ASSOCIATION CONSTANTS OF 5,8,11,14-TETRAOXA-2,17-DITHIABICYCLO[16.4.1]TRICOSA-1(22),18,20-TRIEN-23-ONE FOR VARIOUS METAL IONS†

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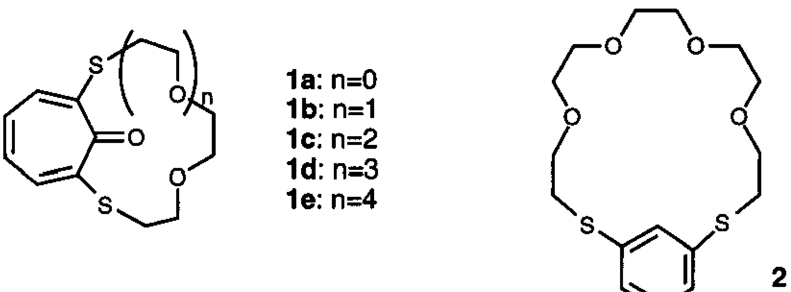
Abstract—With the regard to the pronounced mercurophilicity of dithio-crown ethers incorporated into seven-membered conjugated systems, the association constants of 5,8,11,14-tetraoxa-2,17-dithiabicyclo[16.4.1]tricosa-1(22),18,20-trien-23-one, the most effective carrier of mercury(II) salt, were determined with various metal salts. An increasing order of the association constants was $Na^+ < K^+ < NH_4^+ < Li^+ < Mg^{2+} < Zn^{2+} < Cd^{2+} < Hg^{2+} < Ba^{2+} < Ca^{2+}$ in acetonitrile.

Considerable attention has been paid to develop the effective separation and extraction of metal ions by means of complex formation; *e.g.*, Bacon and Kirch[1] have studied transport of heavy metal ions such as Hg^{2+} and Pb^{2+} through a liquid membrane, and Izatt *et al.*[2] and Gokel *et al.*[3] have also studied transport of metal ions by the crown and aza-crown ethers through chloroform membrane.

Currently, we have been interested in the pronounced mercurophilic properties of dithio-crown ethers incorporated into seven-membered conjugated systems.[4,5] Particularly, the exclusive transport of Hg^{2+} through a U-type cell with water-chloroform system was remarkable. Since the transport phenomenon is a



1a: n=0
1b: n=1
1c: n=2
1d: n=3
1e: n=4

2

Chart 1

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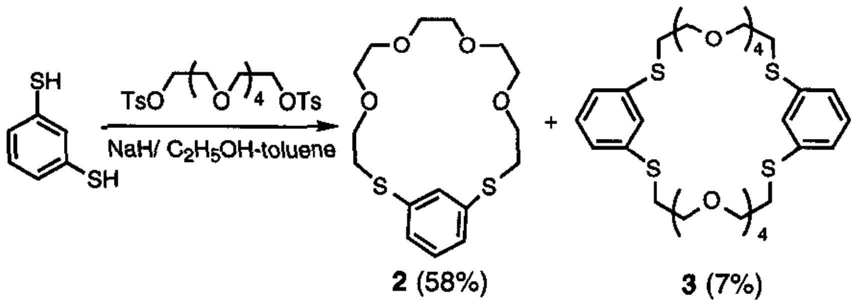
† This paper is dedicated to the memory of the late Professor Shun-ichi Yamada.

combined process of complexation, diffusion, liberation, and extraction, it is important to determine the association constants for the first step of the process between such tropone derivatives and various metal ions.

Among the dithio-crown derivatives synthesized by our hands, 5,8,11,14-tetraoxa-2,17-dithiabicyclo-[16.4.1]tricosa-1(22),18,20-trien-23-one (**1d**) was the most effective mercurophilic dithio-crown tropone derivative.[5] Herein, we describe the results on the metal complexation by **1d** and the role of the tropone carbonyl group by the comparison with the corresponding benzenoid derivative.

