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SYNTHESIS, COMPLEXATION AND FLUORESCENCE BEHAVIOR OF DIAZA-12-CROWN-4 CARRYING TWO NAPHTHYL PENDANTS

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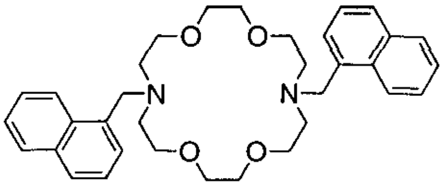
Abstract–*N,N'*-Bis(1-naphthylmethyl)-4,10-diaza-12-crown-4 (**2**) was found to display unique photophysical properties in the presence of the guest metal salts. The diazacrown (**2**) exhibited high Zn^{2+} enhancement selectivity and in the presence of this cation the host fluorescence intensities were increased by a factor of 43. The guest cation-induced fluorescence recovery of **2** was higher than *N,N'*-bis(1-naphthylmethyl)-4,13-diaza-18-crown-6 (**1**).

The development of photoinduced electron transfer (PET) systems for guest cations has recently gained much attention.[1] There are extensive investigations toward the characterization of fluoroionophores including ionophore with naphthalene, anthracene, umbelliferon, and pyrene fluorophore.[2,3] It was found that the azacrown ethers act as electron donors in a typical exciplex-forming system that involves an appropriate electron acceptor.[4,5] The addition of metal salts enhanced the fluorescence emission intensity of *N,N'*-bis(1-naphthylmethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**1**) by a factor of 41.[6] However, the emission intensities of **1** in the presence of the guest salts were lower than the standard substances (1-methylnaphthalene, 1-MN). As an effective PET fluoroionophore is designed, it is some important factors that the PET fluoroionophores have low emission quantum yield by PET from amine donor to excited chromophore, high emission quantum yield in complexation with guest molecules and high binding constant. Thus, it is interesting to investigate the complex formation with metal salts of PET fluoroionophores. As an approach to the manipulation of PET sensor, we now report the fluorescence behavior of the diaza-12-crown-4 (**2**) with two naphthyl pendants in the presence of guest salts.



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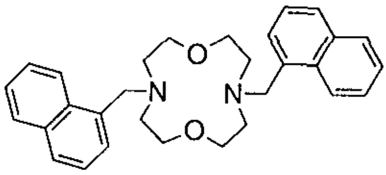

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The naphthalene-functionalized diazacrown ether (**2**) was prepared by the *N*-alkylation of 1,7-diaza-12-crown-4 with 1-chloromethylnaphthalene in triethylamine-toluene-tetrahydrofuran solution. The structure and purity of **2** were ascertained by NMR spectroscopy and elemental analysis.

Fluorescence spectral behavior of **1** and **2** (2.00 x 10^{-5} M) gave weak emission band at 333 nm. The emission-band intensities of **2** was reduced to approximately one-59th that of standard substance (1-methylnaphthalene: 4.00 x 10^{-5} M). This indicates that the quenching of the excited-state naphthalene chromophore by the azacrown unit proceeds in a mechanism similar to that for the classical naphthalene-aliphatic amine system.[7] The quenching efficiency ($I_2/I_{1\text{-MN}}$: 1.7 x 10^{-2}) of **2** is lower than that ($I_1/I_{1\text{-MN}}$: 2.3 x 10^{-3})[6] of **1**. This means that the smaller macrocycle ring inhibits the PET occurring from the nitrogen atoms in the crown to excited fluorescent moieties.

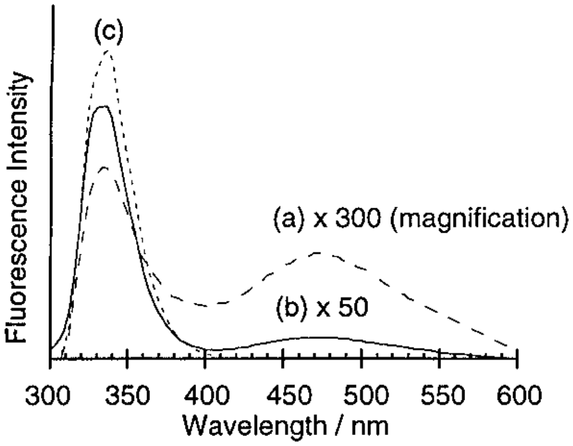


Figure 1. Fluorescence spectra of (a) **1**, (b) **2** (2.00 x 10^{-5} M) and (c) 1-methylnaphthalene (4.00 x 10^{-5} M) in methanol at room temperature, as excited at 280 nm.

