HETEROCYCLES, Vol. 14, No. 9, 1980

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

Lynda L. Box, Vernon G.S. Box* and Earle V.E. Roberts
Chemistry Department, University of the West Indies
Kingston 7, Jamaica, West Indies.

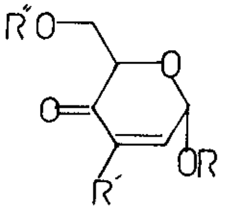
Abstract - An efficient synthesis of the title compounds from methyl 4,6-O-benzylidene-α-D-glucopyranoside is described, thus making available a versatile group of intermediates for the syntheses of branched-chain sugars.

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 recognised[1].

These compounds have been synthesised by the oxidation of the allylic alcohols (2) using MnO_2, 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-glucopyranoside[2].

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 al[5], in 92% yield. Reduction of the ketone with CH_3MgI gave the alloside (6)[4] in 84% yield, which was acetylated using Ac_2O/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-CH_3, $COCH_3$ and -O-CH_3 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).

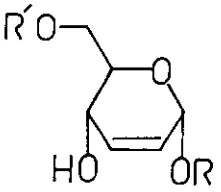
Dehydration of (7) using $SOCl_2$/pyridine at 0°C yielded the olefin (8) in 97% yield. (8) m.p. 112-113°C showed ν_{max} 1740 and 1720 (sh) cm^{-1}, δ_{CDCl_3} 1.68 (3H, m, $W_{1/2}$ = 2Hz, $CH_3\text{-C=C}$), 2.10, 3.45 (each 3H, s, -CO-CH_3 and -O-CH_3 respectively), 5.03 (1H, d, J = 4.5 Hz, H-1), 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 NH_3 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. NH_3 solution, reduced to dryness on a rotary evaporator and the residue triturated with hot $CHCl_3$ to recover the organic matter, thus yielding crude (3). Recrystallisation from benzene/



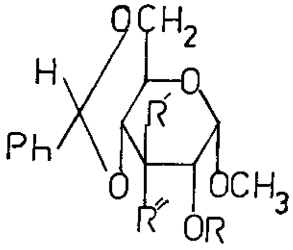
(1) R = CH_3 or C_2H_5, R' = R" = H

(3) R = R' = CH_3, R" = H

(9) R = R' = CH_3, R" = Bz



(2) R = CH_3 or C_2H_5, R' = H

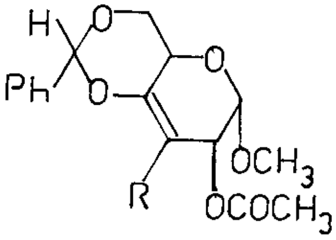


(4) R = Bz, R' = OH, R" = H

(5) R = Bz, R' = R" = O

(6) R = H, R' = CH_3, R" = OH

(7) R = Ac, R' = CH_3, R" = OH



(8) R = 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, $W_{\frac{1}{2}}$=3.5 Hz, $CH_3\text{-}C=C$), 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, $\text{-}C\underline{H}_2\text{-}OH$), 4.40 (1H, t, J = 4.0 Hz, $\underline{H}\text{-}C\text{-}CH_2\text{-}OH$), 5.07 (1H, d, $J \simeq 4.0$ Hz, H-1) and 6.57 (1H, m, H-2).

In the acid hydrolysis the complete loss of the benzylidene group and the acetoxyl 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, $CH_3\text{-}\overset{|}{C}=\overset{|}{C}\text{-}$), 3.48 (3H, s), 4.73 (3H,s,$\text{-}O\text{-}C\underline{H}_2\text{-}\overset{|}{C}\underline{H}\text{-}$), 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-compounds[6], thus we envisage the preparation of a range of derivatives of (3) where R^1 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.

1. (a) B. Fraser-Reid, A. McLean and E.W. Usherwood, J. Amer. Chem. Soc., 91, 5392 (1969).
   (b) Specialist Periodical Report, Carbohydrate Chemistry, The Chemical Society, London, Vol. 10 (1978), Chapters 2 and 14.
   (c) R.C. Anderson, B. Fraser-Reid and J.L. Primeau, J.C.S. Chem. Comm., 6 (1980).
2. B. Fraser-Reid and B. Boctor, Can. J. Chem., 47, 393 (1969).
3. L.L. Box, V.G.S. Box and E.V.E. Roberts, Carbohydr. Res., 69, C1-C3, (1979).
4. F.A. Carey and K.O. Hodgson, Carbohydr. Res., 12, 463 (1970).
5. P.J. Garegg and B. Samuelsson, Carbohydr. Res., 67, 267 (1978).
6. C. Shin, K. Kobayashi, K. Sato and J. Yoshimura, Bull. Chem. Soc. (Japan), 46, 1515 (1973).

Received, 28th May, 1980