

## Macroheterocycles. The Oxetane Function Spiro to Macrocyclic Polyether Rings

Carl G. Krespan

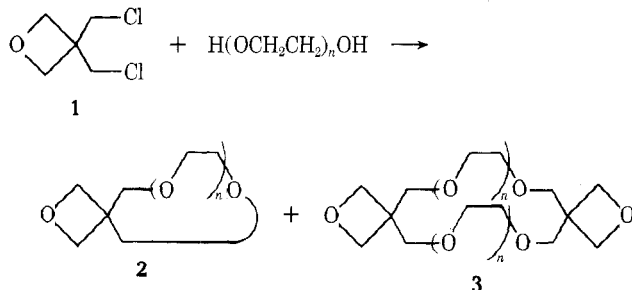
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Macrocyclic polyethers bearing one and two spirooxetane rings are easily obtained in one step from polyethylene glycols and 3,3-bis(halomethyl)oxetanes. Crystalline complexes of these cyclic polyethers are readily obtained from alkali and alkaline earth metal thiocyanates or iodides. For complexes with KSCN, incorporation of the carbon bearing a spirooxetane ring is shown to cause a 10- to 100-fold decrease in stability constant. Some new macrocycles containing sulfide groups are also described.

The original work by Pedersen<sup>1</sup> and subsequent studies by Frensdorff<sup>2</sup> established that macrocyclic polyethers of appropriate ring size complex strongly with cations of the alkali and alkaline earth metals. In only a few cases has later work on macrocyclic polyethers dealt with rings having additional functionality. In particular, the problem of incorporating a polymerizable function into such molecules has apparently been approached exclusively through substituted benzo derivatives. In one case,<sup>3</sup> a dibenzocrown polyether was converted to a mixture of isomeric diamines which was then incorporated into polyamides. In another case,<sup>4</sup> styrene analogs of monobenzocrowns were prepared and homopolymerized. Since these syntheses require several steps to produce the functionalized macrocyclic polyether, a more direct route seemed desirable. This paper describes the one-step synthesis of macrocyclic polyethers containing a spirooxetane unit starting from available materials.

**Synthesis.** 3,3-Bis(chloromethyl)oxetane (1), readily obtained from pentaerythritol<sup>5</sup> and itself polymerizable cationically,<sup>6</sup> is subject to anionic displacement of chlorine, leaving the oxetane ring intact.<sup>5</sup> Polyethylene glycols have now been found to react with 1 in the presence of strong base to yield macrocyclic polyethers of types 2 and 3 in up to 60% yield of isolated product. Dipolar aprotic



solvents such as dimethylformamide can be used, but *tert*-butyl alcohol has proved most convenient, since it can be used as purchased and is easily removed after reaction is complete. At reflux in *tert*-butyl alcohol, reaction of 1 with a polyethylene glycol salt is complete in 4-5 days. Under similar conditions, 3,3-bis(bromomethyl)oxetane reacts in less than 1 day to give similar products. Potassium *tert*-butoxide was used in most cases, but it has been demonstrated that sodium hydroxide or potassium hydroxide can be employed with only a slight yield loss. The yields cited were obtained at concentrations of ca. 10 wt % of each reactant, providing evidence that a template effect<sup>7</sup> is operating even in the protic solvent, *tert*-butyl alcohol. Except where excess *tert*-butoxide was included as a reactant, no trace of butoxy group was seen in the volatile products.

The product ratio 2:3 is governed by ring size. For cases in which 2 contains a macrocyclic polyether ring of 10 or

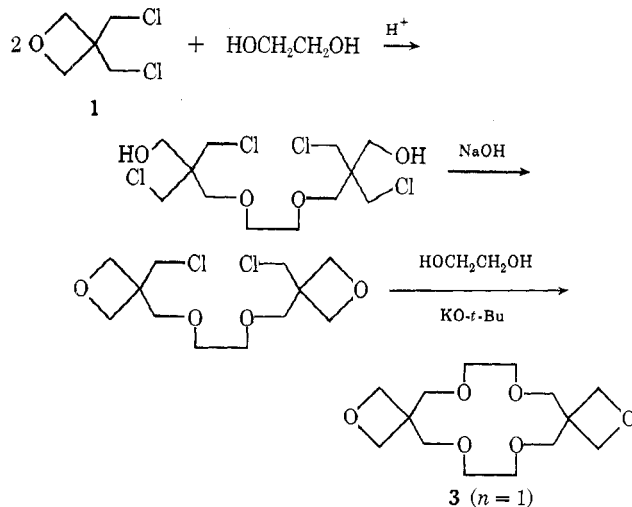
**Table I**  
Spirooxetanes from the Glycols HO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>n</sub>H

<i>n</i>	Glycol registry no.	2, % yield	Registry no.	3, % yield	Registry no.
1	107-21-1	42	51652-65-4	0.7	51652-71-2
2	111-46-6	0.2	51652-66-5	47	51652-72-3
3	112-27-6	30-35	51065-93-1	20-25	51065-94-2
4	112-60-7	53	51652-67-6		
5	4792-15-8	60	51652-68-7		
7	5617-32-3	35	51652-69-8	3	51652-73-4
9	3386-18-3	11	51652-70-1		

13 atoms, *i.e.*, products derived from diethylene glycol and triethylene glycol where *n* = 2 and 3, steric crowding results in a low ratio. For *n* > 3, formation of 2 is favored and the ratio is correspondingly high. The special case of glycol leads mainly to 2 (*n* = 1) with less than 1% of 3 (*n* = 1).

Table I shows the isolated yields for each glycol studied. For most *n* > 3, the yield of 3 was not determined; crystallization of 3 (*n* = 7) led to the isolation of this 50-membered-ring product in low but significant yield.

