DOI: 10.1002/ejoc.200901281

C_{3v} (Trimethyl) *p*-(Benzyloxy)calix[6]arene: A Versatile Platform for the Synthesis of Functionalized C_{3v} Calix[6]arenes

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Keywords: Calixarenes / Alkylation / Quinones / Macrocycles

Partial methylation of *p*-(benzyloxy)calix[6]arene leads to the corresponding trimethylated C_{3v} derivative. This compound was used for the synthesis of new functional calixarenes. The presence of the *p*-(benzyloxy) substituent allows this new C_{3v} derivative to be directly oxidized to the tris(quinone). These new C_{3v} derivatives open the way to new supramolecular receptors, bearing easily derivatized hydroxy groups at the upper rim position.

Introduction

Calixarenes have received much attention during the last decades due to the tremendous possibilities offered by these easily accessible macrocycles.[1–4] (Let us consider, for example, ions and/or molecule recognition phenomena,[5–13] supramolecular assemblies,[14,15] nanoparticles synthesis,[16–20] etc.) Trimethylated C_{3v} *p*-(*t*Bu)calix[6]arene derivatives (Figure 1) were shown to be especially interesting, as they are easily converted into conformationally rigid cone derivatives, showing exceptional characteristics for the selective formation of inclusion complexes.[21–27] In most cases, the suitable recognition groups are introduced at the so-called "small rim" position. "Large-rim"-functionalized C_{3v} derivatives were also described.[28–34] These new calixarene receptors, functionalized at both rim positions, hold great promise for the synthesis of new supramolecular hosts (Figure 2).[27,29,30,34–37]

Up to now, these useful C_{3v} platforms are only described starting from the parent (*p*-*t*Bu)calix[6]arene (Figure 1).[28–34] In this case, the substitution of the *p*-(*t*Bu) group is usually obtained by electrophilic cleavage. Although useful, this approach often requires harsh conditions and/or the use of aggressive reagents. Moreover, the limited number of electrophilic agents able to cleave the *p*-(*t*Bu) group without altering the otherwise sensitive phenolic units makes this approach difficult to generalize. The possibility to use others starting calixarene platforms should thus be of great value for the community.

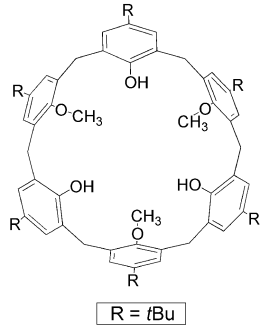

Figure 1. C_{3v}-Symmetric calix[6]arene.

Within this frame, we wish to report here on the synthesis and characterization of such a new calixarene family, starting from *p*-(benzyloxy)calix[6]arene (Scheme 1).[7] We show here that *p*-(benzyloxy)calix[6]arene may be converted into the corresponding trimethylated C_{3v} derivative on a preparative scale. We also describe the simple and high-yield synthesis of useful derivatives from this new C_{3v} *p*-(benzyloxy)calix[6]arene (Schemes 2–4). The presence of the large benzyloxy groups at the *para* positions first allows the simple synthesis of new receptors with a deeper hydrophobic cavity. Second, new possibilities are opened for easy derivatization of these positions after Pd-catalyzed hydrogenolysis, as already demonstrated for other *p*-(benzyloxy)-functionalized calixarenes.[7,15,20,38]

Results and Discussion

The starting *p*-(benzyloxy)calix[6]arene (**2**) was first obtained in very low yields during the base-catalyzed condensation of *p*-(benzyloxy)phenol (**1**) as a byproduct of the *p*-(benzyloxy)calix[8]arene synthesis.[7] An optimized synthetic procedure is provided (see the Experimental Section) and will be detailed in a forthcoming paper.[39]

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200901281.

