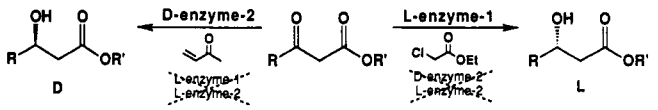
Scheme II



retain only 14%. Thus, D-enzyme-2 is virtually solely responsible for the catalysis of the reduction. Consequently, the D product is afforded stereoselectively. The introduction of an alkyl α-haloacetate shifts the stereoselectivity of the reduction toward formation of the L product.[9] It is believed, therefore, that such compounds inhibit the activity of D-enzyme. However, as the results shown in Figure 8 and listed in Table III demonstrate, ethyl chloroacetate inhibits not only the activity of D-enzyme-2 but also that of L-enzyme-2. On the other hand, the activity of L-enzyme-1 is unaffected by this additive. So, it can be concluded that, in the presence of ethyl chloroacetate, the reduction by bakers' yeast is catalyzed only by L-enzyme-1.

Of course, the results obtained from in vitro studies do not satisfactorily account quantitatively for the results obtained in vivo. Because the location of the enzymes within the yeast cell, the permeability of the cell wall toward organic reagents, and many other complex biological phenomena must be taken into consideration to understand the behavior of living microbes, the difference in the results of in vitro and in vivo studies is not surprising. Nevertheless, at least qualitatively, it is apparent that the activities of the enzymes of bakers' yeast are specifically inhibited by certain compounds. Thus, the stereospecificity of reductions by bakers' yeast can be changed. The effects of additives on the stereoselectivity of the reduction can be summarized by the reactions shown in Scheme II.

Studies of the enzymatic reduction of other substrates and the application of the purified enzymes described here to organic synthesis are now in progress. The results will be reported elsewhere.

Acknowledgment. We thank the Ministry of Education, Science and Culture for financial support (Grants-in-Aid No. 01470022, 01303007, and 02303004).

Registry No. D-β-keto ester reductase, 114705-02-1; L-α-keto ester reductase, 114705-03-2; ethyl 4-chloro-3-oxobutanoate, 78-94-4; ethyl chloroacetate, 105-39-5.

Calixarenes. 25. Conformations and Structures of the Products of Arylmethylation of Calix[4]arenes

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The arylmethylations of calix[4]arenes reported in this paper serve as companion pieces to an earlier study of the effects of reaction conditions and the structure of the derivatizing agent on the conformational outcome of the aroylation of calix[4]arenes. In contrast to the aroylation reaction, where a significant and predictable relation is observed between the para substituent of the aroyl chloride and the ratio of conformers formed, the arylmethylation reaction shows only a small and much less easily predictable dependence of the conformer ratio on the para substituent of the arylmethyl halide. Also, whereas the products of aroylation are the cone and/or 1,3-alternate conformers, those of arylmethylation are the cone and/or partial cone conformers. While no rationale has yet emerged to explain this difference, a study of the benzylation of dibenzyl and tribenzyl ethers of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene has established that the conformations of the tetraethers are not completely established until the third step in some cases and the fourth step in others.

Calixarenes are conformationally mobile macrocyclic compounds that are the focus of considerable attention because of their ability, when appropriately functionalized, to serve as ionophores and enzyme mimics.[1] The possibility for conformational isomerism in the calix[4]arenes was first recognized by Megson[2] and Ott and Zinke;[3] the concept was sharpened by Cornforth and co-workers;[4] and the process of conformational interconversion has now been studied in detail by several groups of researchers including Kämmerer et al.,[5,6] Munch,[7] Gutsche et al.,[8,9] Shinkai et al.,[10-13] Ungaro et al.,[14] and Reinhoudt et al.[15] The four "up-down" conformers that are possible have been designated as cone, partial cone, 1,2-alternate, and 1,3-alternate, as depicted in Figure 1.

Upon replacement of the phenolic hydrogens with sufficiently large groups, the calix[4]arenes become conformationally inflexible, existing as discrete entities in one or another of the conformations.[16,17] A study of the aroylation of calix[4]arenes carried out in this laboratory[18]

(1) Gutsche, C. D. *Calixarenes*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989.
(2) Megson, N. R. L. *Oesterr. Chem.-Ztg.* **1953**, *54*, 317.
(3) Ott, R.; Zinke, A. *Oesterr. Chem.-Ztg.* **1954**, *55*, 156.
(4) Cornforth, J. W.; D'ArcyHart, P.; Nicholls, G. A.; Rees, R. J. W. *Br. J. Pharmacol.* **1955**, *10*, 73.
(5) Kämmerer, H.; Happel, G.; Caeser, F. *Makromol. Chem.* **1972**, *162*, 179.
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(7) Munch, J. H. *Makromol. Chem.* **1977**, *69*, 178.
(8) Gutsche, C. D.; Bauer, L. J. *Tetrahedron Lett.* **1981**, *22*, 4763.
(9) Bauer, L. J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1985**, *107*, 6052, 6063.
(10) Araki, K.; Iwamoto, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 1747.
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(12) Shinkai, S.; Iwamoto, K.; Araki, K.; Matsuda, T. *Chem. Lett.* **1990**, 1263.
(13) Iwamoto, K.; Fujimoto, K.; Matsuda, T.; Shinkai, S. *Tetrahedron Lett.* **1990**, *49*, 7169.
(14) Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R. *Gazz. Chim. Ital.* **1989**, *119*, 335.
(15) Grootenhuis, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreetti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165.
(16) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782.
(17) Bocchi, V.; Foina, D.; Pochini, A.; Ungaro, R.; Andreetti, G. D. *Tetrahedron* **1982**, *38*, 373.

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Table I. Effect of Time, Temperature, and Benzyl Halide: Tetrabenzyl Ethers of *p*-H-Calix[4]arene and *p*-*tert*-Butylcalix[4]arene Prepared in THF–DMF (9:1) Solvent

				tetraether		
arylmethyl halide	calixarene	time, h	temp, °C	cone (%)	partial cone (%)	ratio
$PhCH_2Br$	2	1	70	63	8	89:11
	2	2	70	65	7	90:10
	2	18	24	73	6	92.5:7.5
	2	168	5	83	–	–
	1	1	70	27	19	58:42
	1	168	5	55	3	96:4
$PhCH_2Cl$	2	5	70	66	9	88:12
$PhCH_2I$	2	1	70	79	5	94:6

Table II. Effect of Solvent: Di- and Tetrabenzyl Ethers of *p*-*tert*-Butylcalix[4]arene (2) Prepared from Benzyl Bromide

			tetraether			
solvent	time, h	temp, °C	cone (%)	partial cone (%)	diether	ratio
acetone[a]	24	56	–	–	77	0:0:100
THF	2	65	5	–	59	9:0:91
	8	65	28	17	13	48:29:23
	24	65	45	17	–	72:28:0
THF–DMF (1:1)	1	65	79	–	–	100:0:0
DMF	1	65	83	–	–	100:0:0
DMF[b]	1	65	70	–	–	100:0:0

[a] Anhydrous K_2CO_3 was used as the base. [b] Starting material was *p*-H-calix[4]arene (1).

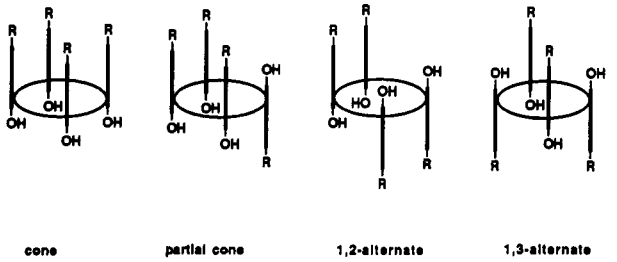


Figure 1. The "up–down" conformers of tetrahydroxycalix[4]-arenes.

showed that the particular conformation in which a calix[4]arene is fixed upon derivatization is dependent, inter alia, on the temperature, the solvent, the para substituent of the calixarene, and the reactivity of the aroylating agent. The results were interpreted in terms of a competition between the rate of conformational interconversion and the rate of derivatization, the more reactive the aroylating agent (i.e., *p*-nitrobenzoyl chloride), the greater the amount of cone conformer and, conversely, the less reactive the aroylating agent (i.e., *p*-methoxybenzoyl chloride), the greater the amount of 1,3-alternate conformer. The present investigation is an extension of this earlier work and involves the use of a variety of para-substituted benzyl halides to assess the effects of para substituents and reaction conditions on the conformational outcome in the ether-forming benzylation reaction.

The conformation of a derivatized calix[4]arene can be readily established on the basis of its ^1H NMR spectrum, particularly from the patterns arising from the methylene protons joining the aromatic rings of the cyclic array;[1,18] the cone conformer shows one pair of doublets, the partial cone conformer two pairs of doublets or a pair of doublets and a singlet,[19] the 1,2-alternate conformer one singlet and two doublets, and the 1,3-alternate conformer one singlet. In the first part of the present study, arylmethyl ethers were prepared from an arylmethyl halide (8–12 mmol),

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

(19) In the latter instance the partial cone conformer can be distinguished from the 1,2-alternate conformer by the presence of three *tert*-butyl resonances in a 2:1:1 ratio in contrast to the single resonance for the 1,2-alternate conformer.

