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SYNTHESIS AND MERCUROPHILIC PROPERTIES OF DITHIOCROWN ETHERS HAVING AN AZULENE PENDANT†

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Abstract – Dithiocrown ether derivatives (**3**) having an azulene pendant were synthesized by regioselective reaction of 8,8-dicyanoheptafulvene derivatives with malononitrile in the presence of sodium ethoxide to examine their extraction and transport of Hg(II) ion through a liquid membrane. The transport was driven by acidic conditions and was capable of moving metal cations ‘up-hill’. Thus, it was possible to follow the transport of Hg(II) ion from the aqueous source phase to the organic layer and from the organic layer to the receiving phase. The carrier (**3**) displayed remarkable selectivity for Hg(II) ion.

Considerable attention has been devoted to the effective separation and recovery of heavy metal ions. The development of selective ion recognition systems has been of much concern because of a solution to environmental pollution. Liquid membrane methods are useful for assessing the partitioning of metals into and out of organic phases and are of considerable importance in medicine, water purification, and metallurgy.[1] A liquid membrane, which consists of an organic solvent system placed at the bottom of a U-tube, has been widely used in order to study ion transport from one water compartment to the other, a process requiring, of course, passage through the chloroform barrier. On the other hand, macrocyclic ligands are of great interest both because they are able to impose unusual coordination numbers and geometries on metal ions and because they serve as models for metal ion transport thorough a membrane.

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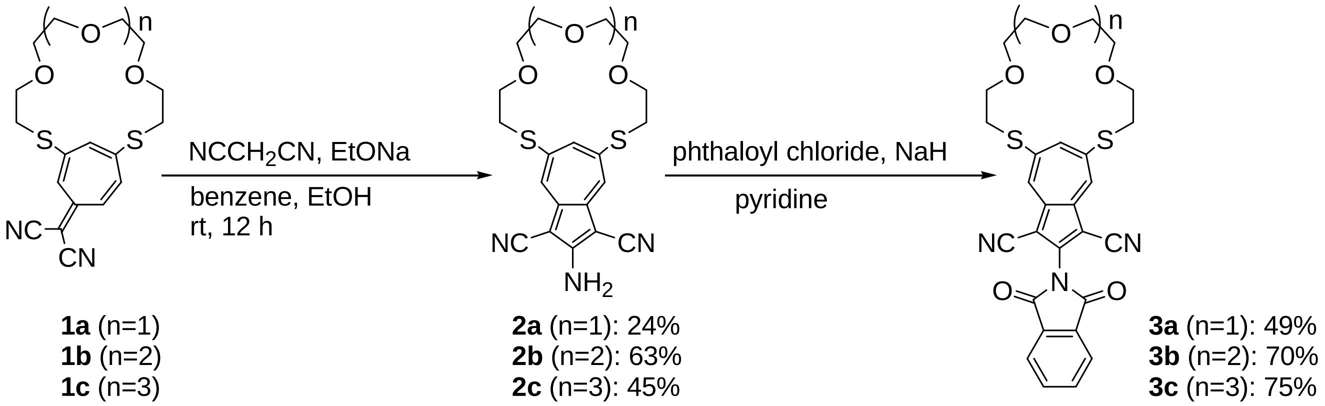
†Dedicated to Professor Dr. Ryoji Noyori on the occasion of his 70th birthday.

Bacon has reported transport of heavy metal ions such as Hg(II) and Pb(II) ions through a liquid membrane[2,3] and Izatt and Gokel have investigated transport of metal cations by the crown and aza-crown ethers through a chloroform membrane.[4-6] Costero *et al.* have been reported the transport of Hg(II) by bis-cyclic crown ether derived from biphenyl through a liquid membrane.[7] Recently, we have been interested in synthesizing dithio-crown ethers having a tropone[1,8-10] and 8,8-dicyanoheptafulvene pendant (**1**),[11] since these molecules are excellent carriers of Hg(II) ion through a liquid membrane. The efficiency of transport rate of the dithiocrown ethers was dependent on the cavity size of the crown ethers. The transport rate of **1c** was fastest in the crown ether derivatives under the same conditions. Furthermore it was ascertained by the X-ray analyses of $HgCl_2$ complexes[12,13] that the transport rate was largely dependent on the structures of its Hg(II) ion complex. The Hg(II) ion of **1c**-$HgCl_2$ exists in a pentagonal bipyramidal coordination with five oxygen atoms of the dithiocrown ring and two chloride anions to form a normal penetrated complex. In this paper, we describe synthesis and properties of dithiocrown ether derivatives (**3**) having an azulene pendant that serves as a new transporting agent of Hg(II) ion through a liquid membrane.

