133.27, 131.56, 130.99, 130.67, 129.40, 128.39, and 128.20 (Ar), 61.41, 60.84, and 59.19 (OCH_3), 34.86, 29.98, 26.18, and 25.74 (CH_2 and $COCH_3$); ^{13}C NMR (Me_2SO-d_6, 150 °C) δ 195.53 (C=O), 160.83, 133.05, 131.00, and 129.54 (Ar), 59.45 (OCH_3), 31.43 (CH_2), 25.10 (CH_3). Anal. Calcd for $C_{40}H_{40}O_8 \cdot {}^1/_4CH_3SOCH_3$: C, 72.80; H, 6.22. Found: C, 73.00; H, 6.37.

5,11,17,23-Tetrabromo-25,26,27,28-tetrahydroxycalix[4]arene (31). A solution of 0.5 g of 5,11,17,23-tetrabromo-25,26,27,28-tetramethoxycalix[4]arene (**15**) in 40 mL of benzene was treated dropwise with 15 mL of BBr_3[37] in CH_2Cl_2, and the mixture was stirred at room temperature for 18 h in an atmosphere protected from moisture. The reaction mixture was poured into 100 mL of H_2O, stirred for 1.25 h, and the organic layer was evaporated and triturated with acetone to leave 0.39 g (84%) of a white powder. Crystallization from pyridine/toluene yielded a yellow powder as the first fraction and a white powder as the second fraction: mp >480 °C; IR (KBr) 3135 cm^{-1} (OH stretching); ^1H NMR (pyridine-d_5) δ 9.72 (s, 4, OH), 7.25 (s, 8, Ar H), 4.0 (br s, 8, $ArCH_2Ar$). Anal. Calcd for $C_{28}H_{20}O_4Br_4 \cdot {}^1/_4C_5H_5N$: C, 46.22; H, 2.79. Found: C, 46.46; H, 2.61.

(37) Tashiro, M.; Yoshiya, H.; Fukatas, G. *J. Org. Chem.* **1982**, *47*, 4425.

Acknowledgment. We are indebted to the National Institutes of Health for a grant (GM-23534) that provided essential financial support of this work.

Registry No. **3**, 92887-22-4; **5**, 92887-20-2; **6**, 99033-30-4; **7**, 99033-31-5; **8**, 99033-32-6; **9**, 99033-33-7; **10**, 99033-34-8; **11**, 99033-35-9; **13**, 74568-07-3; **14**, 99095-68-8; **15**, 99033-36-0; **16**, 99033-37-1; **18**, 99033-46-2; **19**, 99033-47-3; **20**, 99033-40-6; **21**, 99146-80-2; **22**, 99052-67-2; **23**, 99052-68-3; **24**, 99033-41-7; **25**, 99033-42-8; **26**, 99033-43-9; **27**, 97998-56-6; **28**, 99052-69-4; **29**, 99033-44-0; **30**, 99052-70-7; **31**, 97998-58-8; *p*-phenylphenol, 92-69-3; formaldehyde, 50-00-0; allyl bromide, 106-95-6; bis(trimethylsilyl)acetamide, 10416-58-7; *p*-*tert*-butylcalix[4]arene, 60705-62-6; 5,11,17,23-tetrabromo-25,26,27,28-tetrabenzoyloxycalix[4]arene, 99033-39-3; 25,26,27,28-tetrabenzoyloxycalix[4]arene, 99033-38-2; 25,26,27,28-tetramethoxymethylcalix[4]arene, 99033-45-1; calix[4]arene, 281-54-9; chloromethyl methyl ether, 107-30-2; 5,11,17,23-tetraactyl-25,26,27,28-tetramethoxycalix[4]arene, 99052-71-8.

Calixarenes. 17. Functionalized Calixarenes: The Claisen Rearrangement Route

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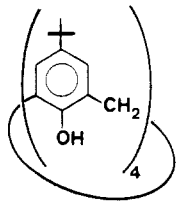
Department of Chemistry, Washington University, St Louis, Missouri 63130

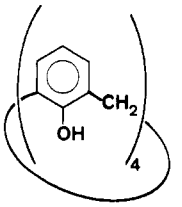
Received May 29, 1985

Methods for the preparation of a variety of para-substituted calix[4]arenes via the Claisen rearrangement route are described. Starting with the readily available *p*-*tert*-butylcalix[4]arene **1**, the *tert*-butyl groups are removed by an $AlCl_3$-catalyzed retro-Friedel–Crafts reaction, and the calix[4]arene **2** that is formed is converted to the tetraallyl ether **3**. This compound undergoes a heat-induced Claisen rearrangement to yield *p*-allylcalix[4]arene **4**, which is a useful starting material for the introduction of functional groups. Along one route, the tosylate of **4** is ozonized to the aldehyde **7**, the aldehyde is reduced to the alcohol **8**, the alcohol is converted to the bromide **10** and then to the azide **11**, and the azide is reduced with diborane to *p*-(2-aminoethyl)calix[4]arene **12**, a compound of interest as a chelating species. Along a second route, the tosylate of **4** is rearranged to *p*-(1-propenyl)calix[4]arene **16** and ozonized to *p*-formylcalix[4]arene **17** from which the oxime **18** can be prepared.

p-*tert*-Butylcalix[4]arene **1** has become one of the most accessible of all of the known macrocyclic cavity-containing compounds, obtainable in greater than 50% yield from the base-induced condensation of *p*-*tert*-butylphenol and formaldehyde.[1] Aluminum chloride-catalyzed de-*tert*-butylation has been shown to proceed in excellent yield,[2,3] making calix[4]arene **2** an extremely attactive starting material for the preparation of various para-substituted calix[4]arenes. To our surprise and disappointment, however, direct introduction of functional groups via electrophilic or nucleophilic substitution reactions has failed in most cases. The only successes that have been achieved are the sulfonation of calix[6]arene by Shinkai and co-workers[4] and the aminomethylation of calix[4]arene in our laboratories.[5] To effect facile bromination and Friedel–Crafts acylation it is necessary to convert calix[4]arene to an ether, such as the methyl ether, as described in the preceeding paper.[6]



