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Note

Selective acetylation of D-mannose and D-xylose

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Our investigations on the direct selective acetylation of some aldopyranoses[1,2] have provided useful syntheses of intermediates not otherwise readily available Treatment of D-mannose with 5 7 mol. of acetic anhydride in the presence of anhydrous sodium acetate at room temperature gave a mixture of products from which the syrupy penta-acetate (~60%) and 1,2,3,6-tetra-*O*-acetyl-α,β-D-mannopyranose (**1**, 29%) were isolated by chromatography on silica gel The penta-acetate was mainly the α anomer, the H-1α signal appeared at τ 3 86, and there was a much weaker signal for H-1β at τ 4 08

In the tetra-acetate, the relative intensities of the H-1 resonances at τ 3 92 and 4 11 indicated the α β ratio to be ~2·1 Methylation of the tetra-acetate with diazomethane–boron trifluoride etherate[3] gave crystalline 1,2,3,6-tetra-*O*-acetyl-4-*O*-methyl-β-D-mannopyranose (**2**), and 4-*O*-methyl-D-mannose was the only sugar isolated after deacetylation

The isolation of the 1,2,3,6-tetra-acetate in useful yield shows that HO-4 of D-mannose is the least reactive hydroxyl group under the designated reaction conditions, in agreement with the reported[5] selective acylation of benzyl α-D-mannopyranoside Also, HO-4 was least reactive in the selective acylation of methyl α-D-mannopyranoside with benzoyl chloride[4]

Acetylation of D-xylose with 5 3 mol of acetic anhydride gave crystalline tetra-*O*-acetyl-β-D-xylopyranose (27%) and a syrupy triacetate fraction (**3**, ~29%), from which 1,2,4-tri-*O*-acetyl-β-D-xylopyranose (**4**, 7 2%) was isolated by fractional crystallisation The structure of **4** was established by methylation with diazomethane–boron trifluoride etherate in dichloromethane, and was confirmed by n m r spectrometry of the derived, crystalline 3-phenylcarbamate **6** Irradiation at the high-field portion (τ 4 80–5 10) of the pattern due to H-2,3,4 decoupled the H-5 signals, maximum decoupling occurred with irradiation at τ 5 06, so this was taken as the centre of the H-4 signal Similarly, by decoupling H-1, the H-2 signal was shown to be centred at τ 4 97 Thus, H-3 was centred at τ 4 86 In the spectrum[6] of 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose in acetone-d_6 at 100 MHz, the signal for H-3 was a triplet (τ 4 71) The upfield shift (0 15 p p m) in the H-3 signal of **6** relative to

that of H-3 of the tetra-acetate is to be expected, since the C_6H_5-NH group should decrease the anisotropic deshielding effect of the C=O group Methylation of the triacetate fraction, followed by deacetylation, yielded 3-*O*-methyl-D-xylose and traces of 2-*O*-methyl-D-xylose and D-xylose, the 2-methyl ether was not detected by alkaline triphenyltetrazolium chloride

Thus, the selective acetylation of D-xylose provides a useful preparation of 1,2,4-tri-*O*-acetyl-*β*-D-xylopyranose

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage and are uncorrected Solutions were concentrated under diminished pressure below 50° T l c was performed on Silica gel F-254 (Merck) with benzene–methanol (96 4–9 1), and detection with ferric hydroxamate or charring with sulphuric acid Column chromatography was carried out on Silica gel (Grace, mesh 50–100) N m r spectra were measured with a Jeol JNM-MH-100 spectrometer, and optical rotations with a Perkin–Elmer Model-241 polarimeter

Partial acetylation of D-*mannose* — A mixture of D-mannose (10 g, 55 mmol), anhydrous sodium acetate (3 g), and acetic anhydride (30 ml, 317 mmol) was stirred for 2 days at room temperature, and then filtered, diluted with water, and concentrated The syrupy residue was partitioned between chloroform and water The aqueous phase (2 86 g) contained D-mannose and sodium acetate T l c of the chloroform phase (~18 g) revealed two major components, and a portion (5 2 g) was eluted from a column (42 × 4 cm) of silica gel, fractions (150 ml) were monitored by t l c

