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Synthesis and X-Ray Crystal Structures of Three Isomeric Macrobicyclic Polyethers having similar Melting Points and different Complexing Power for Alkali-metal Cations

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Summary Three isomeric macrobicyclic polyethers, $C_{28}H_{42}O_8$, each substituted by one benzene and two cyclohexane rings and melting at *ca.* 133 °C, have been characterised by X-ray crystal structure analyses and the relative configurations correlated with the large differences in stability constant with alkali-metal salts; one isomer forms a 1:1 methanol solvate.

WE have shown that neutral bicyclic polyethers which contain two¹ or three² benzene rings as substituents are powerful complexing agents for alkali-metal cations. To investigate factors which influence the selectivity we have now synthesised three isomeric macrobicyclic polyethers having one benzene and two cyclohexane rings as substituents which differ only in the relative configurations at the cyclohexane ring junctions.

Hydrogenation of the dibenzo-14-crown-4-*cis*-diol (1) with a ruthenium catalyst gave a mixture from which the three possible isomers, (2a)–(2c), expected from *cis*-hydro-

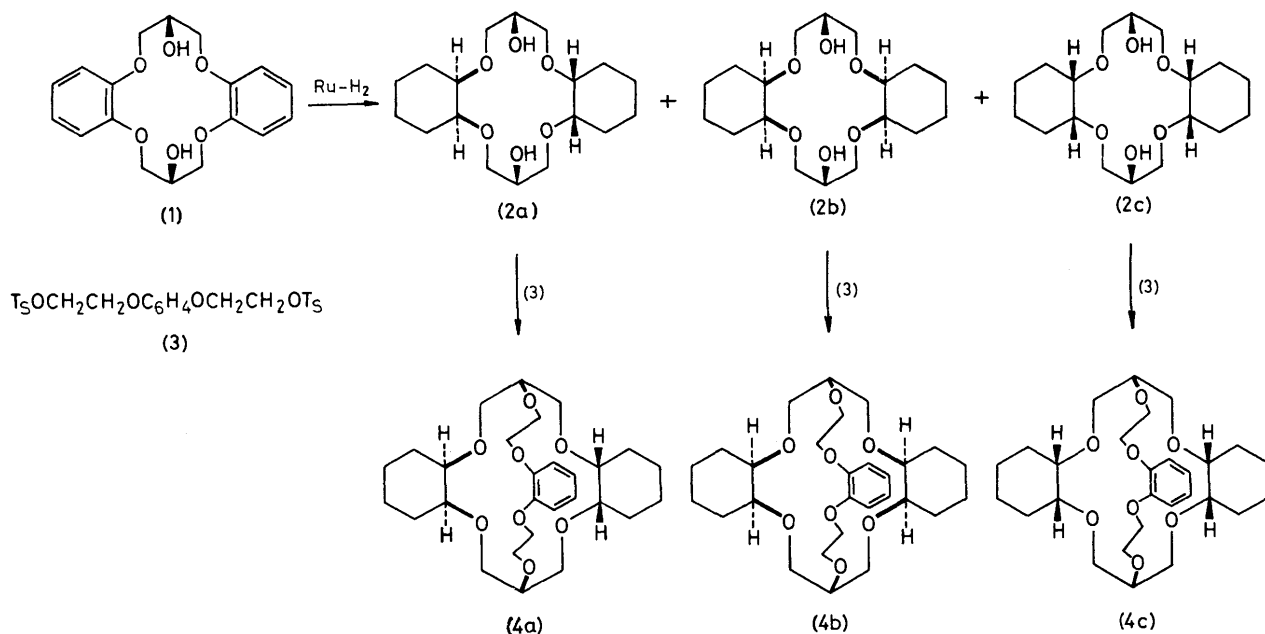
genation across the ring junctions, have been isolated by fractional crystallisation. They can be distinguished by their melting points, see the Table. Each was subsequently treated with the ditosylate (3) to yield the corresponding macrobicyclic polyethers (4a)–(4c) (Scheme). These may be recrystallised from various solvents to yield unsolvated compounds each of which melts at *ca.* 133 °C; there are significant differences in the 'fingerprint' region of the i.r. spectra; one characteristic band for each isomer is given in the Table. Satisfactory elemental analyses have been obtained. The isomer (4c) was sparingly soluble in methanol from which it deposited crystals having 1:1 stoichiometry of MeOH to (4c); these have a subtly different i.r. spectrum to that of the pure compound and show a sharp band at ν 3555 cm^{-1} (OH).

Formation constants for 1:1 complexes between compounds (4a)–(4c) and alkali-metal halides in methanol were determined by the e.m.f. method.³ The values, see the Table, show very significant differences between isomers; all highest values occur with potassium.

TABLE

Isomer	M.p. of (2) °C	M.p. of (4) °C	Diagnostic i.r. band ^a of (4) ν/cm^{-1}	Log K_f^b (methanol) at 25 °C			
				NaBr	MX: (4), 1:1 KBr	RbCl	CsCl
a	137	135	980	5.86	6.50	4.62	3.58
b	118	133	1001	7.86	8.18	7.16	5.01
c	170	133	822	4.13	4.65	2.42	1.85

^a In Nujol mull. ^b K_f (1 mol⁻¹) = $[M^+ (4)] / [M^+][(4)]$



SCHEME. (4a): 21*R*,22,23,24,25,26*S*,29*S*,30,31,32,33,34*R*-dodecahydro-1,4,7,14,17,20,28,35-octaoxa[2^{3,29},2^{18,34}][7.7]orthocyclophane. (4b): 21*R*,22,23,24,25,26*S*,29*R*,30,31,32,33,34*S*-dodecahydro-1,4,7,14,17,20,28,35-octaoxa[2^{3,29} *syn*, 2^{18,34} *syn*][7.7]orthocyclophane. (4c): 21*S*,22,23,24,25,26*R*,29*S*,30,31,32,33,34*R*-dodecahydro-1,4,7,14,17,20,28,35-octaoxa[2^{3,29} *anti*, 2^{18,34} *anti*][7.7]orthocyclophane. Ts = tosyl.

