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Note

A synthesis of 1,2-*trans*-related glycofuranosyl acetates

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Although, in particular cases and under specific conditions, it is possible to obtain aldofuranose peresters by direct acylation of the free sugars[1], it is more common to make them by strategies which restrict the products to the five-membered ring forms. Acetylation of 5-*O*-triphenylmethylpentoses[2] and the use of 3,5-di-*O*-acetyl-1,2-*O*-isopropylidene-α-D-xylose[3] exemplify such routes, but these methods are limited and the more general procedures available utilise glycofuranosides or thioglycofuranosides.

A useful method, which gives anomeric mixtures of products, is based on the esterification of alkyl furanosides followed by acetolysis of the glycosidic bonds[4]. However, for the preparation of benzoylated glycofuranosyl 1-acetates, which were required for conversion into their 4-halogenated derivatives[5], we preferred to use 1-thiofuranosides, from which 1,2-*trans*-related products have now been made with high efficiency.

Thio sugar derivatives can be used in several ways as synthetic precursors of furanosyl esters, for example, in the preparation of 5-substituted aldopentoses (which on esterification can only give furanose products) from aldose dithioacetals[2]. Otherwise, 1-thiofuranosides, which, in some cases, are readily available from these dithioacetals, can be acylated and then converted into esterified glycofuranosyl halides and hence 1-esters by way of halogenosulphonium intermediates[6a]. However, since 1-thioglycosides can be used to give glycosides directly by activation with mercury(II) salts[7], it appeared that they might also afford direct access to the 1-esters. Such conversions have been reported previously, but yields have been moderate; thus, for example, ethyl 5-*O*-benzoyl-1-thio-β-L-arabinofuranoside, when treated at room temperature with mercury(II) acetate in acetonitrile, gave[8] the corresponding α-1-acetate (34%), and similar yields were obtained in related cases and with other mercury(II) carboxylates[9]. We now report that treatment of 1,2-*cis*-related 1-thioglycofuranoside esters[6] in acetic acid in the presence of mercury(II) acetate gives the 1,2-*trans*-related 1-acetates with high efficiency. The 1-thioglucofuranoside tetrabenzoate **2**, easily obtained from the dithioacetal **1**, on heating with mercury(II) acetate in acetic acid, gave the β-acetate **3** in almost quantitative yield, and the β-D-*galacto* isomer was obtained with similar

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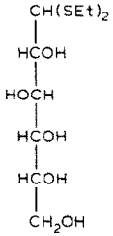
efficiency. The previous method of effecting the conversion **2** → **3** afforded a 52% yield[11]. Likewise, 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose, which is used extensively in nucleoside synthesis, was obtained in 72% yield from D-ribose *via* the diethyl dithioacetal and the ethyl 1-thio-α-furanoside, without isolation or purification of either intermediate.



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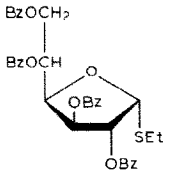

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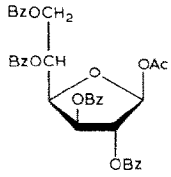

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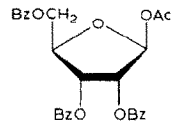

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The usual methods of cyclising aldose dithioacetals to give 1-thiofuranosides involve acid catalysis in aqueous media, but some dithioacetals do not react efficiently under these conditions because the initial products appear to undergo further reaction[6]. In incomplete studies[10], we found that phenyl 1-thio-α-D-glucofuranoside and -D-galactofuranoside can be produced from the diphenyl dithioacetals by using, for example, mercury(II) salts or phenylmercury acetate in alcohols or in such non-hydroxylic solvents as *N,N*-dimethylformamide or acetonitrile, and we suggest that such procedures, in association with the above acetolysis reaction, may offer generally applicable routes to glycofuranosyl esters.