Table III. Effect of Para Substituent in Arylmethyl Bromide: Tetrakis(arylmethyl) Ethers of *p*-*tert*-Butylcalix[4]arene (2) Prepared in THF–DMF (9:1), 1 h at 70 °C

	tetraether		
para substituent	cone (%)	partial cone (%)	ratio
H	63	8	89:11
CH_3	68	6	92:8
tert-Bu	62	9	87:13
Br	70	17	80:20
CN	28	46	38:62
NO_2	30	36	46:54

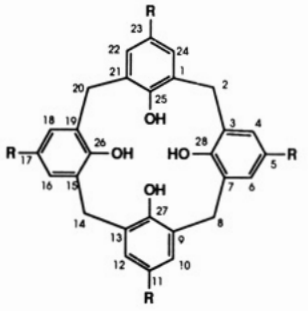
Table IV. Effect of Para Substituent in Arylmethyl Bromide: Tetrakis(arylmethyl) Ethers of *p*-H-Calix[4]arene Prepared in THF–DMF (9:1), 1 h at 70 °C

	tetraether		
para substituent	cone (%)	partial cone (%)	ratio
H	27	19	58:42
CH_3	58	4	93:7
tert-Bu	42[a]	34[a]	55:45
Br	55	15	79:21
CN	74	–	100:0
NO_2	61	–	100:0

[a] Values obtained only by ^1H NMR analysis.

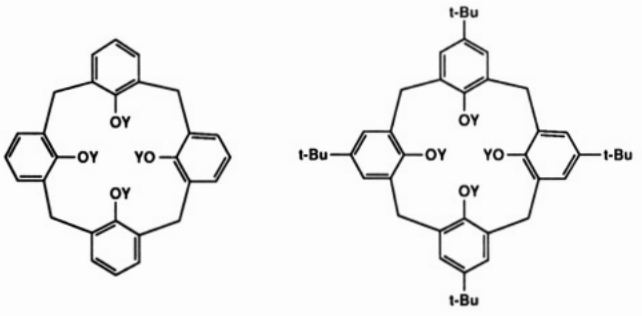
NaH (8–12 mmol), and *p*-H-calix[4]arene (1) or 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix-[4]arene (2) (generally referred to as *p*-*tert*-butylcalix-[4]arene) in 50 mL of a solvent. The arylmethyl ethers were obtained from the crude products by fractional crystallization and/or chromatography, and the structures of the pure materials were established by ^1H NMR spectroscopy combined with elemental analysis. The product ratios shown in Tables I–IV are based, in most cases, on the actual isolated yields of the components, checked by semiquantitative comparison of the ^1H NMR spectrum of the product mixture with the spectra of the pure components. The variables that were studied include time, temperature, solvent, halogen atom of the benzyl halide, para substituent of the benzyl halide, and para substituent of the calix[4]arene.

In contrast to the aroylation reaction, where the para substituents of the aroyl chlorides play an important role



1 (R = H)

2 (R = C(CH$_3$)$_3$)



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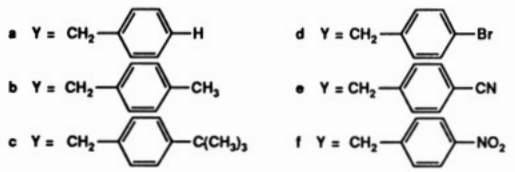


in determining the conformational outcome of the derivatization reactions, the para substituents of the arylmethyl halides in the arylmethylation reaction are seen from the data in Tables III and IV to have a less pronounced effect. This can be ascribed to the differing pathways by which the aroylation and arylmethylation processes occur. The rate-determining step in the aroylation reaction is probably the formation of the tetrahedral intermediate arising from nucleophilic attack by the calixarene oxyanion at the sp^2 carbonyl carbon of the aroylating agent, which is made more electrophilic by electron-withdrawing groups in the para position and less electrophilic by electron-releasing groups. Arylmethylation, on the other hand, is an S_N2 reaction involving nucleophilic attack at an sp^3-hybridized carbon to produce an activated complex whose formation and decomposition are dependent on the characteristics of both the C–halogen and C–oxygen bonds, modified to some degree by the electronic character of the aryl rings of the derivatizing agent and the calixarene. In the case of *p-tert*-butylcalix[4]arene (**2**) a change in the product ratio occurs with the strongly electron withdrawing para substituents CN and NO_2, which lead to less cone and more partial cone conformer than the other arylmethylating agents. *p*-H-Calix[4]arene (**1**), on the other hand, shows a larger cone to partial cone ratio for *p*-cyano- and *p*-nitrobenzyl bromide and, somewhat surprisingly, a lower ratio with benzyl bromide itself. The difficulty of quantitatively assessing the influence of electronic factors in S_N2 processes[20] has often been noted as, for example, in the reaction of $S_2O_3^{2-}$ with benzyl chlorides where both

(20) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper & Row Publishers, Inc.: New York, 1987; pp 327–412.

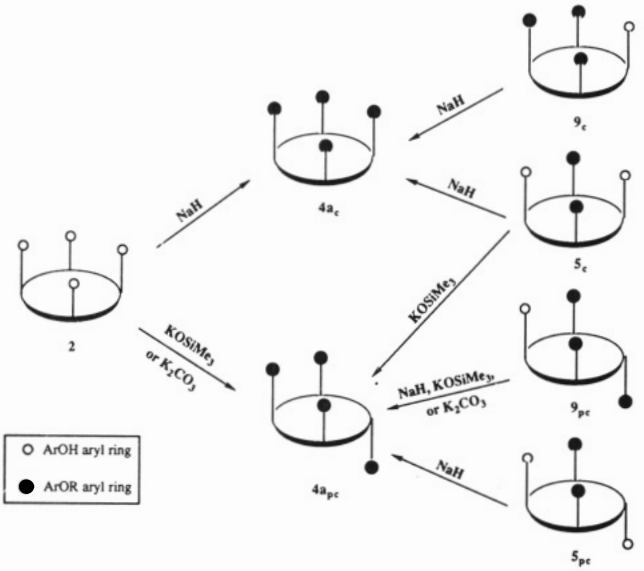


Figure 2. Major pathways of benzylation of calix[4]arene **2** and its di- and triethers.

p-tert-butylbenzyl chloride and *p*-nitrobenzyl chloride react more rapidly than benzyl chloride,[21] the first by a factor of 1.29 and the second by a factor of 2.55. The only conclusion we draw from the data in Tables III and IV, which show that the variation in product ratio covers a rather narrow range of values, is that substituents in the para positions of either the arylmethylating agent or the calixarene have a relatively small and not easily predictable effect on the ratio of cone to partial cone conformer that is formed.

To gain further insight into the steps in the derivatization sequence at which the final conformations are fixed, we carried out a number of benzylation reactions with *p-tert*-butylcalix[4]arene (**2**), the cone and partial cone (vide infra) conformers of its diether **5**, and the cone and partial cone conformers of its triether **9** using NaH (very strong base), $KOSiMe_3$ (strong base), and K_2CO_3 (weak base) as bases and THF–DMF or acetone as solvents. The products consist primarily of the tetraether **4a** in the cone (**4a$_c$**), partial cone (**4a$_{pc}$**), and/or 1,3-alternate (**4a$_{1,3\text{-alt}}$**) conformations accompanied in a few instances by the triether **9**. The detailed results of these experiments are shown in Table V, and the major results are summarized in Figure 2. The most significant observations are as follows: (a) The cone conformations of the diether and triether are retained to a greater extent with NaH than with $KOSiMe_3$ and K_2CO_3. For example, the cone conformer of diether **5$_c$** gives 67% cone conformer of tetraether **4a$_c$** with NaH and 74% partial cone conformer of **4a$_{pc}$** with $KOSiMe_3$; the cone conformer of the triether **9$_c$** gives the cone conformer **4a$_c$** in 85%, 56%, and 36% yields as the base changes from NaH to $KOSiMe_3$ to K_2CO_3. (b) The partial cone conformations of the diether **5$_{pc}$** and the triether **9$_{pc}$** are completely retained in the tetraether **4a$_{pc}$** with NaH and $KOSiMe_3$ and almost completely with K_2CO_3, which also yields a small amount of **4$_{1,3\text{-alt}}$**. (c) The outcome of the benzylation of the parent calixarene **2** reflects that of the benzylations of the di- and triethers, viz., NaH leads primarily to **4a$_c$**, while $KOSiMe_3$ and K_2CO_3 lead primarily to **4a$_{pc}$**.

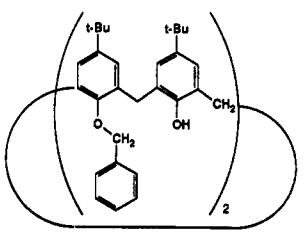
What is believed to be the partial cone conformer of the diether **5$_{pc}$** was obtained in an unexpected fashion. A reaction of the cone conformer of the diether **5$_c$** with a

(21) Fuchs, R.; Carleton, D. M. *J. Am. Chem. Soc.* **1963**, *85*, 104.

Table V. Products Formed in the Benzylation of *p-tert*-Butylcalix[4]arene (2), the Dibenzyl Ether 5, and the Tribenzyl Ether 9 in the Presence of K_2CO_3, $KOSiMe_3$, or NaH

compd	base	solvents	time, h	temp, °C	products, % yields			
					$4a_c$	$4a_{pc}$	$4a_{1,3\text{-alt}}$	9_c
2	NaH	THF-DMF (9:1)	1	reflux	63	8		
2	$KOSiMe_3$	acetone	24	reflux	1	69	2	
2	$KOSiMe_3$	THF-DMF (9:1)	24	reflux	1	71	1	
2	K_2CO_3	acetone	60	reflux	2	50	2	2
5_c	NaH	THF-DMF (9:1)	1	reflux	67	20		
5_c	$KOSiMe_3$	THF-DMF (9:1)	24	reflux	5	74	1	
5_c	K_2CO_3	acetone	60	reflux	4	63	2	7
5_{pc}	NaH	THF-DMF (9:1)	2	rt		83		
9_c	NaH	THF-DMF (9:1)	1	reflux	85			
9_c	$KOSiMe_3$	THF-DMF (9:1)	24	reflux	56	22		
9_c	K_2CO_3	acetone	168	reflux	36	28		22
9_{pc}	NaH	THF-DMF (9:1)	1	reflux		81		
9_{pc}	$KOSiMe_3$	THF-DMF (9:1)	24	reflux		83		
9_{pc}	K_2CO_3	acetone	60	reflux		83	4	

limiting amount of benzyl bromide and $KOSiMe_3$ yields the triether 9_c as the major product accompanied by 10% of a diether different from the starting material. It possesses an elemental analysis and ^1H NMR spectrum compatible with a diether, and upon further benzylation in the presence of NaH it yields the partial cone conformer of the tetraether $4a_{pc}$. However, the pair of equal-intensity resonances arising from the *tert*-butyl groups and the three singlets arising from the $ArCH_2Ar$ methylenes are not easily accommodated to this structure except by assuming that (a) two of the *tert*-butyl resonances are overlapped to appear as a singlet and (b) the J value for the nonequivalent hydrogens in two of the methylene groups is close to 0, resulting in no observable coupling; this might be ascribed to a flattened partial cone conformation. The ^{13}C NMR spectrum indicates the presence of three nonequivalent methylene carbons, compatible with a partial cone structure.



