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SYNTHESIS AND MERCUROPHILIC PROPERTIES OF ACYCLIC AND THIOLARIAT ETHERS HAVING A TROPONE PENDANT

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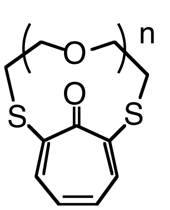
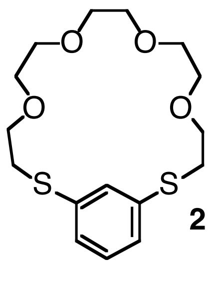
Abstract— Acyclic and thiolariat ether derivatives (**3** and **4**) having a tropone pendant were synthesized. Acyclic and thiolariat ether (**3**, **4a** and **4b**) were used as carriers for transport of Hg^{2+} through a chloroform liquid membrane. Thiolariat (**4c**) did not transport from source phase to receiving phase of Hg^{2+}, but extracted into chloroform layer. Effective Hg^{2+} extractability of **4c** was a result of the synergistic coordination of oxygen and sulfur atoms of the thiolariat ether.

Considerable attention has been devoted to the effective separation and recovery of heavy metal ions. In this respect, Bacon[1] has reported transport of heavy metal ions such as Hg^{2+} and Pb^{2+} through a liquid membrane, and Izatt[2] and Gokel[3] have investigated transport of metal cations by the crown and aza-crown ethers through a chloroform membrane. Recently, we have been interested in synthesizing dithio-crown ethers (**1**) having a troponoid pendant, since these molecules are excellent carriers of Hg^{2+} ion through a liquid membrane.[4] The efficiency of transport of Hg^{2+} with **1** was dependent on the cavity size of the crown ethers. The order of Hg^{2+} transport rate of **1** was **1d** > **1e** > **1b** > **1a** > **1c**. The relationship between the transport rate and the structures of its Hg^{2+} complex was confirmed by the X-Ray analyses of the $HgCl_2$ complexes of **1a**–**1d**;[5] there are two kinds of coordination modes, in which one is a side-on complex and another is a normal penetrated complex. The Hg^{2+} ions of **1a**–**c** are coordinated with both the tropone carbonyl group and the thioether sulfur atom to form a side-on complex, while the Hg^{2+} ion of **1d**-$HgCl_2$ is at the center of dithiocrown ring to form a normal penetrated complex.



1a (n=1)
1b (n=2)
1c (n=3)
1d (n=4)
1e (n=5)



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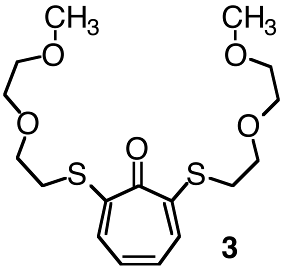

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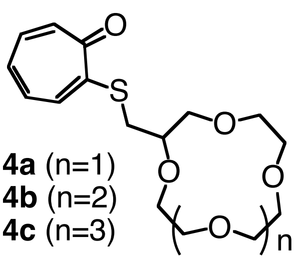


4a (n=1)
4b (n=2)
4c (n=3)

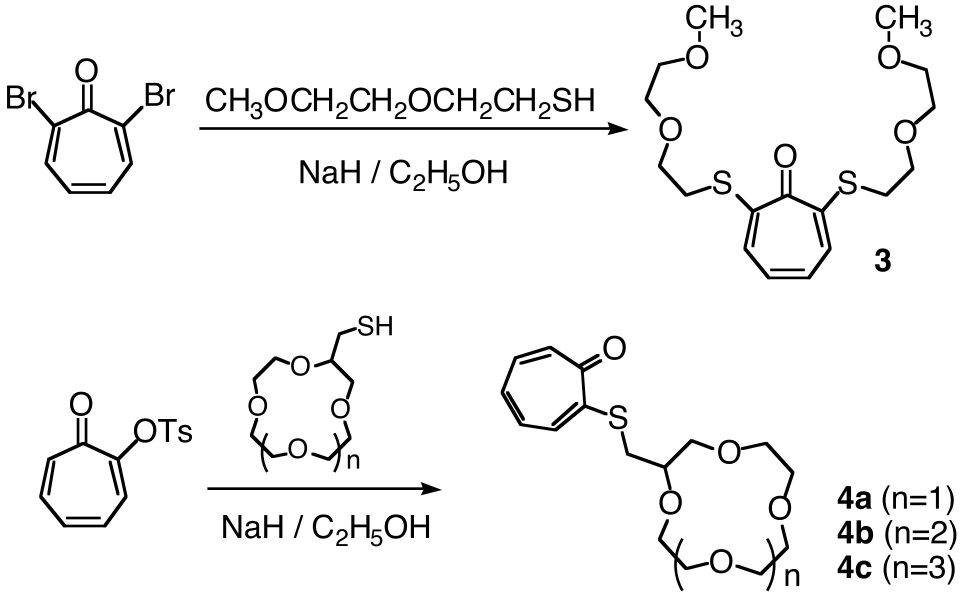
Dedicated to Professor Shô Itô on the occasion of his 77th birthday.

