Pergamon

Tetrahedron, Vol. 53, No. 9, pp. 3287-3300, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00039-2

Calixarenes with *Exo*-hydroxy Groups: Synthesis, Crystal and Molecular Structure of *ortho-tert*-Butylphenol-based Calix[4]-, Calix[6]- and Calix[8]arenes.

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Abstract: *Ortho-tert*-butylcalixarenes **3**, **4** and **5** with *exo*-hydroxy groups were synthesised by tin tetrachloride-promoted condensation of 2,2'-dihydroxy-3,3'-di-*tert*-butyldiphenylmethane **6** with formaldehyde. While ^{1}H NMR analysis of compounds **3**, **4** and **5** revealed a considerable annular flexibility in $CDCl_3$ solution, their X-ray single crystal analysis showed the presence of a strong intramolecular hydrogen bonds between the proximal OH groups.

Introduction

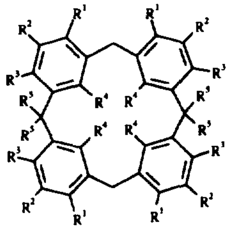
Calix[n]arenes and related macrocycles have been of particular interest in the last twenty years.[1] The interest in these compounds started in the late 1970's when C.D. Gutsche reported an efficient procedure for multigram preparation of calix[n]arenes with controlled ring sizes by direct condensation of *para*-alkylphenols and formaldehyde under basic catalysis.[2]

Some years later, A.G. Högberg reported the one-pot synthesis of a second important class of phenolic macrocycles, the resorcin[4]arenes, by acid-promoted condensation of resorcinol with aliphatic and aromatic aldehydes.[3]

Since that time, calix[n]arenes and resorcin[4]arenes have become the most studied classes of metacyclophanes. In fact these macrocycles can be modified in various ways at the phenolic hydroxy groups or at the phenyl rings and represent, therefore, useful building blocks for the construction of more complex receptors for ions and neutral molecules.[4]

In calix[n]arenes the n OH groups are intra-annular and are appended on the lower rim, while in the resorcin[4]arenes the eight OH groups are extra-annular and are on the upper rim.

Some attention has been furthermore paid to the synthesis and properties of calix[4]arenes with four extra-annular OH groups.



1, 2, 3

	R^1	R^2	R^3	R^4	R^5
1	OH	Bu^t	H	H	Me
2	Me	OH	Me	Me	H
3	OH	Bu^t	H	H	H

Figure 1. Calix[4]arenes with *exo*-cyclic OH groups previously synthesized.

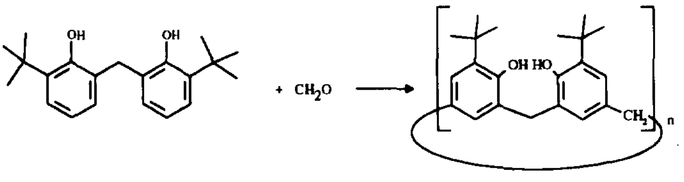
D.W. Chasar reported the synthesis of compound **1** by thermal condensation of 2,2-bis(3-*tert*-butyl-4-hydroxyphenyl)propane with formaldehyde[5] and V. Böhmer described the preparation of compound **3** by using the same procedure.[6] Finally, the fragment synthesis of compound **2** was recently described by S. Pappalardo.[7]

As part of our continuing efforts on studies of regio- and stereocontrolled phenol-aldehyde condensation[8] we have investigated the reaction of different *ortho*-linked bisphenols with aldehydes to produce calixarenes.[9]

We have also found that the *ortho-tert*-butylcalix[4]arene **3** with four extra-annular OH groups could be synthesised in 30% yield by reaction of 2,2'-dihydroxy-3,3'-di-*tert*-butyldiphenylmethane with formaldehyde and $BF_3 \cdot Et_2O$ as promoter.[10]

Since further examination of the reaction mixture has resulted in the isolation of the hitherto unknown hexameric and octameric macrocycles with six and eight extra-annular OH groups, we wished to expand our preliminary findings and examine in more details the macrocyclization process.

In the present paper we describe the useful synthesis, isolation and characterisation, including X-ray structures, of *ortho-tert*-butylphenol-based calix[4]-, calix[6]- and calix[8]arenes **3**, **4** and **5** as well as a few unsuccessful but instructive approaches to them.

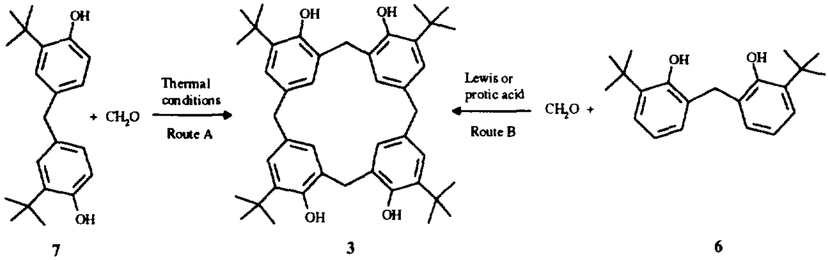


6 **3** (n=2); **4** (n=3); **5** (n=4)

