Isolation, Characterization, and Conformational Characteristics of *p-tert*-Butylcalix[9−20]arenes[1]

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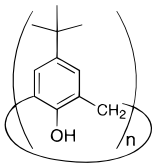
Abstract: *p-tert*-Butylcalix[*n*]arenes in which $n = 9-20$ (designated as "large" calixarenes) have been isolated from both the base-induced and the acid-catalyzed condensation of *p-tert*-butylphenol and formaldehyde. The acid-catalyzed process, previously thought to form linear oligomers as the major or even exclusive products, has been optimized to produce calixarenes in almost quantitative yield, providing a better source of these "large" calixarenes than the base-induced process. Central to the discovery of the calix[9−20]arenes and the optimization of the acid-catalyzed condensation was the development of an HPLC assay that allows baseline resolution of the 17 cyclic oligomers as well as their linear counterparts. Using this assay for guidance, procedures for the obtention of ponderable amounts of *p-tert*-butylcalix[7−20]arenes from the acid-catalyzed process have been developed. Data are adduced that bear on possible mechanistic pathways for calixarene formation under these conditions. A study measuring the amount of each of the linear and cyclic oligomers formed at various stages during an acid-catalyzed condensation suggests that the calixarenes are probably formed from linear oligomers containing the same corresponding number of aryl residues. However, the possibility of *ipso* substitution as a cyclization route was also indicated by an experiment involving the presence of benzyl cations. The conformational mobilities of calix[*n*]arenes ($n = 4-20$), measured by dynamic ^{1}H NMR spectroscopy in $CDCl_3$ solution, show a periodicity in which calixarenes with 4, 8, 12, 16, and 20 aryl residues are more stable than their immediate neighbors, ascribed to particularly efficient hydrogen bonding and molecular packing in these conformers.

Introduction

Calixarenes are [1_n] metacyclophanes (**I**) that have found



I

widespread use as complexation hosts and as frameworks for the construction of more complex structures. Central to these applications is their ready availability in various ring sizes[2] and their protean capacity for assuming a wide variety of shapes. Calixarenes containing four, six, and eight aryl units (the "major" calixarenes[2a]) can be easily prepared in good to excellent yields and high states of purity and in any amount, ranging from milligrams to kilograms. Those containing five and seven aryl units (the "minor" calixarenes[2a]), although obtainable only in lower yields, are also useful starting materials for further structural elaboration. Calixarenes containing more than eight aryl units (the "large" calixarenes[2a]), on the other hand, are far less readily available and for many years were thought not to be present in the reaction mixtures. However, experiments initiated in this laboratory in the late 1980s[3] showed this to be incorrect, and it is now known that calixarenes containing as many as 20 aryl units can, indeed, be formed in the condensation of *p-tert*-butylphenol and formaldehyde. The present paper deals with the isolation, characterization, and conformational properties of these "large" calixarenes

The time-tested method for synthesizing *p-tert*-butylcalixarenes[4] involves the base-induced condensation of *p-tert*-butylphenol with formaldehyde, the choice of reaction conditions dictating whether *p-tert*-butylcalix[4]arene (**[4]**),[5] *p-tert*-butylcalix[6]arene (**[6]**)[6] or *p-tert*-butylcalix[8]arene (**[8]**)[7] is the major product. It was from the residues of the calixarenes prepared by these procedures as well as that for *p-tert*-butylcalix[5]arene (**[5]**)[8] that the "large" calixarenes were first detected and from which mixtures of small amounts of **[9]**−**[14]** were eventually

(1) Paper 52 in the series Calixarenes. For paper 51 cf.: Sharma, S. K.; Gutsche, C. D. *J. Org. Chem.* **1999**, *64*, In press.

(2) For extensive reviews cf.: (a) Gutsche, C. D. Calixarenes Revisited. In Monographs in Supramolecular Chemistry; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1998. (b) McKervey, M. A.; Schwing-Weill, M.-J.; Arnaud-Neu, F. Cation Binding by Calixarenes. In *Comprehensive Supramolecular Chemistry*; Gokel, G., Ed.; Pergamon Press: New York, 1996; Vol. 1, p 537−603. (c) Pochini, A.; Ungaro, R. Calixarenes and Related Hosts. In *Comprehensive Supramolecular Chemistry*; Vögtle, F., Ed.; Pergamon Press: New York, 1996; Vol. 2, pp 103−142. (d) Böhmer, V. Calixarenes, Macrocyclic with (Almost) Unlimited Possibilities. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713−745. (e) Gutsche, C. D. Calixarenes. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989.

(3) Gutsche, C. D.; Rogers, J. S.; Stewart, D. R.; See, K.-A. *Pure Appl. Chem.* **1990**, *62*, 485. Stewart, D. R.; Gutsche, C. D. *Third International Calixarene Conference*; Fort Worth, TX, 1995, Abstract P-42. Gutsche, C. D.; Gibbs, C. G.; Sharma, S. K.; Stewart, D. R.; Wang, J.; Xie, D. *Fourth International Conference on Calixarenes*, Parma, 1997; Abstract IL1.

(4) The calixarenes discussed in this paper, all of which are *p-tert*-butyl substituted, are identified in abbreviated fashion by a bold, bracketed numeral that indicates the number of *p-tert*-butylaryl residues in the cyclic array.

(5) Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1990**, *68*, 234.

(6) Gutsche, C. D.; Dhawan, B.; Leonis, M.; Stewart, D. R. *Org. Synth.* **1990**, *68*, 238.

(7) Munch, J. H.; Gutsche, C. D.*Org. Syntheses* **1990**, *68*, 243.

(8) Stewart, D. R; Gutsche, C. D. *Org. Prep. Proc. Intl.* **1993**, *25*, 137.

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isolated and purified.[3] Although each of these mixtures contains "large" calixarenes, the total amount of these compounds depends to some extent on the particular recipe that is employed (vide supra). The variations in amounts are relatively small, however, and the total amount generally hovers around 1−3% of the "large" calixarenes. The residue from the preparation of **[5]** provides the best source, by a small margin, of the large calixarenes obtainable via the base-induced procedures.[9]

Acid-Catalyzed Condensation of *p-tert*-Butylphenol and Formaldehyde. It was assumed for many years that the acid-catalyzed condensation of *para*-substituted phenols with formaldehyde yields linear oligomers as the major products accompanied by little, if any, calixarene products.[10] It was most surprising, therefore, to discover that a refluxing AcOH solution containing *p-tert*-butylphenol, a slight excess of paraformaldehyde, and a catalytic amount of concentrated HCl produced a 25−30% yield of a mixture of *p-tert*-butylcalixarenes in addition to the expected linear oligomers. Particularly interesting was the fact that the proportion of "large" calixarenes in this mixture was considerably greater than that in the mixtures obtained by base-induced procedures. Efforts, therefore, were made to increase the overall yield by exploring the effects that various acid catalysts, solvents, reaction times, *p-tert*-butylphenol/HCHO ratios, and reactant concentrations have upon the yield of calixarenes. Ultimately, a set of reaction conditions was established that employs fairly high concentrations of *p-tert*-butylphenol, *s*-trioxane (the HCHO source), $CHCl_3$ (the solvent), and *p*-toluenesulfonic acid (TsOH) (the catalyst). These conditions result in a better than 95% conversion of the starting material to calixarenes and now provide the preferred source for the "large" calixarenes as well as the "minor" calixarene **[7]**.[11]

HPLC-Based Assay of Calixarene Mixtures. For guidance of the separation and purification of "large" calixarenes and for mechanistic studies of calixarene formation a rapid and sensitive assay of the product was an essential requirement. For the calixarene mixtures under study the clear choice was HPLC. Although several HPLC analyses of calixarenes have been reported in the literature,[12,13] none were quite sufficient for the mixtures encountered in the present work. Therefore, a nonaqueous reversed phase HPLC assay was developed using the overlapping resolution mapping (ORM) technique,[14] leading to an excellent and fast assay. The plot in Figure 1 shows a representative separation.[15]

The HPLC separation that was developed employs a C18 stationary phase and a mobile phase comprising various ratios of two eluents **A** and **B**. Eluent **A** consisted of MeCN with 1% AcOH;[16] eluent **B** consisted of CH_2Cl_2 and methyl *tert*-butyl ether (MTBE) in a 12:9 ratio and 1% AcOH. The eluent strength was varied in three isocratic steps connected by short linear gradients. Thus, calixarene mixtures containing **[4]**−**[10]**, **[10]**−**[16]**, and **[16]**−**[20]** were isocratically separated in about 10 min with an 80/20, 65/35, and 55/45 mixture of eluents **A**/**B**, respectively. When these isocratic steps were connected by short linear gradients, all sizes of calixarenes were resolved. Additionally, the *p-tert*-butyl linear oligomers with up to five subunits that elute before **[4]** could be resolved with an additional isocratic step at a 90/10 mixture of **A**/**B**. Longer *p-tert*-butyl linear oligomers could also be resolved with the same eluents used to separate **[4]**−**[20]**, but they first had to be separated from the cyclooligomers by flash chromatographing the sample with toluene on silica gel.[10] In general, a linear oligomer elutes near the *p-tert*-butylcalix[*n*]arene that contains $n - 1$ aryl residues. Finally, in contrast to other reported separations,[12,13,17] UV detection at 281 nm rather than at 287 nm was used, because the molar absorbtivities per subunit of calixarenes of various sizes at 281 nm are quite similar, whereas at 287 nm they may differ by a factor as high as two.[18] Therefore, detection at 281 nm gives peak areas that accurately reflect the actual composition (to within ±10%), and the uncorrected peak area percentages are assumed to correspond to the actual composition.

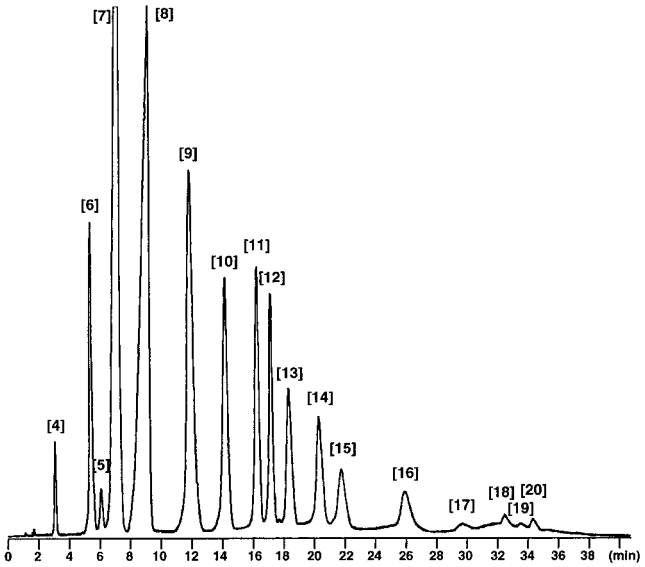


Figure 1. Chromatogram of an HPLC analysis of a crude product from an acid-catalyzed reaction of *p-tert*-butylphenol and *s*-trioxane.

