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Synthesis of 6-deoxy-5-thio-D-glucose [1]

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Abstract

Three routes were investigated for the conversion of D-glucose into the title compound. In the first approach, reduction of the 5,6-thiirane ring of 5,6-dideoxy-5,6-epithio-1,2-*O*-isopropylidene-α-D-glucofuranose (**17**) as well as that of its 3-*O*-allyl derivative (**13**) with lithium aluminium hydride was investigated; **17** afforded the corresponding 6-deoxy derivative besides di-, tri-, and poly-mers, whereas only polymers were formed from **13**. In the second approach, the oxirane ring of 3-*O*-allyl-5,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose was reduced by sodium borohydride and the resulting 6-deoxy derivative was converted into the 5-thiobenzoate; the corresponding hex-4-enofuranose was formed as a byproduct. In the third approach partial mesylation of methyl 5-thio-α-D-glucopyranoside was attempted, but the 6-mesylate **27** could be isolated only in modest yield (28%) together with rearranged 2,5-thioanhydromannofuranoside derivatives. The mechanism of this rearrangement is discussed in detail. The 6-mesylate **27** was converted via the 6-iodo derivative into the title compound. © 1996 Elsevier Science Ltd.

Keywords: 6-Deoxy-5-thio-D-glucose; Reduction of 5,6-thiirane rings with $LiAlH_4$; Rearrangement reactions of mesylated methyl 5-thio-α-D-glucopyranoside; Reaction mechanism: transannular participation of the sulfur atom

1. Introduction

Thio sugars and their derivatives in which the ring oxygen is replaced by a sulfur atom perform some interesting biological activities [1]. For example 5-thio-D-gluco-

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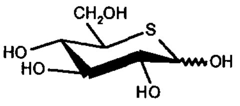
pyranose (**1**) [2] inhibits the release of insulin [3], whereas some glycosides of 5-thio-D-xylopyranose (**2**) proved to be orally active venous antithrombotics [4]. This activity depends strongly on the presence of the ring sulfur atom, as the corresponding oxygen-containing analogues were much less active. Since **2** differs from **1** only in the absence of the equatorial hydroxymethyl substituent, we wished to check the influence of this group on the biological activity by replacing it with a methyl substituent. For the synthesis of 6-deoxy-5-thio-D-glucose (**3**), using D-glucose as starting material, two transformations (*a*) OH-5 → SH (with retention of configuration), and (*b*) OH-6 → H are necessary. The theoretically possible synthetic approaches may differ in the sequence of these transformations.



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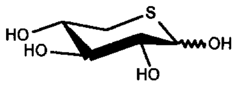

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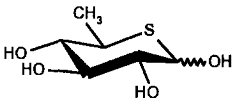

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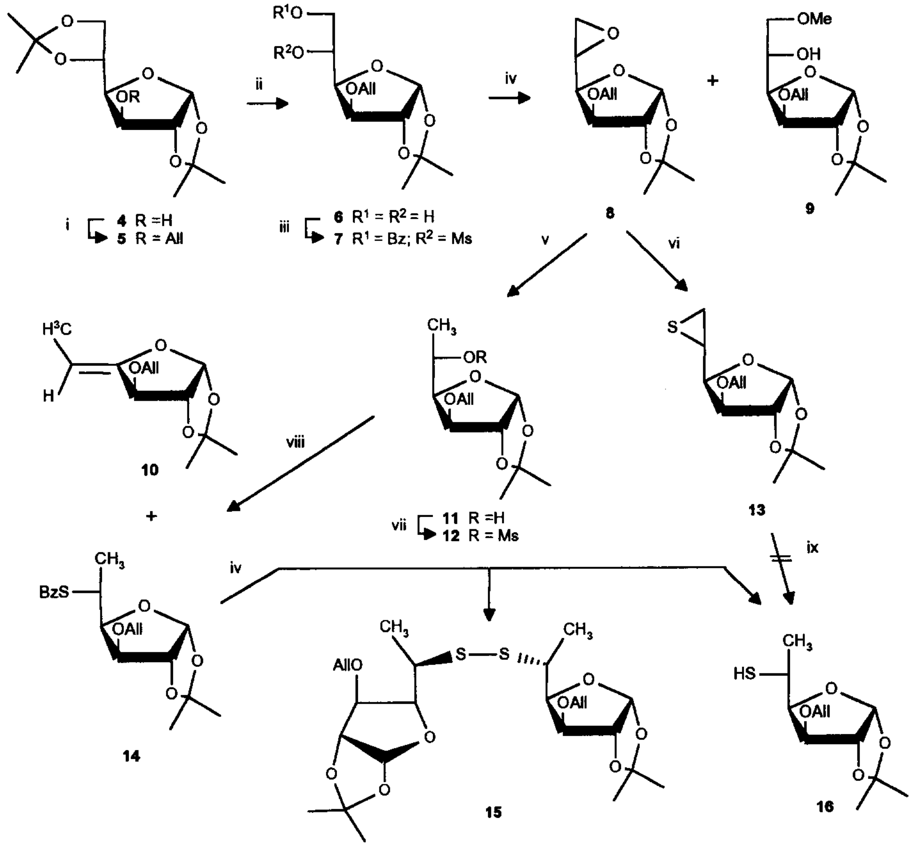
2. Results and discussion

In our first attempt, the sequence (*a*) → (*b*) was investigated. Introduction of the 5-thiol group was carried out along the original synthetic pathway of Whistler and Lake [2] starting from 1,2:5,6-di-*O*-isopropylidene-α-D-glucose (**4**, Scheme 1). However, for the protection of the OH-3 group, the *O*-allyl group (**5**) was chosen [5] instead of the *O*-benzyl group which is somewhat awkward to remove. The diol **6**, obtained after partial hydrolysis of the terminal *O*-isopropylidene group [5], was converted into the 6-*O*-benzoyl-5-*O*-mesyl derivative **7** which, on treatment with methanolic sodium methoxide, gave the corresponding L-*ido* epoxide **8** as the main product (52%) and the corresponding 6-*O*-methyl derivative **9** as a byproduct (7%). Reaction of **8** with thiourea afforded the corresponding 5,6-epithio-D-*gluco* isomer **13** in high yield (83%), but instead of the 6-deoxy derivative **16** only polymers were obtained by reduction of **13** with lithium aluminium hydride under different conditions. Therefore the (*b*) → (*a*) approach was investigated next.

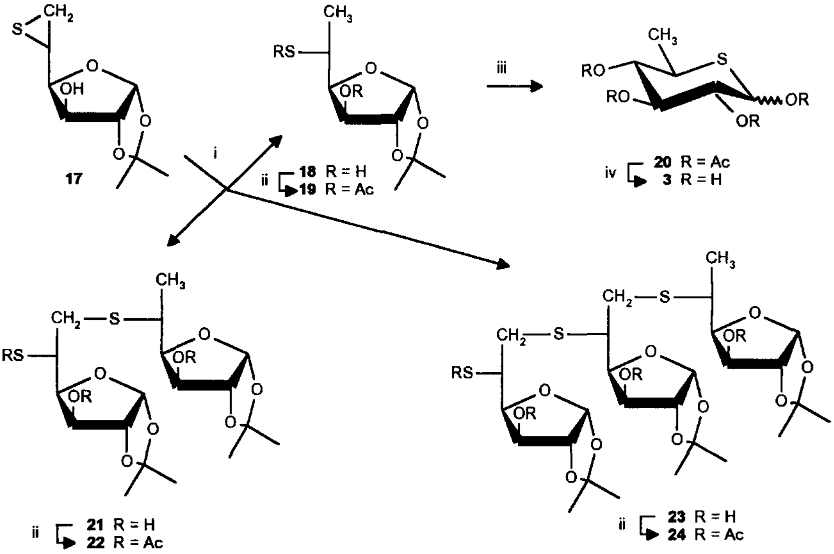
The terminal oxirane ring of **8** could be smoothly reduced with sodium borohydride in ethanol to give the 6-deoxy-L-idofuranose derivative **11**, which after mesylation (**12**) and subsequent treatment with potassium thiolbenzoate in DMF afforded an inseparable mixture, containing, besides the expected 5-*S*-benzoyl-D-*gluco* isomer **14**, the unsaturated 4-ene derivative **10** which according to NMR possessed the *Z* configuration (an NOE effect was observed between H-5 and H-3). Compound **10** must have been formed from **12** by a base-catalyzed, anti elimination of methanesulfonic acid. Debenzoylation of this mixture was attempted by the Zemplén method, but because of the acidity of the thiol group 1.2 equiv of sodium methoxide had to be used to complete the reaction. Under these conditions a thiol **16** was formed, while **10** remained unchanged. These two derivatives could only be separated by column chromatography, but during this process oxidation of **16** into its disulfide **15** could not be avoided. Accordingly **16** was isolated



