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SYNTHESIS OF *p*-NITROBENZYL AND *p*-NITROPHENYL 1-THIOGLYCOPYRANOSIDES*†

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ABSTRACT

Reaction of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (**1**) with thiourea (**2**), followed by reductive cleavage of the product, gave 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranose (**4**). Reaction of **4** with *p*-nitrobenzyl bromide followed by *O*-deacylation yielded *p*-nitrobenzyl 1-thio-β-L-fucopyranoside (**6**). Similar reaction conditions were used for the synthesis of *p*-nitrobenzyl 1-thio-β-D-fucopyranoside (**11**) and 1-thio-α-D-mannopyranoside (**16**). A facile preparation of *O*-acylated *p*-nitrophenyl 1-thioglycopyranosides was achieved by condensing the appropriate glycosyl halide with sodium *p*-nitrobenzenethioxide in *N*,*N*-dimethylformamide.

INTRODUCTION

Glycosidases have been widely used as excellent tools for structural studies of the carbohydrate moiety of glycoproteins and glycolipids. The isolation and purification of these glycosidases by such conventional procedures as gel filtration and ion-exchange chromatography is quite laborious and time-consuming. Much attention has recently been directed to the development and application of affinity chromatography for purification of these glycosidases[1]. For this technique, a substrate, or, preferably, a competitive inhibitor, is covalently linked to an insoluble matrix at an appropriate "arm length". When a crude extract containing the enzyme in a buffer solution is applied to the derivatized medium, the enzyme binds to the desired ligand, whereas unbound contaminants are removed by washing with the same buffer. The enzyme is then eluted off with a buffer at different pH or salt concentration, or a buffer containing the substrate. For ready application of affinity chromatography, it is essential that the ligands needed be conveniently available. As a result, synthetic investigations have focused on the facile preparation of 1-thioglycopyranosides, as these are known to be competitive inhibitors for glycosidases[2].

*Carbohydrate Derivatives for Affinity Chromatography. II. Our previous publication, Ref. 7, should be considered to be Part I of this series.

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The pseudothiourea derivatives prepared by reaction of acylated glycosyl halides with thiourea[3,4] offer a potential approach to the synthesis of 1-thioaldosides. A number of such synthetic sugar derivatives have recently been synthesized[5,6], and we have reported the synthesis of *p*-nitrobenzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranosides and related compounds[7]. In the present study, such derivatives of 1-thio-L-fucose, -D-fucose, and -D-mannose have been prepared by a similar reaction-sequence.

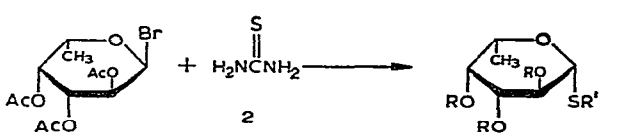
The synthesis of *p*-substituted-phenyl tetra-*O*-acetyl-1-thioglycopyranosides has generally been achieved by reaction of the appropriate, acylated glycosyl halide with a *p*-substituted benzenethiol in alkaline media[8–10]. In the present investigation, we have conveniently prepared such derivatives by condensation of glycosyl halides with sodium *p*-nitrobenzenethioxide in anhydrous *N,N*-dimethylformamide.

RESULTS AND DISCUSSION

The general procedure for the preparation of acetylated pseudothiourea derivatives involves refluxing a solution of a glycosyl halide and powdered thiourea in acetone. Interestingly, the resulting derivatives of such sugars as D-galactose, D-glucose, 2-acetamido-2-deoxy-D-glucose, and D-xylose crystallize out during the refluxing. However, a solution of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (**1**) and thiourea (**2**) in acetone did not produce a solid on boiling, but compound **3** may be isolated as a solid by keeping the mixture overnight at 0°. The procedure for isolation of the desired product was modified as described in the Experimental section.