Scheme 1

Results and Discussion

As mentioned above, it was known that the calix[4]arene **3** in which four *ortho*-*tert*-butylphenol units are interconnected at the *ortho* and *para* positions with methylene bridges, could be synthesised by thermal condensation of the *para*-linked dimer **7** with formaldehyde (Scheme 2, route A).[6] However, following our previous successful strategy we have preferred to approach this compound *via* the modified route **B** starting from the more easily accessible *ortho*-linked isomer **6** and formaldehyde under typical Friedel-Crafts conditions.[9,10]



Scheme 2

In fact, while **6** is obtained in 90% yield by thermal condensation of 2-*tert*-butylphenol and formaldehyde,[11] the preparation of **7** requires a multistep process from 2-bromo-6-*tert*-butylphenol.[12]

Our studies began investigating the reaction of **6** with formaldehyde under various conditions in order to achieve the optimum yield of the target compound **3**. The reactions were carried out in dichloromethane and in 1,2-dichlorobenzene or in nitromethane at 25°C under Lewis or protic acid catalysis using about 1 : 1 substrate **6** : formaldehyde molar ratio. Some experiments were also carried out in glacial acetic acid or in ethanol. After usual work-up (see experimental section) yields were estimated by weighting the products after separation by silica gel chromatography (eluant: hexane / ethyl acetate 15%). Results are summarised in Table 1.

The use of a catalytic amount of tin tetrachloride in methylene chloride gave the best results with 46% yield of **3**, 16% yield of **4** and approximately 9% yield of **5** (entry h). Reactions carried out in 1,2-dichlorobenzene or nitromethane under the same conditions produced mixtures of **3**, **4** and **5** with lower yields (entries i and j). The other Lewis acids investigated gave less satisfactory results (entries a, d and e) and aluminum trichloride induced the reaction but yielded a mixture of linear oligomers (entries b and c). The use of protic acids gave mixtures of linear high molecular weight telomers (entries k and l). The use of 1,3,5-trioxane in ethanol under conditions recently claimed for the synthesis of resorcin[6]arenes,[10] resulted in the production of a tar material with only traces of **3** and **4**. To increase the efficiency of the process, we utilised the *para*-linked dimer **7**, early used by Chasar and more recently by Böhmer for the synthesis of **3** *via* thermal condensation with formaldehyde. The reaction was carried out under the best condition for the synthesis of **3** (see Table 1, entry h).

Table 1: Conditions and yields of the macrocyclization reaction of **6** with paraformaldehyde.

Entry	Catalyst	Molar ratio catalyst / 6	Solvent	Time (h)	Temp. (°C)	Conversion (%)	Yield 3 (%)	Yield 4 (%)	Yield 5 (%)
a	$ZnCl_2$	1	CH_2Cl_2	2	38	77	8	10	5
b	$AlCl_3$	1	“	2	25	98	--	-	-
c	“	0.2	“	2	"	98	--	-	-
d	$BF_3{\cdot}Et_2O$	“	“	2	"	80	30	25	5
e	$TiCl_4$	1	“	2	"	90	37	17	6
f	$SnCl_4$	0.1	“	2	"	80	35	12	7
g	“	0.2	“	2	"	98	30	18	8
h	“	0.1	“	6	“	98	46	16	9
i	“	“	1,2-diClC$_6$H$_4$	6	"	87	13	4	9
j	“	“	CH_3NO_2	2	"	100	13	4	-
k	HCl	1	EtOH	72	"	25	-	-	-
l	H_2SO_4	0.2	CH_3COOH	6	"	75	-	-	-

The production of a mixture of linear telomers without any cyclic compound demonstrates the crucial role played by the *ortho*-linked dimer **6** in the acid-promoted reaction. These results run apparently counter to those recently reported by Böhmer. The rationale could be that in non polar solvents the *para*-linked dimer **7** is able to coordinate formaldehyde by hydrogen bond which activates the reagents and favours the *ortho*-alkylation.[11] This effect and the formation of two new intramolecular O-H ···· O-H bonds in the product are responsible for the easy production of **3** under Chasar and Böhmer conditions. On the contrary, with the *ortho*-linked dimer **6** both these effects do not play any role and the synthesis of **3** can only be performed by protic or Lewis acid activation of formaldehyde. Evidently under these conditions the formation of intramolecular hydrogen bonds is not a crucial point.