1



2

Synthesis of *p*-Allylcalix[4]arene 4. Concomitant with the investigation reported in the preceding paper, we explored another route for the introduction of functional groups into the para position. The Claisen rearrangement is the prototype of the electrocyclic reaction and furnishes an extremely useful method for converting allyl phenyl ethers to *o*-allylphenols.[7] In those cases where both of the ortho positions are blocked, a two-step rearrangement occurs to yield *p*-allylphenols. Since all of the ortho positions in calix[4]arene are occupied by the methylene bridges, this would be the expected pathway of rearrangement for 25,26,27,28-tetrakis(allyloxy)calix[4]arene

(1) Gutsche, C. D.; Iqbal, M.; Stewart, D. S., unpublished observations.
(2) Gutsche, C. D.; Levine, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 2652.
(3) Gutsche, C. D.; Lin, L.-g. *Tetrahedron*, in press.
(4) Shinkai, S.; Mori, S.; Tsubaki, T.; Sone, T.; Manabe, O. *Tetrahedron Lett.* **1984**, 5315.
(5) Gutsche, C. D.; Nam, Kye Chun, unpublished observations.
(6) Gutsche, C. D.; Pagoria, P. F. *J. Org. Chem.*, preceding paper in this issue.
(7) Claisen, L. *Ann.* **1919**, *418*, 69.

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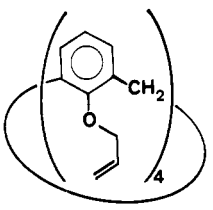
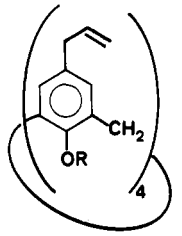
3. The tetraallyl ether **3** was prepared in 74% yield by treatment of calix[4]arene with NaH and allyl bromide[3] in DMF–THF solution, following a general procedure of Stoochnoff and Benoiton.[8] When a solution of **3** in di-



3



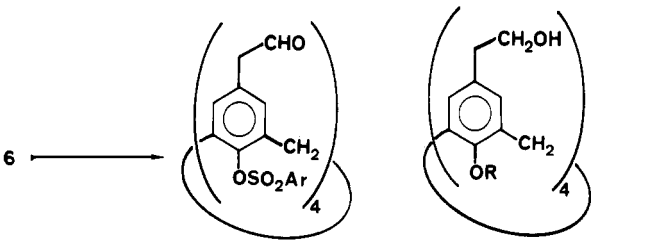
4 (R = H)
5 (R = $SiMe_3$)
6 (R = $SO_2C_7H_7$)

methyl aniline is refluxed, 5,11,17,23-tetraallylcalix[4]arene **4** is, indeed, obtained in 74% yield as colorless crystals.[9] This was previously described in work[2] that also reported the conversion of **4** to the tetrakis(trimethylsilyl) ether **5** in the "cone" conformation.[10]

Attempts to convert **4** to the methyl ether with CH_3I, to the ethyl ether with C_2H_5I, and to the benzyl ether with benzyl chloride produced viscous oils containing mixtures of products. Substituting benzyl tosylate for benzyl chloride and using K_2CO_3 as the base gave the dibenzyl ether, as reported previously.[10b] Although the tetrakis-(trimethylsilyl) ether can be prepared, it is too susceptible to decomposition to be useful as a protecting group while alterations of the allyl group are made. The *p*-toluenesulfonate **6** proved more stable in this respect and could be prepared in 80% yield by the reaction of **4** with *p*-toluenesulfonyl chloride in the presence of NaH in THF solution. The ^1H NMR spectrum of **6** displays a pair of doublets arising from the methylene groups, indicating that the compound is frozen into the cone conformation.

Reactions of the *p*-Toluenesulfonate of *p*-Allylcalix[4]arene (6). We investigated the ozonolysis of **6** in some detail but were unsuccessful in isolating a pure sample of the aldehyde **7**. When a methylene chloride–methanol solution of **6** was treated with ozone at −77 °C and then reduced with NaI in acetic acid an intractible mixture was obtained which showed an unresolved set of ^1H NMR resonances. Although an IR absorption band at 1725 cm^{-1} indicated the presence of a carbonyl group, attempts to confirm this by the preparation of a 2,4-dinitrophenylhydrazone, an oxime, or a dimethylacetal were unsuccessful. Other methods for decomposing the ozonide, including Zn in acetic acid or dimethyl sulfide, failed to yield an isolable sample of **7**, but when sodium borohydride was employed the corresponding alcohol **8** was produced as a crystallizable compound possessing spectral properties commensurate with the assigned structure. Base-induced hydrolysis of **8** yielded *p*-(hydroxyethyl)calix[4]arene **9**.

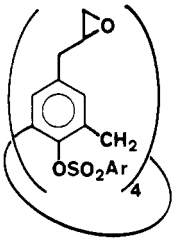
As an alternative to ozonolysis, the oxidation of **6** with $KMnO_4$ and KIO_4[11] was considered but was abandoned



7

8 (R = $SO_2C_7H_7$)
9 (R = H)

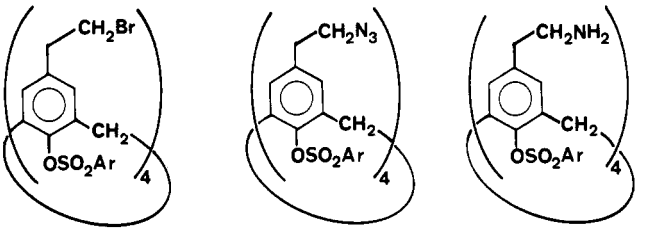
when the action of this reagent on the model compound 4-allyl-2,6-dimethylphenol was found to yield a brown tar which seemed to be the result of overoxidation. Oxidation of **6** with *m*-chloroperbenzoic acid, on the other hand, proceeded smoothly to yield a crystalline solid, which possesses an ^1H NMR spectrum commensurate with the epoxide structure **10**. However, TLC analysis indicated



10

a mixture of at least two compounds, probably diastereoisomers, since four chiral centers are introduced in the expoxidation reaction. Attempts to convert the epoxide **10** to an aldehyde by treatment with BF_3 etherate[12] yielded a white, cellulose-like material that was insoluble in all of the usual organic solvents.