Separation and Purification of Calixarene Mixtures. The separation and purification of the "large" calixarenes from either the base-induced or acid-catalyzed reaction mixtures were effected by a combination of trituration, chromatography, and crystallization procedures as detailed in the Experimental Section. By these means samples of greater than 95% purity were obtained for the "large" *p-tert*-butylcalixarenes **[9]**−**[16]** and **[20]** and greater than 75% purity for **[17]**−**[19]**. Isolated yields range from 9.0% to 0.2% for **[9]**−**[20]**, respectively[19]

(9) A recent report (Dumazet, I.; Regnouf de Vains, J-B.; Lamartine, R. *Synth. Commun.* **1997**, *27*, 2547) describes the isolation of *p-tert*-butylcalix-[9−12]arenes in 1−1.5% yields from a mixture obtained by treating the "precursor" used in the preparation of *p-tert*-butylcalix[6]arene[6] with a linear trimer. Although their melting points differ substantially from those reported in the present paper, other data are in good agreement.

(10) Ludwig and Bailie detected ca. 5% of calixarenes **[4]**−**[8]** in the product mixture that consisted mainly of linear oligomers: Ludwig, L. B.; Bailie, A. G., Jr. *Anal. Chem.* **1986**, *58*, 2069.

(11) *p-tert*-Butylcalix[7]arene (**[7]**) can be isolated from the acid-catalyzed reaction mixture in yields as high as 25%. Vocanson et al. report the formation of [**7**] in 16.8% yield from a base-induced reaction: Vocanson, F.; Lamartine, R.; Lanteri, P.; Longeray, R.; Gauvrit, J. Y. *New J. Chem.* **1995**, *19*, 825.

(12) A third HPLC separation using a chemically bonded C-60 stationary phase has been reported (Saito, Y.; Ohta, H.; Terasaki, H.; Katoh, Y.; Nagashima, H.; Jinno, K.; Itoh, K.; Trengove, R. D.; Harrowfield, J.; Li, S. F. Y. *HRC-J. High Res. Chromatogr.* **1996**, *19*, 475).

(13) Ludwig, F. J.; Bailie, A. G., Jr. *Anal. Chem.* **1984**, *56*, 2081.

(14) Snyder, L. R.; Glajch, J. L.; Kirkland, J. J. *Practical HPLC Method Development*; John Wiley & Sons: New York, **1988**, p 37.

(15) In some of the HPLC assays small, broad peaks beyond **[20]** were observed, presumably indicating the presence of even larger calixarenes.

(16) Acetic acid is added to suppress the ionization of the calixarenes, which are rather strong acids.

(17) Vocanson, F.; Lamartine, R.; Duchamp, C.; Regnouf de Vains, J. B. *Chromatographia* **1995**, 41, 204.

(18) Casiraghi, G.; Cornia, M.; Ricci, G.; Balduzzi, G.; Casnati, G. *Makromol. Chem.* **1983**, *184*, 1363.

(19) The isolated yield of 0.2% for **[20]** is for a reaction run at 50% (w/v). The isolated yield of **[20]** can be increased to at least 0.5% by employing the most concentrated reaction conditions.

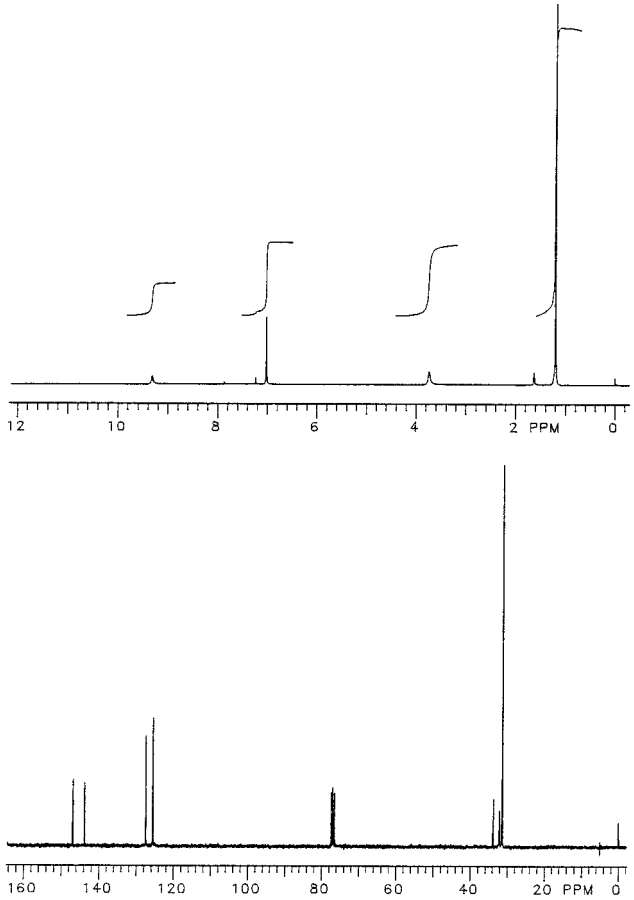


Figure 2. ^{1}H and ^{13}C NMR spectra of *p-tert*-butylcalix[14]arene (**[14]**).

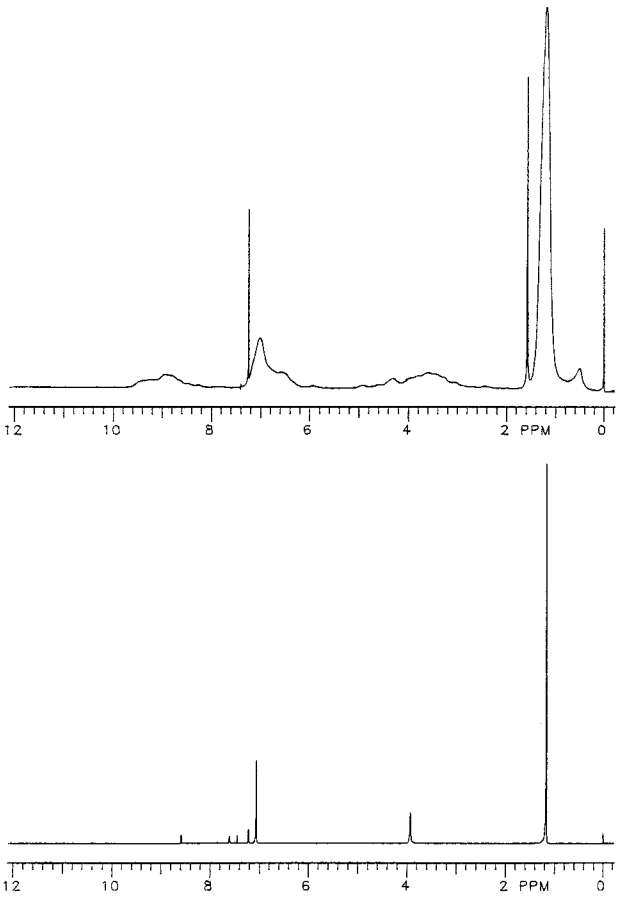


Figure 3. ^{1}H NMR spectra of *p-tert*-butylcalix[20]arene (**[20]**) in $CDCl_3$ and $CDCl_3$:pyridine-d_5 (6:1).

(HPLC yields ranging from 13.8% to ca. 2%; cf. Table 2). After further purification good elemental analyses were obtained for **[9]**−**[16]** and **[20]**, but not for calixarenes **[17]**−**[19]** for which only very small amounts are available. Interestingly, the chromatographic properties of **[20]**[20] allow it to be more easily purified than **[17]**−**[19]** and, accordingly, to give a satisfactory elemental analysis.

Characterization of [9]−[20] as Calixarenes. The compounds isolated as described above were clearly established as calixarenes by ^{1}H NMR, ^{13}C NMR, and mass spectral analyses. The ^{1}H NMR spectra in $CDCl_3$ solution for all but **[20]** show the characteristic pattern containing a single sharp resonance at ca. δ 1.25 for the *tert*-butyl protons, a somewhat broadened singlet at ca. δ 3.8 for the methylene protons, a singlet at ca. δ 7.1 for the aromatic protons, and a resonance varying from sharp to broad at *ca.* δ 9 for the hydroxyl protons; the spectrum of **[14]** shown in Figure 2 (top) is typical of the entire series except for **[20]**. Like the ^{13}C NMR for **[14]** in Figure 2 (bottom), the ^{13}C NMR spectra for **[9]** to **[19]** all display seven lines (one for $C(CH_3)_3$, one for $C(CH_3)_3$, one for $ArCH_2Ar$, and four for the aryl carbons). Missing in the ^{13}C NMR was any indication of a resonance near δ 115 which is characteristic of a H−C aryl carbon *ortho* to the HO−C aryl carbon of the phenolic ring, i.e. a terminal residue in a linear oligomer.[18] Also, the mass spectra of calixarenes **[9]**−**16]** and **[20]** all show a strong molecular ion peak at the expected *m*/*e* ratio.

As shown in Figure 3 (top), **[20]** differs from all of the other large calixarenes in showing many very broad signals in the ^{1}H NMR spectrum in $CDCl_3$ solution. Upon addition of 0.1 mL of pyridine-d_5 to the solution, however, the spectrum becomes dramatically sharper, as shown in Figure 3 (bottom). This observation, along with the mass spectrum containing a parent peak at *m*/*e* 3242.0 (calcd 3242.8), provides compelling evidence that **[20]** is, indeed, a calixarene albeit different in some fashion from its smaller relatives. The realization that **[8]** is unexpectedly immobile as the result of particularly favorable intramolecular hydrogen bonding suggested that a comparable situation might exist for **[20]**. Two other possibilities for consideration are the topological isomers: (a) a catenane derived from a pair of **[10]** molecules and (b) a trefoil knot. Molecular mechanics calculations indicate that while the energies or these are higher than that of a "planar" calixarene, they may be within the range of possibility. Arguing against the catenane, however, is the fact that the melting point decomposition products of partially decomposed **[20]** do not include any larger a proportion of **[10]** than do the decomposition products of other sizes of calixarenes; also, the mass spectrum of **[20]** shows no signal for **[10]** at *m*/*e* 1620. The trefoil structure remains a possibility, but no experimental support has yet been adduced.[21]

Physical Properties. The solubilities of the *p-tert*-butylcalix[4−20]arenes in various solvents, listed in Table 1, show that surprising differences exist in some cases for cyclooligomers that differ by only a single aryl unit (*cf.* **[15]** with **[16]**). Calixarenes **[4]**−**[20]** all are white crystalline or microcrystalline materials that generally show appreciable shrinkage before

(20) In EtOAc/hexane **[20]** elutes before **[18]**, **[16]**, **[14]**, **[15]**, **[12]**, and **[19]**, respectively.

(21) Recognizing that the trefoil structure of **[20]** possesses chirality, the ^{1}H NMR spectrum of the compound was measured in the presence of a chiral shift reagent. However, the shift reagent, just like pyridine, changes the spectrum to the pattern shown in Figure 3 (bottom), and no doubling of resonances was observed. Thus, although casting doubt on the trefoil structure, the results are somewhat inconclusive.