Scheme 1. (i) AllBr/NaH/DMF. (ii) AcOH/H_2O. (iii) (1) BzCl/Py, (2) MsCl/Py. (iv) NaOMe/MeOH. (v) $NaBH_4$/EtOH. (vi) $(NH_2)_2CS$/MeOH. (vii) MsCl/Py. (viii) KSBz/DMF. (ix) $LiAlH_4$/THF.

in a yield of only 5%, making this approach unsuitable for the preparation of the target compound **3**.

In our next attempt, **4** was converted by known methods [6] into the 5,6-dideoxy-5,6-epithio-D-glucofuranose derivative **17** and the reduction of the thiirane ring with lithium aluminium hydride in THF was studied in detail, since according to the literature [7] this reaction afforded the corresponding 6-deoxy-5-thio derivative in the case of the analogous L-*ido* isomer. When the reduction was carried out at low temperature (0 °C), besides traces of the 5-thiol **18**, a mixture of different di-, tri-, and poly-mers was formed from which the dimer **21** and the trimer **23** could be separated (Scheme 2). For structure elucidation both were converted into their crystalline peracetates (**22** and **24**). The chirality of the C-5 atoms could not be established unambiguously by NMR, but it is very unlikely that inversion at the C-5 centres would take place under these conditions. This tendency towards polymerization is not surprising [8], as thiol **18** once formed is present in the reaction mixture as its Li-thiolate salt. As the thiolate anion is a much stronger nucleophile than the hydride anion, the latter can hardly compete successfully in the ring-opening reaction. The yield of **18** could be increased substan-

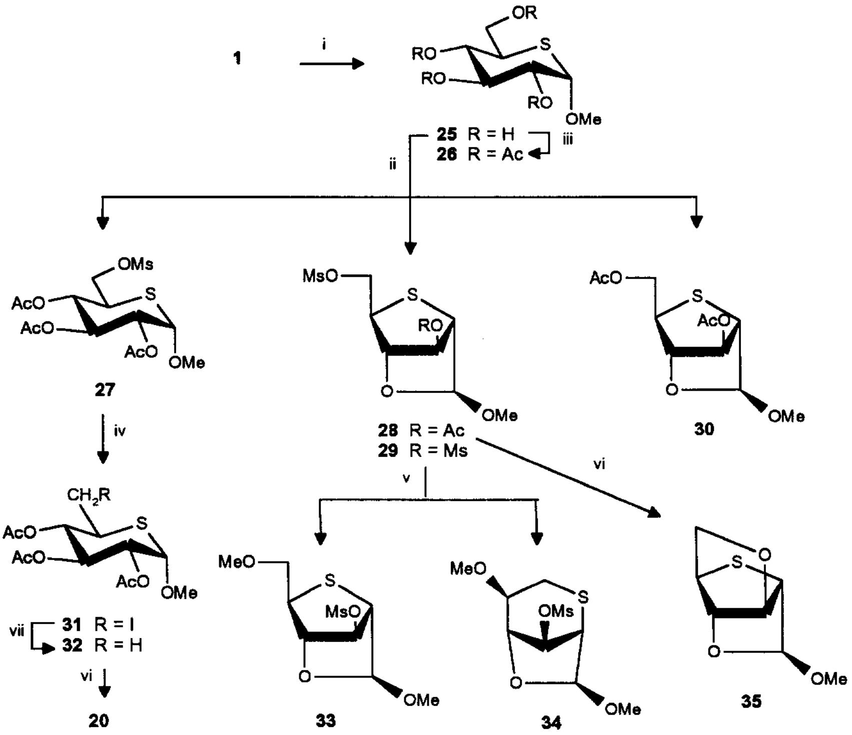


Scheme 2. (i) $LiAlH_4$/THF. (ii) Ac_2O/Py. (iii) (1) HCl/AcOH, (2) Ac_2O/Py. (iv) NaOMe/MeOH.

tially (31.5%) by carrying out the reduction in boiling THF when **21** and **23** were formed in yields of 32 and 7%, respectively. Hydrolysis of **18** and subsequent acetylation afforded tetraacetate **20** in high yield (84%). Deacetylation of the latter by Zemplén's method gave **3**.

Because of the relatively low yield of the reduction step (**17** → **18**) a totally different synthetic approach was investigated. The thiirane intermediate **17** was converted [6] into methyl 5-thio-α-D-glucopyranoside (**25**), which was treated with 1.2 equiv of mesyl chloride and subsequently with acetic anhydride in pyridine (Scheme 3). From the resulting complex mixture, besides the peracetylated starting material **26** (30%), the 6-mesylate **27** (27.5%) as well as two rearranged furanosides **28** (7%) and **30** (12%) could be isolated. The latter two contained, according to NMR, a 2,5-thioanhydro bridge, an OAc group at C-3, and differed only in the substituent at C-6 which was OMs for **28** and OAc for **30**. The yield of monomesylate **27** could not be increased by using a higher ratio (5 equiv) of mesyl chloride; in this case the dimesylate **29** of the rearranged furanoside was formed as the main product (64%). The structures of **28** and **29** could be proved by chemical methods, since treatment of **28** with 1.2 equiv of methanolic sodium methoxide gave the expected 3,6-anhydro derivative **35**, while **29** could be converted in boiling methanol in the presence of barium carbonate into a 1:1 mixture of the 6-*O*-methyl derivative **33** and the rearranged 2,6-thioanhydro derivative **34**. The former proved to be unstable and decomposed on standing at room temperature, giving the known [6] thiophene derivative **47** via elimination of methanesulfonic acid and methanol.

