present case, higher transport rate enhancements are observed which may be due to chemical redox but may also result from use of the little-studied solid-supported, liquid membrane system. In our experience, the solid-supported system permits better control of experimental parameters. Previous electrochemical results reported from our laboratories necessitated the use of bulk liquid membrane models for the experiments to succeed. These are plagued with stirring and convection problems as well as interfacial disruptions.

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^{13}C NMR Chemical Shifts. A Single Rule To Determine the Conformation of Calix[4]arenes

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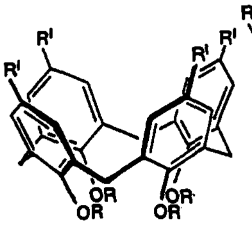
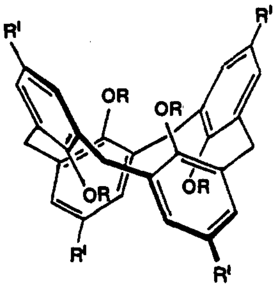
The conformations of calix[4]arenes can be deduced from the ^{13}C NMR chemical shift of the methylene groups connecting each pair of aromatic rings. Inspection of 24 cases revealed that when the phenol rings beside each methylene are in a syn orientation (i.e., in cone conformations), the methylene signals appear around δ 31, whereas they appear around δ 37 when both phenol rings are anti oriented (i.e., in 1,3-alternate conformations). Steric effects are believed to be the main cause of such large differences.

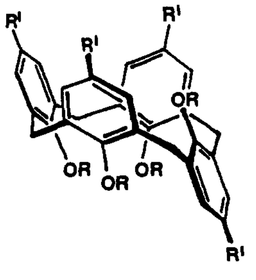
The conformations of calix[4]arenes in solution have long been studied since the pioneering work of Gutsche.[1] Among the number of methods that can be used,[2] those based on the ^{1}H NMR methylene or aromatic signals and their multiplicities have been shown to be the most useful to distinguish the four main conformations of these cyclic tetramers of phenols.[3] For calix[4]arenes with the same substituent at each para position, an AB system is usually observed below the coalescence temperature for the methylene protons in the cone (A) conformation, whereas a singlet is observed in the 1,3-alternate (B) conformation.



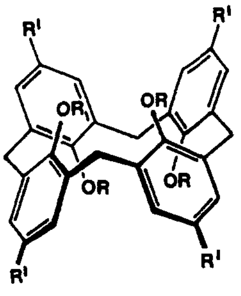
(A)



(B)

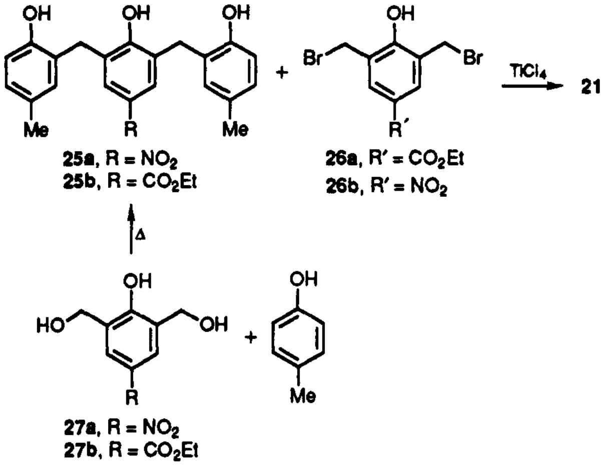


(C)



(D)

Scheme I



Both singlet and AB systems should be present in partial cone (C) or in 1,2-alternate (D) conformations, and the number and multiplicity of aromatic signals could be used to differentiate them. Since most calix[4]arenes coalesce above room temperature in a broad range of solvents, these observations are usually enough to ascertain the preferred

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

(2) (a) NOE experiments: Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R. *Gazz. Chim. Ital.* 1989, *119*, 335. (b) Dipole moments measurement: Elguero, J.; Fayet, J. P.; de Mendoza, J.; Nieto, P. M.; Prados, P.; Sánchez, C.; Vertut, M. C. To be published. (c) For X-Ray crystal structures, see ref 3.

(3) Gutsche, C. D. In "Calixarenes"; Stoddart, J. F., Ed.; Monographs in Supramolecular Chemistry; The Royal Society of Chemistry; London, 1989; Vol. 1.

(4) (a) Gutsche, C. D.; Lin, L. G. *Tetrahedron* 1986, *42*, 1633. (b) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Sangermano, V. *J. Chem. Soc., Perkin Trans. 2*, 1984, 1979.

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

(6) Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* 1981, *103*, 3782.

0022-3263/91/1956-3372$02.50/0

conformation. However, such symmetry-controlled patterns are absent in stepwise assembled calixarenes with *different* substituents in the phenol rings. For example, cone and 1,3-alternate conformations could not be distinguished by ^{1}H NMR chemical shifts in cases of R^1–R^2–R^1–R^2, R^1–R^2–R^1–R^3, or R^1–R^2–R^3–R^4 para substitutions; the same number of signals should appear for both conformations in aromatic or methylene protons as well.

