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Synthesis of L-gulose, L-galactose, and their acetylated *aldehydo* forms from 6-*S*-phenyl-6-thio-D-hexoses

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ABSTRACT

Methyl 6-*S*-phenyl-6-thio-α-D-glucopyranoside, prepared in high yield from methyl α-D-glucopyranoside by the action of diphenyl disulfide and tributylphosphine in pyridine, was converted into 6-*S*-phenyl-6-thio-D-glucitol pentaacetate (7) by sequential hydrolysis, borohydride reduction, and acetylation. Oxidation of 7 with 3-chloroperoxybenzoic acid gave the corresponding *S*-epimeric sulfoxides, which underwent Pummerer rearrangement to 1-epimeric L-gulose *S*-phenyl monothiohemiacetal hexaacetates. Boron trifluoride-catalyzed reaction of the latter with thiophenol gave the analogous diphenyl dithioacetal, whereas base-catalyzed methanolysis led to free L-gulose. Treatment of 7 with *N*-chlorosuccinimide afforded 1-epimeric 1-chloro-1-*S*-phenyl-1-thio-L-gulitol pentaacetates, which were hydrolyzed to provide *aldehydo*-L-gulose pentaacetate. The same reaction sequences were performed with 6-*S*-phenyl-6-thio-D-galactose, synthesized in two steps from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, furnishing ultimately L-galactose, its diphenyl dithioacetal pentaacetate, and *aldehydo*-L-galactose pentaacetate. Similar reaction sequences for the chain-terminal interchange of oxidation state in other ω-*S*-phenyl-ω-thioaldoses may prove useful for the preparation of less-common sugar derivatives.

INTRODUCTION

The Pummerer rearrangement of sulfoxides was first extended to carbohydrate synthesis by McElhinney and co-workers[1], who obtained 4-thiofuranoses from thiolane-3,4-diol *S*-oxides. In our own laboratories, an array of 4,4-disubstituted tetrahydrothiopyrans have been converted, *via* their *S*-oxides, into C-3 branched, 5-thio-D,L-pentopyranoses (Scheme 1,a)[2], and it was discovered that Pummerer reaction of 2-deoxy-3,4:5,6-di-*O*-isopropylidene-2-*C*-nitromethyl-1-*S*-phenyl-1-thio-D-glucitol *S*-oxide leads either to the expected *O*-acetyl-*S*-phenyl monothiohemiacetal or to a phenyl 1-thioglycoside, depending on the conditions employed (Scheme 1,b)[3]. In view of these results it was reasoned that rearrangement of simple hexitols bearing a phenylsulfinyl group at C-6 might be a convenient route to certain rare carbohydrate derivatives, considering that such a process involves an interchange of oxidation state between the termini of the hexose chain. Thus, in principle, 6-*S*-phenyl-6-thio-D-glucose should be convertible by simple operations into thio derivatives of L-gulose (Scheme 1,c), and

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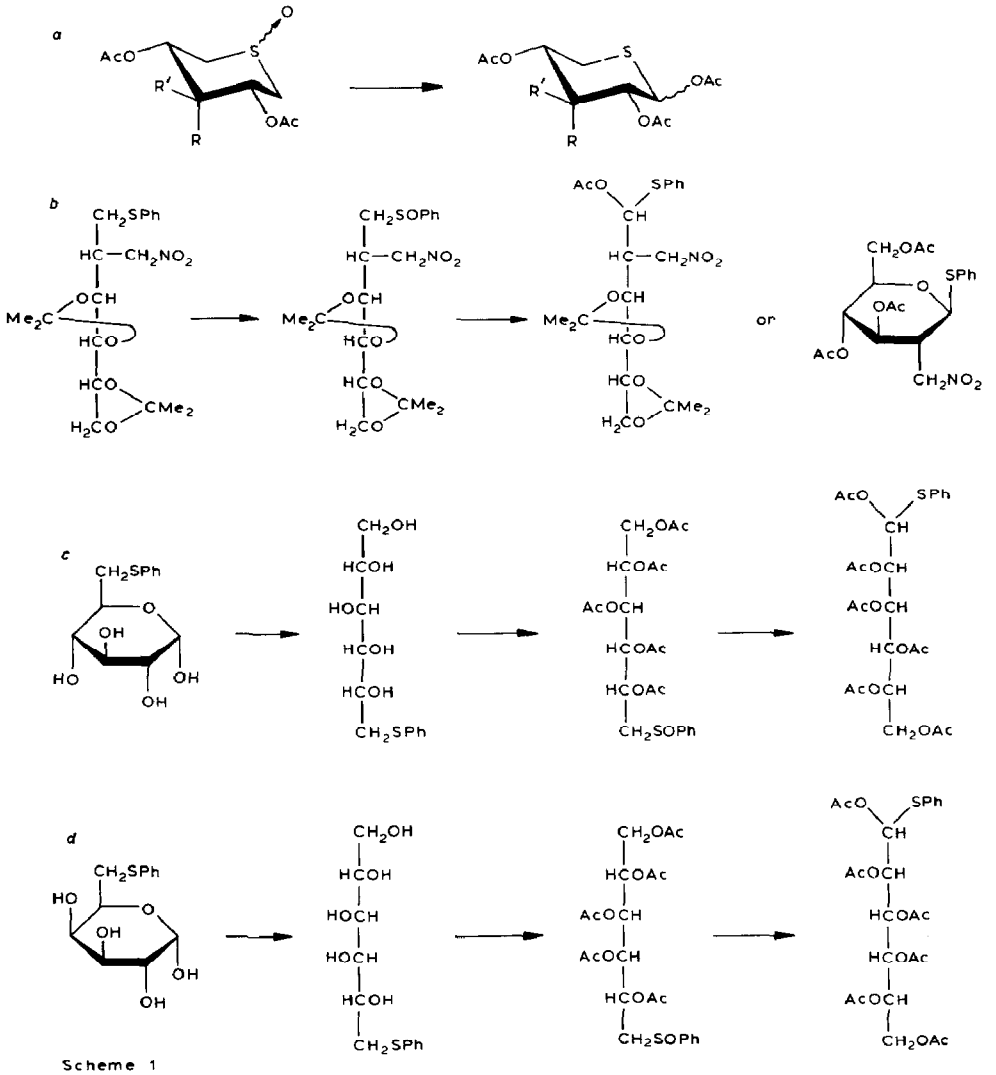
similarly, 6-*S*-phenyl-6-thio-D-galactose should provide derivatives of L-galactose (Scheme 1,d). The realization of this concept is reported here.



Scheme 1

RESULTS AND DISCUSSION

In order to procure the required 6-*S*-phenyl-6-thio-D-glucose (**5**), methyl 6-chloro-6-deoxy-α-D-glucopyranoside (**2**), prepared from methyl α-D-glucopyranoside (**1**), was treated with sodium thiophenoxide in refluxing methanol for 3.5 days. The crystalline 6-*S*-phenyl-6-thioglycoside **3** obtained in 96% yield was acetylated to give the triacetate **4**. A more-direct procedure, circumventing the chlorodeoxy sugar **2**,

consisted of treating **1** with[4] diphenyl disulfide in the presence of tributylphosphine and pyridine (16 h at 25°), which smoothly gave **3**, isolated after acetylation as **4** (82%) and recovered by Zemplén deacetylation (92%).

The glycoside **3** was hydrolyzed with hydrochloric acid to afford syrupy 6-*S*-phenyl-6-thio-*α,β*-D-glucose (**5**). Sodium borohydride reduction then gave crystalline 6-*S*-phenyl-6-thio-D-glucitol (**6**), which was acetylated, and the pentaacetate **7** was oxidized quantitatively with 3-chloroperoxybenzoic acid to furnish the sulfoxide **8** as a mixture of *S*-epimers. Zemplén deacetylation of **8** provided the pentols **9**.

