From Sugars to Carbocycles. 2.[1] Three- to Seven-Membered Rings from Mannose by Addition of 1,3-Dithiane Followed by Intramolecular Displacement Reaction

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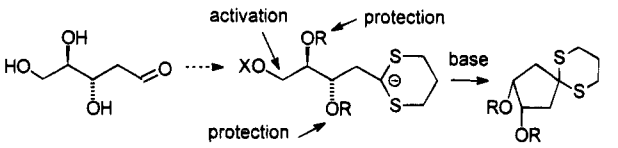
A new methodology for the conversion of sugars to three-, four-, six-, and seven-membered rings is presented. The sequence of transformations is demonstrated with mannose (**1**) and involves addition of 2-lithio-1,3-dithiane to the acetonide **2** followed by elimination and reduction to the 2-deoxydithiane **6**. Starting from this intermediate, appropriate activation (tosylate, epoxide) and protection (acetonide, methyl ether) yields **8**, **18**, and **23**, the starting materials for carbocyclization, which are converted by nucleophile displacement to the optically active cyclopropane **9**, cyclobutane **19**, cyclohexane **24**, and cycloheptane **25**, respectively. The cyclopropyl-1,3-dithane **9** can be desulfurized to the cyclopropane **10**.

The use of carbohydrates in the construction of functionalized carbocyclic ring systems is an emerging new field in carbohydrate chemistry. Ferrier and Middleton,[2] in a recent comprehensive review on the conversion of sugars to cyclopentanes and cyclohexanes, state that more than 80% of the papers relevant to the subject were published in the last decade. The use of sugars for incorporation in condensed ring systems[3] or in radical cyclizations[4] has also recently been reviewed.

In 1991 we published a first paper on the synthesis of three- to five-membered carbocycles from 2-deoxyribose.[1] The principle of the reaction sequence is shown in Scheme 1. The electrophilic aldehyde functionality (in equilibrium with the cyclic hemiacetal) of 2-deoxyribose is converted into a nucleophilic 1,3-dithiane group by reaction with 1,3-propanedithiol (umpolung); then one of the hydroxy groups is rendered electrophilic by conversion into a good leaving group (e.g. tosylation or conversion into an epoxide), the remaining hydroxy groups are protected, and cyclization is induced by treatment with a base (*n*-BuLi). This work showed, in spite of some limitations in the choice of the 2-deoxygenated starting materials, that sugar-derived 1,3-dithianes not previously used in this context can successfully undergo intramolecular cyclizations to carbocycles.

We now report on the extension of our previous methodology that expands the scope and flexibility of the reaction and also reduces limitations in the choice of carbohydrate starting materials by addition of 1,3-dithiane to protected sugars such as 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**2**)[5] followed by deoxygenation to **6**. Transacetalization of known alcohol **3**[6,7] to the triacetonide **4** was achieved by treatment with acetone and acid (84%). This facile protection of the open-chain 1,3-dithiane sugar derivatives by conversion to triacetonides is presumably quite independent of specific sugar configurations as demonstrated with glucose in the following paper.[8] The next two steps can be performed in one reaction vessel: elimination to the transient thioketene acetal **5** is initiated by treatment with 2 equiv of *n*-BuLi and subsequent reduction to the saturated alcohol **6** with 1.2 equiv of LAH (Scheme 2, overall yield 90%).[9]

Scheme 1



At this point it is worth noting that a minor side product (**7**) (3%) could be isolated that resulted from the addition of *n*-BuLi to the intermediate hydroxy ketene acetal **5**. We rationalize this unusual reaction by addition of the nucleophile to a lithium-complexed intermediate and are presently investigating the generality of this process, which could give an easy access to branched sugars. The stereochemistry at C-2 of **7** was deduced from the coupling of $J_{1,2} = 5.5$ Hz; much larger couplings have been found for similar *threo*-configurated compounds.[10]

Cyclopropane Derivatives. Cyclopropane derivatives show unique chemical and physiological properties as exemplified by chrysanthemic acids. They are accessible by our strategy in a very short reaction sequence (six steps from mannose, Scheme 2). Thus, the LAH reduction product **6** is tosylated to the monotosylate **8** (96%) and then cyclized by treatment of **8** with 1 equiv of *n*-BuLi to the crystalline cyclopropane derivative **9** in 77% yield (Scheme 3). The product showed typical signals for the cyclopropane methylene protons in the ^{1}H

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(1) Previous communication: Krohn, K.; Börner, G. *J. Org. Chem.* **1991**, *56*, 6038–6043.

(2) Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779–2831.

(3) Hale, K. J. In *Rodd's Chemistry of Carbon Compounds, 2nd Supplement*; Elsevier: Amsterdam, 1993; Vol. 1, p 315.

(4) Fraser-Reid, B.; Tsang, R. *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: New York, 1989; Vol. 2, pp 123–162.

(5) Schmidt, O. Th. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1963; Vol. II, p 319.

(6) Paulsen, H.; Schüller, M.; Nashed, M. A.; Heitmann, A.; Redlich, H. *Liebigs Ann. Chem.* **1986**, 675–686.

(7) Paulsen, H.; Schüller, M.; Nashed, M. A.; Heitmann, A.; Redlich, H. *Tetrahedron Lett.* **1985**, *26*, 3689–3692.

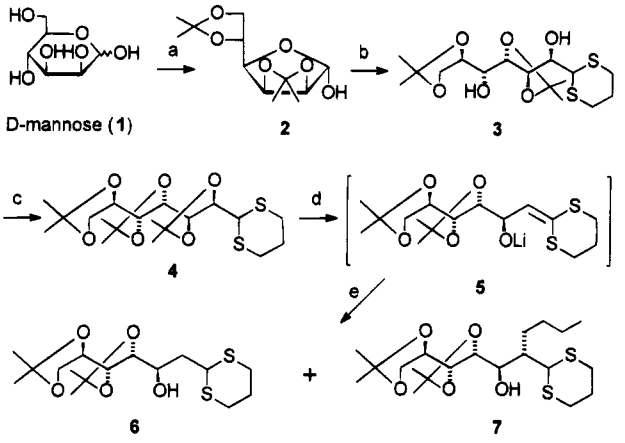
(8) Krohn, K.; Börner, G.; Gringard, S. *J. Org. Chem.* **1994**, *59*, following paper in this issue.

(9) Wong, M. Y.; Gray, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 3548–3553.

(10) Redlich, H.; Thormählen, S. *Tetrahedron Lett.* **1985**, *26*, 3685–3688.

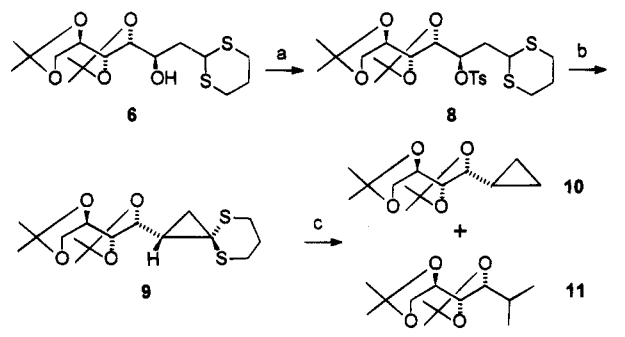
0022-3263/94/1959-6063$04.50/0

Scheme 2



[a] (a) Reference 5; (b) ref 6; (c) CH_3COCH_3, H_2SO_4 (84%); (d) *n*-BuLi, −40 to −20 °C; (e) LAH, 0 °C (90% **6**, 3% **7**).

