Syntheses and Conformations of the *p-tert*-Butylcalix[4]arenethiols[1]

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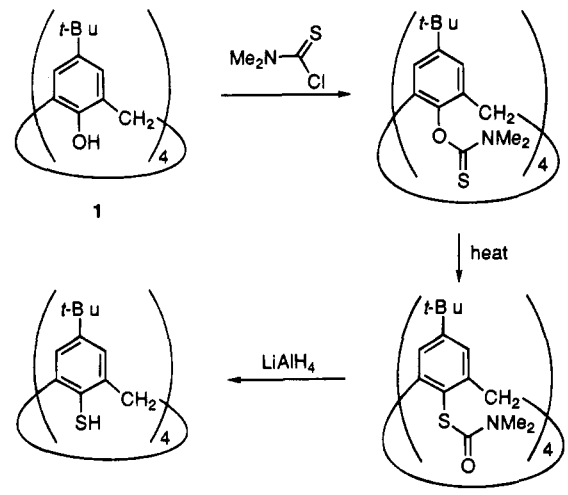
The reaction of dimethyl(thiocarbamoyl) chloride with *p-tert*-butylcalix[4]arene under various conditions yields mixtures from which most of the conformers of the mono-, bis-, tris-, and tetrakis-(dimethyl(thiocarbamoyl))oxy compounds have been isolated and purified. Thermal rearrangement of these compounds produces the (dimethylcarbamoyl)thio compounds which, upon reduction with $LiAlH_4$, afford the tetrathiol **14**, the trithiol **16**, the 1,3-dithiol **21**, and the monothiol **24**. X-ray crystallographic structure determinations and variable-temperature ^1H NMR studies show that the tetrathiol exists as an immobile 1,3-alternate conformer, the trithiol as a semimobile partial cone/1,3-alternate conformer, the 1,3-dithiol as a mobile flattened cone conformer, and the monothiol as a mobile cone conformer. Although the tetrakis((dimethylcarbamoyl)thio) compound exists in three noninterconverting forms comprising the 1,2-alternate **13**, partial cone **18**, and 1,3-alternate **19** conformers, all three yield the same tetrathiol **14** upon reduction. Similarly, the *syn* **22** and *anti* **20** conformers of the 1,3-bis((dimethylcarbamoyl)thio) compound yield the same dithiol **21**. Molecular mechanics calculations for each of the conformers of the mono-, 1,3-di-, tri-, and tetrathiols show general agreement with the X-ray data.

During the past decade much research effort has been expended in embellishing calixarene frameworks[2] with functional groups. Attention has been focused primarily on attachments to the *p*-carbons at the upper rim and the oxygens at the lower rim, and relatively few attempts have been reported concerning the replacement of the OH groups with other groups. Most of these have dealt with replacement of one to four of the OH groups with H in the calix[4]arene system.[3] Replacement of one or two of the OH groups with amino[4] and mercapto groups[5] has also been reported, and replacement of all four OH groups with mercapto groups was first accomplished recently in this laboratory.[6] The present paper provides a detailed account of this work.

Scheme 1. Overall Process



Attempts to replace the OH groups of calixarenes with SH groups were initiated in our laboratories in the mid 1980s, employing the Newman–Kwart method for converting phenols to thiophenols.[7] Treatment of *p-tert*-butylcalix[4]arene (**1**) with dimethyl(thiocarbamoyl) chloride was carried out with the expectation of obtaining only the tetrasubstituted compound which was then to be thermally rearranged and reduced to the tetrathiol as shown in Scheme 1. Unfortunately, no set of reaction conditions investigated at that or any subsequent time has given a tetrakis(dimethyl(thiocarbamoyl))oxy compound unmixed with various other compounds. When the reaction mixture obtained in this early experiment was strenuously heated in sulfolane, a black tar was obtained from which a few crystals separated that were identified by X-ray crystallography as the tetrakis-(dimethylcarbamoyl)thio compound in the 1,2-alternate

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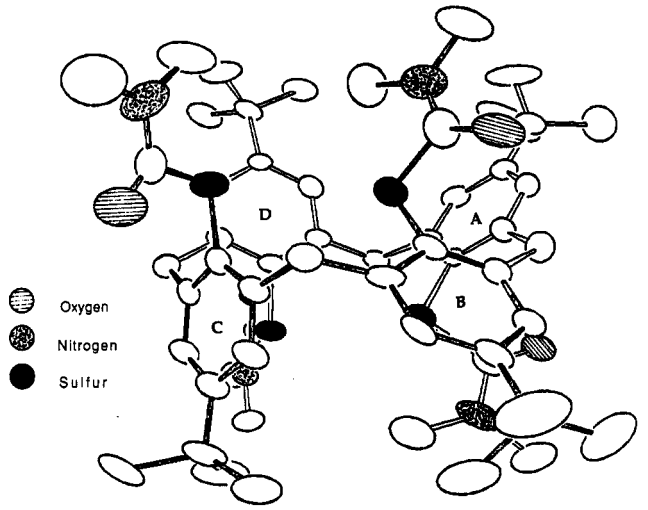

Figure 1. X-ray crystallographic structure of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethylcarbamoyl)thio)calix-[4]arene (1,2-alternate conformation) (**13**).

conformation.[8] Although this was a unique conformational observation at the time, a detailed account of this work[9] was held in abeyance until a clearer understanding of the process could be gained. In the meantime, several other examples of calix[4]arenes in 1,2-alternate conformations have been reported.[10,11] A careful reinvestigation of the reaction of *p-tert*-butylcalix[4]arene with dimethyl-(thiocarbamoyl) chloride has now provided some insight in what has proved to be a much more complicated reaction pattern than had been anticipated at the outset.

The reactions of Scheme 1 have been most successfully accomplished using the following procedures. Treatment of *p-tert*-butylcalix[4]arene (**1**) with NaH and dimethyl-(thiocarbamoyl) chloride in diglyme at 130−135 °C for 18 h yields a mixture from which a product can be isolated by flash chromatography in 43% yield whose ^{1}H NMR spectrum clearly indicates it to be the 1,2-alternate conformer. Thermal rearrangement of this material can be effected in 42% yield[12] by heating in di-*p*-tolyl ether at gentle reflux for 24−30 h. The ^{1}H NMR spectrum of the product showed that it, too, is the 1,2-alternate conformer, as had previously been established by X-ray crystallography[6,8] (Figure 1). Lithium aluminum hydride reduction produces the tetrathiol in 64% yield as a crystalline solid. Although the reactions shown in Scheme 1 represent the successful completion of the initial goal, the system proved proved to be considerably more complex than this simple presentation might suggest.

Synthesis of ((Dimethyl(thiocarbamoyl))oxy)-calix[4]arenes. As shown in Scheme 2, the reaction of *p-tert*-butylcalix[4]arene (**1**) with Me_2NCSCl and NaH in diglyme at elevated temperature produces, in addition to a 43% yield of the 1,2-alternate conformer of the tetrasubstituted compound **2**, a 9% yield of the tetrasubstituted compound in the partial cone conformation **3**, a 3% yield of the *anti*-1,3-disubstituted compound[13] **4**, and a 5% yield of the trisubstituted compound in the partial cone/1,3-alternate conformation[13] **5**. Conversion of the disubstituted compound **4** and the trisubstituted compounds **5** and **10** to tetrasubstituted compounds was effected by further treatment with Me_2NCSCl and NaH. In the case of **5**, a mixture containing 40% of the partial cone conformer **3** and 28% of the 1,3-alternate conformer **6** was obtained. The tetrasubstituted cone conformer was obtained in a more circuitous fashion. Treatment of **1** with Me_2NCSCl using K_2CO_3 in refluxing Me_2CO for 24 h yields a mixture from which the *syn* and *anti* 1,3-disubstituted compounds **8** and **4** and the trisubstituted compounds in the partial cone/1,3-alternate conformation **5**, partial cone/1,2-alternate conformation **10**, and cone/partial cone conformation **11** can be chromatographically separated. Further treatment of **11** with Me_2NCSCl and NaH produces a mixture from which the tetrasubstituted compounds in the partial cone conformation **3** and the cone conformation **12** can be chromatographically separated. A third compound was also isolated from this mixture and is designated as **3′**, because it closely resembles **3** yet is not identical with it (*vide infra*). The same treatment of **8** yields a similar mixture that also contains the 1,3 alternate conformer **6**. Alkylation of calixarenes with $Ba(OH)_2 \cdot 8H_2O$ generally leads to the di- and/or tri-O-substituted products,[14] so it was surprising to obtain the monosubstituted compound **7** in moderately good yield (55%) mixed with a small amount of unreacted starting material when this reagent was used. Anhydrous $Ba(OH)_2$, on the other hand, yields more extensive mixtures containing **4**, **5**, and **7**−**11** in varying amounts depending on the ratio of reagents. Pure samples of each of these compounds were obtained by chromatographic separation.