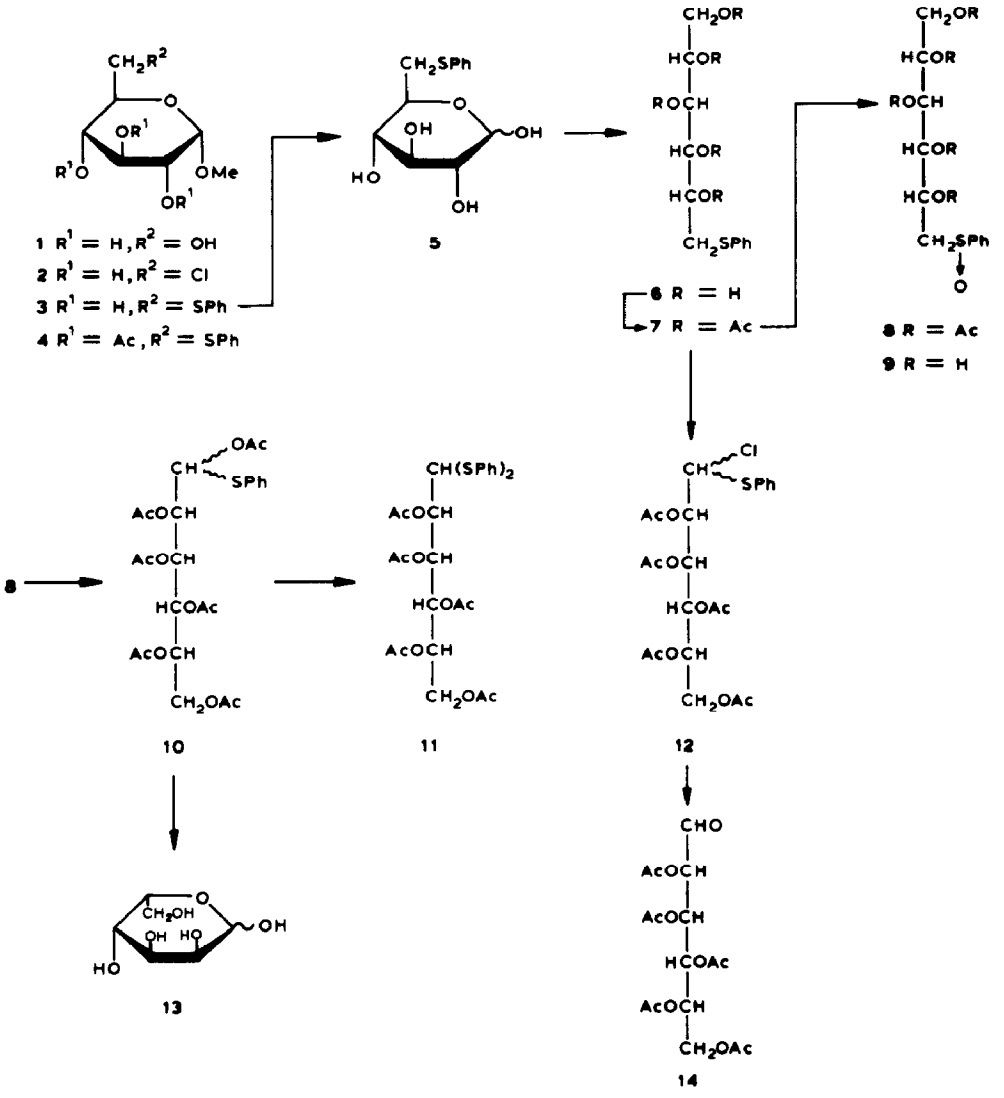
Treatment of the penta-*O*-acetyl sulfoxides **8** with boiling acetic anhydride in the presence of anhydrous sodium acetate effected the Pummerer rearrangement, to give an 85% yield of 1,2,3,4,5,6-hexa-*O*-acetyl-L-gulose *S*-phenyl monothiohemiacetals (**10**) as a 2:1 mixture of 1-epimers. The major component was isolated crystalline, whereas the minor one remained syrupy. Rearrangement of **8** performed by use of acetic anhydride and *p*-toluenesulfonic acid in refluxing dichloromethane generated the epimeric products **10** in 98% yield, but in a ratio of 1:4. Reaction of **10** with thiophenol under catalysis by boron trifluoride gave a 90% yield of 2,3,4,5,6-penta-*O*-acetyl-L-gulose diphenyl dithioacetal (**11**), and methoxide-promoted methanolysis of **10** furnished free L-gulose (**13**), characterized as the crystalline calcium chloride adduct of the *α* anomer.

Reaction of the acetylated thioglucitol **7** with *N*-chlorosuccinimide produced 2,3,4,5,6-penta-*O*-acetyl-1-chloro-1-*S*-phenyl-1-thio-L-gulitol (**12**) as a mixture of 1-epimers. The chloro sulfide was hydrolyzed in aqueous acetonitrile in the presence of cupric acetate and cupric oxide (to oxidize the thiophenol formed[5]), to afford *aldehydo*-L-gulose pentaacetate (**14**).

Similar experiments were performed starting from D-galactose. Its 1,2:3,4-di-*O*-isopropylidene derivative (**15**) was converted with 95% yield into the 6-*S*-phenyl-6-thio derivative **16** by the diphenyl disulfide procedure. Deacetalation with trifluoroacetic acid, followed by borohydride reduction and acetylation, furnished in turn the free 6-*S*-phenyl-6-thio-D-galactose (**17**), the corresponding D-galactitol **18**, and the pentaacetate **19**. Oxidation of **19** with 3-chloroperoxybenzoic acid gave a mixture of *S*-epimeric, penta-*O*-acetyl sulfoxides (**20**), which was deacetylated (Zemplén) to the corresponding pentols **21**. All of these reactions proceeded with excellent yields (86–96%).

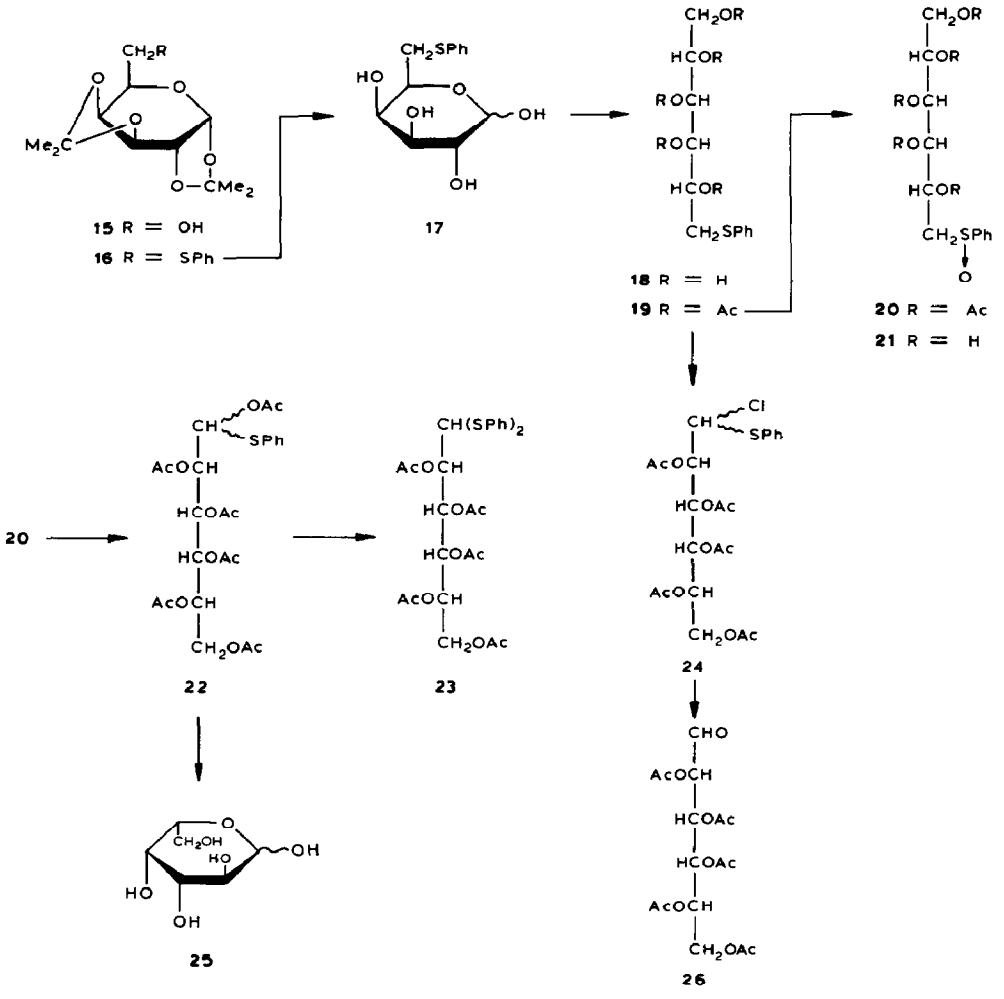
Pummerer reactions of **20** with boiling acetic anhydride in the presence of sodium acetate, or with acetic anhydride and *p*-toluenesulfonic acid in refluxing dichloromethane, gave 1,2,3,4,5,6-hexa-*O*-acetyl-L-galactose *S*-phenyl monothiohemiacetal (**22**) as mixtures of separable 1-epimers, the components being isolated in yields of 48 and 32%, and 72 and 23%, respectively. Conversions of **22** into 2,3,4,5,6-penta-*O*-acetyl-L-galactose diphenyl dithioacetal (**23**; yield, 65%) and free L-galactose (**25**; yield, 76%) were performed as described for the aforementioned, analogous L-gulose derivatives.

Action of *N*-chlorosuccinimide upon **19** gave 2,3,4,5,6-penta-*O*-acetyl-1-chloro-1-*S*-phenyl-1-thio-L-galactitol (**24**) as a mixture of 1-epimers (84%). Hydrolysis of **24** in the presence of cupric ion produced *aldehydo*-L-galactose pentaacetate (**26**) in 70% yield.



In summary, we have shown that readily-prepared 6-*S*-phenyl derivatives of 6-thio-D-glucose and 6-thio-D-galactose are convenient starting points for high-yielding syntheses of L-gulose and L-galactose, their (acetylated) *aldehydo* tautomers, and their acetylated *S*-phenyl monothiohemiacetals, with key operations involving the Pummerer rearrangement of 6-deoxy-6-phenylsulfinylalditols and the related reaction of *S*-phenylthioalditols with *N*-chlorosuccinimide. It may be suggested that some of the new thio sugar intermediates **10–12** and **22–24** should prove useful for further synthetic transformations in the L-*gulo* and L-*galacto* series, in view of the various, interesting reactions[6] which such types of compounds are known to undergo. Applications of this chemistry to D-allose or D-altrose (both conveniently prepared from D-glucose) should offer new entries into the less-common L-allose or D-talose series, and similar inter-

change of chain-terminal functionality might become an attractive device in the synthesis of higher-carbon sugars.