Synthesis of the *p*-Toluenesulfonate of *p*-(2-Aminoethyl)calix[4]arene (13). Although primary alcohols are reported to react with diphenylphosphoryl azide in the presence of diethyl azodicarboxylate and triphenylphosphine to yield azides,[13] **8** failed to react in this fashion to yield **13**. Therefore, a less direct route involving replacement of the hydroxyl group by a better leaving group was employed. Treatment of **8** with triphenylphosphine dibromide in CH_3CN solution[14] yielded 70–80% of the *p*-toluenesulfonate of *p*-(2-bromoethyl)calix[4]arene **11** as a crystalline solid. Treatment of **11** with NaN_3 in

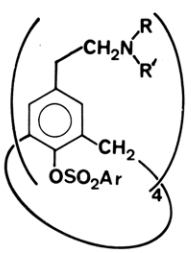


11 12 13

aqueous DMF resulted in a clean conversion to the *p*-toluenesulfonate of *p*-(azidoethyl)calix[4]arene **12** in 95% yield. Attempts to convert **12** to the amine **13** by catalytic reduction, using 10% Pd–C as catalyst, yielded only re-

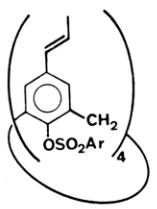
(8) Stoochnoff, B. A.; Benoiton, N. L. *Tetrahedron Lett* **1973**, 21.
(9) To obtain a colorless product it is necessary to work up the reaction mixture as quickly as possible. The crude material changes, on standing, from white or pale yellow to red or violet, and chloroform solutions of the crude product show a similar color change. Once-recrystallized material, however, remains colorless.
(10) For discussions of the conformations of the ethers and esters of calix[4]arenes cf. (a) Bocchi, V.; Foina, D.; Pochini, A.; Ungaro, R. *Tetrahedron* **1982**, *38*, 373; (b) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409.
(11) von Rudloff, E. *Can. J. Chem.* **1955**, *33*, 1714; *Can. J. Chem.* **1956**, *34*, 1413.
(12) Reif, D. J.; House, H. O. *Org. Syn.* **1963**, Coll. Vol. IV, 375.
(13) Lal, B.; Pramanik, B. N.; Manhas, M. S.; Bose, A. K. *Tetrahedron Lett* **1977**, 1977.
(14) Schaefer, J. P.; Higgins, J. G.; Shenoy, P. K. *Org. Syn.* **1973**, Coll. Vol V, 249.

covered starting material, and $LiAlH_4$ or $NaBH_4$ reduction produced gelatinous materials which could not be adequately characterized. Reduction with diborane in THF solution, however, proceeded smoothly to yield ca. 80% of a product which was isolated as the amine hydrochloride, from which the free amine **13** was obtained by treatment with aqueous K_2CO_3. The IR spectrum of the free amine showed the complete disappearance of the 2100-cm^{-1} stretching bands of the N_3 moiety, and the IR spectrum of the hydrochloride showed a strong absorption at 3210 cm^{-1}, characteristic of the ammonium group. The ^1H NMR and ^{13}C NMR spectra of **13** are in accord with the assigned structure, but a TLC analysis indicated that the product contains one major component accompanied by three minor components. Attempts to obtain a completely pure product have been unsuccessful. Separation by column chromatography has been attempted, but the compound decomposed in the process. Recrystallization of the free amine **13** or its hydrochloride has yielded only brown powders. Precipitation from a CH_2Cl_2–hexane solution yielded a white powder, which, however, displayed a less well-resolved ^1H NMR spectrum than the crude material; that this might be due to contamination with traces of a paramagnetic metal ion was suggested by the fact that the resolution was improved by washing the material with a CH_2Cl_2 solution of EDTA. To more fully characterize **13** the benzal and acetyl derivatives were prepared. The benzal derivative **14** was obtained as a white powder possessing the expected IR and NMR spectral properties, but it decomposed upon attempted recrystallization. The acetyl derivative **15** was also obtained as a white powder whose ^1H NMR, ^{13}C NMR, and IR characteristics are commensurate with the assigned structure and whose elemental analysis is in fair agreement with the molecular formula.

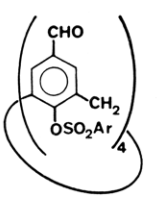


14 (RR' = $=CHC_6H_5$)
15 (R = $COCH_3$, R' = H)

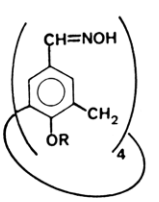
Other Reactions of the *p*-Toluenesulfonate of *p*-Allylcalix[4]arene (6). The *p*-toluenesulfonate of *p*-allylcalix[4]arene (**6**) could be rearranged to the *p*-toluenesulfonate of *p*-(1-propenyl)calix[4]arene (**16**) in 68–80% yield by treatment with tris(triphenylphosphine)rhodium(I) chloride in refluxing toluene.[15]



16 (Ar = C_7H_7)



17 (Ar = C_7H_7)



18 (R = $SO_2C_7H_7$)
19 (R = H)

Ozonolysis of **16** affords a 57% yield of the *p*-toluenesulfonate of *p*-formylcalix[4]arene (**17**), which, in contrast to the homologous aldehyde **7**, is amenable to isolation as white needles, which could be purified and characterized. Treatment of **17** with hydroxylamine yields the *p*-toluenesulfonate of *p*-[(hydroxyimino)methyl]calix[4]arene (**18**) from which the tosyl groups can be selectively removed by base-induced hydrolysis to afford **19** in 35% yield.