When submitted to reductive cleavage as described by Cerny *et al.*[3], crystalline **3** gave 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranose (**4**) in 62% yield. On reaction with *p*-nitrobenzyl bromide in the presence of potassium carbonate, compound **4** gave *p*-nitrobenzyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside (**5**). The optical rotation and n.m.r. spectrum supported assigning of the β-L configuration to compound **5**. Treatment of **5** with a catalytic amount of sodium methoxide in methanol afforded *p*-nitrobenzyl 1-thio-β-L-fucopyranoside (**6**) (see Scheme I).

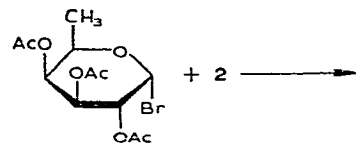
Condensation of 2,3,4-tri-*O*-acetyl-α-D-fucopyranosyl bromide (**7**) with **2** similarly gave *p*-nitrobenzyl 1-thio-β-D-fucopyranoside (**11**), as shown in Scheme II.



1 2

3 R = Ac, R' = C(=NH)–NH2 · HBr
4 R = Ac, R' = H
5 R = Ac, R' = $CH_2C_6H_4NO_2$-*p*
6 R = H, R' = $CH_2C_6H_4NO_2$-*p*

Scheme I

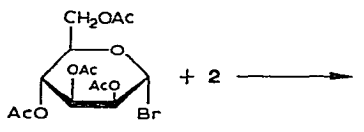


7

8 R = Ac, R' = C(=NH)—NH$_2$·HBr
9 R = Ac, R' = H
10 R = Ac, R' = $CH_2C_6H_4NO_2$-*p*
11 R = H, R' = $CH_2C_6H_4NO_2$-*p*

Scheme II

Starting from 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**12**), we synthesized *p*-nitrobenzyl 1-thio-α-D-mannopyranoside (**16**) by Scheme III. (Reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide with potassium ethylxanthate has been found to give the pure β-D anomer in quite low yield[11].) However, in the present study, no attempt was made to isolate any β anomer from the mother liquor of the crystalline 2-*S*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-2-thiopseudourea hydrobromide (**13**) obtained by the usual procedure.

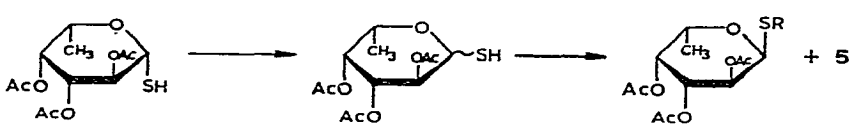


12

13 R = Ac, R' = C(=NH)—NH$_2$·HBr
14 R = Ac, R' = H
15 R = Ac, R' = $CH_2C_6H_4NO_2$-*p*
16 R = H, R' = $CH_2C_6H_4NO_2$-*p*

Scheme III

As our interest lay in the preparation of an appropriate ligand for α-L-fucosidase, we planned to develop an alternative approach for its synthesis. Like other 1-thio-aldose derivatives, 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-glucopyranose has been found[12] to mutarotate in aqueous solvent: $[\alpha]_D$ −8 → +47° (*c* 1.5, 90% ethanol). This unique phenomenon offered us an alternative route for the synthesis of *p*-nitrobenzyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-fucopyranoside from pure **4**. A solution of **4** in 90% ethanol was kept for 4 days under a nitrogen atmosphere until the optical rotation became constant, $[\alpha]_D$ −26.3 → −83° (*c* 1, 90% ethanol). The solvent was removed and, on treatment with *p*-nitrobenzyl bromide as already described, the syrupy product gave