A mixture of dithiocrown ethers with 8,8-dicyanoheptafulvene (**1**) and malononitrile was stirred in the presence of sodium ethoxide to give a single red-colored crystalline azulene derivative (**2**). The symmetrical structures of azulene derivatives were clarified by NMR spectroscopy as depicted in Scheme 1; in the ^{1}H NMR spectra all of these **2a**-**c** had two seven-membered ring aromatic signals [7.78 (1H, t, *J*=1.5 Hz) and 7.87 (2H, d, *J* =1.5 Hz) for **2a**, 7.51 (1H, t, *J* =1.3 Hz) and 7.57 (2H, d, *J* =1.3 Hz) for **2b**, 7.61 (1H, t, *J* =1.5 Hz) and 7.78 (2H, d, *J* =1.5 Hz) for **2c**], and the number of the ^{13}C NMR signals.[14]



Scheme 1

The structure[15] of **2c** was also checked by X-ray crystallographic analysis as shown in Figure 1. A single crystal of **2c** was obtained by prolonged standing at room temperature to remove off $CHCl_3$ solvent. The color of the complex obtained was dark red. The azulene ring is nearly planar; the respective deviations of each atom from the least squares plane A defined by C1– C10 atoms are -0.011(3), 0,037(3), 0.030(3), -0.009(4), -0.058(3), -0.015(3), 0.064(3), 0.029(3), -0.050(3), and -0.027(4) Å. The azulene plane A makes an angle of 69° with the crown ether ring defined by atoms S1, O2-O5, S2. The conformation of the ethereal moiety is S1(*t*)C13(*g*)C14(*t*)O1(*t*)C15(*g*)C16(*t*)O2(*t*)C17(*g*)C18(*t*)O3(*t*)C19(*g*)C20(*g*)O4(*t*) C21(*g*)C22(*g*)O5(*t*)C23(*t*)C24(*g*)S2, where *t* and *g* denote trans and gauche forms, respectively.

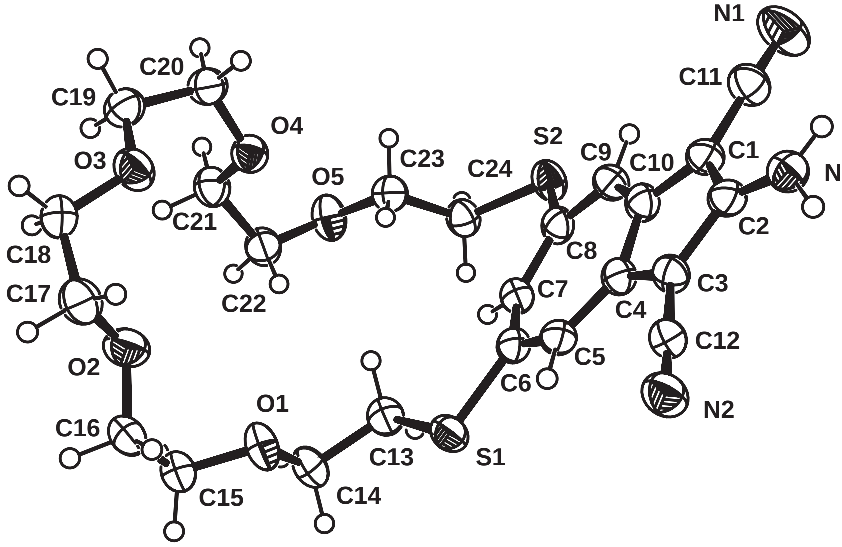


Figure 1. An ORTEP drawing of **2c** showing 50% probability displacement ellipsoids.

The reaction of **2a**-**c** with phthalolyl chloride and sodium hydride furnished the phthalimide derivatives (**3a**-**c**). The structures of **3a**-**c** were ascertained by NMR and MS spectral data.[16] ^{1}H NMR spectral screening experiments of **3** (5.0 x 10^{-5} mol dm^{-3}) suggested a complexation with various metal salts (1.0 x 10^{-2} mol dm^{-3}). These kinds of metal salts (LiSCN, NaSCN, $Mg(SCN)_2$, $Ca(SCN)_2$, $Ba(SCN)_2$, $Zn(SCN)_2$, $Co(SCN)_2$, $NiCl_2$, $CuCl_2$, $AgNO_3$, and CdI_2) revealed no indication of NMR spectral changes, but $HgCl_2$ showed a spectral change. This result suggests that **3** has an observable binding ability with Hg(II) ion.

