Synthesis and Conformational Properties of Calix[6]arenes Bridged on the Lower Rim: Self-Anchored Rotaxanes

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Abstract: The 1,4-di-*p*-tolyl ether of *p-tert*-butylcalix[6]arene can be converted to transannularly bridged esters by treatment with diacid chlorides ranging from succinoyl to suberoyl and including terephthaloyl. The parent compounds *p-tert*-butylcalix[6]arene and *p*-H-calix[6]arene can also be transannularly bridged by treatment with bis-halomethylaryl compounds by using $KOSiMe_3$ as the base. Methylation of the resulting calix[6]arenes containing 1,4-CH_2ArCH_2 bridging moieties produces the corresponding tetramethyl ethers. When Ar is anthrylene the conformation of the starting material is retained, but when Ar is phenylene the conformation changes; when Ar is duryl a mixture of conformers is obtained. ^1H NMR analysis and molecular modeling studies suggest that, when Ar is phenyl or durylene, the system is capable of undergoing a conformational transformation in which the bridging moiety becomes threaded through the annulus of the macrocyclic ring to produce a "self-anchored rotaxane". Employing a new scheme for denoting calixarene conformations, this is designated as a (**u**,u,u,u,u,u) to (u,u,d,d,d,u) transformation. The apparent driving force for the conformational change is the greater spatial separation of the OMe groups in the (**u**,u,d,d,d,u) conformation as compared with the (**u**,u,u,u,u,u) conformation, resulting in a more favorable electrostatic energy contribution to the total energy of the former.

Introduction

Calix[4]arenes[1] have provided the major testing ground for the development of general methods for functionalizing the class of macrocyclic compounds collectively known as calixarenes.[2] As the study of these compounds approaches maturity, increasing attention is being devoted to some of the larger members of the family, and the easy accessibility of *p-tert*-butylcalix[6]arene makes it the next logical candidate for close scrutiny. As the present results show, however, the increased flexibility of this system presents new problems and may also produce unexpected results. An earlier paper in this series[3] discussed the O-benzylation of *p-tert*-butylcalix[6]arene (**1**) and pointed out that when NaH is used as the base the products are 1,2,4,5-tetraethers but that when Me_3SiOK is used as the base the products are 1,4-diethers.[4-6] The study also demonstrated that the 1,4-diether **3** reacts with succinoyl chloride to yield the lower rim-bridged compound **4**. The present paper extends this study and deals with (a) the bridging of 1,4-diethers with several other dialkanoyl halides, (b) the direct introduction of lower rim ether bridges into the parent calix[6]arenes, and (c) the methylation of the lower rim-bridged compounds.

(1) The term "calixarene" is variously employed in different contexts. In colloquial usage (as employed in the Discussion section), it implies the presence of hydroxyl groups, as, for instance, in "*p-tert*-butylcalix[6]arene" for **1** and "*p*-H-calix[6]arene" for **2**. In the more precise and complete specification of a compound (as used in the Experimental Section), it implies only the basic skeleton to which the substituents, including the OH groups, are attached at positions designated by appropriate numbers.

(2) *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1991. Gutsche, C. D. *Calixarenes*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989. Gutsche, C. D. Calixarenes and the Art of Molecular Basketmaking. In *Synthesis of Macrocycles: The Design of Selective Complexing Agents*; Izatt, R. M., Christensen, J. J., Eds.; John Wiley & Sons: 1987; pp 93–165. Gutsche, C. D. In *Host Guest Complex Chemistry: Macrocycles;* Vögtle, F., Weber, E., Eds.; Springer-Verlag: Berlin, 1985; pp 375–421.

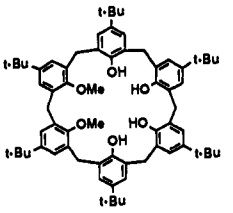
(3) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3160.

Conformational Notation

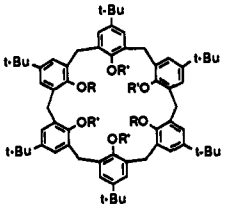
The conformational notation used in this paper presents a scheme that may find general utility in the calixarene field. Although calix[6]arenes are used as the representative examples, the scheme is applicable to calixarenes of other sizes as well. The following conventions are employed:

(A) The orientation of an aryl group of a calixarene ring is designated as "up" or "down" relative to the average plane of the molecule, as determined by its methylene groups, using the

(4) The formation of the 1,2,4,5-tetrabenzyl ether and the 1,4-dibenzyl ether stands in contrast to the reported formation of the 1,3,5-trimethyl ether.[5] Repetition of the work by Casnati *et al.*[5] confirmed their reported isolation of the trimethyl ether in *ca.* 35% yield and also resulted in the isolation of a second compound in 18% yield. On the basis of its elemental analysis and ^1H NMR spectrum, this compound is identified as the 1,2-dimethyl ether of *p-tert*-butylcalix[6]arene (**A**). That it is neither the 1,4-dimethyl ether (**B**) nor the 1,2,4,5-tetramethyl ether (**E**) was shown by independent syntheses of these materials: **B** by Me_3SiOK-induced methylation of **1** and **E** by methylation of the 1,4-dibenzyl ether **C** to give **D** followed by removal of the benzyl groups.



A



B (R = Me, R' = H)

C (R = CH_2Ar, R' = H)

D (R = CH_2Ar, R' = CH_3)

E (R = H, R' = CH_3)

(5) Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1991**, 1413.

(6) It has been reported that alkylation of **1** with 2-(chloromethyl)pyridine using $BaO/Ba(OH)_2$ produces the 1,4-diether in high yield as a barium complex: Neri, P.; Pappalardo, S. *J. Org. Chem.* **1993**, *58*, 1048.

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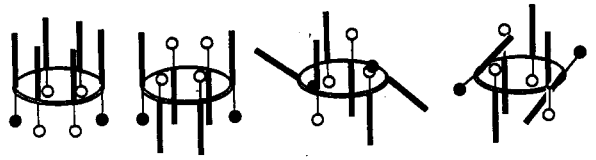
descriptors "**u**" (up) and "**d**" (down). Recognizing that in most instances the orientations of the aryl groups are not truly perpendicular, the "up" and "down" designations can be indicated as "**uo**" (up and out), "**do**" (down and out), "**ui**" (up and in), or "**di**" (down and in) when the angle of inclination is appreciable (*i.e.* 45° or more from the perpendicular). When the angle of inclination is close to 90° from the perpendicular, the group can be designated as "**o**" (out).

(B) The aryl moiety carrying the highest priority substituent (using the Cahn–Ingold–Prelog convention) at any position other than the two attached to the bridging methylene groups is designated as the *reference group*. For calixarenes the highest priority substituent will generally be the oxygen-containing function attached at the intraannular position between the methylene groups; for calixresorcinarenes it will generally be the oxygen-containing functions attached at the extraannular positions adjacent to the methylene groups.

(C) Representing the calixarene ring system as a pseudo-three-dimensional ellipse oriented horizontally (*i.e.* a side view of the average plane of the calixarene ring system), the reference group is affixed to the left-hand ("in plane of page") position and given the appropriate descriptor to designate its orientation.

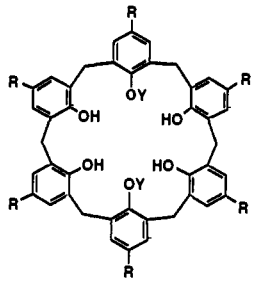
(D) Progressing, in clockwise sequence, from the left-hand ("in plane of page") position occupied by the reference group to the "behind the plane of page" positions, then to the right-hand "in plane of page" position (if present), and finally to the "in front of the plane of page" positions, the orientations of the aryl moieties are assigned the appropriate descriptors.

