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CALIXARENES 12

THE SYNTHESIS OF FUNCTIONALIZED CALIXARENES

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Abstract—Procedures are described for the removal of the *p*-t-butyl groups from *p*-t-butylcalix[4]arene, *p*-t-butylcalix[6]arene, and *p*-t-butylcalix[8]arene and the introduction of functional groups in their place. Although attempts to functionalize the *p*-positions of the calixarenes have generally failed, the corresponding methyl ethers are amenable to facile acetylation to provide syntheses of the *p*-acetyl-, *p*-carboxy-, and *p*-carbomethoxycalix[6]arenes and calix[8]arenes. Acetylation and benzoylation of calix[4]arene and calix[6]arene occur at the phenolic oxygens rather than the *p*-positions, leading under most reaction conditions to the completely O-substituted product. Calix[4]arene reacts with benzoyl chloride in the presence of pyridine, however, to yield the tribenzoate. Conversion of the tribenzoate to the corresponding tribenzoyloxy monoallyl ether followed by a Claisen rearrangement and hydrolysis yields monoallylcalix[4]arene, a compound of particular interest because of its potential for the synthesis of calixarenes containing a single substituent on the "upper rim".

Calixarenes, which are basket-shaped compounds of potential interest for host–guest complexation studies,[1] have been synthesized in a variety of ways. Those methods of synthesis that can be grouped under the heading of "one-step" procedures (involving the base-catalyzed reactions of *p*-substituted phenols and formaldehyde) offer the advantage of the ease with which the calixarene framework can be obtained. In practice, however, only a few *p*-alkyl-substituted phenols give products from which pure calixarenes can be isolated in reasonable yield.[2] Furthermore, calixarenes so obtained are constrained, by the nature of the reaction, to be symmetrically substituted. Those methods of synthesis that come under the heading of "multi-step", originally devised by Hayes and Hunter[3] and more recently exploited by Kämmerer *et al.*,[4] offer the advantage of considerably greater flexibility and the potential for the construction of unsymmetrically substituted calixarenes. However, they suffer the disadvantages of being long and tedious and of generally giving rather low overall yields. One solution to this problem has been the development of convergent "multi-step" routes, as exemplified by those devised by Böhmer *et al.*[5] and by No and Gutsche.[6] The purpose of the present work is to exploit the possibility of adapting the "one-step" synthesis to the preparation of functionalized calixarenes, including those in which the pattern of functionalization is unsymmetrical.

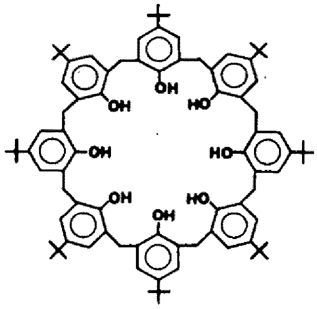
Among the several *p*-alkyl-substituted phenols that undergo "one-step" condensation with paraformaldehyde and base to produce calixarenes, *p*-t-butylphenol yields the most tractible products in a process that can be controlled through adjustments of the reaction conditions.[2] Thus, *p*-t-butylcalix[4]arene (**1**), *p*-t-butylcalix[6]arene (**2**), and *p*-t-butylcalix[8]arene (**3**) are all readily accessible materials, and these compounds provide the starting points for the present investigation. The removal of the t-butyl groups from **1** has been shown to proceed smoothly[7] to afford calix[4]arene (**4**) in reasonably good yield, and this compound would appear to be perfectly adapted to functionalization in the aryl ring at the positions *para* to the hydroxyl groups. However, our initial attempts to achieve *p*-substitution by means of conventional electrophilic substitution reactions failed to yield products that could be purified, and characterized. Therefore, a more circuitous route involving the preparation and subsequent rearrangement of the tetra-allyl ether was developed,[8] represented by the sequence **1** → **4** → **15** → **18**. The possibility of employing electrophilic substitution reactions remains attractive, however, and some success with this approach is demonstrated in the present work.

Acetylation and benzoylation of calixarenes

Treatment of phenols with acetic anhydride in the presence of a small amount of a strong acid is the conventional method for producing aryl acetates and was first described for calixarenes by Zinke and Ziegler.[9] Treatment of calix[4]arene (**4**) under these conditions yields a mixture of tetraacetates,[10] one in the "partial cone" conformation (**7a**) and one in the "1,3-alternate" conformation (**7b**).[11] Because of the conformational mobility of the larger ring system, calix[6]arene (**5**) and calix[8]arene (**6**) yield the hexaacetate (**8**) and octaacetate (**9**), respectively, as single, pure compounds rather than mixtures of conformers.

Acylation or aroylation in the presence of pyridine can be used as an alternative to the acid-catalyzed procedures. Benzoyl chloride in the presence of pyridine, for example, reacts with calix[6]arene to afford a high yield of the hexabenzoate (**11**) as a single compound.[12] To our surprise, however, calix[4]arene yields only a tribenzoate (**29**) under these conditions, even upon prolonged exposure to the benzoylating agents. This unexpected but easy access to the tribenzoate affords a means for the selective functionalization of a calixarene, as discussed in a later section of this paper.

It was anticipated that in the presence of aluminum chloride the treatment of the calixarenes with acetyl chloride or benzoyl chloride might yield the *p*-acetyl or



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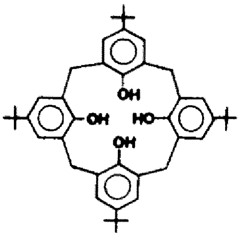

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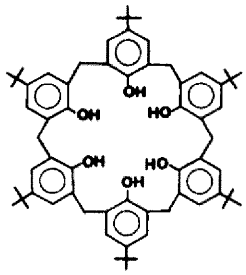

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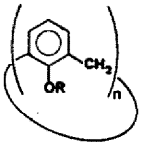
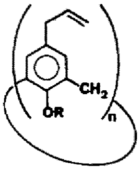
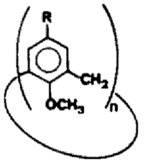


4 (n = 4, R = H)
5 (n = 6, R = H)
6 (n = 8, R = H)
7 (n = 4, R = $COCH_3$)
8 (n = 6, R = $COCH_3$)
9 (n = 8, R = $COCH_3$)
10 (n = 4, R = COC_6H_5)
11 (n = 6, R = COC_6H_5)
12 (n = 4, R = CH_3)
13 (n = 6, R = CH_3)
14 (n = 8, R = CH_3)
15 (n = 4, R = $CH_2CH{=}CH_2$)
16 (n = 6, R = $CH_2CH{=}CH_2$)
17 (n = 8, R = $CH_2CH{=}CH_2$)

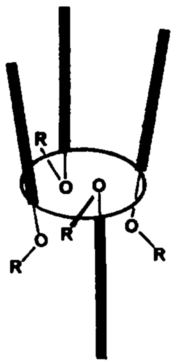


18 (n = 4, R = H)
19 (n = 6, R = H)
20 (n = 8, R = H)
21 (n = 6, R = CH_3)



