Synthesis, and *X*-Ray Crystal and Molecular Structure of a Novel Macrobicyclic Ligand: Crowned *p*-t-Butyl-calix[4]arene

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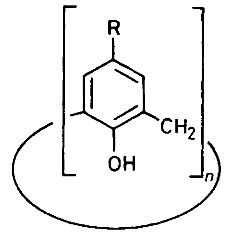
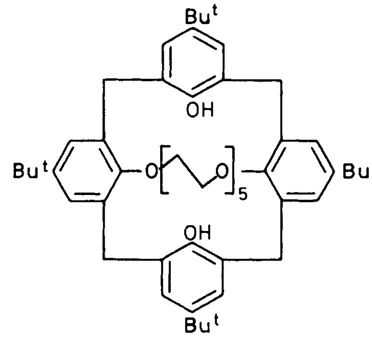
Capping of *p*-t-butyl-calix[4]arene (**1a**) with pentaethylene glycol ditoluene-*p*-sulphonate and Bu^tOK in benzene leads to the first member of a new class of macrobicyclic crown compounds (**2**), which possess two cavities (one hydrophilic and one lypophilic) and two additional, ionizable binding sites.

The search for new synthetic hosts having the ability to form selective inclusion complexes with ions and neutral molecules is very active. Compounds with enforced cavities called cavitands,[1] macropolycyclic hollow molecules called speleands,[2] and other synthetic molecular receptors[3] have been recently designed and their syntheses and properties reported. On the other hand crown ethers with pendant ionizable groups have been synthesized in order to achieve selectivity in the separation of alkali and alkaline earth cations[4] or to act as catalysts in selected reactions.[5]



(1) R = H, Bu^t, octyl, n = 4–8
(1a) n = 4; R = Bu^t



(2)

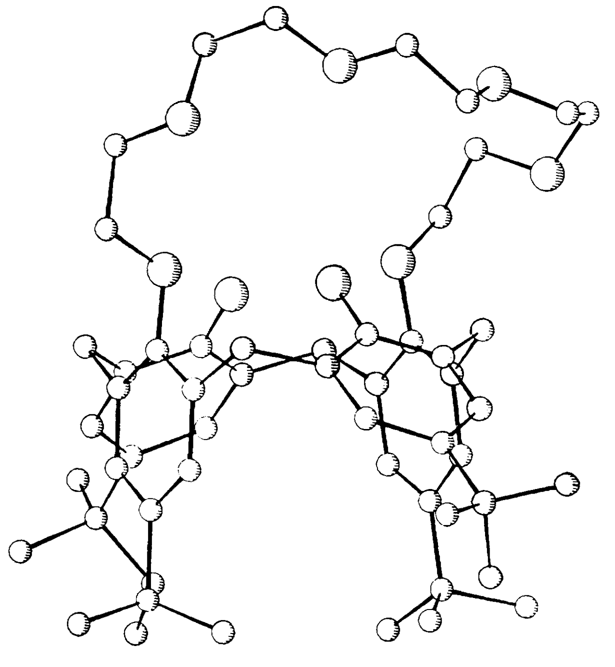


Figure 1. Perspective view of the molecule (**2**) showing the conformation of the crown chain and the shape of the calixarene cavity. Bond distances and angles show normal values.

Calixarenes (**1**) are able to form inclusion complexes with several organic neutral molecules[6–8] and we have also used some of them as 'ordered building blocks' for open chain cation ligands (polypodands).[9]

We report here the synthesis and *X*-ray crystal and molecular structure of the first 'crowned' calixarene (**2**) which has been obtained from *p*-t-butyl-calix[4]arene (**1a**). This macrocycle has been chosen because it is the smallest in the calixarene family and can be obtained in reasonable yields from the base catalysed condensation of *p*-t-butylphenol and formaldehyde;[6–7] it is easily separated from the reaction mixture by exploiting its ability to form intramolecular inclusion complexes with toluene and other aromatic guests.[6]

Moreover, Corey–Pauling–Koltun (CPK) molecular models of the 'crowned' macrocycles derived from (**1a**) show that a rather circular ring can be created by linking two opposite OH groups with a suitable polyethereal chain, whereas two additional and potentially ionizable hydroxy groups still remain above and below the plane of the polyethereal ring. Finally the high lipophilicity of (**1a**) makes the resulting crowns attractive for extraction and transport studies.

