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Unexpected Single-Step Formation of 1,2-*anti*-Heterodisubstituted Calix[4]arenes upon Alkylation of a Tribenzoyl Precursor

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Abstract: The selective preparation and complete structural characterization of a small series of 1,2-*anti*-heterodisubstituted calix[4]arenes has been accomplished. These compounds were obtained in two steps from unsubstituted *p-tert*-butylcalix[4]arene by tribenzoylation and a subsequent one-pot, two-step sequence involving alkylation with simultaneous partial deacylation, resulting in heterodisubstituted calixarenes carrying an alkyl and an aroyl group. The monoalkyl−tribenzoyl intermediate, prior to in situ deprotection, could also be isolated.

Functionalized calixarenes[1] are useful building blocks and molecular platforms for supramolecular applications such as molecular recognition[2] and formation of capsular entities.[3] To achieve these goals, however, full control over the calixarene conformations by means of selective introduction of functional groups is an essential requirement. Conformations of calix[4]arenes (cone, partial cone, 1,3-alternate, and 1,2-alternate) have been extensively studied.[4] Introduction of bulky groups or chains longer than ethyl on the phenol positions at the lower rim effectively prevents a "through-the-annulus" interconversion between the different conformer families.[5]

The lower rim O-functionalization of calix[4]arenes has been well-developed, and simple synthetic procedures are known for monosubstituted,[6] 1,3-*syn*-disubstituted,[7] and fully substituted analogues.[8] Selective proximal *homo*-1,2-dialkylation of calix[4]arenes can also be achieved,[9] though significantly fewer examples are known as compared with the case of their 1,3-distal-alkylated regioisomers. A rather limited number of examples of hetero-1,2-disubstituted versions have been reported, but full conformational evidence was not provided in these particular cases.[10] In this note we wish to report the selective formation of 1,2-*anti*-heterodisubstituted calix[4]arenes and a detailed conformational study of these derivatives and of their tribenzoyl precursor.

Chawla et al.[11] first reported the tribenzoylation of *p-tert*-butylcalix[4]arene **1** (Scheme 1) (benzoyl chloride (4 equiv)/pyridine, 1 M calixarene). The isolated product (87% yield) was described as two conformationally different tribenzoyl derivatives (cone and partial cone conformations) in a ca. 1:3 ratio. For larger-scale preparation, we decided to use a much higher dilution (32.5 mM) and a different workup. The isolated crude material (13.49 g, 84% overall yield) was partially dissolved in methanol upon trituration. Both the resulting solid and the solution were found to contain the same three components in different ratios (84:15:1 for the solid (10.05 g) and 1:88:11 in solution (3.44 g) by NMR integration). Overall, the three components were present in a 63:34:3 ratio. The major components of both fractions were obtained as pure materials by a single crystallization step. The identity of the third, not isolated minor

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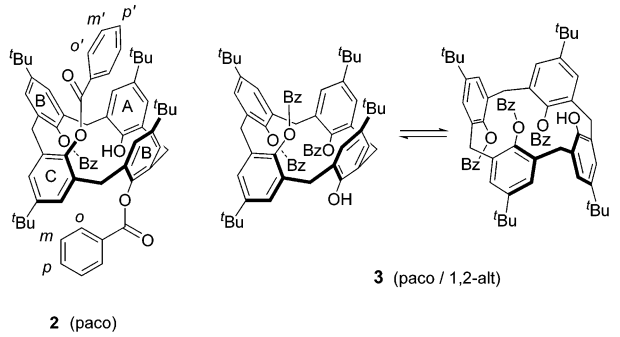
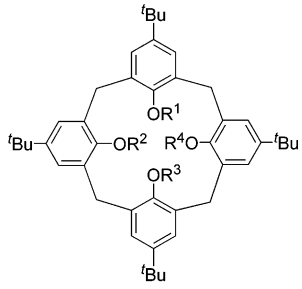


FIGURE 1. Structures of the tribenzoyl derivatives **2** and **3**.

SCHEME 1. Synthesis of Calixarene Compounds 2−6



1 $R^1 = R^2 = R^3 = R^4 = H$

↓ BzCl, Pyridine, r. t.

2 $R^1 = H$ $R^2 = R^3 = R^4 = Bz$ (paco symmetric)
3 $R^1 = H$ $R^2 = R^3 = R^4 = Bz$ (paco/1,2-alt asymmetric)

↓ R^1X (X = Br, I) NaH, DMF, r. t.

