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1-O-MESYL DERIVATIVES OF D-GLUCOPYRANOSE AND THEIR APPLICATION TO α-D-GLUCOPYRANOSIDE SYNTHESIS[1)]

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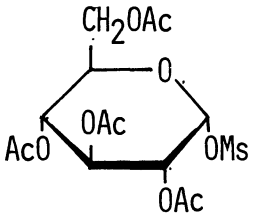
1-O-Mesyl-D-glucopyranose derivatives were synthesized by a reaction between the corresponding α-D-glucopyranosyl bromides and silver methanesulfonate. Alcoholysis of the 1-O-mesyl derivatives was attempted.

1-O-Tosyl derivative of D-glucopyranose was first prepared by Helferich and Gootz[2)] in 1929 and later 1-O-mesyl-D-glucopyranose derivative was synthesized by Helferich and Gnüchtel,[3,4)] by a reaction between metallic salts of the corresponding sulfonic acid and 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide (1).[5)] After that, no attention has been paid on these compounds for a long time, owing to their instabilities and an ambiguity of configurations on the anomeric carbon atom.

Very recently, Eby and Scherch[6)] have described a preparation of several 1-O-tosyl-D-glucopyranose derivatives and their usefulness in α-D-glucopyranoside synthesis.

In the present letter, we wish to report a preparation of 2,3,4,6-tetra-O-acetyl-1-O-mesyl-α-D-glucopyranose (2) and 2-O-benzyl-1-O-mesyl-3,4,6-tri-O-p-nitrobenzoyl-β-D-glucopyranose (5) and their applications to α-D-glucopyranoside synthesis which have been demonstrated with methanol, isopropyl alcohol and cyclohexanol.

2,3,4,6-Tetra-O-acetyl-1-O-mesyl-α-D-glucopyranose (2) was prepared by the method of Helferich and Gnüchtel[3)] by treating a dry benzene solution of 1 with silver methanesulfonate under ice cooling in a yield of 60%, and the crystalline product 2, mp 102°C, $[\alpha]_D^{20}$ +100° (c 1.0, chloroform), decomposed gradually at room temperature. The α-D-configulation of compound 2 has been determined by PMR



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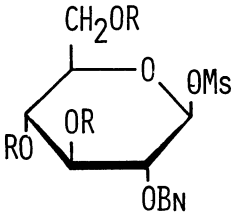

R=p-$NO_2C_6H_4CO$

5

spectrum[7]. That is, the spectrum revealed a doublet at τ 4.00 having a comparatively small coupling constant between H-1 and H-2 ($J_{1,2}$=3.5 Hz) which is characteristic of an equatorial proton on the anomeric carbon atom in the Cl (D) chair conformation. This assignment is also supported by its large positive optical rotation.

Alcoholysis of 2 in methanol in the presence of calcium carbonate gave methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (3)[8] in 71% yield.

Successful attempts to synthesize α-D-glucopyranoside by solvolysis of D-glucopyranosyl bromides having a benzyl group on C-2 have been described by Ishikawa and Fletcher[9].

Along this line, in the present experiments, the β-D-anomer of the 1-O-mesyl derivative having non-participating group on C-2 has been prepared in a crystalline state. To a dry benzene solution of 2-O-benzyl-3,4,6-tri-O-p-nitrobenzoyl-α-D-glucopyranosyl bromide (4)[9,10], silver methanesulfonate was added and the mixture was agitated overnight under ice cooling. The mixture was filtered and the filtrate was evaporated under reduced pressure at room temperature. The residue was crystallized in ethyl acetate to give 2-O-benzyl-1-O-mesyl-3,4,6-tri-O-p-nitrobenzoyl-β-D-glucopyranose (5), mp 153°C, $[\alpha]_D^{20}$ -4° (c 1.0, dichloromethane) in 76% yield. Anal. Calcd. for $C_{35}H_{29}N_3O_{17}S$(796): C, 52.83; H, 3.67; N, 5.28; S, 4.03%. Found: C, 53.11; H, 3.97; N, 5.42; S, 4.29%.

The PMR spectrum of 5 revealed a doublet at τ 4.34 with a large coupling constant ($J_{1,2}$=8 Hz), indicating that 5 is the β-D-anomer.

Compound 5 can be recrystallized from ethyl acetate without serious decomposition and stored in a vacuum desicator in a refrigerator for a week or so.

Alcoholysis of 5 was carried out in boiling methanol for 4 hrs. in the presence of calcium carbonate afforded methyl 2-O-benzyl-3,4,6-tri-O-p-nitrobenzoyl-α-D-glucopyranoside (6), mp 174°C, $[\alpha]_D^{20}$ +20° (c 1.0, dichloromethane), in 92% yield. PMR spectrum of 6 revealed a doublet at τ 5.10 with $J_{1,2}$=3.5 Hz indicating that 6 is the α-D-anomeric isomer. De-O-acylation of 6 in methanolic sodium methoxide gave methyl 2-O-benzyl-α-D-glucopyranoside (7), mp 112°C, $[\alpha]_D^{28}$ +78° (c 0.5, ethanol), in 79% yield. Hydrogenolysis of 7 in the presence of palladium charcoal in hydrogen atomosphere afforded methyl α-D-glucopyranoside (8) in 78% yield, which was identified with an authentic sample[11].

Alcoholysis of 5 in isopropyl alcohol in the analogous procedure gave isopropyl 2-O-benzyl-3,4,6-tri-O-p-nitrobenzoyl-α-D-glucopyranoside (9), mp 136°C, $[\alpha]_D^{20}$ +12° (c 1.0, chloroform), in 74% yield. PMR spectrum of 9 showed a doublet at τ 4.82 ($J_{1,2}$=4 Hz) characteristic of the α-D-anomer. De-O-acylation of 9, followed by catalytic hydrogenation and subsequent acetylation afforded isopropyl 2,3,4,6-tetra-O-acetyl-α-D-glucopyranoside (10), mp 85°C, $[\alpha]_D^{22}$ +140° (c 1.0, ethanol), in 44% yield. (Lit.[12] mp 86.5°C, $[\alpha]_D$ +143°).

Alcoholysis of 5 in cyclohexanol afforded cyclohexyl 2-O-benzyl-3,4,6-tri-O-p-nitrobenzoyl-α-D-glucopyranoside (11), mp 116°C, $[\alpha]_D^{20}$ +14° (c 1.0, chloroform), in 76% yield. A doublet characteristic of α-D-anomer was observed at τ 4.76 ($J_{1,2}$=3.5 Hz) in the PMR spectrum. De-O-acylation of 11, followed by catalytic hydrogenation afforded cyclohexyl α-D-glucopyranoside (12), mp 120°C, $[\alpha]_D^{21}$ +135° (c 1.0, ethanol), in 36% yield. (Lit.[13] mp 125°C, $[\alpha]_D^{33}$ +136°).

All the products obtained in the alcoholysis gave correct elementary analyses.

REFERENCES AND FOOTNOTES

1) A part of this work was presented at the 27th Annual Meeting of the Chemical Society of Japan, Nagoya, October, 1972 (See Abstracts of Papers of the Meeting, Vol. I, p. 136).

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