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Carbohydrate Research 282 (1996) 207–221

CARBOHYDRATE RESEARCH

Novel conversion of aldopyranosides into 5-thioaldopyranosides via acyclic monothioacetals with inversion and retention of configuration at C-5

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Received 9 September 1995; accepted 15 November 1995

Abstract

A new strategy for synthesis of 5-thioaldopyranosides was developed. This included the ring opening of D-aldopyranosides with dimethylboron bromide and thioacetic acid, giving the acyclic monothioacetals, followed by the intramolecular cyclization between C-5 and 1-S. Cyclization with inversion of configuration at C-5 was achieved by simultaneous *S*-deacetylation and intramolecular nucleophilic substitution of the 5-methanesulfonylated monothioacetal to give 5-thio-L-aldopyranosides. The 5-hydroxymonothioacetal underwent cyclization with the Mitsunobu reagents to give the same 5-thio-L-aldopyranosides. Syntheses of 5-thio-D-glucopyranosides were achieved by double inversion of C-5. The glycos-5-ulose derivatives of the monothioacetals spontaneously cyclized on *S*-deacetylation to give 5-*C*-hydroxyl-5-thio-D-glucopyranosides, which were deoxygenated at C-5 to give 5-thio-D-glucopyranosides, with net retention of configuration at C-5 from the monothioacetal. Stereoselective reduction of the glycos-5-ulose followed by intramolecular cyclization with the Mitsunobu reagents also gave 5-thio-D-glucopyranosides. The strategy for L enantiomers was applied to the synthesis of 5-thio-L-galactose. The inhibitory effect of 5-thio-L-galactose toward α-L-fucosidase (K_i 960 μM) is also reported.

Keywords: Thio sugar; 5-Thio-D-glucose; 5-Thio-L-idose; 5-Thio-L-galactose; Fucosidase inhibitor

1. Introduction

In both chemical and biochemical conversions of carbohydrates, cleavage and formation of carbon–oxygen bonds at the anomeric center are the most important

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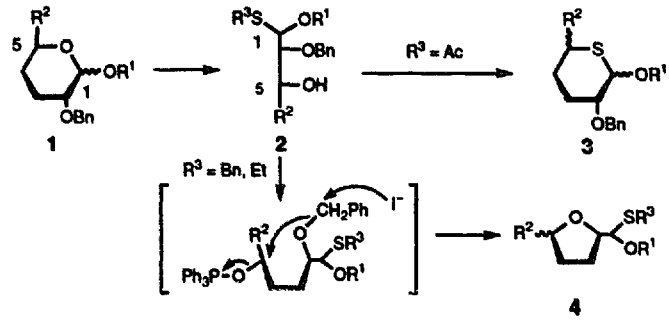
SSDI 0008-6215(95)00386-X



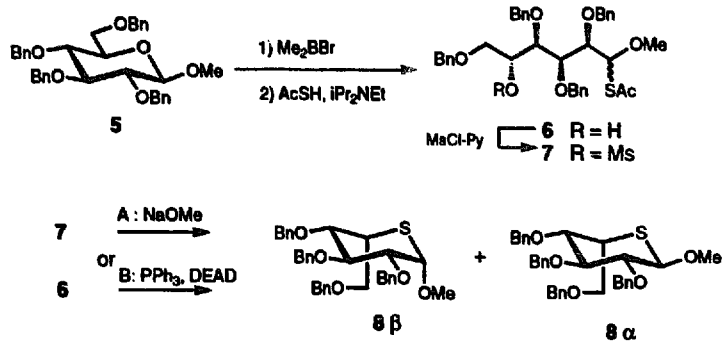
Scheme 1.

reactions, and the ring oxygen in the furanose or pyranose structure plays a decisive role. In this sense "pseudo sugars" which have atoms in the ring other than oxygen have attracted attention, and a number of nitrogen (imino sugar) [1], sulfur (thio sugar) [2–12], phosphorus [13] as well as carbon (carba sugar) [14] analogs have been synthesized. It is well known that protonated "imino sugars" can interact with catalytic site of glycosidases and inhibit enzyme activities so strongly that, in some cases, slight modification of the structure leaves the activity intact [1]. The number of synthetic reports on "imino sugars" has increased enormously during the past ten years. On the other hand, the synthesis of "thio sugars" has a longer history, and examples have been reported over a longer time-interval. The D-xylose analog was first reported in 1961 [2], followed by analogs of D-glucose [3] and D-ribose [4] in the 1960s. Those of L-arabinose [5], D-fructose [6], L-rhamnose [7], *N*-acetylglucosamine [8], and D-galactose [9] were described in the 1970s, and that of *N*-acetylneuraminic acid [10] in 1987. Recently, D-mannose [11] and L-fucose [12] analogs were added to the list by us. In addition, these two analogs showed new aspects of the chemistry of "thio sugars", that is, the former is the first naturally occurring thio sugar [15], and the latter was found to be a potent inhibitor of bovine α-L-fucosidase. However, synthesis of these analogs requires quite a tedious and long synthetic route; namely, conversion of the pyranose structure into a furanose in order to introduce sulfur at C-5. We therefore determined to establish a facile synthetic strategy for 5-thiopyranosides.

Guindon and Anderson have recently reported an attractive method for ring opening of pyranosides with dimethylboron bromide (Me_2BBr) [16]. This method involves introduction of a sulfur function at C-1 and simultaneous differentiation of the 5-hydroxy group. Subsequent carbon–sulfur bond formation between these two functional groups may thus provide a novel and effective synthetic method for 5-thiopyranoses, namely, by conversion of pyranoside **1** into 5-thiopyranoside **3** via monothioacetal **2** [17], as shown in Scheme 1.

2. Results and discussion

S-Benzyl and *S*-ethyl acyclic monothioacetals **2** ($R^3 = PhCH_2$, CH_3CH_2) could not be converted into 5-thiopyranoside **3** by the method used for the synthesis of 5-thiopen-



Scheme 2.

topyranosides employing triphenylphosphine and triiodoimidazole, instead the undesired 2,5-anhydro derivative **4** was obtained, probably through the mechanism shown in Scheme 1. On the other hand, the *S*-acetyl derivative **2** (R^3 = Ac) proved useful as an intermediate for the preparation of **3**, as described below.

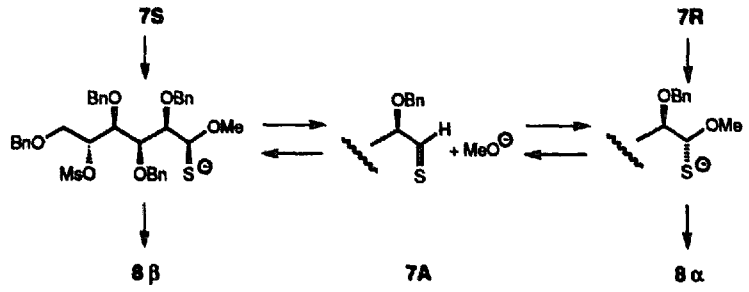
Conversion of methyl D-*glucopyranoside into methyl 5-thio-*L-*idopyranoside.*—Treatment of per-*O*-benzylated methyl β-D-glucopyranoside (**5**) with Me_2BBr and then AcSH-iPr_2NEt gave the *S*-acetyl *O*-methyl monothioacetal **6** as a diastereomeric mixture with a 1.2–1:1 ratio of the *S*-isomer (**6S**) and the *R*-isomer (**6R**), the ratio depending on the reaction temperature of the second step. Each isomer, as well as a 1:1 diastereomeric mixture, was methylsulfonylated and treated with sodium methoxide in methanol to give the desired 5-thio-L-idopyranoside (**8**) as shown in Scheme 2 and Table 1 (Method A). Because this cyclization should proceed with inversion and retention of configuration at C-5 and C-1, respectively, the configuration at C-1 in monothioacetal **2** can be confirmed by the anomeric configuration in 5-thiopyranoside **3**. As shown in Table 1, however, partial isomerization at C-1 occurred, probably through the thioaldehyde (**7A** in Scheme 3).

