Tetrahedron Vol. 43, No. 21, pp 4917 to 4930, 1987
Printed in Great Britain.

0040-4020/87 $3.00+.00

CALIXARENES 21. THE CONFORMATIONS AND STRUCTURES OF THE PRODUCTS OF AROYLATION OF THE CALIX[4]ARENES

MUZAFFAR IQBAL, THOMAS MANGIAFICO, and C. DAVID GUTSCHE*

Contribution from the Department of Chemistry, Washington University,
St Louis, Missouri 63130

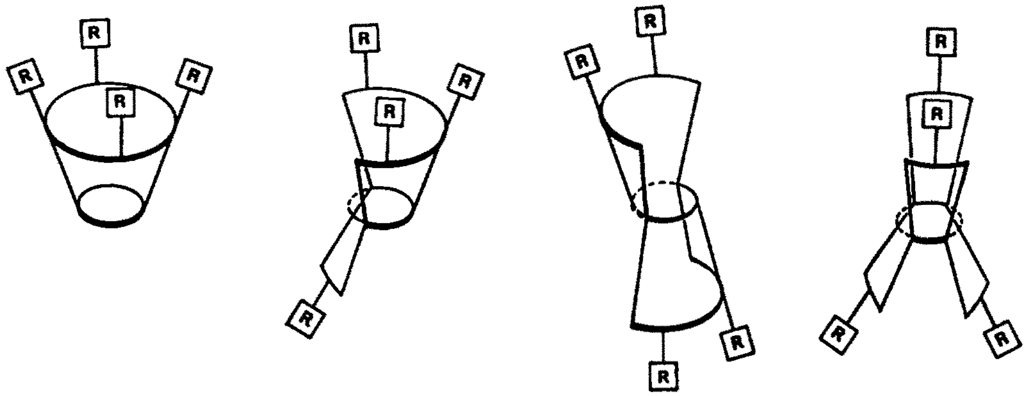
(*Received in UK* 9 *February* 1987)

Abstract- The aroylation of calix[4]arene (1), p-tert-butylcalix[4]arene (2) and p-allylcalix[4]arene (3) with benzoyl chloride and a variety of p-substituted benzoyl chlorides has been carried out via $AlCl_3$-catalyzed reaction and NaH-induced reaction. The products are tetra-aroylates that exist in the cone, partial cone, and/or 1,3-alternate conformation. It is shown that the distribution among these conformers is dependent on a variety of factors including temperature, aroylating agent, calixarene, and solvent. When 1 is esterified by the $AlCl_3$ procedure lower temperature tends to slightly favor the partial cone conformation, while higher temperature favors the 1,3-alternate conformation. When 3 is esterified by the NaH method aroyl chlorides carrying electron-releasing p-substituents favor the 1,3-alternate conformers; those carrying electron-withdrawing substituents favor the cone conformers, the distribution between the conformers correlating quite well with the Hammett σ constants for the p-substituents of the aroylating agents. When 2 is esterified by the NaH method it shows a greater tendency to produce the cone conformer than does 3, the former undergoing slower conformational inversion than the latter. On the basis of these observations it is postulated that the conformer distribution is dependent on the relative rates of the conformational inversion process and the aroylation process, viz. faster aroylation leading to cone conformers or partial cone conformers and slower aroylation leading to 1,3-alternate conformers.

Calixarenes[1] are conformationally mobile macrocyclic compounds that are of interest, inter alia, because of their potential as polyfunctional catalysts. Conformational isomerism in the calix[4]arenes was first suggested by Megson[2] and Ott and Zinke[3] and was made explicit by Cornforth and coworkers[4] who pointed out that four discrete forms can exist. We have designated these[5] as "cone", "partial cone", "1,2-alternate", and "1,3- alternate" conformations as pictured in Fig 1, and we abbreviate them in the designation of the structures in this paper as [c], [pc], [1,2-alt], and [1,3-alt], respectively. The facile interconversion of these conformers was demonstrated by Kämmerer and coworkers[6,7] who used dynamic ^1H NMR measurements on a number of p-alkylcalix[4]arenes, and the results of these studies have been substantiated and extended by subsequent workers[8,9,10]. The facile interconversion among conformers disappears, however, upon transformation to the ethers and esters of the calix[4]arenes, because the interconversion process requires that the aryl rings rotate around the C-2/C-6 bonds in a direction that brings the oxygen end of the aryl moiety through the annulus of the macrocyclic ring. Thus, derivatization freezes the calix[4]arene system into one or more of the four conformations[5,11], and in

---

Dedicated to Professor Hans Wynberg on the occasion of his 65th birthday.



Cone Partial Cone 1,2-Alternate 1,3-Alternate

Fig 1. The conformations of calix[4]arenes

many instances quite high yields of one particular conformer can be obtained by appropriate choice of derivatizing agent. For example, acetylation often favors the "partial cone" conformation; benzylation and trimethylsilylation generally favor the "cone" conformation. In this paper we report the results of a study of the effects that the derivatizing reagent and the reaction conditions have on the conformations and the structures of the calix[4]arene aroylates that are obtained via $AlCl_3$-catalyzed and NaH-induced aroylation. The aroylation process was chosen for study because of the possibility it affords for making graded changes in the derivatizing agent via the *p*-substituents in the benzene ring. In studying the conformational outcome of these reactions advantage was taken of the easy distinction among conformers that is made possible by ^1H NMR measurements. The characteristic ^1H NMR patterns arising from the CH_2 groups of particular conformations are indicated in Table 1, and several typical spectra are shown in Fig 2.

Conformation	**^1H NMR Pattern**
Cone	One pair of doublets
Partial Cone	Two pairs of doublets (ratio 1:1) or one pair of doublets and one singlet (ratio 1:1)
1,2-Alternate	One singlet and two doublets (ratio 1:1)
1,3-Alternate	One singlet

Table 1. ^1H NMR patterns for the CH_2 protons of calix[4]arenes in various conformations.

Tetra-aroylates via Aluminum Chloride-Catalyzed Aroylation. Room temperature benzoylation of calix[4]arene (**1**) with benzoyl chloride and $AlCl_3$ in CH_2Cl_2 solution yields a mixture of materials from which two pure substances can be isolated. The higher melting (mp $>450^{\circ}$ C) acetone-insoluble compound was identified as the tetrabenzoate of calix[4]arene in the 1,3-alternate conformation {**4[1,3-alt]-a**} and the lower melting (mp 302-4° C) acetone-soluble compound as the corresponding partial cone conformer {**4[pc]-a**}. With these pure materials as reference compounds, the compositions of crude mixtures of the benzoylation products obtained at