Elution with ether–benzene (5 95) (fractions 1–8), followed by ether–benzene (1 9) (fractions 9–12), gave syrupy penta-*O*-acetyl-D-mannose (3 g), $[\alpha]_D$ +28° (*c* 1, chloroform) The $[\alpha]_D$ values of the various crops obtained by fractional crystallisation of the syrup from ether–light petroleum indicated an α β ratio of ~2.1. N m r. data τ 3 86 (d, $J_{1\ 2}$ ~1.8 Hz, H-1α) and 4 08 (d, $J_{1\ 2}$ ~1 2 Hz, H-1β) Fractions 13–15, eluted with ether–benzene (15 85), contained a mixture of the penta-acetate and the tetra-acetate **1**

Continued elution with ether–benzene (15 85) (fractions 16–41) gave **1** (1 2 g), $[\alpha]_D$ +23° (*c* 1, chloroform) N.m r data ($CDCl_3$) τ 3.92 (bd, J ~2 Hz, H-1α), 4 11 (bd, J < 2 Hz, H-1β), 6 96 (bs, 1 H, OH), and 7 84–7 96 (12 H, 4 AcO)

Anal Calc for $C_{14}H_{20}O_{10}$ C, 48 28, H, 5 74 Found C, 48 20, H, 5 65

Fractions 42–50, eluted with ether–benzene (1·4), contained tetra-acetate and, presumably, triacetate

1,2,3,6-Tetra-O-*acetyl-4*-O-*methyl-β*-D-*mannopyranose* (**2**) — To a solution of **1** (467 mg) in dichloromethane (5 ml) at −5°, boron trifluoride etherate (0 02 ml) was added The solution was kept at −5° during the addition of excess of diazomethane in dichloromethane and for a further 0 5 h at −5° to allow all colour to discharge T l c then showed ~60% conversion into the faster-moving product The mixture was filtered and concentrated, and a solution of the syrupy residue in benzene

(~10 ml) was extracted with water (6 × 10 ml) to remove **1** (110 mg), and then concentrated to a syrup (313 mg), $[\alpha]_D$ +32° (*c* 0 45, chloroform) N m r data ($CDCl_3$). τ 6 55 (OMe) and 7 86–7 96 (12 H, 4 AcO)

Crystallisation from di-isopropyl ether occurred slowly to yield **2**, m p 136–140°, $[\alpha]_D$ −46 5° (*c* 0 43, chloroform), lit [7] m p 75–76°, $[\alpha]_D$ +59° (chloroform), for the α-D isomer of this compound

Anal Calc for $C_{15}H_{22}O_{10}$ C, 49 72, H, 6 08 Found 49 20, H, 6 17

Attempts to recrystallise the material recovered after the measurement of the specific rotation failed A solution of syrupy **2** (20 mg) in methanol (3 ml) was treated with 0 1M methanolic sodium methoxide (1 ml) for 4 h at room temperature Cations were removed from the solution with Amberlite IR-120 (H^+) resin, and the solution was then concentrated to give chromatographically homogeneous (detection with aniline hydrogen phthalate) 4-*O*-methyl-D-mannose as a viscous syrup, $[\alpha]_D$ +18 5° (*c* 0 82, water), M_G 0 56, which was identified by comparison with 4-*O*-methyl-D-mannose {lit [8] $[\alpha]_D$ +22° (water)} prepared from benzyl 2,3,6-tri-*O*-acetyl-α-D-mannopyranoside[5]

Partial acetylation of D-*xylose* — A mixture of D-xylose (15 g, 100 mmol), sodium acetate (7 5 g), and acetic anhydride (50 ml, 525 mmol) was stirred for 6 days at room temperature T l c revealed tetra-acetate and triacetate (major products), and a smaller proportion of diacetate The slurry was filtered and the solids were rinsed with chloroform The combined filtrate and washings were diluted with a large volume of ethanol and concentrated Fractional crystallisation of the residue (24 9 g) from ethanol gave tetra-*O*-acetyl-β-D-xylopyranose (8 5 g), m p and mixture m p 124–126°, lit [9] m p 124 5–126°.

