Heteroatom Chemistry
Volume 12, Number 4, 2001

Synthesis and Metal Transport Ability of a New Series of Thiamacrocycles Containing Thiol and Disulfide Groups inside the Ring

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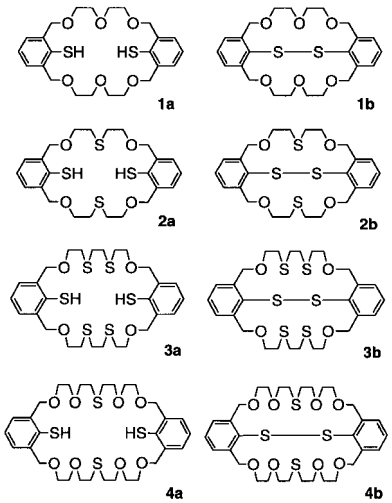
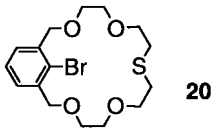
Received 15 December 2000; revised 12 February 2001

ABSTRACT: *Synthetic methods for thiamacrocycles containing two thiol groups or a disulfide linkage and their abilities to effect single heavy-metal-ion transport across a liquid membrane were examined. High Ag^+ selectivity was accomplished by the thiol or disulfide hosts, although all the corresponding crown ether analogs bearing a disulfide group showed no Ag^+ selectivity. The difference of the transport preferences among the thiacrown ethers prepared here is considered to be reflected by the position and the number of the sulfur atoms ligating to Ag^+ and the cavity size of the hosts.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:276–281, 2001

Incorporation of a gate into a recognition site of a host is an extremely effective way to control the binding affinity toward a specific guest [1]. The open state recognizes the guest via the cavity of the host, while the closed state does not. Consequently, an all-or-none type of switching can be achieved if the gate is respondent to a certain external stimulus. We have designed macrocycles **1** containing thiol groups and a disulfide linkage inside the cavity to prove that the gating concept is useful for ion recognition [1,2]. The reduced form, namely the open state, binds to and transports Ag^+ very selectively. In contrast, the oxidized form shows no affinity for Ag^+. Generally, the replacement of oxygen atoms of crown ethers by sulfur atoms drastically affects the binding strength and selectivity [3–7]. Thus, the concept of the redox gate may be extended to the regulation of heavy metal ions by the use of thiamacrocycles. We report here the synthesis and metal-transport abilities of the novel thiamacrocycles **2–4** that possess thiol groups and a disulfide linkage.



All the thiamacrocycles were prepared from the tribromide **5** [8,9] (Scheme 1–3). Treatment of **5** with Na and ethylene glycol afforded the diol **6**. The ditosylate **7** obtained from **6** reacted with **5** under high dilution conditions to give the cyclic dibromide **8**. The dithiol host **2a** was obtained by lithiation of **8**, followed by the reaction with elemental sulfur. Oxidation of **2a** with hydrogen peroxide in the presence of K_2CO_3 produced the disulfide **2b**. In the preparation of the hosts **3** and **4**, one hydroxy group of thiaethylene glycol oligomers **9** and **14** was protected as a THP ether and then used for the reaction with **5**. The compounds **11** and **16** thus obtained were deprotected under acidic conditions to give the diols **12** and **17**. Cyclization of **5** with **12** yielded the dibromide **13**. In a similar fashion, the macrocyclic dibromide **19** was synthesized (method A), whereas the cyclization of the ditosylate **18** using Na_2S resulted in a low yield of **19** due to the formation of the cyclic monobromide **20**. The bromides **13** and **19** were converted to the hosts **3a** and **4a** according to a procedure similar to the preparation of **2a**. The dithiols **3a** and **4a** were oxidized by hydrogen peroxide to give the disulfide hosts **3b** (70%) and **4b** (92%), respectively.



