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New Functionalized Derivatives of Sulfur- and Oxygen-Containing Hexacyclic Cage Compounds

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Several new sulfur- and oxygen-bridged hexacyclic cage compounds have been obtained *via* transannular cyclization of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (**1**). Thus, cage-annulated thiapodands **9** and **10** were prepared *via* reaction of ditosylate **6** with 2-mercaptoethylamine (**7**) or 2-mercaptoethanol (**8**), respectively. Other ditosylate **11** was reacted with thiourea to afford the corresponding dimercapto podand **12**. An optically active podand **(*R*,*R*)-14** was prepared in similar fashion by reacting ditosylate **6** with (*R*)-2-amino-1-butanol **(*R*)-(13)**. Functionalized 4-thiahexacyclo[5.4.1.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecanes **17a–b** and **18a–b** were prepared *via* reactions of **1** with 2-chloro- (**15**) or 2-bromoethanol (**16**), respectively in the presence of H_2S(g) and HCl(g). The corresponding reaction of **1** with 2 equivalents of **8** produced the corresponding bisthioacetal **20**, which subsequently was changed into a spiro-cage-annulated dithiacrown ether **22**.

Key words: cage systems, sulfur heterocycles, synthetic methods, crown derivatives

Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (**1**) was first prepared in 1958 [1]. Subsequently, the chemistry of this unusual cage dione has been explored extensively [2]. In particular, a number of 4-oxa- [3], 4-aza- [4], and 4-thiahexacyclo[5.4.1.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecanes [5] have been prepared from **1** *via* transannular cyclization processes. Some 4-oxahexacyclo-[5.4.1.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane derivatives **2** and **3** have been shown to function effectively as calcium channel antagonists [6].

Recently, the reaction of **1** with gaseous H_2S and HCl in methanol was described [5]. The results thereby obtained were found to depend critically upon reaction conditions. Both sulfur-bridged compounds **4** and **5** were isolated and characterized as products of this reaction.

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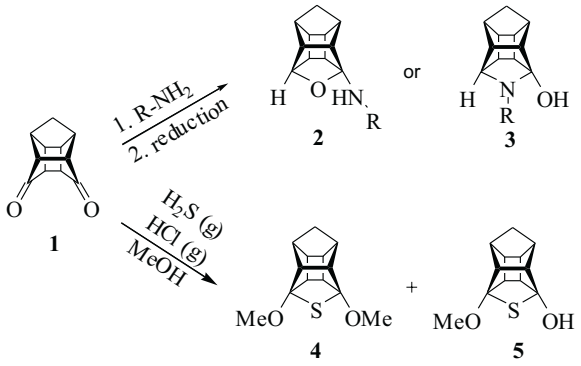
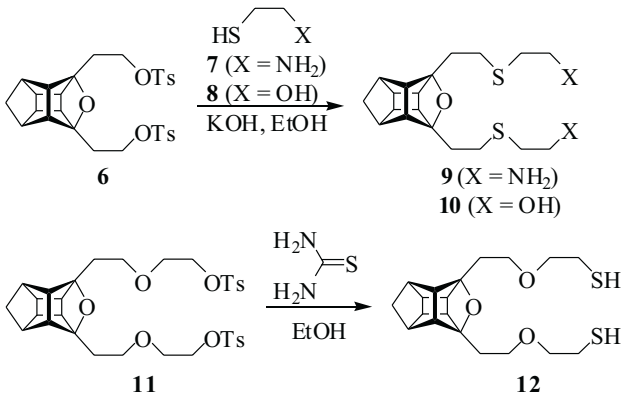
Scheme 1



RESULTS AND DISCUSSION

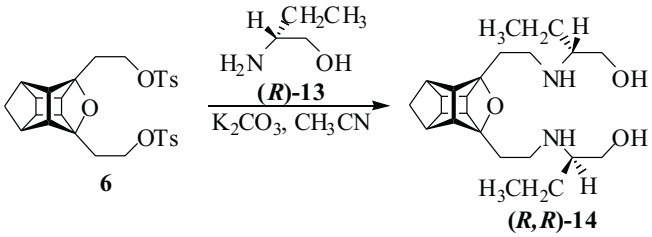
Synthesis of cage-annulated thiapodands. Cage-annulated thiapodands **9** and **10** were prepared *via* reaction of ditosylate **6** [7] with 2-mercaptoethanol (**7**) and 2-mercaptoethylamine (**8**), respectively. Subsequent reaction of extended ditosylate **11** [8] with thiourea afforded cage-annulated podand **12**. Compounds of the type **9**, **10**, and **12** serve as key intermediates for preparing cage-annulated crown ethers and cryptands [9].

