Calixarenes. 29. Aroylation and Arylmethylation of Calix[6]arenes

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Aroylations and arylmethylations of *p-tert*-butylcalix[6]arene have been carried out using a variety of para-substituted aroyl chlorides and arylmethyl halides to determine the effect of para substituents on the structural and/or conformational outcome of the reactions. When an excess of derivatizing agent is used with NaH as the base the products in all cases are the 1,2,4,5-tetrasubstituted compounds in the 1,2,3-alternate conformation. However, with Me_3SiOK as the base the products of arylmethylation are the 1,4-diethers. By varying the reaction conditions it is possible in some cases to prepare hexaethers as well as monoethers. By means of ^1H NMR spectral measurements it has been shown that any aroyl moiety or any para-substituted phenylmethyl moiety is large enough to prevent its rotation through the annulus of the calix[6]arene, thus partially, or in some cases completely, freezing the conformation. The unsubstituted benzyl moiety, however, is small enough to pass through the annulus farily easily, thus allowing complete conformational interconversion to occur. The synthetic utility of these derivatives is adumbrated by the selective de-*tert*-butylation of a tetraester and the intramolecular bridging of a diether.

The preceding paper[1] describes the *p*-nitrobenzoylation of *p-tert*-butylcalix[6]arene (**1**),[2] which produces a high yield of the 1,2,4,5-tetraester **3j** as a single structure and conformer. A previous study[3] of the aroylation of *p-tert*-butylcalix[4]arene showed that the conformational outcome in this system is quite dependent on the reactivity of the aroylating agent, the very reactive *p*-nitrobenzoyl chloride yielding the cone conformer and the much less reactive *p*-methoxybenzoyl chloride yielding the 1,3-alternate conformer. An analogous study[4] of the arylmethylation of *p-tert*-butylcalix[4]arene shows that the *p*-substituent plays a similar role in this case as well, although to a much less significant extent. It is of interest, therefore, to compare and contrast the tetrameric and hexameric calixarenes with regard to the influence on the structure and conformation of the products of the para substituents of aroylating and arylmethylating reagents.

Aryolation of *p-tert*-Butylcalix[6]arene (1) with 4-R-Benzoyl Chlorides 2

Two procedures were used to effect the aroylation of **1**, one employing the aroyl halide **2** and NaH in a THF–DMF solvent and the other employing the aroyl halide **2** and 1-methylimidazole in acetonitrile as solvent. The yields from the NaH procedure (42–62%) do not appear to correlate with the structural features of the aroyl halide, but those from the 1-methylimidazole procedure (26–76%) are appreciably higher when electron-withdrawing groups (e.g., CN, F_3C, NO_2) are the para substituents in the aroyl chloride. The products in all cases are very-high-melting solids (mp 385 ± 25 °C) possessing elemental analyses compatible with a tetraester and showing ^1H NMR spectra containing a pair of doublets and a singlet arising from the methylene protons. As discussed in detail in the accompanying paper,[1] these data are in agreement with a 1,2,4,5-tetraester structure in a 1,2,3-alternate conformation. Thus, in contrast to *p-tert*-butylcalix[4]arene, where the conformational outcome is strongly dependent on the para substituent of the aroylating agent, the conformational outcome with *p-tert*-butylcalix[6]arene appears to be insensitive to this feature.

To rationalize the conformational outcome of aroylations of *p-tert*-butylcalix[4]arene it has been postulated[3] that a competition exists between the rate of conformational interconversion and the rate of aroylation, the more reactive aroylating agents capturing the system in the cone conformation and the less reactive ones capturing it in the 1,3-alternate conformation. Calix[6]arenes, however, are more conformationally flexible than calix[4]arenes, the $\Delta G^{\ddagger}$ values for conformational inversion of the *p-tert*-butyl compounds in $CDCl_3$ being 13.3 (11 °C)[5a] and 15.7 (53 °C) kcal/mol,[5b,6] respectively. Thus, it is postulated that under aroylation conditions the rate of conformational interconversion in the cyclic hexamer is more rapid than the rate of aroylation in *all* cases, with the result that the same conformer (presumably the most stable one) is formed in every instance regardless of the reactivity of the aroylating agent.

Arylmethylation of *p-tert*-Butylcalix[6]arene (1) with 4-R-Arylmethyl Halides 4

Two procedures were used for the arylmethylation of **1**, one using the arylmethyl chloride or bromide **4** in THF–DMF solution with NaH as the base[7] and the other using Me_3SiOK as the base. The ^1H NMR spectra of the products from the first procedure all show two *tert*-butyl resonances in a 2:1 ratio and an $ArCH_2Ar$ pattern consisting of a pair of doublets and a singlet in a 2:1 ratio, in agreement with a 1,2,4,5-tetraether structure in the 1,2,3-alternate conformation, i.e., the same type of structure and conformation that is formed from the aroylation of **1**. The yields of arylmethyl ethers in most cases are quite good (ranging from 71% for **5i** to 94% for **5d**), and the products have moderately high melting points (mp ca. 260 ± 30 °C) that are ca. 100 °C lower than those of the corresponding esters. A competition experiment using *p-tert*-butylcalix[4]arene and equivalent amounts of *p*-

(1) Rogers, J. S.; Gutsche, C. D. *J. Org. Chem.*, previous paper in this issue.

(2) The term "calixarene" is variously employed in different contexts. In colloquial usage (as employed in the Discussion), it implies the presence of hydroxyl groups as, for instance, in "*p-tert*-butylcalix[6]arene" for **1a** and "*p*-H-calix[6]arene" for **1b**. In the 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 the positions that are designated by appropriate numbers.

(3) Iqbal, M.; Mangiafico, T.; Gutsche, C. D. *Tetrahedron* **1987**, *43*, 4917.

(4) Gutsche, C. D.; Reddy, P. A. *J. Org. Chem.* **1991**, *56*, 4783.

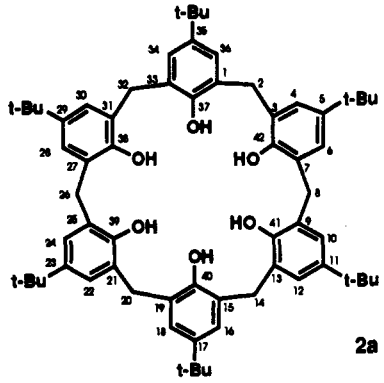
(5) Gutsche, C. D. *Calixarenes*; Stoddart, J. F. Ed.; Monographs in Supramolecular Chemistry; Royal Society of Chemistry, Cambridge, 1989; (a) p 98, (b) p 92, (c) pp 110–111.

(6) A value of 16.4 (>55 °C) is reported from line-shape analysis by: Araki, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 581.

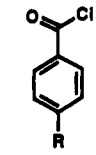
(7) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409.

