Carbohydrate Research, 94 (1981) 91–99
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

SYNTHESIS OF THIOLACTOSE (4-*S*-β-D-GALACTOPYRANOSYL-4-THIO-D-GLUCOPYRANOSE)

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(Received October 10th, 1980; accepted for publication in revised form, January 14th, 1981)

ABSTRACT

The potential enzyme-inducer, 4-*S*-β-D-galactopyranosyl-4-thio-D-glucopyranose, thiolactose (**20**), was synthesized *via* two routes. The intermediate, methyl 2,3,6-tri-*O*-benzoyl-4-*S*-cyano-4-thio-α-D-glucopyranoside (**5**), was obtained in high yield from methyl α-D-galactopyranoside. Reaction of the sodium salt of methyl 4-thio-α-D-glucopyranoside, derived from **5**, with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide in hexamethylphosphoric triamide produced a methyl thiolactoside derivative that could be selectively benzoylated to give 2,6-di-*O*-benzoyl-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-thio-α-D-glucopyranoside (**14**), which was directly crystallized from a complex mixture of products produced in the coupling reaction. Selective acetolysis of the methyl glycoside linkage of **14** (or of the derived heptaacetate), followed by transesterification, afforded **20**.

INTRODUCTION

As an approach to the treatment of certain diseases that result from inherited glycosidase deficiencies, we are currently investigating the possible induction of certain of these enzymes by appropriate thiodisaccharides. Accordingly, we describe herein the synthesis of one such compound, thiolactose (4-*S*-β-D-galactopyranosyl-4-thio-D-glucopyranose) (**20**). Reports of thiodisaccharides containing a reducing sugar terminus are limited[1,2], although several methyl glycosides of closely related thiodisaccharides have recently been reported[3,†]. In spite of our extensive efforts to optimize the yield of the coupling reaction, we obtained distinctly lower yields of the substituted methyl thiolactosides than were reported by Blanc-Muesser *et al.*[3], for very similar compounds. Our observation that the methyl glycoside residue could be selectively acetolyzed under quite vigorous conditions contrasted with that of Hutson[1] who found, in his work on thiogentiobiose, that a thioglycosidic linkage was more

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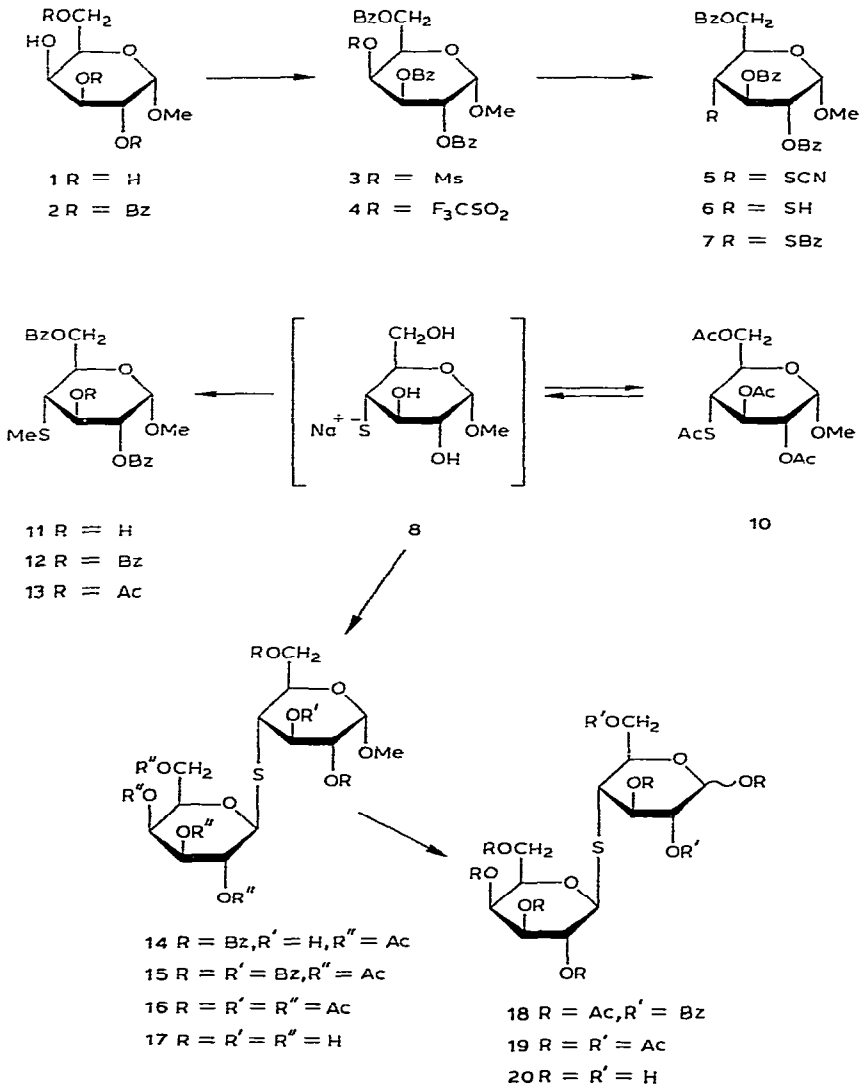
†We were informed by a referee that related work and, in particular, the use of the 4-triflate of D-galactose for the preparation of thiodisaccharides was reported by Defaye *et al.* at the Xth International Symposium on Carbohydrate Chemistry, Sydney, Australia (1980); these abstracts were unavailable to us when this manuscript was prepared.