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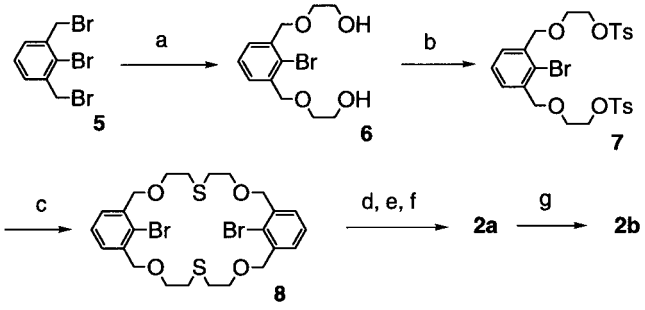
The metal-transport ability of the novel hosts **2–4** were examined by single-ion transport experiments using a dual cylindrical apparatus [10]. The 1,2-dichloroethane layer used as a liquid membrane contains one of the hosts (2×10^{-4} M). A solution of a metal nitrate (0.01 M) and deionized water were employed for the source and receiving phases, respectively. Concentrations of the metal ions transported into the receiving phase were determined by atomic absorption spectroscopy. The transport values after 24 hours are summarized in Table 1. All the hosts besides **2b** exhibit effective and selective Ag^+ transport. In the hosts **2**, the thiol form carries Ag^+ more preferentially than the corresponding disulfide **2b**, as seen for **1** [1]. Thiol-containing crown ethers are reported to show a high Ag^+ selectivity, while the transport ability is extremely decreased in the corresponding disulfide containing hosts [1,11]. In contrast to the thiamacrocycles **2**, the disulfide hosts **3b** and **4b** transport Ag^+ more effectively than the dithiol hosts **3a** and **4a**. This tendency, opposite to that observed in **1** and **2**, is probably due to the fact that the cavities of **3b** and **4b** are sufficiently large and preorganized to bind Ag^+. The cavities of **3a** and **4a** seem to be too large for effective coordination to Ag^+. Compared to **3a** and **3b**, rates of Ag^+ transport by **4a** and **4b** are lower, respectively. However, the degree of the selectivity enhancement in **4** is larger than in **3**. The difference of the binding preferences among the crown ethers **1** and the thiacrown ether derivatives **2–4** is probably reflected by the position and the number of the sulfur atoms ligating to Ag^+ and the cavity size of the hosts. We are now preparing crystals of the complexes to clarify the interactions between the hosts and Ag^+ by X-ray crystallography.



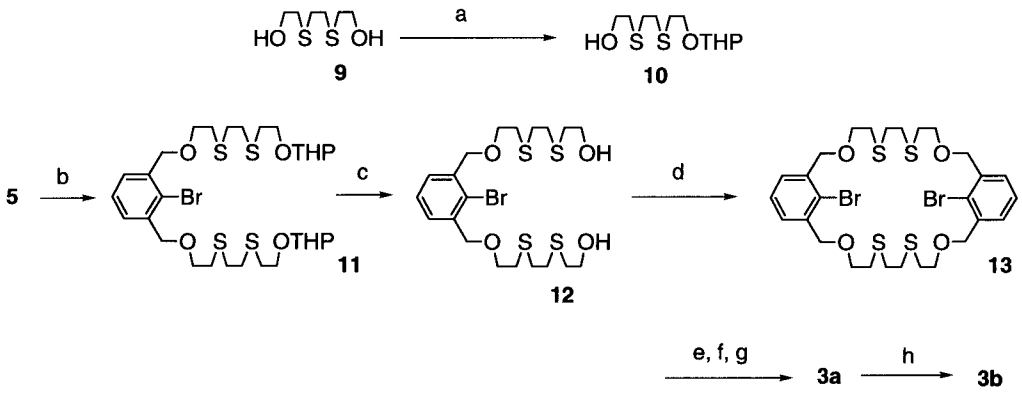
SCHEME 1 (a) Na, ethylene glycol, 60°C, 2 days, 79%; (b) TsCl, NaOH, THF/H_2O, −10°C, 82%; (c) $Na_2S{\cdot}9H_2O$, THF/EtOH, reflux, 2 days, 29%; (d) BuLi, THF, −78°C; (e) S_8, −78°C ∼ rt; (f) HCl, 48%; (g) H_2O_2, K_2CO_3, CH_2Cl_2/H_2O, rt, 73%.

