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# Conformational Characteristics of *p-tert*-Butylcalix[6]arene Ethers[1]

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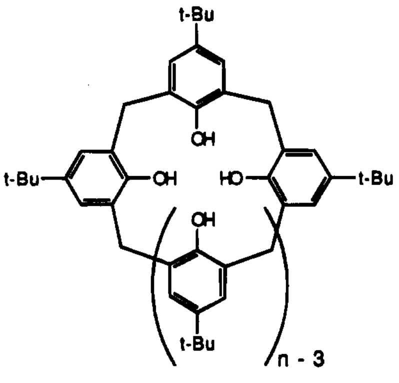
The conformational characteristics of a variety of O-substituted *p-tert*-butylcalix[6]arenes have been studied by means of the $^1H$ NMR patterns arising from their $ArCH_2Ar$ methylene protons and from the position of the $^{13}C$ NMR lines arising from the carbons bearing these protons. On the basis of this information, the tribenzyl trimethyl ether **13**, the bis-calixarenes **15** and **16**, the monobenzyl ether **3**, the monobenzyl pentamethyl ether **10**, and the hexakis(*p*-cyanobenzyl) ether **19b** are established as having cone conformations at ambient temperature. The tetrabenzyl dimethyl ether **14**, the tetrabenzoyl esters **17a–d**, the tetraarylmethyl ethers **18a–d**, and the bridged ether **21**, on the other hand, are found to possess 1,2,3-alternate conformations. The conformational mobilities of these compounds were assessed by variable temperature $^1H$ NMR spectral measurements, leading to the classification of the structures as immobile, semimobile, or mobile with respect to conformational interconversion via the "lower rim through the annulus" pathway.



**1a** (n = 4)
**1b** (n = 5)
**1c** (n = 6)

The synthesis of *p-tert*-butylcalix[6]arene (**1c**) was first described in 1981 in an early paper in this series,[2] and in subsequent publications four years later[3,4] the conformational properties of **1c** and several of its esters and ethers were reported. Other aspects of the chemistry of the calix[6]arenes were explored at a relatively relaxed pace during the 1980's, with particular attention to the functionalization of the upper[5] and lower[6] rims and to the establishment of the conformations of the parent compound and several hexa-O-substituted derivatives.[7] With the rapidly escalating interest in the calixarenes in the 1990's, the situation has changed dramatically, and research efforts in numerous laboratories are currently directed to these compounds. "It always happens", said Mark Twain,[8] "that when a man seizes upon a neglected and important idea, people inflamed with the same notion crop up all around". This is aptly illustrated by the almost simultaneous publication of four independent reports concerning the methyl ethers of the calix[6]arenes[9-12] which provide one part of the background for the present paper. The second part is provided by the benzyl ethers of **1c** which have been studied in this laboratory[13] as a corollary to an investigation of the corresponding aroylates.[14-16] Concomitantly, Shinkai and co-workers[17] and Pappalardo and co-workers[18] have studied the synthesis and conformational properties of the 2-pyridylmethyl ethers of **1c** in careful detail. It is the combination of the benzylation and the methylation of **1c** that provides the basis for the present investigation which seeks to interpret the effects of O-substituents on

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(1) Paper 36 in the series entitled Calixarenes. For paper 35 *cf.* Sharma, S. K.; Gutsche, C. D. *Synthesis* 1994, in press. A significant portion of this work was reported at the 2nd International Workshop on Calixarenes and Related compounds, Kurume, Japan, June 1993.

(2) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782.

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(9) Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Ugozzoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. *Synthesis* **1993**, 380.

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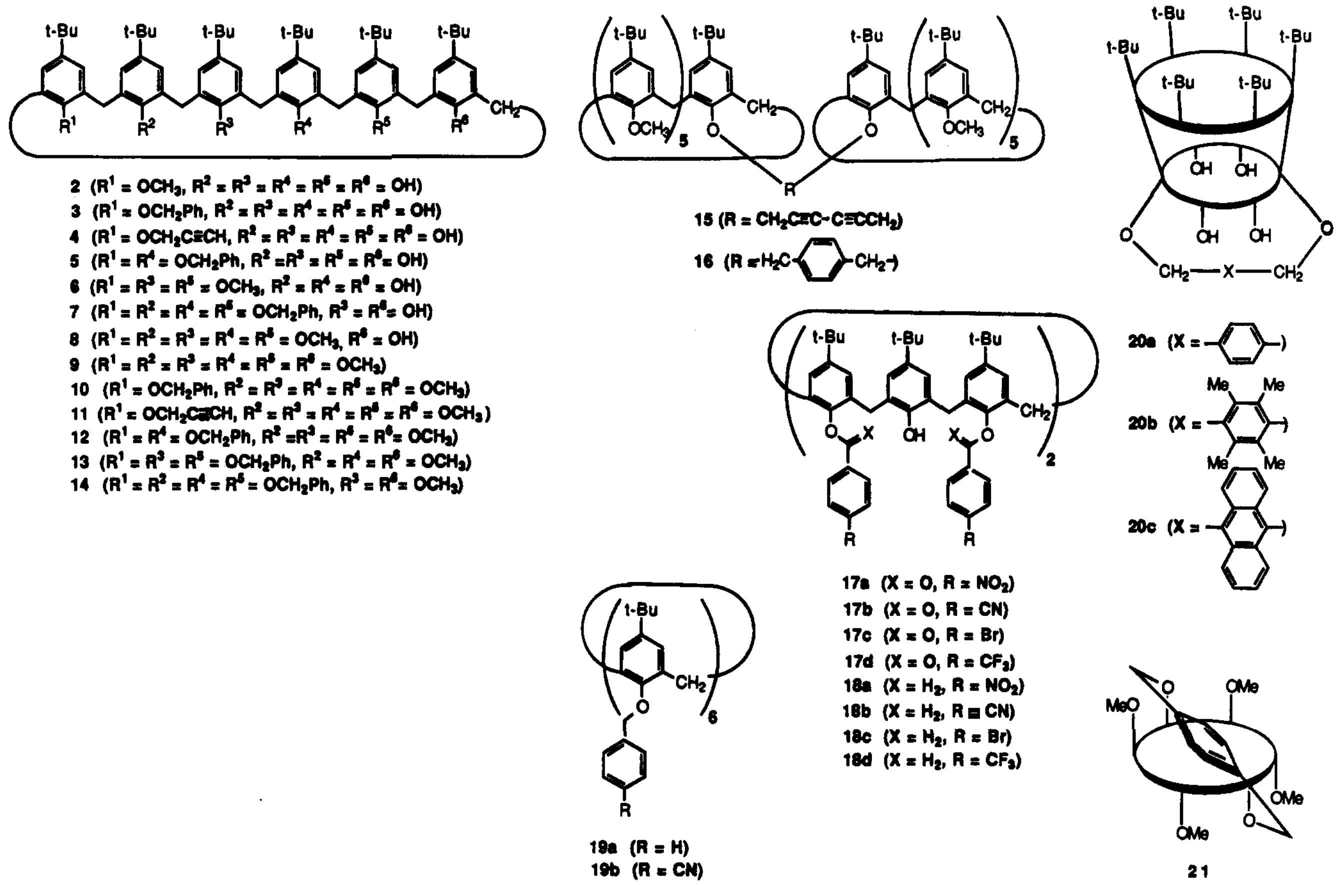
0022-3263/94/1959-3871$04.50/0

Chart 1



the conformational state and mobility of the *p-tert*-butylcalix[6]arenes.

Two pathways are potentially available for the conformational inversion of calixarenes. One involves a "lower rim through the annulus" motion in which the OR functions swing through the annulus, and the other involves an "upper rim through the annulus" motion in which the para-substituents swing through the annulus. Only the first of these is available to the calix[4]arenes, the latter pathway being precluded even when the para-substituents are hydrogens. The calix[6]arenes, on the other hand, were shown some years ago[4] to be able to employ the "upper rim through the annulus" pathway when the para-substituents are hydrogens, and recent work[19,20] has shown that it remains available even with the much larger *p-tert*-butyl groups. The $\Delta G^{\ddagger}$ in the latter instance, however, is sufficiently high that apparent conformational "fixing" can be observed when various substituents are attached to the oxygens of the calixarene, and it is with this aspect of the conformation of *p-tert*-butylcalix[6]arenes that the present work is concerned.