Scheme 2



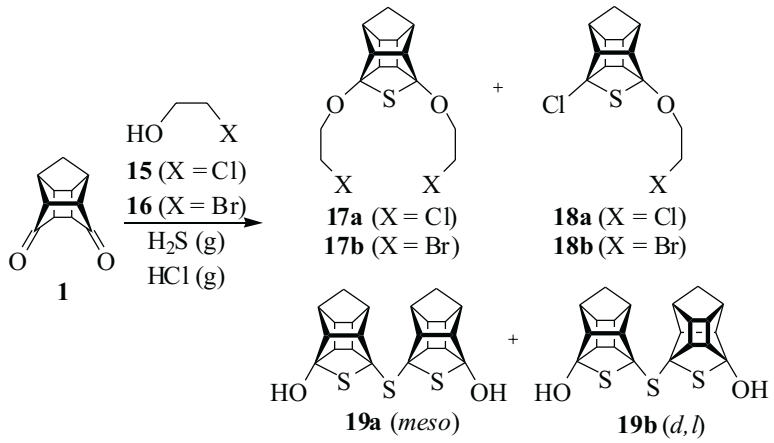
In addition, an optically active podand **(*R*,*R*)-14**, was prepared in similar fashion. Thus, reaction of ditosylate **6** with (*R*)-2-amino-1-butanol **(*R*)-13** produced **(*R*,*R*)-14** in good yield.

Scheme 3



Synthesis of functionalized 4-thiahexacyclo[5.4.1.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecanes. Thia-bridged hexacyclododecanes were prepared *via* reactions of cage dione **1** with 2-chloro- and 2-bromoethanol (**15** and **16**, respectively). Initially, a mixture of H_2S (g) and HCl (g) was bubbled through a solution of **1** in excess of 2-haloethanol during 4 h. Work-up of the reaction mixtures afforded **17a** and **17b** in low yield (8–9%). Two additional products were identified as **18a**/**18b** (*ca.* 40%) from each reaction and a dimeric product **19**, which was obtained as a mixture of *meso*- and *d,l*-diastereoisomers **19a** and **19b**, respectively (*ca.* 10% yield).

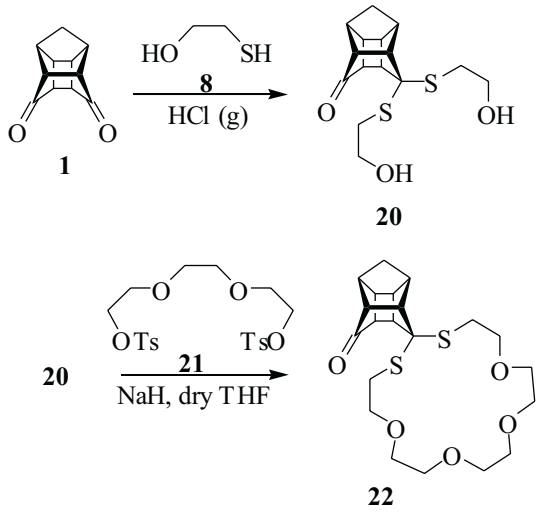
Scheme 4



Subsequently, the reaction of 2-chloroethanol (**15**) with dione **1** was carried out by using H_2S (g) in the presence of $BF_3 \cdot Et_2O$ instead of HCl (g). Under these conditions, the yield of **17a** increased to 18% at the expense of **18a**, which was not formed.

Synthesis of spiro-cage-annulated bisthioacetals. Interestingly, the corresponding reaction of **1** with 2-mercaptoethanol (**8**) in the presence of H_2S (g) and HCl (g) proceeded in an entirely different manner. Thus, instead of producing a thia-bridged hexacyclic product, reaction occurred at only one of the two available carbonyl groups in the substrate, thereby affording the corresponding bisthioacetal **20**. Subsequent base-promoted reaction of **20** with triethylene glycol ditosylate **21** produced the corresponding dithiacrown ether **22**, in 53% yield [10].

