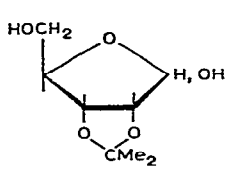
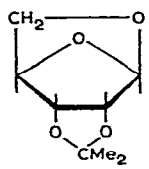
Notes

New isopropylidene derivatives of D-ribose: 1,2:3,4-di-*O*-isopropylidene-D-ribopyranose and 1,2-*O*-isopropylidene-D-ribopyranose

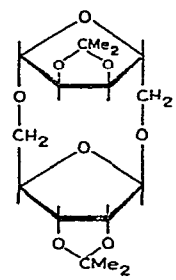
Levene and Stiller first examined the reaction of D-ribose with acetone and observed the formation of 2,3-*O*-isopropylidene-D-ribofuranose (I) together with two anhydro-compounds[1]. The structures of these two latter compounds have been shown to be 1,5-anhydro-2,3-*O*-isopropylidene-D-ribofuranose (II) and di-(2,3-*O*-isopropylidene-*β*-D-ribofuranose) 1,5′:1′,5-dianhydride (III)[2]. Barker and Spoors[3] also observed the formation of the monomeric anhydride (II) and showed that the major product, 2,3-*O*-isopropylidene-D-ribofuranose (I), condensed with benzaldehyde to give a 1,5-*O*-benzylidene-2,3-*O*-isopropylidene-D-ribofuranose (IV). Toluene-*p*-sulphonylation of the crude isopropylidene compound (I) gave a small yield of di-ester which was shown by Mills[4] to be 1,2-*O*-isopropylidene-3,5-di-*O*-toluene-*p*-sulphonyl-D-ribofuranose (V) and to have arisen from a small amount of 1,2-*O*-isopropylidene-D-ribofuranose (VI) present in the crude compound (I). More recently, the 1,2-ketal (VI) has been synthesised from 5-*O*-benzoyl-1,2-*O*-isopropylidene-D-xylofuranose by selective oxidation of the 3-hydroxyl group, followed by reduction and debenzoylation[5].



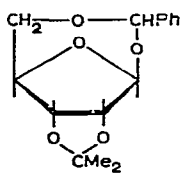
(I)



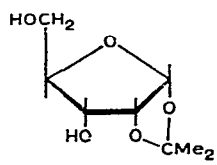
(II)



(III)



(IV)

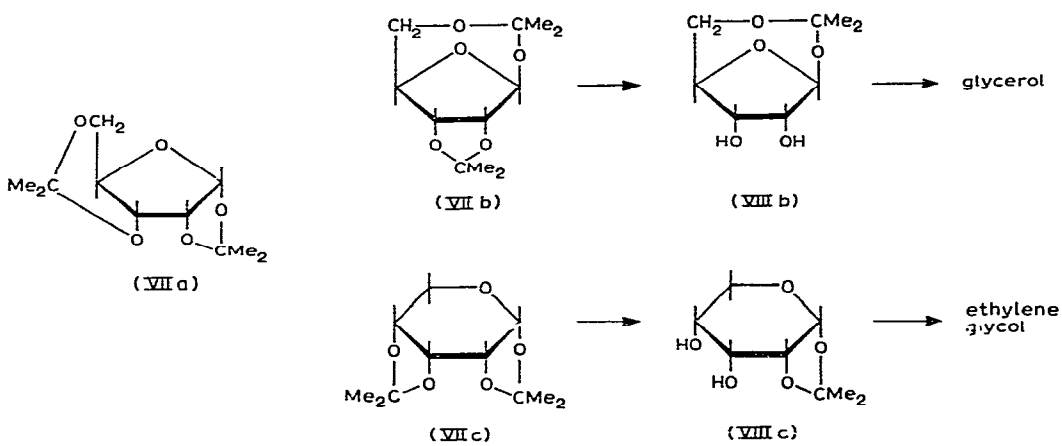


(VI)

In the present work D-ribose was condensed with acetone in the presence of sulphuric acid as catalyst. The crude product was purified by silica chromatography,

when three distinct fractions were obtained. The first fraction was shown by thin-layer chromatography to contain three compounds which could not be separated by further column chromatography but were resolved by repeated micro-sublimation. Two of the compounds were identified as the monomeric and dimeric anhydro-compounds (II) and (III). Only traces of the latter compound were formed. However, when the 2,3-ketal (I) was stored in acetone in the presence of sulphuric acid for longer periods of time the anhydro-compounds (II) and (III) were both formed in greater yield. The second fraction contained only the 2,3-ketal (I), whilst the third fraction contained the 1,2-isomer (VI) and disaccharide compounds. The wide separation of these two isomers on the silica column is probably due to strong intramolecular hydrogen bonding between the 5- and 1-(β)-hydroxyl groups in the 2,3-ketal (I); similar bonding is not possible in the 1,2-ketal (VI).