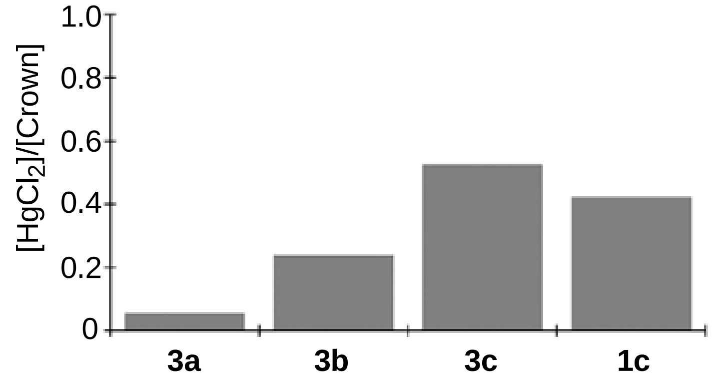


Figure 2. Molar ratio of Hg(II) extraction with **1c** and **3**.

The extraction experiment of the dithiocrown ethers toward $HgCl_2$ was examined using a $CHCl_3$-water system. The molar ratios of the Hg(II) ion extracted with **3** are 0.06 for **3a**, 0.24 for **3b**, and 0.53 for **3c**, respectively. The extraction amount of Hg(II) ion with **3c** is larger than that (0.42) of **1c** in the similar conditions. This means that the dithiocrown ether with an azulene pendant had an excellent extraction ability of Hg(II) ion than that with 8,8-dicyanoheptafulvene. The electron density of hetero atoms of crown ethers should be responsible to the extraction of Hg(II) ion. When the electron density of the sulfur atoms is compared between heptafulvenes **1** and azulenes **3**, the former has poorer electron density than the latter because the calculated (PM3) dipole moment of 8,8-dicyanoheptafulvene (6.47 D) is larger than 2-phthaloylimino-1,3-dicyanoazulene (2.85 D).

Transport experiments were performed using a liquid membrane system.[17] The Hg(II) ion concentrations in the aqueous compartments were monitored as a function of time by means of the colorimetric method. No transport of Hg(II) ion through the chloroform was observed unless a carrier was used. Hg(II) ion transport with **3a-c** was promoted by the counterflow of protons from the receiving to the source phase, although proton concentration was not quantitatively investigated. When an aqueous solution of $HgCl_2$ (source phase) was brought into contact with a $CHCl_3$ solution of **1** or **3**, stirring with a magnetic bar, the concentration of Hg(II) ion in the source phase decreased. The Hg(II) ion was transported to the $CHCl_3$ layer and could be extracted by aqueous 2 M HCl into the receiving phase.