0008-6215/81/0000–0000/$ 02.50,

labile to acetolysis than a methyl glycoside linkage. This emphasizes the important chemical difference between (1→4)- and (1→6)-linked thiodisaccharides.

RESULTS AND DISCUSSION

Two preparations of thiolactose derivatives were considered: (a) the sodium salt of methyl 4-thio-α-D-glucopyranoside could be condensed with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide; and (b) the sodium salt of 1-thio-β-D-galactopyranoside could be coupled in an SN2 reaction to C-4 of an appropriate D-galactose derivative. Both methods should provide the desired methyl 4-*S*-β-D-galactopyranosyl-



4-thio-α-D-glucopyranoside derivative; indeed, both general approaches were employed successfully by Hutson[1] for the synthesis of thiogentiobiose.

The necessary intermediate methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside[4,5] (**2**) was obtained in a significantly improved yield by selective benzoylation of methyl α-D-galactopyranoside (**1**). Compound **2** was mesylated[5] or triflated[6,7] to give the highly crystalline methyl 2,3,6-tri-*O*-benzoyl-4-*O*-mesyl- (**3**) or 4-*O*-triflyl-α-D-galactopyranoside (**4**), in 91 and 99% yields, respectively. Displacement of the mesyloxy group of **3** with a precise stoichiometric amount of potassium thiocyanate in *N*,*N*-dimethylformamide required 42 h at 140°, and, after column chromatography, provided methyl 2,3,6-tri-*O*-benzoyl-4-*S*-cyano-4-thio-α-D-glucopyranoside[8] (**5**), in 68% yield, whereas the triflyloxy group of **4** could be displaced in 12 h at 80°, and provided the thiocyanate **5** in 85% yield, without chromatography. The overall yield of the important thiocyanate intermediate **5** from methyl α-D-galactopyranoside (**1**) was, therefore, increased from 35% by the previous sequence[4,5,9] to 60%. Thiocyanate **5** could be reduced with zinc in acetic acid to the thiol **6**, which was characterized as the *S*-benzoyl derivative[10] **7**, but every attempt to employ the sodium salt of the blocked thiol* **6** to prepare thiolactose derivatives met with total failure. Ultimately, the thiocyanate **5** provided the necessary sodium salt **8** of methyl 4-thio-α-D-glucopyranoside that was subsequently used in coupling reactions.