EXPERIMENTAL

General methods. — Column chromatography was performed on Silica Gel Merck 7734 (100–200 mesh). The following solvent combinations (v/v) were used: (*A*) 1:20 MeOH–$CHCl_3$; MeOH–EtOAc, (*B*) 3:1, and (*C*) 1:1; (*D*) 1:1 MeOH–ether; EtOAc–hexane, (*E*) 2:1, and (*F*) 1:1; ether–hexane, (*G*) 3:1, (*H*) 2:1, (*I*) 1:1, (*J*) 1:3, and (*K*) 1:7. Melting points were determined in capillaries with a Gallenkamp electrothermal apparatus. Optical rotations were measured at ~25° with a Perkin–Elmer 241 polarimeter and refer to $CHCl_3$ solutions unless otherwise specified. I. r. data (ν_{max}) were

recorded with a Perkin–Elmer model 783 spectrometer. Mass-spectral data (m/z) were obtained in the chemical-ionization mode, using ether as the ionizing gas. The ^{1}H- and ^{13}C-n.m.r. data refer to spectra obtained at 300 and 75.43 MHz, respectively, from solutions in $CDCl_3$ unless otherwise indicated.

*Methyl-6-S-phenyl-6-thio-α-*D*-glucopyranoside* (**3**) *and its 2,3,4-triacetate* **4**. — *A. From* **2**. To chilled, 1.3M methanolic NaOMe (30 mL) was added PhSH (4.0 g) followed by a solution of chloro glycoside[7] **2** (2.51 g) in MeOH (25 mL). The mixture was boiled under reflux in an N_2 atmosphere for 3.5 d, the solvent evaporated, and an aqueous solution of the residue extracted with EtOAc (6 × 50 mL). The dried ($MgSO_4$) extract was concentrated, and the crude product purified by column chromatography (solvent *A*), to give syrupy **3** (3.85 g, 96%), $[\alpha]_D$ +150° (*c*, MeOH), which crystallized from 99% EtOH–ether at −18°, or from ether–hexane or EtOAc–hexane on careful concentration of the solutions; m.p. 74–75° (with sintering at 66–67°), raised to 76–77° by recrystallization; m/z 286 (M^+) and 255 (M^+ − OMe); ^{1}H-n.m.r. (after D_2O exchange): δ 7.35–7.1 (m, 5 H, Ph), 4.70 (d, $J_{1,2}$ 3.9 Hz, H-1), 3.73 (m, H-5), 3.64 (t, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 3.48 (dd, H-2), 3.45 (dd, $J_{5,6}$ 2.5 $J_{6,6'}$ 13.6 Hz, H-6), 3.37 (t, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 3.35 (s, 3 H, OMe), and 3.03 (dd, $J_{5,6'}$ 8.3, $J_{6,6'}$ 13.6 Hz, H-6').

Anal. Calc. for $C_{13}H_{18}O_5S$ (286.3): C, 54.53; H, 6.33; S, 11.19. Found: C, 54.39; H, 6.47; S, 11.31.

The *triacetate* **4** was obtained as a syrup (260 mg, 95%) after acetylation of **3** (190 mg) with Ac_2O (3 mL) and pyridine (2 mL) during 16 h at 25°, followed by conventional processing; $[\alpha]_D$ +116° (*c* 0.7); m/z 413 (M^+ + 1) and 381 (M^+ − OMe); ^{1}H-n.m.r.: δ 7.35–7.15 (m, 5 H, Ph), 5.42 (dd, $J_{2,3}$ 9.9, $J_{3,4}$ 9.25 Hz, H-3), 4.95 (dd, $J_{3,4}$ 9.25, $J_{4,5}$ 10 Hz, H-4), 4.90 (d, $J_{1,2}$ 3.7 Hz, H-1), 4.86 (dd, $J_{1,2}$ 3.7, $J_{2,3}$ 9.9 Hz, H-2), 3.95 (ddd, $J_{5,6}$ 3, $J_{5,6'}$ 8.5, $J_{4,5}$ 10 Hz, H-5), 3.34 (s, 3 H, OMe), 3.09 (dd, $J_{5,6}$ 3, $J_{6,6'}$ 13.8 Hz, H-6), and 2.99 (dd, $J_{5,6'}$ 8.4, $J_{6,6'}$ 13.8 Hz, H-6'); ^{13}C-n.m.r.: δ 169.9, 169.85, 169.6 (*Me*CO), 136.0, 129.3, 128.9, 126.6 (Ph), 96.4 (C-1), 72.0, 70,9. 70.0, 68.2 (C-2,3,4,5), 55.3 (*O*Me), 35.9 (C-6), and 20.7 (*CO*Me).

Anal. Calc. for $C_{19}H_{24}O_8S$ (412.5): C, 55.33; H, 5.86; S, 7.77. Found: C, 55.56; H, 5.83; S, 7.57.

B. From **1**. A mixture of methyl *α*-D-glucopyranoside (**1**, 1.94 g), PhSSPh (3.27 g), Bu_3P (3.06 g), and dry pyridine (5 mL) was kept for 24 h at room temperature, cooled (0°), and treated with Ac_2O (5 mL) and 4-dimethylaminopyridine (~10 mg). After 30 min, the mixture was kept for 17 h at room temperature, poured into ice–water, and extracted with CH_2Cl_2 (200 mL). The organic phase was washed with 5% HCl (2 × 100 mL), aq. $NaHCO_3$ (2 × 100 mL), and water (50 mL), dried ($MgSO_4$), and concentrated, to give crude **4** which was purified by column chromatography (solvent *J*), furnishing 3.38 g (82%) of pure **4** identical (n.m.r.) with the product from procedure *A*. Treatment of **4** (3.30 g) with MeOH (60 mL) containing a catalytic amount of NaOMe during 1 h at room temperature, followed by deionization of the solution with a cation-exchange resin and evaporation, gave **3** (2.10 g, 91.7%; dried in a high vacuum), m.p. 63–65° (from EtOAc–hexane), identified by its mass spectrum and ^{1}H-n.m.r. data.

*6-S-Phenyl-6-thio-α,β-*D*-glucose* (**5**). — Glycoside **3** (3.0 g) was boiled in M HCl (60

mL) for 7 h. The cooled hydrolyzate was neutralized with $NaHCO_3$, saturated with NaCl, and extracted with EtOAc (10 × 50 mL). The dried ($MgSO_4$) extract was evaporated, and the residue purified by column chromatography (solvent *A*), to give **5** (2.2 g, 77%) as a colorless syrup; $[\alpha]_D$ +117° (*c* 1, MeOH); *m/z* 272 (M^+) and 255 (M^+ − OH); ^{1}H-n.m.r. (Me_2SO-d_6, D_2O): δ 5.65 (d, *J* ~4 Hz, H-1*α*), and 5.04 (d, *J* ~8 Hz, H-1*β*); ^{13}C-n.m.r. (Me_2SO-d_6): δ 137.4–125.0 (4 pairs of Ph signals), 96.9 (C-1*β*), 92.3 (C-1*α*), 76.2–70.0 (8 peaks for C-2,3,4,5 of the two anomers), 35.1 and 35.0 (C-6*α*, *β*).

Anal. Calc. for $C_{12}H_{16}O_5S$ (272.3): C, 52.93; H, 5.92; S, 11.77. Found: C, 52.79; H, 6.06; S, 11.66.

6-S-Phenyl-6-thio-D-glucitol (**6**). — Sodium borohydride (0.30 g) was added portionwise during 15 min to a solution of **5** (1.10 g) in EtOH (50 mL). After 2 h, water (25 mL) was added, and the solution was deionized with Amberlite IR-120 (H^+) resin and evaporated. Portions of MeOH (7 × 25 mL) were sequentially added to, and evaporated from, the residue, which was then purified by column chromatography (solvent *A*) to give **6** (0.90 g, 81%), m.p. 98–99° (from EtOAc), $[\alpha]_D$ +56° (*c* 2, MeOH); *m/z* 275 (M^+ + 1), 274 (M^+), 257 (M^+ + 1 − H_2O), 239 (M^+ + 1 − 2 H_2O), and 221 (M^+ + 1 − 3 H_2O); ^{1}H-n.m.r. (Me_2SO-d_6): δ 7.3–7.1 (m, 5 H, Ph); exchangeable OH signals at 4.98 (d, *J* 6.4 Hz), 4.63 (m, 2 H), 4.52 (t, *J* 5.5 Hz), and 4.16 (d, *J* 6.8 Hz); 3.7–3.3 (m, H-1 to H-6) and 2.90 (dd, $J_{5,6'}$ 8.5, $J_{6,6'}$ 13.1 Hz, H-6′).

Anal. Calc. for $C_{12}H_{18}O_5S$ (274.3): C, 52.54; H, 6.61; S, 11.69. Found: C, 52.33; H, 6.48; S, 11.49.

