Synthesis and Metal-Ion Binding Properties of Monoazathiacrown Ethers

Mutsuo Tanaka,*,† Makoto Nakamura,§ Tomokazu Ikeda,‡ Kiyomi Ikeda,† Hisanori Ando,† Yasuhiko Shibutani,‡ Setsuko Yajima,§ and Keiichi Kimura*,§

Special Division for Human Life Technology, National Institute of Advanced Industrial Science and Technology, 1-8-31, Midorigaoka, Ikeda, Osaka 563-8577, Japan, Department of Chemistry, Faculty of Engineering, Osaka Institute of Technology, 5-16-1, Ohmiya, Asahi-ku, Osaka 535-8585, Japan, and Department of Applied Chemistry, Faculty of Systems Engineering, Wakayama University, 930, Sakae-dani, Wakayama, Wakayama 640-8510, Japan

mutsuo-tanaka@aist.go.jp

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Synthetic procedures for monoazathiacrown ethers were explored, and monoazatrithia-12-crown-4, monoazatetrathia-15-crown-5, and monoazapentathia-18-crown-6 were obtained in moderate yields by the reaction of bis(2-chloroethyl)amine with the appropriate dithiols in the presence of lithium hydroxide in THF. To evaluate metal-ion binding properties of the monoazathiacrown ethers by solvent extraction, lipophilic dodecyl and dodecanoyl groups were incorporated onto the monoazathiacrown ethers. The solvent extraction experiments suggested that monoazathiacrown ethers have Ag^+ and Hg^{2+} selectivities and that the relative selectivity between Ag^+ and Hg^{2+} depends on their nitrogen atom properties and numbers of sulfur atoms reflecting the respective affinities of nitrogen and sulfur atoms to Hg^{2+} and Ag^+. An interesting ability to bind Mg^{2+} was observed in the case of *N*-dodecyl monoazatrithia-12-crown-4.

Introduction

Since crown ethers were first recognized to have selective metal-ion binding properties by Pedersen,[1] various crown ethers have been prepared and their metal-ion binding properties have been studied extensively. Of particular note are commercially available monoaza- and hydroxymethyl-crown ethers used as building blocks to induce a metal-ion-selective function in supramolecular systems.[2] At the same time, various thiacrown ethers have also been prepared[3] and their heavy-metal-ion binding properties are well-known.[4] However, little use seems to have been made of thiacrown ethers as building blocks in supramolecular systems because there are few thiacrown ethers that have functional groups to incorporate into a supramolecule.[5] To the best of our knowledge, general procedures for preparing monoazathiacrown ethers, which could be quite useful to incorporate into a supramolecule, have not been reported yet. In this paper, therefore, we report the synthesis of monoazathiacrown ethers and their metal-ion binding properties evaluated by solvent extraction for the purpose of their application as building blocks in supramolecular systems.

Results and Discussion

Preparation of Monoazatrithia-12-crown-4. First, we examined cyclization of diethanolamine derivatives with 3-thiapentane-1,5-dithiol in the preparation of monoazatrithia-12-crown-4 by three methods shown in Schemes 1−3. In method 1 (Scheme 1), the reaction of diethanolamine with *p*-toluenesulfonyl chloride in pyri-

* Corresponding authors. E-mail for K. Kimura: kimura@sys.wakayama-u.ac.jp.
† National Institute of Advanced Industrial Science and Technology.
‡ Osaka Institute of Technology.
§ Wakayama University.

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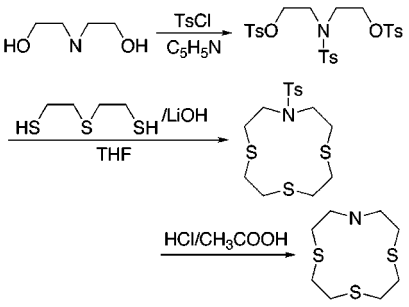
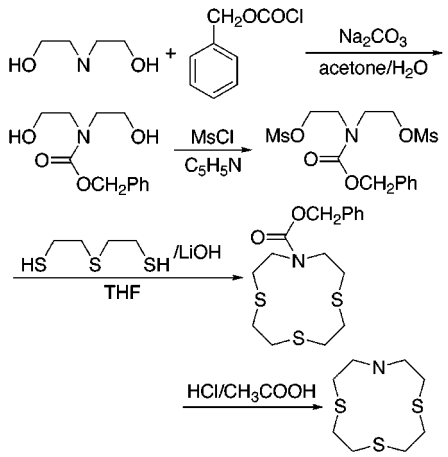
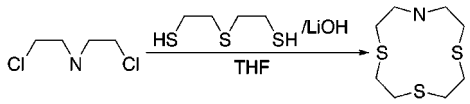
Scheme 1. Method 1