Subsequently, we turned our attention to the larger-scale preparation of the main compound **3** by using the best protocol reported in Table 1 (entry h). As mentioned above, the preparation of macrocyclic compounds was accompanied by the concomitant production of varying amounts of linear telomers. Although product **3** could readily be separated by thin layer or column chromatography, these purification techniques were unpractical for the large-scale preparation prompting further refinement of the methodology. After some experiments with different solvents we found that separation of **3** from other cyclic and linear telomers was not anymore a difficult task due to the markedly different solubility properties of this compound in CH_3CN with respect to the other reaction products. The yellow slurry obtained after removal of the solvent from the quenched reaction mixture, was stirred at room temperature with CH_3CN giving pure **3** as a white powder which could be separated and purified by filtration and washing with small amount of CH_3CN. While this protocol provided a convenient entry to calix[4]arene **3**, the further isolation and purification of calix[6]- and calix[8]arenes **4** and **5** was more difficult. Thus concentration of the filtrate yielded a second yellow material from which macrocycles **4** and **5** could be obtained by column chromatography (SiO_2 and a gradient of ethyl acetate in hexane from 5% to 20%). The first eluted fractions contained the monooxidized calix[4]arene **8** (3% yield) (figure 2) followed by calix[4]arene **3** (3% yield), calix[6]arene **4** (16% yield) and calix[8]arene **5** (9% yield).Compounds **3**, **4** and **5** were studied by IR spectroscopy in order to gain information on the intramolecular hydrogen bonding between the OH groups on the adjacent phenol rings. The observed values of the OH stretching frequencies are as follows: 3435 cm^{-1} (**3**), 3430 cm^{-1} (**4**) and 3433 cm^{-1} (**5**). These values are closer to those found by Konishi for some calix[4]arenes and resorcin[6]arenes (3432 cm^{-1} and 3420 cm^{-1} respectively[13]) rather than to the values early reported by Gutsche for *para-tert*-butylcalix[4]arene, *para-tert*-butylcalix[6]arene and *para-tert*-butylcalix[8]arene (3160, 3150 and 3200 cm^{-1} respectively[2,14]). In fact in calixarenes **3**, **4** and **5** as well as in resorcinarenes the OH groups cannot form a strong isodromic hydrogen bond as observed in *para-tert*-butylcalixarenes.

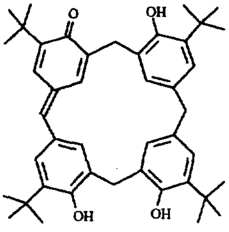


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Figure 2

Moreover temperature-dependent ^1H NMR analysis demonstrated a large conformational mobility of these compounds in $CDCl_3$ solution. In fact at 298 K the methylene hydrogens of **3**, **4** and **5** appear as pairs of sharp singlets at 3.79 and 3.81 ppm, 3.78 and 3.86 ppm, 3.77 and 3.79 ppm respectively and no appreciable changing of the signal pattern was observed when samples were cooled to 183 K or heated to 363 K, indicating fast interconversion.

X-Ray Structural Analysis.

Crystals of the macrocycles synthesised were obtained by slow evaporation of the appropriate solvent. Compound **3** was grown from methylene chloride, compound **4** from dimethylformamide and compound **5** from a mixture of nitromethane and ethanol.

The *exo*-calix[4]arene **3** adopts an almost regular cone conformation in the solid state (Figure 3) that is energetically the most stable[6b] and is very similar to that recently reported by Böhmer et al[6c] in which the disordered acetonitrile host molecule probably determines the crystallization in a different crystal system. In **3**, as in the above mentioned structure, the hydroxy H atoms are equally disordered over two sites and the major conformation determining feature is the presence of the strong intramolecular O-H···O hydrogen bonds between the proximal phenolic OH groups (2.660(3) Å). The macrocycle has crystallographic C_{2v} symmetry with the two independent methylene groups lying on two mirror planes. The dihedral angles between the aromatic rings and the plane of the four methylene carbon atoms are equal because of symmetry (126.55(9)°) (interplanar angles >90° indicate that the aromatic ring system is tilted so that its OH group is directed away from the ring cavity)

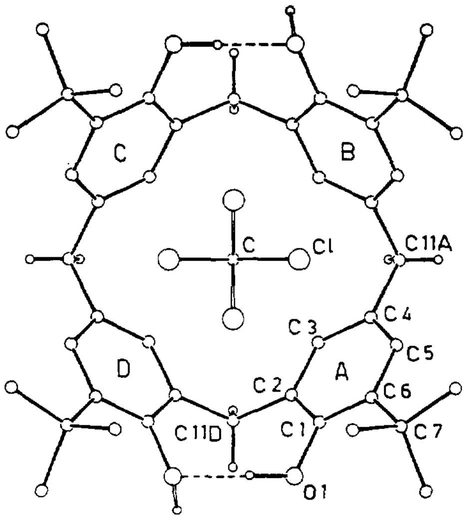

Figure 3. Projection of the *exo*-calix[4]arene (3) along b, with the labeling scheme. For clarity the atoms are drawn with arbitrary size. The B, C, D units are related to the unit A by the symmetry operations: *x, y, 1/2-z; -x, y, 1/2-z; -x, y, z*.

and the angles between the ring A and the rings B, C and D are 111.35(8)°, 73.10(9)° and 110.20(9)°, respectively. The strong intramolecular hydrogen bond blocks the conformation of the 2,2'-dihydroxy-3,3'-di-*tert*-butyldiphenylmethane moiety. The orientation of the hydroxy H atoms which determines the intermolecular hydrogen bond (2.726(3) Å) is restrained by the presence of the methylene and *tert*-butyl groups. Moreover the *tert*-butyl conformation is constrained by the OH group. The cavity is filled by a disordered CH_2Cl_2 molecule with host-guest interactions near to the Van der Waals radii sum. The four C(3) atoms define the rectangular base of the calix with C3...C3B and C3...C3D distances of 3.621(4) and 3.700(5) Å, respectively.

The hydrogen bond distance values and the polymeric zig-zag hydrogen-bonded ribbon conformation are very similar in the two compounds. The only significative difference is the increasing of the inclination angle value of the aromatic rings with respect to the four CH_2 groups [126.55(9)° against 123.7(1)°] owing to the bulky host molecule.

