

METHYL 2,3-DIDEOXY- α -D-GLYCERO-HEX-2-ENO-PYRANOSID-4-ULOSE

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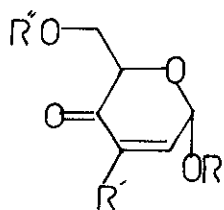
Abstract - An efficient synthesis of the title compounds from methyl 4,6-O-benzylidene- α -D-glucopyranoside is described; thus making available a versatile group of intermediates for the syntheses of branched-chain sugars.

There have been numerous examples of the use of the compounds (1), and their simple derivatives, in the syntheses of rare and unusual sugars, and the potential synthetic applications of these compounds have been well recognised¹.

These compounds have been synthesised by the oxidation of the allylic alcohols (2) using MnO₂, in yields of about 50%^{1a}. The syntheses of (2) have been achieved in low overall yield from methyl 4,6-O-benzylidene- α -D-glucopyranoside².

Our interest in the syntheses of branched-chain sugars has led us to the synthesis of (3) by a route which should prove generally applicable to the syntheses of the other homologues or derivatives i.e. (3), R = alkyl or aryl. Starting from the available 2-benzoate (4)³, we prepared the 3-keto-compound (5)⁴ by the method due to Garegg et al⁵, in 92% yield. Reduction of the ketone with CH₃MgI gave the alloside (6)⁴ in 84% yield, which was acetylated using Ac₂O/pyridine to produce the compound (7)⁶, quantitatively. (7), m.p. 96-97°C showed ν_{\max} 1740 cm⁻¹, δ_{CDCl_3} 1.30, 2.14 and 3.40 (each 3H, s, 3-C-CH₃, COCH₃ and -O-CH₃ respectively), 4.70 and 4.83 (each 1H, d, J = 3.5 Hz, H-1 and H-2), 5.48(1H, s, benzylidene proton) and 7.23 (5H, m).

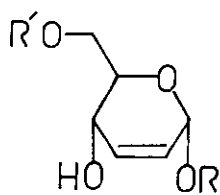
Dehydration of (7) using SOCl₂/pyridine at 0°C yielded the olefin (8) in 97% yield. (8) m.p. 112-113°C showed ν_{\max} 1740 and 1720 (sh) cm⁻¹, δ_{CDCl_3} 1.68 (3H, m, $W_{1/2}$ = 2Hz, CH₃-C=C), 2.10, 3.45 (each 3H, s, -CO-CH₃ and -O-CH₃ respectively), 5.03 (1H, d, J = 4.5 Hz, H-1), 5.43 (1H, m, H-2), 5.50 (1H, s, benzylidene proton). Treatment of a 1% solution of (8) in 95% aqueous methanol with a catalytic amount of concentrated HCl for 15 minutes, followed by neutralisation of the acid with concentrated aqueous NH₃ solution yielded the compound (3) in 96% yield. In a typical reaction, (8), 0.615 g, was dissolved in 95% aqueous methanol (62 mls) and to the well stirred solution 0.5 ml of conc. HCl was added. After 15 minutes the reaction was neutralised with conc. NH₃ solution, reduced to dryness on a rotary evaporator and the residue triturated with hot CHCl₃ to recover the organic matter, thus yielding crude (3). Recrystallisation from benzene/



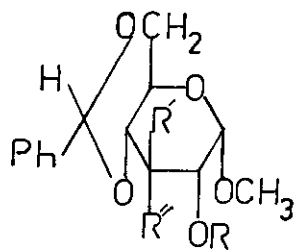
(1) $R = \text{CH}_3$ or C_2H_5 , $R' = R'' = \text{H}$

(3) $R = R' = \text{CH}_3$, $R'' = \text{H}$

(9) $R = R' = \text{CH}_3$, $R'' = \text{Bz}$



(2) $R = \text{CH}_3$ or C_2H_5 , $R' = \text{H}$

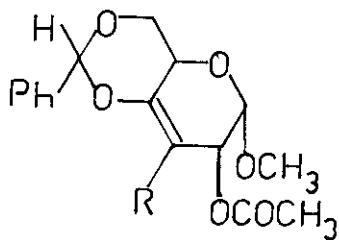


(4) $R = \text{Bz}$, $R' = \text{OH}$, $R'' = \text{H}$

(5) $R = \text{Bz}$, $R' = R'' = \text{O}$

(6) $R = \text{H}$, $R' = \text{CH}_3$, $R'' = \text{OH}$

(7) $R = \text{Ac}$, $R' = \text{CH}_3$, $R'' = \text{OH}$



(8) $R = \text{CH}_3$

60-80° petrol provide white needles of (3), 0.329 g, m.p. 98-100°C, ν_{\max} 1690 cm^{-1} , λ_{\max} 225 nm (3.87), δ_{CDCl_3} 1.80 (3H, m, $W_{1/2}=3.5$ Hz, $\text{CH}_3\text{-C=C}$), 2.37 (1H, m, exchanged with D_2O), 3.47 (3H, s, $-\text{O}-\text{CH}_3$), 3.93 (2H, d, $J=4.0$ Hz, $-\text{CH}_2\text{-OH}$), 4.40 (1H, t, $J = 4.0$ Hz, $\text{H-C-CH}_2\text{-OH}$), 5.07 (1H, d, $J \approx 4.0$ Hz, H-1) and 6.57 (1H, m, H-2).

In the acid hydrolysis the complete loss of the benzylidene group and the acetoxy group at C-2 had been achieved. It was noteworthy that every proton's resonance was discernible in the NMR spectrum of (3) and that H-1 was long ranged coupled to the 3-C-methyl protons.

Benzoylation of (3) gave the ester (9) m.p. 78-79° ν_{\max} 1693 and 1735 cm^{-1} , δ_{CDCl_3} 1.87 (3H, m, $\text{CH}_3\text{-C=C-}$), 3.48 (3H, s), 4.73 (3H, s, $-\text{O}-\text{CH}_2\text{-CH-}$), 3.07 (1H, d, $J=3.5$ Hz), 6.62 (1H, m), 7.43 (3H, m) and 7.97 (2H, m).

The reduction of the 3-keto-compound (5) by the metal hydrides or simple Grignard reagents is well known to produce the allo-compounds⁶, thus we envisage the preparation of a range of derivatives of (3) where R¹ is introduced via a Grignard reaction, followed by the dehydration and subsequent reactions.

It should be noted that in this synthesis of (3), the lowest yield reaction, the Grignard reaction, proceeded in 84% yield and thus we achieved a 72% overall yield of the desired compound from the 2-benzoate (4).

References and Notes

All new compounds reported gave satisfactory analytical data.

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