Dithio-crown ethers examined are shown in Chart 1.

UV Spectral Changes. The UV-vis spectral changes have been examined by the addition of various metal ions to several tropone-attached dithio-crown ethers and dimeric tetrathioethers, prepared from 2,7-dibromotropone and 2,4,7-tribromotropone and a series of oligoethylene glycol bis(2-mercaptoethyl)-ethers.[5]



Scheme 1

Thioether (**1**) with a smaller cavity did not show much changes by the addition of metal ions. Thioether (**1d**) with a larger cavity showed the appreciable changes by the addition of 100 equivalent of Ca^{2+}, Ba^{2+}, Hg^{2+} and Cd^{2+}, but the slight changes by the addition of Li^+, Na^+, K^+, NH_4^+, Mg^{2+} and Zn^{2+} as shown in the upper spectra in Figure 1. The spectra of **1d** changed accompanying an increase in the absorption in the longer wavelength region as shown in the lower spectra in Figure 1 when the metal ions such as Ca^{2+}, Ba^{2+}, Mg^{2+}, Zn^{2+}, Cd^{2+}, and Hg^{2+} were added in large excess. However, on the addition of Li^+, Na^+, K^+, and NH_4^+, the intensity of the absorption band at 399 nm of **1d** was decreased. There is a remarkable difference in a spectral change caused by addition of different metal ions. This may indicate that the binding sites are different according to the metal ions added.

Association Constants and Transport. Association constants (*Ks*) were determined by using the non-linear curve fitting method[6,7] from the change of absorbance in the UV spectra in acetonitrile (CH_3CN) or the change of chemical shifts in the ^1H NMR spectrum in acetonitrile-d_3 (CD_3CN) by titrating at 298 K. The *Ks* was calculated to be 1023 M^{-1} from the curve-fitting plot of the UV spectral change of **1d** by addition of $Hg(SCN)_2$. Similarly, the *Ks* of **1d** for Li^+, Na^+, K^+, NH_4^+, Ca^{2+}, Ba^{2+}, Zn^{2+}, Mg^{2+}, Cd^{2+}, and Hg^{2+}, calculated from the titration curves, are summarized in Table 1. The increasing order of *Ks* of **1d** was $Na^+ < K^+ < NH_4^+ < Li^+ < Mg^{2+} < Zn^{2+} < Cd^{2+} < Hg^{2+} < Ba^{2+} < Ca^{2+}$ in CH_3CN. The larger complexation constants for Ca^{2+} and Ba^{2+} over Hg^{2+} are not apparently consistent to the results