Scheme 2. Method 2



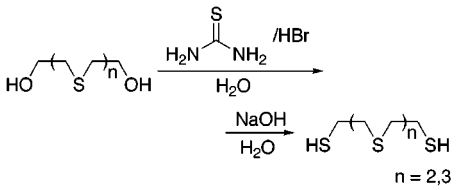
Scheme 3. Method 3



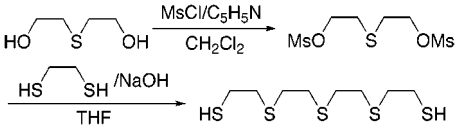
dine gave *N*-tosyldiethanolamine ditosylate in an excellent yield (>95%). Subsequent cyclization of *N*-tosyldiethanolamine ditosylate with 3-thiapentan-1,5-dithiol in THF in the presence of lithium hydroxide produced *N*-tosylmonoazatrithia-12-crown-4 in a 25% yield. Attempts to remove the *N*-protecting tosyl group with various reagents such as sulfuric acid at various concentrations (47 wt % hydrobromic acid−acetic acid and 35 wt % hydrochloric acid−ethanol) resulted in decomposition or no reaction. Finally, 35 wt % hydrochloric acid−acetic acid gave monoazatrithia-12-crown-4, but the yield was only 10%.

In method 2 (Scheme 2), the benzyloxycarbonyl group was introduced to diethanolamine as the *N*-protecting group. Selective reaction of benzyloxycarbonyl chloride with the amino group of diethanolamine was attained in acetone−water in the presence of sodium carbonate with a 58% yield. Methanesulfonyl chloride was chosen to react with *N*-benzyloxycarbonyldiethanolamine, as methanesulfonyl chloride (>95%) gave a better yield than *p*-toluenesulfonyl chloride (75%). Cyclization of *N*-benzyloxcarbonyldiethanolamine dimesylate with 3-thiapentan-1,5-dithiol was carried out under conditions similar

Scheme 4



Scheme 5



to those in method 1, but the yield was only 14%. Subsequent removal of the *N*-protecting group was accomplished with 35 wt % hydrochloric acid−acetic acid in a 70% yield.[6]

Method 3 (Scheme 3) is a one-step preparation of monoazatrithia-12-crown-4, namely, the cyclization reaction of commercially available bis(2-chloroethyl)amine with 3-thiapentan-1,5-dithiol. The reaction was carried out under conditions similar to those in method 1, and the yield was 39%.

On the basis of the high total yield and simplicity, method 3 appears to be the most promising procedure. In light of this, various combinations of solvent and bases such as lithium, sodium in ethanol, lithium hydroxide, sodium hydroxide, potassium hydroxide, sodium hydride in THF, and cesium carbonate in DMF were examined according to method 3. Lithium hydroxide in THF gave the best yield at 39%. Cesium carbonate in DMF has been reported to give excellent yields in thiacrown ether preparation;[7] however, no improvement was observed in this study.

Preparation of Monoazathiacrown Ethers and Their Derivatives. To prepare monoazatetrathia-15-crown-5 and monoazapentathia-18-crown-6, syntheses of 3,6-dithiaoctan-1,9-dithiol and 3,6,9-trithiaundecan-1,11-dithiol were carried out according to reported procedures (Scheme 4).[8] The cleavage of thioether bonds[9] resulted in a low yield of 22% in the case of 3,6-dithiaoctan-1,9-dithiol preparation, and 3,6,9-trithiaundecan-1,11-dithiol was not formed by this method. Therefore, a modified procedure for 3,6,9-trithiaundecan-1,11-dithiol preparation was examined as shown in Scheme 5, and the yields were 53 and 51% for the first and second steps, respectively.