The second and more efficient method (B) was found during treatment of **6** with triphenylphosphine and diethyl azodicarboxylate (DEAD) in the presence of benzoic acid with the intention of inverting the configuration at C-5. Instead of the desired 5-benzoate, the 5-thio-L-idopyranoside was obtained without any epimerization at C-1.

Table 1
Cyclization of monothioacetal to 5-thiopyranoside

Method [a]	Monothioacetal		5-Thiopyranoside	
	Compound	*S*/*R*	8β/8α	Yield (%)
A	**7**	1:1	1:1	59
A	**7**	1:0	7:3	69
A	**7**	0:1	1:4	73
B	**6**	3:4	4:3	64
B	**6**	1:0	1:0	56
B	**6**	0:1	0:1	64

[a] A: MeONa/MeOH; B: PPh_3, DEAD.



Scheme 3.

as shown in Table 1. Since the corresponding *S*-benzyl monothioacetal did not react at all under the same conditions, the mechanism of this reaction is presumably the one depicted in Fig. 1. The conformation of 5-thio-L-idopyranosides **8β** and **8α** was confirmed to be $^{4}C_{1}$ from the coupling constants of their ring protons, as shown in Table 2, where the dihedral angles were calculated from the modified Karplus equation [18]. This result stands in sharp contrast to the ring oxygen analogs, which have the $^{1}C_{4}$ conformation [19]. Recently Hughes reported the same results for per-*O*-acetylated methyl 5-thio-L-idopyranoside and attributed it to the "hockey stick" effect of the ring sulfur atom [20].

Conversion of a D-*glucopyranoside into a 5-thio*-D-*glucopyranoside.*—If the configuration of C-5 in monothioacetal **6** could be inverted, the same methods as just described might provide thio sugars having the D-*gluco* configuration. However, attempts at conventional substitution reactions ended in formation of the 2,5-anhydro derivative **4**. Thus, two methods via glycos-5-ulose derivatives (**9**), which were obtained by Swern oxidation of **6**, were developed. On *S*-deacetylation of the glycos-5-ulose **9S** with

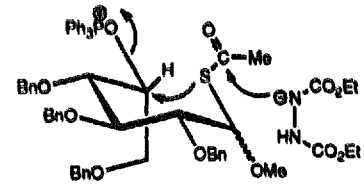
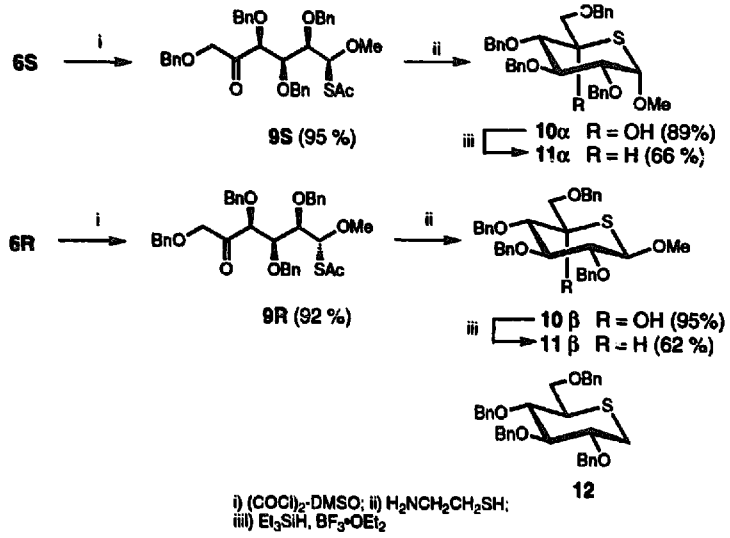


Fig. 1. Possible mechanism of the cyclization of **6** with the Mitsunobu system.

Table 2
Dihedral angles between ring protons of **8α** and **8β** calculated from the coupling constants using the modified Karplus equation [a]

		H1-H2	H2-H3	H3-H4	H4-H5
8α	*J* (Hz)	8.4	8.2	5.6	5.2
	φ (°)	168	198	167	−48
8β	*J* (Hz)	3.2	9.3	9.5	4.3
	φ (°)	53	190	175	−53

[a] Ref. [18].



Scheme 4.

2-aminoethanethiol, cyclization occurs spontaneously by nucleophilic attack of sulfur to give the thermodynamically stable D-*gluco* isomer **10**α. Treatment of **10**α with triethylsilane (Et_3SiH) in the presence of boron trifluoride etherate ($BF_3 \cdot OEt_2$) gave the corresponding 5-thio-α-D-glucopyranoside **11**α in 66% yield. In the same manner, the epimer **6R** was converted into the 5-thio-β-D-glucopyranoside **11**β, as shown in Scheme 4.

The deoxygenation reaction of **10** with Et_3SiH proved to be rather sensitive to the conditions used, especially the amount of acid. $BF_3 \cdot OEt_2$ gave better results than trifluoromethanesulfonic acid, as shown in Table 3. While the less-reactive α anomer **10**α requires 4 equiv of $BF_3 \cdot OEt_2$ for the best yield (entry 6), only 1.2 equiv, even at a lower temperature, is enough for the β anomer **10**β (entry 8). As shown in entry 7, the higher equivalent of acid gave demethoxylated (**12**) and anomerized (**11**α) products,

Table 3
Reduction of **10** with Et_3SiH in the presence of acid

Entry	Substrate	Reagent		Condition			Yield (%) of product			
		Et_3SiH (equiv)	Acid [a]	Solvent	Temp (°C)	Time (h)	**11**α	**11**β	**12**	SM
1	**10**α	2	A (3)	CH_3CN	rt	24	15			
2	**10**α	2	A (1)	CH_3CN	rt	24	40			
3	**10**α	2	A (0.3)	CH_3CN	rt	24	0			
4	**10**α	1	B (2)	CH_3CN	−40 to 0	3.3	23			
5	**10**α	4	B (1.5)	CH_2Cl_2	−10	1.2	52			30
6	**10**α	6	B (4)	CH_2Cl_2	−10	1	66		8.5	8
7	**10**β	6	B (4)	CH_2Cl_2	−10	1	11	16	25	
8	**10**β	1.2	B (1.2)	CH_2Cl_2	−45 to −15	2	trace	62	trace	

[a] A: CF_3CO_2H (M); B: $BF_3 \cdot OEt_2$ (equiv.).

