236. *Acetylated Sugars with a Free α-Position, and Synthetic Experiments with 2 : 3 : 4 : 6-Tetra-acetyl Glucose and Similar Compounds.*

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THE conversion of acetohalogenoses into acetylated sugars with a free α-position by interaction with moist silver carbonate is not very convenient and the yields are not always satisfactory.

The following rather unexpected reaction has been observed. If an acetone solution of tetra-acetylglucosidyl bromide is shaken with an aqueous solution of sodium nitrite (2 mols.) for several days at the ordinary temperature, and the acetone layer is removed and evaporated, a 70% yield of pure 2 : 3 : 4 : 6-tetra-acetyl glucose is obtained:

$$C_{14}H_{19}O_9Br + NaNO_2 + H_2O = NaBr + HNO_2 + C_{14}H_{19}O_9{\cdot}OH$$

The nitrous acid decomposes and nitric oxide is evolved.

Pure crystalline hepta-acetyl lactose was obtained in the same way in equally satisfactory yield, but tetra-acetyl galactose has been isolated only as a syrupy mass and characterised by its optical rotation.

The sodium nitrite seems to act as a mild alkali and catalyse the hydrolysis of the glucosidyl bromide. If the reaction is stopped after 24 hours, a new crystalline substance, $C_{14}H_{19}O_{11}N$, can be isolated from the acetone solution. Since the new substance is hydrolysed by water to tetra-acetyl glucose and nitrous acid, it is a *tetra-acetyl glucosidyl nitrite*. The above reaction, therefore, apparently proceeds in two stages:

$$C_{14}H_{19}O_9Br + NaNO_2 \longrightarrow C_{14}H_{19}O_9{\cdot}O{\cdot}NO + NaBr;$$
$$C_{14}H_{19}O_9{\cdot}O{\cdot}NO + H_2O \longrightarrow C_{14}H_{19}O_9{\cdot}OH + HNO_2$$

In view of these facts, the classical reaction between silver carbonate and acetylated glucosidyl bromides probably leads to a carbonic acid derivative of the sugar, which is subsequently hydrolysed.

The velocity of hydrolysis of the glucosidyl nitrite is interesting from a theoretical standpoint. Esters of inorganic acids are easily hydrolysed, but doubtless the presence of many acetoxy-groups in the close neighbourhood of the ester linkage accelerates the rate of hydrolysis (compare Ingold, Jackson, and Kelly, J., 1931, 2035).

The tetra-acetyl glucose was required for experiments in connexion with earlier investigations (*Compt. rend.*, 1929, **189**, 104; 1930, **190**, 268; *Z. physiol. Chem.*, 1929, **184**, 241; *Bull. Soc. chim.*, 1932, **51**, 212) on the synthesis of α-aminoacyl 2 : 3 : 4 : 6-tetra-acetyl glucose. Although we have not yet achieved our purpose, we report the experiments so far carried out in order to secure the possibility of continuing them, since such substances have recently been prepared by Bergmann, Zervas, and Overhoff (*Z. physiol. Chem.*, 1934, **224**, 52). Our suggested method is the condensation of 2 : 3 : 4 : 6-tetra-acetyl glucose with α-halogenated acyl chlorides and subsequent displacement of the α-halogen atom by means of ammonia or an amine.

Through the interaction of bromoacetyl bromide and tetra-acetyl glucose a well-crystallised *bromoacetyl* derivative was obtained, apparently different from that of Brauns (*J. Amer. Chem. Soc.*, 1925, **47**, 1297); it could be converted into the corresponding *iodo*-compound by means of sodium iodide in acetone.

In the same way diacetone-glucose can be converted into a bromoacetyl diacetone-glucose, and the latter into an *iodo*-compound (during the latter conversion one acetone group is split off). Monoacetone-glucose (Freudenberg and co-workers, *Ber.*, 1926, **59**, 100, 107; 1928, **61**, 1735) gives in the same way a *trisbromoacetyl* and a *trisiodoacetyl monoacetone-glucose.*

Other α-halogenated acyl chlorides can be used instead of bromoacetyl bromide; *e.g.*, the condensation *product* of 2 : 3 : 4 : 6-tetra-acetyl glucose and α-bromo*iso*hexoyl bromide was easily prepared.

