Selective Lower Rim Reactions of 5,17-Upper Rim-Disubstituted Calix[4]arenes[1]

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p-tert-Butylcalix[4]arene,[2] easily accessible via base-induced condensation of *p-tert*-butylphenol and formaldehyde, provides a convenient starting material for the preparation of calixarenes carrying a wide variety of groups on the upper and lower rims.[3] The selective introduction of these groups, however, continues to be a challenge to the synthetic chemist, and several approaches to this problem have appeared in the literature. The work described in this paper employs one that involves the preparation of calix[4]arenes disubstituted on the upper rim followed by selective substitution on the lower rim to yield calix[4]arenes that can be captured in one of three conformations.

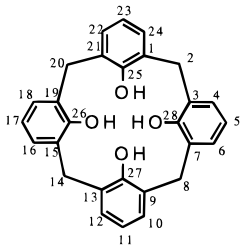
The introduction of nitro groups into the *para* positions of calixarenes was first described by Shinkai and co-workers who treated *p*-sulfonatocalix[4,6,8]arenes with nitric acid.[4] Direct nitration of calix[4]arene was subsequently accomplished by No and Noh,[5] and *ipso* nitration of the tetrapropyl ether of *p-tert*-butylcalix[4]arene has more recently been described by Reinhoudt and co-workers[6]. The latter reaction provides a mixture of fully nitrated and partially nitrated compounds that requires separation by column chromatography. However, the 5,-17-dinitro-11,23-di-*tert*-butyl compound is more cleanly prepared by *ipso* nitration of the 25,27-dipropyl ether of *p-tert*-butylcalix[4]arene,[6] the *p-tert*-butyl groups *para* to the free OH groups being the ones more readily replaced. The greater reactivity of these positions has been used to advantage in other procedures for selective functionalization of the upper rim,[4,7−9] and it is this general scheme that is employed in the present work.

Starting with dibenzyl ether **1** obtained by treatment of calix[4]arene with benzyl bromide and K_2CO_3 using previously described procedures,[10] nitration yields 5,17-dinitro-25,27-dibenzyl ether **2** (Scheme 1). The benzyl groups of **2** can be removed by treatment with $AlCl_3$ to give 5,17-dinitrocalix[4]arene (**3**)[11] and can be restored by treatment of **3** with benzyl bromide and Me_3SiOK, the benzylation occurring on the less acidic phenol moieties which provide the more nucleophilic phenolate anions. O-Methylation of **2** with NaH proceeds smoothly to give **5** from which the benzyl groups can be selectively removed to yield **6**, isomeric with the compound obtained by Reinhoudt and co-workers[7] in which the methyl ether groups are on the phenolic rather than the *p*-nitrophenolic rings. Conformational control can be exerted in the conversion of **2** to the corresponding tetrabenzyl ether. When the reaction is carried out with weak bases such as K_2CO_3[12] or Cs_2CO_3, the product is fixed in the 1,3-alternate conformation (**8**), whereas with a stronger base such as NaH the cone conformer (**7**) is produced. The products of esterification of **2** proved to be dependent on the esterifying reagent. Whereas acetyl chloride and butyryl chloride yield tetrasubstituted compounds **4a** and **4b**, benzoyl chloride yields only trisubstituted compound **9**, as previously noted.[13]

As mentioned above, benzylation of **3** in the presence of Me_3SiOK produces 1,3-dibenzyl ether **2** even when an excess of benzyl bromide is employed. When the weaker base K_2CO_3 is used, only monobenzylation occurs to yield **11** in which the benzyl group resides on a *p*-nitrophenolic oxygen (Scheme 2). Here, also, a large excess of benzyl bromide fails to alter the outcome. The structure of **11** was based on the elemental analysis and the appearance in the ^{1}H NMR spectrum of resonances at δ 10.04 and 8.72 in a 1:2 ratio for the OH groups and resonances at δ 7.98 and 7.91 in a 1:1 ratio for the Ar-H protons of the *p*-nitrophenyl rings. The conformation was established as the cone on the basis of four doublets at δ 4.53, 4.22, 3.56, and 3.54 in the ^{1}H NMR spectrum arising from the $ArCH_2Ar$ methylene hydrogens[3a] and a resonance at δ 31.67 in the ^{13}C NMR spectrum arising from the $ArCH_2$-Ar methylene carbons.[14] Further benzylation of monobenzyl ether **11** using Me_3SiOK as base yielded tribenzyl ether **13**, once again the result of the weaker phenolic moieties providing the more nucleophilic oxyanions. Its structure is based on the elemental analysis and the

(1) Paper 45 in the series Calixarenes. For paper 44, *cf.* Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1996**, *61*, 2511.

(2) The term "calixarene" is variously employed in different contexts. In colloquial usage (as employed in the Discussion section), it implies the presence of hydroxyl groups. In the more precise and complete specification of a compound (as used in the Experimental Section), it implies only the basic skeleton to which the substituents, including the OH groups, are attached at positions designated by appropriate numbers as shown in the following structure.



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(11) Attempts to prepare a dinitrocalix[4]arene by nitration of calix-[4]arene or its ethyl ether led to mixtures of the tetranitro and dinitro compounds (see Experimental Section).

(12) When K_2CO_3 (50 equiv) was employed in very dilute solution, the product was the 1,3-alternate conformer, but the cone conformer was the major product when a more concentrated solution was used.

