Synthesis of Macrobicyclic Polyethers with Carbon Bridgeheads

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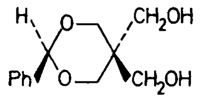
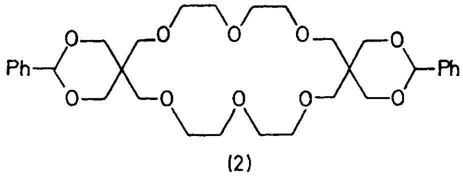
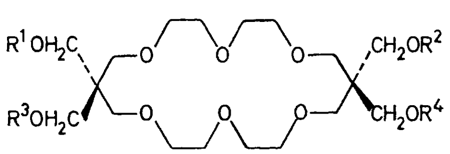
Summary A macrobicyclic polyether (**4**) has been synthesised from pentaerythritol in four steps and is a suitable precursor to related compounds where the nature of the functional groups attached to the bridgehead carbon atoms can be varied.



(1)

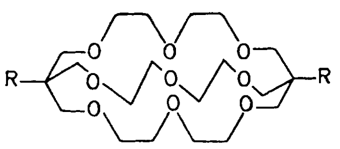


(2)



(3a) $R^1 = R^2 = H$; $R^3 = R^4 = CH_2Ph$

(3b) $R^1 = R^4 = H$; $R^2 = R^3 = CH_2Ph$



(4) $R = CH_2OCH_2Ph$

(5) $R = CH_2OH$

(6) $R = CH_2OMs$

RECENTLY macrocyclic[1] and macrobicyclic[2] polyethers containing bridgehead nitrogen atoms have attracted considerable attention because of their surprising ability to form stable complexes with metal cations. We now report a general synthesis of macrobicyclic polyethers where carbon atoms occupy the bridgehead positions.

Pentaerythritol can be converted[3] into its *O*-benzylidene derivative (**1**) in good yield. Reaction of this diol (**1**) with NaH and $TsOCH_2CH_2OCH_2CH_2OTs$[4] in Me_2SO at 50° for 70 h afforded a product, m.p. 99°, with the constitution† (**2**) in 15% yield after chromatography (Et_2O) on alumina. Treatment of (**2**) with $LiAlH_4$–BF_3[5] in Et_2O yielded the two diastereomeric diols (**3a**) and (**3b**), as colourless oils after chromatography (EtOAc) on silica gel. The second diol eluted from the column was assigned to the configurational isomer (**3a**) [^1H n.m.r. ($CDCl_3$): τ 2·79 (10H, br s, 2 × Ph), 5·59 (4H, s, 2 × $PhCH_2O$), 6·21—6·79 (32H, other CH_2 protons), and 7·35 (2H, br s, 2 × OH)] with *cis*-CH_2OH groups, since this compound underwent reaction with NaH and $TsOCH_2CH_2OCH_2CH_2OTs$[4] in $MeOCH_2CH_2OMe$ at 50° for 24 h to give the dibenzyl ether (**4**), m.p. 48—49°, in 30% yield after chromatography (Et_2O) on silica gel. Hydrogenation (10% Pd–C) of (**4**) afforded quantitatively the diol (**5**), m.p. 64—65°, which was characterised as the dimesylate (**6**) [m.p. 90—91°; ^1H n.m.r. ($CDCl_3$): τ 5·76 (4H, s, 2 × $MsOCH_2$), 6·40 (36H, br s, other CH_2 protons), and 7·03 (6H, s, 2 × Me)].

The macrobicyclic polyethers (**4**)—(**6**) are of interest because their properties are liable to complement those of the diaza-macrobicyclic polyethers,[2] *e.g.* ^1H n.m.r. spectroscopy indicates that the dibenzyl ether (**4**) forms complexes with NaI and KI in $CDCl_3$ and preliminary observations show that (**4**) solubilises $KMnO_4$ in benzene (*cf.* ref. 6).

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† Although it is suspected that this product is a mixture of diastereomeric dispiro-compounds, it exhibits a sharp m.pt., migrates as a homogeneous component on t.l.c., and has a ^1H n.m.r. spectrum characteristic of one compound.

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