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SYNTHESIS AND COMPLEXING PROPERTIES OF THIACROWNOPHANES

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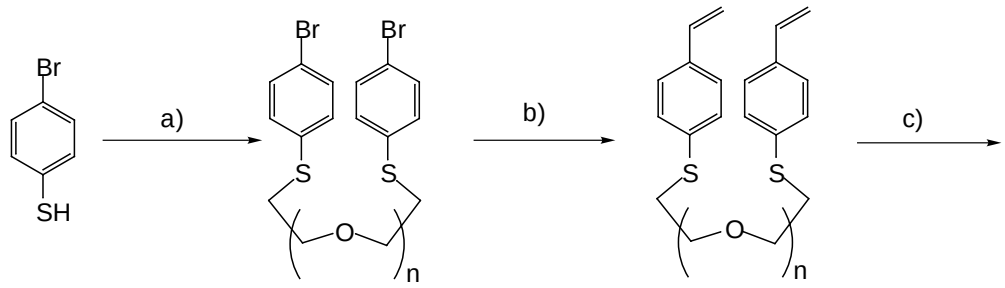
Abstract- Novel thiacrownophanes (**1**) (*cis*-form) and (**2**) (*trans*-form) were prepared by means of intramolecular [2 + 2] photocycloaddition of styrene derivatives. The ratio of **1**:**2** was significantly dependent on the oxyethylene chain length of the linkage between the two aromatic nuclei of precursors. In a liquid-liquid extraction, thiacrownophanes (**1c**) possessing three ethereal oxygens showed perfect selectivity with high efficiency toward Ag^+ ion. From ESI-MS analysis, **1c** was found to form a 1:1 complex with Ag^+ ion in MeCN-H_2O homogeneous system.

Crownophanes possessing both cyclophane and crown ether moieties in the molecule were found to show unique host-guest interaction with many kinds of metal cations and organic compounds in organic media.[1-9] They were conveniently prepared by efficient intramolecular photocycloaddition of styrene derivatives. Recently, we found a quite astonishing results in the preparation of thiacrownophanes, because it formed *cis*-isomers (**1**) and/or *trans*-isomers (**2**)**,** although the photochemical method has always exclusively given *cis*-isomer like **3**.[6] In this communication, we report the relationship between the ratio of **1**:**2** and linkage length of precursors, and complexing ability of the thiacrownophanes toward heavy metal cations.

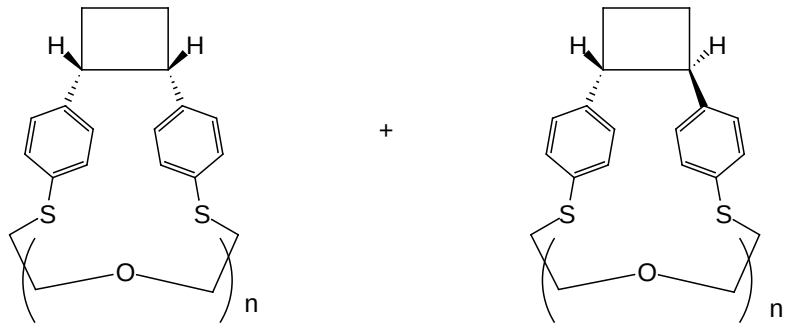
Thiacrownophanes (**1**) and (**2**) were prepared by the sequence shown in Scheme 1. Thus, compounds (**4a-d**) were obtained in good yields from thioetherification of 4-bromothiophenol with oligoethyleneglycol ditosylate, and then converted to **5a-d** by Migita-Kosugi-Stille reaction[10] in moderate yields. Finally thiacrownophanes were synthesized by the photoreaction.[1] Analytical data of new compounds prepared are given.[11] Photoreaction of **5a** and **5b** exclusively afforded *cis*-isomers (**1a**) (18%) and (**1b**) (15%), respectively. In contrast with these data, irradiation to **5c** produced both *cis*-

isomer (**1c**) (19%) and *trans*-isomer (**2c**) (5%). Surprisingly, **5d** exclusively gave *trans*-isomer (**2d**) (12%). Thus, it was found that product isomer ratio significantly depended on the length of oxyethylene linkage. In the case of prototypical crownophanes, which have only ethereal oxygens in the linkage, *cis*-isomer was exclusively formed in the photoreaction even if the precursor has six ethereal oxygens in the linkage.[1]



