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SYNTHESIS AND MERCUROPHILIC PROPERTIES OF 5,8,14,17-TETRAOXA-2,11,20-TRITHIABICYCLO[19.4.1]HEXACOSA-21,23,25-TRIEN-26-ONE

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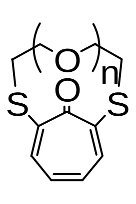
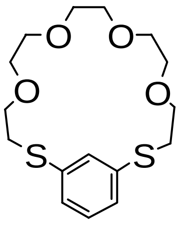
Abstract—Base-mediated condensation reaction of 2,7-dibromotropone with 3,6,12,15-tetraoxa-9-thiaheptadecane-1,17-dithiol afforded 1:1 and 2:2 condensates (**4** and **5**). Troponoid trithiocrown ether (**4**) was used as a carrier through a chloroform liquid membrane. However, the guest selectivity of **4** was lower than that of the corresponding dithiocrown ether derivative (**1e**).

The development of selective ion recognition systems has been of much concern because of a solution to environmental pollution. Macrocyclic ligands are of great interest because they serve as models for metal ion transport through a membrane. [1] We are currently interested in synthesizing metal ion-capturing ionophores having a tropone ring (**1**).[2] Particularly noteworthy are their reversible complexation behaviors with mercury(II) salts to enable transport of mercury(II) ions through a liquid membrane. As a matter of efficiency in transport of Hg^{2+} ion, transport rates of the troponoid dithiocrown derivatives (**1**) depended 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[3,4] of the $HgCl_2$ complexes of **1a-d**; there are two kinds of coordination modes, one of which is a side-on complex[3] and another is a normal penetrated one.[4] The Hg^{2+} ions of **1a-c** are coordinated with both the tropone carbonyl group and one of the thioether sulfur atoms to form a side-on complex, whereas the Hg^{2+} ion of **1d**-$HgCl_2$ is at the center of the thiocrown



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



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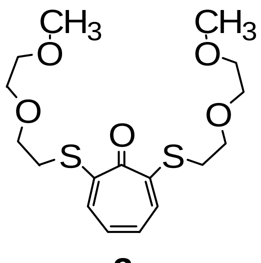

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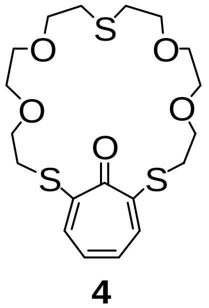

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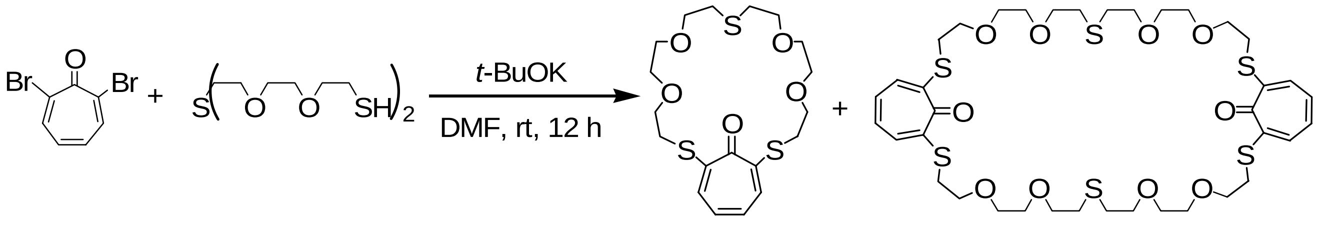
Dedicated to Professor Leo A. Paquette on the occasion of his 70th birthday.

ring to form a normal penetrated complex. The transport rate of **1d** for Hg^{2+} is faster than that of the corresponding benzenoid (**2**),[5] suggesting that the tropone part participates in the liberation of Hg^{2+}. On the other hand, the transport rate of troponoid acyclic ether (**3**)[6] was slower than that for troponoid dithiocrown ether (**1d**), suggesting that the dithiocrown ether part also plays an important role in the complexation. Indeed, it is interesting to investigate the selectivity on the mercurophilicity of several troponoid ionophores. As an approach to the manipulation of sulfur-containing troponoid ionophores, we now report the synthesis and complexation behavior of trithiocrown ether (**4**) having a tropone pendant.

