

Macrocyclic Polyether Sulfide Syntheses. Preparation of Thia(crown-6, -7, and -8) Compounds^{1,2}

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Macrocyclic polyether sulfides have been prepared by treating an oligoethylene glycol dichloride with a dimercaptan as reported in previous papers.^{3,4} The following new compounds were prepared: 1,5-dithia(19-crown-6) (1); 3-hydroxy-1,5-dithia(19-crown-6) (2); 1,4-dithia(21-crown-7) (3); 3-hydroxy-1,5-dithia(22-crown-7) (4); and 1,4-dithia(24-crown-8) (5). 1,13-Dithia(24-crown-8) (6) which has previously been reported,⁹ was also prepared.

In previous papers³⁻⁵ we have reported the syntheses of sulfur-containing polydentate compounds including the thia(crown-3, -4, -5, -6, and -7) compounds. A calorimetric investigation⁶ of the cation complexing properties of several of the thia(crown-5) compounds show them to form much more stable (as measured by log *K*) complexes in aqueous solution with Ag⁺ and Hg²⁺ than with Tl⁺ and Pb²⁺. Also, 2:1 ligand-metal complexes are found for reactions of these cations with thia(crown-3, -4, and -5) ligands. Dalley and coworkers⁷ have studied the crystalline structures of three of the thia(crown-4, -5, and -6) compounds. In each case, the larger sulfur atoms were directed away from the ring cavity. We are interested in investigating the cation selectivities of the larger crown rings containing one or at the most two sulfur atoms. We have, therefore, synthesized (see Chart I) thia(crown-6, -7, and -8) compounds

thia(24-crown-8) (5). In addition, we prepared 1,13-dithia(24-crown-8) (6), which was previously reported.⁹ The determination of log *K*, Δ*H*^o, and Δ*S*^o values for the reactions of these compounds with metal ions is underway. This paper reports on their synthesis.

Results and Discussion

The compounds shown in Chart I were prepared from the appropriate dimercaptans and oligoethylene glycol dichlorides. For example, compound 2 was prepared from 1,3-dimercapto-2-propanol and pentaethylene glycol di-

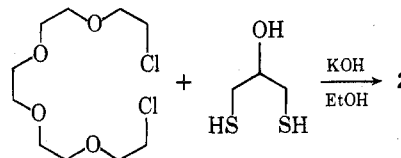
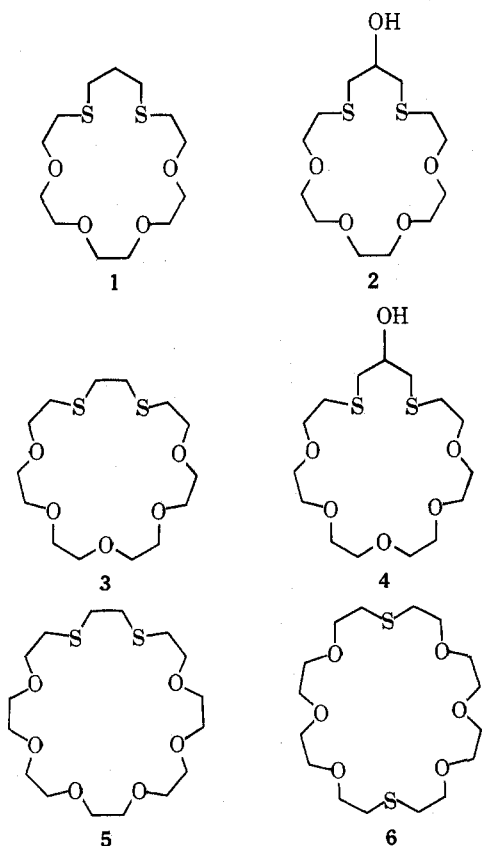


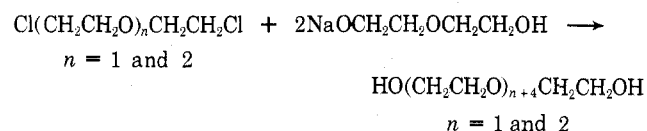
Chart I



with two sulfur atoms, namely, 1,5-dithia(19-crown-6) (1),⁸ 3-hydroxy-1,5-dithia(19-crown-6) (2), 1,4-dithia(21-crown-7) (3), 3-hydroxy-1,5-dithia(22-crown-7) (4), and 1,4-di-

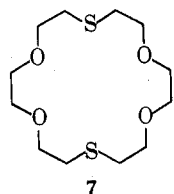
chloride.^{3,9} The reactions were carried out in ethanol using potassium or sodium hydroxide as a base. Since the mercaptan is a stronger acid than alcohol or water¹⁰ and the resulting sulfide is a stronger nucleophile than the oxide,¹¹ we would expect only the sulfide products. Running the reaction at high dilution ensures a good yield of the cycloaddition products.⁹ The yields varied from 5% for compound 5 to 24% for compound 1. Because of their high boiling points, these compounds were isolated by column chromatography.