4	R^1 = 4-I-$C_6H_4CH_2$	$R^2 = H$	$R^3 = H$	$R^4 = Bz$
5	R^1 = 4-I-$C_6H_4CH_2$	$R^2 = Bz$	$R^3 = Bz$	$R^4 = Bz$
6	R^1 = 4-I-$C_6H_4CH_2$	$R^2 = H$	$R^3 = H$	$R^4 = H$
7	$R^1 = C_6H_5CH_2$	$R^2 = H$	$R^3 = H$	$R^4 = Bz$
8	R^1 = Pr	$R^2 = Bz$	$R^3 = Bz$	$R^4 = Bz$
9	R^1 = Pr	$R^2 = H$	$R^3 = H$	$R^4 = Bz$
10	$R^1 = H$	$R^2 = H$	$R^3 = Bz$	$R^4 = Bz$
11	R^1 = Pr	$R^2 = H$	$R^3 = H$	$R^4 = H$

component, could not be established. The ^{1}H NMR and NOESY spectra at 500 MHz indicated that the major component was the symmetric partial cone isomer **2** (Scheme 1), whereas the earlier reported partial cone isomer[11] showed much resemblance with the minor isolated component (Scheme 1, **3**). In contrast to the results obtained under Chawla's conditions,[11] no *cone* isomer could be detected.[12]

For compound **2**, medium to strong NOE contacts were observed between the *t*Bu^B group and benzoyl protons H_o', H_m', and H_p', whereas *t*Bu^A showed contacts only with H_m', suggesting that this benzoyl group is partially included into the cavity (Figure 1). On the other hand, strong NOEs were noted between benzoyl hydrogens H_o, H_m, and H_p and the *t*Bu^C group. Finally, the free phenol hydrogen showed a strong through-space contact with the benzoyl proton H_o, a fact that unambiguously confirms the structure of **2** as a symmetric partial cone conformation.

The minor component **3** was identified as an asymmetric species, since four distinct *tert*-butyl groups were observed in the ^{1}H and ^{13}C{^{1}H} NMR spectra. This latter observation suggested that the three benzoyl groups should occupy both rims of this calixarene in either a (u,u,d) or (d,d,u) fashion.[13] The NOESY spectrum showed clear NOE interactions with two H_o protons from distinct benzoyl groups as well with both H_{eq} and H_{ax} protons of one of the methylene AB systems. The observation of additional well-defined through-space contacts was complicated due to strong overlap of signals. Nevertheless, the simplicity of the *tert*-butyl region in the ^{1}H and ^{13}C{^{1}H} spectra of **3** suggested either the presence of a single asymmetric species or a fast equilibrium between a partial cone and a 1,2-alternate conformation. Likely, the equilibrium takes place by rotation of the free phenol ring through the annulus.

The inherent chirality of the two proposed conformers was established by ^{1}H NMR (**(**$CDCl_3$, 500 MHz) by addition of an excess of Pirkle's chiral shift reagent ((*R*)-(−)-2,2,2-trifluoro-1-(9-anthracyl)ethanol) to **3**, which caused splitting of the OH group, the benzoyl protons, and the AB patterns corresponding to the methylene fragments. One of the *tert*-butyl signals was also split.

Benzylation of **2** with 4-iodobenzyl bromide (NaH, DMF, rt) and subsequent workup under acidic conditions yielded a mixture of three components in a 78:15:7 ratio (**4**−**6**, Scheme 1). The major component **4** was isolated in a 30% yield as a pure, microcrystalline solid.

The ^{1}H NMR spectrum of **4** displayed a nonsymmetric structure (four distinct signals for the CH_2 and *tert*-butyl groups) and revealed the presence of a single benzoyl group and two free phenol rings (singlet resonances at δ = 8.91 and 7.89 ppm). Clearly, two benzoyl groups were hydrolyzed during the benzylation process. A NOESY experiment showed a strong contact between OH_B and OH_C protons, implying a syn orientation of both adjacent phenol rings. Furthermore, additional strong contacts were observed for OH_B and both benzylic CH_2 protons (H_3 and H_4) as well as with the aromatic H_5 proton, a fact that provided evidence that the benzyl substituent resides on the same face of the calixarene framework as the phenol hydrogens. As for **2**, the benzoyl protons H_o, H_m, and H_p displayed medium to weak NOE contacts with the *t*Bu^A, *t*Bu^B, and *t*Bu^C groups, which indicated again that the benzoyl moiety is pointing toward the (upper rim) cavity (Figure 2). The ^{13}C{^{1}H} NMR spectrum of **4** showed two methylene carbon resonances in the region around 39 ppm, indicating that the remaining aromatic ring of the calixarene system carrying the benzoyl group must be in an anti orientation[14] with respect to the benzyl and the hydroxyl groups. Thus, a partial cone assignment was fully supported by the NMR data.