Monoazatetrathia-15-crown-5 and monoazapentathia-18-crown-6 were prepared according to method 3 with 34 and 26% yields, respectively, and two noncyclic analogues were also prepared for comparison (Scheme 6). To evaluate the metal-ion binding properties of monoazathiacrown ethers by solvent extraction, lipophilic groups such as dodecyl and dodecanoyl groups were introduced onto monoazathiacrown ethers by the reaction of dodecyl halide and dodecanoyl halide in the presence of bases. Similarly, noncyclic analogues were converted

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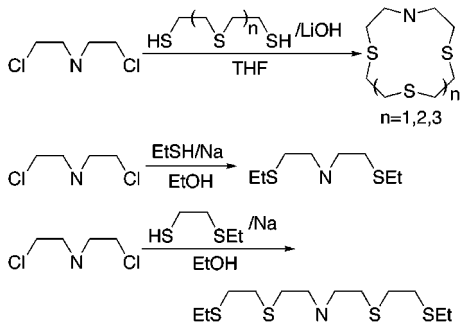
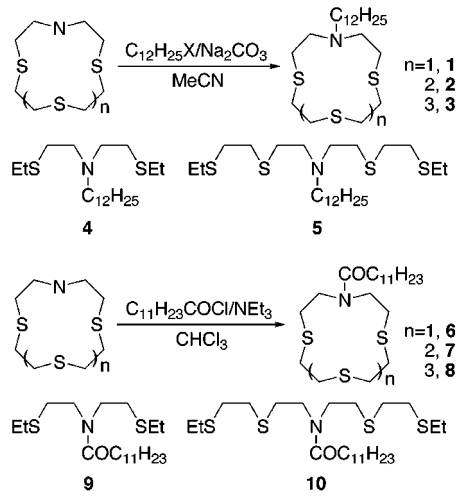
Scheme 6



Scheme 7



to the corresponding dodecyl and dodecanoyl derivatives (Scheme 7).

Solvent Extraction. Solvent extraction experiments were carried out using metal picrate salts in a chloroform−water system at 30 °C, and the extracted metal-ion % was determined from the decrease in the picrate concentration in the aqueous phase by UV measurement. The percentages of extracted metal ions are summarized in Table 1. There was no significant metal-ion extraction of alkali metal ions with any of the thiacrown ethers as anticipated. For alkaline-earth metal ions, small amounts of Ca^{2+} were extracted with **1**−**5**. However, **6**−**10** extracted only small amounts of alkaline-earth metal ions, even though the thiacrown ether concentration was 10-fold that of **1**−**5**. In the case of **6**−**10**, the electron-withdrawing carbonyl group suppressed the metal-ion binding of the nitrogen atom of the crown ethers. An interesting tendency was exhibited by **1**: it extracted a small amount of Mg^{2+}, which is generally difficult to extract from aqueous to organic phases. This result implies that the monoazatrithia-12-crown-4 unit has some binding ability for Mg^{2+}. Among the heavy metal ions studied, Ag^+ and Hg^{2+} were extracted effectively by the thiacrown ethers as expected,[10] but significant differences in selectivities were observed between groups **1**−**5** and **6**−**10**. While dodecyl derivatives **1**−**5** showed Hg^{2+} selectivities, the selectivities of dodecanoyl derivatives **8** and **10** were for Ag^+. The Ag^+ selectivities relative to Hg^{2+}, the ratio of $Ag^+/(Ag^+ + Hg^{2+})$ in the organic phase, are also summarized in Table 1. Among **1**−**3**, the relative Ag^+ selectivities to Hg^{2+} were 34, 36, and 41%, respectively, indicating that the relative Ag^+ selectivity is proportional to the number of sulfur atoms. This tendency was observed with other hosts. When the relatively low Hg^{2+} extractability of **6**−**10** bearing an amide carbonyl group is considered, the Hg^{2+} selectivity of **1**−**5** seems to be derived from an affinity of their amine nitrogen atoms for Hg^{2+}. On the other hand, the comparison between cyclic and noncyclic thiacrown ethers did not show any meaningful difference.

In conclusion, the syntheses of monoazatrithia-12-crown-4, monoazatetrathia-15-crown-5, and monoazapentathia-18-crown-6 were attained by the reaction of bis(2-chloroethyl)amine with the corresponding dithiols in the presence of lithium hydroxide in THF in moderate yields. Solvent extraction experiments suggested that monoazathiacrown ethers have Ag^+ and Hg^{2+} selectivities and that relative selectivity between Ag^+ and Hg^{2+} depends on their nitrogen atom properties and sulfur atom numbers. An interesting ability to bind Mg^{2+} was observed in the case of dodecyl monoazatrithia-12-crown-4.

Experimental Section

All chemicals were of available purity and used without further purification. Prepared monoazathiacrown ethers, noncyclic analogues, and **1**−**5** tended to suffer from oxidation, but **6**−**10** were quite stable. We prepared 3,6-dithiaoctan-1,8-dithiol according to ref 8.