At first, 2,7-dibromotropone was condensed with 3,6,12,15-tetraoxa-9-thiaheptadecane-1,17-dithiol mediated by *t*-BuOK to give 1:1 and 2:2 condensates (**4** and **5**). Structures of **4** and **5** were clarified as depicted in Scheme 1 by NMR spectroscopy and FAB MS spectrometry.[7]



4 (62%)

5 (24%)

Scheme 1

^1H NMR spectral screening experiments of **1e** and **4** suggested a complexation with metal ions (10 eq.). The complex formation of **1e** and **4** was examined with various metal salts, i.e., alkali metal ions (LiCl, NaCl, KCl, RbCl, and CsCl), alkaline earth metals ($MgCl_2$, $CaCl_2$, and Ba Cl_2), and some transition metal ions ($NiCl_2$, $CuCl_2$, and $CdCl_2$) showed no ^1H NMR spectral changes in $CDCl_3$. The ^1H NMR spectra of **4**, however, changed by the complex formation of $HgCl_2$ and $AgNO_3$ although the selectivity of **4** was lower than **1**. Remarkable ^1H NMR spectral feature was observed in Figure 1.

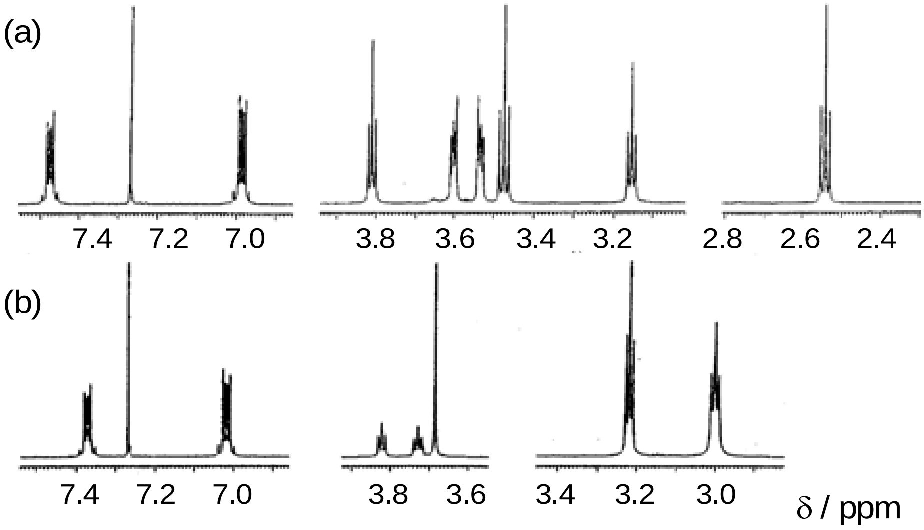


Figure 1. ^1H NMR spectrum of (a) **4** (6.0 mM) and (b) **4** (6.0 mM) in the presence of $HgC1_2$ (18 mM).

When $HgCl_2$ was added, the original proton signals of **4** changed depending on the guest concentrations. The ^{1}H NMR spectrum of the mercury complex is as follows: ^{1}H NMR ($CDCl_3$): δ=3.00 (4H, t, J=5.7 Hz), 3.22 (4H, t, J=5.7 Hz), 3.69 (8H, s), 3.73 (4H, t, J=5.7 Hz), 3.82 (4H, t, J=5.7 Hz), 7.00-7.04 (2H, m), and 7.35-7.39 (2H, m). The methylene proton signals bearing the trithiocrown ether group shifted downfield and the aromatic proton signals shifted upfield or downfield. The spectral patterns are similar to those of **1d**, **1e**,[2] and 23-dicyanomethylene-5,8,11,14,17-pentaoxa-2,20-dithiabicyclo[19.4.1]-hexacosa-1(26),21,24-triene.[8] This result means that the Hg^{2+} ion of **4**-$HgCl_2$ is at the center of the thiocrown ring to form a normal penetrated complex in pentagonal bipyramidal coordination.

The extraction experiment[9] of the troponoid ionophores toward $HgCl_2$ was examined using a $CHC1_3$-water system. The molar ratio of the extracted Hg^{2+} with **4** is 0.23, that is smaller than **1e** (0.30). Further transport experiments[10] were performed using a liquid membrane system. When an aqueous solution of $HgCl_2$ (source phase) was brought into contact with a $CHC1_3$ solution of **1e** 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 5 M HCl into the receiving phase. Figure 2 shows the results of transport experiments of Hg^{2+} with **1e** and **4** . It is also noteworthy that the transport rate for **4** was slower than **1e**. These results means that the stability of **4**-$HgCl_2$ complex in pentagonal bipyramidal coordination is lower than that of **1e**. The additional sulfur atom of **4** inhibited the complexation with Hg^{2+}. Thus, the crown ether part in the dithiocrown ether (**1e**) played an important role in the complexation of Hg^{2+}.