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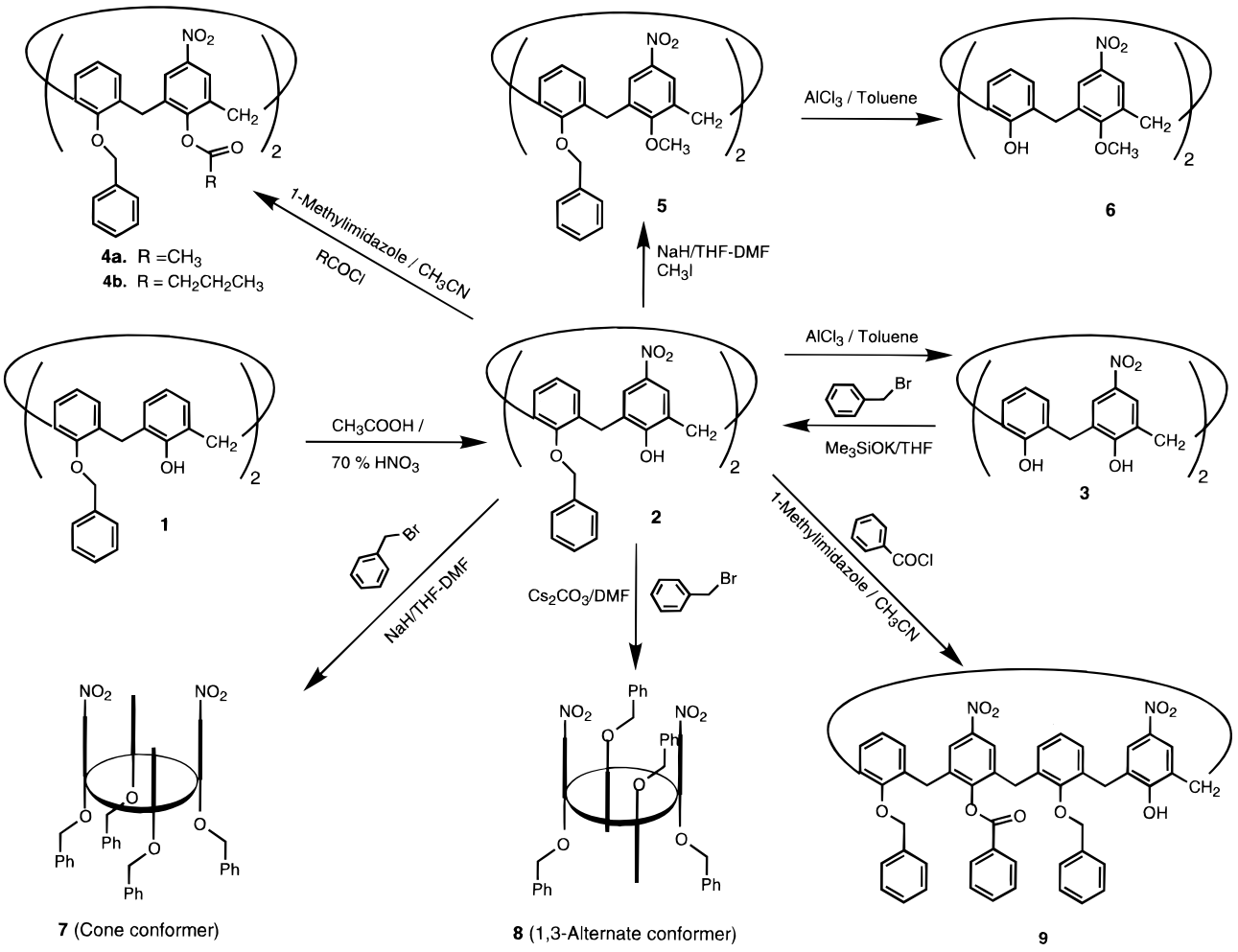
0022-3263/96/1961-2564$12.00/0

Scheme 1



appearance in the ^{1}H NMR spectrum of singlets at δ 8.02 and 7.94 in a 1:1 ratio for the Ar-H protons of the *p*-nitrophenyl rings, a singlet at δ 7.84 for the lone proton on the OH group, a pair of doublets at δ 5.03 and 4.85 from the methylene groups (diastereotopic H) of the two equivalent benzyl groups on the phenol moieites, and a singlet at δ 4.78 for the methylene group (equivalent H) of the benzyl group on the *p*-nitrophenol moiety. The conformation was established as a partial cone ("up, down, up" orientation with respect to the three benzylated moieties) on the basis of four doublets at δ 3.99, 3.82, 3.68, and 3.30 for the $ArCH_2Ar$ methylene protons in the ^{1}H NMR spectrum along with a pair of signals at δ 37.48 and 30.75 for the $ArCH_2Ar$ methylene carbons in the ^{13}C NMR spectrum.

Treatment of **3** with benzoyl chloride and $AlCl_3$ produces 1,3-diester **12** in a flattened cone conformation (a pair of doublets at δ 4.01 and 3.68 in the ^{1}H NMR spectrum and a singlet at δ 34.59 in the ^{13}C NMR spectrum), while with NaH or 1-methylimidazole tetraester **10** in the 1,3-alternate conformation is the major product (close-lying pair of doublets centered at δ 3.46). Although Cs_2CO_3 is generally the required base for directing alkylations to produce the 1,3-alternate conformation,[15] acylation and aroylation are known to follow this pathway under a variety of conditions.[13,16] Tetraester **10** is also produced when 1,3-diester **12** is treated with benzoyl chloride. However, an attempt to convert diester **12** to a mixed benzyloxy−benzoyloxy compound failed, the only product formed being the tetrabenzyl ether as a mixture of conformers.

To explore the monobenzylation reaction of **3** in more detail, 5,17-bis-*tert*-butylcalix[4]arene (**15**) was treated with benzyl bromide under the conditions used to convert **3** to **11**. However, the only product isolated was 1,3-dibenzyl ether **14** in which, in contrast with **11**, the benzyl groups are attached to the unsubstituted phenolic moieties. This is rationalized by the assumption that the phenolic moieties are slightly stronger acids than the *p*-*tert*-butylphenolic moieties and, with a weak base, are preferentially removed in the formation of the mono- or dianion. The structure of **14** was established on the basis of the elemental analysis and the constancy of the position of the ^{1}H NMR resonance of the *tert*-butyl hydrogens in starting compound **15** and product **14**.[17] Benzoylation of **15**, on the other hand, introduces the benzoyl groups on the oxygens of the *p*-*tert*-butyl moieties to give diester **16**, as indicated by the shift in the resonance position of the *tert*-butyl hydrogens from δ 1.24 in the starting material **15** to δ 1.08 in the product **16**.