4

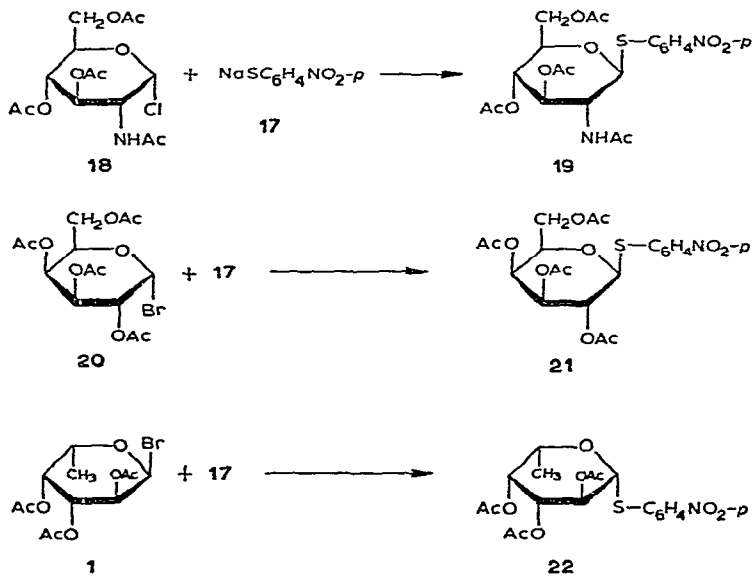
5a R = $CH_2C_6H_4NO_2$-*p*

Scheme IV

a mixture of **5** and **5a** (see Scheme IV). A pure sample of compound **5a** was isolated by preparative t.l.c. Use has been made of mutarotation in the synthesis of β-L-fucopyranosyl phosphate from 2,3,4-tri-*O*-acetyl-β-L-fucopyranose, the oxygen analog[13] of **4**.

Affinity chromatography has been successfully applied for the purification of α-L-fucosidase from human placenta[14] and human liver[15] by use of *N*-(6-aminohexanoyl)-β-L-fucopyranosylamine as the affinity ligand. Binding of α-L-fucosidase to this inhibitor may be due to the presence of a small proportion of the α-L anomer in the commercially available ligand[15].

Synthesis of various *p*-substituted-phenyl 1-thioglycopyranosides has been accomplished by reaction of the appropriate per-*O*-acetylglycosyl halides with *p*-substituted benzenethiol in alkaline solution. However, it has been reported that some *O*-deacylation of the product may occur under these conditions of coupling[16]. Based upon these observations, Shah and Bahl[9] preferred to subject the crude reaction product to acetylation with acetic anhydride–pyridine for the isolation of crystalline, acetylated 1-thioglycosides. Interestingly, synthesis of *p*-aminophenyl 1-thio-β-D-galactopyranoside has been achieved by reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with *p*-aminobenzenethiol in sodium hydroxide[5]. However, this procedure has been found quite inconvenient for the synthesis of other *p*-aminophenyl 1-thioglycosides[5]. The synthesis of such thio derivatives was, in fact, based on the method for the synthesis of the corresponding oxygen analog. The corresponding oxygen analog can be obtained from 2-acetamido-2-deoxy-D-glucose in better yields by reaction of the acetylated D-glucosyl halide with the sodium or



Scheme V

potassium salt of *p*-nitrophenol in *N,N*-dimethylformamide[17]; this prompted us to try such reaction-conditions for the synthesis of *p*-nitrophenyl 1-thioglycosides. Sodium *p*-nitrobenzenethioxide (**17**) was obtained on treatment of *p*-nitrobenzenethiol with sodium powder in anhydrous ether. Reaction of **17** with a per-*O*-acetylglycosyl halide (of D-galactose, L-fucose, or 2-acetamido-2-deoxy-D-glucose) provided the protected thio derivatives, which were readily isolated (see Scheme V).

EXPERIMENTAL

General. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer Model 457 spectrophotometer. N.m.r. spectra were recorded with a Varian HA-100 spectrophotometer; chloroform-*d* was the solvent, and tetramethylsilane, the internal standard. Optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. The purity of the compounds was established by ascending thin-layer chromatography (t.l.c.), conducted on plates coated with a 250-μm layer of silica gel HF-254 (Merck, Darmstadt). The components were located by exposure to iodine vapor. The solvents for t.l.c. were: (*a*) 9:1 acetone–petroleum ether (b.p. 38.3–48.8°); (*b*) 5:1 benzene–ethyl acetate; (*c*) 9:1 benzene–methanol; (*d*) 4:1 benzene–methanol; and (*e*) 3:2 benzene–methanol. The pseudothiourea derivatives were examined by t.l.c. in solvent *a*. For acetylated derivatives, solvents *b* and *c* were used, and solvents *d* and *e* for the *O*-deacylated products. Silica gel (Davison grade 923) was used for column chromatography. The elementary analyses were performed by Robertson Laboratory, Florham Park, New Jersey.