The *exo*-calix[6]arene **4** adopts a conformation with a pseudo-symmetry *C*, except for the OH and *tert*-butyl substituents. The pseudo-mirror plane bisects perpendicularly the B and E phenyl rings (Figure 4).

All the constrains found in **3** are observed in **4**, but the presence of the polar DMF solvent in the crystals causes the disruption of one of the three intramolecular hydrogen bonds. The macrocycle binds through hydrogen bonds four DMF molecules (range 2.561(7)-2.767(7) Å) while a fifth interacts only with Van der Waals contacts. The macrocycle may be considered as formed by two trimeric subunits [A-B-C] and [D-E-F] linked by the hinge C11C···C11F of length of 4.465(5) Å that roughly corresponds to the span of one unit (5.03 Å).

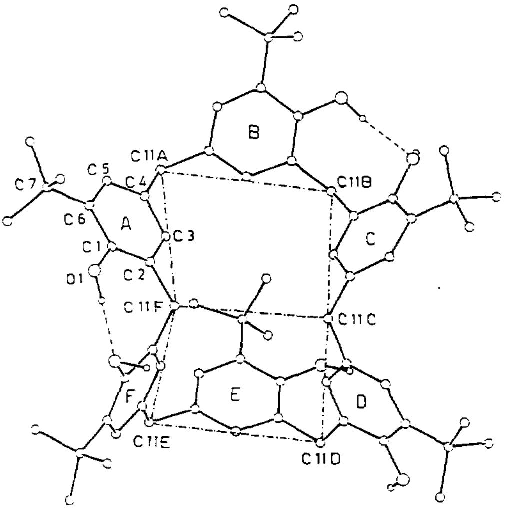

Figure 4. Perspective view of the *exo*-calix[6]arene (**4**) with labeling scheme. For clarity the atoms are drawn with arbitrary size.

So every trimeric subunit can be described as a pseudo calix[4]arene with the fourth position occupied by the other trimeric subunit. As in **3** we can define a plane formed by the methylene carbon atoms C11A, C11B, C11C, C11F for the first moiety and C11C, C11D, C11E, C11F for the second (max. dev. 0.089(4) Å). For the first trimeric subunit the dihedral angles between the plane of the four methylene carbon atoms and the phenyl rings A, B, C are 151.14(9)°, 119.06(9)° and 136.55(10)°, respectively and with the plane of the four methylene carbon atoms of the other trimeric subunit, 87.39(7)°. The conformation can be described as partial cone (three dihedral angles >90° and one <90°). For the second moiety the corresponding dihedral angles with the phenyl rings D, E, F are 146.87(9)°, 87.83(11)° and 122.18(9)°, respectively and with the other trimeric subunit, 87.39(7)°, indicative of a flattened 1,3-alternate conformation (>90°, <90°, >90°, <90°).

The crystal structure of the *exo*-calix[8]arene **5** shows the presence of two independent centrosymmetric macrocycles, the first with an approximate C_{2h} symmetry and the other only with the crystallographic C_i symmetry (the first labelled with capital letters, the second with small letters, Figures 5 and 6).

Unlike **4** the two independent calix[8]arene molecules **5** preserve all the intramolecular hydrogen bonds, so it is possible to envisage the macrocycles as formed by four dimeric subunits with almost constant conformational parameters.

The four methylene carbon atoms that link the four dimeric subunits determine a plane and define an almost regular rhombohedral parallelogram for both the macrocycle (C11A-C11C 7.256(12) Å, C11C-C11A' 7.580(9)Å, C11A-C11C-C11A' 122.5(1)°; C11a-C11c 7.602(10) Å, C11c-C11a' 7.456(10) Å, C11a-C11c-C11a'