Two general coupling-methods were investigated, the first utilizing the sodium salt of 1-thio-β-D-galactopyranose, which was generated by cleavage of the 1-*S*-acetyl[11], the 2-thiopseudourea hydrobromide[12,13], or the ethyl xanthate[14] derivative of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose, and condensed with the triflate compound **4**. Acetylation or benzoylation of this reaction produced an intractable mixture of products, some of which were believed to be associated with a competing elimination of the triflyloxy group of **4**.

A more satisfactory process for the production of a thiolactose derivative was the coupling between the sodium salt **8** and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**9**) in hexamethylphosphoric triamide, followed by an *in situ* selective benzoylation[15] to yield a dibenzoate, to which was ascribed the structure methyl 2,6-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-thio-α-D-glucopyranoside (**14**) based on the known order of reactivity of OH-2, -3, and -6 of D-lactose derivatives towards benzoylation[15]. Compound **14** was directly crystallized from the complex mixture in 25% yield, and an additional 5% could be obtained by chromatography of the mother liquors. It is important to note that, in view of the complexity of the reaction mixture, it was not desirable to produce the 2,3,6-tri-*O*-benzoyl analog **15** since this was not a crystalline compound (as was shown by its preparation), and was, therefore, difficult to separate from the reaction mixture even with medium-pressure liquid chromatography. The coupling method followed the

*This blocked thiol salt was generated either by warming **6** with one equivalent of sodium hydride in hexamethylphosphoric triamide or by addition of one equivalent of sodium methoxide to **5** dissolved in 1,2-dimethoxyethane.

procedures described by Blanc-Muesser *et al.*[3], except for the use of **5** as a source of **8**, and for the use of selective benzoylation as a means of isolation of the coupled product. Our attempts to isolate the coupled product *via* acetylation gave very low yields of the peracetylated thiolactoside **16**, largely due to the difficulty in separating **16** from the complex reaction mixture.

Although the use of hexamethylphosphoric triamide seemed to enhance the coupling reaction relative to other solvents*, it also methylated a substantial proportion of the starting material **8**. Separation of the coupling reaction mixture (after benzoylation) afforded a low to moderate yield of two oils to which, based on their t.l.c. behavior and n.m.r. spectra, were assigned structure **11** and **12**, respectively. The 2,6-dibenzoate structure assigned to **11** was again based on the known order of reactivity of OH-2, -3, and -6 of D-glucose towards benzoylation[4]. Although rigorous purification of **11** and **12** was not performed, **11** was acetylated and characterized as the crystalline methyl 3-*O*-acetyl-2,6-di-*O*-benzoyl-4-*S*-methyl-4-thio-α-D-glucopyranoside (**13**). The use of methyl 2,3,6-tri-*O*-acetyl-4-*S*-acetyl-4-thio-α-D-glucopyranoside[16] (**10**), as employed by Blanc-Muesser *et al.*[3] to generate the sodium salt **8** for subsequent use in the coupling reaction, had no useful effect on the yield.

Acetolysis[17] of **14** with 5% sulfuric acid in acetic anhydride and acetic acid at 40° for 5 min produced 1,3-di-*O*-acetyl-2,6-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-thio-α,β-D-glucopyranose (**18**) in 85% yield as an anomeric mixture in which the α anomer predominated according to ^{1}H-n.m.r. spectrometry. Interestingly, the intersugar linkage remained intact under these conditions, although prolonged heating (>1 h) completely destroyed that linkage. Acetolysis of the peracetylated compound **16** proceeded similarly and gave 96% of the octaacetate **19**. Transesterification of either of the acetolysis products **18** or **19**, afforded free thiolactose (**20**), which could be crystallized from anhydrous methanol to give a white hygroscopic solid.

Previous experience with the action of sulfur-containing nucleophiles on 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide indicates the formation of a β-D intersugar linkage[3,18]. Additional proof for the structure of these compounds is provided by (a) elemental analysis, (b) ^{13}C- and ^{1}H-n.m.r. spectrometry, (c) the lack of an *S*-acetyl band at 1680 cm^{-1} in the i.r. spectrum, and (d) degradation of the compound.