Synthesis of ((Dimethylcarbamoyl)thio)calix[4]-arenes. Several of the (dimethyl(thiocarbamoyl))oxy compounds described above, including the monosubstituted compound **7**, the disubstituted compounds **4** and **8**, the trisubstituted compound **5**, and the tetrasubstituted compounds **2**, **3**, and **6**, were subjected to the Newman−Kwart thermal rearrangement to convert them to the corresponding (dimethylcarbamoyl)thio compounds, as shown in Scheme 3. However, the rearrangements did not proceed with equal facility in all cases. In the tetrasubstituted series gentle refluxing of the 1,2-alternate conformer **2** and the 1,3-alternate conformer **6** in di-*p*-tolyl ether for 30−48 h produced the rearrangement products **13** (1,2-alternate conformer) and **19** (1,3-alternate conformer) in 42% and 49% yields, respectively. On the other hand, similar treatment of the partial cone conformer **3** resulted in rearrangement of only three of the groups and replacement of the fourth group by OH to give the trisubstituted compound in the partial cone/1,3-alternate conformation **15** identical with that ob-

(8) The atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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(13) The phenolic units in calix[4]arenes are conformationally mobile and can easily swing between the "up" and "down" orientations. While the *anti* disposition of the substituted phenol units in the 1 and 3 positions in **4** remains fixed, the conformational mobility of the unsubsubstituted phenol units makes possible both the 1,2-alternate and the partial cone conformations. Similarly, other calixarenes containing one or more phenol units can exist in two or more rapidly equilibrating conformations.

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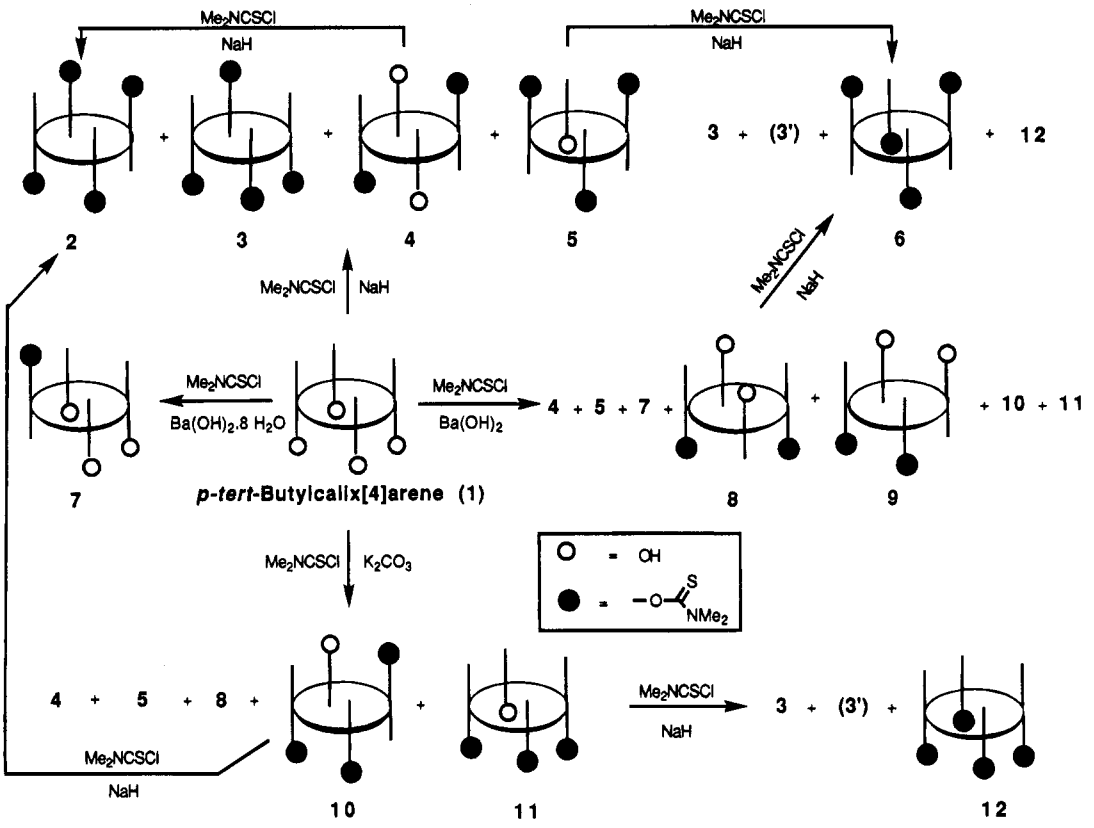
Scheme 2. Synthesis of ((Dimethyl(thiocarbamoyl))oxy)calix[4]arenes



tained by rearrangement of the trisubstituted compound **5**. The replacement reaction occurred even when scrupulously dried reagents were used, and the pathway for this reaction remains unclear. Treatment of **15** with Me_2NCSCl and NaH reintroduces a (dimethyl(thiocarbamoyl))oxy group to give compound **17** which when refluxed in di-*p*-tolyl ether for only 7 h produces the tetrasubstituted (dimethylcarbamoyl)thio compound (partial cone conformer) **18** in 77% yield. In comparable fashion, the disubstituted compounds **4** and **8** and the monosubstituted compound **7** were thermally rearranged to the (dimethylcarbamoyl)thio compounds **20**, **22**, and **23**, respectively, in yields ranging from 16 to 70%.

Synthesis of Calix[4]arenethiols. The final step in the overall process involves $LiAlH_4$-induced cleavage of the (dimethylcarbamoyl)thio compounds **13**, **15**, **18**–**20**, **22**, and **23** to produce the four calix[4]thiols **14**, **16**, **21**, and **24**, as shown in Scheme 3. Clearly, the conformational integrity of the carbamoylthio compounds is not retained in this process, for all three of the conformers of the tetrasubstituted compound yield the same calix[4]arenetetrathiol **14** (1,3-alternate conformation) and both of the conformers of the 1,3-disubstituted compound yield the same calix[4]arenedithiol **21** (flattened cone conformation). The trisubstututed compound **15** (partial cone/1,3-alternate conformation) yields the calix[4]arenetrithiol **16** (1,3-alternate conformation), and the monosubstituted compound **23** yields the calix[4]arenemonothiol **24** (cone conformation).

Hosseini and co-workers[12] have found that the thermal rearrangement of **2** to **13** can be effected in 88% yield by heating the compound neat at 310–320 °C in an argon atmosphere. However, their attempts to extend this procedure to the thermal rearrangement of **4** to **21**, which we have shown to proceed smoothly in solution, failed under neat conditions.[15] They instead resorted to protection of the free OH groups by methylation and thermolysis to produce a mixture of compounds that included the previously reported[5] dimethoxy dithiol and then deprotection to give **21**. Thus, thermolyses neat and in solution complement one another.

Characterization of Compounds 2–24. Structures and conformations were established in all cases by a combination of elemental analysis, ^1H NMR/^{13}C NMR spectroscopy, and X-ray crystallography. The NMR probes are especially useful for establishing solution state conformations, taking advantage of the well-documented patterns of the ^1H NMR resonances[2a] (particularly those arising from the *tert*-butyl and the $ArCH_2Ar$ groups) and the positions of the ^{13}C NMR resonances associated with these same groups.[16,17]

Conformation and Conformational Flexibility of the Calix[4]arenethiols. The tetrathiol **14** was established as the 1,3-alternate conformer on the basis of a singlet in the ^1H NMR spectrum for the $ArCH_2Ar$ methylene protons, a signal at δ 45.71 in the ^{13}C NMR spectrum for the $ArCH_2Ar$ methylene carbons,[16] and an X-ray crystallographic structure.[6,8,12] The ^1H NMR spec-

