Synthesis and Reactivity of Calix[4]arene-Based Copper Complexes[1]

Dejian Xie and C. David Gutsche*

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

Received June 1, 1998

The interaction of copper and oxygen with calix[4]arenes carrying one or two chelating moieties on the upper rim has been investigated. The chelating moieties include pyrazolylethyl and pyridylethyl functions attached to an amino nitrogen separated from the calixarene rim by one or two methylene groups. The products obtained by treatment of the pyrazole-based calixarenes with Cu(I) and Cu(II) are stable to oxidation (by O_2) and reduction (by MeOH), respectively. Those produced by treatment of the pyridine-based calixarenes with Cu(I), however, are more reactive and undergo intramolecular oxidation at the benzylic carbon of the chelate-containing side chain. Putative pathways for the decomposition of the dicopper−dioxygen complexes are discussed.

The interaction of dioxygen with copper-containing complexes is a vigorously studied topic in bioorganic chemistry,[2,3] much of the research focusing on the structure of the copper−dioxygen species and the way in which they transfer oxygen to an acceptor site, either intramolecularly or intermolecularly. A striking intramolecular example was reported by Karlin and coworkers[4] who showed that the dicopper−dioxygen complex prepared from a compound containing two chelating arms attached to a *m*-xylyl framework undergoes oxidation at the 2-position of the xylyl moiety to yield a phenolic function after removal of the copper. This provided the incentive for the present investigation which sought to achieve the *inter*molecular oxidation of a guest molecule captured within the cavity of a host molecule. Although this goal has yet to be realized, some useful approaches to the synthesis of dinuclear complexing agents have been developed, and the oxidation products resulting from their interaction with copper and oxygen are of interest.

Calix[4]arenes, which are cavity-containing molecules easily obtainable in good yield from the base-induced condensation of *p-tert*-butylphenol and formaldehyde,[5] were chosen as the putative hosts. When appropriately modified they provide attractive platforms to which to attach chelating moieties for metal ion complexation. In the present work two types of ligands have been attached to the upper rim of calix[4]arenes, viz. bis[2-(3,5-dimethyl)-1-pyrazolylethyl]amine moieties[6] (the pyrazole series) and bis(2,2′-pyridylethyl)amine moieties[7] (the pyridine series).

Synthesis of Calix[4]arenes Carrying Pyrazole Ligands on the Upper Rim. A calix[4]arene carrying a single pyrazole-containing chelating moiety on the upper rim was prepared as shown in Scheme 1 starting with the previously described[8] *p*-bromobenzenesulfonate (abbreviated as "brosylate") of 5-cyanomethylcalix[4]arene (**1**). Acid-catalyzed hydrolysis of **1** proceeded smoothly to yield the brosylate of 5-carboxymethylcalix[4]arene (**2**) to which bis[2-(3,5-dimethyl)-1-pyrazolylethyl]amine was then attached either via the acid chloride **3** or directly from **2** via the dicyclohexylcarbodiimide (DCC) procedure. The product **4** was reduced with diborane[9] to afford an 88% yield of the desired product **5**. A calix[4]arene carrying a pair of pyrazole-containing moieties on the upper rim (**7**) was prepared in similar fashion, starting with the brosylate of 5,17-dicyanomethyl-11,23-di-*tert*-butylcalix[4]arene[10,11] and using the DCC method for introducing the pyrazole moieties. In this case attempts to prepare the diacid chloride of the di-carboxymethyl compound resulted in the formation of the anhydride **8** which was subsequently shown to be very useful in the preparation of a variety of upper rim-functionalized calixarenes.[11] The analogue of **7** lacking the *p-tert*-butyl groups was prepared in like fashion starting with the brosylate of 5,17-dicyanomethylcalix[4]arene (**9**) and converting it to **12** via the bis-carboxymethyl compound **10** and then to the bis-amide **11**.

(1) Paper No. 49 in the series entitled "Calixarenes". For paper no. 48, see: Wang, J.; Gutsche, C. D. *J. Am. Chem. Soc.* **1998**, *120*, 12226−12231.

(2) For general reviews, cf: (a) Karlin, K. D.; Tyeklár, Z.; Zuberbühler, A. D. In *Bioinorganic Catalysis*; Reedijk, J., Ed.; Marcel Dekker: New York, 1992; Chapter 9. (b) Sorrell, T. N. *Tetrahedron* **1989**, *45*, 3.

(3) For recent reviews, cf: (a)Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737. (b) Karlin, K. D., Kaderli, S.; Zuberbühler, A. D. *Acc. Chem. Res.* **1997**, *30*, 139. (c) Tolman, W. B. *Acc. Chem. Res.* **1997**, *30*, 227.

(4) Cf. refs 1−6 in Karlin, K. D.; Nasir, M. S.; Cohen, B. I.; Cruse, R. W.; Kaderli, S.; Zuberbühler, A. D. *J. Am. Chem. Soc.* **1994**, *116*, 1324.

(5) For reviews, cf: (a) Gutsche, C. D. Calixarenes Revisited. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1998. (b) Böhmer, V. Calixarenes, Macrocycles with (Almost) Unlimited Possibilties. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 713−745. (c) Gutsche, C. D. Calixarenes. *Aldrichimica Acta* **1995**, *28*, 3−9. (d) *Calixarenes, A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer: Dordrecht, The Netherlands 1991. (e) Gutsche, C. D. Calixarenes. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: London, 1989.

(6) Sorell, T. N.; Malachowski, M. R.; Jameson, D. L. *Inorg. Chem.* **1982**, *21*, 3251.

(7) Brady, L. E.; Freifelder, M.; Stone, G. R. *J. Org. Chem.* **1961**, *26*, 4757.

(8) (a) Alam, I.; Sharma, S. K.; Gutsche, C. D. *J. Org. Chem.* **1994**, *59*, 3716. (b) Sharma, S. K.; Alam, I.; Gutsche, C. D. *Synthesis* **1995**, 1089.

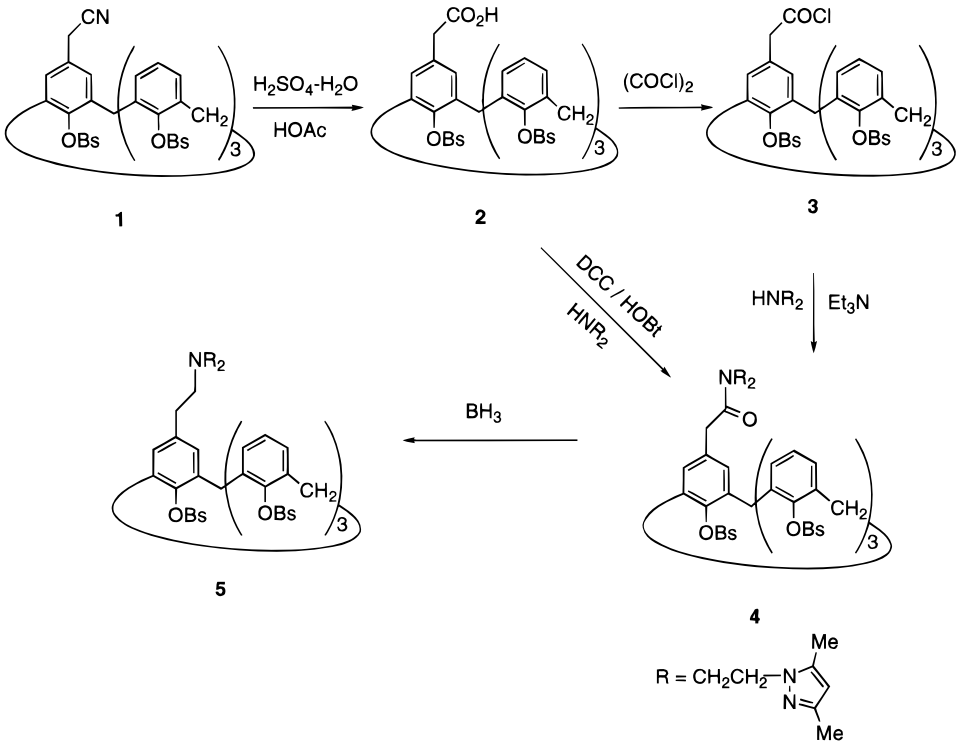
(9) Longer reaction times result in the formation of additional compounds, presumably the result of reduction of the 3,5-dimethlyl pyrazole ring. The preferred procedure for this reaction uses a large excess of diborane to force the reduction to go to completion but a short reaction time at room temperature to avoid over reduction.

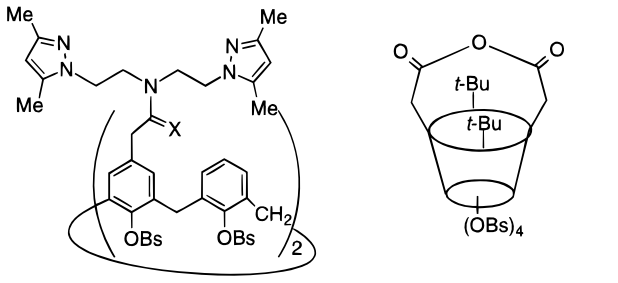
(10) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1995**, *60*, 6070.

(11) Xie, D.; Gutsche, C. D. *J. Org. Chem.* **1997**, *62*, 2280.