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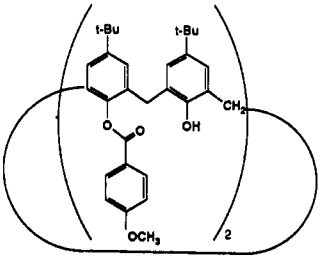

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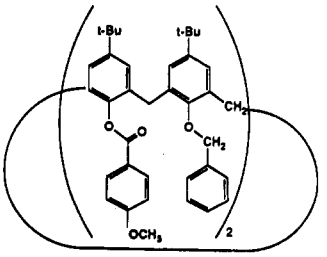

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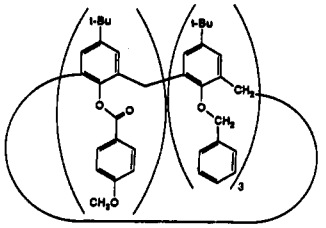

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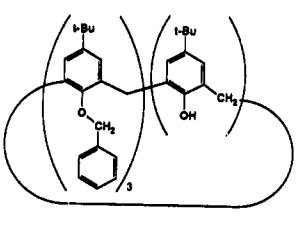

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Shinkai and co-workers[10,22] have found that the alkylations of *p-tert*-butylcalix[4]arene (2) with MeI, EtI, and PrI yield the partial cone conformer as the exclusive products in the first two cases and the major product in the third. They also observed that as the size of the R group of the alkylating agent increases, the ratio of cone to partial cone conformer increases (i.e., 0:100 for Et, 45:55 for Pr, 53:47 for Bu) as the conformational flexibility of the system decreases. The earlier observation that the tetramethyl ethers of tetrahydroxycalix[4]arenes are as flexible as the parent compounds[23] was corroborated, and it was also shown that the tetraethyl ethers retain considerable conformational flexibility at elevated temperatures. The tetrapropyl ethers, however, have fixed conformations, as must certainly be the case with the tetrabenzyl ethers. Although *complete* conformational interconversion in a calix[4]arene is curtailed as soon as only one R group larger than Et is introduced, *partial* conformational change remains a possibility until the fourth R group is introduced. Thus, in spite of the fact that the 1,3-dibenzyl ether 5_c appears to be conformationally frozen in the cone conformation,[23] treatment of 5_c with benzyl bromide yields both cone and partial cone conformers of the tetraether **4a**. Similarly, although the triether 9_c appears to be conformationally inflexible, it yields both cone and partial cone tetraether products. In each case the aryl moiety undergoing inversion is assumed to be the one containing the free OH group, as depicted in Figures 2 and 3. As suggested in the earlier paper dealing with the aroylation process,[18] these results can be interpreted as a competition between the rates of conformational inversion and derivatization. Thus, if (a) $k_{-a} \gg k_a$ (i.e., K for the cone to partial cone interconversion $\ll 1$), (b) k_{-a} and $k_a > k_1$, k_2, and k_3 (i.e., conformational equilibration is faster than derivatization), and (c) k_2 and/or $k_3 \gg k_1$, the major product would be the partial cone conformer of the triether. However, if k_{-a} and $k_a < k_1$, k_2, and k_3 (i.e., conformational equilibrium is slower than derivatization), a greater amount of cone conformer of the triether would be expected from 5_c, whereas 5_{pc} should yield a greater amount of partial cone conformer. Similar arguments can be adduced for the subsequent conversion of the triethers to the tetraethers, although, not surprisingly, the conformational interconversion appears to be slower for the triethers than the diethers (i.e., k_c and $k_{-c} < k_a$ and k_{-a}).

(22) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.*, in press. We are indebted to Professor Shinkai for making the details of this work available to us prior to their publication.

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

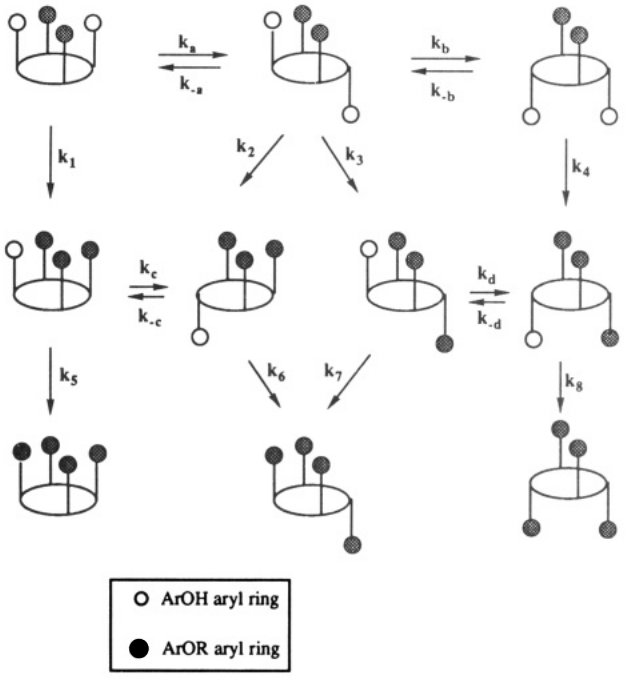

Figure 3. Rates of conformational interconversion and derivatization of calix[4]arenes.

Thus, $4a_c$ is the major though not exclusive product from 9_c under all conditions, and $4a_{pc}$ is the only product from 9_{pc} under all conditions. On the basis of these results it can be concluded that the conformation in the arylmethylation reaction is established primarily but not completely in the third step, the fourth step also playing a role at least in some cases. A similar conclusion has been reached by Shinkai et al.[22] for the propylation reaction.

The products of arylmethylation partition principally between the cone and partial cone conformers, while those of aroylation partition principally between the cone and 1,3-alternate conformers. Molecular dynamics studies of the pathway for conformational interconversion of calix[4]arenes[15] indicate that the molecule first goes to the partial cone conformer and then to the 1,2- and/or 1,3-alternate conformer, the second step being especially facilitated by a polar solvent (H_2O used in the MD simulation studies). Thus, the arylmethylation reactions might be (a) more rapid than the slower of the aroylation reactions, allowing them to intercept the calixarene at the earlier point on the pathway of conformational interconversion, but (b) slower than the faster of the aroylation reactions, which give cone conformer as the exclusive product. That there is only a narrow range of reactivity among the arylmethylating agents is indicated by the data cited above,[21] which show only a 3-fold difference in rate between *p-tert*-butylbenzyl chloride and *p*-nitrobenzyl chloride with $S_2O_3^{2-}$. A much greater spread in reactivities is expected in the aroylation reaction, and it might be argued that none of the aroyl halides used in the NaH method in the previous study[18] have precisely the right degree of reactivity to produce the partial cone conformation; i.e., some are too reactive, leading to cone conformer, and others are too unreactive, leading to 1,3-alternate conformer. This rationalization appears to be untenable, however, because a reaction mixture containing 1 mmol of **2** and 8 mmol each of *p*-methoxybenzoyl chloride (a low-reactivity aroyl chloride), *p*-methylbenzyl bromide, and NaH yields 54% of the diester (**6**) as the only isolable product; at most, only traces of *p*-methylbenzyl ethers are present, so even the relatively unreactive *p*-methoxybenzoyl chloride outcompetes the benzyl halide. It is interesting to note, though, that the same reaction carried out in the absence of the benzyl halide gives the diester in 65% yield. Further reaction of the diester with benzyl bromide in the presence of NaH yields a mixture of at least five compounds, including 36% of the cone conformer of the mixed ester ether 7_c as the major product accompanied by small amounts (3–8%) of the partial cone and 1,3-alternate conformers 7_{pc} and $7_{1,3\text{-alt}}$, the tribenzyl ether monoester (**8**), and the tetrabenzyl ether ($4a_c$). In contrast, reaction of the dibenzyl ether **5** with *p*-methoxybenzoyl chloride produces 7_c in 97% yield.

In terms of the reaction scheme depicted in Figure 3, the formation of tetraesters in the 1,3-alternate conformation requires that k_4 and/or k_8 be faster than k_2, k_3, k_6, and k_7 in the aroylation process but slower in the arylmethylation process. If the rates of conformational equilibrium are the same in the aroylation and arylmethylation processes, it is difficult to reconcile the experimental data with this scheme. However, the picture is further complicated by the fact that the disubstituted compounds can also exist as mono- and dianions and the trisubstituted compounds can also exist as monoanions. That the conformational mobility of the anions is different from that of the neutral species has been shown by recent work from this laboratory in which 1, 2, 3, and 4 equiv of butyllithium are added to DMSO solutions of a calix[4]arene.[24] Whether such data can provide a rationale for the formation of 1,3-alternate conformers in the aroylation reaction must await further exploration of the mechanistic subtleties of these processes.

