

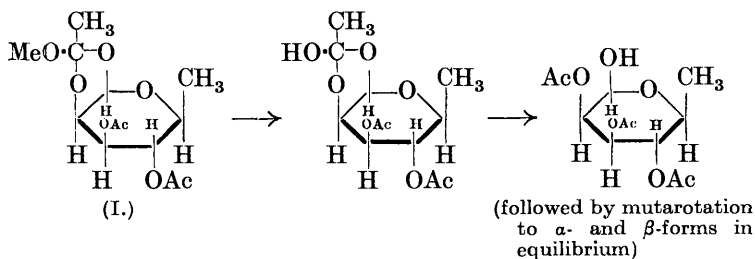
CCCC.—*The Third Variety of Triacetyl Methyl-rhamnoside.*

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A NEW modification of the procedure given by Fischer, Bergmann, and Rabe (*Ber.*, 1920, **53**, 2362) for the preparation of the so-called " γ "-methylrhamnoside triacetate is herein described. This has enabled its preparation to be carried out with ease, and has afforded opportunity for a more detailed study of this interesting substance which, as was shown in an earlier paper (Haworth, Hirst, and Miller, *J.*, 1929, 2469), must not be confused with the γ -sugar series inasmuch as it has been shown to be a rhamnopyranoside. In a later paper (Bott, Haworth, and Hirst, *J.*, 1930, 1395) the constitution of this product was given as (I). Further evidence of this structure is now provided in that it is shown that, whilst the acetyl groups at positions 3 and 4 are eliminated with cold alkali, the substituting residues at positions 1 and 2, though stable to hot alkali, are extremely labile in the presence of very dilute acid. From a mathematical analysis of the polarimetric data (for which we are indebted to Mr. E. Gordon Cox) it appeared that two consecutive reactions were initiated by the action of $N/100$ - or $N/1500$ -acid at 20° on the so-called " γ "-monoacetyl methylrhamnoside. The first of these changes is occasioned by hydrolysis of the methoxyl residue of the orthoacetic ester group and was catalysed by hydrogen ion. The value of the velocity coefficient was approximately $k_1 = 5.5$ (in terms of mins. and natural logarithms and for $N/100$ -acid). The specific rotation of the product given by this reaction was $[\alpha]_D^{20} + 47^\circ$. For the second reaction, which was influenced by the hydrogen-ion concentration to a much smaller extent, the velocity coefficient was approximately $k_2 = 0.11$ (in terms of mins. and natural logarithms). From the figures given by Moelwyn-Hughes for the ordinary glucosides (*Trans. Faraday Soc.*, 1929, **25**, 81), the first reaction proceeds some 10^{11} times as quickly as the hydrolysis of α -methylglucoside under comparable conditions.

Once the above consecutive reactions are initiated they proceed simultaneously and we were able to associate the first reaction with the removal of a methyl residue. (At this stage the product reduces Fehling's solution.) At the end of the second reaction an acetyl group is still largely intact at position 2, and the 2-acetyl residue is removable under conditions similar to those which eliminate acetyl groups from positions 3 and 4 in the original " γ "-triacetyl methyl-

rhamnoside. The consecutive changes may be represented by the following formulæ :



We have again examined the behaviour of the " γ "-monoacetyl dimethyl methylrhamnoside and have confirmed the observation in the earlier paper (Haworth, Hirst, and Miller, *loc. cit.*) that the substituent group at position 2 is eliminated during methylation in contact with sodium hydroxide. The hydrolysis of the resistant acetyl group does not proceed appreciably at 70° (after 3 hours' treatment with *N*/10-sodium hydroxide solution), but at 80° it occurs to the extent of 64%. This explains also the observation of Bott, Haworth, and Hirst (*loc. cit.*) that in the case of the analogous " γ "-tetra-acetyl methylmannoside the whole of the acetyl groups and the methyl group are removed during methylation with methyl sulphate and alkali, and that during this procedure the solution became dark. The latter effect was evidently due to the removal of the orthoacetic ester group from positions 1 and 2 with the formation of the reducing sugar, which then underwent complete methylation by the re-introduction of a methoxyl residue at position 1. Under the conditions now given, it was possible to follow these consecutive changes. There is no disturbance of the pyranose ring structure, since methyl groups already occupy positions 3, 4, and 6 of the mannose residue before the removal of the orthoacetic ester group is initiated.

E X P E R I M E N T A L.