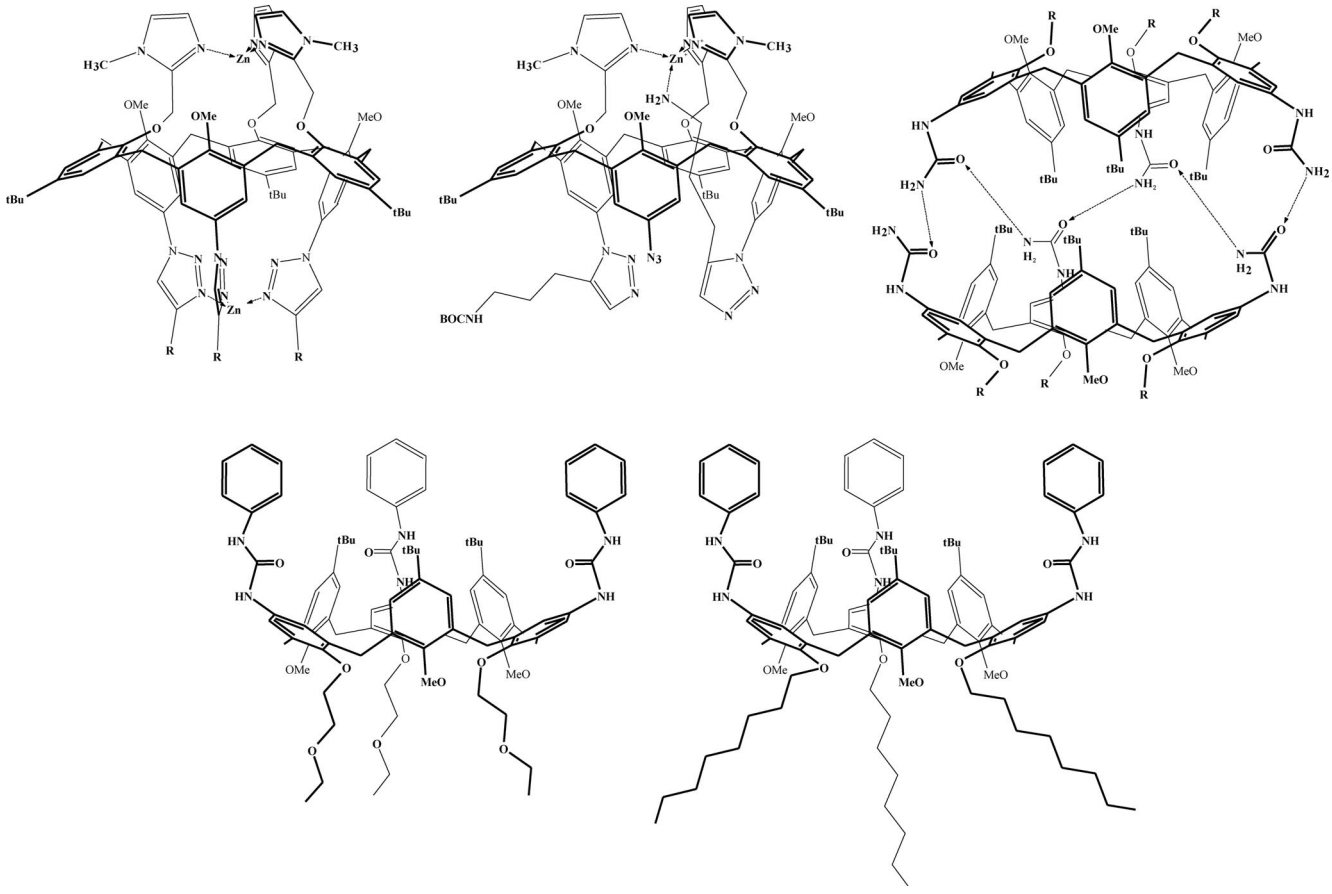
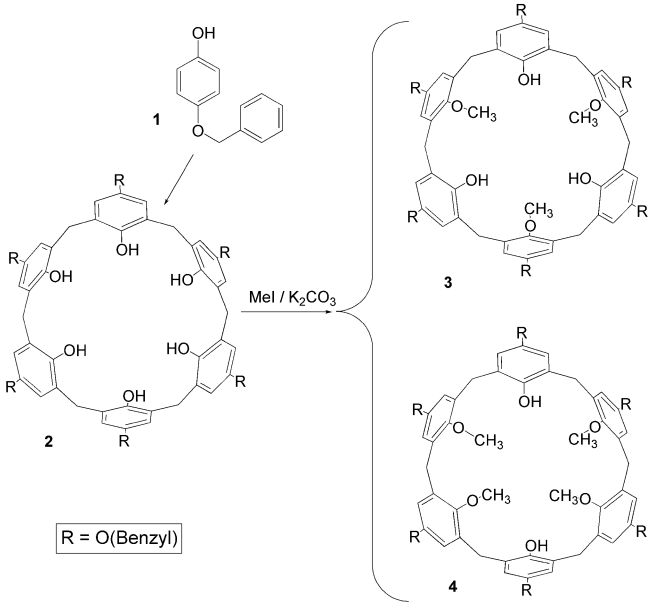


Figure 2. Some already described examples of "large-rim"-functionalized calix[6]arenes.[27,29,30,34–36]



Scheme 1. Synthesis of C_{2v}-tetramethylated **3** and C_{3v}-trimethylated **4** *p*-(benzyloxy)calix[6]arenes.

Alkylation of **2** with methyl iodide {according to the procedure already described for *p*-(*t*Bu)calix[6]arene[40]} results in a very complex mixture of partly alkylated products. Fortunately, the expected trimethoxy C_{3v} derivative is observed as one of the main components.

The crude reaction media shows two phases (white precipitate along with a limpid supernatant). Both phases were analyzed separately. The precipitate appears to comprise the (1,2,4,5)-tetramethyl *p*-(benzyloxy)calix[6]arene derivative (**4**; Scheme 1, final yield 25%). This assignment is based on mass spectrometry (MALDI) analysis, along with the observed symmetry of the NMR spectra (Supporting Information, Figure S1c). The high-field region shows one singlet along with a pair of doublets, with a characteristic ^4J coupling constant of 4 Hz. The region around 5 ppm shows the presence of two singlets with the expected 2:1 ratio, corresponding to the two benzyloxy-type methylenes. The very low solubility of this tetraalkylated C_{2v}-symmetric compound makes this product easy to purify and readily available.

C_{3v}-Trimethylated *p*-(benzyloxy)calix[6]arene (**3**; Scheme 1) is recovered from the corresponding filtrate as a white solid in 20% yield, by combining selective precipitation from acetone and chromatography over deactivated alumina (see the Experimental Section). The remaining chromatographic fractions (probably a mixture of more highly methylated calix[6]arene derivatives) were not further analyzed. This product was fully characterized by NMR spectroscopy and mass spectrometry (Supporting Information). The ^{1}H

NMR spectrum clearly shows the expected C_{3v} symmetry, as observed for the analogous *p*-(*t*Bu) trimethylated C_{3v} derivative (Supporting Information, Figure S1a).

