832. *A Synthesis of* 3 : 4-*Dimethyl* D-*Xylose and* 4-*Methyl* D-*Xylose.*

By L. HOUGH and J. K. N. JONES

3 : 4-Dimethyl D-xylose and 4-methyl D-xylose have been synthesised from D-arabinose *via* 2 : 3-anhydro-β-methyl-D-riboside. Crystalline derivatives suitable for their characterisation are described.

3 : 4-DIMETHYL D-XYLOSE has been reported to occur in the fission products of methylated tragacanthic acid (James and Smith, *J.*, 1945, 739), of methylated mucilages (Mullan and Percival, *J.*, 1940, 1501; Nelson and Percival, *J.*, 1942, 99), and of a methylated aldobiuronic acid, namely, 2-(4-methyl D-glucuronopyranosyl)-D-xylose, obtained from aspen wood (Jones and Wise, *J.*, 1952, 3389). We attempted the synthesis of this xylose derivative since it was not well characterised and a synthesis described by Robertson and Speedie (*J.*, 1934, 825) is ambiguous. 2 : 3-Anhydro-β-methyl-D-riboside (Honeyman, *J.*, 1946, 990; Kent, Stacey, and Wiggins, *J.*, 1949, 1234) was prepared from D-arabinose and methylated by Purdie's reagents to give a readily crystallised 4-methyl derivative. Treatment of the latter with sodium methoxide gave a dimethyl methylpentoside. As expected from the results of Honeyman (*loc. cit.*), Mukherjee and Todd (*J.*, 1947, 969), and Kent, Stacey, and Wiggins (*loc. cit.*), the product contained largely 3 : 4-dimethyl-β-methyl-D-xyloside and not the arabinose derivative. Proof of identity was obtained by methylation to 2 : 3 : 4-trimethyl β-methyl-D-xyloside which on hydrolysis gave 2 : 3 : 4-trimethyl D-xylose. Hydrolysis of 3 : 4-dimethyl methylxyloside gave 3 : 4-dimethyl D-xylose as a syrup, which gave a crystalline xylosylamine derivative and lactone. Recently, we became aware of an independent synthesis by another route of 3 : 4-dimethyl D-xylose by Percival and Zobrist and, through the kindness of Dr. E. E. Percival, details of this work appear concurrently with this publication. We have compared samples and, from mixed m. p. data and paper chromatograms, the products are clearly identical and resemble those described by James and Smith (*loc. cit.*).

Aqueous alkaline hydrolysis of 4-methyl 2 : 3-anhydro-β-methyl-D-riboside afforded crystalline 4-methyl β-methyl-D-xyloside. The methylglycoside consumed one mol. of periodate, gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside on methylation, and depressed the melting point of 2-methyl β-methyl-D-xyloside. Acidic hydrolysis of the methylglycoside gave syrupy 4-methyl D-xylose which was converted into the crystalline osazone.

EXPERIMENTAL

M. p.s are uncorrected. Microanalyses are by Mr. B. S. Noyes of Bristol. Evaporations were carried out under reduced pressure.

4-Methyl 2 : 3-Anhydro-β-methyl-D-riboside.—β-Methyl-D-arabinoside (4·8 g.) was converted into the 3 : 4-*iso*propylidene derivative by Honeyman's method (*loc. cit.*). The crude product (5·4 g.) was treated in pyridine (25 c.c.) with toluene-*p*-sulphonyl chloride (7 g.). After 24 hours at 20°, the solution was poured on ice, and the precipitate of crude 3 : 4-*iso*propylidene 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside was recrystallised from aqueous ethanol. The product (7·8 g.), m. p. 136°, was dissolved in boiling acetone (25 c.c.), and the *iso*propylidene residue removed by addition of 0·1N-formic acid (50 c.c.), during 2 hours. Evaporation of the solvent afforded syrupy 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside (4·4 g.), which was dissolved in