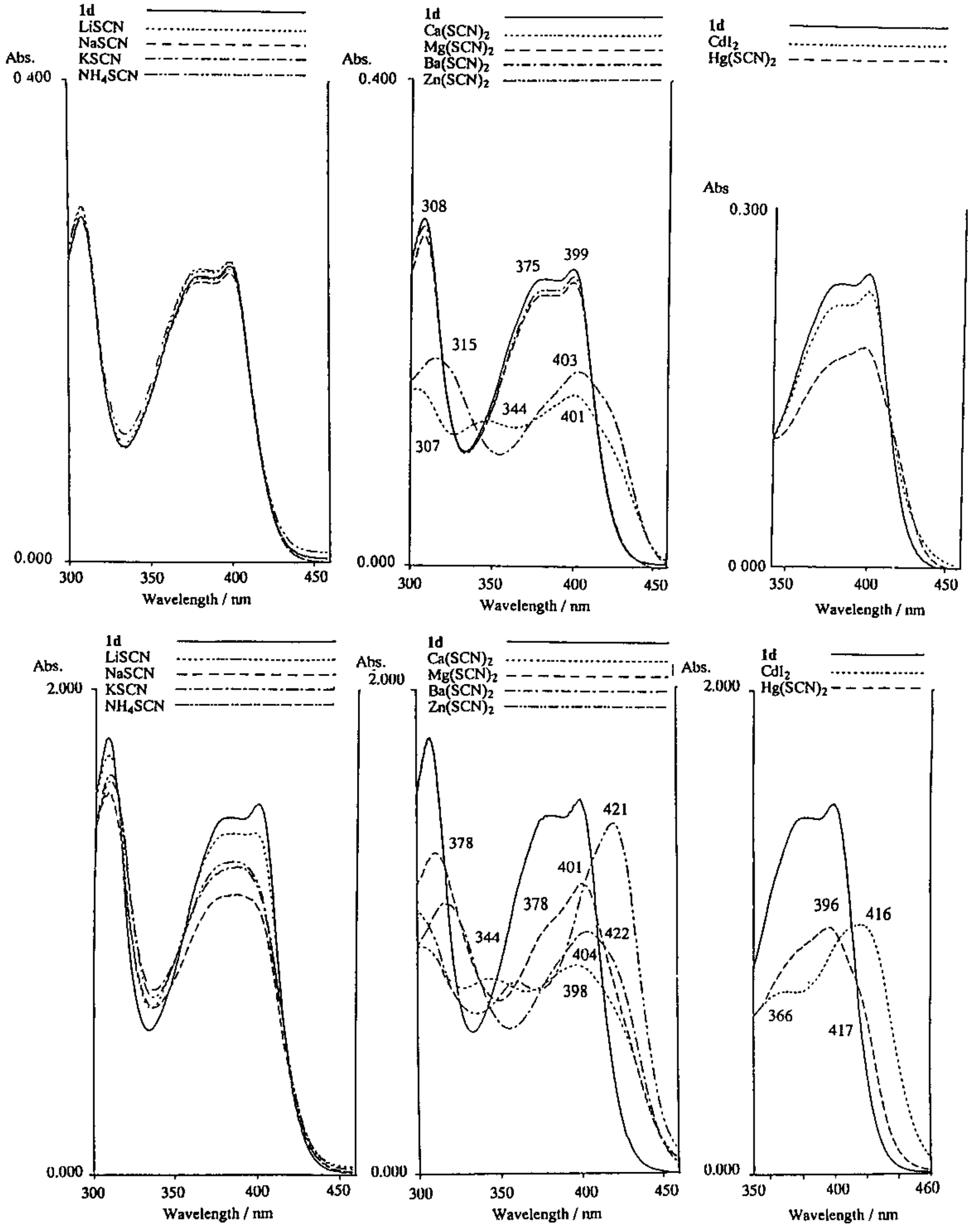


Figure 1. UV Spectral changes of **1d** in the presence of various metal ions in acetonitrile. The upper spectra were measured in the presence of 100 equivalent of metal ions and the lower ones in the presence of 5000 equivalent of metal ions. In the case of Hg^{2+}, however, 300 equivalent of $Hg(SCN)_2$ was used due to low solubility.

complexes of Ca^{2+} and Ba^{2+} are not soluble in chloroform (the solvent for the transport experiment) because extraction of these ions into the chloroform-*d* ($CDCl_3$) solution was not observed by ^1H NMR spectroscopy.

Table 1. Association constants of the 1 : 1 complexes of **1d** and various metal ions

	Method[a]	Salts	K_s	Log K_s	R[b]
1d	A	LiSCN	30	1.48	0.999
	A	NaSCN	4	0.56	0.993
	A	KSCN	13	1.10	0.994
	A	NH_4SCN	11	1.06	0.991
	A	$Ca(SCN)_2$	7250	3.86	0.999
	A	$Mg(SCN)_2$	20	1.30	0.999
	A	$Ba(SCN)_2$	5540	3.73	0.999
	A	$Zn(SCN)_2$	24	1.37	0.999
	A	CdI_2	73	1.86	0.999
	A	$Hg(SCN)_2$	1023	3.01	0.999
	B	$Hg(SCN)_2$	1090	3.04	0.999
1e	B	$Hg(SCN)_2$	354	2.55	0.999
2	B	$Hg(SCN)_2$	516	2.71	0.995

a) Curve-fitting method, Method A: UV spectrum, Method B: ^1H-NMR titration

b) R factor for the curve fitting. Conditions: CH_3CN or CD_3CN at 298 K.