1,2,3,4,5-Penta-O-acetyl-6-S-phenyl-6-thio-D-glucitol (**7**). — Compound **6** (0.50 g) was treated with Ac_2O (6 mL) and pyridine (4 mL) during 16 h at room temperature. After conventional processing, column chromatography (solvent *H*) of the crude product gave syrupy **7** (0.85 g, 96%), $[\alpha]_D$ +13.3° (*c* 2); *m/z* 484 (M^+), 425 (M^+ + 1 − AcOH), and 364 (M^+ − 2 AcOH); ^{1}H-n.m.r. (assignments corroborated by comparison with data[8] for D-glucitol hexaacetate): δ 7.35–7.15 (m, 5 H, Ph), 5.43 (dd, $J_{3,4}$ 4.0, $J_{4,5}$ 6.0 Hz, H-4), 5.39 (dd, $J_{3,4}$ 4.0, $J_{2,3}$ 6.4 Hz, H-3), 5.14 (dt, $J_{1,2}$ 4, $J_{1',2}$ ~ $J_{2,3}$ ~ 6.2 Hz, H-2), 5.07 (ddd, $J_{4,5}$ 6.0, $J_{5,6}$ 4.5, $J_{5,6'}$ 7.2 Hz, H-5), 4.33 (dd, $J_{1,2}$ 4.0, $J_{1,1'}$ 12 Hz, H-1), 3.98 (dd, $J_{1',2}$ 6.0, $J_{1,1'}$ 12.1 Hz, H-1′), 3.15 (dd, $J_{5,6}$ 4.5, $J_{6,6'}$ 14.4 Hz, H-6), 3.05 (dd, $J_{5,6'}$ 7.2, $J_{6,6'}$ 14.4 Hz, H-6′), 2.11, 2.05, 2.04, 2.03, and 1.84 (5 s, 3 H each, 5 OAc); ^{13}C-n.m.r.: δ 170.2–169.5 (*Me*CO), 135.0. 130.6, 129.0, and 126.9 (Ph), 70.4, 70.0, 69.4, 68.4 (C-2,3,4,5), 61.8 (C-1), 34.9 (C-6), and 20.9–20.6 (*CO*Me).

Anal. Calc. for $C_{22}H_{28}O_{10}S$ (484.5): C, 54.53; H, 5.82; S, 6.61. Found: C, 54.73; H, 6.01; S, 6.45.

1,2,3,4,5-Penta-O-acetyl-6-deoxy-6-phenylsulfinyl-D-glucitol (**8**). — Compound **7** (300 mg) in CH_2Cl_2 (20 mL) was treated at −10° with 3-chloroperoxybenzoic acid (125 mg) for 30 min. The solvent was evaporated and **8** isolated quantitatively (310 mg), by column chromatography (solvent *I*), as a syrupy mixture of *S*-epimers; $[\alpha]_D$ +17.3° (*c* 2); *m/z* 501 (M^+ + 1), 459 (M^+ + 1 − CH_2O), 441 (M^+ + 1 − AcOH), 425 (M^+ + 1 −AcOH − O), 375 (M^+ − PhSO) and 257 (not assigned). The ^{1}H- and ^{13}C-n.m.r. spectra ($CDCl_3$) were similar to those of **7**, but the number of signals present indicated two epimers; C-6 resonated downfield from its position in **7**, giving signals at δ 58.7 and 56.4.

Anal. Calc. for $C_{22}H_{28}O_{11}S$ (500.5): C, 52.79; H, 5.64; S, 6.40. Found: C, 53.00; H, 5.86; S, 6.17.

*6-Deoxy-6-phenylsulfinyl-*D*-glucitol* (**9**). — Compound **8** (0.95 g) was deacetylated in MeOH (30 mL) containing a catalytic amount of NaOMe (2 h, 25°). Deionization with Amberlite IR-120 (H^+) resin and evaporation of the solution gave solid **9** (0.55 g, 100%), presumably a mixture of *S*-epimers. Recrystallization from MeOH gave a single epimer, m.p. 155–157° $[\alpha]_D$ +159° (*c* 1, water); ν_{max}^{KBr} 3450, 3250 (bd), and 1090–1000 cm^{-1} (several bands); *m/z* 291 ($M^+ + 1$) and 273 ($M^+ + 1 - H_2O$); ^{1}H-n.m.r. (D_2O): δ 7.7–7.6 (m, 5 H, Ph), 4.24 (~septet, *J* 2.45, 7.3, and 10.5 Hz), 3.85–3.69 (m, 4 H), 3.62 (dd, *J* 6.1 and 11.7 Hz), 3.42 (dd, $J_{5,6}$ 2.45, $J_{6,6'}$ 13.8 Hz, H-6), and 3.10 (dd, $J_{5,6'}$ 10.7, $J_{6,6'}$ 13.7 Hz, H-6'); ^{13}C-n.m.r. (D_2O): δ 141.4, 133.0, 130.5, 125.2 (Ph), 74.2, 73.4, 70.3, 66.4 (C-2,3,4,5), 63.1 (C-1), and 61.4 (C-6).

Anal. Calc. for $C_{12}H_{18}O_6S$ (290.3): C, 49.64; H, 6.25. Found: C, 49.55; H, 6.39.

*1,2,3,4,5,6-Hexa-*O*-acetyl-*L*-gulose S-phenyl monothiohemiacetals* (**10**). — *A. Procedure I.* A mixture of **8** (0.80 g), anhydrous NaOAc (1 g), and Ac_2O (10 mL) was boiled under reflux for 10 h, cooled, treated with MeOH (10 mL), and concentrated with repeated addition of MeOH (10 mL). The residue was taken up in ether (25 mL), insoluble material was removed, and the solution concentrated for column chromatography (solvent *I*), which gave **10** (0.74 g, 85%) as a 2:1 mixture of 1-epimers (^{1}H-n.m.r.) showing two closely-spaced spots (R_F ~0.5) in t.l.c. (solvent *G*, triple irrigation).

Anal. Calc. for $C_{24}H_{30}O_{12}S$ (542.5): C, 53.13; H, 5.57; S, 5.91. Found: C, 52.92; H, 5.63; S, 6.01.

The marginally more-polar, *major epimer* was isolated (392 mg) by crystallization of the mixture from ether (4 mL) and hexane (16 mL); m.p. 104–105° $[\alpha]_D$ +18° (*c* 1); ν_{max}^{KBr} 1750, 1740, 1365, 1269, 1210, 1094, 1045, 1027, 951, 838, and 690 cm^{-1}; *m/z* 483 ($M^+ + 1$ − AcOH), 433 ($M^+ + 1$ − PhSH), 423 ($M^+ + 1 - 2$ AcOH), and 381 ($M^+ + 1 -$ 2 AcOH − CH_2CO); ^{1}H-n.m.r.: δ 7.5–7.3 (m, 5 H, Ph), 6.15 (d, $J_{1,2}$ 3.3 Hz, H-1), 5.43 (dd, $J_{1,2}$ 3.3, $J_{2,3}$ 8.5 Hz, H-2), 5.36 (dd, $J_{3,4}$ 5.7, $J_{4,5}$ 9.2 Hz, H-4), 5.34 ($J_{3,4}$ 5.7, $J_{2,3}$ 8.5 Hz, H-3), 5.07 (m, H-5), 4.33 (dd, $J_{5,6}$ 3.3, $J_{6,6'}$ 12.3 Hz, H-6), 4.08 (dd, $J_{5,6'}$ 5.7, $J_{6,6'}$ 12.3 Hz, H-6'), 2.08, 2.06, 2.06, 2.05, 2.03, and 2.01 (6 s, 18 H total, 6 OAc); ^{13}C-n.m.r.: δ 170.2, 169.7, 169.6, 169.6, 169.3, 169.0 (*Me*CO), 134.4, 130.5, 129.1, 128.9 (Ph), 78.3 (C-1), 70.1, 69.5, 68.1, and 67.7 (C-2,3,4,5), 62.0 (C-6), and 20.9–20.7 (*CO*Me).

The material in the mother liquor of crystallization was chromatographed on a small column of silica gel (solvent *I*), yielding 85 mg of the pure, slightly less-polar, *minor epimer* as a syrup, $[\alpha]_D$ −16° (*c* 2); ν_{max}^{film} 1750, 1368, 1210, 1040, and 1020 cm^{-1}; *m/z* 483 ($M^+ + 1$ − AcOH), 433 ($M^+ + 1$ − PhSH), 423 ($M^+ + 1 - 2$ AcOH), and 381 ($M^+ +$ 1 − 2 AcOH − CH_2CO); ^{1}H-n.m.r.: δ 7.4–7.2 (m, 5 H, Ph), 6.13 (d, $J_{1,2}$ 4.1 Hz, H-1), 5.54 (dd, $J_{3,4}$ 3.8, $J_{2,3}$ 6.9 Hz, H-3), 5.42 (dd, $J_{3,4}$ 3.8, $J_{4,5}$ 6.6 Hz, H-4), 5.19 (dd, $J_{1,2}$ 4.1, $J_{2,3}$ 6.9 Hz, H-2), 5.13 (m, H-5), 4.34 (dd, $J_{5,6}$ 4.3, $J_{6,6'}$ 12.1 Hz, H-6), 4.07 (dd, $J_{5,6'}$ 5.7, $J_{6,6'}$ 12.1 Hz, H-6'), 2.12, 2.07, 2.05, 2.04, 2.035, and 2.03 (6 s, 18 H total, 6 OAc); ^{13}C-n.m.r.: δ 170.1, 169.6 (3 peaks), 169.1, and 169.0 (6 *Me*CO), 133.5, 131.1, 129.1, 128.7 (Ph), 80.3 (C-1), 70.9, 69.4, 69.2, 68.3 (C-2,3,4,5), 61.7 (C-6) and 20.9–20.5 (*CO*Me).