(E) It is recommended that the reference group descriptor be bold faced and that it be listed first in the sequence, although it should be recognized that the first and last descriptors represent adjacent groups. This can be explicitly designated by connecting these two descriptors (*i.e.* (u,u,d,d,d,u), which is identical with (u,u,u,d,d,d), (d,u,u,u,d,d), etc.). However, the parentheses are intended to imply this feature, obviating the necessisity of showing the connector. It should also be recognized that a pair of reciprocal designations (*i.e.* (**u**,u,d,u,d,d) and (**d**,d,u,,d,u,u)) specify identical conformations and, depending on the symmetry of the molecule, represent either meso or enantiomeric forms. Four representative examples are shown below.[7]



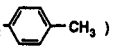
Bridged Calix[6]arenes

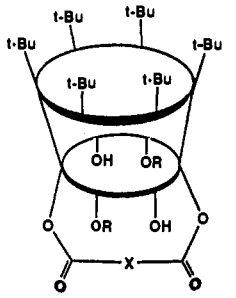
The 1,4-ditolyl ether of *p-tert*-butylcalix[6]arene (**3**) is converted in modest yields (28–55%) to the diester-bridged diethers **4–8** by treatment with the appropriate diacid chloride

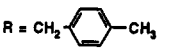


1 (R = *t*-Bu, Y = H)

2 (R = Y = H)

3 (R = *t*-Bu, Y = )



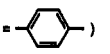
R = 

4 (X = CH_2CH_2)

5 (X = $(CH_2)_4$)

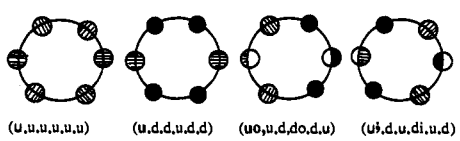
6 (X = $(CH_2)_5$)

7 (X = $(CH_2)_6$)

8 (X = )

in the presence of triethylamine. The compounds were characterized by their elemental analyses and ^1H NMR spectra and, in several cases, their mass spectra. Preliminary X-ray crystallographic data[8] obtained for **5** show it to be intramolecularly bridged, as has been observed in a number of instances in the calix[4]arene series.[9] Included among the features of the ^1H NMR spectra of **4–8** are (a) three singlets near δ 1, in accord with three sets of nonequivalent *p-tert*-butyl groups, (b) three sets of pairs of doublets in the δ 4.75–3.0 region, in accord with three sets of nonequivalent $ArCH_2Ar$ groups, and (c) a pair of doublets in the δ 5 region associated with the $ArCH_2O$ moieties in which the CH_2 hydrogens bear a diastereotopic relationship to one another. Similar observations have been reported for the $ArCH_2O$ protons of the 1,2,4,5-tetrakis(2-pyridylmethyl) ether[10] and 1,2,4,5-tetrabenzyl ethers of calix[6]arenes,[3] although the patterns for some of the latter compounds appear as triplets or broadened singlets.[11,12] Included among the diacid chlorides that produce the bridged calix[6]arenes is terephthaloyl chloride, which in the case of *p-tert*-butylcalix[4]arene reacts intermolecularly to join two calixarenes together to give a double calixarene.[13]

(7) The conformational notations can be rendered in two-dimensional fashion by employing the shadow projected when light is cast downward from the upper rim of the calixarene. A cross-hatched circle denotes a group projecting toward the light (a "**u**" group), a solid circle denotes a group projecting away from the light (a "**d**" group), a circle cross-hatched in the half outside the calixarene ring denotes a group projecting up and outward (a "**uo**" group), a circle cross-hatched in the half inside the calixarene ring denotes a group projecting up and inward (a "**ui**" group), a circle solid-filled in the half outside the calixarene ring denotes a group projecting down and outward (a "**do**" group), a circle solid-filled in the half inside the calixarene ring denotes a group projecting down and inward (a "**di**" group), and an unfilled circle denotes a group projecting outward (an "**o**" group).



(8) We are indebted to Professor William H. Watson and Dr. Ram P. Kashyap for carrying out the X-ray crystallographic determination.

(9) Alfieri, G.; Dradi, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1075. Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.-E.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567. Beer, P. D.; Keefe, A. D.; Böhmer, V.; Goldmann, H.; Vogt, W.; Lecocq, S.; Perrin, M. *J. Organomet. Chem.* **1991**, *421*, 265. Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 4527.

(10) Neri, P.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B.; Pons, M.; Molins, M. A.; Giunta, L.; Pappalardo, S. *J. Am. Chem. Soc.* **1992**, *114*, 7814.

(11) The methylene protons of the benzyl groups in the 1,2,4,5-tetrabenzylcalix[6]arenes show ^1H NMR patterns ranging from well-separated pairs of doublets, to triplets, to broad singlets. In ref 3 it was stated that these patterns arise from the "nonequivalent hydrogens of the CH_2 groups of the benzyloxy moieties". It is more precise, however, to state that the hydrogens bear a diastereotopic relationship to one another. Application of the "substitution test"[12] (*i.e.* changing a benzyl H to G) makes the benzyl group a PhC(H,G)O moiety, rendering it chiral and, concurrently, different from the other three benzyl groups. This, in turn, confers chirality on the calixarene itself (*i.e.*, a calix[6]arene substituted in an "*abcacc*" pattern is chiral), verifying the diastereotopic relationship of the methylene protons. In similar fashion, the methylene protons of the benzyl groups of **4–8** are characterized as diastereotopic. In contrast, the CH_2 hydrogens of the benzyloxy moieties of 1,4-disubstituted calix[6]arenes bear an equivalent relationship and appear as singlets.

(12) Mislow, K.; Raban, M. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Eds.; Interscience: New York, 1967; Vol. 1, pp 1–38.

(13) Kraft, D.; van Loon, J.-D.; Owens, M.; Verboom, W.; Vogt, W.; McKervey, M. A.; Böhmer, V.; Reinhoudt, D. N. *Tetrahedron Lett.* **1990**, *31*, 4941. For a study of inter- *vs* intramolecular bridging in the calix[4]arenes, *cf.* van Loon, J.-D.; Kraft, D.; Ankone, M. J. K.; Verboom, W.; Harkema, S.; Vogt, W.; Böhmer, V.; Reinhoudt, D. N. *J. Org. Chem.* **1990**, *55*, 5176.

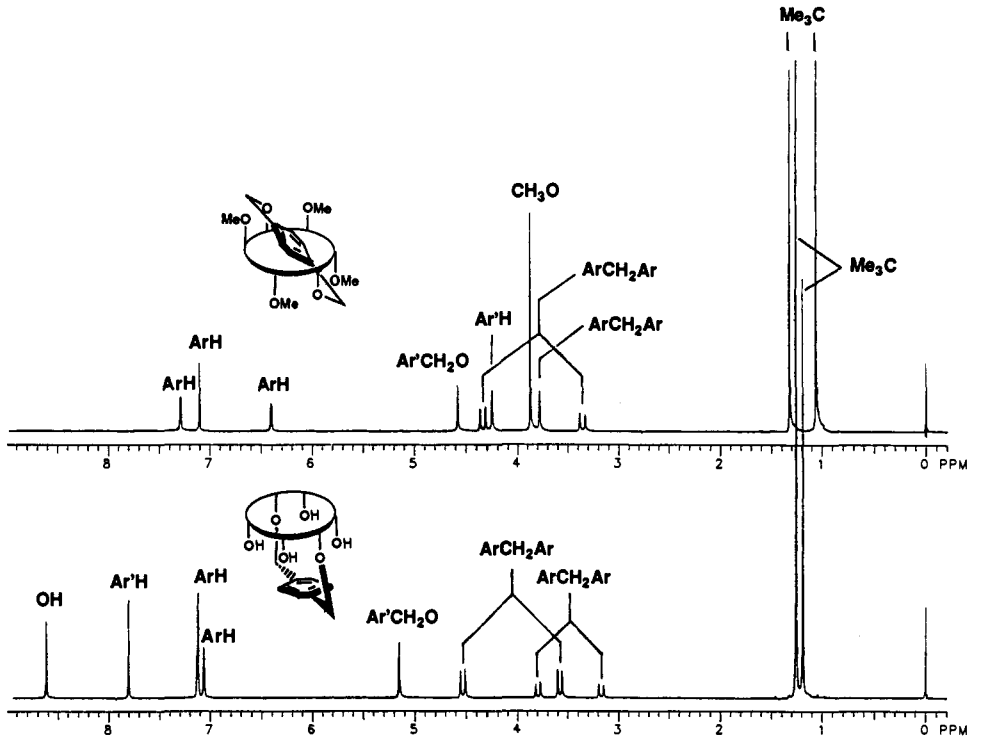
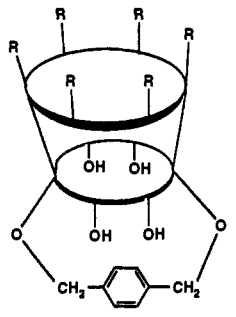


Figure 1. ^{1}H NMR spectra of **9** and **15** at room temperature in $CDCl_3$ at 300 MHz.

Apparently, the greater flexibility of the calix[6]arene ring system allows the transannular OH groups to approach each other closely enough to allow intramolecular bridging to occur instead.