Scheme 3



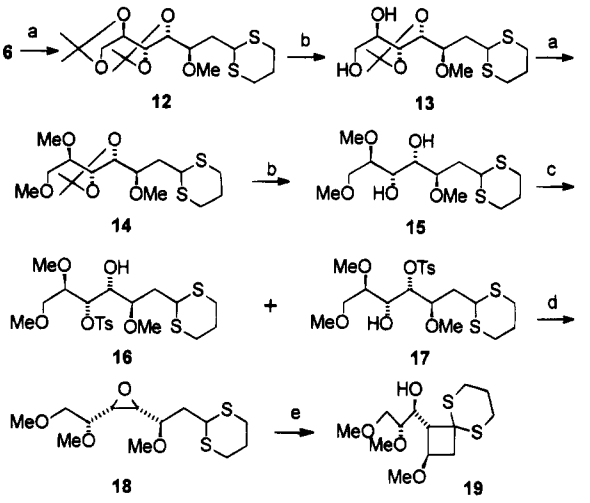
[a] (a) Py/TsCl/DMAP, 24 h, 20 °C (96%); (b) THF, *n*-BuLi, −40 °C to 20 °C, 2 h; (77%); (c) Ra−Ni, EtOH, 76 °C, 30 min (51% **9**, 44% **10**).

NMR spectrum at δ 1.01 (t, J = 6.4 Hz) and 1.20 (dd, J = 6.3 und 9.0 Hz).

At this occasion we wanted to study the desulfurization of cyclopropane dithioacetals. No reports of this transformation have appeared in the literature. Not unexpectedly, treatment of **9** with mercury salts only leads to open-chain products. However, desulfurization with Raney nickel (activity W2, 30 min reflux in ethanol) was successful. Two products could be isolated. The major compound (51%) was identified as the chiral cyclopropane derivative **10** showing two typical cyclopropane signals at δ 2.34 and 2.41 for secondary carbons in the ^{13}C NMR spectrum. The minor product (44%) could be assigned the open-chain structure **11**, displaying two doublets for the methyl groups at δ 0.90 and 0.93 in the ^1H NMR spectrum.

Cyclobutane Derivative. In our previous communication[1] the yield of cyclobutanes was low (18%). To investigate if the yields could be improved by the new methodology, we required an epoxide such as **18** (Scheme 4). From the work of Stork et al.[11] on epoxy nitrile cyclization, it was known that the smaller four-membered ring was formed preferentially to the alternative cyclopentane. The required epoxide **18** was prepared starting from the common intermediate **6**. The hydroxy group at C-2 was protected as methyl ether **12** (96%) and the primary acetonide of **12** cleaved selectively to afford the diol **13** (68%). Protection as methyl ether **14** (96%),

Scheme 4



[a] (a) THF, NaH, MeI, 18 h, 20 °C (96% **12**, 96% **14**); (b) MeOH, HCl (68% **13**, 90% **15**); (c) Py/TsCl/DMAP, 2 h, 20 °C (25% **16**, 56% **17**); (d) NaOMe/MeOH, 18 h, 20 °C (95%); (e) THF, *n*-BuLi, −40 to 20 °C, 18 h (34%).

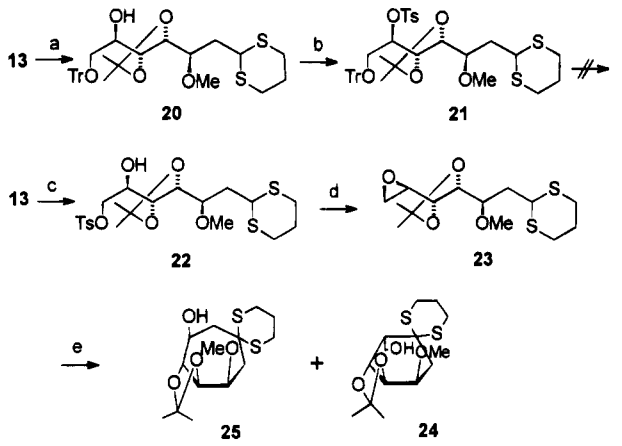
cleavage of the acetonide to the diol **15** (90%), and tosylation afforded a mixture of the 5-*O*-monotosylate **16** (25%) and as the major product the 4-*O*-monotosylate **17** (56%). Cyclization of the two monotosylates via their corresponding epoxides would lead to the products that are isomeric at the C-1 of the cyclobutane. In this investigation we only used the major tosylate **17** which was converted to the epoxide **18** by treatment with NaOMe in MeOH (95%). Employing the usual conditions for deprotonation of the 1,3-dithiane (1 equiv of *n*-BuLi in THF, −40 °C), cyclobutane derivative **19** was isolated in 34% yield. The structure was deduced from the ^1H−^1H and ^1H−^{13}C COSY NMR spectra and also by the chemical shift of the quaternary carbon ring atom at δ 44.57 by comparison with related cyclobutane and cyclopentane chemical shifts.[1] No cyclopentane derivates could be detected in the unpolar fraction, in agreement with Stork's observation[11] and the Baldwin rules.[12] Thus, although the yield could be doubled, cyclobutanes are still formed in relatively low yield using the dithiane methodology.

Cyclohexanes and Cycloheptanes. The diol **13** can also be used to selectively activate the position at C-6 and C-7 for the anticipated nucleophilic ring closure. A selective activation of 6-OH can be achieved by protection of the primary hydroxy group by tritylation to afford the trityl ether **20** in 82% yield. The remaining secondary hydroxy group was then tosylated to **21** (86%). This monotosylate could in principle be a substrate for ring closure to chiral cyclohexanes. However, even under prolonged reaction times no cyclization products could be observed. Only compounds that probably resulted from the *ortho*-metalation of the aromatic ring could be detected. A related observation has been made by Seebach et al. in intermolecular reactions with tosylated 1,3-dithianes.[13] The failure of this cyclization reaction demonstrates that tosylates are not good substrates for intramolecular nucleophilic displacement if the electrophile bears two neighboring electronegative substituents. This is confirmed with a less hindered analogous mesy-

(11) Stork, G.; Cama, L. D.; Coulson, D. R. *J. Am. Chem. Soc.* **1974**, *96*, 5268−5270.

(12) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734−736.
(13) Seebach, D.; Wilka, E.-M. *Synthesis* **1976**, 476−477.

Scheme 5



[a] (a) TrCl/Py/DMAP, 2 d, 20 °C, (82%); (b) TsCl/Py/DMAP, 2 d, 20 °C (86%); (c) Py/TsCl 18 h, 3 °C (73%); (d) NaOMe/MeOH, 2 h, 20 °C, (97%); (e) THF, *n*-BuLi, 4 h −40 °C − 20 °C (55% **24**, 12% **25**).

late in the following paper, showing that the failure of these cyclizations is not due to purely steric factors.[8]

Consequently, we investigated the behavior of the primary epoxide **23**. The synthesis of **23** started from the diol **13**, which was selectively tosylated at the primary position (73%) and subsequently treated with NaOMe in MeOH to afford the epoxide **23** quantitatively. The reaction of this epoxide with *n*-BuLi gave two crystalline products (55 and 12%) that could be identified as the six- and seven-membered ring systems **24** and **25** by their spectra. The ratio of the carbocycles could be influenced by the reaction conditions. The reaction in favor of the cyclohexane **24** could be increased to 12:1 if the reaction temperature was maintained at −40 to −20 °C, making the reaction highly selective (Scheme 5). Again, the result is in agreement with the Baldwin rules since 6-*exo-tet* and -*trig* as well as 7-*endo trig* processes are favored.[12]

In summary, we have shown that appropriately activated and protected open-chain 1,3-dithianes derived from addition of 1,3-dithiane to sugars such as mannose acetonide (**2**) can be converted to chiral three-, four-, six-, and seven-membered carboxycles very flexibly in few reaction steps.

Experimental Section

The following instrumentation was used: polarimeter (Perkin-Elmer 241); IR spectrometer (Nicolet 320 FT-IR); NMR spectrometer (Bruker AMX-200; Brucker AMX 300, and Brucker AM-400, in $CDCl_3$, δ, TMS as internal standard), the multiplicity in the ^{13}C NMR spectra are deduced from the DEPT spectra; MS spectrometer (Finnegan MAT 8430). Elemental analyses were performed by Ilse Beetz, Kronach, Germany, and W.-D. Karrasch, Univ. GH Paderborn). For TLC silica gel on aluminum foils (Merck Mo. 5562) and for column chromatography silical gel 60 (Merck, Germany) were used.

