Tricalixarenes and Pentacalixarenes: Synthesis and Complexation Studies[1]

Jianshe Wang and C. David Gutsche*

Department Chemistry, Texas Christian University, Fort Worth, Texas 76129

d.gutsche@tcu.edu

Received November 15, 2001

Tricalix[4]arene **4**, tricalix[5]arene **14**, and pentacalix[4]arene **10** have been synthesized from *O*-alkylcalixarene mono- and dialdehydes by a two-step conversion to the corresponding monoethynyl ketones or diethynyl ketones followed by aryne trimerization in refluxing DMF containing a dialkylamine. The tricalixarenes **4** and **14** were converted, in turn, to calixarenes **6** and **16**, which carry OH groups on the lower rim and methylenes as the bridging moieties to the benzene ring. Complexation studies with the tricalix[5]arene **16** show that it forms (a) a 1:3 complex with *N*,*N*-dimethylethylenediamine in which each calixarene unit contains a molecule of the amine, (b) a 1:1 complex with tris(aminomethyl)amine in which each calixarene unit contains one of the three arms of the guest, and (c) a 1:1 complex with C_{60} in which the guest presumably resides in the cavity provided by the three calixarene units acting cooperatively.

Calixarenes, which are macrocyclic compounds containing cavities of molecular-sized dimensions, have engendered extensive research effort because of their capacity for forming complexes with a variety of guests.[1,2] Particular interest attends calixarenes containing two or more binding sites, and the present work was undertaken to assess the complexation properties of tricalixarenes synthesized by an aryne cyclotrimerization process.

Synthesis of Tricalix[4]arene 4

The cyclotrimerization of alkynes provides a very useful method for synthesizing 1,3,5-trisubstituted benzene compounds, and the utility of this reaction is enhanced by the fact that it can be effected simply by heating ethynyl ketones in refluxing DMF without the aid of a transition-metal catalyst.[3−5] The application of the process to the construction of tri- and pentacalixarenes is demonstrated by the work described below.

As shown in Scheme 1, the requisite calixarene ethynyl ketone **2** was prepared by treating calix[4]arene monoaldehyde **1**, synthesized by a literature procedure,[6] with ethynylmagnesium bromide in THF at 0 °C. Without purification the crude product was oxidized to the ketone with the Jones reagent. According to the well-established mechanism of the trimerization reaction of aryl ethynyl ketones,[3−5] **2** should be convertible to the calix[4]arene trimer **4** either by refluxing it in DMF or by first treating it with dialkylamine to convert it to the enamine **3** followed by refluxing with 2 equiv of **2** in toluene. In the present case both routes gave the desired product in moderate yield (55−65%), and purification of the product was easily achieved by chromatography on silica gel.

Elemental analysis and ^{1}H NMR, ^{13}C NMR, and MALDI mass spectral data all support the structure assigned to **4**. The ^{1}H NMR spectrum shows the three calixarene subunits to be identical, at least on the NMR time scale, and to exist in cone conformations in a molecule possessing C_3 symmetry. The bridge CH_2 groups exhibit two sets of pairs of doublets at δ 4.53, 4.47, 3.20, and 3.14 ppm, respectively. The progress of the cyclotrimerization is conveniently followed by the disappearance of the ethynyl proton signal of the starting material and the appearance of a new singlet at δ 7.75 ppm that indicates the formation of the new benzene ring residing in the center of the molecule. Reduction of the carbonyl groups of **4** to methylene groups was achieved with B_2H_6 in THF, yielding compound **5**, which has greater conformational flexibility than **4**. Removal of the alkyl groups on the lower rims of the calixarene moieties was effected by treating **4** with an excess of BBr_3 in CH_2Cl_2, forming **6** (Scheme 1). Both **5** and **6** have spectral characteristics and elemental analyses compatible with the assigned structures.

(1) For general reviews of calixarene chemistry cf. the following: (a) *Calixarenes 2001*, Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2001. (b) Gutsche, C. D. In *Calixarenes Revisited*; Stoddart, J. F., Ed.; Monographs in Supramolecular Chemistry; Royal Society of Chemistry: London, 1998. (c) Böhmer, V. Calixarenes, Macrocycles with (almost) Unlimited Possibilities. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713−745. (d) Gutsche, C. D. Calixarenes. *Aldrichimica Acta* **1995**, *28*, 3-9. (e) *Calixarenes, A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1991. (f) Gutsche, C. D. In *Calixarenes*; Stoddart, J. F., Ed.; Monographs in Supramolecular Chemistry; Royal Society of Chemistry: London, 1989.

(2) For previous complexation studies from our laboratories cf. the following: (a) Wang, J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1998**, *120*, 12226. (b) Gibbs, C. G.; Wang, J. S.; Gutsche, C. D. Synthesis and Fullerene Complexation Studies of *p*-Allylcalix[5]arenes. In *Calixarenes for Separations*; Lumetta, G. J., Rogers, R. D., Gopalan, A. S., Eds.; ACS Symposium Series 757; American Chemical Society: Washington, DC, 2000; p 313. (c) Wang, J.; Gutsche, C. D. *J. Org. Chem.* **2000**, *65*, 6273. (d) Wang, J.; Bodige, S. G.; Mendez-Rojas, M.; Watson, W. H.; Gutsche, C. D. *J. Org. Chem.* **2000**, *65*, 8260.

(3) Balasubramanian, K. K.; Selvaraj, S. *Synthesis* **1980**, 29.

