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Preparation of methyl 2,3-di-*O*-mesyl-4,6-thioanhydro-α-D-galactopyranoside and methyl 2-*O*-mesyl-4,6-thioanhydro-α-D-gulopyranoside☆

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Dedicated to Professor Günther Wulff on the occasion of his 65th birthday.

Abstract

Two 2-oxa-7-thiabicyclo[4.2.0]octane derivatives, **4** and **10**, with the D-*galacto* and D-*gulo* configuration, respectively, were obtained from methyl α-D-glucopyranoside. The thietane cyclization involved a thio-Mitsunobu reaction resulting in a 6-thioacetate, which underwent selective base-catalyzed intramolecular nucleophilic substitution at a C-4 mesylate. The structures of **4** and **10** were elucidated by X-ray diffraction analysis.

Keywords: Mitsunobu reaction; Thiosugars; 2-Oxa-7-thiabicyclo[4.2.0]octanes; X-ray diffraction analysis; $^1C_4$-α-D-Gulopyranose derivative

1. Introduction

Primary hydroxyl groups of carbohydrates can be transformed into thioacetates with complete chemoselectivity [2] via the thio-Mitsunobu reaction [3]. Secondary hydroxyl groups are much less reactive under the applied conditions and, therefore, do not need to be protected. We took advantage of this for the preparation of anhydro-thiosugars, which represent useful starting derivatives for the stereocontrolled synthesis of highly functionalized heterobicyclic compounds [2].

Thus, methyl α-D-glucopyranoside (**1**) yielded the 6-thioacetate **2** on reaction with diisopropyl azodicarboxylate (DIAD) and thioacetic acid in the presence of triphenylphosphine. The yield was only moderate[1] and **2** is not a very stable compound. However, prompt base-catalyzed reaction with mesyl chloride yielded 71% of the trimesylate, which is more convenient to handle. The thioacetate **3** was cleaved with sodium hydrogencarbonate in boiling aqueous 2-methoxyethanol under

☆ Thiosugars, Part 3. For Part 2 see Ref. [1].

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[1] The yield of only 38% might be improved by a different protocol of addition, since DIAD is able to oxidize thiols to disulfides [4]. We thank the referee for this valuable hint. Our procedure, however, gave good yields in other similar cases.

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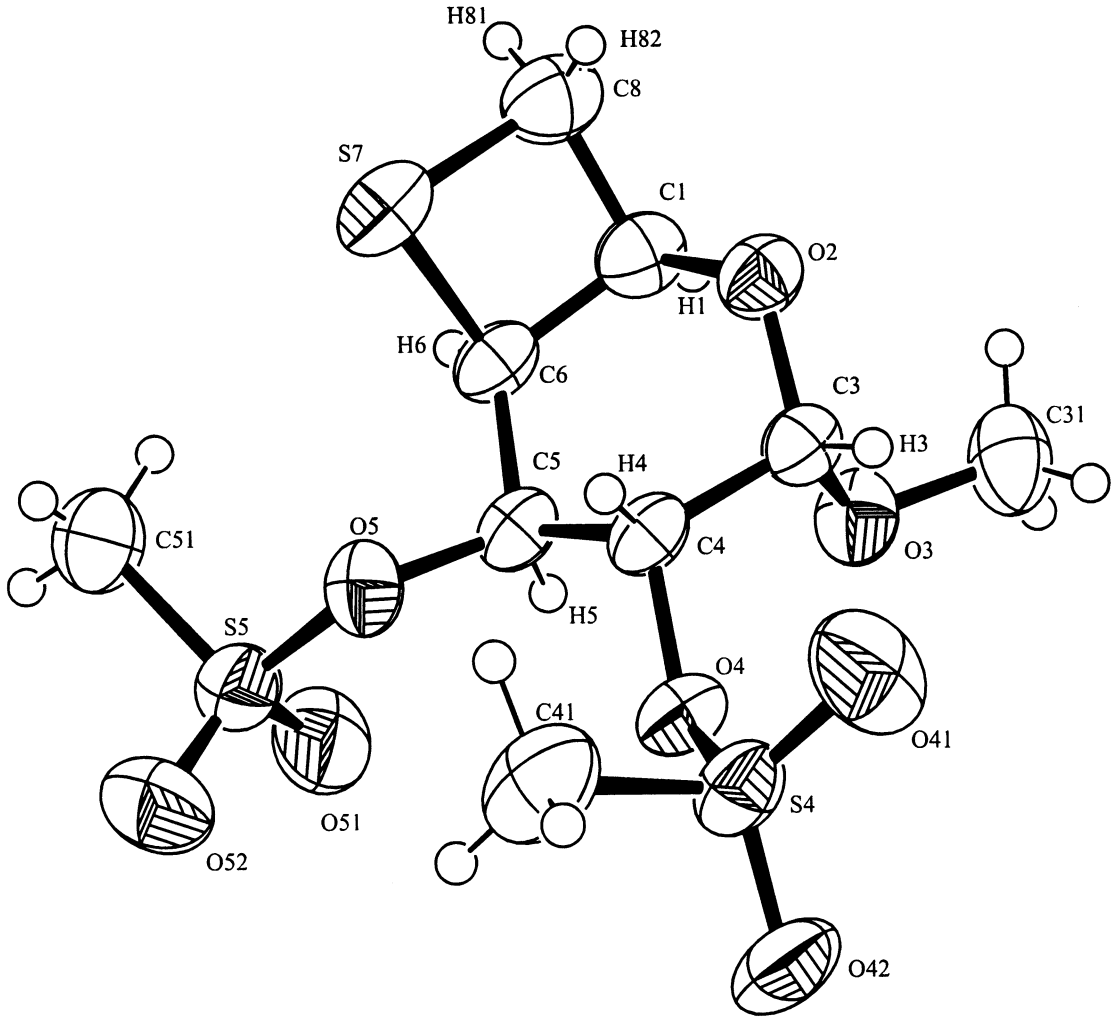
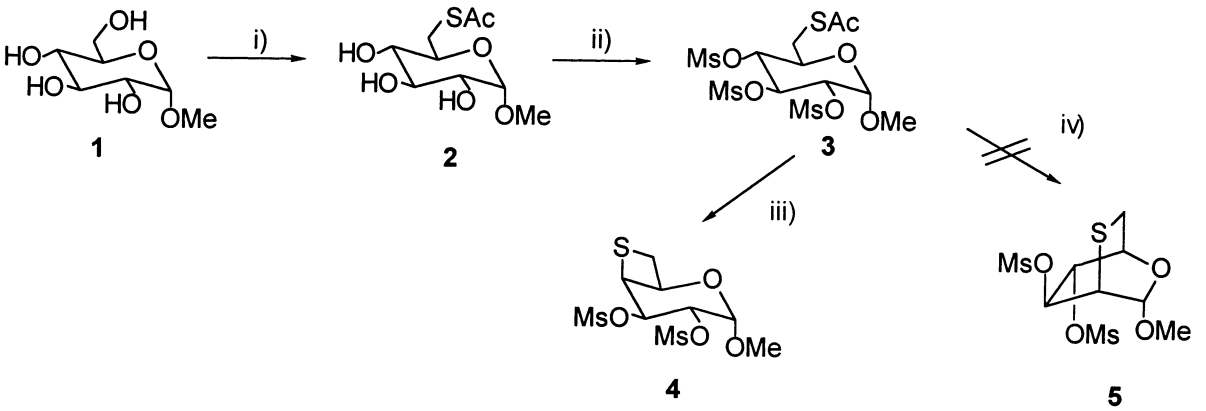