A definite confirmation of the proposed structure for **4** was obtained by X-ray crystallography. The benzoyl group is pointing inside the upper rim cavity, in agreement with the high-field shifts found for the H_o and H_m

(12) In our hands, at 1 M calixarene concentration (Chawla's conditions), a mixture of the symmetrical partial cone isomer **2** (49%), the asymmetric partial cone isomer **3** (26%), and the cone isomer (25%) in an 83% isolated yield was obtained.

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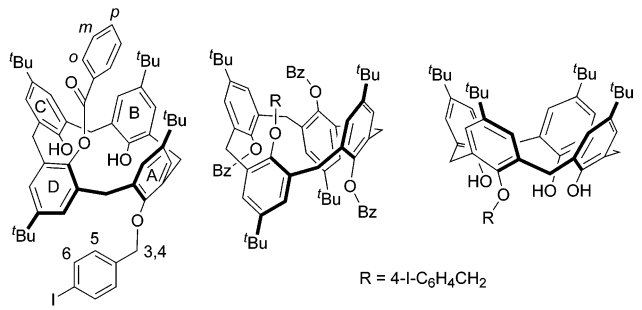

4 (paco) **5** (1,3-alt) **6** (cone)

FIGURE 2. Structures of the products **4**−**6** obtained after alkylation of **2**.

protons in NMR. Furthermore, as earlier suggested by the NMR study, the two phenol OHs are linked by a hydrogen bond (see Supporting Information).

The structures of isolated **5** and **6** (Figure 2) could be readily assigned by 1D and 2D NMR spectroscopy. Thus, data for **5** agreed with a 1,3-alternate conformation, as evidenced by the ^{13}C NMR spectrum, which showed two signals for the calixarene CH_2 groups at 38.9 and 38.4 ppm, respectively,[14] while the ^1H NMR spectrum displayed two different AB systems for these groups. Furthermore, MALDI-TOF mass spectrometric analysis confirmed the presence of three benzoyl groups in **5**. On the contrary, **6** was fully depleted of benzoyl groups and showed a cone conformation. Its structure was assigned by comparison with previously published data.[15]

Other alkylating agents produced a comparable set of derivatives from **2**, also yielding 1,2-*anti*-heterodisubstituted products as the major component. Thus, treatment of **2** with benzyl bromide yielded the desired monobenzyl−monobenzoyl product **7** in 47% after crystallization (Scheme 1). With propyl iodide, however, a mixture of components resulted. The identity of all components, isolated by column chromatography, was established by NMR and MALDI-TOF-MS to be compounds **8**−**11** (Scheme 1). Interestingly, the two main products in this propylation reaction were **8**[16] and the nonalkylated, fully deacylated starting material **1** (both isolated in 27% yield), whereas the other (minor) products **9**−**11**[17,18] were isolated in 13, 5, and 3% yield, respectively.

CPK model inspection suggests that the formation of species **4**, **7**, and **9** is related to the faster hydrolysis of the benzoyl moieties in their more crowded, tribenzoyl compounds. On the other hand, the less reactive halides (i.e., propyl iodide) give rise to more complex mixtures. Although the mechanism for the formation of **4**, **7**, and **9** remains unclear, there are some precedents of base-induced cleavage and/or rearrangement processes that involve aroyl substituents in calixarene compounds.[19] More details about the mechanistic aspects of the above transformations are currently under investigation.

In summary, we have described the selective formation of 1,2-*anti*-heterodisubstituted calix[4]arenes carrying both benzyl/alkyl and benzoyl groups. The difference in reactivity of the anchored groups may be used to furnish a number of predefined calixarene structures with conformational features potentially useful as building blocks in supramolecular chemistry.

