1,5,9-Trioxacyclododecane and 3,3,7,7,11,11-Hexamethyl-1,5,9-trioxacyclododecane: Novel Lithium Cation Complexing Agents

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12-Crown-3 and its hexamethyl derivative, obtained in good yield from oxetane and from 3,3-dimethyloxetane, give stronger complexation than the corresponding 16-crown-4 ligands, and the high selectivity for lithium as compared with sodium and magnesium is retained for Me_6-12-crown-3, but is lost for 12-crown-3 owing to the formation of sandwich complexes; *X*-ray crystal structures are reported for 12-crown-3·LiNCS, Me_6-12-crown-3·$LiClO_4$, and Me_6-12-crown-3.

The crown ethers with a 1,4-relationship between neighbouring ether oxygen atoms have a natural geometry that best matches alkali and alkaline-earth metal cations of intermediate size (Na^+, K^+, Rb^+, Ca^{2+}, Sr^{2+}, or Ba^{2+}). They therefore show a marked, although far from complete, selectivity against the smaller Li^+ and Mg^{2+} cations and the larger Cs^+ cation.[1] When neighbouring ether oxygen atoms have a 1,5-relationship, their natural geometry should allow a tighter folding to fit smaller cations, and it has in fact been found[2,3] that 1,5,9,13-tetraoxacyclohexadecane and its 3,3,7,7,11,11,15,15-octamethyl derivative complex Li^+ with a high selectivity against Na^+ and K^+. However, the complexation was too weak to compete with solvation of Li^+ in water and in methanol, and had to be studied in $CHCl_3$ or $ClCH_2CH_2Cl$.

These 16-crown-4 compounds have been known for a long time as major crystalline tetrameric by-products when oxetane and 3,3-dimethyloxetane are polymerized with BF_3.[4] The corresponding trimeric products have never been isolated, although 12-crown-3 has been recognized analytically by g.l.c.–mass spectrometry as a minor product in the polymerization of oxetane.[5,6]

We now report that 12-crown-3 can be isolated in 40% yield as a liquid, b.p. 101—102 °C at 12 mmHg, from 0.05 M solutions of oxetane in CH_2Cl_2 that have been left at room temperature for 1 day with BF_3 as catalyst; the yield of 16-crown-4 is only 10%. With 3,3-dimethyloxetane the reaction is slower (15 days), and BF_3 must be replenished repeatedly. When the crude product was neutralized immediately with NH_3, g.l.c.–mass spectrometry revealed that substantial quantities of a homologous series of fluorohydrins, especially 11-fluoro-4,8-dioxa-2,2,6,6,10,10-hexamethylundecan-1-ol, were present along with the cyclic oligomers. If additional BF_3 is introduced when the monomer has been consumed, the fluorohydrins cyclize to the corresponding crown ethers, and Me_6-12-crown-3, m.p. 55—56 °C, can be isolated in a total yield of 20%; the yield of Me_8-16-crown-4 is only 5%.

Titration of 12-crown-3 in CD_3CN–CD_3OD (95 : 5) with solid $LiClO_4$ monitored by ^{13}C n.m.r. spectroscopy resulted in a 4.5 p.p.m. downfield shift for the α-CH_2 signal [Figure 1(a)]. The curve shape indicated a strong 1 : 1 complex (K >1000) and a weaker 2 : 1 complex. A similar titration of 16-crown-4 [Figure 1(b)] indicated a weak 1 : 1 complex (K *ca.* 100), and competition experiments confirmed that Li^+ selects the twelve-membered in preference to the sixteen-membered ring. Me_6-12-crown-3 [Figure 1(c)] gave a much weaker complex (K *ca.* 5), while Me_8-16-crown-4 did not respond in this medium. When $NaClO_4$ was used, no shift displacement was observed for the 16-crown-4 ligands or Me_6-12-crown-3,

