guest cations (Li^+, Na^+, K^+, Rb^+, Cs^+, Ca^{2+}, Ba^{2+}, Zn^{2+}, Mg^{2+} and NH_4^+). When the guest cations were added (10^4 molar equivalents), the relative fluorescence intensity ($I_{complex}/I_{2c}$), being used as a measure of the molecular recognition sensing, changed from 1 to 38 depending on the nature of guest cations as shown in Figure 2 and Table 1.

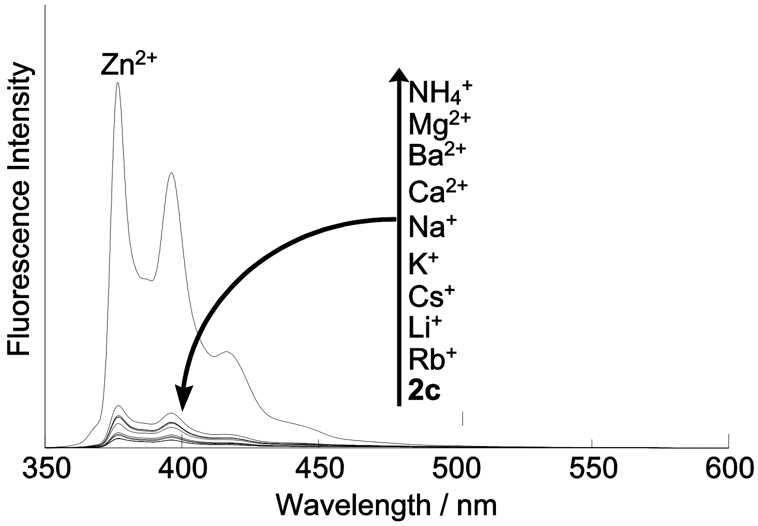

Figure 2. Fluorescence spectra of **2c** (1.0 x 10^{-6} M) with and without various metal cations (1.0 x 10^{-2} M) in MeOH-CHCl$_3$ (9:1 *v/v*) at room temperature.

Interestingly, the fluorescence intensity ratio ($I_{complex}/I_{2c}$) was different among bound guest cations and decreased in the following order: Zn^{2+} (38) > NH_4^+ (4.4) > Ba^{2+} (3.4) > Ca^{2+}, Mg^{2+} (3.2) > Na^+ (2.5) > K^+ (1.6) > Cs^+ (1.4) > Li^+ (1.3) > Rb^+ (1.0). The order of $I_{complex}/I_{2c}$ is similar to that of $I_{complex}/I_{2a}$[10,12] and $I_{complex}/I_{2b}$.[11,12] In Table 1 is illustrated the fluorescence intensity ratio ($I_{complex}/I_{1\text{-}MP}$) of guest

Table 1. The fluorescence intensity ratio ($I_{\mathbf{2c}\text{-zinc cation complex}}/I_{\mathbf{1\text{-}MP}}$) at 377 nm of the guest cation complexes of **2**[a]

	2a[10,12]		**2b**[11,12]		**2c**	
	$I_{\text{complex}} / I_{\mathbf{1\text{-}MN}}$	$I_{\text{complex}} / I_{\mathbf{2a}}$	$I_{\text{complex}} / I_{\mathbf{9\text{-}MA}}$	$I_{\text{complex}} / I_{\mathbf{2b}}$	$I_{\text{complex}} / I_{\mathbf{1\text{-}MP}}$	$I_{\text{complex}} / I_{\mathbf{2c}}$
Free	1.7×10^{-2}	-	5.1×10^{-3}	-	1.9×10^{-2}	-
LiSCN	1.9×10^{-2}	1.1	6.1×10^{-3}	1.2	2.1×10^{-2}	1.3
NaSCN	2.0×10^{-2}	1.2	6.6×10^{-3}	1.3	4.9×10^{-2}	2.5
KSCN	2.0×10^{-2}	1.2	6.6×10^{-3}	1.3	3.1×10^{-2}	1.6
RbSCN	1.7×10^{-2}	1.0	5.1×10^{-3}	1.0	2.0×10^{-2}	1.0
CsSCN	2.0×10^{-2}	1.2	5.5×10^{-3}	1.1	2.8×10^{-2}	1.4
NH_4SCN	2.9×10^{-2}	1.7	1.7×10^{-2}	3.3	8.5×10^{-2}	4.4
$Mg(SCN)_2$	2.7×10^{-2}	1.6	1.9×10^{-2}	3.7	6.1×10^{-2}	3.2
$Ca(SCN)_2$	2.7×10^{-2}	1.6	2.1×10^{-2}	4.2	6.2×10^{-2}	3.2
$Ba(SCN)_2$	2.2×10^{-2}	1.3	1.1×10^{-2}	2.2	6.5×10^{-2}	3.4
$Zn(SCN)_2$	0.73	43	0.93	182	0.74	38

[a]Standard substance (**1-MN**: 1-methylnaphthalene, **9-MA**: 9-methylanthracene, **1-MP**: 1-methylpyrene).