In order to elucidate the roles of the tropone part as a Hg^{2+} carrier, the corresponding benzenoid derivative (**2**) was sysnthesized.[6] The transport rate of **2** for Hg^{2+} is slower than that of **1d**, suggesting that the tropone part plays an important role in the liberation. Indeed, it is interesting to investigate the selectivity on the mercurophilicity of several troponoid ionophores having acyclic and thiolariat ether derivatives as well as the generality for Hg^{2+} ion.

As an approach to the manipulation of sulfur-containing troponoid ionophores, we now report the sysnthesis and complexation behavior of acyclic (**3**) and thioarmed crown ether (**4**) having a tropone pendant.

Synthesis of Troponoid Ionophores

At first, 2,7-dibromotropone was condensed with 2-mercaptoethyl methoxyethyl ether[7] mediated by NaH to give 1:2 condensate (**3**). Structure of **3** was clarified as depicted in Scheme 1 by NMR spectroscopy; in the ^1H NMR spectra, **3** had an A_2B_2 pattern of the aromatic protons, and their overlapped ^{13}C NMR signals showed it to be symmetrical. Next, thiolariat ether derivatives (**4**) were obtained by condensation from NaH-mediated mercaptomethyl crown ether[8] and 2-(*p*-toluenesulfonyloxy)tropone.



Scheme 1

Complex Formation with Mercury(II) Salt

^1H NMR spectral screening experiments of **3** and **4** suggested a complexation with metal ions (10 eq.). The complex formation of **3**, **4a**, and **4b** was 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 (Ni^{2+}, Fe^{3+}, Cu^{2+}, Cd^{2+}, Ag^+, and Hg^{2+}) showed no indication of ^1H NMR spectral changes in $CDCl_3$.

The ^1H NMR spectra of **4c**, however, changed by the complex formation of Hg^{2+} and Ag^+ although the selectivity of **4c** was lower than **1d**. Remarkable ^1H NMR spectral feature was observed in Figure 1. The intensities of the original (free host) signals decreased, and the intensities of new resonance peaks (the corresponding complex) at lower field region increased as Hg^{2+} concentration increased. The new signals are corresponding to the mercury complex. In respects of the chemical shift differences, $\Delta\delta$, between **4c** and its mercury complex, which were measured in $CDCl_3$ solution obtained by extraction from an aqueous mercury solution [^1H NMR ($CDCl_3$): δ=3.27 (1H, dd, J=12.6, 4.2 Hz), 3.49–3.88 (23H, m), 4.06 (1H, dd, J=8.6, 7.7 Hz), 6.94 (1H, dd, J=10.6, 9.0 Hz), 7.07 (1H, d, J=12.1 Hz), 7.09 (1H, dd, J=10.6, 9.6 Hz), 7.23 (1H, dd, J=12.1, 9.0 Hz), and 7.34 (1H, d, J=9.6 Hz), and ^{13}C NMR: δ=29.93, 67.94, 69.84, 69.90, 69.94, 69.96, 69.98, 70.01, 70.02, 70.07, 70.23, 71.08, 77.43, 128.27, 130.16, 132.79, 134.85, 136.25, 158.30, and 183.48], the complexation caused a dramatic change; e.g., the methylene carbon bearing the thioether group (Δδ=3.9 ppm). These result indicated that sulfur and oxygen atoms of the thiolariat crown ether coordinated with Hg^{2+} strongly.