EXPERIMENTAL

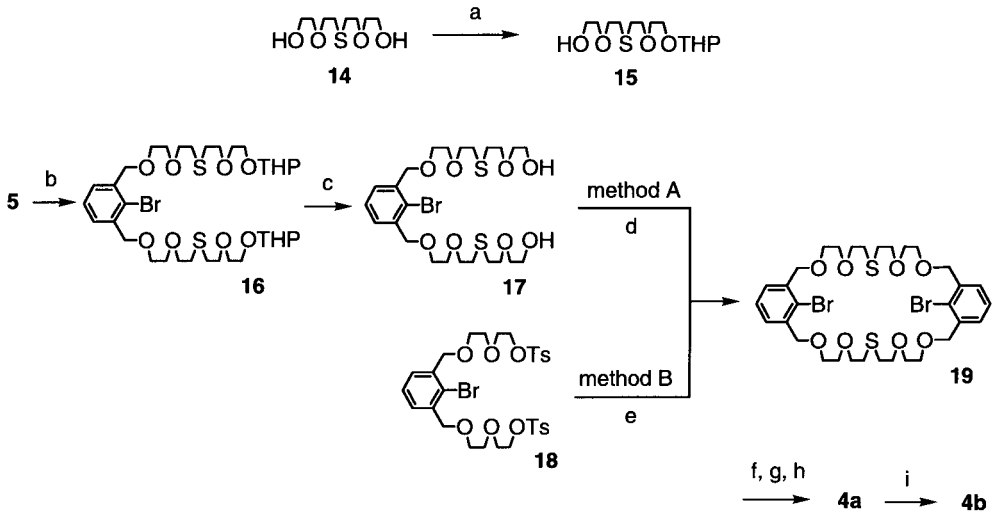
For the general methods, see Ref. [6]. Coupling constants (J) are reported in Hz.

Compound 6. Tribromide **5** was added to a solution prepared by dissolution of Na (5.745 g, 0.2499 mmol) in diethlylene glycol (70 g) at room temperature. The mixture was then stirred at 60°C for 2 days. The mixture was treated with 3 N HCl (100 mL) and extracted with $CHCl_3$ (70 mL × 3). The extracts were washed with H_2O (100 mL × 2) and saturated aqueous NaCl (100 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue thus obtained was purified by column chromatography (SiO_2, AcOEt-MeOH, 5:2) to give **6** (3.51 g, 79%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.05 (t, J = 5.9 Hz), 3.68–3.86 (m, 8H), 4.66 (s, 4H), 7.30–7.45 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 61.8, 71.9, 72.8, 123.4, 127.3, 128.5, 137.8. IR (NaCl) 3400 (br), 2870, 1429, 1352, 1130, 1071 cm^{-1}. MS (EI) m/z 304 (M^+), 306 (M + 2).

Compound 7. A solution of TsCl in tetrahydrofuran (THF) (40 mL) was added dropwise at −10°C to a mixture of the diol **6** in THF (40 mL) and NaOH



SCHEME 2 (a) 3,4-dihydro-2H-pyran, TsOH, CH_2Cl_2/THF, 0°C, 4 hours, 67%; (b) **10,** NaH, THF, reflux, 20 hours, 70%; (c) 3 N HCl, MeOH/THF/$CHCl_3$, rt, 39 hours, 74%; (d) **5,** NaH, THF, reflux, 5 days, 29%; (e) BuLi, THF, −78°C; (f) S_8, −78°C ∼ rt. (g) HCl, 36%; (h) H_2O_2, K_2CO_3, CH_2Cl_2/H_2O, rt, 70%.