Table 1. Qualitative Solubilities of *p-tert*-Butylcalix[4−20]arenes in Seven Common Solvents[a]

cmpd no.	MeOH	acetone	EtOAc	CH_2Cl_2	$CHCl_3$	toluene	hexanes
[4]	insol	insol	insol	δ sol	δ sol	insol	insol
[5]	insol	sol	sol	sol	sol	sol	insol
[6]	insol	insol	insol	sol	sol	insol	insol
[7]	insol	sol	sol	v sol	v sol	v sol	δ sol
[8]	insol	insol	insol	insol	δ sol	insol	insol
[9]	insol	insol		δ sol	sol	insol	insol
[10]	insol	insol	insol	sol	sol	insol	insol
[11]	insol	sol	δ sol	sol	sol	δ sol	sol
[12]	insol	sol		sol	sol	δ sol	insol
[13]	insol	sol	sol	sol	sol	sol	insol
[14]	insol	insol	insol	sol	sol	sol	sol
[15]	insol	sol	sol	sol	sol	sol	insol
[16]	insol	insol	insol	sol	sol	δ sol	insol
[20]				sol	sol		

[a] Approximate values for the solubility classes: insol, <1 mg/mL; δ sol, 1 mg/mL; sol, 3 mg/mL; v sol, >10 mg/mL.

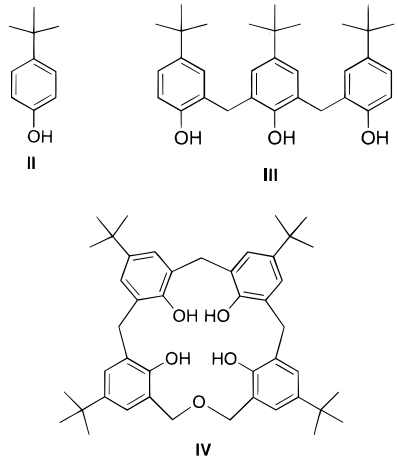
melting, probably due to changes in crystal morphology and/or decomposition (cf. Experimental Section). That decomposition does occur upon melting was shown by comparing the HPLC traces from unmelted and melted materials, the former showing a single peak corresponding to the pure *p-tert*-butylcalix[*n*]arene and the latter showing a multiplicity of peaks arising, inter alia, from smaller calixarenes.

Effect of Reaction Conditions in the Acid-Catalyzed Procedure. Replacement of AcOH and HCl of the acid-catalyzed preparation described above with toluene and TsOH[22] increased the yield to 50−55%, and replacement of toluene with $CHCl_3$ increased it to 80−90%.[23] Still higher yields were obtained when *s*-trioxane was used in place of paraformaldehyde, and almost quantitative yields were then realized by optimizing the molar ratios of *p-tert*-butylphenol, formaldehyde (as *s*-trioxane), and TsOH (1.00:1.15:0.10) with a *p-tert*-butylphenol concentration of 10% (wt of phenol/mL of $CHCl_3$). At higher and lower reactant concentrations 1 equiv of formaldehyde (as *s*-trioxane) was used plus a small additional amount to establish an excess concentration of 0.09 M of HCHO at the end of the reaction. If more than this slight excess of HCHO is present, the reaction mixture becomes much darker, the yields of "large" calixarenes decrease, and the yield of **[8]** increases. At other reactant concentrations the same concentration of TsOH was used as in the 10% reaction.

A study of the effect of reactant concentration on the product composition was carried out with the initial concentration of *p-tert*-butylphenol being varied from 1% to 75% w/v (weight of phenol/volume of solvent). The data presented in Table 2 show that the amount of large calixarenes climbs sharply between concentrations of 1−10% and then considerably more slowly between concentrations of 10−75%. The choice of concentration in a given experiment, therefore, is dictated by the particular group of calixarenes desired for isolation. For the isolation of **[7]**, for example, a concentration near 5% would be chosen to minimize the presence of other difficult to remove calixarenes. If calixarenes **[11]**−**[14]** are the target molecules the preferred concentration is ca. 20%. For the isolation of **[15]**−**[20]** the highest concentration is best, although ca. 60% is the practical experimental limit. Calixarenes **[9]** and **[10]** are easily isolated from any acid-catalyzed reaction mixture regardless of the concentration at which the reaction is carried out.

"Mechanism" of the Acid-Catalyzed Condensation. The progress of an acid-catalyzed condensation (phenol concentration 60%) was followed by removing aliquots at various times. Each aliquot was analyzed by HPLC and by ^1H and ^{13}C NMR spectral measurements and then separated into cyclic and linear fractions which were weighed. In no case was there any indication of the presence of CH_2OH or $ArCH_2OCH_2Ar$ moieties in the products. Peaks in the ^{13}C NMR spectra at δ 115 were observed only in fractions containing appreciable amounts of linear oligomers, and they decreased in relative intensity as the reaction proceeded. After an induction period there is an inverse correspondence between the disappearance of linear oligomers and the appearance of cyclic oligomers, with calixarene formation beginning near 100 minutes and ending after 200 min.

The concentrations of linear oligomers with four to six residues (**L4**−**L6**) successively increase and then decrease during the first 100 min of the reaction.[24] At about 150 min, however, their concentration falls abruptly and is accompanied by a concurrent appearance of only trace amounts of **[4]**−**[6]**. On the other hand, the concentrations of linear oligomers with more than six residues (**L7**−**L12**) rise and fall more evenly, and the maxima are reached between 130 and 150 min with an inverse correspondence between the disappearance and appearance of the linear oligomers and cyclic oligomers containing seven to twelve residues. While this does not prove that the cyclooligomers arise only from linear oligomers containing the same corresponding number of aryl moieties, it suggests that this may at least partly be the case. The fact that only small amounts of **[4]**−**[6]** are found indicates that either the reaction conditions favor continued linear oligomerization or that the linear precursors to **[4]**−**[6]** do not cyclize as readily as do their larger counterparts. Since only small amounts of **[4]**−**[6]** are observed in all but the most dilute concentrations (cf. Table 2), the latter explanation is probably correct.



In the hope of gaining further insight into these processes a comparison was made of the product composition of mixtures obtained by starting with *p-tert*-butylphenol (**II**), the linear trimer of *p-tert*-butylphenol (**III**), or *p-tert*-butyldihomooxacalix[4]-

(22) Acids such as H_2SO_4 were avoided because of the probable reaction with *p-tert*-butylphenol (i.e. sulfonation, *de-tert*-butylation). With CF_3CO_2H no reaction was observed, while with the ion-exchange resin Amberlyst-15 the reaction proceeded mainly to give short hydroxymethylated linear oligomers along with trace amounts of the smallest calixarenes (**[4]** was isolated from the reaction mixture).

(23) A change to a more inert solvent was suggested when a series of singlets near δ 2.3 were observed in an ^1H NMR spectrum of the noncalixarene fraction of an acid-catalyzed reaction mixture in which toluene was used as the solvent. These singlets were interpreted as arising from the methyl protons of the toluene residues in the linear oligomers.

(24) Linear oligomers with two and three residues evolve similarly, and *p-tert*-butylphenol decreases in a pseudo-first-order fashion during the first 60 min of the reaction.

Table 2. Final Composition and Average Molecular Weights of Mixtures from Acid-Catalyzed Reactions of *p-tert*-Butylphenol with *s*-Trioxane in $CHCl_3$ Performed at Concentrations of 1−75% w/v (wt of phenol per mL of $CHCl_3$)

rxn concn, % w/v	percent of *p-tert*-butylcalix[4−20]arenes in the final reaction mixture[a,b]														av MW[d]
	[4]	**[5]**	**[6]**	**[7]**	**[8]**	**[9]**	**[10]**	**[11]**	**[12]**	**[13]**	**[14]**	**[15]**	**[16]**	**[17−20]**[c]	
1	13.9	8.8	19.3	21.1	19.9	8.6	3.7	1.7	1.1	0.0	0.0	0.0	0.0	0.0	1083
5	5.1	3.7	14.3	23.6	26.2	12.8	5.0	2.9	2.3	1.3	1.1	0.3	0.2	0.0	1235
10	2.5	1.8	10.2	25.0	23.4	13.8	7.0	4.8	3.4	2.8	2.2	1.0	0.5	0.8	1351
20	1.5	1.2	7.5	25.2	22.5	13.6	7.8	5.8	4.3	3.4	2.8	1.8	1.1	1.0	1418
30	1.2	1.0	6.5	23.9	22.2	13.1	7.2	5.7	4.3	3.6	3.3	2.4	1.9	2.7	1464
40	0.9	0.7	4.9	23.7	21.8	12.5	6.9	5.7	4.9	4.1	4.2	2.5	1.9	4.5	1511
50	0.8	0.7	4.3	22.3	19.9	11.8	6.9	6.3	5.1	4.9	4.7	3.7	2.9	5.1	1595
60	0.7	0.6	3.9	21.9	19.3	11.8	7.1	6.1	5.1	4.8	4.3	3.4	2.2	8.1	1639
75	0.6	0.5	3.6	19.9	17.6	11.0	6.8	5.9	5.1	5.1	5.0	3.7	2.8	11.5	1728

[a] Peak area percents are obtained from one HPLC chromatogram of the final crude reaction mixture. [b] The remaining percentage of the reaction mixture (<2%) is due to rounding of values and/or the presence of linear or unknown components. [c] Calculated as the sum of the fraction of each size of calixarene present multiplied by its MW. The MW of [**18**] was used for the contribution of [**17**]−[**20**] to the average MW. [d] The percentage of [**17**]−[**20**] for reactions at 60 and 75% includes some later-eluting peaks. At 60% the amounts of [**17**]−[**20**] are 1.2%, 1.4%, 1.9%, and 1.8%, respectively.

Table 3. Composition of the Final Reaction Mixture (As Determined by HPLC Analysis) from the Acid-Catalyzed Reaction of *p-tert*-Butylphenol (**II**), *p-tert*-Butyl Linear Trimer (**III**), and *p-tert*-Butyldihomooxacalix[4]arene with HCHO in $CHCl_3$

starting cmpd	rxn concn[c]	percent of *p-tert*-butylcalix[4−20]arenes in the final reaction mixture[a,b]													
		[4]	**[5]**	**[6]**	**[7]**	**[8]**	**[9]**	**[10]**	**[11]**	**[12]**	**[13]**	**[14]**	**[15]**	**[16]**	**[20]**
II	30%	1.2	1.0	6.5	23.9	22.2	13.1	7.2	5.7	4.3	3.6	3.3	2.4	1.9	2.7
III	30%	0.7	0.6	6.9	15.7	17.0	20.1	5.7	5.7	7.5	4.0	4.1	4.3	1.8	5.4
II	10%	5.1	3.7	14.3	23.6	26.2	12.8	5.0	2.9	2.3	1.3	1.1	0.3	0.2	0.0
IV[d]	10%	18.3	5.2	12.3	12.5	11.7	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

[a] Peak area percents are obtained from one HPLC chromatogram of the final crude reaction mixture. [b] The remaining percentage of the reaction mixture (<2%) is due to rounding of values and/or the presence of linear or unknown components. [c] % w/v (wt of phenol per mL of $CHCl_3$). [d] No HCHO source was used with **IV**. Final mixture contained 24.3% of **IV** after 24 h.