Conclusion. The present work shows that nitration of the 25,27-dibenzyl ether of calix[4]arene (**1**) yields the

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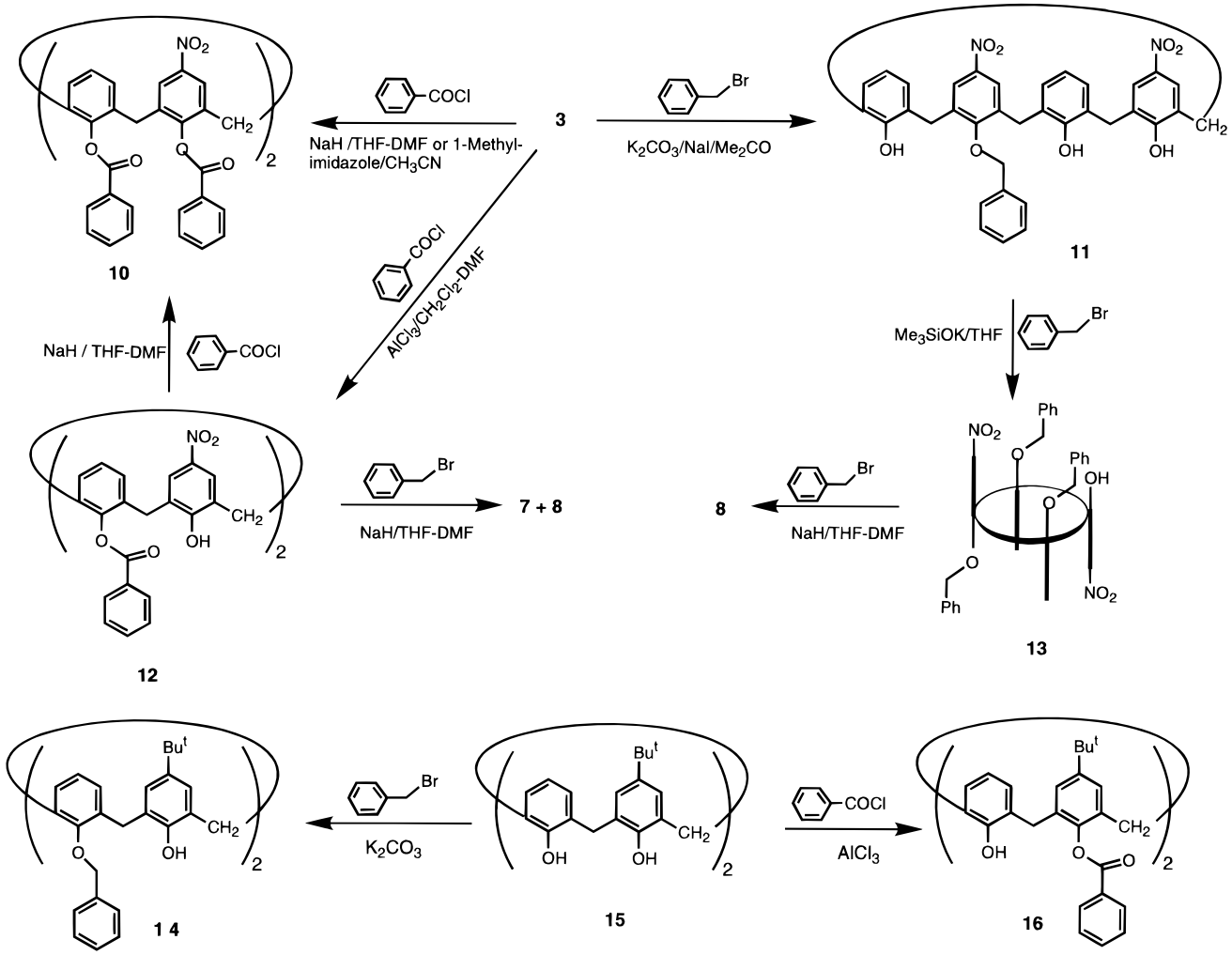
(16) Iqbal, M.; Mangiafico, T.; Gutsche, C. D. *Tetrahedron* **1987**, *21*, 4917.

(17) When O-benzylation takes place on the *p*-*tert*-butylphenolic rings the ^{1}H NMR resonance of the *tert*-butyl groups generally moves upfield from its position at δ 1.24 in the starting material.

Scheme 2



corresponding 5,17-dinitro compound **2** from which the benzyl groups can be removed to produce 5,17-dinitrocalix[4]arene (**3**). Alkylation and acylation reactions have been carried out with **2** and **3** under a variety of conditions to yield products in which one (**11**), two (**12**), three (**9**, **13**), or all four (**4**, **5**, **7**, **8**, **10**) of the phenolic oxygens carry substituent groups and in which the systems are fixed in cone (**1**−**3**, **7**, **11**, **12**), partial cone (**13**), or 1,3-alternate (**8**) conformations. Benzylation of 5,17-di-*tert*-butylcalix[4]arene (**15**) takes place on the oxygens at the 25,27 positions (**14**), while benzoylation takes place on the oxygens at the 26,28 positions (**16**).