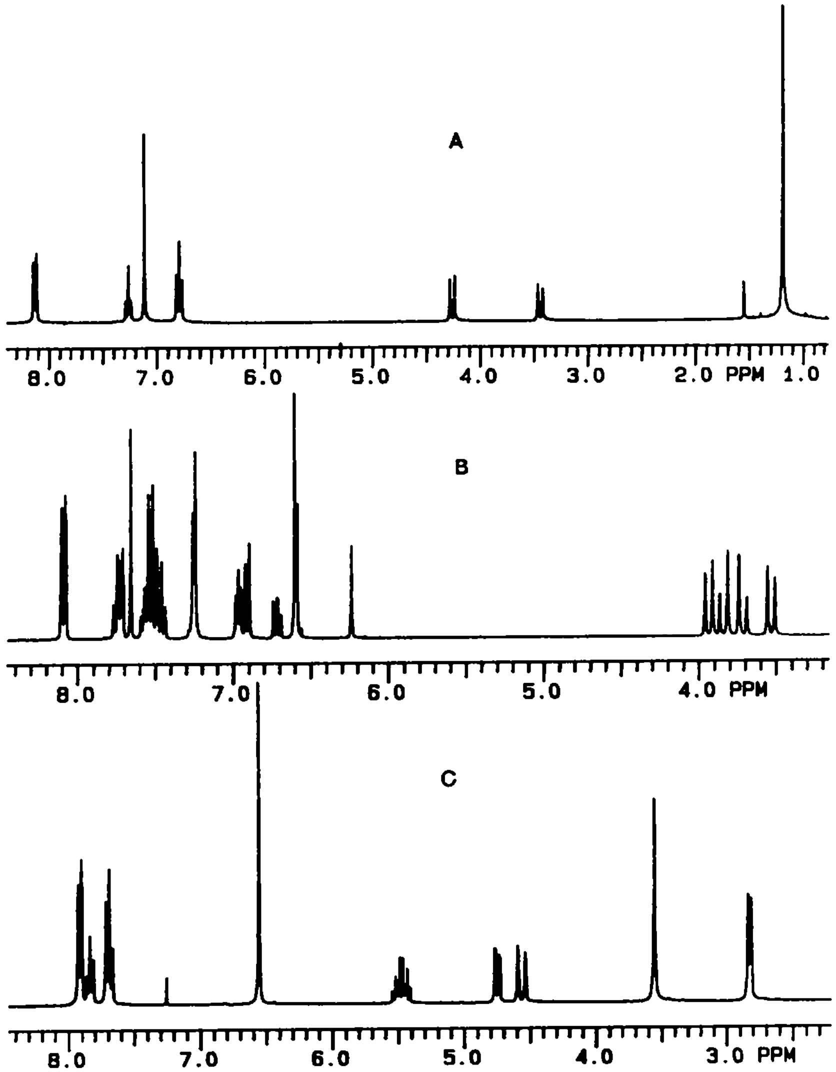
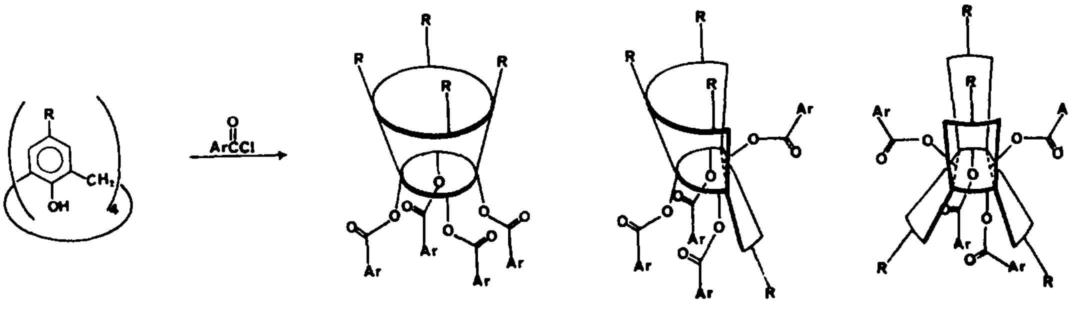


Fig 2. ^{1}H NMR spectra at 300 MHz of tetra-aroylates: (A) tetrabenzoate of p-tert-butylcalix[4]arene in the cone conformation, (B) tetrabenzoate of calix[4]-arene in the partial cone conformation, (C) tetrabenzoate of p-allylcalix-[4]arene in the 1,3-alternate conformation.

various temperatures were then established by means of HPLC, giving the results shown in Table 2. It is clearly evident from these data that higher temperatures favor the formation of the 1,3-alternate conformer, although the wide variation between replicate determinations (± 8% in some cases) produces some uneveness in the data over the range of 0°C to the reflux temperature of the solvent.

In the hope of determining the effect of electronic factors on the conformational outcome of the aroylation process, reactions were next carried out with a number of p-substituted benzoyl chlorides. Although benzoyl chlorides carrying electron-releasing substituents in the p-position reacted quite smoothly and gave products that could be assayed for the distribution between partial cone and 1,3-alternate conformers (see Table 3), benzoyl chlorides carrying electron-withdrawing substituents (e.g. p-nitro, p-cyano, and p-trifluoromethyl) either failed to react or gave such low yields of intractible mixtures that the results were of little use.

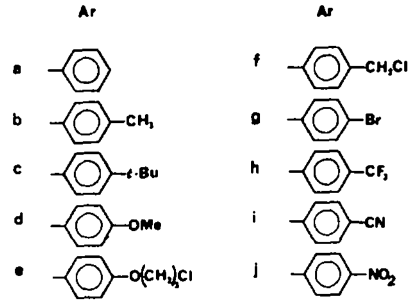


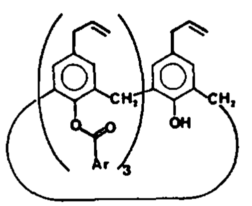
1 (R = H)
2 (R = CMe$_3$)
3 (R = CH$_2$CH=CH$_2$)

4[c] (R = H)
5[c] (R = CMe$_3$)
6[c] (R = CH$_2$CH=CH$_2$)

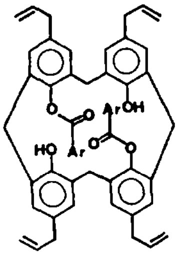
4[pc] (R = H)
5[pc] (R = CMe$_3$)
6[pc] (R = CH$_2$CH=CH$_2$)

4[1,3-alt] (R = H)
5[1,3-alt] (R = CMe$_3$)
6[1,3-alt] (R = CH$_2$CH=CH$_2$)





7



8

The changes that occur in the conformer distribution of the aroylates with changes in temperature suggest that the rate of conformational inversion of the calixarene might play a key role in determining the conformer distribution of the derivatization product. That we are dealing with competitive rates - viz. the rate of conformational inversion vs the rate of aroylation - is further indicated by the fact that electron-releasing p-substituents in the aroylating agent (which might be expected to reduce the reaction rate) give a higher proportion of the 1,3-alternate conformer. Thus, whereas benzoyl chloride produces a mixture of conformers even at reflux temperature and p-methylbenzoyl chloride gives a mixture at room temperature,

Temperature	**Partial Cone, %**	**1,3-Alternate, %**
reflux	23	67
40	19	77
35	23	74
30	43	55
25	54	45
0	76	22

Table 2. Effect of temperature on the ratio of partial cone to 1,3-alternate conformers formed in the benzolyation of calix[4]arene

p-Substituent of Benzoylation Agent	Temperature, °C	Product Distribution
H	0	22% 1,3-Alternate/76% Partial Cone
	Reflux	68% 1,3-Alternate/23% Partial Cone
CH_3	0	100% Partial Cone
	25	Mixture of 1,3-Alternate & Partial Cone
	Reflux	100% 1,3-Alternate
$(CH_3)_3C$	25	100% 1,3-Alternate
CH_3O	25	100% 1,3-Alternate
$Cl(CH_2)_3O$	25	100% 1,3-Alternate

Table 3. Effect of temperature and the structure of the aroylating agent on the conformer distribution in the aroylation of calix[4]arene

p-tert-butyl, p-methoxy, and p-3-chloropropoxy analogs all produce pure 1,3-alternate product at room temperature. These data provide the basis for the following hypotheses: (a) the 1,3-alternate conformers of the tetra-aroylates are more conformationally stable than the cone or partial cone conformers, a fact that finds some corroboration in the work of Högberg on the extra-annular octahydroxycalix[4]arenes[12], (b) if the rate of conformational inversion is slow relative to the rate of derivatization the cone or partial cone conformer will be formed, and (c) if the rate of conformational inversion is fast relative to the rate of derivatization the 1,3-alternate conformer will be formed. As described in the next section, these hypotheses were subsequently explored in greater detail with the NaH method of derivatization which not only gives better yields and cleaner products than the $AlCl_3$ method in some cases (e.g. p-tert-butylcalix[4]arene and p-allylcalix[4]arene) but also permits the use of a wider assortment of aroylating agents, including those carrying electron-withdrawing, rate-enhancing p-substituents. Curiously, the $AlCl_3$ method gives better yields than the NaH method in the case of calix[4]arene; the conformational outcome is approximately the same with the two methods when benzoyl chloride is the aroylating agent but different when p-tert-butyl-, p-methoxy- and p-methylbenzoyl chlorides are used.