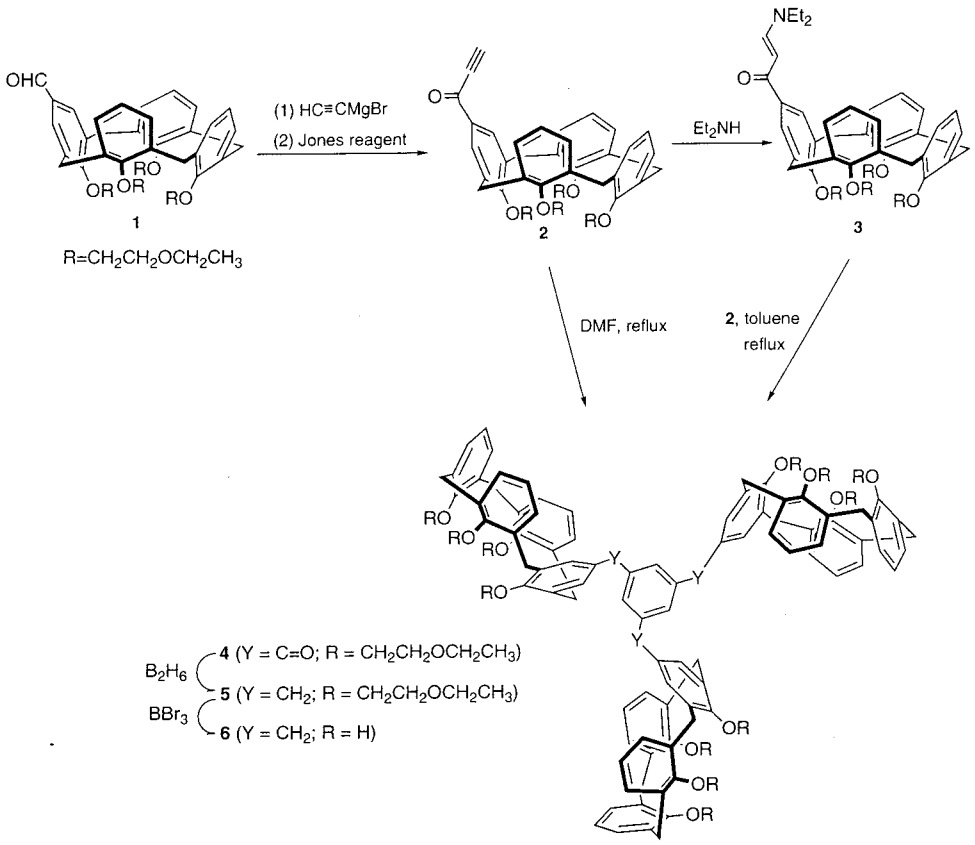
(4) Matsuda, K.; Nakamura, N.; Iwamura, H. *Chem. Lett.* **1994**, 1765.

(5) (a) Pigge, F. C.; Ghasedi, F.; Zheng, Z.; Rath, N. P.; Nichols, G.; Chickos, J. S. *J. Chem. Soc., Perkin Trans. 2* **2000**, 2458. (b) Pigge, F. C.; Ghasedi, F. *Tetrahedron Lett.* **2000**, *41*, 6547. (c) Pigge, F. C.; Ghasedi, F.; Rath, N. P. *Tetrahedron Lett.* **1999**, *40*, 8045. (d) Pigge, F. C.; Zheng, Z.; Rath, N. P. *New J. Chem.* **2000**, *24*, 183.

(6) Arduini, A.; Fanni, S.; Manfredi, G.; Pochini, A.; Ungaro, R.; Sicuri, A. R.; Ugozzoli, F. *J. Org. Chem.* **1995**, *60*, 1448.

10.1021/jo0110808 CCC: $22.00
Published on Web 05/18/2002

Scheme 1



Synthesis of Pentacalix[4]arene 10

Following the method used to synthesize the tricalix[4]arene **4** but starting with calix[4]arene 5,17-dialdehyde **7**, compound **8** carrying two upper rim ethynylcarbonyl groups was obtained in 90% yield as shown in Scheme 2. Compound **8** was treated with diethylamine in chloroform to give the addition product, enamine **9**, in quantitative yield. Refluxing **9** with an excess of **2** in toluene for 3 days resulted in a pair of double trimerization reactions to afford the desired pentacalix[4]arene **10** in 43% yield accompanied by a small amount (~10%) of **4** as a side product formed as the result of catalysis by the diethylamine eliminated in the initial trimerization reaction. Compound **10** was isolated from the crude reaction mixture and purified by standard chromatographic techniques.

Compound **10** contains five calixarene moieties, among which the central one is disubstituted on the upper rim and shows an ^{1}H NMR spectral pattern different from that of the other four. The fact that the protons on the two unsubstituted benzene rings are high-field-shifted to δ 6.20−6.15 ppm and the protons on the other two rings are low-field-shifted to δ 7.91 ppm indicates that the central calixarene unit is in a pinched cone conformation. The other four calixarene subunits behave similarly to those in the tricalixarene **4**.

Synthesis of Tricalix[5]arene 16

The tricalix[5]arene **16** was synthesized by the reactions shown in Scheme 3.

The selective monoformylation of the pentamethyl ether of calix[5]arene **11** was accomplished in 89% yield by reaction with $SnCl_4$ and $CHCl_2OCH_3$ in CH_2Cl_2 at 5 °C, representing a significant advantage over the previously used methods.[2c] Employing a reaction sequence similar to the one used for the preparation of the tricalix[4]arene **4**, the analogous compound, the tricalix[5]arene **14**, was synthesized. The three carbonyl groups in **14** were reduced in high yield (95%) to methylene groups by $NaBH_4$ and CF_3CO_2H.[7] Demethylation of **15** by BBr_3 in CH_2Cl_2 gave a 75% yield of the tricalix[5]arene **16**.

The structures of tricalix[5]arenes **14**−**16** were confirmed by ^{1}H NMR, ^{13}C NMR, and FAB-MS spectra and by elemental analyses. The ^{1}H NMR spectra show that the three appendages in these molecules are all conformationally flexible. The two protons of the CH_2 groups between the calixarene subunits and the central phenyl ring in **15** and **16** are equivalent on the ^{1}H NMR time scale, showing singlets at δ 3.69 ppm for **15** and δ 3.72 ppm for **16**.

Complexation Behavior of Tricalixarenes

The tricalix[4]arene **6** and tricalix[5]arene **16** each possess three cavities which have the potential for complexing either three guest molecules using the three cavities independently (type A in Scheme 4) or a single guest molecule using the three cavities cooperatively (types B and C in Scheme 4). Accordingly, three types of compounds were selected as putative guest molecules, viz., *N*,*N*-dimethylethylenediamine ($Me_2NCH_2CH_2NH_2$) (DMED) for type A, tris(aminoethyl)amine ($[H_2NCH_2CH_2]_3N$) (TREN) for type B, and fullerenes for type C.

(7) (a) Ketcha, D. M.; Gribble, G. W. *J. Org. Chem.* **1985**, *50*, 5451. (b) Gribble, G. W.; Kelly, W. J.; Emery, S. E. *Synthesis* **1978**, 763. (c) Gribble, G. W.; Leese, R. M. *Synthesis* **1977**, 172.

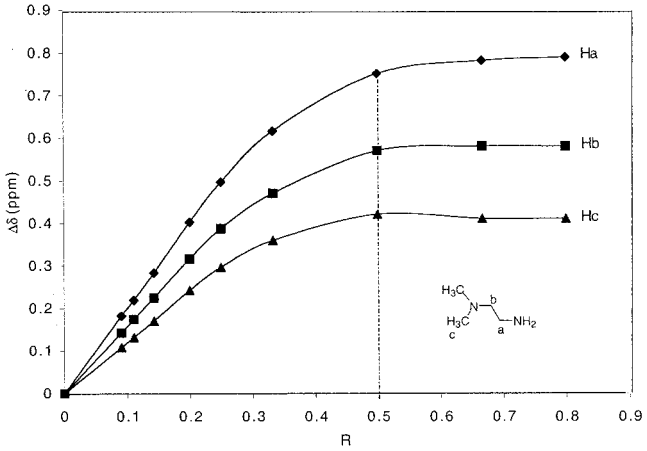


Figure 1. Complexation of calix[5]arene and DMED in $CDCl_3$–CD_3CN (5:1).