2,3:4,5:6,7-Tri-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptose Trimethylene Dithioacetal (4). A solution of the dithiane derivative[6] **3** (2.60 g, 6.83 mmol) in dry acetone (50 mL) was treated at 0 °C with concd sulfuric acid (1 mL) and was stirred for 90 min at 20 °C (TLC control). The mixture was neutralized with solid Na_2CO_3 and filtered, the filtrate was evaporated at reduced pressure, and the residue was crystallized from petroleum ether to afford **4** (2.40 g, 84%): mp 77 °C; $[\alpha]^{20}_D$ −21° (*c* 0.35, CH_2Cl_2); IR (KBr) 1383 (C-H-deformation, ketal) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35−1.46 (m, 18 H, 6 × CH_3), 1.93−2.13 (m, 2 H, SCH_2CH_2), 2.66−2.83 (ddd, 2 H, SCH_2), 2.98−3.12 (ddd, 2 H, SCH_2), 3.98 (dd, J = 5.6 Hz and 8.3 Hz, 1 H), 4.03−4.27 (m, 6 H) 4.38 (dd, J = 4.1 and 6.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.34 (q, CH_3), 25.72 (t, SCH_2CH_2), 26.48, 27.20, 27.25, 27.42, 27.63 (all q, CH_3), 28.54 and 28.96 (t, SCH_2), 47.13 (d, C-1), 66.40 (t, C-7), 76.30, 78.65, 79.42 79.97, 82.56 (all d, C-2/3/4/5/6), 109.65, 110.38, 110.50 (all s, $C(CH_3)_2$); MS (70 eV) *m*/*z* (rel intensity) 420 (16) [M^+], 405 (29) [$M^+ - CH_3$], 243 (100), 199 (59), 185 (80), 155 (88), 141 (76), 119 (48), 85 (48). Anal. Calcd for $C_{19}H_{32}O_6S_2$: C, 54.26; H, 7.67. Found: C, 53.96; H, 7.35.

2-Deoxy-4,5:6,7-di-*O*-isopropylidene-D-*manno*-heptose Trimethylene Dithioacetal (6). A solution of *n*-BuLi (3.56 mL, 1.6 N in *n*-hexane, 2 equiv) was added under argon at −40 °C to a solution of the triacetonide **4** (2.18 g, 5.18 mmol) in dry THF (50 mL). TLC monitoring showed that the educt was completely converted to the ketene dithioacetal after 1 h. The solution was then treated at 0 °C portionwise with LAH (0.24 g, 1.2 equiv), and the solution was diluted after 2 h with diethyl ether (50 mL) and then cautiously hydrolyzed with a saturated aqueous solution of $NaHSO_4$ (5 mL). The mixture was filtered through a column of Celite, and the filtrate was evaporated to dryness at reduced pressure. The crude product was purified by colum chromatography on silica gel (diethyl ether/pentane = 1:1) to afford from the polar fraction **6** (1.70 g, 90%), mp 55−60 °C, and from the less polar fraction **7** (65 mg, 3%) as an oil.

Data for 6: $[\alpha]^{20}_D$ 27° (*c* 0.55, CH_2Cl_2); IR (KBr) 3430 (br, OH), 1381 (ketal) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 9 H, 3 × CH_3), 1.42 (s, 3 H, CH_3), 1.84−1.92 (m, 2 H, SCH_2CH_2), 2.07−2.16 (m, 2 H, 2-H), 2.81−2.90 (m, 4 H, SCH_2), 3.37 (br s, 1 H, OH), 3.71−3.73 (m, 2 H, 7-H), 3.91−3.97 (m, 2 H), 4.03 (ddd, J = 2.2/6.0/11.7 Hz, 1 H), 4.17 (dd, J = 6.0 and 8.3 Hz, 1 H), 4.33 (dd, J = 4.1 and 10.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.05 (q, CH_3), 25.98 (t, SCH_2CH_2), 26.34 (q, CH_3), 26.75 (q, 2 × CH_3), 29.65 and 30.17 (t, SCH_2), 39.28 (t, C-2), 43.35 (d, C-1), 67.94 (t, C-7), 68.81, 76.42, 80.68, 83.13 (d, C-3/4/5/6), 109.36 and 110.10 (s, $C(CH_3)_2$); MS (70 eV) *m*/*z* (rel intensity) 364 (14) [M^+], 349 (19) [$M^+ - CH_3$], 243 (34), 199 (48), 185 (36), 155 (66), 142 (62), 119 (45), 71 (100). Anal. Calcd for $C_{15}H_{28}O_5S_2$: C, 52.72; H, 7.74. Found: C, 52.69; H, 7.61.

2-Deoxy-2-*C*-butyl-4,5:6,7-di-*O*-isopropylidene-D-*glycero*-D-*talo*-heptose Trimethylene Dithioacetal (7): ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J = 7.0 Hz, 3 H, CH_2-CH_3), 1.34 (s, 6 H, 2 × CH_3-acetonide), 1.36 , 1.44 (s, 6 H, 2 × CH_3-acetonide), 1.47−1.98 (m, 7 H, 3 × CH_2 butyl, 2-H), 2.05−2.19 (m, 2 H, SCH_2CH_2), 2.79−3.00 (m, 4 H, SCH_2), 3.18 (d, J = 2.3 Hz, 1 H, OH), 3.80 (m_c, 2 H), 3.95 (dd, J = 5.6 and 8.1 Hz, 1 H), 4.03−4.11 (m, 2 H), 4.16 (dd, J = 6.2 and 8.1 Hz, 1 H), 4.32 (d, $J_{1,2}$ = 5.5 Hz, 1 H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.02 (q, CH_2-CH_3), 22.94, 24.68, 26.23, 30.49, 31.05, 31.18 (6 × t, 3 × CH_2 butyl, SCH_2CH_2), 25.20, 26.34, 26.87, 26.93 (q, CH_3-acetonide), 44.68 (d, C-1), 51.99 (d, C-2), 67.56 (t, C-7), 72.69, 76.34, 80.11, 81.68 (d, C-3/4/5/6), 109.46, 110.12 (s, 1,3-dioxolane-C's).

2-Deoxy-4,5:6,7-di-*O*-isopropylidene-3-*O*-tosyl-D-*manno*-heptose Trimethylene Dithioacetal (8). *p*-Toluenesulfonyl chloride (1.09 g, 1.1 equiv) and DMAP (ca. 0.05 g) were added to a solution of the alcohol **6** (1.90 g, 5.21 mmol) in dry pyridine (30 mL). After 24 h the solution was poured into ice-cold 1 N HCl (40 mL) and extracted three times with CH_2Cl_2 (15 mL). The organic phase was washed with concd aqueous $NaHCO_3$ (5 mL) and then water (5 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The crude product was filtered through a short column of silica gel (CH_2Cl_2) to afford **8** (2.59 g, 96%): mp 83−84 °C; $[\alpha]^{20}_D$ 31° (*c* 0.66, CH_2Cl_2); IR (film) 1376 (C-H-deformation, ketal), 1180 (SO_2 valence) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30, 1.33, 1.37, 1.43 (s, 12 H, 4 × CH_3-acetonide), 1.72−2.31 (m, 4 H, 2-H and SCH_2CH_2), 2.45 (s, 3 H, CH_3-Ar), 2.40−2.96 (m, 4 H, SCH_2), 3.60−4.21 (m, 6 H, 1/4/5/6/7-H), 5.08 (m, 1 H, 3-H), 7.35 (d, J = 8.1 Hz, 2 H, H-Ar), 7.88 (d, J = 8.1 Hz, 2 H, H-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.55 (q, CH_3-Ar), 25.25 (q, CH_3-acetonide), 25.56 (t, SCH_2CH_2), 26.60, 26.80, 26.88 (q, 3 × CH_3-acetonide), 29.13, 29.70 (t, SCH_2), 35.16 (t, C-2), 42.25 (d, C-1), 67.58 (t, C-7),

76.74, 77.93, 78.34, 80.94 (d, C-3/4/5/6), 109.78, 110.33 (s, CCH_3), 128.16, 129.60 (d, each 2 C, C-Ar), 133.69, 144.68 (s, C-Ar); MS (70 eV) m/z (rel intensity) 518 (23) [M^+], 503 (39) [$M^+ - CH_3$], 445 (6), 395 (4), 359 (12), 346 (17), 315 (11), 288 (14), 230 (14), 187 (29), 143 (100), 119 (55), 101 (33), 91 (50). Anal. Calcd for $C_{23}H_{34}O_7S_3$: C, 53.26; H, 6.61. Found: C, 52.84; H, 6.82.