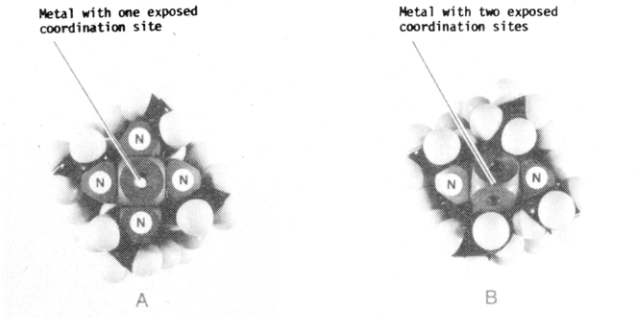


Figure 1. Space filling molecular models of two modes of complexation between compound **13**, metal ions, and external nucleophiles.

Interaction of the *p*-Toluenesulfonate of *p*-(2-Aminoethyl)calix[4]arene with Metal Ions. The tetraamine **13** is interesting, because space filling molecular models suggest that it should be able to form a complex with certain metal ions in which the four amino groups of **13** occupy the planar coordination sites of the metal, leaving one of the apical sites available for coordination with an external nucleophile and the other apical site accessible only through the cavity of the calixarene, as illustrated by structure A in Figure 1. It is possible that a complex of this structure might serve as an oxygen carrier and, thus, a heme mimic. However, a preliminary study of the interaction of **13** with Ni^{+2}, Cu^{+2}, and Co^{+2} in Me_2SO solution, comparing the electronic spectra with those of complexes of known geometry,[16] suggests that another mode of complexation might also be possible, viz., one in which two of the coordination sites can be occupied by external nucleophiles, as illustrated by structure B in Figure 1. The results of these studies will be reported in detail in a separate publication.

Experimental Section[17]

25,26,27,28-Tetrahydroxycalix[4]arene (2). A hot solution of 5.00 g (6.75 mmol) of *p-tert*-butylcalix[4]arene **1**[1,20] in 250 mL

(15) Birch, A. J.; Subba Rao, G. S. R. *Tetrahedron Lett.* **1968**, 3797.

(16) Drago, R. S.; Purcell, K. F. in "Non-Aqueous Solvent Systems", Waddington, T. C., ed., Academic Press, 1965, p. 211–251.

(17) The melting points of all compounds melting above 250 °C were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) using a 500 °C thermometer calibrated against a thermocouple. Infrared (IR) spectra were determined on a Perkin-Elmer 283B spectrometer. Proton nuclear magnetic resonance spectra (^1H NMR spectra) were recorded on a Hitachi Perkin Elmer R-24B spectrometer or a JEOL FX-100 spectrometer. Carbon nuclear magnetic resonance spectra (^{13}C NMR) were obtained on the latter instrument. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0) as an internal standard. Visible spectra were measured with a Cary 119 spectrometer. Mass spectra were obtained on a Varian Atlas MAT CH-7 mass spectrometer. Osmometric molecular weight determinations[18] were made on a Wescan Model 232A apparatus using concentrations of ca 10^{-3}M in $CHCl_3$ solution. Microanalyses were carried out by Industrial Testing Laboratories, St Louis, MO and MicAnal Laboratories, Tuscon, AZ. Thin layer chromatographic analyses were carried out on silica gel plates (absorbent thickness 250 um). Flash chromatography[19] was carried out with E. Merck silica gel (230–400 mesh ASTM) on columns of 80 mm diameter (for more than 5 g of sample), 50 mm diameter (for 1–5 g of sample) and 30 mm diameter (for less than 1 g of sample) filled to a height of 6 in. Elution rates were 2 in/min; fractions of ca 50 mL were collected from the two larger columns and of 20–30 mL from the smallest collumn.

(18) We are indebted to Alice Gutsche for carrying out the osmometric molecular weight determinations.

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

of toluene was placed in a 500-mL three-necked, round-bottomed flask fitted with a mechanical stirrer and a gas inlet tube. The solution was cooled to 50–55 °C, treated with 5.0 g (37 mmol) of anhydrous $AlCl_3$, and stirred for 2 h at 50–55 °C in an inert atmosphere. The mixture was cooled in an ice bath and stirred with 125 mL of 1 N HCl for 30 min, and the organic phase was separated and washed, dried, and evaporated to leave a yellow residue. This was triturated with 500 mL of ether, and the insoluble material was recrystallized from $CHCl_3$–CH_3OH to yield 1.89 g (66%) of **2** as off-white microcrystals, mp 313–318 °C. An analytical sample was obtained by recrystallization from acetone as opaque, trapezoidal plates: mp 315–318 °C; IR (KBr) 3120 cm^{-1} (OH stretching); ^1H NMR ($CDCl_3$) δ 10.19 (s, 4, OH), 7.22–6.64 (s, 12, Ar H), 3.63 and 3.48 (br d, 8, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 148.18, 129.0, 128.2, and 122.2 (Ar), 31.7 (CH_2); osmometric M_r ($CHCl_3$, 37 °C) 450 (calcd for **2** with $^1/_4$ mol of acetone 439); mass spectrum, *m/e* 424 (calcd *m/e* 424). Anal. Calcd for $C_{28}H_{24}O_4 \cdot {}^1/_4C_3H_6O$: C, 78.67; H, 5.81. Found: C, 78.68; H, 5.88.

