14b, 42541-96-8; $CH_2{=}CHCH_2I$, 556-56-9; $CH_2{=}CHCH_2Br$, 106-95-6; $PhCH_2I$, 620-05-3; $PhCH_2Br$, 100-39-0; PhSeCl, 5707-04-0; $CH_3CH{=}CHCH_2Br$, 4784-77-4; $CH_3CH_2C{\equiv}CH_2I$, 34498-11-8; $CH_3O_2C(CH_2)_3C{\equiv}CCH_2I$, 31776-12-2; $CH_3O_2C(CH_2)_3CH{=}CHCH_2I$, 64493-06-7; (tributylstannyl)lithium, 4226-01-1.

Supplementary Material Available: ^1H NMR spectra for compounds 5c, 6d, 6e, and 6f (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Calixarenes. 28. Synthesis, Structures, and Conformations of Aroylates of Calix[6]arenes

Janet S. Rogers and C. David Gutsche*

Departments of Chemistry of Texas Christian University, Fort Worth, Texas 76129, and Washington University, St. Louis, Missouri 63130

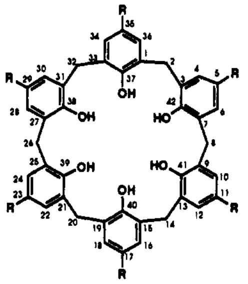
Received November 20, 1991

A study of the aroylation of calix[6]arenes under a variety of conditions has shown that the reaction often yields the 1,2,4,5-tetraester as a major product but that the outcome is dependent both on the aroylating agent and the calixarene. The best results have been obtained with *p*-nitrobenzoyl chloride which reacts with *p*-*tert*-butylcalix[6]arene (**1a**) to yield a separable mixture containing ca. 40% tetraester **2a** and 30% pentaester **3** when NaH is used as the base or up to 85% of the tetraester when 1-methylimidazole is used as the base. In comparable fashion benzoyl chloride and *p*-nitrobenzoyl chloride react with **1a** and **1b**, respectively, to yield the tetraesters **2b** and **2c**, whereas *p*-allylcalix[6]arene (**1c**) reacts under the same conditions to produce the hexaester **6**. With limiting amounts of *p*-nitrobenzoylating agent the diesters **4** and **5** have been isolated in low yields. 3,5-Dinitrobenzoyl chloride gives less satisfactory results, producing mixtures containing six or more esters from which only small amounts of the 1,2,4,5-tetraester **2d** have been isolated. The structure and conformation of the products have been established by elemental analysis, mass spectral measurements, and ^1H NMR techniques. In the case of **2a** this includes difference NOE and transient NOE determinations which show that the compound exists in a conformation in which two of the aroylated moieties are canted inward so that their *p*-*tert*-butyl groups occupy the two faces of the calix[6]arene cavity, thus self-complexing the compound and preventing intermolecular complexation.

The increasing attention currently being devoted to the $[1_n]$metacyclophanes known as calixarenes[1] is focusing principally on the calix[4]arenes, these members of the series possessing the minimum of functionality and conformational flexibility. Although the larger calixarenes have received a modicum of attention, their higher degree of functionality and greater conformational flexibility complicate their chemistry and make isolations and characterizations an often difficult task. The present work addresses this problem in the case of certain aromatic esters of *p*-*tert*-butylcalix[6]arene (**1a**), *p*-H-calix[6]arene (**1b**), and *p*-allylcalix[6]arene (**1c**).[2] First, the syntheses of these compounds are presented, followed by discussions of their structures, conformations, and complexing characteristics.

Synthesis of Aroylates of Calix[6]arenes

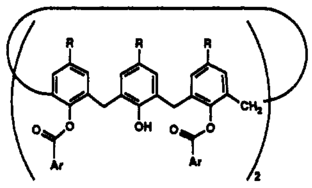
3,5-Dinitrobenzoates. The work described in this paper had its inception in the hope that calix[6]arenes **1** could be selectively esterified with 3,5-dinitrobenzoylating agents in a manner analogous to the calix[4]arenes[3] and thus provide a starting material for the synthesis of double-cavity calix[6]arenes.[4] However, early attempts in the present investigation to isolate pure materials from reaction mixtures obtained by the action of 3,5-dinitrobenzoylating agents on *p*-*tert*-butylcalix[6]arene (**1a**) and *p*-H-calix[6]arene (**1b**) gave difficultly separable mixtures. For example, products containing from 6 to 10 or more components were obtained when **1a** was treated with 3,5-dinitrobenzoyl chloride in the presence of NaH or 1-methylimidazole or with 3,5-dinitrobenzoic acid in the presence of phenyl dichlorophosphate. Only late in the investigation was a compound obtained in low yield from one of these reaction mixtures that was identified as the tetraester **2d**.



1a (R = *tert*-Butyl)

1b (R = H)

1c ($R = CH_2CH{=}CH_2$)



2a (R = *tert*-Butyl, Ar = $-C_6H_4-NO_2$)

2b (R = H, Ar = $-C_6H_5$)

2c (R = *tert*-Butyl, Ar = $-C_6H_4-NO_2$)

2d (R = *tert*-Butyl, Ar = $-C_6H_3(NO_2)_2$)

---

[1] Gutsche, C. D. *Calixarenes*; Stoddart, F. J., Ed.; Monographs in Supramolecular Chemistry; The Royal Society of Chemistry: Cambridge, 1989, Vol. 1.

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

[3] See, K. A.; Fronczek, F. R.; Watson, W. H.; Gutsche, C. D. *J. Org. Chem.* 1991, *56*, 7256.

[4] Gutsche, C. D.; See, K. A. To be published.

0022-3263/92/1957-3152$03.00/0

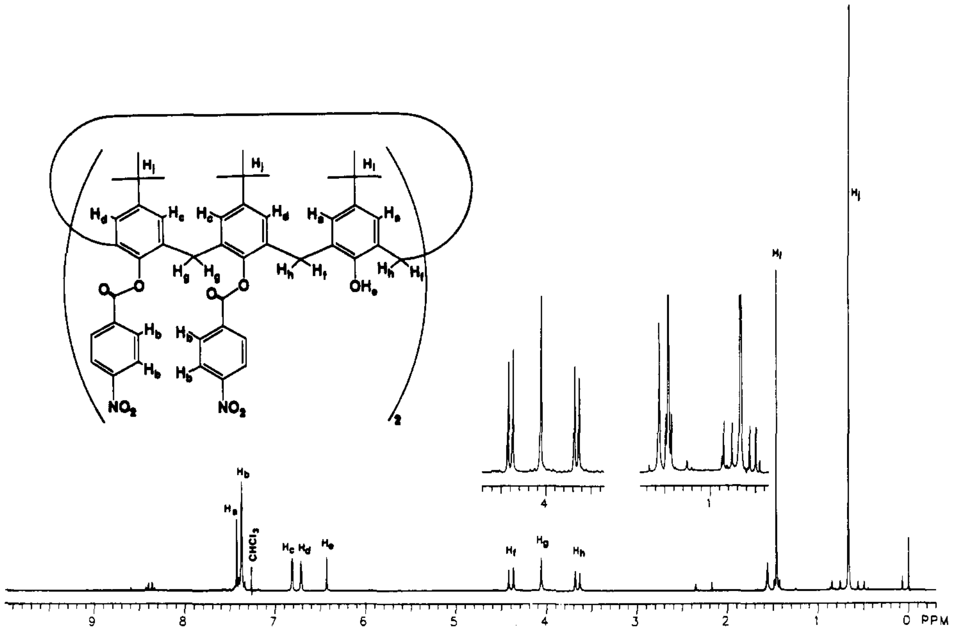
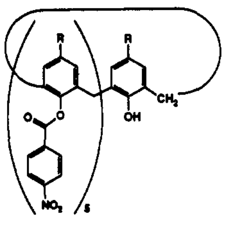


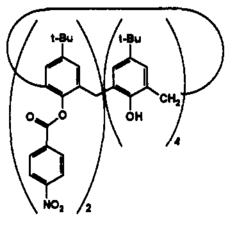
Figure 1. ^{1}H NMR spectrum of **2a** in CDCl$_3$ (300 MHz, 25 °C).

