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SYNTHESIS OF 4-THIO-D-MANNOSE

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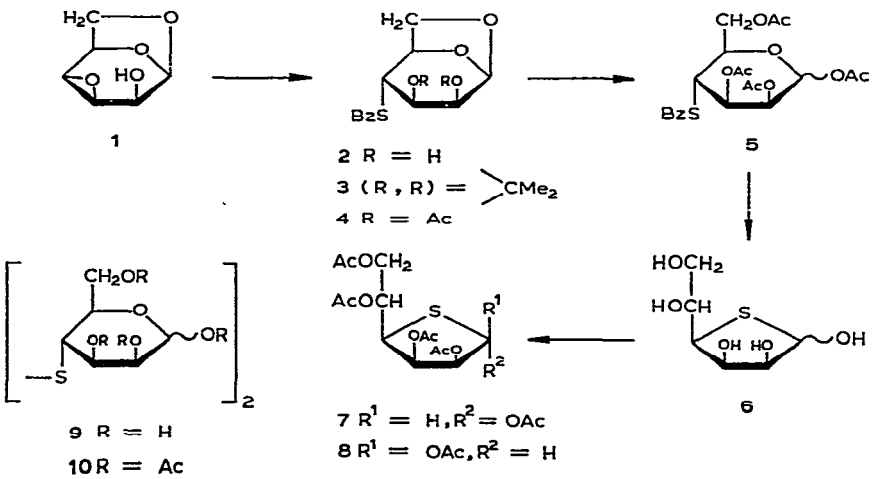
ABSTRACT

1,6-Anhydro-4-*S*-benzoyl-4-thio-β-D-mannopyranose, obtained by treatment of 1,6:3,4-dianhydro-β-D-talopyranose with pyridinium thiolbenzoate in *N*,*N*-dimethylformamide, was converted into its 2,3-di-*O*-acetyl derivative, which was acetolyzed to give 1,2,3,6-tetra-*O*-acetyl-4-*S*-benzoyl-4-thio-D-mannopyranose. Deacylation of the last-named compound with sodium methoxide in methanol gave syrupy 4-thio-D-mannose, which was characterized as 1,2,3,5,6-penta-*O*-acetyl-4-thio-α- and -β-D-mannofuranose.

INTRODUCTION

The alkyl[1–5], aryl[1,6–9], and aralkyl[10,11] glycosides derived from 1-thio sugars have been widely studied as inhibitors of glycosidases. However, except for the inhibition[12] of β-D-xylosidase and α-L-arabinosidase (both enzymes from hemicellulase) by 5-thio-D-xylopyranose, similar studies involving other glycosidases and derivatives



of other sugars bearing a thiol function at a non-anomeric position do not appear to have been reported. We describe here the synthesis of 4-thio-D-mannose (**6**) as a potential inhibitor of α-D-mannosidase. A previous attempt to obtain **6** by acid hydrolysis of 1,6-anhydro-4-thio-β-D-mannopyranose was reported to be unsuccessful[13].

RESULTS AND DISCUSSION

The reaction of 1,6:3,4-dianhydro-β-D-talopyranose[14] (**1**) with pyridinium thiolbenzoate in *N*,*N*-dimethylformamide for 1 h at 115° caused diaxial opening of the 3,4-anhydro ring and gave 1,6-anhydro-4-*S*-benzoyl-4-thio-β-D-mannopyranose (**2**) in 72.5% yield. When **1** was fused with pyridinium thiolbenzoate, according to conditions employed by Kocourek[15] for opening of the oxirane ring of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside, a 61% yield of **2** was obtained. Conversion of **2** into its isopropylidene ketal **3** was achieved by stirring its solution in acetone with anhydrous copper sulfate. A trace of material, identical in mobility with that of **2**, remained unchanged during isopropylidenation, and presumably was the isomeric product resulting from the diequatorial epoxide-opening of **1**, namely, 1,6-anhydro-3-*S*-benzoyl-3-thio-β-D-idopyranose; in contrast to **2**, the D-*ido* isomer is incapable of forming an isopropylidene ketal, because of the 1,3-diequatorial disposition of its hydroxyl groups. Owen and Ragg[13] obtained 1,6-anhydro-4-*S*-benzyl-4-thio-β-D-mannopyranose by opening the oxirane ring of **1** with sodium α-toluenethioxide. We preferred the *S*-benzoyl group for **2**, because of the convenience and ease whereby it may be removed by deacylation with sodium methoxide in methanol.