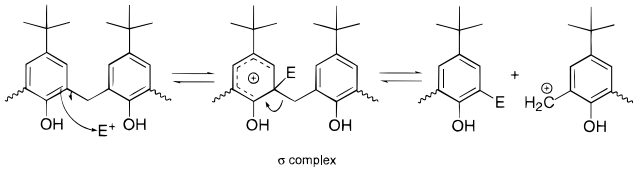


Figure 4. Reaction pathway for electrophile-induced fragmentation of linear oligomers.

arene (**IV**). The results are shown in Table 3. The expectation was that when starting with the linear trimer (**III**) the *p-tert*-butylcalix[$m \times 3$]arenes ($m = 1, 2, 3, ...$) would be the only products. While it does turn out that the *p-tert*-butylcalix[$m \times 3$]arenes are formed in somewhat larger amounts from the linear trimer than from the monomer at the same reaction concentration, substantial amounts of all of the other sizes of calixarenes are present as well, indicating that fragmentation/recombination processes are occurring to a significant extent.[25] The fact that **IV** undergoes fragmentation but reacts only sluggishly, with 24% of starting material remaining after 24 h at reflux, may indicate that the dibenzyl ether bridge is not formed under these conditions. One pathway along which fragmentation might take place involves *ipso* attack of an electrophile (E^+) to yield a σ-complex which can then fragment, as illustrated in Figure 4. Thus, as illustrated in Figure 5, a linear oligomer has several available reaction pathways, including (a) hydroxymethylation at one terminus followed quickly by carbocation formation[26] and intramolecular attack at the other terminus to form a cyclic oligomer without loss of an aryl residue, (b) hydroxymethylation at one terminus followed by carbocation formation and intra-

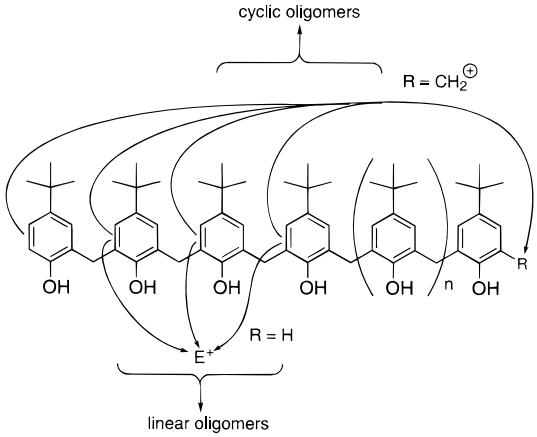


Figure 5. Reaction pathways for linear oligomers of *p-tert*-butylphenol and HCHO with electrophiles.

molecular *ipso* attack to form a cyclic oligomer with loss of one or more aryl residues, and (c) external attack by an electrophile to form other linear oligomers. Among the available electrophiles are H^+, $ArCH_2^+$, and $H_2C{=}OH^+$. However, H^+ proves to be a rather ineffective electrophile, for treatment of **[8]** with TsOH in refluxing $CHCl_3$ or toluene for 24 and 48 h, respectively, yielded only starting material and no other calixarenes. Similarly, **[7]** with TsOH in refluxing $CHCl_3$ for 84 h underwent no change, although treatment of **[7]** with triflic acid in CH_2Cl_2 at room temperature for 32 h did effect some decomposition. Treatment of a mixture of **[5]**, **[7]**, and TsOH in refluxing $CHCl_3$ with *s*-trioxane gave equivocal results, the solution becoming intensely colored and some change in the calixarene composition occurring. More definitive results were obtained when a solution of **[5]**, **[7]**, and TsOH was treated with benzyl alcohol (1 equiv per 6 ArOH groups) in refluxing $CHCl_3$ for 24 h, producing a mixture of more than 10 components from which calixarenes **[4]** and **[8]** were isolated. Clearly, benzyl

(25) Fragmentation/recombination has been shown to play a dominant role in the base-induced condensation of *p-tert*-butylphenol and formaldehyde (Dhawan, B.; Chen, S.-I.; Gutsche, C. D. *Makromol. Chem.* **1987**, *188*, 921 and ref 2a) and the acid-catalyzed preparation of calixrescorcarenes (ref 2e, p 33).

(26) In the aliquot study no oligomers with hydroxymethyl groups were detected.

Table 4. Coalescence Temperatures, ^{1}H NMR Data, and $\Delta G^{\ddagger}$ Values for the Conformational Inversion of *p-tert*-butylcalix[4−16]arenes ([**4**]−[**16**]) in $CDCl_3$ at 300 MHz

p-tert-butylcalix [*n*]arene	T_c (°C)	$\Delta\nu$ (Hz)	k_c (s^{-1})	$\Delta G^{\ddagger}$ (±0.3 kcal/mol)
[4]	65	225	505.3	15.7
[5]	21	180	406.8	13.2
[6]	11	210	472.4	13.1
[7]	14	216	485.5	12.3
[8]	66	246	551.4	15.7
[9]	17	240	538.2	13.4
[10]	−18	255	571.2	11.6
[11]	−37	216	485.5	10.8
[12]	−14	225	505.3	11.9
[13]	−31	270	604.2	11.0
[14]	−29	270	604.2	11.1
[15]	−31	240	538.2	11.1
[16]	0	255	571.2	12.5

cation is a more effective electrophile for calixarene fragmentation than the H^+ and, possibly, formyl cations.

Conformational Properties. The parent calixarenes, i.e., those containing *endo*-OH groups[27] on *all* of the aryl moieties, are conformationally mobile, from the smallest member **[4]** to the very largest member. While mobility often complicates the life of the calixarene chemist, it has the redeeming feature of providing cyclooligomers possessing cavities and crevices of highly varied contour. Calix[4]arenes have four "up/down" conformations that are readily identified and are designated as cone, partial cone, 1,2-alternate, and 1,3-alternate. Of these, the most stable conformation for the parent calixarene is the cone, ascribed to its structural compactness and the especially strong intramolecular hydrogen bonding that exists among its four OH groups. Similarly, the parent calix[5]arenes adopt the cone conformation, although their baskets, larger by one arylmethylene moiety, have less strong hydrogen bond stabilization. With the parent calix[6]arenes the cone conformation is no longer favored because of its unfavorable dihedral angles and its consequent inability to afford the most effective hydrogen bonding array. Instead, the calix[6]arenes adopt more contorted conformations,[28] one of which is called a "pinched cone". These same conformational conditions also prevail for the parent calix[7]arenes. Additional conformations come into play with the calix[8]arene, one of which is called a "pleated loop" in which the strength of the intramolecular hydrogen bonding is comparable to that of the cone conformation of the calix[4]arenes. Quite coincidentally the barriers to conformational inversion for **[4]** and **[8]** are almost identical, and both are higher than those of any of the other sizes of parent calixarenes (see Table 4). Thus, the cone and the pleated loop provide the best conformation-stabilizing structures in the calixarene family, and it is postulated that all of the other parent calixarenes incorporate as many cone-like and/or pleated loop-like conformational segments as possible.

The earliest studies of the temperature-dependent ^{1}H NMR behavior of the calixarenes were carried out in the early 1970s by Kämmerer and co-workers[29] on cyclooligomers prepared by stepwise syntheses. Their studies showed that the pair of doublets arising from the CH_2 protons of *p*-methylcalix[4]arene at room temperature changes to a sharp singlet at higher temperatures, indicating that at higher temperatures the two types

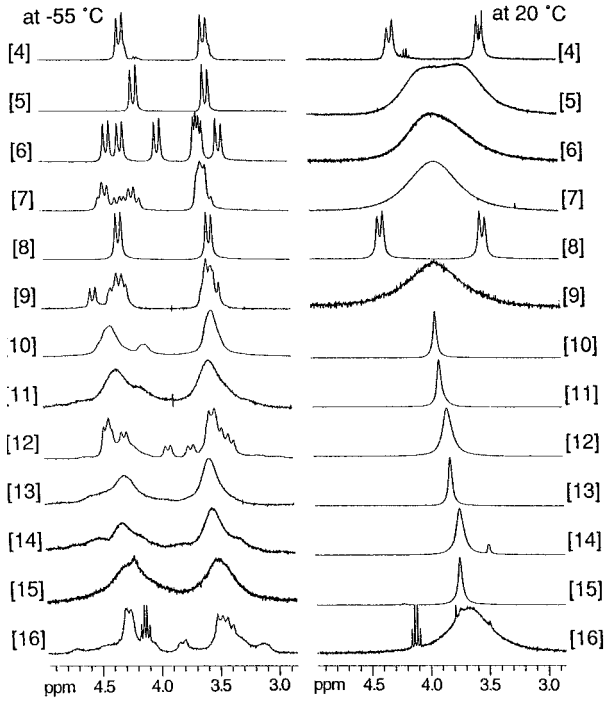


Figure 6. ArCH_2Ar resonances near 20 and −55 °C for *p-tert*-butylcalix[4−16]arenes (**[4]**−**[16]**) in $CDCl_3$.

of protons are exchanging environments rapidly on the NMR time scale. Employing well-established techniques for the quantitative treatment of coalescence phenomena of this type,[30] a free energy of activation for conformational inversion was calculated. This method for studying the conformational mobility of calixarenes has become very widely used and has been applied with particular vigor to the "major"[31] and "minor"[32] calixarenes. It provides the basis for the present study, even though it is realized that in many instances the calculated values represent only an average free energy of activation for assemblies that generally contain nonidentical molecular segments. Figure 6 shows the room temperature and low temperature (−55 °C) patterns for the ArCH_2Ar methylene protons of calixarenes **[4]**−**[16]**, and Table 4 shows the coalescence temperatures (T_c) for each of the members of the *p-tert*-butylcalix[*n*]arene family from $n = 4$ to 16, determined from a series of stacked spectra acquired every 1−2 °C near the coalescence temperature. From these data, the $\Delta G^{\ddagger}$ values shown in Table 4 were calculated using the standard equations[33] incorporating the values for $\Delta\nu$, J_{AB}, and T_c. A graphical display of these data is shown in Figure 7.

Inspection of the $\Delta G^{\ddagger}$ values in Table 4 and the plot in Figure 7 shows that the barriers to conformational interconversion generally trend downward as the size and concomitant flexibility of the calixarene increases. The major exception is **[8]** which, as discussed above, adopts the particularly stable pleated loop conformation.[34] The dominant role played by intramolecular hydrogen bonding in maintaining the pleated loop conformation of **[8]** is revealed by the failure of this compound to show decoalescence to a pair of doublets in pyridine-d_5 solution as the temperature is lowered to −90 °C.[35] It is interesting to

(27) For nomenclature cf. p 7 of ref 2a.
(28) See p 60 of ref 2a for an enumeration of the conformers of calix[6]arenes
(29) Kämmerer, H.; Happel, G.; Caesar, F. *Makromol. Chem.* **1972**, *162*, 179. Happel G.; Mathiasch, B.; Kämmerer, H. *Makromol. Chem.* **1975**, *176*, 3317.
(30) Kurland, R. S.; Rubin, N. B.; Wise, W. B. *J. Chem. Phys.* **1964**, *40*, 2426.
(31) Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6052.
(32) Kämmerer, H.; Happel, G. *Makromol. Chem.* **1980**, *181*, 2049. Kämmerer, H.; Happel, G. *Monaatsh. Chem.* **1981**, *112*, 759. Kämmerer, H.; Happel, G.; Mathiasch, B. *Monastsh. Chem.* **1981**, *182*, 1685. Stewart, D. R.; Krawiec, M.; Kashyap, R. P.; Watson, W. H.; Gutsche, C. D. *J. Am. Chem. Soc.* **1995**, *117*, 586.