EXPERIMENTAL

1-O-Acetyl-2,3,5,6-tetra-O-benzoyl-β-D-glucofuranose (**3**). — To a solution of ethyl 2,3,5,6-tetra-*O*-benzoyl-1-thio-α-D-glucofuranoside[11] (**2**, 4.30 g) in dry glacial acetic acid (40 mL) was added mercury(II) acetate (4.30 g), and the mixture was heated under reflux for 0.75 h, cooled, filtered, and concentrated, to leave a colourless syrup which was partitioned between chloroform (50 mL) and saturated aqueous sodium chloride (50 mL). Pyridine (2 mL) was shaken with the mixture, and the resulting gelatinous precipitate was removed by filtration through Celite and washed with chloroform (50 mL), and the washings were added to the organic phase of the filtrate. The aqueous phase was extracted with chloroform (50 mL), and the combined organic solutions were washed with dilute hydrochloric acid (50 mL), saturated aqueous sodium hydrogencarbonate (50 mL), and water (50 mL), and then dried. Removal of the solvent and trituration of the residue with ether caused crystallisation of the product; recrystallisation from alcohol yielded **3** (3.93 g, 92%), m.p. 127–128°, $[\alpha]_D$ −29.5° (*c* 1, chloroform); lit.[11] m.p. 130.5°, $[\alpha]_D$ −34°. The ^{1}H- and ^{13}C-n.m.r. data are reported elsewhere[5].

Ethyl 2,3,5,6-tetra-O-benzoyl-1-thio-α-D-galactofuranoside. — Ethyl 1-thio-α-D-galactofuranoside[12] (1.89 g) was treated conventionally with pyridine (10 mL) and benzoyl chloride (5.0 mL). Column chromatography of the product gave the syrupy tetrabenzoate (5.09 g, 94%). Preparative t.l.c. gave material having $[\alpha]_D$ +77° (*c* 1, chloroform). N.m.r. data [$(CD_3)_2CO$]: ^1H, δ 1.25 (t, 3 H, *J* 7.4 Hz, CH_3), 2.75 (q, 2 H, SCH_2), 4.75 (dd, 1 H, $J_{5,6'}$ 6.1, $J_{6,6'}$ 12.1 Hz, H-6'), 4.75 (t, 1 H, $J_{3,4}$ 5.2, $J_{4,5}$ 5.2 Hz, H-4), 4.95 (dd, 1 H, $J_{5,6}$ 4.1 Hz, H-6), 5.80–6.16 (m, 4 H, H-1,2,3,5), and 7.20–8.15 (m, 20 H, 5 Ph); ^{13}C, δ 15.5 (CH_3), 26.0 (SCH_2), 64.2 (C-6), 71.5 (C-5), 78.0, 79.2 (C-2,3), 81.6 (C-4), and 87.4 (C-1).

Anal. Calc. for $C_{36}H_{32}O_9S$: C, 67.5; H, 5.0; S, 5.0. Found: C, 67.6; H, 5.0; S, 5.2.

1-O-Acetyl-2,3,5,6-tetra-O-benzoyl-β-D-galactofuranose. — A solution of the foregoing tetrabenzoate (4.67 g) and mercury(II) acetate (4.64 g) in glacial acetic acid (50 mL) was heated under reflux for 10 min. The solvent was then removed *in vacuo*, and the syrupy residue was shaken with chloroform (100 mL), pyridine (2 mL), and saturated aqueous sodium chloride (100 mL). After filtration through Celite, the two layers were separated, the filter-cake was washed with chloroform (100 mL), and the filtrate was used to extract the aqueous phase. The combined extracts were washed with dilute hydrochloric acid (200 mL), saturated aqueous sodium hydrogencarbonate (200 mL), and water (200 mL), dried, filtered, and concentrated *in vacuo*. The colourless, syrupy residue crystallised on the addition of a small amount of ether. Recrystallisation from ethanol then gave the title compound (4.27 g, 92%), m.p. 121–122°, $[\alpha]_D$ −6° (*c* 1, chloroform). The ^1H- and ^{13}C-n.m.r. data are given elsewhere[5].

Anal. Calc. for $C_{36}H_{30}O_{11}$: C, 67.7; H, 4.7. Found: C, 67.7; H, 5.0.