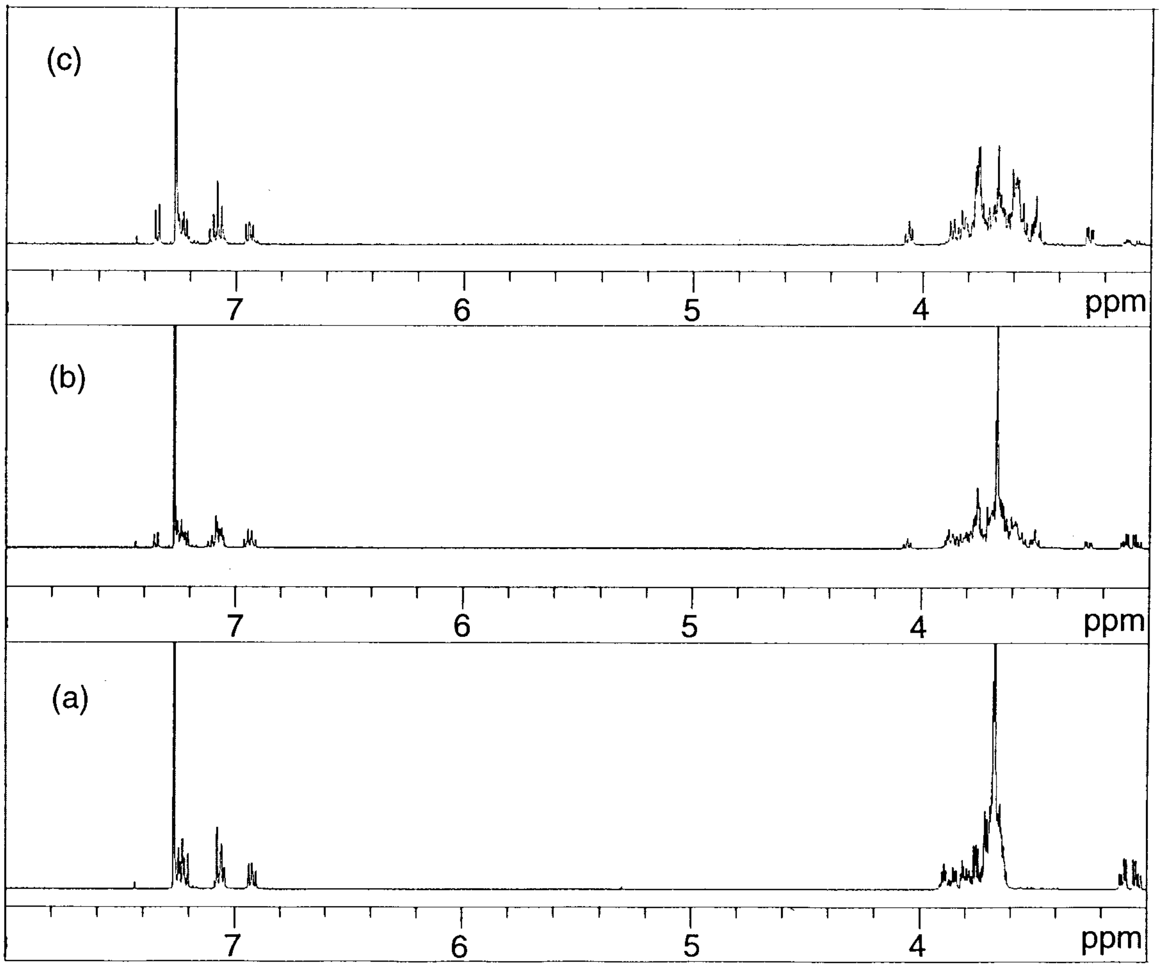


Figure 1. ^1H NMR Spectral changes of **4c** (5.0 mM) with and without $HgCl_2$ (a: 0 mM, b: 2.5 mM, c: 5.0 mM).