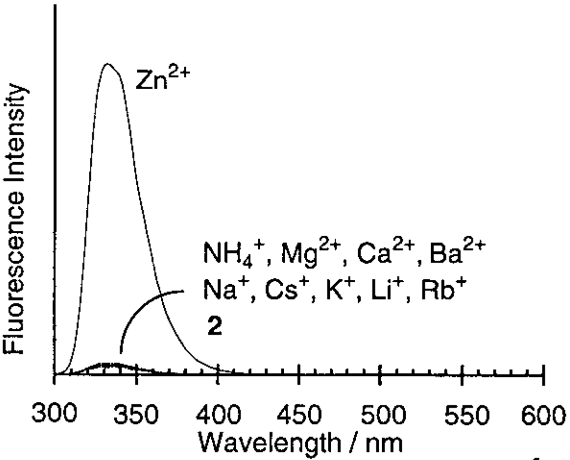


Figure 2. Fluorescence spectra of **2** (2.00 x 10^{-5} M) with and without various guest cations (5.00 x 10^{-4} M) in methanol, as excited at 280 nm.

In Figure 2 is illustrated the relative fluorescence spectral behavior of guest cation complexes **2** (2.00 x 10^{-5} M) in methanol at room temperature. A dramatic change in the emission intensity of **2** (I_2) 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 (25 molar equivalent), the relative emission intensity ($I_{complex}/I_2$), being used as a measure of the molecular recognition sensing, changed from 1 to 43 depending on the nature of guest cations as shown in Figure 2. Figure 3 illustrates the relative emission intensity of **2** against the guest cations concentration. Clearly, the emission intensity increases with an increase in the guest cation concentration. Interestingly, the intensity ratio ($I_{complex}/I_2$) was different among bound guest cations and decreased in the following order: Zn^{2+} (43) > NH_4^+ (1.7) > Mg^{2+}, Ca^{2+} (1.6) > Ba^{2+} (1.3) > Na^+, K^+, Cs^+ (1.2) > Li^+ (1.1) > Rb^+ (1.0). The order of $I_{complex}/I_2$ differs from that of $I_{complex}/I_1$ (Ba^{2+} (41) > Ca^{2+} (15) > Zn^{2+} (5.4) > NH_4^+ (4.9) > Mg^{2+} (3.5) > K^+ (2.8) > Na^+ (2.2) > Rb^+ (1.5) > Li^+ (1.2) and Cs^+ (1.2))[6]. Zinc ion binding can then cause high fluorescence recovery. This recovery is due to coordination from the nitrogen atoms of the diazacrown to the zinc ion. The strength of this binding interaction modulates the PET from the amine to naphthalene.

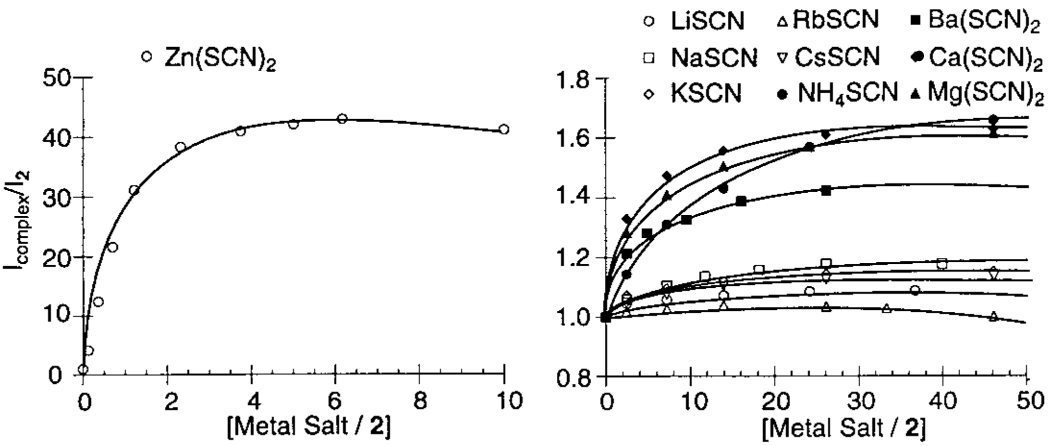


Figure 3. Dependence of fluorescence intensities of **2** (2.00×10^{-5} M) at 332 nm on concentration of various guest cations (added as thiocyanate salts) in methanol.