## Syntheses

The previously unreported compounds employed in this study were obtained in the following manner. The monobenzyl pentamethyl ether **10** was prepared in 84% yield by methylation of the monobenzyl ether of *p-tert*-butylcalix[6]arene (**3**), which has been reported by Janssen *et al.*[9] who obtained it in 78% yield by treating an acetone solution of **1c** with benzyl chloride and $K_2CO_3$. In an analogous sequence **1c** was converted to the monopropargyl ether **4** in 61% yield and exhaustively methylated to produce the monopropargyl pentamethyl ether **11** in 72% yield, a compound amenable to oxidative coupling with $Cu(OAc)_2{\cdot}H_2O$ in pyridine/MeCN solution to provide the bis-calixarene **15** in 78% yield. A similar bis-calixarene was prepared by treating the pentamethyl ether **8** with *p*-xylylene dibromide to yield 52% of **16**.[21] The tribenzyl trimethyl ether **13**, also reported by van Duynhaven et al.,[20] was prepared by benzylation of the trimethyl ether **6**,[12 22] and in similar fashion the dibenzyl tetramethyl ether **12** and the tetrabenzyl dimethyl ether **14** were obtained in 94 and 87% yields by methylation of the dibenzyl ether **5** and the tetrabenzyl ether **7**,[13] respectively.

## ¹H NMR Studies

The curious effect on the conformational behavior of *p-tert*-butylcalix[4]arene resulting from partial methylation was first observed with the 1,3-dimethyl ether, which is less mobile than either the parent compound or the corresponding tetramethyl ether.[23] The other methyl ethers of **1a** have subsequently been prepared, and it has

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[19] Otsuka, H.; Araki, K.; Shinkai, S. *Chem. Express* **1993**, *8*, 470. Otsuka, H.; Araki, K.; Sakaki, T.; Nakashima, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 7275.

[20] van Duynhoven, J. P. M.; Janssen;, R. G.; Verboom, W.; Franken, S. M.; Casnati, A.; Pochini, A.; Ungaro, R.; de Mendoza, J.; Nieto, P. M.; Prados, P.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, in press. We are indebted to these authors for making a preprint of this work available to us prior to publication.

[21] Single-bridged double calix[4]arenes have been reported by (a) McKervey, M. A.; Owens, M.; Schulten, H.-R.; Vogt, W.; Böhmer, V. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 280. (b) Ohseto, F.; Sakaki, T.; Araki, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 2149.

[22] Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R. *J. Chem. Soc. Chem. Commun.* **1991**, 1413.

[23] Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409.

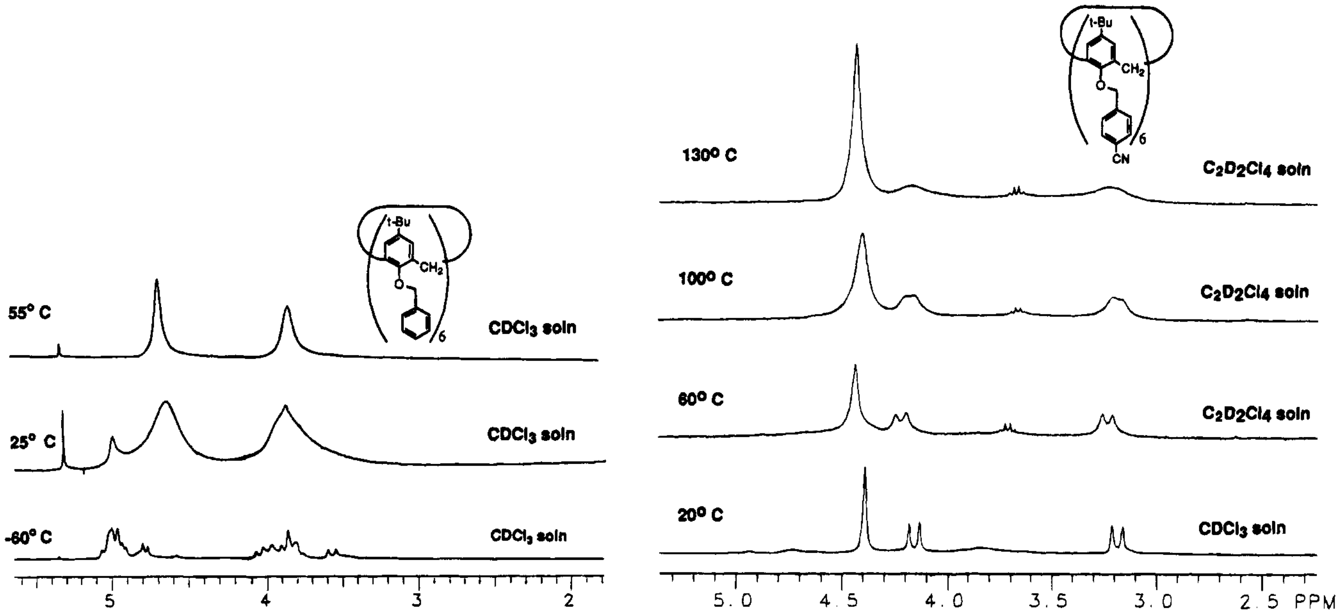

**Figure 1.** Variable temperature $^1$H NMR spectra of the hexabenzyl ether **19a** and the hexakis(*p*-cyanobenzyl) ether **19b** in $CDCl_3$ and $C_2D_2Cl_4$ solution at 300 MHz.

been shown[24] that they likewise are less mobile than **1a** or the tetramethyl ether. The conformational mobility of these compounds can be interpreted as the result of the interplay of intramolecular hydrogen bond attractions and steric repulsions. Intramolecular hydrogen bonding is at a maximum in the parent compound but entirely absent in the tetramethyl ether, while steric hindrance is at a minimum in the former and a maximum in the latter. Both factors contribute to the reduction of conformational mobility in the case of the partially methylated compounds. The steric hindrance factor can be magnified, of course, by attaching larger groups to the phenolic oxygen, and it may quickly become the dominant factor. Thus, the tetraethyl ether of **1a** is considerably less mobile than the tetramethyl ether of **1a**, and the tetrapropyl ether of **1a** is, for all practical purposes, conformationally fixed at room temperature.[25] Comparable steric hindrance effects with the next larger member of the calixarene series, *p-tert*-butylcalix[5]arene (**1b**), require larger OR groups.[26] The minimum size necessary for conformational fixing of a penta-substituted derivative of **1b** falls between the penta-*n*-butyl ether and the pentabenzyl ether (or between the penta-*n*-butanoate and the pentaisobutanoate). For a monosubstituted derivative of **1b** it falls between the *n*-propyl ether and the monobenzyl ether.[26] The present work addresses the question of how large the OR groups must be to induce similar consequences in the hexasubstituted and monosubstituted derivatives of *p-tert*-butylcalix[6]arene (**1c**).

The $^1$H NMR spectral patterns associated with the $ArCH_2Ar$ methylene protons of calixarenes provide a useful measure of conformational identity, and their temperature dependence allows an assessment of the rates of conformational inversion.[27] In $CDCl_3$ solution both *p-tert*-butylcalix[5]arene (**1b**) and *p-tert*-butylcalix[6]arene (**1c**) show this resonance as a broad singlet at room temperature, conformational inversion occurring at a rate that is fast on the NMR time scale. Variable temperature $^1$H NMR spectral measurements on **1b** and **1c** show that at lower temperatures the singlet resolves to a multiplet, from which $\Delta G^‡$ values of 13.2 and 13.3 kcal mol$^{-1}$, respectively, can be calculated[27,28] for the inversion process. The cyclic tetramer, *p-tert*-butylcalix[4]arene (**1a**), on the other hand, shows a pair of doublets at room temperature, its rate of conformational inversion being slower than that of **1b** and **1c**. Variable temperature measurements of the $^1$H NMR spectrum of **1a** give a $\Delta G^‡$ of 15.7 kcal mol$^{-1}$. As discussed above, the tetramethyl ether of **1a** is comparable in mobility to the parent compound. The pentamethyl ether of **1b** and the hexamethyl ether of **1c**, however, are much more mobile than their respective parents. In contrast to the calix[4]arene system, the larger annuli of **1b** and **1c** do not allow the small steric effect of the methyl groups to offset the loss of hydrogen bonding. To observe the interplay of steric hindrance and hydrogen bond factors in the calix[6]arenes, therefore, substituents larger than methyl are required. As the following observations indicate, the dividing line for a hexasubstituted calix[6]arene falls between a benzyl and a para-substituted benzyl group. Thus, the hexabenzyl ether **19a** derived from **1c** shows a broad singlet at room temperature (see Figure 1) that sharpens upon heating.[4,13] The coalescence temperature for its conformational inversion is estimated to be *ca.* 10 °C corresponding to a $\Delta G^‡$ of *ca.* 12.9 kcal mol$^{-1}$. The hexakis(*p*-cyanobenzyl) ether **19b**, on the other hand, shows a pair of doublets at room temperature[13] (see Figure 1). This pattern persists at temperatures up to *ca.* 100 °C at which point the doublets start to become broad singlets although showing no movement toward one another, even at 130 °C. Such behavior is in

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[24] Groenen, L. C. Ph.D. Thesis, University of Twente, Enschede, The Netherlands, 1992. For a short abstract *cf. Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 197.