Scheme 5



In conclusion, the new cage-annulated podands **9**, **10**, and **12** have been easily prepared starting from well known dione **1**. An optically active podand **14** was prepared in similar fashion by reacting ditosylate **6** with (*R*)-2-amino-1-butanol (**13**). In addition, several reactions of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (**1**) with sulfur-containing nucleophiles have been studied. Thus, functionalized 4-thiahexacyclo[5.4.1.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]-dodecanes were prepared *via* reactions of **1** with 2-chloro- (**15**) and with 2-bromoethanol (**16**), respectively in the presence of mixture of H_2S (g) and HCl (g). The corresponding reaction of **1** with 2-mercaptoethanol (**8**) produced the corresponding bisthioacetal **20**, which subsequently was converted into a spiro-cage-annulated dithiacrown ether **22**.

The cage-annulated podands prepared herein are of interest as key intermediates that can be used to prepare novel, cage-annulated crown ethers, cryptands, and molecular boxes, all of which can serve as "host" molecules for the study of molecular recognition and inclusion phenomena. It is of particular interest to incorporate "soft" Lewis base atoms, such as sulfur, into molecules of this type, as this should render the resulting hosts suitable for use as soft Lewis acid complexants. Applications to environmental remediation are envisioned, *e.g.*, for selective complexation and transport of divalent heavy metal cations that are ubiquitous groundwater contaminants.

EXPERIMENTAL

Melting points were determined using capillary apparatus and were uncorrected. High-resolution mass spectral data reported herein were obtained at the Mass Spectrometry Facility at the Department of Chemistry and Biochemistry, University of Texas at Austin by using a ZAB-E double sector high-resolution mass spectrometer (Micromass, Manchester, England) that was operated in the chemical ionization mode. ^{1}H and ^{13}C NMR spectra were recorded at 199.975 and 50.289 MHz, respectively by using a Varian

Gemini 200 NMR spectrometer. NMR spectra were recorded in $CDCl_3$ (or DMSO-d_6) by using residual $CHCl_3$ (or DMSO) as an internal standard at 20°C. ^{13}C NMR peak assignments were made on the basis of APT experiments. Infrared spectra were obtained by using a Micac Fourier transform IR spectrophotometer.

Ditosylate **6** and extended ditosylate **11** were prepared according to literature protocol [7] and [8], respectively.

Base-promoted reaction of 6 with 7. To a solution of KOH (300 mg, excess) in EtOH (15 ml) the aminoethanethiol hydrochloride (**7**) (170 mg, 1.5 mmol) was added and the resulting mixture was stirred at ambient temperature during 15 minutes. Ditosylate **6** (280 mg, 0.5 mmol) was then added, and the resulting mixture was refluxed with stirring during 4 h. The reaction mixture was allowed to cool gradually to ambient temperature, and the reaction was quenched by addition of ice-cold water (50 ml). The EtOH was evaporated and the resulting aqueous suspension was extracted with CH_2Cl_2 (3×50 ml). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on neutral alumina by using a 3–10% MeOH-$CHCl_3$ gradient elution scheme. Pure **9** (150 mg, 75%) was obtained as a colorless, viscous oil; IR (film): cm^{-1} = 3356 (br, s), 3294 (br, s), 2958 (vs), 2860 (s), 1668 (s), 1579 (s), 1471 (s), 1377 (m), 1323 (s), 1298 (m), 898 (m); ^1H NMR ($CDCl_3$): δ = 1.49 (AB, J_{AB} = 10.4 Hz, 1 H), 1.68 (br s, 4 H), 1.84 (AB, J_{AB} = 10.4 Hz, 1 H), 1.97–2.05 (m, 4 H), 2.36–2.69 (m, 12 H), 2.83 (t, J = 6.3 Hz, 4 H); ^{13}C NMR ($CDCl_3$): δ = 27.4 (t), 33.1 (t), 36.2 (t), 41.0 (t), 41.6 (d), 43.5 (t), 44.3 (d), 47.8 (d), 58.5 (t), 95.3 (s); HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{19}H_{30}N_2OS_2$: m/z 367.1878. Found: m/z 367.1882.