The 6-mesylate **27** could be smoothly converted with sodium iodide in boiling 3-pentanone into the 6-iodo derivative **31** (93%) which on reduction with sodium borohydride–nickel chloride gave the 6-deoxyglycoside **32**. Acetolysis of the latter afforded the tetraacetate **20** already mentioned. Because of the low yield of the



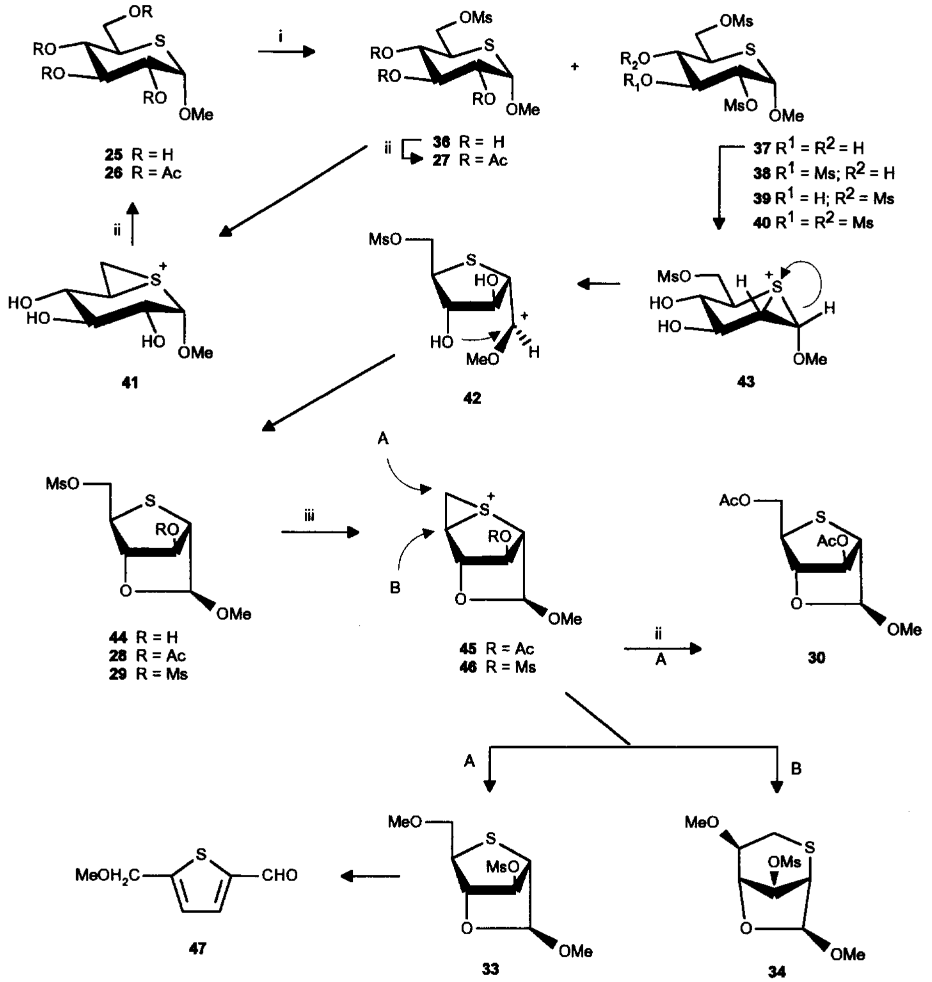
Scheme 3. (i) HCl/MeOH. (ii) (1) MsCl/Py, (2) Ac_2O/Py. (iii) Ac_2O/Py. (iv) NaI/3-pentanone. (v) $BaCO_3$/MeOH. (vi) NaOMe/MeOH. (vii) $NaBH_4$/$NiCl_2$/EtOH.

mesylation reaction (**25** → **27**) this approach proved to be economically less useful than the aforementioned one.

Structure determination of the rearranged products by NMR spectroscopy.—By comparing the ^{13}C NMR data of the two 6-mesylates **27** and **28** it is obvious that the thioether bridge is shifted from C-1 to C-2, as the corresponding signals appear at δ 81.12 and 74.48 in the former and at 108.95 and 49.60 in the latter. As similar values were found for these atoms in **33**, **34**, and **35** (C-1: δ 108.46, 107.68, 108.92; and C-2: δ 49.48, 44.55, 53.28) the rearranged thioether bridge must be present in all of them. The *S* configuration of C-1 in **28**, **29**, **30**, **33**, **34**, and **35** was proved by the $J_{1,2}$ value ~ 0 Hz, reflecting the ~ 90° dihedral angle between H-1 and H-2 in these rigid bridged systems. Consequently the oxocarbenium ion **42** formed as an intermediate (see Scheme 4) is attacked by the 4-OH group from the *Si* face exclusively. This means that the rotation of the planar charged C-1 atom around the C-1–C-2 bond is a much slower process than the ring-closure reaction.

The presence of the 2,5-thioanhydro bridge and the furanoid structure of compounds **28**, **29**, **30**, and **33** was revealed by semiselective INEPT long-range experiments. The H-1 resonance gave long-range correlations with C-3 and C-4. Moreover, in the 2D spectra, correlation was observed between H-2 and C-5.

The structure and stereochemistry of the other bridged system containing a six- and a



Scheme 4. (i) MsCl/Py. (ii) Ac_2O/Py. (iii) $BaCO_3$ /MeOH.

five-membered ring (**34**) was also assigned with the help of the NMR data. Firstly, the geminal coupling value of H-6a and H-6b (13.6 Hz) was characteristic of a six-membered ring. Secondly, selective irradiation of H-1 gave NOE intensity enhancements on the signals of H-2 and H-6a. Finally, long-range heterocorrelation was found between H-1 and C-4, and H-2 and C-6, respectively. The chirality of C-3 could be established by DNOE measurements, proving the sterically close arrangement of the methoxy group at C-1 and the H-3 proton.

The presence of a third bridge in compound **35** was identified on the basis of the geminal coupling of the H-6 methylene protons (8.0 Hz). This structure was corroborated by the long-range connectivity observed between H-6 protons and C-3.

The mechanism of the rearrangement reactions.—The products formed during the mesylation and subsequent acetylation of methyl 5-thio-α-D-glucopyranoside (**25**) can be explained by the general mechanism suggested [9] for the rearrangement reactions of different sulfonate esters of 5-thio-hexose derivatives, taking part via transannular participation of the ring sulfur atom. As the reactivity order of the hydroxyl groups in **25** should not differ significantly from that for methyl α-D-glucopyranoside (6-OH > 2-OH > 3-OH ~ 4-OH) it can be expected that the 6-mesylate **36** and the 2,6-dimesylate **37** are formed in the first step of the reaction. In **37**, the mesyloxy group at C-2 is oriented exo to the sulfur atom and will act as a leaving group. The very fast intramolecular attack of the sulfur atom leads to the episulfonium intermediate **43** which rearranges to the 2,5-thioanhydro oxocarbenium ion **42**. In **42**, HO-4 is in favourable cis arrangement with the charged C-1 atom; therefore an instant ring closure takes place, yielding furanoside **44** after deprotonation. In the second stage of the reaction the free HO-3 group of **44** is acetylated and the mixed ester **28** so formed can be isolated from the reaction mixture. However, the terminal mesyloxy group in **44** is still a leaving group and consequently a second episulfonium ion **45** might be formed, which can be attacked by the acetate ion present in the reaction mixture. Theoretically both bridge atoms (C-5 and C-6) could be attacked, but under the mild conditions (room temperature) used attack at the less-hindered C-6 atom (route A) is preferred, leading to diacetate **30**. It is obvious that when only 1.2 equiv of mesyl chloride are present formation of dimesylate **37** will consume part of it; consequently some of the starting material must remain unchanged and will be acetylated in the second stage of the reaction, forming tetraacetate **26**. The high amount (30%) of isolated **26** suggests, however, that even the 6-mesylate **36** can form an episulfonium ion **41**, which will be opened by the acetate anion at C-6 to give **26** after subsequent acetylation.

When a larger amount (5 equiv) of mesyl chloride is applied, the reaction is shifted towards the dimesylate **37**, which immediately undergoes the rearrangement reaction mentioned above. This must be a very fast process, as neither the theoretically possible 2,4,6-trimesylate **39** (or its acetate) nor the tetramesylate **40** was formed. That means that HO-4 is blocked by the anhydro ring formation, therefore further mesylation can take place only at O-3 (**38**), leading, after rearrangement, to **29** which could be isolated as the main product (64%) of the reaction.