[25] Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955.

[26] Stewart, D. R.; Gutsche, C. D., unpublished

[27] Gutsche, C. D. *Calixarenes*; Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989.

[28] The rate constant ($k_c$ in s$^{-1}$) for conformational interconversion at the coalescence temperature was calculated from the equation $k_c = 2.22\ (\Delta\nu^2 + 6J_{AB}^2)^{1/2}$. The free energy barrier to conformational interconversion in kcal/mol was calculated from the equation: $\Delta G^‡ = 4.58T_c\ (10.32 + \log T_c/k_c)/1000$. Assuming an accuracy of ± 5 °C for the value of $T_c$, an accuracy of ±15 Hz for the value of $\Delta\nu$, and an accuracy of ±2 Hz for the value of $J_{AB}$, it is estimated that $\Delta G^‡$ is accurate to ± 0.4 kcal/mol.

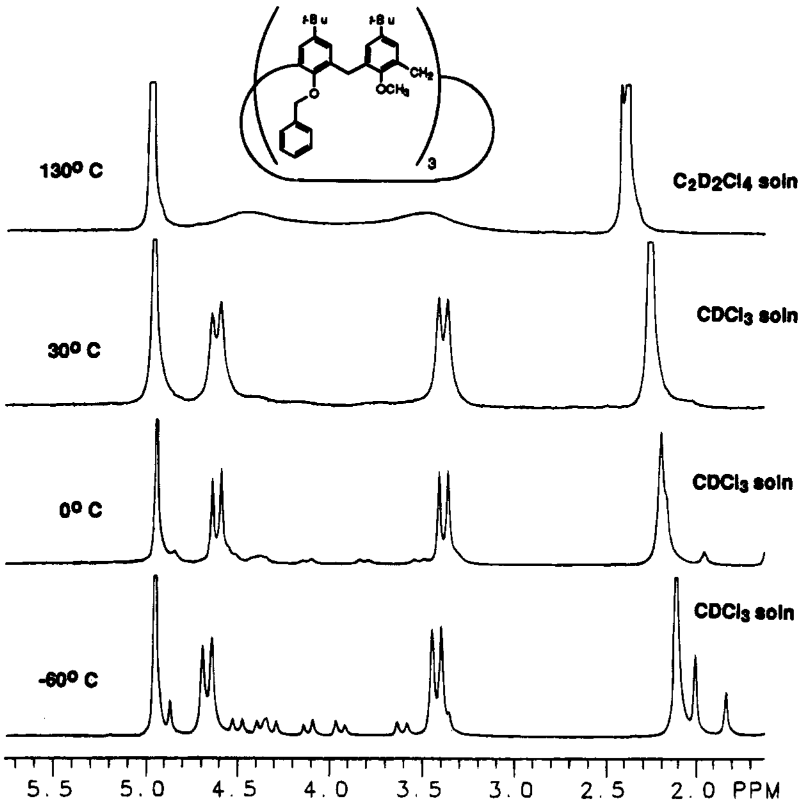

**Figure 2.** Variable temperature $^1$H NMR spectrum of the tribenzyl trimethyl ether **13** in $CDCl_3$ and $C_2D_2Cl_4$ at 300 MHz.

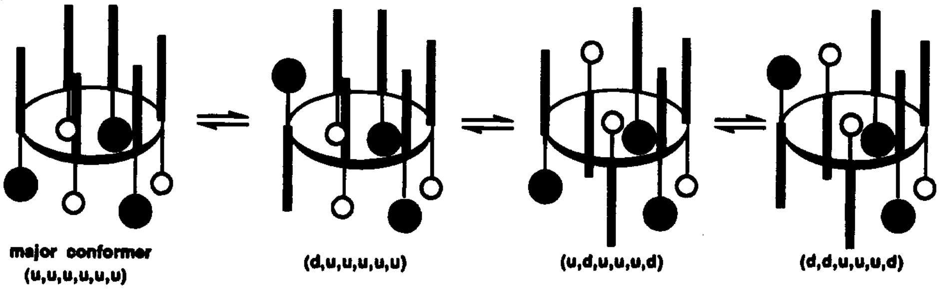

**Figure 3.** Conformers of the tribenzyl trimethyl ether **13**.

agreement with a cone conformation for which the $\Delta G^{\ddagger}$ for conformational interconversion via the "lower rim through the annulus" pathway is considerably greater than 18 kcal mol$^{-1}$. Inspection of CPK models of **19a** and **19b** shows that an $ArOCH_2C_6H_5$ moiety can just squeeze through the annulus, whereas an $ArOCH_2C_6H_4CN$ moiety cannot do so because of the increased steric hindrance arising from the *p*-cyano group.

Also existing in the cone conformation are the hexasubstituted compounds derived from the 1,3,5-trimethyl ether **6**, as first demonstrated by Ungaro and co-workers[22] who converted **6** to a hexaether by treatment with *tert-butyl* α-bromoacetate. It is demonstrated again in the present work by the conversion of **6** to the 1,3,5-tribenzyl-2,4,6-trimethyl ether **13**, the room temperature $^1$H NMR spectrum of which contains a pair of doublets arising from the $ArCH_2Ar$ methylene resonances (see Figure 2). At higher temperatures this patttern changes to a pair of broad resonances which at 130 °C are starting to move together, indicative of a $T_c$ well above this temperature and a $\Delta G^{\ddagger}$ greater than 18.5 kcal mol$^{-1}$. Upon cooling below room temperature, the spectrum becomes considerably more complex because it arises from a mixture of a major and a minor constituent. The major consituent shows *tert*-butyl resonances at δ 1.40 and 0.79 (1:1 ratio), a single OMe resonance at δ 2.11, and $ArCH_2Ar$ resonances as a pair of doublets centered at δ 4.67 and 3.48. The minor constituent shows *tert*-butyl resonances at δ 1.34, 1.18, 1.06, and 0.92 (1:2:2:1 ratio), OMe resonances at δ 2.01 and 1.84 and probably another pair buried under the OMe resonance of the major conformer, and $ArCH_2Ar$ resonances as 12 lines between δ 4.50 and 3.60 corresponding to three sets of nonequivalent methylenes. The $^1$H NMR pattern of the major constituent is that of a cone conformer (**u**,u,u,u,u,u)[29] [actually, a flattened cone (**u**,uo,u,uo,u ,uo)]; that of the minor constituent fits any of several noncone $C_s$ conformers, three of which are shown in Figure 3. A distinction among these has been made by van Duynhoven *et al.*[20] on the basis of quantitative NOE data from NOESY and ROESY spectra which show the minor constituent to be the 1,2,3-alternate conformer [(**d**,d,u,u,u,d) in Figure 3]. On the basis of the relative areas of their resonance envelopes, the major and minor constituents are estimated to be present at −60 °C in a ratio of *ca.* 2.6:1. At low temperatures the interconversion between these two conformers is slow on the $^1$H NMR

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[29] For a description of a conformational notation scheme, see Kanamathareddy, S.; Gutsche, C. D. *J. Am. Chem. Soc.* **1993**, *115*, 6572.