The ^{13}C-n.m.r. spectrum of the thiolactoside **17** was completely consistent with those obtained for similar compounds by Blanc-Muesser *et al.*[3]. The spectrum accounted for the 13 carbon atoms and had appropriate signals for C-1 and C-1′ (100.67 and 85.53 p.p.m., respectively), for OCH_3 (56.48 p.p.m.), and for the distinctly shielded[19] C-4 at 48.53 p.p.m. The spectrum of thiolactose (**20**) was similar to that of lactose in the number of total peaks, but differed substantially in the position of

*Several other solvents were used including *N,N*-dimethylformamide, tetrahydrofuran, acetonitrile, 1,2-dimethoxyethane, and methanol. Several nonpolar solvents were also used in conjunction with 18-Crown-6.

those peaks as a result of the shielding effects of the sulfur[19] bridging-atom. A total of 18 different signals appeared in the spectrum; indicative of the presence of two anomers and two C-1 peaks for the D-glucose residue (C-1α, 97.02; and C-1β, 93.52 p.p.m.), the two C-4 peaks for the D-glucose residue (C-4α, 48.72; and C-4β, 53.72 p.p.m.), and a single C-1′ peak for the D-galactose moiety at 85.77 p.p.m. were especially significant.

The ^{1}H-n.m.r. spectrum of the octaacetate **19** again clearly showed the presence of two anomers with anomeric proton doublets at δ 6.35 ($J_{1,2}$ 3.5 Hz) and 5.7 ($J_{1,2}$ 7 Hz) for the α- and β-D anomers, respectively. Integration of the doublets suggested that the α to β ratio was 2.5:1. The spectrum of **19**, as well as the spectra of other thiolactose derivatives, were distinguished by the presence of an upfield doublet of doublets centered at δ 3.1 ($J_{3,4}$ 10 and $J_{4,5}$ 12 Hz) for H-4 as a result of the shielding effect of the sulfur atom[19].

Attempts to hydrolyze and identify the hydrolysis products from the octaacetate **19** were only partially successful owing to the instability of the 4-thioglucose residue to hot acid. D-Glucose derivatives substituted at C-4 with amino and thio groups are known to cyclize to pyrrolidine[20] and tetrahydrothiophene[21] compounds, respectively. Further exposure of these compounds to acid results in elimination and resinification[20,21]. However, the acid hydrolysis of **19** did permit identification of the D-galactose residue by t.l.c. Prolonged acetolysis of **14** similarly resulted in severe darkening and decomposition of the sulfur-containing carbohydrates product.

EXPERIMENTAL

General methods. — Melting points were determined with a Meltemp apparatus and are uncorrected. Organic solvents were dried over 3A molecular sieves where this method was appropriate[12]. N.m.r. spectra were recorded with Varian EM-360A (^{1}H) and Varian CFT-20 (^{13}C) spectrometers at 60 and 20 MHz, respectively, for solutions in chloroform-*d*, unless otherwise noted: chemical shifts are listed in the δ scale. Optical rotations were measured with a Perkin–Elmer model 141 automatic polarimeter. I.r. spectra were recorded with a Beckman Acculab-4 spectrometer using potassium bromide discs for solids, and chloroform or carbon tetrachloride solutions for non-solid materials. Column chromatography employed SilicAR-cc-7 40–60 mesh, (Mallinckrodt) silica gel at atmospheric pressure. Medium-pressure liquid chromatography[23] was performed with Polygosil 60-4063 40–63 mesh (Macherey-Nägel), at pressures ranging from 0.7–3.5 · 10^5Pa. T.l.c. separations were performed in a short bed–continuous development chamber (Regis), using Brinkman Polygram Sil G/UV_{254} plates; the spots were detected with u.v. light or a 10% aqueous sulfuric acid spray; the solvent system was 1:2:6 (v/v) ethyl acetate–chloroform–hexane, unless otherwise noted. T.l.c. separations of unblocked sugar derivatives were performed on Whatman MKC_{18}F, reverse-phase plates with 85% aqueous isopropyl alcohol as the developing solvent, in a standard development chamber, and with a silver nitrate–ethanolic sodium hydroxide detection spray[24].