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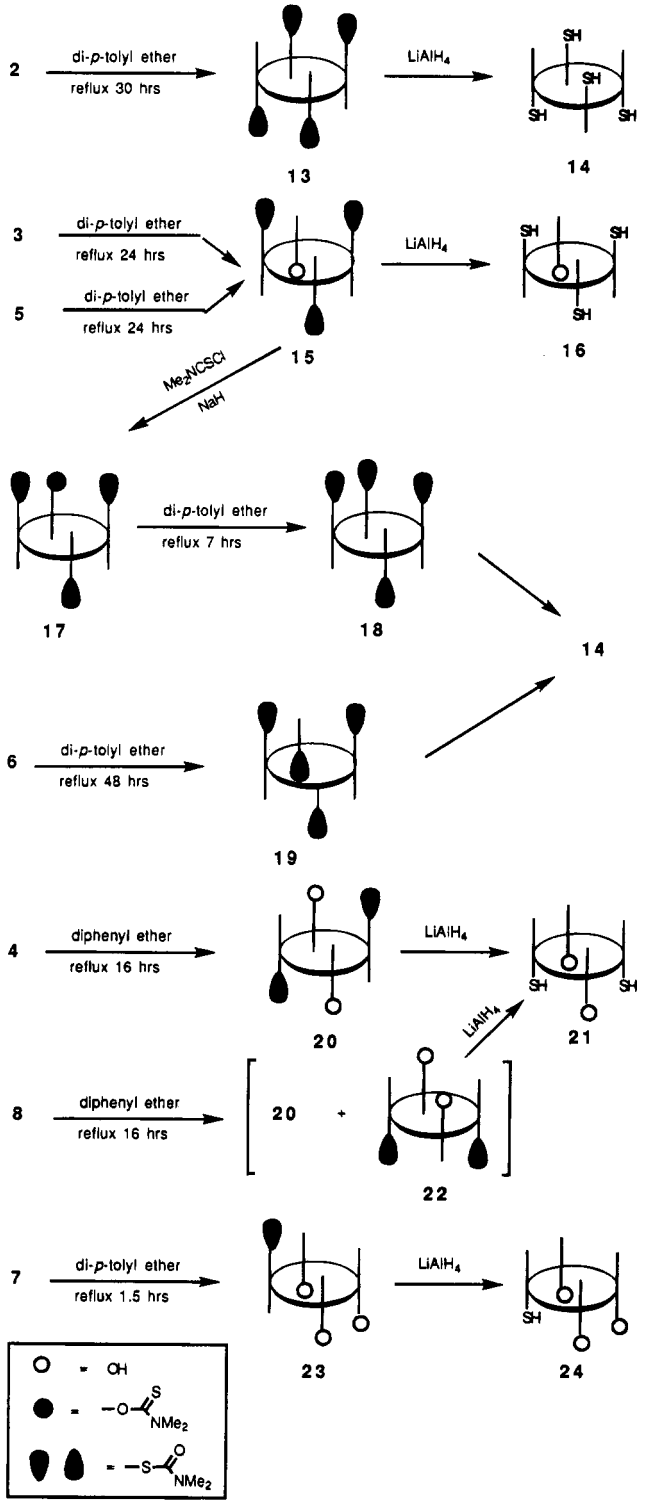
(16) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sanchez, C. J. *Org. Chem.* **1991**, *56*, 3372 found that a resonance near δ 31 appears when the aryl groups are *syn* to one another and near δ 37 when they are *anti*.

(17) The position of the ^{13}C NMR methylene resonances for *syn* and *anti* ArOR moieties[16] holds true for the (dimethyl(thiocarbamoyl))oxy compounds studied in the present work. For the (dimethylcarbamoyl)-mercapto compounds, however, the resonances are displaced downfield. On the basis of the data in the literature and that accumulated in the present work the following predictive assignments can be made:

	ArSR/ArSR	ArSR/ArOR	ArOR/ArOR[16]
syn	39.5 ± 0.5	36 ± 2	31
anti	46.8 ± 2.0	*ca.* 45 (extrapolated)	37

Scheme 3. Rearrangement of ((Dimethyl(thiocarbamoyl))oxy)calix[4]arenes to *N,N*-((Dimethylcarbamoyl)thio)calix[4]arenes and Reduction to Calix[4]arenethiols



tral pattern remains invariant over the temperature range −60 to +100 °C, commensurate either with a pair of rapidly interconverting cone conformers or a noninterconverting 1,3-alternate conformer; the latter is more likely.

The X-ray crystallographic structure[8] of the trithiol **16** (Figure 2) shows that the three ArSH groups are oriented "up,down,up" in the solid state. The compound possesses a poorly resolved ^{1}H NMR spectrum at room temperature

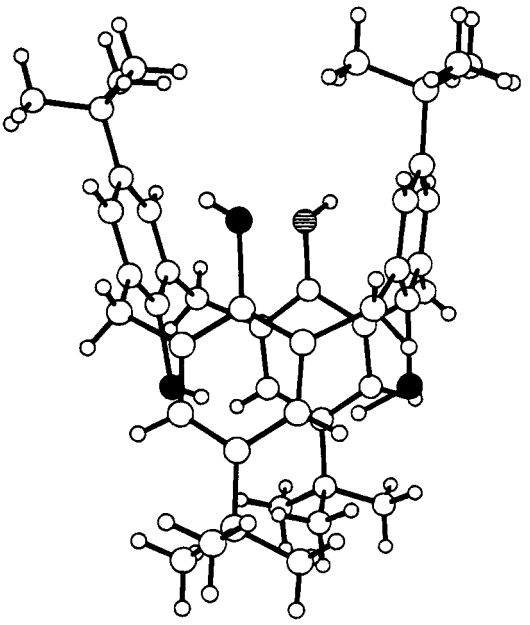


Figure 2. X-ray crystallographic structure of 5,11,17,23-tetra-*tert*-butyl-25,26,27-trithiocalix[4]aren-28-ol (**16**).

that becomes more highly resolved at −60 °C, showing two pairs of doublets. Heating to 100 °C simply results in further line broadening with no indication of coalescence. The ^{13}C NMR spectrum shows signals at δ 45.53 and 38.65 arising from the $ArCH_2Ar$ methylene carbons, suggesting a partial cone conformation.[16,17] Inspection of CPK models indicates that the ArOH moiety in **16** should be conformationally mobile, and it is probably the interconversion between the partial cone and 1,3-alternate conformations that accounts for the broadening of the ^{1}H NMR spectrum upon heating.

The X-ray crystallographic structure[8] of the 1,3-dithiol **21**[15] indicates it to be a flattened cone conformation in which the two ArSH rings are almost parallel and the two ArOH rings are canted outward. The ^{1}H NMR spectrum shows a pair of methylene doublets that sharpen upon heating to 105 °C to a broad singlet at δ 4.00, suggesting that in this system complete cone−cone interconversion occurs with a $\Delta G^{\ddagger}$ of 17.6 kcal/mol, a somewhat higher value than that reported by Delaigue *et al.*[15] Concurrently, some other process (oxidation?) occurs at the elevated temperature, giving rise to a new pair of doublets at δ 3.62 and 4.42 which persist upon cooling.

Although the X-ray structure of the monothiol **24** is poorly refined, it quite clearly shows the compound to be in a cone conformation in the solid state. In solution the ^{1}H NMR spectrum (Figure 3) contains doublets at δ 4.50, 4.17, 3.70, and 3.50 arising from the $ArCH_2Ar$ protons, and the ^{13}C NMR spectrum contains a pair of lines at δ 37.64 and 32.68 commensurate with a cone conformation. Decoupling studies indicate that the coupling occurs between the doublets at δ 4.50 and δ 3.70 and between the doublets at δ 4.17 and δ 3.50. Upon being heated to 135 °C, the δ 4.50/3.70 set broadens but does not coalesce, while the δ 4.17/3.50 set coalesces to a broad singlet at δ 3.70. It is postulated that the δ 4.17/3.50 ($\Delta\delta$ = 0.67) set arises from the methylene groups flanked on both sides by ArOH and that the δ 4.50/3.70 ($\Delta\delta$ = 0.30) set arises from the methylene groups flanked by one ArSH and one ArOH. The variable temperature behavior suggests that cone−cone interconversion is

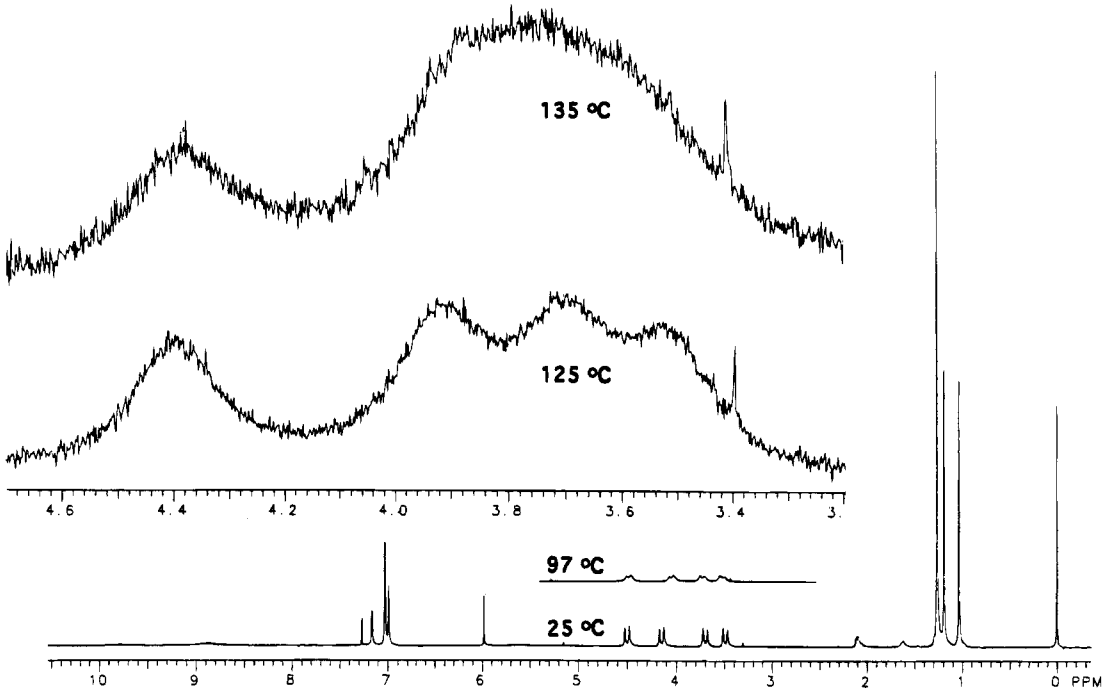


Figure 3. Variable temperature ^{1}H NMR spectrum of the monothiol **24** in $CDCl_3$ or $CDCl_2CDCl_2$ at 300 MHz.

possible in this system, with the ArOH groups passing through the annulus more easily than the ArSH group.[18] Were it possible to go to higher temperatures it is anticipated that a pair of singlets would be observed for the two sets of $ArCH_2Ar$ protons.

