General Synthesis of Substituted and Unsubstituted Crown Ethers

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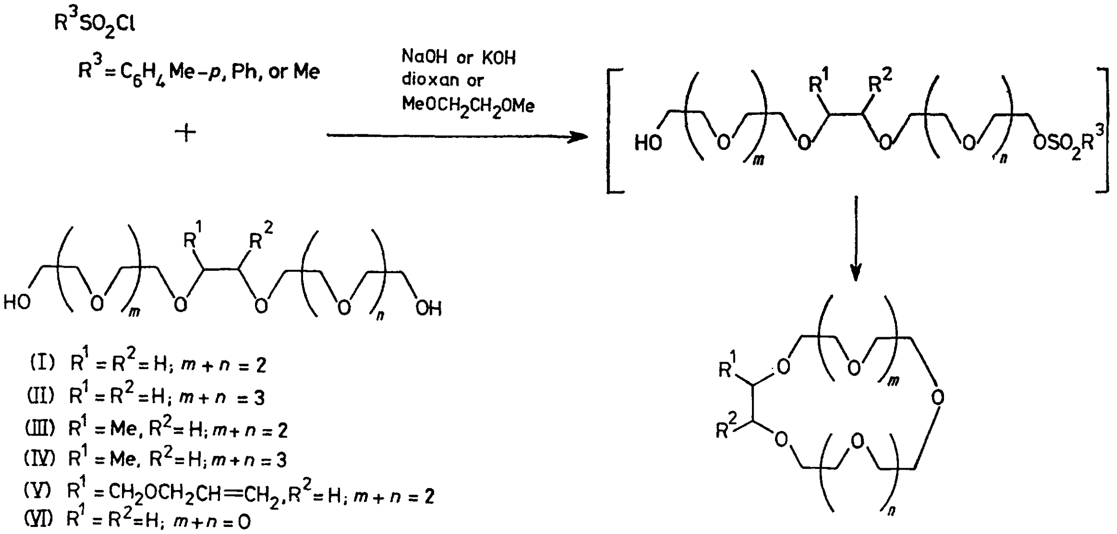
Summary Substituted and unsubstituted crown ethers were prepared in good yields by treatment of the corresponding polyethylene glycols with sulphonyl chlorides in the presence of alkali metal hydroxides, the metal ion acting as the template atom.

NUMEROUS examples of the use of crown ethers and other macrocyclic compounds have been reported recently.[1] The most widely adopted methods for the preparation of crown ethers are the reactions of aromatic *ortho*-dihydroxy compounds or polyethylene glycols with polyoxyethylene dichlorides or ditosylates.[2] However, because of synthetic difficulties, only a limited number of types of crown ethers are available. We report a convenient method for the preparation of various crown ethers with or without substituents.

Reactions of unsubstituted or substituted polyethylene glycols having suitable ethylenoxy units with sulphonyl chlorides such as toluene-*p*-sulphonyl chloride or methanesulphonyl chloride in the presence of an alkali metal hydroxide in an aprotic solvent afforded the corresponding crown ethers in fair to good yield.

For example, a solution of equimolar amounts of the polyether (I) (4·7 g) and toluene-*p*-sulphonyl chloride (3·8 g) in 20 ml of dioxan was slowly added with stirring to a suspension of powdered sodium hydroxide (3·2 g) in dioxan (50 ml) at room temperature. The product was filtered off, washed with dichloromethane, and, after removal of solvent, sodium chloride or sodium toluene-*p*-sulphonate complexes of 15-crown-5 were obtained as viscous liquids (6·1 g). 15-Crown-5 (2·2 g) was liberated by pyrolysis of the complexes *in vacuo*. Similarly, 18-crown-6 was obtained from (II) in 75% yield.