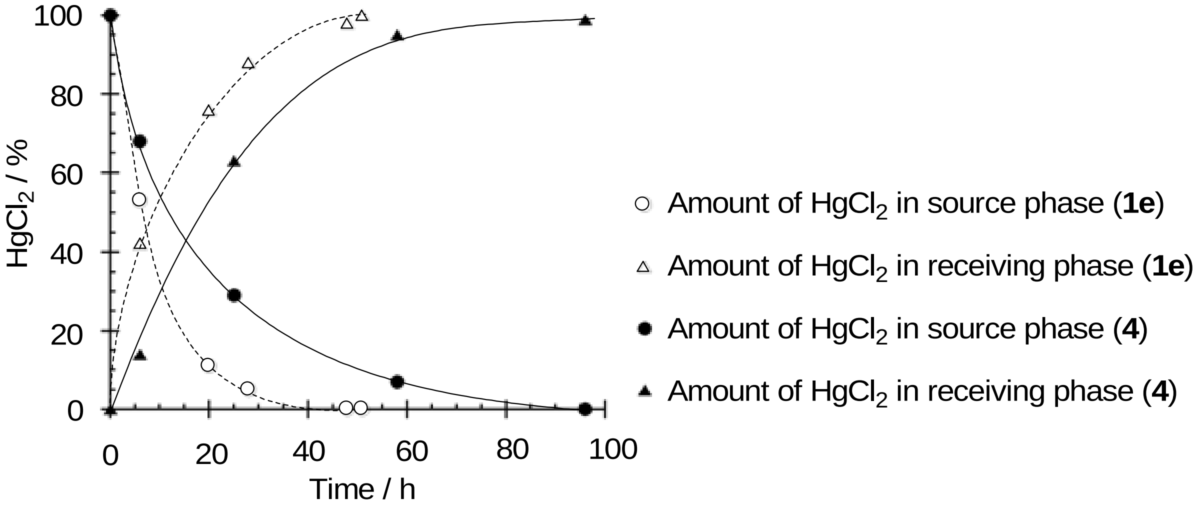


Figure 2. Transport of Hg^{2+} with **1e** and **4** using 5 M HCl.

In conclusion, a new carrier (**4**) was synthesized. But the extractability and transport rate for **4** were slower than those for the corresponding troponoid dithiocrown ether (**1e**). This result makes it possible to design more effective carriers for Hg^{2+} separation.

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7. Synthetic details and physical properties will be reported elsewhere. **4**: yellow oil, ^{1}H NMR (270 MHz, $CDCl_3$) δ=2.52 (4H, t, J=6.6 Hz), 3.14 (4H, t, J=5.9 Hz), 3.46 (4H, t, J=6.6 Hz), 3.50-3.60 (8H, m), 3.79 (4H, t, J=5.9 Hz), 6.92-7.02 (2H, m), and 7.41-7.51 (2H, m). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ=31.7 (2C), 32.0 (2C), 69.9 (2C), 70.6 (2C), 70.8 (2C), 128.3 (2C), 129.3 (2C), 150.1 (2C), and 179.1. HR FAB MS. Found: 433.1175. Calcd for $C_{19}H_{28}O_5S_3$: 433.1177. **5**: yellow crystals (EtOAc-hexane), 87-88 °C, ^{1}H NMR (270 MHz, $CDCl_3$) δ=2.77 (8H, t, J=6.6 Hz), 3.09 (8H, t, J=5.9 Hz), 3.60-3.66 (16H, m), 3.67 (8H, t, J=6.6 Hz), 3.77 (8H, t, J=6.6 Hz), 6.96-7.00 (4H, m), and 7.23-7.27 (4H, m). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ=31.6 (4C), 31.9 (4C), 68.8 (4C), 70.3 (4C), 70.6 (4C), 128.2 (4C), 128.4 (4C), 150.5 (4C), and 178.7 (2C). HR FAB MS. Found: 865.2284. Calcd for $C_{38}H_{56}O_{10}S_6$: 865.2276.
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9. A standard aqueous solution (10 mL) containing $HgC1_2$ (13.6 mg, 50 μmol) was shaken with $CHC1_3$ solution (10 mL) of **1e** and **4** (each 50 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%).
10. The apparatus is the same to one used in the previous study.[2] The metal ions dissolved in water (50 μmol, 10 mL, Aq. I) and 5 M HCl solution (10 mL, Aq. II) is connected with 20 mL of $CHCl_3$ layer containing **1e** and **4** (50 μmol) and stirred with a magnetic bar. Occasionally, aliquots of Aq I and Aq II were taken for the measurement of UV spectrophotometry.