Caution! Mustard gaslike materials such as 3-thiapentan-1,5-dimesylate and bis(2-chloroethyl)amine hydrochloride (purchased from Tokyo Kasei Kogyo) are blistering agents. Some materials have the potential to become a blistering agent during the preparation process.

Preparation of Monoazathiacrown Derivatives. 3-Thiapentan-1,5-dimesylate. 3-Thiapentan-1,5-diol (1.22 g, 10 mmol), pyridine (4.0 g, 50 mmol), and dichloromethane (50 mL) were put into a three-necked flask at room temperature. A dichloromethane solution (10 mL) of methanesulfonyl chloride (3.44 g, 30 mmol) was added dropwise to the mixture, and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was poured into water, and the organic layer was separated. The aqueous layer was extracted with chloroform once. After solvent evaporation, THF (30 mL) was poured into the obtained crude product and the insoluble pyridinium salt was filtrated. The crude product (53%) was obtained as a colorless liquid by solvent evaporation and was used for the subsequent preparation after drying.

3,6,9-Trithiaundecan-1,11-dithiol. Caution! This material is a blistering agent! Under a nitrogen atmosphere, dithioethyleneglycol (4.71 g, 50 mmol), powdered sodium hydroxide (2.0 g, 50 mmol), and THF (50 mL) were put into a three-necked flask, and the mixture was refluxed. A THF solution (10 mL) of crude 3-thiapentan-1,5-dimesylate (2.78 g, 10 mmol) was added dropwise, and the reaction mixture was then refluxed for 12 h under a nitrogen atmosphere. The cooled reaction mixture was poured into 5 wt % aqueous hydrochloric acid, and the product was extracted with chloroform. The resulting precipitate was filtrated. The colorless, solid product (51%) was purified by recrystallization with chloroform.

3-Thiapentan-1-thiol. Under a nitrogen atmosphere, dithioethyleneglycol (65.8 g, 0.7 mol), powdered sodium hydroxide (8.40 g, 210 mmol), and THF (700 mL) were put into a three-necked flask, and the mixture was refluxed. A THF solution (280 mL) of ethyl iodide (21.88 g, 140 mmol) was added dropwise, and the reaction mixture was refluxed for 1 h under a nitrogen atmosphere. The residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform twice. The colorless liquid product (95%) was purified by vacuum distillation.

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Table 1. Percentage of Metal Ion Extracted from Aqueous to Organic Phases[a]

host	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Ag^+	Tl^+	Pb^{2+}	Hg^{2+}	Zn^{2+}	Cu^{2+}	Ag^+ selectivity[b]
1	0	0	0	0	0	7	8	0	0	23	5	7	45	0	4>	34
2	0	0	0	0	0	0	8	0	0	20	1>	4>	36	0	3>	36
3	0	0	0	0	0	0	9	0	0	31	7	8	45	0	6	41
4	0	0	0	0	0	0	7	0	0	6	2>	4>	20	0	3>	23
5	0	0	0	0	0	0	5	0	0	25	0	4>	28	0	0	47
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	−
7	0	0	0	0	0	0	3>	0	0	9	4>	0	11	0	0	45
8	0	0	0	0	0	0	0	0	0	41	0	0	8	0	0	84
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	−
10	0	0	0	0	0	0	4>	0	0	21	0	0	10	0	0	68

[a] Host = 1×10^{-4} mol dm^{-3} for **1**−**5** and 1×10^{-3} mol dm^{-3} for **6**−**10**, and MPic and $M(Pic)_2 = 5 \times 10^{-5}$ mol dm^{-3}; $CHCl_3$(10 mL)/H_2O(10 mL); 30 °C. [b] Ag^+ selectivity represents the Ag^+ selectivity relative to that for Hg^{2+}, which is defined as the ratio of $Ag^+/(Ag^+ + Hg^{2+})$ in the organic phase.

***N*-Tosyldiethanolamine Ditosylate.** Diethanolamine (1.05 g, 10 mmol) and pyridine (20 mL) were put into a three-necked flask at 0 °C. A pyridine solution (20 mL) of *p*-toluenesulfonyl chloride (8.57 g, 45 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 12 h. The reaction mixture was poured into ice−water and neutralized by hydrochloric acid. The product was extracted with chloroform twice. The obtained crude brown liquid product (>95%) was used for the subsequent preparation after drying.