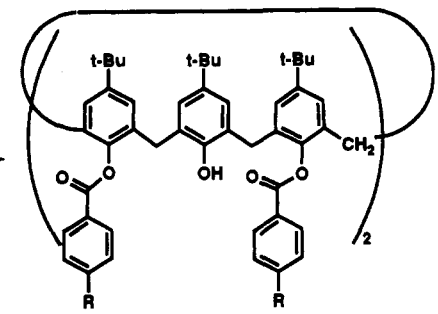
0022-3263/92/1957-3160$03.00/0

Scheme I



1

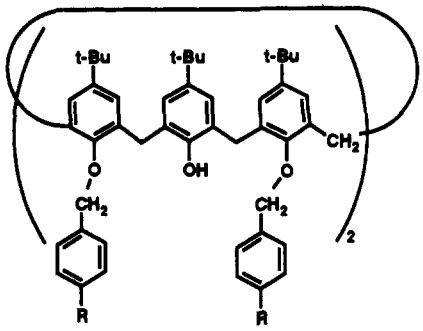


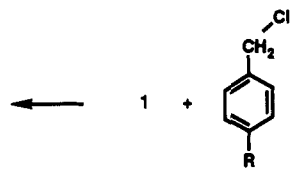


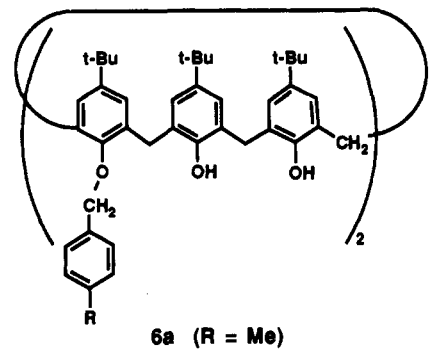
2a (R = H)
2b (R = OMe)
2c (R = Me)
2d (R = *tert*-Bu)
2e (R = CN)
2f (R = F_3C)
2g (R = Br)
2h (R = Cl)
2i (R = F)
2j (R = NO_2)

3a (R = H)
3b (R = OMe)
3c (R = Me)
3d (R = *tert*-Bu)
3e (R = CN)
3f (R = F_3C)
3g (R = Br)
3h (R = Cl)
3i (R = F)
3j (R = NO_2)

Scheme II







5a (R = H)
5b (R = Me)
5c (R = *tert*-Bu)
5d (R = CN)
5e (R = F_3C)
5f (R = Br)
5g (R = Cl)
5h (R = F)
5i (R = NO_2)

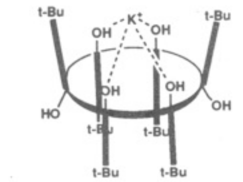
4a (R = H)
4b (R = OMe)
4c (R = Me)
4d (R = *tert*-Bu)
4e (R = CN)
4f (R = F_3C)
4g (R = Br)
4h (R = Cl)
4i (R = F)
4j (R = NO_2)

6a (R = Me)
6b (R = *tert*-Bu)
6c (R = CN)
6d (R = F_3C)
6e (R = Br)
6f (R = NO_2)

methoxybenzoyl chloride (a low reactivity aroylating agent) and *p*-methylbenzyl bromide has been shown[4] to produce the ester to the virtual exclusion of the ether, indicating the greater rate of aroylation as compared with arylmethylation. Thus, if product determination depends on the relative rates of conformational inversion and derivatization it would be predicted that the regiochemically identical products (i.e., 1,2,4,5-tetrasubstituted) from the arylmethylation and aroylation of *p*-*tert*-butylcalix[6]arene should all have the same conformation, in contrast to the case with *p*-*tert*-butylcalix[4]arene.

Surprisingly, the products of arylmethylation using Me_3SiOK as the base are diethers rather than tetraethers and are obtained in yields of 69–87%. The ^1H NMR spectra of these materials all show two *tert*-butyl resonances in a 2:1 ratio and an $ArCH_2Ar$ pattern consisting of four doublets in a 2:2:1:1 ratio, in agreement with a 1,4-diether structure **6** in which the arylmethyl groups are syn to one another. Since Me_3COK and KH (unpublished observations) also lead to 1,4-diethers in comparable fashion, it is clear that this change in the outcome of arylmethylation arises from the change of cation from Na^+ to K^+. Possibly, calix[6]arenes form a complex with K^+ involving the OH groups at the 2,3,5,6 positions 7, leaving the OH groups at positions 1 and 4 more accessible to reaction with the arylmethyl halide. Some support for this postulate is provided by the fact that even with an excess of arylmethyl bromide only diether, not tetraether, is formed. However, additional study of this and other systems must be carried out to gain insight into these phenomena, such studies providing interesting intellectual challenges as well as the potential for useful product control procedures.

The formation of tetrasubstituted compounds as the major products when an excess of derivatizing agent is used with NaH as the base can be ascribed to the reduced re-



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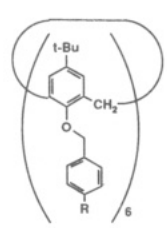
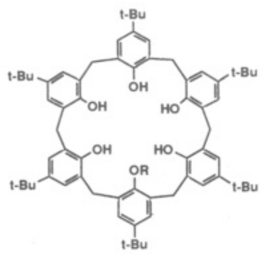
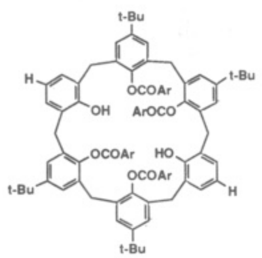


8a (R = H)

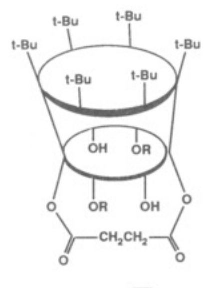
8b (R = CN)



9 (R = CH$_2$-C$_6$H$_4$-OCH$_3$)



10 (Ar = C$_6$H$_4$-NO$_2$)



R = CH$_2$-C$_6$H$_4$-CH$_3$

11

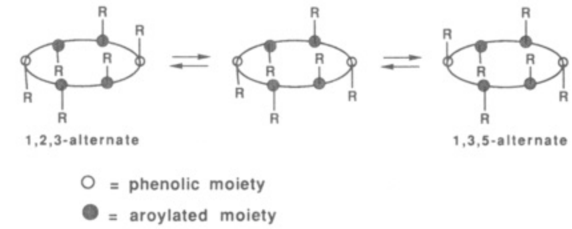


Figure 1.

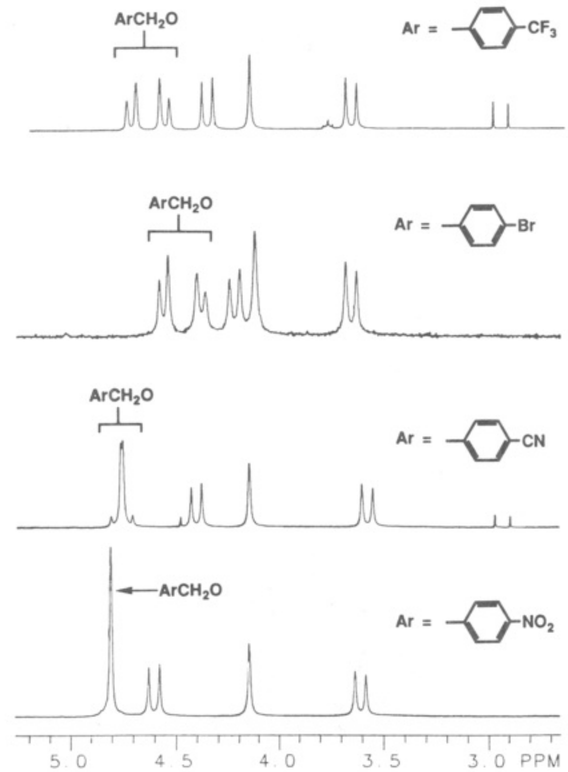


Figure 2.

activity of the remaining two OH groups. By using extended reaction times, however, it is possible in some instances to effect complete substitution. For example, the hexabenzyl ether **8a** and hexakis(*p*-cyanobenzyl) ether **8b** can be made using NaH as the base and allowing the reaction to continue for up to 80 h. Conversely, by using mild conditions and a less reactive benzyl halide it is possible to isolate a monoether, as illustrated by the low-yield conversion of **1** to the mono(*p*-methoxybenzyl) ether **9**. Although the 1,3,5-trimethyl ether of *p*-*tert*-butylcalix[6]arene has been isolated in 30% yield by Casnati et al.,[8] using K_2CO_3 and MeI, triethers or triesters could not be isolated in pure form in the present work.