Inert reaction environments were obtained by use of deoxygenated (pyrogallol solution) dry nitrogen. The acetolysis mixture contained acetic anhydride (65 mL), glacial acetic acid (30 mL), and concentrated sulfuric acid (5 mL). The general processing for all products isolated *via* acetylation, benzoylation, or acetolysis was to pour the reaction mixture into ice-cold, saturated sodium hydrogencarbonate solution, extract with chloroform or dichloromethane (10–15 mL/g), wash with cold 3M hydrochloric acid, then cold aqueous sodium hydrogencarbonate, and then cold water. All organic solutions were dried with magnesium sulfate, and evaporated *in vacuo*, generally $<40°$.

*Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-trifluoromethylsulfonyl-α-*D*-galactopyranoside* (**4**). — To a chilled (—20°), stirred solution of dry dichloromethane (150 mL), pyridine (5.5 mL), and methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside[4,5] (**2**, 19.3 g, 38.4 mmol) was added, dropwise, trifluoromethanesulfonic anhydride (16.8 g, 55.6 mmol). The mixture was allowed to warm to room temperature during about 45 min when t.l.c. showed that the reaction was complete. A conventional work-up, followed by crystallization from ethanol yielded **4** (24.1 g, 99%), m.p. 137–138°, $[\alpha]_D^{28}$ +103.6°; (*c* 1.0, chloroform); n.m.r.: δ 8.1 and 7.4 (m, 15 H, Ar), 6.1 (dd, 1 H, $J_{2,3}$ 11 and $J_{3,4}$ 3 Hz, H-3), 5.6 (m, 2 H), 5.3 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 4.6 (m, 3 H), and 3.48 (s, 3 H, OCH_3).

Anal. Calc. for $C_{29}H_{25}F_3O_{11}S$: C, 54.55; H, 3.95. Found: C, 54.47; H, 3.91.

*Methyl 2,3,6-tri-*O*-benzoyl-4-*S*-cyano-4-thio-α-*D*-glucopyranoside*[8,9] (**5**). — A well-stirred solution of potassium thiocyanate (15.23 g, 156.7 mmol), triflate (33.3 g, 52.15 mmol), and *N*,*N*-dimethylformamide (250 mL) was heated for 21 h at 85°, or until t.l.c. showed the reaction to be complete. It was then stirred into ice–water (600 mL). The crude precipitate was filtered off, washed thoroughly with water, and dissolved in dichloromethane (300 mL). The solution was dried and evaporated, and the residue crystallized from benzene to give the thiocyanate **5** (24.25 g, 84.9%), m.p. 190–191° (lit.[9] m.p. 192–192.5°); ν_{max}^{KBr} 2150 cm^{-1} (SCN); ^{1}H-n.m.r.: δ 8.0 and 7.3 (m, 15 H, Ar), 6.0 (m, 1 H), 5.25 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.05 (m, 1 H), 4.7 (d, 2 H), 4.35 (dt, 1 H), 3.45 (s, 3 H, OCH_3), and 3.35 (dd, 1 H, $J_{3,4}$ 10, $J_{4,5}$ 10.5 Hz, H-4).

*Methyl 2,3,6-tri-*O*-benzoyl-4-thio-α-*D*-glucopyranoside* (**6**). — A mixture of thiocyanate **5** (1.0 g, 1.83 mmol), zinc dust (1.0 g), and glacial acetic acid (10 mL) was heated under reflux with stirring for 16 h. The resulting mixture was stirred into ice–water (200 mL) that contained sodium hydrogencarbonate (14.0 g), and then was extracted with chloroform (100 mL). The chloroform layer was washed with water (100 mL), dried, and evaporated to give a viscous syrup (1.2 g) that showed predominantly one spot on t.l.c. (9:1, v/v, benzene–ether), and a distinct SH absorbance at $\nu_{max}^{CCl_4}$ 2550 cm^{-1}. Compound **6** was characterized as the *S*-benzoyl derivative **7**.