(18) Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. HPLC grade *N*,*N*-dimethylformamide (DMF), acetonitrile, and acetone were used. Tetrahydrofuran (THF) was dried over benzophenone/Na and distilled immediately before using. Column chromatography was carried out by using Aldrich 70−230 mesh, 60 Å silica gel. Thin-layer chromatography (TLC) was performed on 250 μm silica gel plates containing a fluorescent indicator. Melting points were taken in sealed and evacuated capillary tubes on a MEL-Temp apparatus (Laboratory Devices, Cambridge, MA) using a 400 °C thermometer calibrated against a thermocouple and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL-300 spectrometer, and the chemical shifts are reported as δ values in ppm. ^{1}H NMR spectra are referenced to tetramethylsilane (TMS) at 0.00 ppm as an internal standard and recorded at room temperature (20 + 1 °C), and ^{13}C NMR spectra are referenced to either $CDCl_3$ (77.00 ppm), DMSO-d_6 (40.0 ppm), or TMS (0.00 ppm) and also recorded at room temperature (20 ± 1 °C). Microanalytical samples were dried for at least 48−72 h at 111 °C (toluene) or at 140 °C (xylene) 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 and affected the elemental analysis. In such cases, best fits between the analytical values and appropriate increments of the solvents were used.

Experimental Section[18]

25,27-Dibenzylcalix[4]arene-26,28-diol (1) (Cone Conformer). A 15.3 g (115 mmol) sample of anhydrous K_2CO_3 and 2.0 g of NaI were suspended in 200 mL of acetone followed by 21.2 g (50 mmol) of calix[4]arene-25,26,27,28-tetrol. To the stirred reaction mixture was added benzyl bromide (19.7 g, 115 mmol), and the mixture was stirred at rt for 6 h. The solvent was removed under reduced pressure, ice-cold water was added with stirring, the contents were neutrallized with 20% HCl, and a light yellow precipitate formed. It was removed by filtration and washed thoroughly with water. The resulting material was stirred with MeOH, insoluble material was removed by filtration, and the product was purified by column chromatography ($CHCl_3$ eluent) to yield 26.4 g (87%) of **1** as a colorless powder: mp 221−223 °C (lit.[7] mp 220−222 °C).

5,17-Dinitro-25,27-bis(benzyloxy)calix[4]arene-26,28-diol (2) (Cone Conformer). To a slurry of 20.15 g (33 mmol) of **1** in 200 mL of glacial AcOH was added 50 mL of 70% HNO_3 in portions at 0 °C. The reaction mixture was stirred for 2 h and poured into ice-cold water, and the light yellow precipitate was separated by filtration. This material was washed with cold water and triturated with MeOH to afford a single compound pure enough for subsequent reactions. An analytical sample was obtained by passing the product through a silica gel column ($CHCl_3$ eluent), crystallizing from $CHCl_3$−*n*-hexane (1:3), and stirring with MeOH to yield 19.6 g (85%) of a colorless solid: mp 285−286 °C; ^{1}H NMR ($CDCl_3$) δ 8.99 (s, 2H), 8.03 (s, 4H), 7.60−7.57 (m, 4H), 7.44−7.38 (m, 6H), 6.97 (d, 4H, J = 7.4 Hz), 6.86 (t, 2H, J = 6.9 and 8.1 Hz), 5.09 (s, 4H), 4.27 (d, 4H, J = 13.38 Hz), 3.47 (d, 4H, J = 13.44 Hz); ^{13}C NMR ($CDCl_3$) δ 159.46, 151.67, 139.85, 135.83, 131.78, 129.75, 129.00, 128.29, 127.71,

126.10, 124.56 (ArC), 78.98, 31.25. Anal. Calcd for $C_{42}H_{34}N_2O_8 \cdot 0.5H_2O$:[19] C, 71.68; H, 5.01. Found: C, 71.95; H, 5.21.

5,17-Dinitrocalix[4]arene-25,26,27,28-tetrol (3) (Cone Conformer). A 21.4 g (160 mmol) sample of anhydrous $AlCl_3$ and 100 mL of toluene were placed in a 250 mL round-bottomed flask and stirred for 5 min at rt. A slurry of 13.9 g (20 mmol) of **2** in 20 mL of toluene was added with stirring (dark brown semisolid material settled to bottom of flask). The reaction mixture was stirred for 30 min at rt and poured into 200 mL of ice-cold water, and unreacted $AlCl_3$ was destroyed with 20% HCl. The greyish precipitate was removed by filtration, toluene was evaporated from the filtrate, and the remaining aqueous phase was extracted with CH_2Cl_2. Evaporation of the CH_2Cl_2 left a residue which was combined with the greyish precipitate and triturated with MeOH (100 mL) to leave 8.03 g (78%) of a light brown product: 351 °C dec (turns brown at 325 °C); ^{1}H NMR ($CDCl_3$) δ 10.14 (b, 4H), 7.99 (s, 4H), 7.18 (d, 4H, J = 7.5 Hz), 6.87 (t, 2H, J = 7.5 and 7.3 Hz), 4.31 (bs, 4H), 3.72 (bs, 4H); ^{13}C NMR ($CDCl_3$) δ 155.48, 148.35, 141.46, 129.45, 129.07, 127.01, 124.56, 122.69 (ArC), 31.24. Anal. Calcd for $C_{28}H_{22}N_2O_8$: C, 65.37; H, 4.31. Found: C, 66.05; H, 4.40.

5,17-Dinitro-26,28-diacetyl-25,27-bis(benzyloxy)calix[4]arene (4a). A mixture of 0.70 g (1 mmol) of **2**, 1.0 mL of 1-methylimidazole, 50 mL of CH_3CN, and 2 mL of acetyl chloride was stirred for 18 h at rt and poured over ice-cold water to give a white precipitate which was removed by filtration, dried, and purified by column chromatography (CH_2Cl_2 eluent) to give 0.68 g (89%) of **4a** as a mixture of conformers. However, further chromatography (CH_2Cl_2 eluent) followed by crystallization from CH_2Cl_2−MeOH (1:2) gave 0.46 g (58%) of the 1,3-alternate conformer of **4a**: mp 257−258 °C; ^{1}H NMR ($CDCl_3$) δ 7.64 (s, 4H), 7.26−7.22 (m, 6H), 7.04−6.96 (m, 6H), 6.77 (d, 4H, J = 7.2 Hz), 4.75 (s, 4H), 3.75 (d, 4H, J = 16.2 Hz), 3.59 (d, 4H, J = 15.9 Hz), 1.66 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 167.54, 156.28, 152.90, 144.86, 136.01, 134.89, 133.44, 130.40, 128.65, 128.60, 127.35, 124.56, 123.73 (ArC), 72.80, 37.79, 20.78. Anal. Calcd for $C_{46}H_{38}O_{10}N_2$: C, 70.94; H, 4.92. Found: C, 70.89; H, 5.02.