Conformational Characteristics of Calix[6]arene Esters and Ethers

As mentioned above, calix[6]arenes are conformationally more mobile than calix[4]arenes and require larger groups affixed to the oxygen atoms to freeze the conformation (on the ^{1}H NMR time sacle at 25 °C). Space-filling CPK models indicate that any benzoyl moiety or any para-substituted benzyl moiety affixed to the aryloxy oxygen of a calix[6]arene is large enough to prevent rotation through the annulus of a calix[6]arene. Earlier studies[9] have shown that the *p*-*tert*-butyl groups of *p*-*tert*-butylcalix[6]arene prevent the rotation of the aroyloxy moieties in the other direction through the annulus. Thus, hexakis[(*p*-cyanobenzyl)oxy]calix[6]arene (**8b**) is frozen into what appears to be a cone conformation, based on its ^{1}H NMR spectrum which contains a singlet for the *tert*-butyl protons and a pair of doublets for the CH_2 protons. Similarly, the tetraesters **3a**–**3j** and the tetraethers **5b**–**5i** possess room-temperature ^{1}H NMR patterns that remain invariant upon heating. In the case of the tetrasubstituted compounds the two underivatized phenolic residues remain free to rotate, allowing the possibility of conformational equilibration between the three conformations shown in Figure 1. On the basis of the experiments reported in the preceding paper[1] it appears that at room temperature it is the 1,2,3-alternate conformer that is the major contributor in such an equilibrated system.

Even a single benzoyl moiety or para-substituted benzyl moiety is sufficient to prevent complete conformational inversion at room temperature. For example, the mono(*p*-methoxybenzyl) ether **9** possesses a ^{1}H NMR spectrum that shows four *tert*-butyl resonances (2:2:1:1) and six doublets from the CH_2 protons, reflecting the presence of a mixture of conformers in a system that is incapable of complete conformational inversion. If complete conformational interconversion were possible the system would contain three sets of equivalent CH_2 groups, each of which would give rise to a singlet resonance in the ^{1}H NMR.

Benzyl groups themselves, however, appear to be at the borderline for conformational freezing, for the room temperature spectrum of the tetrabenzyl ether **5a** shows a partially resolved set of lines which only at lower temperature sharpens to a pattern that is characteristic for the 1,2,3-alternate conformation. Even six benzyl residues are insufficient to completely freeze the calix[6]arene at

(8) Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1991**, 1413.
(9) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6059.

Table I. ^{1}H NMR Resonances for $ArCH_2Ar$ and $ArCH_2O$ Protons of the 1,2,4,5-Tetraethers of *p-tert*-Butylcalix[6]arene (5)

compd	para substituent	$ArCH_2Ar$ resonances			$\Delta\delta$	$ArCH_2O$ resonances
		doublet	singlet	doublet		
5a	H	4.18	4.00	3.66	0.52	very broad singlet
5b	Me	4.16	3.98	3.65	0.51	multiplet
5c	*t*-Bu	4.21	4.02	3.68	0.53	broad multiplet
5d	CN	4.40	4.14	3.57	0.83	distorted quartet
5e	F_3C	4.33	4.13	3.63	0.70	quartet
5f	Br	4.21	4.11	3.64	0.57	quartet
5g	Cl	mixture of conformations				
5h	F	mixture of conformations				
5i	NO_2	4.60	4.15	3.60	1.00	sharp singlet

room temperature, for the ^{1}H NMR spectrum of the hexabenzyl ether **8a** shows a broadened set of resonances that sharpen upon heating.

The ^{1}H NMR patterns arising from the nonequivalent hydrogens of the CH_2 groups of the benzyloxy moieties are very dependent on the para substituents. For example, as illustrated in Figure 2, the *p*-(trifluoromethyl)benzyl tetraether **5e** shows a relatively undistorted AB quartet, while the *p*-cyanobenzyl tetraether **5d** shows a highly distorted AB quartet and the *p*-nitrobenzyl tetraether **5i** shows an apparent singlet. It is not possible for these protons to achieve time-averaged equivalence, because this would require complete conformational inversion of the calixarene. Thus, the observed patterns arise from the time-averaged differences in nonequivalent environments for the two hydrogens, the differences in environment depending, inter alia, on the conformation of the calixarene. Although the resonance patterns arising from the $ArCH_2Ar$ hydrogens indicate that the 1,2,3-alternate conformation is present in all of the tetraethers **5**, the $\Delta\delta$ between the doublets of these patterns suggest that the ethers adopt somewhat different shapes within this framework. In the calix[4]arene series a correlation has been made[5c] between the $\Delta\delta$ value and the conformation, a high value (e.g., 1 ppm or greater) indicating a cone conformation, an intermediate value (e.g., 0.5 ppm) indicating a flattened cone conformation, and a low or zero value indicating a 1,3-alternate conformation. As shown in Table I, the $\Delta\delta$ values between the calixarene CH_2 hydrogens of the tetraethers **5** range between 0.51 and 1.00. The "distortion" in the $ArCH_2O$ resonances appears to correlate with the $\Delta\delta$ values, the higher the $\Delta\delta$ value the greater the "distortion". The $\Delta\delta$ also correlates with the polarity of the para substituent, *p*-NO_2 being the most strongly electron-withdrawing group and showing the largest $\Delta\delta$ value with *p*-CN, the next most highly electron-withdrawing group, showing the next largest $\Delta\delta$ value. And, it is these two ethers that show the most singlet-like $ArCH_2O$ patterns. We postulate that dipole repulsion between adjacent *p*-nitrobenzyl moieties forces the calix[6]arene into a conformation that has greater "up, down" character, as reflected by the greater $\Delta\delta$ value, and that this, in turn, confers environments on the CH_2 hydrogens of the (arylmethyl)oxy group that are more similar than in those conformations in which the aryl moieties are more "outward" oriented.

The major purpose for undertaking this investigation was to provide the groundwork for fashioning calix[6]arenes into polyfunctionalized baskets, and to this end a few exploratory experiments have been carried out. One of these involves the selective de-*tert*-butylation, a reaction that has been used to good advantage in the calix[4]arene series. Treatment of the tetrakis(*p*-nitrobenzoyl) ester **2j** with $AlCl_3$ in a CH_2Cl_2 solution containing phenol yields 85% of compound **10** in which the *tert*-butyl groups para to the free OH functions have been removed, making these positions available for functionalization by any of the several methods that have been devised for this purpose.[10] Another experiment involves the addition of a bridge to the lower rim of the calix. Starting with the 1,4-bis(*p*-methylbenzyl) ether **6a**, a bridge containing 4 carbon atoms has been introduced onto the lower rim using succinoyl dichloride to give compound **11**. That the bridge forms intramolecularly rather than intermolecularly is established by a mass spectral molecular weight determination. The scope and limitations of the bridging reaction will be reported in detail in a future paper.