***N*-Tosylmonoazatrithia-12-crown-4.** Under a nitrogen atmosphere, lithium hydroxide (960 mg, 40 mmol) and dry THF (300 mL) were put into a three-necked flask, and the mixture was refluxed. A dry THF solution (20 mL) of 3-thiopentan-1,5-dithiol (1.54 g, 10 mmol) and crude *N*-tosyldiethanolamine ditosylate (5.67 g, 10 mmol) was added dropwise, and the reaction mixture was refluxed for 24 h under a nitrogen atmosphere. The residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform and then purified by gel permeation chromatography to give a pale-yellow solid (25%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.43 (3H, s, CH_3), 2.7−2.8 (12H, m, SCH_2), 3.4−3.5 (4H, m, NCH_2), 7.32 (2H, d, J = 8.5 Hz, ArH), 7.70 (2H, d, J = 8 Hz, ArH).

Monoazatrithia-12-crown-4 (Method 1). Under a nitrogen atmosphere, *N*-tosylmonoazatrithia-12-crown-4 (189 mg, 0.5 mmol), 35 wt % aqueous hydrochloric acid (20 mL), and acetic acid (10 mL) were put into a three-necked flask, and the reaction mixture was stirred at 100 °C for 24 h. The cooled reaction mixture was poured into 20 wt % aqueous sodium hydroxide (100 mL), and the product was extracted with chloroform three times. The product was purified by recrystallization with hexane to give a colorless solid (10%). Mp: 80−83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.59 (1H, s, NH), 2.7−3.0 (16H, m, SCH_2, NCH_2).

***N*-Benzyloxycarbonyldiethanolamine.** Diethanolamine (1.16 g, 11 mmol), sodium carbonate (2.65 g, 25 mmol), acetone (25 mL), and water (25 mL) were put into a three-necked flask at 0 °C. Benzyloxycarbonyl chloride (1.71 g, 10 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was poured into water, and the product was extracted with chloroform. The crude colorless liquid product (58%) obtained by solvent evaporation was used for the subsequent preparation after drying.

***N*-Benzyloxycarbonyldiethanolamine Dimesylate.** Crude *N*-benzyloxycarbonyldiethanolamine (478 mg, 2 mmol), pyridine (474 mg, 6 mmol), and chloroform (50 mL) were put into a three-necked flask at 0 °C. Methanesulfonyl chloride (687 mg, 6 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was poured into water, and the product was extracted with chloroform. The crude colorless liquid product (>95%) obtained by solvent evaporation was used for the subsequent preparation after drying.

***N*-Benzyloxycarbonylmonoazatrithia-12-crown-4.** Under a nitrogen atmosphere, lithium hydroxide (960 mg, 40 mmol) and dry THF (300 mL) were put into a three-necked flask, and the mixture was refluxed. A dry THF solution (20 mL) of 3-thiopentan-1,5-dithiol (1.54 g, 10 mmol) and crude *N*-benzyloxycarbonyldiethanolamine dimesylate (3.95 g, 10 mmol) was added dropwise, and the reaction mixture was refluxed for 24 h under a nitrogen atmosphere. The residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform and then purified by gel permeation chromatography to give a colorless liquid (14%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.7−2.9 (12H, m, SCH_2), 3.5−3.6 (4H, m, NCH_2), 5.13 (2H, s, CH_2), 7.3−7.4 (5H, m, ArH).

Monoazatrithia-12-crown-4 (Method 2). Under a nitrogen atmosphere, *N*-benzyloxycarbonylmonoazatrithia-12-crown-4 (179 mg, 0.5 mmol), 35 wt % aqueous hydrochloric acid (20 mL), and acetic acid (10 mL) were put into a three-necked flask, and the reaction mixture was stirred at 100 °C for 3 h. The cooled reaction mixture was poured into 20 wt % aqueous sodium hydroxide (100 mL), and the product was extracted with chloroform three times. The product was purified by recrystallization with *n*-hexane to give a colorless solid (70%).

Monoazatrithia-12-crown-4 (Method 3). Under a nitrogen atmosphere, 3-thiopentan-1,5-dithiol (308 mg, 2 mmol), bis(2-chloroethyl)amine hydrochloride (357 mg, 2 mmol), lithium hydroxide (288 mg, 12 mmol), and dry THF (150 mL) were put into a three-necked flask, and the reaction mixture was refluxed for 24 h. Residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform twice. The product was purified by recrystallization with hexane to give a colorless solid (39%).

