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SYNTHESIS OF 1,2-O-ISOPROPYLIDENE-α-D-APIO-D-FURANOSE AND D-APIOSE

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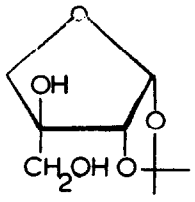
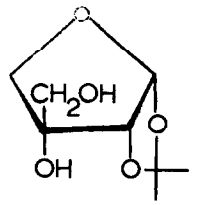
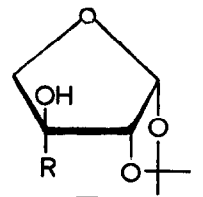
Two 1,2-O-isopropylidene derivatives of D-apiose are possible, namely 1,2-O-isopropylidene-α-D-apio-L-furanose (I) and its C-3 epimer (II) (1,2-O-isopropylidene-α-D-apio-D-furanose) (1). Recently, Carey et al. (2) characterised compound (I) which was obtained by selective acid hydrolysis of 1,2:3:5-di-O-isopropylidene-α-D-apio-L-furanose. Now we describe a new synthesis of compound (II) which was required as an intermediate in the synthesis of the disaccharide component of apiin (3). Jones et al. (4) have defined the stereochemistry at C-3 in the apiose part of apiin and have demonstrated that the sugar has the D-apio-D-furanose configuration. However, the configuration of the disaccharide linkage in apiin has not been established unequivocally,



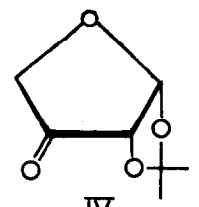
I



II



III(R= H)
V(R=OH)



IV

1,2-O-Isopropylidene-β-L-threofuranose (III) (5) was oxidised with ruthenium tetroxide in carbon tetrachloride to afford crystalline material (40%), m.p. 52-60°, $[\alpha]_D$ + 151° (c 1.9, chloroform), $\nu_{max.}$ 3400 (OH) and 1780 (C=O) $cm.^{-1}$, which was a mixture of 1,2-O-isopropylidene-α-D-glycero-tetros-3-ulose (IV) (6)

and its gem-diol (V). After being shaken in chloroform solution with molecular sieve (4A) the material showed loss of absorption at 3400 cm.$^{-1}$ and increase in the $>C=O$ absorption at 1780 cm.$^{-1}$. Consequently its n.m.r. spectrum* was measured on a solution in CCl_4 which had been treated with molecular sieve. The signals assigned were as follows: τ 4.0 (1H, doublet), $J_{1,2}$ 4.3Hz (H-1); 5.80 (1H, doublet) (H-2); an AB system centred at τ 5.87, $J_{4y,4x}$ 17.0Hz (H-4y, H-4x); two singlets of 3 protons each at τ 8.53 and 8.63 (methyl groups of isopropylidene residue).

Crystallisation of the oxidation product from wet ether gave pure diol (V),† m.p. 65-80° (with loss of water), $[\alpha]_D$ + 79.5° (c 1, chloroform), $\nu_{max.}$ 3400 cm.$^{-1}$, n.m.r. spectrum (measured in $(CD_3)_2SO$) showed signals at τ 3.90 (2H, singlet, lost on addition of D_2O and assigned to OH groups); 4.27 (1H, doublet), $J_{1,2}$ 3.8Hz (H-1); 5.93 (1H, doublet) (H-2); an AB system centred at τ 6.39, $J_{4y,4x}$ 8.5Hz (H-4y, H-4x); two singlets of 3 protons each at τ 8.57 and 8.75 (isopropylidene methyl groups).

Treatment of the mixture (1V/V) with diazomethane in methanol-ether (1:1) afforded quantitatively an epimeric mixture of epoxides in which the major component was 1,2-O-isopropylidene-3,1'-anhydro-α-D-apio-D-furanose (V1), whereas epoxidation with dimethylsulphoxonium methylide (7,8) gave a 1:1 mixture of the epimerides, but in poor yield.