Fig. 1. ORTEP plot of the molecular structure of **4**. Thermal ellipsoids are drawn at the 50% probability level. Numbering is given according to the bicycloalkane rather than the carbohydrate nomenclature. Selected bond lengths (pm), angles (°) and torsion angles (°): C-1–C-6 150.5, C-6–S-7 184.9, S-7–C-8 182.7, C-1–C-8 152.2, C-6–S-7–C-8 75.2, C-6–C-1–C-8 95.5, C-1–C-6–S-7 91.0, C-1–C-8–S-7 91.4, C-8–S-7–C-6–C-1 18.1, C-6–S-7–C-8–C-1 17.9, C-8–C-1–C-6–S-7 21.2, C-6–C-1–C-8–S-7 21.5.

nitrogen atmosphere[2]. The thiolate that is formed intermediately reacted via intramolecular nucleophilic attack at a C-4 mesylate yielding the 2-oxa-7-thiabicyclo[4.2.0]octane derivative **4** (methyl 2,3-di-*O*-mesyl-4,6-thioanhydro-α-D-galactopyranoside) as the only product. Formation of the four-membered thietane ring is strongly favored over the ring closure between the thiolate and the 2-position since S_N2 displacement of a mesylate leaving group adjacent to the anomeric centre is known to be restricted [7]. Moreover, attack upon C-2 would lead to a 2-oxa-5-thiabicyclo[2.2.2]octane derivative (**5**) containing three six-membered rings with boat conformation. Attack upon the 3-position with formation of a 2-oxa-6-thiabicyclo[3.2.1]octane should be unlikely on account of the syn-position of the leaving group.

The ^1H and ^{13}C NMR spectra are in agreement with the structure **4** but cannot consistently be assigned to **5**. In particular, the observed large vicinal coupling constant of 9.4 Hz is indicative of the trans-diaxial configuration of two protons (H-2 and H-3) in a pyranose ring with chair conformation and cannot occur for protons at C-2 or any other protons in **5**. Furthermore, the ^{13}C chemical shift of δ 41.95 must be assigned to the bridgehead carbon atom of a thietane ring in the bicyclo[4.2.0] system of **4** according to our

[2] We applied sodium hydrogencarbonate, which in fact is transformed into the stronger base sodium carbonate in boiling methoxyethanol. It is the better choice as compared with sodium acetate, which leads to the formation of other products such as acetates, disulfides, and sulfides besides **4** [5,6].



Scheme 1. (i) AcSH, DIAD, Ph_3P; (ii) MsCl, NEt_3; (iii) $NaHCO_3$, glyme–H_2O; (iv) $NaCO_3$.

previous experiences with related 2-oxa-6-thiabicyclo[3.2.0]heptanes [2,6].

Eventually, the structure of **4** was unequivocally proven by an X-ray structural analysis. The ORTEP plot of **4** is shown in Fig. 1. The α-D-galactopyranose ring of **4** is close to the $^4C_1$ chair conformation, with Cremer–Pople puckering parameters $Q = 0.510$ Å, $\Theta = 156.1°$, and $\Phi = 112.5°$ for the atom sequence O–C-5–C-4–C-3–C-2–C-1 (Scheme 1).