Monoazatetrathia-15-crown-5. The preparation procedure was the same as that used for monoazatrithia-12-crown-4, except 3,6-dithiooctan-1,8-dithiol (428 mg, 2 mmol) was used instead of 3-thiopentan-1,5-dithiol to give a colorless solid (34%). Mp: 60−62 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.68 (1H, s, NH), 2.7−3.0 (20H, m, SCH_2, NCH_2).

Monoazapentathia-18-crown-6. The preparation procedure was the same as that used for monoazatrithia-12-crown-4, except 3,6,9-trithioundecan-1,11-dithiol (548 mg, 2 mmol) was used instead of 3-thiopentan-1,5-dithiol to give a colorless solid (26%). Mp: 53−56 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.7−3.0 (24H, m, SCH_2, NCH_2).

3,9-Dithia-6-monoazaundecane. Under a nitrogen atmosphere, sodium (4.60 g, 200 mmol) was dissolved in ethanol (200 mL), and ethanethiol (7.44 g, 120 mmol) was added to the solution. An ethanol solution (100 mL) of bis(2-chloroethyl)amine hydrochloride (7.14 g, 40 mmol) was added dropwise with refluxing, and the reaction mixture was refluxed for 2 h under a nitrogen atmosphere. The residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform twice. The product was purified by vacuum distillation to give a colorless liquid (84%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.27 (6H, t, J = 7.2 Hz, CH_3), 1.68 (1H, s, NH), 2.55 (4H, q, J = 7.3 Hz, SCH_2CH_3), 2.70 (4H, t, J = 6.4 Hz, SCH_2), 2.83 (4H, t, J = 6.6 Hz, NCH_2).

3,6,12,15-Tetrathia-9-monoazaheptadecane. Under a nitrogen atmosphere, sodium (5.75 g, 250 mmol) was dissolved in ethanol (250 mL), and 3-thiapentan-1-thiol (18.3 g, 150 mmol) was added to the solution. An ethanol solution (150 mL) of bis(2-chloroethyl)amine hydrochloride (8.93 g, 50 mmol) was

added dropwise with refluxing, and the reaction mixture was refluxed for 4 h under a nitrogen atmosphere. The residue obtained by solvent evaporation was poured into water, and the product was extracted with chloroform twice. The crude brown liquid product (71%) obtained by solvent evaporation was used for the subsequent preparation after removing low-boiling material under vacuum conditions at 100 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.27 (6H, t, J = 7.6 Hz, CH_3), 1.69 (1H, s, NH), 2.58 (4H, q, J = 7.3 Hz, SCH_2CH$_3$), 2.7−2.8 (12H, m, SCH_2), 2.84 (4H, t, J = 6.2 Hz, NCH_2).

***N*-Dodecylmonoazatrithia-12-crown-4 (1).** Under a nitrogen atmosphere, monoazatrithia-12-crown-4 (446 mg, 2 mmol), bromododecane (747 mg, 3 mmol), sodium carbonate (530 mg, 5 mmol), and acetonitrile (50 mL) were put into a three-necked flask, and the reaction mixture was refluxed for 48 h. The cooled reaction mixture was poured into 5 wt % aqueous sodium hydroxide, and the product was extracted with chloroform. The product was purified by gel permeation chromatography to give a 15% yield of **1** as a colorless solid. Mp: 54−56 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.0 Hz, CH_3), 1.2−1.4 (18H, m, $(CH_2)_9$), 1.48 (2H, m, NCH_2CH_2), 2.46 (2H, m, NCH_2CH_2), 2.6−2.9 (16H, m, SCH_2, NCH_2). Anal. Calcd for $C_{20}H_{41}NS_3$: C, 61.38; H, 10.49; N, 3.58; S, 24.55. Found: C, 61.15; H, 10.47; N, 3.54; S, 24.05. *m/z*: 391 (M^+). IR (neat, cm^{-1}): 2915, 2845 (−CH_2−).

***N*-Dodecylmonoazatetrathia-15-crown-5 (2).** The preparation procedure was the same as that used for **1**, except monoazatetrathia-15-crown-5 (566 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 74% of **2** as a colorless solid. Mp: 37−38 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.0 Hz, CH_3), 1.2−1.4 (18H, m, $(CH_2)_9$), 1.45 (2H, m, NCH_2CH_2), 2.50 (2H, t, J = 7.5 Hz, NCH_2CH_2), 2.6−2.9 (20H, m, SCH_2, NCH_2). Anal. Calcd for $C_{22}H_{45}NS_4$: C, 58.54; H, 9.98; N, 3.10; S, 28.38. Found: C, 58.48; H, 9.98; N, 3.08; S, 28.22. *m/z*: 451 (M^+). IR (neat, cm^{-1}): 2920, 2845 (−CH_2−).