To the best of our knowledge, this is the first time that a partial methylation procedure is successfully applied to a calix[6]arene not functionalized at the upper rim by *t*Bu groups. This shows that the general behavior of the *p*-(*t*Bu)-functionalized calixarenes is similar to that of the *p*-(benzyloxy)-functionalized derivative.

In order to explore the potential of compound **3**, the synthesis of a representative panel of derivatives was undertaken (Schemes 2–4, compounds **5**–**10**). All these new compounds were fully characterized by ^{1}H and ^{13}C NMR spectroscopy, IR spectroscopy, and mass spectrometry.

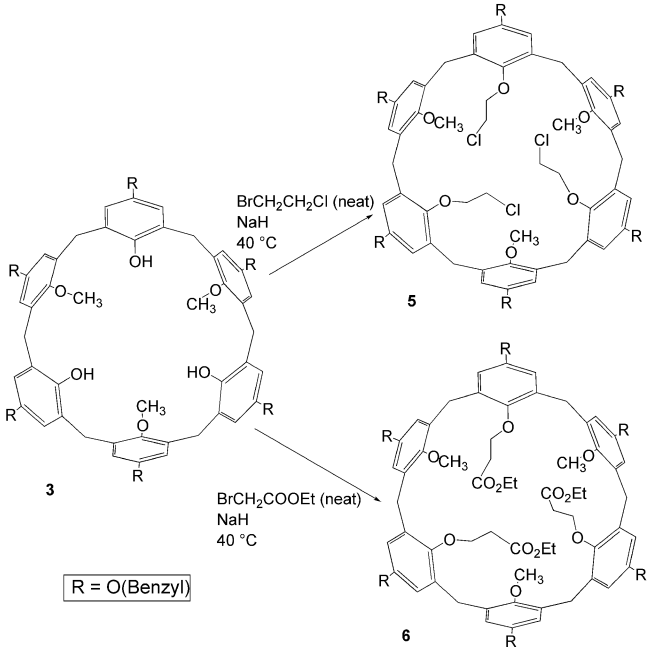
It is noteworthy to mention that some of these new *p*-(benzyloxy)calixarenes (although exhibiting the expected C_{2v} or C_{3v} symmetry) are showing broadened NMR signals relative to those of the analogously functionalized *p*-(*t*Bu)calixarenes. This provides evidence that the bulkier *p*-(benzyloxy)-functionalized phenolic subunits rotate more slowly. In the extreme cases of thioester **8** and ester **6** derivatives, the conformational flexibility is reduced to such an extent that very broad signals are observed, probably the result of the existence (on the NMR timescale) of several, slowly interconverting conformations. If necessary, variable-temperature NMR experiments were used to overcome these problems.

Alkylation of compound **3** by 1-bromo-2-chloroethane and ethyl bromoacetate (used as both solvents and reagents, see Experimental Section) lead to compounds **5** and **6**, respectively (Scheme 2). These alkylation reactions proceed smoothly in quantitative yields with NaH as a base. However, the addition of a small amount of DMF was found to be crucial, otherwise these alkylation reactions do not proceed at all, and unreacted starting products are recovered.

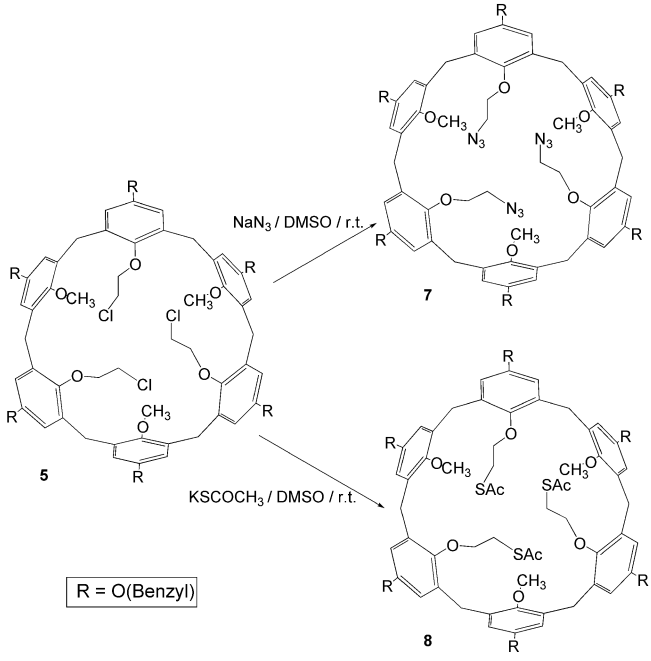
Interestingly, the NMR spectra of compound **6** are completely different from those of the corresponding *p*-(*t*Bu)-functionalized analog.[41,42] The expected C_{3v} symmetry is not observed. The reason for such a difference is not clear. Maybe the increased bulkiness of the *p*-(benzyloxy) substituents allows some others conformations to be "frozen" during the course of the alkylation reaction. This may be reinforced by the fact that compound **6** is obtained at a temperature close to the ambient one (whereas the corresponding compound in the *p*-(*t*Bu) series is obtained in refluxing THF[41,42]). This may allow different conformations to be observed, as the conformational equilibriums are strongly influenced by temperature. Moreover, the solvents used in these two cases are different [pure ethylbromoacetate (this work) or THF]. This may also influence the conformational equilibria.