The 1,3-alternate conformer of the tetrabenzoate of calix[4]arene {**4[1,3-alt]-a**} displays some interesting ^1H NMR features. At room temperature the resonance pattern at 6.7 arising from the aryl hydrogens on the calixarene is a multiplet, as would be predicted for an A_2A' system. At -45° C, however, this pattern changes to a sharp singlet, apparently the result of accidental equivalence of these protons. Because the elemental analysis of **4[1,3-alt]-a** indicated the inclusion of solvent, a 2D NOE spectrum in $CDCl_3$ was obtained. As shown in Fig 3-B, it displays off-diagonal resonances corresponding to a moderately strong interaction between $CHCl_3$ and the aromatic protons of the benzoyl groups. A 2D HOMCOR spectrum of this same material in $CDCl_3$ (Fig 3-A) shows only the expected J coupling patterns between the protons within the molecule. The 2D NOE spectrum can be interpreted in terms of a complex between $CHCl_3$ and **4[1,3-alt]-a** in which

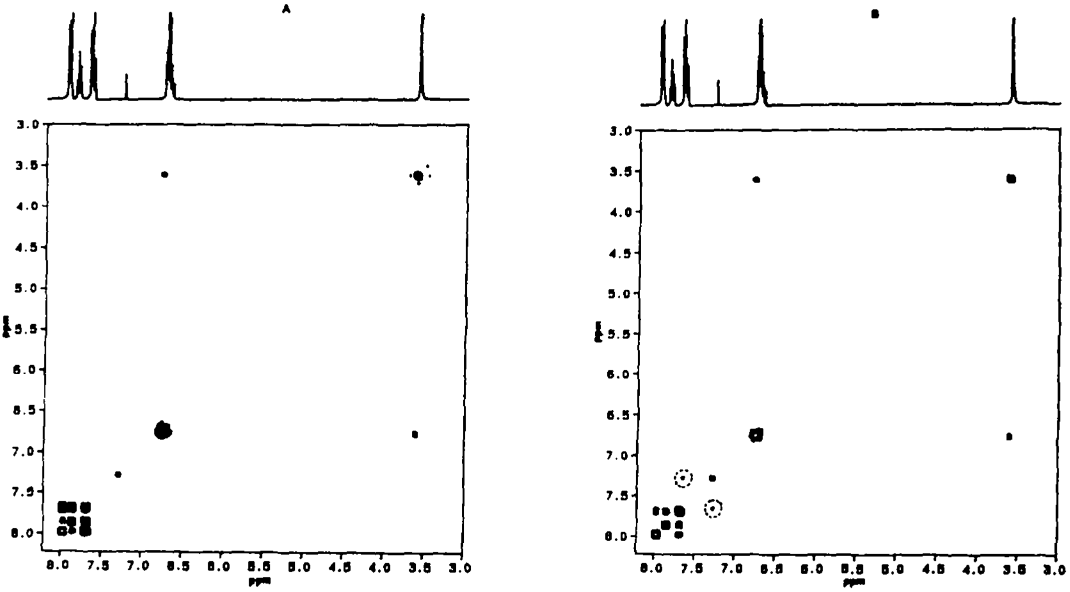


Fig 3. 2D ^{1}H NMR spectra of the tetra-benzoate of calix[4]arene in the 1,3-alternate conformation in CDCl$_3$ solution: *(A) HOMCOR spectrum, (B) NOE spectrum*

molecules of CHCl$_3$ reside inside the cavities of the calixarene tetrabenzoate, comparable to the complex that is proposed for the endo-calix complexes of the parent calixarenes[13] with amines.

Tetra-aroylates via Sodium Hydride-Induced Aroylation. The most extensive set of aroylation experiments in the present study was carried out with p-allylcalix[4]arene because of the synthetic interest in using the allyl groups to introduce functionality[14] on the calixarene ring. p-Allylcalix[4]arene (3) in THF solution was treated with 8 equivalents of NaH and 5 equivalents of the appropriate benzoyl chloride to yield products whose compositions were established by inspection of their ^{1}H NMR spectra. The results are shown in Table 4. A similar, though less extensive study was then carried out using p-tert-butylcalix[4]arene (2) to determine whether the p-substituent of the calixarene has any effect on the conformational outcome of the reaction. That it does is indicated by the data in Table 5 which show that there is a considerably greater preference for the formation of the cone conformer in the case of p-tert-butylcalix[4]arene than in the case of p-allylcalix[4]arene, even with benzoyl chlorides containing electron-releasing groups.

Studies of the conformational behavior of the calixarenes[10] have shown that the rate of conformational inversion, as measured by the coalescence temperatures obtained from ^{1}H NMR spectral measurements, depends on the p-substituent of the calix[4]arene as well as on the solvent. To provide comparative data among the compounds used in the present study, the coalescence temperatures for calix[4]arene (1), p-tert-butylcalix[4]arene (2), and p-allylcalix[4]arene (3) were measured in CD$_2$Cl$_2$, THF-d$_8$, and DMF-d$_7$; these results, along with those from the earlier investigation, are shown in Table 6. In agreement with earlier observations[10], the coalescence temperatures are lower for all three of the calixarenes in the more polar solvents (i.e. conformational inversions are faster in these than in nonpolar solvents). Quantitatively, the effects are greater for calix[4]arene and p-allylcalix[4]arene

p-Substituent of the Benzoylating Agent	σ_{para}	Product Composition
OCH_3	-0.27	1,3-Alternate Conformation*
$C(CH_3)_3$	-0.20	1,3-Alternate Conformation
CH_3	-0.17	1,3-Alternate Conformation
H	0.00	1,3-Alternate Conformation
CH_2Cl		1,3-Alternate Conformation
Br	0.23	1,3-Alternate Conformation
CF_3	0.54	1,3-Alternate Conformation (67%) Cone Conformation (33%)
CN	0.66	Cone Conformation (major product) Partial Cone Conformation (minor product)
NO_2	0.78	Cone Conformation (95%) 1,3-Alternate Conformation (5%)

* Because of the reduced reactivity of this aroylating agent the product is a mixture of tetra-aroyl (6-d), tri-aroyl (7-d) and di-aroyl (8-d) compounds.

Table 4. The product composition from the aroylation of p-allylcalix[4]arene with benzoyl chloride and various p-substituted benzoyl chlorides.

than for p-tert-butylcalix[4]arene, supporting the idea that the p-tert-butyl group is particularly effective in maintaining the cone conformation. A puzzling feature in the behavior of p-tert-butylcalix[4]arene was discovered when a sample was used in which the toluene of crystallization had been removed by drying under vacuum at high temperature. In $CDCl_3$, THF-d_8 and pyridine-d_5 solutions the coalescence temperatures for the more soluble toluene-complexed sample and the less soluble toluene-free sample of p-tert-butylcalix[4]arene are identical, as would be anticipated. However, in DMF-d_7 solution the coalescence temperature of the toluene-free sample is ca 20° lower than that of the toluene-complexed sample. Even after the NMR solutions

p-Substituent of Benzoylating Agent	σ_{para}	Product Composition
OCH_3	-0.27	Cone Conformation (90%) Partial Cone Conformation (5%) 1,3-Alternate Conformation (5%)
$C(CH_3)_3$	-0.20	Cone Conformation (80%) 1,3-Alternate Conformation (20%)
CH_3	-0.17	Cone Conformation (90%) 1,3-Alternate Conformation (5%) Tri-substituted Compound (5%)
H	0.00	Cone Conformation (98%) 1,3-Alternate Conformation (trace)
Br	0.23	Cone Conformation
NO_2	0.76	Cone Conformation

Table 5. The product composition from the aroylation of p-tert-butylcalix[4]arene with benzoyl chloride and various p-substituted benzoyl chlorides.

are heated, the difference in coalescence temperatures persists, negating the idea that the difference might be ascribed to slow entry and/or exit of toluene from the cavity of the calixarene. That no chemical change occurs upon removal of the the toluene is shown by the ability to reconstitute the toluene-complexed material by recrystallizing the toluene-free calixarene from toluene. Further work will be necessary to provide an explanation for this phenomenon.