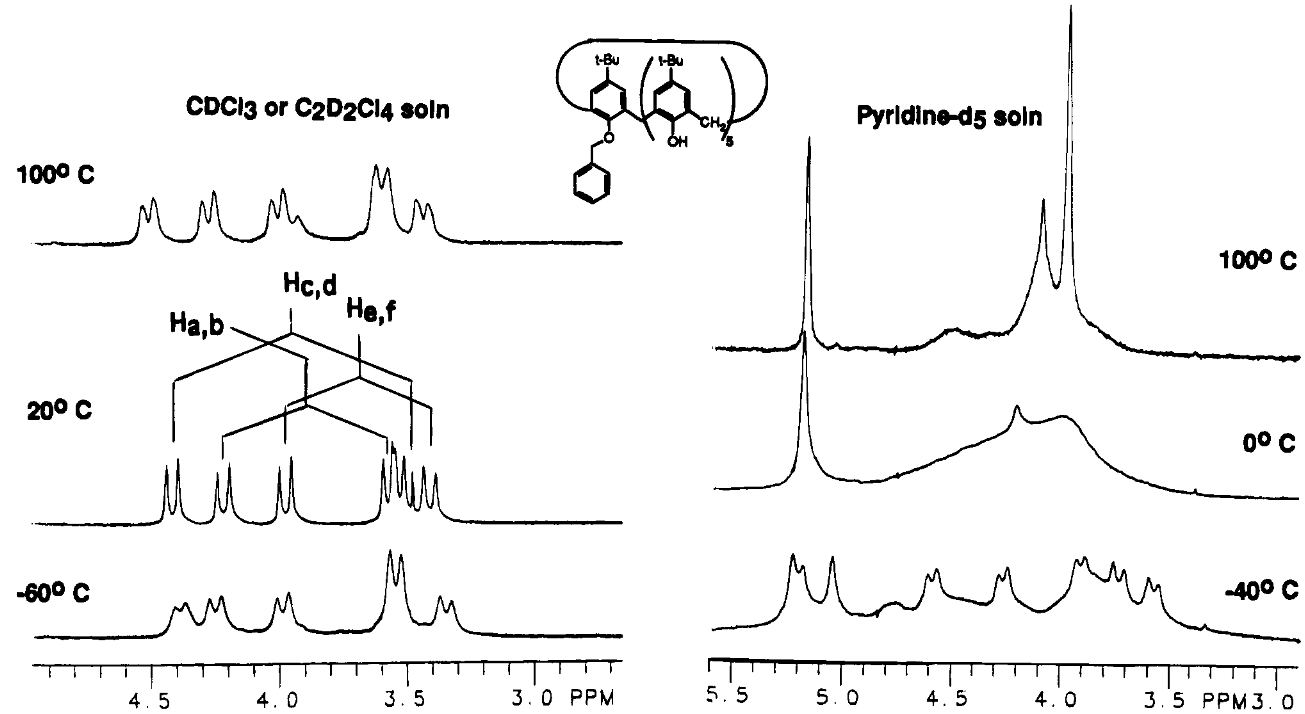

**Figure 4.** Variable temperature $^1$H NMR spectrum of the monobenzyl ether **3** in $CDCl_3/C_2D_2Cl_4$ and pyridine-$d_5$ at 300 MHz. The splitting pattern was determined by double-resonance experiments.

time scale, with the result that they are observed as discreet species. As the temperature rises, however, the equilibrium shifts in favor of the cone conformer which becomes the increasingly dominant species. At ambient temperature the minor constituent is barely visible. If it were retaining its identity and simply undergoing increasingly rapid conformational inversion to its mirror image as the temperature rises, the eventual appearance of 3 singlets clustered near δ 4.2 would have been expected.

The ambient temperature $^1$H NMR spectra of the monobenzyl ether **3** and the benzyl pentamethyl ether **10**, as shown in Figures 4 and 5, contain three pairs of doublets arising from the $ArCH_2Ar$ methylene protons. The Δδ separations[30] (0.90 for $H_{a,b}$, 0.69 for $H_{c,d}$, 0.72 for $H_{e,f}$ in **3**; 0.94, 0.50, 0.21 for **10**) are sufficiently large as to indicate that the aryl moieties adjoining the $CH_2$ groups are *syn* to one another,[31] and this is corroborated (*vide infra*) by the $^{13}$C NMR spectra which show three $ArCH_2Ar$ methylene resonances near δ 31 but none near δ 37. These data are in agreement with a cone conformation for both **3** and **10**.

The variable temperature $^1$H NMR spectra of the monobenzyl ether **3** and the benzyl pentamethyl ether **10** resemble that of the tribenzyl trimethyl ether **13** in general detail, showing well-resolved sets of $ArCH_2Ar$ resonances at ambient temperature that broaden upon cooling as well as heating. Compounds **3** and **10** differ from one another, however, in that the degree of heat-induced broadening is considerably greater for the latter, indicating the benzyl pentamethyl ether **10** is the more mobile. Thus, the spectrum of **3** retains a reasonably well-resolved set of resonances at 100 °C, whereas that of **10** is already severely broadened at 85 °C and is approaching a coalescence point at 125 °C, corresponding to a $\Delta G^{\ddagger}$ of 18.45 kcal mol$^{-1}$. Apparently, the intramolecular hydrogen bonding of five OH groups is more effective in curtailing conformational interconversion than the steric hindrance arising from five OMe groups. That hydrogen bonding is, indeed, an important factor in establishing the conformational character of **3** is shown by the dramatic increase in conformational mobility that occurs in pyridine-$d_5$ solution. In this solvent a $T_c$ of *ca.* 0 °C is observed, corresponding to a $\Delta G^{\ddagger}$ of 12.8 kcal mol$^{-1}$.

In contrast to the low temperature spectra of the monobenzyl ether **3** and the tribenzyl trimethyl ether **13**, which show well-resolved methylene resonances, that of the benzyl pentamethyl ether **10** is much less well-defined. The two pairs of "interior" methylene doublets (δ 4.17/4.02; 3.81/ 3.67) observed in the 20 °C spectrum collapse to broad singlets at −40 °C, while the "exterior" doublet (δ 4.46/3.52) retains its resolution until −60 °C at which temperature it, too, becomes a broad singlet.[32] This can probably be ascribed to two or more conformers that are present at low tempature and which interconvert slowly on the $^1$H NMR time scale. These conformers may

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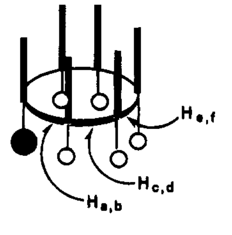
[30] The coupling patterns for the $ArCH_2Ar$ methylene protons were determined by double resonance experiments. The assignments $H_{a,b}$, $H_{c,d}$, and $H_{e,f}$ are based on the rationale that the molecule is inflexible in the portion proximate to the benzyl-containing aryl moiety, maintaining the *syn* orientation in this region, but flexible in the region distal to these moieties, allowing *syn*/*anti* transformations to occur.

[31] *Cf.* ref 27, pp 110−111 for comments on Δδ values. The methylene groups in **3** and **10** are designated as indicated in the following picture:



[32] That the line broadening observed at low temperaures is not simply due to increased solvent viscosity is indicated by the well-resolved spectrum observed for the tetramethyl ether of **20c** at −60 °C, as reported in ref 11.

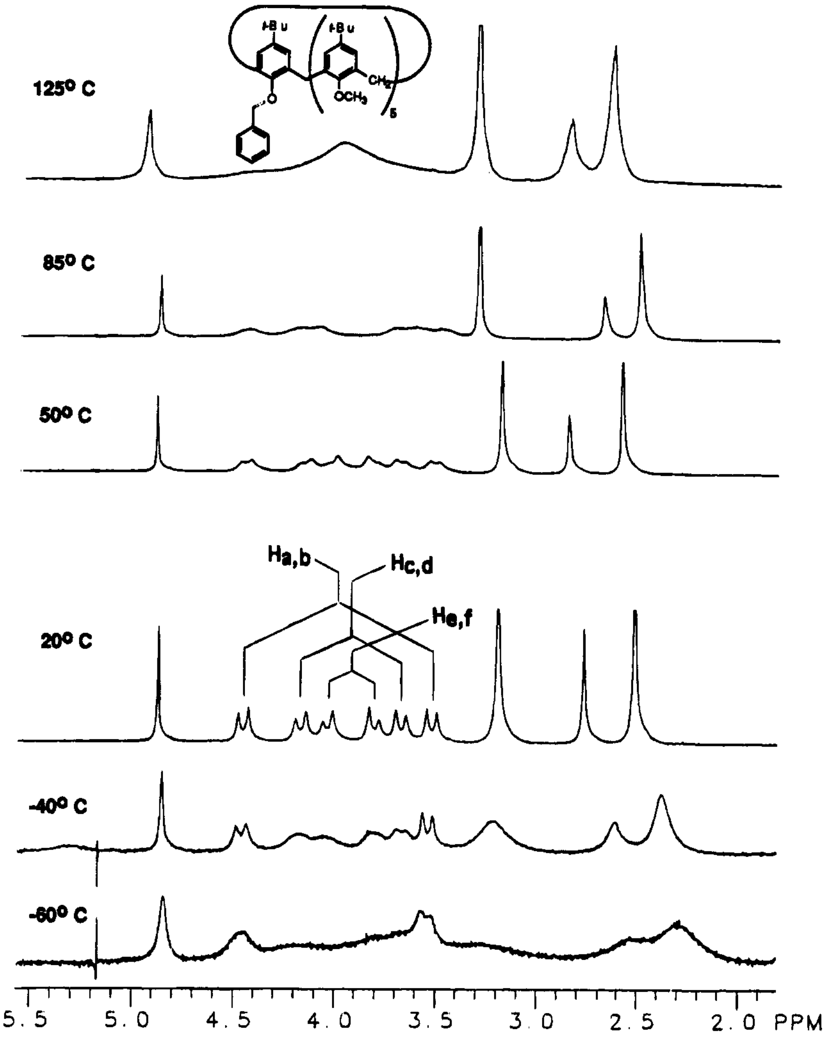


**Figure 5.** Variable temperature $^1$H NMR spectrum of the benzyl tetramethyl ether **10** in $CDCl_3$ and $C_2D_2Cl_4$ at 300 MHz. The splitting pattern was determined by double-resonance experiments.

include not only those involving up/down orientations of the aryl units but inside/outside orientations of the OMe groups as well. A downfield shift of the OMe resonances (room temperature resonances at $\delta$ 3.20, 2.77, 2.51 in a 2:1:2 ratio) is, in fact, observed upon heating, and an upfield shift is observed upon cooling.