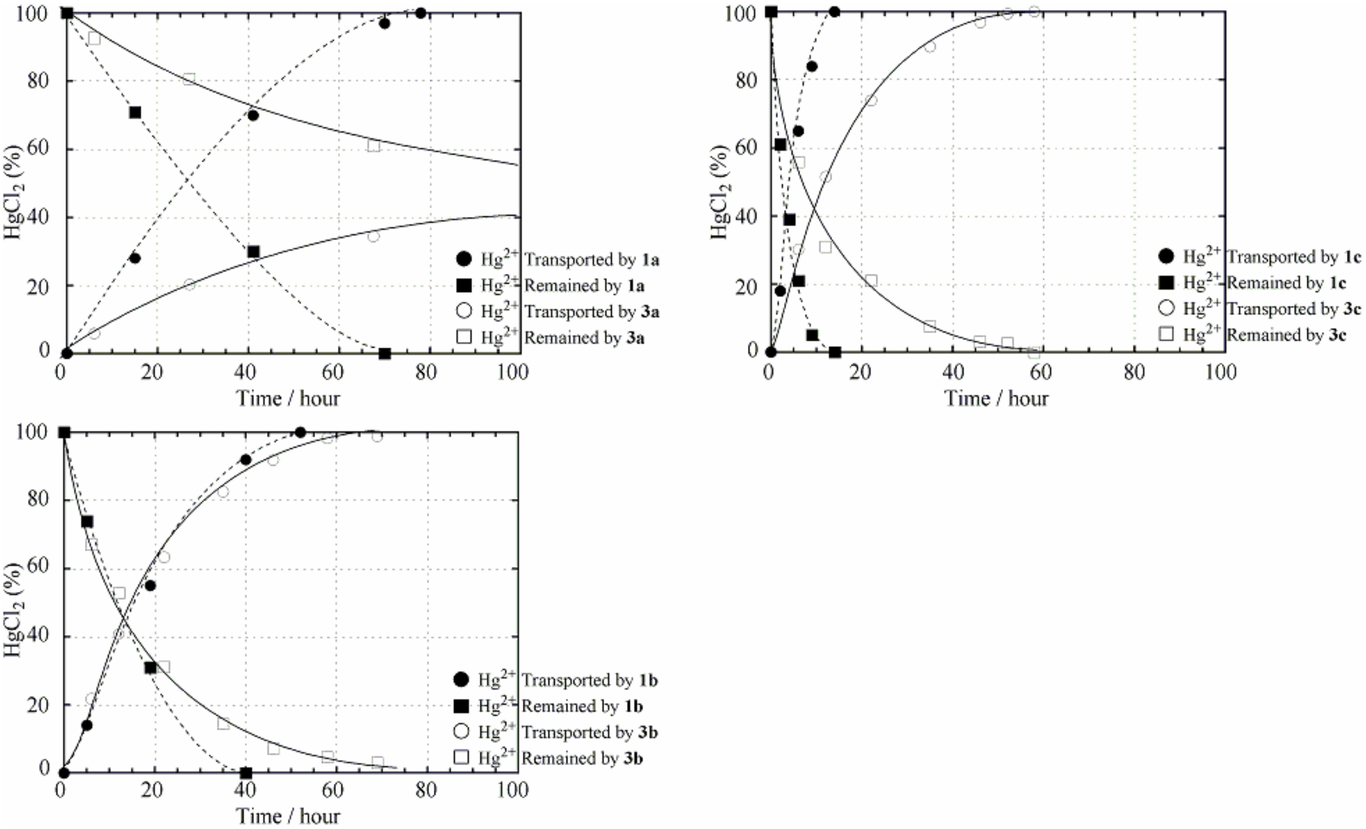


Figure 3. Transport of Hg(II) with **1** and **3** using 2 M HCl.

Figure 3 shows the results of transport experiments of Hg(II) ion with **1** and **3**. The order of Hg(II) ion transport rate is **3c** > **3b** > **3a** and the transport rate for **3** was slower than **1**. It is worthy of note that the Hg(II) ion transport rates are not correlated with the extraction experiment data. It is reasonable that the extraction process of Hg(II) ion into the $CHCl_3$ layer is faster than the release process to the receiving phase. Then, the latter process is the rate-determining process. The protonation of the aromatic part is responsible for the ready release of Hg(II) ion by generating a 6π-cationic system with the seven-membered ring to cause Coulomb repulsion with the complexed Hg(II) ion. Therefore, since in the azulene derivatives the generation of a 6π-cationic system might be less favored than 8,8-dicyanofulvenes in acidic conditions, azulenes **3** are less effective Hg(II) ion transport carriers. Moreover, in transport experiment with **3c**, Cu(II), Zn(II), Ni(II), and Ag(I) ions were not transported under the same conditions. In conclusion, a new carrier was synthesized. The dithiocrown ethers having an azulene pendant were selective and effective for Hg(II) ion transport through a liquid membrane. The extractability for azulene derivative (**3c**) was higher than that for the corresponding 8,8-dicyanoheptafulvene derivative (**1c**). But the Hg(II) ion transport rate for **3c** was slower than that for **1c**. The result of Hg(II) ion extractability was not parallel to the result of the transport. Thus, the large dipole moment of 8,8-dicyanoheptafulvene and tropone would play an important role in Hg(II) ion transport through a liquid membrane.