Most of the starting materials used in this study were readily available. However, hexaethylene glycol and heptaethylene glycol were prepared by reacting di- and triethylene glycol dichloride with diethylene glycol and sodium.¹² The yield of these was poor (27-34%).



The structures of all crown products were consistent with those derived from the NMR spectra, elemental analyses, and in most cases molecular weight determinations. The NMR spectra exhibited peaks at δ 2.73 ± 0.01 (triplet, CH₂ α to sulfur but β to oxygen), 2.84 ± 0.01 (singlet, ethylene between sulfur atoms for compounds 3 and 5), and 3.65 ± 0.05 (CH₂ next to oxygen). In addition the middle CH₂ of the propylene moiety in compound 1 exhibited a peak at δ 1.95. Hydroxy bands were observed in the ir spectra for compounds 2 and 4.

In the x-ray diffraction structural studies of 1,10-dithia(18-crown-6) (7), Dalley and co-workers found that the donor atoms were nearly coplanar and they formed an elliptical cavity. The molecule is located about a center of



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symmetry with the sulfur atoms directed out of the cavity. The shortest distance across the cavity, 4.6 Å, is between the symmetry-related oxygen atoms.⁷

The important aspect of the structure is the fact that the sulfur atoms are directed away from the cavity. This fact is in harmony with the structure determinations for polyethylene oxide and polyethylene sulfide. Tai and Tadokoro found that polyethylene oxide has a helical form while the polyethylene sulfide has a glide form.¹³ They attribute this to differences in bond lengths of the C–O (1.43 Å) and C–S (1.815 Å) bonds and in the van der Waals radii for oxygen (1.52 Å) and sulfur (1.85 Å) atoms. Thus it is understandable that sulfur would be displaced from the normal cavity position of an oxygen atom. This may be beneficial in large thia(crown) compounds. Compound 3, for example, could have a cavity size similar to that of 18-crown-6 but have quite different cation complexing properties owing to the presence of the sulfur atoms. Work is now in progress to determine the complexing properties of these compounds.

Experimental Section

All infrared (ir) spectra were obtained on a Perkin-Elmer 457 spectrometer. A Varian A-60A spectrometer was used to obtain the nuclear magnetic resonance (NMR) spectra. Elemental analyses and molecular weights were performed by M-H-W Laboratories, Garden City, Mich. Thin layer chromatography R_f values were obtained using Eastman 13181 silica gel sheets with fluorescent indicator and reagent chloroform as eluent.

General Synthesis. All macrocyclic polyether sulfides were prepared by treating oligoethylene glycol dichlorides with the appropriate dimercaptans in base as previously reported.^{3,4} We used chloroform to dilute the initial reaction residue rather than ether. The starting materials were used as purchased. The dihalides were prepared from the corresponding glycols:^{3,4} 1,11-dichloro-3,6,9-trioxaundecane (from tetraethylene glycol, Eastman Kodak), 1,14-dichloro-3,6,9,12-tetraoxatetradecane (from pentaethylene glycol, Columbia Organic Chemicals), 1,17-dichloro-3,6,9,12,15-pentaoxaheptadecane (from hexaethylene glycol), and 1,20-dichloro-3,6,9,12,15,18-hexaoxaicosane (from heptaethylene glycol). All the dimercaptans were purchased from Aldrich Chemical Co. except 1,3-propanedithiol, which was made from 1,3-dichloropropane by the method of Urquhart.¹⁴