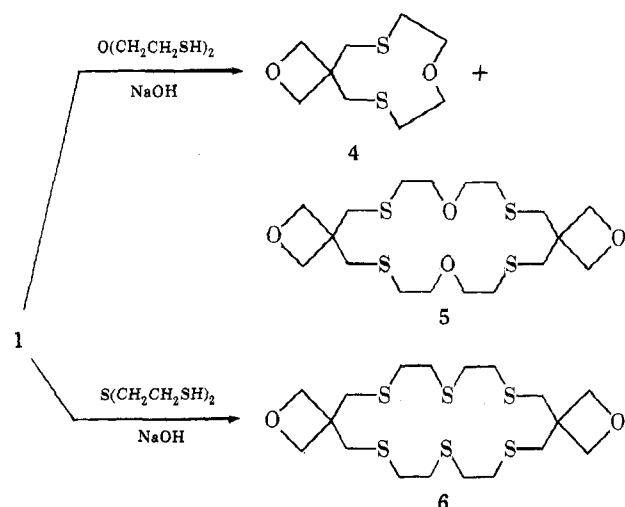
Dispirooxetanes which are difficult to obtain in reasonable yield by the one-step procedure, as well as dispirooxetanes having two different polyether bridges, can be made by a three-step route in which the two glycol molecules are introduced separately. An example is the synthesis of 3 (*n* = 1) according to the following scheme.



Even at temperatures over 100°, sulfuric acid is an ineffective catalyst for the first step, presumably because intermediate sulfate ester derived from the oxetane does not solvolyze readily. Trifluoromethanesulfonic acid proved to be a useful catalyst.

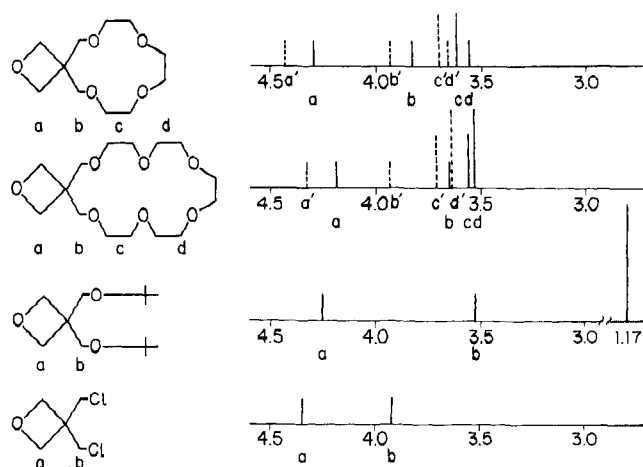
Extension of the one-step synthesis to dimercaptans was feasible, although a pronounced tendency to form polymer necessitated the use of dilute solutions. A greatly reduced

template effect is not surprising, since sulfur coordinates poorly to alkali metal ions.<sup>2</sup> Bis(2-mercaptoethyl) ether gave both monooxetane **4** and dioxetane **5**, while bis(2-mercaptoethyl) sulfide gave only dioxetane **6**.



Determination of the mono- and dispirooxetane structures rested on their nmr spectra, as well as on elemental analyses, infrared spectra, and molecular weight measurements. For products containing only oxygen as heteroatom, the isolated methylene and ethylene units appear as singlets at positions progressively further upfield as the distance from the oxetane ring increases. All ethylene units beyond those nearest the oxetane ring appear together as a broadened singlet. Figure 1 schematically illustrates some observed spectra along with those of reference oxetanes. Infrared absorption(s) at 10–10.5  $\mu$  are characteristic of the oxetane ring.<sup>5</sup>

**Complex Formation.** Stuart-Briegleb models indicated a minimum amount of space available inside the four-oxygen macrocycle, **2** ( $n = 3$ ). In accord with the model, lithium thiocyanate formed a stable, crystalline, 1:1 complex with **2** ( $n = 3$ ), whereas sodium thiocyanate formed a weak complex easily disrupted by ether extraction of the macrocycle, and a solid complex with potassium thiocyanate could not be obtained. The polyethers **2** ( $n = 4$ ) and **2** ( $n = 5$ ) formed well-defined 1:1 complexes with sodium



**Figure 1.**  $^1\text{H}$  chemical shifts observed with and without  $\text{K}^+$  present. Shifts are given in parts per million for 20% solutions in acetone- $d_6$ . Dotted lines designated by primed letters are for chemical shifts with 1 equiv of KSCN present.

and potassium thiocyanate, but lithium thiocyanate gave glassy complexes which resisted attempts at crystallization. These 1:1 complexes are assumed to involve a near-planar structure in which the cation is centrally located inside the ring with oxygen atoms oriented toward the cation, similar to the structures determined for other 1:1  $\text{M}^+$ -macrocyclic polyether complexes.<sup>8a</sup> Note that in the case of **2** ( $n = 4$ ) and KSCN, the addition of one carbon atom to the ring allows  $\text{K}^+$  to fit inside sufficiently well to favor a 1:1 complex, whereas crown polyethers containing five oxygen atoms form 2:1 sandwich structures with  $\text{K}^+$ .<sup>8b</sup>

The dispirooxetane **3** ( $n = 3$ ) preferentially forms 2:1 alkali metal thiocyanate-polyether complexes, a stoichiometry apparently not observed by Pedersen,<sup>1</sup> and reported by Truter, *et al.*, for similar 2:1 complexes involving  $\text{K}^+$ , but not  $\text{Na}^+$ . The smaller polyether ring in **3** ( $n = 2$ ) accommodates fewer sodium ions and even fewer potassium ions.

Ability to complex alkaline earth metal ions was demonstrated in one case; calcium iodide formed a 1:1 complex with **2** ( $n = 5$ ).