The 4-thiolbenzoate (**2**) was acetylated with acetic anhydride in pyridine, and the resulting, crystalline diacetate **4** was acetolyzed to give syrupy 1,2,3,6-tetra-*O*-acetyl-4-*S*-benzoyl-4-thio-D-mannopyranose (**5**) in ~97% yield. T.l.c. and optical rotatory (+102°) data suggested that **5** was predominantly (~90%) the α anomer; however a slightly slower-moving component (~10%), presumably the β anomer, was also present. Both the elemental analysis and the i.r. spectral data were in accord with the structure **5**.

The retention of the *S*-benzoyl group and the lack of contraction of the pyranose ring to the furanose form during acetolysis of **4** stand in contrast to the behavior of methyl 2,3-di-*O*-acetyl-4-*S*-benzoyl-4-thio-β-D-[16] (**11**) and -L-ribopyranoside[16] (**12**), and methyl 2,3-di-*O*-benzoyl-4-*S*-benzoyl-4-thio-α-D-xylopyranoside[17] (**13**) during similar treatment. Reist *et al.*[16,17] reported that, during acetolysis, these pentopyranosides suffer an essentially complete loss of the 4-*S*-benzoyl group with simultaneous contraction to the sulfur-containing furanose ring. Vegh and Hardegger[18] reported the conversion of 2,3-di-*O*-acetyl-4-*S*-acetyl-1,6-anhydro-4-thio-β-D-glucopyranose (**14**) into 4-thio-α-D-glucopyranose pentaacetate by acetolysis without concomitant ring-contraction to the thiofuranose form. During acetolysis, under essentially identical conditions, methyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-deoxy-4-

thio-α-D-idopyranoside[19] (**15**) undergoes ring contraction to form 6-deoxy-4-thio-α,β-D-idofuranose tetraacetate in 43% yield, whereas, in contrast, the 6-deoxy-D-*altro*[19] (**16**) and 6-deoxy-D-*gulo*[20] (**17**) analogs of **15** do not, but afford the anomeric 4-thio-6-deoxyhexopyranose pentaacetates in 54 and 70% yields, respectively; a 3% yield of tetra-*O*-acetyl-6-deoxy-4-thio-α,β-D-gulofuranose was also obtained[20] from **17**. Acetolysis of methyl 4-*S*-acetyl-6-deoxy-2,3-di-*O*-methyl-4-thio-β-D-glucopyranoside (**18**) leads to the formation, with ring contraction, of 6-deoxy-2,3-di-*O*-methyl-4-thio-α,β-D-glucopyranose diacetate in 45% yield[13] as compared with the pyranose-ring retention during acetolysis of the 4-thio-D-glucopyranose derivative[18] (**14**).

Gross and Oriez suggested[19] that the D-*ido* derivative **15** undergoes ring contraction during acetolysis, but the D-*altro* isomer **16** does not because the 4-thiol group in the latter is equatorial, and hence not close enough for the sulfur atom to attack the carbonium ion at C-1 to form the intermediate required by the mechanism proposed[16] by Reist *et al.*[16,17] to explain the formation of thiofuranose acetates from 4-thiopentopyranosides **11**–**13**. The virtual absence of ring contraction during acetolysis of 6-deoxy-4-thio-D-guloside **17** was explained by Boigegrain and Gross[20] in terms of the instability of the resulting, anomeric, 6-deoxy-4-thio-D-gulofuranose tetraacetates, especially of the α anomer, in which all four substituents are on the same side of the thiofuranose ring; a small amount (3% yield) of the anomeric tetra-*O*-acetyl 6-deoxy-4-thio-D-gulofuranose does, however, arise, because of the axial orientation of the 4-*S*-acetyl group. It is possible that, in addition to the presence of the axial 4-*S*-acetyl group, the greater stabilities of the anomeric 6-deoxy-4-thio-D-idofuranose tetraacetates relative to those of their pyranose analogs enhances the proclivity of methyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-deoxy-4-thio-α-D-idopyranoside (**15**) to undergo ring contraction during acetolysis[19]. In the $^4C_1$(D) conformation, the α anomer of 1,2,3-tri-*O*-acetyl-4-*S*-acetyl-6-deoxy-4-thio-D-idopyranose is destabilized by two *syn*-diaxial interactions, whereas the β anomer is destabilized by one *syn*-diaxial interaction and the anomeric effect[21,22] arising from equatorial orientation of the 1-acetoxyl group.