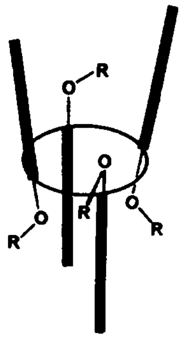
22 (n = 4, R = $COCH_3$)
23 (n = 6, R = $COCH_3$)
24 (n = 8, R = $COCH_3$)
25 (n = 6, R = CO_2H)
26 (n = 8, R = CO_2H)
27 (n = 6, R = CO_2CH_3)
28 (n = 8, R = CO_2CH_3)

p-benzoyl compounds. Instead, reaction occurs only on the phenolic functions to yield esters. It was then anticipated that the esters, once formed, might undergo Friedel–Crafts acylation or aroylation on the benzene rings, but such was not the case. When calix[4]arene (**4**) is treated with aluminum chloride and acetyl chloride a mixture is obtained that contains the same pair of tetraacetates that are obtained using acetic anhydride and sulfuric acid. The ^{1}H-NMR spectrum of the lower melting isomer (m.p. 405–406°) indicated that it is the "1,3-alternate" conformation (**7b**); that of the higher melting isomer (m.p. 408–411°) indicated that it is the "partial cone" conformation (**7a**). To date, only a few other calixarenes have been isolated in the "1,3-alternate" conformation; most of the O-substituted calixarenes prefer the "partial cone" or the "cone" conformation.[11] Prolonged treatment of the tetraacetate with acetyl chloride and aluminum chloride failed to yield detectable amounts of any *p*-acetyl products.



Partial cone

7a (R = $COCH_3$)
10a (R = COC_6H_5)



1,3-Alternate

7b (R = $COCH_3$)
10b (R = COC_6H_5)

In a similar fashion, the aluminum chloride-catalyzed benzoylation of calix[4]arene with benzoyl chloride yields a mixture of tetrabenzoates that can be separated into a lower-melting isomer (m.p. 301–303°) possessing the "partial cone" conformation (**10a**) and a higher-melting isomer (m.p. > 450°) possessing the "1,3-alternate" conformation (**10b**).

Acetylation and transformation of calixarene ethers

Although the calixarene esters fail to undergo Friedel–Crafts acylation or aroylation at the *p*-positions, it was hoped that the corresponding ethers might behave differently. Substance to this hope was provided by the Hammett sigma constants for an OCH_3 group in the *p*-position (-0.27) as compared with an $OCOCH_3$ group in the *p*-position[13] ($+0.31$). Experiment confirmed the expectation, for the calixarene ethers do, indeed, undergo C-acylation at the *p*-positions. In the case of the cyclic tetramer, however, the process is complicated by concomitant demethylation, leading to a mixture of materials that required **22** to be separated by column chromatography.† In contrast, the cyclic hexamer and cyclic octamer undergo smooth acetylation to afford 60–65% yields of easily purified **23** and **24**. With the *p*-acetyl compounds **23** and **24** in hand, efforts were then made to transform the acetyl groups to other functions. Several possibilities were explored, but only the haloform conversion to carboxyl groups was successful, leading to hexacarboxycalix[6]arene (**25**) and octacarboxycalix[8]arene (**26**); these compounds were characterized as their methyl esters **27** and **28**, respectively. Carboxylic acids **25** and **26** along with tetra-*p*-carboxycalix[4]arene,[14] the tetracarboxymethyl ether of *p*-t-butylcalix[4]arene[15] and the hexasulfonatocalix[6]arene[16] constitute the presently known group of aqueous base soluble calixarenes.

Synthesis of allylcalixarenes

The utility of the Claisen rearrangement as a means for introducing a proto-functional group into the *p*-positions of calixarenes has previously been demonstrated with calix[4]arene.[8] In the present work the possibility of extending this process to the cyclic hexamer and cyclic octamer was explored. Conversion of calix[6]arene (**5**) to the hexaallyl ether (**16**) with allyl bromide and NaH in a THF–DMF solution proceeds in 89% yield. Treatment of this material with refluxing N,N-diethylaniline for several hours results in complete rearrangement, as indicated by ^{1}H-NMR and IR spectral data, although only a 21% yield of pure *p*-hexaallylcalix[6]arene (**19**) could be isolated. Attempts to improve the isolation procedure have failed to increase the yield, in spite of the fact that significantly greater amounts of **19** appear to be present in the crude product. In a similar fashion, calix[8]arene (**6**) can be converted to the octaallyl ether **17**, which undergoes what appears (on the basis of spectral indications) to be complete rearrangement when heated in refluxing N,N-diethylaniline. However, all attempts to isolate a pure sample of *p*-octaallylcalix[8]arene (**20**) from the crude product have been unavailing.

The fortuitous synthesis of the tribenzoate of calix[4]arene (**29**), as described above, provides the possibility of preparing mono-allylcalix[4]arene via the Claisen rearrangement route. Treatment of the tribenzoate with allyl bromide gives a 58% yield of pure 25-allyloxy-26,27,28-tribenzoyloxycalix[4]arene (**30**), and Claisen rearrangement of this material affords a crystalline sample of 5 - allyl - 25 - hydroxy - 26,27,28 - tribenzoyloxycalix[4]arene (**32**) in 62% yield. Methylation of **32** yields the corresponding methyl ether **33**, and hydrolysis in aqueous alcoholic NaOH produces 5 - allyl - 25,26,27,28 - tetrahydroxycalix[4]arene (**34**) in 72.5% yield. Alternatively, the benzoyl groups can be removed prior to the Claisen rearrangement, yielding 25 - allyloxy - 26,27,28 - trihydroxycalix[4]arene (**31**). Treatment of this material in refluxing N,N-diethylaniline produces the same monoallylcalixarene **34**.

Conformational properties of compounds **30**, **31**, **32**, *and* **34**

4 - Allyl - 25,26,27,28 - tetrahydroxycalix[4]arene (**34**) shows a temperature-dependent ^{1}H-NMR behavior characteristic of calix[4]arenes, namely a singlet at *ca* 60°, arising from the methylene groups which resolves into a broad doublet at room temperature and a pair of doublets at lower temperature, as shown in Fig. 1. 25 - Allyloxy - 26,27,28 - trihydroxycalix[4]arene (**31**), on the other hand, surprisingly is conformationally stable. Even at 60° the methylene resonances give rise to a pattern of six sharp lines, as shown in Fig. 2, which can be interpreted as two sets of overlapping pairs of doublets. Comparable conformational stability has been noted for the trimethyl and dimethyl ethers of calix[4]arenes[11] and has been interpreted in terms of "flattened" conformations. In the case of **31** the magnitude of the chemical shift between the centers of the doublets (0.95 and 0.85 ppm), reflecting the differences in the environments of the hydrogens attached to the methylene groups, is commensurate with a "cone" conformation. Although a "partial cone" conformation cannot be ruled out, the hydrogens on the methylene groups adjacent to the allyloxy ring would be in quite similar environments in this conformation and a much smaller chemical shift would be expected.