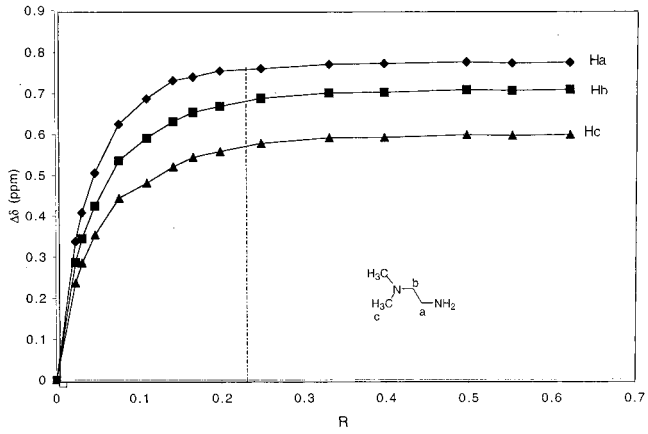
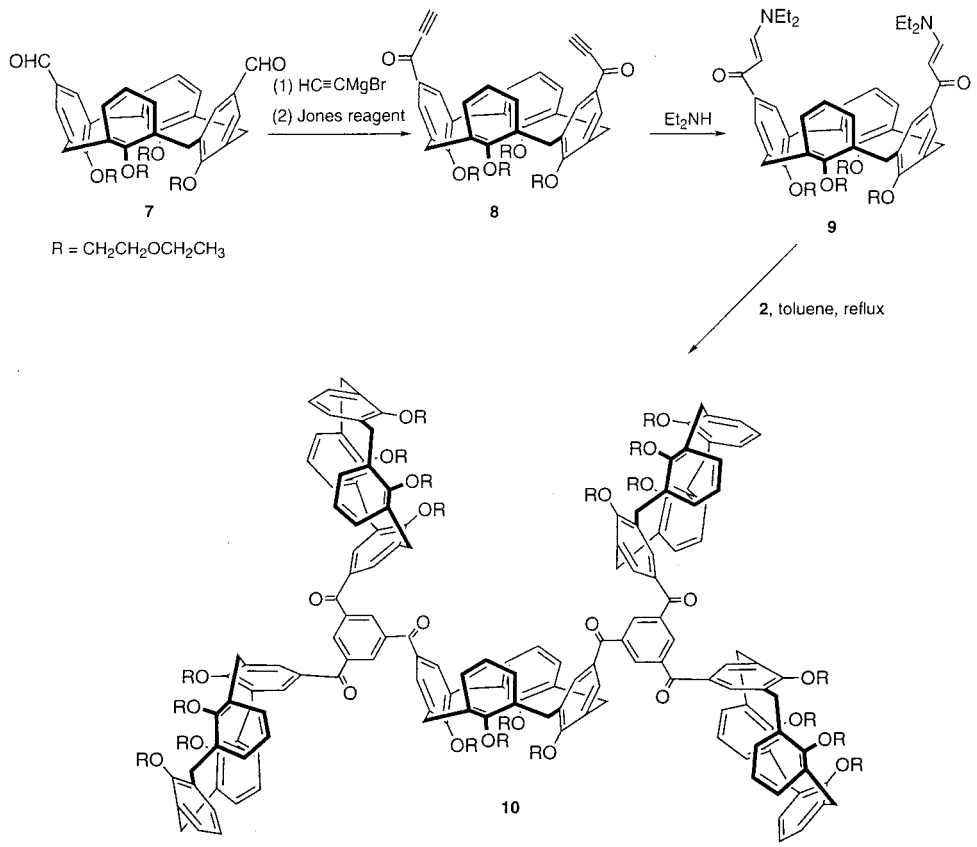


Figure 2. Complexation of tricalix[5]arene **16** and DMED in $CDCl_3$–CD_3CN (5:1).

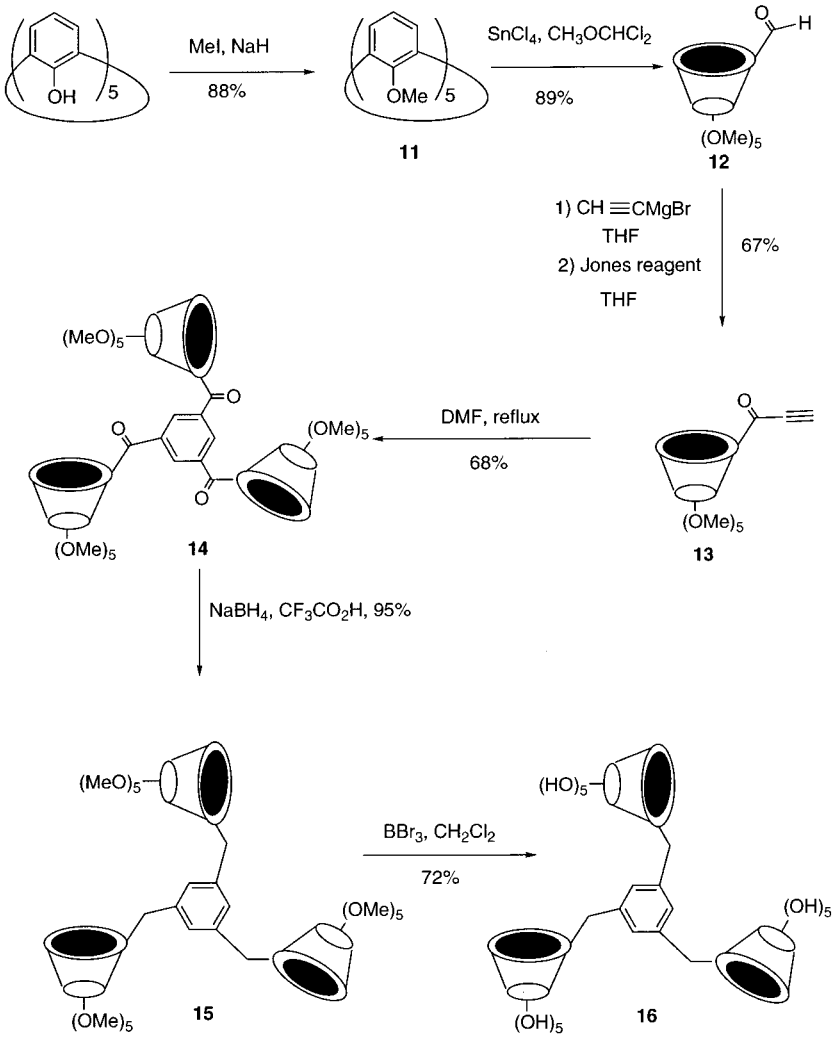
With DMED no measurable complexation was observed with calix[4]arene itself or its tri analogue **6**, although some proton transfer appeared to take place as evidenced by the proton signals of DMED, which were shifted to slightly lower field. With calix[5]arene itself and its tri analogue **16**, on the other hand, the proton signals of DMED were shifted to higher field immediately upon mixing. Plots of this chemical shift change $\Delta\delta$ ($\delta_0 - \delta_1$, where δ_0 and δ_1 represent the chemical shift values of DMED before and after the addition of calixarene) versus the calixarene mole fraction (X = [calixarene]/([calixarene] + [amine])) are shown in Figures 1 and 2. In both cases the plots can be divided into two portions, one portion in which $\Delta\delta$ increases with increasing X and a second portion in which there is no change in $\Delta\delta$ with increasing X. The point of intercept of the two portions of the plots approximates the complexation ratio of the two components. Thus, with $X = 0.5$ for the first case, a 1:1 complex between calix[5]arene and DMED is indicated, and with $X = 0.25$ in the second case, a 1:3 complex between **16** and DMED is indicated, in agreement with expectation.