(I) $R^1 = R^2 = H$; $m + n = 2$
(II) $R^1 = R^2 = H$; $m + n = 3$
(III) $R^1 = Me$, $R^2 = H$; $m + n = 2$
(IV) $R^1 = Me$, $R^2 = H$; $m + n = 3$
(V) $R^1 = CH_2OCH_2CH{=}CH_2$, $R^2 = H$; $m + n = 2$
(VI) $R^1 = R^2 = H$; $m + n = 0$

TABLE. Synthesis of substituted and unsubstituted crown ethers

Starting materials	Reagents[a]	Product	% Yield[b]	
(I)	TsCl, NaOH, dioxan	15-Crown-5[c]	50	(68)
"	$MeSO_2Cl$, NaOH, dioxan	"	41	(48)
"	$PhSO_2Cl$, NaOH, glyme	"	44[d]	(96)
(II)	TsCl, KOH, dioxan	18-Crown-6[e]	75	(92)
(VI)	$PhSO_2Cl$, NaOH, dioxan	"	34	(52)
(III)	TsCl, NaOH, dioxan	Methyl-15-crown-5[f]	41	(—)
(IV)	TsCl, KOH, glyme	Methyl-18-crown-6[g]	53	(—)
(V)	TsCl, NaOH, dioxan	Allyloxymethyl-15-crown-5[h]	41	(—)

[a] Ts = *p*-$MeC_6H_4SO_2$; glyme = $MeOCH_2CH_2OMe$. [b] Yield of isolated crowns. Values in parentheses are determined by g.l.c. [c] *m/e* 220 (M^+); δ (CCl_4) 3·53 (s). [d] Complex could not be completely pyrolysed at *ca.* 200 °C. [e] *m/e* 264 (M^+); δ (CCl_4) 3·50 (s). [f] *m/e* 234 (M^+); δ (CCl_4) 1·04 (d, 3·2H) and 3·20—3·60 (s + m, 19H). [g] *m/e* 278 (M^+); δ (CCl_4) 1·06 (d, 3H) and 3·20—3·60 (s + m, 23H). [h] *m/e* 290 (M^+) and 219 ($M^+ - CH_2OCH_2$-$CH{=}CH_2$); δ (CCl_4) 3·40—3·68 (s + m, 21H), 3·92 (d, 1·9H), 5·13 (m, 1H), 5·22 (m, 1H), and 5·80 (m, 0·9H); $\nu_{max.}$ (neat) 2880, 1645, 1470, 1450, 1350, 1295, 1140—1080, 980, and 920 cm^{-1}.

Substituted polyethylene glycols (III), (IV), and (V) were prepared by the reaction of propane-1,2-diol and 3-allyloxymethylpropane-1,2-diol with ethylene oxide in the presence of $BF_3{\cdot}Et_2O$ and by successive fractional distillation under reduced pressure. From these adducts, as shown in the Table, substituted crown ethers were prepared as almost colourless liquids by procedures analogous to those described above.

Furthermore, 18-crown-6 was obtained in 34% yield from the reaction of (VI) with benzenesulphonyl chloride. This shows that cyclization occurs after the dimerization of the monobenzenesulphonated triethylene glycol.

(*Received*, 6*th March* 1978; *Com.* 233.)

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[1] J. J. Christensen, D. J. Eatough, and R. M. Izatt, *Chem. Rev.*, 1974, **74**, 351; G. W. Gokel and H. D. Durst, *Synthesis*, 1976, 168; *Aldrichimica Acta*, 1976, **9**, 3; F. Jeanne and A. Trichet, *Information Chimie*, 1976, **155**, 327; F. Vogtle and E. Weber, *Kontakte*, 1977, 11.

[2] C. J. Pedersen, *J. Amer. Chem. Soc.*, 1967, **89**, 7017; J. O. Dale and P. O. Christiansen, *Chem. Comm.*, 1971, 670; *Acta. Chem. Scand.*, 1972, **26**, 1471; R. N. Greene, *Tetrahedron Letters*, 1972, 1793; F. L. Cook, T. C. Caruso, M. P. Bryne, C. W. Bowers, D. H. Speck, and C. L. Liotta, *ibid.*, 1974, 4029; G. Jones, C. R. Ransom, and C. B. Reese, *Synthesis*, 1976, 515.