1-O-Acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (**4**). — Ethanethiol (10.0 mL) was added to a solution of D-ribose (9.6 g) in conc. hydrochloric acid (10.0 mL), and the mixture was stirred at 0° for 1 h and then neutralised with 2M sodium hydroxide. The solvent was removed, the residue was dissolved in water (120 mL), mercury(II) oxide (14.1 g) was added, and then a solution of mercury(II) chloride (8.7 g) in water (100 mL) was added dropwise with stirring during 0.3 h. After a further 1.5 h, pyridine (5 mL) was added, and the mixture was filtered with the aid of Celite and then concentrated *in vacuo*. A solution of the residue in pyridine (120 mL) and benzene (75 mL) was dried azeotropically for ~2 h with the addition of benzene, and the benzene and some of the pyridine (20 mL) were then distilled off. Benzoyl chloride (25 mL, 3.3 mol. equiv.) was added, the mixture was left overnight at room temperature, water (100 mL) was added, and the mixture was extracted with dichloromethane (3 × 160 mL). The combined extracts were washed with dilute hydrochloric acid (400 mL), which was then back-extracted with dichloromethane (120 mL). The combined extracts were washed with saturated aqueous sodium hydrogencarbonate (300 mL) and water (300 mL), dried, and concentrated *in vacuo*. A solution of the syrupy residue in warm acetic acid (200 mL) containing mercury(II) acetate (30 g) was stored for 1 h at 20° and then concen-

trated *in vacuo*. The residue was shaken with chloroform (300 mL), saturated aqueous sodium chloride (300 mL), and pyridine (15 mL), and filtered with the aid of Celite. The aqueous phase was extracted with chloroform (2 × 100 mL), and the combined extracts were washed successively with dilute hydrochloric acid (400 mL), saturated aqueous sodium hydrogencarbonate (400 mL), and water (400 mL), dried, and concentrated. The product (23.3 g, 72%) crystallised upon the addition of ethanol–ether (1:1). It was homogeneous (t.l.c. and ^{1}H-n.m.r.) and had m.p. 120–124°, $[\alpha]_D$ +40° (*c* 1, chloroform). Recrystallisation from ethanol gave material having m.p. 127–128°, $[\alpha]_D$ +45°; lit.[13] m.p. 131–132°, $[\alpha]_D$ +44.2°. The ^{1}H- and ^{13}C-n.m.r. data are given elsewhere[5].

*Phenyl 1-thio-α-*D*-glucofuranoside.* — A solution of phenylmercury acetate (5.4 g, 1.2 mol) in hot dry ethanol (50 mL) was added to a solution of D-glucose diphenyl dithioacetal (5 g) in boiling ethanol (100 mL), and the mixture was heated under reflux for 5 min. The precipitated phenylmercury thiophenate [4.7 g, 93% based on the acetal; m.p. 102–103° (lit.[14] m.p. 106°, 103°)] and the solvent were removed, and the residual syrup was extracted with water. The aqueous phase was taken to dryness with several additions of ethanol, and the residue crystallised on trituration with ether to give the title compound (2.6 g, 73%). Recrystallisation from ethanol–pentane gave material having m.p. 120–123°, $[\alpha]_D$ +206° (*c* 0.5, pyridine); lit.[15] m.p. 119–121°, $[\alpha]_D$ +216° (pyridine); yield, 61%.

The preparation could also be completed by using ethanol with mercury(II) chloride and mercury(II) oxide, or mercury(II) acetate in *N,N*-dimethylformamide or methanol.

*Phenyl 1-thio-α-*D*-galactofuranoside.* — Mercury(II) oxide (100 g) and a solution of mercury(II) chloride (4.7 g) in hot acetonitrile (300 mL) were added to a stirred solution of D-galactose diphenyl dithioacetal (20 g) under reflux. Heating was continued for 10 min, the solids were then removed, and the filtrate was concentrated to half volume to precipitate mercury salts (20.1 g). These were removed and the filtrate was concentrated to dryness to leave a solid residue which was extracted with water. The extract was concentrated to dryness, and the syrupy residue (10 g) was fractionated on a column of silica gel to give the title compound (4.5 g, 32%), which, after crystallisation from chloroform, had m.p. 123–125°, $[\alpha]_D$ +176° (*c* 0.8, pyridine). ^{1}H-N.m.r. data (C_5D_5N): δ 4.15–5.05 (m, 6 H, H-2,3,4,5,6,6′) and 6.12 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1).

Anal. Calc. for $C_{12}H_{16}O_5S$: C, 53.0; H, 5.9; S, 11.8. Found: C, 52.7; H, 6.1; S, 11.7.

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