Treatment of dimesylate **29** according to the literature [8] in boiling methanol with barium carbonate led to the formation of the postulated episulfonium intermediate **46**. Attack of methanol at the less-hindered C-6 bridge atom of **46** (route A) gives **33**, while attack at C-5 (route B) yields the rearranged furanoside **34** containing a six-membered thioanhydro bridge (Scheme 4).

3. Experimental

General methods.—Organic solutions were dried over $MgSO_4$ and concentrated under diminished pressure at or below 40 °C. TLC: Merck precoated Silica Gel 60 F_{254} plates, with hexane–EtOAc mixtures (*A*, 1:1; *B*, 2:1; *C*, 4:1) and benzene–MeOH mixtures (*D*, 4:1; *E*, 9:1); detection by spraying the plates with 0.02 M I_2/0.30 M KI in aq 10% H_2SO_4 followed by heating at ca. 200 °C. For column chromatography Kieselgel 60 was used. Melting points are uncorrected. Optical rotations were determined on 0.5% solutions in $CHCl_3$ at 20 °C unless stated otherwise. NMR spectra were recorded with a Varian XL-400 spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) or with a Bruker Ac 250 spectrometer at 250 MHz (^{1}H) and 62.9 MHz (^{13}C) on solutions in $CDCl_3$ (internal Me_4Si) unless stated otherwise. Multiplicities of the ^{13}C NMR spectra were obtained from DEPT experiments. The assignments of the protons were based on homonuclear decoupling and DNOE experiments. Connectivities between identified protons and protonated carbons were observed by means of HETCOR experiments.

*6-Deoxy-5-thio-*D*-glucose* (**3**).—Deacetylation of tetraacetate **20** (1.2 g, 3.4 mmol) with M NaOMe (0.1 mL) in MeOH (10 mL) yielded, after deionsation with Dowex 50WX and concentration, **3** as a syrup (0.58 g, 95%); $[\alpha]_D$ +157° (c 1.0, pyridine); R_f 0.3 (solvent D). Anal. Calcd for $C_6H_{12}O_4S$: C, 39.99; H, 6.71; S, 17.79. Found: C, 40.14; H, 6.89; S, 17.68.

*3-*O*-Allyl-1,2:5,6-di-*O*-isopropylidene-α-*D*-glucofuranose* (**5**).—To a mixture of **4** (26.0 g, 100 mmol) in DMF (100 mL) and 50% NaH in oil (5.2 g, 108 mmol) was added allyl bromide (9.6 mL, 110 mmol), the mixture was stirred at room temperature for 30 min, then MeOH (20 mL) and water (20 mL) were added, and stirring was continued for 30 min. The solution was extracted with ether, and the organic layer was washed with brine and concentrated to give **5** as a syrup (29.3 g, 97%); $[\alpha]_D$ −31°; R_f 0.6 (solvent C); NMR data identical with lit. data [5].

*3-*O*-Allyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**6**).—Partial hydrolysis of **5** (29.3 g, 97.5 mmol) was carried out according to ref. [5] to give **6** as a syrup (22.1 g, 87%); $[\alpha]_D$ −48°; R_f 0.3 (solvent A); NMR data identical with lit. data [5].

*3-*O*-Allyl-6-*O*-benzoyl-1,2-*O*-isopropylidene-5-*O*-methanesulfonyl-α-*D*-glucofuranose* (**7**).—To a solution of **6** (22.0 g, 84.5 mmol) in CH_2Cl_2 (160 mL) and pyridine (40 mL) was added a solution of benzoyl chloride (10.0 mL, 86 mmol) in CH_2Cl_2 (90 mL) at −15 °C. The solution was stirred at room temperature for 4 h and mesyl chloride (7.5 mL, 96.9 mmol) was added. The mixture was kept overnight at room temperature, then water (30 mL) was added. The organic layer was separated and processed in the usual way to give **7** (23.9 g, 64%); mp 130–132 °C (EtOH); $[\alpha]_D$ −15°; R_f 0.5 (solvent B); ^{1}H NMR: δ 8.10 (d, 2 H, aromatic), 7.60–7.40 (m, 3 H, aromatic), 5.95 (m, 1 H, OAll), 5.34 (m, 1 H, OAll), 5.22 (m, 1 H, OAll), 4.15 (m, 2 H, OAll), 3.02 (s, 3 H, OMs), 1.51, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 165.91 (C=O), 133.76, 133.22, 129.66, 129.66, 128.45, 128.45 (aromatic and $-O-CH_2-CH=CH_2$), 117.89 ($-O-CH_2-CH=CH_2$), 71.31 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{20}H_{26}O_9S$: C, 54.29; H, 5.92; S, 7.25. Found: C, 54.41; H, 6.03; S, 7.38.

*3-*O*-Allyl-5,6-anhydro-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**8**) *and 3-*O*-allyl-1,2-*O*-isopropylidene-6-*O*-methyl-β-*L*-idofuranose* (**9**).—To a solution of **7** (21.2 g, 47.9 mmol) in $CHCl_3$ (750 mL) was added 3 M NaOMe in MeOH (50 mL) and the mixture was stirred for 3 h at room temperature. The solution was concentrated, the residue was dissolved in $CHCl_3$, and the solution was washed with water and brine. Column chromatography (solvent B) of the residue obtained on concentration gave **8** (6.0 g, 52%); $[\alpha]_D$ −60° (c 1.0, $CHCl_3$); R_f 0.6 (solvent B); ^{1}H NMR: δ 5.88 (m, 1 H, OAll), 5.30 (m, 1 H, OAll), 5.22 (m, 1 H, OAll), 4.18 (m, 1 H, OAll), 4.02 (m, 1 H, OAll), 1.47, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 133.61

Table 1
Selected ^1H NMR data for solutions in $CDCl_3$

Compound	Chemical shifts (δ)						
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
7	5.94	4.63	4.03	4.45	5.38	4.93	4.50
8	5.98	4.60	3.95	3.81	3.25	2.84	2.65
9	5.98	4.59	3.95	4.22	4.15		3.41
10	6.06	4.51	4.16		4.63		1.68
11	5.97	4.59	3.88	3.98	4.14		1.22
12	5.95	4.60	3.82	4.18	4.90		1.40
13	5.96	4.60	3.92	3.58	3.20	2.66	2.42
15	5.90	4.55	4.00	4.00	3.20		1.50
16	5.90	4.56	4.03	4.03	3.20		1.45
18	5.92	4.51	4.36	3.95	3.15		1.48
20 [a]	6.05	5.23	5.40	5.08	3.35		1.20
27	4.50	5.17	5.50	5.39	3.50	4.44	4.24
28	4.94	3.62	5.43	4.55	3.57	4.54	4.25
29	4.96	3.61	5.37	4.65	3.63	4.50	4.27
30	4.92	3.59	5.39	4.48	3.50	4.35	4.14
31	4.66	5.18	5.30	5.16	3.20	3.40	3.20
32	4.58	5.18	5.45	5.05	3.17		1.15
33	4.93	3.56	5.32	4.56	3.52	3.72	3.45
34	5.18	3.23	5.34	4.46	3.72	3.17	2.69
35	4.89	3.54	4.80	4.72	3.50	4.18	4.15

Compound	Coupling constants (Hz)						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
7	3.6	~0	3.2	8.1	2.0	6.3	12.8
8	3.8	~0	3.5	6.2	2.7	4.3	4.8
9	3.8	~0	3.6	5.4	nd	nd	5.1
10	3.3	~0	–	–	6.8		
11	3.8	~0	3.4	6.2	7.0		
12	3.8	~0	3.5	6.2	7.0		
13	3.8	~0	3.1	8.8	6.1	5.3	1.2
15	3.6	~0	nd [b]	nd	6.9		
16	3.6	~0	nd	nd	6.9		
18	3.7	~0	2.7	9.6	6.9		
20 [a]	3.2	10.2	9.7	10.6	6.8		
27	2.8	10.1	9.6	10.7	4.7	3.2	10.7
28	~0	2.1	2.7	0.7	9.1	6.8	10.4
29	~0	2.2	2.9	0.8	9.5	7.2	10.9
30	~0	2.2	2.8	0.8	8.5	7.2	11.2
31	2.7	9.5	9.8	nd	nd	nd	nd
32	2.9	10.3	9.7	10.7	7.0		
33	~0	2.3	3.0	0.8	7.3	7.4	9.4
34	~0	5.5	6.0	4.0	5.0	3.7	13.6
35	~0	2.9	3.5	2.0	1.5	0.7	8.0

[a] α anomer.