4-Nitrobenzoates. With the realization that well-defined 3,5-dinitrobenzoates of calix[6]arenes are not easily attained, attention was turned to the *p*-nitrobenzoates, since these compounds also possess the potential for carrying out bridging reactions with the corresponding amines. The results in this case were more rewarding, treatment of *p-tert*-butylcalix[6]arene (**1a**) with *p*-nitrobenzoyl chloride and NaH in THF producing a mixture that affords, upon chromatographic separation, ca. 40% of a higher-melting component identified as the tetraester **2a** and ca. 30% of a lower-melting component identified as the pentaester **3**. Roughly comparable results are obtained using **1a** and *p*-nitrobenzoic acid in the presence of phenyl dichlorophosphate, but with *p*-nitrobenzoyl chloride in the presence of 1-methylimidazole[3] **2a** is obtained in yields as high as 85%.

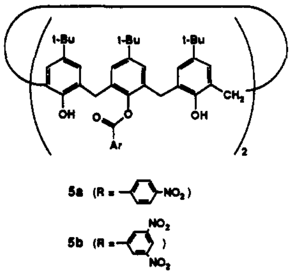
The relative simplicity of the product mixtures obtained with an excess of *p*-nitrobenzoylating agent prompted further investigation using smaller amounts in the hope of securing less highly esterified calix[6]arenes. When the NaH procedure is used with a limiting amount of *p*-nitrobenzoyl chloride a mixture is produced from which two compounds have been isolated. These are identified as the 1,2-diester **4**, obtained in ca. 1% yield; and the 1,4-diester **5**, obtained in 10% yield. Considerably higher yields (ca. 39%) of **4** are obtained from **1a** and *p*-nitrobenzoic acid in the presence of diphenyl chlorophosphate and pyridine, this procedure having the further advantage of requiring only a simple workup rather than a chromatographic separation. Attempts to isolate mono- and/or tri-*p*-nitrobenzoates of **1a** have been unsuccessful, although the presence of what is assumed to be the monoester is indicated by HPLC analyses of the crude reaction mixture.

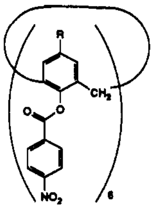


3



4





6

In contrast to *p-tert*-butylcalix[6]arene (**1a**), the calixarene lacking the *tert*-butyl group (**1b**) reacts with *p*-nitrobenzoylating agents to give mixtures from which it has not yet been possible to isolate pure compounds. *p*-Allylcalix[6]arene (**1c**), on the other hand, undergoes complete esterification with *p*-nitrobenzoyl chloride in the presence of NaH to afford the hexaester **6**.

Benzoates. Gutsche and Lin[5] reported that treatment of *p*-H-calix[6]arene (**1b**) with benzoyl chloride in the presence of pyridine yields a high melting compound which they assumed to be the hexaester **6**, although no substantiating analytical data were reported.

In the present investigation the reaction of **1b** with benzoyl chloride in the presence of NaH yielded a compound possessing analytical data more compatible with the tetraester **2b** than a hexaester or a pentaester. Similarly, *p-tert*-butylcalix[6]arene (**1a**) gives the tetrabenzoate **2c** as the major product, isolated in 78% yield.

Structure and Conformation of Aroylates of Calix[6]arenes

Tetrakis(4-nitrobenzoate) of *p-tert*-Butylcalix[6]arene (2a). The elemental analysis and mass spectral data of the major product obtained by the action of *p*-nitrobenzoyl chloride on **1a** in the presence of NaH or 1-methylimidazole provide clear evidence for a tetraester. This is supported by the ^{1}H NMR spectrum of **2a**, shown in Figure 1. Of particular relevance are the pair of high-field singlets in a ratio of 2:1 arising from the *tert*-butyl protons and the pair of doublets with an intervening singlet in the δ 4–5 region arising from the methylene protons. Of the 54 structure/conformation possibilities for a tetraester[6] only the four conformational isomers of

---

(5) Gutsche, C. D.; Lin, L.-G. *Tetrahedron* **1986**, *42*, 1633.

Table I. Difference NOE Values for 2a Based on Peak Integrals

proton saturated	proton observed A	B	C	D	E	F	G	H	I	J
A	–	−11.3	−0.3	4.8	1.3	−0.2	0.0	3.3	1.5	0.0
B	−8.5	–	0.6	2.2	10.1	1.3	0.4	0.6	0.3	0.3
C	0.8	0.3	–	−14.9	−1.1	−1.0	4.4	0.8	−0.1	0.4
D	3.9	0.5	−9.5	–	−2.3	−1.0	0.1	1.4	−0.1	0.8
E	0.3	2.9	−1.7	−11.1	–	3.1	0.5	0.2	0.3	0.1
F	−0.7	1.4	0.8	0.0	10.6	–	−5.4	18.1	0.4	0.1
G	−0.6	0.1	17.0	0.4	0.4	−4.2	–	0.6	0.5	0.0
H	10.1	−0.1	0.3	4.6	0.6	17.7	−2.9	–	0.3	0.2
I	6.3	0.6	−0.1	0.7	−0.5	1.4	0.4	0.5	–	−0.9
J	−0.6	0.9	6.3	8.4	−0.1	−0.1	−0.4	0.1	−0.2	–

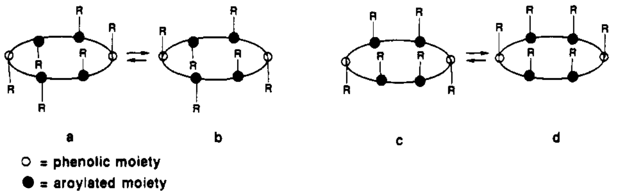


Figure 2. Structure/conformation possibilities for a 1,2,4,5-tetraester possessing a ^{1}H NMR spectrum showing two *tert*-butyl resonances in a 2:1 ratio.

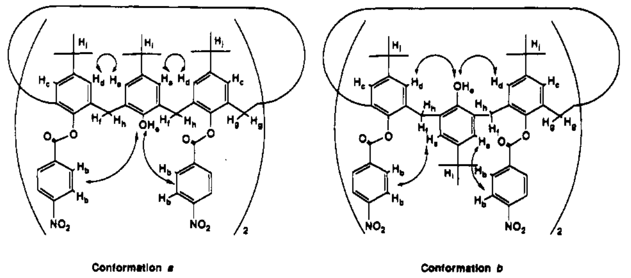


Figure 3. Expected NOE enhancements for conformations a and b of **2a**.

a calix[6]arene substituted in a 1,2,4,5-fashion, as illustrated in Figure 2, would be predicted to generate a pair of *tert*-butyl resonances in a 2:1 ratio. Among these four, only structures a and b in which the adjacent aroyl moieties are anti to one another would generate the pattern shown in Figure 1, thus quickly reducing the structure/conformation determination of **2a** to a choice between the 1,2,3-alternate conformation (structure a) and the 1,3,5-alternate conformation (structure b). Although structures a and b are interconvertible by rotation of the phenol moieties through the annulus of the calix[6]arene one of the structures is likely to be sufficiently more stable than the other to constitute the major conformer at room temperature.[7] To select between these two possibilities, nuclear Overhauser effect (NOE) experiments were undertaken.