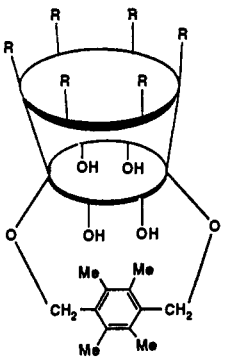
Taking advantage of the earlier observation[3] that 1,4-diethers of calix[6]arenes are produced when a potassium base is used, *p-tert*-butylcalix[6]arene (**1**) and *p*-H-calix[6]arene (**2**) are converted in fair to good yield (40–75%) to the 1,4-bridged ethers **9–13** by treatment with the appropriate bis-arylmethyl halide in the presence of $KOSiMe_3$. The ^{1}H NMR spectra of compounds **9–13** are illustrated by that of **9** (see Figure 1), which shows singlets for OH, ArH of the bridging phenyl, and benzyl CH_2 protons; two pairs of very close-spaced doublets (2:1 ratio) for ArH of the calixarene phenyls; two sets of pairs of doublets (2:1 ratio) for calixarene CH_2 protons; and two singlets (2:1 ratio) for *p-tert*-butyl protons. A survey of the possible conformations for substituted calix[6]arenes[14] indicates that there is only one disubstituted calix[6]arene that clearly possesses two sets of pairs of doublets (2:1 ratio) arising from the methylene resonances, *viz.* a 1,4-disubstituted calix[6]arene with the (u,u,u,u,u,u) conformation. A 1,4-disubstituted calix[6]arene with the (u,d,d,u,d,d) conformation might also possess two sets of pairs of doublets (2:1 ratio) but more likely would have only one pair of doublets along with a singlet (1:2 ratio), Therefore, the (u,u,u,u,u,u) cone-like conformation is chosen as the more likely one for the bridged compounds **9–13.** This stands in contrast to the 1,2,4,5-tetraaroylates, which in an earlier investigation[14] were shown to exist in the (u,u,d,d,d,u) conformation (designated as the "1,2,3-alternate" conformation). It also stands in contrast to the 1,2,4,5-tetrakis(2-pyridylmethyl)oxycalix[6]arene, which is stated to possess a (u,d,d,u,d,u) conformation.[10,15]

Treatment of the bridged ring compounds **9**, **11**, and **13** with MeI and NaH affords the corresponding tetramethyl ethers, isolated in the case of **15** (from **9**) and **18** (from **13**) as single



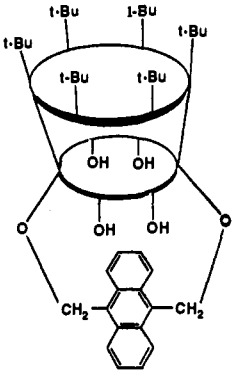
9 (R = *t*-Bu)

10 (R = H)



11 (R = *t*-Bu)

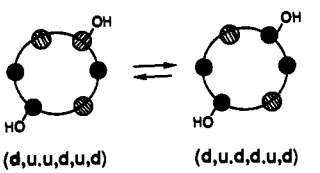
12 (R = H)



13

(14) Rogers, J. S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3152. See supplementary material.

(15) The (d,u,u,d,u,d) and (d,u,d,d,u,d) conformers (conformers A and A1 in ref 8) described by Pappalardo *et al.*[10] (shown below in projection representation with the positions of the OH-containing aryl moieties explicitly designated)



(d,u.u,d,u,d) (d,u.d,d.u,d)

contain three sets of nonequivalent aryl rings and might be expected to display three singlets for the *tert*-butyl protons in a 1:1:1 ratio. The observed pair of singlets in a 2:1 ratio perhaps can be ascribed to accidental equivalence, a possibility that colors all of the conformational assignments of calixarenes made on the basis of NMR spectral observations.

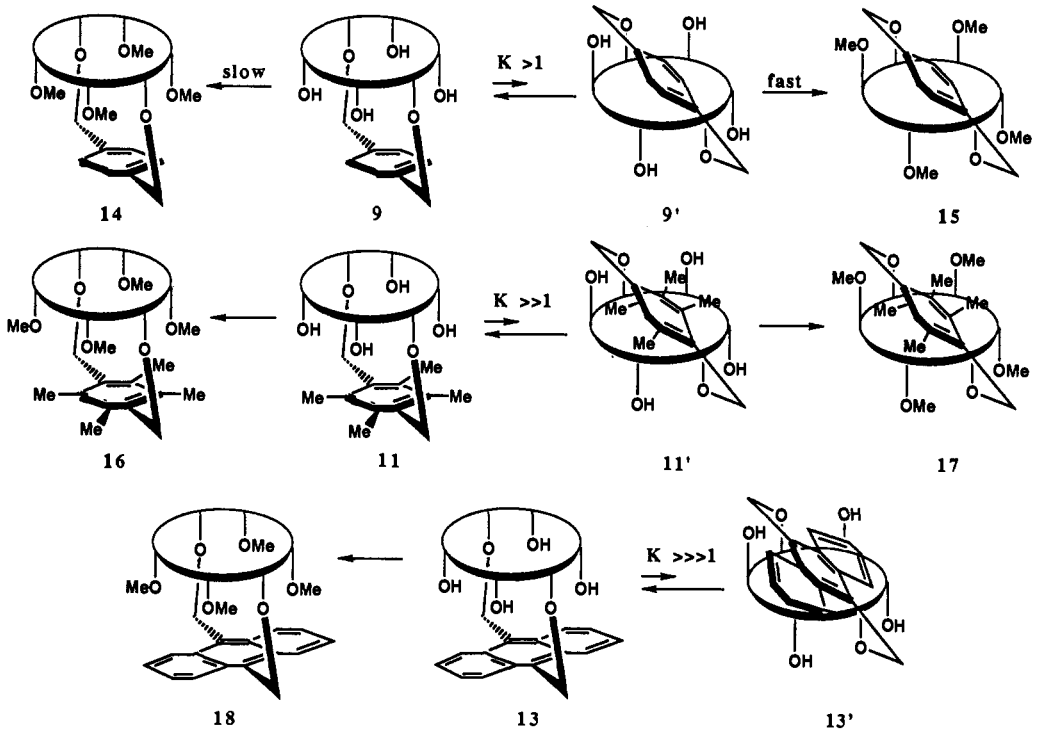


Figure 2. Methylation of 1,4-bridged calix[6]arenes.

compounds in 77% and 81% crude yields, respectively. Compound **11**, on the other hand, produces a mixture of ethers from which pure compounds were not obtained. The ^{1}H NMR of the tetramethoxy anthrylene-bridged compound **18** is quite similar to that of its precursor **13**, indicating that starting material and product have the same conformation; for example, both possess two sets of pairs of doublets for the calixarene methylene protons, commensurate with the (u,u,u,u,u,u) conformation shown in Figures 1 and 2. The ^{1}H NMR of **15**, however, is quite different from that of its precursor **9**. The ArH resonances of the bridging phenyl ring move upfield from δ 7.80 to δ 4.25,[16] the resonance of the CH_2 protons of the bridging moiety moves upfield from δ 5.15 to δ 4.57, the pattern for the calixarene CH_2 protons changes to a pair of doublets and a singlet (ratio 2:1), and the two *p-tert*-butyl resonances move slightly, one upfield and one downfield. A survey of the possible conformations for substituted calix[6]arenes[14] shows that there is only one disubstituted calix[6]arene that clearly possesses one pair of doublets and a singlet (2:1 ratio); *viz.* the (u,u,d,d,d,u) 1,2,3-alternate conformation, as shown in Figures 1 and 2. A 1,4-disubstituted calix[6]arene with the (u,d,u,d,u,d) conformation (designated as the 1,3,5-alternate conformation) might also possess a pair of doublets and a singlet (2:1 ratio) but more likely would have only 2 singlets (2:1 ratio). Thus, the ^{1}H NMR spectrum of **15** appears to demand the same conformation that is adopted by the 1,2,4,5-tetraaroylates of calix[6]arenes, one that might seem unlikely in the present case in that it requires the bridging moiety to be threaded through the annulus of the macrocyclic ring system. Such a conformation can be viewed as a rotaxane-type molecule (*i.e.* an axle threaded through a ring) in which the two ends of the axle are bonded to the ring (*i.e.* a "self-anchored rotaxane"). The differing conformational behavior of the bridged compounds **9**, **11**, and **13** upon methylation can be interpreted as the result of the relative sizes of the bridging moieties. Phenylene, the smallest of the bridges, should be the one most easily accommodated by the annulus; anthrylene, the largest of the bridges, should be the one least easily accommodated; durylene, intermediate in size, is less easily accommodated than phenylene but more easily than anthrylene. The sequence of events depicted in Figure 2 rationalizes the observed results by postulating that (a) the **9** → **9'** interconversion is faster than methylation, (b) the **13** → **13'** interconversion is slower than methylation (or does not occur), and (c) the **11** → **11'** interconversion represents an intermediate situation where conformational changes and methylation are comparable in rate.