Although the 4-*S*-acyl groups of 2,3-di-*O*-acetyl-1,6-anhydro-4-thio-β-D-glucopyranose[18] (**14**) and -mannopyranose (**4**) are axial, neither of these two derivatives undergoes ring contraction during acetolysis with the formation of thiofuranose acetate products. This must arise from the fact that the generation of the C-1 carbonium ion by cleavage of the 1,6-anhydro bridge is accompanied by reversion to the $^4C_1$(D) conformation, in which the 4-*S*-acyl group is equatorial. For the 4-thio-D-mannose derivative **4**, another factor that deters the formation of thiofuranose acetates may be (as in the acetolysis of methyl 2,3-di-*O*-acetyl-4-*S*-acetyl-6-deoxy-4-thio-α-D-gulopyranoside[20], **17**) the instability of such products (especially of the β anomer, **8**) because of crowding of all of the substituents on the same side of the ring.

It is somewhat surprising that, in contrast to **14** (ref. 18), methyl 4-*S*-acetyl-6-deoxy-2,3-di-*O*-methyl-4-thio-β-D-glucopyranoside (**18**) is susceptible to ring contraction and forms[13] 1,5-di-*O*-acetyl-6-deoxy-2,3-di-*O*-methyl-4-thio-α,β-D-gluco-

furanose as the sole product, despite the fact that the 4-*S*-acetyl group in the favored conformation [$^4C_1$(D)] of **18** is equatorial. An explanation for this behavior lies in the possibility that the *gauche* interaction (steric and electronic) between the bulky *O*-methyl groups at O-2 and O-3, as well as that between the 3-*O*-methyl and the 4-*S*-acetyl groups, destabilizes the pyranose products, and that the adoption of the thiofuranose ring helps overcome this instability. Similar interactions, as well as the anomeric effect[21] of the equatorial, anomeric methoxyl group, destabilize the $^4C_1$(D) conformation of **18**, which must facilitate inversion (during acetolysis) to form the $^1C_4$(D) conformer in which S-4 is axial and suitably placed to attack the glycosyl carbonium ion.

Deacylation[23] of **5** with sodium methoxide in methanol under nitrogen afforded a quantitative yield of syrupy 4-thio-D-mannose, which may exist[16] in, besides **6**, the tautomeric pyranose and aldehydo forms. The disulfide **9** was formed (as judged by t.l.c. in solvent *D*) when deacylation with sodium methoxide in methanol was performed in the presence of air; the $R_{Mannose}$ value of **9** was 0.92 as compared with 1.1 for 4-thio-D-mannose. Acetylation of **9** gave the octaacetate **10**, whose disulfide structure was evident from its i.r. spectrum (no *S*-acetyl) and from its considerably lower mobility as compared with those of the pentaacetates **7** and **8**. Apparently, **10** was present as an anomeric mixture, as it showed two, closely spaced spots in t.l.c.