For the type B complex the three-armed guest molecule tris(aminoethyl)amine (TREN) was explored in the thought that each of the arms would occupy a separate calixarene moiety. When equal amounts of **16** and TREN were mixed in an NMR tube in the solvent $CDCl_3$–CD_3CN (5:1), a precipitate immediately formed. Removal of the precipitate by filtration left a clear solution with an ^1H NMR spectrum showing two broad peaks in the high-field area arising from the methylene groups of TREN.

Scheme 2



Scheme 3



When this solution was heated to 30−60 °C, a more finely resolved spectrum was observed, presumably the result of the increased rate of conformational interconversions. This spectrum revealed a large change in the chemical shifts in the resonances of both the host and guest molecules, as shown in Table 1. Since protonation of the amino groups of TREN with trifluoroacetic acid in CD_3CN shifted the CH_2 signals to lower field, the large shifts to higher field for the protons of TREN in the presence of tricalix[5]arene **16** indicate that something more than simple protonation has occurred, viz., that a strong complex between **16** and TREN is formed. On the basis of an investigation carried out several years ago in this laboratory[8] involving the interaction of *p*-allylcalix[4]arene and *tert*-butylamine, it is postulated that the overall complexation process with **16** can be viewed as proceeding in the two steps shown in Scheme 5, a proton transfer from each of the quite strongly acidic calixarene subunits to each of the strongly basic amino groups of TREN to form the triammonium compound **17** and the calixarene trianion **18** followed by interaction of the anion and cation to form the *endo*-cavity complex **19**. This complex may be too tight to allow solvent molecules to penetrate the cavity, perhaps accounting for its insolubility in $CDCl_3$–CD_3CN.

(8) (a) Bauer, L. J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1985**, *107*, 6063. (b) Gutsche, C. D. Iqbal, M.; Alam, I. *J. Am. Chem. Soc.* **1987**, *109*, 4314.

For the type C complex shown in Scheme 4 the globular fullerene molecules C_{60} and C_{70} are attractive guests. Complexation studies employing UV−vis spectroscopic analysis (color change from magenta to red with C_{60} and from red to colorless with C_{70}) show that while tricalix[4]arene **6** fails to form complexes with these fullerenes, its larger analogue tricalix[5]arene **16** forms strong complexes in toluene solution at 25 °C. A Benesi−Hilderbrand treatment of the spectrometric measurements established the binding constants as $283 \pm 24\ M^{-1}$ for C_{60} and $320 \pm 25\ M^{-1}$ for C_{70}. These values are 10 and 7 times larger, respectively, than those for the binding constants of the parent calix[5]arene.[2a]

In summary, novel tri- and pentacalixarenes have been synthesized via the trimerization of calixaryl ethynyl ketones, employing dialkylamines as catalysts. The complexation properties of tricalix[5]arene **16** with various guest molecules have been studied, and the results indicate that binding occurs when the guest is the simple amine DMED, the three-armed amine TREN, or the globular guest C_{60}.

Experimental Section[9]

The syntheses of compounds **1** and **7** were performed following the procedures described in the literature.[6] Compound **12** was first synthesized in this laboratory by a multistep sequence in ca. 20% overall yield.[2c] For the present work, however, it was synthesized in much higher yield by direct formylation.

Scheme 4. Schematic Representation of Supramolecular Complexation of Tricalixarene with Various Guest Molecules

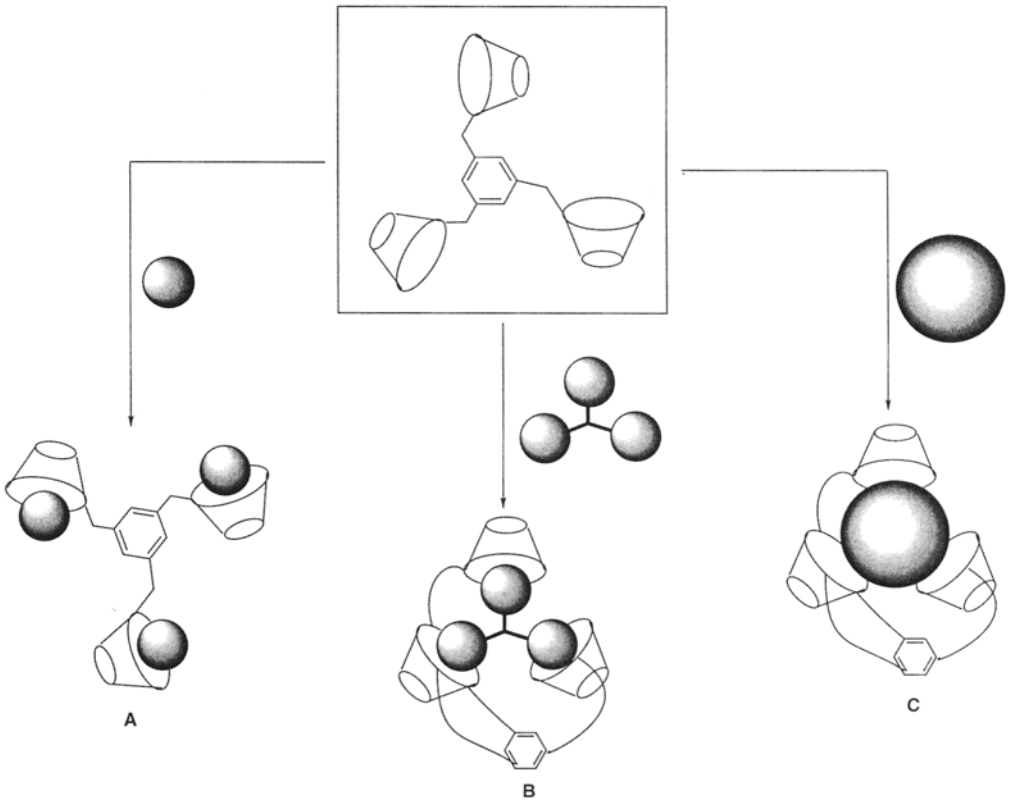


Table 1. Chemical Shift Values of the Protons in TREN in the Presence and Absence of Additives