In Table 1 is illustrated the fluorescence intensity ratio ($I_{complex}/I_{1\text{-MN}}$) of guest cation complexes for 1-methylnaphthalene, as a measure of the guest cation-induced fluorescence recovery. The fluorescence intensity ratio ($I_{2\text{-guest cation complex}}/I_{1\text{-MN}}$) of **2** was larger than that ($I_{1\text{-guest cation complex}}/I_{1\text{-MN}}$) of **1**. This means that the diaza-12-crown-4 derivative (**2**) is more excellent PET fluoroionophore than the diaza-18-crown-6 (**1**).

Guest concentration dependence of the emission intensity (Figure 3) allowed us to determine the association constants (K) by the non-linear curve-fitting method[3,6,8] (Table 2). The K values of **2** for various metal ions were larger than those of **1**.[5] This means that the two naphthalene rings of **2** having smaller macrocycle ring may not block the incorporation of guest cations in **2**. The azacrown (**2**) showed the following cation selectivity: $NH_4^+ < Cs^+ < Rb^+ < K^+ < Na^+ < Mg^{2+} < Ba^{2+} < Li^+ < Ca^{2+} < Zn^{2+}$.

Table 1. Fluorescence intensity ratio of guest cation complex for 1-methylnaphthalene (1-MN)

	$I_1/I_{1\text{-MN}}$	$I_2/I_{1\text{-MN}}$
Free	2.3×10^{-3}	1.7×10^{-2}
LiSCN	2.7×10^{-3}	1.9×10^{-2}
NaSCN	5.0×10^{-3}	2.0×10^{-2}
KSCN	6.4×10^{-3}	2.0×10^{-2}
RbSCN	3.4×10^{-3}	1.7×10^{-2}
CsSCN	2.7×10^{-3}	2.0×10^{-2}
NH_4SCN	1.1×10^{-2}	2.9×10^{-2}
$Zn(SCN)_2$	1.2×10^{-2}	7.3×10^{-1}
$Mg(SCN)_2$	8.0×10^{-3}	2.7×10^{-3}
$Ca(SCN)_2$	3.4×10^{-2}	2.7×10^{-2}
$Ba(SCN)_2$	9.3×10^{-2}	2.2×10^{-2}

Table 2. Association constants (K / M^{-1}) of **1** and **2** for guest salts in methanol

	1	**2**
LiSCN	27 ± 5	13100 ± 3300
NaSCN	123 ± 9	9390 ± 610
KSCN	1850 ± 320	9320 ± 1600
RbSCN	305 ± 26	5120 ± 2210
CsSCN	97 ± 30	4940 ± 960
NH_4SCN	1490 ± 165	4670 ± 180
$Zn(SCN)_2$	126 ± 13	190000 ± 10000
$Mg(SCN)_2$	3240 ± 200	10200 ± 400
$Ca(SCN)_2$	61 ± 4	21300 ± 1100
$Ba(SCN)_2$	710 ± 114	11100 ± 3900

The association constants of **1** and **2** for various guest cations are depending upon the nature of ionophore properties.[9]

Binding interactions of the host **2** with guest cations were examined using ^{1}H NMR spectroscopy.