4-Thio-D-mannose (**6**) was acetylated with pyridine and acetic anhydride to give a mixture of the furanose pentaacetates (**7** and **8**) in quantitative yield; these were separated by chromatography on silica gel. There was no evidence for formation of the peracetylated 4-thio-D-mannopyranose derivative. The 100-MHz n.m.r. spectra of both **7** and **8** showed the presence of five acetoxyl signals between τ 7.90 and 8.02 and no *S*-acetyl signal between τ 7.57 and 7.75. The anomeric configurations of **7** and **8** were assigned on the basis of Hudson's isorotation rules[24]. The anomeric 9-(4-thio-β-D-xylofuranosyl)adenines and their 3′,5′-isopropylidene ketals also conform[17] to the isorotation rules[24] and, accordingly, in each instance, the α anomer is more dextrorotatory than the β anomer; $[\alpha]_D^{21-24}$ (2-methoxyethanol): α anomer, +15° and β anomer, −29° (for the unsubstituted nucleoside); α anomer, +19° and β anomer, −0.6° (for the 3′,5′-isopropylidene ketal of the nucleoside)[17]. Confirmatory evidence for the anomeric assignments of **7** and **8** was obtained from the relative chemical-shifts of H-1 of the two anomers; the H-1–H-2 coupling constants of **7** and **8** are of a magnitude [$J_{1,2}$: α anomer (**7**), 6.6 Hz; β anomer (**8**), 5.0 Hz] that precludes[25] distinction between *cis* and *trans* H-1–H-2 and hence could not be employed for assigning the anomeric configurations. In this respect, 4-thio-D-mannofuranose (**6**) is similar to 5-*O*-methyl-D-mannofuranose, the two anomers of which have identical[26] H-1–H-2 coupling constants (5.0 Hz), and to the anomeric methyl D-mannofuranosides[27] ($J_{1,2}$: α anomer, 4.0 Hz; β anomer 4.5 Hz). Stevens and Fletcher[25] have surmised that, when H-1 and H-2 are *cis*, the chemical shift of the anomeric proton of the pentofuranose derivatives lies at a lower field than when they are *trans*. Accordingly, the H-1 resonance of **7** (τ 3.95) was located at higher field than that of **8** (τ 3.80).

Whereas the acetylation of 4-thio-D-mannose (**6**) with pyridine and acetic anhydride gave the thiofuranose pentaacetates (**7** and **8**) exclusively, both the pyranose and thiofuranose acetates are formed[18] from 4-thio-D-glucose in a ratio of 1:1.5. As neither D-glucose[28] nor D-mannose[29] shows a significant tendency to form the furanose pentaacetates on acetylation with pyridine and acetic anhydride, the preponderance of the thiofuranose pentaacetates from 4-thio-D-glucose and 4-thio-D-mannose (**6**) must be ascribed[30] to the increased formation of the thiofuranose ring because of the greater nucleophilicity of the sulfur atom, as compared with that of an oxygen atom, on C-4. However, this rationale cannot be the entire explanation, as the effect of the presence of sulfur at C-4 is unequal for 4-thio-D-glucose and -mannose, and is considerably more pronounced for the latter, where no evidence for the presence of the pyranose acetates could be detected. There is evidence[31] in support of a repulsive interaction between an axial oxygen atom in the pyranoid ring and the electron pair on the ring-oxygen atom as having a destabilizing influence on the pyranoid structure. Hence, as the only structural difference between 4-thio-D-glucose and -mannose is in the configuration at C-2, it may be reasoned that the presence of the (less-electronegative) sulfur atom in place of an oxygen atom on a carbon atom (C-4) adjacent to the one linked to the pyranose-ring oxygen atom intensifies the repulsive interaction between the axial [in the $^4C_1$(D) conformation] oxygen atom at C-2 and the electron pair on the ring-oxygen atom of 4-thiomannose, and as a consequence, the pyranoid form of this sugar is considerably less stable than that of 4-thioglucose.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at room temperature in a 1-dm cell with a Perkin–Elmer Model 241 automatic polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 257 spectrophotometer. ^{1}H-N.m.r. spectra were measured at 100 MHz in chloroform-*d* with tetramethylsilane as internal reference with a Varian XL-100 n.m.r. spectrometer equipped with a Nicolet NIC-80 data-system. The chemical shifts and coupling constants given are first-order values, except those given in parentheses for the geminal protons on C-6, which were calculated by ABX analysis[32]. The R_F values were determined on t.l.c. plates of silica gel G (layer thickness, ~0.25 mm) in the following solvents: *A*, 100:4 chloroform–methanol; *B*, 100:2 benzene–methanol; *C*, 3:1 light petroleum–acetone; and *D*, 2:1:1 1-butanol–acetic acid–water. The spots on t.l.c. plates were made visible by exposure to iodine vapor and/or by charring with sulfuric acid (5% v/v) in methanol. Silica gel G was obtained from Sigma Chemical Company, St. Louis, Missouri. Column chromatography was performed on Hi-Flosil, 60–200 mesh (Applied Science Laboratories, State College, Pennsylvania). Prior to use, *N*,*N*-dimethylformamide was dried over Davison No. 4A molecular sieves, 14–30 mesh. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, Georgia. Ivory-nut mannan, for the

preparation of 1,6:3,4-dianhydro-β-D-talopyranose[14], was a generous gift of Pfanstiehl Laboratories, Waukegan, Illinois.