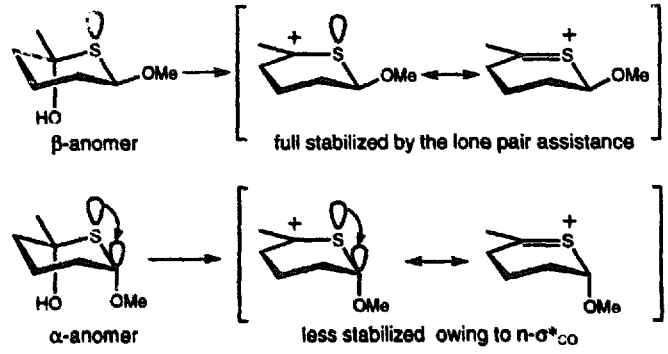


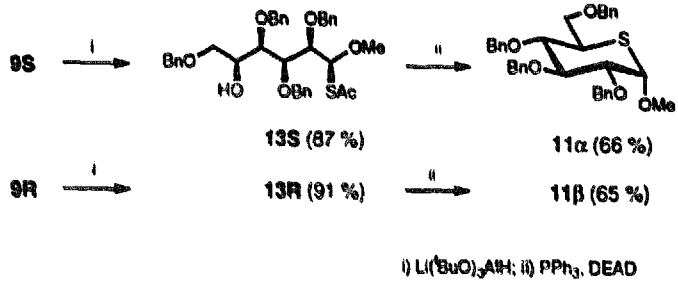
Fig. 2. Difference between α and β anomers in stabilization of the C-5 carbenium ion by the ring sulfur atom in the deoxygenation reaction of **10**.

together with the desired product **11β**. Thus this deoxygenation seems to require optimization of conditions according to the substrate.

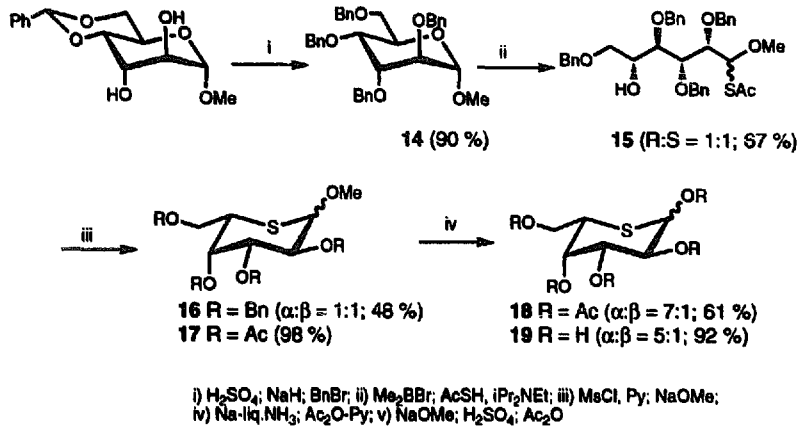
The reactivity difference between the α and β anomers is explainable by the anomeric effect as follows (Fig. 2). The driving force of the reaction obviously is the stabilization of the carbenium or radical intermediate by lone-pair participation from the ring sulfur atom. It is well documented that the ring sulfur atom of α-glycosides is less nucleophilic than that of β-glycosides because the orbital energy of the lone pair is lowered by back donation to the glycosidic bond (n–σ^*_{CO}) in the case of the α-glycosides [21]. This nucleophilicity difference may be reflected by the participation ability of the ring sulfur atom to the carbenium ion or radical center at C-5, thereby lowering the stability of the carbenium or radical intermediate for the α anomer. This could be a new example that shows a reactivity difference attributable to an anomeric effect in a position other than the anomeric center [22].

As an alternative method of inversion, reduction of the glycosulose **9** with lithium tri-*tert*-butoxyaluminum hydride was found to be highly stereoselective, giving the L-*ido* derivative **13** preferentially with diastereomeric ratios of 94:6 and 95:5 for the *S*- and *R*-isomers, respectively. Cyclization of **13S** and **13R** with the Mitsunobu reagents as already described gave 5-thio-α-D-glucopyranoside **11α** and its β anomer **11β**, respectively, as shown in Scheme 5.

*Synthesis of 5-thio-*L*-galactose.*—5-Thio-L-fucose is a potent inhibitor of α-L-fucosidase from the bovine kidney (K_i 84 μM) [12]. To understand the reason for such



Scheme 5.



Scheme 6.

a high affinity, it is desirable to synthesize a number of derivatives and compare their inhibitory activities. 5-Thio-L-galactose (**19**) is a 6-hydroxy derivative of 5-thio-L-fucose and may provide information about the recognition mechanism. Thus the already described method, with inversion of configuration at C-5 of a D-altropyranoside, was applied to the synthesis of **19** (Scheme 6). Treatment of per-*O*-benzylated methyl α-D-altropyranoside (**14**), prepared from methyl 4,6-*O*-benzylidene-α-D-altropyranoside [23], with Me_2BBr and then AcSH-iPr_2NEt, gave the *S*-acetyl *O*-methyl monothioacetal (**15**) as a diastereomeric mixture in 1:1 ratio. The monothioacetal **15** was cyclized by Method A, as shown in Scheme 2, to give 5-thio-L-galactopyranoside **16** (α:β = 1:1) in 48% yield. Birch reduction of **16** followed by acetylation gave a mixture of peracetylated methyl 5-thio-α-L- and β-L-galactopyranosides (**17**α and **17**β), whose physical and spectral data coincide with those of the corresponding D enantiomers [9] except for the sign of their optical rotations ($[\alpha]_D = -242°$ and $-5.8°$ for **17**α and **17**β, and

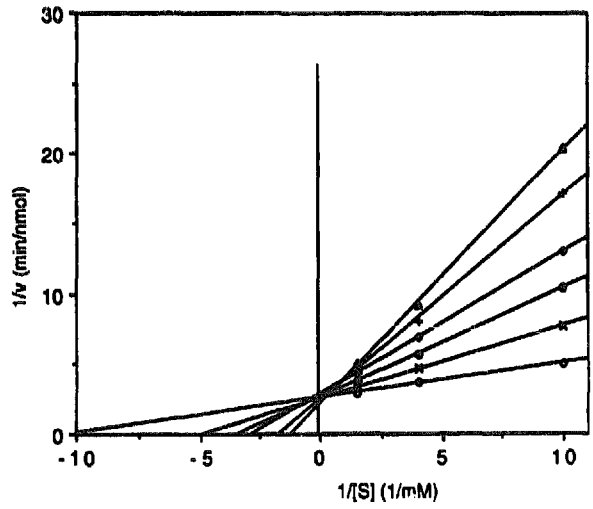


Fig. 3. Lineweaver–Burk plot showing inhibition of α-L-fucosidase from the bovine kidney with 5-thio-L-galactose (**19**): [*I*] (mM): ○ 0, × 1.5, ● 3.0, ◆ 4.5, + 6.0, ▲ 7.5.

+225.5° and +9.5° for the corresponding D enantiomers). Hydrolysis of **17** and subsequent acetylation afforded per-*O*-acetylated 5-thio-L-galactose (**18**), deacetylation of which gave 5-thio-L-galactose (**19**). We confirmed that **19** could be converted into the known per-*O*-acetylated 5-thio-L-fucopyranose [12] in 4 steps through deoxygenation of the 1,2;3,4-di-*O*-isopropylidene-6-*O*-tosyl derivative.