The temperature needed to restore the C_{3v} symmetry is so high that the product rapidly decomposes, resulting in the appearance of secondary peaks, and their intensity rapidly increases within minutes (Supporting Information, Figure S5b).

The tris(chloroethyl) derivative **5** proved to be a versatile platform for the synthesis of functionalized calixarenes. As an example, the reaction with sodium thioacetate and sodium azide in DMSO at ambient temperature leads to the corresponding azido and thioester derivatives in quantitative yields (compounds **7** and **8**, Scheme 3).



Scheme 2. Synthesis of compounds **5** and **6**.



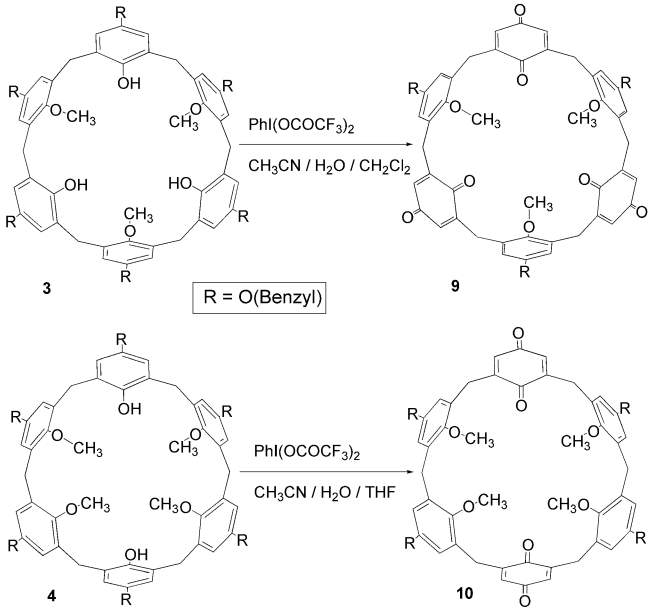
Scheme 3. Synthesis of the azide and thioacetyl derivatives of compound **5** (compounds **7** and **8**).

The MALDI mass spectrum of the tris(azide) is especially interesting. Along with the expected molecular ion, three successive azide-to-amine reduction processes are also

observed (R-N_3 → R-NH_2). These reduction processes are made possible by the strongly reducing conditions associated with MALDI-type mass spectrometry analyses.[43]

An analogous tris(azido) derivative has very recently been described starting from the corresponding C_{3v}-symmetrical trimethylated *p*-(*t*Bu)calix[6]arene.[44] It was shown that this new compound is a very useful platform for the synthesis of new supramolecular receptors. Within this frame, the successful synthesis of the corresponding *p*-(benzyloxy) derivative significantly reinforces the synthetic potential of this new family of azido-functionalized calixarenes.

Along with these "classical" alkylation-based functionalization strategies, the presence of the benzyloxy groups opens the possibility to explore more specific chemistry. Oxidation of compounds **3** and **4** with bis(trifluoroacetoxy)iodosobenzene results in the one-step formation of the expected quinone derivatives in quantitative yields at ambient temperature (compounds **9** and **10**, Scheme 4).



Scheme 4. Synthesis of the oxidized C_{2v}-tetramethylated and C_{3v}-trimethylated *p*-(benzyloxy)calix[6]arene derivatives (compounds **9** and **10**).

The simplicity and efficiency of this protocol is in contrast to that previously described for calixquinone synthesis {using either multistep de-*tert*-butylation-based processes or direct oxidation with toxic/unstable reagents [such as thallium(III) salts or chlorine dioxide[45]]}. Moreover, the yields of the calixquinones are not always satisfactory.

The NMR spectra confirm the disappearance of one type of benzyloxy signal in both cases, while preserving the overall symmetry of the compounds (Supporting Information, Figures S6a and S7).

As calixquinones are prone to undergo well-defined redox processes in solution,[46–48] a rich redox behavior may be anticipated for these new quinone derivatives. As an example, the MALDI mass spectra of **9** and **10** show that these two polyquinones undergo a full reduction process during the analysis. Two successive two-electron/two-proton reductions in the case of compound **10** and three two-electron/two-proton reductions for compound **9** are observed. These reduction processes are probably the result of complex electron-transfer phenomena from the matrix during its initial laser-induced electronic excitation. These new calixquinones also open interesting possibilities for the synthesis of new supramolecular receptors, as calixquinones-type macrocycles were shown to exhibit rich chemistry.[49]

Conclusions

In conclusion, alkylation of *p*-(benzyloxy)calix[6]arene with methyl iodide results in a complex mixture of partly alkylated products, from which trimethylated C_{3v}-derivative **3** and tetramethylated derivative **4** are recovered on a preparative scale. These new calixarenes were used for the synthesis of new functional derivatives. Compound **3** was used for the synthesis of a first set of derivatives by "conventional" alkylation reactions of the phenolic groups. By using the alkylating agent as a reagent and as a solvent, these reaction proceeds in quantitative yield in the presence of "off-the-shelf" DMF. Moreover, the presence of the *p*-(benzyloxy) substituents opens the possibility to directly convert these new C_{3v} and C_{2v} derivatives into tris(quinone) **9** and bis(quinone) **10**, respectively.

