CLXXXII.—*The Conversion of* 1 : 2 : 3 : 4-*Tetra-acetyl* β-d-*Glucose into* 2 : 3 : 4 : 6-*Tetra-acetyl* β-*Methyl-glucoside.*

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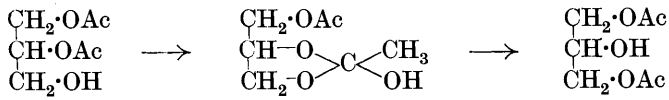
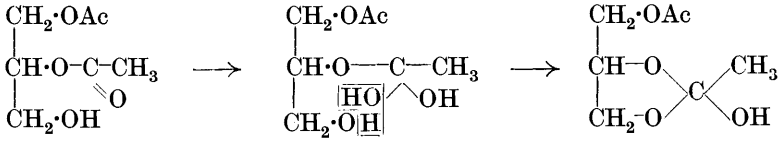
VARIOUS examples are known of the wandering of acyl groups linked with polyhydric alcohol residues. One of the first to observe this change was Fischer (*Ber.*, 1920, **53**, 1624), who suggested that the mechanism of the wandering of acyl groups might be explained

by the intermediate formation of an ortho-carbonic ester group of the type shown below :

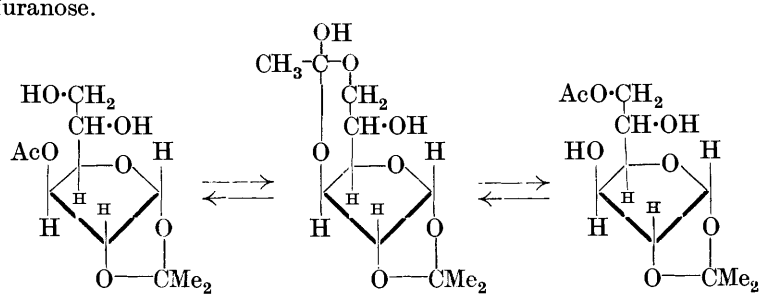


This view may be expanded by including the assumption that the addition and elimination of water takes place in the following way :



Similar instances of acyl wandering are known in the glycerides of higher fatty acids (Grün, *Ber.*, 1921, **54**, 290; Fairbourne and Cowdrey, J., 1929, 129; Fairbourne, *ibid.*, pp. 1151, 2232; Hibbert and Carter, *J. Amer. Chem. Soc.*, 1929, **51**, 1607) and also in the sugar group (Ohle, *Ber.*, 1924, **57**, 403; Ohle and Dickhäuser, *Ber.*, 1925, **58**, 2593). A benzoyl or acetyl residue at position 3 in glucose is shown to be capable of translation to position 6, especially under the influence of faintly alkaline solutions, and the conditions under which this change is effected have been studied (Josephson, *Annalen*, 1929, **472**, 217).

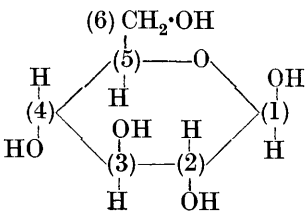
If the above mechanism be admitted, it would appear that the cases studied by the last author may be expressed as follows, where positions 1 and 2 are linked by an acetone group in gluco-furanose.



The spatial proximity of the hydroxyls at positions 3 and 6 which are situated at the same side of the plane constituting the glucose ring apparently facilitates this interchange, and these stereochemical considerations are probably of importance also in other cases. In the course of our work on the properties of 1 : 2 : 3 : 4-tetra-acetyl β-glucose (I) (Oldham, J., 1925, **127**, 2840; Helferich and Klein, *Annalen*, 1926, **450**, 219) we were impressed by the similar