Since the three conformers **13**, **18**, and **19** of the tetrasubstituted (dimethylcarbamoyl)thio compounds yield the same 1,3-alternate conformer of the tetrathiol **14** and the two conformers **20** and **22** of the disubstituted carbamoylmercapto compounds yield the same cone conformer of the dithiol **21**, a sulfur-containing moiety of some sort must be able to swing through the cavity of a calix[4]arene. In the thought that it might be S^- the temperature ^{1}H NMR spectrum of the monothiol **24** in DMSO solution containing *n*-BuLi was investigated. However, the anion proves to be even less conformationally flexible than the parent compound, similar to calix[4]arenetetrols such as *p*-allylcalix[4]arene.[19]

It is interesting to compare the conformational behavior of the calix[4]arenethiols with the calix[4]arene alkyl ethers. In the case of the methyl ethers of *p-tert*-butylcalix[4]arene (**1**), conformational stability reaches a maximum with the diethers,[11c,14a,20] and in contrast to the tetrathiol **14** the tetramethyl ether of **1** is as flexible as **1** itself. The tetraethyl ether of **1**, though still capable of conformational interconversion, is less flexibile than the tetramethyl ether, while the tetra-*n*-propyl ether appears to be truly inflexible[11b] (with a conformer composition comprising cone, partial cone, and a small amount of 1,3-alternate). In this context, the SH group appears to be conformationally comparable to the propoxy group. Inspection of CPK models, however, suggests that the mode of hindrance from OR groups is different from that from SH groups. With OR groups the hindrance is between the R substituent and the aryl residues of the calixarene ring, whereas with the SH group it is between the sulfur atom and the aryl residues. Although the oxygen atom of OR can easily slide past the flanking aryl residues, making possible an "up" to "down" transformation when R is sufficiently small, the motion of the sulfur atom of SH is much more restricted because of its larger size.

Hill et al.[21] have adsorbed **14** onto a rough silver surface and, through the use of surface-enhanced Raman scattering, observed complete disappearance of the S–H stretching bands at 2540 cm^{-1}. This is in agreement with conversion of the 1,3-alternate conformer of **14** to the cone conformer. As discussed in the following section, the calculated energy difference between the 1,3-alternate and cone conformations of the tetrathiol is *ca.* 4 kcal/mol. Thus, although the cone conformer would be undetectable by ^{1}H NMR spectral measurements in an equilibrium mixture of the two conformers, the energy difference between the two is small enough to make credible the stabilization of the cone conformer by adsorption on a silver surface.

(18) We are indebted to a reviewer for valuable comments pertaining to this interpretation.

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(21) Hill, W.; Wehling, B.; Gibbs, C. G.; Gutsche, C. D.; Klockow, D. *Anal. Chem.* **1995**, *34*, 3187.

(22) Molecular mechanics calculations were carried out on a Silicon Graphics IRIS 4D 210 VGX computer using the QUANTA 3.2/CHARMm 21.3 program package which gives energies in kcal mol^{-1}. Except for the Ar–SH bond, the default parameters supplied with the program were used; for the Ar–SH bond a bond angle of 98° was chosen.[23] Within QUANTA a radially dependant dielectric function (RDIE), proportional to $1/r^2$, was used with a weighting factor of 1.00. After the structures were imported from ChemNote, the energy was first minimized and the desired up/down conformer was generated by breaking one $Ar-CH_2$ bond, appropriately adjusting the macrocyclic torsions to the desired values, and reforming the broken bond, and the energy of the new up/down conformer was then minimized with the ABNR routine to an rms force of *ca.* 0.3. The resulting structure was subjected to a systematic conformational search in which all ArSH/ArOH bonds and at least two $Ar-C(CH_3)_3$ bonds were varied between the initial value and +180° and the energies then minimized to an rms force of 1×10^{-7} or less.

Table 1. Total Energies of the Cone, Partial Cone, 1,2-Alternate, and 1,3-Alternate Conformations of the Monothiol 24, 1,3-Dithiol 21, Trithiol 16, and Tetrathiol 14

compd	cone	partial cone	1,2-alternate	1,3-alternate
monothiol	48.10	49.78,[a] 52.87,[b] 49.77[c]	53.47	50.92
1,3-dithiol	48.54	50.97,[d] 53.10[e]	53.44	51.85
trithiol	53.80	52.86,[f] 52.47,[g] 53.89[h]	57.10	52.97
tetrathiol	58.90	54.74	57.68	54.74

[a] S(d),O(d),O(d),O(u); [b] S(d),O(d),O(u),O(d); [c] S(d),O(u),O(u),O(u); [d] S(d),O(d),S(d),O(u); [e] S(d),O(d),S(u),O(d); [f] S(d),S(d),O(d),S(u); [g] S(d),O(d),S(d),S(u); [h] S(d),S(d),S(d),O(u) where S is sulfur, O is oxygen, u designates "up", and d designates "down".

Molecular Modeling. Molecular mechanics calculations[22,23] were carried out on the mono-, di-, tri-, and tetrathiols in each of their four possible conformations, and the total energies for these compounds are shown in Table 1. For the monothiol- and 1,3-dithiol the cone conformers are lowest in energy, in agreement with the X-ray structures. For the trithiol the energies of the cone, partial cone, and 1,3-alternate are all within 1 kcal/mol of one another, and for the tetrathiol the partial cone and 1,3-alternate have virtually identical energies. The X-ray structures show both of these compounds to be in the 1,3-alternate conformation in the solid state, in general agreement with the molecular mechanics calculations. However, the molecular mechanics calculations suggest that a conformational mixture might be expected to be observed in solution for the trithiol and tetrathiol, but this appears not to be the case.

Experimental Section[24]

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethyl(thiocarbamoyl))oxy)calix[4]arene (2) (1,2-Alternate Conformer). (A) From 1. To a suspension of 3.84 g (96 mmol) of NaH (60% oil dispersion rinsed with dry hexane) in 300 mL of anhydrous, freshly distilled diglyme[25] was added 8.9 g (12 mmol) of recrystallized *p-tert*-butylcalix[4]arene (**1**),[26] and the mixture was heated to 130–135 °C for 1.5 h. A solution of 12.6 g (96 mmol) of dimethyl(thiocarbamoyl) chloride in 60 mL of dry diglyme was added dropwise to the stirred mixture at a rate to maintain the temperature at 130 °C. After addition, the reaction mixture was stirred at 130–135 °C for 18 h, cooled, poured into a large volume of water, and filtered and the crude solid air dried to give 12.9 g containing disubstituted, trisubstituted, and tetrasubstituted products. Flash chromatography[27] was accomplished by dissolving the crude solid in CH_2Cl_2, adding 10 to 15 times its weight of silica gel, and evaporating to dryness. This material was slurried in a small amount of CH_2Cl_2–petroleum ether (60:40) and added to a prepared column made up of the same solvent system. Elution[28] with a gradient solvent system (CH_2Cl_2–petroleum ether to 100% CH_2Cl_2 in 10% incremental steps) gave, after trituration with a small amount of MeOH, 5.2 g (43%) of the tetrasubstituted product **2** in the 1,2-alternate conformation. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 378–379 °C; ^{1}H NMR ($CDCl_3$) δ 7.26 (d, 4, J = 2.0 Hz), 7.01 (d, 4, J = 2.2 Hz), 3.8 (s, 4), 3.64 (d, 2, J = 13.2 Hz), 3.35 (d, 2, J = 13.4 Hz), 3.20 (br s, 12), 2.11 (br s, 12), 1.34 (s, 36); ^{13}C NMR ($CDCl_3$) δ 186.74, 149.08, 147.63, 134.20, 133.49, 126.18, 126.04, 43.43, 37.71, 38.60, 29.47, 34.42, 31.60. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.46; H, 7.70; N, 5.52.

(B) From 4. To a suspension of 0.26 g (6.6 mmol) of NaH (60% oil dispersion rinsed with dry hexane) in 100 mL of dry THF and 10 mL of dry DMF was added 1.81 g (2.2 mmol) of the disubstituted compound **4**, and the mixture was heated at reflux for 0.5 h. A solution of 0.82 g (6.6 mmol) of *N,N*-dimethyl(thiocarbamoyl) chloride in 10 mL of dry THF was added dropwise, and the mixture was heated at reflux for 6 h. The solvent was evaporated, dilute HCl was added, and the mixture was extracted with CH_2Cl_2. After drying, the solvent was evaporated to give, after trituration with MeOH, 1.75 g (80%) of **2**.