methanol containing sodium methoxide (from 1 g. of sodium). Overnight, sodium toluene-*p*-sulphonate separated. It was filtered off, and the filtrate was diluted with water, neutralised with sulphuric acid (phenolphthalein), and extracted continuously with chloroform. Concentration of the chloroform extract yielded syrupy 2 : 3-anhydro-β-methyl-D-riboside (2·2 g.). This material was methylated by two treatments with silver oxide and methyl iodide with the formation of crystalline 4-*methyl* 2 : 3-*anhydro*-β-*methyl*-D-*riboside* (2·2 g.) which on recrystallisation from light petroleum (b. p. 40—60°) gave long needles, m. p. 75—77°, $[\alpha]_D^{19}$ −7° (*c*, 1·49 in water) (Found : C, 52·8; H, 7·3; OMe, 38·8. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5; OMe, 38·8%). The product sublimes at 90—100°.

3 : 4-*Dimethyl* β-*Methyl*-D-*xyloside*.—The latter anhydro-compound (0·7 g.) was heated in methanol (25 c.c.) containing sodium (1·5 g.) for 24 hours. The solution was evaporated to a small volume, diluted with water, and extracted continuously with chloroform. Evaporation of the extract gave crystals (0·7 g.) of 3 : 4-*dimethyl* β-*methyl*-D-*xyloside*, which on recrystallisation from ether–light petroleum (b. p. 40—60°) had m. p. 89—90°, not depressed on admixture with a sample provided by Dr. E. E. Percival, $[\alpha]_D^{19}$ −71° (*c*, 1·53 in water) (Found : C, 49·8; H, 8·0; OMe, 48·3. $C_8H_{16}O_5$ requires C, 50·0; H, 8·3; OMe, 48·4%).

Methylation of a portion (0·15 g.) of this substance with Purdie's reagents gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside (0·14 g.), m. p. and mixed, m. p. 47—48°, $[\alpha]_D^{19}$ −68·5° (*c*, 1·36 in chloroform), after recrystallisation from light petroleum (b. p. 40—60°). Acid hydrolysis in the usual manner gave 2 : 3 : 4-trimethyl D-xylose, which was isolated on a tile and recrystallised from ether–light petroleum (b. p. 40—60°), then having m. p. and mixed m. p. 89—90°, $[\alpha]_D^{21}$ +46° ⟶ −24° (constant; *c*, 0·67 in chloroform) (Found : OMe, 46·9. Calc. for $C_8H_{16}O_5$: OMe, 48·4%).

3 : 4-*Dimethyl* D-*Xylose*.—3 : 4-Dimethyl β-methyl-D-xyloside was hydrolysed with hydrochloric acid (0·5N) on the boiling-water bath for 12 hours ($[\alpha]_D$ +12° at equilibrium). The solution was neutralised with silver carbonate, then filtered, and the solution concentrated to syrupy 3 : 4-dimethyl D-xylose (0·53 g.), $[\alpha]_D$ +13° (*c*, 1·6 in methanol) (Found : OMe, 34·7. Calc. for $C_7H_{14}O_5$: OMe, 34·8%), which moved at the same rate on paper chromatograms, in a variety of solvents, as did authentic 3 : 4-dimethyl D-xylose (for details see Jones and Wise, *loc. cit.*). A portion of the syrup (96 mg.) was heated under reflux with alcoholic aniline for 1 hour, and on removal of the solvent a crystalline xylosylamine derivative was formed. This material was unstable, rapidly darkening in the air, and was difficult to purify by recrystallisation. It was purified by partition chromatography on Whatman No. 1 paper, with *n*-butanol–ethanol–water (40 : 11 : 19) as mobile phase. The xylosylamine derivative, which was detected by using the *p*-anisidine hydrochloride spray reagent (Hough, Jones, and Wadman, *J.*, 1950, 1702), moved at a slower rate than the coloured impurities and aniline, and faster than 3 : 4-dimethyl D-xylose. Extraction of the appropriate section of the paper chromatogram yielded *N*-phenyl-D-xylosylamine 3 : 4-dimethyl ether, m. p. 126° and mixed m. p. 124° with a specimen previously prepared (Jones and Wise, *loc. cit.*).