B. Procedure II. A solution of **8** (300 mg), Ac_2O (5 mL), and *p*-toluenesulfonic acid

trihydrate (300 mg) in dry CH_2Cl_2 (20 mL) was boiled under reflux for 8 h, cooled, diluted with CH_2Cl_2 (50 mL), washed with aq. $NaHCO_3$ (2 × 75 mL), dried ($MgSO_4$), and evaporated. Column chromatography (solvent *H*) of the residue gave **10** (320 mg, 98%) as a syrup showing a preponderance of the *less-polar* epimer (t.l.c. with solvent *G*, triple irrigation). The ^{1}H-n.m.r. spectrum revealed a 4:1 epimer ratio.

*2,3,4,5,6-Penta-*O*-acetyl-*L*-gulose diphenyl dithioacetal* (**11**). — To a solution of **10** (320 mg, epimer mixture) in CH_2Cl_2 (25 mL) was added PhSH (1 mL) and 10 drops of $BF_3{\cdot}Et_2O$, at room temperature. After 15 min the mixture was washed with aq. $NaHCO_3$ (30 mL) and water, dried, and evaporated. Column chromatography (solvent *I*) of the product gave syrupy **11** (316 mg, 90.4%), $[\alpha]_D$ −28° (*c* 2); ν_{max}^{film} 1750, 1580, 1370, 1260–1190, 1070–1025, 750, and 690 cm^{-1}; *m/z* 483 (M^+ + 1 − PhSH) and 423 (M^+ + 1 − PhSH − AcOH); ^{1}H-n.m.r.: δ 7.5–7.25 (m, 10 H, 2 Ph), 5.73 (dd, $J_{3,4}$ 2.1, $J_{2,3}$ 7.6 Hz, H-3), 5.45 (dd, $J_{3,4}$ 2.1, $J_{4,5}$ 7.9 Hz, H-4), 5.32 (dd, $J_{1,2}$ 3.9, $J_{2,3}$ 7.6 Hz, H-2), 5.10 (ddd, $J_{5,6}$ 3.4, $J_{5,6'}$ 5.6, $J_{4,5}$ 7.9 Hz, H-5), 4.44 (d, $J_{1,2}$ 3.9 Hz, H-1), 4.37 (dd, $J_{5,6}$ 3.4, $J_{6,6'}$ 12.3 Hz, H-6), 4.07 (dd, $J_{5,6'}$ 5.6, $J_{6,6'}$ 12.3 Hz, H-6'), 2.03, 2.02, 2.01, 1.98, and 1.93 (5 s, 3 H each, 5 OAc); ^{13}C-n.m.r.: δ 170.2, 169.7, 169.65, 169.6, 169.3 (*Me*CO), 133.6–127.6 (multiple signals, 2 Ph), 71.9, 69.7, 69.5, 68.1 (C-2,3,4,5), 62.1 (C-6), 60.8 (C-1), 20.8, 20.75, 20.7, 20.66, and 20.57 (*CO*Me).

Anal. Calc. for $C_{28}H_{32}O_{10}S_2$ (592.7): C, 56.74; H, 5.44; S, 10.82. Found: C, 56.16; H, 5.57; S, 10.76.

*2,3,4,5,6-Penta-*O*-acetyl-1-chloro-1-*S*-phenyl-1-thio-*L*-gulitol* (**12**). — A mixture of **7** (0.77 g), *N*-chlorosuccinimide (0. 23 g) and CCl_4 (20 mL) was stirred for 16 h at room temperature, after which t.l.c. (solvent *I*, triple irrigation) revealed 2 spots, R_F 0.4 and 0.35. Filtered from suspended succinimide, the solution was evaporated to give crude **12** as a mixture of epimers. Column chromatography (solvent *I*) gave 3 syrupy fractions weighing 122 mg (chiefly the faster-moving epimer), 520 mg (both epimers), and 36 mg (chiefly the slower epimer), for a total of 678 mg (88%). The middel fraction had $[\alpha]_D$ −2°, $[\alpha]_{365}$ −25° (*c* 1).

Anal. Calc. for $C_{22}H_{27}ClO_{10}S$ (518.95): C, 50.91; H, 5.25. Found: C, 51.15; H, 5.30.

The *faster-moving epimer* had ν_{max}^{film} 1750, 1368, 1240–1200, 1045, 966, and 690 cm^{-1}; *m/z* 482 (M^+ − HCl), 461 and 459 (M^+ + 1 − AcOH), and 423 (M^+ + 1 − HCl − AcOH); ^{1}H-n.m.r.: δ 7.53–7.36 (m, 5 H, Ph), 5.70 (dd, $J_{3,4}$ 2.1, $J_{2,3}$ 8.0 Hz, H-3), 5.45 (dd, $J_{1,2}$ 3.6, $J_{2,3}$ 8.0 Hz, H-2), 5.44 (dd, H-4), 5.28 (d, $J_{1,2}$ 3.6 Hz, H-1), 5.13 (ddd, *J* 3.4, 5.5, and 8 Hz, H-5), 4.40 (dd, $J_{5,6}$ 3.4, $J_{6,6'}$ 12.4 Hz, H-6), 4.10 (dd, $J_{5,6'}$ 5.5, $J_{6,6'}$ 12.4 Hz, H-6'), 2.15, 2.10, 2.07, 2.06, and 2.03 (5 s, 15 H, 5 OAc); ^{13}C-n.m.r.: δ 170.2; 169.7, 169.6, 169.5, 169.1 (*Me*CO), 137.8, 133.5, 131.8, 129.2 (Ph), 72.9 (C-2 or C-4), 70.8 (C-1), 69.6 (C-5), 69.2 (C-3), 68.0 (C-4 or C-2), 62.0 (C-6), and 21.0–20.7 (*CO*Me).

The *slower-moving epimer* had ν_{max}^{film} 1750, 1370, 1213, 1050, 964, and 690 cm^{-1}; *m/z* 483 (M^+ + 1 − HCl), 461 and 459 (M^+ + 1 − AcOH), and 423 (M^+ + 1 − HCl − AcOH); ^{1}H-n.m.r.: δ 7.55–7.36 (m, 5 H, Ph), 5.57 (dd, $J_{3,4}$ 2.1, $J_{2,3}$ 7 Hz, H-3), 5.47 (2 dd, H-2,4), 5.30 (d, $J_{1,2}$ 5.0 Hz, H-1), 5.14 (ddd, *J* 3.6, 5.5, and 7.7 Hz, H-5), 4.40 (dd, $J_{5,6}$ 3.6, $J_{6,6'}$ 12.4 Hz, H-6), 4.06 (dd, $J_{5,6'}$ 5.5, $J_{6,6'}$ 12.4 Hz, H-6'), 2.12, 2.10, 2.07, 2.04, and 2.03 (5 s, 15 H, 5 OAc); ^{13}C-n.m.r.: δ 170.2, 169.7, 169.65, 169.4, 169.25 (*Me*CO), 133.6, 130.6,

129.2, 123.9 (Ph), 71.6, 69.6, 69.3, 68.5, 67.9 (C-1,2,3,4,5), 61.9 (C-6), and ~20.7 (several peaks, *CO*Me).

L-*Gulose* (**13**). — A solution of **10** (400 mg) in MeOH (30 mL) containing a catalytic amount of NaOMe was kept for 1 h at room temperature, deionized with Amberlite IR-120 (H^+), and evaporated. The material was passed through a column of silica gel; elution with EtOAc (100 mL) removed PhSH, and solvent *C* then eluted **13** (100 mg) as a syrup, $[\alpha]_D$ +17° (*c* 5, water), lit.[9] +20° (*c* 13.6, water). The crystalline $CaCl_2$ addition compound, prepared as directed[9], had m.p. 200–203° (dec.) as reported.

