Calixarene Anhydrides as Useful Synthetic Intermediates[1]

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The introduction of functionality into calixarenes continues to be one of the major goals in the rapidly expanding chemistry of the these compounds,[2] and a number of methods have been devised for the synthesis of calixarenes containing two or more different functional groups on the upper rim.[3] The present work adds to this list, making use of calixarene anhydrides for achieving this goal.

The starting compound for these syntheses is 5,17-bis(cyanomethyl)-11,23-di-*tert*-butylcalix[4]arene-25,26,-27,28-tetrol (**1**),[4] prepared by the quinone methide route.[5] Brosylation of **1** (*i.e.*, treatment with *p*-bromobenzenesulfonyl chloride) to give **2** was chosen to fix the calix[4]arene in the cone conformation, because benzylation is known to also involve the α-carbons of the cyanomethyl groups.[6] Acid-catalyzed hydrolysis of the cyano groups of **2** proceeds smoothly to yield the dicarboxylic acid **3** without disruption of the brosylate moieties (Scheme 1). Treatment of **3** with oxalyl chloride leads to the diacid chloride **5**, the anhydride **4**, or a mixture thereof depending on the reaction conditions. If oxalyl chloride is used as both reagent and solvent the diacid chloride **5** is obtained in 95% yield along with a small amount of anhydride. However, if a dilute solution of **3** (lower than 0.01 M) in CH_2Cl_2 is treated with oxalyl chloride the anhydride **4** is obtained in quantitative yield.

The anhydride **4** is stable at room temperature and undergoes only very slow decomposition upon standing in a humid atmosphere. However, it reacts smoothly with a variety of nucleophiles such as alcohols to give half esters **6a**−**d**, and amines to give half amides **7a**−**e**. A particularly useful aspect of the latter is the reaction of **4** with α-amino esters to give calixarenes carrying a chiral moiety on the upper rim. For example, (*R*)-(−)-2-phenylglycine methyl ester hydrochloride reacts with **4** in the presence of Et_3N in refluxing CH_2Cl_2 to afford a 95% yield of the half amide **8a**, a compound in which groups that are ^{1}H NMR-equivalent in **7a**−**e** (*e.g.*, methylenes, *tert*-butyls) now become diastereotopic, as reflected in the increased multiplicity of the ^{1}H NMR spectrum. In a similar fashion, other amino acid moieties can be introduced onto the top rim of the calixarene to give, for example, **8b** and **8c.**

The carboxyl groups in **6**−**8** can, in turn, be converted to other functional groups, *e.g.*, esters and amides, to produce a variety of difunctionalized calixarenes. This has been explored in two particular cases, one in which the second group is both structurally and stereochemically identical with the first and the other in which the second group is structurally identical but stereochemically enantiomeric with the first. Thus, introduction of a second phenylglycine methyl ester moiety into **8a**, using the dicyclohexylcarbodiimide method for amide formation from a carboxylic acid and an amine, yields the (*R,R*) compound **9a** when the (*R*)-(−) enantiomer of the α-amino ester is used and the (*R,S*) compound **9b** when its (*S*)-(+) enantiomer is used. The ^{1}H NMR spectra of **9a** and **9b** present an interesting comparison (Figure 1). The optically active (*R,R*) compound **9a** contains a C_2 symmetry axis. The methylene groups of the calixarene ring in **9a** labeled 1 and 3 are equivalent; those labeled 2 and 4 are equivalent; but, the 1,3-set is diastereotopic with the 2,4-set. As a consequence, two sets of pairs of doublets are observed in the ^{1}H NMR spectrum arising from the $ArCH_2Ar$ groups, one centered near δ 3.75 and the other at δ 2.47. Similarly, the CH_2CONH methylene groups are equivalent but their hydrogens are diastereotopic, giving rise to a pair of very close-lying doublets at δ 2.87. The CO_2Me groups are equivalent and appear as a sharp singlet at δ 3.69, and the *p*-*tert*-butyl groups also are equivalent and appear as a singlet at δ 1.22. The optically inactive (*R,S*) compound **9b** is a *meso* structure with a plane of symmetry. The methylene groups of the calixarene ring in **9b** labeled 1 and 2 are enantiotopic; those labeled 3 and 4 are enantiotopoic; but, the 1,2 -set is diastereotopic with the 3,4-set. Thus, just as with the (*R,R*) compound, two sets of doublets are observed at δ 3.73 and 2.48. The CH_2CONH groups are enantiotopic, but their hydrogens are diastereotopic and should appear as a pair of doublets. The apparent singlet at δ 2.86 must, therefore, be the result of accidental overlap. In contrast to **9a**, the *tert*-butyl groups in **9b** are not equivalent but are diastereotopic, and a pair of singlets is observed at δ 1.26 and 1.20.

The bisanhydride, prepared[7] from the 1,3-alternate conformer of the tetrabenzyl ether of *p*-(carboxymethyl)-calix[4]arene, forms much less easily than does the monoanhydride **4**. The reactions of the bisanhydride will be described in a subsequent paper.

Experimental Section[8]

5,17-Bis(cyanomethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (2). To a solution of 2.15 g (3.5 mmol) of 5,17-bis(cyanomethyl)-11,23-

(1) Calixarenes. 46. Part 45: Sharma, S. K.; Gutsche, C. D. *J. Org. Chem.* **1996**, *61*, 2511.

(2) Böhmer, V. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713. Gutsche, C. D. *Aldrichim. Acta* **1995**, *28*, 3. *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Böhmer, V., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, 1991. Gutsche, C. D. Calixarenes. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989.

(3) *(3) Cf.* for example: Timmerman, P.; Verboom, W.; Reinhoudt, D. N.; Arduini, A.; Grandi, S.; Sicuri, A. R.; Pochini, E.; Ungaro, R. *Synthesis* **1994**, 185. Shu, C.-m.; Yuan, T.-s.; Ku, M.-c.; Ho, Z.-c.; Liu, W.-c.; Tang, F.-s.; Lin, L.-g. *Tetrahedron* **1996**, *52*, 9805. For a review of the prior literature *cf.*: van Loon, J.-D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proced. Int.* **1992**, *24*, 437.

(4) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1995**, *60*, 6070.

(5) Gutsche, C. D.; Nam, K. C. *J. Am. Chem. Soc.* **1988**, *110*, 6153.