The bis-calixarene decamethyl ethers **15** and **16** are somewhat less conformationally mobile than the related benzyl pentamethyl ether **10**, showing no change in the $ArCH_2Ar$ resonance patterns upon heating to 60 °C but exhibiting behavior identical with that of **10** upon cooling. The intermolecular link beween the two calixarene units constitutes a much larger group than benzyl and, consequently, is more effective in curtailing the conformational interconversions.

The 1,2,4,5-tetrabenzyl ether **7** has been previously reported[13] as showing a partially resolved set of $ArCH_2Ar$ resonances at room temperature that sharpen at lower temperatures to the characteristic pattern for a 1,2,3-alternate conformation. Above ambient temperature the pattern becomes increasingly diffuse and at 60 °C shows a pair of broad singlets (2:1 ratio), commensurate with a system at its coalescence temperature for the interconversion between a 1,2,3-alternate conformer and its mirror image. The addition of two methyl groups to produce the tetrabenzyl dimethyl ether **14** results in a compound that is much less mobile than **7**. Its behavior is similar to that described above for the benzyl pentamethyl ether **10**, the NMR spectrum showing a well-resolved $ArCH_2Ar$ pattern consisting of a pair of doublets and a singlet that is characteristic of a 1,2,3-alternate conformation that persists from room temperature down to −60 °C. By 100 °C, however, the methylene pattern has changed to three broad singlets, possibly the result of partial inversion involving only the ArOMe moieties swinging through the annulus. Noteworthy is the upfield position ($\delta$ 1.48) of the OMe resonance in **14**, commensurate with an "inside" orientation of these groups. The conformational stabilization observed with **14** is similar to that of the tribenzyl trimethyl ether **13**. That four benzyl groups are more effective than four methyl groups in curtailing conformational interconversion is shown by the lower mobility of the tetrabenzyl dimethyl ether **14** as compared with the dibenzyl tetramethyl ether **12**.

## $^{13}$C NMR Studies

de Mendoza and co-workers[33] correlated the conformations of two dozen calix[4]arenes with the chemical shift values of the $^{13}$C NMR resonances arising from the $ArCH_2Ar$ methylene carbons and showed that a resonance near $\delta$ 31 appears when the aryl groups are *syn*

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(33) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sanchez, C. *J. Org. Chem.* **1991**, *56*, 3372.

**Table 1. $^{13}$C NMR Resonances (ppm) of O-Substituted *p-tert*-Butylcalix[6]arenes**

| compound[a] | $OCH_3$ | $OCH_2Ar$ | $ArCH_2Ar$ | $\Delta\delta$ | conformation |
|---|---|---|---|---|---|
| **10** | 60.02<br>59.94<br>59.83 | 74.36 | 31.25<br>30.65<br>30.35 | | cone |
| **15** | 60.01<br>59.92<br>59.84 | | 31.05<br>30.18 | | cone |
| **16** | 60.03<br>59.96<br>58.82 | 74.28 | 30.70<br>30.52<br>30.42 | | cone |
| **13** | 60.17 | 74.56 | 29.84 | | cone |
| **A*** | | | 30.00 | | cone |
| **B**** | | | 30.00 | | cone |
| **19b**[13] | | 73.73 | 29.45 | | cone |
| **14** | 58.93 | 74.48 | 33.03<br>29.92 | 3.11 | 1,2,3-alternate |
| **17a**[16] | | | 38.53<br>30.36 | 8.17 | 1,2,3-alternate |
| **17b**[13] | | | 38.45<br>30.43 | 8.02 | 1,2,3-alternate |
| **17c**[13] | | | 38.52<br>30.42 | 8.10 | 1,2,3-alternate |
| **17d**[13] | | | 38.56<br>30.14 | 8.42 | 1,2,3-alternate |
| **18a**[13] | | 70.77 | 38.96<br>30.57 | 8.39 | 1,2,3-alternate |
| **18b**[13] | | 71.03 | 38.98<br>30.60 | 8.38 | 1,2,3-alternate |
| **18c**[13] | | 72.06 | 38.99<br>30.67 | 8.32 | 1,2,3-alternate |
| **18d**[13] | | 71.58 | 39.04<br>30.46 | 8.58 | 1,2,3-alternate |
| **20a**[11] | | 77.88 | 33.84<br>33.00 | | flattened cone |
| **20b**[11] | | 72.45 | 33.82<br>32.56 | | flattened cone |
| **20c**[11] | | 69.23 | 33.78<br>32.53 | | flattened cone |
| **21**[11] | 60.00 | 72.21 | 34.02<br>28.84 | 5.18 | 1,2,3-alternate |

[a] (*) $R^1 = R^3 = R^5 = OCH_3$, $R^2 = R^4 = R^6 = OCH_2CO_2C(CH_3)_3$ (ref 22). (**) $R^1 = R^3 = R^5 = OCH_3$, $R^2 = R^4 = R^6 = OCH_2CON(C_2H_5)_2$ (ref 22).

to one another and near $\delta$ 37 when they are *anti*. This difference is ascribed to steric rather than electronic factors (*i.e.* no para-substituent effect) or solvent influences. While it does not follow categorically that a similar correlation should be observed in the larger calixarenes, it is reasonable to expect this to be the case, and the data in Table 1 appear to support this. The compounds to which cone conformations (*i.e.* all $ArCH_2Ar$ orientations *syn*) are assigned on the basis of $^1$H NMR patterns include the tribenzyl trimethyl ether **13**, the biscalixarenes **15** and **16**, the monobenzyl pentamethyl ether **10**, the hexaethers prepared by Casnati *et al.*[22] from the 1,3,5-trimethyl ether, and the hexakis(*p*-cyanobenzyl) ether **19b**. In all of these compounds the $^{13}$C NMR signal for the $ArCH_2Ar$ methylene carbon falls at 30.35 ± 0.90. The compounds to which 1,2,3-alternate conformations (*i.e.* $ArCH_2Ar$ orientations both *syn* and *anti*) are assigned on the basis of $^1$H NMR patterns include tetrabenzyl dimethyl ether **14**, the tetrabenzoyl esters **17a–d**, the tetraarylmethyl ethers **18a–d**, and the bridged ether **21**. In these compounds two $^{13}$C NMR signals for the $ArCH_2Ar$ methylene carbons are observed, the one at higher field at 30.05 ± 0.40 and the one at lower field ranging from 33.03 to 39.04. The chemical shift difference between the higher and lower field resonances ($\Delta\delta$) ranges between 3.11 and 8.58 ppm. The 1,4-bridged compounds **20a–c** represent an equivocal case, their close-lying pairs of resonances falling between $\delta$ 32.53 and 33.84. The $^1$H NMR spectra of these compounds show two pairs of doublets for the $ArCH_2Ar$ methylene protons ($\Delta\delta$ 0.94 and 0.62 for **20a**; 1.23 and 0.52 for **20c**), in best agreement with a flattened cone conformation. This is also supported by inspection of CPK models. Although the absolute positions of the $^{13}$C NMR signals may generally be used to establish the conformation of a calix[6]arene, the more significant feature might be the $\Delta\delta$ between signals when two or more are observed. If the $\Delta\delta$ is greater than 3 ppm, it is probably safe to assume that both *syn* and *anti* conformations are present, but if $\Delta\delta$ is less than 1 ppm it may be safe to assume that the $ArCH_2Ar$ conformations are either all *syn* or all *anti*.