SCHEME 3 (a) 3,4-dihydro-2H-pyran, TsOH, CH_2Cl_2, −10°C, 2.5 hours, 38%; (b) **15,** NaH, THF, reflux, 2 days, 55%; (c) 3 N HCl, MeOH/THF, rt, 34 hours, 85%; (d) **5,** NaH, THF, reflux, 4 days, 35%; (e) $Na_2S{\cdot}9H_2O$, THF/EtOH, reflux 1 day, 8%; (f) BuLi, THF, −78°C; (g) S_8, −78°C ∼ rt; (h) HCl, 27%; (i) H_2O_2, K_2CO_3, CH_2Cl_2/H_2O, rt, 92%.

in H_2O (40 mL). The reaction mixture was poured into ice water (100 mL), extracted with CH_2Cl_2 (50 mL), and dried over anhydrous $MgSO_4$. The residue obtained after evaporation of the solvent was purified by column chromatography (S:O_2, $CHCl_3$–AcOEt, 10:1) to give **7** (16.9 g, 82%) as a colorless oil: m.p. 74–75°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.44 (s, 6H), 3.76 (t, J = 4.8 Hz, 4H), 4.25 (t, J = 4.6 Hz, 4H), 4.54 (s, 4H), 7.27–7.34 (m, 7H), 7.80 (d, J = 8.3 Hz, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.58, 68.24, 69.31, 72.65, 122.68, 127.45, 128.18, 128.25, 130.11, 133.20, 137.63, 145.19. IR (NaCl) 2874, 1734, 1599, 1357, 1170, 1140, 1021, 922 cm^{-1}. fast atom bombardment mass spectrometry (FABMS) *m/z* 613 ([M + H]$^+$). Anal. Calcd for $C_{26}H_{29}BrO_8S_2$: C, 50.90; H, 4.76. Found: C, 50.80; H, 4.65.

Compound 8. A solution of **7** (5.544 g, 9.036 mmol) in 50 mL of THF and 50 mL of EtOH was added dropwise over a period of 3 hours, under reflux, to a solution of $Na_2S{\cdot}9H_2O$ (2.278 g, 9.458 mmol) in 580 mL of EtOH. After the addition, the mixture was refluxed for 2 days. The solvent was removed in vacuo, and the residue was mixed with 200 mL of CH_2Cl_2 and 150 mL of H_2O. The organic layer was washed with 100 mL of H_2O and 100 mL of brine, dried over anhydrous $MgSO_4$, and then concentrated in vacuo. The crude product was purified by silica gel column chromatography using CH_2Cl_2/AcOEt (50:1) as an eluent to give **8** (0.795 g, 29%) as a white powder: m.p. 100–102°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.83 (t, J = 6.5 Hz, 8H), 3.73 (t, J = 6.6 Hz, 8H), 4.51 (s, 8H), 7.11–7.36 (m, 6H). ^{13}C NMR (50

TABLE 1 Single Ion Transport for Heavy Metal

	Conc. of Metal Ion in the Receiving Phase ($\times 10^{-5}$ M)[a]							
Host	Ag^+	Mn^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}
2a	6–9[b]	0	0	0	0	0.3	0	0
2b	0.6	0	0	0	0	0	0	0
3a	13.6[b]	0	0	0	0	0	0	0
3b	25.6[b]	0	0	0	0	0	0	0
4a	4.2	0	0	0	0	0.1	0	0
4b	18.1	0	0	0	0	0	0	0

[a]The values were determined after 24 hours [Host] = 2×10^{-4} M in the liquid membrane, [metal nitrate] = 0.01 M in the source phase.
[b]Precipitates were observed.