Inhibitory effect of 5-thio-L-galactose (**19**) *toward α-L-fucosidase.*—As shown in the Lineweaver–Burk plot (Fig. 3), **19** showed competitive inhibition toward α-L-fucosidase from the bovine kidney and K_i was determined to be 960 μM from the second plot. This result indicates that the α-L-fucosidase strictly recognizes the methyl residues of L-fucose and 5-thio-L-fucose, and the presence of the hydroxyl group at C-6 disturbs the recognition. The free energy of the disturbance is estimated to be 1.5 kcal/mol from the difference in K_i between 5-thio-L-fucose and 5-thio-L-galactose. This value may originate from the absence of the hydrophobic effect of methyl group and repulsion between the recognition site and 6-OH.

3. Experimental

Melting points were measured with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Jasco DIP-4 polarimeter. Column chromatography was performed on Merck Kieselgel 60 (Art 7734) or Wako gel C-300 with the solvent systems specified. ^{1}H NMR spectra were recorded with a JEOL JNM-FX-90Q, JNM-PS-100, JNM-EX-270, or JNM-GX-500 spectrometer. ^{13}C NMR spectra were recorded with a JEOL JNM-FX-90Q or JNM-EX-270 spectrometer. Chemical shifts were recorded as δ values in parts per million (ppm) from tetramethylsilane as an internal standard in $CDCl_3$. In D_2O, acetone (δ^1_H = 2.23 ppm and δ^{13}_C = 30.6 ppm) was used as an internal standard.

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-D-glucose S-acetyl O-methyl monothioacetal (**6S** *and* **6R**).—To a stirred solution of **5** (3.00 g, 5.4 mmol) in CH_2Cl_2 (60 mL) was added a 1.0 M solution of Me_2BBr in CH_2Cl_2 (10.8 mL) at −78 °C under Ar. After 30 min, iPr_2NEt (2.37 mL, 13.6 mmol) and then AcSH (1.14 mL, 16.1 mmol) were added. The temperature was gradually increased to room temperature during 90 min. Ice–water was added and the mixture was extracted with CH_2Cl_2, which was then successively washed with aq $NaHCO_3$, 5% HCl, and H_2O. The organic layer was dried over $MgSO_4$, evaporated, and chromatographed on a silica gel (10:1–5:1 hexane–EtOAc) to give **6S** (1.49 g, 44%) and **6R** (1.24 g, 36%), respectively, as a syrup.

6S: $[\alpha]_D^{25}$ +24.3° (*c* 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.49 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 4.95–3.58 (m, 14 H, H-2,3,4,5,6, PhCH_2), 3.25 (s, 3 H, OMe), 2.96 (bs, 1 H, OH), 2.33 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 195.8 (S*C*=O), 138.6, 138.3, 138.1, 128.4, 128.2, 128.1, 127.9, 127.7, 127.5 (Ar), 88.8 (C-1), 82.3, 79.7, 77.9, 75.1, 74.9, 73.4, 73.1, 71.4, 70.5 (C-2,3,4,5,6, PH*C*H_2), 56.4 (OMe), 31.1 (SAc). Anal. Calcd for $C_{37}H_{42}O_7S$: C, 70.45; H, 6.71; S, 5.08. Found: C, 70.10; H, 6.77; S, 4.85.

6R: $[\alpha]_D^{25}$ −15.3° (*c* 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.62 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 4.93–3.60 (m, 14 H, H-2,3,4,5,6, PhCH_2), 3.30 (s, 3 H,

OMe), 2.96 (bs, 1 H, OH), 2.37 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 196.2 (S*C*=O), 138.1, 138.0, 128.4, 128.1, 127.9, 127.7 (Ar), 86.9 (C-1), 81.5, 79.1, 77.6, 75.4, 74.8, 73.4, 73.2, 71.3, 70.9 (C-2,3,4,5,6, Ph*C*H_2), 56.7 (OMe), 31.1 (SAc). Anal. Calcd for $C_{37}H_{42}O_7S$: C, 70.45; H, 6.71; S, 5.08. Found: C, 70.34; H, 6.73; S, 4.55.

*(1S)-2,3,4,6-Tetra-*O*-benzyl-5-*O*-methanesulfonyl-*D*-glucose* S*-acetyl* O*-methyl monothioacetal* (**7S**).—To a stirred solution of **6S** (155 mg, 0.246 mmol) in pyridine (3 mL) was dropped methanesulfonyl chloride (29 μL, 0.38 mmol) at 0 °C. After 12 h at room temperature, the mixture was evaporated and partitioned between CH_2Cl_2 and H_2O. The organic layer was dried over $MgSO_4$, evaporated, and chromatographed on a silica gel (5:1 hexane–EtOAc) to give **7S** (148 mg, 85%) as a syrup: $[\alpha]_D^{21}$ +41.3° (*c* 3.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.40 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1), 4.96–3.67 (m, 14 H, H-2,3,4,5,6, PhCH_2), 3.25 (s, 3 H, OMe), 2.91 (s, 3 H, OMs), 2.39 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 195.8 (S*C*=O), 138.5, 138.0, 137.8, 128.6, 128.4, 128.3, 128.1, 127.8, 127.7, 127.5 (Ar), 88.0 (C-1), 83.9, 82.2, 80.4, 80.1, 75.5, 74.8, 74.6, 73.3, 69.3 (C-2,3,4,5,6, Ph*C*H_2), 56.3 (OMe), 38.2 (OMs), 31.1 (SAc). Anal. Calcd for $C_{38}H_{44}O_9S_2$: C, 64.38; H, 6.26; S, 9.05. Found: C, 64.33; H, 6.37; S, 9.57.

*(1R)-2,3,4,6-Tetra-*O*-benzyl-5-*O*-methanesulfonyl-*D*-glucose* S*-acetyl* O*-methyl monothioacetal* (**7R**).—Compound **6R** (96 mg, 0.153 mmol) was treated with methanesulfonyl chloride (18 μL, 0.23 mmol) as just described for **6S** to give **7R** (106 mg, 98%) as a syrup: $[\alpha]_D^{21}$ −9.2° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.53 (d, 1 H, $J_{1,2}$ 2.6 Hz, H-1), 4.92 (m, 1 H, H-5), 4.8–4.4 (m, 8 H, PhCH_2), 4.1–3.7 (m, 5 H, H-2,3,4,6), 3.35 (s, 3 H, OMe), 2.90 (s, 3 H, OMs), 2.36 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 195.9 (S*C*=O), 138.0, 137.9, 137.7, 128.3, 128.2, 127.7 (Ar), 86.3 (C-1), 83.2, 81.1, 80.3, 79.1, 75.3, 74.9, 74.8, 73.3, 69.2 (C-2,3,4,5,6, Ph*C*H_2), 56.9 (OMe), 38.3 (OMs), 31.1 (SAc). Anal. Calcd for $C_{38}H_{44}O_9S_2$: C, 64.38; H, 6.26; S, 9.05. Found: C, 64.01; H, 6.35; S, 8.94.

*Methyl 2,3,4,6-Tetra-*O*-benzyl-5-thio-α- and β-*L*-idopyranoside* (**8a** *and* **8b**).—*Method A*. To a stirred solution of **7S** (148 mg, 0.208 mmol) in MeOH (3 mL) was dropped 0.36 M NaOMe (1.16 mL, 0.42 mmol). After being stirred for 10 h at room temperature, the mixture was neutralized with Dowex 50 (H^+) ion-exchange resin. After removal of the insoluble material, the filtrate was evaporated and chromatographed on silica gel (10:1 hexane–EtOAc) to give **8α** (18 mg, 15%) and **8β** (68 mg, 58%), respectively, as syrups.