5,11,17,23-Tetraallyl-25,26,27,28-tetrahydroxycalix[4]arene (4). 25,26,27,28-Tetrakis(allyloxy)calix[4]arene (**3**) was obtained as previously described[10b] as colorless needles in 74% yield after recrystallization from 95% ethanol, mp 183–184 °C (lit.[10b] mp 184–185 °C). A solution of 1.66 g (2.84 mmol) of **3** in 25 mL of *N,N*-diethylaniline was heated at reflux for 2 h in an inert atmosphere. The solution was cooled, poured into 250 mL of ice–water, stirred with 250 mL of concentrated HCl, and filtered to yield a crude product, which was crystllized from isopropyl alcohol to afford 1.22 g (74%) of off-white needles, mp 245–248 °C. A second recrystallization from isopropyl alcohol yielded an analytical sample as colorless needles, mp 250.5–252 °C; IR (KBr) 3150 cm^{-1} (OH stretching); ^1H NMR ($CDCl_3$) δ 10.1 (s, 4, OH), 6.8 (s, 8, Ar H), 6.1–5.5 (m, 4, =CH), 5.2–5.0 (m, 4, =CH), 5.0–4.8 (m, 4, =CH), 4.1–3.3 (br d, 8, $ArCH_2Ar$), 3.17 (d, 8, $CH_2CH{=}CH_2$); ^{13}C NMR ($CDCl_3$) δ 147.0 (Ar), 137.5 (=C), 133.4, 128.9, and 128.2 (Ar), 115.5 (=CH_2), 39.3 (*C*C=C), 31.7 (Ar*C*H_2Ar); osmometric M_r ($CHCl_3$, 37 °C) 590 (calcd 585). Anal. Calcd for $C_{40}H_{40}O_4$: C, 82.16; H, 6.90. Found: C, 82.25; H, 7.02.

5,11,17,23-Tetraallyl-25,26,27,28-tetrakis[(trimethylsilyl)oxy]calix[4]arene (5). Employing the method of Klebe et al.,[21] a solution of 0.305 g (0.522 mmol) of **4** and 1.6 g (7.9 mmol) of *N,O*-bis(trimethylsilyl)acetamide in 10 mL of dry CH_3CN was refluxed in an inert atmoshere for 16 h. The solution was cooled, and the solid material was collected by filtration and recrystallized from CH_3OH–H_2O to yield **5** as fine, colorless needles: mp 173–181 °C; ^1H NMR ($CDCl_3$) δ 6.43 (s, 8, Ar H), 6.03–5.43 (m, 4, HC=), 5.13 (br s, 4, =CH_2), 4.93–4.63 (m, 4, =CH_2), 4.31 (d, 4, J = 12 Hz, $ArCH_2Ar$), 3.12 (br s, 9, $CH_2C{=}C$), 3.02 (d, 4, J = 12 Hz, $ArCH_2Ar$), 0.26 (s, 36, $Si(CH_3)_3$). Anal. Calcd for $C_{52}H_{72}O_4Si_4$: C, 71.50; H, 8.31. Found: C, 71.49; H, 8.45.

5,11,17,23-Tetraallyl-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (6). A solution of 2.09 g (3.57 mmol) of **4** in 100 mL of dry THF was treated with 1.0 (42 mmol) of NaH followed by 4.0 g (21 mmol) of *p*-toluenesulfonyl chloride, and the mixture was heated at reflux for 1.5 h. The solvent was removed by evaporation to leave a light brown oil, which was dissolved in 100 mL of $CHCl_3$, cooled in an ice bath, and treated with 100 mL of ice–water. The organic phase was dried and evaporated, and the residue was recrystallized from isopropyl alcohol to yield 3.41 g (79.5%) of **6** as pale yellow needles. An analytical sample was obtained by another recrystallization, which afforded fine white needles: mp 224.5–226 °C; IR (KBr) 1375 and 1175 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 7.83, 7.70, 7.38, and 7.23 (AA′BB′ system, 16, Ar H of OSO_2Ar), 6.32 (s, 8, calixarene Ar H), 5.9–5.3 (m, 4, =CH), 5.2–4.8 (m, 4, =CH_2), 4.7–4.5 (m, 4, =CH), 3.82 (d, 4, J = 14 Hz, $ArCH_2Ar$), 2.95 (d, 8, $CH_2C{=}C$), 2.43 (s, 12, $ArCH_3$), 2.36 (d, 4, J = 14 Hz, $ArCH_2Ar$). Anal. Calcd for $C_{68}H_{64}O_{12}S_4$: C, 67.98; H, 5.37. Found: C, 67.72; H, 5.25.

5,11,17,23-Tetrakis(2-hydroxyethyl)-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (8). A solution of 3.50 g of the *p*-toluenesulfonate of *p*-allylcalixarene (**4**) in 60 mL of CH_2Cl_2 and 40 mL of CH_3OH was cooled in a dry ice–acetone bath and treated with O_3 until it retained a blue color (10–15 min). Nitrogen was bubbled through the solution until the blue color disappeared, and 2 g of $NaBH_4$ was added. The solution was stirred at room temperature for 3–4 h, poured into ice cold, dilute HCl solution, and worked up in conventional fashion to yield a crude sample of **8** as a white resin. Recrystallization from 3:5 acetone–hexane produced 1.51 g (43%) of microcrystals, from which an analytical sample of **8** was obtained as white needles by a second recrystallization from ethanol–hexane: mp 235–237°; ^1H NMR ($CDCl_3$) δ 7.80, 7.71, 7.37, and 7.29 (AA′BB′ system, 16, Ar H of OSO_2Ar), 6.51 (s, 8, Ar H), 3.88 (d, 4, J = 14 Hz, $ArCH_2Ar$), 3.50 (t, 8, $ArCH_2CH_2OH$), 2.5–2.3 (m, 24, $ArCH_2Ar$, $ArCH_3$, and $ArCH_2CH_2OH$): ^{13}C NMR (Me_2SO-d_6) δ 135.17, 127.57, 125.13, 122.74, 120.01, 119.62, and 119.13 (Ar), 52.36 ($ArCH_2Ar$), 20.88 ($ArCH_2CH_2OH$), 11.62 ($ArCH_2CH_2OH$). Anal. Calcd for $C_{64}H_{64}O_{16}S_4 \cdot {}^1/_2H_2O$: C, 62.69; H, 5.34. Found: C, 62.69; H, 5.42.