With perseverance a CPK model of **15** (u,u,d,d,d,u conformation) can be constructed which, although quite rigid, appears to be without serious strain. The two aryl rings and the bridging moiety to which they are attached are arranged in a "Z" fashion, and the four OMe groups enjoy a relatively unhindered environment. CPK models are known to be "harder" and less flexible and resilient than the molecules they represent, a case in point being the tetramethyl ether of *p-tert*-butylcalix[4]arene, which undergoes conformational inversion far more easily than the CPK model would predict.[17] Thus, the capacity for the CPK model of **15** to be constructable provides evidence that this molecule can, indeed, adopt the (u,u,d,d,d,u) conformation, as indicated by its ^{1}H NMR spectrum, even though it is not possible to convert the CPK model of the (u,u,u,u,u,u) conformation to the (u,u,d,d,d,u) conformation without breaking bonds. In contrast to **15**, the CPK model of the tetramethyl ether of the anthrylene-bridged compound **13**, while constructable in the (u,u,u,u,u,u) conformation,[18] cannot be constructed in the (u,u,d,d,d,u) conformation. Inspection of the CPK models of the tetramethoxy ethers **14** (u,u,u,u,u,u conformation) and **15** (u,u,d,d,d,u conformation) indicates that the OMe groups are forced closer to one another in **14** than in **15**. In the case of the parent compounds **9** and **9'** the forced proximity is advantageous in that it promotes hydrogen bonding, but in the ethers it constitutes an electrostatic disadvantage (see below).

The ^{1}H NMR spectra of the tetramethoxy anthrylene-bridged compound **18** at various temperatures (Figures 3 and 4) show interesting changes that can be rationalized in terms of the following conformational interconversions: (a) The two *tert*-

(16) The positions of the upfield-shifted resonances arising from the ArH and the CH_2 protons of the bridging moiety are arbitrarily assigned; they may be the reverse.

(17) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409.

(18) More accurately specified as the (uo,u,u,uo,u,u) conformation.

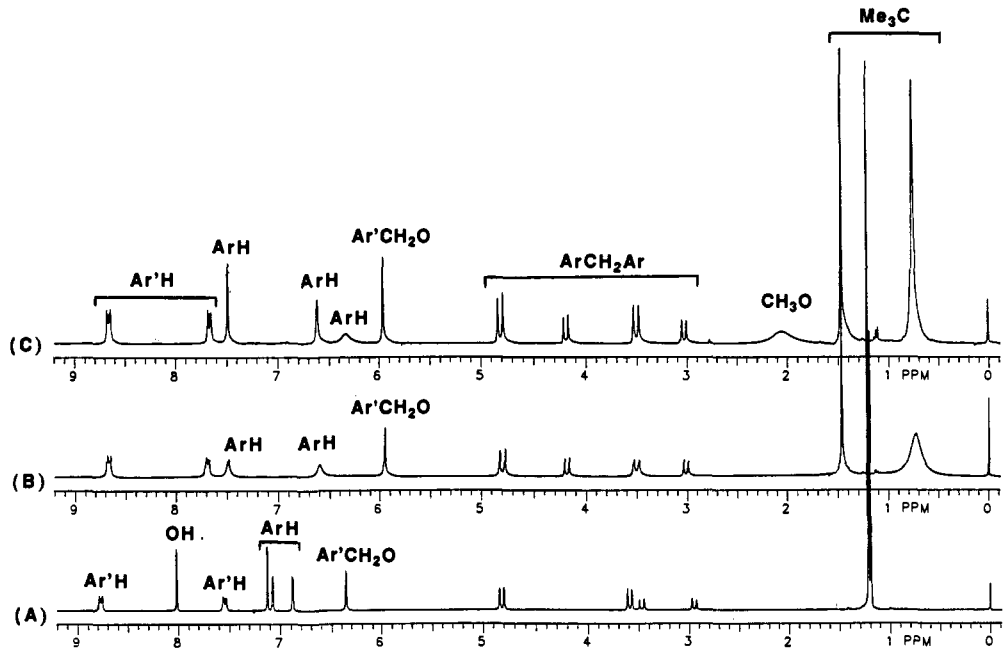


Figure 3. ^{1}H NMR spectra in $CDCl_3$ at 300 MHz: (A) **13** at room temperature; (B) **18** at room temperature; (C) **18** at 55 °C.

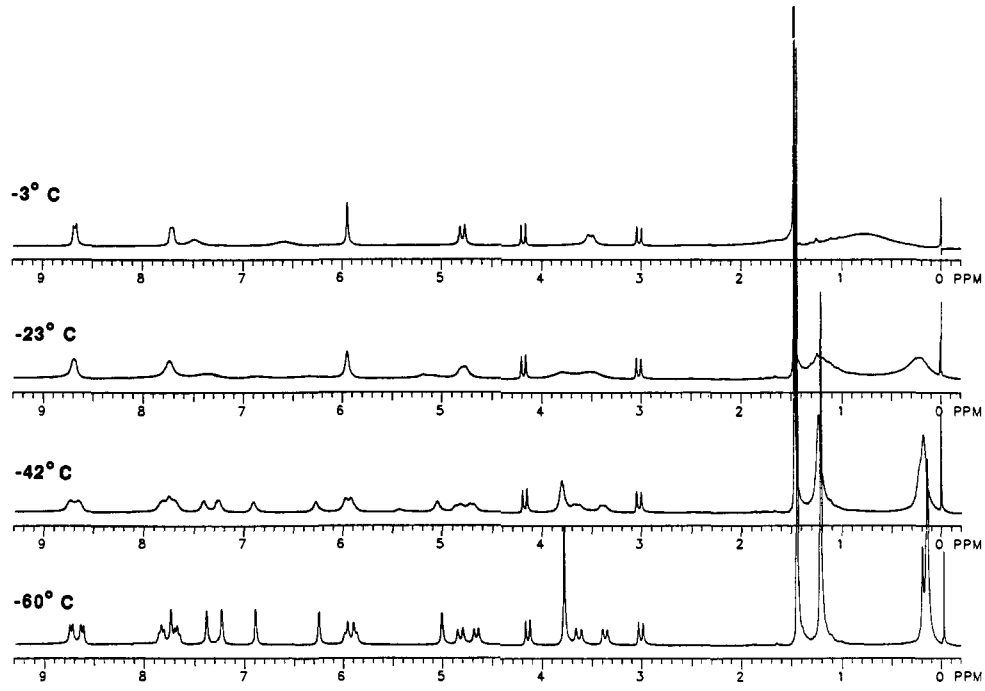


Figure 4. ^{1}H NMR spectra in $CDCl_3$ at 300 MHz of **18** at low temperatures.

butyl resonances at δ 0.75 and 1.46 in the spectrum at 55 °C change to three resonances at δ 0.14, 1.18, and 1.42 in the –60 °C spectrum, the coalescence temperature for the δ 0.14 and 1.18 lines being *ca.* 0 °C. These changes can be attributed to "inside the cavity" (δ 0.14) and "outside the cavity" (δ 1.18) orientations for one or more of the *tert*-butyl groups, the transformation between these conformations being rapid on the NMR time scale at 55 °C but slow at –60 °C. The CPK model of **18**, in fact, is assembled most easily with one of the aryl moieties orientied so that its *tert*-butyl group fills the cavity. (b) The room temperature spectrum of **18** appears to lack an OMe resonance, but at 55 °C a broad band attributable to this group appears at δ 2.05, which splits at –60 °C into two resonances at δ 0.19 and 3.78. This behavior can likewise be explained in terms of "inside the cavity" (δ 0.19) and "outside the cavity" (δ 3.78) orientations for the OMe group, with the coalescence temperature for this conformational interconversion probably being near 0 °C. (c) The $ArCH_2Ar$ resonance consists of two sets of pairs of doublets at 55 °C (centered at δ 3.05, 3.50, 4.20, and 4.81) and three sets of pairs of doublets at –60 °C (centered at δ 3.05, 3.36, 3.64, 4.20, 4.66, and 4.81). A molecule of **18** undergoing conformational interconversion that is rapid on the NMR time scale possesses only two sets of $ArCH_2Ar$ methylenes that are structurally nonequivalent regardless of the conformation, accounting for the two sets of pairs of doublets that are observed at 55 °C. A molecule of **18** in which one of the *tert*-butyl groups occupies the cavity, however, possesses three sets of nonequivalent $ArCH_2Ar$ methylenes, giving rise to the three sets of pairs of doublets observed at –60 °C, where the rate of conformational interconversion is slow on the NMR time scale. The coalescence temperature for this transformation appears to be *ca.* –30 °C. (d) The $ArCH_2O$ resonance consists of a singlet at δ 5.95 at room temperature but becomes a close-lying pair of doublets at δ 5.92 at –60 °C with a coalescence temperature in the vicinity of –40 °C. For the