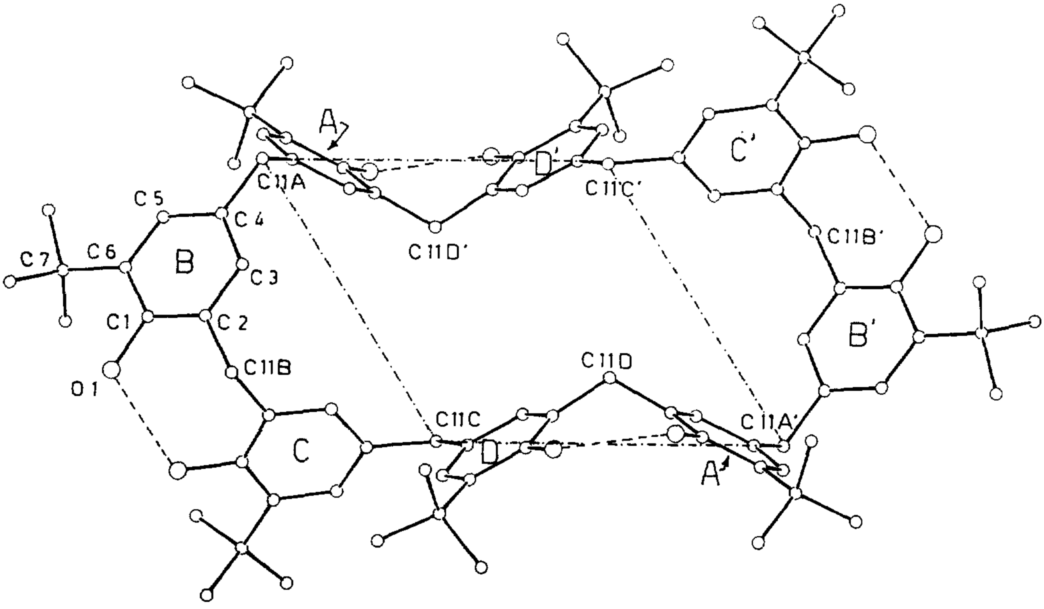

Figure 5. Projection of the first independent molecule of the *exo*-calix[8]arene (**5**) in the plane defined by the four methylene carbon atoms C11A, C11C, C11A', C11C', with the labeling scheme. For clarity the atoms are drawn with arbitrary size. The primed symbols are related to the unprimed ones by the symmetry operation 1-*x*, 1-*y*, 1-*z*.

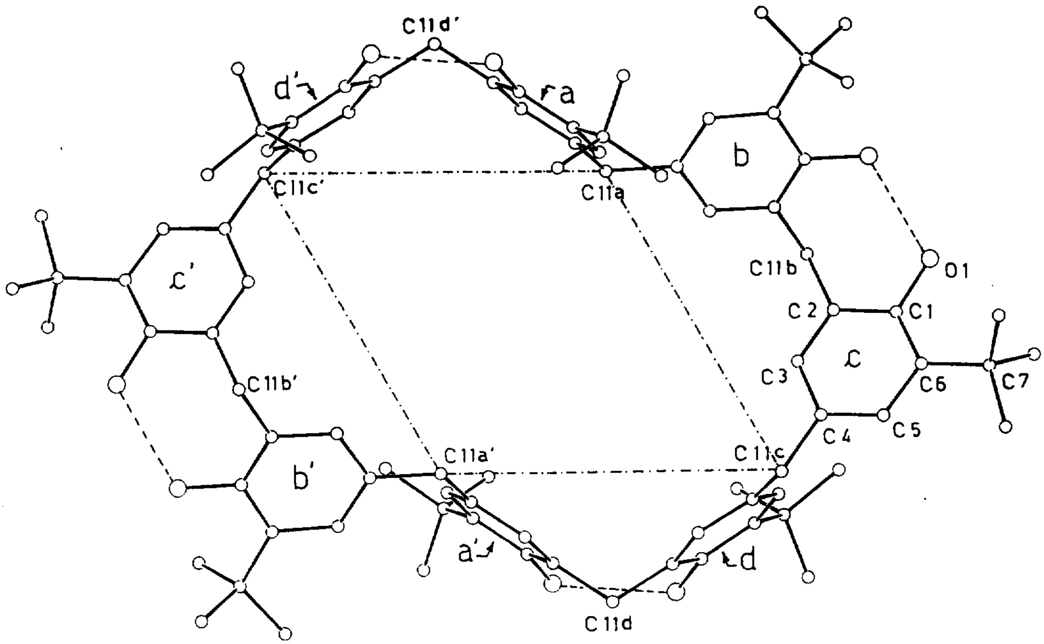

Figure 6. Projection of the second independent molecule of the *exo*-calix[8]arene (5) in the plane defined by the four methylene carbon atoms C11a, C11c, C11a', C11c', with the labeling scheme. For clarity the atoms are drawn with arbitrary size. The primed symbols are related to the unprimed ones by the symmetry operation 2-*x*, 1-*y*, 2-*z*.

120.0(1)°). The three methylene carbon atoms of each dimeric subunit define a plane that allows to describe the conformation of the macrocycles. The internal dihedral angles between the C11A C11B C11C and C11C C11D C11A' planes and the C11A C11C C11A' C11C' plane are 149.0(2)° and 64.2(1)°, respectively, C11B and C11D atoms being on the same half-space. Consequently the train of the dihedral angles is 149.0(2)°, 64.2(1)°, 31.0(2)°, 115.8(1)°, so the first macrocycle adopts a 1,2-alternate envelope conformation (with an internal acute dihedral angle) as shown in figure 7.

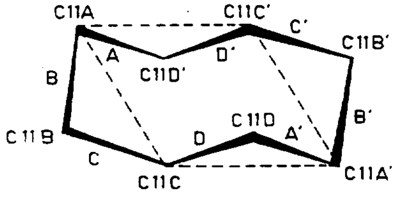

Figure 7. Schematic representation of 1,2-alternate envelope conformation of the *exo*-calix[8]arene (internal acute dihedral angle).

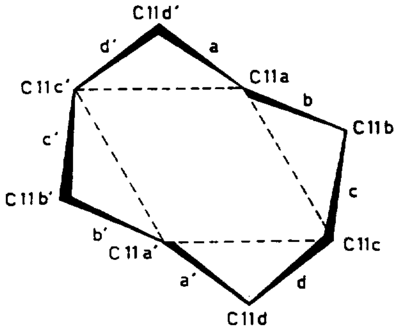

Figure 8. Schematic representation of 1,2-alternate envelope conformation of the *exo*-calix[8]arene (internal obtuse dihedral angle).

