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Synthesis of Polymethyl Crown Ethers. A New Class of Lipophilic Crown Ethers

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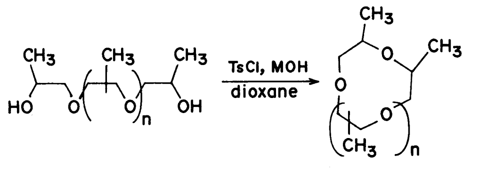
Synopsis. A new class of lipophilic polymethyl crown ethers were synthesized from oligopropylene glycols *via* the intramolecular cyclization, and the stability constants of some complexes in methanol were determined.

Crown ethers show a superior ability as catalyst in nucleophilic substitution reaction of solid-liquid phase-transfer systems. In the case of liquid-liquid systems, however, quaternary onium salts usually show a better performance than ordinary crown ethers. The differences in effectiveness as phase transfer catalysts between crown ethers and quaternary salts may be attributed to the difference of lipophilicity between crown complexed cations and quaternary onium cations.

To overcome this unsatisfactory ability of crown ethers, some investigators[1—4)] introduced a lipophilic group, such as an alkyl group or an acyl group, into the crown ether molecule. Although these lipophilic crown ethers also show excellent performance in the extraction and the transportation of salts, their preparation is tedious and require the use of uncommon reagents.

Previously we reported a new method for the preparation of crown ethers by the intramolecular cyclization of substituted and unsubstituted oligoethylene glycols.[5—7)] Now we have found that the intramolecular cyclization method could be successfully applied to the preparation of polymethyl crown ethers which have not been prepared previously except for tetramethyl-12-crown-4,[8)] from oligopropylene glycols. Introduction of polymethyl groups on the crown ring endows an additional lipophilicity in a different way from the known substituents and may improve the function of the crown ethers. The raw materials, penta-, hexa-, and heptapropylene glycol, were isolated from polypropylene glycol ♯400 by fractional distillations.

In the cyclization reaction of oligopropylene glycols, three kinds of condensations may generally take place, since the glycols are made up of three combinations of primary and secondary hydroxyl groups, depending on the origin of the oligopropylene glycols. Among these three kinds of condensations, there should be differences in reactivity and selectivity. Therefore, it is necessary to determine the ratio of the primary to secondary hydroxyl groups in the glycols. ^{1}H-NMR of acetylated hexapropylene glycol, examined as an example, showed a sextet signal at $\delta=4.91$ and no signal at around $\delta=4.0$—4.6, indicating the absence of primary hydroxyl group at least in the extent of NMR precision [CCl_4, δ; 1.0—1.3 (two d, 18H), 1.96 (s, 6H), 3.2—3.7 (m, 16H), 4.91 (sxt, 2H)]. Good yields of the polymethyl crown ethers prove the successful application of the intramolecular cyclization method to glycols which have two secondary hydroxyl groups.



1a-c 2a-c

a; n=3, M=Na **b**; n=4, M=K **c**; n=5 M=K

Scheme

The yields of polymethyl crown ethers seemed to be somewhat low compared with those of the cyclization of oligoethylene glycols in which two primary hydroxyl groups were concerned. This depended on the production of allyl ethers as by-product *via* elimination reaction.

To inspect the influences of polymethyl substitution on the complexation with metal cation, stability constants with sodium and potassium cations in methanol were determined and compared with those of unsubstituted crown ethers (Table 2). Polymethyl groups

Table 1. Preparation of polymethyl crown ethers

Crown ether	Yield[a)] / %	Bp θ_b/°C (Torr)
Pentamethyl-15-crown-5 (**2a**)	30	100 (0.1)
Hexamethyl-18-crown-6 (**2b**)	37	105 (0.05)
Heptamethyl-21-crown-7 (**2c**)	27	115 (0.05)

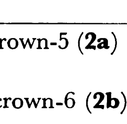
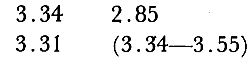
a) Yield of pure, isolated product; not optimized. b) Kugelrohr distillation. c) Satisfactory microanalyses obtained (C±0.34, H±0.06). The ^{1}H-NMR spectra (CCl_4) of **2** showed two signals at $\delta=1.04$ (d, $3(n+2)$H, CH_3) and at $\delta=3.0$—4.0 (m, $3(n+2)$H, OCH_2CHO). The mass spectra showed the parent peak, $m/e=117$  and $m/e=59$  respectively.