2-S-(2,3,4-Tri-O-acetyl-β-L-fucopyranosyl)-2-thiopseudourea hydrobromide (**3**). — A solution of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (**1**; 9 g) and thiourea (**2**; 1.94 g) in anhydrous acetone (30 ml) was boiled under reflux for 25 min, cooled, and evaporated under diminished pressure. The residue was stirred with chloroform (200–250 ml) and cooled; the mixture was filtered, the filtrate evaporated to dryness, and the residue crystallized from acetone containing a few drops of ethyl acetate; yield 6.3 g (58%), m.p. 167–169°, $[\alpha]_D^{20}$ −19.2° (*c* 1, methanol).

Anal. Calc. for $C_{13}H_{21}BrN_2O_7S$: C, 36.37; H, 4.92; Br, 18.61; N, 6.52; S, 7.46. Found: C, 36.33; H, 5.19; Br, 18.61; N, 6.68; S, 7.56.

2,3,4-Tri-O-acetyl-1-thio-β-L-fucopyranose (**4**). — A solution of potassium pyrosulfate ($K_2S_2O_7$) (1.03 g) in water (4 ml) was heated at 85° under a reflux condenser, and chloroform (6 ml) was introduced, followed by compound **3** (2.0 g). The mixture was boiled for 15–20 min with constant stirring, and cooled; the organic layer was separated, washed with water, dried (sodium sulfate), and evaporated, and the white, solid residue crystallized from methanol; yield 1.32 g (92.5%), m.p. 117–220°, $[\alpha]_D^{20}$ −26.3° (*c* 1, methanol).

Anal. Calc. for $C_{12}H_{18}O_7S$: C, 47.05; H, 5.92; S, 10.47. Found: C, 46.88; H, 5.99; S, 10.64.

p-Nitrobenzyl 2,3,4-tri-O-acetyl-1-thio-β-L-fucopyranoside (**5**). — To a solution

of **4** (1.15 g) in acetone (4 ml) was added *p*-nitrobenzyl bromide (0.82 g). A solution of potassium carbonate (0.42 g) in water (4 ml) was added, and the mixture was shaken for 1.5 h, poured into ice-cold water (50 ml), and stirred vigorously. The aqueous phase was extracted with chloroform (4 × 25 ml), and the extract was washed with water (3 × 25 ml), dried (sodium sulfate), and evaporated, to give **5** as a syrup (1.39 g; 86.5%), $[\alpha]_D^{20}$ +57.5° (*c* 1, methanol); ν_{max}^{neat} 1745 (ester), 1520, 1370 (nitro), 1600 and 720 cm^{-1} (aromatic); n.m.r. data: τ 1.78–2.53 (m, 4 H, $-C_6H_4NO_2$), 5.65 (d, 1 H, $J_{1,2}$ 10 Hz, H-1), 7.79–8.0 (m, 9 H, OAc), and 8.78 (d, 3 H, *J* 6.5 Hz, CMe).

p-*Nitrobenzyl 1-thio-β-*L*-fucopyranoside* (**6**). — To a solution of compound **5** (1.45 g) in absolute methanol (10 ml) was added sodium methoxide (0.5 ml of a solution of 0.1 g of sodium in 10 ml of methanol), and the mixture was kept at room temperature. After 3 h, fine crystals of material appeared; after a further 2 h, the mixture was made neutral with dil. acetic acid, cooled, filtered, and the crystals washed with cold methanol. The filtrate and washings were combined and evaporated, and the residue was crystallized from methanol, and recrystallized from the same solvent, to give pure **6**; yield 0.90 g (87.5%), m.p. 169–172°, $[\alpha]_D^{20}$ +138° (*c* 1, methanol); ν_{max}^{KBr} 3600–3150 (broad, OH), 1530, 1350 (nitro), 1610 and 715 cm^{-1} (aromatic).