Base-promoted reaction of 6 with 8. To a solution of KOH (300 mg, excess) in EtOH (15 ml) the 2-mercaptoethanol (**8**) (130 mg, excess) was added and the resulting mixture was stirred at ambient temperature during 15 minutes. Ditosylate **6** (280 mg, 0.5 mmol) was then added, and the resulting mixture was refluxed with stirring during 12 h. The reaction mixture was allowed to cool gradually to ambient temperature, and the reaction was quenched by addition of ice-cold water (50 ml). The reaction mixture was concentrated on a rotary evaporator to remove EtOH, and the resulting aqueous suspension was extracted with CH_2Cl_2 (3×50 ml). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on neutral alumina by using a 10–30% EtOAc-hexane gradient elution scheme. Pure **10** (160 mg, 80%) was obtained as a colorless, viscous oil; IR (film): cm^{-1} = 3340 (br, vs), 2960 (vs), 2862 (s), 1435 (m), 1371 (m), 1292 (m), 1226 (m), 1130 (m), 1045 (s), 1008 (s), 927 (m), 898 (m); ^1H NMR ($CDCl_3$): δ = 1.43 (AB, J_{AB} = 10.4 Hz, 1 H), 1.77 (AB, J_{AB} = 10.4 Hz, 1 H), 1.90–1.99 (m, 4 H), 2.30–2.53 (m, 8 H), 2.61 (t, J = 6.2 Hz, 4 H), 3.13 (br s, 2 H), 3.61 (t, J = 6.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$): δ = 27.2 (t), 32.8 (t), 34.7 (t), 41.3 (d), 43.3 (t), 44.0 (d), 47.5 (d), 58.2 (d), 60.5 (t), 94.2 (s); HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{19}H_{28}O_3S_2$: m/z 369.1558. Found: m/z 369.1566.

Reaction of 11 with thiourea. A solution of ditosylate **11** [8] (650 mg, 1.0 mmol) and thiourea (200 mg, excess) in EtOH (15 ml) was refluxed with stirring during 48 h. The reaction mixture was concentrated on a rotary evaporator to remove EtOH, and then saturated aqueous $NaHCO_3$ (10 ml) was added, and the resulting mixture was refluxed 3 h with stirring. The reaction mixture was allowed to cool gradually to ambient temperature and then was acidified by careful, dropwise addition of 2 N aqueous HCl up to pH ~5. The resulting mixture was extracted with CH_2Cl_2 (3×50 ml), dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 10–40% EtOAc-hexane gradient elution scheme. Pure **12** (160 mg, 80%) was obtained as a colorless, viscous oil; IR (film): cm^{-1} 2960 (vs), 2862 (s), 2546 (w), 1481 (w), 1417 (w), 1361 (m), 1294 (m), 1109 (s), 1026 (m), 931 (m); ^1H NMR ($CDCl_3$): δ = 1.45 (AB, J_{AB} = 10.4 Hz, 1 H), 1.54 (t, J = 8.1 Hz, 1 H), 1.81 (AB, J_{AB} = 10.4 Hz, 1 H), 2.03 (t, J = 7.0 Hz, 4 H), 2.33 (br s, 2 H), 2.46–2.67 (m, 10 H), 3.49 (t, J = 6.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$): δ = 24.3 (t), 32.6 (t), 41.7 (d), 43.3 (t), 44.3 (d), 48.3 (d), 58.7 (d), 67.8 (t), 72.3 (t), 94.2 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{19}H_{28}O_3S_2$: m/z 369.1558. Found: m/z 369.1558.

Base-promoted reaction of 11 with (*R*)-13. To a solution of **11** (690 mg, 1.0 mmol) in CH_3CN (20 ml) the **(*R*)-13** (1.1 g, excess) and K_2CO_3 (1.3 g, excess) was added and the resulting mixture was refluxed with stirring during 12 h. The reaction mixture was allowed to cool gradually to ambient temperature, and the reaction was quenched by addition of ice-cold water (100 ml). The resulting mixture was extracted with CH_2Cl_2 (3×50 ml); the combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a

30–40% EtOAc-hexane gradient elution scheme. Pure **(*R,R*)-14** (150 mg, 75%) was obtained as a colorless, viscous oil; IR (film): cm^{-1} = 3340 (br, vs), 2962 (vs), 2877 (s), 1651 (m), 1462 (vs), 1371 (s), 1296 (s), 1273 (m), 1221 (m), 1136 (s), 1053 (s), 958 (m), 916 (m), 869 (m), 752 (s); ^{1}H NMR ($CDCl_3$): δ = 0.81 (t, J = 7.6 Hz, 6 H), 1.14–1.48 (m, 5 H), 1.79–1.91 (m, 5 H), 2.25–2.51 (m, 16 H), 3.17–3.26 (m, 2 H), 3.50–3.57 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ = 10.4 (q), 23.4 (t), 32.0 (t), 41.3 (d), 41.4 (d), 43.4 (t), 43.6 (d), 44.0 (d), 47.5 (d), 47.7 (d), 58.1 (d), 58.3 (d), 60.8 (d), 62.7 (t), 95.8 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{23}H_{32}N_2O_3$: m/z 391.2961. Found: m/z 391.2962.