2,3,4,5,6-Penta-O-*acetyl*-aldehydo-L-*gulose* (**14**). — To a solution of **12** (400 mg) in CH_3CN (20 mL) and water (7 mL) was added $Cu(OAc)_2$ (0.5 g) and CuO (0.5 g). The mixture was vigorously stirred for 40 min at 60°. T.l.c. (solvent *E*) revealed the absence of **12** (R_F 0.8, u.v. positive) and presence of **14** (R_F 0.2, u.v. negative). The mixture was cooled, concentrated, taken up in water (15 mL), and filtered. Extraction of the filtrate with EtOAc (4 × 50 mL), drying and concentration of the extract, and passage of the residue over a silica gel column with solvent *E* gave syrupy **14** (132 mg, 44%), $[\alpha]_D$ −5° (initial) → −7° (2 h, final; *c* 2); ν_{max}^{film} 3600–3300, 1750, 1370, 1220, and 1045 cm^{-1}; *m/z* 391 (M^+ + 1) and 331 (M^+ + 1 − AcOH); ^{1}H-n.m.r.: δ 9.45 and 5.11 (d and dd, 0.3 H each, $J_{1,2}$ 1, $J_{2,3}$ 5.5 Hz, H-1 and H-2 of *aldehydo* form), 5.6–5.2 and 4.9 (ill-resolved multiplets, ~4.4 H, H-1,2 of hydrate and H-3,4,5 of both forms), 4.32 (dd, 1 H, $J_{5,6}$ 4.3, $J_{6,6'}$ 12.1 Hz, H-6), 3.99 (dd, 1 H, $J_{5,6'}$ 5.8, $J_{6,6'}$ 12.1 Hz, H-6'), 2.10–2.04 (multiple s, 15 H, 5 OAc), and 1.9 (broad, OH); ^{13}C-n.m.r.: 196.2 (C-1, *aldehydo* form), 170.8–169.8 (9 peaks, *Me*CO), 74.7 (C-1, hydrate), 69.4–68.4 (8 peaks, C-2,3,4,5, both forms), 61.5 (C-6), and 20.5–20.1 (multiple peaks, *CO*Me).

1,2:3,4-Di-O-*isopropylidene-6*-S-*phenyl-6-thio-α*-D-*galactopyranose* (**16**). — Diphenyl disulfide (8.8 g) and Bu_3P (20 mL) were added to a solution of 1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose[10] (7.0 g) in dry pyridine (14 mL). The mixture was kept for 20 h at room temperature, and then diluted with CH_2Cl_2 (100 mL), washed with 5% HCl (2 × 100 mL), aq. $NaHCO_3$ (100 mL), and water (50 mL), dried (K_2CO_3), and concentrated. The crude product was chromatographed on a column by use of hexane (1 L) followed by solvent *K* to give syrupy **16** (9.00 g, 95%); R_F 0.7 (t.l.c., solvent *I*), $[\alpha]_D$ −110° (*c* 1); ν_{max}^{film} 3060, 1580, 1480, 1455, 1440, 1300–800 (multiple bands), 732, and 685 cm^{-1}; *m/z* 353 (M^+ + 1), 352 (M^+), and 295 (M^+ + 1 − Me_2CO); ^{1}H-n.m.r.: δ 7.38–7.11 (m, 5 H, Ph), 5.50 (d, $J_{1,2}$ 5.1 Hz, H-1), 4.57 (dd, $J_{2,3}$ 2.4, $J_{3,4}$ 8 Hz, H-3), 4.37 (dd, $J_{4,5}$ 1.8, $J_{3,4}$ 8 Hz, H-4), 4.26 (dd, $J_{2,3}$ 2.4, $J_{1,2}$ 5.1 Hz, H-2), 3.81 (dt, $J_{4,5}$ 1.5, $J_{5,6} = J_{5,6'}$ = 7 Hz, H-5), 3.15 (d, 2 H, *J* 7 Hz, H-6,6'), 1.44, 1.33, 1.26, and 1.21 (4 s, 3 H each, 4 *C*Me); ^{13}C-n.m.r.: δ 135.6, 129.4, 128.9, 126.1 (Ph), 109.3 and 108.5 (Me_2CO_2), 96.6 (C-1), 71.3, 70.9, 70.5, 66.1 (C-2,3,4,5), 33.3 (C-6), 26.1, 25.7, 25.0, and 24.5 (2 Me_2C).

Anal. Calc. for $C_{18}H_{24}O_5S$ (352.5); C, 61.34; H, 6.86: S, 9.09. Found: C, 61.53; H, 7.09; S, 8.96.

6-S-*Phenyl-6-thio*-D-*galactose* (**17**). — Compound **16** (8.3 g) was boiled for 2.5 h under reflux, in a mixture of 1,4-dioxane (50 mL), water (30 mL), and CF_3CO_2H (15 mL). The solvents were evaporated and the solid product was washed with ether and dried in a desiccator, to give **17** (5.8 g, 90.4%), m.p. 146–147° (from EtOAc–hexane), $[\alpha]_D$

$-1.3°$, $[a]_{365}$ $-6.0°$ (*c* 1, CH_3OH); ν_{max}^{KBr} 3500–3160, 1140, 1110, and 1070 cm^{-1}; *m/z* 272 (M^+), 271 ($M^+ - 1$), 255 ($M^+ + 1 - H_2O$), 237 ($M^+ + 1 - 2H_2O$), and 213; ^{1}H-n.m.r. (D_2O): 7.5–7.3 (m, 5 H, Ph), 5.25 (d, ~0.3 H, *J* 3.2 Hz, H-1, *α* anomer), and 4.51 (d, ~0.7 H, *J* 7.6 Hz, H-1, *β* anomer); ^{13}C-n.m.r. (Me_2SO-d_6): δ 136.4, 129.0, 127.8, 125.5 (Ph), 97.5 (C-1), 73.3, 72.8, 71.7, 69.0 (C-2,3,4,5), and 31.7 (C-6). It appears that **17** crystallized as the *α* anomer and underwent anomerization in aqueous solution but not in Me_2SO.

Anal. Calc. for $C_{12}H_{16}O_5S$ (272.3): C, 52.93; H, 5.92; S, 11.77. Found: C, 52.71; H, 5.95; S, 11.73.

*6-S-Phenyl-6-thio-*D*-galactitol* (**18**). — To a stirred solution of **17** (5.0 g) in MeOH (250 mL) was added $NaBH_4$ (1.4 g), in portions. After 2 h, water (25 mL) was added, the solution deionized with Amberlite IR-120 (H^+) resin and concentrated, and boric acid removed by repeated evaporations of MeOH from the product which was then washed with 2:1 water–MeOH (50 mL) and ether (50 mL), to give **18** (4.7 g, 93%); m.p. 180–182° (from methanol), $[a]_D$ + 5.5°, $[a]_{365}$ +14° (*c* 1, pyridine); ν_{max}^{KBr} 3400, 3200, 1100, 1090, 1080, 1050, 1030, 1028, and 730 cm^{-1}; *m/z* 275 ($M^+ + 1$), 274 (M^+), 257 ($M^+ + 1 - H_2O$), 239 ($M^+ + 1 - 2H_2O$), 221 ($M^+ + 1 - 3H_2O$), 203 ($M^+ + 1 - 4H_2O$), and 165 ($M^+ + 1$ − PhSH); ^{1}H-n.m.r. (Me_2SO-d_6): δ 7.3–7.15 (m, 5 H, Ph), 4.58 (d, *J* 7 Hz, OH), 4.43 (t, *J* 5.4 Hz, OH-1), 4.39 (d, *J* 7.3 Hz, OH), 4.14 (d, *J* 6.8 Hz, OH), 4.06 (d, *J* 7.3 Hz, OH), 3.9–3.4 (m, 6 H, H-1 to H-5), 3.10 (dd, *J* 6.8 and 13.1 Hz, H-6), and 3.02 (dd, *J* 6.9 and 13.1 Hz, H-6′); ^{13}C-n.m.r. (Me_2SO-d_6): δ 137.0, 128.8, 127.3, 125.0 (Ph), 70.25, 70.0, 69.3, 68.1 (C-2,3,4,5,), 63.1 (C-1), and 36.1 (C-6).

Anal. Calc. for $C_{12}H_{18}O_5S$ (274.3): C, 52.54; H, 6.61; S, 11.69. Found: C, 52.41; H, 6.70; S, 11.56.

*1,2,3,4,5-Penta-O-acetyl-6-S-phenyl-6-thio-*D*-galactitol* (**19**). — Compound **18** (4.7 g) was treated with Ac_2O (15 mL) and pyridine (8 mL) at room temperature during 16 h. Coevaporation of the reagents with added PhMe, followed by column chromatography (solvent *F*) of the crude product gave **19** (7.1 g, 85.5%), m.p. 121–123° (from EtOAc–hexane), $[a]_D$ −10° (*c* 2); ν_{max}^{KBr} 1750–1730, 1575, 1230–1200, 1070–1035, 950, 860, 833, and 730 cm^{-1}; *m/z* 425 ($M^+ + 1$ − AcOH); ^{1}H-n.m.r.: δ 7.4–7.1 (m, 5 H, Ph), 5.40 and 5.27 (dd, 1 H, and m, 2 H, H-2,3,4), 5.11 (septet, $J_{4,5}$ 1.7 Hz, H-5), 4.25 (dd, $J_{1,2}$ 4.6, $J_{1,1'}$ 11.6 Hz, H-1), 3.79 (dd, $J_{1',2}$ 7.2 Hz, $J_{1,1'}$ 11.6 Hz, H-1′), 2.97 (dd, $J_{5,6}$ 7.4, $J_{6,6'}$ 14.1 Hz, H-6), 2.85 (dd, $J_{5,6'}$ 6.3, $J_{6,6'}$ 14.1 Hz, H-6′), 2.11, 2.07, 2.00, 1.99, and 1.99 (5 s, 15 H, 5 OAc); ^{13}C-n.m.r.: δ 170.3; 170.15, 170.1, 169.8, 169.6 (*Me*CO), 134.9, 130.2, 128.9, 126.7 (Ph), 68.8, 68.5, 67.8, 67.7 (C-2,3,4,5), 62.3 (C-1), 34.9 (C-6), and 20.8–20.6 (Me*CO*).