On the basis of previous observations[11] the

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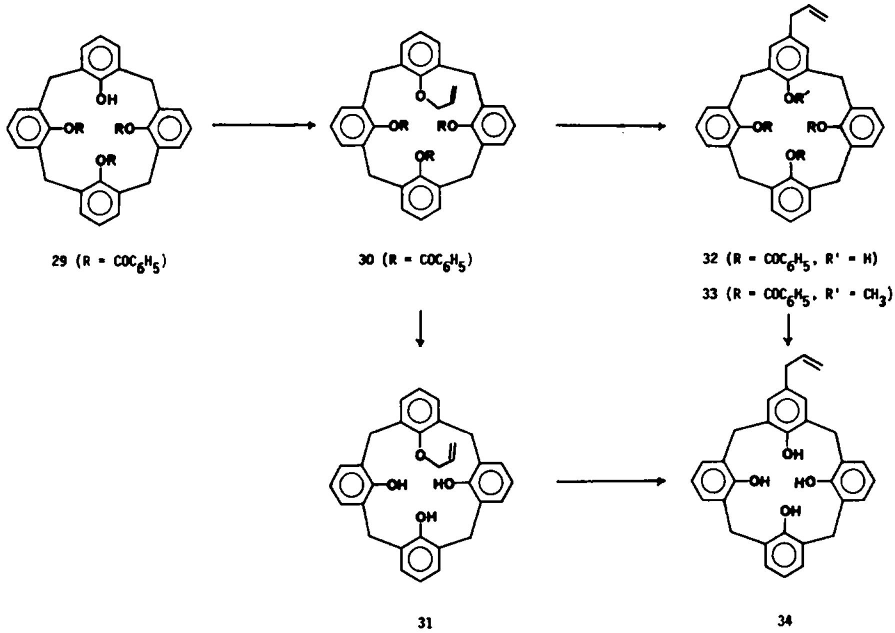
† We are indebted to Dr P. F. Pagoria for carrying out these experiments.



29 ($R = COC_6H_5$)

30 ($R = COC_6H_5$)

32 ($R = COC_6H_5$, $R' = H$)

33 ($R = COC_6H_5$, $R' = CH_3$)

31

34

tribenzoates **30** and **32** would be expected to show no conformational mobility even at elevated temperatures, and this proves to be the case. The ^{1}H-NMR spectra of these compounds suggest that they exist in the "1,3-alternate" conformation, and evidence in support of this is provided by an X-ray crystallographic determination of 5 - allyl - 25 - methoxy - 26,27,28 - tribenzoyloxycalix[4]arene (**33**).[17]

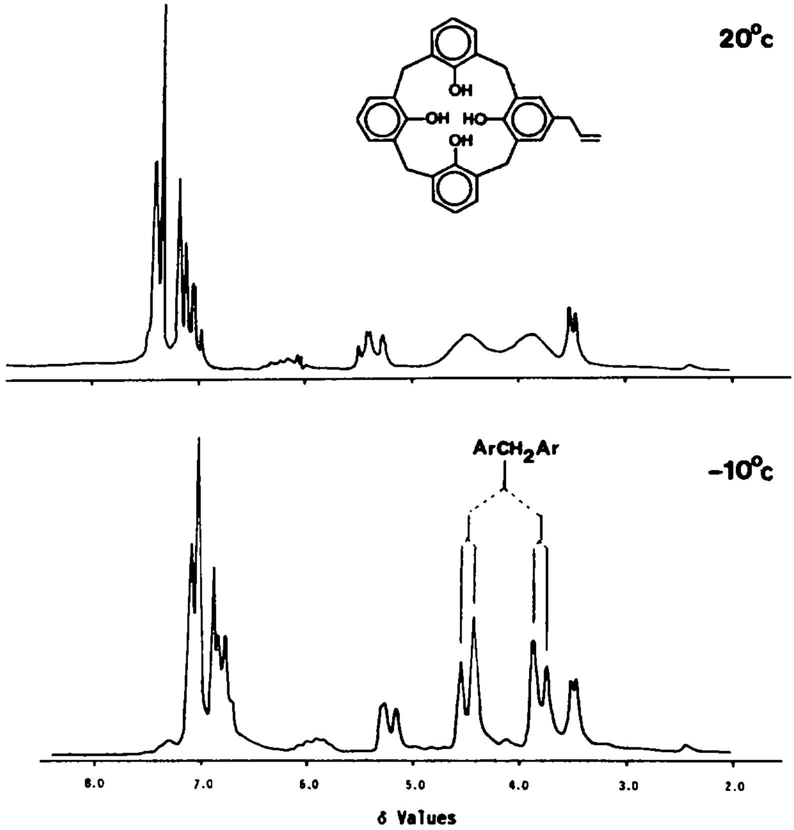


Fig. 1. ^{1}H-NMR spectra (100 MHz) of 5-allyl-25,26,27,28-tetrahydroxycalix[4]arene (**34**) in $CDCl_3$ at 20° and −10°.

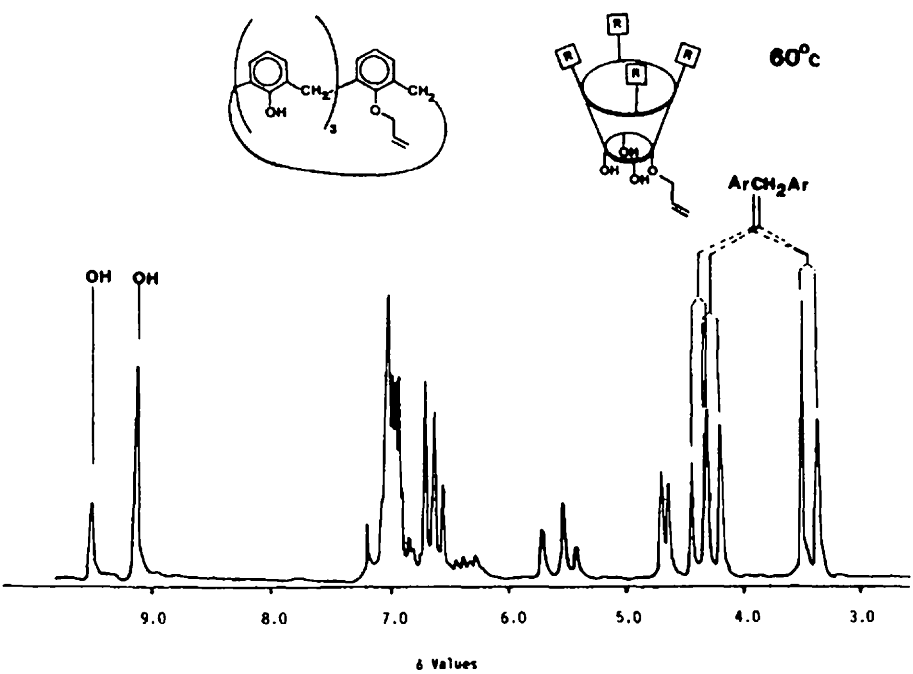


Fig. 2. ^{1}H-NMR spectrum (100 MHz) of 25-allyloxy-26,27,28-trihydroxycalix[4]arene (31) in $CDCl_3$ at 60°.

