10. *The Reaction of Some Sugar Acetates with Ammonia.*

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The reaction of *aldehydo*-sugar acetates with ammonia is discussed.

ISBELL and FRUSH (*J. Amer. Chem. Soc.*, 1949, **71**, 1579) showed that reaction of *aldehydo*-L-arabinose tetra-acetate with ammonia in methanol or with concentrated aqueous ammonia gives *NN*-diacetyl-L-arabinosylamine. A mechanism was suggested to account for the formation of this derivative. This postulated the addition of ammonia to the *aldehydo*-form of the sugar, followed by migration of a neighbouring acetyl group to the amino-nitrogen by way of an intermediate ortho-ester (cf. Fischer, *Ber.*, 1920, **53**, 1621; Hibbert *et al.*, *J. Amer. Chem. Soc.*, 1929, **51**, 1601; *Canad. J. Res.*, 1931, **4**, 254; Farmer, *Ann. Reports*, 1930, **27**, 103; see Hirst and Peat, *ibid.*, 1934, **31**, 172, for evidence of the mechanism). The diacetamido-derivative could be formed from the monoacetamido-derivative by replacement of the hemiacetal hydroxyl group with ammonia, followed by a further migration of the neighbouring acetyl group (cf. Hockett, Deulofeu, and Defarrari, *J. Amer. Chem. Soc.*, 1950, **72**, 1840; cf. Deulofeu and Defarrari, *Nature*, 1951, **167**, 42).

The reaction seems to be general since it has been shown in this department in collaboration with Dr. A. S. Jones that treatment of *aldehydo*-D-galactose penta-acetate with methanolic ammonia results in the formation of *NN*-diacetyl-D-galactosylamine which can be characterised as its penta-acetate. However, it has been demonstrated that the migration of the acetyl groups to $C_{(1)}$ occurs only from $C_{(2)}$ or $C_{(3)}$. There is no migration, for instance, if the hydroxyl groups at $C_{(2)}$ and $C_{(3)}$ are blocked by other residues. 2 : 3-Dimethyl *aldehydo*-D-glucose 4 : 5 : 6-triacetate was prepared from 2 : 3-dimethyl D-glucose (cf. *Canad. J. Res.*, 1942, **20**, *B*, 175) by the usual sequence of reactions (cf. Wolfrom, *J. Amer. Chem. Soc.*, 1930, **52**, 2464) involving the formation of 2 : 3-dimethyl D-glucose diethyl mercaptal and its triacetate. Removal of sulphur from the latter compound afforded 2 : 3-dimethyl *aldehydo*-D-glucose 4 : 5 : 6-triacetate. Treatment of this with methanolic ammonia gave a nitrogen-free product shown to be 2 : 3-dimethyl D-glucose chromatographically and by preparation of the diethyl mercaptal and *p*-toluidide. No trace of a mono- or di-acetamido-derivative of 2 : 3-dimethyl D-glucose was detected.

EXPERIMENTAL

NN-Diacetyl-D-galactosylamine 2 : 3 : 4 : 5 : 6-penta-acetate. *aldehydo*-D-Galactose penta-acetate (1 g.; Wolfrom, *J. Amer. Chem. Soc.*, 1930, **52**, 2464) was dissolved in dry methanol (40 c.c.), and the solution was saturated at 0° with gaseous ammonia. After being kept at 0° for 18 hours the solution was evaporated to dryness. Ammonium acetate was removed from the residue at 70—80°/0·005 mm. The gelatinous product, dissolved in dry pyridine (6 c.c.), was cooled at −5°. Freshly distilled acetic anhydride (3 c.c.) was added and the mixture was kept at 0° for 24 hours and then for a further 24 hours at room temperature. After being poured into water, the mixture was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated to dryness. The residue was kept *in vacuo* over concentrated sulphuric acid and phosphoric oxide until quite dry. Thereafter it was dissolved in warm acetic acid and passed through a small column of alumina. On addition

of light petroleum to the eluate, needles separated. Recrystallisation from acetic acid–light petroleum gave NN-*diacetyl*-D-*galactosylamine penta-acetate* (0·3 g.) as colourles needles, m. p. 205°, $[\alpha]_D^{19}$ −38·9° (*c*, 1·0 in chloroform) (Found : C, 48·3; H, 6·2; N, 5·5. $C_{20}H_{30}O_{12}N_2$ requires C, 48·8; H, 6·2; N, 5·7%).

2 : 3-*Dimethyl* D-*glucose* p-*toluidide*. 2 : 3-Dimethyl D-glucose (0·5 g.) (Freudenberg, Toepffer, and Andersen, *Ber.*, 1928, **61**, 1750) was boiled under reflux for 3 hours with *p*-toluidine (0·5 g.) in absolute ethanol (100 c.c.). Evaporation to dryness then afforded a syrup which slowly crystallised at 0°. Recrystallisation from aqueous ethanol afforded the *p*-toluidide as long colourless needles, m. p. 151°, $[\alpha]_D^{21}$ +26·6° (equilibrium) (*c*, 1·13 in ethanol) (Found : C, 61·0; H, 7·1. Calc. for $C_{15}H_{23}O_5N$: C, 60·6; H, 7·7%).