Anal. Calc. for $C_{22}H_{28}O_{10}S$ (484.5): C, 54.53; H, 5.82; S, 6.62. Found: C, 54.57, H, 5.90; S, 6.63.

*1,2,3,4,5-Penta-O-acetyl-6-deoxy-6-phenylsulfinyl-*D*-galactitol* (**20**). — 3-Chloroperoxybenzoic acid (1.25 g) in CH_2Cl_2 (50 mL) was added dropwise, at 15°, to **19** (3.0 g) in CH_2Cl_2 (50 mL). After 1 h, t.l.c. (ether) revealed complete consumption of the fast-moving **19** and showed a slow-moving spot for **20**. The solvent was evaporated, and the solid residue triturated several times with ether to free it from acid, to give **20** (2.61 g). Additional **20** (0.3 g, for a total yield of 94%) was obtained on chromatographic

processing of the ether washings; m.p. 179–181° (from ether–hexane), $[\alpha]_D$ −35.5° (*c* 2); ν_{max}^{KBr} 1740, 1375, 1220, 1055, 1025, and 960 cm^{-1}; *m/z* 501 ($M^+ + 1$), 459 ($M^+ + 1 - CH_2CO$), 441 ($M^+ + 1 - AcOH$), 425 ($M^+ + 1$ AcOH − O), 375 ($M^+ + 1 - PhSOH$), 369, and 257. The ^{1}H-n.m.r. spectrum showed separate signals (2:3 intensity ratio) for some of the corresponding protons of *S*-epimers, designated *a* and *b*: δ 7.7–7.5 (m, 5 H, Ph*a,b*), 5.63 (ddd, *J* 1.9, 2.8, and 8.9, H-5*a*), 5.40 (ddd, *J* 1.9, 4.4, and 8.5, H-5*b*), 5.32–5.18 (m, 3 H, H-2*a,b*, 3*a,b*, 4*a,b*), 4.28 (dd, *J* 4.6 and 7.8 Hz, H-1*a*), 4.24 (dd, *J* 4.5 and 7.7 Hz, H-1*b*), 3.80 (dd, *J* 3.2 and 7.5 Hz, H-1′*b*), 3.76 (dd, *J* 3.2 and 7.6 Hz, H-1′*a*), 2.99 (dd, *J* 8.5 and 13.6 Hz, H-6*b*), 2.94 (*J* 2.8 and 13.8 Hz, H-6*a*), 2.90 (dd, *J* 4.4 and 13.6 Hz, H-6′*b*), 2.73 (dd, *J* 8.9 and 13.8 Hz, H-6′*a*), and 2.12–1.99 (10 s, total 15 H, 5 OAc*a,b*); ^{13}C-n.m.r.: δ 170.3–169.6 (*Me*CO), 143.4, 131.4, 129.35, 129.3, 124.2, 123.9 (Ph), 70.1, 69.3, 67.6, 67.6, 67.5, 67.45, 65.0, 64.8 (C-2,3,4,5), 62.3 and 62.2 (C-1), 60.5 and 59.3 (C-6), and 20.7 (Me*CO*).

Anal. Calc. for $C_{22}H_{28}O_{11}S$ (500.5): C, 52.79; H, 5.64; S, 6.40. Found: C, 52.74; H, 5.80; S, 6.14.

6-Deoxy-6-phenylsulfinyl-D-*galactitol* (**21**). – Compound **20** (1.0 g) was treated with a catalytic amount of NaOMe in MeOH (50 mL) during 2 h at room temperature. Evaporation of the deionized solution, and trituration of the resulting solid with MeOH, gave **21** [376 mg, plus 180 mg (96%) from the mother liquor by column chromatography with solvent *D*], m.p. 226–228°, $[\alpha]_D$ +74° (*c* 1, pyridine); ν_{max}^{KBr} 3400–3300, 1440, 1398, 1300–1190, 1090–970, 847, and 685 cm^{-1}; *m/z* 291 ($M^+ + 1$); ^{13}C-n.m.r. (Me_2SO-d_6): δ 145.5, 130.5, 129.2, 123.5 (Ph), 72.0, 69.9, 69.3, 64.5 (C-2,3,4,5), 64.1 and 63.0 (C-1,6).

Anal. Calc. for $C_{12}H_{18}O_6S$ (290.3): C, 49.64; H, 6.25; S, 11.04. Found: C, 49.78; H, 6.33; S, 10.88.

1,2,3,4,5,6-Hexa-O-*acetyl*-L-*galactose* S-*phenyl thiohemiacetals* (**22**). — *A. Procedure I.* A mixture of **20** (1.0 g), Ac_2O (12 mL), and anhydrous NaOAc (1.2 g) was efficiently stirred for 12 h at the reflux temperature. Processing and column chromatography as described for **10** gave **22** as 2 homogeneous fractions consisting of epimer I (eluted first) and epimer II.

Epimer I (0.52 g, 48%) had m.p. 82–83° (from ether at 0°), $[\alpha]_D$ −36° (*c* 2); ν_{max}^{film} 1750, 1480, 1440, 1370, 1250–1200, 1040, 750, and 690 cm^{-1}; *m/z* 483 ($M^+ + 1 - AcOH$), 433 ($M^+ + 1 - PhSH$), and 423 ($M^+ + 1 - 2$ AcOH); ^{1}H-n.m.r.: δ 7.45–7.30 (m, 5 H, Ph), 5.95 (d, $J_{1,2}$ 7.8 Hz, H-1), 5.48 (dd, $J_{2,3}$ 1.9, $J_{3,4}$ 9.9 Hz, H-3), 5.35 (dd, *J* 1.9 and 7.8 Hz, H-2), 5.20 (dd, $J_{4,5}$ 1.9, $J_{3,4}$ 9.9 Hz, H-4), 5.15 (m, H-5), 4.25 (dd, $J_{5,6}$ 4.8, $J_{6,6'}$ 11.7 Hz, H-6), 3.77 (dd, $J_{5,6'}$ 7.3, $J_{6,6'}$ 11.7 Hz, H-6′), 2.11, 2.06, 2.05, 2.03, 1.99, and 1.98 (6 s, 3 H each, 6 OAc); ^{13}C-n.m.r.: δ 170.2, 170.1, 169.7, 169.6, 169.5, 168.9 (*Me*CO), 134.0, 130.7, 128.9, 128.6 (Ph), 78.8 (C-1), 69.3, 67.8, 67.6, 66.8 (C-2,3,4,5), 62.3 (C-6), and 21.0–20.7 (*CO*Me).

Anal. Calc. for $C_{24}H_{30}O_{12}S$ (542.5): C, 53.15, H, 5.57; S, 5.91. Found: C, 53.10; H, 5.71; S, 5.73.

Epimer II was obtained as a syrup (0.35 g, 32%) that crystallized slowly on being kept; m.p. 71–72°, $[\alpha]_D$ +72° (*c* 2). The i.r. and mass spectra were similar to those of

epimer I; ^{1}H-n.m.r.: δ 7.54–7.35 (m, 5 H, Ph), 5.93 (d, $J_{1,2}$ 9 Hz, H-1), 5.71 (dd, $J_{2,3}$ 1.8, $J_{3,4}$ 9.5 Hz, H-3), 5.17 (dd, J 1.8 and 9 Hz, H-2), 5.12 (m, 2 H, H-4,5), 4.21 (dd, $J_{5,6}$ 5.1, $J_{6,6'}$ 11.7 Hz, H-6), 3.79 (dd, $J_{5,6'}$ 7.1, $J_{6,6'}$ 11.7 Hz, H-6'), 2.12, 2.09, 2.04, 2.02, 1.99, and 1.90 (6 s, 3 H each, 6 OAc); ^{13}C-n.m.r.: δ 170.3, 170.1, 169.5, 169.5, 169.2, 168.5 ((*Me*-CO), 134.3, 129.7, 129.1, 128.9 (Ph), 77.4 (C-1), 69.1, 67.8, 67.65, 67.0 (C-2,3,4,5), 62.1 (C-6), and 20.9–20.55 ((*CO*Me).

Anal. Calc. as for epimer I. Found: C, 53.27; H, 5.70; S, 5.78.

B. Procedure II. A solution of **20** (0.63 g), Ac_2O (10 mL), and *p*-toluenesulfonic acid trihydrate (0.60 g) in CH_2Cl_2 (40 mL) was heated under reflux for 10 h. Processing (as described for **10**, procedure II) and column chromatography (solvent *I*) of the product gave epimer I (0.49 g, 72%), m.p. 82–83°, and syrupy epimer II (0.16 g, 23%), identified by their ^{1}H-n.m.r. spectra.