10.1021/jo981038l CCC: $15.00
Published on Web 11/17/1998

Scheme 1

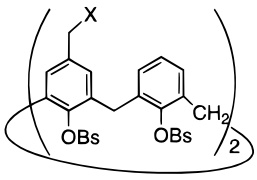




6: X = O

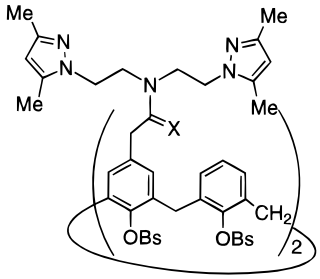
7: X = H_2

8



9: X = CN

10: X = COOH



11: X = O

12: X = H_2

In compounds **5**, **7**, and **12**, the tertiary amine nitrogens are separated from the *p*-positions of the calixarene by two carbons. In the thought that the host properties of the pyrazole-containing calixarenes might be altered if this separation is a single carbon,[12] the synthesis of **16** was carried out as shown in Scheme 2. Starting with 5,17-bis-*tert*-butylcalix[4]arene[10] (**13**), chloromethylation[13] produced **14** which was treated with bis[2-(3,5-dimethyl)-1-pyrazolylethyl]amine (the same reagent used in the previous synthesis), and the resulting product (**15**) was converted to the brosylate **16**. The choice of solvent proved to be important for this last step, only an intractable mixture being obtained when the reaction was carried out in THF but a clean reaction occurring in CH_2Cl_2. It is postulated that brosylation more effectively competes with decomposition of **15** to a *p*-quinonemethide (by loss of the amine moieties) in the less polar CH_2Cl_2 than in the more polar THF, producing the cone conformer.

Interaction of Calix[4]arene-Based Pyrazole with Copper. Calixarenes **5**, **7**, **12**, and **15** were treated with $[Cu(ClO_4)_2]6H_2O$, but in no case was there any indication that the presumed Cu(II) complexes are reduced to Cu(I) complexes in MeOH solution.[14] This contrasts with the observations by Nolte and co-workers with compounds containing a pair of pyrazole-containing moieties attached to a diaza-18-crown-6 framework[15] or a diphenylglycouril framework,[16] both of which effect oxidation of substrate molecules such as MeOH (oxidized to HCHO) and benzyl alcohols (oxidized to benzaldehydes). The same calixarenes were treated[17] with $[Cu(CH_3CN)_4]PF_6$, but again there was no indication that the presumed Cu(I) complexes were oxidized when O_2 was bubbled through CH_2Cl_2 solutions. In addition to Nolte's work, studies with pyrazole-containing copper complexes have

(12) Martens, C. F.; Schenning, A. P. H. J.; Feiters, M. C.; Berens, H. W.; van der Linden, J. G. M.; Admiraal, G.; Beurskens, P. T.; Kooijman, H.; Spek. A. L.; Nolte, J. M. *Inorg. Chem.* **1995**, *19*, 4735.

(13) Almi, M.; Arduini, A.; Casnati, A.; Pochini, A.; Ungaro, R. *Tetrahedron* **1989**, *45*, 2117.

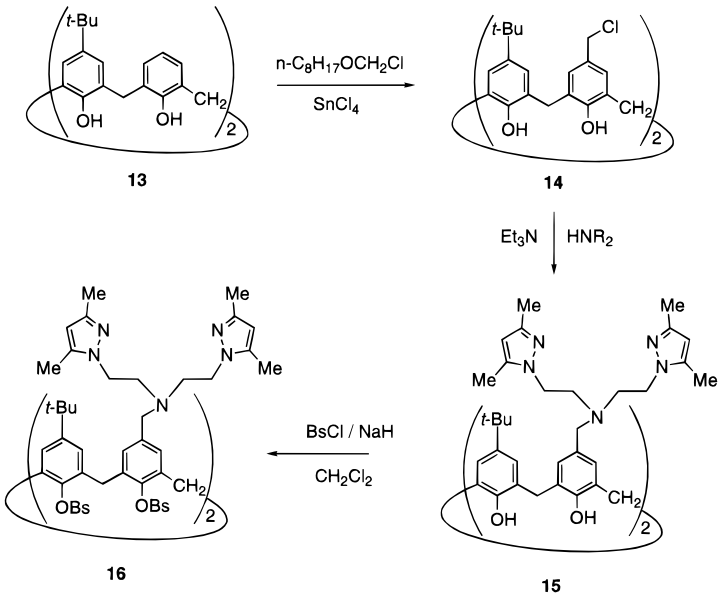
(14) This reaction is easily followed by the color of the solution, reduction resulting in the green solution (Cu(II) species) changing to colorless or pale yellow (Cu(I) species). Also see refs 6 and 7.

(15) Martens, C. F.; Schenning, A. P. H. J.; Klein Gebbink, R. J. M.; Feiters, M. C.; van der Linden, J. G. M.; Heck, J.; Nolte, R. J. M. *J. Chem. Soc., Chem. Commun.* **1993**, 88.

(16) Martens, C. F.; Klein Gebbink, R. J. M.; Feiters, M. C.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1994**, *116*, 5667.

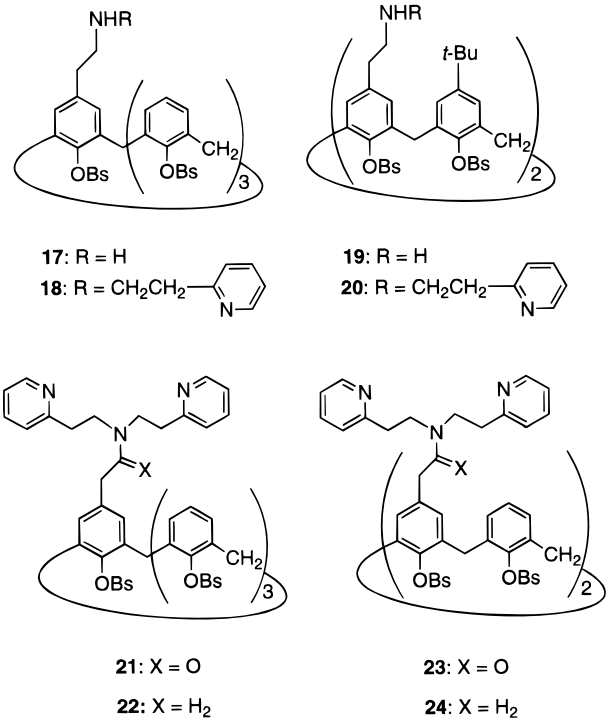
(17) Kubas, G. J. *Inorg. Synth.* **1979**, *19*, 90.

Scheme 2

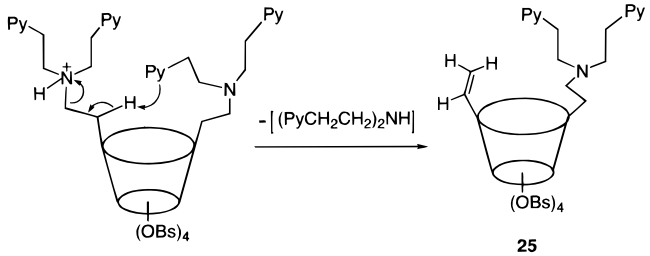


also been reported by several other research groups. Kitajima and co-workers,[18] for example, provided the first demonstration of a synthetic model of hemocyanin, showing that a sterically hindered tris(pyrazolyl)borate copper complex reversibly binds dioxygen and can oxidize various substrates such as cyclohexene (e.g., to cyclohexene-3-ol). However, Sorrell and co-workers[19] found that dicopper(I) complexes of bis{bis[2-(1-pyrazolyl)ethyl]-amino}-*m*-xylene and related molecules do not effectively bind dioxygen and are devoid of oxidizing capacity. The reasons for the differences among these various pyrazole-containing systems, particularly between the seemingly analogous diphenylglycouril- and calixarene-derived compounds, are not obvious but must arise in some fashion from the different geometries of the frameworks.

Synthesis of Calix[4]arenes Carrying Pyridyl Ligands on the Upper Rim. Attempts to prepare the target molecules **22** and **24** by treatment of amines **17** and **19** with 2-vinylpyridine were unsuccessful, the reactions stopping at the stage of monosubstitution to give **18** and **20**. Treatment of **18** and **20** with a large of excess of 2-vinylpyridine yielded only starting materials, confirming the difficulty of introducing a second pyridylethyl group onto a nitrogen already carrying this moiety. Attention, therefore, was directed to the synthesis pathways described above for the pyrazole series. Thus, treatment of the brosylate of 5-carboxymethylcalix[4]-arene with bis(2,2-pyridylethyl)amine using the DCC procedure yielded **21**, and diborane reduction converted it to **22**. In like fashion, the brosylate of 5,17-bis-carboxymethylcalix[4]arene yielded **24**. Surprisingly, the diborane reductions of **21** and **23** proceeded in somewhat different yields, viz. 80% in the first case but only 65%



in the second case in which a minor product was also isolated in 8% yield. On the basis of its elemental analysis and its ^{1}H NMR, ^{13}C NMR, and 2D COSY NMR spectra the side product was identified as **25**, a compound in which one of the dipyridylamine moieties of **24** has been extruded to produce a vinyl group. It is postulated