The data in Tables I and II also reveal the effects of temperature, the arylmethylating agent, and the solvent. Although the product ratios for cone vs partial cone formed from benzyl bromide and *p-tert*-butylcalix[4]arene (**2**), as shown in Table I, are close to one another, the isolable amount of cone conformer increases as the reaction temperature is lowered. An analogous result was encountered in the earlier work,[18] where it was found that the ratio of partial cone to 1,3-alternate conformer in the $AlCl_3$-catalyzed benzoylation increases as the reaction temperature decreases. In both cases the data can be interpreted as the results of a competition between the rate of conformational interconversion and the rate of derivatization, with the conformational inversion process having a greater temperature dependence. The halogen of the benzyl halide has only a minor influence on the conformational outcome, benzyl iodide giving a slightly higher cone to partial cone ratio than benzyl bromide or benzyl chloride. A somewhat greater difference was found by Shinkai et al.[10] with propyl bromide vs propyl iodide. The solvent used in most of the arylmethylations in the present study was THF–DMF (9:1). When pure THF is used, the formation of the tetraether becomes much slower, and the 1,3-diether is formed as the major product in the reaction carried out for 2 h at 65 °C, as shown in Table II. Only after 24 h at this temperature is the diether completely converted to a mixture of cone and partial cone tetraether. Increasing the amount of DMF increases the rate of the reaction and, concomitantly, the amount of cone conformers, reinforcing the idea that the faster the reaction, the greater is the amount of cone conformer formed.

(24) Gutsche, C. D.; Iqbal, M.; Nam, K.-C.; See, K. A.; Alam, I. *Pure Appl. Chem.* **1988**, *60*, 483.

Experimental Section[25]

Cone Conformer of 25,26,27,28-Tetrakis(benzyloxy)calix[4]arene ($3a_c$). To a suspension of 0.48 g (12 mmol) of NaH (60% oil dispersion) washed with two 2-mL portions of hexane in 40 mL of THF–DMF (7:1, v/v) was added 0.636 g (1.5 mmol) of *p*-H-calix[4]arene (1)[27] with stirring at room temperature in an atmosphere of N_2. After 15 min a solution of 2.05 g (12 mmol) of benzyl bromide in 10 mL of THF was introduced, and the reaction mixture was stirred and refluxed for 1 h. After cooling, a few drops of MeOH were added, and the solvent was removed on a rotary evaporator. The residue was poured onto 100 mL of water, and the gummy material that separated was partitioned between water and $CHCl_3$. The $CHCl_3$ extract was washed with water and brine, then dried over Na_2SO_4, and evaporated to give an oil. Flash chromatography (gradient elution with CCl_4–CH_2Cl_2 from 9:1 to 17:3) yielded two compounds, one of which was crystallized from CH_2Cl_2–hexane to give 0.315 g (27%) of $3a_c$ as colorless needles: mp 152–154 °C (lit.[28] mp 135–136 °C); ^1H NMR ($CDCl_3$) δ 7.31–7.18 (m, 20, ArH), 6.59–6.51 (m, 12, ArH), 4.93 (s, 8, OCH_2Ph), 4.21 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 2.95 (d, 4, J = 13.6 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{56}H_{48}O_4$: C, 85.68, H. 6.16. Found: C, 85.36; H, 6.21.

Partial Cone Conformer of 25,26,27,28-Tetrakis(benzyloxy)calix[4]arene ($3a_{pc}$). The second compound obtained from the chromatographic separation described above was crystallized from CH_2Cl_2–hexane to give 0.225 g (19%) of $3a_{pc}$ as colorless crystals: mp 129–130 °C; ^1H NMR ($CDCl_3$) δ 7.39–7.17 (m, 18, ArH), 7.11–6.97 (m, 7, ArH), 6.88–6.77 (m, 3, ArH), 6.46–6.26 (m, 4, ArH), 4.88 (s, 2, OCH_2Ph), 4.66 (s, 4, OCH_2Ph), 4.46 (s, 2, OCH_2Ph), 3.81 (d, 2, J = 13.6 Hz, $ArCH_2Ar$), 3.56 (d, 2, J = 13.1 Hz, $ArCH_2Ar$), 3.51 (d, 2, J = 13.1 Hz, $ArCH_2Ar$), 2.85 (d, 2, J = 13.6 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{56}H_{48}O_4$: C, 85.68; H, 6.16. Found: C, 85.63; H, 6.09.

Cone Conformer of 25,26,27,28-Tetrakis[(*p*-methylbenzyl)oxy]calix[4]arene ($3b_c$). Treatment of 1 with 2.22 g (12 mmol) of 4-methylbenzyl bromide by the procedure described above for the preparation of **3a** yielded 0.92 g of crude product as a white powder after trituration with MeOH. Repeated fractional crystallization from CH_2Cl_2–MeOH afforded 0.67 g of $3b_c$ as colorless prisms: mp 187–189 °C; ^1H NMR ($CDCl_3$) δ 7.17 (d, 8, J = 8.0 Hz, ArH), 7.10 (d, 8, J = 8.0 Hz, ArH), 6.56–5.50 (m, 12, ArH), 4.88 (s, 8, OCH_2Ar), 4.22 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 2.94 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 2.32 (s, 12, Me). Anal. Calcd for $C_{60}H_{56}O_4$: C, 85.68; H, 6.71. Found: C, 85.69; H, 6.71. Concentration of the filtrate followed by preparative TLC (1:3 CH_2Cl_2–hexane) furnished 0.06 g of the $3b_c$ (overall yield 58%).

Partial Cone Conformer of 25,26,27,28-Tetrakis[(*p*-methylbenzyl)oxy]calix[4]arene ($3b_{pc}$). A second compound isolated from the preparative TLC experiment describes above consisted of 0.055 g (4%) of $3b_{pc}$, which was obtained as a white solid: mp 70–75 °C; ^1H NMR ($CDCl_3$) δ 7.33–7.13 (m, 14, ArH), 6.97–6.79 (m, 10, ArH), 6.41 (t, 2, J = 7.6 Hz, ArH), 6.21 (d, 2, J = 6.3 Hz, ArH), 4.86 (s, 2, OCH_2Ar), 4.62 (s, 4, OCH_2Ar), 4.38 (s, 2, OCH_2Ar), 3.81 (d, 2, J = 13.6 Hz, $ArCH_2Ar$), 3.55 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 3.49 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 2.84 (d, 2, J = 13.6 Hz, $ArCH_2Ar$), 2.40 (s, 3, Me), 2.36 (s, 6, Me), 2.28 (s, 3, Me). Anal. Calcd for $C_{60}H_{56}O_4$: C, 85.68; H, 6.71. Found: C, 85.80; H, 6.73.

Cone Conformer of 25,26,27,28-Tetrakis[(*p*-*tert*-butylbenzyl)oxy]calix[4]arene ($3c_c$). Treatment of 1 with 2.71 g (12 mmol) of 4-*tert*-butylbenzyl bromide by the procedure described above for the preparation of **3a** yielded 1.23 g (76%) of a colorless solid after flash chromatography (1:2 CH_2Cl_2–hexane), the ^1H NMR spectrum of which indicated it to be a mixture containing 55% of $3c_c$ and 45% of $3c_{pc}$. Anal. Calcd for $C_{72}H_{80}O_4$ as a mixture of conformers: C, 85.67; H, 7.99. Found: C, 85.62; H, 8.06. Repeated fractional crystallization from CH_2Cl_2–MeOH–acetone yielded 0.36 g of $3c_c$ as colorless prisms: mp 193–195 °C; ^1H NMR ($CDCl_3$) δ 7.26 (d, 8, J = 8.3 Hz, ArH), 7.20 (d, 8, J = 8.3 Hz, ArH), 6.55–6.43 (m, 12, ArH), 4.87 (s, 8, OCH_2Ar), 4.25 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 2.95 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 1.27 (s, 36, CMe_3). Anal. Calcd for $C_{72}H_{80}O_4$: C, 85.67; H, 7.99. Found: C, 86.16; H, 8.00.

Cone Conformer of 25,26,27,28-Tetrakis[(*p*-bromobenzyl)oxy]calix[4]arene ($3d_c$). Treatment of 1 with 3.0 (12 mmol) of 4-bromobenzyl bromide by the procedure described above for the preparation of **3a** yielded 1.36 g of a white powder after trituration with MeOH. Repeated fractional crystallization from $CHCl_3$–MeOH–acetone and CH_2Cl_2–MeOH yielded two compounds, one of which was 0.90 g (55%) of $3d_c$ as colorless glistening flakes: mp 199–201 °C; ^1H NMR ($CDCl_3$) δ 7.35 (d, 8, J = 8.4 Hz, ArH), 7.10 (d, 8, J = 8.4 Hz, ArH), 6.60–6.46 (m, 12, ArH), 4.82 (s, 8, OCH_2Ar), 4.10 (d, 4, J = 13.6 Hz, $ArCH_2Ar$), 2.96 (d, 4, J = 13.6 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{56}H_{44}Br_4O_4$: C, 61.11; H, 4.03. Found: C, 61.14; H, 3.83.

Partial Cone Conformer of 25,26,27,28-Tetrakis[(*p*-bromobenzyl)oxy]calix[4]arene ($3d_{pc}$). The other compound obtained in the experiment described above was 0.24 g (15%) of $3d_{pc}$ as colorless prisms: mp 172–175 °C; ^1H NMR ($CDCl_3$) δ 7.38 (d, 6, J = 8.3 Hz, ArH), 7.27 (d, 2, J = 8.3 Hz, ArH), 7.20 (d, 2, J = 7.4 Hz, ArH), 7.10–6.91 (m, 8, ArH), 6.87 (d, 2, J = 8.4 Hz, ArH), 6.78 (d, 2, J = 8.3 Hz, ArH), 6.64 (dd, 2, J = 7.2, 1.8 Hz, ArH), 6.45–6.34 (m, 4, ArH), 4.58 (d, 2, J = 11.5 Hz, OCH_2Ar), 4.57 (s, 2, OCH_2Ar), 4.45 (d, 2, J = 11.5 Hz, OCH_2Ar), 4.40(s, 2, OCH_2Ar), 3.75 (d, 2, J = 13.2 Hz, $ArCH_2Ar$), 3.60 (d, 2, J = 13.9 Hz, $ArCH_2Ar$), 3.54 (d, 2, J = 13.9 Hz, $ArCH_2Ar$), 2.86 (d, 2, J = 13.2 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{56}H_{44}Br_4O_4$: C, 61.11; H, 4.03. Found: C, 61.03; H, 3.87.