**Table II**  
 $K_{\text{stab}}$  for  $\text{K}^+$ - $\text{CH}_3\text{OH}$  Systems at 25°

Polyether	Log stability constant	Compd	Log stability constant
	2.20		2.08
	3.60		3.81
	5.00		2.43
	3.49		1.67
	6.10		<0.7

Complexation with alkali metal cations produced only small (ca. 0.1–0.3 ppm) downfield shifts in the large ring proton nmr positions.<sup>9</sup> Furthermore, the deshielding of protons on the oxetane ring was as great as or greater than that of the macrocyclic protons. In one case, that of 2 ( $n = 5$ )-KSCN, where a particularly stable complex with potassium ion was present (*vide infra*), splitting of the protons in one ethylene unit was induced by the fixed geometry. The effects of metal ions on the <sup>1</sup>H nmr spectra are exemplified in Figure 1.

Ability to form crystalline complexes with well-defined melting points and stoichiometry is, of course, not a reliable indicator of relative stability. Although the macrocyclic polyethers prepared in this work form such complexes, their stability in the presence of such strongly coordinating solvents as water and methanol can be expected to vary greatly. Stability constants of selected spirooxetane derivatives with potassium ion in methanol solution are presented in Table II.<sup>10</sup> For comparison, similar values for an acyclic polyether and several crown ethers are also included in Table II. Just as has been observed with the crown ethers, cyclic polyethers containing an additional carbon bearing a spirooxetane unit form the most stable complexes with K<sup>+</sup> when six ether oxygen atoms are present. Inspection of Table II reveals that a penalty of one to two powers of ten in stability constant results from each spirooxetane unit incorporated into the ring.

Rather surprisingly, polysulfide 5 forms a crystalline complex with sodium thiocyanate. The 2:1 ligand-NaSCN stoichiometry suggests that, unlike complexes of the related polyethers, this complex has a sandwich structure with Na<sup>+</sup> in the center coordinated to four ether oxygen atoms. Both 5 and 6 form complexes with mercuric chloride with well-defined 1:1 stoichiometry.<sup>11</sup>

### Experimental Section<sup>12</sup>

**2,6,9-Trioxaspiro[3.6]decane (2,  $n = 1$ ) and 2,6,9,13,16,19-hexaoxadispiro[3.6.3.6]eicosane (3,  $n = 1$ ).** A solution of 12.4 g (0.20 mol) of glycol, 47.0 g (0.42 mol) of potassium *tert*-butoxide, and 31.1 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane in 500 ml of *tert*-butyl alcohol was stirred and refluxed under nitrogen for 2 days. The mixture was cooled, addition of the three reactants repeated, and reaction continued for an additional 5 days. Evaporation of volatiles to 50° (0.5 mm) and continuous extraction of the residue with pentane gave 58.9 g of high-boiling oil along with 0.8 g of 2,6-dioxaspiro[3.3]heptane as a volatile solid. Sublimation of this solid gave 0.31 g (0.8%) of pure dioxaspiroheptane: mp 89–90° subl (lit.<sup>5</sup> mp 90°); mass spectrum  $m/e$  100 (parent<sup>+</sup>), 70 (P<sup>+</sup> - CH<sub>2</sub>O); ir (Nujol) 10.31 and 10.92  $\mu$  (oxetane ring); <sup>1</sup>H nmr  $\delta$  4.70 ppm (s).

Distillation of the high-boiling oil gave 24.2 g (42%) of 2,  $n = 1$ : bp 97–99° (10 mm); ir 3.41 and 3.48 (saturated CH), 8.8–9.1 (COC), 10.19 and 10.85  $\mu$  (oxetane ring); <sup>1</sup>H nmr  $\delta$  4.36 (s, 1, oxetane CH<sub>2</sub>), 3.99 (s, 1, CCH<sub>2</sub>), and 3.63 ppm (s, 1, OCH<sub>2</sub>CH<sub>2</sub>O).

*Anal.* Calcd for C<sub>7</sub>H<sub>12</sub>O<sub>3</sub>: C, 58.32; H, 8.40; O, 33.29. Found C, 57.99; H, 8.23; O, 32.89.

Isolation of solid from the distillation residue gave, after recrystallization from ether, 0.42 g (0.7%) of 2,6,9,13,16,19-hexaoxadispiro[3.6.3.6]eicosane (3,  $n = 1$ ), mp 163–165°, recrystallized from acetone for analysis: mass spectrum  $m/e$  288 (weak parent<sup>+</sup>), 289 (weak P + H<sup>+</sup>), 258 (strong P<sup>+</sup> - CH<sub>2</sub>O); ir (Nujol) 8.7–9.1 (COC), 10.29, 10.42, and 10.68  $\mu$  (oxetane); <sup>1</sup>H nmr  $\delta$  4.30 (s, 1, oxetane CH<sub>2</sub>), 3.80 (s, 1, CCH<sub>2</sub>), and 3.63 ppm (s, 1, OCH<sub>2</sub>CH<sub>2</sub>O).

*Anal.* Calcd for C<sub>14</sub>H<sub>24</sub>O<sub>6</sub>: C, 58.32; H, 8.40. Found: C, 58.88, 58.92; H, 8.05, 8.47.

**Stepwise Synthesis of 3,  $n = 1$ .** As catalyzed by sulfuric acid, the reaction of polyethylene glycols with bis(chloromethyl)oxetane is unusually sluggish. However, trifluoromethanesulfonic acid at elevated temperatures does catalyze the addition of glycol to this oxetane to form 2,2,9,9-tetrakis(chloromethyl)-4,7-dioxadecane-1,10-diol as a major product. Reaction of the bulk mixture gave only 10% of crude 3-chloromethyl-3-[6-(3'-chloromethyl-3'-oxetanyl)-2,5-dioxaheptyl]oxetane after treatment with base, a low yield owing to excessive polymerization in the first step. Use of a

solvent (CH<sub>2</sub>Cl<sub>2</sub> glyme, or CHCl<sub>2</sub>CHCl<sub>2</sub>) resulted in a yield of bis-oxetane of 32–42%.