1,6-Anhydro-4-S-benzoyl-4-thio-β-D-mannopyranose (**2**). — To a solution of 1,6:3,4-dianhydro-β-D-talopyranose[14] (**1**, 0.50 g) in dry *N,N*-dimethylformamide (1.6 mL) were added thiolbenzoic acid (2.1 mL) and pyridine (1.6 mL). The mixture was heated for 1 h at 115°, at which time t.l.c. in solvent *A* indicated the absence of **1**. The mixture was cooled to room temperature, mixed with chloroform (25 mL), and washed successively with water, 5% aqueous sodium hydrogencarbonate solution, and water. The dried (magnesium sulfate) chloroform solution was evaporated, traces of *N,N*-dimethylformamide and pyridine being removed by evaporation of several portions of xylene from the residue. The residue was chromatographed on a column (22.5 × 2 cm) of silica gel with chloroform as solvent. Fractions (monitored by t.l.c. in solvent *A*) containing the 4-*S*-benzoyl derivative **2** were pooled and evaporated to a residue (0.71 g, 72.5%) that crystallized spontaneously. Recrystallization from ethanol afforded colorless needles, m.p. 133°, $[\alpha]_D$ −102° (*c* 0.16, chloroform); R_F 0.37 (*A*), 0.17 (*B*), 0.74 (*C*); ν_{max}^{KBr} 3440 and 3300 (OH), 1658 (*S*-benzoyl C=O), 1595, 1580 and 1446 (phenyl C=C), 1212 and 903 (*S*-benzoyl[33]), and 773 and 688 cm^{-1} (monosubstituted phenyl).

Anal. Calc. for $C_{13}H_{14}O_5S$: C, 55.31; H, 5.00; S, 11.36. Found: C, 55.23; H, 5.07; S, 11.26.

When **1** (0.072 g) was fused (in the absence of *N,N*-dimethylformamide) with thiolbenzoic acid (0.1 mL) and pyridine (0.04 mL) for 45 min at 128° and the crude mixture chromatographed on silica gel as already described, 86 mg (61.0%) of the chromatographically homogeneous 4-*S*-benzoyl derivative **2**, identical with **2** already prepared (according to t.l.c. in solvent *A*) was obtained. This product was further characterized by conversion into the 2,3-isopropylidene ketal **3** (see later).

1,6-Anhydro-4-S-benzoyl-2,3-O-isopropylidene-4-thio-β-D-mannopyranose (**3**). — A solution of **2** (86 mg) in dry acetone (5 mL) was stirred for 46 h at room temperature with anhydrous copper sulfate (0.30 g). T.l.c. at this stage in solvent *A* showed a major product (corresponding to **3**) at the solvent front and a trace of a component having an R_F value (0.37, solvent *A*) coincident with that of **2**; further addition of anhydrous copper sulfate (1.3 g) and continued stirring for an additional 146 h had no effect on the presence of the slow-moving component, indicating that it was not **2**.

After a total reaction period of 192 h, the copper sulfate was filtered off and thoroughly washed with chloroform. The combined filtrates were evaporated to a yellow syrup, which crystallized spontaneously. The crystalline residue was triturated with light petroleum, and the nearly colorless **3** collected by filtration; yield 74 mg (75.7%), m.p. 91–94°, $[\alpha]_D$ −61.9° (*c* 0.16, chloroform); R_F 1.00 (*A*), 0.95 (*B*), and 1.00 (*C*); ν_{max}^{KBr} 1663 (*S*-benzoyl C=O), 1592, 1580, and 1445 (phenyl C=C), 1378 and 1368 (*gem*-dimethyl), 1213 and 910 (*S*-benzoyl[33]), and 775 and 688 cm^{-1} (monosubstituted phenyl).