EXPERIMENTAL

The m.ps of all compounds melting above 250° were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, Massachusetts) using a 500° thermometer calibrated against a thermocouple. IR spectra were determined on a Perkin–Elmer 283B spectrometer. ^{1}H-NMR spectra were recorded on a Hitachi Perkin–Elmer R-24B spectrometer or a JEOL FX-100 spectrometer. Chemical shifts are reported as δ values in ppm relative to TMS (δ 0.0) as an internal standard. Osmometric molecular weight determinations† were made on a Wescan Model 232A apparatus using concentrations of *ca* 10^{-3} M in $CHCl_3$ soln. Microanalyses were carried out by Industrial Testing Laboratories, St Louis, Missouri, and MicAnal Laboratories, Tuscon, Arizona. TLC analyses were carried out on silica gel plates (absorbant thickness 250 μm). Flash chromatography[18] was carried out with E. Merck silica gel (230–400 mesh ASTM) on columns of 80 mm diam (for more than 5 g of sample), 50 mm diam (for 1–5 g of sample) and 30 mm diam (for less than 1 g of sample) filled to a height of 6 in. Elution rates were 2 in min^{-1}; fractions of 50 ml were collected from the two larger columns and of 20–30 ml from the smallest column. Analytical samples were dried for at least 36 hr at 140° and 1–2 mmHg of pressure. In a number of instances, however, solvent of crystallization was retained, considerably affecting the elemental analyses. In such cases best fits between the analytical values and appropriate fractional increments of solvent were sought, leading sometimes to seemingly adventitious amounts of solvent.

5,11,17,23 - *Tetra* - t - *butyl* - 25,26,27,28 - *tetrahydroxycalix*[4]*arene* (1). Compound 1 was synthesized as described previously[2] and obtained as colorless plate-like crystals after recrystallization from toluene: m.p. 344–346° (lit.[2] 344–346°).

5,11,17,23,29,35 - *Hexa* - t - *butyl* - 37,38,39,40,41,42 - *hexahydroxycalix*[6]*arene* (2). Compound 2 was synthesized as described previously[2] and obtained as fine, colorless crystals: m.p. 380–381° (lit.[2] m.p. 380–381°).

5,11,17,23,29,35,41,47 - *Octa* - t - *butyl* - 49,50,51,52,53,54,55,56 - *octahydroxycalix*[8]*arene* (3). Compound 3 was synthesized as described previously[2] and obtained as colorless needles after crystallization from $CHCl_3$; m.p. 410–411° (lit.[2] m.p. 411–412°).

25,26,27,28 - *Tetrahydroxycalix*[4]*arene* (4). A slurry of 13.3 g (20 mmol) of *p*-t-butylcalix[4]arene, 9.02 g of phenol (96 mmol) and 14 g of $AlCl_3$ (105 mmol) was stirred in 125 ml of toluene at room temp for 1 hr in an inert atmosphere. The mixture was poured into 250 ml of 0.2 N HCl, the organic phase was separated, and the toluene was evaporated. Upon the addition of MeOH a ppt formed, which was removed by filtration to give 7.54 g of a solid. Recrystallization from MeOH–$CHCl_3$ afforded 6.77 g (78%) of colorless crystals: m.p. 313–315° (lit.[8] 315–318°).

37,38,39,40,41,42 - *Hexahydroxycalix*[6]*arene* (5). A slurry of 10.54 g (11 mmol) of *p*-t-butylcalix[6]arene, 6.19 g (66 mmol) of phenol, and 11.75 g (88 mmol) of $AlCl_3$ in 125 ml of toluene was stirred for 1 hr in an N_2 atmosphere at room temp. The reaction was quenched by the addition of 100 ml of ice water, and the organic phase was separated. The toluene was removed by evaporation, and the residue was triturated with 70 ml of MeOH to leave 6.81 g of a crude, colorless product. This was recrystallized from MeOH–$CHCl_3$ to afford 6.13 g (89%) of a white powder: m.p. 417–418°; IR(KBr) 3300 cm^{-1} (OH stretching); ^{1}H-NMR ($CDCl_3$) δ 10.4 (s, 1, ArOH), 6.7–7.4 (m, 3, ArH), 4.0 (s, 2, $ArCH_2Ar$); osmometric mol wt ($CHCl_3$, 37°), 655 (calc, 636; with 1/3 mol MeOH, 647). (Found: C, 78.57; H, 5.68. Calc for $C_{42}H_{36}O_6 \cdot 1/3$ CH_3OH: C, 78.52; H, 5.78%.)

49,50,51,52,53,54,55,56 - *Octahydroxycalix*[8]*arene* (6). A slurry of 10.0 g (7.7 mmol) of *p*-t-butylcalix[8]arene, 5.8 g (62 mmol) of phenol, and 12.35 g (93 mmol) of $AlCl_3$ in 150 ml of toluene was treated as described above for the cyclic hexamer and tetramer to give 11.4 g of a crude product as an orange solid. This was washed, in succession, with acetone–HCl, MeOH, $CHCl_3$, acetone, and ethyl ether to afford 6.10 g (93%) of a light gray solid: m.p. > 450° (lit.[19] m.p. > 350°); ^{1}H-NMR (pyridine-d_5) δ 6.0–7.0 (m, 3, ArH), 3.5 (br s, 2, $ArCH_2Ar$).

25,26,27,28 - *Tetraacetoxycalix*[4]*arenes* (7a and 7b). A soln containing 2.41 g (18 mmol) of $AlCl_3$ and 3.1 ml (44 mmol) of acetyl chloride in 25 ml of CH_2Cl_2 was slowly added to a soln of 0.75 g (1.7 mmol) of calix[4]arene in 25 ml of CH_2Cl_2 at

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† We are indebted to Alice Gutsche for carrying out the osmometric molecular weight determinations.

reflux temp. After 2 hr of reflux the mixture was poured into ice water, and the organic layer was separated and dried over Na_2SO_4. Evaporation of the solvent and recrystallization from MeOH–$CHCl_3$ gave 0.60 g (59%) of a mixture of conformers of the tetraacetate. Passage through a flash chromatographic column using a 1:4 mixture of acetone and n-hexane as the eluent gave (a) 0.39 g (38%) of the 1,3-alternate conformer (**7b**) as almost colorless needles: m.p. 405–406°; IR(KBr) 1750 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.9 (s, 3, ArH), 3.6 (s, 2, $ArCH_2Ar$), 1.4 (s, 3, $COCH_3$) and (b) 0.19 g (18%) of the partial cone conformer (**7a**) as colorless plates: m.p. 408–411°; IR(KBr) 1750 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) 7.2 (s, 6, ArH), 6.6–7.0 (m, 6, ArH), 3.6 (s, 4, $ArCH_2Ar$), 3.1–3.6 (pair d, 4, $ArCH_2Ar$), 2.3 (s, 6, $COCH_3$), 2.0 (s, 3, $COCH_3$), 1.8 (s, 3, $COCH_3$).