Cone Conformer of 25,26,27,28-Tetrakis[(*p*-cyanobenzyl)oxy]calix[4]arene ($3e_c$). Treatment of 1 with 2.59 g (12 mmol) of 4-cyanobenzyl bromide by the procedure described above for the preparation of **3a** yielded 1.17 g of a white powder after trituration with MeOH. Recrystallization from $CHCl_3$–MeOH afforded 0.985 g (74%) of $3e_c$ as colorless prisms: mp 244–246 °C; ^1H NMR ($CDCl_3$) δ 7.55 (d, 8, J = 8.2 Hz, ArH), 7.36 (d, 8, J = 8.2 Hz, ArH), 6.64–6.53 (m, 12, ArH), 4.95 (s, 8, OCH_2Ar), 3.97 (d, 4, J = 13.7 Hz, $ArCH_2Ar$), 2.92 (d, 4, J = 13.7 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{60}H_{44}N_4O_4$: C, 81.43; H, 5.01. Found: C, 81.37; H, 4.95.

Cone Conformer of 25,26,27,28-Tetrakis[(*p*-nitrobenzyl)oxy]calix[4]arene ($3f_c$). Treatment of 1 with 2.05 g (12 mmol) of 4-nitrobenzyl bromide by the procedure described above for the preparation of **3a** yielded 1.30 g of a yellow powder after trituration with MeOH. Recrystallization from acetone–petroleum ether (bp 37–55 °C) afforded 0.45 g of $3f_c$ as pale yellow crystals, from which an analytical sample was obtained by another recrystallization from $CHCl_3$–petroleum ether (bp 37–55 °C): mp 222–224 °C; ^1H NMR ($CDCl_3$) δ 8.08 (d, 8, J = 8.7 Hz, ArH), 7.44 (d, 8, J = 8.7 Hz, ArH), 6.67–6.54 (m, 12, ArH), 5.01 (s, 8, OCH_2Ar), 4.04 (d, 4, J = 13.8 Hz, $ArCH_2Ar$), 2.97 (d, 4, J = 13.8 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{56}H_{44}N_4O_{12}$: C, 69.70; H, 4.59. Found: C, 69.01; H, 4.50. Concentration of the filtrate gave a residue, which was flash chromatographed (3:1 $CHCl_3$–hexane)

(25) Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. *N,N*-Dimethylformamide (DMF) was distilled and stored over 3-Å or 4-Å molecular sieves. Tetrahydrofuran (THF) was distilled over Na/benzophenone. Flash chromatography[26] was carried out by using J. T. Baker 40 m silica gel. Column chromatography was carried out by using Aldrich 70–230-mesh, 60-Å silica gel. Thin-layer chromatography (TLC) was carried out on 250 μm silica gel plates, and preparative thin-layer chromatography (PTLC) on 1000 μm silica gel plates containing fluorescent indicator. Melting points of compounds melting above 250 °C were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) with a 500 °C thermometer calibrated against a thermocouple. Proton nuclear magnetic resonance spectra (^1H NMR) were measured on a Varian XL-300 spectrometer. Chemical shifts are reported as δ values (ppm) relative to tetramethylsilane (δ 0.0) as an internal standard. Microanalytical samples were dried for at least 36 h at 111 °C at 1–2 mm, and the analyses were carried out by Desert Laboratories, Tucson, AZ. Solvent of crystallization was retained in some of the analytical samples, affecting of elemental analyses. In such cases best fits between the analytical values and appropriate increments of solvents were used. The term "calixarene" is variously employed in different contexts. In colloquial usage, it implies the presence of hydroxyl groups as, for instance, in "*p*-*tert*-butylcalix[4]arene" for compound 2 and "*p*-H-calix[4]arene" for compound 1. In the precise and complete specification of a compound, however, it implies only the basic skeleton to which the substituents, including the OH groups, are attached at the positions designated by appropriate numbers.

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

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

to yield a yellow gum, which was crystallized from acetone–petroleum ether (bp 37–55 °C) to give an additional 0.435 g of product (overall yield 61%).

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis(benzyloxy)calix[4]arene ($4a_c$). To a suspension of 0.32 g (8 mmol) of NaH (60% oil dispersion) washed with two 2-mL portions of hexane in 40 mL of THF–DMF (7:1, v/v) was added 0.648 g (1 mmol) of *p*-*tert*-butylcalix[4]arene (**2**)[28] with stirring in an atmosphere of N_2. After 15 min a solution of 1.37 (8 mmol) of benzyl bromide in 10 mL of THF was introduced, and the reaction mixture was refluxed and stirred for 1 h. After cooling, a few drops of MeOH were added, and the solvent was removed on a rotary evaporator. The residue was poured into 100 mL of water, and the material that precipitated was removed by filtration and stirred with 10 mL of MeOH to leave 0.80 g of a white powder. Repeated recrystallization from $CHCl_3$–MeOH afforded 0.50 g (50%) of $4a_c$ as colorless needles: mp 250–252 °C (lit.[23] mp 230–231 °C); ^1H NMR ($CDCl_3$) δ 7.30–7.21 (m, 20, ArH), 6.71 (s, 8, ArH), 4.85 (s, 8, OCH_2Ph), 4.17 (d, 4, J = 12.8 Hz, $ArCH_2Ar$), 2.84 (d, 4, J = 12.8 Hz, $ArCH_2Ar$), 1.06 (s, 36, CMe_3). Anal. Calcd for $C_{72}H_{80}O_4$: C, 85.67; H, 7.99. Found: C, 85.98; H, 7.92. An additional 0.14 g of $4a_c$ was obtained from the chromatographic separation described below, bringing the total yield to 63%.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis(benzyloxy)calix[4]arene ($4a_{pc}$). The filtrate from the experiment described above was concentrated, and the residue was flash chromatographed (gradient elution with $CHCl_3$–hexane, 1:3 to 1:1) to give 0.08 g (8%) of $4a_{pc}$ as colorless crystals after recrystallization from $CHCl_3$–MeOH: mp 196–198 °C; ^1H NMR ($CDCl_3$) δ 7.31 (s, 10, ArH), 7.22–7.09 (m, 10, ArH), 6.96–6.93 (m, 4, ArH), 6.71 (d, 2, J = 2.5 Hz, ArH), 6.56 (d, 2, J = 2.5 Hz, ArH), 4.70 (d, 2, J = 11.3 Hz, OCH_2Ph), 4.65 (d, 2, J = 11.3 Hz, OCH_2Ph), 4.56 (s, 2, OCH_2Ph), 4.17 (s, 2, OCH_2Ph), 3.83 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 3.63 (s, 4, $ArCH_2Ar$), 2.75 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 1.26 (s, 9, CMe_3), 1.18 (s, 9, CMe_3), 0.88 (s, 18, CMe_3). Anal. Calcd for $C_{72}H_{80}O_4$: C, 85.67; H, 7.99. Found: C, 85.34; H, 7.81.