(6) Sharma, S. K.; Gutsche, C. D. *Tetrahedron Lett.* **1993**, *34*, 5389; *Tetrahedron* **1994**, *50*, 4087.

(7) Sharma, S. K.; Gutsche, C. D. Unpublished observations.

(8) 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 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. ^{1}H NMR and ^{13}C NMR spectra[9] were recorded on a Varian XL-300 spectrometer at 300 and 75 MHz, respectively. TLC analyses were carried out on Analtech silica gel plates (absorbent thickness 250 μm) containing a fluorescent indicator. Chromatography was carried out with J. T. Baker silica gel no. JT7042-2 (40−64 μm particles) on columns filled to a height of *ca.* 6 in. Elution rates were 2 in./min. Analytical samples were dried at least 36 h at 100−140 °C and 1−2 mmHg of pressure.

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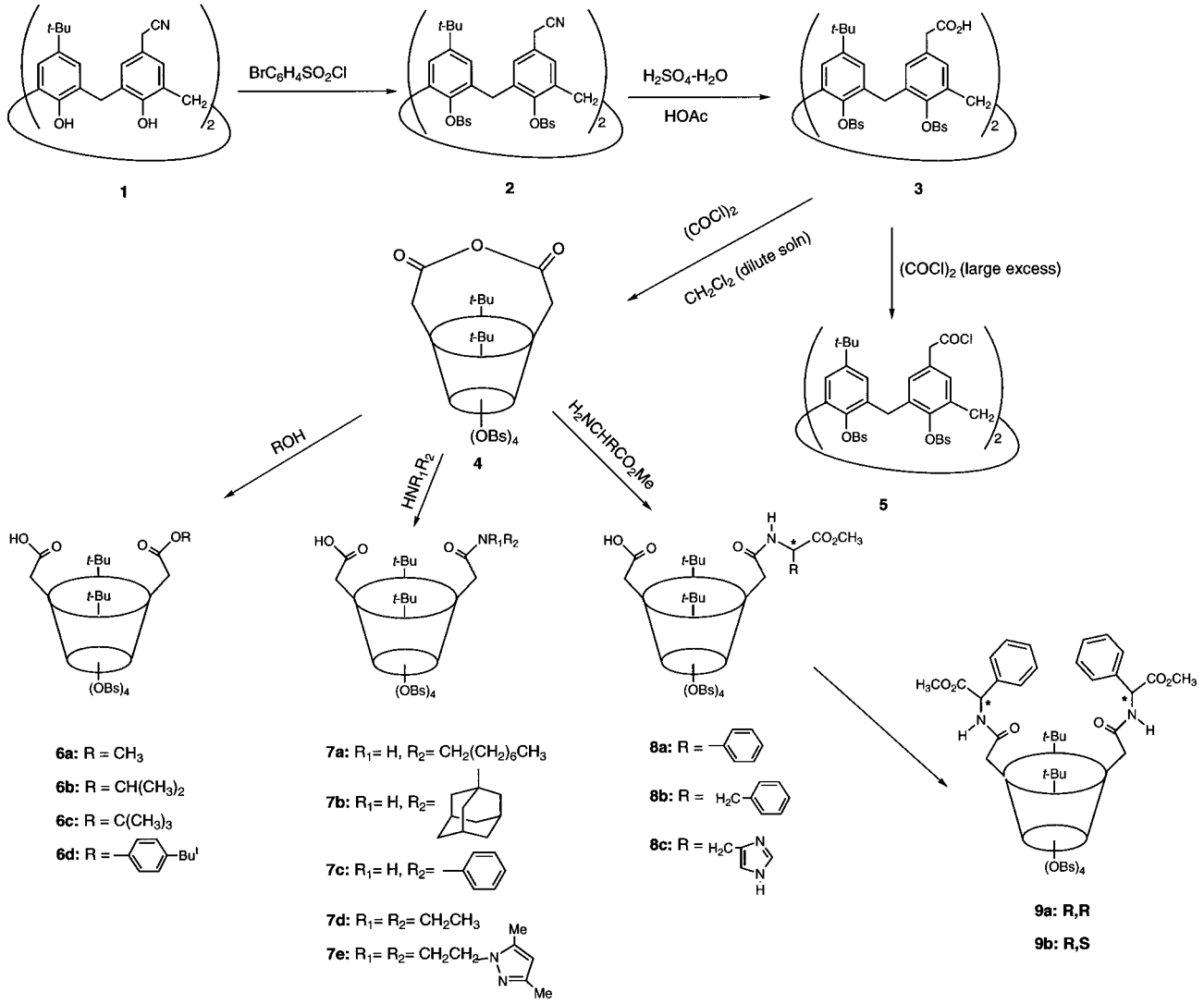
Scheme 1



di-*tert*-butylcalix[4]arene-25,26,27,28-tetrol (**1**) in 100 mL of THF was added 2.25 g of NaH (60% oil dispersion, 56 mmol). The reaction mixture was stirred for 30 min, treated with 4.48 g (18.2 mmol) of *p*-bromobenzenesulfonyl chloride, and allowed to stir at rt for 3 h. The solvent was removed under vacuum, and the residue was treated with 80 mL of $CHCl_3$ and poured into 80 g of crushed ice. The organic layer was separated, washed with H_2O and brine, and dried over Na_2SO_4 and the solvent removed by evaporation, leaving a residue that was triturated with hexane and recrystallized from CH_2Cl_2−MeOH to give 4.5 g (87%) of **2** as white crystals: mp 280−281.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.93 (d, 4, J = 8.5 Hz), 7.80 (d, 4, J = 8.6 Hz), 7.66 (m, 8), 7.04 (s, 4), 6.08 (s, 4), 3.80 (d, 4, J = 14.3 Hz), 3.26 (s, 4), 2.54 (d, 4, J = 14.5 Hz,), 1.35 (s, 18); ^{13}C NMR ($CDCl_3$) δ 150.46, 143.58, 143.46, 135.60, 134.54, 134.44, 134.17, 132.87, 132.39, 131.24, 130.60, 129.70, 129.37, 127.87, 127.81, 127.18, 117.72, 34.49 , 31.46 , 31.30, 22.87 Anal. Calcd for $C_{64}H_{54}N_2O_{12}Br_4S_4$: C, 51.55; H, 3.62. Found: C, 51.63; H, 3.69.