(4*S*,5*R*,4′*R*)-5-((*S*)-(4,8-Dithiaspiro[2.5]oct-1-yl)-2,2,2′,2′-tetramethyl-[4,4′]bi[1,3]dioxolanyl (9). A solution of the tosylate **8** (700 mg, 1.38 mmol) in dry THF (15 mL) was treated at −40 °C under argon with *n*-BuLi (0.86 mL, 1.6 M in *n*-hexane, 1.1 equiv). The solution was allowed to warm to 20 °C and was hydrolyzed after 2 h with a saturated aqueous solution of NH_4Cl (5 mL). The mixture was extracted with diethyl ether (10 mL), and the combined organic phases were dried ($MgSO_4$), evaporated at reduced pressure, and purified by silica gel colunm chromatography (diethly ether/pentane, 1:1) to yield **9** (420 mg, 77%): mp 67.3 °C; $[\alpha]^{20}_D$ −32° (*c* 1.6, CH_2Cl_2); IR (KBr) 1455 and 1370 (ketal), 910 (dithiane) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, *J* = 6.4 Hz, 1 H, 2a-H), 1.20 (dd, *J* = 6.3 and 9.0 Hz, 1 H, 2b-H), 1.32 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 1.53 (ddd, *J* = 6.4 and 2 × 9.1 Hz, 1 H, 1-H), 1.91−2.25 (m, 2 H, SCH_2CH_2), 2.58−2.68, 2.72−2.83, 3.00−3.12, 3.30−3.42 (4 × m, each 1 H, SCH_2), 3.76 (dd, *J* = 6.8 and 9.4 Hz, 1 H, 5″a-H), 3.88 (dd, 2 × *J* = 7.1 Hz, 1 H, 5″b-H), 3.95−4.17 (m, 3 H, 5′/4′/4″-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.53 (t, C-2), 25.14 (q, CH_3), 25.81 (t, SCH_2CH_2), 26.66, 27.14, 27.41 (q, 3 × CH_3), 29.54 (t, SCH_2), 30.24 (s, C-3), 30.68 (t, SCH_2), 35.36 (d, C-1), 67.25 (t, C-5″), 76.58, 80.67, 81.56 (d, C′-5′/4′/4″), 109.06, 109.42 (s, CCH_3); MS (70 eV) m/z (rel intensity) 346 (16) [M^+], 331 (30) [$M^+ - CH_3$], 288 (12), 273 (13), 230 (10), 187 (21), 145 (12), 143 (100), 132 (20), 101 (19), 85 (17). Anal. Calcd for $C_{16}H_{26}O_4S_2$: C, 55.46; H, 7.56. Found: C, 55.77; H, 7.34.

Desulfurization of the Cyclopropyl Derivative 9. (4*R*,4′*R*,5*R*)-5-Cyclopropyl-2,2,2′,2′-tetramethyl[4,4′]bi-[1,3]dioxolanyl (10) and (4*R*,4′*R*,5*R*)-5-Isopropyl-2,2,2′,2′-tetramethyl[4,4′]bi[1,3]dioxolanyl (11). Raney nickel (ca. 1 g, activity W-2) was added to a solution of the thioacetal **9** (140 mg, 0.404 mmol) in ethanol (10 mL) and refluxed for 30 min. The mixture was filtered through a batch of celite and the filtrate was evaporated to dryness at reduced pressure. The crude product was purified by flash chromatography (silica gel, EtOAc/pentane, 1:9) to afford from the polar fraction **10** (50 mg, 51%) as an oil and from the less polar fraction **11** (43 mg, 44%) as an oil.

Data for 10: $[\alpha]^{20}_D$ 3° (*c* 0.9, CH_2Cl_2); IR (film) 3086 (C-H-valence, cyclopropane), 1456 and 1372 (C-H-deformation, ketal) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.36−0.63 (m, 4 H, CH_2-cyclopropyl), 0.95−1.03 (m, 1 H, CH-cyclopropyl), 1.34 (s, 6 H, 2 × CH_3-acetonide), 1.42 (s, 6 H, 2 × CH_3-acetonide), 3.33 (t, *J* = 7.5 Hz, 1 H, 5-H), 3.79−3.85 (m, 1 H), 3.94−4.12 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.34, 2.91 (t, 2 × CH_2-cyclopropyl), 13.71 (d, CH-cyclopropyl), 25.32, 26,70, 27.02, 27.25 (q, 4 × CH_3-acetonide), 67.61 (t, C-5′), 76.76, 81.45, 83.94 (d, C-4/4′/5), 108.69, 109.50 (s, 1,3-dioxolane-C); MS (70 eV) m/z (rel intensity) 242 (3) [M^+], 227 (68) [$M^+ - CH_3$], 185 (18), 169 (47), 157 (34), 141 (11), 127 (25), 109 (45), 101 (100), 83 (62). Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.68; H, 9.56.

Data for 11: ^1H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, *J* = 3.7 Hz, 3 H, CH-CH_3), 0.93 (d, *J* = 3.8 Hz, 3 H, CH-CH_3), 1.28, 1.29, 1.31, 1.34 (s, 12 H, 4 × CH_3-acetonide), 1.76−1.87 (m, 1 H, CH-CH_3), 3.65−4.07 (m, 5 H, 4/5/4′/5′-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.89, 18.83 (q, 2 × CH-CH_3), 24.32, 25.58, 26.39, 26.53 (q, 4 × CH_3-acetonide), 29.51 (d, CH-CH_3), 66.42 (t, C-5′), 76.34, 78.27, 84.24 (d, C-4/5/4′), 107.86, 108.50 (s, 1,3-dioxolane-C).

2-Deoxy-4,5:6,7-di-*O*-isopropylidene-3-*O*-methyl-D-*manno*-heptose Trimethylene Dithioacetal (12). A suspension of NaH [370 mg (80%), 12.3 mmol, 1.5 equiv] in dry THF (80 mL) was treated with a solution of the 2-deoxy-3-hydroxy-dithiane **6** (3.00 g, 8.2 mmol) in dry THF (30 mL), and the mixture was stirred for 1 h. Then MeI (0.8 mL, 1.5 equiv) was added, stirring was continued for 18 h at 20 °C, and the solution was hydrolyzed by addition of a saturated aqueous solution of NH_4Cl (10 mL). The solid was filtered off, the THF was distilled off, and the aqueous phase was extracted three times with diethyl ether, and the combined organic phases were washed with a saturated solution of $KHSO_3$ (10 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure to afford **12** (2.97 g, 96%) as colorless crystals, mp 84 °C (MeOH/H_2O): $[\alpha]^{20}_D$ 38° (*c* 0.64, CH_2Cl_2); IR (KBr) 2838 (methyl ether), 1461 and 1378 (ketal) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34, 1.36, 1.40 and 1.43 (all s, 4 × 3 H, CH_3-acetonide), 1.83−1.93 (m, 2 H, SCH_2CH_2), 2.04−2.16 (m, 2 H, 2-H), 2.79−2.97 (m, 4 H, SCH_2), 3.49 (s, 3 H, OMe), 3.72−3.77 (m, 2 H, 7-H), 3.93−3.97 (dd, *J* = 4.7 and 7.8 Hz, 1 H), 4.04−4.19 (m, 3 H), 4.23 (dd, *J* = 4.4 and 10.2 Hz, 1 H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.24 (q, CCH_3), 26.00 (t, SCH_2CH_2), 26.69, 27.04, 27.15 (q, 3 × CCH_3), 29.82 and 30.32 (t, SCH_2), 35.75 (t, C-2), 43.77 (d, C-1), 58.49 (q, OCH_3), 67.58 (t, C-7), 77.11, 77.27, 78.14, 80.71 (d, C-3/4/5/6), 109.70 and 109.86 (s, $C(CH_3)_2$); MS (70 eV) m/z (rel intensity) 378 (33) [M^+], 363 (40) [$M^+ - CH_3$], 346 (16), 288 (15), 219 (22), 187 (22), 175 (68), 143 (80), 132 (48), 119 (100), 101 (36). Anal. Calcd for $C_{17}H_{30}O_5S_2$: C, 53.94; H, 7.99. Found: C, 53.99; H, 7.91.