An attempt to obtain NOE data for **2a** from a 2D-NOESY experiment showed only an interaction between the coupled *gem* protons, a consequence of the particular size of **2a** which places its molecular correlation time in a region where the ^{1}H NOE is at a minimum.[8] Therefore, a 1D-NOE experiment was carried out on a degassed sample of **2a**, producing the results shown in Table I. The large negative values arise from peaks adjacent to the resonance lines that are being irradiated, and they are probably the result of partial saturation by the irradiating pulse. Figure 3 shows the groups that would be expected to experience NOE enhancement if **2a** is in conformations a and b. In choosing between these alternatives attention is focused particularly on the interaction between protons H_a/H_d and H_b/H_e (conformer a in Figure 3) and protons H_a/H_b and H_d/H_e (conformer b in Figure 3). The observation is that when H_a is irradiated enhancements occur in the signals for H_d and H_h; when H_b is irradiated H_e shows a significant enhancement and H_d shows a small enhancement. Reciprocally, irradiation of H_d causes enhancement of H_a and, to a lesser extent, H_h; irradiation of H_e affects the signals of H_b and H_f. Thus, conformation a appears to be the proper representation for compound **2a**. Other NOE interactions having less relevance to the choice between conformers a and b are also noted. For example, irradiation of H_c enhances the methylene protons H_g (reciprocally, irradiation of H_g enhances H_c); irradiation of H_f gives sizeable enhancements to H_e and H_h; and irradiation of H_h affects H_a, H_d, and H_f. Irradiations of the *tert*-butyl protons H_i and H_j involve only the aromatic protons ortho to the *tert*-butyl groups; H_i affects H_a, and H_j affects H_c and H_d. The most pertinent of the NOE enhancements noted above were further verified by measuring difference NOE spectra which showed positive results for the H_a/H_d and H_b/H_e sets of interactions and negative results for the H_a/H_b and H_d/H_e sets of interactions.

Table II. Proton–Proton Distances in 2a at 25 °C in $CDCl_3$ (the Values in Brackets Are Calculated from the SYBYL Molecular Modeling Program)

proton observed	proton saturated J r, Å	I r, Å	E r, Å
A	2.80	[2.74]	[4.71]
B	2.89	3.15	4.34
C	[2.74]	3.95	5.54
D	[2.74]	3.39	5.64
E	2.72	[5.79]	–
F	3.08	3.51	4.36
G	3.28	4.14	4.92
H	3.18	4.31	5.52
I	2.63	–	[5.79]
J	–	5.08	4.64

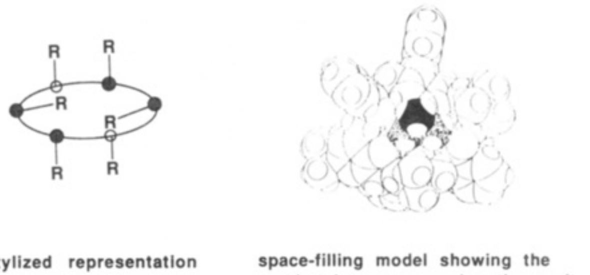
The NOE diminishes by the sixth power of the distance and generally can be observed only when no more than ca. 5 Å separates the interacting nuclei.[8] Through the use of transient NOE techniques the actual distance between the

---

(6) The supplementary material includes a tabulation of the ^{1}H NMR patterns that would be expected from each of the 144 regiochemical/conformational possibilities for *p-tert*-butylcalix[6]arenes that are monosubstituted (equivalent to pentasubstituted), disubstituted (equivalent to tetrasubstituted), or trisubstituted. The conformations are expressed in terms of the aryl moieties being "up" or "down" with respect to the average plane for the system. For each of the "up, down" conformations, however, many additional conformations are possible in which one or more of the aryl moieties assume positions away from the vertical, the limit being an "out" orientation in which the aryl moiety is parallel with the average plane of the system.

(7) The interconvertibility of partially esterified calixarenes is illustrated by the exmaple of a bis(3,5-dinitrobenzoyl) ester of *p-tert*-butylcalix[4]arene which exists in solution predominantly in the 1,3-alternate conformation but crystallizes in the partial cone conformation.[3]

(8) Wüthrich, K. *NMR of Proteins and Nucleic Acids*; John Wiley & Sons: New York, 1986.



stylized representation

space-filling model showing the *tert*-butyl group covering the cavity

Figure 4. Schematic representation and space-filling model of twisted 1,2,3-alternate conformation of **2a**.

Table III. Distances between H_j and Other Protons in 2a (the Values in Brackets Are Calculated from the SYBYL Molecular Modeling Program)

proton observed at 40 °C	r, Å at −15 °C	r, Å at 40 °C
H_a	2.43	2.41
H_b	3.56	2.54
H_c	[2.74]	[2.74]
H_d	[2.74]	[2.74]
H_e	2.78	3.28
H_f	3.80	2.63
H_g	3.49	2.89
H_h	3.21	2.72
H_i	2.37	2.62

interacting nuclei can be approximated with moderate accuracy. Using a pulse sequence involving an equilibrium delay, a selective 180° pulse, a variable delay, and a nonselective pulse the distances in **2a** were calculated from the equation

$$r = (\text{slope of standard/slope of unknown})^{1/6}(r_{\text{std}})$$

where r_{std} is a fixed, known distance within the molecule, r is the unknown distance, and the slopes are values obtained from plots of the NOE versus time. Experiments were performed involving the irradiation of the *tert*-butyl protons H_i and H_j and the hydroxyl proton H_e to give the results shown in Table II. The r_{std} is the distance between the center of the *tert*-butyl group and the aromatic hydrogen ortho to it, calculated from the SYBYL molecular modeling program. While some of the distances provided by the transient NOE measurements clearly are inaccurate, the fact that the distance between H_e and H_b is shorter than that between H_e and H_i is commensurate with conformation a. The proximity of the *tert*-butyl group of the aroylated moiety to the OH group of the adjacent moiety (2.72 Å when H_j is irradiated; 4.64 Å when H_e is irradiated) suggests that two of the aroylated moieties are canted inward so that their *tert*-butyl groups fill the the cavity of the calixarene on both faces, as illustrated in Figure 4. The distances between H_j and the other protons in **2a** at 40 and −15 °C are shown in Table III. While there appear to be some changes in distances upon cooling, the distance between H_j and H_g diminishing and the distances between H_j and the methylene protons H_f, H_g, and H_h increasing, the changes are relatively small and are in accord with a conformationally inflexible system (see later discussion).

Almost imperceptible in the ^{1}H NMR spectrum of **2a** as it is ordinarily displayed but becoming apparent upon magnification (see insert in Figure 1) are six additional singlets (ratio 1:1:1:1:1:1) in the *tert*-butyl region along with additional multiplets in the methylene region. These resonances are thought to be due to the presence of a small amount of one of the 29 other tetrakis(*p*-nitrobenzoates) of *p*-*tert*-butylcalix[6]arene that would show six *tert*-butyl resonances of equal intensity.[6] That the compound is a tetraester is indicated by the ratio of the combined integrals for the six *tert*-butyl resonances and the two OH resonances.