Anal. Calc. for $C_{13}H_{17}NO_6S$: C, 49.51; H, 5.42; N, 4.44; S, 10.16. Found: C, 49.34; H, 5.54; N, 4.41; S, 10.06.

*2-*S*-(2,3,4-Tri-*O*-acetyl-β-*D*-fucopyranosyl)-2-thiopseudourea hydrobromide* (**8**). — A solution of syrupy **7** (16.0 g) and **2** (3.5 g) in acetone (15 ml) was boiled for 20 min, and then kept overnight at 0°. The resulting, fine crystals of **8** were filtered off, and washed with cold acetone; yield 7.5 g. The mother liquor was evaporated to a syrup which, on stirring with chloroform (200 ml), gave crystalline, unreacted thiourea. The suspension was filtered, the filtrate was evaporated, and the residue was dissolved in hot acetone (30 ml) and nucleated with crystals of **8** to give a further crop (2.5 g) of **8**; total yield 10.0 g (51.4%), m.p. 156–158°, $[\alpha]_D^{20}$ +18.4° (*c* 1, methanol).

Anal. Calc. for $C_{13}H_{21}BrNO_7S$: C, 36.37; H, 4.92; Br, 18.61; N, 6.52; S, 7.46. Found: C, 36.29; H, 5.06; Br, 18.78; N, 6.33; S, 7.27.

*2,3,4-Tri-*O*-acetyl-1-thio-β-*D*-fucopyranose* (**9**). — Crystalline **7** (7.0 g) was heated at 85° with a mixture of potassium pyrosulfate (3.5 g) in water (15 ml) and chloroform (25 ml) for 15 min, and the mixture was processed as described for the preparation of **4**. Compound **9** thus isolated was recrystallized from methanol; yield 3.1 g (62%), m.p. 116–118°, $[\alpha]_D^{20}$ +26.4° (*c* 1, chloroform).

Anal. Calc. for $C_{12}H_{18}O_7S$: C, 47.05; H, 5.92; S, 10.47. Found: C, 47.05; H, 6.05; S, 10.64.

p-*Nitrobenzyl 2,3,4-tri-*O*-acetyl-1-thio-β-*D*-fucopyranoside* (**10**). — A solution of compound **9** (3.0 g) and *p*-nitrobenzyl bromide (2.2 g) in acetone (12 ml) was treated with potassium carbonate (1.4 g) in water (12 ml). Syrupy **10** was isolated as described for **5**; yield 4.0 g (92.5%), $[\alpha]_D^{20}$ −80° (*c* 1, chloroform); ν_{max}^{neat} 1745 (ester), 1520, 1369 (nitro), 1605 and 720 cm^{-1} (aromatic); n.m.r. data: τ 1.79–2.55 (m, 4 H,

$C_6H_4NO_2$), 5.65 (d, 1 H, $J_{1,2}$ 10 Hz, H-1), 7.8–8.0 (m, 9 H, OAc), and 8.8 (d, 3 H, CMe).

p-*Nitrobenzyl 1-thio-β-*D*-fucopyranoside* (**11**). — Compound **10** (4.41 g) in anhydrous methanol was treated with a catalytic amount of sodium methoxide in methanol. Compound **11** was isolated by the usual procedure as crystals, yield 2.6 g (82.5%); m.p. 164–166°, $[\alpha]_D^{20}$ −136.5° (*c* 1, methanol); ν_{max}^{KBr} 3600–3180 (OH), 1532, 1345 (nitro), 1610 and 710 cm^{-1} (aromatic).

Anal. Calc. for $C_{13}H_{17}NO_6S$: C, 49.51; H, 5.42; N, 4.44; S, 10.16. Found: C, 49.55; H, 5.21; N, 4.37; S, 10.03.

