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Note

Access to septanoside diacetals from methyl *α*-D-glucopyranoside

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Pyridinium chloride has been known as a reagent for dealkoxylation, dehydration, isomerisation, and ring-opening reactions[1]. Its catalytic properties in an acetalation reaction have also been demonstrated[2]. However, its use in carbohydrate chemistry has not been well developed, although an adduct with methyl 4,6-*O*-benzylidene-*α*-D-glucopyranoside has been reported[3]. Previous papers from this laboratory have shown that treatment of mono-, oligo- and poly-saccharides with pyridinium salts, and particularly pyridinium chloride, was an easy procedure for preparing 5-hydroxymethyl-2-furaldehyde[4]. This work was later extended to the synthesis of substituted furans from *C*-alkylated derivatives of D-fructose[5]. We describe herein a ring-expansion of a six-membered ring achieved by the action of pyridinium chloride on methyl 4,6-*O*-isopropylidene-*α*-D-glucopyranoside, which leads to glucoseptanosides (seven-membered ring). The seven-membered ring form of monosaccharides is usually present in trace quantities at equilibrium in solution[6]; their synthesis, especially by those processes described by Stevens and co-workers[7,8], generally requires several steps and gives very low yields. We show herein that treatment of the protected glucopyranoside with pyridinium chloride provides a very simple, mild and ready access to the corresponding glucoseptanoside, by a process which does not require a large amount of solvent.

Direct heating of 4,6-*O*-isopropylidene-*α*-D-glucopyranoside (**1**) with anhydrous pyridinium chloride, both in solid phase for 90 min at 90°, affords in 43% yield a mixture of two compounds. (This yield is calculated without taking into account the fact that one mole of the starting monoacetal can give theoretically only 0.5 mole of the corresponding diacetal under these reaction conditions.) These two compounds **2** and **3** are separated (column chromatography), and their structures are assigned respectively as 2,3:4,5-di-*O*-isopropylidene-*α*- and *β*-D-glucoseptanosides, on the basis of ^{1}H-n.m.r. spectral data and by comparison of their physical data with those previously published[8]. The ^{1}H-n.m.r. spectra, in particular, show for each compound signal for the two isopropylidene groups, the methoxyl group, and a doublet at low field corresponding to the anomeric proton, with a coupling constant in concordance with the respective

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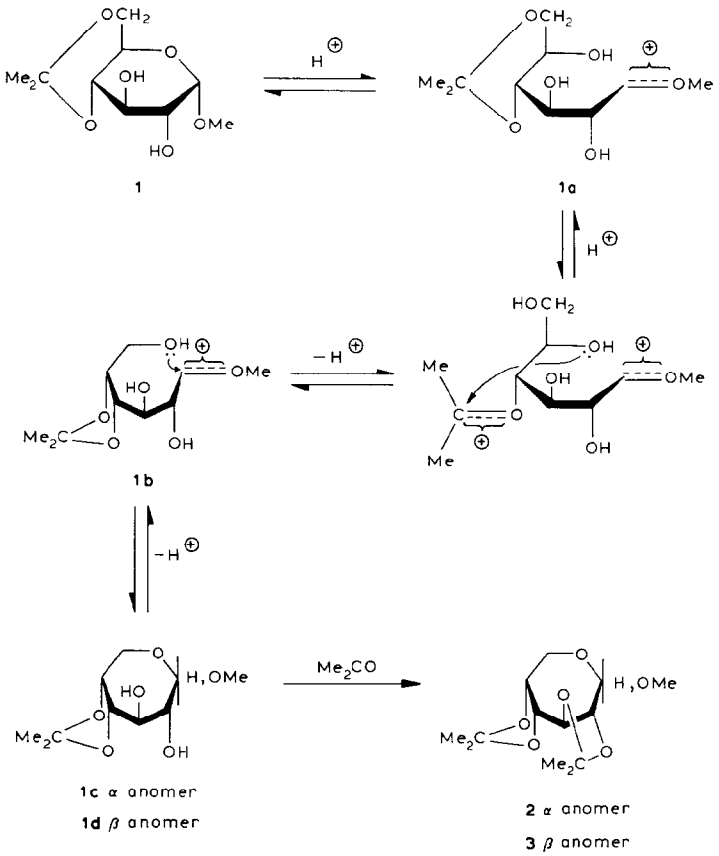