*2,3,4,5,6-Penta-*O*-acetyl-*L*-galactose diphenyl dithioacetal* (**23**). — Compound **22** (epimer mixture, 0.28 g), and PhSH (0.8 mL) in CH_2Cl_2 (20 mL) were treated at room temperature with $BF_3{\cdot}Et_2O$ (8 drops) during 30 min. Processing and chromatography as described for **11** gave **23** (0.20 g, 65%), m.p. 153–155° (from ether–hexane), $[\alpha]_D$ +37° (*c* 2); ν_{max}^{KBr} 1750, 1370, 1250–1200, 1075–1020, 750, and 690 cm^{-1}; *m/z* 483 (M^+ + 1 − PhSH), and 423 (M^+ + 1 − PhSH − AcOH); ^{1}H-n.m.r.: δ 7.40–7.30 (m, 10 H, 2 Ph), 5.73 (dd, $J_{2,3}$ 1.7, $J_{3,4}$ 9.7 Hz, H-3), 5.24 (dd, $J_{2,3}$ 1.7, $J_{1,2}$ 5.5 Hz, H-2), 5.22 (m, H-5), 5.20 (dd, $J_{4,5}$ 2.1, $J_{3,4}$ 9.7 Hz, H-4), 4.48 (d, $J_{1,2}$ 5.5 Hz, H-1), 4.23 (dd, $J_{5,6}$ 4.9, $J_{6,6'}$ 11.7 Hz, H-6), 3.79 (dd, $J_{5,6'}$ 7.9, $J_{6,6'}$ 11.7 Hz, H-6'), 2.09, 2.08, 2.05, 1.99, and 1.93 (5 s, 3 H each, 5 OAc); ^{13}C-n.m.r.: δ 170.3, 170.2, 170.0, 169.8, 169.6 (*Me*CO), 134.2–127.7 (multiple signals, 2 Ph), 70.3, 68.2, 67.9, 67.65 (C-2,3,4,5), 62.3 (C-6), 60.1 (C-1), 21.3, 20.9, 20.73, 20.7, and 20.57 (*CO*Me).

Anal. Calc. for $C_{28}H_{32}O_{10}S_2$ (592.7): C, 56.74; H, 5.44; S, 10.82. Found: C, 56.55; H, 5.64; S, 10.61.

*2,3,4,5,6-Penta-*O*-acetyl-1-chloro-*S*-phenyl-1-thio-*L*-galactitol* (**24**). — A solution of **19** (1.0 g) in CCl_4 (25 mL) was stirred for 18 h at room temperature with *N*-chlorosuccinimide (0.28 g), filtered, and evaporated to give a crude material that was purified by column chromatography (solvent *H*), yielding solid **24** (0.90 g, 84%); m.p. 135–136°, $[\alpha]_D$ +52° (*c* 2); ν_{max}^{KBr} 1750, 1370, 1220, 1045, 955, and 765 cm^{-1}; *m/z* 483 (M^+ − Cl), 461 and 459 (M^+ + 1 − AcOH), and 423 (M^+ − Cl − AcOH). The ^{1}H-n.m.r. spectrum suggested the presence of epimers in 1:3 ratio: δ 7.5–7.3 (m, 5 H, Ph), 5.86 (dd, 0.25 H, J 1.7 and 9.7 Hz), 5.70 (dd, 0.75 H, J 1.8 and 9.6 Hz), 5.46 (dd, 0.75 H, J 1.8 and 6.1 Hz), 5.25–5.16 (m, 3.25 H), 4.28 (2 almost coincident dd, ratio 1:3, 1 H, $J_{5,6}$ 4.8, $J_{6,6'}$ 11.6 Hz, H-6 of both epimers), 3.82 (dd, 0.25 H, $J_{5,6'}$ 7.2 Hz, H-6' of one epimer), 3.81 (dd, 0.75 H, $J_{5,6'}$ 7.1 Hz, H-6' of the other epimer), and 2.15–2.00 (5 major and 4 minor singlets, 15 H total, 5 OAc); ^{13}C-n.m.r.: δ 170.3, 170.1, 169.7, 169.7, 169.5, (*Me*CO), 133.8–128.8 (multiple signals, Ph), 71.6, 69.4, 68.0, 67.6, and 67.6 (C-1,2,3,4,5, major epimer), 70.6–67.0 (5 signals for the minor epimer), 62.2 (C-6, major epimer), 62.1 (C-6, minor epimer), and 21.0–20.7 (*CO*Me).

Anal. Calc. for $C_{22}H_{27}ClO_{10}S$ (518.95): C, 50.91; H, 5.25; S, 6.18. Found: C, 50.80; H, 5.36; S, 6.19.

L-*Galactose* (**25**). — A solution of **22** (400 mg) in MeOH (30 mL) was treated at 25° with a catalytic amount of NaOMe (1 h), deionized, and concentrated for column chromatography. Elution with EtOAc first removed PhSH, and subsequently, elution with solvent *B* produced solid **25** (101 mg, 76%); m.p. 158–159°, raised to 166–167° by recrystallization from 96% EtOH, $[\alpha]_D$ −82° (*c* 1, water); lit.[11] m.p. 163–165°, $[\alpha]_D$ −78° and m.p. 165°, $[\alpha]_D$ −81°.

2,3,4,5,6-Penta-O-*acetyl*-aldehydo-L-*galactose* (**26**). — Compound **24** (0.57 g) was treated with $Cu(OAc)_2$ and CuO in MeCN–water, and the mixture was processed as described for the preparation of **14** from **12**. There was obtained crystalline **26** (0.30 g, 70%); m.p. 108–109° (from acetone–hexane) and 109–110° (from PhMe–hexane), $[\alpha]_D$ +19° (initial) → −11° (2 h, final; *c* 1); lit.[12] for the D enantiomer, m.p. 120–121°, $[\alpha]_D$ −25° → +10° (mutarotation attributed to reaction with EtOH present in the solvent $CHCl_3$); ν_{max}^{KBr} 2850, 1755, 1745, 1737, 1230, 1210, 1056, and 965 cm^{-1}; *m/z* 391 ($M^+ + 1$), 331 ($M^+ + 1 - AcOH$), and 271 ($M^+ + 1 - 2\,AcOH$); ^{1}H-n.m.r.: δ 9.43 (s, H-1), 5.62 (dd, $J_{2,3}$ 1.8, $J_{3,4}$ 9.9 Hz, H-3), 5.45 (dd, $J_{4,5}$ 2, $J_{3,4}$ 9.9 Hz, H-4), 5.34 (ddd, *J* 2.0, 5.1, and 7.5 Hz, H-5), 5.24 (d, $J_{2,3}$ 1.8 Hz, H-2), 4.25 (dd, $J_{5,6}$ 5.1, $J_{6,6'}$ 11.6 Hz, H-6), 3.88 (dd, $J_{5,6'}$ 7.5, $J_{6,6'}$ 11.6 Hz, H-6'), 2.19, 2.10, 2.09, 2.02, and 2.01 (5 s, 3 H each, 5 OAc); ^{13}C-n.m.r.: δ 193.2 (C-1), 170.2, 170.0, 169.8, 169.6, 169.2 (*Me*CO), 75.7, 67.45, 67.4, 66.2 (C-2,3,4,5), and 20.7–20.4 (*CO*Me).

Anal. Calc. for $C_{16}H_{22}O_{11}$ (390.3): C, 49.23; H, 5.68. Found: C, 49.16; H, 5.60.

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REFERENCES

1 J. E. McCormick and R. S. McElhinney, *J. Chem. Soc., Chem. Commun.*, (1969) 171–172; *J. Chem. Soc., Perkin Trans. 1*, (1976) 2533–2540; J. O. Jones and R. S. McElhinney, *J. Chem. Res.*, (1982) (S) 116; (M) 1368; (1984) (S) 146–147; (M) 1501–1517.
2 F. Santoyo González, P. Garcia Mendoza, and F. J. López Aparicio, *Carbohydr. Res.*, 183 (1988) 227–240.
3 H. H. Baer and F. Santoyo González, *Carbohydr. Res.*, 1990, in press.
4 I. Nakagawa and T. Hata, *Tetrahedron Lett.*, (1975) 1409–1412; I. Nakagawa, K. Aki, and T. Hata, *J. Chem. Soc., Perkin Trans. 1*, (1983) 1315–1318.
5 K. Narasaka, T. Sakashita, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 45 (1972) 3724; P. Bakuzis, M. L. F. Bakuzis, C. C. Fortes, and R. Santos, *J. Org. Chem.*, 41 (1976) 2769–2770.
6 D. Horton and J. D. Wander, in W. Pigman and D. Horton (Eds.), the *Carbohydrates*, Academic Press, New York, Vol. 1B (1980), pp. 799–842; M. L. Wolfrom, *ibid.*, Vol. IA (1972), pp. 355–390; J. D. Wander and D. Horton, *Adv. Carbohydr. Chem. Biochem.*, 32 (1976) 15–123.
7 R. L. Whistler and A. K. M. Anisuzzaman, *Methods Carbohydr. Chem.*, 8 (1980) 227–231.
8 S. J. Angyal, R. Le Fur, and D. Gagnaire, *Carbohydr. Res.*, 23 (1972) 121–134.
9 J. C. Sowden and H. O. L. Fischer, *J. Am. Chem. Soc.*, 67 (1945) 1713–1716.
10 R. S. Tipson, *Methods Carbohydr. Chem.*, 2 (1963) 246–250; O. T. Schmidt, *ibid.*, pp. 318–325.

11 C. Araki and K. Arai, *Methods Carbohydr. Chem.*, 1 (1962) 122–126.
12 M. L. Wolfrom, *J. Am. Chem. Soc.*, 52 (1930) 2464–2473; M. L. Wolfrom and W. H. Decker, *Justus Liebigs Ann. Chem.*, 690 (1965) 163–165.