Anal. Calc. for $C_{16}H_{18}O_5S$: C, 59.61; H, 5.63; S, 9.95. Found: C, 59.57; H, 5.65; S, 9.99.

2,3-Di-O-acetyl-1,6-anhydro-4-S-benzoyl-4-thio-β-D-mannopyranose (**4**). — To a solution of **2** (0.100 g) in pyridine (1.7 mL) was added acetic anhydride (0.7 mL). After 1 h at room temperature (t.l.c. of an aliquot at this stage indicated the absence of **2**), the mixture was evaporated to dryness, traces of pyridine and acetic anhydride being removed by evaporation of toluene from the residue. Crystallization of the residue from ether–light petroleum afforded 0.120 g (92.3%) of **4**, m.p. 115–117°. Recrystallization from the same solvent provided analytical **4**, m.p. 120°, $[\alpha]_D$ −94.4° (*c* 0.13, chloroform); R_F 0.77 (*B*) 0.92 (*C*); ν_{max}^{KBr} 1752 and 1747 (*O*-acetyl C=O), 1667 (*S*-benzoyl C=O), 1592, 1582 and 1449 (phenyl C=C), 1375 (*C*-methyl), 1248 and 1233 (acetate C-O-C), 1216 and 900 (*S*-benzoyl[33]), and 785 and 689 cm^{-1} (monosubstituted phenyl).

Anal. Calc. for $C_{17}H_{18}O_7S$: C, 55.73; H, 4.95; S, 8.75. Found: C, 55.72; H, 4.98; S, 8.77.

1,2,3,6-Tetra-O-acetyl-4-S-benzoyl-4-thio-α-D-mannopyranose (**5**). — 2,3-Di-*O*-acetyl-1,6-anhydro-4-*S*-benzoyl-4-thio-β-D-mannopyranose (**4**, 0.120 g) was dissolved in an ice-cold mixture (8.5 mL) of 0.5% (v/v) sulfuric acid in 2.4:1 acetic anhydride–acetic acid, and the mixture was kept for 24 h at room temperature. Anhydrous sodium acetate (0.30 g) was added to the mixture, following which the mixture was evaporated to dryness with the aid of toluene to remove traces of acetic acid and acetic anhydride. The residue was partitioned between chloroform (20 mL) and water (10 mL). The chloroform layer was washed with water (4 × 10 mL), dried (magnesium sulfate), and evaporated to yield syrupy **5**; 0.150 g (97.4%), $[\alpha]_D$ +102° (*c* 0.17, chloroform); R_F 0.69 (*B*), 0.88 (major, ~90%) and 0.85 (minor, ~10%) (*C*); ν_{max}^{film} 1750 (*O*-acetyl C=O), 1677 (*S*-benzoyl C=O), 1597, 1582 and 1450 (phenyl C=C), 1372 (*C*-methyl), 1240–1215 (acetate C-O-C, *S*-benzoyl[33]), 905 (*S*-benzoyl[33]), and 760 and 690 cm^{-1} (monosubstituted phenyl).

Anal. Calc. for $C_{21}H_{24}O_{10}S$: C, 53.84; H, 5.16; S, 6.84. Found: C, 54.76; H, 5.46; S, 6.62.

4-Thio-D-mannose (**6**). — To a solution of **5** (0.254 g) in dry methanol (20 mL) was added 0.6 mL of 0.4M methanolic sodium methoxide. The mixture was kept under nitrogen for 30 min and then made neutral by stirring with methanol-washed, Amberlite IR-120 (H^+) resin. The resin was removed by filtration, and the filtrate was evaporated to dryness, methyl benzoate being removed from the residual, syrupy **6** by extraction with benzene (2 × 5 mL); yield, 0.107 g (100.2%), $[\alpha]_D$ +41.8° (*c* 0.13, water); (no mutarotation observed); R_F 0.69 and $R_{Mannose}$ 1.1 (*D*); ν_{max}^{film} 3315 cm^{-1} (broad, OH).

Anal. Calc. for $C_6H_{12}O_5S \cdot 0.5H_2O$: C, 35.11; H, 6.38. Found: C, 35.20; H, 6.40.