Reaction of 1 with 15 in the presence of H_2S (g)-HCl (g). A solution of **1** (1.00 g, 5.75 mmol) in excess of **15** (20 ml) was placed in a 100 ml round-bottom flask that had been fitted with a gas bubbler apparatus. Hydrogen sulfide (g) and hydrogen chloride (g) were bubbled simultaneously and slowly through the reaction mixture at ambient temperature during 4 h. The reaction mixture then was poured into ice-water (200 ml), and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 × 100 ml). The combined organic layers were washed with brine (3× 100 ml), dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by using a 0–70% CH_2Cl_2-ligroin gradient elution scheme. Work-up of the first chromatography fraction obtained afforded pure **18a** (700 mg, 42%) as a colorless, viscous oil; IR (film): cm^{-1} = 2978 (vs), 2870 (s), 1452 (m), 1321 (s), 1297 (s), 1292 (s), 1270 (m), 1192 (s), 1124 (vs), 1005 (m), 927 (m), 812 (s), 742 (m); ^{1}H NMR ($CDCl_3$): δ = 1.62 (AB, J_{AB} = 10.7 Hz, 1 H), 1.94 (AB, J_{AB} = 10.7 Hz, 1 H), 2.62–2.76 (m, 6 H), 3.03–3.08 (m, 2 H), 3.57 (t, J = 5.8 Hz, 2 H), 3.79 (t, J = 6.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ = 40.2 (d), 41.5 (d), 41.6 (t), 42.3 (t), 45.1 (d), 45.2 (d), 51.1 (d), 56.8 (d), 60.3 (d), 66.4 (d), 69.1 (t), 81.7 (s) 110.2 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{13}H_{15}Cl_2OS$: m/z 289.0221. Found: m/z 289.0229.

Continued elution of the chromatography column afforded a second fraction. Work-up of the second chromatography fraction obtained afforded pure **17a** (160 mg, 8.5%) as a colorless, viscous oil; IR (film): cm^{-1} = 2972 (vs), 2866 (s), 1454 (m), 1315 (s), 1295 (s), 1270 (m), 1190 (s), 1122 (vs), 1066 (m), 1030 (m), 814 (s), 670 (m); ^{1}H NMR ($CDCl_3$): δ = 1.60 (AB, J_{AB} = 10.8 Hz, 1 H), 1.92 (AB, J_{AB} = 10.8 Hz, 1 H), 2.61–2.77 (m, 4 H), 2.99–3.02 (m, 4 H), 3.58 (t, J = 5.3 Hz, 4 H), 3.80 (t, J = 5.5 Hz, 4 H); ^{13}C NMR ($CDCl_3$): δ 41.1 (d), 41.6 (t), 42.5 (t), 45.1 (d), 49.9 (d), 59.6 (d), 68.8 (t), 108.4 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{15}H_{18}Cl_2O_2S$: m/z 333.0483. Found: m/z 333.0490.

Continued elution of the chromatography column with 100% EtOAc afforded a third fraction. Work-up of the third chromatography fraction obtained afforded **19a** and **19b** (mixture of *meso*- and *d,l*-diastereoisomers, 130 mg, 11%) as a colorless microcrystalline solid: m.p. 230°C (dec.); IR (KBr): cm^{-1} = 3229 (br, vs), 2982 (vs), 2866 (s), 1454 (s), 1311 (s), 1296 (s), 1263 (s), 1248 (s), 1186 (m), 1109 (vs), 1003 (s), 887 (s), 808 (s), 748 (m); ^{1}H NMR (DMSO-d_6): δ = 1.52 (AB, J_{AB} = 10.9 Hz, 2 H), 1.89 (AB, J_{AB} = 10.9 Hz, 2 H), 2.51–2.78 (m, 12 H), 2.87–2.96 (m, 1 H), 3.06–3.19 (m, 3 H), 3.29 (br s, 1 H, OH), 3.36 (br s, 1 H, OH); ^{13}C NMR (DMSO-d_6): δ = 40.15 (d), 40.18 (d), 41.0 (t), 44.2 (d), 44.8 (d), 51.7 (d), 52.2 (d), 53.1 (d), 53.9 (d), 61.3 (d), 61.7 (d), 62.1 (d), 63.0 (d), 72.5 (s), 72.7 (s) 105.2 (s), 105.3 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{22}H_{22}O_2S_3$: m/z 415.0820. Found: m/z 415.0840.

