Synthesis of a Cation Complexing Doubly *N,N'*-Bridged Bis-(1,7-dioxa-4,10-diazacyclododecane)

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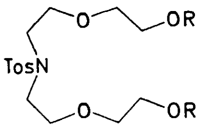
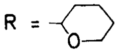
Summary Two molecules of diaza-12-crown-4 can be linked by two ethylene bridges between nitrogen atoms in two controlled steps, the last of which needs Li cation as a template, although Na cation is most strongly complexed by the tricyclic cryptand-like product.

RECENTLY we have reported[1] the synthesis of organic ligands consisting of two mono-aza-12-crown-4 rings linked together by a single alkylene bridge between nitrogen atoms. Very enhanced complexation of alkali cations was observed, in particular of the Na cation when the bridge is $-CH_2CH_2-$

We now report the synthesis of a cryptand-like ligand (**8**) consisting of two diaza-12-crown-4 rings joined by two such bridges.†

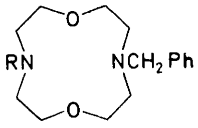


(1) R =



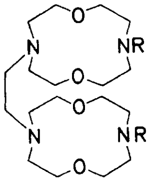
(2) R = H

(3) R = SO_2Me



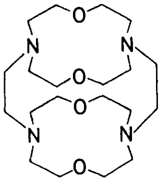
(4) R = Tos

(5) R = H



(6) R = CH_2Ph

(7) R = H



(8)

Tos = p-$MeC_6H_4SO_2$

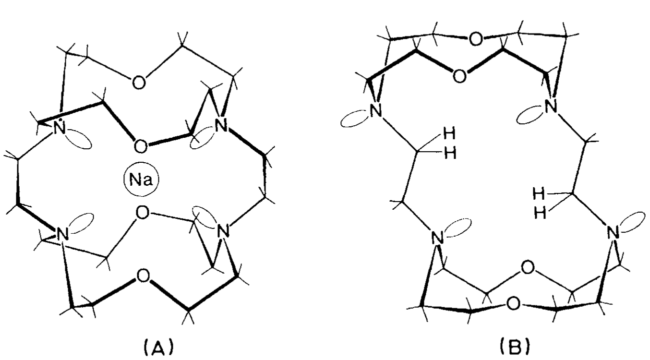
The tetrahydropyran-2-yl ether of 2-(2-chloroethoxy)-ethanol (2 equiv.) reacted with toluene-*p*-sulphonamide in dimethylformamide in the presence of suspended NaH to give the bis-tetrahydropyran-2-yl ether (**1**). Treatment with toluene-*p*-sulphonic acid in methanol yielded the free diol (**2**), which was converted into the bis-methanesulphonate (**3**) with methanesulphonyl chloride in pyridine. Compounds (**1**)—(**3**) were oils whose purity was checked by n.m.r., and mass spectroscopy and t.l.c. Adapting our procedure[1,2] for preparing *N*-alkyl derivatives of mono-aza-12-crown-4 by double alkylation of primary amines with 1,11-di-iodo-3,6,9-trioxaundecane, we treated the bis-methanesulphonate (**3**) with benzylamine in refluxing acetonitrile containing suspended Na_2CO_3 for 48 h to give the unsymmetrically disubstituted diazacrown (**4**), m.p. 95 °C in 58% yield based on (**1**). $LiAlH_4$ reduction in tetrahydrofuran yielded the mono-substituted diaza-crown (**5**), m.p. 48—50 °C (91%).

The first bridge was established by refluxing an acetonitrile solution containing the diaza-crown (**5**) and ethylene bistoluene-*p*-sulphonate, in the presence of suspended Na_2CO_3, for 48 h. The crude product was an oil which solidified on standing and had the correct spectral data for the bis-crown (**6**) (*m/e* 554). It was directly debenzylated by hydrogenolysis over Pd/C to yield the bis-crown (**7**) (distilling with a bath temp. rising to 240 °C at 0·05 mmHg, m.p. 98—100 °C, *m/e* 374) in a yield of 85% based on (**5**).