Table 2. Association constants (log K / M^{-1}) of **1** and **2** for guest salts in $MeOH:CHCl_3$ (9:1 *v/v*) [a] and MeOH [b]

	Log K (M^{-1})			
	1[12,13]	**2a**[10,12]	**2b**[11,12]	**2c**
LiSCN	0.48 ± 0.07^{a}	4.12 ± 0.13^{b}	-	-
NaSCN	2.59 ± 0.04^{a}	3.97 ± 0.03^{b}	-	2.89 ± 0.05^{a}
KSCN	3.38 ± 0.01^{a}	3.97 ± 0.08^{b}, 3.45 ± 0.03^{a}	-	-
RbSCN	2.54 ± 0.03^{a}	3.71 ± 0.25^{b}	-	-
CsSCN	2.07 ± 0.01^{a}	3.69 ± 0.09^{b}	-	-
NH_4SCN	1.70 ± 0.04^{a}	3.67 ± 0.02^{b}	3.26 ± 0.05^{a}	3.25 ± 0.02^{a}
$Mg(SCN)_2$	3.15 ± 0.05^{a}	4.01 ± 0.02^{b}	3.13 ± 0.09^{a}	3.61 ± 0.09^{a}
$Ca(SCN)_2$	2.16 ± 0.04^{a}	4.33 ± 0.02^{b}	3.58 ± 0.04^{a}	3.80 ± 0.03^{a}
$Ba(SCN)_2$	2.15 ± 0.05^{a}	4.05 ± 0.19^{b}	3.24 ± 0.05^{a}	2.83 ± 0.10^{a}
$Zn(SCN)_2$	0.85 ± 0.07^{a}	5.28 ± 0.02^{b}	4.46 ± 0.09^{a}	4.93 ± 0.02^{a}

cation complexes for **1-MP**, as a measure of the guest cation-induced fluorescence recovery. The fluorescence intensity ratio ($I_{\mathbf{2c}\text{-zinc cation complex}}/I_{\mathbf{1\text{-}MP}}$) of **2c** was 0.74. Zinc cation binding can then cause high fluorescence recovery. This recovery is due to coordination from the nitrogen atoms of the diazacrown to the Zn^{2+}. The strength of this binding interaction modulates the PET from the amine to pyrene. The order of Zn^{2+}-induced fluorescence recovery ($I_{\mathbf{2}\text{-zinc cation complex}}/I_{\text{standard substance}}$) is **2b** > **2c**

> **2a**. This means that the 9-anthrylmethyl derivative (**2b**) is more excellent PET fluoroionophore for Zn^{2+}.

Guest concentration dependence of the fluorescence intensity allowed us to determine the association constants (*K*) by the non-linear curve-fitting method[13,16] (Table 2). The *K* values of diaza-12-crown-4 derivative (**2c**) for various guest cations were larger than those of **1**. The order of *K* values for Zn^{2+} is **2a** > **2c** > **2b**. This means the two larger aromatic rings may block the incorporation of guest cations in host. The diazacrown derivative (**2c**) showed the following cation selectivity: $Zn^{2+} > Ca^{2+} > Mg^{2+} > NH_4^+ > Na^+ > Ba^{2+}$. Comparison of the selectivity order for **1** and **2c** confirms that the size and electronic property of ionophore attached with aromatic pendants. The pendants may control the selectivity of the host toward guest cations in a delicate manner.

In conclusion, the cation binding to the pyrene-attached diaza-12-crown-4 (**2c**) did not show the excimer fluorescence enhancement. However the diaza-12-crown-4 (**2c**) exhibited high Zn^{2+} selectivity and fluorescence selectivity. The diaza-12-crown-4 having two 1-pyrenylmethyl pendants may be utilized as a PET fluorescent sensor for Zn^{2+}.