## Molecular Modeling Studies

Molecular modeling studies were carried out on a Silicon Graphics terminal using the CHARMm program, minimizing structures by the Adopted Basis Newton Raphson program followed by the Newton Raphson program to a rms value of 0.05 or lower. Conscientious attempts were made to find conformational minima, but given the structural complexity of the molecules under study there is no assurance that this was successful in all cases. Consequently, the conclusions drawn from these studies should be viewed as interesting and heuristic but not definitive.[34]

Molecular modeling studies of the monobenzyl ether **3** indicate that the minimum-energy structure is a cone-like conformation in which the OH groups are a little too far apart to engage in the very strong hydrogen bonding observed in the parent compound **1c**. This is experimentally supported by the OH stretching frequency for **3** of 3400 cm$^{-1}$, which is much higher than the 3150 cm$^{-1}$ value for **1c**. Nevertheless, the experimental data discussed above indicate that intramolecular hydrogen bonding must play a significant role in maintaining the conformational rigidity of **3**. The molecular modeled structure of **3** lacking a $CHCl_3$ molecule occluded in its cavity shows one of the aryl moieties to be canted so that its *tert*-butyl group resides in the cavity of the cone. When a $CHCl_3$ is occluded in the cavity, however, the aryl moiety assumes an "up" orientation.

Molecular modeling studies of the benzyl pentamethyl ether **10** show that in the absence of $CHCl_3$ it also possesses a cone-like conformation for which the energies increase progressively as the orientations of the OMe groups are changed from inward to outward. The structure in which all five OMe groups project inward is more stable by 12 kcal mol$^{-1}$ than the one in which all five OMe groups project outward. However, in the presence of a $CHCl_3$ molecule these distinctions become blurred, and the most-stable structure appears to be the one in which two OMe groups are oriented inward and three are oriented outward. In both circumstances, though, a structure carrying at least some inward-directed OMe groups is favored, and this may provide a rationale for the difference in conformational mobility of the hexabenzyl ether **19a**, which undergoes conformational inversion more readily than the monobenzyl pentamethyl ether **10**. For there to be sufficient room in the annulus to allow an $ArOCH_2C_6H_5$ moiety to pass through it, *all* of the other ether moieties must adopt "outside" orientations. Inspection of CPK models indicates that even a single OMe group in the "inside" orientation is

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[34] Lipkowitz, K. B.; Peral, G. *J. Org. Chem.* **1993**, *58*, 6729 urge "extreme caution" when using molecular modeling to predict calixarene structures and energies.

sufficient to block the passage of the $ArOCH_2C_6H_5$ moiety. The probability that all five of the OMe groups in **10** will simultaneously adopt the"outside" position is low,[35] whereas the probability that five of the six benzyl groups in **19a** will occupy "outside" positions is much greater. Paradoxically, OMe groups are more effective in curtailing complete conformational inversion than are the larger benzyl groups.

The ability of the hexabenzyl ether **19a** to undergo conformational inversion more easily than the tribenzyl trimethyl ether **13** may similarly be ascribed to the smaller size of the OMe group. Molecular modeling studies of **13** indicate that the most-stable cone-like conformer possesses two OMe groups oriented outward and one inward in the absence of a molecule of $CHCl_3$ but all three oriented outward in the presence of a molecule of $CHCl_3$ which occupies the cavity. However, X-ray crystallography of the closely related compound containing three $Et_2NCOCH_2$ moieties instead of the three benzyl moieties shows that in the solid state structure all three OMe groups are directed inward,[36] providing support for the idea that the orientation of the OMe groups plays a key role in the conformational mobility of the calix[6]arene methyl ethers.

## Conclusions

Although it is now known that *p-tert*-butylcalix[6]-arenes can undergo conformational interconversion via the "upper rim through the annulus" pathway, the $\Delta G^\ddagger$ for this process is sufficiently high (> 21 kcal $mol^{-1}$) that the ease with which conformational interconversion occurs via the "lower rim through the annulus" pathway can play an important role in determining how these compounds behave as ion binders and enzyme mimics. On the basis of the data reported in this and other papers the conformational mobility of the ethers and esters of *p-tert*-butylcalix[6]arene via the "lower rim through the annulus" pathway can be characterized as immobile, semimobile, or mobile on the $^1H$ NMR time scale. Falling in the immobile category are the hexakis-(*p*-cyanobenzyl) ether **19b**, the monobenzyl ether **3**, the tetrabenzyl dimethyl ether **14**, and possibly the tribenzyl trimethyl ether **13** ($\Delta G^\ddagger$ > 18.5 kcal $mol^{-1}$). Falling in the semimobile category are the monobenzyl pentamethyl ether **10** ($\Delta G^\ddagger$ 18.45 kcal $mol^{-1}$ in $C_2D_2Cl_4$; 12.8 kcal $mol^{-1}$ in pyridine-$d_5$), the bis-calixarene decamethyl ethers **15** and **16**, the dibenzyl tetramethyl ether **12**, and the tetrabenzyl ether **7**. Falling in the mobile category are the hexabenzyl ether **19a** ($\Delta G^\ddagger$ = 12.3 kcal $mol^{-1}$), the parent compound **1c** ($\Delta G^\ddagger$ = 13.3 kcal $mol^{-1}$), and the hexamethyl ether **9** ($\Delta G^\ddagger$ = 9.3 kcal $mol^{-1}$). The varying conformational stabilities of these systems can be interpreted in terms of the interplay between intramolecular hydrogen bond attractions and steric hindrances where the methoxyl group provides an interesting example of "small being better than large" in some cases.

## Experimental Section[37]

**5,11,17,23,29,35-Hexa-*tert*-butyl-37-(propargyloxy)-38,39,40,41,42-pentahydroxycalix[6]arene (4).** To a solution of 0.97 g (1 mmol) of **1c** in 25 mL of DMF was added 0.38 g (3 mmol) of $KOSi(CH_3)_3$. After stirring for 10 min, 0.25 mL of an 80% (by weight) solution of propargyl bromide in toluene was added, and the reaction mixture was allowed to stand at rt for 16 h. The contents were poured into 100 mL of cold 1 N HCl, and the precipitate was removed by filtration and dried. Chromatography of the crude product over silica gel (100–230 mesh; 2.5 cm diameter column filled to 30 cm) using hexane–$CH_2Cl_2$ (1:2) gave 0.62 g (61%) of **4**. An analytical sample was recrystallized from $CH_2Cl_2$–MeOH: mp 194–195 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 9.74 (s, 2), 9.54 (s, 1), 8.52 (s, 2), 7.13 (s, 6), 7.10 (s, 2), 7.08 (s, 2), 6.98 (s, 2), 4.83 (d, 2, $J$ = 2.4 Hz), 4.02 to 3.72 (b, 12), 2.70 (t, 1, $J$ = 2.4 Hz), 1.28 and 1.25 (2s, each 18), 1.21 and 1.13 (2s, each 9). Anal. Calcd for $C_{69}H_{86}O_6 \cdot 0.5H_2O$: C, 81.22; H, 8.59. Found: C, 81.01; H, 8.31.

**5,11,17,23,29,35-Hexa-*tert*-butyl-37-(benzyloxy)-38,39,-40,41,42-pentamethoxycalix[6]arene (10).** To a solution of 0.53 g (0.5 mmol) of the monobenzyl ether **3**[9] in 25 mL of THF–DMF (80:20) was added 0.24 g of 60% NaH dispersion in oil. The contents were stirred for 15 min, and 0.62 mL of $CH_3I$ (10 mmol) was then added. The reaction mixture was heated at 80 °C for 6 h, THF was removed under reduced pressure, cold water was added, and the reaction mixture was acidified with HCl. The precipitate was removed by filtration and dried to give 0.48 g (84%) of **10**. An analytical sample was recrystallized from $CH_2Cl_2$–MeOH: mp 372–373 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 7.55–7.35 (m, 5), 7.23 (d, 2, $J$ = 2.4 Hz), 7.11 (s, 2), 7.08 (d, 2, $J$ = 2.3 Hz), 6.90 (d, 2, $J$ = 2.2 Hz), 6.87 (s, 2), 6.84 (d, 2, $J$ = 2.2 Hz), 4.88 (s, 2), 4.46 (d, 2, $J$ = 14.4 Hz), 4.17 (d, 2, $J$ = 14.7 Hz), 4.02 (d, 2, $J$ = 14.5 Hz), 3.81 (d, 2, $J$ = 14.5 Hz), 3.67 (d, 2, $J$ = 14.6 Hz), 3.52 (d, 2, $J$ = 15.0 Hz), 3.20 (s, 6), 2.77 (s, 3), 2.51 (s, 6), 1.25 and 1.02 (2s, each 18), 1.23 and 0.97 (2s, each 9); $^{13}C$ NMR($CDCl_3$) $\delta$ 154.28, 153.56, 151.99, 145.89, 145.70, 145.62, 137.83, 133.87, 133.55, 133.37, 133.21, 133.17, 128.42, 127.77, 127.74, 127.30, 126.82, 126.73, 125.17, 124.99, 124.53 (ArC), 74.36 (t, $OCH_2Ph$), 60.02, 59.93, and 59.83 ($OCH_3$), 34.15 and 34.07 [$C(CH_3)_3$], 31.49, 31.31 and 31.25 [$C(CH_3)_3$], 30.65 and 30.35 (2t, $ArCH_2Ar$). Anal. Calcd for $C_{78}H_{100}O_6$: C, 82.64; H, 8.89. Found: C, 82.72; H, 8.76.