The macrobicyclic compound (**2**) has been obtained in *ca.* 30% yield (not optimized) from *p*-t-butyl-calix[4]arene (**1a**) and pentaethylene glycol ditoluene-*p*-sulphonate (1 equiv.) in refluxing benzene (48 h) using 2 equiv. of Bu^{t}OK (added stepwise in two 1 equiv. portions). After preparative t.l.c. (ethyl acetate–tetrahydrofuran, 95:5) compound (**2**)† has been recrystallized from methanol to give prismatic crystals, m.p. 232—234 °C, suitable for *X*-ray analysis.‡ Figure 1 shows the conformation of the molecule. In the polyethereal chain the O–C–C–O torsion angles range from 71.1(9) to 82.9(11)°, average value 76.1(10)°. The C–O–C–C torsion angles range from 156.9(12) to 178.8(9)° [average 172.2(10)°], with the exception of one of 92.9(9)° which folds the chain in the right part of the molecule (Figure 1). The inclination of the phenyl rings with respect to the axis of the calix is 176.2(8) and 176.9(9)° for the rings carrying the crown and 136.9(9) and 139.5(10)° for those carrying the OH groups to be compared with 123° observed in the toluene clathrate of (**1a**).[6] With the reciprocal orientation of the phenyl rings the OH groups do not form intramolecular hydrogen bonds and the O · · · O contacts of the oxygens of the calix[4]arene moiety in (**2**) are from 2.944(15) to 3.128(18) Å with a lengthening of about 0.3 Å with respect to those observed in the calix[4]arene (**1a**).[6] This seems to be a common behaviour for 1,3-diether derivatives of *p*-t-butyl-calix[4]arene and it has been also observed

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† Satisfactory elemental analyses were obtained for (**2**); M^+ m/z 850 (100%). ^{1}H n.m.r. spectrum (100 MHz, $CDCl_3$, Me_4Si), δ 0.92 (s, 18H, CH_3), 1.32 (s, 18H, CH_3), 3.31 (s, 4H, $ArCH_2Ar$), 4.39 (d, 4H, $ArCH_2Ar$, J_{AB} 13 Hz), 3.78—4.25 (m, 20H, $-OCH_2CH_2O-$), 6.78 (s, 4H, ArH), 7.10 (s, 4H, ArH), and 7.02 (s, 2H, OH).

‡ *Crystal data.* $C_{54}H_{74}O_8$, M = 851.2, triclinic, a = 14.457(8), b = 16.615(12), c = 12.083(9) Å, α = 71.38(5), β = 111.93(6), γ = 98.15(6)°, U = 2550(3) Å^3, Z = 2, D_c = 1.108 g cm^{-3}, space group $P\bar{1}$. Intensity diffraction data were collected up to θ = 70° by using the ω–2θ step-scanning mode with Ni-filtered Cu-K_α radiation (λ = 1.5418 Å). The reflection profiles were analysed with the Lehmann–Larsen algorithm (R. H. Blessing, P. Coppens, and P. Becker, *J. Appl. Crystallogr.*, 1974, **7**, 488). A total of 9035 reflections was collected, 4527 of which [$I > 2\sigma(I)$] were considered observed and used in the structure analysis and refinement. The structure was solved by direct methods and refined by full-matrix anisotropic least-squares techniques. Hydrogen atoms were placed in their geometrical positions with C–H = 1.08 Å. The final R-index was 0.085 [R_w = 0.097, $w = 1/\sigma^2(F)$]. Atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

in the analogous dimethyl compound both in the solid state and in solution.§

Compound (**2**) is able to act as "neutral" ligand toward metal and ammonium picrates which are easily extracted in organic media and transported through a liquid (CH_2Cl_2) membrane (selectivity: $K^+ > NH_4^+ > Na^+ > Cs^+ > Li^+$; $Ba^{2+} >> Ca^{2+}$). On the other hand (**2**) is a very efficient carrier (CH_2Cl_2 membrane) of alkali cations from a basic aqueous source (pH 12—13) to a receiving acidic phase (HCl, 0.1 M). As observed also in other systems,[10] the presence in the same molecule (**2**) of two ionizable phenolic OH groups and a crown macrocycle greatly improves the transport ability of the carrier in these conditions.

In fact neither the starting calix[4]arene (**1a**) nor dibenzo-18-crown-6 are able to transfer Na^+ and K^+ from basic to acid aqueous solutions.

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§ The *X*-ray, and ^1H and ^{13}C n.m.r. data obtained in conformational studies of these derivatives will be published shortly.

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