[b] nd, Not determined.

Table 2
Selected ^{13}C NMR data for solutions in CDCl$_3$

Compound	Chemical shifts (δ)								
	C-1	C-2	C-3	C-4	C-5	C-6	*C*Me$_2$	C*Me*$_2$	Others
7	105.33	81.44*	80.87*	78.11*	75.35	64.02	112.17	26.78, 26.22	39.12 (OMs)
8	105.22	82.69*	82.30*	81.97*	49.88	43.04	111.66	26.66, 26.12	
9	104.58	82.73*	82.14*	79.69	68.98	73.26	111.56	26.57, 26.10	59.40 (OMe)
10	106.32	83.17*	80.55*	152.10	100.04	10.22	113.45	27.85, 27.25	
11	104.82	84.19*	82.35*	82.29*	66.13	18.49	111.66	26.69, 26.21	
12	104.99	82.07*	81.45*	81.30*	79.22	17.87	111.66	26.64, 26.14	38.20 (OMs)
13	105.63	86.46*	82.49*	82.49*	29.61	25.25	111.76	26.77, 26 15	
15	104.94	83.25*	82.00*	81.40*	43.01	17.88	111.50	26.74, 26.20	
16	105.41	86.74*	81.75*	81.75*	32.25	22.45	111.43	26.73, 26.17	
18	105.07	86.05*	84.93*	75.14*	32.80	22.57	111.64	26.70, 26.13	
20	76.18	73.22*	71.14*	70.37*	35.06	15.31			
27	81.12	74.48*	71.72*	70.63*	38.18	65.42			56.73 (OMe), 37.58 (OMs)
28	108.95	49.60	75.29*	75.22*	50.33	67.78			55.21 (OMe), 37.73 (OMs), 20.79 (OAc)
29	108.43	49.93	78.54	75.72	49.96	68.06			38.50 (OMs), 37.59 (OMs), 55.34 (OMe)
30	108.63	49.08	74.94	75.47	50.40	63.48			54.82 (OMe), 20.46 (OAc), 20.53 (OAc)
31	81.12	75.00*	74.79*	70.44*	40.80	2.00			56.54 (OMe)
32	81.35	76.70	74.98	70.55	33.49	15.36			56.37 (OMe)
33	108.46	49.48	78.73	76.38	51.39	72.39			55.14 (OMe), 58.85 (OMe), 38.46 (OMs)
34	107.68	44.55	72.72	71.83	77.55	25.16			55.29 (OMe), 57.79 (OMe), 38.43 (OMs)
35	108.92	53.28	78.14	78.30	49.36	76.80			55.31 (OMe)

* Arbitrary assignment.

(-O-CH$_2$-*C*H=CH$_2$), 117.50 (-O-CH$_2$-CH=*C*H$_2$), 70.82 (-O-*C*H$_2$-CH=CH$_2$), for further data see Table 2. Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.41; H, 7.63.

Concentration of the second fraction gave **9** (0.9 g, 7%); $[\alpha]_D$ −47° (*c* 1.0, CHCl$_3$); R_f 0.3 (solvent *B*); ^{1}H NMR: δ 5.88 (m, 1 H, OAll), 5.30 (m, 1 H, OAll), 5.22 (m, 1 H, OAll), 4.16 (m, 1 H, OAll), 4.00 (m, 1 H, OAll), 3.40 (s, 3 H, OMe), 3.14 (s, 1 H, OH), 1.50, 1.32 (2 s, 6 H, CMe$_2$), for further data see Table 1; ^{13}C NMR: δ 133.18 (-O-CH$_2$-*C*H=CH$_2$), 117.97 (-O-CH$_2$-CH=*C*H$_2$), 70.58 (-O-*C*H$_2$-CH=CH$_2$). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 57.11; H, 8.22.

3-O-Allyl-6-deoxy-1,2-O-isopropylidene-β-L-idofuranose (**11**).—To a solution of **8** (6.0 g, 24.8 mmol) in EtOH (50 mL) was added NaBH$_4$ (4.7 g, 124 mmol) and the mixture was stirred for 5 h at 40 °C. The solvent was evaporated, the residue was dissolved in $CHCl_3$, and the solution was washed with water and concentrated to give **11** (5.0 g, 83%); $[\alpha]_D$ −59.5°, R_f 0.2 (solvent *C*); ^1H NMR: δ 5.87 (m, 1 H, OAll), 5.30 (m, 1 H, OAll), 5.23 (m, 1 H, OAll), 4.18 (m, 1 H, OAll), 3.95 (m, 1 H, OAll), 2.78 (s, OH), 1.50, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 133.36 ($-O-CH_2-CH=CH_2$), 118.12 ($-O-CH_2-CH=CH_2$), 70.75 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 59.11; H, 8.38.

3-O-Allyl-6-deoxy-1,2-O-isopropylidene-5-O-methanesulfonyl-β-L-idofuranose (**12**). —To a solution of **11** (2.6 g, 10.6 mmol) in pyridine (15 mL) was added mesyl chloride (0.9 mL, 11.6 mmol), the mixture was stirred for 3 h at room temperature and then poured into water, and the crystalline product was filtered off and washed with water to give **12** (2.4 g, 70%); mp 69–71 °C; $[\alpha]_D$ −47.5°; R_f 0.8 (solvent *E*); ^1H NMR: δ 5.85 (m, 1 H, OAll), 5.30 (m, 1 H, OAll), 5.25 (m, 1 H, OAll), 4.15 (m, 1 H, OAll), 3.90 (m, 1 H, OAll), 3.10 (s, 3 H, OMs), 1.50, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 133.00 ($-O-CH_2-CH=CH_2$), 118.71 ($-O-CH_2-CH=CH_2$), 70.77 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{13}H_{22}O_7S$: C, 48.44; H, 6.88; S, 9.94. Found: C, 48.61; H, 6.93; S, 9.88.

3-O-Allyl-5,6-dideoxy-5,6-epithio-1,2-O-isopropylidene-α-D-glucofuranose (**13**).—To a solution of **8** (6.0 g, 24.8 mmol) in MeOH (220 mL) was added thiourea (2.75 g, 36.1 mmol) and the mixture was kept at room temperature for 2 days. After concentration the residue was dissolved in $CHCl_3$, and the solution was washed with water and concentrated to yield **13** (5.3 g, 83%); R_f 0.7 (solvent *B*); ^1H NMR: δ 5.90 (m, 1 H, OAll), 5.34 (m, 1 H, OAll), 5.22 (m, 1 H, OAll), 4.10 (m, 2 H, OAll), 1.45, 1.31 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 133.86 ($-O-CH_2-CH=CH_2$), 117.82 ($-O-CH_2-CH=CH_2$), 71.52 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{12}H_{18}O_4S$: C, 55.79; H, 7.02; S, 12.41. Found: C, 55.67; H, 7.09; S, 12.38.