**5,11,17,23,29,35-Hexa-*tert*-butyl-37-(propargyloxy)-38,-39,40,41,42-pentamethoxycalix[6]arene (11)** was prepared in 72% crude yield following the procedure described above for **10**. An analytical sample was recrystallized from $CH_2Cl_2$–MeOH: mp 267–268 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 7.18 (d, 2, $J$ = 2.2 Hz), 7.09 (s, 2), 7.08 (d, 2, $J$ = 2.2 Hz), 6.95 (d, 2, $J$ = 2.1 Hz), 6.91 (s, 2), 6.90 (s, 2), 4.19 (s, 2, $OCH_2$), 3.98 (s, 4), 3.93 (s, 8), 3.14 (s, 6), 2.81 (s, 3), 2.68 (s, 6), 2.35 (bs, 1, $C{\equiv}CH$), 1.25 and 1.07 (2s, each 18), 1.22 and 1.02 (2s, each 9). Anal. Calcd for $C_{74}H_{96}O_6$: C, 82.18; H, 8.95. Found: C, 82.17; H, 8.79.

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-bis(benzyloxy)-37,38,40,41-tetramethoxycalix[6]arene (12).** The dibenzyloxy compound **5** was prepared according to the general procedure described for 1,4-bis(arylmethyl) ethers.[13] To a solution of 0.97 g (1 mmol) of *p-tert*-butylcalix[6]arene in 100 mL of THF containing 10 mL of DMF was added 0.77 g (6 mmol) of $Me_3SiOK$ at 0 °C under $N_2$. After stirring for 10 min, 1.02 g (6 mmol) of benzyl bromide in 5 mL of THF was introduced via an addition funnel. The reaction was continued at 0 °C for 1.5 h and warmed to rt, THF was removed under vacuum, and 100 mL of cold 0.1 N HCl was added. The precipitate was removed by filtration, dried, and treated with MeOH to give 0.98 g (85%) of **5**, the $^1H$ NMR ($CDCl_3$) of which shows it to be a mixture of conformers: $\delta$ 8.43 and 7.79 (OH), 7.45–6.78 ArH), 5.08 and 4.87 ($OCH_2Ph$), 4.26–3.50 (m, $ArCH_2Ar$), 1.23, 1.17 and 1.03 [$C(CH_3)_3$]. This material was

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[35] Assuming that the resonance for an OMe ouside the cavity appears at $\delta$ 3.20 and that the $\delta$ 2.24 resonance for **13** corresponds to 100% of the OMe being inside the cavity, a resonance at $\delta$ 2.35 corresponds to a weighted average of 11% OMe outside and 89% OMe inside the cavity.

[36] We are indebted to Professor Rocco Ungaro for making this unpublished information available.

[37] Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. THF was freshly distilled from Na–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. $^1H$ NMR spectra were recorded at 300 MHz. TLC analyses were carried out on Analtech silica gel plates (absorbant thickness 250 $\mu$m) containing a fluorescent indicator. Chromatography was carried out with J. T. Baker silica gel no. JT7042-2 (40 $\mu$m particles) on columns 50 $\mu$m 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 mm of pressure.

converted to **12** in 94% crude yield following the procedure described above for **10.** An analytical sample was recrystallized from $CH_2Cl_2$-MeOH: mp 323–324 °C; $^1H$ NMR ($CDCl_3$) δ 7.56–7.35 (m, 10), 7.22 (s, 4), 6.99 (s, 4), 6.88 (s, 4), 4.90 (s, 4), 4.29 (bd, 4, $J$ = 13.3 Hz), 3.83 (bs, 4), 3.60 (bd, 4, $J$ = 13.6 Hz), 2.66 (bs, 12, $OCH_3$), 1.13 (s, 36), 1.06 (s, 18). Anal. Calcd for $C_{84}H_{104}O_6$: C, 83.40; H, 8.67. Found: C, 83.71; H, 8.60.

**5,11,17,23,29,35-Hexa-*tert*-butyl-37,39,41-tris(benzyloxy)-38,40,42-trimethoxycalix[6]arene (13)**[20] was prepared in 65% yield following the procedure described above for **10** starting with 1,3,5-trimethyl ether **6**[22] and using benzyl bromide instead of $CH_3I$. An analytical sample was recrystallized from $CH_2Cl_2$–MeOH: mp 218–219 °C; $^1H$ NMR ($CDCl_3$) δ 7.55 to 7.31 (bm, 15), 7.27 (s, 6), 6.69 (s, 6), 4.95 (s, 6), 4.62 (d, 6, $J$ = 14.5 Hz, $ArCH_2Ar$), 3.40 (d, 6, $J$ = 15.1 Hz, $ArCH_2Ar$), 2.24 (s, 9, $OCH_3$), 1.38 and 0.81 (2s, each 27); $^{13}C$ NMR ($CDCl_3$) δ 154.49, 151.67, 145.78, 145.68, 137.70, 133.83, 133.15, 128.43, 128.24, 127.98, 127.81, 123.57 (ArC), 74.56 (t, $OCH_2$), 60.18($OCH_3$), 34.21 and 34.00 [$C(CH_3)_3$], 31.62 and 31.19 [$C(CH_3)_3$], 29.84 (t, $ArCH_2Ar$). Anal. Calcd for $C_{90}H_{108}O_6$: C, 84.07; H, 8.47. Found: C, 84.30; H, 8.47.

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dimethoxy-37,-38,40,41-tetrakis(benzyloxy)calix[6]arene (14)** was prepared from **7**[13] in 87% crude yield following the procedure described above for **10**. An analytical sample was recrystallized from $CH_2Cl_2$–MeOH: mp 322–323 °C; $^1H$ NMR ($CDCl_3$) δ 7.63 to 7.34 (m, 20), 7.31 (d, 4, $J$ = 2.3 Hz), 7.18 (s, 4), 6.56 (d, 4, $J$ = 2.1), 4.99 (d, 4, $J$ = 11.0 Hz), 4.86 (d, 4, $J$ = 11.0 Hz), 4.47 (d, 4, $J$ = 15.5 Hz), 3.89 (s, 4), 3.43 (d, 4, $J$ = 15.5 Hz), 1.48 (s, 6, $OCH_3$), 1.34 (s, 18), 0.88 (s, 36); $^{13}C$ NMR ($CDCl_3$) δ 154.65, 152.18, 146.02, 145.71, 137.96, 133.98, 133.23, 132.64, 128.51, 127.99, 127.80, 126.70, 123.39, (ArC), 74.47 (t, $OCH_2Ph$), 58.92 ($OCH_3$), 34.17 and 34.00 [$C(CH_3)_3$], 31.55 and 31.15 [$C(CH_3)_3$], 33.03 and 29.92 (2t, $ArCH_2Ar$). Anal. Calcd for $C_{96}H_{112}O_6$: C, 84.66; H, 8.29. Found: C, 84.65; H, 8.22.