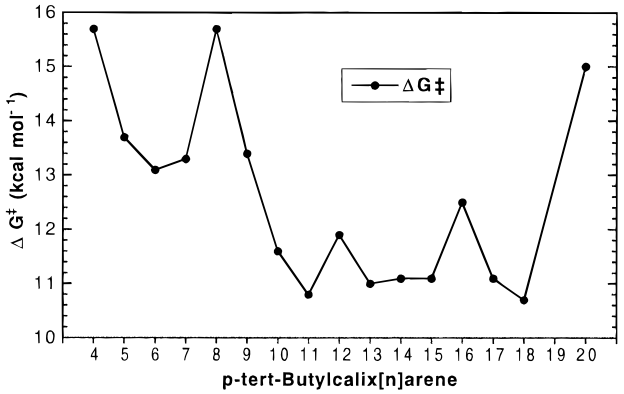
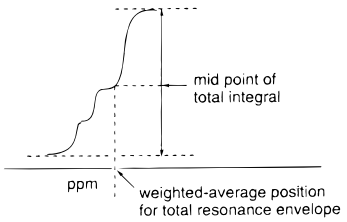


Figure 7. Plot of the $\Delta G^{\ddagger}$ values for *p-tert*-butylcalix[4−20]arenes (**[4]**−**[20]**) in $CDCl_3$ solution.

observe that **[4]** is more conformationally stable than **[5]**, that **[8]** is more conformationally stable than either of its immediate neighbors, and that **[12]** and **[16]** are both conformationally more stable than their immediate neighbors, although to a lesser extent. The increased conformational stability shown by these calixarenes, all containing $m \times 4$ ($m = 1, 2, 3, ...$) aryl residues, is ascribed to their greater ability to incorporate cone-like and/or pleated loop-like segments into the cyclic arrays of [**12**], [**16**], and [**20**] and also to the ability of these structures to adopt a particularly compact zigzag structure in which one molecular segment tessylates with another (see Supporting Information).

In contrast to the general trend toward lower coalescence temperatures as the size of the ring increases from 4 to 16, Figure 8 shows that **[20]** appears to have an unexpectedly high coalescence temperature. At room temperature broad envelopes arising from the OH, ArH, $ArCH_2Ar$, and *t*-Bu protons of **[20]** are observed which sharpen to four singlets only above 70 °C, suggesting a conformational mobility comparable to that of **[4]** and **[8]**. At temperatures between −16 and −54 °C a plethora of fairly sharp resonances is observed, while below −54 °C the resonances again broaden to very ill-defined envelopes at −92 °C. The data in support of a calixarene structure for **[20]** appear to be quite solid, so this variable-temperature ^{1}H NMR behavior suggests that **[20]** may possess a conformation and/or structure (vide supra) different from that of the other "large" calixarenes.

(33) The NMR determinations were carried out in $CDCl_3$ on a 300 MHz Varian XL-300 spectrometer. The rate constants (k_c in s^{-1}) for conformational interconversion at the coalescence temperature were calculated from the equation $k_c = 2.22(\Delta\nu^2 + 6J^2_{AB})^{1/2}$. The free energy barrier to conformational interconversion in kcal mol^{-1} was calculated from the equation $\Delta G^{\ddagger} = 4.58T_c(10.32 + \log T_c/k_c)/1000$. The $\Delta\nu$ values are shown in Table 4; the J_{AB} value used was 14 Hz. Assuming an accuracy of ±5 °C for the value of T_c, ±15 Hz for the value of $\Delta\nu$, and ±1 Hz for the value of J_{AB}, it is estimated that the $\Delta G^{\ddagger}$ values are accurate to ±0.4 kcal mol^{-1}. However, since this treatment was not designed for multisite exchange phenomena, the variations in the values obtained may be larger. The $\Delta\nu$ values were measured between the weighted-average positions of the two low-temperature resonance envelopes for the $ArCH_2Ar$ methylene protons, as illustrated below for one such envelope:



(34) Gutsche, C. D.; Gutsche, A. E.; Karaulov, A. I. *J. Incl. Phenom.* **1985**, *3*, 447.

(35) Gutsche, C. D.; Bauer, L. J. *Tetrahedron Lett.* **1981**, *22*, 4763

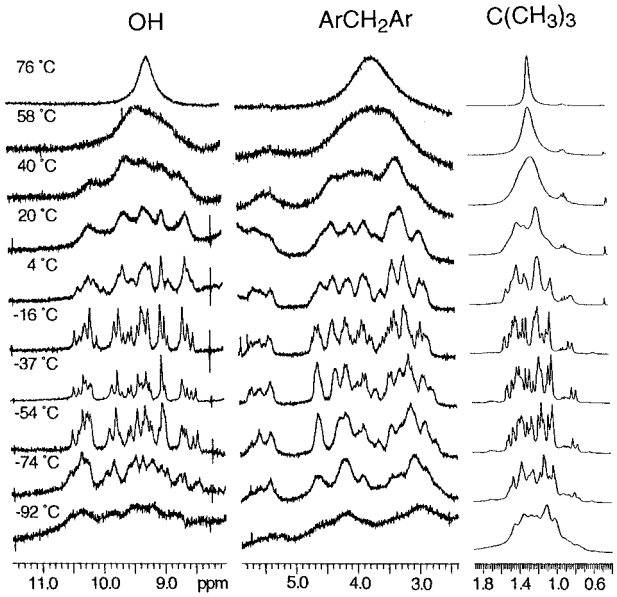


Figure 8. Temperature-dependent ^{1}H NMR spectra of *p-tert*-butylcalix[20]arene in toluene-d_8.

Table 5. IR Stretching Frequencies and ^{1}H NMR Positions for OH Resonances of *p-tert*-Butylcalix[*n*]arenes

		^{1}H NMR		
calixarene	IR (ν_{cm})	δ_{OH}(rt)	δ_{OH}(cold)	peaks (cold)
[4]	3155	10.35	10.43	1
[5]	3285	8.67	8.83	1
[6]	3155	10.53	10.5−10.9	3
[7]	3180	10.34	9.9−11.5	7
[8]	3240	9.64	9.85	1
[9]	3260	9.78 (br)	9.4−10.4	9
[10]	3255	9.24	8.8−9.5	5
[11]	3285	9.50	8.6−10.8	>16
[12]	3260	9.53	9.4−10.7	6
[13]	3335	9.45	9.0−11.0	9
[14]	3325	9.32	8.8−11.0	>20
[15]	3325	9.13	7.6−10.8	*ca.* 18
[16]	3310	9.02	8.3−9.7	7 (2 major)
[17]		9.02		
[18]	3400	8.98		
[19]		9.06		
[20]	∼3340	*ca.* 8−10 (br)	8.4−10.7	>26

The intramolecular hydrogen bond character of the individual calixarenes is reflected both in the low OH stretching frequencies in the IR spectra and the far downfield OH positions in the ^{1}H NMR spectra, as shown in Table 5 and Figure 9. Interesting differences in the number of OH resonances in the ^{1}H NMR are noted. While the calixarenes **[4]**, **[5]**, and **[8]** each have a single sharp OH resonance, **[6]** has three resonances, and **[7]** has seven. All of the "large" calixarenes have multiple OH resonances, generally more for the odd-numbered members than for the even-numbered members. For example, **[9]** shows nine equal lines, while **[10]** shows only five equal lines; **[11]** shows more than 16 lines of varying heights, while **[12]** shows only six equal lines. At −92 °C in CH_2Cl_2 solution, **[13]** shows nine singlets in a 1:2:2:1:2:2:1:1:1 ratio. The number of OH resonances observed for a particular calixarene can be ascribed to its symmetry, or lack thereof, and whether it exists as a single conformer or a mixture of conformers at low temperature.

Experimental Section[36]

HPLC analyses were performed using a Perkin-Elmer instrument consisting of a Series 4 pump, an LC-85B UV/VIS detector set at 281 nm, an LCI-100 integrator/plotter, and a 3.9 mm i.d., 25 cm, E. Merck

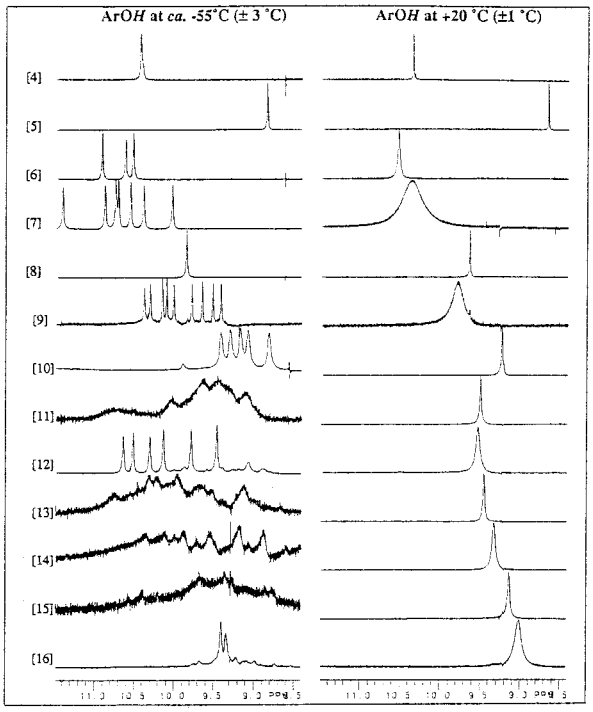


Figure 9. ArOH resonances near 20 and −55 °C for *p-tert*-butylcalix-[4−16]arenes (**[4]**−**[16]**) in $CDCl_3$ solution.

Hibar RP-18 Lichrosphere column packed with 5 μm, non-end-capped, silica-based particles. The separation of *p-tert*-butylcalix[4−20]arenes was accomplished with a mixture of two eluents, **A** and **B** at a flow rate of 2 mL/min and a pressure of 11 MPa. Eluent **A** was a 99:1 mixture of MeCN and AcOH; eluent **B** was a 12:9 mixture of CH_2Cl_2 and methyl *tert*-butyl ether (MTBE) with 1% AcOH. A 80/20 mixture of **A** and **B** was run isocratically for 8 min followed by a 3 min linear gradient to a 65/35 mixture of **A** and **B**, and the column was isocratically eluted for 12 min with this mixture. Next, the column was eluted with a 3 min linear gradient to a 55/45 mixture of **A** and **B** and then isocratically eluted for 6 min with this mixture. Finally, the column was cleaned and reequilibrated with a 3 min linear gradient to a 40/60 mixture of **A** and **B** followed by a 3 min linear gradient to an 80/20 mixture of **A** and **B**. After ca. 5 min the column was ready for another sample. The entire separation and reequilibration requires about 40 min.