The third compound in the first fraction gave ribose on acidic hydrolysis and analysed for a di-isopropylideneribose (VII). Three structures are possible for this compound: 1,2:3,5-di-*O*-isopropylidene-D-ribofuranose (VIIa); 1,5:2,3-di-*O*-isopropylidene-D-ribofuranose (VIIb); and 1,2:3,4-di-*O*-isopropylidene-D-ribopyranose (VIIc). The first is unlikely since it contains a five-membered ring *trans*-fused to a six-membered ring. The second is similar to the benzylidene-isopropylidene compound (IV), and the third is remarkable in having a pyranose ring structure. Partial acidic hydrolysis gave a mono-isopropylidene compound (VIII) which was non-reducing, consumed one mol. of periodate, and was not identical with the 1,2-*O*-isopropylidene-D-ribofuranose (VI), thus eliminating structure (VIIa). Borohydride reduction of the periodate-oxidation product followed by acidic hydrolysis gave ethylene glycol and no glycerol. This is in accord with structures (VIIc) and (VIIIc).



(VII a) (VII b) (VIII b) (VII c) (VIII c)

1,2:3,4-Di-*O*-isopropylidene-D-ribopyranose (VIIc) possesses a *cis*, *syn*, *cis*, arrangement of rings. Mills pointed out that in such a structure there would be steric repulsion between the ketal groups[4] and this may account for the preferential hydrolysis of the 3,4-isopropylidene group. In 1,2:3,4-di-*O*-isopropylidene-L-arabino-

pyranose and in 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, which have a *cis, anti, cis* arrangement of rings, no such preference is observed[6].

In the above acetonation of D-ribose, and in the previous cases mentioned, a strong-acid catalyst was present. With other sugars, variations in the reaction products have been obtained when such non-acidic catalysts as copper sulphate[7] and zinc chloride[8] have been used. When these catalysts were employed with D-ribose, the only marked difference was the absence of the anhydro-compounds (II) and (III) in the products; the yield of the diketal (VIIc) was also reduced.

EXPERIMENTAL

Silica gel, Hopkin and Williams, M.F.C., and Merck, G. grade, respectively, were used for column and thin-layer chromatography. The solvent system, butanol–water (86:14, v/v), was used for paper chromatography.

Condensation of D-*ribose and acetone in the presence of concentrated sulphuric acid*

D-Ribose (12 g) was added with stirring to acetone (240 ml) containing concentrated sulphuric acid (3 ml). Within 5 min the ribose had dissolved, and after 1 h the solution was neutralised with excess of solid sodium carbonate. The solution was filtered and concentrated to a syrup (13 g), which was dissolved in benzene (50 ml) and chromatographed on silica (250 g). Three fractions were obtained:

Fraction A [2.2 g, eluted by benzene–ether (9:1)] was shown by t.l.c. to consist of two major components and traces of a third. The two major components were separated by repeated micro-sublimation. The more volatile 1,5-anhydro-2,3-*O*-isopropylidene-D-ribofuranose (II) (1.3 g, 9 %) sublimed at 25–35°/0.1 mm and had m.p. 61°, $[\alpha]_D^{20}$ −62° (*c* 0.78, methanol) (lit.,[2] m.p. 61°, $[\alpha]_D$ −63°). The second component, 1,2:3,4-di-*O*-isopropylidene-D-ribopyranose (VIIc) (0.6 g, 3 %), sublimed at 35–40°/0.1 mm and had m.p. 68–69°, $[\alpha]_D^{20}$ −51° (*c* 0.6, chloroform) (Found: C, 57.8; H, 7.8. $C_{11}H_{18}O_5$ calc.: C, 57.4; H, 7.8 %). The trace component was not isolated but had the same mobility as di-(2,3-*O*-isopropylidene-*β*-D-ribofuranose) 1,5′:1′,5-dianhydride (III) on thin-layer chromatograms.