(C) From 10. The procedure described above for **4** was repeated using 1.82 g (2 mmol) of **10**. Workup and flash chromatography as previously described gave 1.3 g (65%) of **2**.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethyl(thiocarbamoyl))oxy)calix[4]arene (Partial Cone Conformer) (3). A 1.1 g (9.2%) sample of the tetrasubstituted partial cone conformer **3** was obtained by chromatography of the reaction mixture described above for the preparation of **2**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 355.5–356.5 °C; ^{1}H NMR (CD_2Cl_2) δ 7.41 (d, 2, J = 2.4 Hz), 7.30 (s, 2), 7.14 (s, 2), 6.84 (d, 2, J = 2.4 Hz), 3.91 (d, 2, J = 13.1 Hz), 3.82 (d, 2, J = 17.1 Hz), 3.75 (d, 2, J = 16.7 Hz), 3.46 (d, 2, J = 13.1 Hz), 3.34 (s, 6), 3.10 (very broad base line envelope, 12), 2.89 (s, 3), 1.37 (s, 9), 1.30 (s, 9), 1.26 (s, 18), 0.19 (s, 3); ^{13}C NMR (CD_2Cl_2) δ 189.38, 187.60, 183.47, 150.17, 148.60, 148.43, 148.37, 147.59, 146.66, 136.38, 135.44, 134.60, 132.69, 126.92, 126.41, 125.81, 125.27, 43.79, 36.11, 38.99, 34.55, 31.42, 34.67, 34.60, 31.80, 31.75. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.45; H, 7.74; N, 5.65.

5,11,17,23-Tetra-*tert*-butyl-26,28-bis((dimethyl(thiocarbamoyl))oxy)calix[4]arene-25,27-diol (*anti* arrangement) (4) was obtained by chromatography of the reaction mixture described above for the preparation of **2**, and 0.26 g (2.6%) of product was isolated. Recrystallization from CH_2Cl_2–MeOH gave a white solid: mp 348–349 °C; ^{1}H NMR ($CDCl_3$) δ 7.26 (s, 4), 7.07 (s, 4), 4.82 (s, 2), 3.99 (d, 4, J = 15.1 Hz), 3.63 (d, 4, J = 15.0 Hz), 3.21 (s, 6), 1.72 (s, 6), 1.32 (s, 18), 1.29 (s, 18); ^{13}C NMR ($CDCl_3$) δ 184.73, 149.79, 149.14, 147.29, 142.78, 133.10, 126.37, 125.06, 43.36, 36.71, 34.38, 33.97, 34.25, 31.79, 31.44. Anal. Calcd for $C_{50}H_{66}N_2O_4S_2$: C, 72.95; H, 8.08; N, 3.40. Found: C, 72.71; H, 7.91; N, 3.47.

5,11,17,23-Tetra-*tert*-butyl-26,27,28-tris((dimethyl(thiocarbamoyl)oxy))calix[4]aren-25-ol (partial cone/1,3-alternate conformer) (5) was obtained by chromatography of the reaction mixture from the procedure described above for the preparation of **2**, and 0.55 g (5%) of **5** was isolated. Recrystallization from CH_2Cl_2–MeOH gave a white solid:[29] mp 349–350 °C; ^{1}H NMR ($CDCl_3$) δ 7.15 (s, 2), 7.14 (d, 2, J = 2.3 Hz), 7.05 (s, 2), 6.89 (d, 2, J = 2.3 Hz), 5.29 (s, 1), 3.92 (d, 2, J = 16.9 Hz), 3.84 (d, 2, J = 16.9 Hz), 3.78 (d,

(23) Although the default value for the C–S–H angle in the QUANTA/CHARMm program is 109°, literature values are generally below 100°. For example, *p*-benzenedithiol shows a C–S–H angle of 96.5° (Portalone, G.; Domenicano, A.; Schultz, G.; Hargittai, I. *THEOCHEM* **1989**, *55*, 185). When the 109° angle was used in the present calculations energies well above those calculated with the 98° angle were obtained.

(24) Unless otherwise noted, starting materials were obtained from commercial sources and used without further purification. THF was always freshly distilled from Na–benzophenone. All reactions were carried out in an inert atmosphere of nitrogen. The melting points of all compounds were taken in sealed and evacuated capillary tubes on a Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) with the use of a Fluka 51 K/J thermometer (John Fluke Mfg. Co., Inc., Everett, WA). ^{1}H and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. TLC analyses were carried out on Analtech silica gel plates (absorbent thickness 250 μm) containing a fluorescent indicator. Flash chromatography was carried out with J. T. Baker silica gel No. JT7042-2 (40 μm particle diameter). Analytical samples were dried 24 h at 138 °C and 1–2 mm pressure. Diglyme was refluxed over Na for 24 h and distilled onto 4 Å molecular sieves just prior to use.

(25) Anhydrous diglyme from commercial sources when used undistilled gave inconsistent and erratic results, with the tetrasubstituted calix[4]arene usually being a minor product.

(26) Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1989**, *68*, 234.

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

(28) The order of compound elution is **4**, **5**, **2**, and **3**.

(29) The mother liquor sometimes contains small amounts of the trisubstituted compound **10** in the partial cone/1,2-alternate conformation.

2, J = 13.8 Hz), 3.44 (br s, 6), 3.41 (d, 2), 3.07 (s, 3), 2.79 (br s, 6), 1.38 (s, 9), 1.28 (s, 9), 1.22 (s, 18), 0.56 (s, 3); ^{13}C NMR ($CDCl_3$) δ 186.46, 149.64, 148.57, 148.17, 147.49, 143.01, 134.27, 133.81, 132.33, 127.35, 126.18, 126.05, 125.33, 124.82, 43.72, 36.84, 38.45, 34.28, 32.40, 34.40, 33.95, 31.81, 31.64, 31.52. Anal. Calcd for $C_{53}H_{71}N_3O_4S_3$: C, 69.92; H, 7.86; N, 4.62. Found: C, 70.13; H, 8.02; N, 4.58.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethyl(thiocarbamoyl))oxy)calix[4]arene (1,3-Alternate Conformer) (6). The procedure described above using NaH in THF/DMF was repeated with 2.23 g (2.4 mmol) of **5**, 0.3 g (7.3 mmol) of 60% NaH, and 0.9 g (7.3 mmol) of *N,N*-dimethyl(thiocarbamoyl) chloride. Workup and flash chromatography as described above gave 0.9 g (40%) of **3**, 0.02 g of **5**, and 0.66 g (28%) of the tetrasubstituted compound (1,3-alternate conformation) **6**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 401–402 °C; ^{1}H NMR ($CDCl_3$) δ 7.00 (s, 8), 3.65 (s, 8), 3.41 (s, 12), 2.28 (s, 12), 1.28 (s, 36); ^{13}C NMR ($CDCl_3$) δ 185.55, 150.40, 146.87, 134.60, 126.25, 43.64, 38.91, 37.88, 34.34, 31.62. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.48; H, 7.60; N, 5.54.

5,11,17,23-Tetra-*tert*-butyl-28-((dimethyl(thiocarbamoyl))oxy)calix[4]arene-25,26,27-triol (Partial Cone Conformer) (7). A suspension of 2.2 g (2.97 mmol) of *p-tert*-butylcalix[4]arene (**1**), 1.87 g (5.94 mmol) of $Ba(OH)_2 \cdot 8\ H_2O$, and 1.47 g (11.9 mmol) of *N,N*-dimethyl(thiocarbamoyl) chloride in 50 mL of DMF was stirred at 70 °C for 18 h. The reaction mixture was poured into H_2O and filtered. The resulting solid was flash chromatographed as described above to give 0.19 g of starting calix[4]arene and 1.09 g (55%) of the monosubstituted compound **7**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 281–282 °C; ^{1}H NMR ($CDCl_3$) δ 8.33 (s, 1), 7.38 (s, 2), 7.07 (s, 2), 7.06 (d, 2, J = 2.5 Hz), 6.81 (d, 2, J = 2.3 Hz), 6.67 (s, 2), 4.13 (d, 2, J = 13.5 Hz), 4.05 (d, 2, J = 16.5 Hz), 3.96 (d, 2, J = 16.4 Hz), 3.42 (d, 2, J = 13.6 Hz), 2.89 (s, 3), 1.42 (s, 9), 1.24 (s, 9), 1.18 (s, 18), 0.33 (s, 3); ^{13}C ($CDCl_3$) δ 182.55, 149.94, 149.03, 148.62, 146.87, 144.28, 143.48, 132.11, 128.25, 127.82, 127.39, 125.89, 125.42, 124.64, 43.00, 34.98, 38.30, 31.41, 34.56, 33.97, 33.85, 31.58, 31.52, 31.48. Anal. Calcd for $C_{47}H_{61}NO_4S$: C, 76.69; H, 8.25; N, 1.90. Found: C, 76.70; H, 8.25; N, 1.62.