Scheme 1.

structures of α- and β-D-glycosides. These diacetals **2** and **3** are clearly distinct (t.l.c., physical, and spectral data) from both methyl 2,3:4,6-di-*O*-isopropylidene-α- and β-D-glucopyranosides, which have been recently prepared and studied[9]. Looking into the byproducts of the reaction, we found that the starting material had been partially transformed into methyl α-D-glucopyranoside, which could be recovered as its peracetate by direct acetylation of the residue that was obtained after treatment of the crude mixture with dichloromethane to remove the septanosides.

This reaction to form septanosides can be tentatively explained by the mechanism proposed in Scheme 1. In the first step, the acidic medium would give the oxocarbenium ion **1a**, isomerisation of which is now possible and would lead to the 4,5-*O*-isopropylidene ion **1b**. The driving force of this isomerisation should be the greater stability of a 1,3-dioxolane in respect to the corresponding 1,3-dioxane, which is formed as soon as the acetal carbon atom is disubstituted and an equilibrium is possible, due to a *syn*-axial interaction between the methyl groups and axial protons. This interaction, assumption of which had been previously expressed by the Brown–Brewster–Shechter rule[10], was experimentaly demonstrated in our laboratory[11], then quantitatively estimated by

Eliel[12]. The non-stereospecific attack of the primary hydroxyl group on the oxocarbenium ion gives the glycosides **1c** and **1d**. The last step would then be the simple acetalation of **1c** and **1d** by the acetone produced by the partial decomposition of the starting material under acidic conditions.

EXPERIMENTAL

General methods. — Melting points were determined on a Büchi apparatus. Evaporations were performed under diminished pressure. Optical rotations were measured on a Perkin–Elmer 141 polarimeter in 1-dm tubes. Column chromatography was performed with Kieselgel-60 (Merck), and t.l.c. was carried out on precoated plates (Merck 5724), with detection by charring with sulfuric acid. ^{1}H-n.m.r. spectra were recorded on a Varian T-60 spectrometer. Peak multiphities are given by: s, singlet; d, doublet; t, triplet; m, multiplet. Chemical shift data are given in δ-units (p.p.m.), and spin–spin coupling data are in Hz.

2,3:4,5-Di-O-isopropylidene-α and *β-D-glucoseptanosides (**2** and **3**).* — Methyl 4,6-*O*-isopropylidene-α-D-glucopyranoside **1** (5 g, 21 mmol, ref. 13) and anhydrous pyridinium chloride[4] (5 g, 47 mmol) were mixed at room temperature and then heated under anhydrous conditions on an oil bath at 90°. In the first few min, the solid mixture melted, and the reaction was then monitored by t.l.c. After 90 min, the mixture was cooled to room temperature, and the crude material was treated with dichloromethane. The soluble part was separated, and the solvent was evaporated. The residue was then treated with 1:1 ethyl acetate–hexane for better elimination of the excess pyridinium chloride. After concentration of the extract, column chromatography (1:1 ethyl acetate–hexane) of the residue gave 0.7 g (12%) of **2**, 1.1 g (17%) of **3**, and 0.7 g (12%) of a mixture of **2** and **3**. Total yield: 43%. Physicochemical data for **2**: m.p. 77–79°, lit.[7b] 65°; $[\alpha]_D^{20}$ +134° (*c* 0.1, chloroform), lit.[7b] +137° (*c* 0.1, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 4.87 (1 H, d, H-1, $J_{1,2}$ = 2.5 Hz), 3.44 (3 H, s, OMe), 1.37 and 1.44 (12 H, 2 s, CMe_2). Physicochemical data for **3**: m.p. 68–69°, lit.[7b] 71°; $[\alpha]_D^{20}$ −103° (*c* 0.1, chloroform), lit.[7b] −112° (*c* 0.1, chloroform); ^{1}H-n.m.r. data ($CDCl_3$): δ 4.50 (1 H, d, H-1, $J_{1,2}$ = 6.8 Hz), 3.50 (3 H, s, OMe), 1.40, 1.44, and 1.57 (12 H, 3 s, CMe_2).

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