Method B. To a stirred solution of **6S** (78 mg, 0.124 mmol) and PPh_3 (130 mg, 0.496 mmol) in benzene (5 mL) was dropped DEAD (75 μL, 0.50 mmol) at 0 °C. After being stirred for 15 h at room temperature, the reaction mixture was evaporated and chromatographed on a silica gel (10:1–8:1 hexane–EtOAc) to give **8b** (40 mg, 56%) as a syrup.

8α: $[\alpha]_D^{25}$ −67.2° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 4.86 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.84, 4.73 (each d, each 1 H, *J* 11.0 Hz, PhCH_2), 4.73 (s, 2 H, PhCH_2), 4.67, 4.60 (each d, each 1 H, *J* 11.6 Hz, PhCH_2), 4.59 (s, 2 H, PhCH_2), 3.93 (dd, 1 H, $J_{3,4}$ 8.6, $J_{4,5}$ 5.2 Hz, H-4), 3.86 (dd, 1 H, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 9.5 Hz, H-6a), 3.76 (dd, 1 H, $J_{2,3}$ 8.2 Hz, H-3), 3.73 (dd, 1 H, $J_{5,6b}$ 4.0 Hz, H-6b), 3.68 (t, 1 H, H-2), 3.50 (s, 3 H, OMe), 3.13 (dd, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 138.9, 138.3, 128.0,

127.9, 127.7, 127.6 (Ar), 85.6, 84.7, 81.9, 81.7 (C-1,2,3,4), 73.1 (PhCH$_2$), 69.5 (C-6), 58.7 (OMe), 40.9 (C-5). Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.65; H, 6.71; S, 5.62. Found: C, 73.32; H, 6.93; S, 5.37.

8β: $[\alpha]_D^{25}$ −23.2° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 4.86, 4.80 (each d, each 1 H, *J* 10.2 Hz, PhCH_2), 4.78, 4.65 (each d, each 1 H, *J* 11.9 Hz, PhCH_2), 4.68, 4.64 (each d, each 1 H, *J* 11.4 Hz, PhCH_2), 4.55 (s, 2 H, PhCH_2), 4.36 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.01 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 4.3 Hz, H-4), 3.92 (dd, 1 H, $J_{5,6a}$ 5.2, $J_{6a,6b}$ 9.5 Hz, H-6a), 3.84 (t, 1 H, $J_{2,3}$ 9.4 Hz, H-3), 3.83 (t, 1 H, $J_{5,6b}$ 9.6 Hz, H-6b), 3.77 (dd, 1 H, H-2), 3.38 (s, 3 H, OMe), 3.21 (m, 1 H, H-5); ^{13}C NMR ($CDCl_3$): δ 139.0, 138.4, 128.5, 128.3, 128.1, 128.0, 127.6 (Ar), 84.1, 83.7, 83.0, 78.9 (C-1,2,3,4), 73.4, 73.3 (PhCH$_2$), 69.8 (C-6), 56.3 (OMe), 43.2 (C-5). Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.65; H, 6.71; S, 5.62. Found: C, 73.56; H, 7.01; S, 6.10.

(1S)-2,3,4,6-Tetra-O-*benzyl*-D-xylo-*hexos-5-ulose* S-*acetyl* O-*methyl monothioacetal* (**9S**).—To a stirred solution of oxalyl chloride (84 μL, 0.99 mmol) in CH_2Cl_2 (2 mL) was slowly added Me_2SO (140 μL, 1.97 mmol) in CH_2Cl_2 (4 mL) at −78 °C. After the mixture had been stirred for 10 min, a solution of **6S** (415 mg, 0.657 mmol) in CH_2Cl_2 (2 mL) was slowly added and the mixture was stirred for further 1 h. Triethylamine (273 μL, 1.97 mmol) was added and the mixture was stirred for 30 min. After checking completion of the reaction by TLC the temperature was gradually increased to room temperature. The mixture was diluted with CH_2Cl_2, washed successively with 5% HCl, satd $NaHCO_3$, and H_2O, dried ($MgSO_4$), evaporated, and chromatographed on silica gel (10:1 hexane–ethyl acetate) to give **9S** (391 mg, 95%) as a syrup: $[\alpha]_D^{18}$ +12.0° (*c* 2.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.1 (m, 20 H, Ar), 5.35 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.9–4.0 (m, 13 H, H-2,3,4,6, PhCH_2), 3.21 (s, 3 H, OMe), 2.33 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 206.9 (C-5), 195.9 (S*C*=O), 138.5, 137.8, 137.4, 137.1, 128.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.5 (Ar), 88.3 (C-1), 82.9, 81.8, 80.5, 75.4, 75.2, 74.5, 73.9, 73.3 (C-2,3,4,6, PH*C*H$_2$), 56.3 (OMe), 31.2 (SAc). Anal. Calcd for $C_{37}H_{40}O_7S$: C, 70.68; H, 6.41; S, 5.10. Found: C, 70.76; H, 6.59; S, 5.11.

(1R)-2,3,4,6-Tetra-O-*benzyl*-D-xylo-*hexos-5-ulose* S-*acetyl* O-*methyl monothioacetal* (**9R**).—Compound **6R** (154 mg, 0.243 mmol) was treated with oxalyl chloride (31 μL, 0.37 mmol), Me_2SO (78 μL, 1.1 mmol), and Et_3N (101 μL, 0.73 mmol) as already described for the synthesis of **9S** to give **9R** (141 mg, 92%) as a syrup: $[\alpha]_D^{26}$ −45.9° (*c* 2.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.1 (m, 20 H, Ar), 5.52 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 4.9–3.9 (m, 13 H, H-2,3,4,6, PhCH_2), 3.28 (s, 3 H, OMe), 2.37 (s, 3 H, SAC); ^{13}C NMR ($CDCl_3$): δ 206.7 (C-5), 195.8 (S*C*=O), 137.8, 137.0, 128.4, 128.3, 128.1, 127.8 (Ar), 86.4 (C-1), 82.0, 80.0, 75.1, 75.0, 74.5, 73.8, 73.3 (C-2,3,4,6, PhCH_2), 56.8 (OMe), 31.1 (SAc). Anal. Calcd for $C_{37}H_{40}O_7S$: C, 70.68; H, 6.41; S, 5.10. Found: C, 70.33; H, 6.30; S, 5.21.

Methyl 2,3,4,6-tetra-O-*benzyl-5*-C-*hydroxy-5-thio*-α-D-*glucopyranoside* (**10α**).—To a stirred solution of **9S** (195 mg, 0.309 mmol) in CH_3CN (10 mL) was added 2-aminoethanethiol (29 mg, 0.371 mmol) at 65 °C under Ar. After 2 h, the mixture was evaporated and chromatographed on silica gel (6:1 hexane–EtOAc) to give **10α** (161 mg, 89%) as a syrup: $[\alpha]_D^{16}$ +28° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 4.98, 4.86 (each d, each 1 H, *J* 10.5 Hz, PhCH_2), 4.91, 4.62 (each d, each 1 H,

J 11.2 Hz, PhCH_2), 4.84, 4.68 (each d, each 1 H, *J* 11.9 Hz, PhCH_2), 4.5–4.4 (m, 3 H, PhCH_2, H-1), 4.24 (t, 1 H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H-3), 4.23 (s, 1 H, OH), 4.00 (d, 1 H, H-4), 3.89 (dd, 1 H, $J_{1,2}$ 3.1 Hz, H-2), 3.68 (d, 1 H, $J_{6a,6b}$ 9.8 Hz, H-6a), 3.49 (s, 3 H, OMe), 3.45 (d, 1 H, H-6b); ^{13}C NMR ($CDCl_3$): δ 138.9, 138.4, 138.1, 137.6, 128.6, 128.3, 128.2, 128.0, 127.8, 127.6 (Ar), 83.6 (C-5), 86.3, 86.2, 85.1, 84.1, 80.1, 76.4, 73.6, 73.4, 72.4 (C-1,2,3,4,6, Ph*C*H_2), 57.4 (OMe). Anal. Calcd for $C_{35}H_{38}O_6S$: C, 71.65; H, 6.53; S, 5.47. Found: C, 71.57; H, 6.67; S, 5.41.