5,17-Dinitro-26,28-dibutyryl-25,27-bis(benzyloxy)calix[4]arene (4b). A mixture of 0.70 g (1 mmol) of **2**, 1.0 mL of 1-methylimidazole, 50 mL of CH_3CN, and 2 mL of butyryl chloride was stirred for 18 h at rt and poured over ice-cold water to give a white precipitate which was removed by filtration, dried, and purified by column chromatography (CH_2Cl_2 eluent) to give 0.70 g (84%) of **4b** as a mixture of conformers in which the 1,3-alternate was the dominant form: mp 259−261 °C; ^{1}H NMR ($CDCl_3$) δ 8.01 (s, 1H), 7.57 (m, 4H), 7.33 (s, 1H), 7.23−7.14 (m, 6H), 6.95−6.84 (m, 4H), 6.72−6.60 (m, 4H), 4.70−4.50 (m, 4H), 3.76−3.10 (m, 8H), 1.72−1.68 (m, 4H), 1.52−1.48 (m, 4H), 0.90−0.85 (m, 6H).

5,17-Dinitro-26,28-dimethoxy-25,27-bis(benzyloxy)calix[4]arene (5). A 0.6 g (15 mmol) sample of NaH (60% in oil dispersion) was placed in a 150 mL round-bottomed flask and treated with a mixture of dry, freshly distilled THF and DMF (60 mL, 5:1 ratio) followed by 0.69 g (1 mmol) of **2** and stirred for 3 min at rt. Methyl iodide was added, and the reaction mixture was stirred an additional 18 h at rt. It was poured over ice-cold water and neutralized with 20% HCl to produce a light yellow semisolid which was extracted into CH_2Cl_2. The organic layer was separated, concentrated, and triturated with *n*-hexane (50 mL) to give a white precipitate which was purified by column chromatography ($CHCl_3$ eluent) to yield 0.61 g (85%) of a colorless powder: mp 142−143 °C; ^{1}H NMR ($CDCl_3$) δ 7.83 (s, 2H), 9.38 (bs, 8H), 7.20−6.80 (m, 10H), 4.89−4.77 (m, 4H), 4.35−2.90 (m, 14H). O-Debenzylation of **5** (*vide infra*) yielded **6**, for which elemental analytical data are given.

5,17-Dinitro-26,28-dimethoxycalix[4]arene-25,27-diol (6) (Cone Conformer). A mixture of 0.68 g (5 mmol) of anhydrous $AlCl_3$, 15 mL of toluene, and 0.36 g (0.5 mmol) of **5** was stirred for 10 min in a 150 mL round-bottomed flask and worked up as described above for **3** to give a light yellow compound which was purified by column chromatography ($CHCl_3$ eluent). The product was triturated with anhydrous MeOH (30 mL) and dried under reduced pressure to give 0.20 g (77%) of a white powder: mp 336−338 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.82 (s, 4H), 7.54 (s, 2H), 7.16 (d, 4H, J = 7.5 Hz), 6.77 (t, 2H, J = 7.5 Hz), 4.34 (d, 4H, J = 13.2 Hz), 4.07 (s, 6H), 3.52 (d, 4H, J = 13.2 Hz); ^{13}C NMR ($CDCl_3$) δ 157.15, 151.74, 143.79, 133.59, 128.23, 127.18, 123.77, 119.19, 63.18, 30.21. Anal. Calcd for $C_{30}H_{26}N_2O_8$: C, 66.41; H, 4.83. Found: C, 66.43; H, 4.88.

5,17-Dinitro-25,26,27,28-tetrakis(benzyloxy)calix[4]arene (7) (Cone Conformer). A 0.60 g (15 mmol) sample of NaH (60% in oil dispersion) was placed in a 150 mL round-bottomed flask followed by dry, freshly distilled THF (40 mL) and DMF (10 mL). To this was added 0.69 g (1 mmol) of **2**, and the mixture was stirred for 5 min at rt. A solution of benzyl bromide (1.71 g, 10 mmol) in 10 mL of dry THF was added, and the reaction contents were stirred 12 h. The solvent was removed under reduced pressure on a rotary evaporator, and the concentrated residue was neutralized with ice-cold 20% HCl to produce a light yellow semisolid which was extracted into CH_2Cl_2. The organic layer was separated, concentrated, and triturated with *n*-hexane (50 mL) followed by MeOH (50 mL) to give a white precipitate which was purified by column chromatography ($CHCl_3$ eluent) to yield 0.79 g (91%) of a colorless powder. An analytical sample was obtained by recrystallization from $CHCl_3$−*n*-hexane (1:3): mp 199−201 °C; ^{1}H NMR ($CDCl_3$) δ 7.38 (s, 4H), 7.33−7.20 (m, 20H), 6.68−6.60 (m, 6H), 4.99 (s, 4H), 4.95 (s, 4H), 4.15 (d, 4H, J = 13.8 Hz), 2.95 (d, 4H, J = 14.1 Hz); ^{13}C NMR ($CDCl_3$) δ 160.74, 154.6, 142.62, 136.84, 136.19, 134.38, 129.87, 129.57, 128.88, 128.78, 128.60, 128.42, 128.35, 128.24, 123.48, 123.42 (ArC), 77.00, 76.76, 31.37. Anal. Calcd for $C_{56}H_{46}N_2O_8 \cdot H_2O$:[19] C, 75.32; H, 5.42. Found: C, 75.67; H, 5.16.