EXPERIMENTAL

Melting points were obtained with a Mitamura Riken Kogyo 7-15 Micro Melting Point Apparatus and are uncorrected. NMR spectra were measured on a JEOL JNM-ECA-500 Model spectrometer in $CDCl_3$; the chemical shifts are expressed by an δ unit using tetramethylsilane as an internal standard. The mass spectra were measured with a JEOL JMS-700 spectrometer. IR spectra were recorded on a Shimadzu Prestige-21 infrared spectrophotometer. UV spectra were measured using a Shimadzu Model UV-3150 spectrophotometer. Fluorescence spectra were measured with a JASCO Model FP-6500 spectrofluorimeter. The stationary phase for the column chromatography was supplied by Merck and the eluent was a mixture of ethyl acetate, chloroform, and hexane. The association constants (*K*) were determined by the same procedure in the previous study.[13,16]

Synthesis of 4,10-bis(1-pyrenylmethyl)-1,7-dioxa-4,10-diazacyclododecane (2c)

A THF-toluene solution (10 mL, 1:1 *v/v*) of 1,7-diaza-12-crown-4 (34.8 mg, 0.20 mmol), triethylamine (0.5 mL, 3.6 mmol), and 1-chloromethylpyrene (250 mg, 1.00 mmol) was heated at 80 ˚C for 8 h. The mixture was then diluted with 1.0 M NH_3 solution (30 mL), extracted with $CHCl_3$. The solvent was evaporated and the residue was purified by column chromatography over silica gel using EtOAc and $CHCl_3$ (1:1 *v/v*) as the eluent. The physical and spectral data of **2c** (112 mg, 93%) are given below.

2c: pale yellow crystals, mp 152.0-153.0 ˚C, ^1H NMR ($CDCl_3$) δ = 2.83 (8H, t, *J* = 4.6 Hz), 3.45 (8H, t, *J* = 4.6 Hz), 4.25 (4H, s), 7.93- 8.01 (8H, m), 8.03 (2H, d, *J* = 7.4 Hz), 8.04 (2H, d, *J* = 9.2 Hz), 8.10 (2H, d, *J* = 8.6 Hz), 8.12 (2H, d, *J* = 8.6 Hz), and 8.56 (2H, d, *J* = 9.2 Hz). ^{13}C NMR ($CDCl_3$) δ = 55.5 (4C), 59.2 (2C), 69.4 (4C), 124.4 (2C), 124.5 (2C), 124.7 (2C), 124.8 (2C), 124.9 (4C), 125.7 (2C), 126.9 (2C), 127.0 (2C), 127.4 (2C), 128.1 (2C), 129.8 (2C), 130.6 (2C), 130.9 (2C), 131.3 (2C), and 133.2 (2C). IR (KBr) ν 1036, 1045, 1057, 1123, 1445, 1458, 1685, and 1601 cm^{-1}. UV ($CHCl_3$) λ 242 (ε = 126000), 265 (52000), 276 (82400), 313 (25600), 327 (53400), and 343 (81200) nm. HR FAB MS. Found: 603.3009. Calcd for $C_{42}H_{39}N_2O_2$: 603.3012.

REFERENCES

1. H. G. Löhr and F. Vögtle, *Acc. Chem. Res.*, 1985, **18**, 65.
2. J.-M. Lehn, "*Supramolecular Chemistry*", VCH Verlagsgesellschaft mbH, Weinheim, 1995.
3. A. W. Czarnik, *Acc. Chem. Res.*, 1994, **27**, 302.
4. L. Fabrizzi and A. Poggi, *Chem. Soc. Rev.*, 1995, **95**, 197.
5. B. Valeur and I. Leray, *Coord. Chem. Rev.*, 2000, **205**, 3.
6. K. Kubo, '*Topics in Fluorescence Spectroscopy: Advanced Concepts in Fluorescence Sensing*,' Vol. 9, ed. by C. D. Geddes and J. R. Lakowicz, Springer, New York, 2005, pp. 219–247.
7. A. P. de Silva and S. A. de Silva, *J. Chem. Soc. Chem. Commun.*, 1986, **23** 1709.
8. A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515.
9. K. Kubo, R. Ishige, N. Kato, E. Yamamoto, and T. Sakurai, *Heterocycles*, 1997, **45,** 2365.
10. K. Kubo, E. Yamamoto, and T. Sakurai, *Heterocycles*, 1998, **48,** 2133.
11. K. Kubo, R. Ishige, and T. Sakurai, *Talanta*, 1999, **49**, 339.
12. K. Kubo and T. Sakurai, *Heterocycles*, 2000, **52**, 945.
13. K. Kubo, N. Kato, and T. Sakurai, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 3041.
14. N. Kh. Petrov, A. I. Shushin, and E. L. Frankevich, *Chem. Phys. Lett.*, 1981, **82**, 339.
15. N. Kh. Petrov, V. N. Borisenko, M. V. Alfimov, T. Fiebig, and H. Staerk, *J. Phys. Chem.*, 1996, **100**, 6368.
16. A. Mori, K. Kubo, and H. Takeshita, *Coordination Chem. Rev.*, 1996, **148**, 71.