4 **a**; n=1 Y. 90%
b; n=2 Y. 90%
c; n=3 Y. 75%
d; n=4 Y. 75%

5 **a**; n=1 Y. 50%
b; n=2 Y. 30%
c; n=3 Y. 31%
d; n=4 Y. 40%

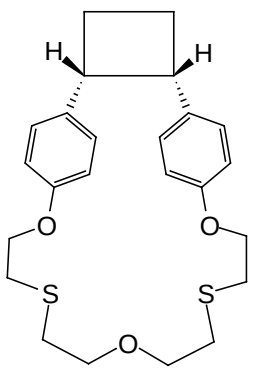


1 **a**; n=1 Y. 18%
b; n=2 Y. 15%
c; n=3 Y. 19%
d; n=4 Y. 0%

2 **a**; n=1 Y. 0%
b; n=2 Y. 0%
c; n=3 Y. 12%
d; n=4 Y. 15%

Scheme 1. Reactions and conditions: a) $TsO(CH_2CH_2O)_{n+1}Ts$, NaOEt/EtOH, rt; b) CH_2=CHSn(n-Bu)$_3$, 2,6-di-*tert*-butyl-4-methylphenol/toluene, reflux; c) hν (> 280 nm)/MeCN, N_2, rt.

Thiacrownophanes obtained were used as extractants for heavy metal cations in a liquid-liquid system. A CH_2Cl_2 solution of a host compound (1×10^{-4} mol dm^{-3}, 5 mL) and an aqueous solution (0.1 mol dm^{-3}, 5 mL), whose pH value was adjusted as high as possible not to precipitate the hydroxides, were shaken in a 20-mL test tube equipped with a ground glass stopper at room temperature for 2 h. After two phases were separated, an aliquot (2 mL) of the organic phase was evaporated, and then HNO_3



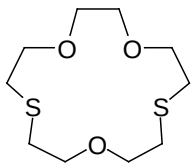
solution (0.1 mol dm^{-3}, 2 mL) was added to the residue. Extracted cation in the acidic aqueous solution was analyzed by atomic absorption spectrometry. Results are summarized in Table 1 with thiacrown reference compounds (**3** and **6**). Both **1a** and **2c** hardly extracted any heavy metal cations examined. Although **1b** with a small cavity to fit Ag^+ ion and **2d** with a strained ligating ring showed a little affinity toward Ag^+ ion, **1c** efficiently and exclusively extracted Ag^+ ion. This efficiency was higher than those of thiacrownophane **3** and conventional dithia-15-crown-5 (**6**).

From the frame work investigation using the space-filling model, two large sulfur atoms directly attached on the aromatic nuclei of **1c** form a nicely arranged cyclic polyether cavity with *ca*. 2.7 Å of diameter. The cavity size is suitable for Ag^+ ion (diameter, 2.32 Å) since an optimaized diameter ratio for cation and crown ether cavity generally becomes 0.9 at complexation.[12]

Table 1. Extraction of heavy metal cations with ligands

	Extractability (%)[a]							
ligand	Ag^+	Pb^{2+}	Cu^{2+}	Mn^{2+}	Zn^{2+}	Ni^{2+}	Co^{2+}	Fe^{3+}
1a	0(6.9)	0(4.5)	0(4.5)	0(6.4)	0(6.8)	0(6.8)	0(7.0)	0(1.5)
1b	13(4.6)	0(5.3)	0(4.3)	0(4.5)	0(5.7)	0(6.9)	0(7.1)	0(1.9)
1c	50(6.5)	0(4.5)	0(4.5)	0(6.0)	0(6.0)	0(7.0)	0(7.0)	0(1.5)
2c	2(5.6)	0(4.9)	0(4.5)	0(4.3)	0(5.5)	0(6.6)	0(6.9)	0(1.5)
2d	14(6.9)	0(4.5)	0(4.5)	0(5.5)	0(5.5)	0(6.9)	0(7.0)	0(1.9)
3	43(4.4)	6(4.8)	0(4.1)	0(6.1)	0(5.3)	2(6.9)	0(7.0)	0(1.7)
6	15(5.0)	0(5.0)	0(4.3)	0(6.2)	0(5.7)	0(7.0)	0(7.0)	0(1.9)

[a] Extraction conditions: Aq. phase (5 mL), [metal nitrate]= 1.0 x 10^{-1} mol dm^{-3}; Org. phase, CH_2Cl_2 (5 mL), [ligand]= 1.0 x 10^{-4} mol dm^{-3}; *ca*. 20 ˚C, shaken for 1 h. The values were based on the concentration of the crown compounds. Values in parentheses were equilibrium pH of aqueous phase. Reproducibility was ±15% which was the average value obtained from three independent runs.



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The ^{13}C NMR chemical shift of two linkage carbons attached to sulfur or ethereal oxygen observed considerably changed with increasing the amount of $AgClO_4$ added to the host solution, but the titration curve was not reached to a plateau up to the **1c**/Ag^+ ratio of 3, indicating a difficulty in determining exact stoichiometric relationships between the host compound and Ag^+ ion in the complexation.

