Note

Convenient synthesis of 2-substituted derivatives of methyl α-D-glucopyranoside preparation of methyl α-D-*arabino*-hexopyranosid-2-ulose

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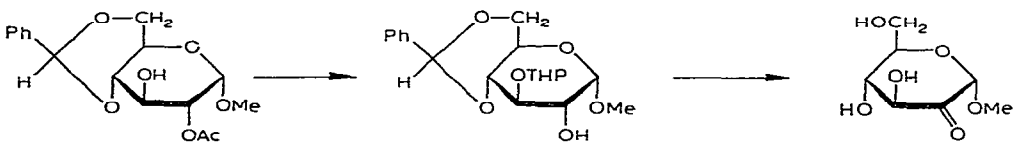
Methyl 4,6-*O*-benzylidene-3-*O*-(tetrahydropyran-2-yl)-α-D-glucopyranoside (**2**) is a useful intermediate for the synthesis of methyl α-D-*arabino*-hexopyranosid-2-ulose (**3**) and may be used for introducing a wide range of substituents at C-2 under basic conditions, since the blocking groups are stable to alkali but readily removed by dilute acid A convenient synthesis of **2** is now reported



1 2 3

Treatment of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside[1] (**1**) (isolated directly from the acetylation mixture by crystallisation) with 3,4-dihydro-2*H*-pyran, followed by removal of the acetate group, afforded **2** as a mixture of diastereoisomers, distinguishable by t l c and n m r The structure of **2** was confirmed by application in sequence of methylation and hydrolysis which gave 2-*O*-methyl-D-glucose

Oxidation of **2** with methyl sulphoxide–acetic anhydride, followed by removal of the benzylidene and tetrahydropyranyl groups with trifluoroacetic acid, gave the 2-ulose **3** in crystalline form, Theander[2] has described the chromatographic properties and reduction products of **3** In contrast to the corresponding 3-ulose derivative, **3** had a very weak i r C=O absorption Two singlets (τ 5 2 and 5 65) for anomeric protons were found in the n m r spectrum (D_2O) of **3** which are assigned, by analogy[3], to the hydrated and non-hydrated forms, respectively

Reduction of **3** with borohydride gave mainly the D-*gluco* isomer (ratio, *gluco*–*manno* 11 1); Lemieux and his co-workers[4] obtained high yields of the D-glucopyranoside on reduction of acetylated 2-oxoglucosides

EXPERIMENTAL

Thin-layer chromatography was performed on Merck Kieselgel F_{254} plates with benzene–methanol (96 4) Paper electrophoresis was performed with 0 1M hydrogen sulphite buffer (pH 4 7) at 25 volts/cm for 30 min The sugars were located with *p*-anisidine at 120°

Methyl 2-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside (**1**) — Methyl 4,6-*O*-benzylidene-α-D-glucoside (31 g) was dissolved in pyridine (150 ml) to which acetyl chloride (7 5 ml) was added dropwise over 20 min at 0° The mixture was stirred at room temperature for 5 h and then poured onto ice and stood overnight The crystals (18 g) were filtered off, washed with water, and dried Two recrystallisations from benzene–light petroleum yielded **1** (9 g), m p 129–131°, lit [5] m p 133–134°

Methyl 4,6-O-benzylidene-3-O-(tetrahydropyran-2-yl)-α-D-glucopyranoside (**2**) The 2-acetate **1** (5 g) was dissolved in chloroform (30 ml) to which 3,4-dihydro-2*H*-pyran (4 ml) and toluene-*p*-sulphonic acid (25 mg) were then added After 3 h, ethanol (50 ml) was added together with fragments of sodium (~250 mg) After 30 min, the mixture was evaporated to small volume, diluted with ethanol (50 ml), and poured into cold water (500 ml) to give, after cooling, **2** (5 g), m p 120–130° Recrystallisation from benzene–hexane afforded material (4 g), m p 135–142°, which was a mixture of diastereoisomers N m r data (60 MHz, chloroform-*d*) τ 2 4–2 6 (5-proton multiplet, phenyl), 4 4 (1-proton singlet, CHPh), 4 75–4 9 (1-proton multiplet, tetrahydropyran H-2), 5 1–5 25 (1 proton, 2 doublets corresponding to H-1 of each diastereoisomer), 8–8 7 (6-proton multiplet, tetrahydropyran H-3,4,5), λ_{max}^{KBr} 3500 cm^{-1} (OH)

Anal Calc for $C_{19}H_{26}O_7$ C, 62,6, H, 7 1 Found C, 61 9, H, 7 1

Treatment of **2** with methyl sulphoxide–methylsulphinyl sodium–methyl iodide[6], followed by acid hydrolysis and conversion of the methylated sugar, gave a product which was identical (*T* 7 9, g l c [7]–m s [8]) with the alditol acetate of 2-*O*-methylglucose

Methyl α-D-arabino-*hexopyranosid-2-ulose* (**3**) — The intermediate **2** (1 2 g) dissolved in methyl sulphoxide (15 ml) was treated with acetic anhydride (3 ml) The reaction was maintained at 50° for 3 5 h, whereafter the solvent was distilled off *in vacuo* at 50° The residue was treated with trifluoroacetic acid (15 ml) and water (2 ml) for 15 min at room temperature, and the mixture was then evaporated The residue was washed twice with warm hexane and then eluted from a column of cellulose with water-saturated butan-1-ol to afford **3** (0 4 g), m p 151–153° (from butanone), $[\alpha]_{578}^{20}$ +141° (*c* 0 5, water) λ_{max}^{KBr} 1740 cm^{-1} (C=O weak)

Anal Calc for $C_7H_{12}O_6$ C, 43 8; H, 6 25 Found C, 43 6, H, 6 3

The 2-ulose **3** (100 mg) was dissolved in ethanol (10 ml) containing a few drops of conc acetic acid 2,4-Dinitrophenylhydrazine (50 mg) was added and the mixture refluxed for 30 min After concentration and cooling, the 2,4-dinitrophenylhydrazone (80 mg) was obtained, m p 181–185°

Anal Calc for $C_{13}H_{16}N_4O_9$ C, 41 9, H, 4 3, N, 14 9 Found C, 42,3, H, 4 5, N, 14 6

Reduction of **3** *with sodium borohydride* — The 2-ulose **3** (20 mg) was dissolved in water (2 ml) and treated with sodium borohydride (30 mg) for 3 h After working up, the product was trimethylsilylated and analysed by g l c on a BDS column The amounts of mannoside and glucoside were 8 and 92%, respectively

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