Acid-Catalyzed Condensation of *p-tert*-Butylphenol with *s*-Trioxane. A solution of 37.6 g (250 mmol) of *p-tert*-butylphenol and 7.69 g (85.4 mmol, 256.1 meq. HCHO) of *s*-trioxane in 75 mL of amylenes-stabilized $CHCl_3$ was brought to reflux in an inert atmosphere in a 3-necked, 125 mL *Ace Glass* "European -style" flask (PN 6961) equipped with a heating mantle, a magnetic stirring bar, a thermometer in the reaction pot, and a Dean−Stark water trap. The water trap, equipped with a distillate-return option (*Ace Glass* PN 7747), a condenser, and a thermometer, was charged with ca. 10 mL of $CHCl_3$. When reflux was attained, 1.50 g (7.89 mmol) of $TsOH{\cdot}H_2O$ was added, and the return stopcock of the trap was adjusted so that the water that forms is collected in the trap while the distilled $CHCl_3$ is returned to the reaction mixture. After ca. 2 h the reaction mixture changed from a colorless clear solution to a colorless cloudy reaction mixture, by which time ca. 3.8 mL of H_2O had collected in the trap. Soon after the mixture became cloudy, it turned to a light brown-violet and the cloudiness increased. After 4−5 h, at which time the reaction mixture was dark violet and the reaction was shown by HPLC analysis to be complete, it was cooled to room temperature and 50 mL of 5% $NaHCO_3$ was added.

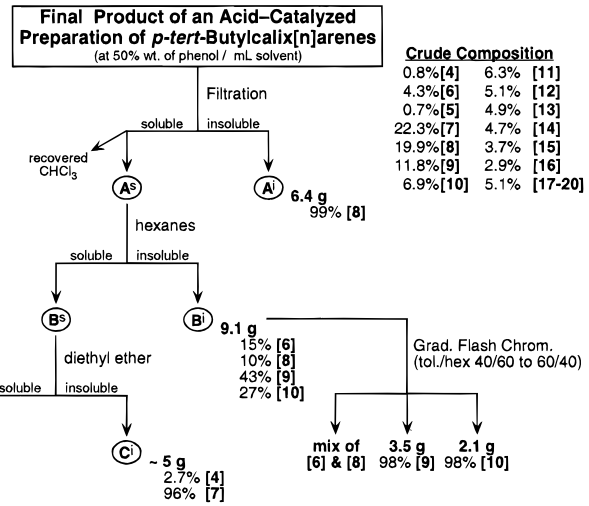


Figure 10. Initial steps in the separation of "large" calixarenes from acid-catalyzed mixture.

Isolation of **[7]** and **[8]** and Fractionation To Obtain a Mixture of **[9]** and **[10]** (See Figure 10**).** The crude product/aqueous $NaHCO_3$ mixture was stirred vigorously for 30 min and filtered to give 6.4 g (16%) of **[8]** as a white powder (**A**$^{\mathbf{i}}$). The $CHCl_3$ layer in the filtrate **A**$^{\mathbf{s}}$ was separated and successively washed with 50 mL of 1 N HCl and 100 mL of H_2O. The $CHCl_3$ layer was dried with $MgSO_4$, and about two-thirds of the solvent was removed in vacuo. The remainder was brought to reflux in an Erlenmeyer flask, and the lost volume of solvent was replaced with hexanes until an appreciable amount of precipitate had formed. Upon cooling, 9.1 g (22%) of a white powder (**B**$^{\mathbf{i}}$) was isolated which consisted of "major" calixarenes as well as **[9]** and **[10]**. The solvent was completely removed in vacuo, and 30 mL of *n*-heptane was added, stirred, and removed in vacuo to eliminate traces of other solvents. The residue **B**$^{\mathbf{s}}$ was refluxed with 100−150 mL of Et_2O for 30 min or until copious amounts of a thick white precipitate formed. Upon cooling to room temperature, the mixture was filtered to give ca.4.5 g (11%) of nearly pure **[7]** as a white powder (**C**$^{\mathbf{i}}$).

Isolation of [9] and most of [10] from B$^{\mathbf{i}}$ (See Figure 10). A 50 mm i.d. column was dry packed with 20 cm of silica gel and eluted with 1.0 L of a 40/60 mixture of toluene/hexanes until the eluent was no longer warm (the warm eluent was discarded). A solution of **B**$^{\mathbf{i}}$ in a 30/40/30 mixture of toluene/hexane/CS_2 was applied by submerged addition, and after the sample was slowly eluted into the column, elution proceeded at about 4 cm/min. Just before the CS_2 eluted, fractions of 75−100 mL were collected. Following the elution of the 40/60 mixture of toluene/hexanes, the column was eluted with 100 mL each of 45/55, 50/50, 55/45, 60/40, 65/35, and 70/30 mixtures of toluene/hexanes. Within 30 min, the **[9]** and **[10]** began to precipitate, and after several hours the precipitates were filtered to give 3.5 g (8.6%) of **[9]** and 2.1 g (5.2%) of **[10]** as fine white powders.

Separation of Remaining [7], [9], and [10] and Preliminary Separation of [11]−[20] from C$^{\mathbf{s}}$ (See Figure 11).[37] A 75 mm i.d. column was packed with 19 cm of silica gel and 1.5 L of a 45/55 mixture of toluene/hexanes; any eluent that was warm when it eluted was discarded. The ca. 36 g of solid filtrate **C**$^{\mathbf{s}}$ from two reaction mixtures was applied to the top of the column but under ca. 7.5 cm of eluent via submerged addition as a 15−20% (w/v) solution in a 25/35/40 mixture of toluene/hexanes/CCl_4. After the sample had been slowly introduced into the column, elution proceeded at about 4 cm/min. When a rapidly moving clear band (CCl_4) was ca. 2.5 cm from the bottom of the column, fractions of 200−250 mL were collected. Following the elution of the 45/65 mixture of toluene/hexanes, the

(36) Unless otherwise noted, starting materials were obtained from commercial suppliers and were used without further purification. The melting points of all compounds melting above 250 °C were measured in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) using a 500 °C thermometer calibrated against a thermocouple. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-300 instrument at 300 and 75 MHz, respectively. TLC analyses were carried out on Analtech silica gel plates (absorbant thickness 250 μm) containing a fluorescent indicator. After being triturated with MeOH for 1 h, analytical samples were dried for at least 36 h at 100−140 °C and 1−2 mm of pressure and analyzed by Desert Analytics, Tucson, AZ.

(37) The bold face letters refer to the various fractions collected; the superscript "i" designates an insoluble fraction; and, the superscript "s" designates a soluble fraction.

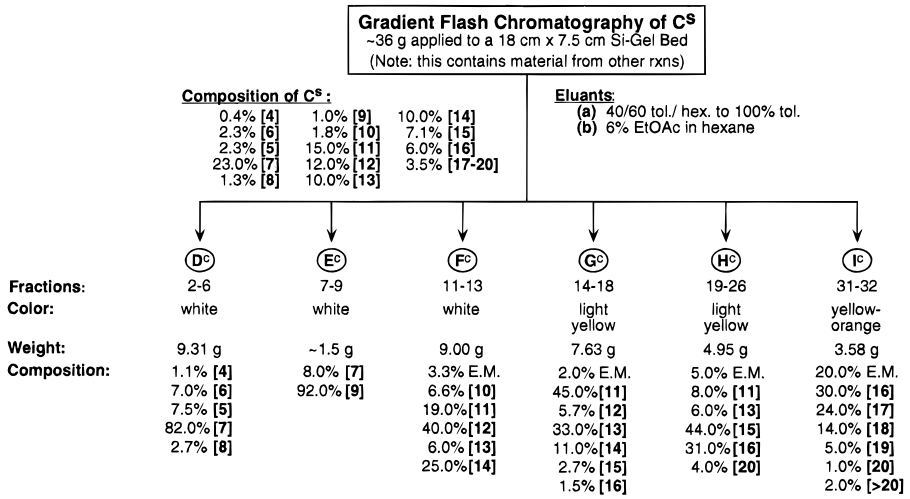


Figure 11. Gradient flash chromatography of the ether soluble portion of the acid-catalyzed preparation of *p-tert*-butylcalixarenes.

column was eluted with 500 mL of a 50/50 mixture of toluene/hexanes and then 250 mL each of 55/45, 60/40, 65/35, and 70/30 mixtures of toluene/hexanes. Then, 500 mL of 75/25, 500 mL of 80/20, 250 mL of 85/15, 500 mL of 90/10, and 250 mL of 95/5 mixtures of toluene/hexanes were successively passed through the column. Subsequently, the column was eluted successively with 1.0 L of toluene, 1.0 L of 6% EtOAc in hexanes, and 1.0 L of 7% EtOAc in hexanes, respectively. Each fraction was analyzed by HPLC and combined with others of similar composition to give the six groups of fractions $\mathbf{D}^c-\mathbf{I}^c$ that are shown in Figure 11. The eluents were removed in vacuo, and the residues were weighed. Group $\mathbf{D}^c$ (9.31 g) contained ca. 80% **[7]** and much smaller amounts of **[4]**, **[5]**, **[6]**, and **[8]**. Group $\mathbf{E}^c$ (ca. 1.5 g) contained ca. 90% **[9]**, while group $\mathbf{F}^c$ (9.00 g) contained appreciable amounts of **[11]**, **[12]**, and **[14]** but only small amounts of **[10]** and **[13]**. Group $\mathbf{G}^c$ (7.63 g) contained appreciable amounts of **[11]** and **[13]** and small or trace amounts of **[12]**, **[14]**, [**15**], and **[16]**. Group $\mathbf{H}^c$ (4.95 g) contained considerable amounts of **[15]** and **[16]** along with small amounts of **[11]**, **[13]**, and **[20]**. Finally, group $\mathbf{I}^c$ (3.58 g) contained **[16]**−**[20]** and perhaps even larger calixarenes.

Isolation of [7] from $\mathbf{C}^i$ and $\mathbf{D}^c$. Since **[7]** is one of the most soluble calixarenes it was necessary to remove less soluble calixarenes before recrystallization. The material from $\mathbf{C}^i$ and $\mathbf{D}^c$ was combined, brought to reflux in ca. 150 mL of acetone, and filtered hot to remove some of the "major and minor" calixarenes. When the solution had cooled to room temperature additional major calixarenes that formed were removed by filtration. The acetone was removed in vacuo and the residue was brought to reflux in 150 mL of $CHCl_3$. The lost volume was replaced with hexanes, and when about 3 volumes of hexanes had been added the solution was allowed to stand at room temperature for 12 h. The mixture was then filtered to give an additional amount of "major and minor" calixarenes. The solvent was removed in vacuo, and the residue was dissolved in 100 mL of hot $CHCl_3$. *i*-PrOH was added to replace lost solvent until the temperature reached 69 °C, and the solution was allowed to stand at room temperature for at least 3 days. After filtration, 7.3 g (>99% pure) of **[7]** as fine white desolvated crystals was collected.

Isolation of [10], [12], and [14] from F^c (See Figure 12**).** Fraction $\mathbf{F}^c$ was dissolved in 15−20 mL of CH_2Cl_2 and cooled to −15 °C. After 8−12 h, it was filtered to give 0.4 g (0.5%) of 88% pure **[10]**. The CH_2Cl_2 from $\mathbf{F}^s$ was removed in vacuo, and the residue was recrystallized from $CHCl_3$−hexanes (mostly hexanes) to give 2.8 g (3.5%) of 98% pure **[12]** ($\mathbf{J}^i$). The solvents were removed in vacuo from $\mathbf{J}^s$, and the residue was dissolved in EtOAc. After several hours a white powder was collected to give 1.5 g (1.9%) of 96% pure **[14]** ($\mathbf{K}^i$).