melting points of this substance, of the 2 : 3 : 4 : 6-tetra-acetyl β-glucose (II) (Fischer and Delbrück, *Ber.*, 1909, **42**, 2778), and of the supposed 1 : 2 : 3 : 6-tetra-acetyl glucose (III) of Helferich and Klein (*Annalen*, 1927, **455**, 173), and by the statement that the pyridine derivative of the supposed 1 : 2 : 3 : 6-tetra-acetyl glucose (III) mutarotates in water from the value $[\alpha]_D$ — 22° to about that of *d*-glucose (+ 53°). Since the simple mutarotation of a compound acetylated in position 1 may be considered unusual, the possibility arose that this last-named compound (III) was structurally closely related to the 2 : 3 : 4 : 6-tetra-acetyl β-glucose (II), which mutarotates from a negative value, in ethyl alcohol, to + 81°, and has a melting point almost identical with that of Helferich's supposed 1 : 2 : 3 : 6-tetra-acetyl glucose (III). We have confirmed, by mixed melting-point determinations, the statement that these two substances are not identical, and another explanation must therefore be provided for the properties of (III). It has been shown already that compound (III) passes by methylation into 2 : 3 : 4 : 6-tetra-acetyl β-methylglucoside (Helferich and Klein, *loc. cit.*) and that the acetylated sugar (III) exists in equilibrium with 1 : 2 : 3 : 4-tetra-acetyl β-glucose (I) in very dilute alkali, and is prepared from the latter by this reaction. Helferich has tentatively suggested that the acetyl group which wanders is that at position 4 in the latter compound (I), but has recognised that a further transposition of acetyl residues must occur when (III) undergoes conversion, although in indifferent yield, into tetra-acetyl β-methylglucoside.

It is seen, however, that position 4 is remote from position 6 in that these hydroxyl groups are situated in different planes in the β-glucopyranose configuration given below.

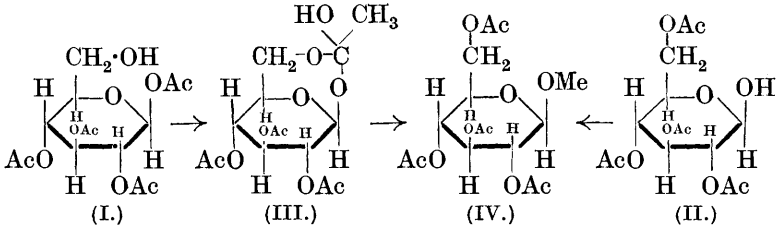


β-Glucopyranose.

The possibility that the exchange of acetyl groups may occur from position 3 to 6 has been considered and rejected by Helferich, since the *p*-toluenesulphonyl derivative of (III) is different from that prepared by Freudenberg and Ivers (*Ber.*, 1922, **55**, 929).

Experiments which we have carried out lead definitely to the view that, in the isomerisation of (I) to give (III), the hydroxyls involved are those at positions 1 and 6. We have submitted both 1 : 2 : 3 : 4-tetra-acetyl β-glucose (I) and 2 : 3 : 4 : 6-tetra-acetyl β-glucose (II) to methylation with methyl iodide and silver oxide and have obtained in both cases 2 : 3 : 4 : 6-tetra-acetyl β-methylglucoside (IV) as our product. It is important to note that the migration is not in any way connected with the actual process of

methylation, but is an example of that type of isomerisation which has been referred to above as taking place in certain partially acylated substances under the influence of alkali. Our observations support the result recorded by Helferich, who has obtained the same product (IV) by methylation of the converted tetra-acetyl glucose (III), and we are therefore of opinion that this evidence points to the formulation of (III) as a derivative of ortho-acetic acid originating from (I) in the following way.



Helferich has demonstrated that the pyranose ring remains undisturbed during the change from (I) to (III), since both give rise on acetylation to the usual penta-acetyl glucose.

At present the evidence of the *p*-toluenesulphonyl derivatives of (I) and (III) throws little light on this view of the structure allocated to (III), although it is not inconsistent with it. Before the problem is finally decided, the toluenesulphonyl derivative of (III) will require further study.