Reaction of 1 with 15 in the presence of H_2S (g)-$BF_3 \cdot Et_2O$. A solution of **1** (1.00 g, 5.75 mmol) and $BF_3 \cdot Et_2O$ (1.60 g, 11.5 mmol) in excess of **15** (20 ml) was placed in a 100 ml round-bottom flask that had been fitted with a gas bubbler apparatus. Hydrogen sulfide (g) and hydrogen chloride (g) were bubbled simultaneously and slowly through the reaction mixture at ambient temperature during 4 h. Work-up of the reaction mixture was performed in the manner described above. The crude product was purified *via* column chromagraphy on silica gel by using a 0–100% CH_2Cl_2-Et_2O gradient elution scheme. Two chromatography fractions were collected; work-up of these fractions afforded pure **17a** (310 mg, 18%) and a diastereoisomeric mixture of **19a** and **19b** (220 mg, 17%). Compound **20a** was not obtained as a product of this reaction.

Reaction of 1 with 16 in the presence of H_2S (g)-HCl (g). A solution of **1** (1.00 g, 5.75 mmol) in excess of **16** (20 ml) was placed in a 100 ml round-bottom flask that had been fitted with a gas bubbler apparatus. Hydrogen sulfide (g) and hydrogen chloride (g) were bubbled simultaneously and slowly through the reaction mixture at ambient temperature during 4 h. Work-up of the reaction mixture was performed in the manner described above. The crude product (CAUTION: STENCH) was purified *via* column chromagraphy on silica gel by using a 0–70% $CHCl_3$-hexane gradient elution scheme. Work-up of the first chromatography fraction obtained afforded pure **18b** (780 mg, 41%) as a colorless, viscous oil; IR (film): cm^{-1} = 2972 (vs), 2868 (s), 1456 (m), 1442 (w), 1315 (s), 1302 (s), 1288 (s), 1271 (s), 1186 (m),

1136 (vs), 1012 (m), 995 (s), 922 (m), 879 (m), 808 (s), 742 (m); ^{1}H NMR ($CDCl_3$): δ = 1.62 (AB, J_{AB} = 10.9 Hz, 1 H), 1.96 (AB, J_{AB} = 10.9 Hz, 1 H), 2.64–2.77 (m, 4 H), 3.04–3.10 (m, 4 H), 3.42 (t, J = 6.3 Hz, 2 H), 3.86 (t, J = 6.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ = 29.8 (t), 40.3 (d), 41.6 (d), 41.7 (t), 45.2 (d), 45.3 (d), 51.2 (d), 56.8 (d), 60.5 (d), 66.5 (d), 69.0 (t), 83.8 (s), 110.2 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{13}H_{14}BrClOS$: m/z 332.9716. Found: m/z 332.9725.

Continued elution of the chromatography column afforded a second fraction. Work-up of the second chromatography fraction thereby obtained afforded pure **17b** (120 mg, 6%) as a colorless, viscous oil; IR (film): cm^{-1} = 2968 (vs), 2866 (s), 1454 (m), 1315 (s), 1294 (s), 1197 (m), 1122 (s), 1008 (m), 808 (m); ^{1}H NMR ($CDCl_3$): δ = 1.61 (AB, J_{AB} = 10.8 Hz, 1 H), 1.92 (AB, J_{AB} = 10.8 Hz, 1 H), 2.62–2.73 (m, 4 H), 2.99–3.02 (m, 4 H), 3.42 (t, J = 6.3 Hz, 4 H), 3.87 (t, J = 6.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$): δ 30.0 (t), 41.1 (d), 41.7 (t), 45.2 (d), 50.0 (d), 59.6 (d), 68.7 (t), 108.3 (s). HRMS exact mass $[M_r + 1]^+$ calcd for $C_{15}H_{18}Br_2O_2S$: m/z 330.9826. Found: m/z 330.9814.