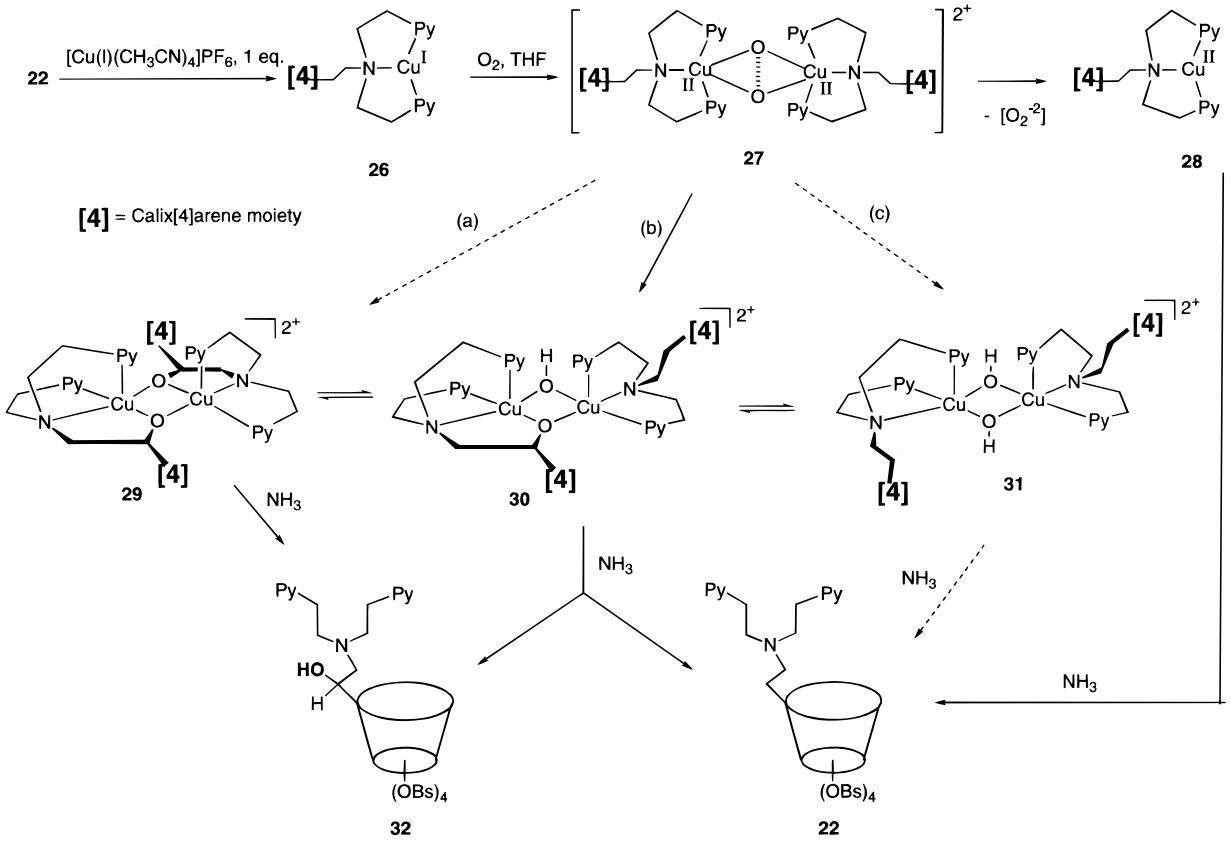


that one of the pyridyl nitrogens of **24** acts as an internal

(18) (a) Kitajima, N.; Koda, T.; Hashimoto, S.; Kitagawa, T.; Moro-oka, Y. *J. Chem. Soc. Chem. Commun.* **1988**, 151. (b) Kitajima, N.; Fujisawa, K.; Moro-oka, Y.; Toriumi, K. *J. Am. Chem. Soc.* **1989**, *111*, 8975. (c) Kitajima, N.; Koda, T.; Iwata, Y.; Moro-oka, Y. *Ibid.* **1990**, *112*, 8833. (d) Kitajima, N.; Fujisawa, K.; Fujimoto, C.; Moro-oka, Y.; Hashimoto, S.; Kitagawa, T.; Toriumi, K.; Tatsumi, K.; Nakamura, A. *Ibid.* **1992**, *114*, 1277.

(19) (a) Sorell, T. N.; Malachowski, M. R.; Jameson, D. L. *Inorg. Chem.* **1982**, *21*, 3251. (b) Sorell, T. N.; Jameson, D. L.; O'Connor, C. J. *Ibid.* **1984**, *23*, 190. (c) Sorell, T. N.; Vankai, V. A.; Garrity, M. L. *Ibid.* **1991**, *30*, 207.

Scheme 3



base to initiate a Hoffmann-type elimination on the neighboring side chain which carries a protonated dipyridylamine moiety that can act as a leaving group. A comparable product is not observed in the pyrazole series, probably because of the lower basicity of the pyrazole nitrogen as compared with the pyridine nitrogen.

Interaction of Calix[4]arene-Based Pyridine with Copper. Calixarene **22**, containing a single chelating ligand, was treated with $[Cu(I)(CH_3CN_4)]PF_6$ in dry THF, and dry O_2 was then bubbled through the solution at room temperature. This resulted in an immediate color change from pale yellow to green, indicating oxidation of Cu(I) to Cu(II). After about 4 h, the green solution became cloudy, and a green powder started to precipitate. The mixture was stirred overnight under an oxygen atmosphere and then filtered to give a green solid (**29**) and a blue-green filtrate. The copper was removed from these complexes by treatment with aqueous NH_4OH followed by extraction with CH_2Cl_2, affording 30% (based on **22**) of **32** from the green solid and 55% of starting material (**22**) along with an additional 5% of **32** from the filtrate.

Product **32** was identified as a compound in which hydroxylation has occurred at the benzylic position, creating a stereogenic center at this carbon. The chiral character of **32** is manifested in its ^{1}H NMR spectrum which is considerably more complex than that of **22**. For example, the $ArCH_2Ar$ methylene protons appear as two pairs of doublets in the spectrum of **22** but as four pairs of doublets in that of **32**. Also of note in the ^{1}H NMR spectrum of **32** is the doublet of doublets centered at δ 4.45 indicating two different coupling constants with the two adjacent diastereotopic protons which are assigned to the proton at the stereogenic carbon. The carbon at this position gives rise to a line at δ 69.9 in the ^{13}C NMR spectrum.

On the basis of the detailed studies of related systems, particularly those investigated by Tolman and co-workers,[20] it is postulated that the benzylic oxidation involves the formation of "side-on" dicopper−dioxygen complexes, as represented by **27**. The exact pathway by which **27** leads to benzylic oxidation, however, remains unclear. One possibility is to view the oxidation as a direct insertion process formally analogous to that of carbene with a C−H bond which leads to C−CH_3, both carbene and oxygen atom being neutral entities carrying only six electrons in their outer valence shell. However, stepwise pathways involving radical intermediates appear to be more likely. In the present case a benzyl radical could be generated by abstraction of a benzyl hydrogen by one of the oxygens of **27** followed by attachment of the benzyl radical to the other oxygen, resulting in the formation of **30**. Removal of the copper by treatment of **30** with ammonia should then yield the hydroxylated compound **32** as well as starting material **22**, both of which are, in fact, isolated. The green precipitate, however, yields *only* the hydroxylated compound **32** and, therefore, is formulated as **29**, support for which is provided by an elemental analysis that is in close agreement with the calculated values and a FAB mass spectrum that shows signals at 3265 for the parent ion (calcd for **29**, 3265) and the parent ion + PF_6 at 3408. Although the formation of **29** from **27** (pathway a, Scheme 3) is commensurate with a direct insertion process, pathway-b involving radical intermediates is considered to be the more likely. To account for

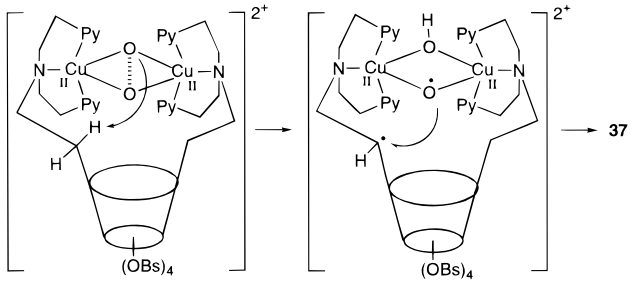
(20) Mahapatra, S.; Halfen, J. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11575.

the formation of **29** it is postulated that **30** undergoes disproportionation (two molecules of **30** yielding one molecule of **29** and one molecule of **31**), driven perhaps by the precipitation of **29** from the reaction mixture. Such a scheme accommodates the formation of both hydroxylated product and recovered starting material without recourse to the solvent as a source of hydrogen atom (i.e., pathway c).

Several other examples of benzylic oxidations in copper-containing complexes have been reported.[20] One that is particularly pertinent to the present work involves the Cu(I)−dioxygen complex of *N*,*N*-bis[2-(2-pyridyl)ethyl]-2-phenylethylamine studied by Itoh and co-workers.[21,22] When the Cu(I) complex of this compound is directly generated, treatment with O_2 affords a 50% yield of benzylic oxidation product. However, when the Cu(I) complex is generated in situ by treatment of the Cu(II) complex with a reducing agent (e.g., benzoin) followed by O_2 a 100% yield of benzylic oxidation product is observed. A very careful and detailed study[22] of this system, including isotopic labeling experiments (using $^{18}O_2$ in crossover experiments and D-substituted ligands in deuterium isotope experiments), led to the conclusion that the benzylic oxidation is an intramolecular process that proceeds via a rate-determining O−O bond homolysis of the μ-η^2:η^2 peroxodicopper(II) intermediate (i.e., analogous to **27**). As with the present system,[23] spectroscopic measurements failed to reveal the presence of a bis-μ-oxodicopper(III) intermediate (i.e., analogous to **27** lacking the O−O bond), presumably because of its high reactivity and/or instability.

In similar fashion **24**, containing a pair of chelating ligands, was treated with 2 equiv of $[Cu(I)(CH_3CN_4)]PF_6$ to generate a complex presumed to be **33**, and O_2 was bubbled through the THF solution at room temperature to form a species presumed to be **34**. In contrast to **27** a green precipitate formed from **34** after only a few minutes, and the reaction appeared to be complete in less than 2 h. Removal of copper from the green solid gave a mixture from which 30% (based on **24**) of **36** together with 15% of the starting material **24** were isolated. This contrasts with the decomposition of **29** which yielded *only* the hydroxylated product and *none* of the starting material. From the filtrate an additional 10% of **36** and 28% of **24** were isolated. The structure of the hydroxylated product **36** was established on the basis of its ^1H and ^{13}C NMR spectra which, similar to those of **32**, display complex patterns as a result of the chirality introduced by the benzylic hydroxylation. A doublet of doublets (J = 1.4 and 8.9 Hz, integrating for a single proton) at δ 4.61 is assigned to the proton at the stereogenic carbon, indicating that only one of the chelate-containing appendages is hydroxylated. Confirmation that the species formulated as **37** contains two calix[4]arene moieties, two copper atoms and one O_2 molecule is provided by the electrospray mass spectrum which shows a peak at 983.5 for M/2 (corresponding to a mass of 1867 (calcd 1866).