The closing of the second bridge with ethylene bistoluene-*p*-sulphonate presented difficulties. In the absence of a template cation only polymeric material was formed, while the presence of sodium salts (carbonate or toluene-*p*-sulphonate) led only to complexation of the ligand (**7**) and no reaction. In view of the lower co-ordination number of lithium, it was expected that this cation might leave the two weakest donor atoms (> NH) free to undergo reaction, but still be sufficiently strongly sandwiched intramolecularly to exert a template effect.‡ In fact, reaction took place when a solution of the bis-crown (**7**), dried lithium toluene-*p*-sulphonate, ethylene bistoluene-*p*-sulphonate, and ethyldiisopropylamine in acetonitrile was heated in a sealed tube at 105 °C for 4 days. Contact with a brine solution during work-up led to the isolation in 80% yield of the crystalline sodium toluene-*p*-sulphonate complex ('cryptate') of the cage ligand (**8**) ('cryptand') for which the chemical ionization mass spectrum (isobutane) corresponded to the dissociated protonated ligand [*m/e* 401, $(M + 1)^+$], while the field-desorption mass spectrum corresponded to the cation complex [*m/e* 423, $(M + 23)^+$]. The ^{13}C n.m.r. spectrum of this complex in acetonitrile showed three lines for the ligand in the expected intensity ratio 8 : 4 : 8 with shifts very close to those observed for chemically comparable carbon atoms of the complexed singly bridged bis-crown ligand[1] and the related simple aza-crown carrying a 2-methoxyethyl side arm (Table). These shifts did not change after passage through a cation exchange resin or a mixed-bed ion exchange resin (elution with water, then with aq. dimethylamine). Pyrolysis *in vacuo* (150—220 °C at 0·05 mmHg) liberated the ligand, m.p. 144—149 °C, which had all three ^{13}C lines moved by about 4 p.p.m. downfield, similar to what is observed for the related ligands (Table). This means[3] that the conformation (A) (Figure) of the complexed ligand,

TABLE. ^{13}C N.m.r. chemical shifts in CD_3CN for free and Na^+-complexed aza-crown ligands.

		Ring OCH_2	Ring NCH_2	Bridge NCH_2
4,4′; 10,10′-Bis-ethylene-bis-(1,7-dioxa-4,10-diazacyclododecane) (**8**)	Free	69·3	55·9	56·2
	Compl.	65·8	51·8	52·2
10,10′-Ethylenebis-(1,4,7-trioxa-10-azacyclododecane)[1]	Free	71·1—71·9	56·6	56·0
	Compl.	65·2—66·7	52·4	52·4
10-(2-Methoxyethyl)-1,4,7-trioxa-10-azacyclododecane[2]	Free	71·0—71·8	56·6	56·9
	Compl.	65·6—66·9	51·7	54·4



FIGURE

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† 7,16,21,26-Tetraoxa-1,4,10,13-tetra-azatricyclo[11.5.5.5^{4,10}]octacosane.

‡ Titration of the ligand (**7**) in acetonitrile with $LiClO_4$ revealed complex formation with 1 : 1 stoicheiometry (intramolecular sandwich).

having all nitrogen lone pairs pointing into the cavity, is not retained by the free ligand. Space-filling molecular models do not allow much conformational choice for this tricyclic molecule and suggest that two of the nitrogen lone pairs are turned out and that both 12-membered rings adopt a conformation with downfield δ-interactions and a reduced number of upfield γ-interactions[3] (B, Figure).

When the free ligand is contacted with a salt solution containing Li, Na, and K cations and Br and BF_4 anions, a complex with $NaBF_4$ crystallizes (m.p. > 310 °C). The *X*-ray structure determination[4] confirms the expected cubic arrangement of the eight donor atoms and identical helicity of the ten ethylene units in each molecule. Further complexation studies will be reported in the full paper.

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[3] G. Borgen, J. Dale, K. Daasvatn, and J. Krane, *Acta Chem. Scand., Sect. B.*, 1980, **34**, 249.
[4] P. Groth, unpublished work.