A mixture of 24.8 g (0.40 mol) of glycol, 128.0 g (0.80 mol) of 3,3-bis(chloromethyl)oxetane, 0.5 ml of trifluoromethanesulfonic acid, and 160 ml of *sym*-tetrachloroethane was heated at 110° for 5 days. Solvent was removed under vacuum, 50 ml of xylene was added, and volatiles were again removed under vacuum. The viscous residue was dissolved in 300 ml of *tert*-butyl alcohol, 32.0 g (0.80 mol) of sodium hydroxide was added, and the mixture was stirred and heated. After an initial exothermic reaction carried the temperature to 80°, the mixture was heated at 70° overnight. Neutralization with concentrated HCl showed that 84% of the base had reacted. The mixture was filtered and volatiles were removed from the filtrate to give 127 g of residual oil. Continuous extraction of this oil with pentane yielded 120 g of high boilers in the extract. Distillation of this oil gave 40.2 g (34%) of the bisoxetane: bp 110–115° (0.05  $\mu$ ); ir 3.38 and 3.47 (saturated CH), 9.0 (broad COC), 10.19 (oxetane), and 13.78  $\mu$  (CCl); <sup>1</sup>H nmr  $\delta$  4.36 (s, 2, oxetane), 3.91 (s, 1, CH<sub>2</sub>Cl), 3.77 (s, 1, CCH<sub>2</sub>O), and 3.67 (s, 1, OCH<sub>2</sub>CH<sub>2</sub>O).

*Anal.* Calcd for C<sub>12</sub>H<sub>20</sub>Cl<sub>2</sub>O<sub>4</sub>: C, 48.17; H, 6.74; Cl, 23.70. Found: C, 48.31; H, 6.44; Cl, 23.97.

A solution of 29.9 g (0.10 mol) of the bisoxetane, 6.2 g (0.10 mol) of glycol, and 24.0 g (0.21 mol) of potassium *tert*-butoxide in 500 ml of *tert*-butyl alcohol was stirred and refluxed for 12 days. The reaction mixture was neutralized with concentrated HCl and filtered and the filter cake was extracted with 3 × 100 ml of CH<sub>2</sub>Cl<sub>2</sub>. Evaporation of the CH<sub>2</sub>Cl<sub>2</sub> solution gave 2.8 g of 3,  $n = 1$ . Evaporation of the mother liquor to 50° (0.5 mm), treatment of the residue with 20 ml of ether, and filtration gave 9.9 g of 3,  $n = 1$ . The combined solids were recrystallized by continuous extraction with ether in a Soxhlet, yielding 9.1 g (32%) of 3,  $n = 1$ , mp 163–165°, not depressed by admixture with an authentic sample.

**2,6,9,12-Tetraoxaspiro[3.9]tridecane (2,  $n = 2$ ) and 2,6,9,12,16,19,22,25-Octaoxadispiro[3.9.3.9]hexacosane (3,  $n = 2$ ).** Reaction of 228 g (2.04 mol) of potassium *tert*-butoxide, 106 g (1.00 mol) of distilled diethylene glycol, 155 g (1.00 mol) of 3,3-bis(chloromethyl)oxetane, and 3.0 l. of *tert*-butyl alcohol at reflux was continued for 2 days. Then the addition of *tert*-butoxide, glycol, and oxetane was repeated, and the reaction mixture was refluxed and stirred for 3 days. Another repeat addition was made and reaction was continued for 2 days. A last repeat addition was made, and the reaction mixture was refluxed for 6 days, filtered, and volatiles removed. The residual mixture of solid and oil, 770 g, was kept molten at 90° while being continuously extracted with heptane for 3 days. The cold heptane extract was filtered, and the solid thus isolated was extracted in a Soxhlet with ether. Filtration of the chilled ether extract gave 342 g of 3,  $n = 2$ , mp 84.5–85.5°. Second and third crops raised the yield to 357 g (47%) of purified 3,  $n = 2$ . An analytical sample was prepared by recrystallization from ether: mp 86–87°; ir (Nujol) 8.7–9.1 (COC), 10.05, 10.32, 10.55, and 10.76  $\mu$  (oxetane ring); <sup>1</sup>H nmr  $\delta$  4.36 (s, 1, oxetane CH<sub>2</sub>), 3.73 (s, 1, CCH<sub>2</sub>), and 3.63 ppm (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O).

*Anal.* Calcd for C<sub>18</sub>H<sub>32</sub>O<sub>8</sub>: C, 57.43; H, 8.57; O, 34.00; mol wt, 376.5. Found: C, 58.02; H, 8.79; O, 33.68; mol wt, 390 (ebullioscopic in benzene).

Distillation of the filtrate from a similar preparation of 3,  $n = 2$ , on a 2-mol scale gave 1.44 g of impure 2,  $n = 2$ , bp 100–120° (0.3 mm). The crude distillate was extracted with 20 ml of ligroin, the extracts were evaporated, the residue was dissolved in 20 ml of water and insolubles were removed by extraction with 2 × 2 ml of ligroin. The aqueous layer was evaporated to give 0.68 g (0.2%) of 2,6,9,12-tetraoxaspiro[3.9]tridecane: mass spectrum  $m/e$  188 (weak parent<sup>+</sup>), 189 (weak P + H<sup>+</sup>), and 158 (strong P<sup>+</sup> - CH<sub>2</sub>O); ir 3.45 and 3.52 (saturated CH), 8.7–9.2 (COC), 10.08, and 10.7  $\mu$  (oxetane ring); <sup>1</sup>H nmr  $\delta$  4.28 (s, 1, oxetane CH<sub>2</sub>), 3.92 (s, 1, CCH<sub>2</sub>) and 3.62 ppm (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O) with weak impurity peaks also present.