Isolation of [11] and [13] from $\mathbf{G}^c$, $\mathbf{K}^s$, and $\mathbf{Q}^c$ (See Figure 13). Filtrate $\mathbf{K}^s$ and fraction $\mathbf{G}^c$ were combined and subjected to gradient flash chromatography to remove **[12]** and **[14]**−**[16]** because they interfere with the isolation of **[11]** and **[13].** A 50 mm i.d. column was packed with ca. 20 cm of silica gel and 1.0 L of a 80/20 mixture of toluene/hexanes. A solution of $\mathbf{K}^s$ and $\mathbf{G}^c$ in this eluent was slowly

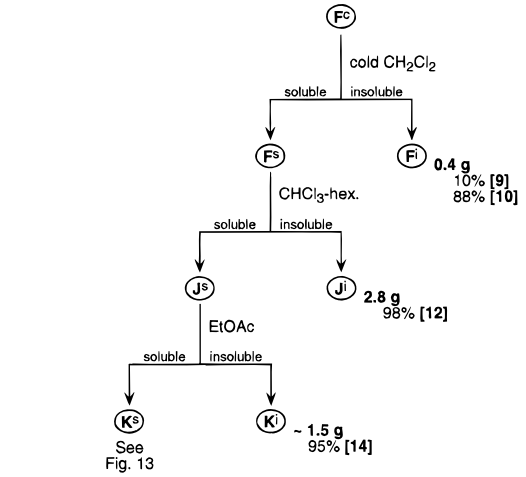


Figure 12. Isolation of **[10]**, **[12]**, and **[14]** from fraction $\mathbf{F}^c$ and isolation of **[15]**, **[16]**, and **[20]** from fraction $\mathbf{H}^c$.

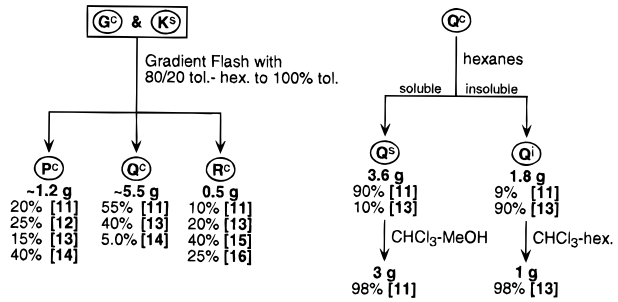


Figure 13. Isolation of **[11]** and **[13]** from fractions $\mathbf{G}^c$, $\mathbf{K}^s$, and $\mathbf{Q}^c$.

introduced into the column. Following the elution of the 80/20 mixture at 3.8 cm/min, 200 mL each of 85/15, 90/10, 95/5, and 100/0 mixtures of toluene/hexanes were successively eluted. After HPLC analysis, similar fractions were combined to give $\mathbf{P}^c$, $\mathbf{Q}^c$, and $\mathbf{R}^c$. Fraction $\mathbf{Q}^c$ was recrystallized from $CHCl_3$−hexanes to give 1.8 g of 90% pure **[13]** as a white solid ($\mathbf{Q}^i$) and 3.6 g of filtrate $\mathbf{Q}^s$ containing 90% pure **[11]**. Recrystallization of $\mathbf{Q}^i$ from $CHCl_3$−hexanes gave 1 g (1.3%) of 98% pure **[13]** as a white powder. Recrystallization of $\mathbf{Q}^s$ from $CHCl_3$−MeOH gave 3 g (3.7%) of **[11]** as a white powder. Fraction $\mathbf{P}^c$ was worked up similarly to fraction $\mathbf{F}^s$ to give additional amounts of **[12]** and **[13]**, and fraction $\mathbf{Q}^c$ was combined with fraction $\mathbf{H}^c$.

Isolation of [15], [16], and [20] from $\mathbf{H}^c$ (See Figure 14). Fraction $\mathbf{H}^c$ was dissolved in ca. 25 mL of EtOAc, and after the mixture stood for 1−3 h a white precipitate formed which was collected to give 1.2 g (1.5%) of 98% pure **[16]** as a white solid ($\mathbf{H}^i$). The EtOAc was removed in vacuo, and the residue was stripped twice with small

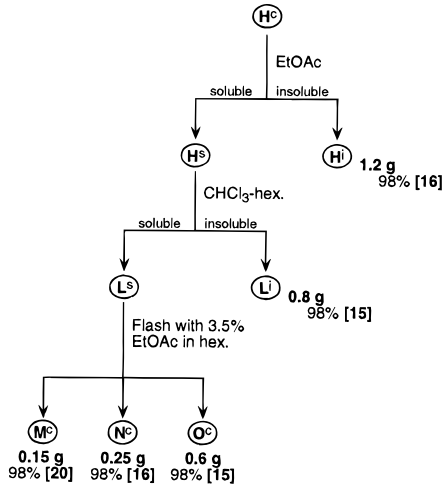


Figure 14. Isolation of **[15]**, **[16]**, and **[20]** from fraction $\mathbf{H}^c$.

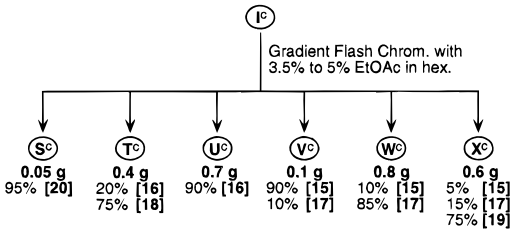


Figure 15. Isolation of **[15]**−**[20]** from fraction $\mathbf{I}^c$.

portions of *n*-heptane to remove any residual EtOAc. The residue was dissolved in hexanes and allowed to remain overnight at room temperature. The white powder that formed was collected to give 0.7 g (0.9%) of **[15]** ($\mathbf{L}^i$). The filtrate $\mathbf{L}^s$ was subjected to flash chromatography on a 50 mm i.d. column packed with 15 cm of silica gel and 1 L of 3.5% EtOAc in hexanes (v/v). After analyzing the fractions by HPLC, similar fractions were combined to give 0.6 g (0.8%) of **[15]** ($\mathbf{O}^c$), 0.25 g (0.3%) of **[16]** ($\mathbf{N}^c$), and 0.15 g (0.2%) of **[20]** ($\mathbf{M}^c$).

Isolation of [15]−[20] from $\mathbf{I}^c$ (See Figure 15). The isolation of calixarenes **[15]**−**[20]** is shown in Figures 11−15. As shown by Figure 14, **[16]** was isolated by triturating fraction $\mathbf{H}^c$ with EtOAc to give fraction $\mathbf{H}^i$. Next, **[15]** was isolated by recrystallizing the residue from this EtOAc filtrate ($\mathbf{H}^s$) from $CHCl_3$−hexane. *p-tert*-Butylcalix[20]arene and additional amounts of **[15]** and **[16]** were isolated when the filtrate $\mathbf{L}^s$ was subjected to flash chromatography. Finally, as shown by Figure 15, calixarenes **[17]**−**[20]** as well as additional amounts of **[15]** and **[16]** were isolated when fraction $\mathbf{I}^c$ of Figure 11 was subjected to flash chromatography using small amounts of EtOAc in hexane. Interestingly, the sequence of elution was as follows: even-membered "large" calixarenes > "minor" calixarenes > odd-membered "large" calixarenes.

Kinetic Study of the Acid-Catalyzed Condensation of *p-tert*-Butylphenol and *s*-Trioxane. A solution of 40.0 g (266 mmol) of *p-tert*-butylphenol and 8.24 g (91.5 mmol, 274 mequiv of HCHO) of *s*-trioxane in amylenes-stabilized $CHCl_3$ was brought to reflux in the same apparatus described above. Once at reflux an aliquot (no. 0) was taken, and 1.91 g (10 mmol) of $TsOH{\cdot}H_2O$ was added. Over the next 8 h, twelve aliquots (nos. 1−12) of 2−3 g each were placed in tared 100 mL round-bottomed flasks and their weights along with the times, reaction temperatures, and trap temperatures were recorded. Each crude aliquot was analyzed by HPLC and then treated, as described below, to remove the TsOH. The $CHCl_3$ was removed under vacuum, the residue was dissolved in $CDCl_3$, and the ^1H and ^{13}C NMR spectra recorded.

Aliquots 4−10 and 12 were each subjected to chromatographic separation of the linear and cyclic components as follows. A 30 mm i.d. column was packed with 18 cm of silica gel and reagent grade toluene. A concentrated toluene solution of the aliquot was added to the column and then washed into the column three times. The column was eluted with 500 mL of toluene or until the HPLC analysis of the aliquots showed no material to be present. The column was eluted with ca. 300 mL of a 2:2:1 solution of acetone, $CHCl_3$, and MeOH, respectively, to obtain the linear oligomers. The cyclic and linear fractions were transferred to tared 500 mL round-bottomed flasks and the eluents were removed in vacuo. The cyclic and linear fractions of each aliquot were dissolved in $CHCl_3$ and analyzed by HPLC. The $CHCl_3$ was removed *in vacuo*, and two 20 mL portions of MeOH were added and successively stripped to assist in the removal of all solvents. The tared flasks were dried at ca. 2 Torr and 80 °C for 30 min on the rotavap and then for at least 24 h at 25 °C and <0.2 Torr. When dry they were weighed, and the weights of the cyclic and linear fractions in each aliquot were determined. HPLC analysis of the "linear" fractions of each aliquot showed that they contained not only linear oligomers but also nearly all of the very large calixarenes **[15]**−**[20]**. Accordingly, the weights of the calixarene fraction and the linear oligomer fraction were adjusted based on the peak area percents of **[15]**−**[20]**. Plots of these data are shown in the Supporting Information.

Treatment of [5] and [7] with Acids and with Benzyl Alcohol. A solution containing 1.0 g of *p-tert*-butylcalix[5]arene and 1.0 g of *p-tert*-butylcalix[7]arene in 50 mL of amylenes-stabilized $CHCl_3$ was brought to reflux in an inert atmosphere in the apparatus described above for the acid-catalyzed condensation. At reflux 0.95 g (5.0 mmol) of $TsOH{\cdot}H_2O$ was added. After 80 min an aliquot was taken, and HPLC analysis showed that no reaction had occurred. At 90 min 0.67 g (0.64 mL, 6.16 mmol) of benzyl alcohol was added. Analysis of subsequent aliquots showed a growing presence of other peaks. After 16 h at reflux the heating was stopped, the solvent was removed in vacuo, and the residue was treated to remove the TsOH as described above. HPLC analysis of this residue showed the presence of at least 10 components. The residue was then triturated with hot $CHCl_3$ and filtered after standing at room temperature for 4 h to give ca. 20 mg of a white powder. HPLC analysis and ^1H NMR and ^{13}C NMR spectral analyses of the white powder indicated it to be a mixture of *p-tert*-butylcalix[4 and 8]arenes (**[4]** and **[8]**).