1,3-Alternate Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis(benzyloxy)calix[4]arene ($4a_{1,3\text{-alt}}$). A slurry of 0.42 g (0.65 mmol) of **2**, 1.37 g (8 mmol) of benzyl bromide in 50 mL of dry acetone, and 4.42 g (32 mmol) of anhydrous K_2CO_3 was stirred under reflux for 60 h in an atmosphere of N_2 to yield 0.43 g of crude product as a white powder. Repeated column chromatography (gradient elution with $CHCl_3$–hexane, 1:3 to 1:1) gave 0.01 g of $4a_c$, 0.33 g (50%) of $4a_{pc}$, and 2% of $4a_{1,3\text{-alt}}$ as colorless microcrystals after recrystallization from CH_2Cl_2–MeOH: mp 224–226 °C; ^1H NMR ($CDCl_3$) δ 7.26–7.23 (m, 12, ArH), 7.04–7.01 (m, 8, ArH), 6.76 (s, 8, ArH), 4.54 (s, 8, OCH_2Ph), 3.45 (s, 8, $ArCH_2Ar$), 0.95 (s, 36, CMe_3). Anal. Calcd for $C_{72}H_{80}O_4$: C, 85.67; H, 7.99. Found: C, 85.42; H, 7.95.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-methylbenzyl)oxy]calix[4]arene ($4b_c$). Treatment of **2** with 1.48 g (8 mmol) of 4-methylbenzyl bromide by the procedure described above for the preparation of **4a** gave 0.91 g of crude product as a white powder. Repeated recrystallization from $CHCl_3$–MeOH gave 0.72 g (68%) of $4b_c$ as a white solid: mp 205–207 °C; ^1H NMR ($CDCl_3$) δ 7.16 (d, 8, J = 7.9 Hz, ArH), 7.02 (d, 8, J = 7.9 Hz, ArH), 6.70 (s, 8, ArH), 4.81 (s, 8, OCH_2Ar), 4.18 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.85 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.34 (s, 12, Me), 1.06 (s, 36, CMe_3). Anal. Calcd for $C_{76}H_{88}O_4$: C, 85.67; H, 8.32. Found: C, 85.99; H, 8.32.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-methylbenzyl)oxy]calix[4]arene ($4b_{pc}$). The filtrate from the experiment described above was concentrated, the residue was flash chromatographed (gradient elution with $CHCl_3$–MeOH, 1:2 to 1:1), and the product was recrystallized from $CHCl_3$–MeOH to give 0.06 g (6%) of $4b_{pc}$ as colorless prisms: mp 164–166 °C; ^1H NMR ($CDCl_3$) δ 7.27–7.07 (m, 16, ArH), 6.90 (d, 4, J = 8.4 Hz, ArH), 6.70 (d, 2, J = 2.5 Hz, ArH), 6.47 (d, 2, J = 2.5 Hz, ArH), 4.64 (d, 2, J = 11.2 Hz, OCH_2Ar), 4.60 (d, 2, J = 11.2 Hz, OCH_2Ar), 4.52 (s, 2, OCH_2Ar), 4.43 (s, 2, OCH_2Ar), 3.83 (d, 2, J = 12.9 Hz, $ArCH_2Ar$), 3.58 (s, 4, $ArCH_2Ar$), 2.76 (d, 2, J = 12.9 Hz, $ArCH_2Ar$), 2.35 (s, 6, Me), 2.34 (s, 3, Me), 2.28 (s, 3, Me), 1.27 (s, 9, CMe_3), 1.15 (s, 9, CMe_3), 0.88 (s, 18, CMe_3). Anal. Calcd for $C_{76}H_{88}O_4$: C, 85.67; H, 8.32. Found: C, 85.79; H, 8.42.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-*tert*-butylbenzyl)oxy]calix[4]arene ($4c_c$). Treatment of **2** with 1.82 g (8 mmol) of 4-*tert*-butylbenzyl bromide by the procedure described above for the preparation of **4a** gave 0.99 g of crude product as a white powder. Fractional crystallization from CH_2Cl_2–MeOH afforded 0.70 g of $4c_c$ as colorless crystals: mp 185–186 °C; ^1H NMR ($CDCl_3$) δ 7.25 (d, 8, J = 8.8 Hz, ArH), 7.21 (d, 8, J = 8.8 Hz, ArH), 6.71 (s, 8, ArH), 4.82 (s, 8, OCH_2Ar), 4.22 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.87 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 1.28 (s, 36, CMe_3), 1.07 (s, 36, CMe_3). Anal. Calcd for $C_{88}H_{112}O_4$: C, 85.66; H, 9.15. Found: C, 85.99; H, 9.30.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-*tert*-butylbenzyl)oxy]calix[4]arene ($4c_{pc}$). From the filtrate of the experiment described above was obtained 0.065 g of $4c_{pc}$ as colorless needles: mp 223–225 °C; ^1H NMR ($CDCl_3$) δ 7.35 (s, 8, ArH), 7.32–7.27 (m, 4, ArH), 7.11 (d, 4, J = 6.4 Hz, ArH), 6.93–6.89 (m, 4, ArH), 6.72 (d, 2, J = 2.5 Hz, ArH), 6.51 (d, 2, J = 2.5 Hz, ArH), 4.65 (d, 2, J = 11.0 Hz, OCH_2Ar), 4.60 (s, 2, OCH_2Ar), 4.57 (d, 2, J = 11.0 Hz, OCH_2Ar), 4.35 (s, 2, OCH_2Ar), 3.90 (d, 2, J = 12.6 Hz, $ArCH_2Ar$), 3.67 (s, 4, $ArCH_2Ar$), 2.82 (d, 2, J = 12.6 Hz, $ArCH_2Ar$), 1.33 (s, 18, CMe_3), 1.32 (s, 9, CMe_3), 1.29 (s, 9, CMe_3), 1.27 (s, 9, CMe_3), 1.04 (s, 9, CMe_3), 0.85 (s, 18, CMe_3). Anal. Calcd for $C_{88}H_{112}O_4$: C, 85.66; H, 9.15. Found: C, 85.91; H, 9.20. The residue obtained by concentrating the filtrate and submitting it to flash chromatography ($CHCl_3$–hexane, 1:4 to 1:3) followed by recrystallization from CH_2Cl_2–MeOH gave 0.07 g of $4c_c$ (overall yield 62%) and 0.05 g of $4c_{pc}$ (overall yield 9%).

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-bromobenzyl)oxy]calix[4]arene ($4d_c$). Treatment of **2** with 1.25 g (8 mmol) of 4-bromobenzyl bromide by the procedure described above for the preparation of **4a** gave 1.25 g of crude product as a white powder. Repeated fractional crystallization from $CHCl_3$–MeOH yielded 0.93 g (70%) of $4d_c$ as colorless crystals: mp 242–244 °C; ^1H NMR ($CDCl_3$) δ 7.34 (d, 8, J = 8.4 Hz, ArH), 7.09 (d, 8, J = 8.4 Hz, ArH), 6.73 (s, 8, ArH), 4.76 (s, 8, OCH_2Ar), 4.09 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.88 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 1.07 (s, 36, CMe_3). Anal. Calcd for $C_{72}H_{76}Br_4O_4$: C, 65.27; H, 5.78. Found: C, 65.31; H, 5.84.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-bromobenzyl)oxy]calix[4]arene ($4d_{pc}$). From the filtrate in the experiment described above was obtained 0.20 g (17%) of $4d_{pc}$ as colorless needles: mp 163–165 °C; ^1H NMR ($CDCl_3$) δ 7.34–7.25 (m, 6, ArH), 7.11 (d, 4, J = 4.8 Hz, ArH), 6.89–6.78 (m, 10, ArH), 6.57 (d, 2, J = 2.5 Hz, ArH), 5.93 (d, 2, J = 8.4 Hz, ArH), 4.54 (d, 2, J = 11.6 Hz, OCH_2Ar), 4.49 (s, 2, OCH_2Ar), 4.39 (d, 2, J = 11.6 Hz, OCH_2Ar), 3.78 (d, 2, J = 12.3 Hz, $ArCH_2Ar$), 3.69 (s, 4, $ArCH_2Ar$), 3.63 (s, 2, OCH_2Ar), 2.83 (d, 2, J = 12.3 Hz, $ArCH_2Ar$), 1.34 (s, 18, CMe_3), 0.78 (s, 18, CMe_3). Anal. Calcd for $C_{72}H_{76}Br_4O_4 \cdot {}^1/_2CHCl_3$: C, 62.89; H, 5.57. Found: C, 62.85; H, 5.61.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-cyanobenzyl)oxy]calix[4]arene ($4e_{pc}$). Treatment of **2** with 1.57 g (8 mmol) of 4-cyanobenzyl bromide by the procedure described above for the preparation of **4a** yielded 1.02 g of crude product as a white powder. Repeated fractional crystallization from CH_2Cl_2–MeOH gave 0.51 g (46%) of $4e_{pc}$ as colorless silky needles: mp 260–262 °C; ^1H NMR ($CDCl_3$) δ 7.47 (d, 6, J = 8.2 Hz, ArH), 7.17 (d, 4, J = 4.5 Hz, ArH), 7.08 (d, 2, J = 8.2 Hz, ArH), 6.91–6.83 (m, 8, ArH), 6.54 (d, 2, J = 2.4 Hz, ArH), 5.82 (d, 2, J = 8.3 Hz, ArH), 4.59 (s, 2, OCH_2Ar), 4.56 (d, 2, J = 12.2 Hz, OCH_2Ar), 4.43 (d, 2, J = 12.2 Hz, OCH_2Ar), 3.82–3.69 (m, 6, $ArCH_2Ar$), 3.46 (s, 2, OCH_2Ar), 2.85 (d, 2, J = 12.3 Hz, $ArCH_2Ar$), 1.41 (s, 9, CMe_3), 1.37 (s, 9, CMe_3), 0.70 (s, 18, CMe_3). Anal. Calcd for $C_{76}H_{76}N_4O_4$: C, 82.28; H, 6.90. Found: C, 81.77; H, 6.77.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-cyanobenzyl)oxy]calix[4]arene ($4e_c$). From the filtrate in the experiment described above was obtained 0.31 g (28%) of $4e_c$ as colorless crystals: mp 256–258 °C; ^1H NMR ($CDCl_3$) δ 7.52 (d, 8, J = 8.3 Hz, ArH), 7.36 (d, 8, J = 8.3 Hz, ArH),

(28) Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1989**, *69*, 234.