Tetrabenzoate of *p*-*tert*-Butylcalix[6]arene (2c) and *p*-H-Calix[6]arene (2b). The product of benzoylation of **1a** has an elemental analysis in agreement with the tetraester **2c**, a mass spectral line at 1390 corresponding to the parent ion of **2c**, and a ^{1}H NMR spectrum showing a methylene region characterized by a pair of doublets at δ 3.55 and 4.35 with an intervening singlet at δ 4.05, diagnostic for a 1,2,4,5-tetraester. The product of benzoylation of **1b** similarly has an elemental analysis consistent with the tetraester **2b**, an osmometric molecular weight of 1059 (calcd 1053), and a ^{1}H NMR spectrum showing a methylene region characterized by a pair of doublets (δ 3.34 and 3.72) and a singlet at δ 3.25. The upfield shifts of the doublets and singlet arising from the methylene protons in **2b** as well as the smaller chemical shift between the doublets as compared with **2a** and **2c** are probably a consequence of changes in the geometry of the 1,2,3-alternate conformation resulting from the replacement of *tert*-butyl groups with hydrogens. It is known that in the calix[4]arenes the magnitude of the chemical shift between the high- and low-field methylene resonances is sensitive to changes in the nature of the cone, increasing in the "parallel" cone conformation and decreasing in the "flattened" cone conformation.[9] This point is discussed in more detail in the following paper.[10]

Tetrakis(3,5-dinitrobenzoate) of *p*-*tert*-Butylcalix[6]arene (2d). The product isolated in low yield from the treatment of **1a** with 3,5-dinitrobenzoyl chloride in the presence of NaH or 1-methylimidazole possesses an elemental analysis commensurate with a tetraester, the C, H, and N values for which differ from those of a triester or pentaester by significant amounts. The identity of the tetraester is further confirmed by the mass spectrum which has strong signals at 1360 (corresponding to a $M^+ - 1$), 1166 (corresponding to the loss of a 3,5-dinitrobenzoyl moiety), and 1148 (corresponding to the loss of a (3,5-dinitrobenzoyl)oxy moiety). The ^{1}H NMR spectrum shows a pair of doublets at δ 3.70 and 3.49 and a broad singlet at δ 4.0 in the methylene region, in reasonable agreement with a 1,2,4,5-tetraester. However, the presence of four *tert*-butyl resonances in the ^{1}H NMR spectrum as well as the appearance of 22 resonances in the ^{13}C NMR spectrum (a tetraester in the 1,2,3-alternate conformation would be expected to have 17) indicates that the product also contains one or more other compounds, presumably conformational isomers of the 1,2,4,5-tetraester.

Pentakis(4-nitrobenzoate) of *p*-*tert*-Butylcalix[6]arene (3). The characterization of the pentaester rests primarily on the elemental analytical and mass spectral data. The ^{1}H NMR spectrum of **3**, shown in Figure 5, displays a surprisingly simple pattern of three lines arising from the *tert*-butyl protons, several pairs of doublets from the methylene protons, and a moderately complex set of resonances from the aromatic protons. The relative simplicity of the spectrum, however, belies the true nature of the product, because HPLC analysis indicates that the pentaester is a mixture of at least three conformers.

Bis(4-nitrobenzoates) of *p*-*tert*-Butylcalix[6]arene 4 and 5. The characterization of the 1,2-diester **4** is based on its elemental analysis, mass spectrum, and ^{1}H NMR spectrum which, as shown in Figure 6, displays three lines from the *tert*-butyl hydrogens and a pattern from the

---

[9] Reference 1, pp 110–11.

[10] Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.*, following paper in this issue.

stylized representation

space-filling model showing the *tert*-butyl group covering the cavity

Figure 4. Schematic representation and space-filling model of twisted 1,2,3-alternate conformation of **2a**.

Table III. Distances between H_j and Other Protons in 2a (the Values in Brackets Are Calculated from the SYBYL Molecular Modeling Program)

proton observed at 40 °C	r, Å at −15 °C	r, Å at 40 °C
H_a	2.43	2.41
H_b	3.56	2.54
H_c	[2.74]	[2.74]
H_d	[2.74]	[2.74]
H_e	2.78	3.28
H_f	3.80	2.63
H_g	3.49	2.89
H_h	3.21	2.72
H_i	2.37	2.62

interacting nuclei can be approximated with moderate accuracy. Using a pulse sequence involving an equilibrium delay, a selective 180° pulse, a variable delay, and a nonselective pulse the distances in **2a** were calculated from the equation

$$r = (\text{slope of standard}/\text{slope of unknown})^{1/6}(r_{\text{std}})$$

where r_{std} is a fixed, known distance within the molecule, r is the unknown distance, and the slopes are values obtained from plots of the NOE versus time. Experiments were performed involving the irradiation of the *tert*-butyl protons H_i and H_j and the hydroxyl proton H_e to give the results shown in Table II. The r_{std} is the distance between the center of the *tert*-butyl group and the aromatic hydrogen ortho to it, calculated from the SYBYL molecular modeling program. While some of the distances provided by the transient NOE measurements clearly are inaccurate, the fact that the distance between H_e and H_b is shorter than that between H_e and H_i is commensurate with conformation a. The proximity of the *tert*-butyl group of the aroylated moiety to the OH group of the adjacent moiety (2.72 Å when H_j is irradiated; 4.64 Å when H_e is irradiated) suggests that two of the aroylated moieties are canted inward so that their *tert*-butyl groups fill the the cavity of the calixarene on both faces, as illustrated in Figure 4. The distances between H_j and the other protons in **2a** at 40 and −15 °C are shown in Table III. While there appear to be some changes in distances upon cooling, the distance between H_j and H_g diminishing and the distances between H_j and the methylene protons H_f, H_g, and H_h increasing, the changes are relatively small and are in accord with a conformationally inflexible system (see later discussion).

Almost imperceptible in the ^1H NMR spectrum of **2a** as it is ordinarily displayed but becoming apparent upon magnification (see insert in Figure 1) are six additional singlets (ratio 1:1:1:1:1:1) in the *tert*-butyl region along with additional multiplets in the methylene region. These resonances are thought to be due to the presence of a small amount of one of the 29 other tetrakis(*p*-nitrobenzoates) of *p*-*tert*-butylcalix[6]arene that would show six *tert*-butyl resonances of equal intensity.[6] That the compound is a tetraester is indicated by the ratio of the combined integrals for the six *tert*-butyl resonances and the two OH resonances.

Tetrabenzoate of *p*-*tert*-Butylcalix[6]arene (2c) and *p*-H-Calix[6]arene (2b). The product of benzoylation of **1a** has an elemental analysis in agreement with the tetraester **2c**, a mass spectral line at 1390 corresponding to the parent ion of **2c**, and a ^1H NMR spectrum showing a methylene region characterized by a pair of doublets at δ 3.55 and 4.35 with an intervening singlet at δ 4.05, diagnostic for a 1,2,4,5-tetraester. The product of benzoylation of **1b** similarly has an elemental analysis consistent with the tetraester **2b**, an osmometric molecular weight of 1059 (calcd 1053), and a ^1H NMR spectrum showing a methylene region characterized by a pair of doublets (δ 3.34 and 3.72) and a singlet at δ 3.25. The upfield shifts of the doublets and singlet arising from the methylene protons in **2b** as well as the smaller chemical shift between the doublets as compared with **2a** and **2c** are probably a consequence of changes in the geometry of the 1,2,3-alternate conformation resulting from the replacement of *tert*-butyl groups with hydrogens. It is known that in the calix[4]arenes the magnitude of the chemical shift between the high- and low-field methylene resonances is sensitive to changes in the nature of the cone, increasing in the "parallel" cone conformation and decreasing in the "flattened" cone conformation.[9] This point is discussed in more detail in the following paper.[10]

Tetrakis(3,5-dinitrobenzoate) of *p*-*tert*-Butylcalix[6]arene (2d). The product isolated in low yield from the treatment of **1a** with 3,5-dinitrobenzoyl chloride in the presence of NaH or 1-methylimidazole possesses an elemental analysis commensurate with a tetraester, the C, H, and N values for which differ from those of a triester or pentaester by significant amounts. The identity of the tetraester is further confirmed by the mass spectrum which has strong signals at 1360 (corresponding to a $M^+ - 1$), 1166 (corresponding to the loss of a 3,5-dinitrobenzoyl moiety), and 1148 (corresponding to the loss of a (3,5-dinitrobenzoyl)oxy moiety). The ^1H NMR spectrum shows a pair of doublets at δ 3.70 and 3.49 and a broad singlet at δ 4.0 in the methylene region, in reasonable agreement with a 1,2,4,5-tetraester. However, the presence of four *tert*-butyl resonances in the ^1H NMR spectrum as well as the appearance of 22 resonances in the ^{13}C NMR spectrum (a tetraester in the 1,2,3-alternate conformation would be expected to have 17) indicates that the product also contains one or more other compounds, presumably conformational isomers of the 1,2,4,5-tetraester.