MHz, $CDCl_3$): δ 32.08, 71.37, 72.65, 123.61, 127.49, 128.71, 138.19. (FABMS) *m/z* 605 ($[M + H]^+$). Anal. Calcd for $C_{24}H_{30}Br_2O_4S_2$: C, 47.54; H, 4.99. Found: C, 47.36; H, 4.87.

*Compound **10***. 3,4-Dihydro-2H-pyran (2.8 g, 33 mmol) was added slowly at 0°C to a mixture of the diol **9** (17.5 g, 96.0 mmol) and *p*-TsOH · H_2O (0.647 g, 3.4 mmol) in 150 mL of CH_2Cl_2: After the mixture had been stirred for 4 hours, resultant precipitates were filtered off and then the solvent was removed in vacuo to give crude **10** (5.876 g) as a colorless viscous oil. The crude product was used without further purification because a small amount of the corresponding dipyranyl polyether as a by-product was included. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.49–1.82 (m, 6H), 2.24 (br, 1H, OH), 2.74–2.83 (m, 8H), 3.49–3.98 (m, 6H), 4.62–4.65 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5, 25.4, 30.6, 31.8, 32.0, 32.6, 35.4, 60.7, 62.3, 67.4, 98.9. IR (NaCl) 3300(br), 2924, 1425, 1348, 1203, 1140, 1030 cm^{-1}; MS (EI) *m/z* 266 (M^+).

*Compound **11***. A solution of the tribromide **5** (4.980 g, 14.52 mmol) in 100 mL of THF was added in several portions under reflux to a suspension of 60% NaH (1.526 g, 38.15 mmol) in 65 mL of THF. After additional reflux for 20 hours, 5 mL of H_2O was added to decompose an excess amount of NaH. The solvent was evaporated under reduced pressure. The residue was mixed with $CHCl_3$ and H_2O. The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue thus obtained was purified by silica gel column chromatography using $CHCl_3$–AcOEt (20:1) to give **11** (7.255 g, 70%) as a pale orange oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.50–1.84 (m, 12H), 2.73–2.85 (m, 16H), 3.46–3.97 (m, 12H), 4.63 (s, 6H), 7.27–7.46 (m, 3H). ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 19.4, 25.4, 30.6, 31.72, 31.82, 32.67, 32.72, 62.3, 67.5, 70.7, 72.6, 98.9, 122.7, 127.3, 128.0, 137.8. IR (NaCl) 2924, 2868, 1734, 1688, 1427, 1352, 1201, 1120, 1081, 1027 cm^{-1}. FABMS *m/z* 713 ($[M + H]^+$).

*Compound **12***. The bromide **11** (7.232 g, 10.13 mmol) was treated with a mixture of 30 mL of MeOH, 40 mL of THF, 10 mL of $CHCl_3$, and 12 mL of 3N HCl at room temperature for 39 hours. After evaporation of the solvent and addition of 50 mL of a 5% NaOH aqueous solution, the mixture was extracted with $CHCl_3$ (50 mL × 3). The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue thus obtained was purified by silica gel column chromatography using $CHCl_3$-AcOEt (2:1) as an eluent to give **12** (4.110 g, 74%) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.20 (br, 2H), 2.70–2.85 (m, 16H), 3.67–3.79 (m, 8H), 4.63 (s, 4H), 7.27–7.46 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7, 31.8, 32.8, 35.3, 60.6, 70.8, 72.6, 123.0, 127.3, 128.2, 137.8. IR (NaCl) 3400(br), 2920, 2868, 1427, 1354, 1292, 1203, 1116, 1025 cm^{-1}. FAB MS *m/z* 545 ($[M+H]^+$).