6.75 (s, 8, ArH), 4.88 (s, 8, OCH_2Ar), 3.97 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.84 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 1.07 (s, 36, CMe_3). Anal. Calcd for $C_{76}H_{76}N_4O_4$: C, 82.28; H, 6.90. Found: 82.38; H, 6.89.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-nitrobenzyl)oxy]calix[4]arene ($4f_{pc}$). Treatment of **2** with 1.73 g (8 mmol) of 4-nitrobenzyl bromide by the procedure described above for the preparation of **4a** gave 1.20 g of crude product as a yellow powder. Flash chromatography (1:3 CH_2Cl_2–hexane to CH_2Cl_2) yielded 0.43 g (36%) of $4f_{pc}$ as pale yellow crystals after recrystallization from $CHCl_3$–hexane: mp 268–269 °C; ^1H NMR ($CDCl_3$) δ 8.02 (d, 4, J = 8.6 Hz, ArH), 8.00 (d, 2, J = 8.7 Hz, ArH), 7.48 (d, 2, J = 8.7 Hz, ArH), 7.21 (d, 4, J = 3.1 Hz, ArH), 7.12 (d, 2, J = 8.7 Hz, ArH), 6.96 (d, 4, J = 8.6 Hz, ArH), 6.89 (d, 2, J = 2.3 Hz, ArH), 6.55 (d, 2, J = 3.0 Hz, ArH), 5.85 (d, 2, J = 8.6 Hz, ArH), 4.64 (d, 2, J = 12.1 Hz, OCH_2Ar), 4.63 (s, 2, OCH_2Ar), 4.50 (d, 2, J = 12.1 Hz, OCH_2Ar), 3.86–3.75 (m, 6, $ArCH_2Ar$), 3.59 (s, 2, OCH_2Ar), 2.91 (d, 2, J = 12.1 Hz, $ArCH_2Ar$), 1.42 (s, 9, CMe_3), 1.39 (s, 9, CMe_3), 0.66 (s, 18, CMe_3). Anal. Calcd for $C_{72}H_{76}N_4O_{12}$: C, 72.71; H, 6.44. Found: C, 72.97; H, 6.33.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis[(*p*-nitrobenzyl)oxy]calix[4]arene ($4f_c$). The other product from the chromatographic separation in the experiment described above was 0.36 g (30%) of $4f_c$ obtained as a colorless solid after recrystallization from $CHCl_3$–MeOH: mp 263–265 °C; ^1H NMR ($CDCl_3$) δ 8.04 (d, 8, J = 8.7 Hz, ArH), 7.45 (d, 8, J = 8.7 Hz, ArH), 6.78 (s, 8, ArH), 4.94 (s, 8, OCH_2Ar), 4.04 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 2.90 (d, 4, J = 12.7 Hz, $ArCH_2Ar$), 1.08 (s, 36, CMe_3). Anal. Calcd for $C_{72}H_{76}N_4O_{12}{\cdot}CH_3OH$: C, 71.78; H, 6.60. Found: C, 71.87; H, 6.26.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,27-bis(benzyloxy)-26,28-dihydroxycalix[4]arene (5_c). A slurry of 0.648 g (1 mmol) of **2**, 1.37 g (8 mmol) of benzyl bromide in 50 mL of dry acetone, and 1.10 g (8 mmol) of anhydrous K_2CO_3 was refluxed for 24 h. The cooled reaction mixture was filtered, and the solid residue was washed several times with small portions of CH_2Cl_2. The combined organic solution was concentrated to an oil, which upon trituration with 10 mL of MeOH containing a trace of CH_2Cl_2 gave 0.70 g of white powder. Recrystallization from CH_2Cl_2–MeOH gave 0.64 g (77%) of **5** as white needles: mp 239–241 °C (lit.[29] mp 216–220 °C); ^1H NMR ($CDCl_3$) δ 7.67–7.64 (m, 4, ArH), 7.38–7.36 (m, 6, ArH), 7.33 (s, 2, OH), 7.05 (s, 4, ArH), 6.80 (s, 4, ArH), 5.06 (s, 4, OCH_2Ph), 4.29 (d, 4, J = 13.1 Hz, $ArCH_2Ar$), 3.27 (d, 4, J = 13.1 Hz, $ArCH_2Ar$), 1.28 (s, 18 CMe_3), 0.95 (s, 18, CMe_3). Anal. Calcd for $C_{58}H_{68}O_4$: C, 84.02; H, 8.27. Found: C, 84.33; H, 8.25.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(*p*-methoxybenzoyl)oxy]-26,28-dihydroxycalix[4]arene (6). (a) In the Presence of 4-Methylbenzyl Bromide. To a stirred suspension of 0.32 g (8 mmol) of NaH (60% oil dispersion) washed with two 2-mL portions of hexane in 40 mL of THF–DMF (7:1, v/v) was added 0.648 g (1 mmol) of calix[4]arene **2**[28] in an atmosphere of N_2. After 15 min a solution of 1.36 g of 4-methoxybenzoyl chloride and 1.48 g (8 mmol) of 4-methylbenzyl bromide in 10 mL of THF was introduced, and the reaction mixture was stirred and refluxed for 2 h. After cooling, a few drops of MeOH were added, the solvent was removed on a rotary evaporator, and the residue was poured onto 100 mL of 1 N HCl. Extraction into CH_2Cl_2 followed by washing with water and brine, drying over Na_2SO_4, and evaporation of the solvent left 0.79 g of a white powder. Flash chromatography with 3:2 CH_2Cl_2–hexane as eluant afforded 0.495 g (54%) of **6** as a white powder. An analytical sample of **6** was obtained as colorless crystals by recrystallization from CH_2Cl_2–EtOH: mp 392–394 °C; ^1H NMR ($CDCl_3$) δ 8.32 (d, 4, J = 8.9 Hz, ArH), 7.03 (s, 4, ArH), 7.01 (d, 4, J = 8.9 Hz, ArH), 6.87 (s, 4, ArH), 5.29 (s, 2, OH), 3.98 (d, 4, J = 14.1 Hz, $ArCH_2Ar$), 3.91 (s, 6, OMe), 3.46 (d, 4, J = 14.1 Hz, $ArCH_2Ar$), 1.20 (s, 18, CMe_3), 0.98 (s, 18, CMe_3). Anal. Calcd for $C_{60}H_{68}O_8$: C, 78.56; H, 7.48. Found: C, 78.65; H, 7.50.

(b) In the Absence of 4-Methylbenzyl Bromide. A reaction carried out as described above with the omission of the 4-methylbenzyl bromide produced **6** in 65% yield.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(*p*-methoxybenzoyl)oxy]-26,28-bis(benzyloxy)calix[4]arene (7_c). (a) To a solution of 0.414 g (0.5 mmol) of dibenzyl ether **5** in 20 mL of THF was added 0.16 g (4 mmol) of NaH (60% oil dispersion) at 0 °C in an N_2 atmosphere. The mixture was stirred at room temperature for 30 min, and 0.255 g (1.5 mmol) of 4-methoxybenzoyl chloride in 10 mL of THF was then introduced. The reaction mixture was stirred and refluxed for 2 h, cooled, and worked up to yield 0.54 g (97%) of 7_c as white, glistening flakes: mp 255–257 °C; ^1H NMR ($CDCl_3$) δ 8.75 (d, 4, J = 8.8 Hz, ArH), 7.14–7.07 (m, 6, ArH), 7.01 (s, 4, ArH), 6.91 (t, 4, J = 7.8 and 7.5 Hz, ArH), 6.69 (s, 4, ArH), 6.65 (dd, 4, J = 7.6 and 1.4 Hz, ArH), 5.02 (s, 4, OCH_2Ph), 3.96 (s, 6, OMe), 3.95 (d, 4, J = 12.9 Hz, $ArCH_2Ph$), 2.97 (d, 4, J = 12.9 Hz, $ArCH_2Ar$), 1.27 (s, 18, CMe_3), 0.90 (s, 18, CMe_3). Anal. Calcd for $C_{74}H_{80}O_8$: C, 80.99; H, 7.35. Found: C, 81.17; H, 7.39.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(*p*-methoxybenzoyl)oxy]-26,28-bis(benzyloxy)calix[4]arene (7_{pc}). A 0.458-g (0.5-mmol) sample of the diester **6** treated with 0.34 g (2 mmol) of benzyl bromide and 0.08 g (2 mmol) of NaH (60% oil dispersion) in 30 mL of THF–DMF (9:1, v/v) by the procedure described above yielded 0.41 g of crude product as a white powder. Repeated column chromatographic separations of the crude product (gradient elution with acetone–hexanes, 1:19 to 1:9) furnished five compounds, including $4a_c$ in 3% yield, 7_c in 36% yield, and three additional compounds, one of which was 7_{pc} obtained in 5% yield as colorless microcrystals after recrystallization from $CHCl_3$–MeOH: mp 282–284 °C; ^1H NMR ($CDCl_3$) δ 8.27 (d, 4, J = 8.8 Hz, ArH), 7.11–6.75 (m, 18, ArH), 6.47 (d, 2, J = 7.1 Hz, ArH), 6.35 (d, 2, J = 7.2 Hz, ArH), 4.63 (s, 2, OCH_2Ph), 4.16 (s, 2, OCH_2Ph), 3.92 (s, 6, OMe), 3.76 (d, 2, J = 12.7 Hz, $ArCH_2Ar$), 3.70 (d, 2, J = 15.5 Hz, $ArCH_2Ar$), 3.62 (d, 2, J = 15.5 Hz, $ArCH_2Ar$), 2.91 (d, 2, J = 12.7 Hz, $ArCH_2Ar$), 1.35 (s, 9, CMe_3), 0.98 (s, 9, CMe_3), 0.89 (s, 18, CMe_3). Anal. Calcd for $C_{74}H_{80}O_8{\cdot}^5/_8CHCl_3$: C, 76.31; H, 6.75. Found: C, 76.06; H, 6.83.

1,3-Alternate Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(*p*-methoxybenzoyl)oxy]-26,28-bis(benzyloxy)calix[4]arene ($7_{1,3\text{-alt}}$). The fourth compound isolated from the experiment described above was $7_{1,3\text{-alt}}$, obtained in 5% yield as colorless microcrystals after recrystallization from $CHCl_3$–MeOH: mp 300–302 °C; ^1H NMR ($CDCl_3$) δ 7.64 (d, 4, J = 8.7 Hz, ArH), 7.28–7.25 (m, 6, ArH), 6.99–6.94 (m, 8, ArH), 6.88 (d, 4, J = 8.7 Hz, ArH), 6.63 (s, 4, ArH), 4.69 (s, 4, OCH_2Ph), 3.89 (s, 6, OMe), 3.46 (s, 8, $ArCH_2Ar$), 1.09 (s, 18, CMe_3), 0.82 (s, 18, CMe_3). Anal. Calcd for $C_{74}H_{80}O_8{\cdot}^1/_4CHCl_3$: C, 79.12; H, 7.17. Found: C, 79.10; H, 7.20.