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-D-*manno*-heptose Trimethylene Dithioacetal (13). A solution of the methyl ether **12** (2.60 g, 6.87 mmol) in MeOH (42 mL) was treated at 20 °C with 0.5 N HCl (14 mL) and stirred for 6−8 h (TLC monitoring). The mixture was then neutralized by addition of solid Na_2CO_3, filtered, and evaporated at reduced pressure to remove the MeOH, and the aqueous phase was extracted three times with diethyl ether (10 mL). The combined organic phases were dried (Na_2SO_4), filtered, and evaporated at reduced pressure, and the residue was chromatographed on silical gel (diethyl ether) to yield **12** (1.59 g, 68%) as an oil: $[\alpha]^{20}_D$ 17° (*c* 1.6, CH_2Cl_2); IR (film) 3422 (br, OH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 and 1.39 (s, 6 H, 2 × CH_3-acetonide), 1.86−1.95 (m, 2 H, SCH_2CH_2), 2.08−2.16 (m, 3 H, OH and 2-H), 2.48 (br s, 1 H, OH), 2.84−2.90 (m, 4 H, SCH_2), 3.49 (s, 3 H, OMe), 3.53−3.87 (m, 5 H), 4.01 (t, *J* = 7.1 Hz, 1 H), 4.24 (t, *J* = 7.2 Hz, 1 H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.78 (t, SCH_2CH_2), 26.81 and 26.84 (q, CCH_3), 30.00 and 30.15 (t, SCH_2), 36.91 (t, C-2), 43.11 (d, C-1), 58.27 (q, OMe), 63.86 (t, C-7), 72.86, 79.25, 79.87 and 80.63 (d, C-3/4/5/6), 109.67 (s, CCH_3); MS (CI/ NH_3, pos) m/z (rel intensity) 356 (12) [$M^+ + NH_4$], 339 (8) [$M^+ + H$], 231 (100). Anal. Calcd for $C_{14}H_{26}O_5S_2$: C, 49.68; H, 7.74. Found: C, 49.48; H, 8.01.

2-Deoxy-4,5-*O*-isopropylidene-3,6,7-tri-*O*-methyl-D-*manno*-heptose Trimethylene Dithioacetal (14). A suspension of NaH (111 mg, 80%, 2.5 equiv) in dry THF (30 mL) was treated under argon at 20 °C with a solution of the diol **13** (500 mg, 1.48 mmol) in dry THF (10 mL). After stirring for 1 h, methyl iodide (0.23 mL, 2.5 equiv) was added and stirring was continued for 18 h. The mixture was hydrolyzed with an aqueous solution of NH_4Cl (10 mL), and the THF was distilled off at reduced pressure. The aqueous phase was then extracted three times with CH_2Cl_2 (10 mL), and the combined organic phases were washed with an aqueous solution of $KHSO_3$ (10 mL), dried ($MgSO_4$), and evaporated to dryness at reduced pressure to yield **14** (520 mg, 96%) as an oil: $[\alpha]^{20}_D$ 36° (*c* 0.3, CH_2Cl_2); IR (film) 2813 (methyl ether), 1426 and 1381 (ketal), 910 (dithiane) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.38, 140 (s, 6 H, 2 × CH_3-acetonide), 1.74−2.19 (m, 4 H, 2-H and SCH_2CH_2), 2.75−3.02 (m, 4 H, SCH_2), 3.37, 3.46, 3.48 (s, 9 H, 3 × OMe), 3.38−3.52 (m, 2 H), 3.60−3.71 (m, 2 H), 3.88−3.95 (m, 1 H), 4.13−4.24 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.43 (t, SCH_2CH_2), 27.52, 27.61 (q, 2 × CH_3-acetonide), 30.24, 30.68 (t, SCH_2), 36.47 (t, C-2), 44.30 (d, C-1), 58.70, 58.99, 59.62 (q, 3 × OMe), 72.21 (t, C-7), 77.52, 78.32, 79.86, 81.87 (d, C-3/4/5/6), 110.14 (s, 1,3-dioxolane-C); MS (70 eV) m/z (rel intensity) 366 (10) [M^+], 351 (16) [$M^+ - CH_3$], 334 (44), 289 (16), 219 (18), 215 (18), 175 (52), 133 (44), 119 (100). Anal. Calcd for $C_{16}H_{30}O_5S_2$: C, 52.43; H, 8.25. Found: C, 52.32; H, 8.10.

2-Deoxy-3,6,7-tri-*O*-methyl-D-*manno*-heptose Trimethylene Dithioacetal (15). A solution of the acetonide **14** (400 mg, 1.09 mmol) in methanol (20 mL) was treated with 2 N HCl (20 mL), and the mixture was refluxed for 1 h (TLC

monitoring). The solution was neutralized by addition of solid Na_2CO_3 and filtered, the methanol was removed under reduced pressure, and the aqueous phase was extracted four times with ethyl ether (40 mL). The combined organic phases were dried, ($MgSO_4$), filtered, evaporated at reduced pressure, and purified by chromatography on silical gel (diethyl ether) to yield **15** (297 mg, 90%) as an oil: $[\alpha]^{20}_D$ −4° (*c* 0.9, CH_2Cl_2); IR (film) 3447 (br, OH) 2828 (methyl ether) 909 (dithiane) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.80−2.04 (m, 4 H, 2-H and SCH_2CH_2), 2.78−3.01 (m, 4 H, SCH_2), 3.07 (d, J = 5.5 Hz, 1 H, OH), 3.14 (d, 1 H, OH), 3.41, 3.49, 3.51 (s, 9 H, 3 × OMe), 3.40−3.92 (m, 6 H, 3/4/5/6/7-H), 4.22 (dd, J = 6.0 Hz and 8.5 Hz, 1 H, 1-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.34 (t, SCH_2CH_2), 30.31, 30.62 (t, SCH_2), 37.54 (t, C-2), 44.09 (d, C-1), 58.96, 59.53, 59.78 (q, 3 × OMe), 70.15, 71.66 (d, C-4/5), 71.83 (t, C-7), 80.12, 81.23 (d, C-3/6); MS (70 eV) *m*/*z* (rel intensity) 326 (6) [M^+], 276 (6), 187 (20), 175 (18), 169 (14), 132 (15), 119 (100). Anal. Calcd for $C_{13}H_{26}O_5S_2$: C, 47.83; H, 8.03. Found: C, 47.89; H, 8.07.