Table I. Energies of 1,4-Bridged Calix[6]arenes Produced by the QUANTA/CHARMm Molecular Modeling and Mechanics Program

compound	conformation	minimized energy, kcal/mol
	Phenylene-Bridged Series	
9	u,u,u,u,u,u (*tert*-butyl "outside cavity")	73.64
9	u,u,u,u,u,u (*tert*-butyl "inside cavity")	61.07
9	u,u,u,u,u,u ($CHCl_3$ "inside cavity")	32.32
9′	u,u,d,d,d,u	72.72
	u,u,d,d,u,d	86.76
14	u,u,u,u,u,u	94.46
14	u,u,u,u,u,u ($CHCl_3$ "inside cavity")	72.86
15	u,u,d,d,d,u	75.53
	u,u,d,d,u,d	90.57
	Anthrylene-Bridged Series	
13	u,u,u,u,u,u (*tert*-butyl "outside cavity)	88.79
13	u,u,u,u,u,u (*tert*-butyl "inside cavity")	81.28
13	u,u,u,u,u,u ($CHCl_3$ "inside cavity")	67.80
18	u,u,u,u,u,u (all OMe "outside cavity")	139.13
18	u,u,u,u,u,u (one OMe "inside cavity")	138.21
18	u,u,u,u,u,u (two OMe "inside cavity")	130.25
18	u,u,u,u,u,u (two OMe and $CHCl_3$ "inside cavity")	115.33

reasons discussed above, the "inside the cavity" orientation of a *tert*-butyl group in **18** confers nonequivalence on the $ArCH_2O$ methylenes, accounting for the pair of doublets at –60 °C. (e) The ArH protons of the calixarene ring appear as three resonances (δ 6.27, 6.59, 7.48) at 55 °C, as two resonances (δ 6.59, 7.48) at room temperature, and as six resonances (δ 5.00, 6.24, 6.88, 7.22, 7.37, 7.73) at –60 °C, with a coalescence temperature of *ca.* 0 °C. The Ar′ resonances of the anthracene ring also show a more complex pattern at –60 °C than at room temperature. These changes similarly are attributable to the unsymmetrical character of the "fixed" conformation at –60 °C.

Molecular modeling studies provide further insight into the conformational possibilities in this series of 1,4-bridged calix[6]arenes. The data shown in Table I indicate the following: (a) The phenylene-bridged calix[6]arene is more stable in the (**u**,u,u,u,u,u) conformation (**9**) than in the (**u**,u,d,d,d,u) conformation (**9′**) even when $CHCl_3$ is not included in the cavity of the latter. (b) The tetramethyl ether of the phenylene-bridged calix[6]arene is more stable in the (**u**,u,d,d,d,u) conformation (**15**) than in the (u,u,u,u,u,u) conformation (**14**) when $CHCl_3$ is not included and comparable in stability when $CHCl_3$ is included. Although the angle energy is higher for **15** than for **14** (39.30 *vs* 23.46 kcal/mol), this is more than offset by the electrostatic energy which is much more favorable for **15** than **14** (–78.67 *vs* –52.96 kcal/mol without $CHCl_3$ in the cavity and –58.87 with $CHCl_3$ in the cavity), in accord with the observation noted above in the discussion of the CPK models that the OMe groups are further from one another in **15** than in **14**. (c) The tetramethyl ether of the anthrylene-bridged calix[6]arene in the (u,u,u,u,u,u) conformation is more stable when two of the OMe groups are oriented "inward" than when one or both are oriented "outward", and the inclusion of $CHCl_3$ in the cavity lowers the energy significantly. When three OMe groups are oriented "inward", the energy-minimization program reorients one of them to an "outward" position.

Attempts to secure crystals of **9**, **13**, **15**, or **18** suitable for X-ray crystallography have so far failed. To this end, the tetraethyl ether of **9** was synthesized and was shown to possess the same ^1H NMR spectral features as **15**; however, it also failed to yield satisfactory crystals. Attempts to make the tetrabenzyl ether from **9** yielded a mixture from which no pure material has been isolated.

Conclusion

^1H NMR spectral evidence, CPK model building, and molecular modeling studies combine to support the following conclusions: (a) A surprising (**u**,u,u,u,u,u) to (**u**,u,d,d,d,u) conformational change occurs when the phenylene-bridged calix[6]arene **9** is converted to its tetramethyl ether **15**, the structure of which is shown in Figure 5 in a three-quarter-view stick and ball model and a top-view CPK model. (b) No major conformational change occurs when the anthrylene-bridged calix[6]arene **13** is converted to its tetramethyl ether **18**, both compounds in this case possessing the (**u**,u,u,u,u,u) conformation. (c) Conformational interconversions with low energy barriers occur in the tetramethyl ether of the anthrylene-bridged calix[6]arene **18** involving the OMe and *tert*-butyl groups in "inward" and "outward" orientations.

Experimental Section[19]

Procedure A: 1,4-Bridged Esters. A solution of 0.24 g (0.2 mmol) of diether **3**, prepared as previously described,[3] in 200 mL of CH_2Cl_2 is treated with 0.2 mL (1.5 mmol) of triethylamine and stirred until a clear solution forms. To this is added, over a period of 15 min, a solution of 0.3 mmol of the acid chloride in 10 mL of CH_2Cl_2. The reaction mixture is allowed to stand at room temperature for 30 min; solvent is then removed, and the product is purified by chromatography on silica gel (70–230 mesh, 60 Å).