*Compound **13***. A mixture of **3** (2.578 g, 7.518 mmol) and **12** (4.102 g, 7.518 mmol) in 75 mL of THF was added dropwise over 24 hours under reflux to a suspension of 60% NaH (1.541 g, 38.52 mmol) in 250 mL of THF. After an additional 2 hours of reflux, a small amount of H_2O was added to the mixture to decompose an excess amount of NaH. The solvent was removed in vacuo, and the residue was mixed with 50 mL of $CHCl_3$ and 50 mL of H_2O. The aqueous layer was separated and extracted with $CHCl_3$ (50 mL × 2). The organic layers were combined, dried over anhydrous $MgSO_4$, and then concentrated in vacuo. The crude product thus obtained was purified by silica gel column chromatography $CHCl_3$–AcOEt–*n*-hexane (8:1:8, v/v) to give **13** (1.585 g, 29%) as a white solid: m.p. 118–119°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.76 (t, J = 6.2 Hz, 8H), 2.83 (s, 8H), 3.72 (t, J = 6.3 Hz, 8H), 4.57 (s, 8H), 7.24–7.41 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.62, 32.79, 71.30, 72.56, 122.78, 127.32, 128.01, 137.81. IR (KBr) 2914, 2892, 2860, 1474, 1420, 1400, 1356, 1349, 1281, 1118, 1087, 1039, 1025, 1014, 770 cm^{-1}. FAB MS *m/z* 725 ($[M+H]^+$). Anal. Calcd for $C_{28}H_{38}Br_2O_4S_4$: C, 46.28; H, 5.27. Found: C, 46.17; H, 5.24.

*Compound **15***. According to a procedure similar to that used for **10**, the alcohol **15** was obtained in 38% yield as a pale yellow oil from **14** (37.989 g, 0.1806 mmol), and *p*-TsOH·H_2O (3.814 g, 20.05 mmol) in CH_2Cl_2 (200 mL). The crude **15** was purified by silica gel column chromatography using $CHCl_3$–AcOEt (5:1), AcOEt-hexane-EtOH (10:8:1), and then AcOEt–MeOH (10:1). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.49–1.90 (m, 6H), 2.78 (t, J = 6.7 Hz, 2H),

2.79 (t, J = 6.4 Hz, 2H,), 2.92 (t, J = 6.3 Hz, 1H), 3.46–3.93 (m, 14H), 4.62–4.66 (m, 1H). ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 19.5, 25.4 30.6, 31.8, 32.1, 61.8, 62.3, 66.7, 70.3, 70.8, 71.2, 72.1, 99.0. IR (NaCl) 3500 (br), 2926, 2870, 1354, 1261, 1203, 1123, 1077, 1036 cm^{-1}.

*Compound **16***. According to a procedure similar to that used for **11**, **16** was prepared in 55% yield as a pale yellow oil from 60% NaH (2.000 g, 50.00 mmol), **5** (6.779 g, 19.77 mmol), and **15** (11.644 g, 39.550 mmol) in THF. Purification of **16** was carried out by silica gel column chromatography using $CHCl_3$–AcOEt (4:1) as an eluent. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.47–1.81 (m, 12H), 2.73–2.82 (m, 8H), 3.47–3.89 (m, 28H), 4.65 (s, 6H), 7.27–7.45 (m, 3H). ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 19.5, 25.4, 30.6, 31.9, 62.3, 66.6, 70.2, 70.3, 71.1, 71.2, 72.8, 99.0, 122.7, 127.2, 128.0, 137.9. IR (NaCl) 2928, 2870, 1123, 1077, 1036 cm^{-1}. FAB MS m/z 769 ($[M+H]^+$).

*Compound **17***. According to a procedure similar to that used for **12, 16** (8.291 g, 10.77 mmol) was deprotected by the reaction with 3 N HCl (69 mL) for 34 hours at room temperature in MeOH (30 mL) and THF (30 mL) to give **17** (5.505 g, 85%) as a pale yellow oil, after silica gel chromatography using AcOEt–hexane–EtOH (10:8:1) as an eluent. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.26 (br, 2H), 2.79 (t, J = 6.5 Hz, 8H), 3.55–3.74 (m, 24H), 4.66 (s, 4H), 7.27–7.47 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 31.95, 32.21, 61.90, 70.37, 70.56, 70.94, 71.45, 72.28, 72.99, 123.14, 127.58, 128.38, 138.30. IR (neat) 3450 (OH), 2868, 2362, 1577, 1352, 1291, 1119, 888, 788, 468 cm^{-1}. FAB MS m/z 601 ($[M+H]^+$).