Scheme 4 depicts the postulated pathways for decomposition of **34**, employing the same assumptions that are discussed above[23] for the decomposition of **27**. Missing from Scheme 4, however, is the counterpart of **29** in Scheme 3, because no doubly hydroxylated material was isolated when starting with **24**. This provides additional support for the pathway discussed for Scheme 3 and pictured below for the conversion of **34** to **37** whereby benzylic oxidation takes place in an entirely intramolecular fashion. In contrast to **30**, compound **37** cannot undergo disproportionation in a comparable fashion, thus accounting for the isolation of both hydroxylated product and starting material by removal of copper from the green precipitate.



34 **39**

Whether the recovered starting material has its genesis only from **37** or whether it might also arise along other pathways is uncertain. That the latter might be possible is suggested by experiments in which benzoin or acetoin are included in the reaction mixture starting with **24**. In these cases the ratio of the yields of hydroxylated product **36** and recovered starting material **24** was ca. 3:1, in contrast to the approximately 1:1 ratio obtained in the absence of these oxidizing agents. This result is similar to that reported by Itoh et al. (vide supra) and may be due to dioxygen-induced oxidation of the dicopper(I)−dioxygen complex **34** to the dicopper(II) complex **35**, the action of the benzoin (or acetoin) being to regenerate the dicopper(I) complex **33** and thereby allow it to again interact with dioxygen and undergo further reaction along the pathway leading to **37**.

The goal of this investigation was to achieve intermolecular oxidation of a guest molecule held in the cavity of the calixarene. It is known that *p*-*tert*-butylcalix[4]arene and toluene do, in fact, form a tight *endo*-calix complex in the solid state,[24] but reactions carried out in THF containing toluene or isopropylbenzene showed no indication of substrate oxidation, either aromatic or benzylic. In THF solution a putative guest molecule must compete with the solvent molecules for occupancy of the cavity of the calix, and the solvent molecules—smaller and in greater abundance—inexorably prevail. However, if intramolecular pathways of decomposition of the dicopper−oxygen complex can be made less available and if the oxidation of a guest molecule can be made sufficiently rapid, solvent competition need not preclude the formation of an intermolecular reaction product. Benzylic oxidation should be curtailed by changing H to

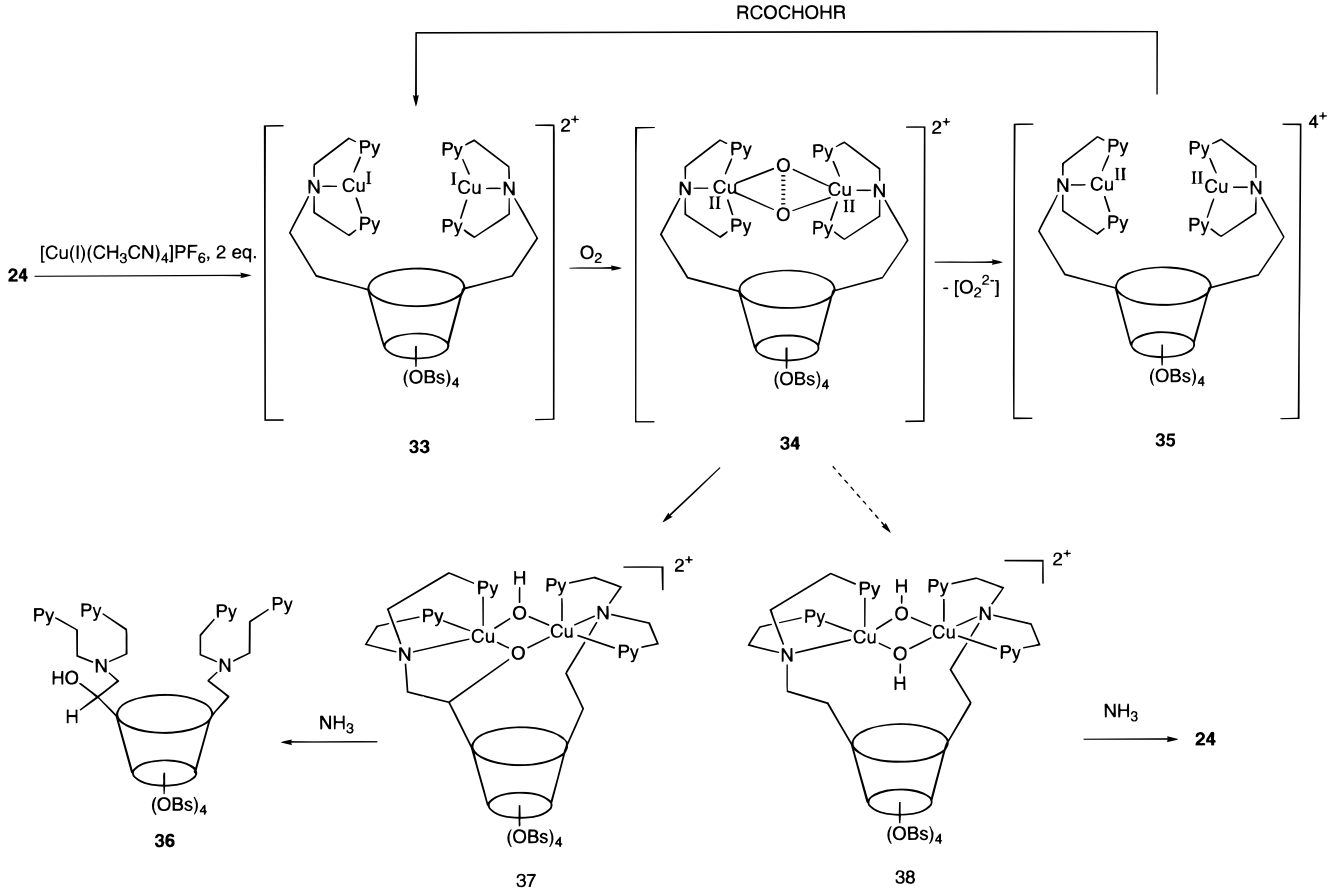
(21) Itoh, S.; Kondo, T.; Komatsu, M.; Ohshiro, Y.; Li, C.; Kanehisa, N.; Kai, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 4714.

(22) Itoh, S.; Nakao, H.; Berreau, L. M.; Kondo, T.; Komatsu, M.; Fukazumi, S. *J. Am. Chem. Soc.* **1998**, *120*, 2890.

(23) We are indebted to Dr. Lisa Berreau, working in the laboratories of Professor William B. Tolman at the University of Minnesota, for investigating the spectroscopic properties of the complexes generated from calixarenes **22** and **24**. Although the slow formation of green solutions was observed, characterized by a broad absorption centered at ca. 660 nm, no evidence for the existence of dioxygen complexes at −76 °C in THF solution was revealed. Dr. Berreau suggests that **34** might adopt a geometry upon metal binding in which steric hindrance at the metal center is reduced compared with the systems of Karlin and Itoh, resulting in a highly reactive (thermally unstable) complex that is not observable at the temperatures employed.

(24) Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1005.

Scheme 4



alkyl in **24**, and the cavity size can be enlarged by increasing the distance between the chelating moieties and the upper rim of the calixarene and/or by using a larger calixarene as the platform. These possibilities provide tha basis for future work.

Experimental Section[25]

5-(Carboxymethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (2). A suspension of 2 g of 5-(cyanomethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}oxy]calix[4]arene (**1**) in 30 mL of HOAc, 3 mL of concentrated H_2SO_4 and 3 mL of H_2O was refluxed for 16 h, becoming clear after 2 h. The reaction mixture was cooled to room temperature, and 30 mL of cold H_2O was added. A precipitate was collected by suction filtration and dried to give a quantitative yield of **2** as a white solid. An analytical sample was obtained by chromatography (eluent, 8% acetone−$CHCl_3$, v/v): mp ca. 177 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.81−7.68 (m, 16H), 6.76−6.77 (m, 3H), 6.52 (d, 2H, J = 7.6 Hz), 6.430 (d, 4H, J = 7.6 Hz), 6.433 (s, 2H), 3.77 (d, 4H, J = 14.6 Hz), 3.32 (s, 2H), 2.54 (d, 4H, J = 14.6 Hz); ^{13}C NMR ($CDCl_3$) δ 176.2, 145.1, 144.8, 144.4, 135.8, 135.7, 135.4, 135.1, 134.4, 132.5, 131.0, 130.9, 130.8, 130.1, 129.4, 129.2, 129.1, 126.2, 125.8, 39.9, 31.3; IR (KBr, cm^{-1}) 1712 (CO), 3385 (OH). Anal. Calcd for $C_{54}H_{38}O_{14}S_4Br_4$: C, 47.72; H, 2.80. Found: C, 47.70; H, 2.73.

5-(Chlorocarbonylmethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}oxy]calix[4]arene (3). A 0.68 g (0.5 mmol) sample of **2** 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. The product decomposes to the mono acid **2** on prolonged storaged in the atmosphere: ^{1}H NMR δ 7.79−7.70 (m, 16H), 6.74−6.69 (m, 3H), 6.53 (d, 2H, J = 7.6 Hz), 6.47−6.43 (m, 6), 3.78 (d + d, 4H, J = 14.5 Hz), 3.80 (s, 2H), 2.54 (d, 4H, J = 14.5 Hz); ^{13}C NMR δ 171.1, 145.0, 144.9, 144.8, 136.3, 135.6, 135.4, 134.9, 134.3, 134.2, 132.6, 132.5, 130.9, 130.8, 130.3, 129.6, 129.4, 129.3, 129.2, 129.1, 126.3; 125.9, 51.9, 31.3; IR (KBr, cm^{-1}) 1792 (CO).

5-[(*N*,*N*-Bis-2-{3,5-dimethylpyrazolyl}ethylamino)-carbonyl]methyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}oxy]calix[4]arene (4). Procedure A (DCC Method). A 1.60 g (1.18 mmol) sample of **2** was mixed with 0.62 g (2.36 mmol) of bis[2-(3,5-dimethyl-1-pyrazoylethyl)]amine, 0.486 g (2.36 mmol) of dicyclohexylcarbodiimide, and 0.32 g of 1-hydroxybenzotriazole in 40 mL of dry CH_2Cl_2, and the mixture was stirred at room temperature for 8 h. After separation of the precipitate by filtration the solvent was removed by evaporation under reduced pressure. The residue was chromatographed by using 1% MeOH−$CHCl_3$ (v/v) to yield 1.65 g (87%) of **4** as a white solid.