The affinities of the sulfur atom of troponoid ionophores toward Hg^{2+} ion were examined by solvent extraction experiment using a $CHCl_3$–water system. When the molar ratios of the extracted Hg^{2+} were compared with each other (Figure 2) in the series of **3** and **4**, **4c** showed the highest value, 1.00, and the others showed inferior figures, 0.29 for **3**, 0.30 for **4a**, and 0.50 for **4b**. The value of extracted molar formation among the homologues, **4c** was most effective in respects of extraction, and significant difference between **4c** and others was noticed. This should be attributable to an appropriate size of the cavity in **4c**. The value for the acyclic derivative, therefore, was smaller than that for **1d**.

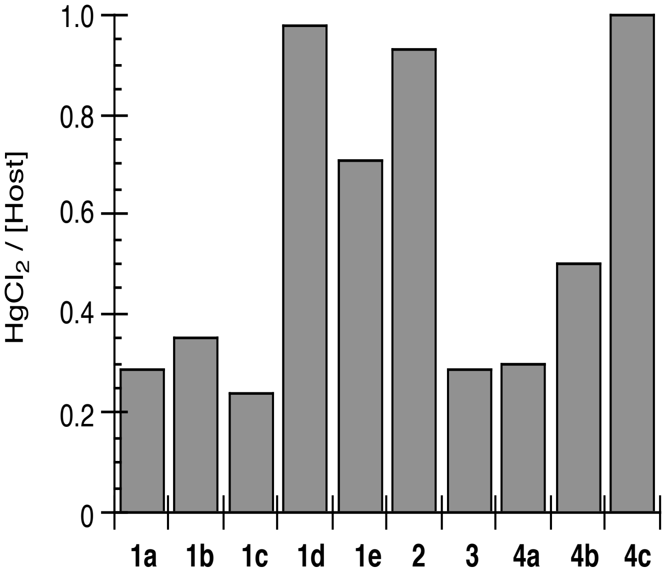


Figure 2. Relative ratio of extracted Hg^{2+} by **1**–**4**.

Transport of Mercury(II) Salt by Troponoid Ionophores

Transport experiments were performed using a liquid membrane system. When an aqueous solution of $HgCl_2$ (source phase) was brought into contact with a $CHCl_3$ solution of **3** or **4**, stirring with a magnetic bar at 25°C, the concentration of Hg^{2+} in the source phase decreased. The Hg^{2+} was transported to the $CHCl_3$ layer and could be extracted by aqueous 2 M HCl into the receiving phase. Figure 3 shows the results of transport experiments of Hg^{2+} with **3**. It is also noteworthy that the transport rate for **3** was slower than **1d** and the amount of the transported Hg^{2+} with **3** at 12 h was less 20% of that with **1d**. Thus, the crown part in the dithiocrown ether (**1d**) played an important role in the complexaion of Hg^{2+}.