Hydrogenolysis of the *p*-(benzyloxy) substituents will open the way to new calixarenes bearing easily derivatized hydroxy groups at the upper-rim position. These new calixarene platforms are promising for the synthesis of new supramolecular hosts. These studies are currently underway within our group.

Experimental Section

General: All reagents were purchased from Aldrich and used as received. All solvents were purchased from Aldrich and used as received, without any supplementary drying or purification procedures. All the NMR spectra were collected with Bruker AMX 250, 300, and 360 MHz spectrometers. IR spectra were collected with a Perkin–Elmer Spectrum 1000 spectrometer. HQ = hydroquinone.

***p*-(Benzyloxy)calix[6]arene (2):** A solution of *p*-(benzyloxy)phenol (20.93 g, 0.104 mol), aqueous RbOH (50 wt-%, 3.8 mL, 0.0323 mol), paraformaldehyde (8 g, 0.267 mol) was heated at reflux in of xylene (mixture of isomers, 300 mL) for 6 h. The resulting suspension was neutralized with HCl (3 M, 100 mL). The organic phase was recovered, and the aqueous phase was washed with chloroform. The combined organic phase was neutralized with $NaHCO_3$, and the solvents were evaporated to dryness. The resulting solid was suspended in CH_2Cl_2 (300 mL) and filtered. The filtrate was evaporated and suspended in ethyl acetate (200 mL). The precipitate was filtered and suspended in acetone to yield **2** in an almost-pure form. A second crop of **2** was recovered by column chromatography of the evaporated acetone filtrate (SiO_2, $CHCl_3$, R_f = 0,5). Overall yield: 40%. Spectroscopic characteristics were in accordance with previously published ones.[7]

***C_{3v}* (Trimethyl) *p*-(Benzyloxy)calix[6]arene (3) and *C_{2v}* (Tetramethyl) *p*-(Benzyloxy)calix[6]arene (4):** A suspension of *p*-(benzyl-

oxy)calix[6]arene (3 g, 2.356 mmol), K_2CO_3 (0.52 g, 3.77 mmol), and methyl iodide (2.57 mL, 41.23 mmol) in acetone (120 mL) was heated at reflux under an atmosphere of argon for 8 h. The resulting suspension was filtered and washed with acetone. The precipitate was suspended in chloroform (30 mL) and filtered. This suspension/filtration procedure was repeated one more time with dichloromethane (30 mL). Compound **4** (0.78 g, 25%) was recovered as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$, 293 K): δ = 3.25 (s, 12 H, OCH_3), 3.78 (br. s, 8 H, $ArCH_2Ar$), 3.88 (br. s, 4 H, $ArCH_2Ar$), 4.74 (s, 4 H, $ArCH_2O$), 4.83 (s, 8 H, $ArCH_2O$) 6.41 (s, 4 H, $Ar_{HQ}H$), 6.60 (d, ^4J = 4 Hz, 4 H $Ar_{HQ}H$), 6.62 (d, ^4J = 4 Hz, 4 H, $Ar_{HQ}H$), 7.2–7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 30.6 ($ArCH_2Ar$), 31.5 ($ArCH_2Ar$), 60.7 (OCH_3), 70.2 ($ArCH_2O$), 70.5 ($ArCH_2O$) 114.2 (Ar_{HQ}-H), 115.1 (Ar_{HQ}-H), 115.6 (Ar_{HQ}-H), 126–130 (ArC-H), 133.7 ($Ar_{HQ}C_{ipso}$-CH_2), 135.5 ($Ar_{HQ}C_{ipso}$-CH_2), 137 (ArC_{ipso}-CH_2), 137.3 (ArC_{ipso}-CH_2), 146.2 ($Ar_{HQ}C_{ipso}$-O), 149.3 ($Ar_{HQ}C_{ipso}$-O), 151.7 ($Ar_{HQ}C_{ipso}$-OBz), 154.9 ($Ar_{HQ}C_{ipso}$-OBz). HRMS (MALDI): calcd. for $C_{88}H_{80}O_{12}K$ [M + K]$^+$ 1367.52814; found 1367.53014.

The different filtrates obtained after the recovery of **4** were then combined, evaporated to dryness, and dissolved in a minimum amount of acetone (about 20 mL). This solution was kept at 2 °C for two weeks. During this time, a precipitate appeared, which was collected by filtration. C_{3v} trimethylated *p*-(benzyloxy)calix[6]arene (**3**; 0.62 g, 20%) was recovered by column chromatography of this precipitate (deactivated Al_2O_3, $CHCl_3$/EtOAc, 3 → 20%) as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$, 293 K): δ = 3.59 (s, 9 H, OCH_3), 3.86 (s, 12 H, $ArCH_2Ar$), 4.69 (s, 6 H, $PhCH_2O$), 4.94 (s, 6 H, $PhCH_2O$), 6.52 (s, 6 H), 6.68 (s, 6 H, $Ar_{HQ}H$), 7.2–<7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 31.4 ($ArCH_2Ar$), 61.5 (OCH_3), 70.1, 70.6 ($ArCH_2$-Obz), 114, 5 (Ar_{HQ}-H), 115.6 (Ar_{HQ}-H), 127.6–128.5 (ArC-H), 128.4 ($Ar_{HQ}C_{ipso}$-CH_2), 134.3 ($Ar_{HQ}C_{ipso}$-CH_2), 136.9 (ArC-CH_2),137.4 (ArC-CH_2), 146.4 ($Ar_{HQ}C_{ipso}$-OH), 148.52 ($Ar_{HQ}C_{ipso}$-OCH_3), 152.2 ($Ar_{HQ}C_{ipso}$-OCH_2), 155.3 ($Ar_{HQ}C_{ipso}$-OCH_2) ppm. HRMS (MALDI): calcd. for $C_{87}H_{78}O_{12}Na$ [M + Na]$^+$ 1337.53855; found 1337.54378.