Experimental Section

General Statements. The presence of solvent molecules in the analytical samples was supported by ^1H NMR spectroscopy. Melting points were measured in open capillaries and are uncorrected.

Synthesis of Tribenzoylated *p-tert*-Butylcalix[4]arene. To a solution of *p-tert*-butylcalix[4]arene **1** (10.53 g, 16.2 mmol) in pyridine (500 mL) was slowly added benzoyl chloride (28 mL, 33.9 g, 241 mmol) at ambient temperature. The homogeneous, salmon-colored reaction mixture was stirred for 72 h, after which the solvent was largely removed under reduced pressure. To the residue was added CH_2Cl_2 (200 mL) and H_2O (200 mL), and the layers were separated. The aqueous layer was once more extracted with CH_2Cl_2 (200 mL), and the combined organic layers were washed with three portions of H_2O (200 mL), dried on $MgSO_4$, filtered, and concentrated to leave a yellowish oil. Trituration at rt with MeOH yielded a first fraction of a white solid (10.05 g). Concentration and cooling (−30 °C) of the MeOH layer furnished a second fraction (3.44 g) of product. Total yield: 13.49 g (14.0 mmol, 84%). Recrystallization of both fractions yielded **2** and **3** as pure materials with spectroscopic and analytical data as given below.

Symmetrical Partial Cone 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,25,27-tris(benzoyloxy)-28-(hydroxy)calix[4]arene (2). Mp (crystals): 310−312 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.10 (d, ^3J = 8.3 Hz, ^4J = 1.2 Hz, 4H, benzoyl-H_o), 7.55 (t, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 2H, benzoyl-H_p), 7.29 (s, 2H, ArH), 7.21 (t, ^3J = 7.8 Hz, benzoyl-H_m), 7.16 (t, ^3J = 7.1 Hz, ^4J = 1.7 Hz, 1H, benzoyl-H_p), 6.99 (d, ^4J = 2.4 Hz, 1H, ArH), 6.95 (s, 1H, ArH), 6.65 (d, ^4J = 2.4 Hz, 1H, ArH), 6.64 (s, 1H, OH, D_2O exchangeable), 6.55−6.60 (dd+d, 4H, benzoyl-H_{o+m}), 4.21 (d, ^2J(A−B) = 13.5 Hz, 2H, CH_2), 4.06 (d, ^2J(A−B) = 16.6 Hz, 2H, CH_2), 3.86 (d, ^2J(A−B) = 16.7 Hz, 2H, CH_2), 3.50 (d, ^2J(A−B) = 13.6 Hz, 2H, CH_2), 1.45 (s, 9H, $C(CH_3)_3$), 0.86 (s, 9H, $C(CH_3)_3$), 0.73 (s, 18H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 164.9, 163.2 (2 × ArC(O)), 150.0, 148.5, 148.0, 145.9, 144.1, 142.9, 133.0, 132.5, 132.4, 132.0, 131.7, 130.3, 129.9, 129.4, 129.0, 128.3, 127.84, 127.80, 126.5, 126.0, 125.53, 125.47 (all ArC), 38.9 (CH_2), 34.1, 33.8, 33.7 (3 × $C(CH_3)_3$, ratio 1:1:2), 32.3 (CH_2), 31.8, 30.9, 30.6 (3 × $C(CH_3)_3$, ratio 1:1:2). MALDI-TOF-MS (ditranol + KI): m/z = 961.4 $(M + H)^+$ (calcd 961.5), 999.4 $(M + K)^+$ (calcd. 999.5). Anal. Calcd for $C_{65}H_{68}O_7 \cdot {}^1/_2H_2O$: C, 80.46; H, 7.17. Found: C, 80.70; H, 7.07.