2 : 3-*Dimethyl* D-*glucose diethyl mercaptal*. 2 : 3-Dimethyl D-glucose (6·04 g.) was shaken for 4·5 hours with ethanethiol (4 c.c.) and concentrated hydrochloric acid (4 c.c.). After being poured into water, the mixture was neutralised by addition of sodium carbonate, and then concentrated to dryness. The solid residue was extracted with hot ethanol. Removal of the solvent yielded a syrup. On distillation (b. p. 190—220°/0·05 mm.) the *diethyl mercaptal* (4·7 g.) was obtained as a yellow viscous syrup, $[\alpha]_D^{20}$ +35·3° (*c*, 0·68 in chloroform) (Found : C, 45·4; H, 8·6. $C_{12}H_{26}O_5S_2$ requires C, 45·8; H, 8·3%). This (4·48 g.) with acetic anhydride (8 c.c.) in dry pyridine (20 c.c.) gave 4 : 5 : 6-*triacetyl* 2 : 3-*dimethyl* D-*glucose diethyl mercaptal* (4·0 g.) as a syrup, b. p. 175—190°/0·05 mm., n_D^{24} 1·4728, $[\alpha]_D^{19}$ +37·6°, +38·8° (*c*, 1·11, 2·06 in chloroform) (Found : C, 49·7; H, 7·2. $C_{18}H_{32}O_8S_2$ requires C, 49·1; H, 7·3%).

4 : 5 : 6-*Triacetyl* 2 : 3-*dimethyl* aldehydo-D-*glucose*. 4 : 5 : 6-Triacetyl 2 : 3-dimethyl D-glucose diethyl mercaptal (4·91 g.) was dissolved in acetone (22·6 c.c.) and water (11·3 c.c.). Cadmium carbonate (15·4 g.) was added to the well-stirred solution and then slowly a solution of mercuric chloride (12·1 g.) in acetone (18 c.c.). The mixture was stirred at room temperature for 24 hours, then filtered on to a small amount of cadmium carbonate. The residue was washed several times with acetone and the combined filtrate and washings were evaporated to dryness in the presence of some cadmium carbonate. The residue was dried by distilling ethanol over it, and then extracted with hot chloroform (3 × 15 c.c.). The chloroform extract was washed with aqueous potassium iodide and then water (4 × 15 c.c.), and dried ($MgSO_4$). After passage through charcoal the solution was evaporated and the syrupy residue was distilled. 4 : 5 : 6-*Triacetyl* 2 : 3-*dimethyl* aldehydo-D-*glucose* (2·5 g.) was obtained as a colourless syrup, b. p. 135—137°/0·02 mm., n_D^{21} 1·4591, $[\alpha]_D^{18}$ +52·4° (*c*, 1·1 in chloroform), $\lambda_{max.}$ 290 mμ, ε, 271 (Found : C, 49·9; H, 6·7; OMe, 18·7. $C_{14}H_{22}O_9$ requires C, 50·4; H, 6·6; OMe, 18·6%). This syrup strongly reduced Fehling's solution.

Action of methanolic ammonia on 4 : 5 : 6-*triacetyl* 2 : 3-*dimethyl* aldehydo-D-*glucose*. A solution of 2 : 3-dimethyl 4 : 5 : 6-triacetyl *aldehydo*-D-glucose (1·88 g.) in dry methanol (100 c.c.) was saturated at 0° with ammonia. The mixture was kept at 0° for 18 hours and then filtered. The filtrate was evaporated at 35°, and the syrupy residue thoroughly dried and then extracted with hot ethyl acetate, ammonium acetate remaining undissolved. After passage through charcoal the ethyl acetate solution was concentrated to dryness and afforded a syrup which was strongly reducing and slowly crystallised on storage *in vacuo*. It then had m. p. 85—90°; Irvine and Scott (*J.*, 1913, **103**, 575) give 85—87° for the α-form and m. p. 121° for the β-form. McClosky and Coleman (*J. Org. Chem.*, 1945, **10**, 184) report m. p. 110° for 2 : 3-dimethyl β-D-glucose. The product was 2 : 3-dimethyl D-glucose since it readily gave 2 : 3-dimethyl D-glucose diethyl mercaptal, b. p. 190—220°/0·02 mm., $[\alpha]_D^{17}$ +33·2° (*c*, 0·48 in chloroform), and the *p*-toluidide, m. p. 151° alone or mixed with a sample prepared as above. 1% Aqueous solutions of the syrupy and the crystalline 2 : 3-dimethyl αβ-D-glucose were run on paper chromatograms with butanol–ethanol–ammonia as eluent (cf. Allerton and Overend, *J.*, 1951, 1480), with 2 : 3-dimethyl D-glucose as a reference compound. The chromatographic behaviour of the samples was identical.

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