*Compound **18***. According to a procedure similar to that used for **7, 18** was obtained as a colorless oil in 91% after being purified by column chromatography (SiO_2, AcOEt–n-hexane–ethanol, 5:4:1, v/v): ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.50 (br. t, 2H), 3.60–3.75 (m, 16H), 4.66 (s, 4H), 7.27–7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 68.7, 69.3, 70.1, 70.7, 72.8, 122.8, 127.3, 127.97, 128.04, 129.8, 132.9, 137.8, 144.8. IR (NaCl) 2874, 1599, 1454, 1357, 1178, 1098, 1019, 922 cm^{-1}; FABMS m/z 701 ($[M+H]^+$).

*Compound **19***. (Method A) According to a procedure similar to that used for **13, 19** was obtained. A solution of **5** (3.053 g, 8.905 mmol) and **17** (5.358 g, 8.906 mmol) in 50 mL of THF was added slowly during 1 day under reflux to a suspension of 60% NaH (0.897 g, 22.4 mmol) in 250 mL of THF. After an additional 3 day of reflux, decomposition of an excess NaH with 10 mL of H_2O, and evaporation of the solvent, the residue was mixed with 50 mL of H_2O and then extracted with $CHCl_3$ (50 mL × 2). The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by silica gel column chromatography using $CHCl_3$–AcOEt (5:1) as an eluent to give **19** as white needles: m.p. 74–75°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.79 (t, J = 6.6 Hz, 8H), 3.66–3.73 (m, 24H), 4.62 (s, 8H), 7.26–7.43 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): 32.29, 70.72, 70.84, 72.03, 73.19, 123.23, 127.85, 128.53, 138.55. IR (KBr) 2936, 2919, 2895, 2872, 1142, 1120, 1100, 1063, 1041 cm^{-1}. FABMS m/z 781 ($[M+H]^+$). Anal. Calcd for $C_{32}H_{46}Br_2O_8S_2$: C, 49.11; H, 5.92. Found: C, 49.32; H, 5.97.

General Experimental Procedure for the Synthesis of **2a, 3a,** *and* **4a**

A *n*-BuLi hexane solution (1.64 M, 3.67 mmol) was added slowly to a stirred solution of bromide **8** (1.67 mmol) in THF (40 mL) at −78°C. After the mixture had been stirred for 1 hour at −78°C, S_8 powder was added. The temperature of the reaction mixture was raised very slowly to 0°C, and then acidified with dilute HCl. The solvent was removed under reduced pressure. The residue thus obtained was mixed with CH_2Cl_2 and washed with H_2O and aqueous NaOH. The organic layer was dried over $MgSO_4$. After the solvent had been evaporated, the crude product was purified by recrystallization from AcOEt to give **2a** as pale yellow crystals (0.807 mmol).

*Compound **2a***. m.p. 137–140°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.81 (t, J = 6.5 Hz, 8H), 3.70 (t, J = 6.6 Hz, 8H), 4.56 (s, 8H), 4.57 (s, 2H), 7.07–7.27 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 31.98, 70.27, 72.82, 125.53, 130.00, 133.68, 137.31. IR (KBr) 2885, 2862, 2796, 2540 (SH), 1476, 1432, 1355, 1280, 1127, 1089, 1054, 1043, 1034, 1007, 782, 768, 726 cm^{-1}. Anal. Calcd for $C_{24}H_{32}O_4S_4$: C, 56.22; H, 6.29. Found: C, 55.95; H, 6.09.