Methyl 2,3,4,6-tetra-O-*benzyl-5*-C-*hydroxy-5-thio-β*-D-*glucopyranoside* (**10β**).—Compound **9R** (51 mg, 0.081 mmol) was treated with 2-aminoethanethiol (9 mg, 0.12 mmol) as already described for the synthesis of **10α** to give **10β** (45 mg, 95%) as a syrup: $[\alpha]_D^{23}$ −115° (*c* 3.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 4.93–4.74 (m, 6 H, PhCH_2), 4.55–4.50 (m, 4 H, PhCH_2, OH, H-1), 3.98–3.84 (m, 3 H, H-2,3,4), 3.56 (d, 1 H, $J_{6a,6b}$ 9.6 Hz, H-6a), 3.53 (s, 3 H, OMe), 3.36 (d, 1 H, H-6b); ^{13}C NMR ($CDCl_3$): δ 138.6, 138.5, 137.8, 137.3, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 127.6 (Ar), 83.4 (C-5), 86.1, 84.2, 83.0, 82.4, 76.2, 75.7, 75.6, 73.7, 73.1 (C-1,2,3,4,6, Ph*C*H_2), 58.9 (OMe). Anal. Calcd for $C_{35}H_{38}O_6S$: C, 71.65; H, 6.53; S, 5.47. Found: C, 71.40; H, 6.36; S, 5.34.

Methyl 2,3,4,6-tetra-O-*benzyl-5-thio-α*-D-*glucopyranoside* (**11α**).—(*1*) To a stirred solution of **10α** (112 mg, 0.190 mmol) in CH_2Cl_2 (5 mL) was added Et_3SiH (182 μL, 1.14 mmol) followed by $BF_3 \cdot OEt_2$ (96 μL, 0.76 mmol) at −10 °C under Ar. After 1 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, evaporated, and chromatographed on silica gel (7:1–4:1 hexane–EtOAc) to give **11α** (72 mg, 66%) and 1,5-anhydro-2,3,4,6-tetra-*O*-benzyl-1-deoxy-5-thio-D-glucitol **12** (9 mg, 8.5%), respectively as a syrup.

(*2*) Compound **13S** (37 mg, 0.059 mmol) was treated with PPh_3 (31 mg, 0.118 mmol) and DEAD (18 μL, 0.12 mmol) as already described for the synthesis of **8** (Method B) to give **11α** (22 mg, 66%) as a syrup.

11α: NMR spectra were in accordance with the literature [24].

12: ^{1}H NMR ($CDCl_3$): δ 7.4–7.1 (m, 20 H, Ar), 5.0–4.5 (m, 8 H, PhCH_2), 3.9–3.3 (m, 5 H, H-2,3,4,6), 2.94 (ddd, 1 H, $J_{4,5}$ 10.2, $J_{5,6a}$ 3.0, $J_{5,6b}$ 5.3 Hz, H-5), 2.79 (dd, 1 H, $J_{1e,1a}$ 13.2, $J_{1e,2}$ 4.5 Hz, H-1e), 2.55 (dd, 1 H, $J_{1a,2}$ 10.9 Hz, H-1a); ^{13}C NMR ($CDCl_3$): δ 139.0, 138.4, 137.9, 128.4, 128.1, 127.9, 127.7 (Ar), 87.8, 82.5, 82.2 (C-2,3,4), 76.1, 73.3, 72.8 (Ph*C*H_2), 68.5 (C-6), 47.4 (C-5), 30.5 (C-1).

Mehtyl 2,3,4,6-tetra-O-*benzyl-5-thio-β*-D-*glucopyranoside* (**11β**).—(*1*) Compound **10β** (57 mg, 0.098 mmol) was treated with Et_3SiH (19 μL, 0.12 mmol) and $BF_3 \cdot OEt_2$ (22 μL, 0.18 mmol) as already described for the synthesis of **11α** to give **11β** (35 mg, 62%) as crystals.

(*2*) Compound **13R** (92 mg, 0.145 mmol) was treated with PPh_3 (76 mg, 0.29 mmol) and DEAD (44 μL, 0.29 mmol) as already described for the synthesis of **8** (Method B) to give **11β** (54 mg, 65%) as crystals.

11β: mp 73–75 °C; $[\alpha]_D^{21}$ +13.9° (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.1 (m, 20 H, Ar), 4.93–4.73 (m, 6 H, PhCH_2), 4.52 (s, 2 H, PhCH_2), 4.46 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1), 3.81–3.73 (m, 4 H, H-2,3,4,6a), 3.6–3.4 (m, 1 H, H-6b), 3.55 (s, 3 H, OMe), 2.90 (ddd, 1 H, $J_{4,5}$ 10.1, $J_{5,6a}$ 3.9, $J_{5,6b}$ 5.2 Hz, H-5); ^{13}C NMR ($CDCl_3$): δ 138.9, 138.7, 138.3, 138.0, 128.4, 128.2, 128.1, 127.7, 127.5 (Ar), 86.4, 86.3, 86.0, 81.9

(C-1,2,3,4), 76.1, 75.4, 73.4 (PhCH$_2$), 68.9 (C-6), 58.7 (OMe), 43.8 (C-5). Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.65; H, 6.71; S, 5.62. Found: C, 73.98; H, 6.84; S, 5.59.

(1S)- and (1R)-2,3,4,6-Tetra-O-benzyl-L-idose S-acetyl O-methyl monothioacetal (**13R** *and* **13S**).—(*1*) To a stirred solution of **11S** (98 mg, 0.156 mmol) in Et_2O (3 mL) was added Li(^{t}BuO)$_3$AlH (79 mg, 0.312 mmol) at −10 °C under Ar. After 1 h, 1 M HCl was added and the mixture was extracted with Et_2O. The organic layer was washed with aq NaCl, dried over $MgSO_4$, evaporated, and chromatographed on silica gel (6:4:1–4:4:1 hexane–benzene–EtOAc) to give **13S** (86 mg, 87%) and **13R** (6 mg, 6%), respectively, as a syrup.

(*2*) **11R** (175 mg, 0.278 mmol) was treated with Li(^{t}BuO)$_3$AlH (142 mg, 0.557 mmol) as described in (*1*) to give **13S** (8.5 mg, 5%) and **13R** (161 mg, 91%), respectively as a syrup.