(Z)-3-O-Allyl-5,6-dideoxy-1,2-O-isopropylidene-β-L-threo-hex-4-enofuranose (**10**), *bis-(3-O-allyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-glucofuranos-5-yl) disulfide* (**15**), *and 3-O-allyl-6-deoxy-1,2-O-isopropylidene-5-thio-α-D-glucofuranose* (**16**).—A mixture of **12** (6.5 g, 20.2 mmol) and KSBz (5.0 g, 28.4 mmol) in DMF (120 mL) was refluxed for 4 h, when according to TLC all starting material was consumed (R_f 0.4 → 0.7, solvent *B*). The residue obtained on concentration of the mixture was dissolved in $CHCl_3$, and the solution was washed with water and brine. Concentration then gave an inseparable syrupy mixture of **10** and **14** (8.2 g). This was dissolved in MeOH (50 mL), 3 M NaOMe in MeOH (8.0 mL) was added under argon, and the mixture was stirred overnight at room temperature. The solution was neutralized with solid CO_2 and concentrated. Column chromatography (solvent *C*) of the residue gave three products: **10** (0.55 g, 12%); $[\alpha]_D$ 0°; R_f 0.7 (solvent *C*); ^1H NMR: δ 5.88 (m, 1 H, OAll), 5.26 (m, 1 H, OAll), 5.18 (m, 1 H, OAll), 4.08 (m, 1 H, OAll), 3.92 (m, 1 H, OAll), 1.45, 1.38 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 134.05 ($-O-CH_2-CH=CH_2$), 117.54 ($-O-CH_2-CH=CH_2$), 69.00 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.87; H, 8.17.

16 (0.25 g, 5%); $[\alpha]_D$ −57°; R_f 0.6 (solvent *C*); ^1H NMR: δ 5.95 (m, 1 H, OAll), 5.30 (m, 1 H, OAll), 5.21 (m, 1 H, OAll), 4.18 (m, 1 H, OAll), 3.96 (m, 1 H, OAll), 1.68 (s, 1 H, SH), 1.52, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: δ 133.89 ($-O-CH_2-CH=CH_2$), 117.66 ($-O-CH_2-CH=CH_2$), 71.07 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{12}H_{20}O_4S$: C, 55.36; H, 7.74; S, 12.31. Found: C, 55.41; H, 7.89; S, 12.48.

15 (1.05 g, 20%); $[\alpha]_D$ −170°; R_f 0.5 (solvent *C*); ^1H NMR: δ 5.95 (m, 2 H, OAll), 5.30 (m, 2 H, OAll), 5.20 (m, 2 H, OAll), 4.18 (m, 2 H, OAll), 3.98 (m, 2 H, OAll), 1.51, 1.33 (2 s, 6 H, CMe_2); for further data see Table 1; ^{13}C NMR: δ 133.98 ($-O-CH_2-CH=CH_2$), 117.75 ($-O-CH_2-CH=CH_2$), 71.30 ($-O-CH_2-CH=CH_2$), for further data see Table 2. Anal. Calcd for $C_{24}H_{38}O_8S_2$: C, 55.58; H, 7.38; S, 12.36. Found: C, 55.71; H, 7.46; S, 12.38.

6-Deoxy-1,2-O-isopropylidene-5-thio-α-D-glucofuranose (**18**), *6-S-(5,6-dideoxy-1,2-O-isopropylidene-α-D-glucofuranos-5-yl)-1,2-O-isopropylidene-5,6-dithio-α-D-glucofuranose* (**21**), *and 6-S-[5-deoxy-6-S-(5,6-dideoxy-1,2-O-isopropylidene-α-D-glucofuranos-5-yl)-1,2-O-isopropylidene-6-thio-α-D-glucofuranos-5-yl]-1,2-O-isopropylidene-5,6-dithio-α-D-glucofuranose* (**23**).—To a stirred solution of 0.65 M $LiAlH_4$ in THF (6.0 mL) under Ar was added **17** (0.44 g, 2.0 mmol) in THF (5 mL) at reflux temperature during 10 min. Reflux was continued for 5 min, then the mixture was cooled to room temperature and EtOAc, water, aq 20% NaOH, and subsequently water were added. The salts were filtered off, the filtrate was concentrated, and the residue submitted to column chromatography (solvent *A*) to give **18** (0.14 g, 32%); mp 98–101 °C; $[\alpha]_D$ −42°; R_f 0.7 (solvent *A*); ^1H NMR: δ 2.60 (s, 1 H, OH), 1.70 (s, 1 H, SH), 1.50, 1.32 (2 s, 6 H, CMe_2), for further data see Table 1; ^{13}C NMR: for data see Table 2. Anal. Calcd for $C_9H_{16}O_4S$: C, 49.07; H, 7.32; S, 14.55. Found: C, 49.23; H, 7.44; S, 14.43.

Acetylation of **18** with Ac_2O–pyridine afforded 3-*O*-acetyl-5-*S*-acetyl-6-deoxy-1,2-*O*-isopropylidene-5-thio-α-D-glucofuranose (**19**); mp 140–143 °C; $[\alpha]_D$ −40° (*c* 0.2, $CHCl_3$); R_f 0.5 (solvent *C*); ^1H NMR: δ 5.92 (d, 1 H, H-1), 5.27 (d, 1 H, H-3), 4.45 (d, 1 H, H-2), 4.21 (dd, 1 H, H-4), 3.90 (dq, 1 H, H-5), 2.28 (s, 3 H, SAc), 2.07 (s, 3 H, OAc), 1.50, 1.30 (2 s, 6 H, CMe_2), 1.45 (d, 3 H, H-6); $J_{1,2}$ 3.7, $J_{2,3}$ ~ 0, $J_{3,4}$ 2.7, $J_{4,5}$ 10.2, $J_{5,6}$ 6.9 Hz; ^{13}C NMR: δ 193.68 (S–C=O), 169.81 (O–C=O), 112.10 (CMe_2), 104.90 (C-1), 83.24, 81.48, 75.52 (C-2,3,4), 36.28 (C-5), 30.65 (SAc), 26.62, 26.12 (CMe_2), 20.78 (OAc), 19.63 (C-6). Anal. Calcd for $C_{13}H_{20}O_6S$: C, 51.30; H, 6.62; S, 10.53. Found: C, 51.23; H, 6.74; S, 10.41.

Concentration of the second fraction gave **21** (0.14 g, 32%); $[\alpha]_D$ −26°; R_f 0.2 (solvent *A*); ^1H NMR: δ 5.93 (d, 1 H, H-1), 5.91 (d, 1 H, H-1′), 4.52 (d, 2 H, H-2, H-2′), 4.38 (dd, 1 H, H-4′), 4.36 (s, 2 H, H-3, H-3′), 3.95 (dd, 1 H, H-4), 3.36 (m, 2 H, H-5, H-6a), 3.10 (dq, 1 H, H-5′), 2.91 (dd, 1 H, H-6b), 1.92 (d, 1 H, SH), 1.50 (s, 6 H, CMe_2), 1.48 (d, 3 H, H-6′), 1.30 (s, 6 H, CMe_2); $J_{1,2} = J_{1',2'} = 3.7$, $J_{2,3} = J_{2',3'} \approx 0$, $J_{3,4} = J_{3',4'} = 2.4$, $J_{4,5} = J_{4',5'} = 10.0$, $J_{5,6b} = J_{5',6'} = 6.8$, $J_{6a,6b}$ 13.0 Hz; ^{13}C NMR: δ 111.90, 111.47 (CMe_2), 105.06, 104.70 (C-1,1′), 84.96, 84.96, 84.74, 84.28, 83.54, 74.80 (C-2,2′,3,3′,4,4′), 39.62, 38.21 (C-5,5′), 37.65 (C-6), 26.70 (C-6′), 26.70, 26.13, 26.13 (CMe_2), 19.92 (C-6′). Anal. Calcd for $C_{18}H_{30}O_8S_2$: C, 49.30; H, 6.90; S, 14.62. Found: C, 49.48; H, 6.93; S, 14.48.