In order to synthesize an original 2-oxa-5-thiabicyclo[2.2.2]octane skeleton, we prepared the thioacetate **9** as precursor, which does not exhibit a leaving group in its 4-position and also should be unable to form a bicyclo[3.2.1]octane system via intramolecular cyclization between the sulfur atom and C-3 because of the syn-disposition of its 3-*O*-mesyl group. The thioacetate **9** was obtained from **1** via methyl 4,6-*O*-isopropylidene-α-D-glucopyranoside (**6**) [8], mesylation to yield the dimesylate **7**, deprotection to form **8**[3], and thio-Mitsunobu reaction of **8**. When **9** was treated with sodium hydrogencarbonate [5,6], a product was obtained that as expected exhibited a free hydroxyl group and one remaining mesylate group. However, its NMR spectrum again did not agree convincingly with the bicyclo[2.2.2]octane structure **11**. At least, they could be equally well assigned to another 2-oxa-7-thiabicyclo[4.2.0]octane, the D-*gulo* derivative **10**. The relatively large difference of 0.6 ppm between the chemical shifts of the two methylene protons is not in good agreement with literature data for related [2.2.2]-bicyclic systems, which have been extensively studied by Toshima et al. [11]. Also, the signal of a tertiary carbon atom at δ 45.1 can be best assigned to the bridgehead center next to sulfur in the bicyclo[4.2.0] skeleton of **10**. Spanish authors [12] have obtained **10** from the 4-*O*-benzoyl derivative of **8** using sodium methoxide. They explained its formation by assuming a 3,4-epoxide as intermediate and ascribed the normal $^4C_1$ conformation to the compound. In order to remove any doubt about our result, we performed an X-ray diffraction analysis, which confirmed the structure of **10** (Fig. 2). Interestingly, the pyranose moiety of **10** exhibits the unusual $^1C_4$ conformation in the crystal (Cremer–Pople puckering parameters $Q = 0.520$ Å, $\Theta = 19.5°$, and $\Phi = 241.3°$ for the atom sequence O–C-5–C-4–C-3–C-2–C-1) with equatorially arranged hydroxy, methoxy, and thioether substituents. The formation of **10** instead of **11** can be explained [7,13] by deprotonation of the hydroxyl group of **9**, $^4C_1 \rightarrow {}^1C_4$ inversion of the pyranose ring, formation of an oxirane (**12**), cleavage of the thioacetate group and, finally, intramolecular ring opening of the epoxide and concomitant ring closure to the thietane [12], which is only possible if **12** and consequently **10** exhibit the $^1C_4$ conformation. Since this reaction cascade implies two intramolecular S_N2 steps at C-3 and C-4, the D-*gluco* configuration of **9** is transformed into

[3] Sinclair [9] as well as Fraser-Reid and Boctor [10] have prepared **8** from the related methyl 4,6-*O*-benzylideneglucoside. Sinclair's ^1H NMR data, which were taken in pyridine at low resolution (100 MHz), do not fully agree with ours, which could be consistently assigned.

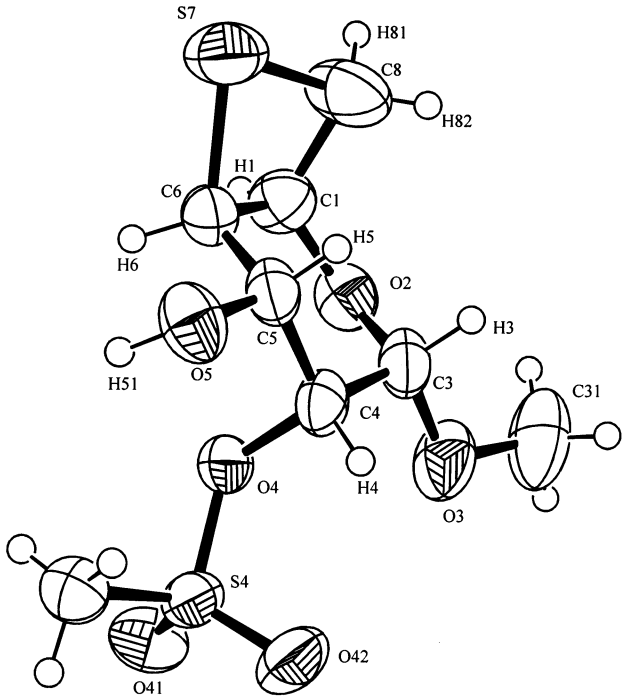
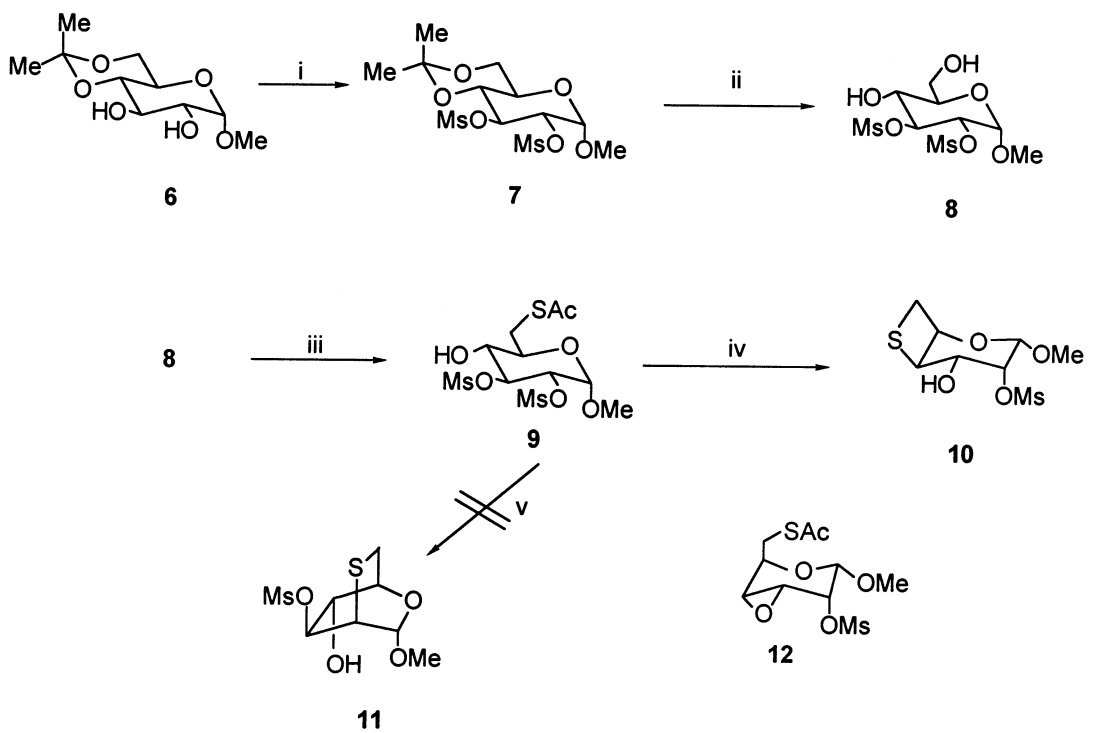