37,38,39,40,41,42 - *Hexaacetoxycalix*[6]*arene* (**8**). A 1.0 g (1.6 mmol) sample of calix[6]arene was dissolved in 26 ml of Ac_2O, treated with 2 drops of conc H_2SO_4 and refluxed for 2.5 hr. The mixture was poured into ice water and worked up in the usual fashion to yield 0.45 g (32%) of a white solid after four recrystallizations from MeOH–$CHCl_3$: m.p. 335–336°; IR(KBr) 1760 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 7.0 (s, 3, ArH), 3.6 (s, 2, $ArCH_2Ar$), 1.9 (s, 3, $COCH_3$); osmometric mol wt ($CHCl_3$, 37°), 890 (calc, 889). (Found: C, 72.93; H, 5.36. Calc for $C_{54}H_{48}O_{12}$: C, 72.97; H, 5.41%.)

49,50,51,52,53,54,55,56 - *Octaacetoxycalix*[8]*arene* (**9**). A 1.00 g (1.2 mmol) sample of calix[8]arene was dissolved in 26 ml of Ac_2O, treated with 2 drops of conc H_2SO_4, and refluxed for 3 hr. The mixture was poured into ice water and worked up in the usual fashion to yield 0.32 g (23%) of colorless needles after three recrystallizations from MeOH–$CHCl_3$: m.p. 327–330°; IR(KBr) 1760 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.0 (s, 3, ArH), 3.6 (s, 2, $ArCH_2Ar$), 2.0 (s, 3, $COCH_3$); osmometric mol wt ($CHCl_3$, 37°), 1210 (calc 1184; with 1/6 mol $CHCl_3$, 1194). (Found: C, 71.87; H, 5.22. Calc for $C_{72}H_{64}O_{16} \cdot 1/6\ CHCl_3$: C, 71.93; H, 5.33%.)

25,26,27 - *Tribenzoyloxy* - 28 - *hydroxycalix*[4]*arene* (**29**). A 4.24 g (10 mmol) sample of calix[4]arene was dissolved in 50 ml of pyridine, and 9.4 ml (81 mmol) of benzoyl chloride was added at ice bath temp. The mixture was stirred at 0° for 1 hr and allowed to slowly warm to room temp for another hour. A 300 ml portion of water was added, and the water insoluble material was collected by filtration. Recrystallization from MeOH–$CHCl_3$ afforded 5.20 g (71%) of thin, colorless plates: m.p. 276–277°; IR(KBr) 3530 (OH stretching), 1730 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.6–8.3 (m, 27, ArH), 15.5 (s, 1, ArOH), 3.4–4.1 (pair d, 4, $ArCH_2Ar$), 3.8 (s, 4, $ArCH_2Ar$); osmometric mol wt ($CHCl_3$, 37°), 790 (calc 736; with 1/3 mol $CHCl_3$, 776). (Found: C, 75.97; H, 4.68 (dried at 115° for 60 hr); C, 75.90; H, 4.73 (dried at 197° for 72 hr). Calc for $C_{49}H_{36}O_7$: C, 79.89; H, 4.89, for $C_{49}H_{36}O_7 \cdot 1/3CHCl_3$: C, 76.28; H, 4.68%.)

25,26,27,28 - *Tetrabenzoyloxycalix*[4]*arene* (**10a** and **10b**)

(A) *From calix*[4]*arene* (**4**). To a soln of 1.00 g (2.36 mmol) of calix[4]arene in 50 ml of CH_2Cl_2 at ice bath temp was added a soln of 1.57 g (11.8 mmol) of $AlCl_3$ and 6.6 ml (7.98 mmol) of benzoyl chloride in 20 ml of CH_2Cl_2. The mixture was allowed to warm to room temp, stirred for 24 hr, and then worked up in the usual fashion to give 1.14 g of crude product. This was dissolved in 75 ml of acetone, filtered, and the filtrate concentrated and then treated with MeOH to yield a ppt of 0.61 g (31%) of **10a** as pale yellow needles: m.p. 301–303°; IR(KBr) 1735 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.1–8.1 (m, 8, ArH), 3.3–4.1 (pair d, 1, $ArCH_2Ar$), 3.6 (s, 1, $ArCH_2Ar$); osmometric mol wt ($CHCl_3$, 37°), 900 (calc 840). (Found: C, 80.24; H, 4.82. Calc for $C_{56}H_{40}O_8$: C, 79.98; H, 4.84%.)

The acetone-insoluble portion was recrystallized from MeOH–$CHCl_3$ to give 0.18 g (9.5%) of **10b** as colorless plates: m.p. >450°; IR(KBr) 1730 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.7–8.1 (m, 32, ArOH), 3.6 (s, 8, $ArCH_2Ar$). (Found: C, 79.31; H, 4.68. Calc for $C_{56}H_{40}O_8$: C, 79.98; H, 4.84%.)

(B) *From* 25,26,27 - *Tribenzoyloxy* - 28 - *hydroxycalix*[4]*arene* (**29**). A soln of 1.84 g (2.5 mmol) of **29** in 30 ml of CH_2Cl_2 was cooled in an ice bath. To this was slowly added a soln of 1.68 g (12.6 mmol) of $AlCl_3$ and 3.5 ml of benzoyl chloride in 20 ml of CH_2Cl_2. The mixture was stirred at room temp for 24 hr and then worked up to yield 1.38 g (66%) of colorless plates after two recrystallizations from MeOH–$CHCl_3$. This material was identical in chemical and physical properties with the higher melting isomer of the tetrabenzoate described above.

37,38,39,40,41,42 - *Hexabenzoyloxy*[6]*arene* (**11**). A soln of 1.59 g (2.5 mmol) of calix[6]arene in 20 ml of pyridine was treated with 5.2 ml (6.33 mmol) of benzoyl chloride at ice bath temp. The mixture was stirred at room temp for 1 hr and worked up to give a material that was insoluble in all of the common organic solvents. When the crude product was washed with $CHCl_3$, MeOH, and acetone 2.19 g of a white powder was obtained: m.p. >400°; IR(KBr) 1730 cm^{-1} (C=O stretching).

25,26,27,28 - *Tetramethoxycalix*[4]*arene* (**12**).[11] Compound **12** was synthesized as described previously and obtained in 64% yield as colorless needles after recrystallization first from MeOH–$CHCl_3$ and then from n-BuOH: m.p. 234–236° (lit.[11] m.p. 234–235°).