1,2,3,5,6-Tetra-O-acetyl-4-thio-α- (**7**) *and -β-D-mannofuranose* (**8**). — A solution of 4-thio-D-mannose (**6**, 0.051 g) in pyridine (5 mL) was treated with acetic anhydride (2.3 mL). After 2 h at room temperature, the mixture was evaporated, traces of pyridine and acetic anhydride being removed by several evaporations of toluene from the residue. The residual syrup was chromatographed on a column of silica gel with chloroform as eluant. Evaporation of appropriate fractions afforded

0.108 g (102%) of the mixture of the anomeric pentaacetates (**7** and **8**); R_F 0.70 (**7**) and 0.56 (**8**) (*B*), 0.90 (**7**), and 0.88 (**8**) (*C*); in each of the two solvents, the ratio of the faster to slower components was visually estimated to be ~55:45. For analysis, the sample was dried overnight at 50° under high vacuum.

Anal. Calc. for $C_{16}H_{22}O_{10}S$: C, 47.29; H, 5.46; S, 7.89. Found: C, 47.50; H, 5.53; S, 7.75.

The two anomers (**7** and **8**) were separated by chromatography of a small amount (~25 mg) of the mixture on a column of silica gel with 100:0.2 benzene–methanol as solvent. The *α anomer* (**7**) had $[\alpha]_D$ +148° (*c* 0.14, chloroform); R_F 0.70 (*B*), 0.90 (*C*); ν_{max}^{film} 1760–1720 cm^{-1} (*O*-acetyl C=O); n.m.r.: τ 3.95 d (H-1), 4.57 q (H-2), 4.30 t (H-3), 5.95 q (H-4), 4.70 m (H-5), 5.62 q (5.62*, H-6), 6.06 q (6.04*, H-6'), 7.90 s, 7.92 s, 7.94 s, 7.95 s, and 8.02 s (15 H, 5 OAc); $J_{1,2}$ 6.6, $J_{2,3}$ 3.4, $J_{3,4}$ 3.9, $J_{4,5}$ 10.0, $J_{5,6}$ 2.6 (2.6*), $J_{5,6'}$ 4.6 (4.4*), and $J_{6,6'}$ 12.4 Hz.

The *β-anomer* (**8**) had $[\alpha]_D$ −103° (*c* 0.15, chloroform); R_F 0.56 (*B*), 0.88 (*C*); ν_{max}^{film} 1760–1720 cm^{-1} (*O*-acetyl C=O); n.m.r.: τ 3.80 d (H-1), 4.77 q (H-2), 4.22 t (H-3), 6.18 q (H-4), 4.65 m (H-5), 5.57 q (5.58*, H-6), 6.02 q (6.02*, H-6'), 7.90 s, 7.91 s, 7.93 s, 7.96 s, and 8.01 s (15 H, 5 OAc); $J_{1,2}$ 5.0, $J_{2,3}$ 4.0, $J_{3,4}$ 4.4, $J_{4,5}$ 10.4, $J_{5,6}$ 2.6 (2.7*), $J_{5,6'}$ 4.6 (4.5*), and $J_{6,6'}$ 12.4 Hz.

4,4'-Dithiobis(D-*mannopyranose*) (**9**) *and its octaacetate* (**10**). — A solution of **5** (10 mg) in 1 mL of dry methanol was treated with 30 μL of 0.87M methanolic sodium methoxide, and for 6 h kept at room temperature, without the exclusion of air with nitrogen. Isolation as described for **6** gave a syrup that showed (t.l.c.) the disulfide **9** as the main component; $R_{Mannose}$ 0.92 (*D*).

The syrupy disulfide **9** was acetylated conventionally with pyridine (0.25 mL) and acetic anhydride (0.12 mL), and the crude product was chromatographed on silica gel with chloroform as the eluant to yield 2.4 mg (30.8% from **5**) of the octaacetate **10**; R_F 0.33 (*B*), 0.50 (major) and 0.48 (minor) (*C*, by visual inspection, the ratio of the major and minor components was estimated to be 4:1); ν_{max}^{film} 1745 cm^{-1} (*O*-acetyl C=O), no band near 1680 cm^{-1} for *S*-acetyl C=O.

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*Calculated by ABX analyses (Ref. 32).

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