Fig. 2. ORTEP plot of the molecular structure of **10**. Thermal ellipsoids are drawn at the 50% probability level. Numbering is given according to the bicycloalkane rather than the carbohydrate nomenclature. Selected bond lengths (pm), angles (°) and torsion angles (°): C-1–C-6 153.2, C-6–S-7 184.7, S-7–C-8 184.2, C-1–C-8 152.9, C-6–S-7–C-8 76.5, C-6–C-1–C-8 96.4, C-1–C-6–S-7 88.6, C-1–C-8–S-7 88.9, C-8–S-7–C-6–C-1 21.2, C-6–S-7–C-8–C-1 21.2, C-8–C-1–C-6–S-7 25.2, C-6–C-1–C-8–S-7 25.3.

the D-*gulo* configuration in product **10** (Scheme 2).

2. Experimental

General.—Melting points were determined by the use of an electrothermal apparatus (values are corrected). IR spectra were measured with an ATI Mattson Genesis spectrometer. NMR spectra were recorded with Bruker AMX 400 and DRX 500 spectrometers. Chemical shifts (ppm) are related to Me_4Si (^1H) and $CDCl_3$ (^{13}C, δ 77.05). Standard correlation techniques were used for assignments. Mass spectra were measured on Varian MAT 311A and VG Analytical 70–250 S (HRMS) spectrometers. Optical rotations were measured by use of a Perkin–Elmer 241 polarimeter ($\lambda = 589$ nm, $l = 10$ cm). Column chromatography was carried out on E. Merck Kieselgel 60 (70–230 mesh). Solvents were purified and dried according to standard laboratory procedures [14]. X-ray structural analyses were performed with a CAD 4 Nonius diffractometer equipped with a graphite monochromator using Cu K_α radiation ($\lambda =$



Scheme 2. (i) MsCl, NEt_3; (ii) H_3O^+; (iii) AcSH, DIAD, Ph_3P; (iv) $NaHCO_3$, glyme–H_2O; (v) $NaHCO_3$.

1.54184 Å). The structures were solved with the direct method SIR 92 [15] and differential Fourier synthesis. Refinement was performed by least-squares methods [16]. The Cremer–Pople puckering parameters [17] were calculated by use of the PLATON program [18].

Methyl 6-S-acetyl-6-thio-α-D-glucopyranoside (**2**).—Triphenylphosphine (8.11 g, 30.9 mmol) was dissolved in dry THF (70 mL) under N_2. Diisopropyl azodicarboxylate (DIAD, 6.25 g, 30.9 mmol) was dropped into the solution at 0 °C and stirred for 1 h. Carefully purified (repeated distillation at 0 °C/ −78 °C) colorless thioacetic acid (2.35 g, 30.9 mmol) was added dropwise to methyl α-D-glucopyranoside (**1**, 5.00 g, 25.75 mmol) in dry THF (50 mL) under N_2 at 0 °C and the suspension obtained was dropped into the above-mentioned DIAD–triphenylphosphine suspension at 0 °C. The mixture was stirred at room temperature (rt) overnight. After removal of THF under diminished pressure, water (100 mL) was added. Triphenylphosphine oxide was filtered off and washed with water. The combined aq solns were washed with five portions (20 mL) of a 1:1 mixture of diethyl ether and petroleum ether (bp 50/70 °C) and the aq soln was evaporated under diminished pressure. After removal of residual water by azeotropic distillation with toluene, the residue was dissolved in EtOAc, the solution was dried over $MgSO_4$ and evaporated to dryness. Purification of the crude product by column chromatography (3:5:1 EtOAc–petroleum ether–EtOH, R_f 0.13) and recrystallization from EtOAc–petroleum ether yielded **2** (2.49 g, 38%) as a colorless powder, mp 94–100 °C (dec). $[\alpha]_D^{20}$ +85° (*c* 1.0, $CHCl_3$). IR: *v* 3520, 3450, 3440, 3280, 3006, 2994, 2925, 2842, 1690 (C=O), 1441, 1413, 1139, 1109, 1053, 1005, 631. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.73 (d, 1 H, H-1), 4.31 (bs, 3 H, OH), 3.75 (dd, 1 H, H-3), 3.72–3.66 (m, 1 H, H-5), 3.55 (dd, 1 H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.5 Hz, H-2), 3.42 (s, 3 H, OCH_3), 3.38 (dd, 1 H, $J_{5,6'}$ 3.0 Hz, H-6′), 3.27 (dd, 1 H, $J_{3,4}$ 9.3, $J_{4,5}$ 9.3 Hz, H-4), 3.18 (dd, 1 H, $J_{5,6}$ 7.0, $J_{6,6'}$ 14.1 Hz, H-6), 2.39 (s, 3 H, CH_3CO). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 197.09 (CO), 99.43 (C-1), 73.75 (C-3), 72.61 (C-4), 72.02 (C-2), 70.03 (C-5), 55.29 (CH_3O), 30.97 (C-6), 30.55 (CH_3CO); FABMS: *m/z* (%) 253 (66) [MH^+], 221 (64) [$M^+ - OCH_3$], 203 (56) [$M^+ - OCH_3 - H_2O$], 161 (100); FABHRMS Calcd for $C_9H_{17}O_6S$: 253.0746. Found: 253.0799.