Pentakis(4-nitrobenzoate) of *p*-*tert*-Butylcalix[6]arene (3). The characterization of the pentaester rests primarily on the elemental analytical and mass spectral data. The ^1H NMR spectrum of **3**, shown in Figure 5, displays a surprisingly simple pattern of three lines arising from the *tert*-butyl protons, several pairs of doublets from the methylene protons, and a moderately complex set of resonances from the aromatic protons. The relative simplicity of the spectrum, however, belies the true nature of the product, because HPLC analysis indicates that the pentaester is a mixture of at least three conformers.

Bis(4-nitrobenzoates) of *p*-*tert*-Butylcalix[6]arene 4 and 5. The characterization of the 1,2-diester **4** is based on its elemental analysis, mass spectrum, and ^1H NMR spectrum which, as shown in Figure 6, displays three lines from the *tert*-butyl hydrogens and a pattern from the

---

(9) Reference 1, pp 110–11.

(10) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.*, following paper in this issue.

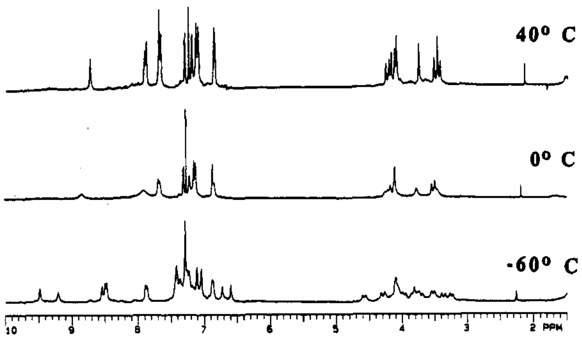


Figure 10. ^{1}H NMR spectrum of 4 in $CDCl_3$ (300 MHz) at 55 to −60 °C.

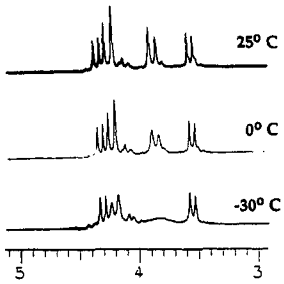


Figure 11. ^{1}H NMR spectrum of the 1,4-diester **5a** in $CDCl_3$ (300 MHz) at 25 to −30 °C.

arc in the vicinity of H_h during its rocking.

The 1,2-diester 4 at room temperature shows a well-resolved 10-line pattern, arising from the CH_2 protons, that remains essentially invariant up to 55 °C. Upon cooling, however, it changes in the manner illustrated in Figure 10, a quasi coalescence point being observed at ca. −40 °C. Below this temperature the system appears to exist as two or more conformers (i.e., nine or more doublets). The temperature-dependent ^{1}H NMR spectrum of the 1,4-diester **5a** presents a more complex picture; upon cooling, only some of the CH_2 resonances broaden while others remain sharp, as shown in Figure 11. A selective broadening of these resonances is also observed at room temperature upon the addition of F_3CCO_2D; concomitantly there is a downfield shift of some of the resonance lines that remain sharp. The reasons for this behavior are not yet understood.

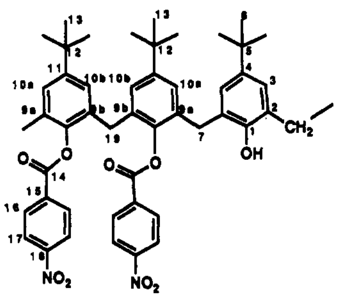
Complexation Studies with Calix[6]arenes

It was hoped that the tetrakis(*p*-nitrobenzoate) of *p*-*tert*-butylcalix[6]arene (**2a**) would form tight complexes with a variety of molecules, particularly flat hydrocarbons that might take advantage of π–π interactions with the *p*-nitrobenzoyl moieties. However, compounds such as naphthalene and anthracene fail to give any indication of complex formation with **2a**, a result that can be ascribed to self complexation of **2a** as revealed by the transient NOE experiments described above. Even amines, which interact with the parent calixarenes, give little if any response with **2a**, although the 1,2-diester 4 does interact with amines such as 1,5-diaminonaphthalene, 1,8-diaminonaphthalene, 1-aminoanthracene, and 1-aminopyrene in $CHCl_3/CH_3CN$ (4:1) solution; the nature of the interaction has not yet been studied in detail.

To assess the nature of a chemical environment Dimroth has made use of pyridinium phenoxides whose spectra are sensitive to the polarity of the medium in which they reside.[12,13] When compounds **2a** and 3 are mixed with these reagents spectral changes are, in fact, noted, although not a shift to the longer wavelength that might be anticipated if the reagent resides inside the cavity of the calixarene. Instead, only the absorptivities are perturbed, providing data that will be published at a later date.

Experimental Section[14]

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(4-nitrobenzoyl)oxy]calix[6]arene (2a). (A) NaH Method. A solution of a 2.00-g (2.05 mmol) sample of *p*-*tert*-butylcalix[6]arene (**1a**)[17] in 300 mL of freshly distilled THF was stirred magnetically under N_2 as 2.08 g (52 mmol) of 60% NaH in mineral oil was added. After the solution was stirred for 30 min a solution of 7.30 g (39 mmol) of 4-nitrobenzoyl chloride in 100 mL of toluene was added dropwise over 1 h, the mixture was brought to reflux, and refluxing was continued for 4.5 h. It was then cooled and neutralized with 250 mL of 0.5 M Na_2CO_3 solution and the resulting layered mixture stirred overnight. The layers were separated, and the organic phase was washed twice with 125 mL of Na_2CO_3 and 125 mL of H_2O and filtered to remove the solid at the interface and then washed again with H_2O and twice with 250 mL of concd NaCl solution. Removal of the solvent left 5.05 g of crude product as a yellow powder which was chromatographed on a silica gel column using CH_2Cl_2–hexane as eluant. The higher R_f fractions were combined and recrystallized from $CHCl_3$–MeOH to give 1.40 g (43%) of **2a** as pale yellow crystals: mp 358 °C dec; IR (KBr, cm^{-1}) 3510 (OH stretching), 1700, 1660 (C═O stretching), 1530, 1345 (NO_2 stretching); ^{1}H NMR ($CDCl_3$) δ 7.40 (s, 4, ArH), 7.36 (d, 8, *p*-NO_2BzH), 7.32 (d, 8, *p*-NO_2BzH), 6.81 (d, 4, J = 2.0 Hz, *p*-NO_2BzOAr*H*), 6.72 (d, 4, J = 2.0 Hz, *p*-NO_2BzOAr*H*), 6.45 (s, 2, OH), 4.33 (d, 4, *p*-NO_2BzArC*H*$_2$ArOH), 4.07 (s, 4, *p*-NO_2BzArC*H*$_2$Ar-*p*-NO_2Bz), 3.60 (d, 4, *p*-NO_2BzArC*H*$_2$ArOH), 1.42 (s, 18, HOArC(C*H*$_3$)$_3$), 0.61 (s, 36, *p*-NO_2BzArC(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$) δ 161.38 (C-14), 149.74 (C-18), 149.60 (C-1), 148.82 (C-11), 145.19 (C-8), 143.84 (C-4), 133.17 (C-15), 132.36 (C-9a), 130.47 (C-16), 129.85 (C-9b), 127.78 (C-16), 126.13 (C-10b), 125.73 (C-2), 125.18 (C-10a), 122.86 (C-17), 38.53 (C-19), 34.40 (C-5), 33.94 (C-12), 31.60 (C-6), 30.61 (C-13), 30.36 (C-7). The assignments of carbons C-9a, C-9b, and C-2 were made by performing a two-bond HETCOR experiment (COLOC): MS (FAB) 1571 (M$^+$), 1421 (M$^+$ − $C_7H_4NO_3$), 1272 (M$^+$ − two $C_7H_4NO_3$). Anal. Calcd for $C_{94}H_{96}N_4O_{18}$: C, 71.92; H, 6.16, N, 3.57. Found: C, 71.54; H, 6.19, N, 3.41.