Solvent	Coalescence Temperature, °C		
	Calix[4]-arene (1)	**p-tert-Butyl-calix[4]arene (2)**	**p-Allyl calix[4]arene (3)**
$CDCl_3$	36	52	37
CD_2Cl_2	37.5	>42*	42
CD_3CN	0	insoluble	2
Acetone-d_6	-5	ca 50	5
Benzene-d_6	15	35	-
Pyridine-d_5	-22	15	7.5
THF-d_8	5	27.5	15
DMF-d_7	-5	60 (40**)	5

*At 42°C a pair of broad resonances can still be observed

**Toluene-free sample

Table 6. Coalescence temperatures in various solvents for calixarenes 1,2, and 3

The hypothesis concerning the relative rates of aroylation and conformational inversion as governing the product composition in the reactions of aroyl halides with calix[4]arenes is hinted at by the results from the $AlCl_3$-catalyzed reactions, and its outlines are sharpened by the results of the NaH-catalyzed reactions. In the $AlCl_3$-catalyzed process the mechanism is assumed to involve the formation of an acylium ion which then interacts with the phenol. Electron-releasing groups such as CH_3O in the p-position of the aroyl halide will enhance the rate at which the acylium ion is formed but diminish its reactivity, once formed. The data in Table 4 correlate nicely with the σ_{para} constants and show that aroyl chlorides carrying electron-releasing groups favor the formation of the 1,3-alternate conformer (i.e. the product of slower reaction) and those carrying electron-withdrawing groups favor the cone conformer (i.e the product of faster reaction). In the NaH-induced process the mechanism is assumed to involve the addition of the phenolate anion to the aroyl carbonyl to form a tetrahedral intermediate which subsequently loses Cl^- to form the product. Electron-releasing groups in the aroyl halide will diminish the electrophilic character of the carbonyl carbon, while electron-withdrawing groups will enhance it. The data in Table 4 and 5 correlate nicely with the σ_{para} constants and again show that aroyl chlorides carrying electron-releasing groups favor the formation of the 1,3-alternate conformer and those carrying electron-withdrawing groups favor the formation of the cone conformer. Thus, it is postulated that in both modes of reaction lower rates result in the formation of 1,3-alternate conformers and faster rates result in the formation of cone conformers. In comparing the data in Tables 4 and 5 we see that the transition between the formation of the 1,3-alternate and cone conformers occurs at a considerably lower value of the σ_{para} constant of the aroylating agent for the reaction with p-*tert*-butylcalix[4]arene than with p-allylcalixarene. This difference correlates well with the difference in ^{1}H NMR coalescence temperature of p-allylcalix[4]arene and p-*tert*-butylcalix[4]arene in THF, the former being somewhat lower than the latter and corresponding to more rapid conformational interconversion. However, the difference in the rate of conformational interconversion corresponding to these two coalescence temperatures is actually quite small, suggesting that the product composition in these reactions is the result of a remarkably delicate balance between the aroylation rate and the conformational inversion rate.

In many of the NaH-induced derivatizations that we have reported in earlier papers in this series the solvent that was used was a mixture of THF and DMF, the latter added in the thought that it solubilized the calixarene. In the light of results of the present study which suggest that (a) the relative rates of aroylation and conformational inversion determine the conformational outcome of the reaction and (b) the coalescence temperature for p-allylcalix[4]arene is lower in DMF than in THF, it became of interest to determine if DMF has any effect on the composition of the reaction product. The benzoylating agent that was chosen for this purpose was p-nitrobenzoyl chloride, because it produces high yields of the cone conformer in THF solution (see Tables 4 and 5). The results shown in Table 7 reveal that DMF does, indeed, have some effect on the conformational outcome, producing less cone conformer and more 1,3-alternate conformer as the proportion of DMF in the solvent mixture increases - in support of the thesis that increasing rate of conformational inversion leads to less cone and more 1,3-alternate conformer. The more profound effect of DMF as a solvent, however, is on the structural outcome of the reaction. As shown in Table 7, as the proportion of DMF in the THF-DMF mixture is increased with p-allylcalix[4]arene as the starting material, the amount of tri-benzoate increases and becomes the sole product (although in low yield) when DMF is used alone. Similar behavior is noted with p-*tert*-butylcalix[4]arene where benzoyl chloride, p-toluoyl chloride, and p-methoxy-benzoyl chloride all give products containing tri-aroylates mixed with various other compounds when THF-DMF is used as the solvent.

Tri-aroylates and Di-aroylates of the Calix[4]arenes. The preparation of the tri-benzoate of p-allylcalix[4]arene through the use of DMF as a solvent, as described above, has little synthetic utility because of very low yields. Pyridine proves to be a much superior solvent (and reactant) for this purpose, as reported in an earlier paper in this series[15]. A subsequent paper will deal with a study of this process as well as with a procedure for preparing the di-aroylates and tri-aroylates.

Solvent	Products
THF (100%)	Tetra-benzoate in the cone conformation (95%) Tetra-benzoate in the 1,3-alternate conformation (5%)
THF (99%) DMF (1%)	Tetra-benzoate: mixture of cone and 1,3-alternate conformers Tri-benzoate (trace)
THF (90%) DMF (10%)	Tetra-benzoate: mixture of cone and 1,3-alternate conformers Tri-benzoate (significant amount)
THF (50%) DMF (50%)	Tri-benzoate (major product) Tetra-benzoate (trace)
DMF (100%)	Tri-benzoate (only isolable product) but in very low yield

Table 7. Product mixtures obtained from the reaction of p-nitrobenzoyl chloride and p-allylcalix[4]arene in various THF-DMF solvent mixtures using 5.0 equivalents of NaH and 5.0 equivalents of aroyl chloride.

Summary.

In a recent review of the calixarenes[1] it was stated that "by appropriate choice of derivatizing agent calix[4]arenes can be fixed either in the cone or partial cone conformation" but "the explanation for the different conformational outcomes upon derivatization is not known, and the roles played by the derivatizing agent and the reaction conditions remain to be determined". The present study of the aroylation reaction with calix[4]arene, p-tert-butylcalix-[4]arene and p-allylcalix[4]arene has now provided some insight into this phenomenon, correlating the rate of conformational interconversion with the rate of derivatization. By extrapolation of these results it is postulated that benzylation and trimethylsilylation tend to give products in the cone conformation because the benzylating and trimethylsilylating reagents that are generally used are quite reactive, therefore outpacing the conformational inversion rate. Acetylation, on the other hand, appears to be a somewhat slower process, resulting in the formation of partial cone and 1,3-alternate conformers.