Acetylation of **21** with Ac_2O–pyridine afforded 3-*O*-acetyl-5-*S*-acetyl-6-*S*-(3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranos-5-yl)-1,2-*O*-isopropylidene-

5,6-dithio-α-D-glucofuranose (**22**); mp 188–192 °C; $[\alpha]_D$ −15° (*c* 0.3, $CHCl_3$); R_f 0.4 (solvent *B*); ^1H NMR: δ 5.88 (d, 1 H, H-1), 5.85 (d, 1 H, H-1′), 5.29 (d, 1 H, H-3), 5.26 (d, 1 H, H-3′), 4.50 (d, 1 H, H-2), 4.44 (d, 1 H, H-2′), 4.38 (dd, 1 H, H-4), 4.10 (dd, 1 H, H-4′), 4.02 (m, 1 H, H-5), 3.17 (m, 1 H, H-5′), 3.04 (dd, 1 H, H-6a), 2.90 (dd, 1 H, H-6b), 2.30 (s, 3 H, SAc), 2.15 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 1.50 (s, 6 H, CMe_2), 1.48 (d, 3 H, H-6′), 1.30 (s, 6 H, CMe_2); $J_{1,2} = J_{1',2'} = 3.7$, $J_{2,3} = J_{2',3'} \approx 0$, $J_{3,4} = J_{3',4'} = 2.8$, $J_{4,5}$ 10.7, $J_{4',5'}$ 10.4, $J_{5,6a}$ 3.7, $J_{5,6b}$ 7.4, $J_{5',6'}$ 6.8, $J_{6a,6b}$ 13.4 Hz; ^{13}C NMR: δ 193.22 (S–C=O), 169.85, 169.72 (O–C=O), 112.38, 111.94 (CMe_2), 104.91, 104.62 (C-1,1′), 83.12, 83.06, 82.62, 79.21, 76.46, 75.32 (C-2,3,4,2′,3′,4′), 42.34, 38.54 (C-5,5′), 33.53 (C-6), 30.61 (SAc), 26.59, 26.59, 26.13, 26.13 ($C\mathit{Me}_2$), 20.99, 20.78 (OAc), 19.46 (C-6′); MS: m/z 565 $[M + H]^+$. Anal. Calcd for $C_{24}H_{36}O_{11}S_2$: C, 51.05; H, 6.43; S, 11.36. Found: C, 51.23; H, 6.64; S, 11.42.

The third fraction gave on concentration **23** (0.03 g, 7%), which after acetylation with Ac_2O–pyridine afforded 3-*O*-acetyl-5-*S*-acetyl-6-*S*-[3-*O*-acetyl-6-*S*-(3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-glucofuranos-5-yl)-5-deoxy-1,2-*O*-isopropylidene-6-thio-α-D-glucofuranos-5-yl]-1,2-*O*-isopropylidene-5,6-dithio-α-D-glucofuranose (**24**); mp 169–172 °C; $[\alpha]_D$ −15° (*c* 0.4, $CHCl_3$); R_f 0.2 (solvent *B*); ^1H NMR: δ 5.85 (m, 3 H, H-1, H-1′, H-1″), 5.30 (m, 3 H, H-3, H-3′, H-3″), 4.50 (m, 2 H, H-2′, H-2″), 4.42 (m, 1 H, H-2), 4.38 (m, 1 H, H-4′), 4.30 (m, 1 H, H-4″), 4.12 (m, 1 H, H-4), 3.98 (m, 1 H, H-5), 3.20–2.80 (m, 6 H, H-5′, H-5″, H-6a, H-6b, H-6a′, H-6b′), 2.30 (s, 3 H, SAc), 2.15 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 1.50 (s, 9 H, CMe_2), 1.48 (m, 3 H, H-6″), 1.30 (s, 9 H, CMe_2); ^{13}C NMR: δ 193.31 (S–C=O), 169.81 (3 O–C=O), 112.38, 112.24, 111.89 (CMe_2) 104.91, 104.63, 104.63 (C-1,1′,1″), 83.15, 83.15, 83.03, 83.03, 82.09, 80.17, 79.30, 76.51, 75.34 (C-2,3,4,2′,3′,4′,2″,3″,4″), 44.93, 42.28, 38.52 (C-5,5′,5″), 34.26, 33.32 (C-6′,6″), 30.63 (SAc), 26.60 (3 $C\mathit{Me}_2$), 26.17 (3 $C\mathit{Me}_2$), 21.01, 21.01, 20.80 (3 OAc), 19.45 (C-6). Anal. Calcd for $C_{35}H_{52}O_{16}S_3$: C, 50.96; H, 6.35; S, 11.66. Found: C, 51.11; H, 6.49; S, 11.42.

*1,2,3,4-Tetra-*O*-acetyl-6-deoxy-5-thio-α,β-D-glucopyranose* (**20**).—(*a*) To a solution of **18** (1.2 g, 5.4 mmol) in aq 50% AcOH (24 mL) was added 4% HCl (6 mL) at 70 °C. The mixture was kept at 70 °C for 3 h, then cooled to room temperature, and aq 6% $NaHCO_3$ (6 mL) was added. After concentration the residue was acetylated in 2:1 pyridine–Ac_2O (30 mL) overnight. The mixture was poured into ice–water and extracted with CH_2Cl_2 to give, after usual processing, **20** as a 4:1 mixture of its α and β anomers (1.6 g, 84%); ^1H NMR: α anomer, for data see Table 1, δ 2.18 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.00 (s, 3 H, OAc); β anomer, δ 5.87 (d, 1 H, H-1), 3.10 (m, 1 H, H-5), 1.22 (d, 3 H, H-6); $J_{1,2}$ 9.3 Hz; ^{13}C NMR: δ 169.75, 169.75, 169.61, 169.61 (C=O), 20.82, 20.44, 20.44, 20.44 (OAc); R_f 0.4 (solvent *B*). Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79; S, 9.20. Found: C, 48.39; H, 5.92; S, 9.38.

(*b*) To a solution of **32** (0.65 g, 2.0 mmol) in acetic anhydride (6.5 mL) was added concd H_2SO_4 (0.1 mL) at 0 °C and the mixture was kept at 0 °C for 1 h, then NaOAc was added to neutralize the sulfuric acid. The mixture was poured into ice–water and extracted with $CHCl_3$ to give after concentration **20** (0.6 g, 85%).

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-methanesulfonyl-5-thio-α-D-glucopyranoside* (**27**), *methyl 3-*O*-acetyl-2,5-anhydro-6-*O*-methanesulfonyl-2-thio-α-D-mannofuranoside* (**28**), *and methyl 3,6-di-*O*-acetyl-2,5-anhydro-2-thio-α-*D*-mannofuranoside* (**30**).—To a solution of **25** (2.1 g, 10 mmol) in pyridine (30 mL) was added mesyl chloride (0.9 mL, 11.6 mmol) in $CHCl_3$ (9.0 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, then acetic anhydride (10 mL) was added and the reaction was kept overnight at room temperature. The mixture was poured into ice–water, then extracted with CH_2Cl_2, and the organic layer was processed in the usual way. The residue obtained on concentration was submitted to column chromatography (solvent B, then A). Concentration of the first fraction gave **30** (0.32 g, 12%); $[\alpha]_D$ +82.5°; R_f 0.5 (solvent B); ^{1}H NMR: δ 3.35 (s, 3 H, OMe), 2.11 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), for further data see Table 1; ^{13}C NMR: δ 170.16, 169.38 (C=O), for further data see Table 2. Anal. Calcd for $C_{11}H_{16}O_6S$: C, 47.82; H, 5.84; S, 11.60. Found: C, 47.95; H, 5.92; S, 11.48.