Nonsymmetrical Partial Cone/1,2-Alternate *rac*-5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,25,27-tris(benzoyloxy)-28-(hydroxy)calix[4]arene (3). Mp (crystals): 286−288 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, ^4J = 2.1 Hz, 1H, ArH), 7.45 (t, ^3J = 7.5 Hz, 1H, benzoyl-H_p), 7.43 (d, ^4J = 2.7 Hz, 1H, ArH), 7.37 (t, ^3J = 7.3 Hz, 1H, benzoyl-H_p), 7.31 (d, ^4J = 2.1 Hz, 1H, ArH), 7.30 (d, ^4J = 2.0 Hz, 1H, ArH), 7.25 (d, ^3J = 7.5 Hz, 2H, benzoyl-H_o), 7.20 (d, ^3J = 7.7 Hz, 2H, benzoyl-H_o), 7.19−7.13 (m, 6H, one ArH + benzoyl-H), 7.04 (t, ^3J = 7.7 Hz, 2H, benzoyl-H_m), 6.84 (d, ^4J = 1.9 Hz, 1H, ArH), 6.82 (d, ^4J = 1.8 Hz, 1H, ArH), 6.80 (d, ^4J = 1.8 Hz, 1H, ArH), 6.64 (t, ^3J = 7.6 Hz, 2H, benzoyl-H_m), 5.16 (s, 1H, OH), 4.02 (d, ^2J(A−B) = 16.7 Hz, 1H, CH_2), 3.95 (d, ^2J(A−B) = 16.8 Hz, 1H, CH_2), 3.92 (d, ^2J not resolved due to strong overlap with other signals, 1H, CH_2), 3.91 (s, 2H, CH_2), 3.89 (d, ^2J(A−B) = 14.2 Hz, 1H, CH_2), 3.58 (d, ^2J(A−B) = 13.6 Hz, 1H, CH_2), 3.52 (d, ^2J(A−B) = 14.0 Hz, 1H, CH_2), 1.43 (s, 9H, $C(CH_3)_3$), 1.18 (s, 9H, $C(CH_3)_3$), 0.98 (s,

(15) Santoyo-González, F.; Torres-Pinedo, A.; Sánchez-Ortega. A. *J. Org. Chem*. **2000**, *65*, 4409−4414.

(16) Compound **8** was actually isolated as a mixture of a 1,3-alternate and a partial cone isomer, which could not be separated by crystallization or column chromatography.

(17) A 1,2-proximal dibenzoyl calix[4]arene has been reported: Dospil, G.; Schatz, J. *Tetrahedron Lett*. **2001**, *42*, 7837−7840. However, in these studies the syn conformer was employed.

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(19) See, K. A.; Fronczek, F. R.; Watson, W. A.; Kashyap, R. P.; Gutsche, C. D. *J. Org. Chem*. **1991**, *56*, 7256−7268.

9H, $C(CH_3)_3$), 0.94 (s, 9H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 165.4, 165.0, 164.2 (3 × ArC(O)), 150.4, 148.8, 148.3, 148.1, 144.9, 144.6, 144.5, 142.3, 134.4, 133.7, 132.9, 132.6, 132.4, 131.9, 131.5, 129.9, 129.6, 128.7, 128.5, 128.3, 128.2, 128.0, 127.8, 126.4, 126.3, 126.00, 125.95, 125.9, 125.8, 125.6, 125.3, 124.3 (all ArC), 38.8, 36.8 (2 × CH_2), 34.4, 34.0, 33.9, 33.7 (4 × $C(CH_3)_3$), 32.5 (CH_2), 31.5, 31.4, 31.0, 30.8 (4 × C(CH_3)$_3$), 30.5 (CH_2). MALDI-TOF-MS (ditranol + KI): m/z = 961.3 $(M + H)^+$ (calcd 961.5), 999.3 $(M + K)^+$ (calcd 999.5). Anal. Calcd for $C_{65}H_{68}O_7 \cdot H_2O$: C, 79.72; H, 7.21. Found: C, 79.58; H, 7.49.