Calix[6]arene Tris(chloroethyl) (5): A 100-mL Schlenk tube was loaded with **3** (0.1 g, 0.076 mmol), bromochloroethane (6 mL), and off-the-shelf DMF (0.3 mL) at 50 °C under an atmosphere of argon. NaH (60%, 43 mg) was added. A transient green color developed and rapidly faded. The system was left at 50 °C for 1 h. A second portion of NaH (60%, 26 mg) was then added, and the resulting white suspension was left overnight at 50 °C under an atmosphere of argon. A third portion of NaH (60%, 26 mg) was added at 50 °C. After 3 h, the system was quenched with distilled water (50 mL) and washed with dichloromethane (3 × 20 mL). The organic phase was recovered, dried with $MgSO_4$, and concentrated. The resulting light-yellow oil on the walls of the balloon was then washed with pentane (100 mL) under vigorous stirring (removal of paraffin and residual bromochloroethane). The colorless pentane supernatant was then discarded, and the light-yellow oil remaining on the walls of the glassware was dried in vacuo to a constant weight. Compound **5** (0.114 g, quant.) was recovered as a pale-yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$, 293 K): δ = 3.1 (s, 9 H, OCH_3), 3.5 (br. t, CH_2Cl), 3.7 (br. t, 6 H, CH_2O), 3.9, (s, 12 H, $ArCH_2Ar$), 4.82/4.83 (12 H, $ArCH_2O$), 6.6 (6 H, $Ar_{HQ}H$), 6.65 (6 H, $Ar_{HQ}H$), 7.2–7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 30.9 ($ArCH_2Ar$), 53.4 (CH_2Cl), 60.3 (OCH_3), 70 ($ArCH_2O$), 72.8 ($ArOCH_2$), 114.8 (Ar_{HQ}-H), 115.1 (Ar_{HQ}-H), 127–128.5 (ArC-H), 134.8 ($Ar_{HQ}C_{ipso}$-CH_2), 135.0, ($Ar_{HQ}C_{ipso}$-CH_2), 137 (ArC-CH_2), 137.2 (ArC-CH_2), 148.2 ($Ar_{HQ}C_{ipso}$-O), 150.2, ($Ar_{HQ}C_{ipso}$-O), 154.4 ($Ar_{HQ}C_{ipso}$-OBz), 154.8, ($Ar_{HQ}C_{ipso}$-OBz) ppm. HRMS: calcd. for $[C_{93}H_{87}Cl_3O_{12}Na]^+$ 1523.5160; found 1523.5210.

Calix[6]arene Tris(ethylester) (6): A solution of **3** (490 mg, 0.33 mmol) in ethylbromoacetate (6 mL) and off-the-shelf DMF (0.5 mL) was prepared under an atmosphere of argon in a 100-mL Schlenk tube. NaH (60%, 150 mg) was then added under strong argon flushing and stirring. The resulting white suspension was left overnight at 50 °C. A second portion of 60% NaH was added at 50 °C under an atmosphere of argon. After 3 h, the product was precipitated with EtOH/CH_3COOH (90:10, 100 mL) and washed with ethanol. The precipitate was recovered by washing with CH_2Cl_2, and the solvents were evaporated to dryness. The resulting oil deposited onto the walls of the glassware was washed with pentane (100 mL) and ethanol (100 mL). Compound **6** (0.51 g, quant.) was recovered as a pale-yellow oil. ^{1}H NMR (400 MHz, DMSO, 360 K): δ = 1.16 (t, 9 H, CH_2CH_3), 3.06 (9 H, OCH_3), 3.89 (br., 12 H, $ArCH_2Ar$), 4.12 (q, 6 H) 4.4 [s, 6 H, $CH_2C(O)$], 4.57 (s, 6H $ArCH_2O$), 5.0 (s, 6H $ArCH_2O$) 6.31 (s, 6H $Ar_{HQ}H$), 6.88 (s, 6H $Ar_{HQ}H$), 7–7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 14.2 (CH_3-C), 31 (br., $ArCH_2Ar$), 60.4 (OCH_3), 60.8 [C(O)O-CH_2] 70.1, ($ArCH_2O$), 70.5, ($ArCH_2O$) 70.4 [OCH_2C(O)-O], 114.8 (Ar_{HQ}-H), 117.1 (Ar_{HQ}-H), 126–130 (ArC-H), 134.8 ($Ar_{HQ}C_{ipso}$-CH_2), 135.4, ($Ar_{HQ}C_{ipso}$-CH_2), 137.6 (Ar*C*-CH_2), 138 (Ar*C*-CH_2), 148.5 ($Ar_{HQ}C_{ipso}$-O), 151.2 ($Ar_{HQ}C_{ipso}$-O), 154.5 ($Ar_{HQ}C_{ipso}$-OBz), 155 ($Ar_{HQ}C_{ipso}$-OBz), 169.1 (C=O) ppm. HRMS: calcd. for $[C_{99}H_{96}O_{18}Na]^+$ 1595.64889; found 1595.65239. IR (KBr): $\tilde{\nu}$ = 1755 (C=O) cm^{-1}.