5,17-Dinitro-25,26,27,28-tetrakis(benzyloxy)calix[4]arene (8) (1,3-Alternate Conformer). A 10.0 g (30 mmol) sample of Cs_2CO_3 was placed in a 150 mL round-bottomed flask followed by DMF (80 mL). To this was added 0.70 g (1 mmol) of **2**, and the contents were stirred at rt. A solution of benzyl bromide (1.40 g, 8 mmol) was added, and the reaction mixture was stirred at rt for 18 h. It was then poured onto ice-cold water and neutrallized with 20% HCl to produce a light yellow oil which was extracted into CH_2Cl_2. The organic layer was removed, concentrated, and poured over *n*-hexane to give a light yellow precipitate which was removed by filtration and triturated with MeOH (100 mL). The resulting material was purified by column chromatography ($CHCl_3$ eluent), and 0.74 g (85%) of an analytical sample was obtained by trituration with MeOH: mp 275−277 °C; ^{1}H NMR ($CDCl_3$) δ 7.65 (s, 4H), 7.42−7.36 (m, 12H), 7.14−7.11 (m, 4H), 7.05−7.03 (m, 4H), 6.72 (d, 4H, J = 7.5 Hz), 6.52 (t, 2H, J = 7.8 Hz), 4.85 (s, 8H), 3.64 (d, 4H, J = 15.0 Hz), 3.55 (d, 4H, J = 14.7 Hz); ^{13}C NMR ($CDCl_3$) δ 161.29, 155.73, 142.48, 136.74, 136.38, 135.25, 132.59, 131.13, 128.56, 128.21, 127.99, 127.83, 127.27, 126.66, 125.71, 122.73 (ArC), 73.02, 36.82. Anal. Calcd for $C_{56}H_{46}N_2O_8 \cdot 0.5H_2O$:[19] C, 76.10; H, 5.36. Found: C, 76.30; H, 5.14.

5,17-Dinitro-25,27-bis(benzyloxy)-26-(benzoyloxy)calix[4]aren-28-ol (9) (Patrial Cone Conformer). A solution of 0.70 g (1 mmol) of **2** and 1.0 mL of 1-methylimidazole in 50 mL of CH_3CN was stirred for 5 min and treated with 1.40 g (10 mmol) of benzoyl chloride. The reaction mixture was stirred 10 h and poured over ice-cold water to give a white precipitate which was removed by filtration and stirred with MeOH (20 mL) to afford 0.76 g which TLC showed to be a mixture of three products. Compound **9** was isolated by column chromatography (CH_2Cl_2 eluent) and purified by stirring with cold acetone to give 0.62 g (78%) of a colorless solid: mp 302−304 °C; ^{1}H NMR ($CDCl_3$) δ 8.19 (s, 2H), 8.01 (s, 2H), 7.97 (s, 1H), 7.70 (m, 1H), 7.30−7.15 (m, 8H), 6.84 (d, 2H, J = 7.8 Hz), 6.65−6.56 (m, 6H), 6.37 (d, 2H, J = 6.9 Hz), 6.07 (t, 2H, J = 7.5 Hz), 4.28 (dd, 4H), 3.77 (d, 2H, J = 13.2 Hz), 3.55 (s, 4H), 3.14 (d, 2H, J = 12.9 Hz); ^{13}C NMR ($CDCl_3$) δ 165.72, 162.53, 154.13, 153.79, 145.39, 145.12, 138.04, 136.16, 135.57, 134.25, 133.33, 132.76, 132.16, 132.03, 130.17, 129.77, 129.38, 128.76, 128.46, 127.71, 127.28, 124.69, 124.17, 123.24 (ArC), 76.81, 38.21, 30.79. Anal. Calcd for $C_{49}H_{38}N_2O_9$: C, 73.67; H, 4.69. Found: C, 74.02; H, 4.69.

5,17-Dinitro-25,26,27,28-tetrakis(benzoyloxy)calix[4]arene (10) (1,3-Alternate Conformer). A solution of 0.25 g (0.5 mmol) of **3** and 0.5 mL of 1-methylimidazole in 20 mL of CH_3CN was stirred 5 min and treated with 1.05 g (7.5 mmol) of benzoyl chloride. The reaction mixture was stirred 6 h and poured over ice-cold water to give a white precipitate which was

(19) The presence of water was qualitatively supported by the appearance of a broad signal in the ^{1}H NMR spectrum at δ 1.5 in $CDCl_3$ or 3.4 in DMSO-d_6.

removed by filtration and triturated with MeOH (20 mL) to afford 0.41 g (91%) of **10** as a colorless powder: mp > 400 °C; ^{1}H NMR ($CDCl_3$−DMSO-d_6) δ 7.66−7.56 (m, 8H), 7.50−7.40 (m, 12H), 7.35−7.30 (m, 4H), 7.24 (s, 2H), 6.57−6.53 (m, 4H), 3.46 (dd, 8H, J = 12.0 and 12.6 Hz). The insolubility of **10** precluded obtention of a ^{13}C NMR spectrum. Anal. Calcd for $C_{56}H_{38}N_2O_{12}\cdot 1.5\ H_2O$:[19] C, 70.21; H, 4.31. Found: C, 70.20; H, 4.39. Compound **10** was also obtained in 84% yield by the reaction of 0.25 g (0.5 mmol) of **3**, 0.5 g of NaH (60% in oil dispersion), and 1.05 g (7.5 mmol) of benzoyl chloride in 60 mL of THF-DMF (5:1) refluxed 5 h.