Partial Cone 1,2-*anti*-Heterodisubstituted 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-(4-iodobenzyloxy)-26-(benzoyloxy)-27,28-bis(hydroxy)calix[4]arene (4). Yield (after crystallization of the crude product): 30%. Mp (crystals): 258−260 °C (turns brown). ^1H NMR (500 MHz, $CDCl_3$): δ = 8.91 (s, 1H, OH), 7.89 (s, 1H, OH), 7.70 (d, ^3J = 8.3 Hz, 2H, ArH iodoaryl group), 7.45 (d, ^4J = 1.7 Hz, 1H, ArH), 7.26 (d, ^4J = 2.3 Hz, 1H, ArH), 7.17 (d, ^4J = 2.3 Hz, 1H, ArH), 7.14 (d, ^4J = 1.6 Hz, 1H, ArH), 6.95 (t, ^3J = 7.4 Hz, 1H, benzoyl-H_p), 6.93 (d, ^4J = 2.2 Hz, 1H, ArH), 6.73 (d, ^4J = 2.3 Hz, 1H, ArH), 6.66 (d, ^3J = 8.3 Hz, 2H, ArH iodoaryl group), 6.61 (d, ^4J = 2.1 Hz, 1H, ArH), 6.58 (d, ^4J = 2.1 Hz, 1H, ArH), 6.30−6.50 (br, 4H, benzoyl-H_{o+m}), 5.20 (d, ^2J(A−B) = 11.1 Hz, 1H, OCH_2), 4.56 (d, ^2J(A−B) = 11.1 Hz, 1H, OCH_2), 4.28 (d, ^2J(A−B) = 16.6 Hz, 1H, CH_2), 4.17 (d, ^2J(A−B) = 13.4 Hz, 1H, CH_2), 4.08 (d, ^2J(A−B) = 17.6 Hz, 1H, CH_2), 4.01 (d, ^2J(A−B) = 17.6 Hz, 1H, CH_2), 3.89 (d, ^2J(A−B) = 16.6 Hz, 1H, CH_2), 3.87 (d, ^2J(A−B) = 13.6 Hz, 1H, CH_2), 3.50 (d, ^2J(A−B) = 13.7 Hz, 1H, CH_2), 3.38 (d, ^2J(A−B) = 13.5 Hz, 1H, CH_2), 1.43 (s, 9H, $C(CH_3)_3$), 1.30 (s, 9H, $C(CH_3)_3$), 0.75 (s, 9H, $C(CH_3)_3$), 0.67 (s, 9H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 163.3 (ArC(O)), 149.7, 149.2, 148.3, 148.0, 146.0, 143.5, 142.3, 137.8, 134.8, 134.0, 132.6, 131.6, 131.5, 130.7, 129.6, 129.2, 129.1, 128.1, 127.5, 127.3, 126.8, 126.4, 125.6, 125.1, 125.0, 124.7, 124.7 (all ArC), 94.2 (ArC−I), 74.4 (OCH_2), 39.2, 39.1 (2 × CH_2), 34.3, 34.1, 33.6, 33.2 (4 × $C(CH_3)_3$), 32.5, 32.4 (2 × CH_2), 31.7, 31.5, 30.8, 30.7 (4 × C(CH_3)$_3$). MALDI-TOF-MS (ditranol + KI): m/z = 969.3 $(M + H)^+$ (calcd 969.4), 1007.2 $(M + K)^+$ (calcd 1007.4). Anal. Calcd for $C_{58}H_{65}IO_5 \cdot {}^1/_2H_2O$: C, 71.23; H, 6.80. Found: C, 71.00; H, 6.67.

Partial Cone 1,2-*anti*-Heterodisubstituted 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-(benzyloxy)-26-(benzoyloxy)-27,28-bis(hydroxy)calix[4]arene (7). This compound was prepared under nearly identical conditions as reported for **4** using benzyl bromide as reagent. Yield (after crystallization of the crude product): 47%. Mp (crystals): 247−248 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 8.98 (s, 1H, OH), 7.88 (s, 1H, OH), 7.47 (s, 1H, ArH), 7.39−7.36 (m, 3H, ArH benzyl), 7.24 (s, 1H, ArH), 7.22 (s, 1H, ArH), 7.16 (s, 1H, ArH), 6.97−6.95 (m, 3H, ArH benzyl + benzoyl-H_p), 6.92 (s, 1H, ArH), 6.73 (s, 1H, ArH), 6.62 (s, 1H, ArH), 6.57 (s, 1H, ArH), 6.50−6.14 (br, 4H, benzoyl-H_{o+m}), 5.30 (d, ^2J(A−B) = 10.6 Hz, 1H, OCH_2), 4.58 (d, ^2J(A−B) = 10.6 Hz, 1H, OCH_2), 4.29 (d, ^2J(A−B) = 16.6 Hz, 1H, CH_2), 4.14 (d, ^2J(A−B) = 13.3 Hz, 1H, CH_2), 4.12 (d, ^2J(A−B) = 17.5 Hz, 1H, CH_2), 4.02 (d, ^2J(A−B) = 17.4 Hz, 1H, CH_2), 3.89 (d, apparent ^2J(A−B) = 14.6 Hz, 2H, 2 × CH_2), 3.48 (d, ^2J(A−B) = 13.5 Hz, 1H, CH_2), 3.35 (d, ^2J(A−B) = 13.3 Hz, 1H, CH_2), 1.42 (s, 9H, $C(CH_3)_3$), 1.34 (s, 9H, $C(CH_3)_3$), 0.75 (s, 9H, $C(CH_3)_3$), 0.66 (s, 9H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 163.3 (ArC(O)), 149.7, 149.6, 148.2, 148.11, 148.09, 146.0, 143.3, 142.3, 135.1, 133.9, 132.6, 131.64, 131.55, 130.7, 129.6, 129.3, 128.7, 128.5, 128.1, 127.7, 127.6, 127.3, 126.9, 126.4, 126.3, 125.6, 125.03, 124.96, 124.8, 124.6 (all ArC), 75.5 (OCH_2), 39.2, 39.1 (2 × CH_2), 34.3, 34.1, 33.6, 33.1 (4 × $C(CH_3)_3$), 32.7, 32.4 (2 × CH_2), 31.7, 31.5, 30.8, 30.7 (4 × C(CH_3)$_3$). MALDI-TOF-MS (ditranol + KI): m/z = 881.6 $(M + K)^+$ (calcd 881.5). Anal. Calcd for $C_{58}H_{66}O_5$: C, 82.62; H, 7.89. Found: C, 82.67: H, 8.27.