In the second macrocycle the internal dihedral angles between the C11a' C11b' C11c' and C11c' C11d' C11a planes and the C11a C11c C11a' C11c' plane are 149.0(1)° and 144.6(1)°, respectively, C11b' and C11d' being on the same side with respect to the rhombohedral parallelogram. The conformation is again 1,2-alternate but much more open and symmetric the train of the dihedral angles being 149.0(1)°, 144.6(1)°, 31.0(1)°, 35.4(1)° (see figure 8).

In the two independent macrocycles all the phenolic O atoms are involved in two hydrogen bonds, one intra- and the other intermolecular. This last interaction occurs towards adjacent macrocycles or water molecules. As in **3** the intramolecular hydrogen bonds (range: 2.644(7)-2.691(7) Å) are stronger than the intermolecular ones (2.705(11)-2.919(8) Å). $MeNO_2$ and EtOH molecules, interacting weakly with the macrocycles, complete the packing. In consequence of the conformations of the *exo*-calixarenes **4** and **5** which do not present a cone conformation, it is not possible to envisage inclusion phenomena.

For all the *exo*-calixarenes **3**, **4** and **5** the bond distances and angles are normal.

In conclusion a convenient method for the preparation of *ortho-tert*-butylphenol-based calixarenes has been described. The reaction of 2,2'-dihydroxy-3,3'-di-*tert*-butyldiphenylmethane with formaldehyde in the presence of tin tetrachloride afforded *ortho-tert*-butylcalix[4]-, -calix[6]- and -calix[8]arenes **3**, **4** and **5** in 46%, 16% and 9% respectively. ^1H NMR analysis of these compounds demonstrated a large conformational mobility in $CDCl_3$ solution, whereas single crystal X-ray analysis revealed the presence of strong intramolecular O-H···O hydrogen bonds between the proximal OH groups in the solid state.

Further work is underway to convert macrocyclic compounds **3**, **4** and **5** into cavitands and ligands for ions and neutral molecules as well as to study the binding properties of these new host molecules.

Experimental

Melting and boiling points were obtained on an Electrothermal melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet PC5 spectrophotometer. ^1H NMR spectra were recorded on a Bruker AMX400 spectrometer at 400 MHz and on a Bruker AC300 at 300 MHz. Chemical shifts are expressed in ppm relative to TMS as internal standard. Mass spectra were obtained on a Finnigan SSQ 710 instrument at 70 eV. Microanalyses were carried out by Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica dell'Università di Parma. TLC analyses and Flash Chromatography were performed on Merck 60 PF_{254} silica gel using mixtures of hexane-ethyl acetate (5-20%). All the reagents were of commercial quality from freshly opened containers. The CH_2Cl_2 was dried on 4 Å molecular sieves before use.

2,2-Dihydroxy-3,3'-di-*tert*-butyldiphenylmethane (6): 1.40 g (90% yield), white powder solid, mp 104-106°C (lit.[15] mp 105-106°C).

Synthesis of 4,4-dihydroxy-3,3'-di-*tert*-butyldiphenylmethane (7): paraformaldehyde (12 mmol, 0.36 g) and 18M aqueous solution of H_2SO_4 (10 mmol, 0.55 ml) were successively added to a solution of 2-*tert*-butylphenol (20 mmol, 3.00 g, 3.1 ml) in glacial acetic acid (50 ml). The resulting mixture was stirred for 6 hours at 25°C, then quenched with water (50 ml) and extracted with diethyl ether (3 x 50 ml). The combined extracts were dried (Na_2SO_4) and the solvent was distilled off. The residue was purified by flash chromatography using hexane : ethyl acetate 90 : 10 as eluant to give 0.24 g (15% yield) of a white powder solid, mp 41-43°C (Found: C, 81.01; H, 8.98. $C_{21}H_{28}O_2$ requires C, 80.73; H, 9.03%); ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.42 (s, 18 H, 2 $(CH_3)_3C$), 3.86 (s, 2 H, CH_2), 4.69 (s, 2 H, 2 OH), 6.57 (d, 2 H, H-5 and H-5', J=8.0 Hz), 6.86 (dd, 2 H, H-6 and H-6', J=8.0 and 2.0 Hz), 7.13 (d, 2 H, H-2 and H-2', J=2.0 Hz); IR (KBr) 3532 (OH); MS (EI) m/e 312 (M^+, 56%), 297 (100), 255 (31).

Synthesis of Calixarenes 3, 4 and 5. General Procedure. To a mixture of the aromatic substrate **6** (20 mmol, 6.20 g) and paraformaldehyde (24 mmol, 0.70 g) in dry CH_2Cl_2 at 25°C under nitrogen, $SnCl_4$ (2 mmol, 0.50 g. 0.2 ml) was added. The resulting mixture was stirred for 6 hours at 25°C, then quenched with 2 N HCl solution (300 ml) and extracted with CH_2Cl_2 (3 x 300 ml). The combined extracts were successively dried (Na_2SO_4) and the solvent was distilled off. The obtained yellow slurry was stirred at room temperature with CH_3CN (100 ml) for 15 minutes giving a yellow solution from which calix[4]arene **3** was obtained as a white powder after filtration and washing with CH_3CN (10 ml) (2.79 g, 43% yield). The remaining solution was concentrated and products separated by column chromatography on silica gel by using a gradient of ethyl acetate in hexane from 5% to 20%. This purification gave the monooxidized compound **8** (0.19 g, 3% yield), a further amount of product **3** (0.19 g, 3% yield) and compounds **4** (1.04 g, 16% yield) and **5** (0.58 g, 9% yield).