---

[12] Dimroth, K.; Reichardt, C.; Siepmann, T.; Bohlmann, F. *Liebigs Ann. Chem.* **1963**, *66*, 1.

[13] Dimroth, K.; Reichardt, C. *Liebigs Ann. Chem.* **1969**, *727*, 93.

[14] Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. THF was freshly distilled from Na–benzophenone. The melting points of all compounds melting above 250 °C were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) with use of a 500 °C thermometer calibrated against a thermocouple. HPLC analyses employed an Analtech reversed-phase C-18 column. ^{1}H NMR spectra were recorded at 300 MHz. Osmometric molecular weight determinations[15] were made on a Wescan Model 232A apparatus using concentrations of ca. 1 mmol/L in $CHCl_3$. TLC analyses were carried out on Analtech silica gel plates (absorbant thickness 250 μm) containing a fluorescent indicator. Flash chromatography[16] was carried out with J. T. Baker silica gel No. JT7042-2 (40-mm particles) on columns 50 mm in diameter filled to a height of 7 in. Elution rates were 2 in./min; fractions of 50 mL were collected. Analytical samples were dried at least 36 h at 100–140 °C and 1–2 mm of pressure.

[15] We are indebted to Alice Gutsche for carrying out the osmometric determinations.

[16] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[17] Gutsche, C. D.; Dhawan, B.; Leonis, M.; Stewart, D. *Org. Synth.* **1989**, *68*, 238.

(B) 1-Methylimidazole Method. A solution of 1.00 g (1.03 mmol) of *p-tert*-butylcalix[6]arene (**1a**), 1.35 g (7.27 mmol) of *p*-nitrobenzoyl chloride, and 1.28 g (15.6 mmol) of 1-methylimidazole in 100 mL of CH_3CN was stirred for 30 min at rt and then neutralized with 50 mL of 2 M HCl. The yellow precipitate was collected by filtration and dried to yield 1.38 g (85%) of **2a**. A reaction carried out for 25 h gave the same product but in a yield of only 68%.

Hydrolysis of 2a. A solution containing 0.95 g (14.4 mmol) of KOH in 6 mL of diethylene glycol and 1 mL of H_2O was heated and stirred as 0.60 g (0.38 mmol) of the tetraester **2a** was added. The mixture was heated at reflux for 7.5 h, and the product was worked up in conventional fashion to yield 0.35 g (95%) of *p-tert*-butylcalix[6]arene (**1a**).

39,42-Dihydroxy-37,38,40,41-tetrakis(benzoyloxy)calix[6]arene (2b). Following the procedure described above for the preparation of **2a** via the NaH method, 0.50 g (0.78 mmol) of calix[6]arene[4] was treated with 0.23 g (5.8 mmol) of 50% NaH and 1.70 g (12.1 mmol) of benzoyl chloride. The reaction mixture was stirred at 0 °C for 30 min and 1 h at rt. The THF was removed on a rotary evaporator, and the residue was suspended in $CHCl_3$ and washed with H_2O. The $CHCl_3$-insoluble material was collected by suction filtration and dried to leave 0.87 g (96%) of a white powder: mp 406–413 °C; IR (KBr, cm^{-1}) 1697 (C=O stretching); ^{1}H NMR ($CDCl_3$, −50 °C) δ 7.63 (t of t, $J_{1,2}$ = 7.4 Hz, $J_{1,3}$ = 2.0 Hz, *p*-BzH), 7.59 (d of d, $J_{1,2}$ = 9.6 Hz, $J_{1,3}$ = 2.0 Hz, *o*-BzH), 7.41 (d of d, $J_{m,p}$ = 7.4 Hz, $J_{o,m}$ = 9.0 Hz, *m*-BzH), 7.28 (t, *p*-HArOH), 7.34 (d, *m-H*ArOH), 6.79 (d, *J* = 10 Hz, *m*-HArBz), 6.60 (t, *p*-HArBz), 6.58 (d, *m*-HArBz), 6.57 (s, OH), 3.72 (d, *J* = 15.9 Hz, BzArCH_2ArOH), 3.34 (d, *J* = 17.6 Hz, BzArCH_2ArOH), 3.25 (s, BzArCH_2 ArBz); Osmometric M_r ($CHCl_3$, 37 °C) 1059 (calcd for tetraester 1053). Anal. Calcd for $C_{79}H_{52}O_{10}$: C, 79.83; H, 4.98. Found: C, 79.59; H, 4.88.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis(benzoyloxy)calix[6]arene (2c). Following the procedure described above for the preparation of **2a** via the NaH method, 5.00 g (5.14 mmol) of *p-tert*-butylcalix[6]arene was treated with 5.14 g (128 mmol) of 50% NaH and 9.00 g (64 mmol) of benzoyl chloride. The mixture was refluxed 4 h and then worked up to yield 5.61 g (78%) of small white crystals after crystallization from $CHCl_3$–MeOH. However, TLC analysis of this material indicated it to be a mixture of several components. Further purification by flash chromatography produced a pure sample of the high R_f material which was recrystallized from $CHCl_3$–MeOH to give 1.45 g (20%) of **2c** as white needles: mp 379–389 °C; IR (KBr, cm^{-1}) 1749 (C=O stretching); ^{1}H NMR ($CDCl_3$) δ 7.31 (s, HOAr*H*), 7.29 (d of d, $J_{1,2}$ = 8.5 Hz, $J_{1,3}$ = 2.1 Hz, *o*-BzH), 6.86 (t of t, $J_{1,2}$ = 7.5 Hz, $J_{1,3}$ = 1.8 Hz, *p*-BzH), 6.56 (d of d, $J_{o,m}$ = 8.65 Hz, $J_{m,p}$ = 7.7 Hz, *m*-BzH), 6.37 (s, OH), 4.35 (d, BzArCH_2ArOH), 4.05 (s, BzArCH_2ArBz), 3.55 (d, BzArCH_2ArOH), 1.40 (s, HOArC(CH_3)$_3$), 0.69 (s, BzArC(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 163.78 (C=O), 149.83, 148.45, 144.10, 143.13, 132.83, 132.06, 130.30, 130.08, 129.17, 127.61, 128.50, 128.02, 127.82, 127.61, 125.99, 125.73, 124.72, 34.16, 33.80, 32.14, 31.43, 30.72; MS(FAB) 1390 (M^+). Anal. Calcd. for $C_{94}H_{100}O_{10}$: C, 81.24; H, 7.25. Found: C, 81.41; H, 7.11. The lower R_f materials are thought probably to be the penta- and hexaesters.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,42-dihydroxy-37,38,40,41-tetrakis[(3,5-dinitrobenzoyl)oxy]calix[6]arene (2d). Following method B described below for the preparation of **4**, a 4.00-g (4.11 mmol) sample of **1a** was treated with 4.27 g (20.1 mmol) of 3,5-dinitrobenzoic acid, 2.0 mL (9.65 mmol) of diphenyl chlorophosphate, and 2.40 mL of pyridine in toluene–DMF solution. The reaction mixture was stirred for 6 h at ice-bath temperature and then neutralized with 25 mL of 0.5 M HCl. Filtration removed a pale yellow powder, and the organic phase was washed four times with 0.5 M HCl, filtered to remove a small amount of solid, dried, and evaporated to leave a yellow, glassy residue. This was triturated with 2-propanol for 24 h, filtered, and dried to leave 2.87 g of product which was dissolved in EtOAc. The solution was heated to boiling, concentrated to ca. 20 mL, treated with 20 mL of hexane, and cooled. The precipitate that formed was collected by filtration and recrystallized a second time to give 0.89 g (9.5%) of **2d** as a white powder: mp 232 °C dec; ^{1}H NMR ($CDCl_3$) δ 9.51, 9.38, 9.26, 7.40, 7.23, 7.19, 7.16, 6.69, 5.50, 4.0 (broad), 3.70 (d, *J* = 16.8 Hz), 3.49 (d, *J* = 15.0 Hz), 1.38, 1.35, 1.27, 0.94; ^{13}C NMR ($CDCl_3$) δ 163.27, 149.92, 149.27, 148.97, 143.57, 143.07, 132.21, 130.26, 127.17, 127.00, 126.46, 126.18, 125.56, 125.46, 124.29, 124.05, 34.25, 34.01, 32.76, 31.68, 31.53, 31.01; MS (FAB) 1360 (M^+), 1166 ($M^+ - C_7H_3N_2O_5$), 1148 ($M^+ - C_7H_3N_2O_6$). Anal. Calcd for $C_{80}H_{88}N_4O_{14}$: C, 70.57; H, 6.51; N, 4.11. Found: C, 70.53; H, 6.48; N, 3.91.

