Tetrahedron Letters No.32, pp. 3805-3807, 1966. Pergamon Press Ltd.
Printed in Great Britain.

METHYL 2, 3:4, 6-DI-O-ISOPROPYLIDENE-α-D-GLUCOPYRANOSIDE

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(Received 26 May 1966)

Acid catalysed formation of cyclic acetals spanning vicinal trans diequatorial hydroxyl groups has hitherto been observed only in certain inositol derivatives (1-5). Angyal and coworkers (1-3) have suggested that a prerequisite for such acetal formation is the presence of a fused ring system which distorts the inositol ring, probably into a twist conformation (5). Mager and Ionescu (4) obtained results which support this proposed condition, observing that scyllo-inositol (three pairs of vicinal trans e-e hydroxyl groups) failed to react with o-nitrobenzaldehyde under conditions which led to formation of a di-O-o-nitrobenzylidene derivative from 1, 2-O-isopropylidene-myo-inositol (one cis e-a pair, spanned by the isopropylidene grouping, and two trans e-e pairs).

Maslinkska and Jedlinski (6) have suggested from conformational considerations that cyclic acetal formation in methyl α-D-glucopyranoside is restricted to the 4 and 6 positions, i. e. that an acetal bridging vicinal trans e-e hydroxyl groups in sugar pyranose rings is highly unlikely.

We now report formation of methyl 2, 3:4, 6-di-O-isopropylidene-α-D-glucopyranoside, in 1-2% yield, when methyl α-D-glucopyranoside is treated with 2, 2-dimethoxypropane and an acid catalyst either in excess dimethoxypropane or in dimethylformamide. The reaction is conveniently carried out by stirring the reactants at room temperature for one day; the yield of diacetal is not increased by carrying out the

reaction at 80°. Thin layer chromatograms of the reaction mixture after one hour and one day were indistinguishable. Methyl 4,6-O-isopropylidene-α-D-glucopyranoside (8) is also formed in the reaction in 79% yield (96% based on unrecovered glucoside).

The crystalline diacetal has m.p. 85° and $[\alpha]_D$ +99° (c 2.0 in benzene). Found: C, 57.07; H, 8.01. $C_{13}H_{22}O_6$ requires C, 56.92; H, 8.08. The n.m.r. spectrum of the compound, in carbon tetrachloride with TMS as internal standard, shows a doublet with J = 3.0 c.p.s. at τ 5.1 for the anomeric proton (1 proton), a poorly resolved group of signals in the region τ 6.0 - 6.8 (9 protons), and three signals at τ 8.50, 8.63, and 8.65 for the isopropylidene protons (7) (12 protons). Molecular weight determinations gave values of 271 by osmometry and 274 by mass spectroscopy.

Graded acidic hydrolysis of the diacetal in glacial acetic acid for 12 hours at room temperature gave methyl α-D-glucopyranoside (30%) and methyl 4,6-O-isopropylidene-α-D-glucopyranoside (8) (70%), both identified by mixed melting points and comparison of their infrared spectra with those of the authentic compounds.

One possible explanation of the low yield of diacetal, even under forcing conditions, is that when the 4,6 acetal ring has been formed the free hydroxyl groups at C-2 and C-3 are held in a conformation which hinders acetal formation whereas if the 2,3 acetal is formed first, with some distortion of the pyranose ring, the hydroxyl groups at C-4 and C-6 are still suitably oriented to participate in acetal formation. We are carrying out studies on various glycosides and cyclitols to elucidate this point.

Base catalysed formation of the 2,3-O-methylidene acetal of methyl 4,6-O-benzylidene-α-D-glucoside has been reported (9). Arguments, based on thermodynamic stability of products, normally used to rationalise products of acetalation reactions do not apply in this

case since this reaction is irreversible. Treatment of methyl 4, 6-O-isopropylidene-α-D-glucoside with 2, 2-dichloropropane in either DMSO-dimethylsulphinyl carbanion or DMF-sodium hydride failed to give any diacetal although addition of dichloromethane to the DMF-sodium hydride reaction mixture led to formation of a crystalline 2, 3-O-methylidene derivative.

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