Procedure B: 1,4-Bridged Ethers. A solution containing 1 mmol of calix[6]arene **1** or **2** in 100 mL of THF and 10 mL of DMF is cooled to 0 °C, treated with 0.77 g (6 mmol) of Me_3SiOK, and stirred for 15 min. A solution of 1.2 mmol of the bis-halomethyl compound in 10 mL of THF is added, and the reaction mixture is stirred at room temperature for 4–6 h and the course of the reaction followed by TLC. The solvent is removed under vacuum, 150 mL of cold 0.1 N HCl is added, the precipitate is removed by filtration, and the dried crude product is purified by recrystallization.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dihydroxy-39,42-(adipoyldioxy)-38,41-bis[(4-methylbenzyl)oxy]calix[6]arene (5) was prepared following procedure A using adipoyl chloride. The fractions eluted with CH_2Cl_2–hexane (80:20) were collected and recrystallized from CH_2Cl_2–MeOH to give 90 mg (37%) of **5**: mp 204–206 °C; MS (FAB) $(M + H)^+$ 1292; ^1H NMR ($CDCl_3$) δ 7.74 (s, 2), 7.41 and 7.24 (each d, 2 × 4, J = 8.0 Hz), 7.37, 7.28, 7.05, 6.99 and 6.78 (each d, 2 × 5, J = 2.3 Hz), 6.54 (d, 2, J = 2.1 Hz), 4.90 (ABq, 4, J = 16 and 10 Hz), 4.12 (d, 2, J = 14.5 Hz), 4.02 (d, 2, J = 13.5 Hz), 3.78 (d, 2, J = 14.2 Hz), 3.49 (d, 2, J = 13.5 Hz), 3.47 (d, 2, J = 14.5 Hz), 3.39 (d, 2, J = 14.2 Hz), 2.40 (s, 6), 1.41, 1.02 and 1.01 (each s, 3 × 18). The protons from the adipoyl ester appeared as multiplets at δ 2.45–2.31 and 1.85–1.55. ^{13}C NMR ($CDCl_3$) δ 172.78 (C=O), 149.47, 147.58, 147.47, 145.29, 141.48, 139.15, 132.40, 132.36, 132.02, 130.72, 126.12 (ArC), 129.62, 129.54, 128.40, 126.86, 125.86, 125.49, 124.29, 123.36 (ArH), 78.18 ($ArCH_2O$), 34.38, 34.07, 33.81, 32.73, 30.84, 30.26, 28.83, 20.45 ($ArCH_2Ar$, $ArCMe_3$, and CH_2), 31.59, 31.41, 31.05 ($ArCMe_3$), 21.32 (ArMe). Anal. Calcd for $C_{88}H_{106}O_8$: C, 81.82; H, 8.27. Found: 81.97; H, 8.41.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dihydroxy-39,42-(pimeloyldioxy)-38,41-bis[(4-methylbenzyl)oxy]calix[6]arene (6) was prepared following procedure A using pimeloyl chloride. Fractions eluted with CH_2Cl_2–hexane (50:50) were collected and recrystallized from CH_2Cl_2–MeOH to give 85 mg (33%) of **6**: mp 301–302 °C; ^1H NMR ($CDCl_3$) δ 7.49 (s, 2), 7.23, 7.20, 7.13 and 6.34 (each b s, 4 × 2), 7.01 to 6.97 (m, 4), 7.03 and 6.72 (each d, 2 × 4, J = 8.0 Hz), 4.76 (d, 2, J = 10.4 Hz), 4.45 (d, 2, J = 10.4 Hz), 4.20 (d, 2, J = 13.4 Hz), 4.16 (s, 4), 3.87 to 3.81 (m, 4), 3.36 (d, 2, J = 13.4 Hz), 2.32 (s, 6), 1.26, 1.22, and 1.05 (each s, 3 × 18). The protons of the pimeloyl ester appeared as multiplets at δ 0.68–0.46 (m, 4), 0.4–0.26 (m, 4), and 0.18–0.08 (m, 2). ^{13}C NMR ($CDCl_3$) δ 170.34 (C=O), 151.48, 150.11, 147.77, 147.42, 146.93, 141.65, 137.94, 133.34, 132.56, 131.30, 130.65, 130.28, 127.63, 124.94 (ArC),

(19) Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. THF was freshly distilled from sodium–benzophenone. The melting points of all compounds melting above 250 °C were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) using a 500 °C thermometer calibrated against a thermocouple. HPLC analyses employed an Analtech reversed-phase C-18 column. ^1H NMR spectra were recorded at 300 MHz. TLC analyses were carried out on Analtech silica gel plates (absorbant thickness 250 mm) containing a fluorescent indicator. Flash chromatography was carried out with J.T.Baker silica gel #JT7042-2 (40-mm particles) on columns 50 mm in diameter filled to a height of *ca.* 7 in. Elution rates were 2 in/min; fractions of 50 mL were collected. Analytical samples were dried at least 36 h at 100–140 °C and 1–2 mmHg of pressure.

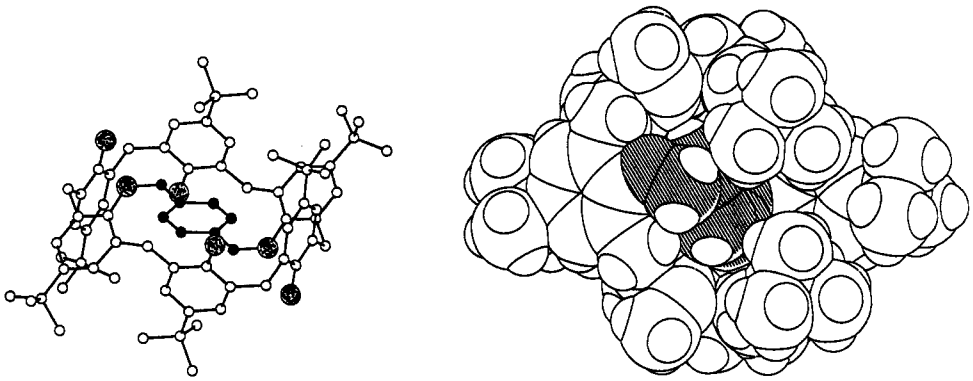


Figure 5. Stick and ball model (left-hand structure) of phenylene-bridged calix[6]arene **9'** and CPK model (right-hand structure) of the tetramethyl ether of the phenylene-bridged calix[6]arene **15**, both in the (u,u,d,d,d,u) conformation.

129.16, 128.16, 127.15, 126.90, 125.83, 125.23, 123.74 (ArH), 75.55 ($ArCH_2O$), 39.28, 34.25, 33.88, 32.38, 31.28, 29.75, 23.80, 19.88 ($ArCH_2Ar$, $ArCMe_3$, and CH_2), 31.42, 31.39 ($ArCMe_3$), 21.22 (ArMe). Anal. Calcd for $C_{89}H_{108}O_8$: C, 81.86; H, 8.34. Found: C, 82.01; H, 8.20.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dihydroxy-39,42-(suberoyldioxy)-38,41-bis[(4-methylbenzyl)oxy]calix[6]arene (7) was prepared following procedure A using suberoyl chloride. Fractions eluted with CH_2Cl_2–hexane (1:1) were collected and recrystallized from CH_2Cl_2–MeOH to give 75 mg (28%) of **7**: mp 257–258 °C; ^{1}H NMR ($CDCl_3$) δ 7.57 (s, 2), 7.25 (s, 2), 7.15 (s, 2), 7.08 (s, 2), 7.03–6.97 (m, 8), 6.71 (d, 4, J = 10.8 Hz), 6.43 (s, 2, ArH), 4.74 (d, 2, J = 10.8 Hz), 4.48 (d, 2, J = 10.8 Hz), 4.13 (b d, 4), 4.05 (b s, 4), 3.94 (d, 2, J = 13.4 Hz), 3.39 (d, 2, J = 13.4 Hz), 2.32 (s, 6), 1.24, 1.23 and 1.05 (each s, 3 × 18). The protons of the suberoyl ester appeared as broad multiplets between δ 0.95 and 0.10. ^{13}C NMR ($CDCl_3$) δ 171.27 (C=O), 151.67, 150.11, 147.65, 147.51, 146.88, 141.91, 137.87, 133.95, 132.51, 131.99, 130.53, 129.95, 128.22, 125.69 (ArC), 129.13, 128.02, 126.79, 125.16, 124.10, 123.77 (ArH), 75.58 ($ArCH_2O$), 39.15, 34.21, 33.89, 32.55, 30.21, 29.90, 26.14 ($ArCH_2Ar$, $ArCMe_3$, and CH_2), 31.48, 31.42 ($ArCMe_3$), 21.56 (ArMe). Anal. Calcd for $C_{90}H_{110}O_8$: C, 81.90; H, 8.40. Found: C, 82.03; H, 8.44.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dihydroxy-39,42-(terephthaloyldioxy)-38,41-bis[(4-methylbenzyl)oxy]calix[6]arene (8) was prepared following procedure A using terephthaloyl chloride. Fractions eluted with CH_2Cl_2 were collected and recrystallized from CH_2Cl_2–MeOH to give 110 mg (42%) of **8**: mp 225–226 °C; MS (FAB) $(M + H)^+$ 1311; ^{1}H NMR ($CDCl_3$) δ 7.47 (d, 2, J = 2.2 Hz), 7.36 (d, 2, J = 2.2 Hz), 7.11 (dd, 4, J = 8.1 Hz), 7.00–6.96 (b m, 4), 6.87 (d, 2, J = 2.2 Hz), 6.54 (d, 2, J = 2.2 Hz), 4.64 (d, 2, J = 10.4 Hz), 4.52 (d, 2, J = 10.4 Hz), 4.37 (s, 2), 4.25 (d, 4, J = 16.6 Hz), 3.70 (d, 2, J = 15.8 Hz), 3.55 (d, 2, J = 16.2 Hz), 3.30 (d, 2, J = 15.0 Hz), 3.27 (d, 2, J = 16.0 Hz), 2.35 (s, 6), 1.47 (s, 18), 1.12 (s, 18), 0.85 (s, 18); ^{13}C NMR ($CDCl_3$) δ 162.95 (C=O), 151.37, 148.86, 148.45, 146.15, 145.48, 141.96, 137.94, 134.17, 133.58, 133.16, 132.79, 131.55, 130.80, 126.46, 123.77 (ArC), 129.25, 129.00, 127.85, 127.25, 127.16, 126.60, 125.15, 124.59, 123.69 (ArH), 74.95 ($ArCH_2O$), 34.61, 34.08, 33.79, 32.24, 30.61, 28.46 ($ArCH_2Ar$ and ArCMe), 31.69, 31.49, 31.32 ($ArCMe_3$), 21.22 (ArMe). Anal. Calcd for $C_{90}H_{102}O_6$: C, 82.41; H, 7.84. Found: C, 82.16; H, 7.81.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-(*p*-xylylenedioxy)calix[6]arene (9) was prepared in 75% crude yield following procedure B using **1** and α,α'-dibromo-*p*-xylene. An analytical sample of **9** was recrystallized from $CHCl_3$–MeOH: mp >318 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.61 (s, 4), 7.80 (s, 4), 7.12 (s, 8), 7.05 (d, 4, J = 2.3 Hz), 5.15 (s, 4), 4.52 (d, 4, J = 13.0 Hz), 3.79 (d, 2, J = 13.6 Hz), 3.58 (d, 4, J = 13.0 Hz), 3.17 (d, 2, J = 13.6 Hz), 1.25 (s, 36), 1.18 (s, 18); ^{13}C NMR ($CDCl_3$) δ 150.10, 148.20, 148.07, 142.05, 137.09, 133.22, 127.03, 126.81 (ArC), 131.02, 126.19, 125.82, 125.58 (ArH), 77.87 ($ArCH_2O$), 34.29, 33.83, 33.45, 33.00 ($ArCH_2Ar$ and Me_3C), 31.63, 31.27 ($ArCMe_3$). Anal. Calcd for $C_{74}H_{90}O_6$: C, 82.64; H, 8.43. Found: C, 82.56; H, 8.62.