5,11,17,23-Tetra-*tert*-butyl-26,28-bis((dimethyl(thiocarbamoyl))oxy)calix[4]arene-25,27-diol (*Syn* Conformer) (8). A suspension of 16.19 g (0.025 mol) of *p-tert*-butylcalix-[4]arene (**1**), 12.4 g (0.1 mol) of *N,N*-dimethyl(thiocarbamoyl) chloride, and 13.8 g (0.1 mol) of anhydrous K_2CO_3 in 600 mL of dry acetone was stirred at reflux for 24 h. The solvent was evaporated, and 100 mL of 1 N HCl was carefully added. The mixture was extracted with CH_2Cl_2 and the organic phase dried. Evaporation of the solvent gave 18.24 g of a white solid consisting of a mixture of disubstituted and trisubstituted products, including **4, 5, 8, 10,** and **11**. Flash chromatography as described previously gave, *inter alia*, 1.64 g (8%) of **4** and 9.12 g (44%) of the disubstituted compound (*syn* arrangement) **8**. Recrystallization from CH_2Cl_2–MeOH gave a white solid: mp 341–342 °C; ^{1}H NMR ($CDCl_3$) δ 7.07 (s, 4), 6.88 (s, 4), 4.79 (s, 2), 3.83 (d, 4, J = 14.9 Hz), 3.48 (d, 4, J = 14.9 Hz), 3.44 (s, 6), 3.13 (s, 6), 1.32 (s, 18), 1.01 (s, 18); ^{13}C NMR δ ($CDCl_3$) 185.6, 150.39,148.66,146.47, 142.30, 132.00, 127.82, 125.97, 125.36, 43.45, 38.21, 33.94, 33.84, 33.49, 31.62, 30.95. Anal. Calcd for $C_{50}H_{66}N_2O_4S_2$: C, 72.95; H, 8.08; N, 3.40. Found: C, 72.63; H, 8.02; N, 3.26.

5,11,17,23,-Tetra-*tert*-butyl-27,28-bis((dimethyl(thiocarbamoyl))oxy)calix[4]arene-25,26-diol (*Syn* Conformer) (9).[30] The reaction was carried out as described above for the preparation of **7** using 0.51 g (2.97 mmol) of anhydrous $Ba(OH)_2$, 1.1 g (1.5 mmol) of *p-tert*-butylcalix[4]arene (**1**), and 0.74 g (6 mmol) of *N,N*-dimethyl(thiocarbamoyl) chloride. Flash chromatography gave 0.94 g (9%) of **7**, 0.74 g (64%) of **8**, and 132 mg (11.5%) of the 1,2-disubstituted compound **9**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 270.5–271.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (d, 2, J = 2.3 Hz), 7.24 (d, 2, J = 2.2 Hz), 7.11 (d, 2, J = 2.4 Hz), 6.91 (d, 2, J = 2.3 Hz), 5.94 (s, 2), 4.04 (d, 1, J = 13.7 Hz), 3.94 (s, 4), 3.72 (d, 1, J = 13.7 Hz), 3.37 (d, 1, J = 13.7 Hz), 3.33 (d, 1, J = 13.6 Hz), 3.17 (s, 6), 2.01 (s, 6), 1.35 (s, 18, C), 1.27 (s, 18); ^{13}C NMR ($CDCl_3$) δ 186.90, 149.84, 149.05, 148.32, 142.80, 134.32, 132.21, 127.95, 127.25, 125.60, 125.40, 125.28, 43.64, 36.79, 38.43, 30.81, 29.51, 34.46, 33.95, 31.66, 31.44. Anal. Calcd for $C_{50}H_{66}N_2O_4S_2$: C, 72.95; H, 8.08; N, 3.40. Found: C, 72.70; H, 8.04; N, 3.35.

5,11,17,23-Tetra-*tert*-butyl-26,27,28-tris((dimethyl(thiocarbamoyl))oxy)calix[4]aren-25-ol (1,2-alternate/partial cone conformer) (10) was obtained as a mixture with **5** in the chromatographic separation of the reaction mixture described above for the preparation of **8** using K_2CO_3 as the base. Fractional crystallization from $CHCl_3$–MeOH gave 2.9 g (12.7%) of **5**. Concentration of the mother liquor gave 5.1 g (22.4%) of **10** as a white solid: mp 326–327 °C; ^{1}H NMR ($CDCl_3$) δ 7.44 (d, 1, J = 2.2 Hz), 7.39 (d, 1, J = 2.3 Hz), 7.29 (s, 2), 7.12 (d, 1, J = 2.2 Hz), 7.03 (d, 1, J = 2.2 Hz), 6.94 (s, 2), 4.67 (s, 1), 4.01 (d, 1, J = 13.2 Hz), 3.93 (d, 1, J = 15.9 Hz), 3.91 (d, 1, J = 17.6 Hz), 3.84 (d, 1, J = 15.7 Hz), 3.81 (d, 1, J = 17.6 Hz), 3.73 (d, 1, J = 13.4 Hz), 3.41 (d, 1, J = 13.6 Hz), 3.28 (d, 1, J = 13.4 Hz), 3.16 (s, 12), 3.02 (s, 3), 1.59 (s, 3), 1.40 (s, 9), 1.35 (s, 9), 1.31 (s, 9), 1.27 (s, 9); ^{13}C NMR ($CDCl_3$) δ 187.99, 185.38, 185.09, 150.16, 148.97, 148.60, 148.40, 148.31, 141.73, 134.72, 134.67, 134.21, 133.94, 133.14, 133.09, 132.93, 128.41, 126.35, 126.18, 126.09, 125.87, 125.51, 125.48, 125.40, 125.15, 43.19, 37.60, 36.90, 38.86, 37.78, 34.38, 29.82, 34.52, 33.96, 31.50, 29.61, 31.74, 31.66, 31.34. Anal. Calcd for $C_{53}H_{71}N_3O_4S_3$: C, 69.92; H, 7.86; N, 4.62. Found: C, 70.27; H, 8.07; N, 4.56.

5,11,17,23-Tetra-*tert*-butyl-25-hydroxy-26,27,28-tris-((dimethyl(thiocarbamoyl))oxy)calix[4]arene (Cone/Partial Cone Conformer) (11). A 1.28 g (5.6%) sample of **11** was obtained in the chromatographic separation of the same reaction mixture described above. Recrystallization from $CHCl_3$-MeOH gave a white solid: mp 336–337 °C; ^{1}H NMR ($CDCl_3$) δ 7.32 (s, 2), 7.04 (s, 4), 6.78 (d, 2, J = 2.2 Hz), 4.12 (s, 2), 3.75 (s, 4), 3.57 (d, 2, J = 13.6 Hz), 3.38 (br s, 12), 3.28 (d, 2, J = 13.7 Hz), 3.21 (br s, 3), 2.68 (br s, 3), 1.42 (s, 9), 1.34 (s, 9), 1.09 (s, 18); ^{13}C NMR ($CDCl_3$) δ 188.43, 187.78, 153.03, 148.55, 147.98, 147.78, 147.49, 141.32, 134.79, 133.34, 131.45, 128.64, 126.40, 126.33 (Ar), 43.91, 43.84, 38.52, 36.84, 30.34, 34.43, 34.11, 31.75, 31.66, 31.22. Anal. Calcd for $C_{53}H_{71}N_3O_4S_3$: C, 69.92; H, 7.86; N, 4.62; S, 10.57. Found: C, 69.90; H, 7.87; N, 4.35.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-((dimethyl(thiocarbamoyl))oxy)calix[4]arene (Cone Conformer) (12). A 910 mg (1 mmol) sample of **11** was treated with 100 mg (1.5 mmol) of 60% NaH and 370 mg (3 mmol) of *N,N*-dimethyl(thiocarbamoyl) chloride in THF/DMF solution. Workup and flash chromatography as described above gave 80 mg of unreacted **11**, 360 mg (39%) of **3**, 0.16 g (17%) of a tetrasubstituted compound also in the partial cone conformation (**3′**),[31] and 60 mg (6.6%) of the tetrasubstituted compound **12**. Recrystallization of **12** from CH_2Cl_2–MeOH gave a white solid: mp 343–344 °C; ^{1}H NMR ($CDCl_3$) δ 7.06 (s, 8), 3.97 (d, 4, J = 13.5 Hz), 3.51 (very br s, 24), 3.39 (d, 4, J = 13.7 Hz), 1.16 (s, 36); ^{13}C NMR ($CDCl_3$) δ 189.03, 147.68, 146.20, 134.10, 125.54, 43.56, 38.88, 34.13, 31.38 31.20. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.11; H, 7.56; N, 5.33.

(30) Compound **9** is sometimes found in the reaction mixture from the $Ba(OH)_2 \cdot 8H_2O$ procedure.