*Methyl 2,3,6-tri-*O*-benzoyl-4-*S*-benzoyl-4-thio-α-*D*-glucopyranoside*[10] (**7**). — To the residue described in the preceding paragraph was added dry pyridine (8 mL) and benzoyl chloride (0.30 mL). The mixture was allowed to stand overnight at room temperature, and then was conventionally processed to give a gum (1.0 g) which,

after two crystallizations from hexane, gave a crystalline solid (0.45 g), m.p. 183°, (lit.[10] m.p. 181.5°); ν_{max}^{KBr} 1720 (OBz) and 1680 cm^{-1} (SBz); ^{1}H-n.m.r.: δ 8.0 and 7.4, (m, 20 H, Ar), 6.1 (m, 1 H), 5.45 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.3 (m, 1 H), 4.7 (d, 2 H), 4.4 (m, 2 H), and 3.5 (s, 3 H, OCH_3).

*Methyl 3-*O*-acetyl-2,6-di-*O*-benzoyl-4-*S*-methyl-4-thio-α-*D*-glucopyranoside* (**13**). — The *S*-methyl derivative **11** (0.75 g), isolated from the coupling reaction products by medium pressure l.c., was conventionally acetylated and processed. Evaporation of the dichloromethane extract gave a syrup (0.78 g) which was purified by medium-pressure l.c. to give a liquid that crystallized, m.p. 97–98°, $[\alpha]_D^{28}$ +90.5° (*c* 1.0, chloroform); ^{1}H-n.m.r.: δ 5.65 (m, 1 H), 5.05 (m, 2 H), 4.7 (m, 2 H), 4.2 (m, 1 H), 3.45 (s, 3 H, OCH_3), 2.8 (dd, 1 H, $J_{3,4}$ 11, $J_{4,5}$ 11 Hz, H-4), 2.15 (s, 3 H, SCH_3), and 2.08 (s, 3 H, OAc).

Anal. Calc. for $C_{24}H_{26}O_8S$: C, 60.74; H, 5.52; S, 6.76. Found: C, 60.18: H, 5.52; S, 6.58.

*Methyl 2,6-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-thio-α-*D*-glucopyranoside* (**14**). — To a stirred solution of sodium methoxide (1.07 g, 19.8 mmol) in methanol (100 mL) under a dry nitrogen atmosphere was added the thiocyanate **5** (10.0 g, 18.3 mL). After 6 h, methanol was evaporated *in vacuo*, and two portions of hexane (50 mL) were added and evaporated to remove any residual methanol. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**9**, 8.0 g, 19.5 mmol) dissolved in hexamethylphosphoric triamide (50 mL) was added, and the mixture was stirred for 20 h and then cooled to −15°. Pyridine (50 mL) was added, and then benzoyl chloride (5.65 g, 40.26 mmol) was slowly added dropwise with stirring, and the mixture was allowed to warm to room temperature. After 24 h, the mixture was stirred into a mixture of crushed ice (200 mL) and saturated sodium hydrogencarbonate solution (200 mL). The product was extracted with ether (350 mL) and processed to give a thin, yellow syrup (23 g). Trituration with two portions of hot hexane (100 mL) removed most of the methyl benzoate from the syrup. Direct crystallization from methanol afforded **14** (3.5 g), and an additional 0.65 g of identical product was recovered by medium-pressure l.c. for a total of 30% of the crystalline glycoside **14**, m.p. 186°, $[\alpha]_D^{28}$ +87.8° (*c* 1.0, chloroform); ^{1}H-n.m.r.: δ 8.15 and 7.6 (m, 10 H, Ar), 5.45 (d, 1 H), 5.25 (d, 1 H), 5.15 (m, 2 H), 4.8 (m, 3 H), 4.15 (m, 5 H), 3.85 (d, 1 H), 3.45 (s, 3 H, OCH_3), 3.05 (dd, 1 H, $J_{3,4}$ 10, $J_{4,5}$ 10 Hz, H-4), and 2.2–1.95 (4 s, 12 H, OAc); ^{13}C-n.m.r.: δ 97.55 (C-1), 85.54 (C-1′), 55.52 (OCH_3), and 52.53 p.p.m. (C-4).