***N*-Dodecylmonoazapentathia-18-crown-6 (3).** The preparation procedure was the same as that used for **1**, except monoazapentathia-18-crown-6 (686 mg, 2 mmol) and iodododecane (888 mg, 3 mmol) were used instead of monoazatrithia-12-crown-4 and bromododecane, respectively, to give 38% of **3** as a pale-yellow solid. Mp: 42−44 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.2−1.4 (18H, m, $(CH_2)_9$), 1.58 (2H, m, NCH_2CH_2), 2.6−2.9 (26H, m, NCH_2CH_2-SCH_2, NCH_2). Anal. Calcd for $C_{24}H_{49}NS_5$: C, 56.36; H, 9.59; N, 2.74; S, 31.31. Found: C, 55.97; H, 9.42; N, 2.67; S, 31.33. *m/z*: 511 (M^+). IR (neat, cm^{-1}): 2920, 2850 (−CH_2−).

***N*-Dodecyl-3,9-dithia-6-monoazaundecane (4).** The preparation procedure was the same as that used for **1**, except 3,9-dithia-6-monoazaundecane (386 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 56% of **4** as a colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.0 Hz, CH_3), 1.2−1.4 (24H, m, SCH_2CH_3, $(CH_2)_9$), 1.54 (2H, m, NCH_2CH_2), 2.58 (4H, q, J = 7.3 Hz, SCH_2CH$_3$), 2.6−2.9 (10H, m, SCH_2, NCH_2). Anal. Calcd for $C_{20}H_{43}NS_2$: C, 66.48; H, 11.91; N, 3.88; S, 17.73. Found: C, 65.83; H, 11.85; N, 3.83; S, 17.43. *m/z*: 361 (M^+). IR (neat, cm^{-1}): 2920, 2850 (−CH_2−).

***N*-Dodecyl-3,6,12,15-tetrathia-9-monoazaheptadecane (5).** The preparation procedure was the same as that used for **1**, except 3,6,12,15-tetrathia-9-monoazaheptadecane (626 mg, 2 mmol) and iodododecane (888 mg, 3 mmol) were used instead of monoazatrithia-12-crown-4 and bromododecane, respectively, to give 12% of **5** as a colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.5 Hz, CH_3), 1.2−1.4 (24H, m, SCH_2CH_3, $(CH_2)_9$), 1.43 (2H, m, NCH_2CH_2), 2.57 (4H, q, J = 7.3 Hz, SCH_2CH$_3$), 2.6−2.8 (18H, m, SCH_2, NCH_2). Anal. Calcd for $C_{24}H_{51}NS_4$: C, 59.88; H, 10.60; N, 2.91; S, 26.61. Found: C, 60.14; H, 10.46; N, 2.81; S, 26.33. *m/z*: 481 (M^+). IR (neat, cm^{-1}): 2920, 2845 (−CH_2−).

***N*-Dodecanoylmonoazatrithia-12-crown-4 (6).** Under a nitrogen atmosphere, monoazatrithia-12-crown-4 (446 mg, 2 mmol), triethylamine (303 mg, 3 mmol), and chloroform (50 mL) were put into a three-necked flask at room temperature. Dodecanoyl chloride (657 mg, 3 mmol) was added dropwise, and the reaction mixture was stirred for 6 h at room temperature under a nitrogen atmosphere. The reaction mixture was poured into water, and the product was extracted with chloroform. The product was purified by gel permeation chromatography to give 90% of **6** as a colorless solid. Mp: 85−86 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.0 Hz, CH_3), 1.2−1.4 (16H, m, $(CH_2)_8$), 1.63 (2H, m, $COCH_2CH_2$), 2.31 (2H, t, J = 8.0 Hz, $COCH_2$), 2.7−2.9 (12H, m, SCH_2), 3.5−3.6 (4H, m, NCH_2). Anal. Calcd for $C_{20}H_{39}NOS_3$: C, 59.26; H, 9.63; N, 3.46; S, 23.70. Found: C, 59.23; H, 9.96; N, 3.43; S, 23.60. *m/z*: 405 (M^+). IR (neat, cm^{-1}): 2920, 2845 (−CH_2−); 1645 (C═O).