Calix[6]arene Tris(azido) (7): To a solution of **5** (0.114 g, 0.076 mmol) in off-the-shelf DMSO (3 mL) in a 50-mL Schlenk tube was added a large excess of sodium azide (30×). The resulting light-orange solution was stirred overnight at ambient temperature (25 °C) under an argon atmosphere. The product was precipitated with water (30 mL), filtered, and washed with water. Compound **7** was recovered in quantitative yield as a light-brown oil. ^{1}H NMR (250 MHz, $CDCl_3$, 293 K): δ = 3.1 (9 H, OCH_3), 3.26, (br. t, 6 H, CH_2N_3), 3.57 (br. t, 6 H, OCH_2), 3.92 (s, 12 H, $ArCH_2Ar$), 4.79 (s, 6 H, OCH_2Ar), 4.84 (s, 6 H, OCH_2Ar), 6.57 (s, 6 H, $Ar_{HQ}H$), 6.66 (s, 6 H, $Ar_{HQ}H$), 7.2–7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 30.9 ($ArCH_2Ar$), 51.0 (CH_2N_3), 60.3 (OCH_3), 70.1 ($ArCH_2O$), 71.3 ($ArCH_2O$), 114.8 (Ar_{HQ}-H), 115.4 (Ar_{HQ}-H), 127–128.5 (ArC-H), 134.8 ($Ar_{HQ}C_{ipso}$-CH_2), 135.0, ($Ar_{HQ}C_{ipso}$-CH_2), 137.2 (ArC-CH_2), 137.3 (ArC-CH_2), 148.3 ($Ar_{HQ}C_{ipso}$-O), 150.4 ($Ar_{HQ}C_{ipso}$-O), 154.5 ($Ar_{HQ}C_{ipso}$-OBz), 154.8, ($Ar_{HQ}C_{ipso}$-OBz) ppm. MS: *m*/*z* = 1522.55 [M + H]$^+$, 1494.55 [M + H$^+$ – N_2]$^+$. Reduction process: *m*/*z* = 1496.55 [M + H]$^+$ – N_2 + 2H, 1468.52 {[M + H]$^+$ – N_2 + 2H} – N_2. Reduction process: *m*/*z* = 1470.51 {[M + H]$^+$ – N_2 + 2H} – N_2 + 2H. HRMS (MALDI): calcd. for [M + Na]$^+$ 1544.63664; found 1544.63173. IR (KBr): $\tilde{\nu}$ = 2103.8 (R–N_3) cm^{-1}.

Calix[6]arene Tris(thioacetyl) (8): To a solution of **5** (0.114 g, 0.076 mmol) in off-the-shelf DMSO (3 mL) in a 50-mL Schlenk tube was added a large excess (30×) of potassium thioacetate. The resulting light-orange solution was stirred overnight at ambient temperature (25 °C) under an argon atmosphere. The product was precipitated with water (30 mL), filtered, and washed with water and methanol. Compound **8** was recovered in quantitative yield as a light-purple oil. ^{1}H NMR (250 MHz, DMSO, 360 K): δ = 2.74 [s, 9 H, $C(O)CH_3$]; 3.01 (9 H, OCH_3), 3.17 (br. t, 6 H, CH_2S), 3.8 (br. t, 6 H, OCH_2), 3.8 (br., 12 H, $ArCH_2Ar$), 4.57 (br. s, 6 H), 4.98 (s, 6H $ArCH_2O$), 6, 32 (s, 6H $Ar_{HQ}H$), 6.78 (s, 6H $Ar_{HQ}H$), 7.2–7.5 (m, 30 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 29.2 [CH_3-C(O)], 30.5 ($ArCH_2Ar$), 53.5 (CH_2S), 60.5 (OCH_3),

70.0, 70.3, 71.6 ($ArCH_2O$), 114.1 (br., Ar_{HQ}-H), 116 (Ar_{HQ}-H), 126–128.5 (ArC-H), 135 (br., $Ar_{HQ}C_{ipso}$-CH_2), 135.3, (br., $Ar_{HQ}C_{ipso}$-CH_2), 137.1 (Ar*C*-CH_2), 137.4 (Ar*C*-CH_2), 147.9 ($Ar_{HQ}C_{ipso}$-O), 150.8 ($Ar_{HQ}C_{ipso}$-O), 154.3 (br., $Ar_{HQ}C_{ipso}$-OBz), 154.8, (br., $Ar_{HQ}C_{ipso}$-OBz), 195.3 (C=O) ppm. HRMS (MALDI): calcd. for $[C_{99}H_{32}S_3O_{15}Na]^+$ 1643,58036; found 1643,58823. IR (KBr): $\tilde{\nu}$ = 1690 (C=O) cm^{-1}.