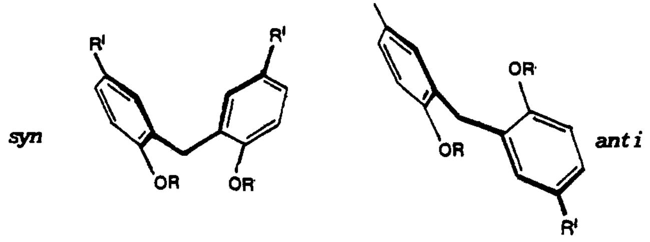
We have examined the ^{13}C NMR spectra of 24 calix[4]arenes (Table I) endowed with para substituents of the following different kinds: alkyl, chloro, carboxy, ester, or nitro groups. In many of them, *O*-acyl or *O*-alkyl groups were also present to fix the conformations.

Most of the calix[4]arenes (**1**–**7**, **10**–**18**) were prepared by described procedures (see references on Table I). The synthesis of the functionalized calix[4]arenes **21** was performed by two different ways, from trimers **25a** or **25b** and the complementary monomeric phenols **26a** or **26b**, respectively, in the presence of $TiCl_4$ (Scheme I). Yields were quite similar in both cases (30% from **25a**; 26% from **25b**). Trimers **25a** and **25b** were, in their turn, prepared in 94% yield by melting phenols **27a** and **27b**, respectively, with an excess of *p*-cresol. The ester functionalities of calix[4]arenes **18** and **21** were easily hydrolyzed with sodium hydroxide in high yields to give the carboxylic acids **20** and **23**. Finally, the O-acetylated derivatives **19**, **22**, and **24** were obtained from the corresponding phenols with acetic anhydride and *p*-toluenesulfonic acid or sulfur acid as catalysts. A single conformer was isolated in each case in yields ranging from 78 to 85%.

Whenever possible (compounds **1**–**7**, **10**–**18**), published ^{1}H NMR patterns were used to ascertain the preferred conformation. Up to three stable conformers were isolated for the *p*-*tert*-butyl-*O*-acetylcalix[4]arene, from which only the partial cone **7**·AcOH conformer was previously reported.[7] The new 1,2-alternate **8** and 1,3-alternate **9** conformers were differentiated from **7** by the number of aromatic signals (see Table I). To our knowledge, **8** represents the second example of a calix[4]arene in a 1,2-alternate conformation.[10] For the rest of the calixarenes, the information provided by the ^{1}H NMR spectra was not sufficient to deduce the preferred conformation.

However, an inspection of the proton-decoupled ^{13}C NMR spectra of all the series revealed that the methylene carbon chemical shift ranged always around two values: ca. δ 31 and 37. The former value was found in calix[4]arenes whose ^{1}H NMR spectra agreed with cone conformations (compounds **1**, **6**, **10**, and **11**) as well as for compounds **13**–**18**, **20**, **21**, and **23**. The latter was found for reported 1,3-alternate conformations (compounds **3**, **5**, and **9**) and also for calixarenes **19**, **22**, and **24**. We can thus conclude that **13**–**18**, **20**, **21**, and **23** are cone conformations, whereas **19**, **22**, and **24** are 1,3-alternate.

In cone conformations, adjacent phenol rings are in a syn orientation, whereas in 1,3-alternate conformations adjacent phenol rings are in an anti orientation. With slight distortions, two syn and two anti orientations are expected in the partial cone and 1,2-alternate calix[4]arenes. Consequently, two ^{13}C NMR signals should be present for the methylene carbon atoms of calix[4]arenes in these conformations. In perfect agreement with this prediction, compounds **2**, **4**, **7**·AcOH and **12** (reported in the literature as partial cones), as well as compound **8** (the 1,2-alternate case), showed two well-differentiated signals of almost equal intensities at ca. δ 31 and 37.



It is important to point out that the previous chemical shifts were quite independent from the para substituent (δ 30.2–32.7 for compounds **1**, **6**, **13**, **15**, **16**, **20**, **21** or δ 36.9–38.2 for compounds **3**, **9**, **19**, **22**, **24**) from the phenol O-protecting group (compare **2** and **4**; **3** and **5**; **6**, **10**, and **11**; **7** and **12**) or from the solvent employed (compounds **3**, **14**, **17**, **20**, **21**, **23**).

The ca. 6 ppm difference in the chemical shifts for the syn and the anti orientations of the phenol rings, which is apparently without exceptions, has no parallel in open-chain bisphenylmethane derivatives.[11] The origin of such differences seems to be more steric than electronic. In fact, the electronic distribution did not change appreciably by rotation, as revealed by an ab initio calculation on bis(2-hydroxyphenyl)methane in both the syn and anti orientations.[12] In good agreement with these calculations, the $^1J_{C-H}$ values for the methylene group were found to be quite uniform (Table II).