Partial Cone 1,2-*anti*-Heterodisubstituted 5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-(propyloxy)-26-(benzoyloxy)-27,28-bis(hydroxy)calix[4]arene (9). Yield (R_f = 0.74): 45.5 mg (13%). ^1H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1H, OH), 8.00 (s, 1H, OH), 7.32 (s, 1H, ArH), 7.27 (s, 1H, ArH), 7.18 (s, ^4J = 2.1 Hz, 1H, ArH), 7.16 (s, 1H, ArH), 6.92 (t, ^3J = 7.2 Hz, 1H, benzoyl-H_p), 6.86 (s, 1H, ArH), 6.73 (s, 1H, ArH), 6.53 (s, 1H, ArH), 6.52 (s, 1H, ArH), 6.45−6.10 (br, 4H, benzoyl-H_{o+m}), 4.25 (d, ^2J(A−B) = 13.4 Hz, 1H, CH_2), 4.16 (d, ^2J(A−B) = 16.6 Hz, 1H, CH_2), 4.01−3.78 (m, 5H, CH_2 + OCH_2), 3.66 (dd, apparent ^3J(A−B) = 8.3 Hz, 1H, OCH_2), 3.51 (d, ^2J(A−B) = 13.7 Hz, 1H, CH_2), 3.39 (d, ^2J(A−B) = 13.5 Hz, 1H, CH_2), 1.42 (s, 9H, $C(CH_3)_3$), 1.41 (s, 9H, $C(CH_3)_3$), 0.68 (s, 9H, $C(CH_3)_3$), 0.63 (s, 9H, $C(CH_3)_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 163.2 (ArC(O)), 149.7, 149.4, 148.2, 147.9, 147.7, 145.9, 143.6, 142.5, 133.5, 132.4, 131.7, 131.6, 130.4, 129.8, 129.3, 128.2, 127.8, 127.3, 126.8, 126.4, 125.7, 125.4, 125.0, 124.8, 124.7 (all ArC), 75.6 (OCH_2), 39.2, 39.0 (2 × CH_2), 34.4, 34.2, 33.6, 33.2 (4 × $C(CH_3)_3$), 32.7, 32.5 (2 × CH_2), 31.8, 31.7, 30.9, 30.7 (4 × C(CH_3)$_3$). MALDI-TOF-MS (ditranol + KI): m/z = 833.7 $(M + K)^+$ (calcd 833.5). Anal. Calcd for $C_{54}H_{66}O_5 \cdot {}^1/_2H_2O$: C, 80.66; H, 8.40. Found: C, 81.21; H, 9.00.

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Supporting Information Available: The ORTEP diagram for the X-ray molecular structure of **4**, copies of ^1H and NOESY (500 MHz) spectra for **2**−**4**, experimental/analytical details and/or workup procedures for **4**, **5**, and **7**−**10**, and CIF file for the X-ray structural data of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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