Procedure B (Acid Chloride Method). A freshly prepared sample of mono acid chloride **3** from 0.54 g (0.4 mmol)

(25) Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. THF was freshly distilled from Na benzophenone. Deoxygenation was effected by bubbling Ar directly through the solvents or reaction mixtures for 30 min.. 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. The melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL-300 spectrometer at 300 and 75 MHz, respectively. Analytical samples were dried in a drying pistol under vacuum for at least 36 h. Microanalyses were performed by Desert Laboratories, Tucson, AZ. Thin-layer chromatography (TLC) was carried out on Analtech silica gel plates (absorbant thickness 250 μm) containing a fluorescent indicator. Column 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. Mass spectral determinations were carried out by the Washington University Resource for Biomedical and Bio-organic Mass Spectrometry, St. Louis, MO.

of **2** was redissolved in 15 mL of dry CH_2Cl_2. The solution was added dropwise to a CH_2Cl_2 solution containing 0.11 g (0.42 mmol) of bis[2-(3,5-dimethyl-1-pyrazoyl-ethyl)]amine and 0.05 g (0.5 mmol) of Et_3N, and the reaction mixture was stirred at room temperature for 3 h. The reaction was then quenched with H_2O. The organic layer was separated, washed with H_2O and brine, and dried over Na_2SO_4, and the solvent was removed by evaporation to leave a residue which was chromatographed to give 0.51 g (80%) of **4**: mp ca. 150 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.82−7.66 (m, 16H), 6.83 (t, 1H, J = 7.6 Hz), 6.64−6.57 (m, 4H), 6.42 (s, 2H), 6.31 (d, 4H, J = 7.6 Hz), 5.79 (s, 1H), 5.74 (s, ^{1}H), 4.12 (t, 2H, J = 5.7 Hz), 3.82 (t, 2H, J = 5.7 Hz), 3.75 (d + d, 4H, J = 14.6 and 14.5 Hz), 3.66 (t, 2H, J = 5.7 Hz), 3.23 (t, 2H, J = 5.7 Hz), 2.94 (s, 2H), 2.53 (d + d, 4H, J = 14.5 and 14.9 Hz), 2.20 (s, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 171.0, 148.3, 145.4, 144.5, 144.3, 139.9, 139.5, 136.1, 135.0, 134.8, 134.5, 134.4, 132.8, 132.6, 132.4, 131.0, 130.8, 130.1, 129.4, 129.0, 126.1, 126.0, 105.6, 105.2, 48.7, 46.7, 46.3, 45.7, 38.6, 31.33, 31.30, 13.6, 13.5, 10.8, 10.7; IR (KBr, cm^{-1}) 1649 (CO), 1552 (pyrazole). Anal. Calcd for $C_{68}H_{59}N_5O_{13}S_4Br_4$: C, 50.97; H, 3.69; N, 4.37. Found: C, 50.92; H, 3.79; N, 4.31.

5-[*N*,*N*-bis-2-(3,5-dimethyl-1-pyrazolyl)ethylamino]-ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]-calix[4]arene (5). To a sample of 0.8 g (0.5 mmol) of **4**, 10 mL of a 1.0 M solution of B_2H_6 in THF was added at 0 °C, and the mixture was stirred at room temperature for 1 h. A few drops of MeOH were then added to destroy the excess B_2H_6. After removal of the solvent by evaporation, the residue was treated with a mixture 3 mL of H_2O, 20 mL of MeOH, and 3 mL of concentrated HCl, and the mixture was refluxed for 1 h. The solvent was removed by evaporation, and the residue was treated with 15 mL of H_2O and neutralized with 20% NaOH to precipitate a white solid. The crude product was collected by suction filtration and chromatographed by using 1% MeOH−$CHCl_3$ (v/v) to yield 0.70 g (88%) of **5** as a white solid: mp ca. 119 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.82−7.68 (m, 16H), 6.81 (t, 1H, J = 7.5 Hz), 6.65−6.60 (m, 4H), 6.30 (m, 6H), 5.76 (s, 2H), 3.84−3.69 (m, 8H), 2.87 (t, 4H, J = 6.7 Hz), 2.60−2.35 (m, 8H), 2.20 (s, 12H); ^{13}C NMR ($CDCl_3$) δ 147.5, 145.3, 144.5, 143.7, 139.0, 138.1, 136.1, 135.7, 135.0, 134.9, 134.5, 134.4, 132.6, 132.4, 131.0, 130.9, 130.8, 129.6, 129.4, 129.3, 129.0, 128.9, 126.0, 104.9, 56.8, 54.5, 47.2, 33.2, 31.4, 31.2, 13.5, 11.1. Anal. Calcd for $C_{68}H_{61}N_5O_{12}S_4Br_4$: C, 51.43; H, 3.87. Found: C, 51.09; H, 3.62.

5,17-Bis[(*N*,*N*-bis-2-{3,5-dimethylpyrazolyl}ethylamino)carbonyl]methyl-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (6). A 1.39 g (0.91 mmol) sample of 5,17-bis(carboxymethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene was mixed with 0.96 g (3.64 mmol) of bis[2-(3,5-dimethyl-1-pyrazoyl-ethyl)]amine and 0.563 g of dicyclohexylcarbodimide and 0.37 g of 1-hydroxybenzotriazole in 40 mL of dry CH_2Cl_2, and refluxed for 12 h. The mixture was worked up in conventional fashion to give 1.37 g (75%) of **6**. An analytical sample was obtained by recrystallization from $CHCl_3$−hexanes as very small colorless needles: mp ca. 167 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.78 (d, 2H, J = 8.7 Hz), 7.68 (d, 2H, J = 8.7 Hz), 7.64 (m, 12H), 6.62 (s, 4H), 6.52 (s, 4H), 5.78 (s, 2H), 5.75 (s, 2H), 4.12 (t, 4, J = 5.6 Hz), 3.78 (d, 4H, J = 14.1 Hz), 3.68 (t, 4H, J = 5.6 Hz), 3.62 (t, 4H, J = 5.6 Hz), 3.24 (t, 4H, J = 5.9 Hz), 3.09 (s, 4H), 2.52 (d, 4H, J = 14.1 Hz), 2.20 (s, 6H), 2.18 (s, 6H), 2.10 (s, 6H), 2.02 (s, 6H)), 0.91 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 170.8, 149.1, 148.2, 148.0, 143.9, 141.9, 140.0, 139.3, 136.0, 134.5, 134.2, 133.6, 132.8, 132.6, 132.2, 131.0, 129.8, 129.3, 125.9, 105.5, 105.2, 49.0, 47.4, 46.3, 45.8, 38.9, 34.0, 31.2, 31.0, 13.6, 13.5, 10.7, 10.6; IR (KBr, cm^{-1}) 1649.2 (CON), 1552.8 (DMP). Anal. Calcd for $C_{92}H_{98}N_{10}O_{14}Br_4S_4$: C, 54.82, H, 4.90; N, 6.95. Found: C, 54.35; H, 4.88; N, 6.67.

5,17-Bis[*N*,*N*-bis-2-(3,5-dimethylpyrazolyl)ethylamino]-ethyl-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (7) was prepared in 85% yield following the procedure described above for **5** using 2 h of reaction time. An analytical sample was obtained by column chromatography using 1.5% MeOH −$CHCl_3$ (v/v)-as an eluent: mp ca. 96 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.78−7.65 (m, 16H), 6.55 (s, 4H), 6.41 (s, 4H), 5.75 (s, 4H), 3.81−3.73 (m, 12H), 2.83 (t, 8H, J = 6.7 Hz), 2.55 (t, 4H, J = 8.1 Hz), 2.47 (d, 4H, J = 14.0 Hz), 2.33 (t, 4H, J = 8.1 Hz), 2.19 (s, 12H), 2.17 (s, 12H), 0.97 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 148.9, 147.4, 143.3, 142.0, 139.0, 138.1, 135.5, 134.6, 134.2, 133.9, 132.7, 132.2, 131.0, 129.3, 125.8, 104.9, 57.2, 54.5, 47.2, 34.1, 33.1, 31.2, 31.1, 13.5, 11.0. Anal. Calcd for $C_{92}H_{102}N_{10}O_{12}Br_4S_4$: C, 55.59, H, 5.17. Found: C, 55.78; H, 4.98.

5,17-Bis(cyanomethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (9). To a solution of 1.22 g (2.4 mmol) of 5,17-bis(cyanomethyl)calix[4]-25,26,27,28-tetrol in 80 mL of THF was added 1.16 g of NaH (60% oil dispersion, 28.8 mmol). The reaction mixture was stirred for 30 min, treated with 3 g (12.2 mmol) of *p*-bromobenzenesulfonyl chloride, and allowed to stir at room temperature for 3 h. The solvent was removed under vacuum, and the residue was treated with 80 mL of CH_2Cl_2 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 was removed by evaporation leaving a residue which was chromatographed (eluent 10% *n*-hexanes−$CHCl_3$ (v/v)) to give 2.66 g (80%) of **9**: mp ca. 181 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.79−7.72 (m, 16H), 6.81 (t, 2H, J = 7.6 Hz), 6.54 (m, 8H), 3.80 (d, 4H, J = 14.5 Hz), 3.50 (s, 4H), 2.55 (d, 4H, J = 14.5 Hz); ^{13}C NMR ($CDCl_3$) δ 144.8, 144.7, 136.3, 134.9, 134.2, 134.1, 132.6, 130.9, 130.8, 129.7, 129.6, 129.4, 128.5, 128.0, 126.6, 117.8, 31.4, 22.6. Anal. Calcd for $C_{56}H_{38}O_{12}Br_4S_4$: C, 48.78; H, 2.78. Found: C, 48.81; H, 2.85.