Experimental[16]

Preparation of Tetra-aroylates via $AlCl_3$-Catalyzed Aroylation of Calix[4]arene

25,26,27,28-Tetra-(benzoyloxy)calix[4]arene (4-a). To a solution of 1.0 g (2.4 mmol) of calix[4]arene (1)[14] in 70 mL of CH_2Cl_2 in a constant temperature bath a mixture of 1.57 g (12.0 mmol) of $AlCl_3$ and 7.98 g (6.6 mL; 56.7 mmol) of benzoyl chloride in 20 mL of CH_2Cl_2 were added over a period of 30 m. The reaction mixture was stirred an additional 2 h at 40° C and then added to 100 mL of cold 6N HCl. The organic layer was separated, dried, concentrated, and treated with 80 mL of methanol to yield 1.64 g of crude product. This was triturated with acetone for 12 h to leave 0.81 g (41%) of of **4[1,3-alt]-a** in the acetone-insoluble fraction: mp > 450° C; ^1H NMR ($CDCl_3$) δ 7.94 (d, 8H, J = 8.7 Hz, Benzoyl ArH), 7.84 (t, 4, J = 7.5 Hz, Benzoyl ArH), 7.67 (t, 8, J = 7.8 Hz, Benzoyl ArH), 6.73 (m, 12, ArH), 3.6 (s, 8, $ArCH_2Ar$); Anal Calcd. for $C_{56}H_{40}O_8$: C, 79.98; H, 4.80. Found: C, 79.22; H, 4.67. The acetone soluble fraction yielded 0.83 g (43%) of **4[pc]-a** which was recrystallized from acetone/methanol to give colorless material: mp 302-304° C; ^1H NMR ($CDCl_3$) δ 8.09 (d, 4, J = 9.3 Hz, Benzoyl ArH), 7.74 (m, 4, Benzoyl ArH), 7.67 (s, 2, Benzoyl ArH), 7.50 (m, 8, Benzoyl ArH), 7.25 (d, 4, J = 4.5 Hz, Benzoyl ArH), 6.97 (t, 2, J = 4.5 Hz, Benzoyl ArH), 6.91 (d, 2, J = 8.1 Hz, Benzoyl ArH), 6.72 (t, 1, J = 7.5 Hz, Benzoyl ArH), 6.60 (d, 4, J = 4.8 Hz, Benzoyl ArH), 6.24 (s, 1, ArH), 3.94 (d, 2, J = 15 Hz, $ArCH_2Ar$), 3.84 (d, 2, J = 14.7 Hz, $ArCH_2Ar$), 3.72 (d, 2, J = 14.7 Hz, $ArCH_2Ar$), 3.53 (d, 2, J = 15 Hz, $ArCH_2Ar$); Anal. Calcd. for $C_{56}H_{40}O_8$: C, 79.97; H, 4.80. Found: C, 79.91; H, 4.78.

25,26,27,28-Tetra-p-methylbenzoyloxy)calix[4]arene (4-b) was prepared by the procedure described above, using p-toluoyl chloride, and obtained in 94% crude yield as a colorless solid. From the acetone-insoluble fraction a 52% yield of the 1,3-alternate conformer (**4[1,3-alt]-b**) was obtained: mp >400° C; ^1H NMR ($CDCl_3$) δ 7.89 and 7.44 (pair d, 16, J = 7.33 and 8.79 Hz, Aroyl ArH), 6.73 (m, 12, ArH), 3.57 (s, 8, $ArCH_2Ar$), 2.63 (s, 12, $ArCH_3$); Anal. calcd. for $C_{60}H_{48}O_8$: C, 80.33; H, 5.39. Found: C, 80.37; H, 5.33.

The acetone-soluble fraction yielded a sample of the partial cone conformer (**4[pc]-b**) that contained a trace of the 1,3-alternate conformer: mp 318-319° C; ^{1}H NMR ($CDCl_3$) δ 7.99 and 7.31 (pair d, 8, J = 8.5 Hz, Aroyl ArH), 7.67 and 7.28 (pair d, 4, J = 8.0 Hz, Aroyl ArH), 7.66 (s, 2, ArH), 7.13 and 7.05 (pair d, 4, J = 8.3 Hz, Aroyl ArH), 6.93 (m, 4, ArH), 6.73 (t, 1, ArH), 6.60 (m, 4, ArH), 6.23 (s, 1, ArH), 3.92, 3.83, 3.70, and 3.50 (four pair d, 8, J = 14.16, 15.03, 15.84, 14.05 Hz), $ArCH_2Ar$), 2.54, 2.45, and 2.42 (three s, 12, intensity ratio 1:1:2, $ArCH_3$); Anal. calcd. for $C_{60}H_{48}O_8$: C, 80.33; H, 5.39. Found: C, 80.09; H, 5.25.

25,26,27,28-Tetra-(*p-tert*-butylbenzoyloxy)calix[4]arene (4-c) was prepared in the manner described above, using *p-tert*-butylbenzoyl chloride, to yield the 1,3-alternate conformer (**4[1,3-alt]-c**) as the only isolable isomer: mp 384-386° C; ^{1}H NMR ($CDCl_3$) δ 7.90 and 7.68 (pair d, 16, J = 8.19 and 8.95 Hz, Aroyl ArH), 6.75 (m, 12, ArH), 3.56 (s, 8, $ArCH_2Ar$), 1.54 (s, 36, $C(CH_3)_3$); Anal. calcd. for $C_{72}H_{72}O_8$: C, 81.17; H, 6.81. Found: C, 80.72; H, 6.64.

25,26,27,28-Tetra-(*p*-methoxybenzoyloxy)calix[4]arene (4-d) was prepared as described above, using *p*-methoxybenzoyl chloride, to yield the 1,3-conformer (**4[1,3-alt]-d**) as the only isolable isomer: mp >400°C; ^{1}H NMR ($CDCl_3$) δ 7.865 and 7.10 (pair d, 16, J = 7.8 and 8.7 Hz, Aroyl ArH), 6.74 (m, 12, ArH), 4.04 (s, 12, OCH_3), 13.57 (s, 8, $ArCH_2Ar$); Anal. calcd. for $C_{60}H_{48}O_{12}$: C, 74.99; H, 5.03. Found: C, 74.73; H, 4.84.

25,26,27,28-Tetra-[*p*-(3-chloropropoxy)benzoyloxy]-calix[4]arene (4-e) was prepared using *p*-(3-chloropropoxy)-benzoyl chloride, to yield the 1,3-alternate conformer (**4[1,3-alt]-e**) as the only isolable isomer: mp 270-272° C; ^{1}H NMR ($CDCl_3$) δ 7.07 (m, 12, ArH), 3.70 (s, 8, $ArCH_2Ar$), 3.64 (t, 8, J = 6.00 Hz, CH_2Cl), 2.01 (m, 8, $CH_2\underline{CH_2}CH_2Cl$), 1.86 (t, 8, J = 6.3 Hz, $\underline{CH_2}CH_2CH_2Cl$); Anal. calcd. for $C_{44}H_{44}O_8Cl_4$: C, 62.72; H, 5.26. Found: C, 62.92; H, 5.17.