Continued elution of the chromatography column with 100% EtOAc afforded a third fraction. Work-up of the third chromatography fraction obtained afforded **19a** and **19b** (mixture of *meso*- and *d,l*-diastereoisomers, 110 mg, 9%) as a colorless microcrystalline solid: m.p. 230°C. The IR and NMR spectra of the mixture of **19a** and **19b** obtained agreed with the corresponding spectra obtained for the mixture of **17a** and **17b** obtained via the reaction of **3** with 2-chloroethanol in the presence of H_2S (g)-HCl (g) (*vide supra*).

Reaction of 1 with 8 in the presence of HCl (g). A solution of **1** (1.00 g, 5.75 mmol) in excess of **8** (20 ml) was placed in a 100 ml round-bottom flask that had been fitted with a gas bubbler apparatus. Hydrogen chloride (g) was bubbled simultaneously and slowly through the reaction mixture at ambient temperature during *ca*. 0.5 h. The reaction mixture then was poured into ice-water (200 ml), and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 ×100 ml). The combined organic layers were washed with brine (3 ×100 ml), dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with $CHCl_3$. Work-up of the eluate thereby obtained afforded pure **20** (1.4 g, 80%) as a colorless, viscous oil; IR (film): cm^{-1} = 3367 (br, vs), 2960 (vs), 2870 (s), 1722 (vs), 1456 (s), 1417 (s), 1284 (s), 1255 (m), 1159 (m), 1140 (m), 1045 (s), 1010 (s), 825 (s), 742 (s); ^{1}H NMR ($CDCl_3$): δ = 1.45 (AB, J_{AB} = 11.0 Hz, 2 H), 1.78 (AB, J_{AB} = 11.0 Hz, 2 H), 2.38–3.10 (m, 8 H), 3.64 (t, J = 5.9Hz, 4 H); ^{13}C NMR: ($CDCl_3$) δ = 33.0 (t), 34.1 (t), 34.5 (d), 36.5 (t), 42.5 (d), 42.9 (d), 43.6 (t), 47.5(t), 48.1 (d), 51.4 (d), 58.1 (d), 60.6 (t), 60.9 (t), 69.1 (s), 213.6 (s). HRMS exact mass $[M_r + 1]^+$ calcd for $C_{15}H_{19}O_3S_2$: m/z 313.0932. Found: m/z 313.0928.

Base-promoted reaction of 20 with triethylene glycol ditosylate 21. To a solution of **20** (150 mg, 0.48 mmol) and ditosylate **21** (220 mg, 0.48 mmol) in dry THF (5 ml) a suspension of NaH (250 mg of a 60% dispersion in mineral oil, excess) in dry THF (30 ml) was added under stirring and the resulting mixture was refluxed during 4 days. The reaction mixture was allowed to cool gradually to ambient temperature and then was quenched by pouring over ice (100 g). The resulting aqueous suspension was extracted with CH_2Cl_2 (3×100 ml); the combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 1% MeOH-$CHCl_3$. Pure **22** (108 mg, 53%) was thereby obtained as a colorless, viscous oil; IR (film): cm^{-1} = 2949 (s), 2866 (vs), 1724 (vs), 1450 (m), 1356 (m), 1286 (m), 1253 (m), 1116 (vs), 985 (m), 825 (m), 742 (m); ^{1}H NMR ($CDCl_3$): δ = 1.39 (AB, J_{AB} = 11.0 Hz, 2 H), 1.66 (AB, J_{AB} = 11.0 Hz, 2 H), 2.31–2.82 (m, 10 H), 2.94–3.07 (m, 2 H), 3.43–3.62 (m, 16 H); ^{13}C NMR ($CDCl_3$): δ = 29.6 (t), 30.4 (t), 34.4 (d), 36.3 (t), 42.2 (d), 42.5 (d), 43.4 (d), 47.0 (d), 48.1 (d), 51.0 (d), 57.4 (d), 68.9 (t), 69.1 (s), 69.4 (t), 69.9 (t), 70.1 (t), 70.4 (t), 70.7 (t), 70.8 (t), 211.5 (s). HRMS: exact mass $[M_r + 1]^+$ calcd for $C_{21}H_{30}O_5S_2$: m/z 427.1613. Found: m/z 427.1604.

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