*Anal.* Calcd for C<sub>9</sub>H<sub>16</sub>O<sub>4</sub>: C, 57.43; H, 8.57. Found: C, 57.38; H, 8.48.

**2,6,9,12,15-Pentaoxaspiro[3.12]hexadecane (2,  $n = 3$ ) and 2,6,9,12,15,19,22,25,28,31-Decaoxadispiro[3.12.3.12]dotriacontane (3,  $n = 3$ ).** A mixture of 233.4 g (2.08 mol) of potassium *tert*-butoxide, 150.2 g (1.00 mol) of triethylene glycol, and 155.0 g (1.00 mol) of 3,3-bis(chloromethyl)oxetane was heated at reflux in 3 l. of *tert*-butyl alcohol. Two additions, each of 75.1 g (0.50 mol) of triethylene glycol, 77.5 g (0.50 mol) of 3,3-bis(chloromethyl)oxetane, and 114.4 g (1.02 mol) of potassium *tert*-butoxide, were made at 2–3-day intervals, and reaction finally continued for 5 days. Filtration and evaporation of volatiles gave residual oil which was extracted continuously with pentane for 3 days. Distil-

lation of the extract through a Vigreux column gave 150.3 g (32%) of 2,6,9,12,15-pentaoxaspiro[3.12]hexadecane and 119.9 g (26%) of crude 2,6,9,12,15,19,22,25,28,31-decaoxaspiro[3.12.3.12]dotriacontane as a distillation residue which largely crystallized.

Redistillation of 2,  $n = 3$ , through a spinning band still gave pure product: bp 97–98° (6  $\mu$ );  $n_D^{25}$  1.4785; ir 3.40 (sh) and 3.47 (saturated CH), 9.0 (COC), and 10.21  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.30 (s, 1, oxetane CH<sub>2</sub>), 3.83 (s, 1, CCH<sub>2</sub>), 3.62 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), and 3.57 ppm (s, 1, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>11</sub>H<sub>20</sub>O<sub>5</sub>: C, 56.88; H, 8.68; O, 34.44; mol wt, 232. Found: C, 56.81; H, 8.73; O, 34.41; mol wt, 232 (field ionization mass spectrum).

A sample of 3,  $n = 3$ , purified by recrystallization from acetone of the complex with KSCN and liberation from the complex by boiling xylene, crystallized, mp 52–53°.

Anal. Calcd for C<sub>22</sub>H<sub>40</sub>O<sub>10</sub>: C, 56.88; H, 8.68; O, 34.44; mol wt, 464. Found: C, 56.91; H, 8.69; O, 34.27; mol wt, 498 (ebullioscopic in benzene).

**3,3-Bis(*tert*-butoxymethyl)oxetane.** Dimethylformamide is also a suitable solvent if all the reactants are added at once. An attempt to carry out the reaction by addition of triethylene glycol and 3,3-bis(chloromethyl)oxetane to a solution of potassium *tert*-butoxide in dimethylformamide resulted in considerable substitution of *tert*-butoxide groups for chlorine in the oxetane.

A solution of 49.2 g (0.44 mol) of potassium *tert*-butoxide in 400 ml of dry dimethylformamide was stirred and heated under a nitrogen atmosphere. At 80–90°, the mixture darkened considerably, so addition of 30.0 g (0.20 mol) of triethylene glycol and 31.0 g (0.20 mol) of 3,3-bis(chloroethyl)oxetane in 200 ml of dimethylformamide was started. The temperature of the reaction mixture rose rapidly to 115° and remained near there until the addition was complete (45 min). After an additional 3 hr at 110°, the solution was cooled and neutralized with 2 ml of acetic acid. After removal of the solvent under reduced pressure, the product was dissolved in chloroform and the solution was filtered. Distillation of the filtrate gave a two-phase mixture of product and triethylene glycol, bp 40–100° (0.1  $\mu$ ). Redistillation of the upper layer gave 5.4 g (12%) of 3,3-bis(*tert*-butoxymethyl)oxetane: bp 44–46° (0.1  $\mu$ ); ir 3.36 and 3.48 (saturated CH), 9.2 (broad COC), 10.20  $\mu$  (oxetane ring);  $^1\text{H}$  nmr (CCl<sub>4</sub>)  $\delta$  4.25 (s, 2, oxetane CH<sub>2</sub>), 3.52 (s, 2, CCH<sub>2</sub>), and 1.17 ppm [s, 9, C(CH<sub>3</sub>)<sub>3</sub>].

Anal. Calcd for C<sub>13</sub>H<sub>26</sub>O<sub>3</sub>: C, 67.78; H, 11.37. Found: C, 67.91; H, 11.56.

**2,6,9,12,15,18-Hexaoxaspiro[3.15]nonadecane** (2,  $n = 4$ ). Reaction of 38.8 g (0.20 mol) of tetraethylene glycol, 47.0 g (0.42 mol) of potassium *tert*-butoxide, and 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane was carried out at reflux in 500 ml of *tert*-butyl alcohol. A second, equivalent addition of the three reagents was made after 1 day. Distillation of the pentane-soluble product in a molecular still gave 58.2 g (53%) of 2,6,9,12,15,18-hexaoxaspiro[3.15]nonadecane as a colorless oil: bp 105–108° (0.2  $\mu$ );  $n_D^{25}$  1.4771; mp 28–30°; ir 3.40 (sh) and 3.47 (saturated CH), 8.7–9.1 (COC), 10.23, and 10.68  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.32 (s, 1, oxetane CH<sub>2</sub>), 3.73 (s, 1, CCH<sub>2</sub>), 3.59 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), and 3.55 ppm (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>13</sub>H<sub>24</sub>O<sub>6</sub>: C, 56.50; H, 8.75; O, 34.74. Found: C, 56.49; H, 8.70; O, 34.78.