5,17-Bis(carboxymethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (3). A suspension of 2 g of **2** in 30 mL of HOAC, 3 mL of concd H_2SO_4, and 3 mL of H_2O was refluxed for 24 h, the solution clearing after 3 h but then depositing a precipitate after 12 h. The mixture was cooled to rt, and 40 mL of cold water was added. The white precipitate was collected by suction filtration and dried to give a quantitative yield of **3**. An analytical sample was obtained by recrystallization from CH_2Cl_2−hexane: mp > 307 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.96 (d, 4, J = 8.7 Hz), 7,83 (d, 4, J = 8.6 Hz), 7.62 (d, 4, J = 8.6 Hz), 7.54 (d, 4, J = 8.6 Hz), 7.05 (s, 4), 6.57 (s, 4), 3.92 (d, 4, J = 13.8 Hz), 3.03 (s, 4), 2.57 (d, 4, J = 14.0 Hz), 1.30 (s, 18); ^{13}C NMR ($CDCl_3$ + 1 drop of DMSO-d_6) δ 172.6, 149.5, 142.8, 142.6, 134.9, 134.3, 134.0, 133.8, 132.4, 132.1, 132.0, 130.9, 130.5, 129.1, 129.0, 126.4, 40.1, 34.1, 31.0; IR (KBr) 1712.9 cm^{-1} (CO_2H). Anal. Calcd for $C_{64}H_{56}O_{16}Br_4S_4$: C, 50.28; H, 3.69. Found: C, 50.58; H, 3.75.

Anhydride of 5,17-Bis(carboxymethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (4). A 0.46 g (0.3 mmol) sample of **3** in 30 mL of dry CH_2Cl_2 containing 1 mL of $(COCl)_2$ (11.5 mmol) was refluxed under N_2 for 2 h. Evaporation of the solvent and excess $(COCl)_2$ gave a white solid in quantitative yield. An analytical sample of **4** was obtained by recrystallization from CH_2Cl_2−hexane: mp 305−306.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.95 (d, 4, J = 8.6 Hz), 7.82 (d, 4, J = 8.2 Hz), 7.59−7.68 (4 lines, 8), 7.02 (s, 4), 6.00 (s, 4), 3.81 (d, 4, J = 14.2 Hz), 3.18 (s, 4), 2.51 (d, 4, J = 14.5 Hz), 1.35 (s, 18); ^{13}C NMR ($CDCl_3$) δ 165.3, 150.2, 143.6, 143.0, 135.7, 134.5, 134.2, 132.9, 132.8, 132.4, 132.3, 131.3, 130.6, 129.6, 129.3, 128.9, 127.0 (Ar: Calcd, 16; found, 16), 42.0, 34.4, 31.4, 31.3 (sp^3: Calcd, 4; found, 4); IR (KBr) 1714.8, 1760.0 cm^{-1} (CO). Anal. Calcd for $C_{64}H_{54}O_{15}Br_4S_4$: C, 50.87; H, 3.60. Found: C, 50.89; H, 3.68.

5,17-Bis[(chlorocarbonyl)methyl]-11,23-di-*tert*-butyl-25,-26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]-arene (5). A 0.23 g (0.15 mmol) sample of **3** in 15 mL of $(COCl)_2$

(9) For the ^{13}C NMR spectra of compounds **4**−**9** the calculated and found numbers of aromatic carbons and sp^3 carbons are included in parantheses. In all cases but one, the number of lines found is equal to or less than the calculated value, ascribable to accidental overlaps. In the case of **7c** one more Ar line than the calculated number appears, the reason for this being unknown.