Methyl 6-S-acetyl-2,3,4-tri-O-mesyl-6-thio-α-D-glucopyranoside (**3**).—Triethylamine (3.55 g, 33.05 mmol) and **2** (1.90 g, 7.53 mmol) were dissolved in CH_2Cl_2 (80 mL). Mesyl chloride (4.02 g, 35.07 mmol) was added to the solution at −20 °C. The mixture was stirred at rt overnight. The solvent was removed and the residue extracted with EtOAc. The extracts were evaporated and the remaining syrup was chromatographed twice: (i) 370 g SiO_2, EtOAc; (ii) 370 g SiO_2, 2:1 EtOAc–petroleum ether) to yield **3** (2.64 g, 72%) as yellowish crystals, mp 132 °C (dec). $[\alpha]_D^{20}$ +93° (*c* 1.0, $CHCl_3$) IR: *v* 3103, 3026, 2943, 2847, 1693 (C=O), 1358, 1177, 1045, 959, 913, 835, 734, 649. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.10 (dd, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 5.05 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.62–4.59 (m, 2 H, H-2, H-4), 3.85 (ddd, 1 H, $J_{4,5}$ 9.1 Hz, H-5), 3.66 (dd, 1 H, $J_{5,6'}$ 2.4 Hz, H-6′), 3.46 (s, 3 H, OCH_3), 3.29 (s, 3 H, CH_3SO_2), 3.21 (s, 3 H, CH_3SO_2), 3.16 (s, 3 H, CH_3SO_2), 2.93 (dd, 1 H, $J_{5,6}$ 9.0, $J_{6,6'}$ 14.3 Hz, H-6), 2.38 (s, 3 H, CH_3CO). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 194.54 (CO), 96.87 (C-1), 76.05, 75.21 (C-3), 74.5, 68.89 (C-5), 55.92 (CH_3O), 39.31 (CH_3SO_2), 39.24 (CH_3SO_2), 38.78 (CH_3SO_2), 30.95 (CH_3CO), 30.16 (C-6). FABMS: *m/z* (%): 487 (12) [MH^+], 317 (100); FABHRMS Calcd for $C_{12}H_{23}O_{12}S_4$: 487.0072. Found: 487.0028.

Methyl 2,3-di-O-mesyl-4,6-thioanhydro-α-D-galactopyranoside [(1R,3S,4R,5R,6S)-4,5-bis(methanesulfonyloxy)-3-methoxy-2-oxa-7-thiabicyclo[4.2.0]octane] (**4**).—A mixture of 2-methoxyethanol (190 mL) and water (10 mL) was refluxed under N_2 for 90 min and during cooling (40 min) N_2 was bubbled through. Compound **3** (2.30 g, 4.73 mmol) and $NaHCO_3$ (0.74 g, 8.8 mmol) were added under N_2 and the solution was refluxed for 6.5 h. The progress of the reaction, which took place under evolution of CO_2, was monitored by thin-layer chromatography (TLC) (1:1 EtOAc–petroleum ether). After cooling and stirring at rt overnight, the solvent was dis-

tilled off under diminished pressure. The residue was dissolved in EtOAc, the solids were filtered off and the crude product obtained after removal of the solvent was chromatographed twice (SiO_2, 1:1 EtOAc–petroleum ether, R_f 0.38) to yield **4** (1.32 g, 80%) as a crystalline solid, mp 152 °C. $[\alpha]_D^{20}$ + 206° (*c* 1.0, $CHCl_3$). IR: *v* 3025, 2930, 2920, 1352, 1177, 1066, 917, 859, 526, 502. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.19 (dd, 1 H, H-2), 5.13 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1), 5.10 (dd, 1 H, $J_{3,4}$ 6.2, $J_{2,3}$ 9.4 Hz, H-3), 4.65–4.61 (m, 2 H, H-4, H-5), 3.55 (dd, 1 H $J_{5,6'}$, 3.8 Hz, H-6′), 3.47 (s, 3 H, OCH_3), 3.14 (s, 3 H, CH_3SO_2), 3.07 (s, 3 H, CH_3SO_2), 2.68 (d, 1 H, $J_{6,6'}$ 10.4 Hz, H-6). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 98.20 (C-1), 75.20 (C-2), 73.31 (C-3), 72.84 (C-5), 56.32 (CH_3O), 41.95 (C-4), 39.05 (CH_3SO_2), 38.62 (CH_3SO_2), 28.10 (C-6). EIMS (70 eV): *m*/*z* (%) 348 (9) [$M^{+\bullet}$], 317 (20) [$M^+ - OCH_3$], 209 (11), 207 (9), 206 (8), 192 (11), 176 (7), 175 (14), 166 (20), 157 (6), 152 (20), 148 (7), 139 (7), 132 (7), 126 (7), 117 (9), 115 (7), 114 (14), 113 (22), 111 (15), 101 (7), 99 (8), 97 (38), 96 (7), 87 (27), 86 (9), 85 (100), 81 (21), 79 (52), 74 (10), 73 (87), 72 (12), 71 (16), 70 (11), 69 (12), 68 (9), 61 (15), 60 (8), 58 (7), 56 (7), 54 (7), 48 (8), 41 (41).