Experimental Section[11]

General Procedures. Procedure A. NaH Method for 1,2,4,5-Tetrabenzoyl Esters of *p-tert*-Butylcalix[6]arene. To 0.97 g (1 mmol) of *p-tert*-butylcalix[6]arene (**1**) in 100 mL of THF containing 10 mL of DMF was added 0.48 g (12 mmol) of a 60% oil dispersion of NaH under an atmosphere of N_2. The reaction mixture was stirred at room temperature for 30 min, and a solution of the benzoyl chloride (6 mmol) in 10 mL of THF was added via an addition funnel. Stirring at rt was continued for 6 h, and the reaction mixture was then poured into 150 mL of cold 0.1 N HCl and extracted with CH_2Cl_2 (4 × 30 mL), and the combined organic layer was washed with water, brine, and dried (Na_2SO_4). Solvent was removed under vacuum, the residue was treated with 20 mL of MeOH, and the resulting white precipitate was removed by filtration and further purified either by fractional crystallizaton from hexane–CH_2Cl_2 or by chromatography over silica gel (70–230 mesh; 60 Å) using CH_2Cl_2–hexane as eluant.

Procedure B. 1-Methylimidazole Method for 1,2,4,5-Tetrabenzoyl Esters of *p-tert*-Butylcalix[6]arene. To benzoyl chloride (6 mmol) in 100 mL of acetonitrile was added 1.23 g (15 mmol) of 1-methylimidazole under N_2, the solution was stirred at rt for 15 min, 0.97 g (1 mmol) of *p-tert*-butylcalix[6]arene was added in one portion, and stirring was continued for 45 min. The mixture was then poured into 150 mL of cold 0.1 N HCl, and the precipitate was removed by filtration, dried, and treated with 20 mL of MeOH. The MeOH-insoluble product was separated by filtration and further purified by fractional crystallization or by chromatography as described in procedure A.

Procedure C. NaH Method for 1,2,4,5-Tetrakis(arylmethyl) Ethers of *p-tert*-Butylcalix[6]arene. 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 treated with 0.48 g (12 mmol) of NaH (60% dispersion in oil) under N_2. The contents were stirred at rt for 30 min, and the arylmethyl bromide (6 mmol) in 10 mL of THF was introduced via an addition funnel. The reaction mixture was stirred at rt for 6–8 h, THF was removed under vacuum, 150 mL of 0.1 N HCl was added with stirring, and the precipitate was collected by filtration. After being dried, the product was treated with 20 mL of MeOH, and the MeOH-insoluble portion was purified by recrystallization.

Procedure D. Me_3SiOK Method for 1,4-Bis(arylmethyl) Ethers of *p-tert*-Butylcalix[6]arenes. 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. The reaction mixture was stirred for 10 min, and a solution of the arylmethyl bromide (6 mmol) in 10 mL of THF was introduced via an addition funnel. Stirring at 0 °C was continued for 1.5 h, the THF was then removed under vacuum, and 150 mL of cold 0.1 N HCl was added with stirring. The precipitate was removed by filtration, dried, and treated with 20

(10) Gutsche, C. D.; Levine, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 2652. Gutsche, C. D.; Lin, L.-G. *Tetrahedron* **1986**, *42*, 1633. Gutsche, C. D.; Pagoria, P. F. *J. Org. Chem.* **1985**, *50*, 5795. Gutsche, C. D.; Levine, J. A.; Sujeeth, P. K. *Ibid.* **1985**, *50*, 5802. Gutsche, C. D.; Nam, K. C. *J. Am. Chem. Soc.* **1988**, *110*, 6153.

(11) For general aspects regarding the Experimental Section, see companion paper (ref 1, footnote 14).