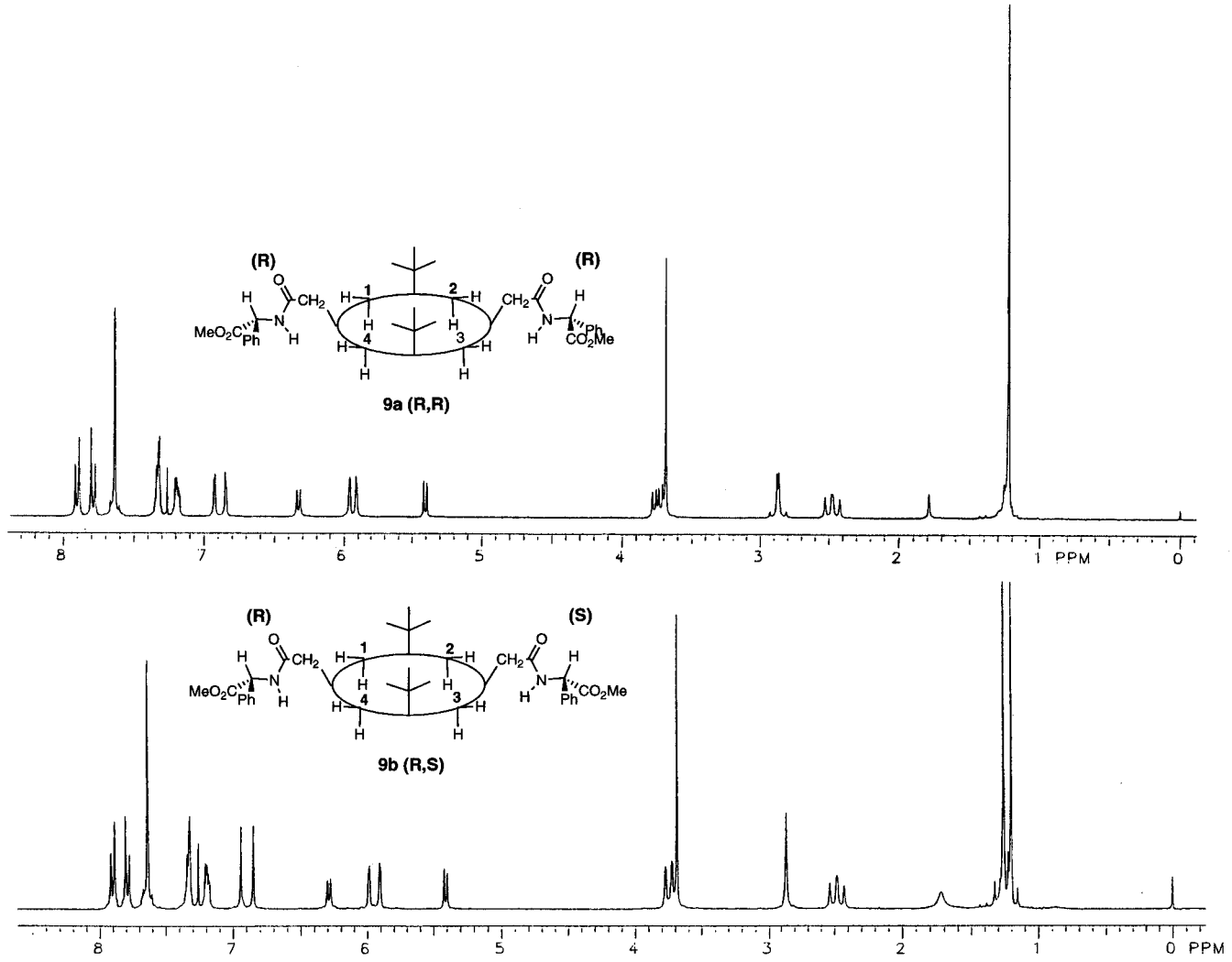


Figure 1. ^{1}H NMR spectra of **9a** and **9b** in $CDCl_3$ at 300 MHz at room temperature.

was refluxed under N_2 for 2 h. Evaporation of the $(COCl)_2$ furnished the diacid chloride **5** as a pale yellow solid in quantitative yield. The product decomposes to the diacid **3** on prolonged storage in the atmosphere: ^{1}H NMR ($CDCl_3$) δ 7.88 (d, 4, J = 8.5 Hz), 7.79 (d, 4, J = 8.6 Hz), 7.64 (d + d, 8, J = 8.5 Hz and 8.2 Hz), 6.92 (s, 4), 6.26 (s, 4), 3.83 (d, 4, J = 14.0 Hz), 3.59 (s, 4), 2.52 (d, 4, J = 14.4 Hz), 1.25 (s, 18); ^{13}C NMR ($CDCl_3$) δ 170.9, 150.1, 143.5, 143.1, 135.0, 134.7, 134.4, 134.0, 132.8, 132.4, 131.2, 130.8, 129.7, 129.6, 129.4, 129.0, 126.8 (Ar: Calcd, 16; found, 16) , 52.0, 34.4, 31.3 (sp^3: Calcd 4; found 3); IR (KBr) 1796 (CO) cm^{-1}.

5-(Carboxymethyl)-17-[(methoxycarbonyl)methyl]-11,-23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)-sulfonyl]oxy]calix[4]arene (6a). A 0.151 g (0.1 mmol) sample of the anhydride **4** was dissolved in 15 mL of CH_2Cl_2. A few drops of MeOH (excess) were added, and the solution was stirred at rt for 3 h. Removal of the solvent gave a quantitative yield of the **6a** as a white solid: mp 180−182 °C; ^{1}H NMR ($CDCl_3$) δ 7.87 (d, 4, J = 8.7 Hz), 7.77 (d, 4, J = 8.7 Hz), 7.67 (m, 8), 6.91 (d, 2, J = 2.4 Hz), 6.98 (d, 2, J = 2.4 Hz), 6.26 (s, 2), 6.14 (s, 2), 3.80 (d + d, 4, J = 14.0 Hz and 14.1 Hz), 3.66 (s, 3), 3.00 (s, 2), 2.51 (d + d, 4, J = 14.1, 14.0 Hz), 1.25 (s, 18); ^{13}C NMR ($CDCl_3$) δ 172.8, 149.8, 143.1, 142.8, 142.7, 135.2, 134.5, 134.3, 134.2, 134.1, 132.7, 132.3, 131.6, 131.3, 131.2, 130.9, 130.8, 129.6, 129.5, 129.3, 128.2, 126.8, 126.6 (Ar: Calcd, 24; found, 22), 52.3, 40.3, 39.3, 34.4, 31.3, 31.2 (sp^3 Calcd, 7; found, 6); IR (KBr) 1739.9 (CO_2Me), 1718.7 cm^{-1} (CO_2H). Anal. Calcd for $C_{65}H_{58}O_{16}Br_4S_4$: C, 50.60; H, 3.79. Found: C, 50.41, H, 3.80.

5-(Carboxymethyl)-17-[(isopropoxycarbonyl)methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)-sulfonyl]oxy]calix[4]arene (6b). A suspension of 0.151 g (0.1 mmol) of **4** in 10 mL of 2-propanol was refluxed for 2 h, the solution becoming clear after 0.5 h. Upon cooling, 0.15 g (95%) of **6b** precipitated as white crystals: mp 180−182 °C; ^{1}H NMR ($CDCl_3$) δ 7.88 (d, 4, J = 8.7 Hz), 7.78 (d, 4, J = 8.6 Hz), 7.60−7.67 (m, 8), 6.95 (d, 2, J = 2.3 Hz), 6.90 (d, 2, J = 2.2 Hz), 6.23 (s, 2), 6.10 (s, 2), 4.98 (5 peaks, 1, J = 6.3 Hz), 3.80 (d + d, 4, J = 14.0 Hz), 3.16 (s, 2), 2.96 (s, 2), 2.50 (dd, 4, J = 14.0 Hz), 1.26 (s, 18), 1.21 (d, 6, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 172.8, 172.1, 149.8, 143.1, 142.7, 142.5, 135.4, 135.3, 134.5, 134.2, 134.1, 134.0, 132.7, 132.3, 132.2, 131.6, 131.2, 130.9, 130.8, 129.6, 129.5, 129.4, 129.3, 128.0, 126.8, 126.6 (Ar: Calcd, 24; found, 24), 68.9, 40.5, 39.6, 34.3, 31.3, 31.2, 21.7 (sp^3: Calcd, 8; found, 7). Anal. Calcd for $C_{67}H_{62}O_{16}Br_4S_4$: C, 51.22; H, 3.98. Found: C, 51.12; H, 4.13.