entry	additive	solvent	$\Delta\delta(N(CH_2CH_2NH_2)_3)$	$\Delta\delta(N(CH_2CH_2NH_2)_3)$
1	none	CD_3CN	2.62	2.40
2	CF_3CO_2H	CD_3CN	3.13 (0.51)	2.74 (0.34)
3	none	$CDCl_3$–CD_3CN (5:1)	2.75	2.50
4	calix[4]arene	$CDCl_3$–CD_3CN (5:1)	2.92 (0.18)	2.71 (0.21)
5	tricalix[4]arene	$CDCl_3$–CD_3CN (5:1)	2.94 (0.19)	2.71 (0.21)
6	calix[5]arene	$CDCl_3$–CD_3CN (5:1)	2.29 (−0.46)	2.15 (−0.35)
7	tricalix[5]arene[a]	$CDCl_3$–CD_3CN (5:1)	1.81 (−0.94)	1.62 (−0.88)

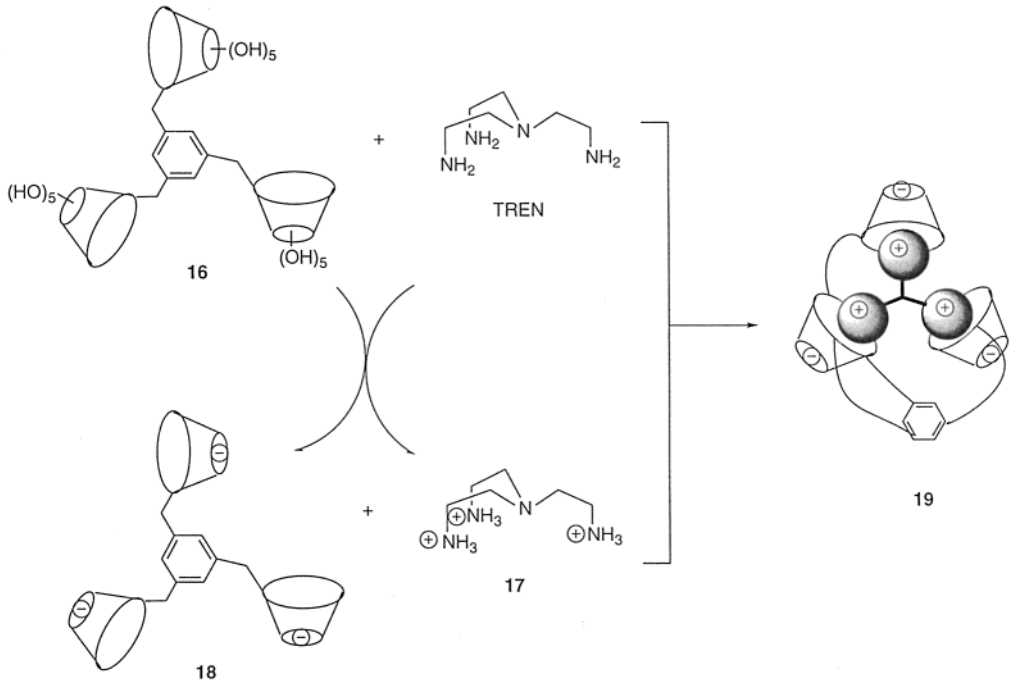
[a] Data at 40 °C.

5-Ethynylcarbonyl-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (2). To a solution of **1** (0.5 g, 0.68 mmol) in 15 mL of dry THF was added dropwise with stirring at −10 °C under an inert atmosphere ethynylmagnesium bromide (2 mmol, 4 mL of stock solution in THF). The reaction mixture was stirred for 1 h at −10 °C and then quenched with 2 mL of acetone. The solution was stirred for 10 min, the Jones reagent was added slowly until the color of the solution was orange, 10 mL of isopropyl alcohol was then added, and stirring was continued another 10 min. The reaction mixture was concentrated under vacuum to leave a residue which was dissolved in $CHCl_3$–H_2O. The organic layer was separated, washed with H_2O and brine, and then dried over Na_2SO_4. Evaporation of the solvent afforded a viscous crude product which was purified by chromatography (silica gel; eluent hexanes−EtOAc, 7:3) to give 0.33 g (64%) of pure product as a viscous oil: ^{1}H NMR ($CDCl_3$) δ 7.43 (s, 2H), 6.63−6.55 (m, 9H), 4.54, 3.22 (d, J = 13.7 Hz, 2H each), 4.47, 3.15 (d, J = 13.6 Hz, 2H each), 4.24 (t, J = 5.3 Hz, 2H), 4.16−4.04 (m, 6H), 3.85−3.77 (m, 8H), 3.57−3.49 (m, 8H), 3.27 (s, 1H), 1.28−1.15 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 176.8, 162.7, 156.3, 156.2, 136.1, 135.2, 135.1, 134.2, 130.6, 130.3, 128.6, 128.3, 128.2, 122.4, 122.3, 80.5, 79.6, 73.6, 73.3, 73.2, 73.1, 69.8, 69.7, 66.4, 30.8, 15.3, 15.2; FAB-MS m/z 766 (M + H). Anal. Calcd for $C_{47}H_{56}O_9 \cdot {}^1/_2H_2O$: C, 72.99; H, 7.36. Found: C, 72.87; H, 7.02.