5,17-Bis(carboxymethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}oxy]calix[4]arene (10) was prepared in quantitative yield by the procedure described for **2**, using **9** as the starting material. An analytical sample was obtained as a white solid by recrystallization from acetone−hexanes: mp ca. 220 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.37 (brs, 2H), 7.79−7.67 (m, 16H), 6.68 (m, 6H), 6.50 (d, 4H, J = 7.6 Hz), 3.83 (d, 4H, J = 14.3 Hz), 3.34 (s, 4H), 2.55 (d, 4H, J = 14.3 Hz); ^{13}C NMR ($CDCl_3$ + 1 drop of DMSO-d_6) δ 177.0, 144.4, 144.3, 136.0, 134.7, 134.4, 134.2, 132.6, 131.4, 131.1, 130.8, 130.3, 129.5, 129.1, 129.0, 126.3, 40.1, 31.2. Anal. Calcd for $C_{56}H_{40}O_{16}Br_4S_4$: C, 47.47; H, 2.85. Found: C, 47.59; H, 2.78.

5,17-Bis[(*N*,*N*-bis-2-{3,5-dimethylpyrazolyl}ethylamino)-carbonyl]methyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}oxy]calix[4]arene (11) was prepared in 77% yield by the procedure described for **6**, using **10** as the starting material. An analytical sample was obtained by column chromatography using 3% MeOH−$CHCl_3$ (v/v) as eluent: mp ca. 140 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.87 (d, 4H, J = 8.6 Hz), 7.72−7.28 (m, 12H), 6.76 (s, 4H), 6.34 (t, 2H, J = 7.6 Hz), 5.97 (d, 4H, J = 7.6 Hz), 5.82 (s, 2H), 5.76 (s, 2H), 4.17 (t, 4H, J = 5.6 Hz), 3.89 (t, 4H, J = 5.4 Hz), 3.71 (m, 8H), 3.33 (t, 4H, J = 5.2 Hz), 3.19 (s, 4H), 2.49 (d, 4H, J = 14.6 Hz), 2.20 (s, 6H), 2.19 (s, 6H), 2.15 (s, 6H), 2.10 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 171.0, 148.3, 148.0, 145.0, 143.6, 139.8, 139.5, 137.1, 134.4, 134.3, 133.6, 133.0, 132.7, 132.2, 131.1, 130.53, 130.49, 129.4, 129.3, 128.5, 125.9, 105.6, 105.2, 48.6, 46.7, 46.3, 45.7, 38.7, 31.2, 13.51, 13.47, 10.7. Anal. Calcd for $C_{84}H_{82}N_{10}O_{14}Br_4S_4$: C, 53.00; H, 4.34. Found: C, 52.95; H, 4.38.

5,17-Bis[(*N*,*N*-bis-2-{3,5-dimethylpyrazolyl}ethylamino)]-ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]-calix[4]arene (12) was prepared in 85% yield by the procedure described for **5**, using **11** as the starting material. An analytical sample was obtained by column chromatography using 2% MeOH−$CHCl_3$ (v/v) as eluent: mp ca. 110 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.85 (d, 4H, J = 8.7 Hz), 7.72 (d, 4H, J = 8.7 Hz), 7.68−7.59 (m, 8H), 6.64 (s, 4H), 6.34 (t, 2H, J = 7.6 Hz), 5.91 (d, 4H, J = 7.6 Hz), 5.77 (s, 4H), 3.86 (t, 8H, J = 6.8 Hz), 3.72 (d, 4H, J = 14.5 Hz), 2.94 (t, 8H, J = 6.8 Hz), 2.69−2.67 (m, 4H), 2.61−2.58 (m, 4H), 2.47 (d, 4H, J = 14.5 Hz), 2.23 (s, 12H), 2.20 (s, 12H); ^{13}C NMR ($CDCl_3$) δ 147.5, 144.6, 143.6, 139.1, 138.5, 136.8, 134.6, 134.4, 133.7, 132.7, 132.2, 131.1, 130.6, 130.1, 129.4, 129.2, 128.4, 125.8, 105.0, 56.9, 54.5, 47.3, 33.4, 31.3, 13.5, 11.1. Anal. Calcd for $C_{84}H_{86}N_{10}O_{12}Br_4S_4$: C, 53.79; H, 4.62. Found: C, 53.64; H, 4.73.

5,17-Bis(chloromethyl)-11,23-di-*tert*-butylcalix[4]arene-25,26,27,28-tetrol (14). To a solution of 1.08 g (2 mmol) of di-*tert*-butylcalix[4]arene-25,26,27,28-tetrol (**13**) in 100 mL of $CHCl_3$ were added 6 mL (31 mmol) of chloromethyl *n*-octyl ether at −10 °C and 2 mL of $SnCl_4$ in 10 mL of $CHCl_3$ dropwise in ca. 15 min. The cooling bath was removed, and stirring was continued at room temperature for 1.5 h. The reaction was quenched by adding H_2O, the red solution changing to pale yellow. The organic layer was washed with H_2O and dried over Na_2SO_4, and the solvent was evaporated to give 0.70 g (55%) of **13** as a white powder. An analytical sample was obtained by recrystallization from CH_2Cl_2−hexane: mp ca. 234 °C (dec); ^{1}H NMR ($CDCl_3$) δ 10.20 (br s, 4H), 7.07 (s, 4H), 7.05 (s, 4H), 4.37 (s, 4H), 4.24 (d, 4H, J = 12.5 Hz), 3.50 (d, 4H, J = 12.5 Hz), 1.23 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 148.9, 146.6, 144.9, 131.0, 129.4, 128.7, 127.2, 126.0, 46.1, 34.1, 32.1, 31.5. Anal. Calcd for $C_{38}H_{42}O_4C_{l2}$: C, 72.03; H, 6.68. Found: C, 72.08; H, 6.74.

5,17-Bis[(*N*,*N*-bis-2-{3,5-dimethylpyrazolyl}ethylamino)]-methyl-11,23-di-*tert*-butyl-calix[4]arene-25,26,27,28-tetrol (15). To a solution of 1.16 g (0.25 mmol) of **14** in 15 mL of THF was added 0.15 g (1.5 mmol) of Et_3N. A blue solution and a white precipitate formed immediately; then, 0.20 g of bis[2-(3,5-dimethyl-1-pyrazoyl-ethyl)]amine was added, and stirring was continued at room temperature for 6 h. The solvent was removed under vacuum, and the residue was treated with 10 mL of H_2O, acidified with 0.1 N HCl to pH = 5, and then extracted by $CHCl_3$ (3 × 10 mL). The $CHCl_3$ solution was washed with H_2O and brine and dried over Na_2SO_4, and the solvent was then evaporated to leave a crude product that was subjected to column chromatography (eluent 3% MeOH−$CHCl_3$, v/v) to give 0.24 g (90%) of **15** as a pale yellow powder: mp ca. 78 °C (dec); ^{1}H NMR ($CDCl_3$) δ 10.07 (br s, 4H), 6.97 (s, 4H), 6.94 (s, 4H), 5.52 (s, 4H), 4.24 (d, 4H, J = 13.7 Hz), 3.74 (t, 8H, J = 7.5 Hz), 3.47 (d, 4H, J = 13.7 Hz), 3.46 (s, 4H), 2.74 (t, 8H, J = 7.5 Hz), 2.15 (s, 12H), 1.43 (s, 12H), 1.02 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 147.9, 146.9, 146.1, 144.9, 138.8, 132.4, 129.4, 128.5, 127.7, 125.5, 104.6, 58.9, 54.1, 47.3, 33.8, 31.8, 31.1, 13.4, 9.6. Anal. Calcd for $C_{66}H_{86}N_{10}O_4$: C, 73.17; H, 8.00. Found: C, 73.13; H, 8.12.

5,17-Bis[(*N*,*N*-bis-2-{3,5-dimethylpyrazolyl}ethylamino)]-methyl-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}-oxy]calix[4]arene (16). To a solution of 1.08 g (1.0 mmol) of **15** in 40 mL of dry CH_2Cl_2 was added 0.64 g of NaH (60% oil dispersion, 16 mmol). The reaction mixture was stirred for 15 min, treated with 1.54 g (6 mmol) of *p*-bromobenzenesulfonyl chloride, allowed to stir at room temperature for 3 h, and poured slowly onto 40 g of crushed ice. The organic layer was separated, washed with water and brine, and dried over Na_2SO_4, and the solvent was removed by evaporation to leave a residue that was subjected to flash chromatography (eluent 1.5% MeOH−$CHCl_3$, v/v) to give 1.27 g (65%) of **16** as a pale yellow powder: mp ca. 100 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.76−7.68 (m, 16H), 6.65 (s, 4H), 6.51 (s, 4H), 5.73 (s, 4H), 3.85 (d, 4H, J = 14.1 Hz), 3.76 (t, 8H, J = 6.6 and 6.8 Hz), 3.29 (s, 4H), 2.74 (t, 8H, J = 6.6 and 6.8 Hz), 2.52 (d, 4H, J = 14.4 Hz), 2.16 (s, 12H), 2.06 (s, 12H), 1.00 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 149.3, 147.3, 143.6, 142.3, 138.7, 136.8, 135.5, 134.3, 132.6, 132.3, 131.0, 129.4, 126.1, 105.0, 58.6, 54.0, 46.9, 34.2, 31.3, 13.5, 10.9. Anal. Calcd for $C_{90}H_{98}N_{10}O_{12}Br_4S_4$: C, 55.16; H, 5.04; Found: C, 55.58; H, 5.09.