Equivalent or better yields were obtained with 3,3-bis(bromomethyl)oxetane. Yields were nearly as high when potassium *tert*-butoxide was replaced by NaOH (52% yield) or KOH (47% yield) in reactions involving 3,3-bis(bromomethyl)oxetane.

**2,6,9,12,15,18,21-Heptaoxaspiro[3.18]docosane** (2,  $n = 5$ ). Pentaethylene glycol was prepared by dropwise addition of 468 g (2.5 mol) of 1,2-bis(2-chloroethoxy)ethane to a solution of 331 g (5.0 mol) of 85% KOH pellets in 930 g (15 mol) of glycol stirred and heated at 110° under nitrogen. The addition was carried out at a rate sufficient to maintain a reaction temperature of 120° with no external heating (2 hr). The mixture was stirred and heated at 120° for an additional 3 hr, cooled, acidified with concentrated HCl, and distilled. Pentaethylene glycol, 213.9 g (36%),  $n_D^{25}$  1.4582, was obtained as a fraction of bp 148–154° (20  $\mu$ ).<sup>13</sup>

A mixture of 600 ml of *tert*-butyl alcohol, 47.0 g (0.42 mol) of potassium *tert*-butoxide, 47.6 g (0.20 mol) of pentaethylene glycol, and 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane was stirred at reflux under nitrogen for 5 days. The mixture was cooled and filtered, and the filter cake was rinsed with *tert*-butyl alcohol and dried to give 30.1 g of KCl. Removal of volatiles from the filtrate to 50° (0.5 mm) afforded 67 g of viscous residue, which was extracted continuously with pentane for 3 days. The extracts yielded 49.3 g of high-boiling residue. Distillation gave 38.5 g (60%) of 2,6,9,12,15,18,21-heptaoxaspiro[3.18]docosane, mainly bp

136–137° (1  $\mu$ ) in a molecular still:  $n_D^{25}$  1.4741; ir 3.40 (sh) and 3.47 (saturated CH), 9.0 (COC), and 10.21  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.29 (s, 1, oxetane CH<sub>2</sub>), 3.65 (s, 1, CCH<sub>2</sub>), 3.56 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), and 3.52 ppm (s, 3, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>15</sub>H<sub>28</sub>O<sub>7</sub>: C, 56.23; H, 8.81. Found: C, 56.51; H, 9.18.

An essentially equivalent result was obtained with 3,3-bis(bromomethyl)oxetane in place of 3,3-bis(chloromethyl)oxetane.

**2,6,9,12,15,18,21,24,27-Nonaoxaspiro[3.24]octacosane** (2,  $n = 7$ ) and **2,6,9,12,15,18,21,24,27,31,34,37,40,43,46,49,52,55-octadeca-oxaspiro[3.24.3.24]hexapentacontane** (3,  $n = 7$ ). To prepare heptaethylene glycol, a mixture of 1590 g (15 mol) of diethylene glycol and 200 g (5.0 mol) of NaOH pellets was stirred and heated to 110° under nitrogen. Dropwise addition of 468 g (2.5 mol) of 1,2-bis(2-chloroethoxy)ethane was carried out at a rate sufficient to keep the temperature near 120° without external heating; addition time was 1.5 hr. The mixture was heated and stirred at 120° for another 3 hr, cooled, filtered, and distilled through a Vigreux column. Heptaethylene glycol was obtained as 270.6 g (33%) of an oil, bp 207–213° (4.5  $\mu$ ),  $n_D^{25}$  1.4627.<sup>13</sup>

Reaction was carried out in 700 ml of *tert*-butyl alcohol using two additions, each of 65.2 g (0.20 mol) of heptaethylene glycol, 47.0 g (0.42 mol) of potassium *tert*-butoxide, and 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane. Distillation of the pentane-soluble products in a molecular still gave 58.0 g (35%) of 2,  $n = 7$ : bp 182–183° (0.3  $\mu$ ); ir 3.48 (saturated CH), 8.7–9.2 (COC), 10.23, and 10.65  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.37 (s, 1, oxetane CH<sub>2</sub>), 3.72 (s, 1, CCH<sub>2</sub>), 3.63 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), and 3.60 ppm (s, 5, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>19</sub>H<sub>36</sub>O<sub>9</sub>: C, 55.87; H, 8.88; O, 35.25. Found: C, 55.62; H, 8.66; O, 35.02.

The distillation residue slowly deposited crystals on standing. The mixture of solid and oil was crystallized from 1:1 ether-ligroin at –80°, from 1:1 ether-acetone at –80°, from 1:1 ether-acetone at 0°, and finally from ether at 0° to give 2.2 g of 3,  $n = 7$ , mp 42–43°. A second crop, 2.1 g, mp 40–41°, was obtained by concentration of the filtrates and two recrystallizations from ether at 0°, bringing the yield to 4.3 g (2.6%): ir (Nujol) 8.7–9.2 (COC), 10.07, 10.29, and 10.37  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.36 (s, 1, oxetane CH<sub>2</sub>), 3.67 (s, 1, CCH<sub>2</sub>), 3.61 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), 3.58 and 3.57 ppm (two singlets, combined area 5, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>38</sub>H<sub>72</sub>O<sub>18</sub>: C, 55.87; H, 8.88; O, 35.25; mol wt, 817. Found: C, 56.39; H, 8.58; O, 34.82; mol wt, 798 (ebullioscopic in benzene).