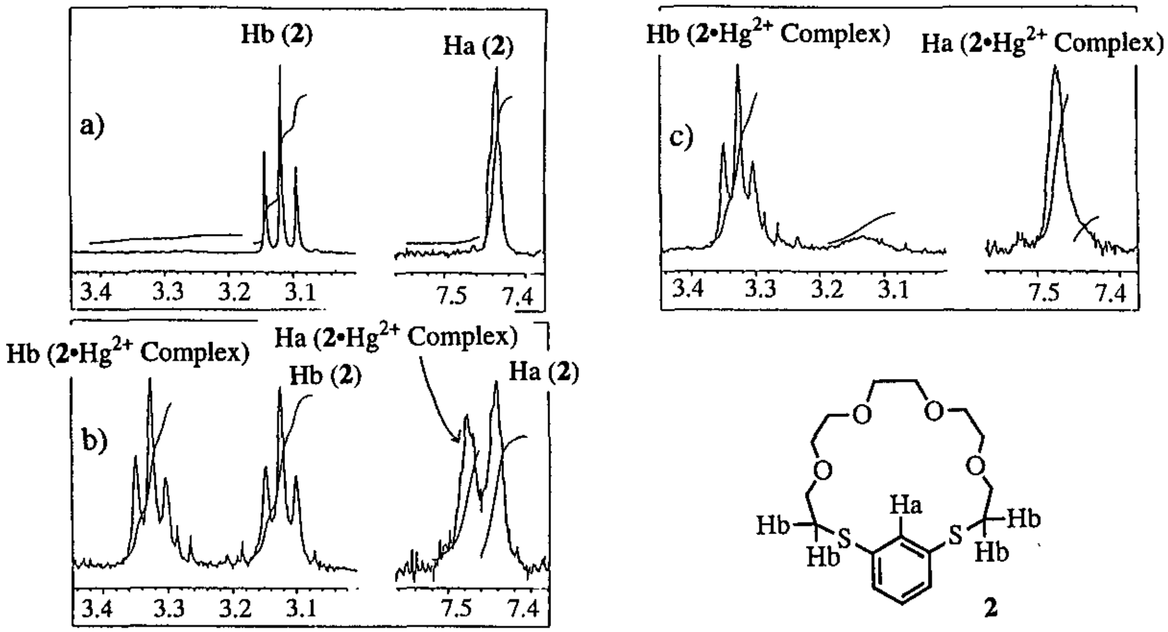


Figure 2. ^1H NMR Spectral changes of **2** upon addition of $Hg(SCN)_2$. a) [complex]/([**2**]+[complex])=0, $[Hg(SCN)_2]$=0, b) [complex]/([**2**]+[complex])=0.49, $[Hg(SCN)_2]$=1.73 c) [complex]/([**2**]+[complex])= 0.83, $[Hg(SCN)_2]$=5.75 mol/L.

The considerably large λ_{max} shifts were observed in **1d** with the increasing order of Ca^{2+}(398 nm) < Hg^{2+}(401 nm) < Mg^{2+}(396 nm) < Ba^{2+}(404 nm) < Cd^{2+}(416 nm) < Zn^{2+}(421 nm) although the observed λ_{max} shifts due to the complexation with metal ions were not parallel to the association constants of the complexes. This is similar to the observation reported by Vögtle.8)

In order to compare the properties with benzenoid analogues, we have prepared a dithio-19-crown-6 ether (**2**) from benzene-1,3-dithiol and pentaethylene glycol bis(*p*-toluenesulfonate) (Scheme 1). It is noteworthy that upon addition of $Hg(SCN)_2$, the ^1H NMR spectrum of **2** exhibited the singals due to the complexed species in addition to the signals of the uncomplexed **2**.