mL of MeOH. The MeOH-insoluble compound was further purified by recrystallization.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-methoxybenzoyl)oxy]calix[6]arene (3b) was prepared following procedures A and B using *p*-methoxybenzoyl chloride (**2b**) and was isolated in 45% and 41% yield, respectively, using hexane–CH_2Cl_2 for fractional crystallization: mp 382–383 °C; ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 4), 7.24 (d, 8, J = 8.8 Hz), 6.78 (d, 4, J = 2.2 Hz), 6.65 (d, 4, J = 2.2 Hz), 6.43 (s, 2), 6.09 (d, 8, J = 8.8 Hz), 4.29 (d, 4, J = 15.3 Hz), 4.01 (s, 4), 3.52 (d, 4, J = 15.3 Hz), 3.42 (s, 12), 1.38 (s, 18), 0.72 (s, 36). Anal. Calcd for $C_{98}H_{106}O_{14}$: C, 77.96; H, 7.21. Found: C, 78.41; H, 7.31.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-methylbenzoyl)oxy]calix[6]arene (3c) was prepared following procedures A and B using *p*-methylbenzoyl chloride (**2c**) and was isolated in 55% and 33% yield, respectively, using hexane–CH_2Cl_2 for fractional crystallization: mp 389–390 °C; ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 4), 7.16 (d, 8, J = 8.2 Hz), 6.76 (d, 4, J = 2.2 Hz), 6.65 (d, 4, J = 2.2 Hz), 6.40 (s, 2), 6.36 (d, 8, J = 8.2 Hz), 4.31 (d, 4, J = 15.3 Hz), 4.01 (s, 4), 3.54 (d, 4, J = 15.3 Hz), 1.88 (s, 12), 1.41 (s, 18), 0.68 (s, 36). Anal. Calcd for $C_{98}H_{108}O_{10}$: C, 81.41; H, 7.53. Found: C, 81.20; H, 7.57.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-*tert*-butylbenzoyl)oxy]calix[6]arene (3d) was prepared following procedures A and B using *p*-*tert*-butylbenzoyl chloride (**2d**) and was isolated in 45% and 26% yield, respectively, by fractional crystallization from hexane–CH_2Cl_2: mp 408–409 °C; ^{1}H NMR ($CDCl_3$) δ 7.34 (d, 8, J = 8.5 Hz), 7.33 (s, 4), 6.78 (d, 4, J = 2.2 Hz), 6.66 (d, 8, J = 8.5 Hz), 6.62 (d, 4, J = 2.2 Hz), 6.38 (s, 2), 4.42 (d, 4, J = 15.3 Hz), 4.05 (s, 4), 3.48 (d, 4, J = 15.3 Hz), 1.41 (s, 18), 0.93 (s, 36), 0.65 (s, 36). Anal. Calcd for $C_{110}H_{132}O_{10}$: C, 81.85; H, 8.24. Found: C, 82.09; H, 8.30.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-cyanobenzoyl)oxy]calix[6]arene (3e) was prepared following procedures A and B using *p*-cyanobenzoyl chloride (**2e**), isolated in 62% and 76% yield, respectively, and purified by chromatography: mp 403–404 °C; ^{1}H NMR ($CDCl_3$) δ 7.40 (s, 4), 7.35 (d, 8, J = 8.4 Hz), 6.86 (d, 8, J = 8.4 Hz), 6.81 (d, 4, J = 2.2 Hz), 6.71 (d, 4, J = 2.2 Hz), 6.33 (s, 2), 4.23 (d, 4, J = 15.3 Hz), 4.04 (s, 4), 3.61 (d, 4, J = 15.3 Hz), 1.45 (s, 18), 0.71 (s, 36). Anal. Calcd for $C_{98}H_{96}N_4O_{10}$: C, 79.01; H, 6.49; N, 3.76. Found: C, 78.84; H, 6.45; N, 3.95.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[[4-(trifluoromethyl)benzoyl]oxy]calix-[6]arene (3f) was prepared following procedures A and B using *p*-(trifluoromethyl)benzoyl chloride (**2f**), isolated in 42% and 72% yield, respectively, and purified by chromatography: mp 393–394 °C; ^{1}H NMR ($CDCl_3$) δ 7.39 (d, 8, J = 8.2 Hz), 7.37 (s, 4), 6.84 (d, 8, J = 8.2 Hz), 6.78 (d, 4, J = 2.2 Hz), 6.66 (d, 4, J = 2.2 Hz), 6.41 (s, 2), 4.30 (d, 4, J = 15.3 Hz), 4.04 (s, 4), 3.57 (d, 4, J = 15.3 Hz), 1.41 (s, 18), 0.66 (s, 36). Anal. Calcd for $C_{98}H_{96}F_{12}O_{10}$: C, 70.83: H, 5.82. Found: C, 70.98; H, 5.63.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-bromobenzoyl)oxy]calix[6]arene (3g) was prepared following procedures A and B using *p*-bromobenzoyl chloride (**2g**), was isolated in 47% and 64% yield, respectively, and was purified by chromatography: mp 430–431 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (s, 4), 7.11 (d, 8, J = 8.5 Hz), 6.78 (d, 4, J = 2.2 Hz), 6.71 (d, 8, J = 8.5 Hz), 6.68 (d, 4, J = 2.2 Hz), 6.34 (s, 2), 4.26 (d, 4, J = 15.3 Hz), 4.01 (s, 4), 3.57 (d, 4, J = 15.3 Hz), 1.45 (s, 18), 0.74 (s, 36). Anal. Calcd for $C_{94}H_{96}Br_4O_{10}$: C, 66.20; H, 5.67. Found: C, 66.30; H, 5.60.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-chlorobenzoyl)oxy]calix[6]arene (3h) was prepared following procedures A and B using *p*-chlorobenzoyl chloride (**2h**) and was isolated in 61% and 51% yield, respectively, and purified by chromatography: mp 409–410 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (s, 4), 7.18 (d, 8 J = 8.4 Hz), 6.78 (d, 4, J = 2.2 Hz), 6.69 (d, 4, J = 2.2 Hz), 6.53 (d, 8, J = 8.5 Hz), 6.34 (s, 2), 4.26 (d, 4, J = 15.3 Hz), 4.01 (s, 4), 3.57 (d, 4, J = 15.3 Hz), 1.44 (s, 18), 0.74 (s, 36). Anal. Calcd for $C_{94}H_{96}Cl_4O_{10}$: C, 73.91; H, 6.33. Found: C, 74.01; H, 6.23.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-fluorobenzoyl)oxy]calix[6]arene (3i) was prepared following procedures A and B using *p*-fluorobenzoyl chloride (**2i**), isolated in 51% and 65% yield, respectively, and purified by chromatography: mp 391–392 °C; ^{1}H NMR ($CDCl_3$) δ 7.34 (s, 4), 7.26 (dd, 8, J = 8.7 Hz), 6.80 (d, 4, J = 2.2 Hz), 6.69 (d, 4, J = 2.2 Hz), 6.34 (s, 2), 6.24 (dd, 8, J = 8.7 Hz), 4.26 (d, 4, J = 15.3 Hz), 4.02 (s, 4), 3.57 (d, 4, J = 15.3 Hz), 1.41 (s, 18), 0.75 (s, 36). Anal. Calcd for $C_{94}H_{98}F_4O_{10}$: C, 77.24; H, 6.62. Found: C, 77.36; H, 6.59.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis(benzyloxy)calix[6]arene (5a) was prepared in 85% yield following procedure C using benzyl bromide (**4a**) and was recrystallized from $CHCl_3$–MeOH: mp 293–294 °C; ^{1}H NMR ($CDCl_3$) δ showed very broad signals at 7.63, 7.35, 7.03, somewhat sharper signals at 6.26 (bs, 2), 5.06 (bs, 8), 4.18 (bd, 4), 4.00 (bs, 4), 3.66 (bd, 4), 1.22 and 0.72 (each bs). Anal. Calcd for $C_{94}H_{108}O_6$: C, 84.64: H, 8.16. Found: C, 85.10; H, 8.20.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-methylbenzyl)oxy]calix[6]arene (5b) was prepared in 79% yield following procedure C using *p*-methylbenzyl bromide (**4c**) and was recrystallized from CH_2Cl_2–MeOH: mp 268–269 °C; ^{1}H NMR ($CDCl_3$), δ 7.51 (d, 8, J = 8.0 Hz), 7.31 (d, 4, J = 2.4 Hz), 7.21 (d, 8, J = 8.0 Hz), 7.02 (s, 4), 7.00 (s, 2), 6.23 (bs, 4), 5.06–5.02 (m, 8), 4.16 (d, 4, J = 15.1 Hz), 3.98 (s, 4), 3.65 (d, 4, J = 15.1 Hz), 2.36 (s, 12), 1.22 (s, 18), 0.61 (s, 36). Although the ^{1}H NMR shows **5b** (in the 1,2,3-alternate conformation) to be the major product, the presence of low-intensity signals indicates that small amounts of other conformers are probably also in the product. Anal. Calcd for $C_{98}H_{116}O_6$: C, 84.68; H, 8.41. Found: C, 84.85; H, 8.37.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[4-(*tert*-butylbenzyl)oxy]calix[6]arene (5c) was prepared in 82% yield following procedure C using *p*-*tert*-butylbenzyl bromide (**4d**) and was recrystallized from $CHCl_3$–MeOH: mp 284–285 °C; ^{1}H NMR ($CDCl_3$) δ 7.57 (d, 8, J = 8.2 Hz), 7.44 (d, 8, J = 8.2 Hz), 7.28 (d, 4, J = 2.4 Hz), 7.08 (s, 2), 7.03 (s, 4), 6.22 (bs, 4), 5.04 (bm, 8), 4.21 (d, 4, J = 15.3 Hz), 4.02 (s, 4), 3.68 (d, 4, J = 15.3 Hz), 1.32 (s, 36), 1.22 (s, 18), 0.56 (s, 36). Anal. Calcd for $C_{110}H_{140}O_6$: C, 84.78; H, 9.06. Found: C, 84.63; H, 9.04.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-cyanobenzyl)oxy]calix[6]arene (5d) was prepared in 94% yield following procedure C using *p*-cyanobenzyl bromide (**4e**) and was recrystallized from CH_2Cl_2–MeOH: mp 225–226 °C; ^{1}H NMR ($CDCl_3$) δ 7.29 (s, 4), 7.28 (s, 2), 6.79 (s, 4), 6.75 (d, 8, J = 8.1 Hz), 6.74 (s, 4), 6.47 (d, 8, J = 8.1 Hz), 4.76 (q, 8, J = 16.4, 13.8 Hz), 4.40 (d, 4, J = 15.3 Hz), 4.14 (s, 4), 3.57 (d, 4, J = 15.3 Hz), 1.46 (s, 18), 0.80 (s, 36). Anal. Calcd for $C_{98}H_{104}N_4O_6$: C, 82.09; H, 7.31; N, 3.91. Found: C, 82.35; H, 7.35; N, 4.25.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[[4-(trifluoromethyl)benzyl]oxy]calix-[6]arene (5e) was prepared in 86% yield following procedure C using *p*-(trifluoromethyl)benzyl bromide (**4f**) and was recrystallized from CH_2Cl_2–MeOH: mp 255–256 °C; ^{1}H NMR ($CDCl_3$) δ 7.44 (s, 2), 7.18 (s, 4), 6.81 (s, 4), 6.79 (s, 4), 6.76 (d, 8, J = 8.1 Hz), 6.42 (d, 8, J = 8.1 Hz), 4.69 (d, 4, J = 13.0 Hz), 4.54 (d, 4, J = 13.3 Hz), 4.33 (d, 4, J = 15.3 Hz), 4.13 (s, 4), 3.63 (d, 4, J = 15.3 Hz), 1.36 (s, 18), 0.80 (s, 36). Anal. Calcd for $C_{98}H_{104}F_{12}O_6$: C, 73.30; H, 6.53. Found: C, 73.23; H, 6.48.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-bromobenzyl)oxy]calix[6]arene (5f) was prepared following procedure C using *p*-bromobenzyl bromide (**4g**) to give 0.72 g (44%) of **5f**, obtained from a mixture of 1.38 g, by chromatography over silica gel (70–230 mesh, 60 Å): mp 267–268 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (s, 2), 7.12 (s, 4), 6.88 (s, 4), 6.83 (s, 4), 6.64 (bs, 8), 6.19 (bs, 8), 4.55 (d, 4, J = 12.0 Hz), 4.37 (d, 4, J = 12.0 Hz), 4.21 (d, 4, J = 15.6 Hz), 4.11 (s, 4), 3.64 (d, 4, J = 15.6 Hz), 1.36 (s, 18), 0.91 (s, 36). Anal. Calcd for $C_{94}H_{104}Br_4O_6$: C, 68.45; H, 6.36. Found: C, 68.45; H, 6.22. After the isolation of **5f**, the remaining portion (0.56 g) showed a very complex ^{1}H NMR spectrum. Increasing the reaction time to 6 h increased the complexity of the product mixture.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-chlorobenzyl)oxy]calix[6]arene (5g) was prepared in 77% yield following procedure C using *p*-chlorobenzyl chloride (**4h**). After the addition of **4h** the reaction mixture was stirred at rt for 2 h and then refluxed for 3 h to give **5h** as a colorless powder: mp 245–247 °C dec; ^{1}H NMR ($CDCl_3$)

