341. 3 : 6-*Dimethyl Glucose: Improved Methods of Synthesis.*

By D. J. Bell.

The method by which 3 : 6-dimethyl glucose was first obtained is both cumbersome and inefficient (cf. Bell, J., 1935, 175). Two other methods employing easily procured materials are described below.

Method 1.—6-Acetyl monoacetone glucose, treated with nitrogen pentoxide, gave a crystalline *dinitrate*, which, subjected to the action of alcoholic dimethylamine, was partly converted into crystalline *monoacetone glucose 5-nitrate*. The latter, after methylation by Purdie's reagents and elimination of the nitrate radical, gave 3 : 6-*dimethyl monoacetone glucose*; following hydrolytic removal of the *iso*propylidene group, crystalline 3 : 6-dimethyl glucose was obtained.

Method 2.—Treatment of 3-methyl monoacetone glucose with 1·1 mols. of *p*-toluenesulphonyl chloride in pyridine gave an amorphous product (probably largely 6-*p*-toluenesulphonyl 3-methyl monoacetone glucose). By the action of sodium methoxide on this, 3 : 6-dimethyl monoacetone glucose was formed; as before, crystalline 3 : 6-dimethyl glucose was obtained on hydrolysis.

Experimental.

Unless otherwise stated, solvents were evaporated under diminished pressure in a vacuum, below 50°, and polarimetric observations were made in chloroform solution in a 2 dm. tube. Substances were recrystallised until a constant m. p. was attained.

6-*Acetyl Monoacetone Glucose* 3 : 5-*Dinitrate* (I).—10 G. of 6-acetyl monoacetone glucose (cf. Fischer and Noth, *Ber.*, 1918, **51**, 321; Bell, this vol., p. 859) were dissolved in 40 ml. of an ice-cold 30% solution of crystalline nitrogen pentoxide in dry chloroform and kept in ice for 2 minutes. The mixture was poured into potassium bicarbonate solution containing ice and shaken until the acid was neutralised. After dehydration over sodium sulphate, the chloroform solution was evaporated, the residue dissolved in benzene, and the solution extracted four times with water. The syrup remaining, after evaporation of the dehydrated benzene solution, rapidly crystallised. Recrystallised from alcohol, the *dinitrate* had m. p. 81·5—82·5°, $[\alpha]_D^{16°}$ − 22·7° (c = 5·8). Yield, 10·6 g. (80%) (Found: N, 7·9. $C_{11}H_{16}O_{11}N_2$ requires N, 7·95%).

Monoacetone Glucose 5-*Nitrate* (II).—To 34 g. of (I), dissolved in 40 ml. of dry benzene, 67 ml. of a 30% solution of dimethylamine in alcohol were added. After 24 hours, the solution was evaporated to dryness below 50° on the water-pump, traces of volatile material being finally distilled at 100°/0·1 mm. The crude product was dissolved in benzene and extracted several times with water; the water was then extracted six times with equal volumes of chloroform, and the chloroform extract dehydrated and evaporated. The residue crystallised on trituration with methyl iodide. Recrystallised from carbon tetrachloride containing a little ether, the *nitrate* had m. p. 86—87°, $[\alpha]_D^{20°}$ − 0·4° in alcohol (c = 4·4). Yield, 12 g. (47%) (Found: N, 4·95. $C_9H_{15}O_8N$ requires N, 5·2%).

This substance exhibited dimorphism: crystallised from 60% alcohol, it melted at 106°; this form, dissolved in hot 60% alcohol, cooled, and seeded with a crystal, m. p. 86—87°, deposited crystals having m. p. 86—88°.

3 : 6-*Dimethyl Monoacetone Glucose* (III).—6 G. of (II) were treated three times with 5 mols. of methyl iodide and 2·5 mols. of silver oxide. The yield was 3·7 g. of an uncrystallisable syrup (OMe, 20%). The low yield could not be accounted for. The syrup was dissolved in alcohol and boiled, until free from nitrate, with a large excess of sodium hydroxide solution previously saturated with hydrogen sulphide. After removal of the alcohol by distillation, the crude product was isolated by six-fold extraction with chloroform. Evaporation of the dehydrated chloroform, followed by distillation of the residue in a high vacuum, gave 3 g. of a colourless syrup, $[\alpha]_D^{20°}$ − 45·9° (c = 5·0) (Found: OMe, 24·8. $C_{11}H_{20}O_6$ requires OMe, 25·0%).

3 : 6-*Dimethyl Monoacetone Glucose from the Crude* 6-p-*Toluenesulphonate of* 3-*Methyl Monoacetone Glucose* (IV).—To 30 g. of 3-methyl monoacetone glucose (Freudenberg, Dürr, and Hochstetter, *Ber.*, 1928, **61**, 1739), dissolved in 150 ml. of dry pyridine, 27 g. (1·1 mols.) of finely powdered *p*-toluenesulphonyl chloride were added. The mixture was kept at 28° for 24 hours, water added, and, after 2 hours, the crude product was extracted with benzene and isolated, after alternate washing with ice-cold 1% sulphuric acid and potassium bicarbonate solution, by evaporation to dryness of the benzene solution. The residual material was dissolved in alcohol, and light petroleum (b. p. 60—80°) added until no more of a dark coloured oil was thrown down. This was rejected, and a light yellow glass obtained after evaporation of the supernatant liquor. 24 G. of this glass were treated with sodium methoxide exactly as described by Levene and Raymond (*J. Biol. Chem.*, 1932, **97**, 751) for the preparation of 6-methyl monoacetone glucose. The crude product (7 g.), obtained after evaporation of a water-washed chloroform solution and distillation in a high vacuum, was a colourless syrup, $[\alpha]_D^{20°}$ − 45·8° (c = 4) (Found: OMe, 24·7. $C_{11}H_{20}O_6$ requires OMe, 25·0%).

3 : 6-*Dimethyl Glucose.*—(a) *From* (III). 1·6 G. were boiled, in 4% concentration, in a mixture of equal parts of alcohol and 5% hydrochloric acid until a constant polarimetric reading was obtained. After neutralisation of the acid with silver carbonate, followed by removal of colloidal silver with norit, the solution was extracted with chloroform to remove unchanged material, evaporated to dryness, and the resulting colourless syrup (1·21 g., 91%) crystallised from dry ethyl acetate. Three fractions were obtained, totalling over 90% of the crude yield. All had m. p. 114—115°, alone or mixed with authentic 3 : 6-dimethyl glucose; $[\alpha]_D^{20°}$ + 61·6° (in water at equilibrium).

(b) *From* (IV). 2·6 G. were treated as above. Yield, 2·34 g. (97%); m. p. 113—115°; $[\alpha]_D^{20°}$ + 61·5° (in water at equilibrium).

The Biochemical Laboratory, Cambridge. [*Received, August 6th*, 1936.]