Preparation of " γ "-Triacetyl Methylrhamnoside.—The following modification of Fischer, Bergmann, and Rabe's process (*loc. cit.*) enabled the preparation of " γ "-triacetyl methylrhamnoside to be carried out with ease and rapidity. A solution of triacetyl rhamnosidyl bromide (10 g.) in dry methyl alcohol containing quinoline (4.4 c.c.) was kept at 16° for 90 minutes until the reaction was complete. After the addition of chloroform (100 c.c.) the quinoline was removed by shaking the solution with *N*/100-sulphuric acid. The chloroform layer was shaken successively with aqueous sodium bicarbonate and with water and was dried over anhydrous magnesium

sulphate. On evaporation under diminished pressure crystalline " γ "-triacetyl methylrhamnoside was obtained. Recrystallisation from ether-light petroleum gave the pure substance, m. p. 83—84°, $[\alpha]_D^{20} + 35^\circ$ in chloroform (*c*, 2.0) (yield, 45% of the theoretical). " γ "-Monoacetyl methylrhamnoside was obtained quantitatively by the action of methyl-alcoholic ammonia on the triacetyl derivative. The substance used in the present experiments had m. p. 140—141°, $[\alpha]_D^{20} + 16.4^\circ$ in water (*c*, 2.0).

Instability of " γ "-Monoacetyl Dimethyl Methylrhamnoside in Alkaline Solution.—When " γ "-monoacetyl methylrhamnoside was methylated by methyl sulphate and alkali the acetyl group was removed and trimethyl methylrhamnopyranoside, b. p. 79°/0.02 mm., n_D^{16} 1.4440, was obtained in good yield (Found : OMe, 54.1. Calc. : OMe, 56.4%). This result was due to the instability of the acetyl group of " γ "-monoacetyl dimethyl methylrhamnoside in alkaline solution. Control experiments in which " γ "-monoacetyl dimethyl methylrhamnoside (Haworth, Hirst, and Miller, *loc. cit.*) was heated under various conditions with *N*/10-sodium hydroxide showed that at 70° there was no appreciable hydrolysis at the end of 90 minutes. At 80° during 3 hours, hydrolysis proceeded to the extent of 64% (Found : CH₃·CO, 11.1%) and at 100° it was complete in 30 minutes (Found : CH₃·CO, 17.6. Calc. for C₁₁H₂₀O₆ : CH₃·CO, 17.3%).

Instability of " γ "-Monoacetyl Methylrhamnoside and its Dimethyl Derivative in Acid Solution.—In neutral aqueous solution " γ "-monoacetyl methylrhamnoside was stable. The rotation $[\alpha]_D + 16^\circ$ remained constant for several days and there was no development of reducing power. In acid solution the substance was extraordinarily labile. Sufficient hydrochloric acid was added at room temperature to a neutral aqueous solution ($[\alpha]_D + 16^\circ$) to make the concentration of acid *N*/100. In less than 30 seconds the rotation had risen to +44°. The acid was neutralised at once, and the solution tested for reducing power by titration with Fehling's solution.

The solution containing the product from 0.10 g. of " γ "-monoacetyl methylrhamnoside was equivalent in reducing power to 0.075 g. of rhamnose. Total hydrolysis of the methylglycosidic group had been effected in less than 30 seconds. The acetyl group was still present but was now readily hydrolysable, and was removed in less than 3 hours at 15° by *N*/10-sodium hydroxide (Found : CH₃·CO, 18.9. Calc. for C₉H₁₆O₆ : CH₃·CO, 19.5%). The rotation value, +45°, was not constant but decreased regularly to a final value, +28°, reached in about 20 minutes. $[\alpha]_D^{20} + 45^\circ$ (30 secs. after addition of acid); +43° (2 mins.); 41° (3 mins.); 39.5°

(4 mins.); 38° (5 mins.); 36° (7 mins.); 34° (9 mins.); 31° (12 mins.); 29° (15 mins.); 28° (20 mins., constant value). The fall in rotation from the maximum value (+ 45°) to the constant value + 28° could not be arrested by neutralising the solution or rendering it alkaline. The end value was the same in each case and the rates of fall were almost identical.

In another experiment, when the acid concentration was reduced to *N*/1500, hydrolysis of the methylglycosidic group was still extremely rapid and the following observations were made: $[\alpha]_D^{20}$ + 17° in water (*c*, 1.0); + 23.5° (40 secs. after addition of acid); + 26° (1 min.); 30.5° (2 mins.); 33.5° (3 mins.); 35° (4 mins.); 36.5° (5 mins.); 36.5° (6 mins.); 36° (7 mins.); 34° (9 mins.); 33° (10 mins.); 31° (12 mins.); 29° (16 mins.); 28° (25 mins., constant value).

Similar results were given by "γ"-monoacetyl dimethyl methyl-rhamnoside. When the substance was dissolved in *N*/100-hydrochloric acid, hydrolysis of the glycosidic group took place so quickly that the reaction could not be followed polarimetrically. The following was a typical experiment: $[\alpha]_D^{20}$ + 36° (in water, constant value); + 48° (1 min. after addition of acid); 44° (2 mins.); 41° (3 mins.); 38° (4 mins.); 35° (6 mins.); 33° (8 mins.); 32° (10 mins.); 30° (15 mins.); 29° (18 mins., constant value).

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