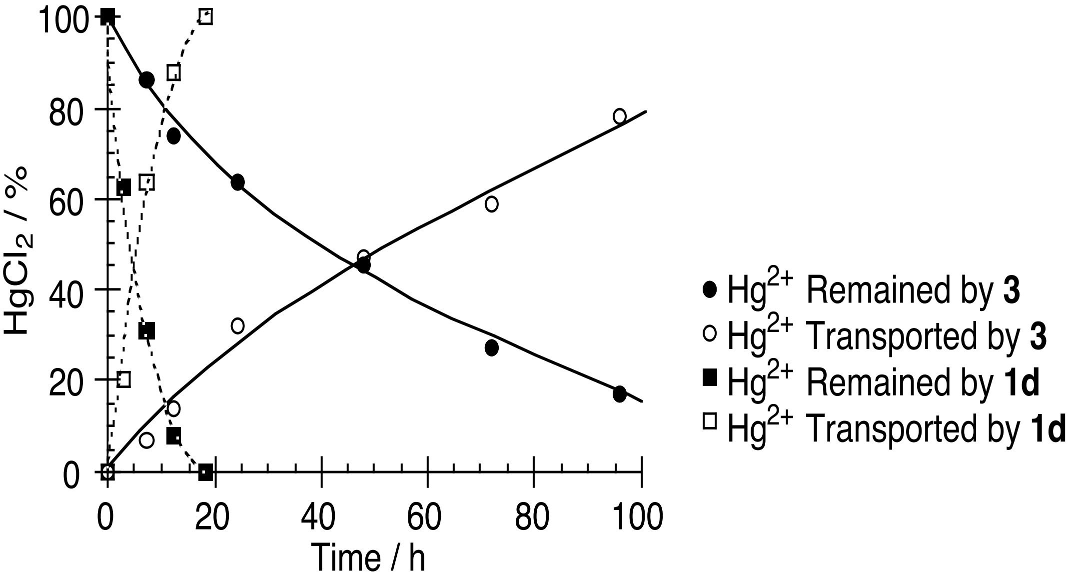


Figure 3. Transport of Hg^{2+} with **1d** and **3** using 2 M HCl

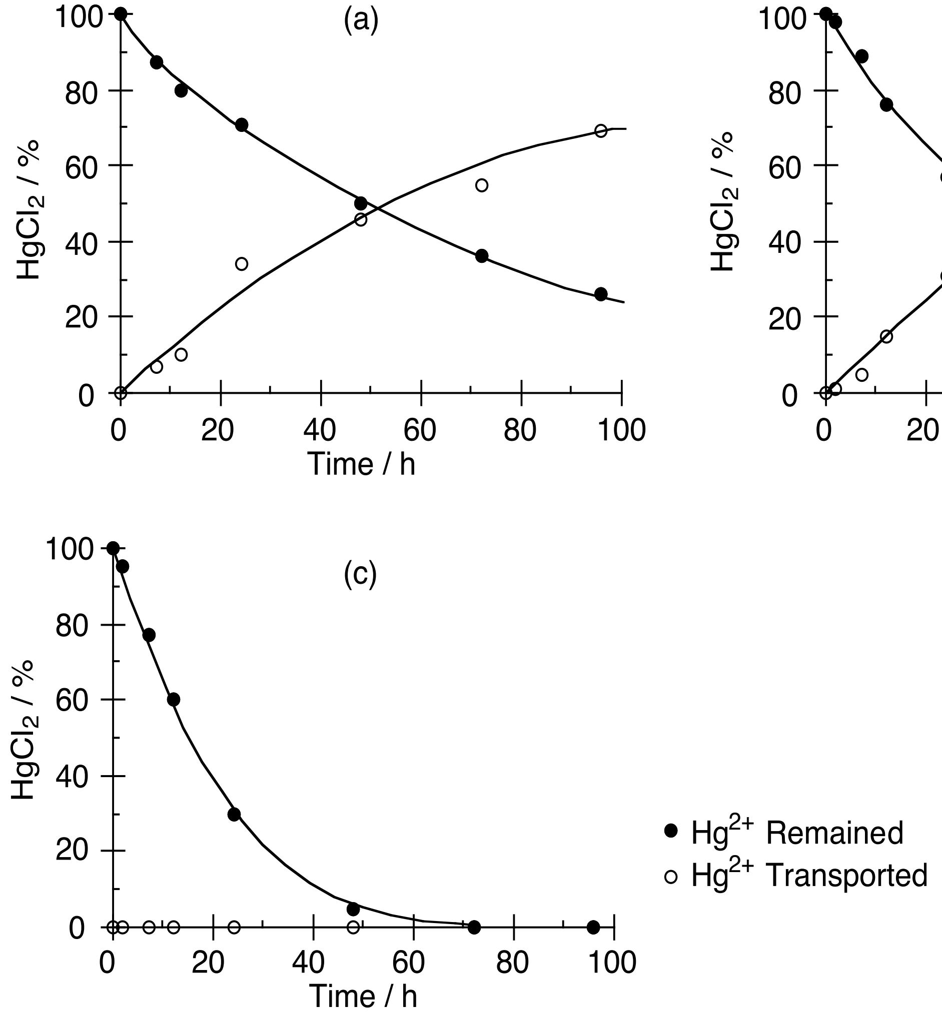


Figure 4. Transport of Hg^{2+} with (a) **4a**, (b) **4b**, and (c) **4c** using 2 M HCl.