This indicated that the complexation and liberation processes with **2** were slow. Namely, the new proton signals of **2** by addition of $Hg(SCN)_2$ appeared at δ 3.32 beside those of the uncomplexed **2** at 3.12, a triplet signal for the ethylene protons adjacent to the sulfur atom (Figure 2). The association constant of **2**, determined by the integral ratio of the protons, was 515 M^{-1}, which is smaller than that (1090 M^{-1}) of **1d**, as being determined from the change of the chemical shift in ^1H NMR spectra. This was in good agreement with the result (1023 M^{-1}) obtained from the UV spectral measurement. The *Ks* (354 M^{-1}) of another crown ether **1e** for Hg^{2+} was smaller than that of **1d**. This result is parallel to our previously reported results of the transport.5

The complex formation of **1d** has been examined with various metal ions, *i.e.*, alkali metal ions (Li^+ and Na^+), alkaline earth metals (Mg^{2+}, Ca^{2+}, and Ba^{2+}), and some transition metal ions (Co^{2+}, Ni^{2+}, Fe^{3+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, and Ag^+) showed no indication of ^1H NMR spectral change in $CDCl_3$. Extraction of Hg^{2+} into the $CDCl_3$ solutions containing **1d** was checked. The ^1H NMR spectra of **2** were changed by the complex formation of Hg^{2+}, Ag^+, and Cd^{2+} although the selectivity of **2** was lower than **1d**.

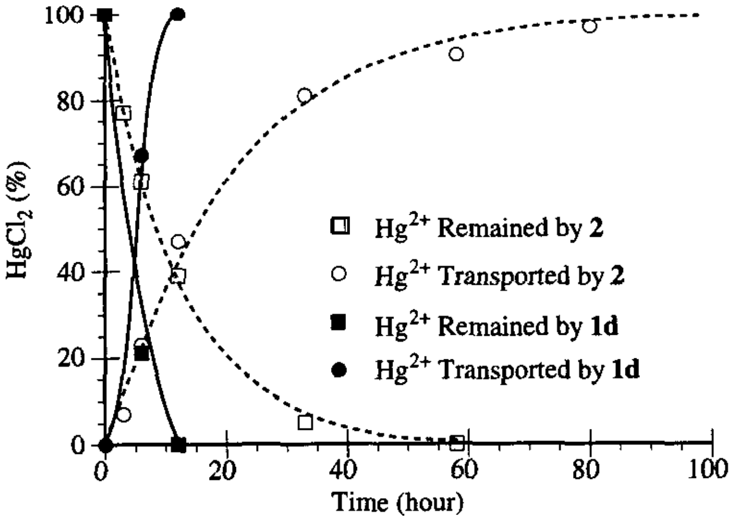


Figure 3. Transport of $HgCl_2$ by **1d** and **2**.

Figure 3 shows the representative results of the transport of Hg^{2+} by **1d** and **2**. It is also noteworthy that the release of Hg^{2+} for **2** from the membrane to the receiving phase is slower than those of **1d** and **1e**. Thus, the tropone function played an important role in the release of Hg^{2+} to the receiving phase.

The generation of a 6π-cationic system was observed by the ^1H NMR spectrum in 5M D_2SO_4 (Figure 4). In respect of the chemical shift differences of **1d**, $\Delta\delta$, between $CDCl_3$ and 5M-D_2SO_4, [^1H NMR (D_2SO_4) δ=3.45 (8H, m), 3.55-3.64 (8H, m), 3.87 (4H, t, J=4.8 Hz), 7.70-7.73 (2H, m), 8.16-8.25 (2H, m)], the generation of a delocalized 6π cationic system caused remarkable down-field shifts for the tropone protons ($\Delta\delta$=-0.78). This result showed the formation of the tropylium ion.