5,11,17,23,29,35-Hexa-*tert*-butyl-42-hydroxy-37,38,39,40,41-pentakis[(4-nitrobenzoyl)oxy]calix[6]arene (3). The lower R_f material obtained from the column chromatographic separation of the product described above in method A for **2a** consisted of 1.27 g (36%) of a yellow powder. This material was dissolved in EtOAc and concentrated to ca. 20 mL by boiling. Boiling hexane was added, and the solution was cooled. The solid that formed was separated by filtration and obtained as 1.01 g (29%) of **3** as yellow crystals: mp 280 °C dec; IR (KBr, cm^{-1}) 1741 (C=O stretching), 1532, 1348 (NO_2 stretching); ^{1}H NMR (DMSO-d_6) δ 8.28 (d, *J* = 8.7 Hz, NO_2ArH), 8.13 (d, *J* = 8.8 Hz, NO_2ArH), 7.96 (d, *J* = 8.7 Hz, NO_2ArH), 7.83 (s), 7.66 (d, *J* = 8.5 Hz, NO_2ArH), 7.59 (s), 7.29 (s), 6.94 (s), 6.82 (d, *J* = 7.4 Hz, NO_2ArH), 4.32 (d, *J* = 16.0 Hz, ArCH_2 Ar), 4.13, 3.88 (d, *J* = 17.0 Hz, ArCH_2Ar), 3.66 (d, *J* = 15.6 Hz, ArCH_2Ar), 3.58 (d, *J* = 17.6 Hz, ArCH_2 Ar), 1.41 (s, $C(CH_3)_3$), 1.32 (s, $C(CH_3)_3$), 0.91 (s, C-(CH_3)$_3$); ^{13}C NMR (DMSO-d_6) δ 163.00, 162.78, 161.91, 151.03, 149.87, 148.72, 147.10, 143.86, 143.65, 133.65, 133.39, 132.42, 132.15, 131.00, 130.82, 130.01, 129.66, 129.46, 128.71, 128.58, 127.96, 124.36, 123.56, 123.26, 123.01, 122.46, 34.49, 34.12, 33.98, 33.79, 31.43, 31.24, 30.80, 30.60, 29.41; MS (FAB) 1737 ($M^+ + H_2O$), 1719 (M^+), 1569 ($M^+ - C_7H_4NO_3$), 1552 ($M^+ - C_7H_4NO_3$ and H_2O), 1419 (M^+ − two $C_7H_4NO_3$). Anal. Calcd for $C_{101}H_{99}N_5O_{21}$: C, 70.57; H, 5.80; N, 4.07. Found: C, 70.57; H, 5.78; N, 3.91. An HPLC analysis (solvent system: 66% CH_3CN, 15% $CH_3OC(CH_3)_3$, 15% CH_2Cl_2, 3% H_2O, 1% HOAc) of six crude reaction mixtures from which **2a** and **3a** were isolated confirmed the presence of these two compounds in the ratio of ca. 1.5:1.0.

5,11,17,23,29,35-Hexa-*tert*-butyl-39,40,41,42-tetrahydroxy-37,38-bis[(4-nitrobenzoyl)oxy]calix[6]arene (4). (A) NaH Method. Following the procedure described above for the preparation of **2a** via the NaH procedure, a 1.03-g (1.06 mmol) sample of *p-tert*-butylcalix[6]arene (**1a**) was dissolved in 300 mL of distilled THF and treated with 0.037 g (0.92 mmol) of 60% NaH followed by 0.20 g (1.08 mmol) of *p*-nitrobenzoyl chloride in 10 mL of toluene. The mixture was heated at reflux for 4 h and then worked up as described above to yield a crude product from which 0.51 g of starting material **1a** was removed by crystallization. Chromatography of the residue afforded 0.14 g (10%) of **4** as a yellow powder after recrystallization from $CHCl_3$–MeOH: mp 320 °C; IR (KBr, cm^{-1}) 3420 (OH stretching), 1743 (C=O stretching), 1530, 1347 (NO_2 stretching); ^{1}H NMR ($CDCl_3$) δ 8.80 (s, 2, OH), 7.90 (d, 4, *J* = 5.7 Hz, NO_2ArH), 7.76 (br s, 2, OH), 7.67 (d, 4, *J* = 8.5 Hz, NO_2ArH), 7.30 (d, *J* = 2.5 Hz, ArH), 7.20 (s, ArH), 7.14 (d, *J* = 2.0 Hz, ArH), 7.10 (d, *J* = 2.3 Hz, ArH), 6.85 (s + d, ArH), 4.24 (d, *J* = 13.7 Hz, ArCH_2Ar), 4.15 (d, *J* = 15.1 Hz, ArCH_2Ar), 4.10 (s, ArCH_2Ar), 3.77 (s, 2, ArCH_2 Ar), 3.51 (d, 2, *J* = 15.1 Hz, ArCH_2Ar), 3.46 (d, 2, *J* = 13.6 Hz, ArCH_2 Ar), 1.34 (s, 18, $C(CH_3)_3$), 1.24 (s, 18, $C(CH_3)_3$), 0.74 (s, 18, $C(CH_3)_3$); ^{1}H NMR in THF-d_8 showed two OH singlets, one at δ 9.21 and the other at δ 8.16: ^{13}C ($CDCl_3$) δ 162.19 (C=O), 150.79 (*Ar*C), 149.57 (*Ar*C), 148.28 (*Ar*C), 144.67 (*Ar*C), 144.61 (*Ar*C), 144.14 (*Ar*C), 133.62 (*Ar*C), 130.20 (*Ar*C), 130.95 (*Ar*H), 130.40 (*Ar*C), 127.31 (*Ar*C), 127.13 (*Ar*H), 126.77 (*Ar*C), 126.57 (*Ar*H), 126.28 (*Ar*C), 125.97 (*Ar*H), 125.92 (*Ar*H), 125.80 (*Ar*H), 125.33 (*Ar*H), 123.58 (*Ar*H; probably 2 carbons), 38.63 ([NO_2Ar]$_2$CH_2), 34.14 (NO_2Ar*C*Me$_3$), 34.02 (HOAr*C*Me$_3$), 33.95 (HOAr*C*Me$_3$), 32.19 (two CH_2), 31.51 (HOArC*Me*$_3$), 31.44 (HOArC*Me*$_3$), 31.19 (CH_2), 30.68 (NO_2ArC*Me*$_3$); MS (FAB) 1290 ($M^+ + H_2O$), 1272 (M^+), 1123 ($M^+ - C_7H_4NO_3$). Anal. Calcd for $C_{80}H_{90}N_2O_{12}$: C, 75.56; H, 7.13; N, 2.20. Anal. Calcd for diester + 3% monoester: C, 76.34; H, 7.22; N, 2.19. Found: C, 76.38; H, 6.98; N, 2.15.