As shown in Figure 4, in the case of thiolariat ethers, **4a** and **4b** were preferable mediators for transport of Hg^{2+}. However, **4c** did not transport Hg^{2+} into the receiving phase; **4c** only extracted Hg^{2+} from aqueous source phase into chloroform. It is quite obvious that the extraction of Hg^{2+} using **4c** from the aqueous source phase into the organic membrane occurred very rapidly. These results suggest that the high Hg^{2+} extractability of **4c** is a result of the synergistic coordination of oxygen and sulfur atoms of the thiolariat ether.[8]

In conclusion, troponoid ionophores (**3** and **4**) displayed a unique selectivity towards Hg^{2+}. Both troponoid acyclic ether (**3**) and lariat derivatives (**4a** and **4b**) were Hg^{2+} transport carriers but the transport rates were slower than that for troponoid dithiocrown ether (**1d**). While lariat 18-crown-6 (**4c**) formed complex with Hg^{2+}, acid treatment with 2 M HCl did not liberate Hg^{2+}. Since the tropone and thiolariat ether coordinate with Hg^{2+} strongly, the tropone and thiolariat ether parts could not release Hg^{2+} from the **4c**-HgCl$_2$ complex. These results also make it possible to design effective carriers for Hg^{2+} separation.

ACKNOWLEDGEMENT

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EXPERIMENTAL

The NMR spectra were measured on JEOL Lambda 400 or 600 Model spectrometer in CDCl$_3$; the chemical shifts are expressed in δ unit. The MS spectra were measured with JEOL 01SG-2 spectrometer. The IR spectra were recorded on a JASCO IR-A102 spectrophotometer with liquid films inserted between NaCl plates for oily materials. The UV spectra were measured using Hitachi U-3400 spectrophotometers. The stationary phase for the column chromatography was Wakogel C-300 and the elution solvents were mixtures of hexane and ethyl acetate.

Synthesis of Acyclic Troponoid Ionophore

To a refluxing mixture of toluene and EtOH (20 + 20 mL) were added a solution of 2,7-dibromotropone (106 mg, 0.4 mmol) in toluene and EtOH (5 + 5 mL) and a solution of 2-mercaptoethyl methoxyethyl ether (136 mg, 1.0 mmol) mediated by NaH (60%, 40 mg, 1.0 mmol) in EtOH (10 mL) through microfeeders in a 3 h period under N_2 atmosphere. After removing the solvent *in vacuo*, the residue was acidified with 2 M HCl and extracted with $CHCl_3$. Silica gel column chromatography of the organic fractions gave 1:2 condensate (**3**) [a yellow oil, 120 mg, 80%, ^{1}H NMR ($CDCl_3$) δ=3.13 (4H, t, J=7.1 Hz), 3.39 (6H, s), 3.55 (4H, m), 3.66 (4H, m), 3.78 (4H, t, J=7.1 Hz), 6.97–7.01 (2H, m), and 7.26–7.30 (2H, m); ^{13}C NMR δ=31.34 (2C), 59.10 (2C), 68.78 (2C), 70.48 (2C), 71.85 (2C), 128.08 (2C), 128.32 (2C), 150.51 (2C), and 178.77; IR (NaCl) ν 669, 702, 739, 771, 849, 909, 977, 1027, 1110, 1197, 1250, 1293, 1343, 1354, 1459, 1563, and 2870; UV (MeOH) λ=206 (13900), 237 (11900), 307 (15800), 357 (9200, sh), 376 (14000), and 401 (15800); HR(EI) MS: *m/z* 374.1219. Calcd for $C_{17}H_{26}O_5S_2$: 374.1222].