The mother liquors were concentrated to a syrup, a solution of which in benzene (100 ml) was filtered and then extracted with water (10 × 10 ml) which removed the lower acetates together with some triacetate The benzene layer was then equilibrated with water, the aqueous solution was extracted with chloroform, and the extract was concentrated to give the syrupy triacetate fraction (8 9 g), $[\alpha]_D$ +5° (*c* 0 47, chloroform) Fractional crystallisation from di-isopropyl ether gave the 1,2,4-triacetate **4** (2 g) as needles, m p 136–137°, $[\alpha]_D$ −17° (*c* 0 19, chloroform) N m r data ($CDCl_3$) τ 4 22 (d, $J_{1,2}$ 7 Hz, H-1), 5 00 (m, H-2,4), 5 80–6 50 (m, H-3,5,5'), 7 18 (bs, 1 H, OH), and 7 90 (s, 3 AcO)

Anal. Calc for $C_{11}H_{16}O_8$ C, 47 82, H, 5 79 Found C, 48 25, H, 5 59

Methylations with diazomethane–boron trifluoride etherate — (*a*) *1,2,4-Tri-O-acetyl-3-O-methyl-β-*D-*xylopyranose* (**5**) To a solution of **4** (350 mg) in dichloromethane (6 ml) at 0° was added boron trifluoride etherate (0 02 ml), and the solution was maintained at 0° during the addition of excess of diazomethane in dichloromethane, and then kept for 1 h to allow all colour to be discharged T l c then showed an almost complete conversion into a faster-moving product The mixture was filtered, and concentrated to give **5** as a syrup (360 mg), $[\alpha]_D$ −42° (*c* 0 2, chloroform)

Anal Calc for $C_{12}H_{18}O_8$ C, 49 65, H, 6 2 Found C, 51 21, H, 5 93

A solution of **5** (80 mg) in dry methanol (3 ml) was treated with a catalytic

amount of sodium methoxide. When deacetylation was complete, the solution was de-ionised and concentrated to a syrup which was dried by distillation with methanol and extracted with acetone The extract was concentrated to dryness The product (~30 mg) migrated at the same rate as an authentic sample of 3-*O*-methyl-D-xylose on electrophoresis in borate buffer, and had M_G 0 70 (lit [10] 0 66)

(*b*) When the procedure in (*a*) was applied to the syrupy triacetate fraction, 3-*O*-methyl-D-xylose was formed together with a trace of the 2-*O*-methyl analogue.

1,2,4-Tri-O-*acetyl-3*-O-*phenylcarbamoyl-β*-D-*xylopyranose* (**6**) — To a solution of **4** (200 mg) in dry toluene (4 ml) were added phenyl isocyanate (0 5 ml) and dry pyridine (0 75 ml) After 24 h at room temperature, t l.c showed almost complete conversion of **4** into material of higher R_F value The solution was treated with water to decompose excess of phenyl isocyanate, kept for 1 h at room temperature, filtered, and concentrated The syrupy residue was extracted with chloroform (30 ml), the extract was filtered and washed with 0 5% aqueous copper sulphate and water to remove pyridine, dried (Na_2SO_4), and concentrated, and the residue was crystallised from the minimal volume of di-isopropyl ether to give **6** as needles (220 mg) Recrystallisation from di-isopropyl ether gave material, m p 150°, $[\alpha]_D$ +8° (*c* 0 2, chloroform) N m r. data ($CDCl_3$) τ 2 75 (m, 5 H, Ph), 3 20 (bs, 1 H, NH), 4 30 (d, 1 H, $J_{1\,2}$ 7 Hz, H-1), 4 80–5 10 (m, 3 H, H-2,3,4), 5 86 (dd, 1 H, $J_{5\,5}$ 11, $J_{5\,4}$ 4 5 Hz, H-5), 6 42 (dd, 1 H, $J_{5\,,5}$ 11, $J_{5',4}$ 9 Hz, H-5'), and 7 92–7 96 (2 s, 9 H, 3 AcO)

Anal Calc for $C_{18}H_{21}NO_9$ C, 54 68; H, 5 32, N, 3 54. Found C, 54.73, H, 5.50, N, 3 43

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