37,38,39,40,41,42 - *Hexamethoxycalix*[6]*arene* (**13**). A soln of 1.10 g (1.7 mmol) of calix[6]arene, 1.01 g (42 mmol) of NaH, and 10.25 g (72 mmol) of CH_3I in 50 ml of THF and 5 ml of DMF was refluxed for 20 hr. The solvent was then removed by evaporation, water was added to the residue, and the solid that was collected was recrystallized from MeOH–$CHCl_3$ to give 1.20 g (96%) of colorless needles: m.p. 326–328°; ^{1}H-NMR ($CDCl_3$) δ 6.9 (s, 3, ArH), 3.9 (s, 2, $ArCH_2Ar$), 3.2 (s, 3, OCH_3); osmometric mol wt ($CHCl_3$, 37°), 760 (calc, 720). (Found: C, 79.03; H, 6.56. Calc for $C_{48}H_{48}O_6$: C, 79.05; H, 6.59%.)

49,50,51,52,53,54,55,56 - *Octamethoxycalix*[8]*arene* (**14**). A mixture containing 4.50 g (5.3 mmol) of calix[8]arene, 4.50 g (188 mmol) of NaH, and 41 g (289 mmol) of CH_3I in 200 ml of THF and 20 ml of DMF was refluxed for 18 hr and then worked up as described above to give 4.60 g (90%) of colorless needles after recrystallization from MeOH–$CHCl_3$: m.p. 256–258°; ^{1}H-NMR ($CDCl_3$) δ 6.8 (s, 3, ArH), 4.0 (s, 2, $ArCH_2Ar$), 3.5 (s, 3, OCH_3); osmometric mol wt ($CHCl_3$, 37°), 963 (calc 960). (Found: C, 80.28; H, 6.73. Calc for $C_{64}H_{64}O_8$: C, 80.00; H, 6.67%.)

37,38,39,40,41,42 - *Hexaallyloxycalix*[6]*arene* (**16**). A soln containing 4.0 g (6.3 mmol) of calix[6]arene, 3.9 g (163 mmol) of NaH, and 33.8 g (280 mmol) of allyl bromide in 75 ml of THF and 15 ml of DMF was refluxed for 6 hr and worked up in the conventional manner to yield 4.9 g (89%) of a white powder. Recrystallization from MeOH–$CHCl_3$ gave a fine, white powder: m.p. 267–269°; IR(KBr) 1650 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.9 (s, 3, ArH), 5.3–5.9 (m, 1, C—CH=C), 4.7–5.1 (m, 2, C=CH_2), 3.9 (s, 2, $ArCH_2Ar$), 3.6–3.8 (d, 2, OCH_2C=C); osmometric mol wt ($CHCl_3$, 37°), 900 (calc, 876). (Found: C, 82.56; H, 6.94. Calc for $C_{60}H_{60}O_6$: C, 82.19; H, 6.85%.)

49,50,51,52,53,54,55,56 - *Octaallyloxycalix*[8]*arene* (**17**). A slurry of 2.10 g (2.5 mmol) of calix[8]arene, 2.05 g of NaH (85 mmol), and 30 g (248 mmol) of allyl bromide in 100 ml of THF and 10 ml of DMF was refluxed for 12 hr and worked up to yield 1.35 g (46.5%) of a white powder after recrystallization from MeOH–$CHCl_3$: m.p. 241–242°; IR(KBr) 1650 cm^{-1} (C=C stretching); ^{1}H-NMR ($CDCl_3$) δ 6.8 (s, 3, ArH), 5.5–6.3 (m, 1, C—CH=C), 4.8–5.4 (m, 2, C=CH_2), 4.0–4.2 (d, 2, OCH_2—C=C), 4.0 (s, 2, $ArCH_2Ar$); osmometric mol wt ($CHCl_3$, 37°), 1170 (calc 1168). (Found: C, 82.30; H, 6.70. Calc for $C_{80}H_{80}O_8$: C, 82.19; H, 6.85%.)

5,11,17,23,29,35 - *Hexaallyl* - 37,38,39,40,41,42 - *hexahydroxycalix*[6]*arene* (**19**). A soln of 5.0 g of hexaallyloxycalix[6]arene in 25 ml of N,N-diethylaniline was refluxed for 4 hr in an argon atmosphere. The N,N-diethylaniline was then removed by washing with dilute HCl, and the crude product was collected and recrystallized from MeOH–CH_2Cl_2 to give 1.06 g (21%) of small, white needles: m.p. 373–374°;

IR(KBr) 3170 (OH stretching), 1640 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 10.3 (s, 1, ArOH), 6.9 (s, 2, ArH), 5.5–6.0 (m, 1, $CH{=}C$), 4.8–5.2 (br d, 2, $C{=}CH_2$), 3.8 (s, 2, $ArCH_2Ar$), 3.2–3.4 (br d, 2, $ArCH_2C{=}C$); osmometric mol wt ($CHCl_3$, 37°), 880 (calc 876). (Found: C, 81.99; H, 6.91. Calc for $C_{60}H_{60}O_6$: C, 82.19; H, 6.85%.)

5,11,17,23,29,35 - *Hexaallyl* - 37,38,39,40,41,42 - *hexamethoxycalix*[6]*arene* (**21**). Compound **21** was prepared from 1.36 g of hexaallylcalix[6]arene and 4.0 ml of CH_3I in 50 ml of THF and 5 ml of DMF in the manner described above and obtained as 1.07 g (72%) of colorless plates after crystallization from MeOH–CH_3Cl: m.p. 162–164°; IR(KBr) 1640 cm^{-1} ($C{=}C$ stretching); ^{1}H-NMR ($CDCl_3$) δ 6.8 (s, 2, ArH), 5.4–6.1 (m, 1, $CH{=}C$), 3.9 (s, 2, $ArCH_2Ar$), 3.2 (br s, 5, $ArCH_2C{=}C$ and OCH_3); osmometric mol wt ($CHCl_3$, 37°), 960 (calc 960). (Found: C, 82.46; H, 7.57. Calc for $C_{66}H_{72}O_6$: C, 82.50; H, 7.50%.)

5,11,17,23 - *Tetraacetyl* - 25,26,27,28 - *tetramethoxycalix*[4]-*arene* (**22**). A soln of 1.2 g (2.5 mmol) of 25,26,27,28-tetramethoxycalix[4]arene in 60 ml of CH_2Cl_2 was cooled to −10° and treated dropwise with a soln of 2.05 g (15 mmol) of $AlCl_3$ and 3.5 ml (50 mmol) of acetyl chloride in 50 ml of CH_2Cl_2. The mixture was stirred at room temp for 3 hr, then treated with 120 ml of cold 1 N HCl, and the two-layer system was stirred overnight. The organic phase was separated, washed, dried, and evaporated, and the residue was recrystallized from acetone–hexane to give 0.75 g (46%) of a white powder which TLC analysis (2:1 hexane–acetone eluant) indicated to be a mixture of three compounds. Flash chromatography on silica yielded 0.47 g (29%) of the desired product as a white powder: m.p. 228–246°; IR(KBr) 1677 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR ($CDCl_3$) δ 6.8–8.1 (broad m, 2, ArH), 2.2–4.4 (broad m, 8, $ArCH_2Ar$, $COCH_3$, OCH_3). (Found: C, 73.00; H, 6.37. Calc for $C_{40}H_{40}O_8\cdot 1/4\ CH_3SOCH_3$: C, 72.80; H, 6.22%.)

