Macroheterocycles; XXIX. Synthesis of Novel Binuclear Crown Ethers

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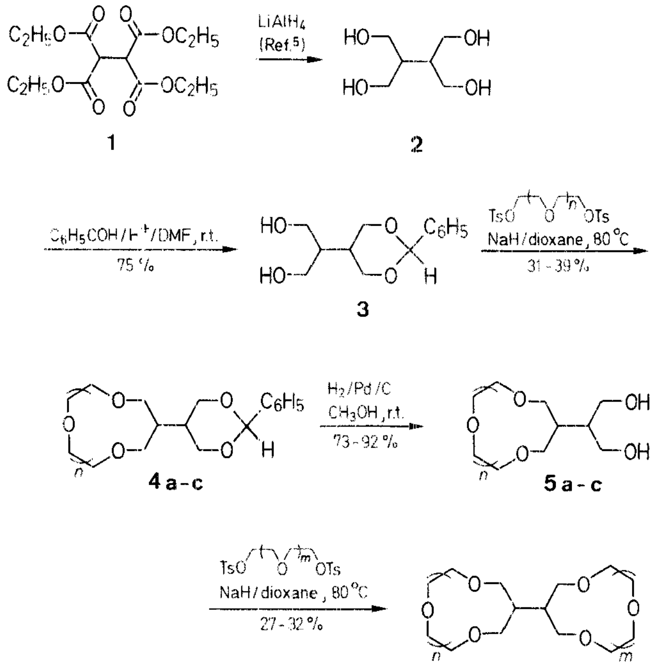
Syntheses of novel binuclear crown ethers from 2,3-dihydroxymethyl-1,4-butanediol is described. Ionic selectivity of the compounds obtained is discussed.

Binuclear crown ethers have received consiberable attention because of their unusual complexing properties[1,2]. We have previously reported the synthesis of some chiral binuclear crown ethers[3]. In continuation of this study, we describe here the synthesis of further novel crown ethers of this type. Starting tetraester **1** was prepared by the dimerization of sodium malonate as described previously[4]. Reduction of **1** by lithium aluminium hydride resulted in tetrol **2**[5]. Reaction of **2** with benzaldehyde, under conditions described for the synthesis of pentaerythritol monoacetal[6], in our case afforded only the bisacetal of tetrol **2**. Monoacetal **3** was prepared by the condensation of **2** with benzaldehyde in dimethylformamide at 25–30 °C. Reaction of **3** with polyethylene glycol ditosylates in the presence of sodium hydride gave crown ethers **4a–c**. Hydrogenolysis of **4a–c** over palladium resulted in bishydroxymethyl crown ethers **5a–c**. Binuclear crown ethers **6a–c** were prepared by the reaction of **5a–c** with polyethylene glycol ditosylates in dioxane in the presence of sodium hydride in about 30% yield. Compounds **3,4,5** and **6** were characterized by microanalyses as well as by mass-, IR and ^{1}H-NMR spectral data. A study of the complexing properties of the title compounds is in progress.

Here we report the results of ion-selectivity measurements carried out on compounds **6**. The cation-binding abilities of non-symmetrical crown ethers (13-crown-4, 16-crown-5 and 19-crown-6) differ greatly from those of the symmetrical ones (3m-crown-m)[7,8]. On the other hand, binuclear crown ethers possess higher selectivities for particular ions as compared with their monocyclic analogues due to cooperative action of two adjacent crown ether rings[9,10]. This suggested that non-symmetrical binuclear crown ethers **6a–e** would possess unusual ion-selectivity properties, and could have interesting practical applications.

The ion-selectives of compounds **6a–e** to alkali and alkaline-earth metal ions were determined potentiometrically[11]. Potentiometrical selectivity coefficients of liquid membranes containing crown ethers (1%-wt solution of a crown ether in chloroform) are illustrated in the following diagram.