δ showed a very complex pattern of signals from 7.62 to 6.48 and 5.03 to 3.48 and several singlets at 1.32, 1.22, 1.20, 1.13, 1.03, 1.02, 0.78, 0.74, 0.60, suggesting that the product is a mixture of several conformers of **5g**. Anal. Calcd for $C_{94}H_{104}Cl_4O_6$: C, 76.72; H, 7.12. Found: C, 77.27; H, 7.27.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-fluorobenzyl)oxy]calix[6]arene (5h) was prepared in 75% yield following general procedure C using *p*-fluorobenzyl bromide (**4i**): mp 277–279 °C; ^1H NMR ($CDCl_3$) showed a very complex signal pattern from δ 7.62 to 6.58 and 5.03 to 3.30 and several singlets at 1.32, 1.23, 1.22, 1.21, 1.14, 1.04, 1.03, 0.78, 0.75, 0.60, suggesting that the product is a mixture of several conformers of **5h**. Anal. Calcd for $C_{94}H_{104}F_4O_6$·MeOH: C, 79.36; H, 7.57. Found: C, 79.21; H, 7.26.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-nitrobenzyl)oxy]calix[6]arene (5i) was prepared in 71% yield following procedure C using *p*-nitrobenzyl bromide (**4j**) and was recrystallized from CH_2Cl_2–MeOH: mp 229–230 °C; ^1H NMR ($CDCl_3$) δ 7.43 (s, 2), 7.33 (d, 8, J = 8.7 Hz), 7.32 (s, 4), 6.79 (s, 4), 6.74 (s, 4), 6.46 (d, 8, J = 8.7 Hz), 4.81 (s, 8), 4.60 (d, 4, J = 15.2 Hz), 4.15 (s, 4), 3.60 (d, 4, J = 15.2 Hz), 1.46 (s, 18), 0.74 (s, 36). Anal. Calcd for $C_{94}H_{104}N_4O_{14}$: C, 74.58; H, 6.92; N, 3.70. Found: C, 74.51; H, 6.91; N, 3.86.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-methylbenzyl)oxy]calix[6]arene (6a) was prepared in 83% yield following procedure D using *p*-methylbenzyl bromide (**4c**) and was recrystallized from $CHCl_3$–MeOH: mp 280–281 °C; ^1H NMR ($CDCl_3$) δ 7.92 (s, 4), 7.38 (d, 4, J = 8.0 Hz), 7.18 (d, 4, J = 8.0 Hz), 7.07 (d, 4, J = 2.4 Hz), 7.04 (d, 4, J = 2.4 Hz), 6.84 (s, 4), 5.04 (s, 4), 4.25 (d, 4, J = 14.8 Hz), 3.89 (d, 2, J = 14.2 Hz), 3.59 (d, 2, J = 14.2 Hz), 3.52 (d, 4, J = 14.8 Hz), 2.32 (s, 6), 1.24 (s, 36), 0.99 (s, 18). Anal. Calcd for $C_{82}H_{100}O_6$: C, 83.35; H, 8.53. Found: C, 83.53; H, 8.69.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-*tert*-butylbenzyl)oxy]calix[6]arene (6b) was prepared in 77% yield following procedure D using *p*-*tert*-butylbenzyl bromide (**4d**) and was recrystallized from $CHCl_3$–MeOH: mp 319–320 °C; ^1H NMR ($CDCl_3$) δ 8.02 (s, 4), 7.44 (d, 4, J = 8.3 Hz), 7.36 (d, 4, J = 8.3 Hz), 7.09 (d, 4, J = 2.4 Hz), 7.06 (d, 4, J = 2.4 Hz), 6.87 (s, 4), 5.06 (s, 4), 4.31 (d, 4, J = 14.5 Hz), 3.84 (d, 2, J = 14.2 Hz), 3.64 (d, 2, J = 14.2 Hz), 3.54 (d, 4, J = 14.5 Hz), 1.29 (s, 18), 1.24 (s, 36), 1.01 (s, 18). Anal. Calcd for $C_{88}H_{112}O_6$: C, 83.50; H, 8.92. Found: C, 83.28; H, 8.72.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-cyanobenzyl)oxy]calix[6]arene (6c) was prepared in 85% yield following procedure D using *p*-cyanobenzyl bromide (**4e**) and was recrystallized from $CHCl_3$–MeOH: mp 226–227 °C; ^1H NMR ($CDCl_3$) δ 7.71 (s, 4), 7.55 (d, 4, J = 8.5 Hz), 7.47 (d, 4, J = 8.5 Hz), 7.10 (d, 8, J = 2.5 Hz), 6.98 (s, 4), 5.14 (s, 4), 4.29 (d, 4, J = 14.0 Hz), 3.91 (d, 2, J = 14.0 Hz), 3.54 (d, 4, J = 14.0 Hz), 3.48 (d, 2, J = 14.0 Hz), 1.25 (s, 36), 1.12 (s, 18). Anal. Calcd for $C_{82}H_{94}N_2O_6$: C, 81.83; H, 7.87; N, 2.33. Found: C, 81.57; H, 8.01; N, 2.10.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[[(4-trifluoromethyl)benzyl]oxy]calix[6]arene (6d) was prepared in 85% yield following procedure D using *p*-(trifluoromethyl)benzyl bromide (**4f**) and was recrystallized from $CHCl_3$–MeOH: mp 234–235 °C; ^1H NMR ($CDCl_3$) δ 8.06 (s, 4), 7.50 (d, 4, J = 8.2 Hz), 7.42 (d, 4, J = 8.2 Hz), 7.11 (s, 8), 6.98 (s, 4), 5.09 (s, 4), 4.32 (d, 4, J = 14.0 Hz), 3.90 (d, 2, J = 14.0 Hz), 3.54 (d, 4, J = 14.0 Hz), 3.52 (d, 2, J = 14.0 Hz), 1.26 (s, 36), 1.10 (s, 18). Anal. Calcd for $C_{82}H_{94}F_6O_6$: C, 76.37; H, 7.35. Found: C, 76.47; H, 7.27.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-bromobenzyl)oxy]calix[6]arene (6e) was prepared in 87% yield following procedure D using *p*-bromobenzyl bromide: mp 261–262 °C; ^1H NMR ($CDCl_3$) δ 7.96 (s, 4), 7.40 (d, 4, J = 8.5 Hz), 7.31 (d, 4, J = 8.5 Hz), 7.08 (s, 8), 6.94 (s, 4), 5.04 (s, 4), 4.28 (d, 4, J = 14.2 Hz), 3.79 (d, 2, J = 14.0 Hz), 3.62 (d, 2, J = 14.0 Hz), 3.51 (d, 4, J = 14.2 Hz), 1.25 (s, 36), 1.07 (s, 18). Anal. Calcd for $C_{80}H_{94}Br_2O_6$: C, 73.27; H, 7.22. Found: C, 73.44; H, 7.27.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-bis[(4-nitrobenzyl)oxy]calix[6]arene (6f) was prepared in 69% yield following procedure D using *p*-nitrobenzyl bromide (**4j**): mp 179–181 °C; ^1H NMR ($CDCl_3$) δ 7.88 (d, 4, J = 8.8 Hz), 7.81 (s, 4), 7.54 (d, 4, J = 8.8 Hz), 7.12–7.09 (m, 8), 7.04 (s, 4), 5.15 (s, 4), 4.36 (d, 4, J = 14.0 Hz), 4.04 (d, 2, J = 14.0 Hz), 3.59 (d, 4, J = 14.0 Hz), 3.43 (d, 2, J = 14.0 Hz), 1.25 (s, 36), 1.14 (s, 18). Anal. Calcd for $C_{80}H_{94}N_2O_{10}$: C, 77.26; H, 7.62; N, 2.25. Found: C, 76.99; H, 7.67; N, 2.24.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40,41,42-hexakis(benzyloxy)calix[6]arene (8a). A 1.2-g (30 mmol) sample of NaH (60% dispersion in oil) in 100 mL of THF containing 20 mL of DMF was mixed with 1.95 g (2 mmol) of *p*-*tert*-butylcalix[6]arene and 5.13 g (30 mmol) of benzyl bromide in 20 mL of THF. The reaction mixture was stirred at rt for 2 h, refluxed for 80 h, and then worked up to give a white solid that was triturated with MeOH to give 2.26 g (74%) of **8a**. An analytical sample was obtained by recrystallization from $CHCl_3$–MeOH: mp 292–293 °C; ^1H NMR ($CDCl_3$) recorded at ambient temperature contains very broad and ill-resolved lines, but as the temperature is raised above 20 °C the resonances sharpen; at 55 °C the spectrum shows resonances at δ 7.17 (s, 30), 6.96 (s, 12), 4.63 (s, 12), 3.80 (s, 12), and 0.96 (s, 54). Upon cooling below ambient temp a very complex, though highly resolved, pattern of peaks is produced. Anal. Calcd for $C_{108}H_{120}O_6$: C, 85.67; H, 7.99. Found: C, 85.64; H, 7.96.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40,41,42-hexakis[(4-cyanobenzyl)oxy]calix[6]arene (8b). A 0.48-g (12 mmol) sample of NaH (60% oil dispersion) was added under N_2 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. After the solution was stirred for 30 min at rt, 1.18 g (6 mmol) of *p*-cyanobenzyl bromide in 10 mL of THF was added. The reaction mixture was boiled under reflux for 68 h, THF was removed under vacuum, 150 mL of cold 0.1 N HCl was added, and the reaction mixture was extracted with CH_2Cl_2 (4 × 25 mL). The combined organic layer was washed with water and brine and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed over silica gel (70–230 mesh, 60 Å). Initial elution with CH_2Cl_2 gave a fraction which upon crystallization from CH_2Cl_2–MeOH afforded 0.25 g (18%) of the tetraether **5d**. Elution with CH_2Cl_2–EtOAc (9.5:0.5) gave a second fraction from which 0.74 g (44%) of the hexaether **8b** crystallized from CH_2Cl_2–MeOH: mp 272–273 °C; ^1H NMR ($CDCl_3$) δ 7.50 (d, 12, J = 8.2 Hz), 7.12 (d, 12, J = 8.2 Hz), 6.87 (s, 12, ArH), 4.39 (s, 12), 4.15 (d, 6, J = 15.0 Hz), 3.17 (d, 6, J = 15.0 Hz), 1.08 (s, 54). Anal. Calcd for $C_{114}H_{114}N_6O_6$: C, 82.28; H, 6.90; N, 5.05. Found: C, 82.70; H, 6.80; N, 5.09. An HPLC analysis of the sample (column: 25 cm Lichrosorb RP-18. Solvent A = CH_3CN (99%)/AcOH (1%); solvent B = CH_2Cl_2 (9 parts)/methyl *tert*-butyl ether (11 parts)) showed that the product is 90% cone conformer with 10% of one or more of the other conformers.