5-(Carboxymethyl)-17-[(*tert*-butoxycarbonyl)methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)-sulfonyl]oxy]calix[4]arene (6c) was prepared by the procedure described for **6b**, with *tert*-butyl alcohol and 12 h reflux, and was obtained in 92% yield as white crystals: mp >180 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.89 (d, 4, J = 8.6 Hz), 7.79 (d, 4, J = 8.6 Hz), 7.56−7.66 (m, 8), 6.97 (d, 2, J = 2.3 Hz), 6.92 (d, 2, J = 2.3 Hz), 6.24 (s, 2), 6.10 (s, 2), 3.82 (d + d, 4, J = 14.2, 14.3 Hz), 3.18 (s, 2), 2.94 (s, 2), 2.50 (d + d, 4, J = 14.0, 14.1 Hz), 1.44 (s, 9), 1.28 (s, 18); ^{13}C NMR($CDCl_3$) δ 172.9, 171.2, 149.9, 143.2, 142.5, 135.4, 134.6, 134.3, 134.2, 133.9, 133.7, 132.8, 132.2, 132.1, 132.0, 131.2, 130.9, 130.8, 129.7, 129.5, 129.4, 129.2, 127.7, 126.9, 126.6 (Ar: Calcd, 24; found, 23), 82.3, 40.7, 40.1, 34.4, 31.4, 31.2, 28.0 (sp^3: Calcd, 8; found 7). Anal. Calcd for $C_{67}H_{64}O_{16}Br_4S_4$: C, 51.16; H, 4.10; Found: C, 51.26; H, 4.04.

5-(Carboxymethyl)-17-[[(*p*-*tert*-butylphenoxy)carbonyl]-methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (6d). A mixture of 0.30 g (0.2 mmol) of the anhydride **4**, 0.034 g (0.22 mmol) of *p*-*tert*-butylphenol, 1 drop of Et_3N, and 20 mL of CH_2Cl_2 was

refluxed for 12 h. The mixture was cooled, washed with 0.2 N HCl, water, and brine, and dried over Na_2SO_4 and the solvent removed by evaporation, leaving a residue that was chromotographed (eluant 4% acetone−CH_2Cl_2 (v/v)) to give 0.30 g (90%) of **6d** as a white solid: mp > 170 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.88 (d, 4, J = 8.6 Hz), 7.78 (d, 4, J = 8.7 Hz), 7.64 (m, 8), 7.38 (d, 2, J = 8.7 Hz), 6.90 (m, 6), 6.20 (s, 4), 3.81 and 3.80 (dd, 4, J = 14.1 Hz), 3.34 (s, 2), 2.96 (s, 2), 2.51 (d, 4, J = 14.5 Hz), 1.32 (s, 9), 1.20 (s, 18); ^{13}C NMR ($CDCl_3$) δ 173.8, 170.3, 149.8, 149.1, 147.9, 143.1, 143.0, 142.9, 135.3, 135.2, 134.4, 134.2, 132.7, 132.3, 131.2, 131.0, 130.8, 130.6, 129.5, 129.4, 129.3, 128.6, 126.8, 126.6, 126.3, 120.4 (Ar: Calcd, 28; found, 24), 40.1, 39.7, 34.5, 34.3, 31.3, 31.2 (sp^3: Calcd, 8; found, 6). Anal. Calcd for $C_{74}H_{68}O_{16}Br_4S_4$: C, 53.50; H, 4.13. Found: C, 53.86; H, 4.18.

5-(Carboxymethyl)-17-[[(*N*-octylamino)carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (7a). To a solution of 0.30 g (0.2 mmol) of the anhydride **4** in 15 mL of dry CH_2Cl_2 was added 0.029 g (0.22 mmol) of octylamine. The reaction mixture was refluxed for 6 h, cooled, washed with 0.2 N HCl, water, and brine, and dried over Na_2SO_4 and the solvent removed by evaporation to give 0.3 g (92%) of **7a** as a white solid: mp > 210 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 4, J = 8.6 Hz), 7.81 (d, 4, J = 8.7 Hz), 7.48−7.68 (m, 8), 6,98 (d, 2, J = 2.1 Hz), 6.94 (d, 2, J = 2.1 Hz), 6.23 (s, 2), 6.06 (s, 2), 5.77 (br t, 1), 3.92 (d, 2, J = 14.0 Hz), 3.70 (d, 2, J = 14.0 Hz), 3.24 (m, 4), 2.89 (s, 2), 2.56 (d, 2, J = 14.0 Hz), 2.43 (d, 2, J = 14.1 Hz), 1.25−1.52 (m, 30), 0.89 (t, 3, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.9, 150.0, 143.2, 142.0, 141.8, 135.4, 134.6, 134.4, 133.9, 133.7, 133.0, 132.9, 132.8, 132.6, 132.2, 132.1, 131.2, 130.8, 130.7, 129.8, 129.5, 129.2, 127.2, 127.1, 126.7 (Ar: Calcd, 24; found, 24), 41.5, 40.2, 39.9, 34.4, 31.8, 31.3, 31.26, 31.1, 29.3, 29.2, 26.8, 22.6, 14.1 (sp^3: Calcd, 14; found 13); IR (KBr) 1734.1 (CO_2H), 1722.5 (sh), 1624.2 cm^{-1} (CONHR). Anal. Calcd for $C_{72}H_{73}NO_{15}Br_4S_4$: C, 52.72; H, 4.49. Found: C, 52.68; H, 4.48.

5-(Carboxymethyl)-17-[[(*N*-adamantylamino)carbonyl]-methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (7b) was prepared in 90% yield following the procedure described above for **7a** using 1-adamantanamine. An analytical sample of **7b** was obtained as white crystals by recrystallization from CH_2Cl_2−hexane: mp >200 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.90 (d, 4, J = 8.7 Hz), 7.80 (d, 4, J = 8.7 Hz), 7.73 (d, 2, J = 8.8 Hz), 7.66 (d, 2, J = 8.8 Hz), 7.61 (d, 2, J = 8.6 Hz), 7.48 (d, 2, J = 8.7 Hz), 7.01 (d, 2, J = 2.3 Hz), 6.97 (d, 2, J = 2.4 Hz), 6.22 (s, 2), 6.01 (s, 2), 5.31 (s, 1), 3.97 (d, 2, J = 14.0 Hz), 3.70 (d, 2, J = 14.1 Hz), 3.20 (s, 2), 2.88 (s, 2), 2.60 (d, 2, J = 14.0 Hz), 2.43 (d, 2, J = 14.1 Hz), 2.11 (br, 3), 2.00 (br, 3), 2.00 (bt, 6), 1.69 (br, 3), 1.33 (s, 18); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.6, 150.1, 143.2, 141.9, 141.6, 135.6, 135.5, 134.7, 134.5, 134.0, 133.8, 133.0, 132.7, 132.1, 131.2, 130.9, 130.7, 129.8, 129.4, 129.1, 127.1, 126.6 (Ar: Calcd, 24; found, 21), 52.8, 41.6, 41.3, 41.0, 36.1, 34.4, 31.5, 31.2, 31.17, 29.3 (sp^3: Calcd, 10; found, 10); IR (KBr) 1714.8 (CO_2H), 1630 cm^{-1} (CONHR). Anal. Calcd for $C_{74}H_{71}NO_{15}Br_4S_4$: C, 53.47; H, 4.31. Found: C, 53.56; H, 4.42.