5-(Diethylaminovinyl)carbonyl-25,26,27,28-tetra(ethoxyethoxy)calix[4]-arene (3). To a solution of **2** (0.76 g) in 10 mL of $CHCl_3$ was added excess diethylamine (10 mmol). The reaction mixture was stirred at rt for 20 min. Evaporation of the solvent to dryness afforded a crude product which was purified by flash chromatography on silica gel with MeOH−$CHCl_3$ (2%) to give 0.8 g (95%) of pure **3** as a viscous oil: ^{1}H NMR ($CDCl_3$) δ 7.64 (d, J = 12.6 Hz, 1H), 7.19 (s, 2H), 6.64−6.52 (m, 9H), 5.44 (d, J = 12.7 Hz, 1H), 4.51 (d, J = 13.4 Hz, 2H), 4.48 (d, J = 13.3 Hz, 2H), 4.16 (t, J = 5.7 Hz, 2H), 4.10 (t, J = 5.4 Hz, 6H), 3.86−3.81 (m, 8H), 3.58−3.49 (m, 8H), 3.28 (q, J = 6.8 Hz, 4H), 3.20 (d, J = 13.7 Hz, 2H), 3.14 (d, J = 13.5 Hz, 2H), 1.25−1.17 (m, 18H); ^{13}C NMR ($CDCl_3$) δ 188.9, 159.1, 156.4, 156.2, 151.3, 135.1, 134.9, 134.8, 134.7, 128.4, 128.2, 128.1, 127.9, 122.2, 92.1, 73.2, 73.1, 73.0, 69.7, 66.4, 30.9,

(9) Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. THF was freshly distilled from Na−benzophenone. The melting points of all compounds melting above 250 °C were measured in sealed and evacuated capillary tubes using a 500 °C thermometer calibrated against a thermocouple. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Many of the compounds show fewer ^{13}C NMR resonances than expected as the result of extensive overlap of lines, particularly in the aromatic region. TLC analyses were carried out on silica gel plates (absorbant thickness 250 μm) containing a fluorescent indicator. Chromatography was carried out with silica gel (40−60 μm particles) on columns filled to a height of ca. 6 in. Elution rates were 2 in./min. Analytical samples were dried for at least 36 h at 100−140 °C and 1−2 mm of pressure and analyzed by Desert Analysis, Tucson, AZ.

Scheme 5



30.8, 15.3. FAB-MS *m/z* 838 (M + H). Anal. Calcd for $C_{51}H_{61}O_9N\cdot{}^1/_2H_2O$: C, 72.36; H, 8.04. Found: C, 72.36; H, 8.02.

1,3,5-Tris(25,26,27,28-tetra(ethoxyethoxy)calix[4]arene-5-carbonyl)benzene (4). Method A. A solution of 0.13 g (0.17 mmol) of **2** in 5 mL of dry DMF was refluxed under a N_2 atmosphere for 30 h. The reaction mixture was treated with $CHCl_3$ (20 mL)−H_2O (20 mL), and the organic layer was washed with water and brine and dried over Na_2SO_4. The resulting crude product was purified by flash chromatography on silica gel with hexanes−EtOAc (3:2) to give 84 mg (65%) of **4**: mp 108−110 °C; ^{1}H NMR ($CDCl_3$) δ 7.65 (s, 3H), 7.29 (s, 6H), 6.62−6.57 (m, 18H), 6.42 (t, J = 7.5 Hz, 9H), 4.53 and 4.57 (d, J = 13.4 Hz, 6H each), 4.15−4.08 (m, 24H), 3.84−3.77 (m, 24H), 3.57−3.49 (m, 24H), 3.20, 3.14 (d, J = 13.5 Hz, 6H each), 1.23−1.15 (m, 36H); ^{13}C NMR ($CDCl_3$) δ 194.2, 161.5, 156.2, 156.1, 138.9, 135.8, 135.2, 134.9, 134.1, 131.6, 131.2, 130.3, 128.7, 128.4, 128.0, 122.5, 122.3, 73.6, 73.2, 73.1, 69.6, 66.3, 30.8, 29.7, 15.3; IR 1657 cm^{-1}; MALDI-FAB-MS *m/z* 2316 (M + Na). Anal. Calcd. For $C_{141}H_{168}O_{27}$: C, 73.8; H, 7.27. Found: C, 73.45; H, 7.27.

Method B. A solution containing 0.084 g (0.1 mmol) of **3** and 0.153 g (0.2 mmol) of **2** in 7 mL of toluene was refluxed under a N_2 atmosphere for 30 h. The reaction mixture was concentrated under vacuum, and the crude product was purified by flash chromatography as described above to afford 0.126 g (55%) of **4**.

1,3,5-Tris(25,26,27,28-tetra(ethoxyethoxy)calix[4]arene-5-methyl)benzene (5). A 170 mg (0.074 mmol) sample of **4** was dissolved in 4 mL of a stock solution of B_2H_6 (1 M in THF) and refluxed under N_2 for 20 h. Another 4 mL of B_2H_6 stock solution was added, and refluxing was continued for an additional 20 h. The reaction mixture was concentrated by evaporation, and the residue was treated with $CHCl_3$ (10 mL)−H_2O (10 mL). The organic layer was separated, washed with brine, and dried over Na_2SO_4 and the crude product purified by flash column chromatography (hexanes−EtOAc, 7:3) to give 0.15 g (88%) of **5** as a viscous oil: ^{1}H NMR ($CDCl_3$) δ 6.74−6.76 (m, 36H), 4.49 and 4.43 (d, J = 13.4 Hz, 6H each), 4.17−4.03 (m, 24H), 3.88−3.80 (m, 24H), 3.61 (s, 6H), 3.57−3.48 (m, 24H), 3.14, 3.07 (d, J = 13.5 Hz, 6H each), 1.26−1.16 (m, 36H); ^{13}C NMR ($CDCl_3$) δ 156.7, 156.0, 154.9, 141.3, 135.5, 135.1, 134.7, 134.6, 134.4, 128.8, 128.4, 128.3, 128.1, 128.0, 127.0, 125.5, 122.2, 122.0, 73.3, 73.0, 72.9, 69.7, 66.4, 66.3, 41.0, 30.9, 30.3, 29.7, 15.3; MALDI-FAB-MS *m/z* 2274 (M + Na). Anal. Calcd for $C_{141}H_{174}O_{24}$: C, 75.17; H, 7.78. Found: C, 75.01; H, 7.75.

1,3,5-Tris(25,26,27,28-tetrahydroxycalix[4]arene-5-methyl)benzene (6). A solution of 200 mg (0.09 mmol) of **5** in 6 mL of dry CH_2Cl_2 was cooled in an ice bath under N_2 and treated dropwise with 5 mL of BBr_3 stock solution (1 M) in CH_2Cl_2. The reaction mixture was stirred for 2 h at this temperature and 20 h at rt, and 10 mL of ice−water was added. The organic layer was separated, washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude product was purified by flash chromatography (silica gel; EtOAc−CH_2Cl_2, 1:4) to yield 63 mg (51%) of **6** as a colorless solid: mp > 215 °C dec; ^{1}H NMR ($CDCl_3$) δ 10.18 (s, 12H), 7.05 (d, 12H, J = 7.6 Hz), 6.98 (d, 6H, J = 7.4 Hz), 6.81 (s, 6H), 6.74−6.68 (m, 12H), 4.24 (br s, 12H), 3.65 (s, 6H), 3.49 (br s, 12H); ^{13}C NMR ($CDCl_3$) δ 150.0, 149.9, 148.2, 141.2, 133.8, 129.7, 129.2, 129.1, 129.0, 127.0, 126.7, 126.6, 126.5, 121.5, 40.6, 31.3, 31.0; MALDI-FAB-MS *m/z* 1409 (M + Na). Anal. Calcd for $C_{93}H_{78}O_{12}\cdot 2H_2O$: C, 78.46; H, 5.81. Found: C, 78.42; H, 6.07.