4,12,16,24-Tetrahydroxy-5,11,17,23-tetra-*tert*-butylcalix[4]arene (**3**): white powder solid, mp 172°C (dec) [lit.[10] mp 172°C (dec)].

4,12,16,24,28,36-Hexahydroxy-5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene (**4**): white powder solid, mp 190°C (dec) (Found: C, 81.70; H, 8.88. $C_{66}H_{84}O_6$ requires C, 81.44; H, 8.70%); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.37 (s, 54 H, 6 $(CH_3)_3C$), 3.78 (s, 6 H, 3 CH_2), 3.86 (s, 6 H, 3 CH_2), 6.10 (s, 6 H, 6 OH), 6.97 (s, 6 H, H arom), 6.99 (s, 6 H, H arom); IR (KBr) 3494 (OH); MS (EI) m/e 973 (MH^+, 10%), 325 (100).

4,12,16,24,28,36,40,48-octahydroxy-5,11,17,23,29,35,41,47-octa-*tert*-butylcalix [8]arene (**5**): white powder solid, mp >200°C (dec) (Found: C, 81.30; H, 8.45. $C_{88}H_{112}O_8$ requires C, 81.44; H, 8.70%); ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.35 (s, 72 H, 8 $(CH_3)_3C$), 3.77 (s, 8 H, 4 CH_2), 3.79 (s, 8 H, 4 CH_2), 6.0 (br s, 8 H, 8 OH), 6.92 (d, 8 H, H arom, J=1.9 Hz), 6.96 (d, 8 H, H arom, J=1.9 Hz); IR (KBr) 3505 (OH); MS (EI) m/e 1298 (MH^++1, 100%), 1283 (23), 649 (28).

5,11,17,23-tetrakis(1,1-dimethylethyl)pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11, 13(27)15,17,19(26),20,22-dodecaene-4,12,16-triol-24-one (**8**): yellow solid, mp 139-141°C (Found: C, 81.83; H, 8.55. $C_{44}H_{54}O_4$ requires C, 81.69; H, 8.41%); ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 1.35 (s, 9 H, $(CH_3)_3C$), 1.45 (s, 9 H, $(CH_3)_3C$), 1.47 (s, 9 H, $(CH_3)_3C$), 1.49 (s, 9 H, $(CH_3)_3C$), 3.48 (s, 2 H, CH_2), 3.87 (s, 2 H, CH_2), 3.96 (s, 2 H, CH_2), 5.9 (br s, 2 H, 2 OH), 6.43 (s, 1 H, CH), 7.0-7.2 (m, 4 H, H arom) 7.04 (d, 1 H, H arom, J=1.8 Hz), 7.27 (d, 1 H, H arom, J=2.1 Hz), 7.45 (d, 1 H, H arom, J=1.8 Hz), 7.60 (d, 1 H, H arom, J=2.1 Hz), 9.21 (s, 1 H, OH); IR (KBr) 3376 (OH); MS (EI) m/e 647 (MH^+, 100%), 632 (25).

X-ray Analysis of *ortho-tert*-butylcalix[4]arene·CH_2Cl_2, *ortho-tert*-butylcalix[6]arene·5DMF, *ortho-tert*-butylcalix[8]arene·3MeNO$_2$·1/2EtOH·H_2O. Intensity data were collected on a Siemens AED diffractometer (Cu Kα radiation, λ = 1.541838 Å, graphite-monochromated **3** and Ni-filtered **4**) and on a Philips PW 1100 diffractometer (Mo Kα radiation, λ = 0.71073 Å, graphite-monochromated **5**) using the θ/2θ scan mode, θ ranges: 3-70° (**3**), 3-60° (**4**), 3-20° (**5**). Precise unit cell dimensions were determined by least-squares refinement on diffractometer angles for 30 carefully centered reflections (18°<θ<40°) for **3**, (18°<θ<30°) for **4**, and 24 (8°<θ<13°) for **5**. No significant decay was noticed over the time of **3** and **4** data collections but a 50% decay was observed for **5**.

Crystal Data. *ortho-tert*-Butylcalix[4]arene·CH_2Cl_2 (**3**): crystal dimensions, 0.22 x 0.25 x 0.33 mm; $C_{44}H_{56}O_4 \cdot CH_2Cl_2$; *Mw* = 733.857; orthorhombic, space group *Cmcm*; a = 23.303(6) Å, b = 7.740(2) Å, c = 23.377(7) Å, V = 4216(2) Å^3; Dc = 1.156 g cm^{-3}; Z = 4; μ(Cu Kα) = 16.87 cm^{-1}; $F(000)$ = 1576; unique observed data ($I \geq 2\sigma(I)$) 1445, unique total data 2104.