In order to evaluate energy differences in conformations not due to dipole moments or hydrogen bonds caused by the functional groups, theoretical calculations were also performed using Allinger's MM2 force field[13] on a calix[4]arene in which all the para substituents (R^1–R^4), as well as the OH groups, were replaced by hydrogen. The results (Table III) showed the preference of this cyclophane system for the cone conformation over the 1,3-alternate. The least stable conformer was the partial cone, although the 1,2-alternate did not differ much from it in stability. Methylene carbons in the cone conformation were more compressed than in the 1,3-alternate, as deduced from their total van der Waals energy (E_{VDW}) and, to some extent, by the magnitude of the C(sp^2)–C(sp^3)–C(sp^2) bond angle (ϕ). Literature X-ray data of calix[4]arenes clearly show that this angle is always smaller[14] for syn orientations (107°–111°) than for anti orientations (111°–118°).[10a,15]

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(7) (a) Ungaro, R.; Bocchi, V.; Foina, D.; Pochini, A.; Andreeti, G. D. *Tetrahedron* **1982**, *38*, 373. (b) Rizzoli, C.; Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Mol. Struct.* **1982**, *82*, 133.

(8) Araki, K.; Iwamoto, K.; Shinkai, S.; Matsuda, T. *Chem. Lett.* **1989**, 1747.

(9) de Mendoza, J.; Nieto, P. M.; Prados, P.; Sánchez, C. *Tetrahedron* **1990**, *46*, 671.

(10) (a) For the first published example, see: Bott, S. W.; Coleman, A. W.; Atwood, J. L. *J. Inclusion Phenom.* **1987**, *5*, 747. (b) An unpublished case of 1,2-alternate calix[4]arene is mentioned in ref 3, page 107.

(11) Acyclic trimer precursors for compounds **13**–**18** already reported,[9] as well as the new trimers **25a** and **25b**, showed ^{13}C NMR chemical shifts for the methylene carbons ranging from 30.2 to 32.1 ppm.

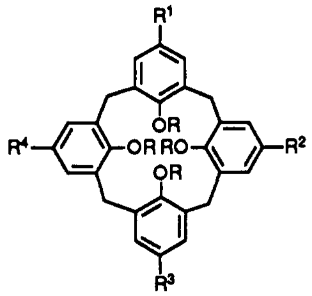
(12) The calculations were made with the X-ray experimental geometry of calix[4]arene **1**[4b] at the Hartree–Fock level of theory and using the STO-3G basis set. Binkley, J. B.; Witheside, R. A.; Krishna, R.; Seeger, R.; De Frees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. GAUSSIAN 80; Department of Chemistry: Carnegie-Mellon University, Pittsburgh, PA, 1980.

(13) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Available from QCPE (PC version by A. Buda) or from Molecular Design, Ltd., 2132 Farallon Dr., San Leandro, CA 94577.

(14) Since in some calix[4]arenes the cones are flattened in the solid state, causing the angles to be unequivalent, the examples were selected from the few 1,2-alternate, partial cone, or 1,3-alternate structures so far described.

(15) Rizzoli, C.; Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Mol. Struct.* **1987**, *82*, 133. Vrielink, A.; Codding, P. W.; Gutsche, C. D.; Lin, L. G. *J. Inclusion Phenom.* **1986**, *4*, 199. Grootenhuis, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; Hummel, G. J.; Ugozzoli, F.; Andreetti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165.

Table I. ^1H and ^{13}C NMR Spectra of Calix[4]arenes[a]