5,11,17,23-Tetra-*tert*-butyl-25-[(*p*-methoxybenzoyl)oxy]-26,27,28-tris(benzyloxy)calix[4]arene (8). The fifth compound isolated from the experiment described above was **8**, obtained in 8% yield as a white solid after recrystallization from CH_2Cl_2–EtOH: mp 249–251 °C; ^1H NMR ($CDCl_3$) δ 8.56 (d, 2, J = 8.7 Hz, ArH), 7.22–7.05 (m, 17, ArH), 6.90 (s, 2, ArH), 6.77 (d, 2, J = 2.0 Hz, ArH), 6.73 (d, 2, J = 2.0 Hz, ArH), 6.66 (d, 2, J = 8.7 Hz, ArH), 4.96 (s, 2, OCH_2Ph), 4.70 (d, 2, J = 11.3 Hz, OCH_2Ph), 4.60 (d, 2, J = 11.3 Hz, OCH_2Ph), 4.29 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 4.12 (d, 2, J = 12.6 Hz, $ArCH_2Ar$), 3.64 (s, 3, OMe), 3.11 (d, 2, J = 12.8 Hz, $ArCH_2Ar$), 2.89 (d, 2, J = 12.6 Hz, $ArCH_2Ar$), 1.23 (s, 9, CMe_3), 1.19 (s, 9, CMe_3), 0.98 (s, 18, CMe_3). Anal. Calcd for $C_{73}H_{80}O_8{\cdot}^1/_4CH_2Cl_2$: C, 81.87; H, 7.55. Found: 82.23; H, 7.48.

Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27-tris(benzyloxy)-28-hydroxycalix[4]arene (9_c). To a stirred and cooled (ice bath) mixture of 0.828 g (1 mmol) of dibenzyl ether 5_c and 0.046 g (1.2 mmol) of NaH (50% dispersion) in 25 mL of DMF was added dropwise 0.126 g (1.0 mmol) of benzyl chloride in 5 mL of DMF. The reaction mixture was stirred at 0 °C for 2 h and poured into 100 mL of 1 N HCl followed by 400 mL of H_2O to afford 0.82 g of a white powder. Column chromatography (gradient elution with $CHCl_3$–hexane, 2:3 to 1:1) gave 0.53 g (58%) of 9_c as colorless needles after recrystallization from CH_2Cl_2–MeOH: mp 207–209 °C; ^1H NMR ($CDCl_3$) δ 7.48–7.20 (m, 15, ArH), 7.09 (s, 2, ArH), 7.00 (s, 2, ArH), 6.58 (d, 2, J = 2.4 Hz, ArH), 6.51 (d, 2, J = 2.4 Hz, ArH), 6.35 (s, 1, OH), 4.93 (s, 2, OCH_2Ph), 4.67 (d, 2, J = 11.6 Hz, OCH_2Ph), 4.60 (d, 2, J = 11.6 Hz,

(29) Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.-E.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567.

OCH_2Ph), 4.18 (d, 2, J = 12.5 Hz, $ArCH_2Ar$), 4.14 (d, 2, J = 12.5 Hz, $ArCH_2Ar$), 3.04 (d, 2, J = 12.5 Hz, $ArCH_2Ar$), 2.98 (d, 2, J = 12.5 Hz, $ArCH_2Ar$), 1.32 (s, 9, CMe_3), 1.29 (s, 9, CMe_3), 0.83 (s, 18, CMe_3). Anal. Calcd for $C_{65}H_{74}O_4 \cdot {}^1/_3CH_2Cl_2$: C, 83.33; H, 7.98. Found: C, 83.04; H, 8.00. In addition, 5% of $\mathbf{4a_c}$ and 12% of starting material ($\mathbf{5_c}$) were isolated in the chromatographic separation.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,26,27-tris(benzyloxy)-28-hydroxycalix[4]arene ($\mathbf{9_{pc}}$). To a stirred and ice-bath-cooled mixture of 0.828 g (1 mmol) of dibenzyl ether $\mathbf{5_c}$ and 0.171 g (1.2 mmol) of $KOSiMe_3$ (90% pure) in an atmosphere of N_2, was added dropwise a solution of 0.188 g (1.1 mmol) of benzyl bromide in 20 mL of THF, and the mixture was stirred at room temperature for 15 h. The solvent was then removed under vacuum, the residue was treated with 100 mL of 1 N HCl, and the gummy residue was extracted into CH_2Cl_2, which was washed with water and brine, dried over Na_2SO_4, and evaporated to give 0.68 g of a white powder. Column chromatography produced (a) 0.095 g (9%) of **4a**, the ^1H NMR spectrum of which indicated it to be an 89:11 mixture of $\mathbf{4a_{pc}}$ and $\mathbf{4a_{1,3\text{-}alt}}$; (b) 0.08 g (10%) of $\mathbf{5_{pc}}$, described below; and (c) 0.435 g (47%) of $\mathbf{9_{pc}}$, obtained as white needles after recrystallization from $CHCl_3$–MeOH: mp 182–185 °C; ^1H NMR ($CDCl_3$) δ 7.39–7.28 (m, 9, ArH), 7.19 (s, 1, OH), 7.10 (s, 2, ArH), 7.04 (s, 2, ArH), 6.90–6.67 (m, 8, ArH), 6.21 (d, 2, J = 7.5 Hz, ArH), 5.09 (d, 2, J = 12.0 Hz, OCH_2Ph), 4.71 (d, 2, J = 12.0 Hz, OCH_2Ph), 4.03 (d, 2, J = 12.9 Hz, $ArCH_2Ar$), 3.90 (d, 2, J = 15.3 Hz, $ArCH_2Ar$), 3.83 (d, 2, J = 15.3 Hz, $ArCH_2Ar$), 3.80 (s, 2, OCH_2Ph), 3.10 (d, 2, J = 12.9 Hz, $ArCH_2Ar$), 1.32 (s, 9, CMe_3), 1.01 (s, 9, CMe_3), 0.77 (s, 18, CMe_3). Anal. Calcd for $C_{65}H_{74}O_4$: C, 84.64; H, 7.99. Found: C, 84.93; H, 8.11.

Partial Cone Conformer of 5,11,17,23-Tetra-*tert*-butyl-25,27-bis(benzyloxy)-26,28-dihydroxycalix[4]arene ($\mathbf{5_{pc}}$). As described above, $\mathbf{5_{pc}}$ was isolated in 10% yield from a reaction of $\mathbf{5_c}$ with benzyl bromide and $KOSiMe_3$ and was obtained as colorless crystals after recrystallization from $CHCl_3$–MeOH: mp 239–241 °C; ^1H NMR ($CDCl_3$) δ 8.29 (s, 2, OH), 7.13 (d, 2, J = 2.3 Hz, ArH), 6.96–6.75 (m, 12, ArH), 6.22 (d, 4, J = 7.8 Hz, ArH), 4.72 (d, 2, J = 11.6 Hz, OCH_2Ph), 4.41 (d, 2, J = 11.6 Hz, OCH_2Ph), 4.07 (s, 2, $ArCH_2Ar$), 3.84 (s, 4, $ArCH_2Ar$), 3.68 (s, 2, $ArCH_2$ Ar), 1.01 (s, 36, CMe_3) (in DMSO-d_6 this signal splits into two singlets of equal intensity at δ 0.99 and 0.96); ^{13}C NMR ($CDCl_3$) δ 151.53, 149.10, 147.05, 142.65, 136.35, 133.68, 132.09, 128.51, 127.79, 127.30, 126.19, 125.35, 125.08, 124.36, 72.16 ($ArCH_2O$), 39.95 ($ArCH_2Ar$), 33.87 ($ArCH_2Ar$), 33.60 ($ArCH_2Ar$), 32.40 (CMe_3), 31.26 (CMe_3), 31.16 (CMe_3). Anal. Calcd for $C_{58}H_{68}O_4 \cdot {}^1/_4CHCl_3$: C, 82.71; H, 8.13. Found: C, 82.84; H, 8.08. A reaction carried out with $\mathbf{5_c}$ as described above but in the absence of benzyl bromide failed to yield any $\mathbf{5_{pc}}$ and gave only recovered starting material.

Benzylation Reactions. (a) The procedures described above for the preparation of $\mathbf{4a_c}$ were used to carry out reactions involving changes in time, temperature, solvent, and benzyl halide, giving the data recorded in Tables I and II. (b). The general procedures described above were followed in treating compounds **2**, $\mathbf{5_c}$, $\mathbf{5_{pc}}$, $\mathbf{9_c}$, and $\mathbf{9_{pc}}$ with benzyl bromide in the presence of NaH, K_2CO_3, or $KOSiMe_3$ in acetone or THF–DMF. The product mixtures were assayed to give the results shown in Table V, where the percentage yields represent in all but two instances the amount of isolated, purified material.

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Notes

Photoinduced Phosphorylation by [α-(Hydroxyimino)benzyl]phosphonates through Fragmentation to Monomeric Metaphosphates

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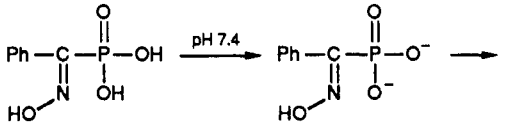
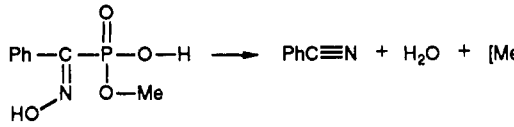
Previously it was reported from one of our laboratories that α-hydroxyimino phosphonic acids and monoesters can serve as precursors to monomeric metaphosphate anion[1] or to alkyl metaphosphates,[2] respectively, and consequently may act as phosphorylating agents. Thus, [α-(hydroxyimino)benzyl]phosphonic acid (**1a**) is unstable as the free acid or as a salt and undergoes facile fragmentation at physiological pH (eq 1).[1] The corresponding monoesters



1a

$$PhC{\equiv}N + OH^- + PO_3^- \quad (1)$$

(e.g., **1b**) are unstable as free acids which undergo spontaneous fragmentation as shown in eq 2. Their salts are



$$PhC{\equiv}N + H_2O + [MeOPO]_2 \quad (2)$$

1b

stable[2] but are unsuitable for use as reagents in organic solvents because of their lack of solubility. Their conversion in situ to the active **1b** would require acid treatment, which could be harmful to some substrates to be phosphorylated. One possible way to avoid this would employ α-hydroxyimino phosphonates with photolabile ester groups,[3] which would liberate the active compounds on irradiation. Benzyloxy groups on phosphorus are

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