Preparation of Tetra-aroylates via NaH-Induced Aroylations of *p*-Allyl-calix[4]arene

5,11,17,23-Tetraallyl-25,26,27,28-tetrabenzoyloxycalix[4]arene (6-a). A solution of 1.00 g (1.71 mmol) of *p*-allylcalix[4]arene[14] in 50 mL of dry THF in a 3-necked flask in which the air was replaced with N_2 was placed in an ice bath, treated with 0.6 g (15 mmol) of NaH (60% oil dispersion), and stirred for 30 m. A solution of 1.2 g (8.5 mmol) of benzoyl chloride in 10 mL of dry THF was then added dropwise over a period of 30 m, and the reaction mixture as stirred an additional 2 h. The solvent was removed on a rotary evaporator, and the residue was neutralized with ca 30 mL of dil HCl. The product was extracted into $CHCl_3$, the $CHCl_3$ solution was washed with water and brine and dried and then evaporated, and the residue was stirred for 30 m with 40 mL of methanol to leave 1.50 g (88%) of crude product. Recrystallization from $CHCl_3$/ CH_3OH afforded a colorless sample of the 1,3-alternate conformer **6[1,3-alt]-a**: mp > 450° C; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 8, J = 9.22 Hz, Benzoyl ArH), 7.94 (t, 4, J = 7.16 Hz, Benzoyl ArH), 7.69 (t, 8, J = 7.21 Hz, Benzoyl ArH), 6.56 (s, 8, ArH), 5.48 (m, 4, CH=C), 4.77, 4.73, 4.59, and 4.54 (pair of d of d, 8, J = 2.2, 10.2, and 17.2 Hz, $C=CH_2$), 3.55 (s, 8, $ArCH_2Ar$), 2.83 (d, 8, J = 6.84 Hz, $CH_2C=C$); Anal. calcd. for $C_{68}H_{56}O_8$: C, 81.58; H, 5.64. Found: C, 81.33; H, 5.65.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-*p*-methylbenzoyloxycalix[4]arene (6-b) was prepared in the manner described above, using *p*-toluoyl chloride, and was obtained in 70% yield as a colorless solid. Recrystallization from $CHCl_3/CH_3OH$ yielded the 1,3-alternate conformer **6[1,3-alt]-b**: mp >400° C; ^{1}H NMR ($CDCl_3$) δ 7.45 and 7.78 (pair d, 16, J = 7.5 and 7.8 Hz, Aroyl ArH), 6.55 (s, 8, ArH), 5.49 (m, 4, CH=C), 4.58 and 4.76 (d of d, 8, J = 2.4, 10.0, and 16.2 Hz, $C=CH_2$), 3.54 (s, 8, $ArCH_2Ar$), 2.84 (d, 8, J = 6.9 Hz, $CH_2C=C$); Anal. calcd. for $C_{72}H_{64}O_8$: C, 81.79; H, 6.10. Found: C, 81.87; H, 5.99.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(*p-tert*-butylbenzoyloxy)calix[4]arene (6-c) was prepared as described above, using *p-tert*-butylbenzoyl chloride, and obtained in 58% yield as a colorless solid after trituration with methanol. Recrystallization from $CHCl_3/CH_3OH$ yielded the 1,3-alternate conformer **6[1,3-alt]-c**: mp > 400° C; ^{1}H NMR ($CDCl_3$) δ 7.73 and 7.87 (pair d, 16, J = 8.2 Hz, Aroyl ArH), 6.55 (s, 8, ArH), 5.52 (m, 4, J = 6.7 Hz, CH=C), 4.74, 4.71, 4.59, and 4.53 (pair of d of d, 8, J = 2.20, 9.66, and 17.20 Hz, $C=CH_2$), 3.51 (s, 8, $ArCH_2Ar$), 2.92 (d, 8, $CH_2C=C$), 1.53 (s, 36, $C(CH_3)_3$); Anal. calcd. for $C_{84}H_{88}O_8$: C, 82.32; H, 7.24. Found: C, 82.21; H, 7.24.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(*p*-methoxybenzoyloxy)calix[4]arene (6-d). Treatment of *p*-allylcalix[4]arene with *p*-methoxybenzoyl chloride by the procedure described above yielded a mixture containing di-substituted, tri-substituted, and tetra-substituted products, with the tri-substituted product present in largest amount. When the ratio of calixarene/NaH/*p*-methoxybenzoyl chloride was changed to 1/17.6/16 the product consisted of a 57% yield of a 50:50 mixture of tri-substituted and tetra-substituted compounds from which a pure sample of the 1,3-alternate conformer of the tetra-substituted compound (**6[1,3-alt]-d**) was obtained by chromatographic separation: mp > 400° C; ^{1}H NMR ($CDCl_3$) δ 7.83 and 7.13 (pair d, 16, J = 8.75 Hz, Aroyl ArH), 6.56 (s, 8, ArH), 5.51 (m, 4, CH=C), 4.79, 4.76, 4.65, and 4.59 (pair of d of d, 8, J = 2.21, 10.18, and 16.33 Hz, $C=CH_2$), 4.02 (s, 12, OCH_3), 3.54 (s, 8, $ArCH_2Ar$), 2.88 (d, 8, J = 6.95 Hz, $CH_2C=C$); Anal. calcd. for $C_{72}H_{64}O_{12}$: C, 77.13; H, 5.75. Found: C, 76.76; H, 5.69.

5,11,17,23-Tetra-allyl-25-hydroxy-26,27,28-tri-(*p*-methoxybenzoyloxy)calix[4]arene (7-d) was obtained by column chromatography from the mixture described above, and the partial cone confomer (**7[pc]-d**) was isolated as a colorless solid: mp 249-251° C; ^{1}H NMR ($CDCl_3$) δ 7.96, and 6.87 (pair d, 12, J = 8.68 Hz, Aroyl ArH), 6.89 and 6.68 (2 s, 4, ArH), 6.75 and 6.42 (2 d, 4 J = 1.5 Hz, ArH), 5.81 (m, 1, CH=C), 5.76 (s, 1, OH), 5.26 (m, 3 CH=), 5.02 (m, 2, $=CH_2$), 4.78 (m, 6, C=CH$_2$), 3.92 - 2.34 (s and 4 pair d, 8, J = 14.05 and 15.52 Hz, ArCH$_2$Ar), 3.88 (s, 9, OCH$_3$), 3.25, 2.70 and 2.56 (m and pair d, 8, J = 6.84 Hz, CH$_2$C=C); Anal. calcd. for $C_{64}H_{58}O_{10}$: C, 77.87; H, 5.75. Found: C, 77.92; H, 6.01.