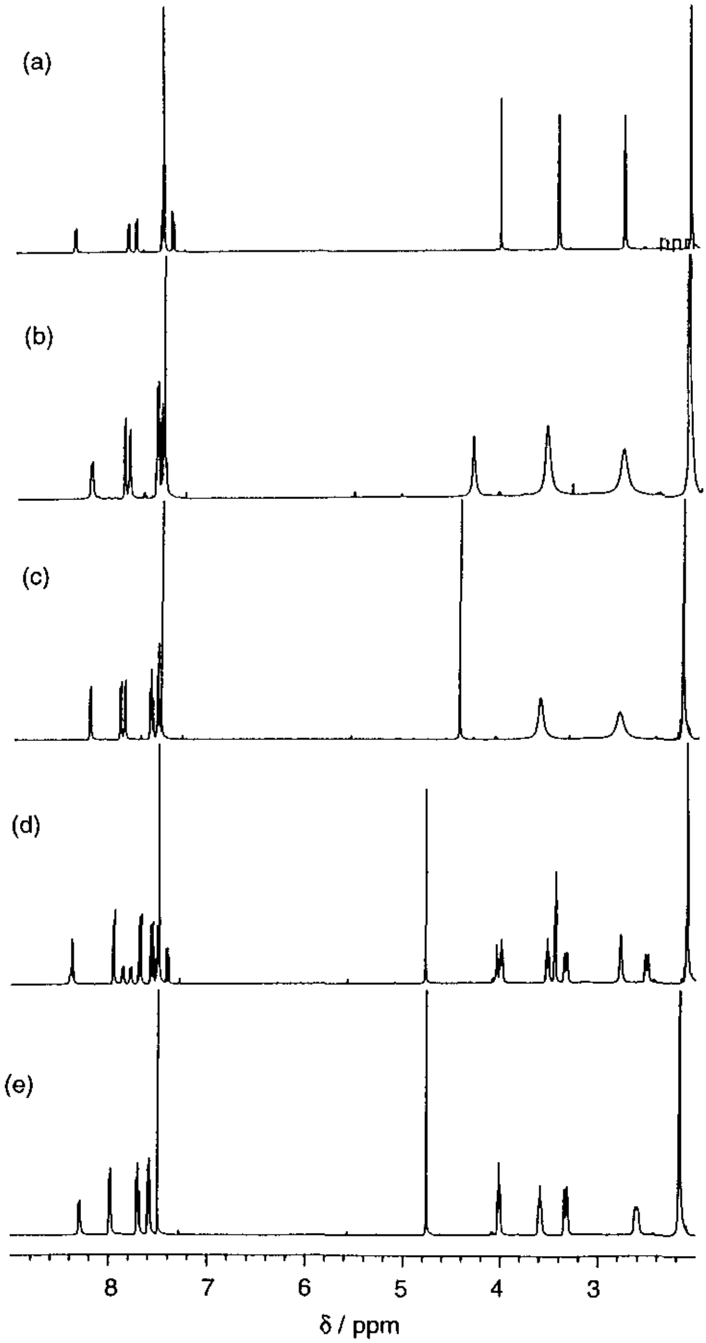
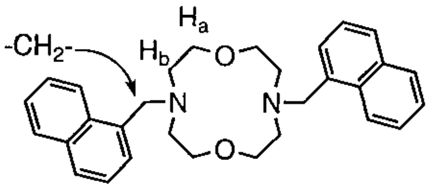


Figure 4. ^{1}H NMR spectral changes of **2** (8.0×10^{-4} M) with LiSCN and $Zn(SCN)_2$ in CD_3CN-$CDCl_3$ (1:1 *v/v*) at 298 K. Concentration of LiSCN and $Zn(SCN)_2$: (a) 0; (b) LiSCN, 5.0×10^{-4}; (c) LiSCN, 1.0×10^{-3}, (d) $Zn(SCN)_2$, 5.0×10^{-4}, and (e) $Zn(SCN)_2$, 1.0×10 M.

When monovalent guest salts were added, the resonance peaks shifted downfield, depending on the nature of the added guest salts (Figures 4a,b,c). While, the addition of bivalent metal ions decreased original-peak intensities, accompanied by an increase in new resonance-peak intensities (Figures 4a,d,e). These spectral changes mean that exchange rates are different between alkali metal and bivalent metal ions. The gradual downfield shift of methylene proton signal of naphthylmethyl group with addded LiSCN (Figures 4a,b,c) indicates that the exchange process between free host and its lithium complex is rapid as compared to the NMR time scale: time-averaged NMR shifts are observed depending upon guest concentrations. On the other hand, original signal intensities at 4.04 ppm decreased and new resonance peak intensities (the corresponding complex, [**2**-Zn^{2+}]) at 4.75 ppm increased as the $Zn(SCN)_2$ concentration was increased. This finding indicates that the exchange process is slow enough even at room temperature, compared with the NMR time scale, to give new signal corresponding to the zinc complex ([**2**-Zn^{2+}]). The difference in exchange rates between Li^+ and Zn^{2+} should be responsible for a large difference in the fluorescence-intensity enhancement for these guest cation complexes (Figure 4). While, the two original signals at 2.77 and 3.44 (*AA'BB'* system) in the diazacrown ether decreased and four new resonance peak intensities (2.60, 3.32, 3.58, and 4.01 ppm, *ABCD* system) increased as the $Zn(SCN)_2$ concentration was increased. This result is attributed to forming the gauche conformation of all methylene protons in the azacrown regions.