5,11,17,23,29,35,41,47,53-Nona-*tert*-butylcalix[9]arene-55,56,57,-58,59,60,61,62,63-nonol ([9]). An analytical sample of **[9]** was recrystallized twice from $CHCl_3$−acetone and once from toluene: mp 317−318.5 °C; ^1H NMR ($CDCl_3$) δ 9.78 (br s, 1, ArO*H*), 7.17 (s, 2, Ar*H*), 3.92 (br s, 2, ArCH_2Ar), 1.25 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.0, 144.3, and 127.8 (Ar), 125.7 (ArH), 34.0 (*C*(CH_3)$_3$), 32.4 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); FAB MS calcd 1459, found 1459. Anal. Calcd for $C_{99}H_{126}O_9$: C, 81.44; H, 8.70. Found: C, 81.13; H, 8.66.

5,11,17,23,29,35,41,47,53,59-Deca-*tert*-butylcalix[10]arene-61,62,-63,64,65,66,67,68,69,70-decol ([10]). An analytical sample of **[10]** was recrystallized once from $CHCl_3$−acetone and three times from toluene: mp 308−310 °C; ^1H NMR ($CDCl_3$) δ 9.24 (s, 1, ArO*H*), 7.14 (s, 2, Ar*H*), 3.91 (br s, 2, ArCH_2Ar), 1.24 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.0, 144.3, and 127.9 (Ar), 125.6 (ArH), 34.0 (*C*(CH_3)$_3$), 32.2 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); FAB MS calcd 1619, found 1619. Anal. Calcd for $C_{110}H_{140}O_{10}$: C, 81.44; H, 8.70. Found: C, 81.72; H, 8.74.

5,11,17,23,29,35,41,47,53,59,65-Undeca-*tert*-butylcalix[11]arene-67,68,69,70,71,72,73,74,75,76,77-undecol ([11]). An analytical sample of **[11]** was recrystallized three times from $CHCl_3$−MeOH: melts and resolidifies between 200 and 250 °C, melts to a glass at 308−310 °C; ^1H NMR ($CDCl_3$) δ 9.50 (s, 1, ArO*H*), 7.12 (s, 2, Ar*H*), 3.88 (s, 2, ArCH_2Ar), 1.23 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.1, 144.1, and 127.5 (Ar), 125.7 (ArH), 33.9 (*C*(CH_3)$_3$), 32.2 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); FAB MS calcd 1781, found 1784. Anal. Calcd for $C_{121}H_{154}O_{11}$: C, 81.44; H, 8.70. Found: C 81.21; H, 8.72.

5,11,17,23,29,35,41,47,53,59,65,71-Dodeca-*tert*-butylcalix[12]arene-73,74,75,76,77,78,79,80,81,82,83,84-dodecol ([12]). An analytical sample of **[12]** was recrystallized three times from $CHCl_3$−MeOH: shrinks near 287 °C, melts to a glass at 294−295.5 °C; ^1H NMR ($CDCl_3$) δ 9.53 (s, 1, ArO*H*), 7.09 (s, 2, Ar*H*), 3.82 (s, 2, ArCH_2Ar), 1.23 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.2, 144.2, and 127.6 (Ar), 125.7 (ArH), 33.9 (*C*(CH_3)$_3$), 32.4 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); MS (FAB) calcd 1945, found 1945. Anal. Calcd for $C_{132}H_{168}O_{12}$: C, 81.44; H, 8.70. Found: C, 82.13; H, 8.80.

5,11,17,23,29,35,41,47,53,59,65,71,77-Trideca-*tert*-butylcalix[13]-

arene-79,80,81,82,83,84,85,86,87,88,89,90,91-tridecol ([13]). An analytical sample of **[13]** was recrystallized three times from $CHCl_3$−MeOH: mp, shrinks at 248 °C then melts at 313−314 °C (if put in at 280 °C the sample immediately melts, refreezes, and then melts again at 313−314 °C); ^{1}H NMR ($CDCl_3$) δ 9.45 (s, 1, ArO*H*), 7.07 (s, 2, Ar*H*), 3.81 (br s, 2, ArCH_2Ar), 1.23 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.2, 144.1, and 127.5 (Ar), 125.7 (ArH), 33.9 (*C*(CH_3)$_3$), 32.2 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); MS (FAB) calcd 2107, found 2108. Anal. Calcd for $C_{143}H_{182}O_{13}$: C, 81.44; H, 8.70. Found: C, 81.49; H, 8.56.

5,11,17,23,29,35,41,47,53,59,65,71,77,83-Tetradeca-*tert*-butylcalix[14]arene-85,86,87,88,89,90,91,92,93,94,95,96,97,98-tetradecol ([14]). An analytical sample of **[14]** was recrystallized three times from CH_2Cl_2−MeOH to give desolvated crystals: mp shrinks at 220 °C, then melts at 317−320 °C (if the sample is put in at ca. 280 °C it immediately melts, then remelts at 317−320 °C); ^{1}H NMR ($CDCl_3$) δ 9.32 (s, 1, ArO*H*), 7.03 (s, 2, Ar*H*), 3.75 (s, 2, ArCH_2Ar), 1.21 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.1, 144.0, and 127.6 (Ar), 125.7 (ArH), 33.9 (*C*(CH_3)$_3$), 32.2 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); MS (FAB) calcd 2271, found 2270. Anal. Calcd for $C_{154}H_{196}O_{14}$: C, 81.44; H, 8.70. Found: C, 81.27; H, 8.48.

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89-Pentadeca-*tert*-butylcalix[15]arene-91,92,93,94,95,96,97,98,99,100,101,102,103, 104,105-pentadecol ([15]). An analytical sample was recrystallized twice from CH_2Cl_2−hexane: mp, shrinks at 222.5−227 °C, turns to a glass, becomes liquid by 295 °C; ^{1}H NMR ($CDCl_3$) δ 9.13 (s, 1, ArO*H*), 7.03 (s, 2, Ar*H*), 3.74 (br s, 2, ArCH_2Ar), 1.21 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.1, 144.0, and 127.6 (Ar), 125.6 (ArH), 33.9 (*C*(CH_3)$_3$), 32.0 (Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); MS (FAB) calcd 2431, found 2431 (stronger signal at 2413). Anal. Calcd for $C_{165}H_{210}O_{15}$: C, 81.44; H, 8.70. Found: C, 81.18; H, 8.69.

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89,95-Hexadeca-*tert*-butylcalix[16]arene-97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112-hexadecol ([16]). An analytical sample of **[16]** was recrystallized twice from EtOAc and once from $CHCl_3$−MeOH: mp, shrinks from 200 to 300 °C, then melts at 310−312 °C (if put in at 300 °C melts quickly implying a phase change at 250−300 °C); ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 1, ArO*H*), 6.98 (s, 2, Ar*H*), 3.69 (v br s, 2, ArCH_2Ar), 1.21 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.0, 143.9, and 127.8 (Ar), 125.5 (ArH), 33.9 (*C*(CH_3)$_3$), 31.9 (Ar*C*H_2Ar), 31.4 (C(*C*H_3)$_3$); MS (FAB) calcd 2593.67, found 2593.7. Anal. Calcd for $C_{176}H_{224}O_{16}$: C, 81.44; H, 8.70. Found: C, 81.05; H, 8.71.

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89,95,101-Heptadeca-*tert*-butylcalix[17]arene-103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119-heptadecol ([17]) was characterized only by ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 1, ArO*H*), 7.02 (s, 2, Ar*H*), 3.71 (br s, 2, ArCH_2Ar), 1.21 (s, 9, C(CH_3)$_3$) and ^{13}C NMR ($CDCl_3$) δ 147.25, 144.00, and 127.63 (Ar), 125.7 (ArH), 33.93 (*C*(CH_3)$_3$), 31.99 (Ar*C*H_2-Ar), 31.50 (C(*C*H_3)$_3$).

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89,95,101,107-Octadeca-*tert*-butylcalix[18]arene-109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126-octadecol ([18]) was characterized only by ^{1}H NMR ($CDCl_3$) δ 8.98 (br s, 1, ArO*H*), 6.99 (s, 2, Ar*H*), 3.70 (br s, 2, ArCH_2Ar), 1.19 (s, 9, C(CH_3)$_3$) and ^{13}C NMR ($CDCl_3$) δ 147.25, 143.97, and 127.63 (Ar), 125.60 (ArH), 33.93 (*C*(CH_3)$_3$), 32.00 (Ar*C*H_2Ar), 31.50 (C(*C*H_3)$_3$).

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89,95,101,107,113-Nonadeca-*tert*-butylcalix[19]arene-115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133-nonadecol ([19]) was characterized only by ^{1}H NMR ($CDCl_3$) δ 9.06 (br s, 1, ArO*H*), 6.99 (br s, 2, Ar*H*), 3.70 (v br s, 2, ArCH_2Ar), 1.19 (s, 9, C(CH_3)$_3$) and ^{13}C NMR ($CDCl_3$) δ 147.23, 143.88, and 127.53 (Ar), 125.58 (ArH), 33.9 (*C*(CH_3)$_3$), 32.0 (Ar*C*H_2Ar), 31.4 (C(*C*H_3)$_3$).

5,11,17,23,29,35,41,47,53,59,65,71,77,83,89,95,101,107,113,119-Eicosa-*tert*-butylcalix[20]arene-121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140-eicosol ([20]). An analytical sample of **[20]** was recrystallized twice from $CHCl_3$−MeOH: mp, shrinks at 279 °C, becomes translucent at 288 °C, melts to a glass at 290−292 °C, becomes a viscous liquid at 309−311 °C and a clear liquid at 325 °C; ^{1}H NMR ($CDCl_3$) δ 8−10 (overlapping br s, 1, ArO*H*), 5.8−7.4 (overlapping br s, 2, Ar*H*), 2.2−4.6 (overlapping br s, 2, ArCH_2Ar), 1.2−1.4 (overlapping br s, 9, C(CH_3)$_3$); ^{1}H NMR ($CDCl_3$:pyridine-d_5 6:1) δ 7.68 (v br s, 1, ArO*H*), 7.05 (s, 2, Ar*H*), 3.88 (s, 2, ArCH_2Ar), 1.18 (s, 9, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147, 144, and 127 (v br s, Ar), 125.4 (ArH), 33.9 (*C*(CH_3)$_3$), 30−32 (v br s, Ar*C*H_2Ar), 31.5 (C(*C*H_3)$_3$); ^{13}C NMR ($CDCl_3$:pyridine-d_5 6:1) δ 150.4, 143.2, 128.6, and 125.9 (Ar), 34.2 (*C*(CH_3)$_3$), 32.4 (Ar*C*H_2-Ar), 31.7 (C(*C*H_3)$_3$); MS (FAB) calcd 3242.0, found 3242.8. Anal. Calcd for $C_{220}H_{280}O_{20}$: C, 81.44; H, 8.70. Found: C, 81.42; H, 8.82.

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Supporting Information Available: Plot of the average molecular weights of the reaction mixtures as a function of concentration in the acid-catalyzed condensation of *p-tert*-butylphenol and *s*-trioxane; plots of concentration of products as a function of time from the acid-catalyzed reaction *of p-tert*-butylphenol and *s*-trioxane; plots of total energies, bond energies, angle energies, Lennard-Jones energies, and electrostatic energies for energy-minimized structures of *p-tert*-butylcalix[*n*]-arenes ($n = 4-20$); and pictures of computer-generated energy-minimized structures for *p-tert*-butylcalix[n]arenes ($n = 4-20$) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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