X-ray structural data. $C_9H_{16}O_8S_3$: crystal dimensions 0.55 × 0.32 × 0.30 mm, orthorhombic, $P2_12_12_1$, $a = 547.6(1)$ pm, $b = 1557.8(2)$ pm, $c = 1722.4(2)$ pm, $\alpha = \beta = \gamma = 90°$, $V = 1.4693(4)$ nm^3, $Z = 4$, $\rho_{calcd} = 1.58$ g cm^{-3}, $\mu = 4.944$ mm^{-1}, $\vartheta - 2\vartheta$ scan, 2775 independent reflections, 2331 significant reflections [$I > 2\sigma(I)$], parameters 210, *R* factor 0.05419, R_w factor 0.1380[4].

*Methyl 4,6-*O*-isopropylidene-2,3-di-*O*-mesyl-α-*D*-glucopyranoside* (**7**).—Methyl 4,6-*O*-isopropylidene-α-D-glucopyranoside (**6**) (3.58 g, 15.3 mmol) [8] was dissolved in CH_2Cl_2 (250 mL). Mesyl chloride (8.92 mL, 13.1 g, 114.5 mmol) was added at − 20 °C. The reaction mixture was stirred at rt for 24 h under monitoring with TLC (3:2 EtOAc–petroleum ether, R_f 0.60). The precipitate was filtered off and the filtrate washed with a satd $NaHCO_3$ soln until it was neutral. After evaporation under diminished pressure, the crude product was chromatographed (370 g SiO_2, 1:1 EtOAc–petroleum ether, R_f 0.45) to yield **7** (4.94 g, 83%) as a yellowish solid, mp 115 °C (dec). $[\alpha]_D^{20}$ + 77° (*c* 1.0, acetone). IR: *v* 3030, 3015, 3005, 2947, 1356, 1201, 1180, 1093, 1049, 987, 908, 849, 717, 523. ^{1}H NMR (400 MHz, acetone-d_6): δ 4.87 (d, 1 H, H-1), 4.71 (dd, 1 H, H-3), 4.56 (dd, 1 H, $J_{2,3}$ 9.6, $J_{1,2}$ 3.7 Hz, H-2), 3.90 (dd, 1 H, $J_{3,4}$ 9.6 Hz, H-4), 3.78 (m, 1 H, H-6′), 3.69 (dd, 1 H, $J_{6,6'}$ 10.4 Hz, H-6), 3.54 (ddd, 1 H, $J_{5,6}$ 5.4, $J_{4,5}$ 10.0, $J_{5,6'}$ 0.5 Hz, H-5), 3.33 (s, 3 H, CH_3O), 3.07 (s, 3 H, CH_3SO_2), 3.06 (s, 3 H, CH_3SO_2), 1.43 (d, 3 H, *J* 0.5 Hz, CH_3), 1.27 (d, 3 H, *J* 0.5 Hz, CH_3). ^{13}C NMR (100.6 MHz, acetone-d_6): δ 100.36 [$(CH_3)_2C$], 99.26 (C-1), 78.13 (C-3), 76.68 (C-2), 72.28 (C-4), 63.9 (C-5), 62.15 (C-6), 55.44 (CH_3O), 38.86 (CH_3SO_2), 37.95 (CH_3SO_2), 28.71 (CH_3), 18.92 (CH_3). FABMS: *m*/*z* (%) 391 (100) [MH^+], 375 (18), 359 (7), 301 (38), 237 (27), 223 (14), 205 (42); FABHRMS Calcd for $C_{12}H_{23}O_{10}S_2$: 391.0733. Found 391.0724.

*Methyl 2,3-di-*O*-mesyl-α-*D*-glucopyranoside* (**8**).—Acetyl chloride (0.20 mL, 0.23 g, 2.90 mmol) was dissolved in MeOH (40 mL). After 30 min stirring, the methanolic HCl soln was added to **7** (4.89 g, 12.52 mmol) and the mixture was stirred for 2 h. Sodium carbonate was added in two portions (2 × 0.18 g, 0.34 mmol) and, after 30 min, the MeOH was removed. The residue was extracted with a sufficient amount of CH_2Cl_2. Drying ($MgSO_4$) and evaporation under diminished pressure yielded **8** (4.12 g, 94%) as a colorless solid, mp 150 °C (dec) (Ref. [8]: 150.6 °C, Ref. [10]: 150–151 °C). $[\alpha]_D^{20}$ + 83° (*c* 1.1, MeOH) [Ref. [9]: $[\alpha]_D^{25}$ + 82.4° (*c*, 1.06, MeOH)] IR: *v* 3533 (OH), 3350, 3040, 2984, 2934, 2887, 2851, 1353, 1341, 1181, 1052, 1010, 971, 849, 771, 731, 660, 562, 501. ^{1}H NMR (400 MHz, D_2O): δ 5.06 (d, 1 H, $J_{1,2}$ 3.1 Hz, H-1), 4.78–4.74 (m, 2 H, H-2, H-3), 3.81 (dd, 1 H, H-6′), 3.71 (dd, 1 H, $J_{4,5}$ 1.5, $J_{3,4}$ 7.3 Hz, H-4), 3.70 (dd, 1 H, $J_{6,6'}$ 12.2 Hz, H-6), 3.66 (dd, 1 H, $J_{5,6}$ 1.8, $J_{5,6'}$

[4] The discrepancy between *R* and R_w is due to the program used for refinement [16]: the weighted *R* index based on F_o^2 is (for compelling statistical reasons) much higher than the conventional *R* index based on F_o with a threshold of $F_o > 4\sigma(F_o)$. For comparison with structures refined against *F*, the latter is, therefore, printed as well. Despite the fact that R_w and not *R* is the quantity minimized, *R* has the advantage that it is relatively insensitive to the weighting scheme [16].