The interaction between 1-iodoacetyl 2 : 3 : 4 : 6-tetra-acetyl glucose and ammonia took an unexpected course. The product, which was also obtained by using hydrazine hydrate instead of ammonia, still contained iodine, and analysis showed it to be isomeric with the initial iodo-compound. The nature of the isomerisation is not yet clear.

EXPERIMENTAL.

2 : 3 : 4 : 6-*Tetra-acetyl Glucose.*—Tetra-acetylglucosidyl bromide (175 g.) in acetone (250 c.c.) and sodium nitrite (80 g.) in water (100 c.c.) were shaken for 5 days, the gas produced being allowed to escape. The acetone layer was separated and evaporated. After remaining for 1 day in a desiccator, the syrupy residue crystallised almost completely; it was then washed on a Buchner funnel with a few c.c. of ice-cold ether. Yield, 70%; m. p. 118°. The tetra-acetyl glucose was identified by acetylation and benzoylation in presence of pyridine, which gave penta-acetyl glucose, m. p. 131·5°, and tetra-acetyl benzoyl glucose, m. p. 146·5°, respectively (Zemplén, *Ber.*, 1915, **48**, 915; 1918, **51**, 1803).

For the above preparation it is not necessary to use pure tetra-acetylglucosidyl bromide; the crude product usually obtained suffices.

Hepta-acetyl Lactose.—Hepta-acetyl-lactosidyl bromide (44 g.) (E. and H. Fischer, *Ber.*, 1910, **43**, 2521) in acetone (150 c.c.) and sodium nitrite (30 g.) in water (100 c.c.) were treated in the described manner. The product was an oil which crystallised in a desiccator after some days; m. p. 83° (Hudson and Sayre, *J. Amer. Chem. Soc.*, 1916, **38**, 1867). Yield, 32 g.

Tetra-acetyl Galactose.—From tetra-acetylgalactosidyl bromide (30 g.) (Fischer and Armstrong, *Ber.*, 1902, **35**, 838; Ohle, Marecek, and Bourjan, *Ber.*, 1929, **62**, 833) in acetone (100 c.c.), tetra-acetyl galactose (22 g.) was obtained as a syrupy mass, $[\alpha]_D$ + 71·54° in chloroform (Unna, Thesis, Berlin, 1911).

2 : 3 : 4 : 6-*Tetra-acetylglucosidyl Nitrite.*—The experiment described above was repeated, but stopped after 24 hours' shaking. The oily residue obtained from the acetone layer began to crystallise rapidly on trituration with ether. The crystals were separated from the remaining oil, the latter consisting of 2 : 3 : 4 : 6-tetra-acetylglucose. The first five crops, recrystallised from benzene–ligroin and then from propyl alcohol, gave rhombic needles, m. p. 108° (Found : C, 44·9; H, 4·9; N, 3·9, 3·9. $C_{14}H_{19}O_{11}N$ requires C, 44·6; H, 5·0; N, 3·7%). The *nitrite* is soluble in chloroform, acetone, and benzene, sparingly soluble in water and ether, and practically insoluble in light petroleum; $[\alpha]_D^{30°} = -4{\cdot}2°$ ($l = 10$ cm.; $c = 5{\cdot}90\%$ in chloroform).