5,17-Dinitro-26-(benzyloxy)calix[4]arene-25,27,28-triol (11) (Cone Conformer). A mixture of 1.40 g (10 mmol) of anhydrous K_2CO_3, 0.3 g of NaI, and 1.03 g (2 mmol) of **3** was suspended in 100 mL of acetone and stirred for 5 min. Benzyl bromide (0.85 g, 5 mmol) was added. The mixture was stirred at rt for 6 h (or refluxed 4 h). Excess solvent was removed under reduced pressure, and the reaction was worked up according to the procedure described above for **8**. The product was purified by column chromatography ($CHCl_3$ eluent), and an analytical sample was obtained by stirring with MeOH to yield 0.98 g (82%) of a colorless solid: mp 166−168 °C; ^{1}H NMR ($CDCl_3$) δ 10.04 (s, 1H), 8.72 (s, 2H), 7.98 (s, 2H), 7.91 (s, 2H), 7.68−7.64 (m, 2H), 7.55−7.53 (m, 3H), 7.16−7.10 (m, 4H), 6.78 (t, 2H, J = 7.5 Hz), 5.29 (s, 2H), 4.53 (d, 2H, J = 13.2 Hz), 4.22 (d, 2H, J = 14.1 Hz), 3.56 (d, 2H, J = 14.1 Hz), 3.54 (d, 2H, J = 13.2 Hz); ^{13}C NMR ($CDCl_3$) δ 156.33, 155.07, 150.47, 145.19, 142.04, 136.08, 129.79, 129.55, 129.51, 129.31, 129.26, 129.14, 126.98, 126.82, 124.97, 124.72, 121.88 (ArC), 80.14, 31.67. Anal. Calcd for $C_{35}H_{28}N_2O_8$: C, 69.53; H, 4.67; N, 4.63. Found: C, 69.78; H, 4.68; N, 4.42.

5,17-Dinitro-25,27-bis(benzoyloxy)calix[4]arene-26,28-diol (12) (Cone Conformer). A mixture of 1.33 g (10 mmol) of anhydrous $AlCl_3$ and 24 mL of CH_2Cl_2 in a 250 mL round-bottomed flask was treated with 6 mL of DMF, stirred for 2 min, and 0.26 g (0.5 mmol) of **3** then added. The reaction mixture was stirred for 5 min, 1.05 g (7.5 mmol) of benzoyl chloride was added, and stirring was continued 6 h at rt. The CH_2Cl_2 was removed under reduced pressure, ice-cold water was added, and the mixture was neutralized with 20% HCl to give a white precipitate which was removed by filtration and triturated with MeOH (20 mL) to give 0.30 g (84%) of a white powder: mp 355−357 °C; ^{1}H NMR (DMSO-d_6) δ 8.67 (s, 2H), 7.83 (t, 2H, J = 7.5 Hz), 7.75 (d, 4H, J = 7.5 Hz), 7.52 (t, 4H , J = 7.5 Hz), 7.46 (s, 4H), 7.30 (d, 4H, J = 7.5 Hz), 7.03 (t, 2H, J = 8.4 Hz), 3.87 (d, 4H, J = 14.4 Hz), 3.53 (d, 4H, J = 14.4 Hz); ^{1}H NMR ($CDCl_3$) δ 8.24 (d, 4H, J = 8.4 Hz), 7.99 (s, 4H), 7.75 (t, 2H, J = 7.5 Hz), 7.55 (t, 4H, J = 7.5 and 8.1 Hz), 7.06−7.00 (m, 6H), 6.34 (bs, 2H), 4.01 (d, 4H, J = 14.7 Hz), 3.68 (d, 4H, J = 14.7 Hz); ^{13}C NMR (DMSO-d_6) δ 163.70, 160.02, 147.56, 138.00, 133.94, 131.47, 130.86, 129.75, 128.88, 128.65, 127.87, 125.12, 124.40 (ArC), 34.59. Anal. Calcd for $C_{42}H_{30}N_2O_{10}\cdot H_2O$:[19] C, 68.10; H, 4.35. Found: C, 67.99; H, 4.10.

5,17-Dinitro-25,26,27-tris(benzyloxy)calix[4]arene-28-ol (13) (Partial Cone Conformer). A 3.35 g (10 mmol) sample of Me_3SiOK was placed in a 150 mL round-bottomed flask followed by dry, freshly distilled THF (90 mL). To this was added 0.61 g (1 mmol) of **11**, and the reaction mixture was stirred at rt for 2 min. A solution of benzyl bromide (1.70 g, 10 mmol) in 10 mL of dry THF was then added, the reaction mixture was stirred at rt for 18 h, and it was worked up as described above for **7** to give a crude product which was recrystallized from $CHCl_3$−*n*-hexane (1:3) to yield 0.63 g (81%) of **13** as a white powder: mp 220−221 °C; ^{1}H NMR ($CDCl_3$) δ 8.02 (s, 2H), 7.94 (s, 2H), 7.84 (s, 1H), 7.40−7.34 (m, 6H), 7.29−7.18 (m, 7H), 6.84−6.76 (m, 4H), 6.66−6.56 (m, 4H), 5.03 (d, 2H, J = 12.0 Hz), 4.85 (d, 2H, J = 12.0 Hz), 4.78 (s, 2H), 3.99 (d, 2H, J = 13.5 Hz), 3.82 (d, 2H, J = 15.0 Hz), 3.68 (d, 2H, J = 15.0 Hz), 3.30 (d, 2H, 13.5 Hz); ^{13}C NMR ($CDCl_3$) δ 159.35, 153.89, 142.73, 139.66, 136.28, 136.05, 135.35, 131.96, 131.60, 130.44, 129.79, 128.72, 128.51, 128.30, 128.07, 127.67, 127.30, 126.72, 126.18, 124.29, 124.23 (ArC), 76.03, 72.47, 37.48, 30.75. Anal. Calcd for $C_{49}H_{40}N_2O_8$: C, 74.99; H, 5.14; N, 3.46. Found: C, 74.62; H, 5.01; N, 3.46.