To establish the constitution of the isomers the crystal structures of (4a), (4b), and 1:1 MeOH:(4c) were determined by *X*-ray diffraction. For all three, intensities were measured on a CAD4 diffractometer with Mo-*K*_α radiation; the phase problem was solved by direct methods and parameters, including anisotropic vibration for the oxygen atoms, obtained by full-matrix refinement.⁴ Hydrogen atoms were located unequivocally.

Crystal data: (4a), C₂₈H₄₂O₈, *M* = 506.6, monoclinic, space group *P*2₁/*a*, *a* = 15.613(2), *b* = 21.492(4), *c* = 8.021(1) Å, β = 96.99(2)°, *U* = 2671.4 Å³, *D*_o = 1.26(1), *D*_c = 1.259 g cm⁻³, *Z* = 4, *R* = 0.066 for 2163 observed reflections, (|*F*| ≥ 4σ*F*). (4b), C₂₈H₄₂O₈, *M* = 506.6, triclinic, space group *P* $\bar{1}$, *a* = 8.842(2), *b* = 16.702(6), *c* = 10.050(3) Å, α = 114.10(3), β = 98.97(2), γ = 91.22(2)°, *U* = 1332.3 Å³, *D*_o = 1.28(1), *D*_c = 1.263 g cm⁻³, *Z* = 2, *R* = 0.060 for

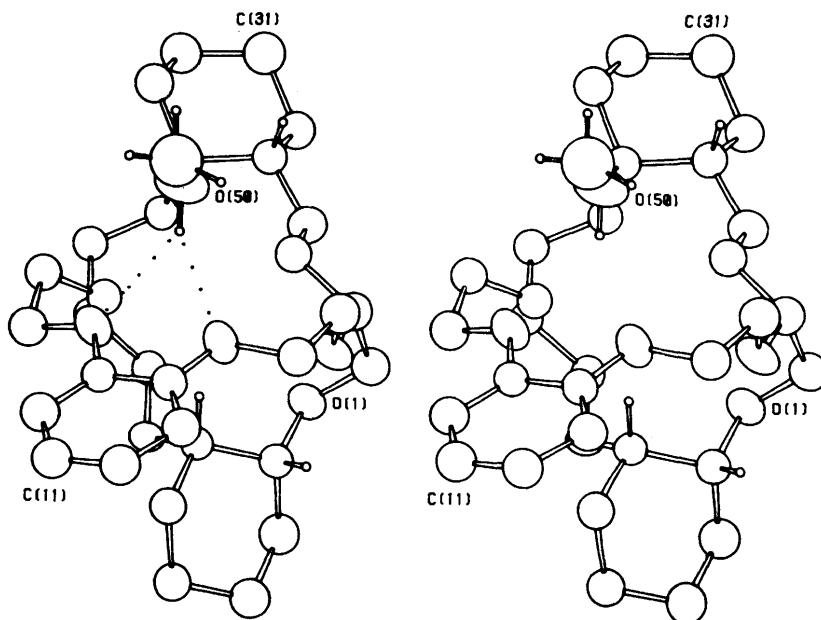


FIGURE. A stereo-diagram of (4c)·MeOH drawn by ORTEP with oxygen atoms as vibration ellipsoids at the 50% confidence level and carbon atoms as spheres, the hydrogen atoms on the cyclohexane bridges and in methanol are shown as small spheres. The hydroxy-group consists of O(51) and its hydrogen atom which is nearly equidistant from the two oxygen atoms O(7) and O(14) on the benzene ring; the bifurcated hydrogen bond is indicated by dotted lines.

2666 observed reflections. (**4c**): methanol, $C_{29}H_{46}O_9$, $M = 538.7$, monoclinic, space group $P2_1/n$, $a = 14.520(2)$, $b = 15.391(3)$, $c = 12.754(2)$ Å, $\beta = 95.02(2)^\circ$, $U = 2839.3$ Å³, $D_o = 1.26(1)$, $D_c = 1.261$ g cm⁻³, $Z = 4$, $R = 0.062$ for 2071 observed reflections.

The crystal structure analyses showed the isomers to have the relative configurations depicted conventionally in the Scheme (with their systematic names). In all three molecules, in the crystalline forms, both cyclohexane rings are in the chair conformation so that one bridge hydrogen is axial and the other equatorial. The relative configurations of the diols (**2a**), (**2b**), and (**2c**) have been assigned from those of the bicyclic molecules.

Isomer (**4c**) is shown in the Figure with the methanol molecule. The hydroxy-group forms a bifurcated hydrogen bond with H . . . O distances of 2.37(10) and 2.31(10) Å and

O(H) . . . O distances of 3.117(7) and 3.023(7) Å. The reduction, 89 cm⁻¹, in the hydroxy-stretching frequency is in the range found⁵ for interaction between methanol and various ethers in dilute solution in tetrachloromethane, and the O . . . O distance calculated from the Bellamy and Owen relationship⁶ would be 3.00 Å for a single hydrogen bond.

The behaviour with metallic cations is consistent with the hypothesis that the hydrogen atoms on the cyclohexane junctions are somewhat electropositive, so that the cavity is most electronegative in (**4b**), least in (**4c**), and intermediate in (**4a**). A similar hypothesis explains the higher formation constants⁷ found by Frensdorff for *cis-syn-cis*-dicyclohexyl-18-crown-6 (isomer A) compared with the *cis-anti-cis*-isomer B.

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