2-Deoxy-3,6,7-tri-*O*-methyl-5-*O*-tosyl-D-*manno*-heptose Trimethylene Dithioacetal (16) and 2-Deoxy-3,6,7-tri-*O*-methyl-4-*O*-tosyl-D-*manno*-heptose Trimethylene Dithioacetal (17). A solution of the diol **15** (210 mg, 0.69 mmol) in dry pyridine (10 mL) was treated at 20 °C with *p*-toluolenesulfonyl chloride (144 mg, 1.1 equiv) and DMAP (20 mg). After 2 d the mixture was poured into 0.5 N HCl/ice−water (20 mL) and extracted three times with CH_2Cl_2 (30 mL). The combined organic phases were washed with an aqueous solution of $NaHCO_3$ (10 mL) and water (10 mL), dried ($MgSO_4$), and filtered, and the solvent was removed at reduced pressure. The crude product was separated by flash chromatography on silica gel (CH_2Cl_2/EtOAc, 95:5) to yield from the less polar fraction the 5-*O*-tosylate **16** (83 mg, 25%, oil) and from the polar fraction the 4-*O*-tosylate **17** (186 mg, 56%, oil).

Data for 16: $[\alpha]^{20}_D$ 7° (*c* 0.9, CH_2Cl_2); IR (film) 3497 (br, OH), 2831 (C-H-valence, methyl ether), 1456 and 1360 (SO_2 valence), 907 (C-H-deformation, dithiane) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.81−2.20 (m, 4 H, 2-H and SCH_2CH_2), 2.47 (s, 3 H, Ar-CH_3), 2.74−2.96 (m, 4 H, SCH_2), 3.35, 3.37, 3.44 (s, 9 H, 3 × OMe), 3.45−3.60 (m, 4 H), 3.78−3.93 (m, 2 H), 4.26 (t, J = 7.0 Hz, 1 H, 1-H), 5.10 (t, J = 2.1 Hz, 1 H, 5-H), 7.37 (d J = 7.9 Hz, 2 H, Ar-H), 7.88 (d, J = 7.8 Hz, 2 H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.05 (q, Ar-CH_3), 26.29 (t, SCH_2CH_2), 30.59 (2d, SCH_2), 36.32 (t, C-2), 43.54 (d, C-1), 57.49 (q, OMe), 59.64 (2q, 2 × OMe), 71.47 (t, C-7), 72.59, 76.76, 79.32, 82.17 (d, C-3/4/5/6), 128.31, 130.09 (2 × 2d, Ar-CH), 134.88, 145.06 (s, Ar-C); MS (70 eV) *m*/*z* (rel intensity) 480 (1) [M^+], 334 (5), 272 (2), 197 (10), 184 (14), 171 (46), 155 (82), 133 (20) 119 (30), 91 (100).

Data for 17: $[\alpha]^{20}_D$ −2° (*c* 1.6, CH_2Cl_2); IR (film) 3476 (br, OH), 2832 (methyl ether), 1360 and 1177 (SO_2), 916 (dithiane) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.82−2.22 (m, 4 H, H-2 and SCH_2CH_2), 2.47 (s, 3 H, Ar-CH_3), 2.78−2.92 (m, 4 H, SCH_2), 3.27−3.36 (m, 2 H, 6-H, OH), 3.37 (s, 3 H, OMe), 3.43 (s, 6 H, 2 × OMe), 3.60 (dd, $J_{6,7a}$ = 2.9 Hz, J_{gem} = 10.6 Hz, 1 H, 7a-H), 3.74 (dd, $J_{6,7b}$ = 3.0 Hz, J_{gem} = 10.6 Hz, 1 H, 7b-H), 3.87−4.02 (m, 2 H, 3/5-H), 4.08 (t, J = 7.3 Hz, 1 H, 1-H), 5.02 (t, J = 1.7 Hz, 1 H, 4-H), 7.37 (d, J = 7.9 Hz, 2 H, Ar-H), 7.88 (d, J = 7.8 Hz, 2 H, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.06 (q, Ar-CH_3), 26.26 (t, SCH_2CH_2), 29.77, 30.19 (t, SCH_2), 37.63 (t, C-2), 43.53 (t, C-1), 57.32, 59.86, 60.18 (q, 3 × OMe), 69.39 (t, C-7), 69.82 (d, C-5), 78.33 (d, C-6), 80.56 (d, C-3), 80.81 (d, C-4), 128.28, 130.29 (d, 4 × CH-Ar), 134.78, 145.22 (s, C-Ar); MS (70 eV) *m*/*z* (rel intensity) 480 (2.5) [M^+], 448 (2.5), 341 (2), 276 (25), 187 (49), 155 (24), 145 (52), 119 (100), 91 (30). Anal. Calcd for $C_{20}H_{32}O_7S_3$: C, 49.48; H, 6.71. Found: C, 49.62; H, 6.63.

4,5-Anhydro-2-deoxy-3,6,7-tri-*O*-methyl-D-*altro*-heptose Trimethylene Dithioacetal (18). A solution of the 4-*O*-tosylate **17** (110 mg, 0.23 mmol) in dry methanol (10 mL) was treated with a 1 N aqueous solution of NaOMe (0.5 mL) and stirred for 18 h at 20 °C. Solid NH_4Cl was added for neutralization and the MeOH was evaporated at reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) filtered, and the solvent was removed at reduced pressure to afford the epoxide **18** (60 mg, 95%) as an oil: $[\alpha]^{20}_D$ 22° (*c* 1.3, CH_2Cl_2); IR (film) 2828 (methyl ether), 909 (dithiane) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.78−2.23 (m, 4 H, 2-H and SCH_2CH_2), 2.78−2.92 (m, 4 H, SCH_2), 2.94−3.08 (m, 3 H, 3/4/5-H), 3.25 (m_c, 1 H, 6-H), 3.33, 3.47, 3.52 (s, 9 H, 3 × OMe), 3.53−3.60 (m, 1 H, 7a-H), 3.75 (dd, J = 2.7 and 10.5 Hz, 1 H, 7b-H), 4.32 (t, J = 7.1 Hz, 1 H, 1-H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.33 (t, SCH_2CH_2), 30.26, 30.82 (t, SCH_2), 38.34 (t, C-2), 43.47 (d, C-1), 53.39, 58.00 (d, C-4/5), 58.62, 59.96, 60.29 (q, 3 × OMe), 72.78 (t, C-7), 76.36, 77.45 (C-3/6); MS (CI/NH_3, pos) *m*/*z* 309 (100) [M^+ + H]. Anal. Calcd for $C_{13}H_{24}O_4S_2$: C, 50.62; H, 7.84. Found: C, 51.01; H, 7.89.

(1*S*,2*R*)-2,3-Dimethoxy-1-((1*S*,2*R*)-2-methoxy-5,9-dithiaspiro[3.5]non-1-yl)propan-1-ol (19). A solution of the epoxide **18** (60 mg, 0.217 mmol) in dry THF (20 mL) was treated at −40 °C under argon with *n*-BuLi (1.6 N in *n*-hexane, 0.136 mL, 1.1 equiv). After 30 min the mixture was allowed to warm to 20 °C and stirring was continued for 18 h (TLC monitoring). The solution was then hydrolyzed by addition of an aqueous solution of NH_4Cl (5 mL), extracted three times with diethyl ether (30 mL), and dried ($MgSO_4$), the solvent was evaporated at reduced pressure, and the crude product was purified by flash chromatography (silica gel, diethy ether/pentane, 6:4) to afford from the unpolar fraction **19** (20 mg, 34%) as an oil: $[\alpha]^{20}_D$ −42° (*c* 0.23, CH_2Cl_2); IR (film) 3447 (br, OH), 2828 (C-H-valence, methyl ether) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.78−2.03 (m, 2 H, SCH_2CH_2), 2.07 (dd, $J_{2,3a}$ = 7.8 Hz, J_{gem} = 11.7 Hz, 1 H, 3a-H), 2.56−2.73 (m, 4 H, 1-H, 3b-H, 2 × SCH_2), 2.96 (d, 1 H, OH, J = 5.2 Hz), 3.02−3.12 (m, 2 H, SCH_2), 3.15 (s, 3 H, OMe), 3.25 (m_c, 1 H, 2′-H), 3.33 (s, 3 H, OMe), 3.42 (s, 3 H, OMe), 3.58−3.61 (m, 3 H, 2-H and 2 × 3′-H), 4.18 (m_c, 1 H, 1′-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.12 (t, SCH_2CH_2), 27.23, 28.12 (t, SCH_2), 43.98 (t, C-3), 44.57 (s, C-4), 55.76, 57.46, 59.50 (q, 3 × OMe), 61.06 (d, C-2), 70.68 (d, C-1′), 71.81 (t, C-3′), 72.31 (d, C-2), 79.94 (d, C-2′); MS (70 eV) *m*/*z* (rel intensity) 308 (5) [M^+], 276 (5) [$M^+ - CH_3O$], 209 (10), 187 (8), 175 (28), 161 (20), 132 (100). Anal. Calcd for $C_{13}H_{24}O_4S_2$: C, 50.62; H, 7.84. Found: C, 50.73; H, 7.96.

