51. *The Isolation of Derivatives of 2-Methyl Glucose and 3-Methyl Glucose from a Partly Methylated Cellulose.*

By W. J. Heddle and E. G. V. Percival.

The products of the hydrolysis of a partly methylated cellulose, prepared according to Piwonka (*Ber.*, 1936, **69**, 1965) by the methylation in the cold of a sodium cupri-cellulose complex, gave 2-methyl glucosephenylhydrazone and 3-methyl glucosazone; the second compound has already been isolated by Piwonka (*loc. cit.*) from the same source. The absence of derivatives of 6-methyl glucose is noteworthy and the possibility that the primary alcohol residues are shielded in some way is strengthened by these observations.

In a previous paper (Heddle and Percival, J., 1938, 1690), it was shown that potassium hydroxide-cellulose on methylation with anhydrous methyl sulphate yielded a partly methylated cellulose (OMe, 5—9%), among the hydrolysis products of which the only monomethyl glucose to be detected was 2-methyl glucose. Attention was drawn to the results of Piwonka (*Ber.*, 1936, **69**, 1965), who, using ramie fibre, isolated a derivative of 3-methyl glucose after methylating a sodium cupri-cellulose complex in aqueous solution and hydrolysing the " hemi-methyl cellulose " obtained. These experiments have been repeated on cotton cellulose and Piwonka's result is confirmed in so far as 3-methyl glucose can certainly be identified (as the glucosazone) in the mixture produced on hydrolysis, but 2-methyl glucosephenylhydrazone also has been isolated in good yield, so there is no doubt that, when cotton cellulose is used, methylation takes place at both these positions in certain of the anhydroglucose units and is not confined exclusively to position 3. No 6-methyl glucosazone nor any dimethyl glucosazone could be detected, although it has been shown that position 6 is the most reactive group in α- and β-methylglucosides (Heddle and Percival, *loc. cit.*), cellobiose (Percival and Ritchie, J., 1936, 1765), and sucrose (Percival, J., 1935, 648). This strengthens the view that in cellulose these residues either are shielded in some way or may be involved in the cross-linkages which are presumed to hold the long chains of β-glucopyranose units together (Cox, *Ann. Reports*, 1937, **34**, 189).

Compton (*J. Amer. Chem. Soc.*, 1938, **60**, 2823), who has methylated cellulose dispersed in dibenzyldimethylammonium hydroxide, has also isolated a crystalline derivative of 2-methyl glucose on hydrolysis of the partly methylated cellulose so obtained, and Lieser (*Annalen*, 1929, **470**, 104) has shown by similar means that position 2 is involved in xanthate formation. Schorigin and Makarowa-Semljanskaja (*Ber.*, 1936, **69**, 1713), by treating cellulose in liquid ammonia with sodium and subsequently with methyl iodide, obtained a partly methylated cellulose, and hydrolysis yielded a mixture of monomethyl glucoses which gave an osazone of low methoxyl content (OMe = 2%). This may be taken as evidence of the presence of a considerable proportion of 2-methyl glucose.

Evidence that the methylation of certain of the primary alcoholic residues in cellulose is hindered in some way is also furnished by Karrer and Escher (*Helv. Chim. Acta*, 1936, **19**, 1192), who found it difficult to introduce the full methoxyl content on methylation of cellulose acetates, and on hydrolysis of the methylated cellulose produced (OMe = 42·5—43%) a dimethyl glucose was obtained which was converted into the crystalline 2 : 3-dimethyl 4 : 6-di-*p*-toluenesulphonyl methylglucoside of Oldham and Rutherford (*J. Amer. Chem. Soc.*, 1932, **54**, 366). These independent observations from a variety of sources appear to agree with our results and support the view that in some anhydroglucose units position 2 is especially reactive and that substitution in position 6 is difficult.

Experimental.

Perparation of Partly Methylated Cellulose.—The methods adopted were identical with those described by Piwonka (*loc. cit.*) as far as could be judged from his paper, except that surgical cotton was used instead of ramie fibre. After treatment with cupric chloride (0·5 mol. per anhydroglucose unit) and 17% sodium hydroxide solution, pressing and drying, a product was obtained containing approximately 5 mols. of sodium hydroxide per anhydroglucose unit, although several trial experiments were necessary to determine the correct degree of the pressing out of the adhering liquid. Methylation at room temperature in aqueous suspension with

methyl sulphate (6·8 mols.) was carried out for 1 hour and the product was filtered off and washed with dilute hydrochloric acid and alcohol until all copper was removed. The dried fibrous products obtained in good yield in this way had methoxyl contents ranging from 9 to 11%.