5,11,17,23-Tetrakis(2-hydroxyethyl)-25,26,27,28-tetrahydroxycalix[4]arene (9). The mother liquor from the recrystallization of **8**, as described above, containing 1.4 g of material, was boiled with 2 mL of 50% NaOH in 100 mL of 95% EtOH for 6 h. The reaction mixture was cooled, neutralized with 10 mL of acetic acid, and poured into ice–water and the precipitate collected by filtration. Recrystallization from CH_3CN gave 0.20 g of colorless crystals: mp 358–360 °C; ^1H NMR (Me_2SO-d_6, 50 °C) δ 11.06 (br s, 4, OH), 9.60 (s, 4, OH), 8.26 (s, 8, Ar H), 5.12 (s, 8, $ArCH_2Ar$), 4.82 (t, 8, $ArCH_2CH_2OH$), 3.83 (t, 8, $ArCH_2CH_2OH$); ^{13}C NMR (Me_2SO-d_6, 50 °C) δ 137.80, 122.69, 119.38, and 118.74 (Ar), 52.56 ($ArCH_2Ar$), 28.78 ($ArCH_2CH_2OH$), 21.27 ($ArCH_2CH_2OH$). Anal. Calcd for $C_{36}H_{40}O_8 \cdot {}^3/_4H_2O$: C, 70.42; H, 6.76. Found: C, 70.42; H, 6.63.

5,11,17,23-Tetrakis(2-bromoethyl)-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (11). A solution of triphenylphosphine dibromide, prepared from 6.5 g (25 mmol) of triphenyphoshine[14] and Br_2, in 150 mL of dry CH_3CN was treated with a solution of **8**, prepared from 3.25 g of **6** as described above, in 50 mL of CH_3CN. The mixture was stirred for 2 h at room temperature and filtered and the solvent removed by evaporation to leave a sticky orange oil. This was stirred with 250 mL of 95% ethanol for 8 h, and 3.10 g (78%) of **10** was collected as a white powder by filtration. An analytical sample was obtained by recrystallization from EtOAc–EtOH as a colorless powder: mp 205 °C (softens, then forms a glass above 147 °C); ^1H NMR ($CDCl_3$) δ 7.80, 7.72, 7.38, and 7.30 (AA′BB′ system, 16, Ar H of OSO_2Ar), 6.39 (s, 8, calixarene Ar H), 3.83 (d, 4, J = 14 Hz, $ArCH_2Ar$), 3.35 (t, 8, J = 7 Hz, $ArCH_2CH_2Br$), 2.77 (t, 8, J = 7 Hz, $ArCH_2CH_2Br$), 2.47 (s, 12, $ArCH_3$); ^{13}C NMR ($CDCl_3$) δ 144.7, 143.8, 136.2, 135.5, 132.4, 129.7, 129.4, and 129.1 (Ar), 37.9 (CH_2CH_2Br), 33.7 ($ArCH_2CH_2Br$), 31.0 ($ArCH_2Ar$), 21.7 ($ArCH_3$). Anal. Calcd for $C_{64}H_{60}Br_4O_{12}S_4$: C, 52.33; H, 4.12. Found: C, 52.57; H, 4.05.

5,11,17,23-Tetrakis(2-azidoethyl)-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (12). A mixture of 2.07 g (1.41 mmol) of **11**, 2.07 g (31.8 mmol) of NaN_3, 50 mL of DMF, and 5 mL of water was stirred for 6 h at room temperature. The mixture was poured into 200 mL of water, and the product was collected by filtration as 1.71 g (92%) of a white powder. Precipitation from benzene–hexane yielded an analytical sample: mp 162–167 °C dec; IR (KBr) 2100 cm^{-1} (N_3 stretching); ^1H NMR ($CDCl_3$) δ 7.82, 7.74, 7.38, and 7.30 (AA′BB′ system, 16, Ar H of OSO_2Ar), 6.38 (s, 8, calixarene Ar H), 3.83 (d, 4, J = 14 Hz, $ArCH_2Ar$), 3.26 (t, 8, J = 7 Hz, $CH_2CH_2N_3$), 2.6–2.4 (m, 20, $ArCH_2CH_2$ and $ArCH_3$), 2.40 (d, 4, J = 14 Hz, $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 144.7, 144.0, 135.7, 135.4, 132.4, 129.6, 129.5, and 129.1 (Ar), 52.0 ($CH_2CH_2N_3$), 34.4 ($ArCH_2CH_2$), 31.1 ($ArCH_2Ar$), 21.7 ($ArCH_3$). Anal. Calcd for $C_{64}H_{60}N_{12}O_{12}S_4$: C, 58.34; H, 4.59; N, 12.76. Found: C, 58.65; H, 4.74; N, 12.44.