Anal. Calc. for $C_{35}H_{40}O_{16}S$: C, 56.14; H, 5.38; S, 4.28. Found: C, 56.05: H, 5.40; S, 4.42.

*Methyl 4-*S*-β-*D*-galactopyranosyl-4-thio-α-*D*-glucopyranoside* (**17**). — To a stirred solution of sodium methoxide (100 mg) in methanol (25 mL) was added the dibenzoate **14** (1.0 g, 1.34 mmol). After 18 h at room temperature, the base was neutralized with Amberlite IR-120 (H^+) cation-exchange resin, and the solution was filtered and evaporated. The resulting residue was partitioned between water and dichloromethane. Evaporation of the aqueous layer *in vacuo* gave the glycoside

(0.46 g, 96%) as a clear glass, $[\alpha]_D^{28}$ +27.1° (*c* 1.0, water); ^{13}C-n.m.r.: δ 100.67 (C-1), 85.53 (C-1'), 62.87 and 62.69 (C-6' and -6), 56.48 (OCH_3), and 48.53 p.p.m. (C-4). Satisfactory analytical data could not be obtained.

*Methyl 2,3,6-tri-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-thio-α-*D*-glucopyranoside* (**16**). — To the syrup described in the preceding paragraph was added pyridine (20 mL) and acetic anhydride (10 mL) at room temperature with stirring. After 18 h, the mixture was processed to yield (0.91 g) a solid residue which slowly crystallized from a dilute solution of 1:1 (v/v) water–methanol to give a crystalline solid (0.78 g, 91%), m.p. 125°, $[\alpha]_D^{28}$ +42.2°, (*c* 1.0, chloroform); ^{1}H-n.m.r.: δ 5.6–5.3 (m, 2 H), 5.25–4.8 (m, 5 H), 4.5 (d, 2 H), 4.15–3.8 (m, 4 H), 2.85 (dd, 1 H, $J_{3,4}$ 11, $J_{4,5}$ 11 Hz, H-4), and 2.0–2.25 (7 s, 21 H, OAc); ^{13}C-n.m.r.: δ 97.26 (C-1), 82.55 (C-1'), 55.65 (OCH_3), and 46.61 p.p.m. (C-4).

Anal. Calc. for $C_{27}H_{38}O_{17}S$: C, 48.65; H, 5.75; S, 4.81. Found: C, 48.38; H. 5.89; S, 4.88.

*1,3-Di-*O*-acetyl-2,6-di-*O*-benzoyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-thio-*D*-glucopyranoside* (**18**). — To the standard acetolysis solution (20 mL) was added the dibenzoate **14** (1.0 g, 1.33 mmol) with stirring. After the solid had dissolved, the mixture was heated for 5 min at 40°, and then was added slowly to a stirred mixture of crushed ice (100 mL) and pyridine (10 mL). The resulting mixture was processed to give an amorphous solid (1.1 g) that showed two, very closely moving spots on t.l.c. Crystallization from tetrachloromethane–hexane gave an amorphous white powder (0.95 g, 84.8%) which was a mixture of anomers; ^{1}H-n.m.r.: δ 6.5 (d, 0.66 H, $J_{1,2}$ 3.5 Hz, H-1α), 5.6 (d, 0.33 H, $J_{1,2}$ 11 Hz, G-1β), 5.35 (m, 1 H), 5.2 (d, 1 H, 4.95 (m, 1 H), 4.75 (m, 2 H), 4.4 (m, 1 H), 4.0 (m, 3 H), 3.85 (m, 2 H), 3.22 (dd, 1 H, $J_{3,4}$ 11, $J_{4,5}$ 11 Hz, H-4), and 2.2–1.9 (6 s, 18 H, OAc).