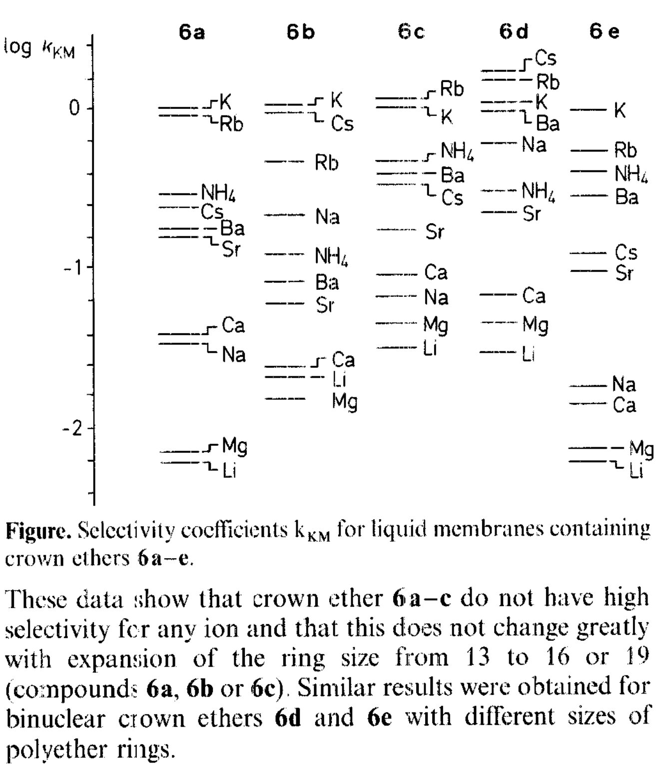


Figure. Selectivity coefficients k_{KM} for liquid membranes containing crown ethers **6a–e**.

These data show that crown ether **6a–c** do not have high selectivity for any ion and that this does not change greatly with expansion of the ring size from 13 to 16 or 19 (compounds **6a**, **6b** or **6c**). Similar results were obtained for binuclear crown ethers **6d** and **6e** with different sizes of polyether rings.

All crown ethers **6a–e** possess higher selectivities towards larger ions K^+, Rb^+, Cs^+ irrespective of the ring size. This is perhaps due to the possibility of sandwich complex formation.

2-Phenyl-5-(2-hydroxy-1-hydroxymethylethyl)-1,3-dioxane (3): Hydrochloric acid (5–7 drops) and benzaldehyde (15.9 g, 0.15 mol) are added to a stirred solution of tetrol **2** (15 g, 0.10 mol) in dry dimethylformamide (100 ml) at 25 °C, and the mixture is stirred for 5 h. After neutralization with a 25% solution of ammonium hydroxide (to pH 7), the solvent is removed under reduced pressure; a solution of sodium carbonate (1.5 g) in water (100 ml) is added to the residue, and the mixture is refluxed for 20 min. Precipitated tetrol **2** bisacetal is filtered, and the filtrate is extracted with chloroform (3 × 100 ml). The combined extracts are dried with sodium sulphate. The solution is concentrated to a volume of 100 ml, cooled and filtered to give dioxane **3**; yield: 11.3 g (75%); m.p. 132 °C.

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Table 1. Crown Ethers **4**, **5** and **6** Prepared.

Product No.	n	m	Yield[a] [%]	m.p. [°C] (solvent)	Molecular Formula[b]	MS (70 eV) m/e (M$^+$)	^{1}H-NMR (CDCl$_3$) δ [ppm]
4a	2	–	39	63–64 (hexane)	$C_{19}H_{28}O_6$ (352.4)	352	1.51 (m, 1H); 2.25 (m, 1H); 2.83–4.45 (m 20H); 5.35 (s, 1H); 7.01–7.5 (m, 5H)
4b	3	–	35	oil	$C_{21}H_{32}O_7$ (396.5)	396	1.51 (m, 1H); 2.33 (m, 1H); 2.75–4.25 (m 24H); 5.33 (s, 1H); 7.08–7.50 (m, 5H)
4c	2	–	31	oil	$C_{23}H_{36}O_8$ (440.5)	440	1.50 (m, 1H); 2.21 (m, 1H); 2.70–4.38 (m 28H); 5.30 (s, 1H); 7.01–7.45 (m, 5H)
5a	2	–	92	oil	$C_{12}H_{24}O_6$ (264.3)	264	1.98 (m, 2H); 3.35–3.85 (m, 22H)
5b	3	–	90	oil	$C_{14}H_{28}O_7$ (308.4)	308	1.95 (m, 2H); 3.25–3.91 (m, 26H)
5c	4	–	73	oil	$C_{16}H_{32}O_8$ (352.4)	352	1.88 (m, 2H); 2.90–3.90 (m, 30H)
6a	2	2	27	117 (hexane)	$C_{18}H_{34}O_8$ (378.4)	378	1.86 (m, 2H); 3.21–3.76 (m, 32H)
6b	3	3	31	oil	$C_{22}H_{42}O_{10}$ (466.6)	466	2.38 (m, 2H); 2.83–3.95 (m, 40H)
6c	4	4	29	oil	$C_{26}H_{50}O_{12}$ (554.7)	554	1.96 (m, 2H); 3.28–3.76 (m, 48H)
6d	2	3	32	oil	$C_{10}H_{38}O_9$ (422.5)	422	2.01 (m, 2H); 3.16–3.75 (m, 36H)
6e	2	4	27	oil	$C_{22}H_{42}O_{10}$ (466.6)	466	1.81 (m, 2H); 3.16–3.83 (m, 40H)