5,11,17,23,29,35 - *Hexaacetyl* - 37,38,39,40,41,42 - *hexamethoxycalix*[6]*arene* (**23**). A slurry of 2.94 g (22 mmol) of $AlCl_3$ in 6.3 ml (89 mmol) of acetyl chloride and 20 ml of CH_2Cl_2 was slowly added to a soln of 1.72 g (2.4 mmol) of hexamethoxycalix[6]arene in 50 ml of CH_2Cl_2 at room temp with stirring. After 1 hr the reaction was quenched by the addition of 300 ml of ice water, the organic layer was separated and evaporated, and the residue was triturated with 50 ml of MeOH to leave 2.00 g of crude, colorless product. Recrystallization from acetone–$CHCl_3$ and then from MeOH–$CHCl_3$ produced 1.48 g (64%) of a white powder: m.p. 320–322°; IR(KBr) 1670 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR ($CDCl_3$) δ 7.7 (s, 2, ArH), 4.1 (s, 2, $ArCH_2Ar$), 3.5 (s, 3, OCH_3), 2.5 (s, 3, $COCH_3$); osmometric mol wt ($CHCl_3$, 37°), 1020 (calc 970; with H_2O, 990). (Found: C, 72.70; H, 6.15. Calc for $C_{60}H_{60}O_{12}\cdot H_2O$: C, 72.73; H, 6.26%.)

5,11,17,23,29,35,41,47 - *Octaacetyl* - 49,50,51,52,53,54,55,56 - *octamethoxycalix*[8]*arene* (**24**). A slurry of 11.69 g (88 mmol) of $AlCl_3$ in 30 ml (422 mmol) of acetyl chloride and 30 ml of CH_2Cl_2 was slowly added to 8.40 g (8.4 mmol) of octamethoxycalix[8]arene in 75 ml of CH_2Cl_2 at ice bath temp, and stirring was continued for 1.5 hr. The mixture was allowed to warm to room temp, stirred for an additional hour, and worked up as described above to give 10.44 g of crude product. Four recrystallizations from MeOH–$CHCl_3$ gave 7.00 g (62%) of a white powder: m.p. 316–318°; IR(KBr) 1680 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR ($CDCl_3$) δ 7.6 (s, 2, ArH), 4.1 (s, 2, $ArCH_2Ar$), 3.6 (s, 3, OCH_3), 2.4 (s, 3, $COCH_3$); osmometric mol wt ($CHCl_3$, 37°), 1370 (calc, 1298; with 1/2 mol MeOH and 1/2 mol $CHCl_3$, 1372). (Found: C, 71.08; H, 6.11. Calc for $C_{80}H_{80}O_{16}\cdot 1/2\ CH_3OH\cdot 1/2\ CHCl_3$: C, 70.85; H, 6.01%.)

5,11,17,23,29,35 - *Hexacarboxy* - 37,38,39,40,41,42 - *hexamethoxycalix*[6]*arene* (**25**). A soln prepared by the addition of 2.0 ml (6.24 g, 39 mmol) of Br_2 to 10 ml of water containing 4.41 g of NaOH was cooled in an ice bath and added dropwise to a soln prepared by dissolving 1.62 g (1.67 mmol) of **23** in 70 ml of hot DMF and then cooling the soln to 0°. The mixture was allowed to warm to room temp and stirred for 1 hr and was then poured into dilute HCl. The yellow ppt was removed and dissolved in acetone, the soln was filtered, and the solvent was evaporated. Trituration with water, $CHCl_3$, n-hexane, and ether left 1.18 g (72%) of a light yellow powder: m.p. >450°; IR(KBr) 3460 (OH stretching), 1700 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR (pyridine-d_5) δ 7.5 (br s, 2, ArH), 3.4 (br, s, 2, $ArCH_2Ar$), 2.7 (br s, 3, OCH_3). (Found: C, 63.57; H, 4.82. Calc for $C_{54}H_{48}O_{18}\cdot 2H_2O$: C, 63.53; H, 5.10%.)

5,11,17,23,29,35 - *Hexacarbomethoxy* - 37,38,39,40,41,42 - *hexamethoxycalix*[6]*arene* (**27**). A suspension of 0.64 g of the hexacarboxy-hexamethoxycalix[6]arene described above in 30 ml of diethyl ether was treated with 50 ml of an ethereal soln of diazomethane at ice bath temp. The mixture was allowed to stand for 16 hr and was then treated with AcOH to destroy the excess diazomethane and worked up in conventional manner to yield 0.42 g of a light yellow powder. This was subjected to flash chromatography (acetone–n-hexane, 2:3), and 0.06 g (9%) of product was obtained as a colorless powder: m.p. 264–267°; IR (KBr) 1720 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR ($CDCl_3$) δ 7.6 (s, 2, ArH), 4.0 (s, 2, $ArCH_2Ar$), 3.8 (s, 3, $COCH_3$), 3.31 (s, 3, CO_2CH_3). (Found: C, 66.49; H, 5.72. Calc for $C_{60}H_{60}O_{18}\cdot 1/6CHCl_3$; C, 66.3; H, 5.53%.)

5,11,17,23,29,35,41,47 - *Octacarboxy* - 49,50,51,52,53,54,55,56 - *octamethoxycalix*[8]*arene* (**26**). A 0.81 g sample of **24** was treated in the manner described above for the corresponding hexamer to yield 0.58 g (71%) of product as a pale yellow solid: m.p. >450°; IR(KBr) 3300 (OH stretching), 1700 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR (pyridine-d_5) δ 7.5 (br s, 2, ArH), 3.4 (br s, 2, $ArCH_2Ar$), 2.9 (br s, 3, OCH_3).

5,11,17,23,29,35,41,47 - *Octacarbomethoxy* - 49,50,51,52,53,54,55,56 - *octamethoxycalix*[8]*arene* (**28**). A 1.48 g sample of **26** described above was converted to the methyl ester by treatment with ethereal diazomethane as described for the corresponding hexamer and obtained as 0.68 g (53.5%) of a white powder: m.p. 343–346°; IR (KBr) 1720 cm^{-1} ($C{=}O$ stretching); ^{1}H-NMR ($CDCl_3$) δ 7.5 (s, 2, ArH), 4.0 (s, 2, $ArCH_2Ar$), 3.7 (s, 3, OCH_3), 3.4 (s, 3, CO_2CH_3). (Found: C, 63.83; H, 5.42. Calc for $C_{80}H_{80}O_{24}\cdot 3/4\ CHCl_3$: C, 64.02; H, 5.33%.)