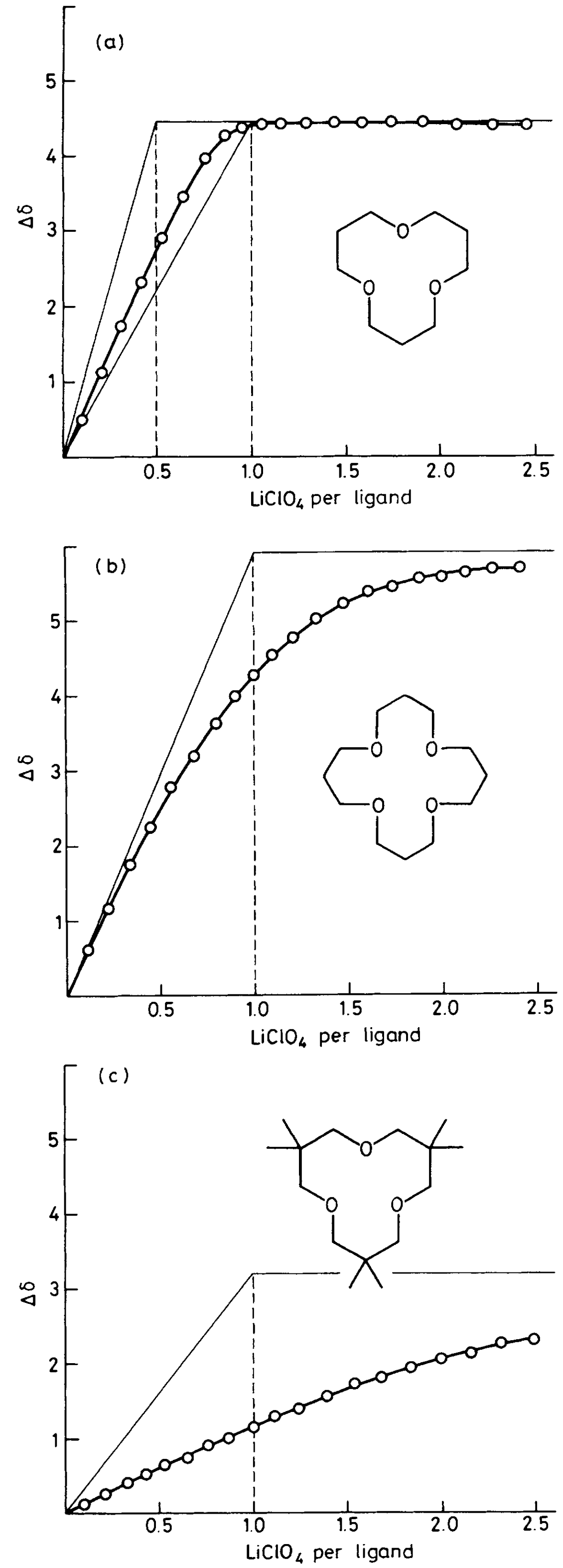

Figure 1. Titration in CD_3CN–CD_3OD (95 : 5) with solid $LiClO_4$ of (a) 12-crown-3, (b) 16-crown-4, and (c) Me_6-12-crown-3.

but a strong 2 : 1 complex (K >1000) was formed with 12-crown-3. Also Mg^{2+}, Ca^{2+}, and K^+ were complexed by 12-crown-3.