4.8 Hz, H-5), 3.38 (s, 3 H, CH_3O), 3.22 (s, 3 H, CH_3SO_2), 3.21 (s, 3 H, CH_3SO_2) [9]. ^{13}C NMR (100.6 MHz, D_2O): δ 97.36 (C-1), 81.33, 76.09, 71.91 (C-5), 67.99 (C-4), 60.36 (C-6), 55.85 (CH_3O), 38.85 (CH_3SO_2), 38.23 (CH_3SO_2). FABMS: m/z (%) 351 (17) [MH^+], 319 (26), 223 (54); FABHRMS Calcd for $C_9H_{19}O_{10}S_2$: 351.0420. Found 351.0411.

*Methyl 6-*S*-acetyl-2,3-di-*O*-mesyl-6-thio-α-*D*-glucopyranoside* (**9**).—The thio-Mitsunobu reaction was performed as described for **2** starting with triphenylphosphine (1.84 g, 7.02 mmol), DIAD (1.80 mL, 1.42 g, 7.02 mmol), thioacetic acid (0.50 mL, 0.53 g, 7.02 mmol) and **8** (2.00 g, 5.71 mmol) in a total vol of 100 mL THF. After a reaction time of 20 h, the solvent was removed under diminished pressure, the residue was dissolved in diethyl ether (40 mL) and most of the triphenylphosphine oxide was precipitated by addition of petroleum ether (40 mL). After filtration, the solvents were removed and the residue chromatographed twice (each 90 g SiO_2, 3:2 EtOAc–petroleum ether, R_f 0.32) to yield **9** (1.49 g, 64%) as a colorless solid, mp 250 °C (dec). $[\alpha]_D^{20}$ +4° (c 1.0, $CHCl_3$). IR: ν 3500, 3031, 2940, 2845, 1694 (C=O), 1358, 1182, 1125, 1100, 907, 848, 773, 633, 524, 476. ^1H NMR (500 MHz, $CDCl_3$): δ 4.93 (d, 1 H, H-1), 4.92 (dd, 1 H, H-3), 4.51 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 9.9 Hz, H-2), 3.90 (ddd, 1 H, H-5), 3.48 (dd, 1 H, $J_{5,6'}$ 3.7 Hz, H-6′), 3.45 (dd, 1 H, $J_{3,4}$ 9.4, $J_{4,5}$ 9.4 Hz, H-4), 3.44 (s, 3 H, CH_3O), 3.19 (s, 3 H, CH_3SO_2), 3.15 (s, 3 H, CH_3SO_2), 3.12 (dd, 1 H $J_{6,6'}$ 14.9, $J_{5,6}$ 3.5 Hz, H-6), 2.44 (s, 3 H, CH_3CO). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 199.62 (CO), 97.96 (C-1), 79.46 (C-3), 75.47 (C-2), 70.35 (C-4), 69.43 (C-5), 55.96 (CH_3O), 38.99 (CH_3SO_2), 38.82 (CH_3SO_2), 30.54 (CH_3CO), 30.52 (C-6).

*Methyl 2-*O*-mesyl-4,6-thioanhydro-α-*D*-gulopyranoside [(1*R*,3*S*,4*R*,5*S*,6*R*)-4-mesyloxy-3-methoxy-2-oxa-7-thiabicyclo[4.2.0]octan-5-ol]* (**10**).—The preparation was performed as described for **4** starting with **9** (1.49 g, 3.65 mmol) and $NaHCO_3$ (0.55 g, 6.55 mmol). The reaction time was 7 h at 110 °C and then 6 h at 130 °C. For purification, the crude product was chromatographed twice (each 100 g SiO_2, 9:1 EtOAc–petroleum ether, R_f 0.63) to yield **10** (0.24 g, 25%) as colorless crystals, mp 140 °C (EtOAc) (Ref. [12]: 147–149 °C. $[\alpha]_D^{20}$ +123° (c 1.0, $CHCl_3$) [Ref. [12]: $[\alpha]_D^{25}$ +129° (c 1.1, $CHCl_3$)]. IR: ν 3480, 3039, 3016, 2972, 2945, 2856, 1348, 1151, 1099, 1059, 966, 920, 845, 528. ^1H NMR (400 MHz, $CDCl_3$): δ 5.26 (dd, 1 H, H-2), 5.04 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), 4.81 (ddd, 1 H, H-5), 4.09 (ddd, 1 H, $J_{4,5}$ 4.6 Hz, H-4), 4.01 (dd, 1 H, $J_{2,3}$ 3.7, $J_{3,4}$ 3.7 Hz, H-3), 3.52 (s, 3 H, CH_3O), 3.51 (dd, 1 H, $J_{5,6}$ 5.5 Hz, H-6), 3.15 (s, 3 H, CH_3SO_2), 2.92 (ddd, 1 H, $J_{6,6'}$, 10.1, $J_{5,6'}$, 2.6, $J_{4,6'}$, 1.0 Hz, H-6′). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 97.61 (C-1), 74.33 (C-2), 70.23 (C-5), 69.80 (C-3), 56.75 (CH_3O), 45.09 (C-4), 39.07 (CH_3SO_2), 30.34 (C-6). EIMS (70 eV): m/z (%) 270 (1) [$M^{+\bullet}$], 224 (5), 152 (47), 148 (23), 131 (7), 129 (5), 118 (14), 116 (9), 115 (6), 114 (34), 113 (8), 103 (7), 101 (10), 97 (13), 89 (20), 87 (11), 86 (10), 85 (50), 81 (18), 79 (17), 75 (8), 74 (25), 73 (100), 72 (33), 71 (24), 70 (37), 69 (27), 68 (23), 61 (25), 60 (7), 59 (19), 58 (11), 57 (16), 45 (61). The spectroscopic data agree with the literature [12].