(31) The compound has a different R_f value than **3** when chromatographed and a different melting point. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 368–369 °C. However, the proton and carbon NMR spectra are very similar to **3**: ^{1}H NMR (CD_2Cl_2) δ 7.41 (d, 2, J = 2.3 Hz), 7.29 (s, 2), 7.12 (s, 2), 6.86 (d, 2, J = 2.3 Hz), 3.91 (d, 2, J = 13.1 Hz), 3.82 (d, 2, J = 17.0 Hz), 3.71 (d, 2, J = 17.2 Hz), 3.46 (d, 2, J = 13.2 Hz), 3.33 (s, 6), 3.1 (very br base line envelope, 12), 2.50 (s, 3), 1.36 (s, 9), 1.29 (s, 9), 1.27 (s, 18), 0.08 (s, 3); ^{13}C NMR (CD_2Cl_2) δ 187.65, 153.12, 148.57, 148.38, 148.30, 147.24, 136.22, 135.25, 134.28, 132.39, 126.95, 126.35, 125.79, 125.23, 38.78, 34.53, 31.37, 36.92, 34.03, 31.76, 31.72. Several attempts to obtain a reasonable elemental analysis gave low carbon values. Calculations which include one-half molecule of $CHCl_3$ per molecule of calix[4]arene gave the best fit. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4 \cdot 1/2CHCl_3$: C, 64.19; H, 7.29; N, 5.30; S, 12.13. Found: C, 64.67; H, 7.40; N, 5.27.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethylcarbamoyl)thio)calix[4]arene (1,2-Alternate Conformer) (13). A mixture of 5.0 g (5 mmol) of the tetrasubstituted compound (1,2-alternate conformation) **2** and 100 g of di-*p*-tolyl ether was heated at gentle reflux for 24–30 h, cooled, diluted with petroleum ether–CH_2Cl_2 (80:20), and suction filtered through a pad of silica gel. The pad was washed with the above solvent mixture to remove di-*p*-tolyl ether which was recovered for reuse. The dry pad was slurried in CH_2Cl_2 and added to a prepared column made up of the same solvent. Flash chromatography with a gradient solvent system (100% CH_2Cl_2 to CH_2Cl_2–EtOAc, 95:5, in 1% incremental steps) gave, after trituration with a small amount of MeOH, 2.1 g (42%) of the rearranged tetrasubstituted compound (1,2-alternate conformation) **13**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 396.5–397.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.36 (d, 4, J = 2.2 Hz), 7.23 (d, 4, J = 2.1 Hz), 4.58 (d, 2, J = 13.2 Hz), 4.12 (s, 4), 3.66 (d, 2, J = 13.3 Hz), 2.89 (br s, 12), 2.72 (br s, 12), 1.31 (s, 36); ^{13}C NMR ($CDCl_3$) δ 167.15, 150.49, 146.75, 146.05, 127.81, 125.19, 124.22, 45.86, 39.04, 36.77, 34.35, 31.27. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.66; H, 7.75; N, 5.60.

5,11,17,23-Tetra-*tert*-butylcalix[4]arene-25,26,27,28-tetrathiol (14). (A) From 13. To a suspension of 2.0 g (2 mmol) of **13** in 150 mL of dry THF was added in one portion 1.28 g (32 mmol) of 95% $LiAlH_4$, and the mixture was refluxed for 8 h. Excess $LiAlH_4$ was destroyed by careful addition of EtOAc, followed by the addition of 150 mL of 10% H_2SO_4. The mixture was extracted with CH_2Cl_2, washed with H_2O and saturated brine, and dried over $MgSO_4$. Flash chromatography of the resulting crude solid using petroleum ether–CH_2Cl_2 (80:20) gave 0.92 g (64%) of the tetramercapto compound **14** in the 1,3-alternate conformation. Recrystallization from petroleum ether–CH_2Cl_2 gave a white solid:[32] mp 406 °C;[33] ^{1}H NMR ($CDCl_3$) δ 7.30 (s, 8), 4.08 (s, 8), 2.32 (br s, 4), 1.25 (s, 36); ^{13}C NMR ($CDCl_3$) δ 146.56, 140.84, 130.42, 127.23, 45.71, 34.11, 31.06. Anal. Calcd for $C_{44}H_{56}S_4$: C, 74.10; H, 7.92; S, 17.98. Found: C, 74.30; H, 7.79; S, 18.24.

(B) From 18. Reduction of 260 mg (0.26 mmol) of **18** as described above gave after workup 160 mg (86%) of **14**.

(C) From 19. Reduction of 770 mg (0.77 mmol) of **19** as described above gave after workup 420 mg (55%) of **14**.

5,11,17,23-Tetra-*tert*-butyl-25,26,27-tris((dimethylcarbamoyl)thio)calix[4]arene-28-ol (15). (A) From 5. A mixture of 1.0 g (1.1 mmol) of **5** and 20 g of di-*p*-tolyl ether was heated at gentle reflux for 24 h, cooled, and worked up in the same manner as for **13** to give, after trituration with MeOH, 0.39 g (39%) of the rearranged trisubstituted compound **15**. Recrystallization from CH_3CN gave a white solid: mp 331–332 °C; ^{1}H NMR ($CDCl_3$) δ 7.46 (s, 2), 7.24 (d, 2, J = 2.2 Hz), 7.06 (d, 2, J = 2.2 Hz), 7.02 (s, 2), 4.14 (s, 1), 4.06 (d, 4, J = 14.5 Hz), 3.98 (d, 2, J = 14.5 Hz), 3.61 (d, 2, J = 14.5 Hz), 3.03 (br s, 12), 2.99 (s, 6), 1.39 (s, 9), 1.30 (s, 9), 1.17 (s, 18); ^{13}C NMR δ ($CDCl_3$) δ 166.97, 166.74, 150.70, 150.08, 149.07, 147.02, 145.57, 145.32, 141.67, 129.94, 129.56, 127.87, 126.19, 126.11, 125.57, 124.43, 45.05, 38.58, 36.91, 34.36, 34.18, 33.76, 31.67, 31.20, 31.01. Anal. Calcd for $C_{53}H_{71}N_3O_4S_3$: C, 69.92; H, 7.86; N, 4.62. Found: C, 69.89, H, 7.83, N, 4.61.

(B) From 3. A mixture of 900 mg (0.9 mmol) of **3** and 15 mL of di-*p*-tolyl ether was heated at gentle reflux for 24 h, cooled, and worked up in the same manner as for **13** to give 172 mg (19%) of **15**. Identical results were obtained when a sample of **3** that had been dried for 24 h at 138 °C in vacuo prior to rearrangement was used.

5,11,17,23-Tetra-*tert*-butyl-25,26,27-trimercaptocalix[4]aren-28-ol (1,3-Alternate Conformer) (16). Reduction of 1.07 g (1.2 mmol) of **15** with $LiAlH_4$ as described above gave after workup and flash chromatography 0.56 g (52%) of **16**. Recrystallization from $CHCl_3$–MeOH gave a white solid:[32] mp 313–314 °C;[33] ^{1}H NMR at −60 °C[34] ($CDCl_3$) δ 7.52 (s, 2), 7.32 (s, 2), 7.17 (s, 2), 7.02 (s, 2), 5.24 (s, 1), 4.20 (d, 4, J = 16 Hz), 4.10 (d, 2, J = 16 Hz), 3.67 (d, 2, J = 14.4 Hz), 3.07 (s, 2), 2.24 (s, 1), 1.35 (s, 9), 1.32 (s, 9), 1.13 (s, 18); ^{13}C NMR δ ($CDCl_3$) 142.04, 130.51, 126.92, 126.08, 45.53, 38.65, 34.16, 34.04, 33.88, 31.56, 31.10, 30.96. Anal. Calcd for $C_{44}H_{56}OS_3$: C, 75.81; H, 8.1; S, 13.8. Found: C, 75.40; H, 8.03; S, 13.2.

5,11,17,23-Tetra-*tert*-butyl-25-((dimethyl(thiocarbamoyl))oxy)-26,27,28-tris((dimethylcarbamoyl)thio)calix[4]arene (Partial Cone Conformer) (17). To a suspension of 70 mg (1.8 mmol) of NaH (60% oil dispersion) in 15 mL of dry DMF was added 550 mg (0.6 mmol) of the trisubstituted compound **15**, and the mixture was stirred at rt for 2 h. A 220 mg (1.8 mmol) sample of *N,N*-dimethyl(thiocarbamoyl) chloride was added in one portion, and the reaction mixture was stirred at rt overnight. The mixture was poured into 50 mL of H_2O, filtered, and air dried to give 540 mg (90%) of **17**. Recrystallization from CH_3CN gave a white solid: mp 369–370 °C; ^{1}H NMR ($CDCl_3$) δ 7.46 (s, 2), 7.25 (s, 2), 7.20 (d, 2, J = 2.0 Hz), 7.04 (d, 2, J = 2.0 Hz), 4.13 (d, 2, J = 13.3 Hz), 4.07 (d, 2, J = 14.5 Hz), 3.92 (d, 2, J = 14.6 Hz), 3.42 (s, 3), 3.39 (d, 2), 3.05 (very br s, 6), 2.99 (s, 12), 2.85 (s, 3), 1.43 (s, 9), 1.37 (s, 9), 1.13 (s, 18); ^{13}C NMR ($CDCl_3$) δ 187.97, 166.77, 166.71, 149.55, 149.51, 148.14, 148.06, 147.73, 146.40, 144.67, 135.36, 129.20, 128.84, 127.28, 125.70, 122.25, 44.85, 43.57, 43.23, 36.92, 36.77, 34.77, 34.59, 34.24, 34.13, 31.60, 31.38, 30.96, 29.61. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.83; H, 7.46; N, 5.57.