13S: $[\alpha]_D^{19}$ +24.4° (*c* 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.66 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.85–4.34 (m, 8 H, PhCH_2), 4.07–3.23 (m, 6 H, H-2,3,4,5,6), 3.25 (s, 3 H, OMe), 2.55 (bs, 1 H, OH), 2.30 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 195.6 (S*C*=O), 138.4, 138.3, 138.0, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5 (Ar), 88.0 (C-1), 81.0, 79.3, 77.9, 74.9, 74.34, 74.27, 73.2, 71.3, 69.7 (C-2,3,4,5,6, PhCH_2), 56.3 (OMe), 31.1 (SAc). Anal. Calcd for $C_{37}H_{42}O_7S$: C, 70.45; H, 6.71; S, 5.08. Found: C, 70.90; H, 6.60; S, 4.95.

13R: $[\alpha]_D^{19}$ −19.6° (*c* 2.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.80 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 4.75–4.35 (m, 8 H, PhCH_2), 4.14–3.25 (m, 6 H, H-2,3,4,5,6), 3.29 (s, 3 H, OMe), 2.46 (bs, 1 H, OH), 2.37 (s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 196.5 (S*C*=O), 138.2, 138.1, 137.9, 137.8, 128.5, 128.3, 128.2, 127.8, 127.7, 127.6 (Ar), 86.4 (C-1), 81.0, 78.1, 74.8, 74.6, 73.9, 73.1, 71.4, 68.9 (C-2,3,4,5,6, PhCH_2), 56.5 (OMe), 31.1 (SAc). Anal. Calcd for $C_{37}H_{42}O_7S$: C, 70.45; H, 6.71; S, 5.08. Found: C, 70.11; H, 6.62; S, 5.28.

Methyl 2,3,4,6-tetra-O-benzyl-α-D-altropyranoside (**14**).—To a stirred suspension of methyl 4,6-*O*-benzylidene-α-D-altropyranoside [23] (16.3 g, 57.6 mmol) in H_2O was added 0.1 M H_2SO_4 (30 mL) at 60 °C. After 4 h, the mixture was neutralized with BaO (460 mg). The insoluble material was removed by Celite filtration and the filtrate was evaporated. The residue was dissolved in DMF (200 mL) and 55% NaH (20.1 g, 460 mmol) was added carefully. After the mixture had been stirred for 2 h at room temperature, benzyl bromide (34.2 mL, 276 mmol) was slowly dropped in at 0 °C. The temperature was gradually increased to room temperature and the mixture was stirred for further 1 h. Ice–water was carefully added and the mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$, evaporated, and chromatographed on silica gel (20:1–7:1 hexane–EtOAc) to give **14** (28.79 g, 90%) as a syrup: $[\alpha]_D^{20}$ +51.4° (*c* 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 4.7–4.4 (m, 9 H, H-1, PhCH_2), 4.24 (dt, 1 H, $J_{4,5}$ 8.9, $J_{5,6a} = J_{5,6b} = 3.6$ Hz, H-5), 3.85 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-4), 3.76 (t, 1 H, $J_{3,4}$ 4.3 Hz, H-3), 3.71–3.69 (m, 3 H, H-2,6), 3.40 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$): δ 138.6, 138.5, 138.1, 128.4, 128.3, 127.9, 127.7, 127.5 (Ar), 100.8 (C-1), 76.2, 73.8, 73.4, 73.0, 72.6, 72.2, 71.7, 69.8, 68.2 (C-1,2,3,4,5,6, PhCH_2), 55.4 (OMe). Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.79; H, 6.91. Found: C, 75.56; H, 6.76.

2,3,4,6-Tetra-O-benzyl-D-altrose S-acetyl O-methyl monothioaceetal (**15**).—Compound **14** (578 mg, 1.04 mmol) was treated with 1.0 M solution of Me_2BBr in CH_2Cl_2

(2.08 mL), iPr_2NEt (0.45 mL, 2.6 mmol), and AcSH (0.22 mL, 3.12 mmol), as already described for the synthesis of **6**, to give **15** (438 mg, 67%) as a 1:1 mixture of diastereomer after silica gel chromatography (8:1 hexane–EtOAc): ^1H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.61 (each d, 1 H, $J_{1,2}$ 2.3 Hz, 3.2, respectively, H-1), 4.82–3.60 (m, 14 H, H-2,3,4,5,6, PhCH_2), 3.33 (s, 3 H, OMe), 2.74 (bs, 1 H, OH), 2.37, 2.35 (each s, 3 H, SAc); ^{13}C NMR ($CDCl_3$): δ 138.8, 138.2, 128.4, 128.2, 128.0, 127.8, 127.7, 127.5 (Ar), 88.9, 87.3 (C-1), 82.6, 82.4, 81.2, 80.4, 80.0, 79.7, 75.2, 75.0, 74.9, 73.4, 72.7, 72.4, 71.6, 71.5, 70.0 (C-2,3,4,5,6, PhCH_2), 56.5 (OMe), 31.2 (SAc). Anal. Calcd for $C_{37}H_{42}O_7S$: C, 70.45; H, 6.71; S, 5.08. Found: C, 70.11; H, 6.72; S, 5.06.

*Methyl 2,3,4,6-tetra-*O*-benzyl-5-thio-*L*-galactopyranoside* (**16**).—To a stirred solution of **15** (27.93 g, 44.8 mmol) in pyridine (200 mL) was added methanesulfonyl chloride and 4-dimethylaminopyridine (100 mg) at 0 °C. After 8 h, the mixture was evaporated. The residue was partitioned between CH_2Cl_2 and H_2O. The organic layer was washed successively with satd $NaHCO_3$, 5% HCl, and H_2O, dried over $MgSO_4$, and evaporated. The residue was dissolved in CH_2Cl_2 (40 mL) and diluted with MeOH (400 mL). To this solution was added 0.89 M NaOMe (150 mL, 133 mmol). After 16 h, the mixture was neutralized with AcOH and evaporated. The residue was dissolved in CH_2Cl_2 and washed with satd $NaHCO_3$. The organic layer was dried over $MgSO_4$, evaporated, and the residue was chromatographed on silica gel (15:1–10:1 hexane–EtOAc) to give **16** (α:β = 1:1, 12.2 g, 48%) as a syrup: ^1H NMR ($CDCl_3$): δ 7.4–7.2 (m, 20 H, Ar), 5.1–4.6 (m, 6 H, PhCH_2), 4.49 (d, 0.5 H, $J_{1,2}$ 7.9 Hz, H-1β), 4.45 (d, 0.5 H, $J_{1,2}$ 3.1 Hz, H-1α), 4.38 (s, 1 H, PCH_2 β), 4.34 (s, 1 H, PhCH_2 α), 4.3–4.2 (m, 1 H, H-2α,4α), 4.17 (t, 0.5 H, $J_{3,4} = J_{4,5}$ = 2.3 Hz, H-4β), 4.10 (t, 0.5 H, $J_{2,3}$ 8.1 Hz, H-2β), 3.88 (dd, 0.5 H, $J_{2,3}$ 10.1, $J_{3,4}$ 2.5 Hz, H-3α), 3.59 (t, 0.5 H, $J_{5,6a} = J_{6a,6b}$ = 9.3 Hz, H-6aβ), 3.54 (dd, 0.5 H, $J_{5,6b}$ 6.4 Hz, H-6bβ), 3.50 (s, 1.5 H, OMeβ), 3.49 (t, 0.5 H, $J_{5,6a} = J_{5,6b}$ = 8.6 Hz, H-6aα), 3.42 (s, 1.5 H, OMeα), 3.39 (dd, 0.5 H, H-3β), 3.37 (dd, 0.5 H, $J_{5,6b}$ 5.2 Hz, H-6bα), 3.34 (ddd, 0.5 H, $J_{4,5}$ 1.2 Hz, H-5α), 3.05 (dt, 0.5 H, H-5β); ^{13}C NMR ($CDCl_3$): δ 139.1, 138.9, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.4 (Ar), 85.7, 83.2, 82.6, 80.2, 75.5, 75.3, 74.7, 74.1, 73.7, 73.4, 73.2 (C-1,2,3,4, PhCH_2), 69.2, 68.4 (C-6), 58.3, 56.7 (OMe), 43.2, 41.1 (C-5). Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.65; H, 6.71; S, 5.62. Found: C, 73.53; H, 6.61; S, 5.53.