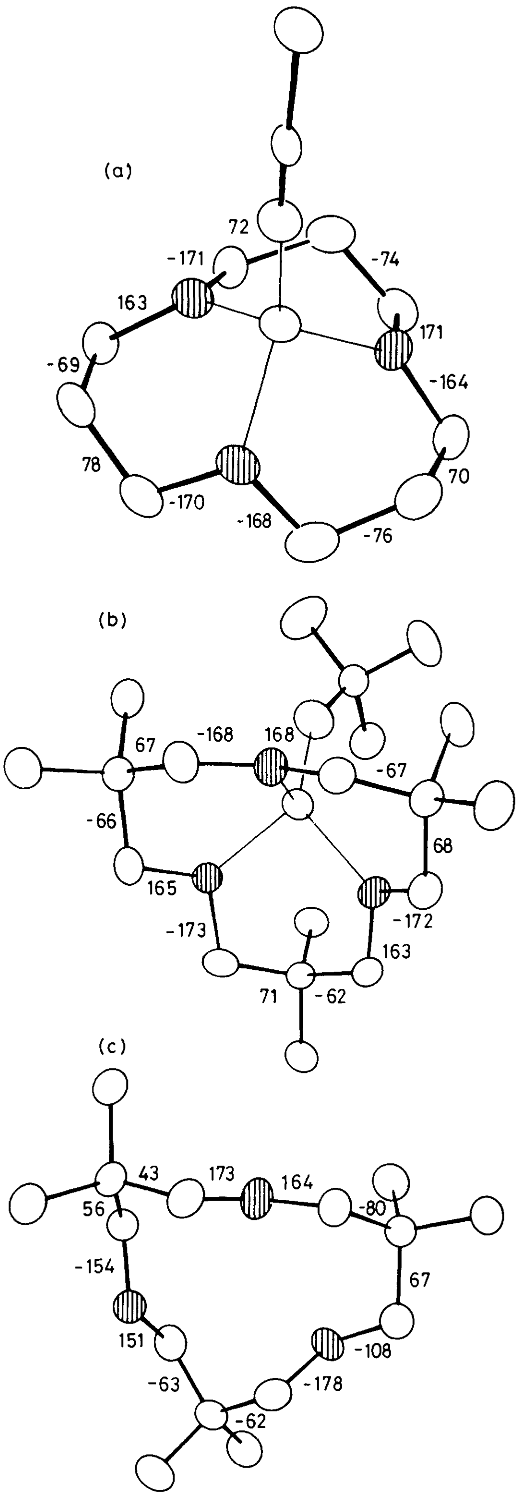

Figure 2. Crystal structures of (a) 12-crown-3·LiNCS, (b) Me_6-12-crown-3·$LiClO_4$, and (c) uncomplexed Me_6-12-crown-3. Ring-skeletal torsion angles are indicated.

The rates of decomplexation were studied by dynamic n.m.r. in $ClCH_2CH_2Cl$ on 1 : 1 mixtures of free ligand and $LiClO_4$ complex. Unexpectedly, the barrier is much lower for the stronger 12-crown-3$^-$ complex than for the weaker Me_6-12-crown-3 complex (<11 against >16 kcal mol^{-1}). A similar observation has already been made for the corresponding sixteen-membered ring complexes[3] (13 kcal mol^{-1} for 16-crown-4 against 17 for Me$_8$-16-crown-4). Also, a comparison between LiClO$_4$ complexes of 12-crown-3 and 16-crown-4 in CDCl$_3$ reveals a lower barrier for the stronger complex (*ca.* 10 against 13 kcal mol^{-1}). This is all in contrast with the parallelism often observed between high complexation strength and slow decomplexation rate.[7,8]

The crystal structures of the LiNCS complex of 12-crown-3 [Figure 2(a)] and the LiClO$_4$ complex of Me$_6$-12-crown-3 [Figure 2(b)] reveal essentially the same non-angular diamond-lattice conformation[9] that is forbidden for cyclododecane (interior hydrogen repulsion) and for the free ligand (oxygen lone-pair repulsion). The Li$^+$ cation is tetrahedrally four-co-ordinated, having contact with the counter-ion. The free ligand [Figure 2(c)] is entirely different and can be characterized[9] as either biangular [84] or quadrangular [4431] with some unfavourable torsion angles.†

We propose that relief of conformational strain in the free 12-crown-3 ligand is part of the driving force for its strong complexation. Such a driving force is absent in 16-crown-4 since the free ligand has already a perfectly strain-free diamond-lattice conformation.[9—11] This explains why complexation is weak even though Li$^+$ attains five-co-ordination (of square pyramidal geometry).[12]

We further propose that the Li$^+$ selectivity found for Me$_6$-12-crown-3 is due to the 'axial' methyl groups hindering sandwich formation for cations with higher co-ordination number requirements. In the 16-crown-4 complexes, the folding of the ligand itself hinders further access to the cation.

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† *Crystal data:* C$_9$H$_{18}$O$_3$·LiSCN [Figure 2(a)], M = 239, monoclinic, space group $P2_1$, a = 7.037(4), b = 13.233(5), c = 7.106(7) Å, β = 104.84(6)°, U = 639.7(7) Å^3, Z = 2, D_c = 1.24 g cm^{-3}. The structure was solved by direct methods and refined to R = 0.052 using 1086 unique reflections with $I > 2.5\sigma(I)$ measured with a Nicolet P3 diffractometer at −150 °C. C$_{15}$H$_{30}$O$_3$·LiClO$_4$ [Figure 2(b)], M = 364, triclinic, space group $P\bar{1}$, a = 8.686(2), b = 10.980(2), c = 10.997(2) Å, α = 113.03(2), β = 90.83(2), γ = 91.61(2)°, U = 964.5 Å^3, Z = 2, D_c = 1.25 g cm^{-3}. The structure was solved by direct methods and refined to R = 0.064 using 1948 unique reflections with $I > 2.5\sigma(I)$ measured with a Nicolet P3 diffractometer at −150 °C. C$_{15}$H$_{30}$O$_3$ [Figure 2(c)], M = 258, monoclinic, space group $P2_1/n$, a = 5.942(1), b = 15.944(4), c = 17.116(4) Å, β = 97.82(2)°, U = 1606.6(5) Å^3, Z = 4, D_c = 1.07 g cm^{-3}. The structure was solved by direct methods and refined to R = 0.046 using 1795 unique reflections with $I > 2.5\sigma(I)$ measured with a Nicolet P3 diffractometer at −150 °C. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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