[a] The purity of all products was determined by GLC. (1.5 m column of SP 2100, 5% on Chromaton N-Super) and was not less than 97%.

[b] Satisfactory microanalyses obtained: C ±0.26, H ±0.20.

Table 2. Selectivity Coefficients, k_{KM}^{Pot}, for Liquid Membranes Containing Crown Ethers **6a–e**

Cation	**6a**	**6d**	**6b**	**6e**	**6c**
Li^+	0.006	0.026	0.021	0.006	0.031
Na^+	0.033	0.574	0.216	0.018	0.062
K^+	1.000	1.000	1.000	1.000	1.000
Rb^+	0.758	1.219	0.444	0.438	1.126
Cs^+	0.231	1.269	0.956	0.125	0.329
NH_4^+	0.281	0.304	0.120	0.413	0.452
Ba^{2+}	0.203	1.030	0.097	0.366	0.430
Sr^{2+}	0.187	0.247	0.074	0.121	0.211
Ca^{2+}	0.017	0.078	0.029	0.018	0.107
Mg^{2+}	0.013	0.051	0.018	0.009	0.053

$C_{13}H_{18}O_4$	calc.	C 65.54	H 7.61
(238.3)	found	65.32	7.59

^{1}H-NMR (CDCl$_3$, HMDS): δ = 1.43 (m, 1H); 2.29 (m, 1H); 3.47–4.57 (m, 8H); 5.46 (s, 1H); 7.41 ppm (m, 5H).

Crown Ethers 4a–c; General Procedure:

A solution of compound **3** (0.025 mol) in dry dioxane (50 ml) is added to sodium hydride suspension (2.4 g, 0.10 mol) in dioxane (150 ml), and the mixture is stirred under nitrogen at 70 °C for 1 h. A solution of polyethylene glycol ditosylate (0.025 mol) in dry dioxane (200 ml) is added and stirring is continued at 80 °C for 10–12 h. After cooling, the excess sodium hydride is destroyed by the addition of cold water (17.5 ml). Dioxane is removed under reduced pressure, and the residue is dissolved in water (50 ml) and extracted with hot hexane (3 × 100 ml). The hexane extracts are combined and dried with magnesium sulfate. The hexane is removed under reduced pressure. Products **4a–c** are isolated by chromatography on alumina with petroleum ether (40–70 °C) / isopropanol, 10:0.25, as eluent.

Crown Ethers 5a–c; General Procedure:

A suspension of crown ether **4** (0.02 mol) and 10% palladium on carbon (1 g) in methanol (100 ml) are hydrogenated at room temperature under 1 atmosphere hydrogen pressure for 5 h. The catalyst is filtered, and solvent is evaporated under reduced pressure to give crown ethers **5a–c**.

Binuclear crown ethers 6a–e; General Procedure:

The reaction of crown ethers **5** (7.5 mmol) with polyethylene glycol ditosylates (7.5 mmol) is carried out at 80 °C for 14–16 h according to the above procedure for crown ethers **4**. Products **6a–e** are isolated by chromatography on alumina (hexane / isopropanol, 10:0.6, as eluent).

Received: August 21, 1985
(Revised form: November 30, 1985)

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