(B) Diphenyl Chlorophosphate Method. A solution of 2.00 mL (9.65 mmol) of diphenyl chlorophosphate in 1.20 mL of DMF was stirred, in a N_2 atmosphere, at 0 °C for 5 min and then treated with a solution of 3.36 g (20.1 mmol) of *p*-nitrobenzoic acid in 25 mL of toluene. The flask was removed from the ice bath and stirred at room temperature for 10 min, and 4.00 g (4.11 mmol) of *p-tert*-butylcalix[6]arene was added. The mixture was stirred an additional 10 min, 2.4 mL of pyridine was added, and the flask was fitted with a condenser and the reaction mixture then refluxed 24 h. After being cooled, the reaction mixture was neutralized with 50 mL of 0.5 M HCl and filtered to give 4.70 g of an off-white powder. Recrystallization from $CHCl_3$ gave 1.86 g (36%) of **4** as a pale yellow powder, identical with the material described above in method A. An additional 0.14 g of **4** was obtained from the initial filtrate, bringing the total yield to 39%.

5,11,17,23,29,35-Hexa-*tert*-butyl-38,39,41,42-tetrahydroxy-37,40-bis[(4-nitrobenzoyl)oxy]calix[6]arene (5a). The chromatographic separation of **4** prepared by method A described above yielded a second compound as a bright yellow powder which was dissolved in 2-propanol/acetone (1:1), filtered, concentrated to ca. 75 mL, cooled, and allowed to stand at room temperature for several days. After filtration, which yielded 0.03 g of a yellow powder, the filtrate was concentrated further and then cooled. Filtration yielded 1.05 g of a yellow powder which was recrystallized twice from 2-propanol to afford 0.24 g (17%) of **5** as clear, yellow crystals which crumbled to a yellow powder upon drying: mp 235 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.12 (s, 4, ArH), 6.77 (s, 12, ArH), 4.31 (d, 2, J = 14.1 Hz, $ArCH_2Ar$), 4.22 (d, 4, J = 17.4 Hz, $ArCH_2Ar$), 3.85 (d, 4, J = 17.4 Hz, $ArCH_2Ar$), 3.53 (d, 2, J = 14.1 Hz, $ArCH_2Ar$), 1.25 (s, 18, CMe_3), 1.02 (s, 36, CMe_3); ^{13}C NMR ($CDCl_3$) δ 161.14 (C=O) [150.41, 150.13, 148.99, 145.99, 143.84, 133.13, 130.45, 126.77, 126.57, 126.07, 125.74, 123.18, 122.61] (Ar) [34.60, 34.00, 33.78, 31.28, 31.15, 30.60] (Alk) [expected for **5** in a cone conformation: 1 C=O, 12 Ar, 6 Alk]; MS (FAB) 1270 (M^+), 1121 ($M^+ - C_7H_4NO_3$), 1103 ($M^+ - C_7H_4NO_4$). Anal. Calcd for $C_{80}H_{90}N_2O_{12}\cdot H_2O$: C, 74.51; H, 7.19; N, 2.17. Found: C, 74.06; H, 6.86; N, 2.24.

5,11,17,23,29,35-Hexaallyl-37,38,39,40,41,42-hexakis[(4-nitrobenzoyl)oxy]calix[6]arene (6). Following the procedure described above for the preparation of **2a** via the NaH method, 1.76 g (2.01 mmol) of *p*-allylcalix[6]arene[4] (**1c**) was dissolved in 150 mL of distilled THF and treated with 11.94 g (48.5 mmol) of 50% NaH followed by 4.47 g (24.1 mmol) of *p*-nitrobenzoyl chloride in 50 mL of toluene. The mixture was refluxed 4.5 h, cooled in ice, and neutralized with 100 mL of 0.5 M Na_2CO_3. The layers were separated, the organic layer was washed twice with 50 mL of 0.5 M Na_2CO_3 and twice with 50 mL of brine, the solent was evaporated, and the yellow residue was dissolved in 50 mL of $CHCl_3/H_2O$ (5:1)). The layers were separated, and the $CHCl_3$ layer was dried over $CaCl_2$, and then concentrated by boiling. Boiling MeOH was added until the solution turned cloudy. The precipitate that formed upon cooling was removed by filtration washed with MeOH, and dried to give 2.09 g (59%) of **6** as a yellow powder: mp 475 °C; IR (KBr, cm^{-1}) 1740 (C=O stretching), 1530, 1348 (NO_2 stretching); ^{1}H NMR ($CDCl_3$) δ [8.34, 8.30, 8.26, 8.18, 8.14, 7.85, 7.81] (NO_2ArH), [6.92, 6.81, 6.69, 6.65, 6.33, 5.86, 5.81] (ArH), 5.69 ($H_2C{=}CHC-$), 5.44 ($H_2C{=}CHC-$), 5.23, 4.86 ($H_2C{=}CHC-$), 4.83 ($H_2C{=}CHC-$), [4.45, 3.94, 3.90, 3.82, 3.53, 3.25]($H_2C{=}CHCH_2-$), 3.05 ($H_2C{=}CHCH_2-$), 2.78, 1.94, 1.53; ^{13}C NMR ($CDCl_3$) δ 162.56 (C=O), 151.12, 143.84, 140.45, 139.02, 139.02, 138.24, 137.88, 135.90, 135.38, 133.72, 133.32, 133.07, 132.57, 131.52, 131.10, 130.74, 130.45, 128.97, 128.43, 127.52, 123.89, 116.60, 113.96, 39.41, 38.96, 38.24, 37.86, 37.73, 36.77, 30.07, 29.70; MS-(FAB) 1772 (M^+). Anal. Calcd. for $C_{102}H_{78}N_6O_{24}$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.28; H, 4.35; N, 4.72.

Spectroscopic Studies. (A) Difference NOE measurements were obtained with a 30.4-mg sample of **2a** in 0.6 mL of $CDCl_3$. The sample was degassed using three or more cycles of the freeze–thaw technique, following which the NMR tube was sealed. The data were collected at 25 °C by interleaving the values obtained from the off-resonance irradiated spectrum and the on-resonance spectrum as a means for eliminating any errors arising from instrument instability. Three runs were performed at each resonance. The NOE data based on peak height, shown in Table I, were obtained by subtracting the transformed spectra. Similar but not identical values resulted from the NOE data based on peak area, obtained by subtracting the free induction decay (FID) signals of the spectra and then transforming the resultant FID.

(B) Transient NOE measurements were made on the same sample used for the difference NOE experiments. The pulse sequence involved an equilibrium delay (6 s), a selective 180° pulse, a variable delay (0.025–1.0 s), and a nonselective pulse (20 μs). The selective 180° pulse was chosen such that the resonances adjacent to the saturated peak would be perturbed by no more than 5%. The values obtained are shown in Table II.

Acknowledgment. We are indebted to the National Institutes of Health (GM-23534) and the Robert A. Welch Foundation (P-1163) for generous support of this work. Thanks are also expressed to Professor William Sherman and the Washington University Mass Spectral facility for providing the mass spectral data and to Dr. Andre d'-Avignon of Washington University for his help with the NOE experiments.

Registry No. 1a, 78092-53-2; **1b**, 96107-95-8; **1c**, 98013-96-8; **2a**, 140175-12-8; **2b**, 140149-05-9; **2c**, 140149-06-0; **2d**, 140175-13-9; **3**, 140149-07-1; **4**, 140149-08-2; **5a**, 140149-09-3; **6**, 140149-10-6; *p*-nitrobenzoyl chloride, 122-04-3; benzoyl chloride, 98-88-4; 3,5-dinitrobenzoyl chloride, 99-33-2.

Supplementary Material Available: Predicted ^{1}H NMR patterns for calix[6]arenes carrying zero, one, two, three, four, five, and six substituents on the phenolic oxygens for all of the possible "up–down" conformations for each of the entries (13 pages). Ordering information is given on any current masthead page.