**2,6,9,12,15,18,21,24,27,30,33-Undeca-oxaspiro[3.30]tetratriacontane** (2,  $n = 9$ ). A mixture of 2252 g (15 mol) of triethylene glycol and 200 g (5.0 mol) of NaOH pellets was treated with 468 g (2.5 mol) of 1,2-bis(2-chloroethoxy)ethane as described above. Distillation through a Vigreux gave 251.2 g (24%) of orange oil, bp 235–249°,  $n_D^{25}$  1.4644. As expected for nonaethylene glycol, the product solidified slowly at 0°.<sup>14</sup>

Two additions, each of 82.8 g (0.20 mol) of nonaethylene glycol, 47.0 g (0.42 mol) of potassium *tert*-butoxide, and 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane, were made to a reaction carried out in 1 l. of *tert*-butyl alcohol as described above. From the pentane-soluble products there was isolated 22.0 g (11%) of 2,  $n = 9$ : bp 250–260° (1  $\mu$ ) in a molecular still; ir 3.45 (saturated CH), 8.7–9.1 (COC), 10.20, and 10.62  $\mu$  (oxetane ring);  $^1\text{H}$  nmr  $\delta$  4.37 (s, 1, oxetane CH<sub>2</sub>), 3.70 (s, 1, CCH<sub>2</sub>), 3.63 (s, 2, OCH<sub>2</sub>CH<sub>2</sub>O), and 3.60 ppm (s, 7, OCH<sub>2</sub>CH<sub>2</sub>O).

Anal. Calcd for C<sub>23</sub>H<sub>44</sub>O<sub>11</sub>: C, 55.63; H, 8.93; O, 35.44. Found: C, 55.88; H, 8.76; O, 35.76.

**2,9-Dioxa-6,12-dithiaspiro[3.9]tridecane** (4) and **2,9,16,22-Tetraoxa-6,12,19,25-tetrathiadispiro[3.9.3.9]hexacosane** (5). A mixture of 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane, 27.7 g (0.20 mol) of bis(2-mercaptoethyl) ether, 3.8 l. of absolute ethanol, and 16.0 g (0.40 mol) of sodium hydroxide pellets was stirred and refluxed under nitrogen for 1 day. Addition of the oxetane, mercaptoethyl ether, and sodium hydroxide was repeated and reaction was continued for another day. The addition was repeated once more and reaction was continued for an additional 3 days. The reaction mixture was filtered, the filtrate was evaporated to 500 ml, and supernatant was decanted. The viscous residue was extracted with 3 × 100 ml of hot ethanol; then the combined supernatant and extracts were evaporated to give high-boiling residue. Continuous ether extraction of this residue, removal of ether from the extracts, and sublimation of the extracted product at 100° (0.1 mm) gave 21.0 g (16%) of 4, mp 102–105°. An analytical sample, mp 104–105°, was prepared by resublimation at 75° (0.025 mm), followed by trituration of the sublimate with ether and drying: ir (Nujol) 9.03 (COC), 10.21, and 10.70  $\mu$

Table III  
Complexes of Macrocyclic Polyethers

Complex <sup>a</sup>	Mp, °C	Yield, %	Registry no.
2 (n = 3) · LiSCN	138–139	57	51652-74-5
2 (n = 3) · NaSCN	164–165	b	51652-75-6
2 (n = 4) · NaSCN	135.5–137	25	51652-76-7
2 (n = 4) · KSCN	105–109	55	51652-77-8
2 (n = 5) · NaSCN	127–128	72	51652-78-9
2 (n = 5) · KSCN	124–126	73	51652-79-0
2 (n = 5) · CaI <sub>2</sub> · H <sub>2</sub> O	176–178	77	51731-29-4
2[3 (n = 2)] · 3NaSCN	70	91	51652-80-3
7[3 (n = 2)] · 8KSCN	103–105	96	51652-81-4
3 (n = 3) · 2LiSCN	192–193	65	51652-83-6
3 (n = 3) · 2NaSCN	165–166	82	51652-84-7
3 (n = 3) · 2KSCN	140–141	55	51652-85-8
2(5) · NaSCN	167.5–169	87	51652-87-0

<sup>a</sup> Satisfactory analyses for C, H, N, and metal were recorded except for the complexes with 2 (n = 3). <sup>b</sup> Deliquescent complex which could not be recrystallized owing to a tendency to lose ligand.

(oxetane); <sup>1</sup>H nmr δ 4.22 (s, 1, oxetane CH<sub>2</sub>), 3.52 (s, 1, CCH<sub>2</sub>S) with rough triplets for AA'BB' at 230, 226, and 220 (1, CH<sub>2</sub>CH<sub>2</sub>O) and 172, 167, and 162 Hz (1, CH<sub>2</sub>CH<sub>2</sub>S).

Anal. Calcd for C<sub>9</sub>H<sub>16</sub>O<sub>2</sub>S<sub>2</sub>: C, 49.05; H, 7.32; S, 29.10; mol wt, 220. Found: C, 49.49; H, 7.31; S, 28.61; mol wt, 221 (ebullioscopic in benzene).

The involatile sublimation residue was kept molten at 90–95° and continuously extracted with heptane for 2 days. Evaporation of heptane from the extract and recrystallization from acetone gave 17.7 g of 5, mp 100–101°. A second crop, 1.9 g, mp 98.5–100°, was also obtained, for a total of 19.6 g (15%) of 5. An analytical sample, mp 100.5–101.5°, was prepared by recrystallization from acetone: ir (Nujol) 9.05 (COC), 10.15, and 10.53 μ (oxetane); <sup>1</sup>H nmr δ 4.35 (s, 1, oxetane CH<sub>2</sub>) and 3.14 (s, 1, CCH<sub>2</sub>S) with rough triplets for AA'BB' at 229, 223, and 217 (1, CH<sub>2</sub>CH<sub>2</sub>O) and 175.5, 169.5, and 163.5 Hz (1, CH<sub>2</sub>CH<sub>2</sub>S).