1-*Bromoacetyl* 2 : 3 : 4 : 6-*Tetra-acetyl Glucose.*—Bromoacetyl bromide (4·3 g.) in chloroform (20 c.c.) was added at 0° to tetra-acetyl glucose (6·6 g.) in chloroform (30 c.c.) and pyridine (1·6 c.c.). The mixture was left for 2 days at the ordinary temperature, then washed with dilute hydrochloric acid, bicarbonate solution, and water, dried, and evaporated; the residue, recrystallised from alcohol, formed needles, m. p. 127°; yield, 92% (Found: Br, 17·0. $C_{16}H_{21}O_{11}Br$ requires Br, 17·1%). $[\alpha]_D^{19°} = -1{\cdot}17°$ in chloroform ($c = 2{\cdot}4\%$).

1-*Iodoacetyl* 2 : 3 : 4 : 6-*Tetra-acetyl Glucose.*—Sodium bromide was precipitated immediately when acetone solutions of the foregoing compound and of sodium iodide in equivalent amounts were mixed. The filtered solution was evaporated, and the residue twice crystallised from ether; m. p. 125—126° (Found : C, 37·9; H, 4·3; I, 24·9. $C_{16}H_{21}O_{11}I$ requires C, 37·2; H, 4·1; I, 24·6%). $[\alpha]_D^{19°} = -16{\cdot}3°$ in chloroform ($c = 1{\cdot}8\%$).

Isomerisation.—A mixture of 1-iodoacetyl 2 : 3 : 4 : 6-tetra-acetyl glucose (5 g.), benzene (15 c.c.), and hydrazine hydrate (1·5 g.) was kept at the ordinary temperature for 24 hours, then heated for 6 hours at 80°. The benzene solution was separated from the oily residue and evaporated in a vacuum, leaving a residue which crystallised from methyl alcohol in needles, m. p. 146° (Found : C, 37·3; H, 3·8. $C_{16}H_{21}O_{11}I$ requires C, 37·2; H, 4·1%). $[\alpha]_D^{19°} = -10{\cdot}14°$ in chloroform ($c = 2{\cdot}8\%$).

1-*Bromoacetyl Diacetone-glucose.*—Diacetone-glucose (1/100 mol.) and pyridine (1/100 mol.) were mixed in chloroform, and bromoacetyl bromide (1/100 mol.) added. The procedure described above gave a crystalline substance, which was recrystallised from chloroform; m. p. 136°.

1-*Iodoacetyl Monoacetone-glucose.*—The *iodo*-compound prepared from the preceding compound in the manner already described lost one acetone group during the process. It crystallised from alcohol–water (1 : 1) in needles, m. p. 74° (Found : I, 32·0. $C_{11}H_{17}O_7I$ requires I, 32·7%. $C_{14}H_{21}O_7I$ requires I, 30·0%).

Trisbromoacetyl Monoacetone-glucose.—Bromoacetyl bromide (25 g.) in chloroform (25 c.c.) was added to monoacetone-glucose (9 g.) and pyridine (10 g.) in chloroform (25 c.c.). The usual procedure gave tetragonal crystals, m. p. 115° (Found: Br, 41·1. $C_{15}H_{19}O_9Br_3$ requires Br, 41·1%). $[\alpha]_D^{19°} = -0·4°$ in chloroform ($c = 2·2\%$).

Trisiodoacetyl Monoacetone-glucose.—Interaction between the foregoing compound and the required amount of sodium iodide in acetone solution gave a product, which separated from alcohol in crystals, m. p. 116° (Found : I, 52·6. $C_{15}H_{19}O_9I_3$ requires I, 52·6%). $[\alpha]_D^{19°} = -1·44°$ in chloroform ($c = 4·8\%$).

1-(α-*Iodo*iso*hexoyl*) 2 : 3 : 4 : 6-*Tetra-acetyl Glucose.*—The condensation product of α-bromo-*iso*hexoyl bromide and tetra-acetyl glucose, obtained in the usual way, was not isolated, but was converted into the *iodo*-derivative, which was crystallised from alcohol; m. p. 112—113° (Found : I, 22·7. $C_{20}H_{29}O_{11}I$ requires I, 22·2%). $[\alpha]_D^{19°} = -2·2°$ in chloroform ($c = 1·6\%$).

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