*2-S-(2,3,4,6-Tetra-*O*-acetyl-α-*D*-mannopyranosyl)-2-thiopseudourea hydrobromide* (**13**). — A solution of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**12**; 60 g) and thiourea (11 g) in acetone (110 ml) was refluxed for 25 min. Compound **13** was extracted by means of chloroform, and the extract evaporated to dryness; the residue was freed of unreacted thiourea as described in the preparation of **3**, the chloroform extract was evaporated, and the residue was crystallized from methanol–petroleum ether to give **13**, yield 30.0 g (41%); m.p. 131–133°, $[\alpha]_D^{20}$ +106.8° (*c* 1, methanol). This product was used for the next step without further purification.

*2,3,4,6-Tetra-*O*-acetyl-1-thio-α-*D*-mannopyranose* (**14**). — Compound **13** (10 g) was treated with potassium pyrosulfate (5 g) in a mixture of water and chloroform as described for **4**, giving **14** as a thick syrup, yield 6.7 g (89.2%); $[\alpha]_D^{20}$ +84.5° (*c* 1, methanol).

p-*Nitrobenzyl 2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranoside* (**15**). — A solution of compound **14** (5 g) and *p*-nitrobenzyl bromide (2.96 g) in acetone (15 ml) was stirred with potassium carbonate (2.1 g) in water (15 ml) for 1.5 h; on processing as usual, crystalline compound **15** was obtained, yield 5.3 g (76.6%); m.p. 128–130°, $[\alpha]_D^{20}$ +160° (*c* 1, methanol); ν_{max}^{KBr} 1740 (ester), 1520, 1370 (nitro), 1600 and 720 cm^{-1} (aromatic); n.m.r. data: τ 1.85–2.55 (m, 4 H, $C_6H_4NO_2$), 6.15 (S, 2 H, SCH_2), and 7.81–8.0 (m, 3 H, OAc).

Anal. Calc. for $C_{21}H_{25}NO_{11}S$: C, 50.50; H, 5.04; N, 2.80; S, 6.51. Found: C, 50.22; H, 5.09; N, 2.82; S, 6.43.

p-*Nitrobenzyl 1-thio-α-*D*-mannopyranoside* (**16**). — A suspension of compound **15** (2 g) in absolute methanol (15 ml) was treated with a small amount of sodium methoxide; a clear solution was obtained after 15 min, and, after 1 h, crystals started to appear. This suspension was kept for 3 h at room temperature, and processed as usual, to give compound **16**, yield 2.2 g (82%); m.p. 150–152°, $[\alpha]_D^{20}$ +336° (*c* 1, methanol); ν_{max}^{KBr} 3600–3100 (broad, OH), 1515, 1350 (nitro), 1600 and 720 cm^{-1} (aromatic).

Anal. Calc. for $C_{13}H_{17}NO_7S$: C, 47.12; H, 5.16; N, 4.22; S, 9.67. Found: C, 46.88; H, 5.29; N, 4.23; S, 9.39.

Synthesis of p-*nitrobenzyl 2,3,4-tri-*O*-acetyl-1-thio-α-*L*-fucopyranoside* (**5a**) *by mutarotation of* **4**. — A solution of pure compound **4** (1.0 g) in 90% ethanol (100 ml) was kept under nitrogen, and its optical rotation was monitored at 24-h intervals; constant after 4 days, $[\alpha]_D^{20}$ −26.3 → −83° (4 days), (*c* 1, 90% ethanol). [For 2,3,4-