ortho-tert-Butylcalix[6]arene·5DMF (**4**): crystal dimensions, 0.21 x 0.28 x 0.35 mm; $C_{66}H_{84}O_6 \cdot 5(CH_3)_2NCHO$; *Mw* = 1338.858; triclinic, space group $P\bar{1}$: a = 13.318(2) Å, b = 16.403(3) Å, c = 20.272(4) Å, α = 83.13(1)°, β = 85.66(1)°, γ = 71.43(1)°,V = 4164(1) Å^3; Dc = 1.068 g cm^{-3}; Z = 2; μ(Cu Kα) = 5.56 cm^{-1}; $F(000)$ = 1456; unique observed data ($I \geq 2\sigma(I)$) 6351, unique total data 12356.

ortho-tert-Butylcalix[8]arene·3MeNO$_2$·1/2EtOH·H_2O (**5**): crystal dimensions, 0.25 x 0.30 x 0.37 mm; $C_{88}H_{112}O_8 \cdot 3CH_3NO_2 \cdot 1/2C_2H_5OH \cdot H_2O$; *Mw* = 1522.018; triclinic, space group $P\bar{1}$; a = 12.661(4) Å, b = 18.131(4) Å, c = 22.005(5) Å, α = 108.16(2)°, β = 95.49(2)°, γ = 103.79(2)°,V = 4582(2) Å^3; Dc = 1.103 g cm^{-3}; Z = 2; μ(Cu Kα) 0.74 cm^{-1}; $F(000)$ = 1646; unique observed data ($I \geq 2\sigma(I)$) 5152, unique total data 8550.

Structure Determination and Refinement of *ortho-tert*-butylcalix[4]arene·CH_2Cl_2, *ortho-tert*-butylcalix[6]arene·5DMF, *ortho-tert*-butylcalix[8]arene·3MeNO$_2$·1/2EtOH·H_2O. The structures were solved by direct methods.

3·CH_2Cl_2 was refined by full-matrix least-squares, first with isotropic thermal parameters and then with anisotropic thermal parameters for all the non-hydrogen atoms. The methylene chloride guest molecule with the carbon atom in the site symmetry *m2m* was found with the chlorine atoms disordered and distributed in two positions of site symmetry *m* with a 3:1 s.o.f. ratio. All the hydrogen atoms, except those of the guest molecule, including the hydroxy H atom found disordered and distributed in two positions, were clearly located in the ΔF map. These hydrogen atoms except the hydroxy ones, introduced as fixed contributors, were refined isotropically. Unit weights were used in all the stages of the refinements. The final *R* and *Rw* were 0.0761 and 0.0655.

4·5DMF was refined first isotropically by full-matrix least-squares then anisotropically by blocked full-matrix least-squares for all non-hydrogen atoms. All the hydroxy H atoms were clearly located in the ΔF map and refined isotropically while the other hydrogen atoms of the calix[6]arene were placed at their geometrically calculated positions and refined "riding" on the corresponding carbon atoms (d C-H = 0.96 Å). In the final cycles of refinement a weighting scheme $w = k[\sigma^2(F_O) + gF_O^2]^{-1}$ was used, at convergence the *k* and *g* values were 1.3742 and 0.00268. The final *R* and *Rw* were 0.0695 and 0.0932.

5·$3MeNO_2$·1/2EtOH ·H_2O was refined first isotropically by full-matrix least-squares then anisotropically by blocked full-matrix least-squares for all non-hydrogen atoms of the calix[8]arene molecules. The structural analysis revealed the presence of two independent macrocycles, both centre-symmetric, nitromethane, ethanol and water solvation molecules. One of the three $MeNO_2$ molecules resulted to be disordered as well as the methylene carbon atom of the EtOH molecule. Only the oxygen atom of the water molecule, the non-hydrogen atoms of the two not disordered $MeNO_2$ molecules, the hydroxy oxygen and the methyl carbon atoms of the EtOH molecule were refined anisotropically, the others isotropically. In each macrocycle only two hydroxy hydrogen atoms among the four independent were clearly located on the ΔF map, as well as the two hydrogen atoms of the methylene carbon which bridges the two centre-symmetric moieties of the calix[8]arene. Only these hydrogen atoms were refined isotropically, all the other macrocycle hydrogen atoms, excluding the hydroxy hydrogen atoms, not clearly located and most probably disordered, were placed at their geometrically calculated positions and refined "riding" on the corresponding carbon atoms (d C-H = 0.96 Å). Unit weights were used in all the stages of the refinements. The final *R* and *Rw* were 0.0734 and 0.0769.

The system of computer programs SIR92, SHELXS-86, SHELX-76, PARST and ORTEP were used.[16] All calculations were carried out on the GOULD POWERNODE and ENCORE 91 of the "Centro di Studio per la Strutturistica Diffrattometrica del C.N.R." Parma, Italy.

Supporting Information Available

Atomic coordinates (Tables SI, SII, SIII, SIV, SV, SVI), thermal parameters (Tables SVII, SVIII, SIX), complete lists of bond distances and angles (Tables SX, SXI, SXII) and experimental data for the X-ray diffraction studies (Table SXIII) have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Acknowledgements

The authors acknowledge the support of the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST), Italy, and the Consiglio Nazionale delle Ricerche (CNR), Italy.

The authors are grateful to the Centro Interdipartimentale Misure (CIM) for the use of NMR and mass spectroscopic instruments.

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(*Received in UK* 5 *December* 1996; *revised* 31 *December* 1996; *accepted* 9 *January* 1997)