Fraction B [9.0 g (59 %), eluted by benzene–ether (1:1)] was shown by t.l.c. to be a single compound, 2,3-*O*-isopropylidene-D-ribose. A sample (0.35 g) was reduced with sodium borohydride and the crude 2,3-*O*-isopropylidene-D-ribitol was benzoylated to give 1,4,5-tri-*O*-benzoyl-2,3-*O*-isopropylidene-D-ribitol (0.55 g), m.p. 94–95° (undepressed on admixture with an authentic sample). Another sample (0.25 g) was oxidised with bromine in aqueous potassium hydrogen carbonate to give 2,3-*O*-isopropylidene-D-ribono-1,4-lactone (0.25 g), m.p. 140–142° (undepressed on admixture with an authentic sample).

Fraction C [1.8 g, eluted by ether–methanol (9:1)] was shown by t.l.c. to consist of several components. Micro-distillation of a sample (105 mg) gave 1,2-*O*-isopropyl-

idene-D-ribofuranose (VI) (50 mg, 6% from D-ribose), b.p. 90°/0.1 mm, which crystallised from benzene–light petroleum as needles, m.p. 86–87° (undepressed on admixture with an authentic sample), $[\alpha]_D^{25}+37°$ (*c* 0.59, chloroform).

1,2-O-Isopropylidene-D-ribopyranose (VIIIc)

(*a*) 1,2:3,4-Di-*O*-isopropylidene-D-ribopyranose (130 mg) was dissolved in methanol (1 ml), 0.15 N-sulphuric acid (1 ml) was added, and the solution was kept at 40° for 3 h. Paper chromatography indicated the presence of ribose (R_F 0.15) and a compound (R_F 0.60) giving a blue-green colour with the periodate–Schiff's reagent[9]. The solution was passed through Dowex-1 (OH^- form) (2 ml) and evaporated to dryness. The residue (20 mg) was purified by micro-sublimation at 70°/0.1 mm to give 1,2-*O*-isopropylidene-D-ribopyranose (VIIIc) (5 mg), m.p. 109–111° (Found: C, 50.6; H, 7.5. $C_8H_{14}O_5$ calc.: C, 50.5; H, 7.4%).

(*b*) A mixture (2.1 g) of 1,2:3,4-di-*O*-isopropylidene-D-ribopyranose and anhydro-compounds (Fraction A above) was dissolved in glacial acetic acid (16 ml) and water (4 ml) was added. After 14 h at room temperature, the solvents were evaporated and the residue (1.84 g) was chromatographed on silica (30 g). Elution with benzene–ether (1:4) gave unchanged anhydro-compounds (II) and (III) (1.41 g) and ether–methanol (9:1) eluted 1,2-*O*-isopropylidene-D-ribopyranose (VIIIc) (0.4 g) which after further purification by sublimation had m.p. 112–114°, $[\alpha]_D^{20}-26°$ (*c* 1.05, water). Periodate uptake: 0.98 mole/mole.

Periodate oxidation and borohydride reduction

1,2-*O*-Isopropylidene-D-ribopyranose (10 mg) was added to water (1 ml) containing sodium periodate (14 mg). The solution was kept for 24 h in the dark at room temperature and then treated with excess of sodium borohydride (20 mg). After a further 40 h the solution was acidified with acetic acid, passed through Dowex-50 (H^+ form), and concentrated to dryness. Borate was removed by repeated distillation of methanol from the residue which was then hydrolysed by 0.1 N-sulphuric acid (1 ml) at 70° for 1 h. Examination of the solution by paper chromatography revealed the presence of ethylene glycol, but not glycerol.

Prolonged treatment of 2,3-O-isopropylidene-D-ribose with acetone and concentrated sulphuric acid

2,3-*O*-Isopropylidene-D-ribose (0.6 g) was dissolved in acetone (10 ml) containing concentrated sulphuric acid (0.1 ml). After 24 h at room temperature, purification as before gave a syrupy residue (0.55 g). Chromatography on silica (20 g) and elution with benzene–ether (9:1) gave a syrup (0.1 g). Further purification of this by micro-sublimation gave, at 30°/0.1 mm, 1,5-anhydro-2,3-*O*-isopropylidene-D-ribofuranose (II) (40 mg), m.p. 61°; and, at 90°/0.1 mm, di-(2,3-*O*-isopropylidene-β-D-ribofuranose) 1,5′:1′,5-dianhydride (III) (30 mg), m.p. 90–93°, $[\alpha]_D^{20}-57°$ (*c* 0.55, chloroform) (lit.,[2] m.p. 86–87° and 97–98°, $[\alpha]_D$ −49°). Between these two fractions, a small amount

of material (25 mg) distilled which appeared to consist mainly of the monomer (II), contaminated with a little of the diketal (VIIc).

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