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-7-*O*-trityl-D-*manno*-heptose Trimethylene Dithioacetal (20). A solution of diol **13** (250 mg, 0.741 mmol) in dry pyridine was treated with trityl chloride (227 mg, 1.1 equiv) and DMAP (30 mg). The solution was stored for 2 d at 20 °C with exclusion of light and moisture and then poured into ice-cold 1 N HCl (25 mL). The mixture was extracted three times with CH_2Cl_2 (30 mL), the combined organic phases were washed with a saturated solution of $NaHCO_3$ (5 mL) and water (5 mL) and dried ($MgSO_4$), and the solvent was evaporated at reduced pressure. The crude product was purified by flash chromtography (silica gel, hexane/EtOAc, 8:2) to afford **20** (361 mg, 82%) as an oil: $[\alpha]^{20}_D$ 13° (*c* 0.5, CH_2Cl_2); IR (film) 3480 (br, OH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30, 1.39 (2 × s, 6H, CH_3-acetonide), 1.80−2.16 (m, 4 H, 2-H and SCH_2CH_2), 2.76−2.94 (m, 5 H, OH and SCH_2), 3.31 (dd, $J_{6,7a}$ = 6.2 Hz, J_{gem} = 9.7 Hz, 1 H, 7a-H), 3.41 (dd, $J_{6,7b}$ = 3.0 Hz, J_{gem} = 9.8 Hz, 1 H, 7b-H), 3.46 (s, 3 H, OMe), 3.69 (ddd, 2 × J = 3.9 Hz, and J = 7.7 Hz, 1 H, 3-H), 3.77 (m_c, 1 H, 6-H), 3.88 (t, J = 7.3 Hz, 1 H, 5-H), 4.18 (dd, J = 4.4 and 6.8 Hz, 1 H, 4-H), 4.23 (dd, J = 5.6 and 8.8 Hz, 1 H, 1-H), 7.20−7.50 (m, 15 H, H-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.00 (t, SCH_2CH_2), 27.13 (q, 2 C, CH_3-acetonide), 29.93, 30.27 (t, SCH_2), 36.42 (t, C-2), 43.85 (d, C-1), 58.28 (q, OMe), 65.20 (t, C-6), 72.82 (d, C-7), 78.14, 78.40, 80.40 (d, C-3/4/5), 86.97 (s, CPh_3), 109.74 (s, 1,3-dioxolane-C), 127.11, 127.31, 127.88, 128.74, 129.11 (d, 15 C, C-Ar), 143.93 (s, 3 × C-Ar); MS (CI/NH_3, pos) *m*/*z* 279 (5) [$M^+ - CPh_3$ − acetone], 258 (36), 217 (56), 200 (100).

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-6-*O*-tosyl-7-*O*-trityl-D-*manno*-heptose Trimethylene Dithioacetal (21). A solution of the trityl ether **20** (220 mg, 0.382 mmol) in dry pyridine (10 mL) was treated with *p*-toluolenesulfonyl chloride (109 mg, 1.1 equiv) and DMAP (30 mg). After 2 d at 20 °C the reaction was worked up as described for **16** to yield **21** (240 mg, 86%) as an oil: $[\alpha]^{20}_D$ 27° (*c* 0.6, CH_2Cl_2); IR (film) 914 (dithiane) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.19, 1.31 (2 × s, 6 H, CH_3-acetonide), 1.72−2.12 (m, 4 H, 2-H and SCH_2CH_2), 2.38 (s, 3 H, CH_3-Ar), 2.70−2.90 (m, 4 H, SCH_2), 3.22 (dd, $J_{6,7a}$ = 3.2 Hz, J_{gem} = 11.2 Hz, 1 H, 7a-H), 3.40 (dd,

$J_{6,7b}$ = 4.2 Hz, J_{gem} = 11.2 Hz, 1 H, 7b-H), 3.46 (s, 3 H, OMe), 3.55 (ddd, 3 × J = 5.8 Hz, 1 H, 3-H), 3.85 (dd, $J_{3,4}$ = 5.9 Hz, $J_{4,5}$ = 7.0 Hz, 1 H), 4.19 (t, J = 7.2 Hz, 1 H, 5-H), 4.25 (dd, J = 4.2 and 7.2 Hz, 1 H, 1-H), 4.88 (m$_c$, 1 H, 6-H), 7.14–7.39 (m, 17 H, H-Ar), 7.79 (d, J = 8.0 Hz, 2 H, H-Ar); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 21.63 (q, CH_3-Ar), 25.92 (t, SCH_2CH_2), 26.84, 29.96 (q, 2 × CH_3-acetonide), 29.66, 30.00 (t, SCH_2), 36.86 (t, C-2), 43.40 (d, C-1), 58.74 (q, OMe), 62.29 (t, C-7), 77.93, 78.29, 79.00, 81.69 (d, C-3/4/5/6), 87.15 (s, CPh_3), 110.25 (s, 1,3-dioxolane-C), 127.05, 127.75, 127.90, 128.66, 129.70 (d, 20 × C-Ar), 143.41, 144.53 (q, C-Ar); MS (FAB, NBA, neg) m/z (rel intensity) 732 (4) [M − 2H], 658 (1), 642 (2), 578 (1.5), 415 (3), 305(4), 243 (4), 171 (100), 153 (19).

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-7-*O*-tosyl-D-*manno*-heptose Trimethylene Dithioacetal (22). A solution of the diol **13** (1.40 g, 4.14 mmol) in dry pyridine (15 mL) was treated at 0 °C with *p*-toluolenesulfonyl chloride (0.87 g, 1.1 equiv). The solution was stored for 18 h at 3 °C (TLC monitoring). Workup was performed as described for **16** to afford after column chromatography (silica gel, diethyl ether/pentane, 3:2) **22** (1.55 g, 73%) as an oil: $[\alpha]^{20}_D$ 22° (*c* 1.4, CH_2Cl_2); IR (film) 3410 (br, OH), 1361 and 1177 (SO_2 valence) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 and 1.31 (s, 6 H, 2 × CH_3-acetonide), 1.80–1.91 (m, 2 H, SCH_2CH_2), 2.00–2.14 (m, 3 H, OH and 2-H), 2.41 (s, 3 H, CH_3-Ar), 2.77–2.91 (m, 4 H, SCH_2), 3.43 (s, 3 H, OMe), 3.51–3.59 (m, 2 H), 3.66–3.79 (m, 2 H), 3.96 (t, J = 6.5 Hz, 1 H), 4.03 (dd, J = 5.6 and 10.3 Hz, 1 H), 4.19 (t, J = 7.2 Hz, 1 H), 4.28 (dd, J = 2.1 and 10.3 Hz, 1 H), 7.32 (d, J = 8.1 Hz, 2 H, H-Ar), 7.78 (d, J = 8.2 Hz, 2 H, H-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.62 (q, Ar-CH_3), 25.77 (t, SCH_2CH_2), 26.77 (q, 2 × CH_3-acetonide), 29.93 and 30.11 (t, SCH_2), 36.66 (t, C-2), 43.10 (d, C-1), 58.29 (q, OMe), 71.65 (t, C-7), 71.44, 78.00, 7875, 80.95 (d, C-3/4/5/6), 109.96 (s, CCH_3), 127.98 and 129.80 (d, 2 × 2 C-Ar), 132.65 and 144.83 (s, C-Ar); MS (CI/ NH_3, pos) m/z 510 (10) [M^+ + NH_4], 493 (8) [M^+ + H], 365 (100). Anal. Calcd for $C_{21}H_{32}O_7S_3$: C, 51.20; H, 6.55. Found: C, 51.01; H, 6.66.