1,20-Dihydroxy-3,6,9,12,15,18-hexaoxaicosane (Heptaethylene Glycol).¹² To diethylene glycol (500 g, excess) at 70°C was added sodium metal (69 g, 3 mol) in parts with stirring under N_2 gas. The heating mantle was removed as the sodium was added and the temperature rose to 180°C during the exothermic reaction. After all the sodium dissolved, the solution was allowed to cool to 110°C and triethylene glycol dichloride (290.2 g, 1.55 mol) was added rapidly. Then the temperature was raised to 170°C until a neutral pH was achieved (1.5 hr). The mixture was cooled to room temperature and filtered through a fritted glass filter. The filtrate was continuously extracted with anhydrous ether on a liquid-liquid extractor equipped with a drying tube (5 days). The ether extract was decolorized with Norit A and the ether was removed on a rotary evaporator. Some diethylene glycol was recovered by distillation, bp 130–140°C (15 mm). The yellow, then later dark-brown, liquid product (95.96 g, 0.29 mol, 19%) was then collected, bp 224–234°C (0.5 mm) [lit. 241–244°C (0.6 mm)].¹⁵ Another run gave a 27% yield. The NMR spectrum exhibited peaks at δ 3.65 (s, 28 H, $HOCH_2CH_2OCH_2$) and 2.95 (s, 2 H, $HOCH_2CH_2O$).

1,17-Dihydroxy-3,6,9,12,15-pentaoxaheptadecane (Hexaethylene Glycol).¹² This compound was prepared as above from diethylene glycol, sodium, and diethylene glycol dichloride to give a 34% yield, bp 180–190°C (0.7 mm) [lit. 203–205°C (0.3 mm)].¹⁵ The ir and NMR spectra were consistent with the assigned structure.

Preparation of Thia(crown) Compounds. **1,5-Dithia(19-crown-6) (8,11,14,17-Tetraoxa-1,5-dithiacyclononadecane, 1).** 1,14-Dichloro-3,6,9,12-tetraoxatetradecane [15 g, 0.054 mol, bp 90–95°C (0.08 mm)] and 1,3-propanedithiol [5.9 g, 0.055 mol, bp 90°C (95 mm)] were mixed with 200 ml of absolute ethanol and added slowly to a stirred solution of an excess of sodium hydroxide in 400 ml of absolute ethanol. The reaction produced 14 g of residue. The residue (3 g) was purified by chromatography on 60 g of alumina (washed with ethyl acetate and dried at 120°C for 48 hr). The column was eluted with 100 ml of hexane and then with 100-ml portions each of 10% chloroform in hexane (v/v), 20, 30, 40, and 50% chloroform, and then 200 ml of pure chloroform. Product 1 (0.85 g, 24%) was found in the 40% chloroform fraction as a viscous oil: R_f 0.70; NMR δ 3.74 (t, 4 H, OCH_2CH_2S), 3.65 (s, 12 H, OCH_2CH_2O), 2.75 (m, 8 H, CH_2SCH_2), and 1.95 (m, 2 H, $SCH_2CH_2CH_2S$). The other fractions (2.1 g) contained mixtures of starting materials and product. No further work was done on these fractions.

Anal. Calcd for $C_{13}H_{26}O_4S_2$: C, 50.29; H, 8.44; S, 20.65; mol wt, 310.48. Found: C, 50.33; H, 8.62; S, 20.73; mol wt, 320.

3-Hydroxy-1,5-dithia(19-crown-6) (3-Hydroxy-8,11,14,17-tetraoxa-1,5-dithiacyclononadecane, 2). 1,14-Dichloro-3,6,9,12-tetraoxatetradecane (17 g, 0.062 mol) and 1,3-dimercapto-2-propanol (7.7 g, 0.062 mol) were treated as above, yielding 16.71 g of residue. The product (8%), purified by chromatography, was a viscous, pale yellow oil: R_f 0.61; NMR δ 3.76 (t, 4 H, OCH_2CH_2S), 3.68 (m, 14 H, $SCH_2CH(OH)CH_2S$, OCH_2CH_2O), and 2.84 (m, 8 H, $CH_2SCH_2CH_2O$).

Anal. Calcd for $C_{13}H_{26}O_5S_2$: C, 47.83; H, 8.03; S, 19.64; mol wt, 326.47. Found: C, 47.61; H, 8.30; S, 19.41; mol wt, 315.