5-(2-Aminoethyl)-25,26,27,28-tetrakis[{(*p*-bromophenyl)-sulfonyl}-oxy]calix[4]arene (17). To a solution of 1.35 g (1.00 mmol) of 5-(cyanomethyl)-25,26,27,28-tetrakis(*p*-bromobenzenesulfonyloxy)calix[4]arene (**1**) in 40 mL of THF was added 20 mL of a 1.0 M solution of B_2H_6 in THF. The mixture was heated at reflux under N_2 for 8 h. The solution was then cooled, excess B_2H_6 was destroyed by MeOH, and the solvent was removed by evaporation. The residue was treated with a mixture of 10 mL of H_2O, 50 mL of MeOH, and 10 mL of concentrated HCl and refluxed for 2 h. The solution was cooled, and MeOH was removed under vacuum. The precipitate was collected by filtration and washed with cold H_2O and MeOH and dried in a vacuum for 2 h to give a 95% yield of **17** as a white powder. The product was pure enough for synthetic purposes. An anlytical sample was prepared by flash chromatography using $CHCl_3$−MeOH (12:1, v/v) as eluent followed by recrystallization from $CHCl_3$−MeOH: mp ca. 245 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.90−7.67 (m, 16H), 6.78 (t, 1H, J = 7.6 Hz), 6.64 (t, 2H, J = 7.6 Hz), 6.56 (d, 2H, J = 7.6 Hz), 6.52 (s, 2H), 6.37 (m, 4H), 5.40 (brs, 2H), 3.81 (d, 2H, J = 14.5 Hz), 3.70 (d, 2H, J = 14.7 Hz), 3.02 (brs, 2H), 2.77 (brs, 2H), 2.63 (d, 2H, J = 14.6 Hz), 2.44 (d, 2H, J = 14.4 Hz); ^{13}C NMR ($CDCl_3$) δ 145.1, 144.6, 144.2, 136.1, 135.7, 135.2, 134.9, 134.4, 134.2, 132.7, 132.5, 132.4, 131.1, 130.9, 129.8, 129.5, 129.4, 129.3, 129.1, 129.0, 126.2, 126.1, 126.0, 41.2, 34.7, 31.4, 31.2. Anal. Calcd. for $C_{54}H_{41}NO_{12}S_4Br_4\cdot H_2CO_3$: C, 46.12; H, 3.06. Found: C, 46.23; H, 3.02.

5-Mono[*N*-2-(2-pyridyl)ethylamino]ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (18). To a solution of 0.67 g (0.5 mmol) of **17** in 30 mL of CH_2Cl_2−CH_3OH (8:2, v/v) were added 0.5 g (5 mmol) of 2-vinylpyridine and 0.15 g (0.25 mmol) of HOAc, and the reaction mixture was refluxed for 5 days. The solvent was evaporated, and the residue was washed with 5% NaOH and extracted with CH_2Cl_2 (3 × 15 mL). The CH_2Cl_2 solution was washed with water and brine and dried over Na_2SO_4, and the solvent was removed by evaporation to leave a residue that was subjected to flash chromatography (eluent 2% MeOH−$CHCl_3$, v/v) to give 0.45 g 67% of **18** as a white solid: mp ca. 133 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.50 (d, 1H, J = 4.3 Hz), 7.79−7.69 (m, 16H), 7.64−7.58 (m, 1H), 7.17−7.11 (m, 2H), 6.75−6.69 (m, 3H), 6.50−6.44 (m, 6H), 6.28 (s, 2H), 3.76 (d + d, 4H, J = 14.6 Hz), 3.04−2.94 (m, 4H), 2.67 (t, 2H, J = 7.2 Hz), 2.57−2.41 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 149.3, 145.0, 144.9, 143.4, 137.8, 136.5, 135.5, 135.4, 135.3, 134.5, 134.4, 132.5, 130.9, 129.4, 129.3, 129.2, 129.1, 126.1, 125.9, 123.3, 121.4, 50.7, 49.1, 38.0, 35.5, 31.3. Anal. Calcd for $C_{61}H_{48}N_2O_{12}S_4Br_4$: C, 50.70; H, 3.35. Found: C, 50.31; H, 3.78.

5,17-Bis(2-aminoethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene-(19) was prepared in 70% yield by the procedure described for **17**, using 5,17-bis(cyanomethyl)-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]-arene as the starting material: mp ca. 190 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.89 (d, 4H, J = 8.5 Hz), 7.79−7.67 (m, 12H), 7.04 (s, 4H), 5.85 (s, 4H), 3.80 (d, 4H, J = 14.2 Hz), 2.65−2.30 (m, 12H), 1.35 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 149.8, 143.7, 142.8, 136.1, 134.4, 134.2, 133.4, 132.8, 132.6, 132.4, 131.2, 130.6, 129.7, 129.4, 128.3, 40.3, 34.5, 33.0, 31.6. Anal. Calcd for $C_{64}H_{62}N_2O_{12}S_4Br_4\cdot CH_3OH$: C, 51.00; H, 4.34. Found: C, 51.62; H, 4.34.

5,17-Bis[*N*-2-(2-pyridyl)ethylamino]ethyl-11,23-di-*tert*-butyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}-oxy]calix[4]arene (20). The procedure described above for **18** was followed, using 0.75 g (0.5 mmol) of **19** and 1.0 g (10 mmol) of 2-vinylpyridine, to give 0.55 g (65%) of **20** as a white solid: mp ca. 143 °C; ^{1}H NMR ($CDCl_3$) δ 8.47 (d, 2H, J = 4.5 Hz), 7.91 (d, 4H, J = 8.7 Hz), 7.77 (d, 4H, J = 8.7 Hz), 7.71−7.61 (m, 10H), 2.27−7.15 (m, 6H), 7.04 (s, 4H), 5.89 (s, 4H), 3.76 (d, 4H, J = 14.4 Hz), 3.39 (t, 4H, J = 6.4 Hz), 3.28 (t, 4H, J = 6.4 Hz), 2.80 (m, 4H), 2.70 (m, 4H), 2.54 (d, 4H, J = 14.5 Hz), 1.39 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 157.0, 150.2, 149.1, 143.6, 142.8, 136.9, 136.0, 134.5, 134.3, 134.1, 133.7, 132.7, 132.3, 131.2, 130.5, 129.6, 129.2, 128.3, 127.1, 123.5, 122.1, 47.8, 46.8, 34.5, 32.6, 31.4. Anal. Calcd for $C_{78}H_{76}N_4O_{12}S_4Br_4\cdot HCl$: C, 53.66; H, 4.45. Found: C, 52.83; H, 4.58.

5-[(*N*,*N*-Bis-2-{2-pyridyl}ethylamino)carbonyl]methyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix-[4]arene (21) was prepared in 80% yield by the procedure described for **4**, using bis[2-(2-pyridyl)ethyl]amine. An analytical sample was obtained by column chromatography using 2% MeOH−$CHCl_3$ (v/v) as eluent: mp ca. 135.0 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.54 (m, 2H), 7.82−7.57 (m, 18H), 7.21−7.10 (m, 4H), 6.87 (t, 1H, J = 7.5 Hz), 6.56 (d, 2H, J = 7.5 Hz), 6.55 (t, 2H, J = 7.5 Hz), 6.49 (s, 2H), 6.27 (d, 4H, J = 7.5 Hz), 3.80−3.71 (m, 6H), 3.56 (t, 2H, J = 7.3 Hz), 3.34 (s, 2H), 3.05 (t, 2H, J = 7.3 Hz), 2.91 (t, 2H, J = 7.3 Hz), 2.52 (d + d, 4H, J = 14.6 and 14.9 Hz); ^{13}C NMR ($CDCl_3$) δ 170.4, 158.9, 157.8, 149.6, 149.3, 145.4, 144.4, 144.2, 136.7, 136.6, 136.1, 134.8,

134.7, 134.4, 134.3, 133.4, 132.5, 132.4, 130.9, 130.7, 129.9, 129.4, 129.3, 129.0, 126.0, 123.6, 121.9, 121.6, 48.2, 46.1, 39.6, 37.3, 36.1, 31.3, 31.2. Anal. Calcd for $C_{68}H_{53}N_3O_{13}S_4Br_4$: C, 52.09; H, 3.41. Found: C, 51.95; H, 3.29.

5-[*N*,*N*-Bis-2-(2-pyridyl)ethylamino]ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (22) was prepared in 81% yield by the procedure described for **5**. An analytical sample was obtained by column chromatography using 2% MeOH−$CHCl_3$ (v/v) as eluent: mp ca. 119 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.53 (m, 2H), 7.81−7.71 (m, 16H), 7.58 (m, 2H), 7.12 (m, 4H), 6.78 (t, 1H, J = 7.4 Hz), 6.62−6.57 (m, 4H), 6.33 (s, 2H), 6.31 (d, 4H, J = 7.4 Hz), 3.74 (d + d, 4H, J = 14.5 and 14.9 Hz), 2.94−2.91 (m, 8H), 2.62−2.43 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 160.4, 149.2, 145.3, 144.5, 143.5, 138.7, 136.3, 136.0, 135.4, 135.0, 134.5, 134.4, 132.5, 132.4, 130.9, 130.8, 130.7, 129.7, 129.3, 129.0, 126.0, 123.3, 121.2 (Ar), 55.7, 53.8, 36.1, 33.0, 31.4, 31.3. Anal. Calcd for $C_{68}H_{55}N_3O_{12}S_4Br_4$: C, 52.56; H, 3.57. Found: C, 52.87; H, 3.31.

5,17-Bis[(*N*,*N*-bis-2-{2-pyridyl}ethylamino)carbonyl]-methyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}-oxy]calix[4]arene (23) was prepared in 75% yield by the procedure described for **6**, using bis[2-(2-pyridyl)ethyl]amine. An analytical sample was obtained by column chromatography using 3% MeOH−$CHCl_3$ (v/v) as eluent: mp ca. 116 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.56−8.53 (m, 4H), 7.86 (d, 4H, J = 8.6 Hz), 7.71−7.57 (m, 16H), 7.20−7.10 (m, 8H), 6.79 (s, 4H), 6.28 (t, 2H, J = 7.7 Hz), 5.96 (d, 4H, J = 7.7 Hz), 3.80 (t, 4H, J = 7.3 Hz), 3.72 (d, 4H, J = 14.5 Hz), 3.64 (t, 4H, J = 7.3 Hz), 3.55 (s, 4H), 3.08 (t, 4H, J = 7.3 Hz), 2.98 (t, 4H, J = 7.3 Hz), 2.48 (d, 4H, J = 14.5 Hz); ^{13}C NMR ($CDCl_3$) δ 170.5, 158.9, 158.0, 149.6, 149.3, 144.9, 143.6, 137.1, 136.8, 136.7, 134.5, 134.3, 133.6, 132.7, 132.2, 131.1, 130.6, 130.2, 129.4, 129.2, 128.6, 125.9, 123.6, 122.0, 121.6, 48.3, 46.1, 39.7, 37.4, 36.1, 31.3. Anal. Calcd for $C_{84}H_{70}N_6O_{14}S_4Br_4$: C, 54.97; H, 3.84. Found: C, 55.05; H, 3.66.