When the diol (V) was likewise treated with diazomethane it also afforded the mixture of exocyclic epoxides. Chromatographic separation on silica gel of the epoxide mixture yielded the major component (V1) as colourless needles, m.p. 68-69°, $[\alpha]_D$ + 91.3° (c 0.8, diethyl ether). The structure of this compound follows from consideration of its reduction with lithium aluminium hydride and of

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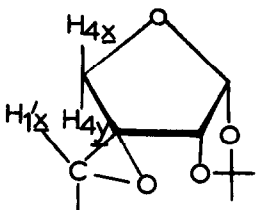
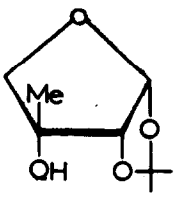
* N.m.r. spectra were recorded on a Varian A-60 spectrometer and peak positions are given in τ units relative to internal tetramethylsilane (for solutions in organic solvents) or to sodium 4,4-dimethyl-4-silapentane sulphonate (for solutions in D_2O).

† Satisfactory elemental analyses were obtained for all compounds described.

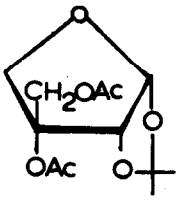
its n.m.r. spectrum. In $CDCl_3$ compound (V1) showed n.m.r. signals at τ 4.05 (1H, doublet), $J_{1,2}$ 4.0 Hz (H-1); 5.66 (1H, doublet) (H-2); 5.69 (1H, doublet), $J_{4x,4y}$, 9.5 Hz (H-4y); 6.29 (1H, doublet) (H-4x); 6.89 (1H, quartet being split by long range coupling), $J_{1'y,4y}$ 1.2 Hz (H-1'y); 7.02 (1H, doublet), $J_{1'x,1'y}$ 5.5 Hz (H-1'x); two singlets of 3 protons each at τ 8.30 and 8.60 (isopropylidene methyl groups).



VI



VII



VIII

Treatment of compound (V1) in tetrahydrofuran with lithium aluminium hydride gave a 1,2-O-isopropylidene-3-C-methyl-α-D-tetrose, m.p. 108-109°, $[\alpha]_D$ + 28° (c 0.8, chloroform), which in solution in CCl_4 showed intramolecular hydrogen bonding ($\nu_{max.}$ 3570 $cm.^{-1}$) thereby indicating that the 3-C-methyltetrose had the D-erythro configuration as shown in formula (V11) (9). Its n.m.r. spectrum (measured in $CDCl_3$) was consistent with this structure [signals at τ 4.21 (1H, doublet), $J_{1,2}$ 3.8Hz (H-1); 5.94 (1H, doublet) (H-2); an AB system centred at τ 6.36, $J_{4y,4x}$ 8.5Hz (H-4y, H-4x); τ 7.36(1H, singlet lost on addition of D_2O) (OH); three singlets of 3 protons each at τ 8.46, 8.66, and 8.70 (three methyl groups)].

When compound (V1) in aqueous methanolic sodium hydroxide was stored for 2 days at room temperature it formed 1,2-O-isopropylidene-α-D-apio-D-furanose (II), m.p. 118-120°, $[\alpha]_D$ + 54.5° (c 1.3, ethanol) [very recently Tronchet and Tronchet (10) reported m.p. 112°-115°, $[\alpha]_D$ - 39.5° (ethanol), for the L-isomer of compound (II) which was prepared essentially by an alternative route involving methods developed in our Laboratory]. Its n.m.r. spectrum (measured on a solution in D_2O)

showed signals at τ 4.06 (1H, doublet), $J_{1,2}$ 4.0Hz (H-1); 5.54 (1H, doublet) (H-2); 6.16 (2H, doublet) ($\rangle CH_2$); 6.39 (2H, singlet) ($\rangle CH_2$); two singlets of 3 protons each at τ 8.39 and 8.60 (methyl groups of isopropylidene residue).

Compounds (I) and (II) were found to be different by mixed m.p. and optical rotation determinations. Acetylation of compound (II) (Ac_2O - C_5H_5N) gave the diacetate (VIII), m.p. 110-111.5°, $[\alpha]_D$ + 64° (c 1.4, chloroform) which differed from the known epimeric diacetate (2) of compound (I).

Acid hydrolysis of compound (II) yield D-apiose identical with an authentic sample.

The synthesis of the disaccharide component of apiin will form the subject of a separate communication.

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