tri-*O*-acetyl-β-L-fucopyranose, Prihar and Behrman[13] reported $[\alpha]_D$ −5.2→ −77° (8 days), (*c* 1, absolute ethanol).] The solution was then evaporated to dryness under diminished pressure. A solution of the resulting syrup in acetone was treated with *p*-nitrobenzyl bromide and aqueous potassium carbonate solution for 1.5 h, and the product was isolated as usual, giving a syrup, $[\alpha]_D$ −29.5° (*c* 1, methanol). T.l.c. (solvent *b*) showed the presence of two clearly distinguishable components (2:3, ratio estimated by eye), along with unidentified, slow-moving, minor impurities. One of the major components corresponded to **5**, and moved slower than its α anomer. A small portion of the syrup was applied to a preparative, thin-layer plate, and developed with solvent *b*. The bands containing **5a** were scraped off separately, and extracted with ethyl acetate; the extracts were combined, and evaporated, to give pure **5a** as a syrup, in 36.7% yield (based upon **4**); $[\alpha]_D^{20}$ −230° (*c* 1, methanol); ν_{max}^{neat} 1745 (ester), 1520, 1370 (nitro), 1600 and 720 cm^{-1} (aromatic); n.m.r. data: τ 1.79–2.59 (m, 4 H, $C_6H_4NO_2$), 4.48 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 7.93–8.0 (m, 9 H, OAc), and 8.91 (d, 3 H, CMe).

Preparation of sodium p-*nitrobenzenethioxide* (**17**). — Sodium (1 g) was stirred vigorously in hot toluene, the liquid was carefully decanted, and the fine particles of sodium were washed with anhydrous ether (2 × 50 ml) to remove toluene. The residue was suspended in anhydrous ether (200 ml), and *p*-nitrobenzenethiol (10 g)) was added; the mixture was stirred for 4 days at room temperature, and the red-brown, crude salt (8 g) was filtered off, washed with anhydrous ether, and stored in a vacuum desiccator.

p-*Nitrophenyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-1-thio-β*-D-*glucopyranoside* (**19**). — A mixture of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride (**18**) (3.65 g) and sodium salt **17** (2.65 g) in anhydrous *N*,*N*-dimethylformamide (40 ml) was stirred for 18 h at room temperature, and then poured into water (600 ml) with stirring. After 4 h, the solid was filtered off, washed with water, dried, and recrystallized twice from chloroform–methanol, to give compound **19** (3.1 g, 65% yield); m.p. 282–284°, $[\alpha]_D^{20}$ −26.8° (*c* 1, *N*,*N*-dimethylformamide); lit.[10] m.p. 285–286°, $[\alpha]_D^{25}$ −26° (*c* 0.89, *N*,*N*-dimethylformamide).

p-*Nitrophenyl 2,3,4,6-tetra*-O-*acetyl-1-thio-β*-D-*galactopyranoside* (**21**). — Treatment of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**20**) (4.1 g) (obtained as semicrystalline material, and used without purification) with **17** (2.65 g) in *N*,*N*-dimethylformamide (40 ml) for 18 h, followed by isolation of the product as described for **19**, gave a solid which was recrystallized from methanol; yield 2.0 g (58%); m.p. 154–155°, $[\alpha]_D^{20}$ −8.2° (*c* 1, chloroform); lit.[9] m.p. 158–159°, $[\alpha]_D$ −7.0° (*c* 9.6, chloroform); lit.[8] m.p. 154–155°, $[\alpha]_D^{23}$ −9.46° (*c* 0.5, methanol).

p-*Nitrophenyl 2,3,4-tri*-O-*acetyl-1-thio-β*-L-*fucopyranoside* (**22**). — A mixture of **1** (1.2 g), sodium salt **17** (1.8 g), and *N*,*N*-dimethylformamide (40 ml) was stirred for 18 h at room temperature, and then processed as usual, giving a solid. T.l.c. of this in solvent *b* indicated fast-moving impurities; consequently, the solid was dissolved in chloroform, and the solution was treated with carbon; the suspension was filtered through a pad of Celite, and the filtrate was evaporated to dryness. In order to remove

other contaminants, a solution of the product in benzene (60 ml) was passed through a column (40 × 2 cm) of silica gel. Benzene (300 ml) eluted the impurities, and the desired material was isolated by elution with 5:1 benzene–ethyl acetate (400 ml), and evaporation. The product crystallized from methanol, yield 0.8 g (55%); m.p. 136–138°, $[\alpha]_D$ +4.5° (*c* 1, chloroform); lit.[18] m.p. 141–141.5°, $[\alpha]_D$ +4.7° (*c* 1, chloroform).

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