Stereospecific Synthesis of the *trans-anti-trans-* and *trans-syn-trans-* Isomers of Dicyclohexyl-18-crown-6

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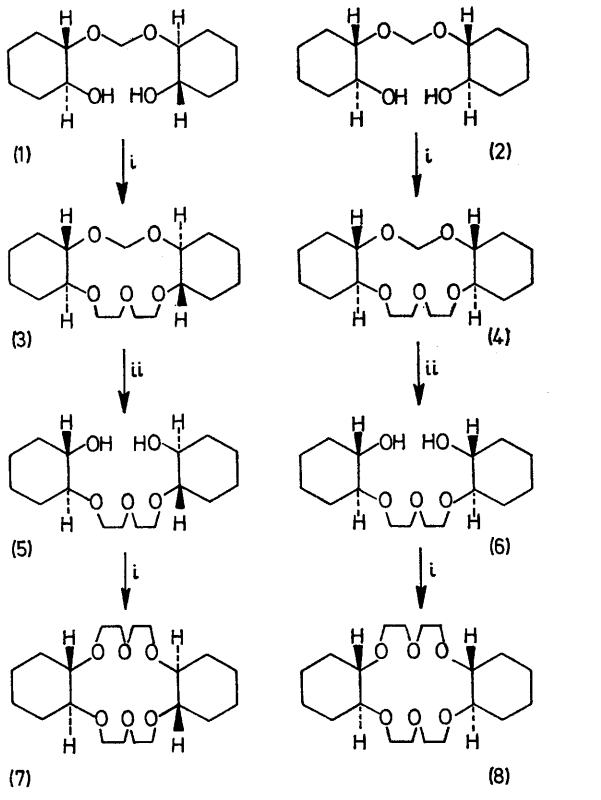
Summary The macrocyclic polyethers, (**7**) and (**8**), have been synthesised stereospecifically from the diastereoisomeric acyclic methylene acetals, (**1**) and (**2**), obtained from (±)-cyclohexane-*trans*-1,2-diol; both (**7**) and (**8**) form stable complexes with metal cations.

OF the many so-called[1,2] crown compounds that were prepared initially by Pedersen,[2] dibenzo-18-crown-6 and dicyclohexyl-18-crown-6 have been the most widely investigated. Two isomers of dicyclohexyl-18-crown-6 have been obtained[1-3] by catalytic hydrogenation of dibenzo-18-crown-6. These have been designated[1,3] as Isomer-A (m.p. 61—62·5°) and Isomer-B (m.p. 69—70°)† in the literature. The assignment of Isomer-A to the *cis-syn-cis*-configuration[4] and Isomer-B to the *cis-anti-cis*-configuration[5] is based on X-ray crystal structure analyses. We now report the stereospecific synthesis of the *trans-anti-trans-* (**7**) and *trans-syn-trans-* (**8**) isomers from the diastereoisomeric acyclic methylene acetals (**1**) and (**2**), respectively.

Acid-catalysed reaction of (±)-cyclohexane-*trans*-1,2-diol with formaldehyde yields, amongst other products, the diastereoisomeric (±)-di-(**1**) and *meso*-di-(*trans*-2-hydroxycyclohexyloxy)methane (**2**), which may be separated by fractional crystallisation.[6] Configurational assignments can be made[7] to these isomers on the basis of the signals observed in the ^{1}H n.m.r. spectra for their dioxymethylene protons.

Treatment of compounds (**1**) and (**2**) in turn with sodium hydride and diethyleneglycol ditosylate[8] in dimethoxyethane–dimethyl sulphoxide (3:1) at 50—55° for 24 h afforded the cyclic acetals (**3**) and (**4**), respectively. Compound (**3**) was obtained in 57% yield as an oil after chrom-



Reagents: i, (p-Me·C$_6$H$_4$·SO$_3$·CH$_2$·CH$_2$)$_2$O; NaH; DME–DMSO; ii, H$^+$–H$_2$O.

† Isomer-B exists in a second crystalline form with m.p. 83—84° (see ref. 3).

atography on silica gel using ether as eluant. Similarly, compound (**4**) was obtained in 21% yield as prisms, m.p. 62—63°. The cyclic acetals (**3**) and (**4**) were hydrolysed quantitatively to the noncrystalline diols (**5**) and (**6**), respectively. Further base-catalysed reactions of the diols (**5**) and (**6**) with diethyleneglycol ditosylate[8] at 50—55° for 16 h yielded the *trans-anti-trans-* (**7**) and *trans-syn-trans-* (**8**) isomers of dicyclohexyl-18-crown-6. Both isomers were purified by silica gel chromatography with ether as eluant. Isomer (**7**) was isolated as needles, m.p. 77—80°, in 25% yield. Isomer (**8**) was isolated as prisms, m.p. 120—121°, in 30% yield. Preliminary observations suggest that isomers (**7**) and (**8**) both form stable crystalline complexes with sodium bromide.

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