Concentration of the second fraction yielded the acetylated starting material **26** [7] (1.15 g, 30%).

Concentration of the third fraction gave **28** as a syrup (0.23 g, 7%); $[\alpha]_D$ +45° (c 0.26, $CHCl_3$); R_f 0.2 (solvent B); ^{1}H NMR: δ 3.38 (s, 3 H, OMe), 3.05 (s, 3 H, OMs), 2.15 (s, 3 H, OAc), for further data see Table 1; ^{13}C NMR: δ 169.42 (C=O), for further data see Table 2. Anal. Calcd for $C_{10}H_{16}O_7S_2$: C, 38.45; H, 5.16; S, 20.53. Found: C, 38.39; H, 5.32; S, 20.38.

Concentration of the fourth fraction gave **27** (1.14 g, 28%); mp 135–137 °C; $[\alpha]_D$ +224°; R_f 0.3 (solvent A); ^{1}H NMR: δ 3.45 (s, 3 H, OMe), 3.05 (s, 3 H, OMs), 2.06 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.00 (s, 3 H, OAc), for further data see Table 1; ^{13}C NMR: δ 170.00, 169.66, 169.66 (C=O), 20.71, 20.51, 20.51 (OAc), for further data see Table 2. Anal. Calcd for $C_{14}H_{22}O_{10}S_2$: C, 40.57; H, 5.35; S, 15.47. Found: C, 40.71; H, 5.52; S, 15.39.

*Methyl 2,5-anhydro-3,6-di-*O*-methanesulfonyl-2-thio-α-*D*-mannofuranoside* (**29**).—To a solution of **25** (0.42 g, 2.0 mmol) in pyridine (7 mL) was added mesyl chloride (0.8 mL, 10.3 mmol) in $CHCl_3$ (8 mL) at 0 °C. The mixture was stirred at room temperature for 3 h, poured into ice–water, and extracted with $CHCl_3$. The organic layer was processed in the usual way to give, after column chromatography (solvent A) of the residue, **29** (0.45 g, 64%); mp 68–70 °C (MeOH); $[\alpha]_D$ +63°; R_f 0.5 (solvent A); ^{1}H NMR: δ 3.38 (s, 3 H, OMe), 3.14 (s, 3 H, OMs), 3.02 (s, 3 H, OMs), for further data see Table 1; ^{13}C NMR, for data see Table 2. Anal. Calcd for $C_9H_{16}O_8S_3$: C, 31.03; H, 4.63; S, 27.61. Found: C, 31.22; H, 4.72; S, 27.49.

*Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-5-thio-α-*D*-glucopyranoside* (**31**).—To a solution of **27** (0.45 g, 1.1 mmol) in 3-pentanone (30 mL) was added NaI (0.3 g, 2.0 mmol), and the mixture was stirred at reflux temperature for 3 h, cooled to room temperature, and filtered. The filtrate was concentrated, the residue was dissolved in $CHCl_3$, and the solution was washed with water to yield after concentration **31** (0.45 g, 93%); $[\alpha]_D$ +150° (c 0.3, $CHCl_3$); R_f 0.5 (solvent B); ^{1}H NMR: δ 3.45 (s, 3 H, OMe), 2.05 (2 s, 6 H, OAc), 2.00 (s, 3 H, OAc), for further data see Table 1; ^{13}C NMR: δ 170.00, 169.63, 169.63 (C=O), 20.73, 20.60, 20.50 (OAc), for further data see Table 2. Anal. Calcd for $C_{13}H_{19}IO_7S$: C, 34.99; H, 4.29; S, 7.18. Found: C, 35.12; H, 4.36; S, 7.34.

*Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-5-thio-α-*D*-glucopyranoside* (**32**).—To a stirred mixture of **31** (1.15 g, 2.6 mmol) and $NaBH_4$ (0.3 g, 7.9 mmol) in EtOH (35 mL) was added $NiCl_2 \cdot 6H_2O$ (30 mg, 0.13 mmol) in EtOH (3 mL) and stirring was continued at room temperature for 30 min. The mixture was neutralized with 4% HCl and filtered, the filtrate was concentrated, and the residue submitted to column chromatography (solvent *B*) to yield **32** (0.65 g, 79%); mp 92–95 °C, $[\alpha]_D$ +236°; R_f 0.5 (solvent *B*); ^1H NMR: δ 3.44 (s, 3 H, OMe), 2.05 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 1.98 (s, 3 H, OAc), for further data see Table 1; ^{13}C NMR: δ 170.07, 169.83, 169.67 (C=O), 20.76, 20.53, 20.53 (OAc), for further data see Table 2. Anal. Calcd for $C_{13}H_{20}O_7S$: C, 48.74; H, 6.29; S, 10.01. Found: C, 48.56; H, 6.03; S, 10.28.

Methyl 2,5-anhydro-3-O-methanesulfonyl-6-O-methyl-2-thio-α-D-mannofuranoside (**33**) *and methyl* 2,6-*anhydro*-3-O-methanesulfonyl-5-O-methyl-2-thio-β-L-*gulofuranoside* (**34**).—To a solution of **29** (0.45 g, 1.3 mmol) in MeOH (30 mL) was added $BaCO_3$ (1.1 g, 5.6 mmol) and the mixture was stirred at reflux temperature for 20 h, then cooled to room temperature. The salts were filtered off, the filtrate was concentrated, and the residue submitted to column chromatography (solvent *B*). Concentration of the first fraction yielded **33** (0.16 g, 44%); mp 73–76 °C (EtOAc–hexane); $[\alpha]_D$ +99°; R_f 0.7 (solvent *A*); ^1H NMR: δ 3.37 (s, 3 H, OMe), 3.36 (s, 3 H, OMe), 3.12 (s, 3 H, OMs), for further data see Table 1; ^{13}C NMR, for data see Table 2. Anal. Calcd for $C_9H_{16}O_6S_2$: C, 38.02; H, 5.67; S, 22.55. Found: C, 38.21; H, 5.72; S, 22.39.

On storage at room temperature **33** decomposed and gave the known [7] 5-(methoxymethyl)thiophene-2-aldehyde (**47**).

Concentration of the second fraction gave **34** as a syrup (0.15 g, 41%); $[\alpha]_D$ +75°; R_f 0.6 (solvent *A*); ^1H NMR: δ 3.42 (s, 3 H, OMe), 3.40 (s, 3 H, OMe), 3.14 (s, 3 H, OMs), for further data see Table 1; ^{13}C NMR, for data see Table 2. Anal. Calcd for $C_9H_{16}O_6S_2$: C, 38.02; H, 5.67; S, 22.55. Found: C, 38.15; H, 5.58; S, 22.44.

Methyl 2,5:3,6-dianhydro-2-thio-α-D-mannofuranoside (**35**).—To a solution of **28** (0.23 g, 0.7 mmol) in MeOH (5 mL) was added 3 M NaOMe in MeOH (0.28 mL), and the mixture was kept overnight at room temperature, then neutralized with solid CO_2, and concentrated. The residue was submitted to column chromatography (solvent *D*) to yield **35** (0.10 g, 78%); $[\alpha]_D$ +219°, R_f 0.7 (solvent *D*); ^1H NMR: δ 3.36 (s, 3 H, OMe), for further data see Table 1; ^{13}C NMR, for data see Table 2. Anal. Calcd for $C_7H_{10}O_3S$: C, 48.26; H, 5.79; S, 18.40. Found: C, 48.15; H, 5.83; S, 18.29.

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