compd (ref)	R	R¹	R²	R³	R⁴	Ar*H*[b]	Ar_2CH_2	no. of aromatic carbons[b]	Ar_2CH_2	conformation
1[4]	H	H	H	H	H	7.06 (d, 8 H) 6.73 (t, 4 H)	4.23 (b s, 4 H) 3.57 (b s, 4 H)	4	31.6	cone
2[4a]	$COCH_3$	H	H	H	H	7.25 (m, 8 H) 6.82 (m, 4 H)	3.65 (s, 4 H) 3.54 (d, 2 H) 3.26 (d, 2 H)	12	37.4 30.7	partial cone
3[4a]	$COCH_3$	H	H	H	H	7.07 (s, 12 H)	3.76 (s, 8 H)	4	37.4	1,3-alternate
3[c,4a]	$COCH_3$	H	H	H	H	7.08 (m, 12 H)	3.60 (s, 8 H)	4	36.7	1,3-alternate
4[5]	COC_6H_5	H	H	H	H	7.25 (d) 6.96 (t) 6.91 (d) 6.72 (t) 6.59 (d) 6.24 (s)	3.93 (d, 2 H) 3.84 (d, 2 H) 3.71 (d, 2 H) 3.53 (d, 2 H)	12	37.4 31.8	partial cone
5[5]	COC_6H_5	H	H	H	H	6.61 (m, 12 H)	3.60 (s, 8 H)	4	36.9	1,3-alternate
6[6]	H	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.03 (s, 8 H)	4.26 (d, 4 H) 3.49 (d, 4 H)	4	32.7	cone
7[7]	$COCH_3$	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.23 (s, 2 H) 7.10 (s, 2 H) 7.05 (d, 2 H) 6.69 (d, 2 H)	3.75 (d, 2 H) 3.64 (d, 2 H) 3.55 (d, 2 H) 3.23 (d, 2 H)	14	37.0[d] 31.1	partial cone
8	$COCH_3$	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.31 (d, 4 H) 7.06 (d, 4 H)	3.81 (s, 4 H) 3.61 (d, 2 H) 3.33 (d, 2 H)	5	38.7[d] 30.2	1,2-alternate
9	$COCH_3$	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.04 (s, 8 H)	3.74 (s, 8 H)	4	38.2[d]	1,3-alternate
10[5]	COC_6H_5	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.11 (s, 8 H)	3.89 (d, 4 H) 3.41 (d, 4 H)	4	30.7[d]	cone
11[5]	$COC_6H_4NO_2$ (*p*)	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.05 (s, 8 H)	4.02 (d, 4 h) 3.42 (d, 4 H)	4	30.6[d]	cone
12[8]	Bu	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	7.21 (s, 2 H) 7.07 (s, 2 H) 6.84 (d, 2 H) 6.57 (d, 2 H)	4.11 (d, 2 H) 3.68 (d, 2 H) 3.62 (d, 2 H) 3.03 (d, 2 H)	11	37.8[d,e] 31.3	partial cone
13[c,9]	H	Cl	Cl	Cl	Cl	7.04 (s, 8 H)	4.15 (b s, 4 H) 3.47 (b s, 4 H)	4	30.2	cone
14[9]	H	*t*-Bu	Cl	*t*-Bu	Cl	7.07 (s, 4 H) 6.99 (s, 4 H)	4.21 (d, 4 H) 3.46 (d, 4 H)	8	31.9[d]	cone
14[c,9]	H	*t*-Bu	Cl	*t*-Bu	Cl	7.17 (s, 8 H)	3.82 (b s, 4 H) 3.36 (b s, 4 H)	8	32.2	cone
15[9]	H	*t*-Bu	CO_2Et	*t*-Bu	CO_2Et	7.74 (s, 4 H) 7.14 (s, 4 H)	4.25 (b s, 4 H) 3.59 (b s, 4 H)	8	31.8[d]	cone
16[9]	H	*t*-Bu	NO_2	*t*-Bu	NO_2	7.98 (s, 4 H) 7.16 (s, 4 H)	4.28 (d, 4 H) 3.64 (d, 4 H)	8	31.8	cone
17[c,9]	H	Cl	NO_2	Cl	NO_2	8.04 (s, 4 H) 7.26 (s, 4 H)	3.60 (b s, 8 H)	8	31.0	cone
18[9]	H	CO_2Et	NO_2	CO_2Et	NO_2	8.06 (s, 4 H) 7.85 (s, 4 H)	4.29 (b s, 4 H) 3.80 (b s, 4 H)	8	31.3	cone
19	$COCH_3$	CO_2Et	NO_2	CO_2Et	NO_2	8.00 (s, 4 H) 7.80 (s, 4 H)	3.84 (s, 8 H)	8	37.0	1,3-alternate
20[c]	H	CO_2H	NO_2	CO_2H	NO_2	7.97 (s, 4 H) 7.75 (s, 4 H)	4.20 (b s, 4 H) 3.59 (b s, 4 H)	7	31.1	cone
21[c]	H	CH_3	NO_2	CH_3	CO_2Et	7.99 (s, 2 H) 7.77 (s, 2 H) 6.93 (d, 2 H) 6.91 (d, 2 H)	4.29 (b d, 4 H) 3.61 (b d, 4 H)	12	31.1 30.9	cone
22	$COCH_3$	CH_3	NO_2	CH_3	CO_2Et	7.96 (s, 2 H) 7.75 (s, 2 H) 6.92 (b s, 2 H) 6.90 (b s, 2 H)	3.83 (d, 2 H) 3.79 (d, 2 H) 3.69 (d, 2 H) 3.66 (d, 2 H)	14	37.3	1,3-alternate
23[c]	H	CH_3	NO_2	CH_3	CO_2H	8.07 (s, 2 H) 7.71 (s, 2 H) 6.85 (d, 2 H) 6.79 (d, 2 H)	3.90 (b s, 8 H)	12	30.7 30.6	cone

Table I (Continued)

compd (ref)	R	R^1	R^2	R^3	R^4	Ar*H*^{b}	Ar$_2$C*H*$_2$	no. of aromatic carbons^b	Ar$_2$CH$_2$	conformation
24	COCH$_3$	CH$_3$	NO$_2$	CH$_3$	CO$_2$H	7.97 (s, 2 H) 7.76 (s, 2 H) 6.92 (b s, 4 H)	3.84 (d, 2 H) 3.81 (d, 2 H) 3.71 (d, 2 H) 3.70 (d, 2 H)	13	37.3	1,3-alternate

[a] Bruker WP-200-SY instrument. Solvent CDCl$_3$ unless otherwise indicated. [b] Aromatic signals of protecting group not counted. [c] Registered in DMSO-d_6. [d] Assigned by a DEPT experiment. [e] Assigned by a 2D ^{1}H–^{13}C experiment.