Table 2. Stability constants of polymethyl crown ethers with metal cations

Crown ether	log K'[a)]	
	Na^+	K^+
Pentamethyl-15-crown-5 (**2a**)	3.34	2.85
15-Crown-5	3.31	(3.34—3.55)[b)]
Hexamethyl- 18-crown-6 (**2b**)	2.94	3.86
18-Crown-6	4.32[c)]	6.10[c)]
Heptamethyl-21-crown-7 (**2c**)	2.34	3.27
21-Crown-7	2.46	4.41[c)]

a) In methanol, 25 °C. b) This value depends on the ratio of K^+ cation and the ligand. Considering the formation of 2 : 1 complex, log $K'_1=3.36$ and log $K'_2=2.62$ were obtained. c) Values reported in Ref.[9)] somewhat inhibit the complexation of crown ring with metal cations, probably due to the steric effect, and thence the rigidity of the crown rings. The stability constants of complexes, however, remained still high especially for hexamethyl-18-crown-6 with potassium cation, log $K'=3.86$, and for pentamethyl-15-crown-5 with sodium cation, 3.34. The catalytic activity and extraction activity of the polymethyl crown ethers are under investigation.

Experimental

The ^{1}H-NMR spectra were taken at 100 MHz on a JEOL JNM-PS-100 spectrometer using the tetramethylsilane internal standard. The infrared spectra were obtained on a Hitachi 260-10 spectrometer. The mass spectra were taken at an ionization potential of 70 eV on a Hitachi RMU-6E mass spectrometer.

Isolation of Oligopropylene Glycol. Commercial polypropylene glyco ♯400 were fractionally distilled to separate penta-, hexa-, and heptapropylene glycol (95—97 °C/0.05 Torr (1 Torr≈133.3 Pa), 116—118 °C/0.005 Torr and 155—158 °C/0.005 Torr, respectively). They showed a single peak in each gas liquid chromatogram (silicone gum SE30 10%, 270 °C).

Polymethyl Crown Ethers. General Procedure: A mixture of hexapropylene glycol (3.6 g, 0.01 mol), tosyl chloride (2.0 g, 0.01 mol) and dioxane (30 ml) was added to a suspension of pulverized potassium hydroxide (2.7 g, 0.04 mol) in dioxane (50 ml) over a period of 2 h under stirring at 60 °C, and stirred for an additional 4 h at the same temperature. The precipitate was separated off by filtration and washed twice with dioxane. After evaporation of the dioxane from the combined solution of filtrate and washings, the resulting viscous pale yellow liquid (4.2 g) was chromatographed on silica gel, and eluted with a mixture of hexane and acetone (95 : 5) to give a colorless liquid (**2b**, 1.3 g, 37%). The yields of the crown ethers are summarized in Table 1. Mutual relations of methyl groups on a macrocycle can not be resolved, because the raw oligopropylene glycols do not have regular structures, which are prepared by addition of propylene oxide to propylene glycol in alkaline conditions.

Isolation of Allyl Ethers. By-product allyl ethers were isolated from the crude product on a silica-gel column (hexane–acetone, 90 : 10), as a following fraction of the objective polymethyl crown ethers, IR (neat film); 3090, 1645, 1000, and 920 cm^{-1}, ^{1}H-NMR (CCl_4, δ); 3.98 (d+m, 2H), 5.02 (d+d, 1H), 5.18 (d+d, 1H), and 5.8 (m, 1H).

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