1,4-Dithia(21-crown-7) (7,10,13,16,19-Pentaoxa-1,4-dithiacycloheptacosane, 3). 1,17-Dichloro-3,6,9,12,15-pentaoxaheptadecane [20.06 g, 0.0627 mol, bp 159–162°C (0.3 mm), lit. 146.5–148°C (1 mm)]¹² and 1,2-ethanedithiol (5.91 g, 0.0627 mol) were treated as before to give 18.14 g of residue. Compound 3 (10%) was purified by chromatography and was a viscous, pale yellow oil: R_f 0.69; NMR δ 3.66 (m, 20 H, $SCH_2CH_2OCH_2CH_2O$), 2.85 (s, 4 H, SCH_2CH_2S), 2.74 (t, 4 H, SCH_2CH_2O).

Anal. Calcd for $C_{14}H_{28}O_5S_2$: C, 49.38; H, 8.29; S, 18.83; mol wt, 340.50. Found: C, 49.26; H, 8.22; S, 18.62; mol wt, 340.

3-Hydroxy-1,5-dithia(22-crown-7) (3-Hydroxy-8,11,14,17,20-pentaoxa-1,5-dithiacyclodocosane, 4). 1,17-Dichloro-3,6,9,12-15-pentaoxaheptadecane (32.1 g, 0.10 mol) and 1,3-dimercapto-2-propanol (12.4 g, 0.10 mol) were treated as for compound 1 to yield 54.11 g of residue. Compound 4 (15%) was purified by chromatography and was a viscous, pale yellow oil: R_f 0.60; NMR δ 3.65 (m, 22 H, $SCH_2CH(OH)CH_2S$, $SCH_2CH_2OCH_2CH_2O$), and 2.78 (m, 8 H, $CH_2SCH_2CH_2O$).

Anal. Calcd for $C_{15}H_{30}O_6S_2$: C, 48.62; H, 8.16; S, 17.31; mol wt, 370.53. Found: C, 48.63; H, 8.36; S, 17.49; mol wt, 386.

1,4-Dithia(24-crown-8) (7,10,13,16,19,22-Hexaoxa-1,4-dithiacyclotetracosane, 5). 1,20-Dichloro-3,6,9,12,15,18-hexaoxaicosane [17 g, 0.0468 mol, bp 167–180°C (0.4 mm)] and 1,2-ethanedithiol (4.4 g, 0.0468 mol) were treated as for compound 1 yielding 7.35 g of residue. Product 5 (5%) was purified by chromatography and was a viscous tan oil: R_f 0.67; NMR δ 3.66 (m, 24 H, $SCH_2CH_2OCH_2CH_2O$), 2.85 (s, 4 H, SCH_2CH_2S), and 2.74 (t, 4 H, SCH_2CH_2O).

Anal. Calcd for $C_{16}H_{32}O_6S_2$: C, 49.97; H, 8.39; S, 16.68. Found: C, 49.80; H, 8.40; S, 16.81.

1,13-Dithia(24-crown-8) (4,7,10,16,19,22-Hexaoxa-1,13-dithiacyclotetracosane, 6). Tetraethylene glycol dichloride (31.8 g, 0.137 mol) and tetraethylene glycol dimercaptan⁴ (30 g, 0.133 mol) were treated as for compound 1 to yield 30 g of residue. The viscous, pale yellow liquid product (1%) was isolated using a silica gel column and eluting as above: R_f 0.63; NMR δ 3.70 (t, 4 H, OCH_2CH_2S), 3.64 (s, 20 H, OCH_2CH_2O), and 2.77 (t, 8 H, CH_2SCH_2).

Anal. Calcd for $C_{16}H_{32}O_6S_2$: C, 49.97; H, 8.39; S, 16.68. Found: C, 50.22; H, 8.66; S, 16.49.

Registry No.—1, 56930-34-8; 2, 56930-35-9; 3, 56930-36-0; 4, 56930-37-1; 5, 56930-38-2; 6, 297-13-2; heptaethylene glycol, 5617-32-3; diethylene glycol, 111-46-6; triethylene glycol dichloride, 112-26-5; hexaethylene glycol, 2615-15-8; diethylene glycol dichloride, 111-44-4; 1,14-dichloro-3,6,9,12-tetraoxatetradecane, 5197-65-9; 1,3-propanedithiol, 109-80-8; 1,3-dimercapto-2-propanol, 584-04-3; 1,17-dichloro-3,6,9,12,15-pentaoxaheptadecane, 52559-90-7; 1,2-ethanedithiol, 540-63-6; 1,20-dichloro-3,6,9,12,15,18-hex-

xaoxaecosane, 56930-39-3; tetraethylene glycol dichloride, 638-56-2; tetraethylene glycol dimercaptan, 2781-02-4.