Table II. $^1J_{C-H}$ (Hz) Coupling Constants of Calix[4]arenes^a

compd	R	R^1	R^2	R^3	R^4	Ar$_2$CH$_2$	$^1J_{C-H}$	conformation
1	H	H	H	H	H	31.6	128.9	cone
3	COCH$_3$	H	H	H	H	37.4	127.9	1,3-alternate
4	COC$_6$H$_5$	H	H	H	H	37.4	129.5	partial cone
						31.8	129.6	
5	COC$_6$H$_5$	H	H	H	H	36.9	128.4	1,3-alternate
8	COCH$_3$	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	38.7	128.4	1,2-alternate
						30.2	*c*	
9	COCH$_3$	*t*-Bu	*t*-Bu	*t*-Bu	*t*-Bu	38.2	130.2	1,3-alternate
13^b	H	Cl	Cl	Cl	Cl	30.2	130.1	cone
19	COCH$_3$	CO$_2$Et	NO$_2$	CO$_2$Et	NO$_2$	37.0	130.1	1,3-alternate

[a] Solvent CDCl$_3$ unless otherwise indicated. For structures, see Table I. [b] Registered in DMSO-d_6. [c] Not measured due to signal overlap.

Table III. MM2 Calculations in a Calix[4]arene Model^a

conformer	rel energy (kcal/mol)	population (%)	methylene carbons	
			E_{VDW}^{b}	ϕ^c
cone	0.00	62.6	0.22521	109.6
1,3-alternate	0.51	26.5	0.19321	109.9
1,2-alternate	1.39	6.0	0.20872	112.6
			0.19432	109.4
partial cone	1.51	4.9	0.21871	111.8
			0.19808	110.0

[a] R^1–R^4 = H; OR replaced by H. For structures, see Table I. [b] Total Van der Waals energy (kcal/mol). [c] C(sp^2)–C(sp^3)–C(sp^2) bond angle.

Consequently, it is reasonable to observe smaller δ values for ^{13}C NMR spectra of the cone than the 1,3-alternate conformer.[16]

Experimental Section

Melting points are uncorrected. Silica gel Alugram Sil G/UV257 was used for thin-layer chromatography. TLC plates were revealed by UV light, by iodine, and/or by ammonium hydroxide. Most chemicals were purchased from Aldrich Co. and used as received without further purification. Organic solvents were purified by standard procedures. Anhydrous dioxane was distilled from benzophenone and sodium under an argon atmosphere immediately prior to use. Compounds **26a**,[17] **26b**,[9] **27a**,[9] and **27b**[18] were obtained according to described procedures. Calculations were performed in VAX-8800 (MM2) and IBM-4738 (ab initio) computers in the Computer Centers of the Universidad Autónoma de Barcelona and Madrid, respectively.