25 - *Allyloxy* - 26,27,28 - *tribenzoyloxycalix*[4]*arene* (**30**). A soln of 6.72 g (9.1 mmol) of 25,26,27-tribenzoyloxy-28-hydroxycalix[4]arene, 0.87 g (36 mmol) of NaH, and 4.8 ml (55 mmol) of allyl bromide in 200 ml of THF and 20 ml of tribenzoyloxycalix[4]arene was refluxed for 6 hr. The solvent was removed by evaporation, and the residue was triturated with MeOH to leave a light yellow powder which was recrystallized from MeOH–$CHCl_3$ to give 4.13 g (58%) of a white powder: m.p. 283–284°; IR(KBr) 1730 ($C{=}O$ stretching), 1645 cm^{-1} ($C{=}C$ stretching); ^{1}H-NMR ($CDCl_3$) δ 6.5–7.9 (m, 27, ArH), 5.9–6.3 (m, 4, $C{-}CH{=}C$), 5.1–5.6 (m, 8, $C{=}CH_2$), 4.2–4.5 (pair d, 2, $ArCH_2Ar$), 3.4–4.0 (pair d, 10, $ArCH_2Ar$ and $OCH_2C{=}C$), 3.6 (s, 4, $ArCH_2Ar$); osmometric, mol wt ($CHCl_3$, 37°), 790 (calc, 776). (Found: C, 80.58; H, 5.35. Calc for $C_{52}H_{40}O_7$: C, 80.41; H, 5.16%.)

25 - *Allyloxy* - 26,27,28 - *trihydroxycalix*[4]*arene* (**31**). A soln containing 0.78 g of 25-allyloxy-26,27,28-tribenzoyloxycalix[4]arene in 50 ml of THF was treated with a soln of 2.48 g of NaOH in 15 ml of water and 35 ml of EtOH, and the mixture was refluxed for 18 hr. The solvent was removed by evaporation, the residue was treated with dilute HCl and the organic material was extracted into $CHCl_3$. Evaporation of the solvent and recrystallization of the residue yielded 0.19 g (41%) of a white solid: m.p. 216–217°; IR(KBr) 3340 (OH stretching), 1640 cm^{-1} ($C{=}C$ stretching); ^{1}H-NMR ($CDCl_3$) δ 9.6 (s, 2, ArOH), 9.2 (s, 2, ArOH), 6.5–7.5 (m, 12, ArH), 6.0–6.5 (m, 1, $C{-}CH{=}C$), 5.4–5.9 (m, 2, $C{=}CH_2$), 4.8, 4.6 (d, 2, $OCH_2C{=}C$), 4.5, 4.3 (d, 2, $ArCH_2Ar$), 4.4, 4.2 (d, 2, $ArCH_2Ar$), 3.5, 3.3 (d, 4, $ArCH_2Ar$); osmometric mol wt ($CHCl_3$, 37°), 480 (calc with 1 mol H_2O, 482). (Found: C, 76.83; H, 6.11. Calc for $C_{31}H_{28}O_4\cdot H_2O$: C, 77.17; H, 6.22%.)

5 - *Allyl* - 25 - *hydroxy* - 26,27,28 - *tribenzoyloxycalix*[4]*arene* (**32**). A soln of 2.50 g of 25 - allyloxy - 26,27,28 - tribenzoyloxycalix[4]arene in 15 ml of N,N-diethylaniline

was refluxed for 4 hr in an atmosphere of N_2. The mixture was poured into 200 ml of dil HCl, and the water-insoluble material was collected by filtration and recrystallized four times from MeOH–$CHCl_3$ to give 1.56 g (62%) of pale orange needles (color from a trace impurity which could not be removed): m.p. 287–289°; IR(KBr) 3540 (OH stretching), 1730 cm^{-1} (C=O stretching); ^{1}H-NMR ($CDCl_3$) δ 6.5–8.2 (m, 27, ArH), 5.4–6.2 (m, 1, C—CH=C), 5.1 (s, 1, ArOH), 4.7–5.1 (m, 2, C=CH_2), 3.3–4.0 (pair d, 4, ArCH_2Ar), 3.7 (s, 4, ArCH_2Ar), 3.0–3.2 (br d, 2, ArCH_2C=C); osmometric mol wt ($CHCl_3$, 37°), 745 (calc, 776). (Found: C, 80.50; H, 5.36. Calc for $C_{52}H_{40}O_7$: C, 80.41; H, 5.15%.)

5 - Allyl - 25 - methoxy - 26,27,28 - tribenzoyloxycalix[4]*arene* (33). Compound 33 was prepared by methylation of 5 - allyl - 25 - hydroxy - 26,27,28 - tribenzoyloxycalix[4]arene with NaH and CH_3I in THF–DMF and obtained as 0.69 g (58%) of colorless needles after recrystallization from MeOH–$CHCl_3$: m.p. 324–326°; ^{1}H-NMR ($CDCl_3$) δ 6.4–7.8 (m, 26, ArH), 4.9–5.9 (m, 1, C—CH=C), 4.3–4.8 (m, 2, C=CH_2), 3.2–4.1 (m, 8, ArCH_2Ar), 2.5–2.7 (m, 2, ArCH_2C=C); osmometric mol wt ($CHCl_3$, 37°), 810 (calc 790). (Found: C, 79.66; H, 5.32. Calc for $C_{57}H_{42}O_7 \cdot 1/2\ CH_3OH$: C, 79.54; H, 5.46%.)

5 - *Allyl* - 25,26,27,28 - *tetrahydroxycalix*[4]*arene* (34)

(A) *From* 25 - *hydroxy* - 26,27,28 - *tribenzoyloxycalix*[4]-*arene* (32). A soln of 0.30 g of 32 in 40 ml of THF was treated with a soln of 1.58 g of NaOH in 5 ml of H_2O and 15 ml of EtOH, and the mixture was refluxed for 18 hr. The solvent was removed on a rotary evaporator, and the residue was triturated with dil HCl and taken up in CH_2Cl_2. Evaporation of the solvent and recrystallization of the residue from MeOH–CH_2Cl_2 gave 0.13 g (72.5%) of colorless, small plates: m.p. 217–219°; IR(KBr) 3200 (OH stretching), 1640 cm^{-1} (C=C stretching); ^{1}H-NMR ($CDCl_3$) δ 6.5–7.3 (m, 11, ArH), 5.5–6.2 (m, 1, C—CH=C), 4.8–5.3 (br d, 2, C=CH_2), 3.5–4.3 (br s, 8, ArCH_2C=C), 3.1–3.3 (d, 2, ArCH_2Ar). (Found: C, 79.33; H, 6.28. Calc for $C_{31}H_{28}O_4 \cdot 1/3\ CH_3OH$: C, 79.15; H, 6.17%.)

(B) *From* 25 - *allyloxy* - 26,27,28 - *trihydroxycalix*[4]*arene* (31). A soln containing 0.50 g of 31 in 15 ml of N,N-diethylaniline was refluxed for 3 hr in an atmosphere of N_2 and worked up, as described above, to give 0.27 g (54%) of material after five recrystallizations which was identical in chemical and spectral properties with the material obtained from procedure A.

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