X-ray structural data. $C_8H_{14}O_6S_2$: Crystal dimensions $0.55 \times 0.29 \times 0.22$ mm, orthorhombic, $P2_12_12_1$, $a = 585.1(1)$ pm, $b = 957.2(1)$ pm, $c = 2040.3(1)$ pm, $\alpha = \beta = \gamma = 90°$, $V = 1.1904(2)$ nm^3. $Z = 4$, $\rho_{calcd} = 1.51$ g cm^{-3}, $\mu = 4.198$ mm^{-1}, $\vartheta - 2\vartheta$ scan, 2106 independent reflections, 2106 significant reflections [$I > 2\sigma(I)$], 189 parameters, R factor 0.0418, R_w factor 0.1160[5].

3. Supplementary material

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 103127 (**4**) and 103126 (**10**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

[5] See footnote 4.

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References

[1] J. Wirsching. J. Voss, *Eur. J. Org. Chem.*, (1999) 691–699.
[2] (a) J. Voss, O. Schulze, F. Olbrich, G. Adiwidjaja, *Phosphorus, Sulfur, Silicon*, 120 (1997) 389–390. (b) O. Schulze, J. Voss, *Phosphorus, Sulfur, Silicon*, 153–154 (1999) 429–430.
[3] (a) O. Mitsunobu, *Synthesis*, (1981) 1–28. (b) R.P. Volante, *Tetrahedron Lett.*, 22 (1981) 3119–3122. (b) D.L. Hughes, *Org. React.* (*NY*), 42 (1992) 335–656. (c) S.H. Kawai, J. Chin, G. Just, *Carbohydr. Res.*, 211 (1991) 245–260. (d) I. Dancy, L. Laupichler, P. Rollin, J. Thiem, *Justus Liebigs Ann. Chem.*, (1993) 343–350. (e) J. Brånalt, I. Kvarnström, B. Classon, B. Samuelsson, *J. Org. Chem.*, 61 (1996) 3604–3610. (f) J. Moravcová, P. Rollin, C. Lorin, V. Gardon, J. Čapková, J. Mazáč, *J. Carbohydr. Chem.*, 16 (1997) 113–127.
[4] D. Camp, I.D. Jenkins, *Aust. J. Chem.*, 43 (1990) 161–168.
[5] (a) K. Polchow, *Diploma Thesis*, University of Hamburg, 1997. (b) J.-S. Brunck, *Dissertation*, University of Hamburg, 1993.
[6] O. Schulze, *Diploma Thesis*, University of Hamburg, 1995.
[7] (a) P. Collins, R. Ferrier, *Monosaccharides. Their Chemistry and Their Roles in Natural Products*, Wiley, Chichester, 1995, p. 194 ff. (b) J. Lehmann, *Kohlenhydrate. Chemie und Biologie*, Thieme Verlag, Stuttgart, 2. Aufl. 1996, p. 115 f. (c) M. Miljkovic, M. Gligorijevic, D. Glišin, *J. Org. Chem.*, 39 (1974) 3223–3226. (d) A.C. Richardson, *Carbohydr. Res.*, 10 (1969) 395–402 and refs therein.
[8] (a) J.K.N. Jones, *Can. J. Chem.*, 34 (1956) 840–842. (b) M.L. Wolfrom, A.B. Diwadkar, J. Gelas, D. Horton, *Carbohydr. Res.*, 35 (1974) 87–96.
[9] H.B. Sinclair, *Carbohydr. Res.*, 50 (1976) 247–256.
[10] B. Fraser-Reid, B. Boctor, *Can. J. Chem.*, 47 (1969) 393–401.
[11] (a) K. Toshima, T. Yoshida, S. Mukaiyama, K. Tatsuta, *Carbohydr. Res.*, 222 (1991) 173–188. (b) K. Toshima, S. Mukaiyama, Y. Nozaki, H. Inokuchi, M. Nakata, K. Tatsuta, *J. Am. Chem. Soc.*, 116 (1994) 9042–9051 and refs. cited therein.
[12] I. Izquierdo Cubero, M.T. Plaza Lopez-Espinosa, *Carbohydr. Lett.*, 1 (1995) 191–198.
[13] P.W. Austin, J.G. Buchanan, E.M. Oakes, *J. Chem. Soc., Chem. Commun.*, (1965) 374-375.
[14] Autorenkollektiv, *Organikum*, 19th ed., Johann Ambrosius Barth Verlag, Leipzig, 1993, pp. 659–681.
[15] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M.C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.*, 27 (1994) 435.
[16] G.M. Sheldrick, SHELXL-97, Program for the Refinement of Crystal Structures, Göttingen, Germany, 1997.
[17] D. Cremer, J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1354–1358.
[18] A.L. Spek, PLATON, A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, 1999.