5,11,17,23-Tetra-allyl-25,27-dihydroxy-26,28-di(p-methoxybenzoyloxy)calix[4]arene (8-d) was obtained by column chromatography from the mixture described above, and the cone conformer (**7[c]-d**) was isolated as a colorless solid: mp 254-256° C; ^{1}H NMR (CDCl$_3$) δ 8.21 and 7.01 (pair d, 8, J = 9.00 Hz, Aroyl ArH), 6.79 and 6.78 (pair s, 8, ArH), 5.81 (m, 4, CH=C), 5.18 (s, 2, OH), 4.8 (m, 8, C=CH$_2$), 3.93 (s, 6, OCH$_3$), 3.89 and 3.50 (pair d, 8, J = 14.1 Hz, ArCH$_2$Ar), 3.13 (t, 8, J = 6 Hz, CH$_2$C=C); Anal. calcd. for $C_{56}H_{52}O_8$: C, 78.85; H, 6.14. Found: C, 78.96; H, 6.17.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(p-chloromethylbenzoyloxy)calix[4]arene (6-f) was prepared as described above, using p-chloromethylbenzoyl chloride, and obtained in 93% yield as a colorless solid. Recrystallization from CHCl$_3$/CH$_3$OH afforded the 1,3-conformer **6[1,3-alt]-f**: mp >400° C; ^{1}H NMR (CDCl$_3$) δ 7.86 and 7.72 (pair d, 16, J = 8.3 Hz, Aroyl ArH), 6.59 (s, 8, ArH), 5.46 (m, 4, CH=C), 4.84 (s, 8, CH$_2$Cl), 4.61, 4.67, 4.77, and 4.81 (pair of d of d, 8, J= 2.1, 10.8, and 16.2 Hz,C=CH$_2$), 3.59 (s, 8, ArCH$_2$Ar), 2.676 (d, 8, J = 6.9 Hz, CH$_2$C=C); Anal. calcd. for $C_{72}H_{60}O_8Cl_4$: C, 72.36; H, 5.06. Found: C, 72.05; H, 4.89.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(p-bromobenzoyloxy)calix[4]arene (6-g) was prepared as described above, using p-bromobenzoyl chloride, and was obtained in 75% yield as the acetone-insoluble material after trituration. Recrystallization from CHCl$_3$/CH$_3$OH yielded the 1,3-alternate conformation **6[1,3-alt]-g**: mp > 400° C; ^{1}H NMR (CDCl$_3$) δ 7.77 and 7.67 (pair d, 16, J = 8.95 and 8.08 Hz, Aroyl ArH), 6.56 (s, 8, ArH), 5.49 (m, 4, J = 6.84 Hz, CH=C),4.88, 4.84, 4.74, and 4.69 (pair of d of d, 8, J = 1.3, 2.3, 10.37, and 17.2 Hz, C=CH$_2$), 3.57 (s, 8, ArCH$_2$Ar), 2.80 (d, 8, J = 6.94 Hz, CH$_2$C=C); Anal. calcd. for $C_{68}H_{52}O_8Br_4$: C, 62.03; H, 3.98. Found: C, 62.10; H, 3.82.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(p-trifluoromethylbenzoyloxy)calix[4]arene (6-h). Treatment of p-allylcalix[4]arene with p-trifluoromethylbenzoyl chloride in the manner described above gave 74% of a product which was indicated by its NMR spectrum to be a mixture containing 34% of the cone conformer and 66% of the 1,3-alternate conformer. The conformers were separated by recrystallization from CHCl$_3$/CH$_3$OH, the 1,3-alternate conformer precipitating first to yield colorless crystals of **6[1,3-alt]-h**: mp > 400° C; ^{1}H NMR (CDCl$_3$) δ 7.97 and 7.91 (pair d, 16, J = 8.3 Hz, Aroyl ArH), 6.57 (s, 8, ArH), 5.42 (m, 4, J = 6.9 Hz, CH=C), 4.82, 4.79, 4.66, and 4.60 (d of d, 8, J = 2.4, 10.2, and 17.2 Hz, C=CH$_2$), 3.61 (s, 8, ArCH$_2$Ar), 2.72 (d, 8, J = 6.9 Hz, CH$_2$C=C); Anal. calcd. for $C_{72}H_{52}O_8F_{12}$: C, 67.92; H, 4.12. Found: C, 67.94; H, 4.04.

The cone conformer (**6[c]-h**) was obtained from the mother liquor of the mixture described above and could not be completely separated from a trace of **6[1,3-alt]-h**: mp > 400° C; ^{1}H NMR (CDCl$_3$) δ 8.18 and 7.44 (pair d, 16, J = 8.4 Hz, Aroyl ArH), 6.79 (s, 8, ArH), 5.81 (m, 4, CH=C), 5.05, 5.02, 4.88, and 4.83 (pair of d of d, 8, J = 1.5, 2.4, 9.9, and 16.2 Hz, C=CH$_2$), 4.07 and 3.36 (pair d, 8, J = 14.1 Hz, ArCH$_2$Ar), 3.17 (d, 8, J = 6.3 Hz, CH$_2$C=C); Aall. calcd. for $C_{72}H_{52}O_8F_{12}$: C, 67.92; H, 4.12. Found: C, 68.04; H, 3.93.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(p-cyanobenzoyloxy)calix[4]arene (6-i) was prepared as described above, using p-cyanobenzoyl chloride, and obtained in 47% yield as a product consisting mostly of the cone conformer (**6[c]-i**) contaminated with a small amount of the partial cone conformer and/or the tri-substituted compound: ^{1}H NMR (CDCl$_3$) δ 8.08 and 7.59 (pair d, 16, J = 8.3 Hz, Aroyl ArH), 6.76 (s, 8, ArH), 5.78 (m, 4, CH=), 5.05 5.02, 4.87, and 4.81 (pair of d of d, 8, J = 1.4, 2.4, 10.36, and 16.8 Hz, C=CH$_2$), 3.97 and 3.35 (pair d, 8, J = 13.8 Hz, ArCH$_2$Ar), 13.15 (d, 8, J = 6.39 Hz, CH$_2$C=C). Difficulties in removal of the tri-substituted compound precluded obtention of an analytical sample for elemental analysis.

5,11,17,23-Tetra-allyl-25,26,27,28-tetra-(p-nitrobenzoyloxy)calix[4]arene (6-j) was prepared as described above, using p-nitrobenzoyl chloride and was obtained in 84% yield as the cone conformer (**6[c]-j**) containing only a trace of the 1,3-alternate conformer: mp 290-291° C; ^{1}H NMR (CDCl$_3$) δ 8.19 and 8.08 (d of d, 16, J = 8.7 Hz, Aroyl ArH), 6.79 (s, 8, ArH), 5.79 (m, 4, CH=C), 5.05, 5.02, 4.87, and 4.81 (pair of d of d, J = 2.4, 10.2, and 17.4 Hz, C=CH$_2$), 4.02 and 4.00 (pair d, 8, J = 14.1 Hz, ArCH$_2$Ar), 3.17 (d, 8, J = 6.9 Hz, CH$_2$C=C); Anal. calcd. for $C_{68}H_{52}O_{16}N_4$: C, 69.15; H, 4.44. Found: C, 69.00; H, 4.39.

Preparation of Tetra-benzoates via NaH-Induced Benzoylations of p-tert-Butylcalix[4]arene

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(benzoyloxy)calix[4]arene (5-a). A solution of 1.00 g (1.54 mmol) of p-tert-butylcalix[4]arene[5,18] in 50 mL of dry THF was added to a 3-necked flask, and the air in the flask was replaced with N$_2$. The flask was put in an ice bath, 1.0 g (25 mmol) of NaH (60% dispersion in oil) was added, the flask was allowed to warm to room temperature, and the contents were stirred for 30 m. A slurry of 1.26 g (8.98 mmol) of benzoyl chloride in 10 mL of dry THF was then added dropwise over a period of 30 m, and the reaction mixture was refluxed for 2 h. The solvent was removed on a rotary evaporator, and the residue was neutralized with ca 30 mL of dil HCl. The product was extracted into CHCl$_3$, and the CHCl$_3$ solution was washed with water and brine, dried, and then evaporated, and the residue was stirred for 30 m with 100 mL of methanol to leave 1.30 g (79%) of crude product from which an analytical sample was obtained by recrystallization from CHCl$_3$/CH$_3$OH to give **5[c]-a**: mp 338-340° C; ^{1}H NMR (CDCl$_3$) δ 8.14 and 8.11 (d of d, 8, J = 1.2 and 8.25 Hz, Aroyl ArH), 7.26 (t, 4, Aroyl ArH), 7.11