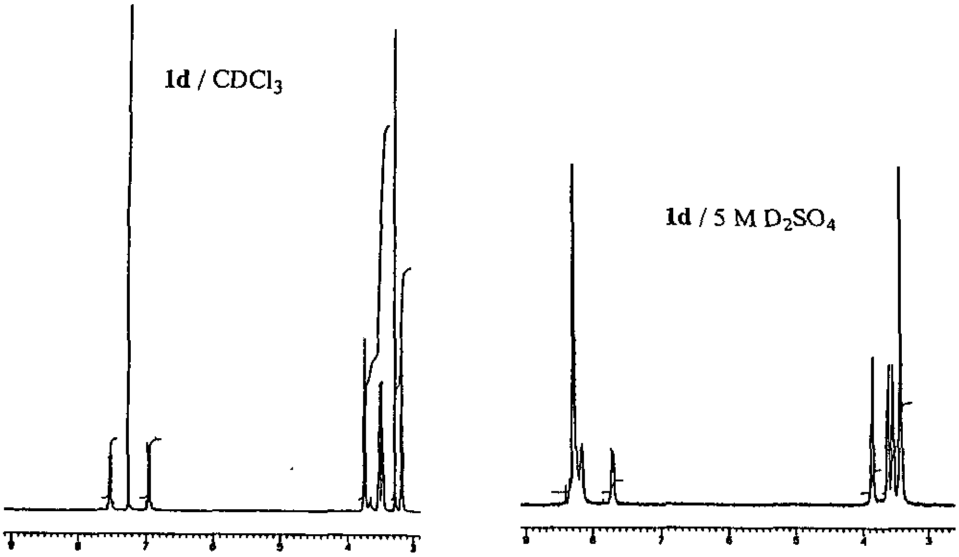


Figure 4. ^1H NMR Spectra of **1d** in $CDCl_3$ and 5 M D_2SO_4.

In conclusion, the troponoid thio-crown ether (**1d**) was more effective carrier of Hg^{2+} than the benzenoid thio-crown ether (**2**) with the similar cavity size. The results clearly showed that protonation is responsible for the ready liberation of Hg^{2+} by generating a 6π cationic system with the seven-membered ring to cause Coulomb repulsion with the complexed Hg^{2+}.

On the other hand, the troponoid thio-crown ethers showed the changes of UV-vis spectra by the addition of various metal ions. It is suggested that the troponoid structure can be utilized as a chromophore on the complex formation.

EXPERIMENTAL

The elemental analyses were performed at the elemental analysis laboratory in the Institute of Advanced Material Study, Kyushu University. The melting points were obtained on a Yanagimoto Micro Melting Point Apparatus and are uncorrected. The NMR spectra were measured on a GSX 270H Model spectrometer in $CDCl_3$ and CD_3CN; the chemical shifts are expressed in δ unit. The mass spectra were measured with a JEOL 01SG-2 spectrometer. The IR spectra were recorded on a JASCO IR-A102 spectrophotometer with KBr disks for crystalline compounds or with liquid films inserted between NaCl plates for oily phase for the column chromatography was Wakogel C-300 and the eluant was a mixture of ethyl acetate, chloroform, and hexane.