5-(Carboxymethyl)-17-[[(*N*-phenylamino)carbonyl]-methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (7c) was prepared in 90% yield following the procedure described above for **7a**, using aniline and a 16 h reflux time. An analytical sample of **7c** was obtained as a white solid by column chromotography using 1.5% MeOH−$CHCl_3$ as eluent: mp >175 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.95 (s, 1), 7.88 (d, 4, J = 8.7 Hz), 7.79 (d, 4, J = 8.6 Hz), 7.59−7.73 (m, 8), 7.48 (dd, 2, J = 7.4, 8.6 Hz), 7.32 (dd, 2, J = 7.6, 8.0 Hz), 7.17 (t, 1, J = 7.4 Hz), 6.99 (d, 2, J = 2.2 Hz), 6.90 (d, 2, J = 2.2 Hz), 6.23 (s, 2), 6.11 (s, 2), 3.95 (d, 2, J = 14.2 Hz), 3.68 (d, 2, J = 14.2 Hz), 3.34 (s, 2), 2.93 (s, 2), 2.57 (d, 2, J = 14.0 Hz), 2.44 (d, 2, J = 14.4 Hz), 1.28 (s, 18); ^{13}C NMR ($CDCl_3$) δ 172.2, 170.6, 150.1, 143.1, 142.0, 141.9, 136.9, 135.5, 135.4, 134.5, 134.2, 134.1, 133.9, 133.2, 132.7, 132.6, 132.3, 132.1, 131.2, 130.8, 130.7, 129.7, 129.6, 129.5, 129.2, 129.0, 127.3, 127.0, 126.7, 125.2, 120.1 (Ar: Calcd, 28; found, 29), 41.3, 41.2, 34.3, 31.3, 31.2, 31.1 (sp^3: Calcd, 6; found 6); IR (KBr) 1719 (CO_2H), 1601 cm^{-1} ($CONR_2$). Anal. Calcd for $C_{70}H_{61}O_{15}NBr_4S_4$: C. 52.41; H, 3.83. Found: C, 52.74; H, 3.90.

5-(Carboxymethyl)-17-[[(*N*,*N*-diethylamino)carbonyl]-methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (7d) was prepared in 95% yield according to the procedure described for **7a**, using diethylamine and a reflux time of 3 h, and obtained as a colorless solid: mp 273.5−275.5 °C; ^{1}H ($CDCl_3$) δ 7.93 (d, 4, J = 8.7 Hz), 7.82 (d, 4, J = 8.7 Hz), 7.50−7.64 (m, 8), 7.03 (d, 2, J = 2.3 Hz), 6.95 (d, 2, J = 2.3 Hz), 6.25 (s, 2), 6.01 (s, 2), 3.93 (d, 2, J = 14.1 Hz), 3.74 (d, 2, J = 14.0 Hz), 3.38 (m, 4), 3.01 (q, 2, J = 7.0 Hz), 2.92 (s, 2), 2.53 (d, 2, J = 14.1 Hz), 2.47 (d, 2, J = 14.4 Hz), 1.33 (s, 18), 1.17 (t, 3, J = 7.0 Hz), 1.02 (t, 3, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 172.5, 171.5, 150.1, 143.2, 141.9, 135.6, 135.4, 134.7, 134.3, 134.1, 133.9, 133.1, 133.0, 132.8, 132.3, 132.0, 131.2, 130.8, 130.7, 129.8, 129.4, 129.2, 127.1, 127.0, 126.6 (Ar: Calcd, 24; found, 23), 42.6, 41.7, 40.2, 36.7, 34.4, 31.5,31.2, 31.3 (sp^3: Calcd, 10; found 8); IR (KBr) 1718 (CO_2H), 1604.9 cm^{-1} ($CONR_2$). Anal. Calcd for $C_{68}H_{65}O_{15}NBr_4S_4$: C, 51.56; H, 4.14. Found: C, 51.56; H, 4.16.

5-(Carboxymethyl)-17-[[*N*,*N*-bis[2-(3,5-dimethylpyrazolyl)-ethyl]amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,-27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]-arene (7e) was prepared in 95% yield following the procedure described for **7a**, using bis[2-(3,5-dimethyl-1-pyrazoyl)ethyl]-amine[10] and a reflux time of 3 h. An analytical sample of **7e** was obtained as a white solid by recrystallization from CH_2Cl_2−MeOH: mp >180 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.94 (d, 4, J = 8.7 Hz), 7.81 (d, 4, J = 8.5 Hz), 7.56−7.65 (m, 8), 6.97 (d, 2, J = 2.2 Hz), 6.95 (d, 2, J = 2.2 Hz), 6.11 (s, 2), 5.88 (s, 2), 5.80 (s, 2), 4.08 (t, 2, J = 5.6 Hz), 3.84 (d, 2, J = 14.4 Hz), 3.66−3.80 (m, 6), 3.10 (t, 2, J = 7.4 Hz), 3.00 (s, 4), 2.51 (d + d, 4, J = 14.4 Hz), 2.23 (s, 3) 2.182 (s, 3), 2.178 (s, 3), 1.88 (s, 3), 1.23 (s, 18); ^{13}C NMR ($CDCl_3$) δ 172.0, 171.9, 149.7, 148.1, 148.0, 143.6, 142.5, 142.2, 140.4, 139.4, 135.9, 135.8, 134.7, 134.3, 133.5, 133.1, 132.9, 132.8, 132.2, 132.1, 131.8, 131.2, 130.7, 129.4, 129.2, 129.1, 128.9, 126.9, 126.8, 105.8, 105.0 (Ar: Calcd, 30; found, 29), 48.8, 47.7, 45.6, 45.3, 39.8, 37.3, 34.3, 31.5, 31.4, 31.2, 13.5, 12.8, 10.6 and 10.5 (sp^3: Calcd 14; found, 14); IR (KBr) 1718.7 (CO_2H), 1653.1 cm^{-1} ($CONR_2$). Anal. Calcd for $C_{78}H_{77}O_{15}N_5Br_4S_4$: C, 52.86; H, 4.38. Found: C, 53.02; H, 4.46.