Anal. Calc. for $C_{38}H_{42}O_{18}S$: C, 55.74; H, 5.17; S, 3.91. Found: C, 55.95; H, 4.98; S, 3.99.

*1,2,3,6-Tetra-*O*-acetyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-thio-*D*-glucopyranose* (**19**). — Peracetylated methyl thiolactoside **16** (0.5 g) was treated with the acetolysis mixture (10 mL) in a procedure similar to that for preparation of **18**. The work-up gave a syrup (0.55 g) that could be crystallized from 1:1 (v/v) water–methanol to give a white amorphous powder (0.50 g) as a mixture of anomers; ^{1}H-n.m.r.: δ 6.3 and 5.7 (2 d, 1 H, $J_{1,2}$ 7 Hz, H-1β; $J_{1,2}$ 3.5 Hz, H-1α), 5.5 (m, 2 H), 5.05 (m, 3 H), 4.8 (d, 1 H), 4.4 (m, 2 H), 4.0 (m, 4 H), 2.0 (dd, 1 H, $J_{3,4}$ 11, $J_{4,5}$ 11 Hz, H-4), and 2.5–2.0 (8 s, 24 H, OAc); ^{13}C-n.m.r.: δ 91.63 (C-1β), 89.54 (C-1α), 82.67 (C-1'), 46.09 (C-4 of α anomer), and 45.89 p.p.m. (C-4 of β anomer).

Anal. Calc. for $C_{28}H_{38}O_{18}S$: C, 48.41; H, 5.51; S, 4.62. Found: C, 48.48; H, 5.52; S, 4.49.

*4-S-β-*D*-Galactopyranosyl-4-thio-*D*-glucopyranose* (**20**). — To a stirred solution of sodium methoxide (50 mg) in methanol (15 mL) was added **18** (100 mg). After 18 h, the base was neutralized with Amberlite IR-120 (H^+) cation-exchange resin, and the mixture was filtered, evaporated, and partitioned between dichloromethane (25 mL) and water (25 mL). Evaporation of water gave a glassy residue (130 mg)

which could be crystallized from anhydrous methanol to give a white, hygroscopic solid (100 mg) as an anomeric mixture, $[\alpha]_D^{33}$ $+5\rightarrow-8°$ (*c* 1.0, water); ^{13}C-n.m.r. (D_2O): δ 97.02 (C-1α), 93.52 (C-1β), 85.77 (C-1), 53.75 (C-4 of β anomer), and 48.72 p.p.m. (C-4 of α anomer).

Anal. Calc. for $C_{12}H_{22}O_{10}S$: C, 40.22; H, 6.18; S, 8.95. Found: C, 40.53; H, 6.86; S, 8.89.

ACKNOWLEDGMENTS

This work was supported by a grant (AM-20219) from the National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health. The authors are indebted to Professor E. Abushanab, College of Pharmacy, University of Rhode Island, for the ^{13}C-n.m.r. spectra and aid in their interpretation. Some of the work was undertaken during the tenure (1977–78) of an Eleanor Roosevelt International Cancer Fellowship awarded by the American Cancer Society to L.G., and one of the authors (L.G.) wishes to acknowledge the support and encouragement of Dr. M. Hubert-Habart in whose laboratory at the Foundation Curie, Institut du Radium, Paris, France, the work was done.

NOTE ADDED IN PROOF

Deacylation of **14** with strong base ion-exchange resin (details of the technique will be reported elsewhere) provided the analytical sample as a crystalline solid (from ethanol), m.p. 213–215°, $[\alpha]_D^{30}$ $+62.5°$ (*c* 1.0, water).

Anal. Calc. for $C_{13}H_{24}O_{10}S$: C, 41.93; H, 6.49; S, 8.61. Found: C, 42.03; H, 6.48; S, 8.28.

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