**1,6-Bis{5,11,17,23,29,35-hexa-*tert*-butyl-38,39,40,41,42-pentamethoxy-37-calix[6]aryloxy}-2,4-hexadiyne (15).** A 0.5 g (2.5 mmol) amount of $Cu(OAc)_2 \cdot H_2O$ was warmed to 65 °C in a mixture of 40 mL of MeCN/pyridine (50:50, v/v).[38] To this mixture was added 0.23 g (0.21 mmol) of **11**, and the reaction mixture was stirred at 65 °C for 10 h, allowed to cool, and poured into 150 mL of 50% aqueous HCl. The precipitate was removed by filtration, washed with water, and dried. The product was dissolved in $CH_2Cl_2$, passed over a small column of silica gel, and further recrystallized from $CH_2Cl_2$–MeOH to give 0.18 g (78%) of **15**: mp 341–342 °C dec; $^1H$ NMR ($CDCl_3$) δ 7.23 (d, 4, $J$ = 2.3 Hz), 7.10 (s, 4), 7.08 (d, 4, $J$ = 2.3 Hz), 6.93 (d, 4, $J$ = 2.2 Hz), 6.87 (s, 4), 6.84 (d, 4, $J$ = 2.2 Hz), 4.42 (s, 4, $OCH_2$), 4.36 (d, 4, $J$ = 14.7 Hz), 4.12 (d, 4, $J$ = 15.2 Hz), 3.98 (d, 4, $J$ = 15.0 Hz), 3.85 (d, 4, $J$ = 15.0 Hz), 3.70 (d, 4, $J$ = 15.5 Hz), 3.55 (d, 4, $J$ = 15.0 Hz), 3.19 (s, 12), 2.77 (s, 6), 2.54 (s, 12), 1.27 and 1.04 (2s, each 36), 1.23 and 0.98 (2s, each 18); $^{13}C$ NMR ($CDCl_3$) δ 154.33, 154.23, 153.64, 151.65, 146.43, 145.81, 145.68, 133.94, 133.66, 133.48, 133.36, 133.22, 133.13, 127.25, 126.95, 126.70, 125.36, 125.06, 124.97 (ArC), 75.56 (s, 2C, $\equiv CCH_2$), 70.99 (s, 2C, $\equiv CC \equiv$), 60.77 (t, $OCH_2$), 60.01, 59.92 and 59.83 ($OCH_3$), 34.20 and 34.10 [ $C(CH_3)_3$], 31.54, 31.50, 31.35 and 31.24 [$C(CH_3)_3$], 31.05 and 30.18 (2t, $ArCH_2Ar$). Anal. Calcd for $C_{148}H_{190}O_{12}$: C, 82.25; H, 8.86. Found: C, 82.34; H, 8.81.

**α,α′-Bis{5,11,17,23,29,35-hexa-*tert*-butyl-38,39,40,41,42-pentamethoxy-37-calix[6]aryloxy}-*p*-xylylene (16).** To a solution of 0.52 g (0.5 mmol) of **8**[9] in 25 mL of THF–DMF (70:30, v/v) was added 0.2 g of 60% dispersion of NaH in oil and it was stirred for 15 min, after which 0.07 g of α,α′-dibromo-*p*-xylene was added and the reaction mixture heated at 80 °C for 12 h. It was allowed to cool, poured into 100 mL of cold water, and acidified and the product extracted into $CH_2Cl_2$ (3 × 25 mL). The combined organic layer was washed with water and brine and dried over $Na_2SO_4$. The residue after removal of the solvent was chromatographed over silica gel (100–230 mesh, 2.5 cm diameter column filled to a height of 30 cm). The fractions eluted with 10% EtOAc in 90% $CH_2Cl_2$ were collected and further recrystallized from $CH_2Cl_2$–MeOH to give 0.28 g (52%) of **16**: mp 238–239 °C; $^1H$ NMR ($CDCl_3$) δ 7.56 (s, 4), 7.24 (d, 4, $J$ = 2.4 Hz), 7.11 (s, 4), 7.08 (d, 4, $J$ = 2.3 Hz), 6.89 (bd, 4), 6.86 (s, 4), 6.84 (d, 4, $J$ = 2.2 Hz), 4.92 (s, 4), 4.46 (d, 4, $J$ = 14.6 Hz), 4.16 (d, 4, $J$ = 15.5 Hz), 4.02 (d, 4, $J$ = 14.7 Hz), 3.82 (d, 4, $J$ =15.0 Hz), 3.68 (d, 4, $J$ = 15.5 Hz), 3.54 (d, 4, $J$ = 14.5 Hz), 3.21 (s, 12), 2.75 (s, 6), 2.50 (s, 12), 1.25 and 1.02 (2s, each 36), 1.23 and 0.96 (2s each 18); $^{13}C$ NMR ($CDCl_3$) δ 154.34, 154.22, 153.58, 152.12, 145.85, 145.69, 145.64, 137.43, 133.91, 133.67, 133.57, 133.32, 133.23, 127.81, 127.41, 126.85, 126.78, 125.15, 125.00, 124.49 (ArC), 74.28 ($OCH_2Ph$), 60.03, 59.96 and 59.82 ($OCH_3$), 34.16 and 34.09 [$C(CH_3)_3$], 31.52, 31.33 and 31.27 [$C(CH_3)_3$], 30.70 and 30.43 (2t, $ArCH_2Ar$). Anal. Calcd for $C_{150}H_{194}O_{12}$: C, 82.30; H, 8.93. Found: C, 82.54; H, 8.87.

The following compounds were previously reported[13] but without $^{13}C$ NMR data:

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[(4-cyanobenzoyl)oxy]calix[6]arene (17b):** $^{13}C$ NMR ($CDCl_3$) δ 161.79, 149.67, 149.20, 145.06, 143.93, 132.08, 131.89, 131.75, 131.60, 129.99, 127.78, 126.20, 125.00, 117.13, 116.05 (ArC and CN), 38.44 and 30.42 (2t, $ArCH_2Ar$), 34.30, 33.89 [$C(CH_3)_3$], 31.68, 30.61 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[(4-bromobenzoyl)oxy]calix[6]arene (17c):** $^{13}C$ NMR ($CDCl_3$) δ 163.13, 149.43, 149.12, 144.22, 144.06, 132.26, 131.35, 131.12, 130.11, 128.34, 127.51, 126.65, 126.00, 125.96, 125.02 (ArC), 38.52 and 30.42 ($ArCH_2Ar$), 34.25, 33.85 [$C(CH_3)_3$], 31.77, 30.62 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[[4-(trifluoromethyl)benzoyl]oxy]calix-[6]arene (17d):** $^{13}C$ NMR ($CDCl_3$) δ 162.37, 149.36, 149.25, 144.60, 144.02, 134.30, 133.87, 132.24, 130.92, 129.94, 127.62, 126.12, 125.89, 125.11, 125.01 (ArC), 38.56 and 30.14 ($ArCH_2Ar$), 34.18 and 33.76 [$C(CH_3)_3$], 31.49 and 30.49 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[(4-nitrobenzyl)oxy]calix[6]arene (18a):** $^{13}C$ NMR ($CDCl_3$) δ 151.06, 150.20, 147.55, 145.97, 144.15, 143.35, 134.14, 130.51, 126.89, 126.49, 125.29, 125.13, 125.00, 122.89 (ArC), 70.77 ($OCH_2Ar$), 38.95 and 30.57 ($ArCH_2Ar$), 34.14 and 33.77 [$C(CH_3)_3$], 31.62, 30.76 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[(4-cyanobenzyl)oxy]calix[6]arene (18b):** $^{13}C$ NMR ($CDCl_3$) δ 151.15, 150.38, 147.51, 143.06, 141.88, 133.76, 131.46, 130.46, 126.79, 126.54, 125.43, 125.20, 124.89, 118.82, 109.65 (ArC & CN), 71.03 ($OCH_2Ar$), 38.98 and 30.60 ($ArCH_2Ar$), 34.15 and 33.83 [$C(CH_3)_3$], 31.81 and 30.85 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[(4-bromobenzyl)oxy]calix[6]arene (18c):** $^{13}C$ NMR ($CDCl_3$) δ 151.95, 150.77, 146.88, 141.87, 135.43, 133.11, 130.91, 130.54, 126.94, 125.54, 125.44, 125.12, 120.15 (ArC), 72.06 ($OCH_2Ar$), 38.98 and 30.66 ($ArCH_2Ar$), 34.10 and 33.86 [$C(CH_3)_3$], 31.83 and 31.01 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,-38,40,41-tetrakis[[(4-trifluoromethyl)benzyl]oxy]calix[6]-arene (18d):** $^{13}C$ NMR ($CDCl_3$) δ 151.62, 150.66, 147.14, 142.33, 140.42, 133.29, 130.71, 126.76, 125.79, 125.33, 125.11, 124.90, 124.52, 124.48 (ArC), 71.58 ($OCH_2Ar$), 39.04 and 30.45 ($ArCH_2Ar$), 34.01 and 33.73 [$C(CH_3)_3$], 31.58 and 30.79 [$C(CH_3)_3$].

**5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40,41,42-hexakis[(4-cyanobenzyl)oxy]calix[6]arene (19b):** $^{13}C$ NMR ($CDCl_3$) δ 151.57, 146.35, 142.50, 132.52, 132.40, 127.80, 125.86, 118.76, 111.28 (ArC & CN), 73.74 ($OCH_2Ar$), 34.17 [$C(CH_3)_3$], 31.40 [$C(CH_3)_3$], 29.45 (t, $ArCH_2Ar$).

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(38) Berscheid, R.; Vögtle, F. *Synthesis* **1992**, 58.