***N*-Dodecanoylmonoazatetrathia-15-crown-5 (7).** The preparation procedure was the same as that used for **6**, except monoazatetrathia-15-crown-5 (566 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 90% of **7** as a colorless solid. Mp: 71−73 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 8.0 Hz, CH_3), 1.2−1.4 (16H, m, $(CH_2)_8$), 1.63 (2H, m, $COCH_2CH_2$), 2.30 (2H, t, J = 7.5 Hz, $COCH_2$), 2.7−2.9 (16H, m, SCH_2), 3.4−3.6 (4H, m, NCH_2). Anal. Calcd for $C_{22}H_{43}NOS_4$: C, 56.77; H, 9.25; N, 3.01; S, 27.53. Found: C, 56.59; H, 9.16; N, 2.97; S, 27.40. *m/z*: 465 (M^+). IR (neat, cm^{-1}): 2920, 2845 (−CH_2−); 1635 (C═O).

***N*-Dodecanoylmonoazapentathia-18-crown-6 (8).** The preparation procedure was the same as that used for **6**, except monoazapentathia-18-crown-6 (686 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 69% of **8** as a colorless solid. Mp: 49−50 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85 (3H, t, J = 7.2 Hz, CH_3), 1.2−1.4 (16H, m, $(CH_2)_8$), 1.61 (2H, m, $COCH_2CH_2$), 2.34 (2H, t, J = 7.6 Hz, $COCH_2$), 2.6−2.9 (20H, m, SCH_2), 3.5−3.7 (4H, m, NCH_2). Anal. Calcd for $C_{24}H_{47}NOS_5$: C, 54.86; H, 8.95; N, 2.67; S, 30.48. Found: C, 55.00; H, 8.90; N, 2.62; S, 30.17. *m/z*: 525 (M^+). IR (neat, cm^{-1}): 2920, 2850 (−CH_2−); 1640 (C═O).

***N*-Dodecanoyl-3,9-dithia-6-monoazaundecane (9).** The preparation procedure was the same as that used for **6**, except 3,9-dithia-6-monoazaundecane (386 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 93% of **9** as a colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 7.0 Hz, CH_3), 1.2−1.4 (22H, m, SCH_2CH_3, $(CH_2)_8$), 1.6−1.7 (2H, m, $COCH_2CH_2$), 2.32 (2H, t, J = 7.5 Hz, $COCH_2$), 2.5−2.6 (4H, m, SCH_2CH$_3$), 2.68 (4H, q, J = 8.0 Hz, SCH_2), 3.50 (4H, t, J = 7.5 Hz, NCH_2). Anal. Calcd for $C_{20}H_{41}NOS_2$: C, 64.00; H, 10.93; N, 3.73; S, 17.07. Found: C, 63.81; H, 11.08; N, 3.74; S, 17.04. *m/z*: 375 (M^+). IR (neat, cm^{-1}): 2940, 2845 (−CH_2−); 1650 (C═O).

***N*-Dodecanoyl-3,6,12,15-tetrathia-9-monoazaheptadecane (10).** The preparation procedure was the same as that used for **6**, except 3,6,12,15-tetrathia-9-monoazaheptadecane (626 mg, 2 mmol) was used instead of monoazatrithia-12-crown-4 to give 37% of **10** as a colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 8.0 Hz, CH_3), 1.2−1.4 (22H, m, SCH_2CH_3, $(CH_2)_8$), 1.6−1.7 (2H, m, $COCH_2CH_2$), 2.32 (2H, t, J = 8.0 Hz, $COCH_2$), 2.5−2.6 (4H, m, SCH_2CH$_3$), 2.7−2.8 (12H, m, SCH_2), 3.5−3.6 (4H, m, NCH_2). Anal. Calcd for $C_{24}H_{49}NOS_4$: C, 58.18; H, 9.90; N, 2.83; S, 25.86. Found: C, 57.92; H, 9.95; N, 2.86; S, 25.86. *m/z*: 495 (M^+). IR (neat, cm^{-1}): 2920, 2845 (−CH_2−); 1650 (C═O).

Solvent Extraction. Equal volumes (10 mL) of a chloroform solution containing a thiacrown ether (1×10^{-4} mol dm^{-3} for dodecyl- and 1×10^{-3} mol dm^{-3} for dodecanoylthiacrown ethers) and an aqueous solution of metal picrates (5×10^{-5} mol dm^{-3}) were thoroughly shaken in a 50 mL flask at 30 °C. The picrate concentration in the organic phase was determined by following its absorbance decrease in the aqueous phase. In control experiments, no distribution of thiacrown ether to the aqueous phase was observed under these conditions.

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