REFERENCES AND NOTES

1. A. Mori, K. Kubo, and H. Takeshita, *Coord. Chem. Rev.*, 1996, **148**, 71.
2. E. Bacon and M. Kirch, *J. Membrane Sci.*, 1985, **24**, 185.
3. E. Bacon and M. Kirch, *J. Membrane Sci.*, 1987, **32**, 159.
4. R. M. Izatt, M. B. Jones, J. D. Lamb, J. S. Bradshaw, and J. J. Christensen, *J. Membrane Sci.*, 1986, **26**, 241.
5. R. M. Izatt, R. L. Bruening, G. A. Clark, J. D. Lamb, and J. J. Christensen, *J. Membrane Sci.*, 1986, **28**, 77.
6. J. C. Hernandez, J. E. Trafton, and G. W. Gokel, *Tetrahedron Lett.*, 1991, **32**, 6269.
7. A. M. Costero, C. Andreu, E. Monrabal, A. Tortajada, L. E. Ochando, and J. M. Amigo, *Tetrahedron*, 1996, **52**, 12499.
8. H. Takeshita, B. Z. Yin, K. Kubo, and A. Mori, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 3451.
9. K. Kubo, N. Kato, A. Mori, and H. Takeshita, *Heterocycles*, 2000, **53**, 535.
10. K. Kubo, A. Mori, and T. Nishimura, *Heterocycles*, 2004, **62**, 149.
11. A. Mori, K. Kubo, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 1094.
12. K. Kubo, A. Mori, N. Kato, and H. Takeshita, *Heterocycles*, 1998, **49**, 385.
13. K. Kubo, N. Kato, A. Mori, and H. Takeshita, *Acta Cryst.*, 2000, **C56**, 644.
14. The synthetic details and physical properties of **2** will be reported elsewhere. **2c**: red crystals, mp 177-179 ˚C. ^{1}H NMR ($CDCl_3$) δ = 3.32 (4H, t, *J*=6.2 Hz), 3.62 (8H, s), 3.64-3.72 (8H, m), 3.84 (4H, t, *J*=6.2 Hz), 6.05 (2H, s), 7.61 (1H, t, *J*=1.5 Hz), and 7.78 (2H, d, *J*=1.5 Hz). ^{13}C-NMR ($CDCl_3$) δ = 34.15, 69.50, 70.58, 70.64, 70.73, 70.83, 80.42, 115.09, 126.95, 129.44, 143.97, 144.44, and 160.82. *Anal.* Calcd for $C_{24}H_{29}N_3O_5S_2$: C, 57.24; H, 5.80; N, 8.34%. Found: C, 57.07; H, 5.82; N, 8.11%.
15. CCDC 633055 contains the supplementary crystallographic data for this paper. These data can be

obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. Crystal data for **2c**: $C_{24}H_{29}O_5N_3S_2$, monoclinic, $P2_1/c$, a = 8.123(4) Å, b = 13.558(5) Å, c = 22.195(9) Å, β = 97.47(3)°, V =2423(1) Å^3, Z = 4, M_r = 494.63, D_x = 1.380 Mgm^{-3}, μ= 23.37 cm^{-1}, T = 173 (1) K, refinement on F^2 (*SHELXL97*),[18] $R[F^2 > 2\sigma(F^2)]$ = 0.080, $wR(F^2)$ = 0.216, S = 1.023.

16. The synthetic details and physical properties of **3** will be reported elsewhere. **3c**: Greenish crystals, mp 167-168.5 °C, ^{1}H NMR ($CDCl_3$) δ = 3.43 (4H, t, J=5.9 Hz), 3.50-3.58 (8H, m), 3.61-3.70 (8H, m), 3.89 (4H, t, J=5.9 Hz), 7.86-7.92 (2H, m), 8.03-8.10 (2H, m), 8.23 (1H, t, J=1.8 Hz), and 8.57 (2H, d, J=1.8 Hz). ^{13}C NMR ($CDCl_3$) δ = 35.56, 70.02, 70.58, 70.77, 70.80, 71.06, 92.41, 114.02, 124.79, 131.62, 134.71, 135.22, 136.81, 140.90, 143.85, 145.23, and 164.33. FAB-MS; 633 ($[M]^+$, 100). HR MS; Calcd for $C_{32}H_{31}N_3O_7S_2$: 634.1682. Found: 634.1679 (M^+).
17. K. Kubo, J. Kubo, C. Kaminaga, and T. Sakurai, *Talanta*, 1998, **45**, 963.
18. G. M. Sheldrick, *SHELXL97*: Program for X-ray crystal structure determination and refinement, Göttingen University, Germany, 1997.