25,26,27,28-Tetraacetoxy-5,11,17,23-tetra-*tert*-butylcalix[4]arene (7–9). A mixture of **6** (0.50 g, 0.77 mmol), acetic anhydride (17 mL), and a catalytic amount of *p*-toluenesulfonic acid was heated at reflux for 20 h. The crude reaction mixture was cooled to room temperature and poured into a 1% (v/v) H$_2$SO$_4$ aqueous solution to give 0.59 g (89%) of a mixture of the acetylated compounds **7–9**. Recrystallization from acetic acid afforded **7**·AcOH (3%): mp >300 °C (lit.[7] mp 320 °C dec); ^{1}H NMR (CDCl$_3$) δ 1.09 (s, 18 H), 1.36 (s, 9 H), 1.40 (s, 9 H), 1.90 (s, 3 H), 1.97 (s, 3 H), 2.32 (s, 6 H), 3.23 (d, 2 H, J = 13.4 Hz), 3.51 (d, 2 H, J = 13.4 Hz), 3.61 (s, 4 H), 6.82 (s, 2 H), 7.06 (s, 2 H), 7.22 (s, 4 H); ^{13}C NMR (CDCl$_3$) δ 21.3, 22.0, 31.1, 31.3, 31.5, 31.7, 34.0, 34.4, 38.0, 125.5, 126.2, 126.8, 127.1, 131.0, 131.8, 133.2, 133.9, 147.0, 147.2, 169.1. An acetic acid free sample of **7** was obtained by recrystallization of **7**·AcOH from benzene: mp 276–277 °C; ^{1}H NMR (CDCl$_3$) δ 1.03 (s, 18 H), 1.36 (s, 9 H), 1.37 (s, 9 H), 1.87 (s, 3 H), 2.22 (s, 3 H), 2.35 (s, 6 H), 3.23 (d, 2 H, J = 13.5 Hz), 3.55 (d, 2 H, J = 13.5 Hz), 3.64 (d, 2 H, J = 14.7 Hz), 3.75 (d, 2 H, J = 14.7 Hz), 6.69 (d, 2 H, J = 2.3 Hz), 7.05 (d, 2 H, J = 2.3 Hz), 7.10 (s, 2 H), 7.23 (s, 2 H); ^{13}C NMR (CDCl$_3$) δ 20.9, 21.7, 22.0, 31.0, 31.1, 31.4, 31.7, 33.8, 34.2, 37.0, 125.7, 125.9, 126.1, 128.1, 131.7, 134.1, 141.8, 143.8, 144.8, 147.8, 148.7, 151.8, 168.8, 170.3. Anal. Calcd for $C_{52}H_{64}O_8$: C, 76.44; H, 7.89. Found: C, 75.93; H, 7.98. Evaporation of the acetic acid filtrate and recrystallization from benzene gave **9** (36%); mp >300 °C; ^{1}H NMR (CDCl$_3$) δ 1.29 (s, 36 H), 1.47 (s, 12 H), 3.73 (s, 8 H), 7.04 (s, 8 H); ^{13}C NMR (CDCl$_3$) δ 20.6, 31.6, 34.4, 38.2, 125.8, 132.3, 146.0, 147.5, 168.1. Calixarene **8** (15%) crystallized on standing from the previous filtrate: mp >300 °C; ^{1}H NMR (CDCl$_3$) δ 1.30 (s, 36 H), 1.41 (s, 12 H), 3.33 (d, 2 H, J = 13.1 Hz), 3.61 (d, 2 H, J = 13.1 Hz), 3.81 (s, 4 H) 7.06 (d, 4 H, J = 2.2 Hz), 7.31 (d, 4 H, J = 2.2 Hz); ^{13}C NMR (CDCl$_3$) δ 20.3, 30.2, 31.5, 34.3, 38.7, 126.2, 131.0, 132.8, 144.7, 147.8, 168.8. Anal. Calcd for $C_{52}H_{64}O_8 \cdot 2H_2O$: C, 73.20; H, 8.03. Found: C, 72.76; H, 7.77.

General Procedures for Acetylation of Calix[4]arenes 18, 21, and 23. Method A. A solution of calix[4]arene (0.60 mmol) in acetic anhydride (32 mL) and a catalytic amount of *p*-toluenesulfonic acid was heated at reflux for 20 h. The crude reaction mixture was cooled to room temperature and poured into cold water. The solid formed was filtered, washed with water, and dried in vacuo over P$_2$O$_5$ to obtain a single conformer.

Method B. A mixture of calix[4]arene (0.28 mmol), acetic anhydride (8 mL), ethyl acetate (2 mL), and a drop of H$_2$SO$_4$ was stirred for 18 h at room temperature. The reaction mixture was poured into water, and the resulting solid was filtered, washed, and dried in vacuo over P$_2$O$_5$ to obtain a single conformer.

25,26,27,28-Tetraacetoxy-5,17-bis(ethoxycarbonyl)-11,23-dinitrocalix[4]arene (19): yield 78% (method A or B); mp >340 °C; MS *m/z* (relative abundance) 700 (M$^+$, 126, 1.2), 697 (1.2), 696 (5.9), 658 (1.2), 654 (54.4), 613 (30.9), 612 (100); ^{1}H NMR (CDCl$_3$) δ 1.38 (t, 6 H, J = 7.0 Hz), 1.70 (s, 12 H), 3.84 (s, 8 H), 4.37 (q, 4 H, J = 7.0 Hz), 7.80 (s, 4 H), 8.00 (s, 4 H); ^{13}C NMR (CDCl$_3$) δ 14.3, 19.9, 37.0, 61.4, 124.5, 127.8, 131.2, 132.5, 134.8, 144.6, 151.2, 152.7, 165.0, 166.5. Anal. Calcd for $C_{42}H_{38}N_2O_{16} \cdot 1.5H_2O$: C, 59.10; H, 4.81; N, 3.28. Found: C, 58.91; H, 4.64; N, 3.10.