Anal. Calcd for C<sub>18</sub>H<sub>32</sub>O<sub>4</sub>S<sub>4</sub>: C, 49.06; H, 7.32; S, 29.10; mol wt, 440.7. Found: C, 49.41; H, 7.75; S, 29.32; mol wt, 438 (ebullioscopic in benzene).

Preparation of 4 and 5 in much more concentrated solution, 0.4 vs. 3.8 l. of absolute ethanol, resulted in only 2% of 4 and 4% of 5 along with considerable polymer.

**2,16-Dioxo-6,9,12,19,22,25-hexathiadispiro[3.9.3.9]hexacosane (6).** A mixture of 31.0 g (0.20 mol) of 3,3-bis(chloromethyl)oxetane, 30.8 g (0.20 mol) of bis(2-mercaptoethyl) sulfide, 16.0 g (0.40 mol) of sodium hydroxide, and 3.8 l. of absolute alcohol was stirred and refluxed under nitrogen for 1 day. Addition of the oxetane, sulfide, and sodium hydroxide was repeated and reaction was continued for another day. The addition was repeated once more and reaction was continued for an additional 3 days. Solvent was removed and the residue was heated at 70° during continuous extraction with benzene for 15 days. Solvent was removed from the extract and the residue was heated at 95° during continuous extraction with heptane for 12 days. Removal of solvent from the extract gave a viscous residue from which only a little oil was volatilized at 100° (0.4 mm). Crystallization of the residue from toluene gave 15.6 g (11%) of 6, mp 129–131°. An analytical sample was prepared by recrystallization from acetone: mp 131–132°; ir (Nujol) 10.21 and 10.57 μ (oxetane); <sup>1</sup>H nmr (benzene-d<sub>6</sub>) δ 4.23 (s, 1, oxetane CH<sub>2</sub>), 2.73 (s, 1, CCH<sub>2</sub>S), 2.54 (s, 2, SCH<sub>2</sub>CH<sub>2</sub>S).

Anal. Calcd for C<sub>18</sub>H<sub>32</sub>O<sub>2</sub>S<sub>6</sub>: C, 45.72; H, 6.82; S, 40.69; mol wt, 473. Found: C, 46.15; H, 6.84; S, 40.83; mol wt, 490 (ebullioscopic in benzene).

**HgCl<sub>2</sub> Complexes of the Macrocyclic Polysulfides 5 and 6.** Solutions of 0.44 g (0.001 mol) of 5 and of 0.54 g (0.002 mol) of mercuric chloride in glyme were mixed and concentrated to 8 ml total volume to give 0.66 g (93%) of the 1:1 complex, mp 174–175°.

Recrystallization from glyme gave an analytical sample, mp 174–174.5°.

Anal. Calcd for C<sub>18</sub>H<sub>32</sub>Cl<sub>2</sub>HgO<sub>4</sub>S<sub>4</sub>: C, 30.35; H, 4.53; Cl, 9.96; Hg, 28.17. Found: C, 30.36; H, 4.47; Cl, 9.89; Hg, 28.75.

A similar reaction of 0.47 g (0.001 mol) of 6 and 0.54 g (0.002 mol) of HgCl<sub>2</sub> gave 0.67 g (90%) of the 1:1 complex, mp ~205° dec.

Anal. Calcd for C<sub>18</sub>H<sub>32</sub>Cl<sub>2</sub>HgO<sub>2</sub>S<sub>6</sub>: C, 29.94; H, 4.33; Cl, 9.53; Hg, 26.95. Found: C, 30.48; H, 4.51; Cl, 9.49; Hg, 27.59.

**Preparation of Complexes.** Derivatives of the macrocyclic polyethers were prepared from alkali metal thiocyanates and calcium iodide starting with homogeneous acetone solutions of the salts. These solutions (filtered in the case of LiSCN to remove insolubles) were added either to the liquid macrocycle or to a solution of macrocycle in acetone. Concentration to low volume under nitrogen and scratching were generally effective in causing crystallization. Recrystallizations were from acetone or acetone-ether. Complexes of the monospiro macrocycles were far more soluble in acetone than those of the dispiro compounds and tended to be hygroscopic. Melting points were characteristically sharp. Ir spectra of the thiocyanate complexes were similar to those of the parent macrocycles with a band for thiocyanate added at ~4.9 μ. Alkali metal analyses by atomic absorption are considered to be less accurate than the other analyses; stoichiometry of the complexes was determined primarily by C, H, and N values. Table III summarizes the results of these syntheses.

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**Registry No.**—1, 78-71-7; 4, 51652-82-5; 5, 51652-86-9; 5 HgCl<sub>2</sub> complex, 51652-88-1; 6, 51652-89-2; 6 HgCl<sub>2</sub> complex, 51652-90-5; LiSCN, 556-65-0; NaSCN, 540-72-7; KSCN, 333-20-0; 2,2,9,9-tetrakis(chloromethyl)-4,7-dioxadecane-1,10-diol, 51652-91-6; 3-chloromethyl-3-[6-(3'-chloromethyl-3'-oxetanyl)-2,5-dioxahexyl]oxetane, 51652-92-7; 1,6-bis(3'-chloromethyl-3'-oxetanyl)-2,5-dioxahexane, 51652-93-8; 3,3-bis(*tert*-butoxymethyl)oxetane, 33867-48-0; 3,3-bis(bromomethyl)oxetane, 2402-83-7; 1,2-bis(2-chloroethoxy)ethane, 112-26-5; bis(2-mercaptoethyl) ether, 2150-02-9; bis(2-mercaptoethyl) sulfide, 3570-55-6; mercuric chloride, 7487-94-7; calcium iodide, 10102-68-8.

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- (10) The author is grateful to Dr. H. K. Frensdorff for determination of these values by potentiometric titration as described in ref 2.
- (11) As has been pointed out by a referee, there is no reason to assume other than the normal covalent structures for adducts of the cyclic polysulfides with mercuric chloride.
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