5,11,17,23-Tetrakis(2-aminoethyl)-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (13). To a solution of 0.711 g (0.54 mmol) of **12** in 15 mL of dry THF was added 14 mL (0.14 mmol) of 1 N B_2H_6 in THF solution, and the mixture was heated at reflux for 2 h. It was then cooled in an ice bath, and 5 mL of acetone was added dropwise with stirring. The solvent was removed by evaporation, and the residue was partitioned between 40 mL of CH_2Cl_2 and 40 mL of 10% aqueous K_2CO_3 solution. The organic phase was separated, washed with 10% K_2CO_3, dried,

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cooled in an ice bath, and treated with HCl gas bubbled through the solution. A precipitate of a hydrochloride of **13** was collected as 0.611 g (83% assuming the formation of a monohydrochloride): IR (KBr) 3220 cm^{-1} (NH_3^+); ^1H NMR (Me_2SO-d_6) δ 7.64, 7.56, 7.46, and 7.37 (AA'BB' system, 16, Ar H of OSO_2Ar), 6.64 (s, 8, calixarene Ar H), 3.84 (d, 4, J = 15 Hz, $ArCH_2Ar$), 2.9–2.2 (m, 32, $ArCH_3$, $ArCH_2CH_2$, CH_2CH_2N, and $ArCH_2$); ^{13}C NMR (Me_2SO-d_6) δ 144.7, 142.6, 135.2, 135.0, 132.0, 129.5, and 128.5 (Ar), 31.8 and 30.2 ($ArCH_2Ar$ and $ArCH_2CH_2$), 21.0 ($ArCH_2CH_2N_3$).

The free base **13** was prepared by stirring the HCl salt with 50 mL of CH_2Cl_2 and 50 mL of an aqueous solution containing 10% K_2CO_3 and 1% EDTA until two clear phases were obtained. The organic phase was washed with water, dried, and evaporated to give a residue which was precipitated from CH_2Cl_2–hexane to yield 0.419 g (64%) of **13** as a white powder: mp >120 °C dec; IR (KBr) 3360 cm^{-1} (NH stretching); ^1H NMR ($CDCl_3$) δ 7.78, 7.65, 7.36, and 7.23 (s, 16, Ar H of OSO_2Ar), 6.44 (s, 8, calixarene Ar H), 3.85 (d, 4, J = 14 Hz, $ArCH_2Ar$), 2.9–2.1 (br s, 40, $ArCH_3$, $ArCH_2CH_2$, CH_2CH_2N, $ArCH_2Ar$, and NH_2); ^{13}C NMR ($CDCl_3$) δ 144.7, 143.4, 137.0, 135.5, 132.6, 129.6, 129.5, and 129.1 (Ar), 43.2 (CH_2CH_2N), 39.0 ($ArCH_2Ar$), 21.8 ($ArCH_3$). Anal. Calcd for $C_{64}H_{68}N_4O_{12}S_4CH_2Cl_2$: C, 60.85; H, 5.33; N, 4.23. Found: C, 60.70; H, 5.49; N, 4.03.

5,11,17,23-Tetrakis[(2-benzalamino)ethyl]-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (14). A mixture of 452 mg (0.332 mmol) of the HCl salt of **13**, 10 mL of benzene, 10 mL of triethylamine, and 0.52 g (4.9 mmol) of benzaldehyde was stirred at room temperature for 24 h. Conventional workup produced an oil, which upon the addition of a few mL of CH_2Cl_2 followed by ca. 50 mL of hexane yielded 281 mg (54%) of **14** as a white powder: mp >110 °C dec; IR (KBr) 1645 (C=N stretching); ^1H NMR ($CDCl_3$) δ 8.01 (s, 4, PhCH=N), 7.9–7.0 (m, 36, Ar H of OSO_2Ar), 6.27 (s, 8, calixarene Ar H), 3.9–3.4 (br m 12, $ArCH_2Ar$ and CH_2CH_2N=), 2.8–2.1 (br m, 24, $ArCH_3$, $ArCH_2CH_2$, and $ArCH_2Ar$); ^{13}C NMR ($CDCl_3$) δ 161.3 (C=N), 144.3, 143.5, 137.1, 136.0, 135.3, 132.6, 130.6, 129.3, 128.6, and 127.9 (Ar), 62.8 (CH_2CH_2N), 36.5 ($ArCH_2CH_2$), 31.1 ($ArCH_2Ar$), 21.7 ($ArCH_3$). Attempts to prepare a dry sample for analysis led to decomposition.

5,11,17,23-Tetrakis(2-acetamidoethyl)-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (15). A mixture of 103 mg (0.085 mmol) of **13**, 5 mL of pyridine, and 0.5 mL of acetic anhydride was stirred at room temperature for 24 h. This was worked up in conventional fashion to yield a solid, which was precipitated from CH_2Cl_2–hexane to afford 78 mg (67%) of **13** as a white powder: mp 165–169 °C; IR (KBr) 3400 and 3300 (NH stretching), 1660 (amide I band), 1550 and 1540 (amide II bands), 1290 (amide III band) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.79, 7.70, 7.34, and 7.27 (AA'BB' system, 16, ArH of OSO_2Ar), 6.79 (br s, 4 NH), 6.36 (s, 8, Ar H), 3.82 (d, 4, J = 15 Hz, $ArCH_2Ar$), 3.07 (br s, 8, CH_2CH_2NH), 2.44 (br s, 24, $ArCH_3$, $ArCH_2CH_2$, and $ArCH_2Ar$), 1.93 (s, 12, $COCH_3$); ^{13}C NMR ($CDCl_3$) δ 170.2 (C=O), 144.4, 143.0, 136.3, 135.9, 133.1, and 129.7 (Ar), 40.4 (CH_2CH_2N), 34.2 ($ArCH_2CH_2$), 30.8 ($ArCH_2Ar$), 23.0 ($COCH_3$), 21.5 ($ArCH_3$). Anal. Calcd for $C_{72}H_{76}N_4O_{16}S_4 \cdot C_6H_{14} \cdot CH_2Cl_2$: C, 61.10; H, 5.97; N, 3.60. Found: C, 61.28; H, 5.51; N, 3.57.