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25,26,27,28-Tetraacetoxy-5-(ethoxycarbonyl)-11,23-dimethyl-17-nitrocalix[4]arene (22): yields 78% (method A), 85% (method B); mp 318 °C dec (methanol); MS *m/z* (relative abundance) 737 (M^+, 0.3), 695 (32.9), 653 (29.1), 607 (88.6), 565 (100), 524 (26.7), 523 (76.5); ^1H NMR ($CDCl_3$) δ 1.37 (t, 3 H, *J* = 7.1 Hz), 1.57 (s, 6 H), 1.63 (s, 3 H), 1.65 (s, 3 H), 2.28 (s, 6 H), 3.66 (d, 2 H, *J* = 16.2 Hz), 3.69 (d, 2 H, *J* = 15.9 Hz), 3.79 (d, 2 H, *J* = 15.9 Hz), 3.83 (d, 2 H, *J* = 16.2 Hz), 4.34 (q, 2 H, *J* = 7.1 Hz), 6.90 (br s, 2 H), 6.92 (br s, 2 H), 7.75 (s, 2 H), 7.96 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.4, 19.9, 20.5, 37.3, 61.2, 124.1, 127.5, 129.9, 130.4, 130.6, 131.4, 132.6, 133.4, 135.0, 135.3, 144.6, 145.7, 151.5, 152.9, 165.4, 166.6, 166.9, 167.7. Anal. Calcd for $C_{41}H_{39}NO_{12}\cdot 0.5H_2O$: C, 65.94; H, 5.40; N, 1.87. Found: C, 65.92; H, 5.11, N. 1.91.

25,26,27,28-Tetraacetoxy-5-carboxy-11,23-dimethyl-17-nitrocalix[4]arene (24): yields 84% (method A), 81% (method B); mp >350 °C; ^1H NMR ($CDCl_3$) δ 1.59 (s, 6 H), 1.63 (s, 3 H), 1.65 (s, 3 H), 2.29 (s, 6 H), 3.70 (d, 2 H, *J* = 16.1 Hz), 3.71 (d, 2 H, *J* = 16.6 Hz), 3.81 (d, 2 H, *J* = 16.6 Hz), 3.84 (d, 2 H, *J* = 16.1 Hz), 6.92 (br s, 4 H), 7.76 (s, 2 H), 7.97 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.0, 20.5, 37.3, 124.1, 126.2, 130.0, 130.4, 131.3, 131.5, 132.5, 133.8, 135.0, 135.3, 144.7, 145.7, 152.4, 166..6, 166.9, 167.7, 169.9. Anal. Calcd for $C_{39}H_{35}NO_{12}\cdot 2.5H_2O$: C, 62.06; H, 5.34; N, 1.85. Found: C, 61.81; H, 4.66; N, 1.87.

General Procedure for Hydrolysis of Ester Groups in Calix[4]arenes 18 and 23. A solution of calix[4]arene (0.132 mmol) and sodium hydroxide (0.053 g, 1.32 mmol) in an ethanol-water mixture (2.6:1 mL) was heated at 90–95 °C for 20 h. The crude reaction mixture was cooled to room temperature, and the solvent was removed in vacuo. The solid obtained was triturated with 6 N hydrochloric acid (5 mL) for 3 h, filtered, and dried in vacuo over P_2O_5.

5,17-Dicarboxy-25,26,27,28-tetrahydroxy-11,23-dinitrocalix[4]arene (20): yield 94%; mp >350 °C; ^1H NMR (DMSO-d_6) δ 3.59 (br s, 4 H), 4.20 (br s, 4 H), 7.75 (s, 4 H), 7.97 (s, 4 H); ^{13}C NMR (DMSO-d_6) δ 31.1, 121.3, 124.3, 139.1, 130.4, 137.6, 158.2, 163.2, 167.3.

5-Carboxy-25,26,27,28-tetrahydroxy-11,23-dimethyl-17-nitrocalix[4]arene (23): yield 97%; mp >340 °C; ^1H NMR (DMSO-d_6) δ 2.02 (s, 6 H), 3.90 (br s, 8 H), 6.79 (d, 2 H, *J* = 1.9 Hz), 6.85 (d, 2 H, *J* = 1.9 Hz), 7.71 (s, 2 H), 8.07 (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 20.0, 30.6, 30.7, 122.4, 124.1, 127.0, 127.8, 128.1, 129.1, 129.3, 130.1, 139.2, 146.4, 155.5, 159.2, 167.0.

2,6-Bis(2-hydroxy-5-methyl-α-tolyl)-4-nitrophenol (25a). A mixture of 4-methylphenol (10.90 g, 0.100 mol) and 2,6-bis(hydroxymethyl)-4-nitrophenol[9] (**27a**; 2.00 g, 0.010 mol) was heated at 100–110 °C for 8 h. The excess of 4-methylphenol was removed by steam distillation, and the resulting solid was filtered, washed with cold water, and dried in vacuo over P_2O_5 to give 3.57 g (93%) of **25a**: mp 212 °C, benzene (lit.[19] mp 219 °C, AcOH); IR (Nujol) 3600–3000, 1515, 1350 cm^{-1}; MS *m/z* (relative abundance) 379 (M^+, 69.6), 272 (17.6), 271 (100), 256 (20.4), 255 (15.4), 254 (82.5), 121 (79.4), 108 (22.5), 107 (16.3); ^1H NMR ($CDCl_3$) δ 2.25 (s, 6 H) 3.93 (s, 4 H), 6.71 (d, 2 H, *J* = 8.0 Hz), 6.89 (dd, 2H, *J* = 1.9, 8.0 Hz), 7.09 (d, 2 H, *J* = 1.9 Hz), 8.09 (s, 2 H); ^{13}C NMR (CD_3OD) δ 20.6, 31.2, 115.9, 124.8, 126.6, 129.3, 130.1, 130.3, 132.3, 141.6, 153.2, 160.0.