5,17-Diethynylcarbonyl-25,26,27,28-tetra(ethoxyethoxy)-calix[4]arene (8) was prepared in 90% yield as a semisolid with a pale yellow color using the procedure described for compound **2** but starting with dialdehyde **7**: ^{1}H NMR ($CDCl_3$) δ 7.82 (s, 4H), 6.38 (t, 2H, J = 6.5 Hz), 6.29 (d, 4H, J = 7.0 Hz), 4.56 and 3.26 (d, J = 13.6 Hz, 4H each), 4.39, 4.00, 3.87 and 3.79 (t, 4H each, J = 5.3 Hz), 3.57 and 3.48 (q, J = 7.0 Hz, 4H each), 3.40 (s, 2H), 1.24 and 1.18 (t, 6H each, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 176.7, 163.8, 155.0, 136.9, 132.9, 130.7, 130.6, 128.1, 122.8, 80.6, 80.1, 73.9, 73.4, 69.9, 69.6, 66.5, 66.2, 30.9, 15.3; FAB-MS *m/z* 817 (M + H). Anal. Calcd for $C_{50}H_{56}O_{10}$: C, 73.51; H, 6.91. Found: C, 73.75; H, 7.30.

5,17-Bis(diethylaminovinylcarbonyl)-25,26,27,28-tetra-(ethoxyethoxy)calix[4]arene (9) was prepared following the procedure described for **3**. Purification was accomplished by flash chromatography (silica gel; MeOH−$CHCl_3$, 3%) to give a semisolid: ^{1}H NMR ($CDCl_3$) δ 7.74 (d, J = 12.5 Hz, 2H), 7.60 (s, 4H), 6.26 (s, 6H), 5.74 (d, J = 12.6 Hz, 2H), 4.52 (d, J = 13.4 Hz, 4H), 4.32 (t, J = 6.0 Hz, 4H), 3.98 (t, J = 5.0 Hz, 4H), 3.88 (t, J = 6.0 Hz, 4H), 3.79 (t, J = 5.5 Hz, 4H), 3.58 (q, J = 7.0 Hz, 4H), 3.50 (q, J = 7.0 Hz, 4H), 3.34 (q, J = 7.2 Hz, 8H), 3.23 (d, J = 13.4 Hz, 4H), 1.27−1.21 (m, 12H), 1.16 (t, J = 7.0 Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 188.6, 160.5, 154.8, 151.9, 136.1, 134.6, 133.2, 128.3, 128.1, 128.0, 122.4, 91.9, 73.7, 72.7, 69.7, 69.6, 66.5, 66.2, 30.9, 15.3, 15.2; FAB-MS *m/z* 936 (M + Li). Anal. Calcd for $C_{58}H_{78}O_{10}N_2\cdot{}^1/_2H_2O$: C, 72.88; H, 8.42. Found: C, 72.66; H, 8.80.

5,17-Bis{3,5-bis[25′,26′,27′,28′-tetra(ethoxyethoxy)calix[4]arene-5′-carbonyl]benzoyl}-25,26,27,28-tetra(ethoxyethoxy)calix[4]arene (10). A solution of 170 mg (0.18 mmol) of **9** and 630 mg (0.82 mmol) of **2** in 7 mL of toluene was refluxed under N_2 for 3 days. The reaction mixture was concentrated under vacuum, and the crude product was purified by flash chromatography (silica gel; hexanes−EtOAc, 70:30 to 40:60) to give 300 mg (43%) of **10** as a colorless solid: mp > 127 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.91 (s, 4H), 7.74 (s, 4H), 7.67 (s, 2H, ArH), 7.22 (s, 8H), 6.67−6.43 (m, 36H), 6.20−6.15 (m, 6H), 4.53 and 4.47 (d, J = 13.4 Hz, 10H each), 4.33−4.05 (m, 40H), 3.90−3.71 (m, 40H), 3.59−3.42 (m, 40H), 3.18 (d, J = 14.6 Hz, 10H), 3.13 (d, J = 14.0 Hz, 10H), 1.25−1.10 (m, 60H); ^{13}C NMR ($CDCl_3$) δ 194.3, 194.1, 163.3, 161.2, 156.3, 156.0, 138.9, 137.3, 135.6, 135.4, 134.6, 134.4, 132.4, 131.9, 131.6, 131.1, 130.4, 130.2, 128.8, 128.3, 128.1, 128.0, 127.9, 122.8, 122.5, 122.3, 74.1, 73.7, 73.3, 73.1, 69.6, 69.5, 66.5, 66.4, 66.3, 66.2, 30.9, 29.7, 15.3, 15.2; MALDI-FAB-MS *m*/*z* 3897 (M + Na). Anal. Calcd for $C_{238}H_{280}O_{46}$: C, 73.74; H, 7.28. Found: C, 73.58; H, 7.28.

31,32,33,34,35-Pentamethoxycalix[5]arene (11). To an ice-bath-cooled solution of calix[5]arene (0.53 g, 1 mmol) in THF (40 mL)−DMF (4 mL) was added NaH (0.48 g, 20 mmol, 60% dispersed in oil). This mixture was stirred for 30 min at rt, MeI (5.0 g, 35 mmol) was added, and the mixture was refluxed for 24 h. The solvent was removed by evaporation under vacuum, the residue was stirred with 20 mL of H_2O, and the solid was collected by filtration. The crude product was purified by flash chromatography with an eluent of EtOAc−CH_2Cl_2 (2%) to afford 0.53 g (88%) of a colorless solid. An analytically pure sample was obtained by recrystallization from MeOH−CH_2Cl_2 as a colorless solid: mp 260−263 °C; ^{1}H NMR ($CDCl_3$) δ 6.97 (d, 10H, J = 7.8 Hz), 6.81 (t, 5H, J = 7.2 Hz), 3.87 (s, 10H), 3.20 (s, 15H); ^{13}C NMR ($CDCl_3$) δ 156.6, 134.5, 129.0, 123.1, 60.5, 31.0; FAB-MS *m*/*z* 600 (M + H). Anal. Calcd For $C_{40}H_{40}O_5$: C, 79.97; H, 6.71. Found: C, 79.59; H:, 6.54.