Synthesis of 1,3-Benzo-19-dithiocrown-6 Ether (2); To a refluxing mixture of toluene (50 mL) and EtOH (50 mL) were added a solution of pentaethyleneglycol bis(*p*-toluenesulfonate) (264 mg, 1 mmol) in toluene (10 mL) and EtOH (15 mL) and a solution of 1,3-benzenedithiol disodium salt [prepared from dithio (142 mg, 1 mmol) and NaH (88 mg, 2.2 mmol)] in EtOH (10 mL) through microfeeders in a 3 h period under N_2 stream. After removing the solvent in vacuo, the residue was acidified with 2M HCl and extracted with $CHCl_3$. Silica gel column chromatography of the organic fractions gave 1,3-benzo-19-dithiocrown-6 ether (**2**) [a colorless oil, 170 mg, 58%. *Anal.* Calcd for $C_{16}H_{24}O_4S_2$: C, 55.78; H, 7.02. Found: C, 55.76; H, 7.05. ^{1}H NMR δ=3.13 (4H, t, J=6.8 Hz), 3.62 (4H, s), 3.63(8H, s), 3.69 (4H, t, J=6.8 Hz), 7.16 (3H, br s), and 7.46 (1H, s); ^{13}C NMR d=33.0 (2C), 69.9 (2C), 70.6 (2C), 70.7 (2C), 70.8 (2C), 127.4 (2C), 128.4, 128.9, and 137.1 (2C); MS *m/z*, 344 (M^+, 20), 168 (66), 154 (44), 153 (56), 136 (74), 135 (100), 134 (55), and 96 (46); IR ν: 2862, 1571, 1463, 1396, 1353, 1291, 1113, 1034, 777, and 685 cm^{-1}; UV λ^{MeOH}_{max}=217 nm (ε=10000), 252.6 (14000), 298.1 (1300), and 308.0 (1000)] and a 2:2-condensate (**3**) [colorless crystals, mp 70-71.5 °C, 20 mg, 7%. *Anal.* Calcd for $C_{32}H_{48}O_8S_4$: C, 55.78; H, 7.02. Found: C, 56.11; H, 7.10. MS *m/z*, 688 (M^+, 100), 212 (41), 195 (48), 194 (82), 169 (52), 168 (86), and 136 (43); ^{1}H NMR δ=3.11 (8H, t, J=6.8 Hz), 3.6-3.65 (24H, m), 3.67(8H, t, J=7.0 Hz), 7.12-7.20 (6H, m), and 7.34 (2H, br s); ^{13}C NMR δ=33.0 (4C), 69.9 (4C), 70.5 (4C), 70.6 (4C), 70.7 (4C), 126.8 (4C), 129.17 (2C), 129.24 (2C), and 137.2 (4C); IR ν: 2876, 1574, 1558, 1466, 1450, 1427, 1392, 1370, 1352, 1283, 1244, 1170, 1119, 1093, 1041, 1022, 948, 936, 909, 886, 834, 786, 769, and 677 cm^{-1}; UV $\lambda^{CHCl_3}_{max}$=255 nm (ε=20900), 298.2 (1800), and 308.8 (1300)].

Determination of Association Constants (*Ks*); The titrations were conducted by adding a crown ether solution (1.3 mol/L in CH_3CN) containing a progressive concentration of excess metal salt, using a 25 or 250 mL syringe, to the cuvette containing 2 mL of the crown ether solution (1.3 mol/L in CH_3CN). The solutions were homogenized by ultrasonic wave for 5 min. The spectrum was recorded after each addition as shown in Figure 1. The added equivalents of the cation were then plotted against the absorption intensity change at a certain wave length around the absorption peak on the spectrum (420-460 nm).[6] Even though the solvent takes part in the association interaction, the solvent concentration is virtually unaffected. The K_S of **1d**, **1e**, and **2** with Hg^{2+} were determined using ^{1}H NMR titration procedure.[7]

Transport Experiments; By the similar procedures as described in a previous paper,[4] transport experiments with standard solution (10 mL, aq I) of $HgCl_2$ (0.05 mmol) were done using a U-type cell consisted of $CHCl_3$ (20 mL) containing **1d** or **2** (0.05 mmol) and 5 M HCl (10 mL, aq II), at rt. Spectrophotometric determinations of metal ions before and after the transport via complexation with **1d** and **2** were carried out.

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Received, 24th March, 1997