5,11,17,23,29,35-Hexa-*tert*-butyl-38,39,40,41,42-pentahydroxy-37-[(4-methoxybenzyl)oxy]calix[6]arene (9). Following procedure C using *p*-methoxy benzyl chloride (**4b**), the reaction mixture was stirred at room temperature for 2 h and then refluxed 2 h (heating the reaction mixture for a longer time produced a complex product mixture). After workup, the product mixture was chromatographed over silica gel (70–230 mesh, 60 Å) using CH_2Cl_2–hexane (1:1) as eluant to give 0.18 of *p*-*tert*-butylcalix[6]arene (**1**) followed by 0.24 g (22%) of **8**: mp 197–198 °C; ^1H NMR ($CDCl_3$) δ 9.88 (bs, 2), 9.70 (bs), 9.11 (bs, 2), 7.66 (d, 2, J = 8.6 Hz), 7.15–7.06 (m, 14), 4.42, 4.22, 3.96, 3.56, 3.52, 3.39 (each d, J = 14.0 Hz), 3.89 (s, 3), 1.27 (s, 18), 1.25 (s, 18), 1.21 (s, 9), 1.17 (s, 9). Anal. Calcd for $C_{74}H_{92}O_7 \cdot {}^1/_2CH_2Cl_2$: C, 78.84; H, 8.38. Found: C, 78.34; H, 8.40.

11,17,29,35-Tetra-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-nitrobenzyl)oxy]calix[6]arene (10). A 1.6-g (12 mmol) sample of $AlCl_3$ was added to 100 mL of CH_2Cl_2 under a N_2 atmosphere. To this slurry was added 1.5 g (1 mmol) of the tetraester (**2j**) followed by 0.19 g (2 mmol) of phenol. The reaction mixture was stirred for 2 h and poured into 200 mL of cold 1 N HCl. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layer was washed with water and brine and dried over anhydrous Na_2SO_4. Removal of the solvent and treatment of the residue with 20 mL of MeOH precipitated a pale yellow compound which was removed by filtration and recrystallized from CH_2Cl_2–hexane to give 1.24 g (85%) of **10**: mp 370–372 °C dec; ^1H NMR ($CDCl_3$) δ 7.45–7.28 (m, 22), 6.81 (d, 4, J = 2.2 Hz), 6.73 (d, 4, J = 2.2 Hz), 6.63 (s, 2), 4.38 (d, 4, J = 15.5 Hz), 4.05 (s, 4), 3.69 (d, 4, J = 15.5 Hz), 0.68 (s, 36). Anal. Calcd for $C_{86}H_{80}N_4O_{18}$: C, 70.87; H, 5.53;