5,17-Bis[*N*,*N*-bis-2-(2-pyridyl)ethylamino]ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix-[4]arene (24) was prepared in 65% yield by the procedure described for **7** and was obtained as the major product after column chromatography (gradient elution 2−6% MeOH−$CHCl_3$, v/v): TLC (silica gel, 2.5% MeOH−$CHCl_3$) R_f = 0.32; mp ca. 98 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.54 (d, 4H, J = 4.3 Hz), 7.88 (d, 4H, J = 8.6 Hz), 7.73 (d, 4H, J = 8.6 Hz), 7.69−7.55 (m, 12H), 7.14−7.10 (m, 8H), 6.66 (s, 4H), 6.30 (t, 2H, J = 7.6 Hz), 5.92 (d, 4H, J = 7.6 Hz), 3.70 (d, 4H, J = 14.5 Hz), 3.68−2.91 (m, 16H), 2.81 (d + d, 4H, J = 6.4 and 7.4 Hz), 2.66 (d + d, 4H, J = 6.4 and 7.4 Hz), 2.45 (d, 4H, J = 14.5 Hz); ^{13}C NMR ($CDCl_3$) δ 160.4, 149.3, 144.4, 143.6, 139.1, 136.6, 136.3, 134.6, 134.5, 133.7, 132.7, 132.3, 131.2, 130.6, 130.1, 129.3, 129.2, 128.5, 125.8, 123.4, 121.2, 55.8, 54.0, 36.2, 33.1, 31.3. Anal. Calcd for $C_{84}H_{74}N_6O_{12}S_4Br_4$: C, 55.82; H, 4.13. Found: C, 55.89; H, 4.14.

5-[*N*,*N*-Bis-2-(2-pyridyl)ethylamino]ethyl-17-ethenyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix-[4]arene (25). The minor product from the chromatographic separation described above was **25**, obtained in 8% yield as a white solid: TLC (silica gel, 2.5% MeOH−$CHCl_3$) R_f = 0.42; mp ca. 118 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.54 (m, 2H), 7.89−7.65 (m, 16H), 7.61−7.56 (m, 2H), 7.14−7.10 (m, 4H), 6.85 (s, 2H), 6.55−6.42 (m, 5H), 6.12 (m, 4H), 5.63 (d, 1H, J = 16.7 Hz), 5.23 (d, 1H, J = 11.1 Hz), 3.73 (d + d, 4H, J = 14.5 and 14.4 Hz), 2.98−2.90 (m, 8), 2.74 (t, 2H, J = 7.2 Hz), 2.57−2.43 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 160.5, 149.3, 145.5, 144.0, 139.1,136.7, 136.3, 136.1, 135.5, 134.5, 134.4, 134.0, 132.7, 132.6, 132.3, 131.1, 130.8, 130.7, 129.9, 129.4, 129.2, 128.8, 128.7, 128.6, 127.2, 125.9, 123.3, 121.2, 114.9, 55.8, 53.9, 36.2, 33.2, 31.4, 31.3. Anal. Calcd for $C_{70}H_{57}N_3O_{12}S_4Br_4$: C, 53.21; H, 3.64. Found: C, 53.45; H, 3.64.

Di-oxygenated Copper(II) Complex (29). To a solution of 250 mg (0.161 mmol) of **22** in 40 mL of THF was added 60 mg (0.161 mmol) of [$Cu(CH_3CN)_4$] PF_6, and the mixture was stirred for 0.5 h under Ar. Dry O_2 was then bubbled through the slightly yellow solution, resulting in a fairly rapid color change from slightly yellow to green, and a green powder solid started to form after ca. 4 h. The mixture was stirred further overnight and filtered, and the precipitate was washed with THF and recrystallized from CH_3CN to give 94 mg (33%) of di-oxygenated copper(II) complex **29** as a green solid: mp ca. 210 °C (dec); FABMS for $C_{136}H_{108}N_6O_{26}S_8Br_8Cu_2PF_6$ [M + PF_6] calcd 3410, obsd 3408; $C_{136}H_{108}N_6O_{26}S_8Br_8Cu_2$ [M] calcd 3265, obsd 3265.Anal. Calcd for $C_{136}H_{108}N_6O_{26}S_8Br_8Cu_2P_2F_{12}$: C, 45.95; H, 3.06. Found: C, 45.94; H, 3.12.

5-Mono[2-{*N*,*N*-bis-2-(2-pyridyl)amino}-1-hydroxy]ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix-[4]arene (32). To a suspension of 94 mg of di-oxygenated copper(II) complex **29** in 10 mL of CH_2Cl_2 was added 5 mL of concentrated aqueous ammonia, and the mixture was stirred vigorously for a few minutes to give a deep blue aqueous layer and a colorless CH_2Cl_2 layer. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 5 mL). The combined CH_2Cl_2 extract was washed with H_2O and brine and dried over Na_2SO_4, and the solvent was removed by evaporation to give a crude product that was then subjected to column chromatography (eluent 2% MeOH−$CHCl_3$, v/v) to give 76 mg of **32** as a white solid: TLC (silica gel, 2.5% MeOH−$CHCl_3$, v/v) R_f = 0.37; mp ca. 134 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.51 (d, 2H, J = 3.8 Hz), 7.87−7.63 (m, 16H), 7.60−7.54 (m, 2H), 7.27−7.10 (m, 2H), 7.03 (d, 2H, J = 7.9 Hz), 6.95 (t, 1H, J = 7.5 Hz), 6.85−6.78 (m, 3H), 6.68 (d, 1H, J = 1.9 Hz), 6.49 (t, 2H, J = 7.6 Hz), 6.21−6.15 (m, 4H), 4.45 (d + d, 1H, J = 2.7 and 10.2 Hz), 3.88−3.64 (7 peaks, 4H), 3.07−2.82 (m, 8), 2.63−2.42 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 160.0, 149.0, 145.6, 144.7, 144.1, 140.7, 136.6, 136.4, 136.2, 135.8, 134.6, 134.5, 134.4, 134.3, 132.6, 132.3, 131.1, 130.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.0, 128.9, 128.8, 127.2, 126.7, 126.4, 126.0, 123.4, 121.3, 69.9, 63.4, 54.1, 35.9, 31.5, 31.3, 31.2. Anal. Calcd for $C_{68}H_{55}N_3O_{13}S_4Br_4$: C, 52.02; H, 3.53. Found: C, 51.97; H, 3.37.

5-[2-{*N*,*N*-Bis-2-(2-pyridyl)amino}-1-hydroxy]ethyl-17-[*N*,*N*-bis-2-(2-pyridyl)ethylamino]ethyl-25,26,27,28-tetrakis[{(*p*-bromophenyl)sulfonyl}oxy]calix[4]arene (36). To a solution of 145 mg (0.08 mmol) of **24** in 30 mL of THF was added 60 mg (0.16 mmol) of [$Cu(CH_3CN)_4$] PF_6, and the solution was stirred for 15 min under Ar. Dry O_2 was then bubbled through the solution, resulting in an immediate color change to green and the formation of a green solid. The mixture was stirred an additional 2 h and filtered, and the precipitate was washed with THF and air-dried. Following treatment with ammonia to remove copper ions, the organic product was subjected to column chromatography to give 44 mg (30%) of **36** (R_f = 0.21, silica gel, 5% MeOH−$CHCl_3$) and 22 mg (15%) of starting material **24** (R_f = 0.12, silica gel, 5% MeOH−$CHCl_3$). The filtrate was concentrated, leaving a residue of a green solid. Following the same demetalation procedure described above, 40 mg (28%) of starting material **24** was recovered, and 15 mg (10%) of **36** was obtained as a white solid: mp ca. 96 °C (dec); ^{1}H NMR ($CDCl_3$) δ 8.53 (m, 4H), 7.93−7.88 (m, 4H), 7.79−7.74 (3 lines, 4H), 7.67−7.55 (m, 14H), 7.15−7.04 (m, 7H), 6.87 (d, 1H, J = 1.6 Hz), 6.70 (s, 1H), 6.69 (s, 1H), 6.27 (t, 2H, J = 7.7 Hz), 5.96−5.87 (m, 4H), 4.61 (d + d, 1H, J = 1.4 and 8.9 Hz), 3.80−3.64 (m, 4H), 3.11−2.43 (m, 26H); ^{13}C NMR ($CDCl_3$) δ 160.4, 160.1, 149.3, 149.0, 145.4, 145.0, 143.5, 140.8, 139.1, 137.2, 136.9, 136.7, 136.6, 136.5, 136.4, 134.7, 134.6, 134.4, 133.6, 133.5, 133.4, 132.7, 132.2, 131.2, 130.6, 130.2, 130.1, 129.4, 129.2, 128.7, 128.6, 128.5, 127.6, 126.9, 125.8, 123.4, 121.3, 70.2, 63.5, 55.8, 54.2, 53.9, 36.3, 35.9, 33.2, 31.4, 31.3, 31.2. Anal. Calcd for $C_{84}H_{74}N_6O_{13}S_4Br_4$: C, 55.33; H, 4.09. Found: C, 55.37; H, 3.95.

Acknowledgment. We are indebted to the Robert A. Welch Foundation and the National Science Foundation for generous support of this research.

JO981038L