6,7-Anhydro-2-deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-D-*manno*-heptose Trimethylene Dithioacetal (23). A solution of the tosylate **22** (760 mg, 1.54 mmol) in dry MeOH (15 mL) was treated at 20 °C dropwise with a 1 N methanolic solution of NaOH (2 mL). Workup was performed after 2 h as described for **18** to yield **23** (479 mg, 97%) as an oil: $[\alpha]^{20}_D$ 26° (*c* 0.81, CH_2Cl_2); IR (film) 3040 (epoxide), 2850 (methyl ether), 910 (dithiane) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 and 1.38 (s, 6 H, 2 × CH_3-acetonide), 1.80–2.13 (m, 4 H, 2-H and SCH_2CH_2), 2.70 (dd, J = 2.6 and 5.0 Hz, 1 H, 7a-H), 2.84–2.77 (m, 5 H, 7b-H and SCH_2), 3.02–3.06 (m, 1 H, 6-H), 3.46 (s, 3 H, OMe), 3.65 (ddd, J = 4.2 Hz, 1 H, 3-H), 3.75 (dd, $J_{4,5}$ = 7.3 Hz, $J_{5,5}$ = 5.3 Hz, 1 H, 5-H), 3.98 (dd, $J_{4,5}$ = 7.3 Hz, $J_{3,4}$ = 4.4 Hz, 1 H, 4-H), 4.17 (dd, J = 5.3 and 9.2 Hz, 1 H, 1-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.72 (t, SCH_2CH_2), 26.47 and 26.63 (2 × q, CCH_3), 29.67 and 30.05 (t, SCH_2), 36.70 (t, C-7), 43.36 (d, C-1), 45.01 (t, C-2), 51.58 (d, C-6), 59.07 (q, OMe), 77.26, 77.57, 80.43 (d, C-3/4/5), 109.60 (s, CCH_3); MS (CI/ NH_3, pos) m/z 338 (4) [M^+ + NH_4], 321 (100) [M^+ + H]. Anal. Calcd for $C_{14}H_{24}O_4S_2$: C, 52.47; H, 7.55. Found: C, 52.41; H, 7.45.

((3a*R*)-7*t*-Methoxy-2,2-dimethyl-(3a*r*,7a*t*)-3a,4,7,7a-tetrahydro-6*H*-spiro[benzo[1,3]dioxole-5,2′-[1,3]dithian]-4*t*-yl)methanol (24) and (3a*R*)-8*c*-Methoxy-2,2-dimethyl-(3a*r*,8a*t*)-3a,4,5,7,8,8a-hexahydrospiro[cyclohepta-[1,3]dioxole-6,2′-[1,3]dithian]-4*c*-ol (25). A solution of the epoxide **23** (220 mg, 0.69 mmol) in dry THF (10 mL) was treated at −40 °C with *n*-BuLi (0.47 mL, 1.6 M in *n*-hexane, 1.1 equiv). The solution was allowed to warm to 20 °C after 10 min and was hydrolyzed after 4 h by addition of a saturated solution of NH_4Cl (3 mL). Workup proceeded as described for **9** to afford after chromatography on silica gel (diethyl ether/pentane, 3:2) from the polar fraction the cyclohexane derivative **24** (120 mg, 55%), mp 171.1 °C, and from the polar fraction the cycloheptane derivative **25** (27 mg, 12%), mp 66.9 °C.

Data for 24: $[\alpha]^{20}_D$ −38° (*c* 1.8, CH_2Cl_2); IR (KBr) 3480 (br, OH), 2815 (methyl ether), 910 (dithiane) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 and 1.48 (s, 6 H, 2 × CH_3-acetonide), 1.71 (dd, J_{gem} = 15.6 Hz, $J_{6eq,7}$ = 2.8 Hz, 1 H, 6eq-H), 1.78–1.89 (m, 1 H, 5′-H), 2.05–2.13 (m, 1 H, 5′-H) 2.41 (dd, J_{gem} = 15.5 Hz, $J_{6ax,7}$ = 1.3 Hz, 1 H, 6ax-H), 2.52–2.65 (m, 2 H, 4′a-H and 6′-H), 2.98–3.14 (m, 2 H, 4′-H and 6′-H), 3.16–3.25 (m, 2 H, OH and 4-H), 3.45 (s, 3 H, OMe), 3.77 (dd, $J_{7,7a}$ = 2.9 Hz, $J_{3a,7a}$ = 10.3 Hz, 1 H, 7a-H), 3.82–3.95 (m, 3 H, 10-H and CH_2OH), 4.73 (dd, $J_{3a,7a}$ = 10.3 Hz, $J_{3a,4}$ = 4.7 Hz, 1 H, 3a-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.42 (t, SCH_2CH_2), 26.57 and 26.85 (q, CCH_3), 26.85 and 27.13 (t, SCH_2), 39.03 (t, C-6), 43.46 (d, C-4), 50.69 (s, C-5), 58.32 (q, OMe), 60.70 (t, CH_2OH), 73.72 (d, C-3a), 75.67 and 75.72 (d, C-7/7a), 109.92 (s, CCH_3); MS (70 eV) m/z (rel intensity) 320 (100) [M^+], 305 (12) [M^+ − CH_3], 289 (24), 262 (20), 231 (19), 188 (38), 175 (94), 159 (25), 155 (31), 140 (30), 125 (26), 111 (25), 97 (52), 85 (44). Anal. Calcd for $C_{14}H_{24}O_4S_2$: C, 52.47; H, 7.55. Found: C, 52.64; H, 7.49.

Data for 25: $[\alpha]^{20}_D$ −51° (*c* 1.5, CH_2Cl_2); IR (film) 3500 (br, OH), 2819 (C-H-valence, methyl ether), 911 (C-H-deformation, dithiane) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38, 1.40 (s, 6 H, 2 × CCH_3), 1.75–2.12 (m, 4 H, SCH_2CH_2,, 7-H, 5-H), 2.50 (ddd, J = 1.6 and 3.8 and 15.1 Hz, 1 H, 7-H) 2.58–2.92 (m, 4 H, OH, 3 × SCH_2), 3.03–3.22 (m, 2 H, 5-H and SCH_2), 3.49 (s, 3 H, OMe), 4.17 (dd, $J_{8,8a}$ = 2.2 Hz, $J_{3a,8a}$ = 9.8 Hz, 1 H, 8a-H), 4.24 (ddd, $J_{3a,4}$ = 4.8 Hz, 2 × $J_{5(a/b),4}$ = 7.6 Hz, 1 H, 4-H), 4.79 (dd, $J_{3a,4}$ = 4.8 Hz, $J_{3a,8a}$ = 9.8 Hz, 1 H, 3a-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.15 (t, SCH_2CH_2), 26.92, 27.81 (t, SCH_2), 27.21, 27.31 (q, CCH_3), 43.19 (t, C-5), 44.02 (t, C-7), 49.10 (s, C-6), 59.58 (q, OMe), 64.64 (d, C-4), 74.50 (d, C-3a), 76.52 (d, C-8a), 77.62 (d, C-8), 109.80 (s, 1,3-dioxolane-C); MS (70 eV) m/z (rel intensity) 320 (100) [M^+], 305 (28) [M^+ − CH_3], 213 (34), 156 (62), 106 (86). Anal. Calcd for $C_{14}H_{24}O_4S_2$: C, 52.47; H, 7.55. Found: C, 52.37; H, 7.47.

Supplementary Material Available: Copies of ^{1}H NMR spectra of **7**, **11**, **16**, **20,** and **21** (5 pages). This material is contained in libaries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.