N, 3.84. Found: C, 71.02; H, 5.48; N, 3.88.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dihydroxy-39,42-(succinyldioxy)-38,41-bis[(4-methylbenzyl)oxy]calix[6]arene (11). A 0.24-g (0.2 mmol) sample of 1,4-bis(*p*-methylbenzyl) ether **6a** was dissolved in 200 mL of CH_2Cl_2, treated with 0.2 mL (1.5 mmol) of triethylamine, and stirred until a clear solution was obtained. A solution of succinoyl chloride (0.3 mmol) in 10 mL of CH_2Cl_2 was introduced over a 15-min period from an addition funnel. After 15–20 min the solvent was removed, and the product was purified by chromatography on silica gel collecting the fractions eluted with CH_2Cl_2–hexane (80:20) which were recrystallized from CH_2Cl_2–MeOH to give 138 mg (55%) of 11: mp 269–270 °C; ^1H NMR ($CDCl_3$) δ 8.10 (s, 2), 7.35 (d, 4, J = 8.0 Hz), 7.33 (bs, 2), 7.30 (bs, 2), 7.22 (d, 4, J = 8.0 Hz), 6.98, 6.93, 6.63 and 6.55 (each bs), 5.02 and 4.87 (each d, J = 10.7 Hz), 4.22 (d, 2, J = 15.6 Hz), 4.07 (d, 2, J = 15.7 Hz), 3.93 (d, 2, J = 14.0 Hz), 3.51 (d, 2, J = 15.7 Hz), 3.41 (d, 2, J = 14.0 Hz), 3.21 (d, 2, J = 15.6 Hz), 2.59 (s, 4), 2.39 (s, 6), 1.42, 1.07 and 0.95 (each s, 54); MS (FAB) $(M + H)^+$ 1263. Anal. Calcd for $C_{86}H_{102}O_8$: C, 81.74; H, 8.14. Found: C, 81.94; H, 8.04.

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Preparation and Cation Complexing Properties of Some Macropolycyclic Ligands

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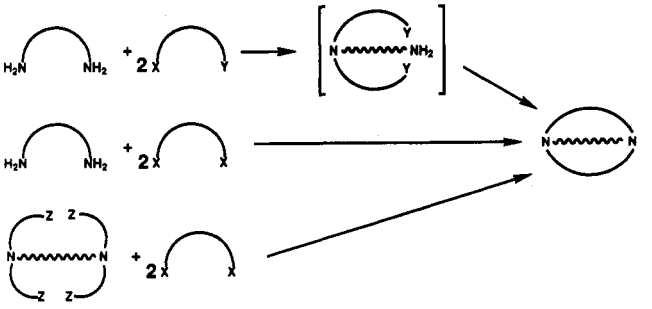
Five new cryptands have been prepared by a 2:1 cyclocondensation of an α,ω-dihalide with an α,ω-diamine. In some cases, other products, such as bis(aza-12-crown-4) ligands and products of a 4:2 cyclocondensation, were isolated also. The structures of the cryptands and bis(aza-crown)s of the same molecular weight were established after careful analysis by ^{13}C NMR and X-ray spectroscopy and a few independent syntheses of the bis(aza-crown) ethers. A new TLC test has been developed to distinguish between the cryptands and the bis(aza-crown)s. Log K values for the interaction of two cryptands, each containing two propylene bridges in one arm, with various cations were determined. The results show a much weaker interaction of the cryptands containing two propylene bridges with various cations than that for the corresponding cryptands with only ethylene bridges. The most stable complexes of these new propylene-containing cryptands were those involving Ba^{2+} and Sr^{2+} ions. X-ray analyses of three cryptands, each of which has the $[18]N_2O_4$ macrocycle as part of its structure, show different organizations for the ring heteroatoms.

Introduction

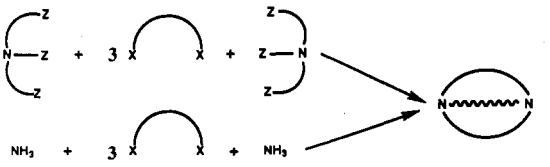
Optimization of synthetic routes to important ligands is critical not only from a financial point of view but also because many synthetic ligands have important chemical applications. The easy access to complicated macrocycles that have hitherto been synthesized in multi steps should be an incentive for a more complete investigation of their physical properties and for finding other chemical and catalytic applications.

The first methods for producing macrocycles were the cyclocondensation of two different difunctionalized linear compounds.[1,2] There is a trend to simplify the total synthesis of macrocycles by using starting materials with only a few atoms, such as ethylene oxide[3] or an aziridine,[4] by cyclopolymerization processes. This idea to react small molecules together in a one-step process has found application in the preparation of the sepulchrates,[5,6] cryptands,[7-15] and bis(aza-crown) ethers.[15]

Scheme I. General Methods To Form the Cryptands A. By 2:1 Cyclocondensations



B. By 3:2 Cyclocondensations



Cryptands usually have been prepared by multi-step processes,[16] but recently, one-step methods from three or five molecules have been studied.[17] Indeed, two difunc-

(1) Krakowiak, K. E.; Bradshaw, J. S.; Zamecka-Krakowiak, D. *J. Chem. Rev.* **1989**, *89*, 929.
(2) Lindoy, L. F. *The Chemistry of Macrocyclic Ligand Complexes*; Cambridge University Press: Cambridge, U.K., 1989.
(3) Dale, J.; Daasvatn, K. *J. Chem. Soc., Chem. Commun.* **1976**, 295.
(4) Hansen, G. R.; Burg, T. E. *J. Heterocycl. Chem.* **1968**, 305.
(5) Creaser, I. I.; Mack, B. J.; Harrowfield, A. J.; Herlt, A. J.; Sargeson, A. M.; Springborg, J.; Geue, R. J.; Snow, R. M. *J. Am. Chem. Soc.* **1977**, *99*, 3181.
(6) Sargeson, A. M. *Pure Appl. Chem.* **1984**, *56*, 1603.
(7) Newkome, G. R.; Majestic, V.; Fronczek, F. R.; Atwood, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 1047.
(8) Newkome, G. R.; Majestic, V. K.; Fronczek, F. R. *Tetrahedron Lett.* **1981**, *32*, 3039.
(9) Rodriguez-Ubis, J. C.; Alpha, B.; Plancherel, D.; Lehn, J.-M. *Helv. Chim. Acta* **1984**, *67*, 2264.
(10) Juanes, O.; de Mendoza, J.; Rodriguez-Ubis, J. C. *J. Chem. Soc., Chem. Commun.* **1985**, 1765.
(11) Alpha, B.; Anklam, E.; Deschenaux, R.; Lehn, J.-M.; Pietraszkiewicz, M. *Helv. Chim. Acta* **1988**, *71*, 1042.
(12) Pietraszkiewicz, M.; Gasiorowski, R.; Kozbial, J. *J. Incl. Phenom.* **1989**, *7*, 309.
(13) Woronkow, M. G.; Kmytow, W. I.; Butin, M. K. *Khim. Geterotsikl. Soedin.* **1989**, 1000.
(14) Krakowiak, K. E.; Bradshaw, J. S.; Izatt, R. M. *J. Heterocycl. Chem.* **1990**, *27*, 1011.
(15) Krakowiak, K. E.; Bradshaw, J. S. *J. Org. Chem.* **1991**, *56*, 3723.
(16) Dietrich, B. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E., MacNichol, D. D., Eds.; Academic Press: London, 1984; Vol. II, p 337.

0022-3263/92/1957-3166$03.00/0