Synthesis of [[(Tropon-2-yl)thio]methyl] crown ethers

To a refluxing mixture of EtOH (10 mL) and toluene (10 mL) was added a solution of 2-(*p*-tolylsulfonyloxy)tropone (55 mg, 0.20 mmol) in toluene (10 mL) and a solution of mercaptomethyl crown ether (56 mg for 12-crown-4, 67 mg for 15-crown-5, 78 mg for 18-crown-6, 0.25 mmol) mediated by NaH (60%, 10 mg, 0.25 mmol) in EtOH (10 mL) for 1 h period by a microfeeder under N_2 atmosphere. Refluxing of the solution was continued for another 3 h. After removing the solvent in vacuo, the residue was acidified with 2 M HCl and extracted with $CHCl_3$. Silica gel column chromatography of the organic fractions gave the desired condensates (**4**).

4a: a yellow oil, 56 mg, 86%, ^{1}H NMR ($CDCl_3$) δ=2.96 (1H, dd, J=12.8, 4.5 Hz), 3.03 (1H, dd, J=12.8, 7.0 Hz), 3.55–3.92 (15H, m), 6.93 (1H, dd, J=11.0, 9.0 Hz), 7.05 (1H, d, J=11.4 Hz), 7.06 (1H, dd, J=11.0, 10.0 Hz), 7.21 (1H, d, J=10.0 Hz), and 7.23 (1H, dd, J=11.4, 9.0 Hz); ^{13}C NMR δ=34.01, 70.36, 70.37, 70.45, 70.62, 71.00, 71.05, 72.66, 77.67, 127.60, 129.97, 132.54, 134.68, 136.16, 158.97, and 183.42; IR (NaCl) ν 680, 776, 916, 986, 1096, 1128, 1250, 1270, 1293, 1358, 1387, 1465, 1561, 1618, 2858, and 2914; UV (MeOH) λ=204 (14100), 226 (13100), 253 (13600), 282 (6500, sh), 326 (7700, sh), 344 (10200), 372 (9600), and 388 (8300, sh); HR (FAB) MS: *m/z* 327.1270, Calcd for $C_{16}H_{22}O_5S$+H: 327.12662.

4b: a yellow oil, 61 mg, 82%, ^{1}H NMR ($CDCl_3$) δ=2.99 (1H, dd, J=13.2, 7.3 Hz), 3.01 (1H, dd, J=13.2, 4.5 Hz), 3.60–3.90 (19H, m), 6.92 (1H, dd, J=10.0, 8.7 Hz), 7.05 (1H, dd, J=10.0, 9.7 Hz), 7.06 (1H, d, J=11.7 Hz), 7.22 (1H, dd, J=11.7, 8.7 Hz), and 7.23 (1H, d, J=9.7 Hz); ^{13}C NMR δ=34.55, 70.40, 70.51, 70.54, 70.60, 70.80, 70.81, 70.91, 71.18, 72.53, 77.96, 127.58, 129.80, 132.58, 134.66, 136.08, 159.32, and 183.52; IR (NaCl) ν 986, 1101, 1250, 1293, 1364, 1467, 1563, 1618, and 2868; UV (MeOH) λ=205 (14800), 226 (14000), 253 (14000), 282 (6700, sh), 327 (7900, sh), 344 (10300), 373 (9600), and 390 (8100, sh); HR (EI) MS: *m/z* 370.1451, Calcd for $C_{18}H_{26}O_6S$: 370.1450

4c: a yellow oil, 66 mg, 80%, ^{1}H NMR ($CDCl_3$) δ=3.04 (1H, dd, J=13.2, 7.0 Hz), 3.10 (1H, dd, J=13.2, 5.0 Hz), 3.58–3.93 (23H, m), 6.93 (1H, dd, J=10.0, 8.7 Hz), 7.06 (1H, d, J=11.7 Hz), 7.07 (1H, dd, J=10.0, 9.4 Hz), 7.22 (1H, dd, J=11.7, 8.7 Hz), and 7.24 (1H, d, J=9.4 Hz); ^{13}C NMR δ=33.83, 70.07, 70.57, 70.61 (3C), 70.67, 70.77, 70.86 (2C), 70.91, 72.43, 77.31, 127.54, 129.77, 132.55, 134.59, 136.07, 159.21, and 183.43; IR (NaCl) ν 949, 986, 1107, 1250, 1293, 1351, 1468, 1565, 1618, and 2870; UV (MeOH) λ=207 (15500), 226 (14700), 253 (14300), 283 (6900, sh), 328 (8100, sh), 344 (10400), 373 (9600), and 390 (8000, sh); HR (EI) MS: *m/z* 414.1711, Calcd for $C_{20}H_{30}O_7S$: 414.1712.

