523. *Ribose and its Derivatives. Part VII.* The Condensation of Methyl* D-*Ribopyranoside with Acetone.*

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By conversion into 3 : 4-di-*O*-methyl-D-ribose, it is shown that the compound originally believed by Levene and Stiller to be methyl 2 : 3-*O*-*iso*propylidene-4-*O*-toluene-*p*-sulphonyl-D-ribopyranoside is methyl 3 : 4-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside.

Levene and Stiller [1] showed that during the condensation of acetone with methyl D-ribopyranoside, approximately fifty per cent. of the material isomerises to a furanoside. They believed the two products to be methyl 2 : 3-*O*-*iso*propylidene-D-ribofuranoside and methyl 2 : 3-*O*-*iso*propylidene-D-ribopyranoside. However, we have previously shown [2] that methylation of the mixed products yields, after hydrolysis, 2-, 4-, and 5-*O*-methyl-D-ribose, suggesting the presence of methyl 3 : 4-*O*-*iso*propylidene-D-ribose amongst the products of the condensation. No estimate was made of the proportions of these sugars. Levene and Stiller treated the mixed condensation products with toluene-*p*-sulphonyl chloride and obtained, besides methyl 2 : 3-*O*-*iso*propylidene-5-*O*-toluene-*p*-sulphonyl-D-ribofuranoside, a crystalline compound which they designated, without proof, as methyl 2 : 3-*O*-*iso*propylidene-4-*O*-toluene-*p*-sulphonyl-D-ribopyranoside. In view of our experiments referred to above, and since the toluene-*p*-sulphonyl derivative is a potentially useful intermediate in the synthesis of partially substituted derivatives of ribose, we have investigated its structure. Material having the same properties as those recorded by Levene and Stiller was obtained by chromatography of the mixed toluene-*p*-sulphonates on alumina. The *iso*propylidene residue was removed and the residual material was methylated and, after reductive fission of the sulphonate and hydrolysis of the glycoside, a syrupy dimethylribose was obtained. This was shown to be 3 : 4-di-*O*-methyl-D-ribose in the following way. Methyl toluene-*p*-sulphonyl-D-riboside, from which the dimethyl-sugar was obtained, was oxidised by one mol. of sodium metaperiodate, thus limiting the free hydroxyl groups available for methylation to the 2 : 3- and 3 : 4-positions. The sugar was distinguished from 2 : 3-di-*O*-methyl-D-ribose by its R_F value (0·53) in *n*-butanol–boric acid and by the fact that it was oxidised by one mol. of periodate with the liberation of titratable acid but of no formaldehyde. The sugar was finally shown to be 3 : 4-di-*O*-methyl-D-ribose by conversion into an osazone the m. p. of which was not depressed by admixture with that derived from authentic 2 : 3 : 4-tri-*O*-methyl-D-ribose with loss of one methoxyl residue. It is interesting to note that on oxidation with periodate, no formic acid was liberated from the 3 : 4-di-*O*-methyl-D-ribose without previous treatment with alkali, suggesting the initial formation of a formyl ester.[3]

The above reactions exclude all other possible structures for the dimethylribose, and

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* Part VI, *J.*, 1956, 1192.

[1] Levene and Stiller, *J. Biol. Chem.*, 1934, **106**, 421.

[2] Barker, Noone, Smith, and Spoors, *J.*, 1955, 1327.

[3] Barker and Smith, *Chem. and Ind.*, 1954, 19.

it is concluded that the crystalline material which Levene and Stiller claimed to be methyl 2 : 3-*O*-*iso*propylidene-4-*O*-toluene-*p*-sulphonyl-D-ribopyranoside was in fact methyl 3 : 4-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside. In view of our previous results,[2] it appears that some material having the former structure may be present in the crude mixture, but none could be isolated.

It seems reasonable to assume that the isomerisation of the pyranoside to the furanoside occurs after condensation with the acetone, since methyl D-ribopyranoside is normally formed from the furanoside under acidic conditions.[4] Also, since, of the 2 : 3- and 3 : 4-hydroxyl groups of methyl D-ribopyranoside, one of each pair is equatorial and one axial, it is to be expected that condensation with acetone will yield both the 2 : 3- and the 3 : 4-*O*-*iso*propylidene derivative in appreciable amounts. It appears probable, therefore, that the presence of the 2 : 3-*O*-*iso*propylidene residue causes the equilibrium between furanose and pyranose to be displaced in favour of the former in the acidic conditions. No such isomerisation is possible with a 3 : 4-*iso*propylidene residue and it is believed that these considerations explain the formation of the products obtained.