4-(Ethoxycarbonyl)-2,6-bis(2-hydroxy-5-methyl-α-tolyl)phenol (25b). A mixture of 4-methylphenol (4.78 g, 44.0 mmol) and 4-(ethoxycarbonyl)-2,6-bis(hydroxymethyl)phenol[18] (**27b**; 1.00 g, 4.40 mmol) was heated at 100–110 °C for 8 h. Workup as for **25a** afforded 1.69 g (94%) of **25b**: mp 183 °C, benzene (lit.[20] mp 185.5 °C, benzene); IR (Nujol) 3600–3000, 1675, 1210 cm^{-1}; MS *m/z* (relative abundance) 406 (M^+, 57.8), 388 (1.9), 363 (1.3), 361 (48.6), 360 (100.0), 333 (13.6), 332 (51.1), 299 (18.3), 298 (69.1), 285 (5.4), 284 (7.2), 225 (40.4), 212 (26.9), 211 (11.7); ^1H NMR ($CDCl_3$) δ 1.40 (t, 3 H, *J* = 7.2 Hz), 2.23 (s, 6 H), 3.89 (s, 4 H), 4.36 (q, 2 H, *J* = 7.2 Hz), 6.70 (d, 2 H, *J* = 8.1 Hz), 6.87 (dd, 2 H, *J* = 2.2, 8.1 Hz), 7.10 (d, 2 H, *J* = 2.2 Hz), 7.90 (s, 2 H), 8.38 (br s, 3 H); ^{13}C NMR ($CDCl_3$) δ 14.5, 20.5, 31.2, 60.9, 115.9, 123.6, 126.2, 127.8, 128.8, 131.0, 131.2, 131.4, 149.6, 154.4, 166.6.

5-(Ethoxycarbonyl)-25,26,27,28-tetrahydroxy-11,23-dimethyl-17-nitrocalix[4]arene (21). Method A. Titanium(IV) chloride (2.19 g, 11.54 mmol) was dissolved under argon in cold (0 °C) dry dioxane (30 mL). The solution was heated to reflux, and solutions of trimer **25b** (0.50 g, 1.23 mmol) in dry dioxane (170 mL) and monomer **26b**[9] (0.3997 g, 1.23 mmol) in dry dioxane (80 mL) were added slowly as follows: 85 mL of trimer solution was added first, and then the monomer solution and finally the rest of the trimer solution were added. Heating was continued for 6 days, and then the solvent was removed, and dichloromethane (400 mL) was added to the residue. The solid obtained was filtered and washed with dichloromethane. The combined filtrate and washings were evaporated in vacuo. The solid was triturated with ethyl ether and filtered to give 0.18 g (26%) of **21**: mp >345 °C (toluene); MS *m/z* (relative abundance) 569 (M^+, 15.0), 524 (36.3), 523 (100.0), 460 (10.0); ^1H NMR (acetone-d_6) δ 1.29 (t, 3 H, *J* = 7.0 Hz), 2.02 (s, 6 H), 3.97 (br s, 4 H), 4.04 (br s, 4 H), 4.26 (q, 2 H, *J* = 7.0 Hz), 6.98 (d, 2 H, *J* = 2.0 Hz), 7.05 (d, 2 H, *J* = 2.0 Hz), 7.87 (s, 2 H), 8.17 (s, 2 H), 9.95 (br s, 4 H); ^{13}C NMR (DMSO-d_6) δ 14.5, 20.3, 30.9, 31.1, 60.4, 121.5, 124.6, 127.8, 128.6, 129.3, 129.5, 129.8, 130.0, 138.5, 147.6, 156.8, 161.9, 165.9. Anal. Calcd for $C_{33}H_{31}NO_8\cdot 2H_2O$: C, 65.44; H, 5.82; N, 2.31. Found: C, 65.99; H, 5.54; N, 2.16.

Method B. The same procedure as in method A was employed with trimer **25a** (0.933 g, 2.46 mmol) in dioxane (460 mL), monomer **26a**[17] (0.867 g, 2.46 mmol) in dioxane (50 mL), and titanium(IV) chloride (2.54 mL, 23.16 mmol) in dioxane (50 mL). The yield of **21** was 0.384 g (30%).

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Supplementary Material Available: Spectra (^1H and ^{13}C NMR) of compounds 8, 9, 20, and 23 (8 pages). Ordering information is given on any current masthead page.

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