References and Notes

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Loss of Water from Ketones in Isobutane Chemical Ionization Mass Spectrometry

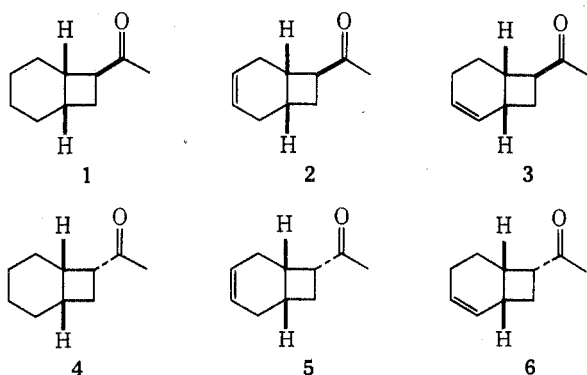
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Isobutane CI mass spectra are reported for 38 ketones containing zero, one, or two carbon-carbon double bonds as the only additional functional groups. An enhanced loss of water in these compounds can be correlated with the structural feature that an allylic hydrogen atom be available and able to approach within 2 Å of the carbonyl oxygen. α,β -Unsaturated ketones fail to show enhanced loss of water, even when this feature is present. Experiments with deuterium-labeled ketones demonstrate that scrambling of hydrogen is rapid relative to loss of water.

Earlier examination of the isobutane chemical ionization (CI) mass spectra of the bicyclic ketones 1-6 revealed a noteworthy variation in the intensity of the $(M + 1 - 18)^+$ ions formed on loss of water from the protonated ketone.¹ Significant loss of water occurs only from the unsaturated, endo-substituted ketones 5 and 6, and we suggested that this result reflected the availability in only these two members of the series of a reactive, allylic hydrogen atom which is accessible to the carbonyl oxygen atom. Through a six-membered (5) or seven-membered (6) transition state this



allylic hydrogen could approach the protonated oxygen atom and be lost subsequently as water. These observations encouraged us to examine the CI mass spectra of a variety of other ketones in order to determine the generality of this process and to study the structural factors influencing it. The results, which are presented in Table I, are discussed below.

The data in Table I are from the isobutane CI mass spectra of 38 monoketones containing zero, one, or two carbon-carbon double bonds as the only additional functional groups. The results indicate that under these conditions

enhanced loss of water can be correlated with three structural requirements. (1) Allylic hydrogens are necessary. Table I contains many pairs of ketones in which the only structural difference involved is the presence or absence of a double bond which provides activation for an appropriately placed (see below) allylic hydrogen. In nearly all cases there is a significant increase in intensity of the $(M + 1 - 18)^+$ ion when allylic hydrogen is present, and many of the ketones lacking the activating double bond show no detectable $(M + 1 - 18)^+$ ion at all.

(2) The allylic hydrogen must be geometrically accessible to the carbonyl oxygen atom. Loss of water occurs only in those ketones of Table I in which allylic hydrogen can approach oxygen closer than 2 Å, as measured on Dreiding models.² Thus no $(M + 1 - 18)^+$ ion is seen in 25 or 27, in which the distance from oxygen to the β allylic hydrogen is ~ 2.3 or ~ 2.5 Å, respectively. Furthermore, there is a qualitative correlation between the intensity of the $(M + 1 - 18)^+$ ion and the expected facility with which the two centers can be brought together. Loss of water is greatest with γ allylic hydrogen, which requires a sterically and entropically favorable six-membered transition state. A related effect is apparent in ketones involving more distant allylic hydrogen. In both 22 and 40 a δ allylic hydrogen is present, but the $(M + 1 - 18)^+$ ion is nearly eight times as intense in 22, in which the activating double bond is situated between the reacting centers rather than beyond the hydrogen atom as it is in 40. This location of the double bond in 22 presumably facilitates formation of the seven-membered transition state by reduction of the available rotational degrees of freedom in the chain. A similar comparison may be made between 24 and 42, where the allylic hydrogen is in the ϵ position. It is also noteworthy that for allylic hydrogen more distant than γ there is little effect of increasing number of methylene groups between the allylic hydrogen and the carbonyl group (compare 40, 42, 44).