5-Formyl-31,32,33,34,35-pentamethoxycalix[5]arene (12). To a solution of pentamethoxycalix[5]arene (1.75 g, 2.9 mmol) and α,α-dichloromethyl ether (0.4 g, 3.5 mmol) in 80 mL of dry CH_2Cl_2 at ice-cold water bath temperature was added dropwise $SnCl_4$ (1.5 g, 5.8 mmol). The mixture was stirred for 30 min, 50 mL of H_2O was added slowly, and the mixture was stirred for 20 min. The organic layer was separated, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. This solution was concentrated under vacuum, and the residue was subjected to flash chromatography with EtOAc−CH_2Cl_2 (1−5%) to yield 0.74 g (89% yield based on the recovered starting material) of **12**. Analytical data are identical with those reported in ref 2c.

5-Ethynylcarbonyl-31,32,33,34,35-pentamethoxycalix[5]arene (13). Following the procedure described for the preparation of **2**, compound **13** was synthesized in 67% yield as a colorless solid: mp > 103 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.83 (s, 2H), 7.00−6.76 (m, 12H), 3.91 (s, 4H), 3.87 (s, 6H), 3.33 (s, 1H), 3.28 (s, 6H), 3.22 (s, 6H), 3.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.0, 159.0, 156.6, 156.5, 135.4, 134.7, 134.5, 134.4, 133.5, 131.4, 131.1, 129.3, 129.0, 128.9, 128.7, 123.4, 123.3, 80.3, 80.2, 60.7, 60.5, 60.4, 60.3, 31.1, 31.0, 30.9, 14.2; FAB-MS *m*/*z* 653 (M + H). Anal. Calcd for $C_{43}H_{40}O_6 \cdot H_2O$: C, 78.4; H, 6.22. Found: C, 78.36; H, 6.08.

1,3,5-Tris(31,32,33,34,35-pentamethoxycalix[5]arene-5-carbonyl)benzene (14). Using method A as described above for the preparation of **4**, compound **14** was prepared in 68% yield: mp > 145 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.34 (s, 3H), 7.71 (s, 6H), 7.69−7.01 (m, 36H), 3.90 (s, 12H), 3.86 (s, 18H), 3.32 (s, 18H), 3.25 (s, 18H), 2.83 (s, 9H); ^{13}C NMR($CDCl_3$) δ 194.3, 162.0, 156.6, 156.3, 138.7, 135.4, 134.6, 134.5, 134.3, 133.4, 133.0, 132.1, 131.3, 129.2, 129.0, 128.9, 128.4, 123.4, 123.2, 60.6, 60.4, 31.2, 31.0, 30.7; MALDI-FAB-MS *m*/*z* 1980 (M + Na). Anal. Calcd for $C_{129}H_{120}O_{18} \cdot H_2O$: C, 78.40; H, 6.22. Found: C, 78.17; H, 6.26.

1,3,5-Tris(31,32,33,34,35-pentamethoxycalix[5]arene-5-methyl)benzene (15). To CF_3CO_2H (4 mL) at 0 °C under N_2 was added, with stirring, over 30 min $NaBH_4$ (0.189 g, 5.1 mmol). The temperature was then raised to 15 °C, and a solution of **14** (100 mg, 0.051 mmol) in 5 mL of CH_2Cl_2 was added dropwise over 30 min. The mixture was stirred overnight at 25 °C, diluted with 10 mL of H_2O, and made basic by addition of NaOH pellets at 0 °C. The two layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum. Purification by flash column chromatography (silica gel; EtOAc−hexane, 6%) gave 93 mg (95%) of **15**: ^{1}H NMR ($CDCl_3$) δ 6.99−6.71 (m, 45H), 3.88 (s, 6H), 3.86 (s, 12H), 3.80 (s, 12H), 3.69 (s, 6H), 3.23 (s, 18H), 3.19 (s, 18H), 3.04 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 157.2, 157.0, 155.6, 141.8, 136.1, 135.1, 135.0, 134.9, 134.8, 130.0, 129.6, 129.5, 129.3, 127.7, 123.6, 61.1, 61.0, 60.9, 41.7, 31.5; MALDI-FAB-MS *m*/*z* 1938 (M + Na). Anal. Calcd for $C_{129}H_{126}O_{15} \cdot 2CH_2Cl_2$: C, 75.42; H, 6.28. Found: C, 75.58; H, 6.28.

1,3,5-Tris(calix[5]arene-5-methyl)benzene (16). Following the procedure described above for the preparation of **6**, compound **16** was obtained in 72% yield as a colorless solid: mp > 230 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.90 (s, 6H), 8.88 (s, 6H), 8.81 (s, 3H), 7.17 (d, J = 7.5 Hz, 6H), 7.13 (d, J = 7.5 Hz, 6H), 7.06 (d, J = 7.5 Hz, 6H), 6.96 (d, J = 7.5 Hz, 6H), 6.91 (s, 6H), 6.81 (t, 6H), 6.72 (s, 3H), 6.65 (t, 6H), 3.75 (bs, 30H), 3.72 (s, 6H). ^{13}C NMR ($CDCl_3$) δ 150.0, 149.9, 148.2, 141.2, 133.8, 129.7, 129.2, 129.1, 129.0, 127.0, 126.7, 126.6, 126.5, 121.5, 40.6, 32.6, 31.3, 31.0; MALDI-FAB-MS *m*/*z* 1728 (M + Na). Anal. Calcd for $C_{114}H_{96}O_{15} \cdot 4H_2O$: C, 77.1; H, 5.79. Found: C, 77.07; H, 5.84.

Measurement of Fullerene Complexation Constants. Complexation constants (K_{assoc}, M^{-1}) were determined in toluene solution with a Cary 3 UV−vis spectrometer at 25 ± 0.5 °C. One set of toluene stock solutions was prepared with a 2.0×10^{-4} M concentration of C_{60} and C_{70}. Another set of toluene stock solutions was prepared containing five different concentrations (2.0, 4.0, 6.0, 8.0, and 10.0×10^{-3} M) of the particular calixarene being measured. For each spectrophotometric determination, identical volumes of the fullerene and calixarene stock solutions were placed in the sample cell, and identical volumes of pure toluene and the calixarene stock solution were placed in the reference cell. The absorption spectra were measured for both C_{60} and C_{70} for each of the five calixarene concentrations. The absorption of a solution of C_{60} in toluene increased in the 400−450 nm region upon the addition of tricalix[5]arene **14**, and the color changed from magenta to red, indicating the formation of a complex. Similarly, the absorption of a solution of C_{70} increased in the 400−450 nm region upon the addition of **14**, and the color changed from red to colorless, again indicating the formation of a complex. The wavelengths for the maximum intensity changes were selected as 430 nm for C_{60} and 420 nm for C_{70}. From the absorption intensities at these wavelengths, along with the concentrations of the host, the complexation constants were calculated using the Benesi−Hildebrand equation.[10]

Acknowledgment. We are indebted to the National Science Foundation and the Robert A. Welch Foundation for generous support of this research and to the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry for the mass spectral analyses.

JO0110808

(10) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703.