EXPERIMENTAL

Methyl 3 : 4-O-iso*Propylidene*-2-O-*toluene*-p-*sulphonyl*-D-*ribopyranoside and Methyl* 2 : 3-O-iso*Propylidene*-5-O-*toluene*-p-*sulphonyl*-D-*ribofuranoside.*—A mixture of the two compounds, prepared from methyl D-ribopyranoside (7·3 g.) as previously described,[1] was dissolved in benzene (100 c.c.) and percolated through alumina (Peter Spence, grade H) (23 × 4·5 cm). Elution with benzene gave, after removal of solvent from successive fractions, methyl 2 : 3-*O*-*iso*propylidene-5-*O*-toluene-*p*-sulphonyl-D-ribofuranoside (2·5 g.), m. p. 84—85·5°, $[\alpha]_D^{20}$ $-34{\cdot}7°$ (*c*, 0·85 in EtOH) (Found : C, 53·4; H, 6·5. Calc. for $C_{16}H_{22}O_7S$: C, 53·6; H, 6·2%), and *methyl* 3 : 4-O-iso*propylidene*-2-O-*toluene*-p-*sulphonyl*-D-*ribopyranoside* (2·2 g.), m. p. 144°, $[\alpha]_D^{20}$ $-113°$ (*c*, 1·0 in EtOH) (Found : C, 53·8; H, 6·1%).

Methyl 3 : 4-*Di*-O-*methyl*-2-O-*toluene*-p-*sulphonyl*-D-*ribopyranoside.*—Methyl 3 : 4-*O*-*iso*propylidene-2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside was converted into methyl 2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside by Levene and Stiller's method.[1] The material (18·7 mg.) in aqueous ethanol (10 c.c.) was set aside at room temperature with sodium metaperiodate (45 mg.). Excess of periodate was determined in aliquot portions at intervals. Reaction was complete after 1 hr. and 0·97 mol. of periodate had then been consumed.

The methyl 2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside (0·45 g.) was refluxed and stirred with methyl iodide (35 c.c.) and silver oxide (0·5 g.) for 6 hr., further quantities (0·5 g.) of silver oxide being added every 30 min. Refluxing and stirring were continued for a further 2 hr., silver salts were removed by filtration and washed with ether, and the combined filtrates were evaporated under reduced pressure to a syrup. The residue (0·51 g.) was dissolved in benzene and percolated through neutral alumina (Peter Spence) (10 × 2·3 cm.). Elution with benzene–ether (3 : 2) yielded, after removal of solvent, syrupy methyl 3 : 4-*di*-O-*methyl*-2-O-*toluene*-p-*sulphonyl*-D-*ribopyranoside* n_D^{24} 1·5080, $[\alpha]_D^{20}$ $-37{\cdot}5°$ (*c*, 0·93 in MeOH) (Found: C, 52·3; H, 6·6; OMe, 26·9. $C_{15}H_{22}O_7S$ requires C, 52·0; H, 6·4; OMe, 27·2%).

3 : 4-*Di*-O-*methyl*-D-*ribose.*—Methyl 3 : 4-di-*O*-methyl-2-*O*-toluene-*p*-sulphonyl-D-ribopyranoside (0·4 g.) in aqueous ethanol (30 c.c.; 80%) was stirred at room temperature with sodium amalgam (20 g.; 3%) for 20 hr. The solution was saturated with carbon dioxide, diluted with water (200 c.c.), and repeatedly extracted with ether. The combined extracts were dried ($MgSO_4$) and evaporated to a thick syrup (0·2 g.). This material (0·15 g.) was refluxed for 5 hr. with ethanol (5 c.c.) and N-hydrochloric acid (5 c.c.). Chloride ions were removed by grinding the product with silver carbonate and filtration (charcoal), and the solvent was then evaporated to yield syrupy 3 : 4-*di*-O-*methyl*-D-*ribose*, $[\alpha]_D^{20}$ $-27{\cdot}0°$ (*c*, 0·44 in MeOH) (Found : OMe, 34·5. $C_7H_{14}O_5$ requires OMe, 34·8%), which was converted into 3 : 4-di-*O*-methyl-D-ribose phenylosazone, having m. p. 138—139° which was not depressed on admixture with a sample prepared from 2 : 3 : 4-tri-*O*-methyl-D-ribose (Found : C, 63·0; H, 7·0; N, 15·7; OMe, 16·7. Calc. for $C_{19}H_{24}O_3N_4$: C, 64·0; H, 7·0; N, 15·7; OMe, 17·4%).

3 : 4-Di-*O*-methyl-D-ribose (10·25 mg.) in aqueous ethanol (10 c.c.; 50%) was set aside at room temperature with sodium metaperiodate (50 mg.). Excess of periodate was determined as before and aliquot portions (1 c.c.) were also withdrawn. After they had been made alkaline with 0·01N-sodium hydroxide (2 c.c.), ethylene glycol (0·1 c.c.) was added and the mixture was

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[4] Levene, Raymond, and Dillon, *J. Biol. Chem.*, 1932, **95**, 699.

warmed at 60° for 10 min. in an atmosphere of nitrogen, cooled, and titrated with 0·01N-hydrochloric acid. Reaction was complete after 1 hr., 1·05 mol. of periodate having been consumed and 0·87 mol. of acid liberated. No formaldehyde was detected by Reeves's method[5] after completion of the oxidation.

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[5] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476.