*Methyl 2,3,4,6-tetra-*O*-acetyl-5-thio-α and β-*L*-galactopyranoside* (**17**α *and* **17**β).—Into a stirred solution of **16** (1.94 g, 3.40 mmol) in THF (100 mL) was liquefied NH_3 (100 mL) at −78 °C. Sodium (1.79 g, 77 mmol) was slowly added during 30 min until the blue color of the solution was maintained over 1 h. Then NH_4Cl (8.6 g, 160 mmol) was carefully added and the temperature was gradually raised to room temperature. The mixture was evaporated and the residue was subjected to conventional acetylation with pyridine (50 mL) and Ac_2O (50 mL). The crude products was chromatographed on silica gel (6:1–4:1 hexane–EtOAc) to give **17**α (423 mg, 33%), **17**β (339 mg, 26%), and a mixture of **17**α and **17**β (α:β = 1:2, 451 mg, 35%), respectively as a syrup. ^1H NMR spectra for **17**α and **17**β were in accord with those for D enantiomers [9].

17α: mp 101–102 °C (from EtOH); $[\alpha]_D^{18}$ −242° (*c* 1.3, $CHCl_3$); lit. for the D enantiomer [9] 96–98 °C (from EtOAc–hexane); $[\alpha]_D$ +225.5° (*c* 1.4, $CHCl_3$).

17β: mp 107–108 °C (from EtOH); $[\alpha]_D^{18}$ −5.8° (*c* 4.9, $CHCl_3$); lit. for the D enantiomer [9] 102–103° (from MeOH); $[\alpha]_D$ +9.5° (*c* 4.2, $CHCl_3$).

1,2,3,4,6-Penta-O-acetyl-5-thio-L-galactopyranose (**18**).—To a stirred solution of **17** ($\alpha:\beta = 1:1$, 2.17 g, 5.73 mmol) in MeOH (90 mL) was added 0.6 M NaOMe (1 mL). After 20 h, the mixture was neutralized with acetic acid and evaporated. The residue was dissolved into H_2O (150 mL) and 6 M H_2SO_4 was added. The mixture was heated for 4 h at 90 °C and neutralized with BaO (1.1 g). The insoluble material was removed by Celite filtration and the filtrate was evaporated. The residue was subjected to standard acetylation with pyridine (90 mL) and Ac_2O (90 mL) and purification by silica gel chromatography (3:1 hexane–EtOAc) to give **18** ($\alpha:\beta = 7:1$, 1.42 g, 61%) as an amorphous: $[\alpha]_D^{19} -199°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.15 (d, 0.9 H, $J_{1,2}$ 2.7 Hz, H-1α), 5.84 (d, 0.1 H, $J_{1,2}$ 7.0 Hz, H-1β), 5.70 (dd, 0.9 H, $J_{3,4}$ 2.6, $J_{4,5}$ 1.6 Hz, H-4α), 5.61 (t, 0.1 H, $J_{3,4} = J_{4,5} = 3.0$ Hz, H-4β), 5.39 (dd, 1 H, $J_{2,3}$ 10.6 Hz, H-2α), 5.29 (dd, 1 H, H-3α), 5.02 (dd, 0.1 H, $J_{2,3}$ 7.6 Hz, H-3β), 4.4–3.8 (m, 3 H, H-5,6), 2.2–2.0 (m, 15 H, OAc); ^{13}C NMR ($CDCl_3$, only signals for the α anomer were shown): δ 170.1, 169.9, 169.8, 169.0 (O*C*=O), 71.3, 69.4, 68.7, 68.1 (C-1,2,3,4), 61.1 (C-6), 39.6 (C-5), 20.9, 20.6 (OAc). Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.47; H, 5.63; S, 8.14.

5-Thio-L-galactose (**19**).—To a stirred suspension of **18** (242 mg, 0.595 mmol) in MeOH (8 mL) was added 0.5 M NaOMe (0.1 mL). After 2 h, the mixture was neutralized with Dowex 50 (H^+) ion-exchange resin. The resin was removed by filtration and the filtrate was evaporated to give a solid, which was recrystallized from EtOH to give **19** (108 mg, 92%) as crystals. Anomeric equilibrium was reached 3 days after the compound had been dissolved in D_2O ($\alpha:\beta = 83:17$, measured by ^1H NMR): mp 178–180 °C (from EtOH); ^1H NMR (D_2O): δ 5.10 (d, 0.8 H, $J_{1,2}$ 3.3 Hz, H-1α), 4.9 (m, 1 H, H-1β), 4.35 (dd, 0.8 H, $J_{3,4}$ 2.8, $J_{4,5}$ 1.3 Hz, H-4α), 4.25 (dd, 0.2 H, $J_{3,4}$ 3.0, $J_{4,5}$ 1.4 Hz, H-4β), 4.09 (dd, 0.8 H, $J_{2,3}$ 10.2 Hz, H-2α), 3.95–3.85 (m, 2.0 H, H-3α,6aα,2β,6aβ), 3.74 (dd, 0.8 H, $J_{5,6b}$ 7.3, $J_{6a,6b}$ 11.3 Hz, H-6bα), 3.72 (dd, 0.2 H, $J_{5,6b}$ 7.6, $J_{6a,6b}$ 11.6 Hz, H-6bβ), 3.62 (dt, 0.8 H, $J_{5,6a}$ 7.3 Hz, H-5α), 3.55 (dd, 0.2 H, $J_{2,3}$ 9.5 Hz, H-3β), 3.39 (ddd, 0.2 H, $J_{5,6a}$ 6.8 Hz, H-5β); ^{13}C NMR (D_2O, only signals for the α anomer were seen): δ 73.8, 71.6, 70.9, 70.5 (C-1,2,3,4), 61.5 (C-6), 43.8 (C-5). Anal. Calcd for $C_6H_{12}O_5S$: C, 36.73; H, 6.16; S, 16.34. Found: C, 36.80; H, 6.24; S, 15.86.

General procedure for enzyme assay.—α-L-Fucosidase (bovine kidney) was purchased from Sigma. *p*-Nitrophenyl α-L-fucopyranoside was purchased from Seikagaku Kogyo Inc. The enzyme assay was performed by essentially the same method as previously reported [12]. The reaction was started by adding the enzyme solution (80 pg) to the mixture of *p*-nitrophenyl α-L-fucopyranoside and 5-thio-L-galactose in citrate buffer (final: 20 mM, pH 5.5, 300 μL) at 25 °C. After 30 min, the reaction was quenched by adding 50 mM glycine buffer (pH 10.0, 500 μL). The amount of liberated *p*-nitrophenol was monitored at 400 nm.

Acknowledgements

This work was supported in part by a Grant-in-aid (No. 06453212) from the Japanese Ministry of Education, Science, Sports and Culture.

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