5-(Carboxymethyl)-17-[[[*N*-[(carbomethoxyphenyl)-methyl]amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,-27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]-arene (8a). A mixture of 0.60 g (0.4 mmol) of anhydride **4**, 0.088 g (0.44 mmol) of (*R*)-(−)-2-phenylglycine methyl ester hydrochloride, 0.1 g of Et_3N, and 20 mL of CH_2Cl_2 was refluxed for 3 h. The mixture was cooled and washed with 0.2 N HCl (2 × 3 mL), water, and brine and the solvent removed by evaporation to give 0.64 g (95%) of **8a** as a white solid: mp > 172 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.94 (d, 4, J = 8.7 Hz), 7.82 (d, 4, J = 8.7 Hz), 7.68 (s, 4), 7.62 (d, 2, J = 8.2 Hz), 7.53 (d, 2, J = 8.6 Hz), 7.36−7.41 (m, 3). 7.24−7.26 (m, 2), 7.0 (d + d, 2, J = 2.3 Hz), 6.93 (d, 1, J = 2.3 Hz), 6.88 (d, 1, J = 7.0 Hz), 6.51 (d, 1, J = 2.3 Hz), 6.24 (d, 1, J = 2.2 Hz), 6.15 (d, 1, J = 2.3 Hz), 6.05 (d, 1, J = 2.2 Hz), 5.79 (d, 1, J = 2.0 Hz), 5.53 (d, 1, J = 7.0 Hz), 3.92 (d, 1, J = 13.7 Hz), 3.89 (d, 1, J = 13.9 Hz), 3.73 (s, 3), 3.71 (d, 1, J = 14.4 Hz), 3.57 (d, 1, J = 14.2 Hz), 3.36 (d, 1, J = 16.7 Hz), 3.20 (d, 1, J = 16.2 Hz), 2.98(d, 1, J = 13.4), 2.81 (d, 1, J = 13.4 Hz), 2.65 (d, 1, J = 14.5 Hz), 2.50 (d, 1, J = 14.5 Hz), 2.39 (d, 1, J = 14.0 Hz), 2.25 (d, 1, J = 14.0 Hz), 1.32 (s, 9), 1.16 (s, 9); ^{13}C NMR ($CDCl_3$) δ 172.1, 171.6, 171.4, 149.9, 143.2, 142.2, 142.1, 135.5, 135.4, 135.3, 134.6, 134.3, 134.1, 134.0, 133.8, 133.25, 133.18, 132.8, 132.4, 132.2, 132.1, 131.7, 131.3, 130.8, 130.7, 129.6, 129.4, 129.2, 129.1, 128.7, 127.6, 127.4, 127.0, 126.8, 126.7 (Ar: Calcd, 40; found, 32), 53.2, 52.6, 41.1, 40.3, 37.7, 34.4, 31.4, 31.3, 31.2, 31.0 (sp^3: Calcd, 12; found, 10); IR (KBr) 1740.0 (CO_2-Me), 1686.5 (CO_2H), 1637.7 cm^{-1} (CONHR). Anal. Calcd for $C_{73}H_{65}O_{17}NBr_4S_4$: C, 52.31; H, 3.91. Found: C, 52.12; H, 3.86.

5-(Carboxymethyl)-17-[[[*N*-[(carbomethoxybenzyl) methyl]amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,-27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]-arene (8b) was prepared by the procedure described for **8a**, using L-phenylalanine methyl ester hydrochloride, and was obtained in 95% yield as a white solid: mp > 160 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.90−7.93 (4 lines, 4), 7.78−7.82 (4 lines, 4), 7.52−7.63 (5 lines, 8), 7.27 (m, 3), 7.01 (m, 4), 6.93 (d, 1, J = 2.2 Hz), 6.90 (d, 1, J = 2.2 Hz), 6.21 (s, 2), 6.13 (d, 1, J = 7.0 Hz), 6.02 (s, 1), 5.96 (s, 1), 4.84 (m, 1), 3.71−3.91 (m, 7), 3.01−3.23 (m, 4), 2.90 (s, 2), 2.44−2.56 (m, 4), 1.314 (s, 9), 1.307 (s, 9); ^{13}C

(10) Sorrell, T. N.; Malachowski, M. R. *Inorg. Chem.* **1983**, *22*, 1883.

NMR ($CDCl_3$) δ 172.1, 171.6, 171.4, 149.9, 143.2, 142.2, 142.1, 135.5, 135.4, 135.3, 134.6, 134.3, 134.1, 134.0, 133.8, 133.2, 132.8, 132.4, 132.2, 132.1, 131.7, 131.3, 130.8, 130.7, 129.6, 129.4, 129.2, 129.1, 128.7, 127.6, 127.4, 127.0, 126.8, 126.7 (Ar: Calcd, 40; found, 31), 53.2, 52.6, 41.1, 40.3, 37.7, 34.3, 31.4, 31.3, 31.2, 31.0 (sp^3: Calcd, 13; found, 10). Anal. Calcd for $C_{74}H_{67}O_{17}NBr_4S_4$: C, 52.59; H, 4.0. Found: 52.41; H, 4.05.