3 : 4-*Dimethyl* D-*Xylonolactone*.—3 : 4-Dimethyl D-xylose (0·33 g.) was oxidised with bromine water at about 30° for 48 hours, and the product isolated in the usual way, to give 3 : 4-dimethyl D-xylonolactone (0·21 g.) which crystallised spontaneously. After recrystallisation from ether, it had $[\alpha]_D^{16}$ −50° (10 mins.; *c*, 1·1 in water) ⟶ −22° (48 hours, constant), m. p. 68°, undepressed on admixture with samples prepared by Jones and Wise (*loc. cit.*) and Dr. E. E. Percival (personal communication) (Found : C, 47·7; H, 6·8; OMe, 35·5. Calc. for $C_7H_{10}O_5$: C, 47·7; H, 6·8; OMe, 35·2%). The derived *phenylhydrazide* had m. p. 132° (Found : C, 54·9; H, 7·0; N, 10·2; OMe, 22·7. $C_{13}H_{20}O_5N_2$ requires C, 54·9; H, 7·0; N, 9·9; OMe, 21·8%).

4-*Methyl* β-*Methyl*-D-*xyloside*.—4-Methyl 2 : 3-anhydro-β-methyl-D-riboside (0·25 g.) was heated with sodium hydroxide (5%; 25 c.c.) on the boiling-water bath for 48 hours. Initially, a bright yellow colour formed, and slowly disappeared. The cooled solution was neutralised with sulphuric acid and extracted exhaustively with chloroform. Concentration of the extract gave crystals of 4-*methyl* β-*methyl*-D-*xyloside* (0·16 g.), m. p. 95° after recrystallisation from ether ($[\alpha]_D^{22}$ −69°; *c*, 0·44 in water) (Found : OMe, 34·7. $C_7H_{14}O_5$ requires OMe, 34·8%). Methylation of a portion (55 mg.) with Purdie's reagents gave 2 : 3 : 4-trimethyl β-methyl-D-xyloside, m. p. and mixed m. p. 46—47°, $[\alpha]_D^{20}$ −66° (*c*, 0·78 in methanol). A further portion (20·8 mg.) in water (5 c.c.) was left with 0·2M-sodium metaperiodate (1 c.c.) in the dark for 24 hours; then the solution (pH 5·0) was treated with saturated solution of sodium hydrogen carbonate and 0·1N-sodium arsenite (5 c.c.). After 0·5 hour, the solution was titrated with 0·01N-iodine (25·5 c.c.) (Found : 1 mole of metaperiodate is consumed by 163 g. of the methylxyloside. $C_7H_{14}O_5$ requires the consumption of 1 mole per 178 g. of the xyloside).

4-*Methyl* D-*Xylose*.—The methylglycoside (44 mg.) was hydrolysed with N-sulphuric acid (20 c.c.) for 6 hours. Then the solution was cooled and neutralised with barium carbonate in the usual way. Evaporation gave syrupy 4-*methyl* D-*xylose* {39 mg.; $[\alpha]_D$ $+9° \pm 2°$ (*c*, 0·66 in water)}. On paper chromatograms, using Whatman No. 1 paper, its rate of movement relative to that of rhamnose was 1·22, 1·11, and 1·28 with (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), (*b*) *n*-butanol–pyridine–water (10 : 3 : 3), and (*c*) *n*-butanol–ethanol–water (40 : 11 : 19) as mobile phase. Solvents (*b*) and (*c*) separate 4-methyl from 2-methyl xylose (rates of movement, 1·43 and 1·24 respectively) and with *p*-anisidine hydrochloride as spray reagent show different colours, a reddish-brown and a mauve respectively.

4-*Methyl* D-*xylosazone* was prepared by heating the sugar (35 mg.) in water (5 c.c.) with phenylhydrazine (0·2 c.c.) and glacial acetic acid (0·2 c.c.) at *ca.* 70° for 3 hours. The reaction mixture was cooled to 2°, and the crystalline osazone filtered off and recrystallised from methanol–water. After drying, it had m. p. 160—161° (Found : OMe, 9·0. $C_{18}H_{22}O_3N_4$ requires OMe, 9·1%).

THE UNIVERSITY, BRISTOL.

[*Received, July 18th*, 1952.]