Since ESI-MS is an appropriate method to observe cation-complexing behavior in solution,[13,14] we investigated the interaction between **1c** and Ag^+ ion in MeCN-H_2O (1:1) by employing the method to

clarify the complexing behavior of the thiacrownophane to Ag^+ ion clearer: The sample solution contained **1c** and $AgClO_4$ salt (1 x 10^{-4} mol dm^{-3} in each). Figure 2 showed that 1:1 (**1c**:Ag^+) complex was quantitatively formed, because free **1c** was hardly detected.

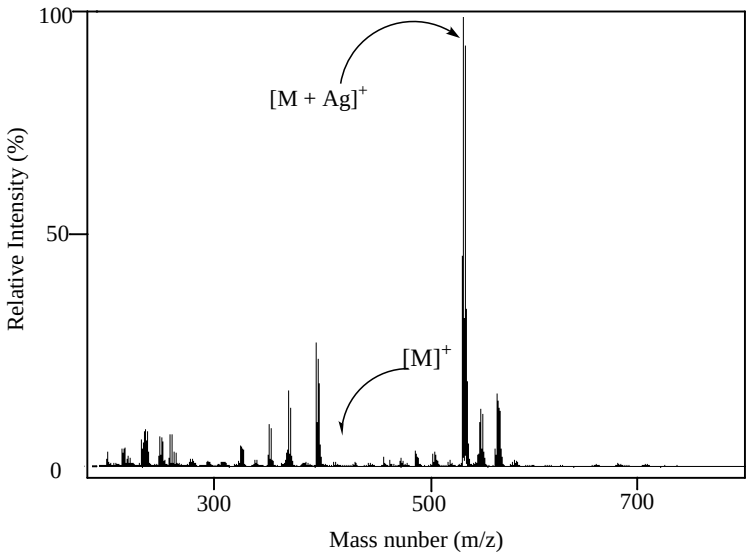

Figure 2. ESI-MS spectra of pyridinocrownophane (**1c**) in 1:1 (v/v) MeCN-H_2O containing $AgClO_4$.

In conclusion, thiacrownophanes was prepared by intramolecular [2 + 2] photocycloaddition, and *trans*-thiacrownophanes were first prepared in the series of crownophanes. In the liquid-liquid extraction, **1c** showed extraordinarily high efficiency and selectivity toward Ag^+ ion. From ESI-MS analysis compound (**1c**) was found to form Ag^+-complex quantitatively in homogeneous solution.

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11. Analytical and spectroscopic data of new compounds prepared: **1a**; white solid (mp 107.2-107.7 ˚C). ^1H NMR ($CDCl_3$, 500 MHz) δ=7.15 (4H, d, *J*=10.0), 6.87 (4H, br s), 4.05 (2H, s), 3.16 (4H, m), 2.76 (4H, m),

2.49 (4H, m). ESI-MS m/z 343.4 ([M + H]$^+$). **1b**; white solid (mp 74.1-74.6 ˚C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ=7.11 (4H, AB*q*, *J*=8.3), 6.79 (4H, AB*q*, *J*=8.3), 3.91 (2H, m), 3.49 (4H, s), 3.38 (4H, t, *J*=7.0), 2.91 (4H, t, *J*=7.0), 2.41 (2H, m,), 2.34 (2H, m). ESI-MS m/z 386.2 (M^+), 387.3 ([M + H]$^+$). **1c**; pale yellow liquid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ=7.13 (4H, AB*q*, *J*=10.0), 6.82 (4H, AB*q*, *J*=10.0), 3.96 (2H, m), 3.65 (4H, m), 3.64 (4H, m), 3.56 (4H, t, *J*=7.5), 2.97 (4H, t, *J*=7.5), 2.43 (2H, m), 2.40 (2H, m). ESI-MS m/z 430.4 (M^+), 431.4 ([M + H]$^+$). **2c**; white solid (mp 102.4-103.2 ˚C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ=7.39 (4H, AB*q*, *J*=10.0), 7.08 (4H, AB*q*, *J*=10.0), 3.55 (4H, m), 3.42 (4H, m), 3.36 (6H, m), 2.99 (4H, m), 2.26 (2H, m), 2.16 (2H, m). ESI-MS m/z 430.4 (M^+), 431.4 ([M + H]$^+$). **2d**; pale yellow liquid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ=7.36 (4H, AB*q*, *J*=8.2), 7.32 (4H, AB*q*, *J*=8.2), 3.74 (2H, m**),** 3.56 (16H, m), 3.01 (4H, t, *J*=7.0), 2.28 (2H, m), 2.11 (2H, m). ESI-MS m/z 474.4 (M^+), 475.3 ([M + H]$^+$). Thiacrownophanes (**1**) were of *cis*-configuration and **2** was *trans*-configuration, which were proved by the specific methine proton signals at δ=3.91-4.04 and 3.36-3.56, respectively.[15]

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