37,38,40,41-Tetrahydroxy-39,42-(*p*-xylylenedioxy)calix[6]arene (10) was prepared in 74% crude yield following procedure B using **2** and α,α'-dibromo-*p*-xylene. An analytical sample was recrystallized from $CHCl_3$–MeOH; mp >320 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.52 (s, 4), 7.85 (s, 4), 7.14–7.06 (m, 12), 6.95 (t, 2, J = 7.0 Hz), 6.70 (t, 4, J = 7.5 Hz), 5.18 (s, 4), 4.55 (d, 4, J = 13.0 Hz), 3.77 (d, 2, J = 13.9 Hz), 3.63 (d, 4, J = 13.0 Hz); ^{13}C NMR ($CDCl_3$) δ 152.39, 150.58, 137.20, 133.83, 127.56 (ArC), 131.05, 129.67, 129.10, 128.79, 126.03, 119.85 (ArH), 78.09 ($ArCH_2O$), 32.35, 32.22 ($ArCH_2Ar$). Anal. Calcd for $C_{50}H_{42}O_6$: C, 81.28; H, 5.73. Found: C, 81.27; H, 6.07.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-[durylenebis(methyleneoxy)]calix[6]arene (11) was prepared in 73% crude yield following a slightly modified procedure B using 0.47 g (0.5 mmol) of **1** and 3,6-bis(chloromethyl)durene in 100 mL of THF containing 10 mL of DMF. An analytical sample was recrystallized from CH_2Cl_2–MeOH: mp >400 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.81 (s, 4), 7.11 (s, 8), 7.03 (d, 4, J = 2.3 Hz), 5.57 (s, 4), 4.80 (d, 4, J = 12.8 Hz), 3.78 (d, 2, J = 13.5 Hz), 3.51 (d, 4, J = 12.9 Hz), 3.15 (d, 2, J = 13.8 Hz), 2.64 (s, 12), 1.25 (s, 36), 1.19 (s, 18); ^{13}C NMR ($CDCl_3$) δ 150.17, 148.27, 147.92, 141.91, 134.76, 133.80, 133.22, 127.16, 126.63 (ArC), 126.09, 126.03, 125.65 (ArH), 72.45 ($ArCH_2O$), 34.20, 33.82, 33.70, 32.54 ($ArCH_2Ar$ and $ArCMe_3$), 31.63, 31.22 ($ArCMe_3$), 18.12 (ArMe). Anal. Calcd for $C_{78}H_{98}O_6$: C, 82.79; H, 8.73. Found: C, 82.64; H, 9.00.

37,38,40,41-Tetrahydroxy-39,42-[durylenebis(methyleneoxy)]calix[6]-arene (12) was prepared in 96% crude yield following procedure B using **2** and 3,6-bis(chloromethyl)durene. An analytical sample was recrystallized from CH_2Cl_2–MeOH: mp >380 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.69 (s, 4), 7.12–7.04 (m, 12), 6.93 (t, 2, J = 7.2 Hz), 6.69 (t, 4, J = 7.5 Hz), 5.61 (s, 4), 4.82 (d, 4, J = 13.0 Hz), 3.77 (d, 2, J = 13.8 Hz), 3.57 (d, 4, J = 13.0 Hz), 3.18 (d, 2, J = 13.8 Hz), 2.65 (s, 12); ^{13}C NMR ($CDCl_3$) δ 152.41, 150.65, 134.80, 134.31, 127.59, 127.54 (ArC), 133.26, 129.59, 129.31, 128.75, 125.95, 119.77 (ArH), 72.69 ($ArCH_2O$), 32.35, 31.87 ($ArCH_2Ar$ and $ArCMe_3$), 18.17 (ArMe). Anal. Calcd for $C_{54}H_{50}O_6 \cdot 1/6CH_2Cl_2$: C, 80.41; H, 6.27. Found: C, 80.14; H, 6.20.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-[9,10-anthrylenebis(methyleneoxy)]calix[6]arene (13) was prepared following procedure B, modified to increase the reaction time to 72 h at room temperature, using **1** and 9,10-bis(chloromethyl)anthracene. The crude reaction mixture was chromatographed over silica gel (70–230 mesh, 60 Å). Elution with CH_2Cl_2–hexane (80:20) gave 40% of **13** followed by 0.12 g of starting material **1**. An analytical sample of **13** was recrystallized from CH_2Cl_2–MeOH: mp 252–253 °C; MS(FAB) $(M + H)^+$ 1175; ^{1}H NMR ($CDCl_3$) δ 8.78–8.75 (m, 4), 8.01 (s, 4), 7.56–7.52 (m, 4), 7.12 (s, 4), 7.07 (d, 4, J = 2.2 Hz), 6.87 (d, 4, J = 2.2 Hz), 6.35 (s, 4), 4.82 (d, 4, J = 12.4 Hz), 3.59 (d, 4, J = 12.6 Hz), 3.47 (d, 2, J = 13.8 Hz), 2.95 (d, 2, J = 13.7 Hz), 1.21 (s, 36), 1.19 (s, 18); ^{13}C NMR ($CDCl_3$) δ 149.96, 148.34, 148.06, 141.63, 133.80, 131.17, 129.33, 127.25, 126.29 (ArC), 126.44, 126.02, 125.76, 125.40, 124.31 (ArH), 69.23 ($ArCH_2O$), 34.24, 33.77, 33.56, 32.53 ($ArCH_2Ar$ and $ArCMe_3$), 31.60, 31.23 ($ArCMe_3$). Anal. Calcd for $C_{82}H_{94}O_6$: C, 83.78; H, 8.06. Found: C, 83.56; H, 8.08.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetramethoxy-39,42-(*p*-xylylenedioxy)calix[6]arene (15). To a solution of 1.07 g of **2** (1 mmol) in 100 mL of THF containing 10 mL of DMF was added 0.48 g of NaH (60% dispersion in oil). After 15-min stirring, 1.0 mL of methyl iodide was added, and the mixture was refluxed for 20 h. The THF was removed under vacuum, 100 mL of cold water was added, and the product was separated by filtration. The white powder was dissolved in $CHCl_3$ and triturated with MeOH to give 1 g (77%) of white powder. An analytical sample was obtained by recrystallization from CH_2Cl_2–MeOH: mp 371–372 °C; ^{1}H NMR ($CDCl_3$) δ 7.26 (s, 4), 7.08 (s, 4), 6.40 (d, 4, J = 2.3