NMR Spectral Screening Experiments

The affinities of troponoid ionophores toward various metal salts were examined by NMR spectral screening using a $CDCl_3$-H_2O biphasic system. The standard aqueous solutions (1 mL) containing metal salt (50 μmol, LiCl, NaCl, $MgCl_2$, $CaCl_2$, $BaCl_2$, $NiCl_2$, $FeCl_3$, $CuCl_2$, $CdCl_2$, $AgNO_3$, $HgCl_2$) were shaken with $CDCl_3$ solution (1 mL) of **3** and **4** (each 5 μmol) for 5 min. The $CDCl_3$ solutions were measured by NMR spectroscopy.

Solvent Extraction of Metal Ions

A standard aqueous solution (5 mL) containing $HgCl_2$ (20 μmol) was shaken with $CHCl_3$ solution (5 mL) of **3** and **4** (each 5 μmol) for 5 min. Aqueous layer was titrated photometrically (490 or 610 nm) in phosphate buffer (10 cm^3, pH =6.0) with added 1,5-diphenylthiocarbazone solution (5 mL, 0.0006%).

Transport Experiment

The apperatus is same to one used in the previous study.[3] The metal ions dissolved in water (50 μmol, 10 mL, Aq I) and 2 M HCl (10 mL, Aq II) connected with 20 mL of $CHCl_3$ layer containing **3** or **4** (50 μmol) and stirred with a magnetic bar. Occasionally, aliquots of Aq I and Aq II were taken for the UV spectrophotometry.

REFERENCES AND NOTES

1. E. Bacon and L. Jung, *J. Membrane Sci.*, 1985, **24**, 185; E. Bacon and M. Kirch, *ibid.*, 1987, **32**, 159.
2. R. M. Izatt, G. A. Clark, and J. J. Christensen, *ibid.*, 1985, **24**, 1; R. M. Izatt, M. B. Jones, J. D. Lamb, J. S. Bradshaw, and J. J. Christensen, *ibid.*, 1986, **26**, 241; R. M. Izatt, R. L. Bruening, G. A. Clark, J. D. Lamb, and J. J. Christensen, *ibid.*, 1986, **28**, 77.
3. J. C. Hernandez, J. E. Trafton, and G. W. Gokel, *Tetrahedron Lett.*, 1991, **32**, 6269.

4. A. Mori, K. Kubo, and H. Takeshita, *Coordination Chem. Rev.*, 1996, **148**, 71; N. Kato, K. Kubo, A. Mori, and H. Takeshita, *Heterocycles*, 1995, **41**, 1901; A. Mori, K. Kubo, and H. Takeshita, *Heterocycles,* 1997, **46**, 509; K. Kubo, A. Mori, N. Kato, and H. Takeshita, *Heterocycles*, 1998, **49**, 385.
5. K. Kubo, A. Mori, N. Kato, and H. Takeshita, *Acta Cryst.*, 1996, **C52**, 1656; A. Mori, K. Kubo, N. Kato, H. Takeshita, M. Shiono, and N. Achiwa, *Heterocycles*, 1998, **47**, 149; K. Kubo, N. Kato, A. Mori, and H. Takeshita, *ibid.*, 2000, **53**, 535.
6. A. Mori, K. Kubo, and H. Takeshita*, Heterocycles,* 1997, **46**, 509
7. T. Nabeshima, T. Takahashi, T. Hanami, A. Kikuchi, T. Kawabe, and Y. Yano, *J. Org. Chem.*, 1998, **63**, 3802.
8. T. Nabeshima, N. Tsukada, K. Nishijima, H. Ohshiro, and Y. Yano, *J. Org. Chem.*, 1996, **61**, 4342.