EXPERIMENTAL.

1 : 2 : 3 : 4-*Tetra-acetyl* β-d-*Glucose*.—This substance was prepared by the action of hydrogen bromide, dissolved in glacial acetic acid, on 6-trityl 1 : 2 : 3 : 4-tetra-acetyl β-*d*-glucose (Helferich and Klein, *Annalen*, 1926, **450**, 219). Crystallisation from ether gave colourless needles, m. p. 127°, $[\alpha]_D^{20°}$ + 13° (*c*, 2·95 in chloroform). These constants and the properties of the substance are in complete agreement with those given by Helferich and Klein, but the m. p. and rotation are very close also to those of 2 : 3 : 4 : 6-tetra-acetyl β-*d*-glucose, which, when prepared from tetra-acetyl glucosidyl bromide by the method of Fischer and Delbrück (*Ber.*, 1909, **42**, 2778), has m. p. 135°, $[\alpha]_D^{20°}$ + 16° (*c*, 0·87 in chloroform); $[\alpha]_D^{20°}$ −1·5° (in ethyl alcohol; *c*, 1·17) ⟶ + 81° in 10 days. The two substances are not, however, identical, since the m. p. of a mixture showed a depression of 20—25°. A similar depression was observed when either 1 : 2 : 3 : 4-tetra-acetyl β-*d*-glucose or 2 : 3 : 4 : 6-tetra-acetyl β-*d*-glucose (m. p. 135°) was mixed with Helferich's supposed 1 : 2 : 3 : 6-tetra-acetyl β-*d*-glucose, prepared from the 1 : 2 : 3 : 4-compound by the action of very dilute alkali.

Methylation of 1 : 2 : 3 : 4-*Tetra-acetyl* β-d-*Glucose.*—A solution of 1 : 2 : 3 : 4-tetra-acetyl β-*d*-glucose (3 g.) in methyl iodide (8 c.c.) was boiled for 8 hours during the gradual addition of dry silver oxide (15 g.) which had been prepared from silver nitrate and barium hydroxide and very thoroughly washed. The product was extracted by boiling chloroform and, on removal of the solvent under diminished pressure, was obtained as a pale yellow viscid syrup (2·8 g.). After being kept for some weeks, this began to crystallise, the rate of crystallisation being increased when the syrup was rubbed with alcohol. The solid was then recrystallised from absolute alcohol, giving colourless needles, m. p. 104—106° (yield, 0·6 g.); $[\alpha]_D^{22°}$ — 18·5° (*c*, 1·62 in chloroform). The substance did not reduce boiling Fehling's solution. It was identified by a mixed m. p. determination as tetra-acetyl β-methylglucoside, which has m. p. 104—105°; $[\alpha]_D^{20°}$ — 18·2° in chloroform (Found : C, 49·8; H, 6·5; OMe, 9·1. Calc. for $C_{15}H_{22}O_{10}$: C, 49·7; H, 6·1; OMe, 8·6%).

The syrup left after removal of the tetra-acetyl β-methylglucoside gave OMe, 14·5%, from which it appeared that the methylation process had been accompanied by simultaneous deacetylation.

Methylation of 2 : 3 : 4 : 6-*Tetra-acetyl* β-d-*Glucose.*—2 : 3 : 4 : 6-Tetra-acetyl β-*d*-glucose (4·2 g.) was dissolved by gentle heating in methyl iodide (15 c.c.). The solution was heated with silver oxide (10 g.) for 6 hours at 45°. The product (4·3 g.), which crystallised spontaneously, m. p. 96°, was mainly 2 : 3 : 4 : 6-tetra-acetyl β-methylglucoside. One crystallisation from alcohol gave pure material, m. p. 105° alone or when mixed with authentic 2 : 3 : 4 : 6-tetra-acetyl β-methylglucoside which had been prepared by the acetylation of β-methylglucoside.

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