Table 3. Change of ^1H NMR chemical shifts of **2** (1.0×10^{-2} M) with various guest salts (1.0×10^{-2} M) in CD_3CN-$CDCl_3$ (1:1 *v/v*)

		Azacrown unit	
	-CH_2-	H_a	H_b
2	4.04	3.44	2.77
LiSCN	4.45 (+0.41)	3.62 (+0.18)	2.81 (+0.04)
NaSCN	4.12 (+0.08)	3.52 (+0.08)	2.75 (-0.02)
KSCN	4.04 (0.00)	3.44 (0.00)	2.76 (-0.01)
RbSCN	4.04 (0.00)	3.44 (0.00)	2.77 (0.00)
CsSCN	4.04 (0.00)	3.44 (0.00)	2.77 (0.00)
NH_4SCN	4.43 (+0.39)	3.49 (+0.05)	3.08 (+0.31)
$Zn(SCN)_2$	4.75 (+0.71)	4.01 3.58	3.32 2.60
$Mg(SCN)_2$	4.71 (+0.67)	4.07 3.57	3.27 2.55
$Ca(SCN)_2$	4.66 (+0.62)	4.03 3.59	3.06 2.49
$Ba(SCN)_2$	4.66 (+0.62)	4.04 3.57	2.95 2.47



The chemical shifts (δ) and induced shifts (Δδ) of the host **2** with and without guest cation are summarized in Table 3. Interestingly, Zn^{2+} produced even more remakable chemical-shift change for the methylene proton signal. The magnitude of guest cation-induced shift for this proton signal decreased in the following order: Zn^{2+} (+0.71) > Mg^{2+} (+0.67) > Ba^{2+}, Ca^{2+} (+0.62) > Li^+ (+0.41) > NH_4^+ (+0.39) > Na^+ (+0.08) > K^+, Rb^+, Cs^+ (0), clearly demonstrating that the nitrogen atom in the azacrown ether has a propensity to strongly coordinate with bivalent cations.

In conclusion, the high association constant for **2** in methanol, the emission intensity of this host was greatly enhanced in the presence of zinc salts, establishing that **2** has a high fluorescence switch-on ability for complexation. The guest cation-induced emision-intensity enhancement originates from the affinity of the nitrogen atom in the azacrown ether for cations, the guest cation-dependent coordinated structure, and exchange rate between the free host **2** and its guest salt complex in the ground state. The diaza-12-crown-4 having two 1-naphthyl pendant may be utilized as a new PET fluorescent sensor for guest cations.

EXPERIMENTAL

Elemental analyses were performed by Perkin Elmer PE2400 series II CHNS/O analyzer. Melting points were obtained with a Yanagimoto Micro Melting Point Apparatus and are uncorrected. NMR spectra were measured on a JEOL JNM-500 Model spectrometer in $CDCl_3$; the chemical shifts are expressed by an δ unit using tetramethylsilane as an internal standard. IR spectra were recorded on a Hitachi Model 270-30 infrared spectrophotometer. UV spectra were measured using a Shimadzu Model UV-2200 spectrophotometer. Fluorescence spectra were measured with a Hitachi Model F-4500 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.[3,6,8]

N,*N'*-Bis(1-naphthylmethyl)-1,7-dioxa-4,10-diazacyclododecane (2).

A THF-toluene solution (10 mL, 1:1 *v/v*) of 1,7-diaza-12-crown-4 (17.0 mg, 0.10 mmol), triethylamine (0.5 mL, 3.6 mmol), and 1-chloromethylnaphthalene (90.0 mg, 0.50 mmol) was refluxed for 6 h. The mixture was then diluted with 1M NH_3 (10 mL), extracted with chloroform. The solvent was evaporated and the residue was purified by column chromatography over silica gel (70-230 mesh, Merck) using hexane and ethyl acetate (1:1 *v/v*) as the eluent. Recrystallization from ethanol gave analytically pure samples with the following physical and spectroscopic properties. colorless crystals, mp 138.5–139.5 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.81 (8H, t, J =4.9 Hz), 3.45 (8H, t, J =4.9 Hz), 4.05 (4H, s), 7.38 (2H, dd, J =7.0, 8.2 Hz), 7.46-7.51 (6H, m), 7.75 (2H, d, J =8.2 Hz), 7.83 (2H, dd, J =2.5, 7.0 Hz), and 8.38 (2H, d, J =7.0 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) = 55.70 (4C), 60.13 (2C), 69.44 (4C), 125.13 (2C), 125.22 (2C), 125.57 (2C), 125.65 (2C), 127.16 (2C), 127.81 (2C), 128.30 (2C), 132.54 (2C), 133.82 (2C), and 135.44 (2C). UV (MeOH): 223 (ε=145000), 270 (12800, sh), 281 (14900), and 293 (10200, sh) nm. IR (KBr): 768, 996, 1046, 1066, 1120, 1300, 1334, 1356, 1436, 1594, 2848, and 2904 cm^{-1}. Anal. Calcd for $C_{30}H_{34}N_2O_2$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.20; H, 7.60; N, 6.12.

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