Isolation of Monomethyl Glucoses.—Simultaneous hydrolysis and glucoside formation was carried out by contact of the partly methylated cellulose (5 g.) with 1% methyl-alcoholic hydrogen chloride after the method of Irvine and Hirst (J., 1923, **123**, 518). A longer period of heating was necessary than for trimethyl cellulose and even after 150 hours at 130° an insoluble residue (1·0 g.) remained, but this was substantially unchanged material (OMe, 8%) and a quantity obtained from several experiments gave on hydrolysis a mixture of sugars similar to that described below. Neutralisation with silver carbonate and evaporation gave a syrup (3·8 g.), from which by distillation at 180—190° (bath temp.)/0·04 mm. a fraction (1·8 g.) was obtained, $[\alpha]_D^{17°}$ + 77° in water (*c*, 0·4), $n_D^{17°}$ 1·4690 (Found: OMe, 30·4. Calc. for $C_8H_{16}O_6$: OMe, 29·8%). This mixture of monomethyl methylglucosides was hydrolysed with 5% hydrochloric acid at 100° until the rotation had fallen to a constant value (2·5 hours), and the sugars were isolated as a clear syrup (1·1 g.) in the usual way. $[\alpha]_D^{17°}$ + 57° in water (*c*, 0·5) (Found: OMe, 15·7. Calc. for $C_7H_{14}O_6$: OMe, 16·0%).

Isolation of 2-Methyl Glucosephenylhydrazone.—The above syrup (0·5 g.) was mixed with water (0·2 c.c.), phenylhydrazine (1·0 g.), and acetic acid (0·05 c.c.) and kept at 0° for 3 days. The white crystals of the phenylhydrazone produced were removed, and addition of dry ether to the filtrate caused the separation of a further crop. Yield, 0·22 g.; m. p. 177°. After recrystallisation from alcohol the product had $[\alpha]_D^{17°}$ —11° in pyridine (*c*, 0·9), and m. p. 179°, unchanged on admixture with an authentic specimen prepared from 2-methyl glucose dibenzylmercaptal. This experiment was twice repeated (Found: C, 54·6; H, 7·3; OMe, 10·6; N, 9·7. Calc. for $C_{13}H_{20}O_5N_2$: C, 54·9; H, 7·1; OMe, 10·9; N, 9·85%).

Osazone Formation. The Isolation of Glucosazone and 3-Methyl Glucosazone.—Another specimen of the mixed methyl glucoses (1·0 g.; OMe, 15·5%) prepared as above was subjected to osazone formation in the usual way. The crude osazone (0·35 g.) had OMe, 4·2%. Recrystallisation from alcohol gave glucosazone, m. p. 200°, unchanged on admixture with an authentic specimen (OMe, nil). A further quantity of the crude osazone (0·8 g.; OMe, 4%) was extracted with chloroform for 4 minutes at 60° and at room temperature for 12 hours. The undissolved material (0·45 g.) was chiefly glucosazone and one recrystallisation from alcohol was sufficient to purify it. The solution was treated with light petroleum (b. p. 60—80°) and after filtration of the product (I) (0·12 g.) a further quantity (II) (0·1 g.) was deposited overnight. The filtrate was evaporated to yield a reddish gum (III) (0·01 g.).

	OMe, %.	M. p.
I	7·3	169—172°
II	7·9	169—172
III	7·6	—

Both (I) and (II) were recrystallised from alcohol and water to give a pale yellow osazone, m. p. 177—178°, which had m. p. 160° on admixture with authentic 6-methyl glucosazone (m. p. 182—183°) and 177° on admixture with authentic 3-methyl glucosazone (m. p. 177—178°) (Found: C, 61·0; H, 6·5; OMe, 7·9; N, 14·9. Calc. for $C_{19}H_{24}O_4N_4$: C, 61·3; H, 6·5; OMe, 8·3; N, 15·0%). It thus appears that the crude osazone is a mixture of 3-methyl glucosazone and glucosazone, the latter having been derived from the 2-methyl glucose in the mixture. These results were twice confirmed.

Thanks are expressed to the Carnegie Trust for the award of a Teaching Fellowship to one of us (E. G. V. P.) and to the Earl of Moray Endowment and Imperial Chemical Industries Ltd. for grants.

KING'S BUILDINGS, UNIVERSITY OF EDINBURGH. [*Received, January 13th,* 1939.]