5,11,17,23-Tetra-1-propenyl-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (16). A mixture of 10 g of the tosylate of *p*-allylcalix[4]arene **6** and 0.5 g of tris(triphenylphosphine)rhodium(I) chloride in 500 mL of toluene was refluxed for 20 h. Half of the toluene was removed by evaporation, and 200 mL of hexane was added. A colored precipitate was removed by filtration, and the filtrate was evaporated to dryness to yield a crude product, which was chromatographed on silica gel (4:4:2 $CHCl_2$–hexane–acetone) and then recrystallized from toluene–heptane to afford 4.5 g of almost white microcrystals, mp 180–185 °C. From the mother liquors an additional 2.3 g of white solid was obtained, bringing the total yield to 6.8 g (68%). An analytical sample was obtained as white, opaque needles: mp 253–254 °C; ^1H NMR ($CDCl_3$) δ 7.9–7.1 (m, 16, Ar H of OSO_2Ar), 6.5–5.7 (m, 16, calixarene Ar H and =CH), 3.77 (d, 4, J = 14 Hz, $ArCH_2Ar$), 2.5–2.2 (m, 16, $ArCH_2Ar$ and $ArCH_3$), 1.75 (d, 12, $=CCH_3$). Anal. Calcd for $C_{68}H_{64}O_{12}S_4$: C, 67.98; H, 5.37. Found: C, 67.78; H, 5.57.

5,11,17,23-Tetraformyl-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (17). A solution of 0.5 g of **16** in 90 mL of 1:2 CH_3OH–CH_2Cl_2 was cooled to −10 °C, and O_3 was added until a blue color persisted (ca. 10 m). Excess O_3 was purged with N_2, and the ozonide was decomposed by treatment with a solution of 5 g of KI in 20 mL of 50% acetic acid. The crude product was recrystallized from 2:1 toluene–heptane to afford 0.205 g (43%) of **17** as opaque, white crystals, mp 315–319 °C. Attempts to obtain additional material from the mother liquor were not successful, but an oxime prepared from the mother liquor indicated the presence of at least an additional 15% of material. An analytical sample was obtained by a second recrystallized from toluene–heptane, which produced white needles: mp 329–330 °C dec; ^1H NMR ($CDCl_3$) δ 9.56 (s, 4, CHO), 7.82, 7.74, 7.69, and 7.43 (AA'BB' system, 16, Ar H of OSO_2Ar), 6.97 (s, 8, calixarene Ar H), 3.92 (d, 4, J = 14 Hz, $ArCH_2$), 2.7–2.5 (m, 16, $ArCH_2$ and $ArCH_3$); ^{13}C NMR ($CDCl_3$) δ 190.50 (C=O), 145.86, 136.91, 133.75, 131.88, 130.12, and 129.36 (Ar), 31.31 ($ArCH_2Ar$), 21.89 ($ArCH_3$). Anal. Calcd for $C_{60}H_{48}O_{16}S_4$: C, 62.49; H, 4.20. Found: C, 62.31; H, 4.32.

5,11,17,23-Tetrakis[(hydroxyimino)methyl]-25,26,27,28-tetrakis[(*p*-tolylsulfonyl)oxy]calix[4]arene (18). A solution of 0.20 g of **17** in 50 mL of CH_3CN was treated with 2.0 g of NH_2OH·HCl followed by 3.0 g of Na_2CO_3 in 15 mL of H_2O. The solution was clarified by adding 10 mL of ethanol and then refluxed for 30 m. After the addition of 3 mL of acetic acid to render the reaction mixture homogeneous it was refluxed an additional 2 h and then worked up in conventional fashion to give a crude product, which was recrystallized from toluene–hexane to yield 0.13 g (65%) of white crystals. A TLC analysis (94:6 CH_2Cl–CH_3OH) showed a major spot (R_f 0.43) and several additional spots, including one with R_f 0.38 and another with R_f 0.43. Isolation of the compounds corresponding to R_f values of 0.43 and 0.38 was accomplished by column chromatography on silica gel. Both compounds melted, with decomposition, at ca. 257 °C, possessed virtually identical NMR patterns, and gave satisfactory elemental analyses: ^1H NMR (CD_3CN) δ 8.65 (s, 4, =NOH), 7.72 (s, 4, HC=N), 7.72, 7.64, 7.45, and 7.36 (AA'BB', 16, Ar H of OSO_2Ar), 6.76 (s, 8, calixarene Ar H), 3.86 (d, 4, J = 14 Hz, $ArCH_2Ar$), 2.46 (d, 4, J = 14 Hz, $ArCH_2Ar$), 2.5 (s, 12, $ArCH_3$); ^{13}C NMR (CD_3CN) δ 147.90, 145.00, 135.95, 129.70, 128.49, 127.10, and 116.90 (Ar), 30.00 ($ArCH_2Ar$), 20.50 ($ArCH_3$). Anal. Calcd for $C_{60}H_{52}N_4O_{16}S_4$: C, 59.39; H, 4.32; N, 4.62. Found: C, 59.17; H, 4.28; N, 4.63.

5,11,17,23-Tetrakis[(hydroxyimino)methyl]-25,26,27,28-tetrahydroxycalix[4]arene (19). A solution of 200 mg of **18** in 95% ethanol was treated with 3 g of NaOH in 3 mL of H_2O and refluxed for 3 h. The mixture was worked up in conventional fashion to give 90 mg of a light brown powder. Purification by passage through a silica gel column yielded 35 mg (36%) of **19** as colorless needles, and recrystallization from CH_3CN gave an analytical sample: mp ca. 230 °C dec; ^1H NMR (CD_3CN) δ 10.05 (s, 4, =NOH), 7.89 (s, 4, HC=N), 7.44 (s, 8, Ar H), 3.98 (br s, 8, $ArCH_2Ar$). Anal. Calcd for $C_{32}H_{28}N_4O_8 \cdot {}^3/_2H_2O$: C, 61.63; H, 5.01; N, 8.99. Found: C, 61.40; H, 4.72; N, 8.68.

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