*Compound **3a***. m.p. 107–108°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.71 (t, J = 6.3 Hz, 8H), 2.76 (s, 8H), 3.65 (t, J = 6.3 Hz, 8H), 4.53 (s, 2H), 4.59 (s, 8H), 7.12–7.31 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 31.78, 32.80, 70.46, 72.66, 125.65, 129.83, 132.88, 137.26; IR (KBr) 2931, 2862, 2843, 2553 (SH), 1446, 1430, 1418, 1400, 1364, 1201, 1091, 1054, 1038, 1026, 1002, 980, 788, 738, 704 cm^{-1}. Anal. Calcd for $C_{28}H_{40}O_4S_6$: C, 53.13; H, 6.37. Found: C, 53.09; H, 6.42.

*Compound **4a***. m.p. 67–68°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.77 (t, J = 6.7 Hz, 8H), 3.62–3.69 (m, 24H), 4.62 (s, 10H), 7.08–7.30 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 32.02, 69.78, 70.43, 71.58, 72.88, 125.49, 129.71, 133.03, 137.30. IR (KBr) 2906, 2868, 2517 (SH), 1115, 1024, 972, 939, 878, 784, 731 cm^{-1}. Anal.

Calcd for $C_{32}H_{48}O_8S_4$: C, 55.79; H, 7.02. Found: C, 55.63; H, 7.02.

General Experimental Procedure for the Synthesis of **2b, 3b,** *and* **4b**

A solution of **2a** (0.268 mmol) in CH_2Cl_2 (50 mL) was stirred vigorously with 7% aqueous H_2O_2 (32 mL) and K_2CO_3 (2.53 mmol). Subsequently, a saturated aqueous NaCl solution (20 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with H_2O (2 × 50 mL) saturated NaCl (50 mL). After evaporation of the solvent, the residue thus obtained was washed with AcOEt and H_2O to give **2b** (0.2 mmol), which was practically pure as seen from the ^{1}H NMR spectrum. Very pure **2b** was obtained by recrystallization from CH_2Cl_2–AcOEt.

*Compound **2b***. m.p. 199–200°C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.84 (t, J = 6.0 Hz, 8H), 3.77 (t, J = 6.1 Hz, 8H), 4.36 (br, 8H), 7.39 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 32.38, 71.53, 71.60, 129.95, 130.61, 136.03, 142.72. IR (KBr) 2910, 2868, 2828, 1349, 1282, 1172, 1102, 1084, 1047, 1006, 803 cm^{-1}. HRMS calcd for $C_{24}H_{30}O_4S_4$ *m/z* 510.1027. Found *m/z* 510.0992.

*Compound **3b***. m.p. 162–163°C (from AcOEt-hexane). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.68 (t, J = 6.2 Hz, 8H), 2.85 (s, 8H), 3.66 (br, 8H), 4.41 (br, 8H), 7.44 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 31.09, 32.88, 70.93, 71.92, 128.38, 130.80, 132.34, 143.43. IR (KBr) 2920, 2863, 1424, 1409, 1352, 1206, 1107, 1054, 1000, 806, 789 cm^{-1}. Anal. Calcd for $C_{28}H_{38}O_4S_6$: C, 53.30; H, 6.07. Found: C, 53.27; H, 6.14.

*Compound **4b***. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.80 (t, J = 6.4 Hz, 8H), 3.60 (s, 16H), 3.68 (t, J = 6.5 Hz, 8H), 4.51 (br, 8H), 7.27–7.46 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 32.00, 70.44, 70.80, 71.56, 72.42, 128.02, 128.11, 132.13, 140.89. IR (KBr) 2857, 1459, 1442, 1407, 1388, 1368, 1340, 1318, 1293, 1247, 1230, 1130, 984, 909, 884, 786, 669, 542 cm^{-1}. FAB MS *m/z* 687 ($[M+H]^+$).

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