Hz), 4.57 (s, 4), 4.33 (d, 4, J = 16.0 Hz), 4.25 (s, 4), 3.87 (s, 12), 3.78 s, 4), 3.36 (d, 4, J = 15.7 Hz), 1.32 (s, 18), 1.06 (s, 36); ^{13}C NMR ($CDCl_3$) δ 153.67, 144.92, 143.75, 132.78, 132.71, 132.63, 132.33 (ArC), 128.50, 128.26, 125.90, 124.27 (ArH), 72.21 ($ArCH_2O$), 60.00 (ArOMe), 34.01, 33.49, 28.84 ($ArCH_2Ar$), 31.63, 31.47 ($ArCMe_3$). Anal. Calcd for $C_{78}H_{98}O_6$: C, 82.79; H, 8.73. Found: C, 82.83; H, 8.91.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetraethoxy-39,42-(*p*-xylylenedioxy)calix[6]arene was prepared in 84% crude yield following the procedure described for **15** but using ethyl iodide. An analytical sample was obtained by recrystallization from CH_2Cl_2–MeOH: mp 365–366 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (d, 4, J = 2.3 Hz), 7.07 (s, 4), 6.39 (b s, 4), 4.58 (s, 4), 4.33 (d, 4, J = 16.0 Hz), 4.30 (s, 4), 3.98 (q, 8, J = 7.0 Hz), 3.78 (s, 4), 3.34 (d, 4, J = 16.0 Hz), 1.59 (t, 12, J = 7.0 Hz), 1.31 (s, 18), 1.05 (s, 36); ^{13}C NMR ($CDCl_3$) δ 152.67, 149.79, 144.74, 143.73, 133.03, 132.77, 132.70, 132.34, 128.45, 128.27, 126.04, 124.16, 72.24, 68.15, 34.07, 34.01, 33.84, 29.00, 31.63, 31.48, 16.26. Anal. Calcd for $C_{82}H_{106}O_6$: C, 82.92; H, 9.00. Found: C, 82.56; H, 9.33.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetramethoxy-39,42-[1,4-anthrylenebis(methyleneoxy)]calix[6]arene (18). Following the procedure described above for the preparation of **15**, the anthracenyl-bridged compound **13** was converted to the tetramethoxy compound **18** in 81% crude yield. An analytical sample was obtained by recrystallization from CH_2Cl_2–MeOH: mp 264–265 °C; ^{1}H NMR ($CDCl_3$) δ 8.68–8.65 (m, 4), 7.70–7.67 (m, 4), 7.48, 6.59, and 6.27 (observed only at 55 °C) [each b s, 3 × 4, ArH], 5.94 (s, 4, $ArOCH_2$), 4.80 (4, J = 15.0 Hz), 4.18 (2, J = 13.5 Hz), 3.50 (d, 4, J = 15.0 Hz), 3.01 (d, 2, J = 13.5 Hz, $ArCH_2Ar$), 2.02 (b s, OCH_3) [observed only at 55 °C; upon addition of DMSO-d_6 the signal sharpens and appears at δ 2.66], 1.46 (s, 18, $C(CH_3)_3$), 0.73 (b s, 36, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) δ 154.85, 153.14, 146.46, 144.65, 134.25, 133.50, 133.11, 131.46, 128.81, 127.60, 126.58, 124.56, 124.15, 124.04 (ArC and ArH), 69.37 (OCH_2Ar), 60.83 (OCH_3)$_3$, 34.35, 33.75, and 32.16 [$ArCH_2Ar$ and $ArC(CH_3)_3$], 31.74 and 31.03 [$ArC(CH_3)$]. Anal. Calcd for $C_{86}H_{102}O_6$: C, 83.86; H, 8.35. Found: C, 84.15; H, 8.62.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40-tetrahydroxy-41,42-dimethoxycalix[6]arene (A) was isolated in 18% yield in addition to 35% of the reported 1,3,5-trimethoxycalix[6]arene, following the procedure reported by Casnati et al:[5] mp 317–318 °C; ^{1}H NMR ($CDCl_3$) δ 8.67 (s, 2, OH), 8.18 (s, 2, OH), 7.12–6.93 (six d, 12, J = 2.2 Hz, ArH), 4.09 (s, 2), 3.90 (s, 4), 3.75 (s, 2), and 3.73 (s, 4) ($ArCH_2Ar$), 3.81 (s, 6, OCH_3), 1.27, 1.24, and 1.1 (three s, 3 × 18, $C(CH_3)_3$). Anal. Calcd for $C_{68}H_{88}O_6$: C, 81.56; H, 8.86. Found: C, 81.86; H, 9.01.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-dimethoxycalix[6]arene (B) was prepared in almost quantitative crude yield following the general procedure described in B with 3 mmol of CH_3I and heating of the reaction mixture at 85 °C for 2 h. An analytical sample was obtained in *ca.* 60% yield by washing the product with methanol followed by chloroform (compound is sparingly soluble in $CHCl_3$/acetone). An identical product was obtained by methylation of the 1,2,4,5-tetrabenzyl ether of **1** followed by debenzylation: mp 371–372 °C; ^{1}H NMR ($CDCl_3$) δ 8.26 (s, 4), 7.11 (d, 4, J = 2.2 Hz), 7.02 (s, 4), 6.97 (d, 4, J = 2.4 Hz), 3.88 (s, 8), 3.86 (s, 4), 3.69 (s, 6), 1.21 (s, 36), 1.16 (s, 18); ^{13}C NMR ($CDCl_3$) δ 152.06, 149.24, 147.69, 142.64, 132.09, 126.91, 126.20, 126.12, 125.77 and 125.50 (ArC), 62.28 (OCH_3), 34.26, 33.92, 32.09 and 31.97 [$ArCH_2Ar$, $C(CH_3)_3$], 31.53 and 31.28 [$C(CH_3)_3$]. Anal. Calcd for $C_{68}H_{88}O_6$: C, 81.56; H, 8.86. Found: C, 81.11; H, 8.75. The ^{1}H NMR of the crude product from the direct methylation is different from that of the analytical sample, showing a broad, ill-resolved set of resonances in the δ 2.5–4.5 and δ 1–1.5 regions which change after several hours at room temperature to sharp resonances at δ 4.4 (d), 3.86 (s), 3.3 (d), 3.2 (d), 2.87 (d), 1.32 (s), and 1.03 (s). Purification effects a further change to the spectrum noted above. Presumably, these changes are the result of conformational transformations.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetramethoxycalix[6]arene (E). A mixture of 2.36 g (2 mmol) of 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-methylbenzyl)oxy]calix[6]arene (C)[3] in 50 mL of THF containing 5 mL of DMF, 0.8 g (20 mmol) of NaH (60% dispersion in oil), and 1.7 g (12 mmol) of CH_3I was heated at 80 °C for 4 h. The THF was removed in vacuum, and 100 mL of cold water was added with stirring. The precipitate was separated by filtration, dried, and treated with MeOH to give 2.14 g (94%) of a white powder as a mixture of conformers of the tetramethoxybis[(4-methylbenzyl)oxy]calix[6]arene **D**. A 1.24-g (1-mmol) portion of this compound was added to a slurry of 0.33 g (2.5 mmol) of $AlCl_3$ in 50 mL of toluene. The contents were stirred for 10 min, and 100 mL of cold water was added. The organic layer was separated, and the aqueous layer was extracted with 25 mL of $CHCl_3$. The combined organic layer was washed with water and brine and dried over Na_2SO_4. Removal of the solvent under vacuum and recrystallization of the residue ($CHCl_3$–MeOH) gave 0.57 g (55%) of tetramethoxycalix[6]arene (E): mp 326–327 °C; ^{1}H NMR ($CDCl_3$) δ 8.02 (s, 2), 7.07 (s, 8), 6.69 (s, 4), 3.97 (s, 4), 3.87 (s, 8), 3.13 (s, 12), 1.18 (s, 36), 0.93 (s, 18); ^{13}C NMR ($CDCl_3$) δ 153.16, 149.36, 146.62, 141.76, 133.94, 132.21, 127.32 (ArC), 126.43, 126.10, 123.87 (ArCH), 61.40 (OCH_3), 34.14, 33.73 ($ArCH_2Ar$), 31.33, 31.26 (CMe_3), 30.95, 30.80 ($CCMe_3$). Anal. Calcd for $C_{70}H_{92}O_6$: C, 81.67; H, 9.01. Found: C, 81.86; H, 9.06.

Molecular Modeling Studies. The structures and energies of the various calix[6]arenes were obtained using the QUANTA and CHARMm programs on a Silicon Graphics IRIS-4D/210VGX. The structures were energy minimized using an Adopted Basis Newton–Raphson prodedure, iterated to an energy gradient of 0.001 kcal/(Å mol). Global minima for each structure were sought by reminimization following various conformational alterations in the starting structures.

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