5-(Carboxymethyl)-17-[[[*N*-(1-carbomethoxy-2-imidazolylethyl)amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (8c). A mixture of 0.5 g (0.34 mmol) of the anhydride **4**, 0.096 g (0.40 mmol) of L-histidine methyl ester dihydrochloride, 0.16 g of Et_3N, and 20 mL of CH_2Cl_2 was refluxed for 3 h. The mixture was cooled and washed with 1 N HCl (2 × 2 mL), water, and brine and the solvent removed by evaporation to give a white solid. Further purification by chromatography (eluant, 5% MeOH−$CHCl_3$, v/v) followed by recrystallization from $CHCl_3$−MeOH gave 0.39 g (70%) of **8c** as white crystals: mp > 180 °C; ^{1}H NMR ($CDCl_3$) δ 8.05 (d, 1), 7.91 (m, 4), 7.79 (m, 4), 7.51−7.65 (m, 9), 7.09 (s, 1), 6.99 (s, 2), 6.93 (s, 1), 6.83 (s, 1), 6.31 (s, 1), 6.26 (s, 1), 6.14 (s, 1), 5.81(s, 1), 4.53 (m, 1), 3.94 (d, 1, J = 14.1 Hz), 3.92 (d, 1, J = 14.0 Hz), 3.69−3.74 (m, 4), 3.54 (d, 1, J = 14.5 Hz), 2.78−3.19 (m, 6), 2.26−2.60 (m, 4), 1.29 (s, 9), 1.27 (s, 9); ^{13}C NMR ($CDCl_3$) δ 173.8, 171.5, 171.0, 149.9, 149.8, 143.6, 143.5, 142.2, 141.9, 136.4, 136.2, 135.4, 135.0, 134.8, 134.7, 134.5, 134.2, 134.1, 133.5, 133.4, 133.2, 133.1, 132.74, 132.66, 132.6, 132.3, 132.2, 131.2, 130.7, 129.8, 129.5, 129.4, 129.24, 129.20, 129.1, 128.8, 128.2, 127.3, 126.5, 114.8 (Ar: Calcd, 39; found, 37), 53.8, 52.3, 40.5, 40.2, 34.3, 31.9, 31.7, 31.3, 31.2, 31.1, 28.2 (sp^3: Calcd, 13; found, 11). Anal. Calcd for $C_{71}H_{65}Br_4O_{17}N_3S_4 \cdot 1.67CHCl_3$: C, 46.45; H, 3.58. Found: C, 46.67. H, 3.68.

(*R*,*R*)-5,17-Bis[[[*N*-[(carbomethoxyphenyl)methyl]amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (9a). A 0.2 g (0.12 mmol) sample of **8a** was mixed with 0.03 g (0.18 mmol) of (*R*)-(−)-2-phenylglycine methyl ester, 0.036 g (0.18 mmol) of dicyclohexylcarbodimide, and 0.024 g (0.18 mmol) of 1-hydroxybenzotriazole in 15 mL of dry CH_2Cl_2. The mixture was stirred at rt for 1 day. After removal of the precipitate by filtration, the solution was treated with 2 mL of 0.1 N HCl, water, and brine and dried over Na_2SO_4 and the solvent removed by evaporation under reduced pressure. The residue was chromatagraphed (0.5% acetone−$CHCl_3$, v/v) and recrystallized from CH_2Cl_2−MeOH to yield 0.18 g (85%) of **9a** as tiny needles: mp 242−244 °C; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 4, J = 8.7 Hz), 7.79 (d, 4, J = 8.6 Hz), 7.64 (m, 8), 7.33 (m, 3), 7.19 (m, 2), 6.93(d, 2, J = 2.2 Hz), 6.85 (d, 2, J = 2.2 Hz), 6.33 (d, 2, J = 7.1 Hz), 5.96 (d, 2, J = 2.0 Hz), 5.92 (d, 2, J = 2.0 Hz), 5.41 (d, 2, J = 7.1 Hz), 3.76 (d, 2, J = 14.2 Hz), 3.74 (d, 2, J = 14.5 Hz), 3.69 (s, 6), 2.87 (dd, 4, J = 15.9 Hz), 2.51 (d, 2, J = 14.6 Hz), 2.45 (d, 2, J = 14.6 Hz), 1.22 (s, 18); ^{13}C NMR ($CDCl_3$) δ 171.1, 170.0, 149.9, 143.5, 143.2, 136.2, 135.7, 135.6, 134.7, 134.6, 134.5, 134.2, 132.7, 132.4, 131.9, 131.2, 130.7, 129.5, 129.3, 129.1, 129.0, 128.9, 128.6, 127.0, 126.9, 126.8 (Ar: Calcd, 24; found, 24), 56.2, 52.8, 42.1, 34.3, 31.4, 31.2 (sp^3: Calcd, 7; found, 6). Anal. Calcd for $C_{85}H_{74}O_{18}N_2Br_4S_4$: C, 54.02; H, 4.09. Found: C, 53.93; H, 4.07

(*R*,*S*)-5,17-Bis[[[N-[(carbomethoxyphenyl)methyl]amino]carbonyl]methyl]-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[[(*p*-bromophenyl)sulfonyl]oxy]calix[4]arene (9b) was prepared by the procedure described for **9a,** using (*S*)-(+)-2-phenylglycine methyl ester, and was obtained in 85% yield as tiny needles: mp 249.5−251.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 4, J = 8.6 Hz), 7.79 (d, 4, J = 8.6 Hz), 7.64 (m, 8), 7.33 (m, 3), 7.19 (m, 2), 6.94 (s, 2), 6.85(s, 2), 6.29 (d, 2, J=7.3 Hz), 5.99 (s, 2), 5.91 (s, 2), 5.41 (d, 2, J = 7.2 Hz), 3.73 (dd, 2, J = 14.0 Hz), 3.69 (s, 6), 2.86 (s, 4), 2.48(dd, 2, J = 15.0 Hz), 1.26 (s, 9), 1.20 (s, 9); ^{13}C NMR ($CDCl_3$) δ 171.1, 170.0, 149.9, 143.5, 143.48, 143.3, 136.2, 135.7, 135.64, 135.60, 134.7, 134.6, 134.5, 134.1, 132.8, 132.4, 131.9, 131.2, 130.7, 129.5, 129.3, 129.2, 129.0, 128.6, 127.0, 126.9, 126.8 (Ar: Calcd, 28; found, 25), 56.2, 52.8, 42.2, 34.39, 34.34, 31.44, 31.28, 31.23 (sp^3: Calcd, 9; found 8). Anal. Calcd for $C_{85}H_{74}O_{18}N_2Br_4S_4$: C, 54.02; H, 4.09. Found: C, 53.83; H, 4.07.

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