5,11,17,23-Tetra-*tert*-butyltetrakis((dimethylcarbamoyl)thio)calix[4]arene (Partial Cone Conformer) (18). A mixture of 400 mg (0.4 mmol) of **17** and 20 g of di-*p*-tolyl ether was heated at gentle reflux for 7 h, cooled, and worked up in the same manner as described above to give 310 mg (77%) of the rearranged tetrasubstituted compound **18**. Recrystallization from CH_3CN gave a white solid: mp 385–386 °C; ^{1}H NMR ($CDCl_3$) δ 7.54 (s, 2), 7.30 (s, 2), 7.21 (d, 2, J = 2.2 Hz), 6.89 (d, 2, J = 2.2 Hz), 4.43 (d, 2, J = 13.3 Hz), 4.05 (d, 2, J = 14.2 Hz), 3.90 (d, 2, J = 14.4 Hz), 3.54 (d, 2, J = 13.1 Hz), 3.13 br shoulder blending into 3.03 (s, 24), 1.42 (s, 9), 1.38 (s, 9), 1.09 (s, 18); ^{13}C NMR ($CDCl_3$) δ 167.73, 167.43, 167.03, 152.58, 149.28, 148.83, 148.58, 147.17, 145.77, 144.83, 129.94, 125.82, 125.36 124.15, 124.11, 44.77, 39.84, 36.93, 36.69, 34.51, 34.42, 34.04, 31.34, 30.9. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.24, h, 7.49; N, 5.72.

5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis((dimethylcarbamoyl)thio)calix[4]arene (1,3-Alternate Conformer) (19). A mixture of 1.07 g (1.07 mmol) of **6** in 20 mL of di-*p*-tolyl ether was heated at gentle reflux for 48 h. Workup as described above gave 0.52 g (49%) of the rearranged tetrasubstituted compound **19**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 397–399 °C; ^{1}H NMR ($CDCl_3$) δ 7.18 (s, 8), 4.07 (s, 8), 2.98 (br s, 12), 2.70 (br s, 12), 1.27 (s, 36); ^{13}C NMR ($CDCl_3$) δ 166.83, 150.13, 147.87, 128.23, 123.65, 45.83, 36.53, 34.07, 31.17. Anal. Calcd for $C_{56}H_{76}N_4O_4S_4$: C, 67.43; H,7.68; N, 5.62. Found: C, 67.38; H, 7.79; N, 5.40.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis((dimethylcarbamoyl)thio)calix[4]arene 26,28-diol (*Anti* Conformer) (20). (A) From 4. A solution of 880 mg (1.07 mmol) of **4** in 20 mL of diphenyl ether was heated at gentle reflux for 16 h. Workup and flash chromatography as previously described gave 380 mg (43%) of the rearranged disubstituted compound **20**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 322.5–323.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.31 (s, 4), 7.05 (s, 4), 4.38 (s, 2), 4.27 (d, 4, J = 14.9 Hz), 3.78 (d, 4, J = 14.6 Hz), 2.94 (br s, 6), 2.78 (br s, 6), 1.31 (s, 18), 1.24 (s, 18); ^{13}C NMR ($CDCl_3$) δ 166.60, 152.28, 150.08, 144.91, 142.06, 127.03, 126.57, 125.56, 124.89, 38.77, 36.77, 34.24, 33.83, 31.64, 30.99. Anal. Calcd for $C_{50}H_{66}N_2O_4S_2$: C, 72.95; H, 8.08; N, 3.40. Found: C, 72.78; H, 8.04; N, 3.36.

(B) From 8. The above reaction was repeated using the disubstituted compound **8**. Although rearrangement took place, the yield of crude product was low (16%), and a mixture of *anti*-1,3-disubstituted compound **20** and *syn*-1,3-disubsti-

(32) Compounds **14**, **16**, and **21** slowly turn yellow upon exposure to light over a period of several weeks.

(33) The melting point apparatus must be heated to just below the melting point prior to dropping in the sealed capillary; otherwise, compound **14** slowly polymerizes and then decomposes above 440 °C.

(34) The ^{1}H NMR of **16** at 20 °C gave very broad and ill-defined peaks.

tuted compound **22** in a 1:3 ratio was obtained. All attempts to separate the two compounds failed: ^{1}H NMR ($CDCl_3$) δ 7.12 (s, 4), 6.86 (s, 4), 4.61 (s, 2),4.34 (d, 4, J = 14.1 Hz), 3.61 (d, 4, J = 14.0 Hz), 3.23 (br s, 6), 3.03 (br s, 6), 1.34 (s, 18), 0.93 (s, 18); ^{13}C NMR ($CDCl_3$) δ 166.37, 151.38, 150.55, 143.85, 142.27, 128.50, 125.96, 125.60, 123.82,37.83, 37.14, 37.06, 34.04, 33.88, 31.66, 30.71.

5,11,17,23-Tetra-*tert*-butyl-25,27-dithiocalix[4]arene-26,28-diol (21). (A) From 20. Reduction of 422 mg (0.513 mmol) of **20** with $LiAlH_4$ as described above gave after workup and flash chromatography 240 mg (69%) of compound **21** in the cone conformation. Recrystallization from ether–hexane gave a white solid:[32] mp 254–255 °C;[33] ^{1}H NMR ($CDCl_3$) δ 7.15 (s, 4), 6.81 (s, 4), 5.83 (s, 2), 4.40 (d, 4, J = 14.38 Hz), 4.21 (s, 2), 3.62 (d, 4, J = 14.00 Hz), 1.34 (s, 18), 0.92 (s, 18); ^{13}C NMR ($CDCl_3$) δ 151.03, 148.97, 142.40, 140.59, 127.68, 126.01, 125.73, 123.42, 37.76, 33.94, 33.86, 31.68, 30.76. Anal. Calcd for $C_{44}H_{56}O_2S_2$: C,77.60; H, 8.29; S, 9.42. Found: C, 76.93; H, 8.32; S, 9.18.

(B) From 20 + 22. Reduction of 235 mg (0.285 mmol) of the mixture of **20** and **22** described above gave 113 mg (58%) of **21**.

5,11,17,23-Tetra-*tert*-butyl-25-((dimethylcarbamoyl)-thio)calix[4]arene-26,27,28-triol (Partial Cone Conformer) (23). A mixture of 0.74 g (1mmol) of the monosubstituted compound **7** in 20 g of di-*p*-tolyl ether was heated at gentle reflux for 1.5 h. Workup and flash chromatography as previously described gave 0.52 g (70%) of the rearranged monosubstituted compound **23**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 254–255 °C; ^{1}H NMR ($CDCl_3$) δ 9.17 (s, 1), 7.79 (s, 2), 7.11 (d, 2, J = 2.2 Hz), 7.03 (s, 2), 7.01 (d, 2, J = 2.3 Hz), 7.00 (s, 2),4.43 (d, 2, J = 13.8 Hz), 4.11 (d, 2, J = 13.9 Hz), 3.68 (d, 2, J = 14.0 Hz), 3.47 (d, 2, J = 14.0 Hz), 3.26 (s, 3), 3.03 (s, 3),1.25 (s, 18), 1.17 (s, 9), 1.03 (s, 9); ^{13}C NMR ($CDCl_3$) δ 166.05, 152.01, 148.82, 146.82, 144.39, 143.79, 143.14, 128.06, 127.79, 126.51, 126.18, 125.98, 125.60, 125.45, 37.45, 32.39, 37.32, 34.00, 33.90, 31.56, 31.34, 30.70. Anal. Calcd for $C_{47}H_{61}NO_4S\cdot H_2O$: C, 74.86; H, 8.42; N, 1.86. Found: C, 74.93; H, 8.33; N, 1.82.

5,11,17,23-Tetra-*tert*-butyl-25-thiocalix[4]arene-26,27,28-triol (Cone Conformation) (24). Reduction of 1.18 g (1.6mmol) of **23** with $LiAlH_4$ gave after workup and flash chromatography 0.93 g (87%) of **24**. Recrystallization from $CHCl_3$–MeOH gave a white solid: mp 211–212 °C; ^{1}H NMR ($CDCl_3$) δ 9.83 (br s, 1), 8.86 (br s, 2), 7.13 (d, 2, J = 2.2 Hz), 7.05 (s, 2), 7.04 (s, 2), 7.00 (d, 2, J = 2.2 Hz), 5.70 (br s, 1), 4.50 (d, 2, J = 14.0 Hz), 4.17 (d, 2, J = 13.9 Hz), 3.70 (d, 2, J = 13.7 Hz), 3.50 (d, 2, J = 14.0 Hz), 1.23 (s, 18), 1.22 (s, 9), 1.10 (s, 9); ^{13}C NMR ($CDCl_3$) δ 149.73, 148.73, 147.20, 143.80, 143.51, 141.14, 127.93, 127.82, 126.40, 126.27, 126.12, 125.88, 125.57, 37.46, 32.68, 34.13, 34.02, 33.93, 31.52, 31.39, 30.82. Anal. Calcd for $C_{44}H_{56}O_3S\cdot 1/2CHCl_3$: C, 73.76; H, 7.86; S, 4.42. Found: C, 73.80; H, 7.79; S, 4.30.

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Supporting Information Available: The assignment of NMR peaks and the molecular mechanics calculations for the calix[4]arenethiols (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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