(Trimethyl) Calix[6]arene Tris(quinone) (9): To solution of **3** (14 mg, 0.0106 mmol) dissolved in a mixture of CH_3CN (0.4 mL), H_2O (0.2 mL), and CH_2Cl_2 (0.1 mL) was added a solution of bis(trifluoroacetoxy)iodosobenzene (0.15 g, 0.035 mmol) in CH_3CN (2 mL) at ambient temperature. The color instantly changed from colorless to deep yellow. The solution was left for 10 min, and then quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL). The organic phase was then recovered, filtered, and concentrated. The product was dissolved in a mixture of CH_3CN (5 mL) and water (1 mL), and the solvents were evaporated to dryness again (removal of benzylic alcohol). The resulting yellow oil was washed overnight with pentane (15 mL). The pentane supernatant was then discarded. After vacuuming, compound **9** (11 mg, quant.) was recovered as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$, 293 K): δ = 3.4 (9 H, OCH_3), 3.66 (s, 12 H, $ArCH_2Ar$), 4.93 (s, 6 H $ArCH_2O$), 6.09 (s, 6 H $Ar_{quinone}H$), 6.63 (s, 6 H $Ar_{HQ}H$), 7.2–7.5 (m, 15 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 30.6 (br., $ArCH_2Ar$), 60.7 (OCH_3), 70.4 ($ArCH_2O$), 114.8 (Ar_{HQ}-H), 116.1 (Ar_{HQ}C-H), 126–130 (ArC-H), 132.3 ($Ar_{HQ}C_{ipso}$-CH_2), 132.5 ($Ar_{quinone}$C-H), 136.7 (ArC_{ipso}-CH_2), 137.6 ($Ar_{HQ}C_{ipso}$-CH_2), 148.1 ($Ar_{HQ}C_{ipso}$-O), 155.1 ($Ar_{HQ}C_{ipso}$-OBz), 186.5 (C=O), 187.1 (C=O) ppm. MS: *m*/*z* = 1061.32 $[C_{66}H_{54}O_{12}Na]^+$. Full reduction: *m*/*z* = 1067.35 $[C_{66}H_{60}O_{12}Na]^+$, 1077.31 $[C_{66}H_{54}O_{12}K]^+$. Full reduction: *m*/*z* = 1083.32 $[C_{66}H_{60}O_{12}K]^+$. HRMS (MALDI): calcd. for $[C_{66}H_{54}O_{12}Na]^+$ 1061.35075; found 1061.34813. IR (KBr): $\tilde{\nu}$ = 1655 (C=O) cm^{-1}.

(Tetramethyl) Calix[6]arene Bis(quinone) (10): To a suspension of **9** (0.5 g, 0.38 mmol) in THF/CH_3CN/H_2O (1:1:1, 20 mL) was added bis(trifluoroacetoxy)iodosobenzene (0.6 g, 1.4 mmol). The resulting pale-yellow suspension was vigorously stirred overnight at ambient temperature. Bis(trifluoroacetoxy)iodosobenzene (0.6 g, 1.4 mmol) was then added, and the resulting orange suspension was vigorously stirred for 6 h. $NaHCO_3$ (2 g) was then added, and the solvents were removed under vacuum. The product was recovered by washing with dichloromethane (2 × 40 mL) and filtering, and the resulting orange solution was evaporated to dryness. The oil on the walls of the glassware was then washed overnight with ethanol (100 mL) under vigorous stirring. The ethanol supernatant was discarded. The orange solid on the walls of the glassware was rinsed one more time with ethanol (100 mL) and dried in vacuo to a constant weight. Compound **10** (0.43 g, quant.) was recovered as an orange solid. ^1H NMR (300 MHz, CDCl3, 293 K): δ = 3.27 (s, 12 H, OCH_3), 3.66 (s, 8 H, $ArCH_2Ar$), 3.87 (s 4 H, $ArCH_2Ar$), 4.96 (s, 8 H $ArCH_2O$), 6.2 (s, 4 H $Ar_{quinone}H$), 6,63/6.64 (d, ^4J = 4 Hz, 4 H, $Ar_{HQ}H$), 6,67/6.68 (d, ^4J = 4 Hz, 4 H, $Ar_{HQ}H$), 7.2–7.5 (m, 20 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ = 30.6 ($ArCH_2Ar$), 31.5 ($ArCH_2Ar$), 60.5 (OCH_3), 70.3 ($ArCH_2O$) 115.4 (Ar_{HQ}-H), 116 (Ar_{HQ}-H), 126–130 (ArC-H), 131.9 ($Ar_{quinone}H$), 132.5 ($Ar_{HQ}C_{ipso}$-CH_2), 137 ($Ar_{HQ}C_{ipso}$-CH_2), 137.3 (ArC_{ipso}-CH_2), 148.5 ($Ar_{HQ}C_{ipso}$-O), 154.7 ($Ar_{HQ}C_{ipso}$-OBz), 186.6 (C=O), 187.9 (C=O). Full reduction: *m*/*z* = 1148.50 $[C_{74}H_{68}O_{12} + H]^+$, 1167.48 $[C_{74}H_{64}O_{12}Na]^+$. Full reduction: *m*/*z* = 1171.50 $[C_{74}H_{68}O_{12}Na]^+$. Full reduction: *m*/*z* = 1187.48 $[C_{74}H_{68}O_{12}K]^+$. HRMS (MALDI): calcd. for $[M + Na]^+$ 1167.42900; found 1167.42694. IR (KBr): $\tilde{\nu}$ = 1654 (C=O) cm^{-1}.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR, HSQC/HMBC, and variable-temperature NMR spectroscopic experiments.

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Received: November 9, 2009
Published Online: March 5, 2010