(s, 8, ArH), 6.79 (t, 8, J = 8.1 Hz, Aroyl ArH), 4.26 and 3.44 (pair d, J = 13.8 Hz, $ArCH_2Ar$), 1.19 (s, 36, $C(CH_3)_3$; Anal. calcd. for $C_{72}H_{72}O_8$: C, 81.17; H, 6.81. Found: C, 81.30; H, 7.12.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(p-methylbenzoyloxy)calix[4]arene (5-b) was prepared as described above, using p-toluoyl chloride. The crude product, obtained in 78% yield, was a mixture that was indicated by its NMR spectrum to contain ca 90% of the cone conformer, 5% of the 1,3-alternate conformer and 5% of the tri-substituted compound. An analytical sample of the cone conformer §5[c]-b† was prepared by recrystallization from $CHCl_3/CH_3OH$: mp 360°; ^1H NMR ($CDCl_3$) δ 8.02 and 6.50 (pair d, 16, J = 7.8 Hz, Aroyl ArH), 7.12 (s, 8, ArH), 4.28 and 3.46 (pair d, 8, J = 12.9 Hz, $ArCH_2Ar$), 2.17 (s, 12, CH_3), 1.20 (s, 36, $C(CH_3)_3$); Anal. calcd. for $C_{76}H_{80}O_8$: C, 81.39; H, 7.19. Found: C, 80.51; H, 6.63.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(p-tert-butylbenzoyloxy)calix[4]arene (5-c) was prepared as described above, using p-tert-butylbenzoyl chloride. The crude product, obtained in 78% yield, was a mixture that was indicated on the basis of its NMR spectrum to contain ca 80% of the cone conformer and 20% of the 1,3-alternate conformer. An analytical sample of the cone conformer (5[c]-d) was prepared by recrystallization from $CHCl_3/CH_3OH$: mp 355-356° C; ^1H NMR ($CDCl_3$) δ 8.31 and 6.87 (pair d, 16, J = 9.3 Hz, Aroyl ArH), 7.14 (s, 8, ArH), 4.33 and 3.14 (pair d, 8, J = 14.1 Hz, $ArCH_2Ar$), 1.09 (s, 36, $C(CH_3)_3$); Anal. calcd. for $C_{88}H_{104}O_8$: C, 81.95; H, 8.13. Found: C, 81.96; H, 8.00.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(p-methoxybenzoyloxy)calix[4]arene (5-d) was prepared as described above, using p-methoxybenzoyl chloride. The crude product, obtained in 78% yield, was indicated on the basis of its NMR spectrum to contain ca 90% of the cone conformer, 5% of the partial cone conformer, and 5% of the 1,3-alternate conformer. An analytical sample of the cone conformer (5[c]-c) was prepared by recrystallization from $CHCl_3/CH_3OH$: mp 375-378° C; ^1H NMR ($CDCl_3$) δ 8.18 and 6.26 (pair d, 16, J = 8.7 Hz, Aroyl ArH), 7.14 (s, 8, ArH), 4.30 and 3.46 (pair d, 8, J = 14.1 Hz, $ArCH_2Ar$), 3.54 (s, 12, OCH_3), 1.19 (s, 36, $C(CH_3)_3$; Anal. calcd. for $C_{76}H_{80}O_{12}$: C, 77.00; H, 6.80. Found: 76.79; H, 6.77.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(p-bromobenzoyloxy)calix[4]arene (5-g) was prepared as described above, using p-bromobenzoyl chloride. The crude product, obtained in 75% yield, was indicated on the basis of its NMR spectrum to be pure cone conformer. An analytical sample was obtained by recrystallization from $CHCl_3/CH_3OH$ to give the cone conformer 5[c]-g: mp 371-373° C; ^1H NMR ($CDCl_3$) δ 7.91 and 7.14 (pair d, 16, J = 9.3 Hz, Aroyl ArH), 4.11 and 3.42 (pair d, 8, J = 13.8 Hz, $ArCH_2Ar$), 1.17 (s, 36, $C(CH_3)_3$; Anal. calcd. for $C_{72}H_{68}O_8Br_4$: C, 62.62; H, 4.96. Found: C, 62.45; H, 5.00.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-(p-nitrobenzoyloxy)calix[4]arene (5-j) was prepared as decribed above, using p-nitrobenzoyl chloride. The crude product, obtained in 86% yield, was indicated on the basis of its NMR spectrum to be pure cone conformer. An analytical sample was obtained by recrystallization from $CHCl_3/CH_3OH$ to give the cone conformer 5[c]-j : mp 360° C (dec); ^1H NMR ($CDCl_3$) δ 8.19 and 8.06 (pair d, 16, J = 8.7 Hz, Aroyl ArH), 7.05 (s, 8, ArH), 4.04 and 3.44 (pair d, 8, J = 14.1 Hz, $ArCH_2Ar$), 1.16 (s, 36, $C(CH_3)_3$); Anal. calcd. for $C_{72}H_{68}O_{16}N_4$: C, 69.44; H, 5.50. Found: C, 69.58; H, 5.56.

2D ^{1}H NMR Determinations. Pulse sequences for 2D HOMCOR and 2D NOE were available in the Varian XL-300 library. The 90° pulse was 22 us, the delay time was 3 s (ca 3 X T_1), and 256 FID and 16 transients were accumulated. With a spectral width of 2619 Hz the data set consisted of 1024 points on each dimension. Diagonal folding was carried out after transformation to remove T_1 noise and spurious peaks.

Acknowledgment. We are indebted to the National Institutes of Health for generous financial support of this work (GM-23534).

References

(1) For general reviews of the calixarenes cf. Gutsche, C. D., Topics in Current Chemistry, **1984**, 123, 1; idem, "Host Guest Complex Chemistry: Macrocycles", Vögtle, F.; Weber, E. eds, Springer, Berlin, **1985**, p. 375; idem, "Synthesis of Macrocycles: Design of Selective Complexing Agents", Izatt, R. M.; Christensen, J. J., eds, John Wiley & Sons, New York, **1987**, p 93-165.

(2) Megson, N. R. L., Oesterr. Chem. Z., **1953**, 54, 317.

(3) Ott, R.; Zinke, A., Oesterr. Chem. Z., **1954**, 55, 156.

(4) Cornforth, J. W.; D'Arcy Hart, P.; Nicholls, G.A.; Rees, R. J. W.; Stock, J. A., Brit. J. Pharmacol., **1955**, 10, 73.

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

(6) Kämmerer, H.; Happel, G.; Caesar, F., Makromol. Chem., **1972**, 162, 179.

(7) Happel, G.; Matiasch, B.; Kämmerer, H., *ibid*, **1975**, *176*, 3317.

(8) Munch, J. H., *ibid*, **1977**, *178*, 69.

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

(10) Gutsche, C. D.; Bauer, L. J., *J. Am. Chem. Soc.*, **1985**, *107*, 6052.

(11) Bocchi, V.; Foina, D.; Pochini, A.; Ungaro, R.; Andreetti, G. D., *Tetrahedron*, **1982**, *38*, 373.

(12) Högberg, A. G. S., *J. Org. Chem.*, **1980**, *45*, 4498; *idem*, *J. Am. Chem. Soc.*,**1980**, *102*, 6046.

(13) Gutsche, C. D.; Iqbal, M.; Alam,l I., *J. Am. Chem. Soc.*, **1987**, *108*, 000.

(14) Gutsche, C. D.; Levine, J. A.; Sujeeth, P. K., *J. Org. Chem.*, **1985**, *50*, 5802.

(15) Gutsche, C. D., Lin, L.-g., *Tetrahedron*, **1986**, *42*, 1633.

(16) The melting points of all compounds melting above 250° C were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) using a 500° C thermometer calibrated against a thermocouple. HPLC analyses were carried out on a Perkin-Elmer Series 4 apparatus using a Fisher Resolvex column and a LC-85B spectrometer. Using a methanol-water (9:1) mobile phase and a flow rate of 1.0 ml/min, the partial cone conformers showed shorter retention times (ca 7 min) than the 1,3-alternate conformers (ca 10 min). Proton nuclear magnetic resonance spectra (^{1}H NMR spectra) were recorded on a Varian XL-300 spectrometer. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (0.0) as an internal standard. Microanalyses were carried out by MicAnal Laboratories, Tuscon, AZ. Flash chromatography[17] was carried out with E. Merck silica gel (230-400 mesh ASTM) on columns 50 mm diameter filled to a height of 6 in. Elution rates were 2 in./min; fractions of 50 mL were collected. Analytical samples were dried for at least 36 h at 140°C and 1-2 mm pressure.

(17) Still, W. C.; Kahn, M.; Mitra, A., *J. Org. Chem.*, **1978**, *43*, 2923.

(18) Gutsche, C. D.; Iqbal, M.; Stewart, D., *J. Org. Chem.*, **1986**, *51*, 742.