5,17-Di-*tert*-butyl-25,27-bis(benzyloxy)calix[4]arene-26,28-diol (14) (Cone Conformer). A mixture of 0.70 g (5 mmol) of anhydrous K_2CO_3, 0.2 g of NaI, and 0.26 g (0.5 mmol) of **15** in 50 mL of acetone was stirred 5 min and treated with 0.8 g (4 mmol) of benzyl bromide in 5 mL of acetone. The mixture was stirred at rt for 18 h and worked up to give a crude product from which an analytical sample was obtained by column chromatography ($CHCl_3$ eluent) and crystallization from $CHCl_3$−*n*-hexane (1:3) as 0.29 g (83%) of a colorless powder: mp 256−258 °C; ^{1}H NMR ($CDCl_3$) δ 7.80 (s, 2H), 7.65 (d, 4H, J = 7.5 Hz), 7.34−7.36 (m, 6H), 7.02 (s, 4H), 6.93 (d, 4H, J = 7.5 Hz), 6.79 (t, 2H, J = 7.5 Hz), 5.05 (s, 4H), 4.30 (d, 4H, J = 12.9 Hz), 3.31 (d, 4H, J = 12.9 Hz), 1.26 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 151.99, 150.94, 141.47, 136.84, 133.55, 129.01, 128.71, 127.97, 127.61, 127.15, 125.46, 125.27 (ArC), 78.44, 33.85, 31.91, 31.70. Anal. Calcd for $C_{50}H_{52}O_4\cdot {}^2/_5CHCl_3$: C, 79.16; H, 6.91. Found: C, 79.25; H, 6.91.

5,17-Di-*tert*-butyl-26,28-bis(benzoyloxy)calix[4]arene-25,27-diol (16) (Cone Conformer). A mixture of 1.0 g (0.75 mmol) of anhydrous $AlCl_3$ and 24 mL of CH_2Cl_2 in a 150 mL round-bottomed flask was treated with 6 mL of DMF and stirred for 2 min. To this was added 0.26 g (0.5 mmol) of **15**, the reaction mixture was stirred for 5 min, 1.05 g (15 mmol) of benzoyl chloride was added, and stirring was continued for 18 h at rt. The crude product was purified by triturating with MeOH to give 0.30 g (79%) of a white solid: mp 348−351 °C; ^{1}H NMR ($CDCl_3$) δ 8.21 (d, 4H, J = 7.2 Hz), 7.73 (d, 2H, J = 6.9 Hz), 7.54 (t, 4H, J = 7.8 Hz), 6.99 (s, 4H), 6.93 (d, 4H, J = 6.9 Hz), 6.59 (t, 2H, J = 7.5 Hz), 5.09 (s, 2H), 3.87 (d, 4H, J = 14.4 Hz), 3.57 (d, 4H, J = 14.4 Hz), 1.08 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 165.12, 153.25, 149.39, 144.39, 134.10, 132.29, 131.05, 129.62, 129.37, 129.03, 128.40, 126.65, 119.97 (ArC), 34.51, 34.20, 31.55. Anal. Calcd for $C_{50}H_{48}O_6$: C, 80.62; H, 6.49. Found: C, 80.63 H, 6.72.

5,11,17,23-Tetranitro-25,26,27,28-tetraethoxycalix[4]arene. To a 1.08 (2 mmol) sample of tetraethyl ether of calix[4]arene in a 150 mL round-bottomed flask were added 15 mL of glacial acetic acid, 40 mL of CH_2Cl_2, and 5 mL of 70% HNO_3. The reaction mixture was stirred at rt for 4 h, turning light yellow and then dark brown. It was poured into ice-cold water to give a light yellow precipitate which was removed by filtration and washed throughly with cold water and triturated with MeOH to give 0.81 g of a light yellow material which TLC showed to be a mixture of the tetranitro and dinitro compounds. The tetranitro compound was separated by column chromatography (3:1 CH_2Cl_2−*n*-hexane eluent). Trituration with MeOH produced 0.61 g (42%) of an analytical sample as a white powder: mp 310−312 °C; ^{1}H NMR ($CDCl_3$) δ 7.62 (s, 8H), 4.55 (d, 4H, J = 13.8 Hz), 4.14 (q, 8H, J = 7.2 Hz), 3.42 (d, 4H, J = 14.1 Hz), 1.50 (t, 12H, J = 6.9 and 6.9 Hz); ^{13}C NMR (DMSO-d_6) δ 161.50, 142.02, 135.98, 123.56 (ArC), 71.06, 29.77, 15.17. Anal. Calcd for $C_{36}H_{36}N_4O_{12}$: C, 60.33; H, 5.06. Found: C, 60.32; H, 5.31.

5,17-Dinitro-25,26,27,28-tetraethoxycalix[4]arene was isolated from the above mixture (9:1 $CHCl_3$−*n*-hexane eluent) and purified by crystallization from CH_2Cl_2−*n*-hexane (1:3) followed by trituration with MeOH which yielded 0.15 g (12%) of a pale yellow powder: mp 225−226 °C; ^{1}H NMR ($CDCl_3$) δ 7.47 (s, 4H), 6.80−6.70 (m, 6H), 4.49 (d, 4H, J = 13.4 Hz), 4.10−4.01 (m, 8H), 3.26 (d, 4H, J = 13.4 Hz), 1.52−1.43 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 161.53, 155.96, 142.57, 136.55, 134.41, 128.89, 123.35, 123.12 (ArC), 70.97, 70.37, 31.10, 15.61, 15.57 Anal. Calcd for $C_{36}H_{38}N_2O_8$: C, 68.99; H, 6.11. Found: C, 68.67; H, 6.06.

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