251. *Studies of Trifluoroacetic Acid. Part XIV.* Reaction of Acyl Trifluoroacetates with* 1 : 6-*Di*-O-*benzoyl*-2 : 4-3 : 5-*di*-O-*methylene*-D-*glucitol.*†

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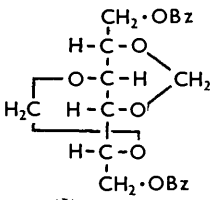
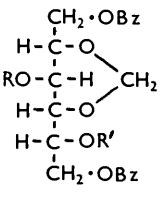
An equimolecular mixture of acetic (or benzoic) acid and trifluoroacetic anhydride reacts at 25° with 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol to give 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (or 1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol). Prolonged reaction at 25° does not cause scission of the βC-ring (see Barker and Bourne [1] for this nomenclature). A ten-fold excess of acetic acid over trifluoroacetic anhydride gives 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol. Conformational analysis is used to explain the position of ring scission and the marked difference in reactivity between the rings.

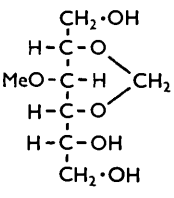
Hann, Hudson, and their co-workers, in their studies on the structures of cyclic acetals of the polyhydric alcohols, treated a number of such acetals with a mixture of acetic anhydride, glacial acetic acid, and concentrated sulphuric acid, which caused rupture of the acetal rings. Acetolysis of a cyclic methylene ether left an *O*-acetyl group on one, and an *O*-acetoxymethyl group on the other, of the oxygen atoms of the polyalcohol which were originally incorporated in the ring (see, *inter alia*, refs. 1—5). Thus, 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (I) gave 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (II) in 72% yield.[4] [When we prepared this compound by this method, its properties differed somewhat from those given by the original authors (see p. 1278), but we assume that both products had structure (II).]



(I)



(II — XII) except (VIII)



(VIII)

	R	R′
II	CH_2·OAc	Ac
III	Ac	Ac
IV	H	H
V	H	Ac

	R	R′
VI	Ac	H
VII	Me	Ac
IX	Bz	Ac

	R	R′
X	H	Bz
XI	Ac	Bz
XII	CH_2·O·CO·CF_3	Ac

It appeared that an equimolecular mixture of trifluoroacetic anhydride and a carboxylic acid might react analogously with a cyclic methylene ether, with the introduction of acyl and trifluoroacetoxymethyl groups, since ions of the type R·CO^+, which are required for acetolysis, are formed in such a mixture:

$$R{\cdot}CO_2H + (CF_3{\cdot}CO)_2O \rightleftharpoons R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 + CF_3{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad (1)$$

$$R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \rightleftharpoons R{\cdot}CO^+ + CF_3{\cdot}CO_2^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

* Part XIII, *J.*, 1957, 315.
† Presented in part at XIVth International Congress of Pure and Applied Chemistry, Zürich, 1955.

[1] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[2] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1906.
[3] Ness, Hann, and Hudson, *ibid.*, pp. 665, 670.
[4] Hann, Wolfe, and Hudson, *ibid.*, p. 1898.
[5] Haskins, Hann, and Hudson, *ibid.*, 1945, **67**, 1800; 1947, **69**, 624.

These equilibria have been suggested previously [6,7] to explain other reactions of mixtures of carboxylic acids and trifluoroacetic anhydride and have been confirmed by conductimetric,[8] infrared,[9] and cryoscopic [9] measurements.

When 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (I) was treated with a nine-fold excess (necessary for complete dissolution) of an equimolecular mixture of acetic acid and trifluoroacetic anhydride for 3 hr. at 25° (the rotation had then become constant), a fluorine-containing syrup was formed. This compound decomposed on exposure to air with the evolution of formaldehyde and trifluoroacetic acid, but on being treated with dry methanol, as described by Bourne, Tatlow, and Tatlow [10] for the removal of *O*-trifluoroacetyl groups, it gave quantitatively a crystalline substance (A), m. p. 149—150°, which analysis indicated was an *O*-acetyldi-*O*-benzoyl-*O*-methylenehexitol. Its catalytic de-esterification with sodium methoxide in methanol gave the known 2 : 4-*O*-methylene-D-glucitol. Acetylation with acetic anhydride in pyridine gave a compound which was shown to be 3 : 5-di-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (III) as follows: 2 : 4-*O*-Methylene-D-glucitol was preferentially benzoylated at the primary hydroxyl groups with 2 mol. of benzoyl chloride in pyridine (a similar technique had been used by Hudson's group [11] to convert 2 : 5-*O*-methylene-D-mannitol into its 1 : 6-di-*O*-benzoyl derivative [12]). The dibenzoate (IV) was acetylated to give the 3 : 5-di-*O*-acetyl derivative (III), which was identical with the compound previously obtained.

Thus, compound (A) was 5-*O*- (V) or 3-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (VI). That it was the former was demonstrated in three ways. First, controlled acidic hydrolysis of 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol [3,4] (II) gave a product identical with (A) in 28% yield. Secondly, methylation of (A) with the Purdie reagents gave an *O*-methyl derivative (VII), which afforded an *O*-methyl-2 : 4-*O*-methylene-D-glucitol (VIII) by catalytic de-esterification: this could not have been the 5-*O*-methyl derivative as it consumed 1 mol. of sodium periodate with evolution of approximately 1 mol. of formaldehyde. Compound (A) is not proved to be the 5-acetate (V) by this etherification procedure alone, however, because of the possibility of acetyl migration from position 3 to position 5 during the methylation.[13] Final confirmation of structure (V) was provided however, as will be described in detail in a subsequent paper, by synthesis from 5-*O*-acetyl-6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-methylene-D-glucitol and benzoic acid–trifluoroacetic anhydride.

Compound (V) could not be benzoylated very successfully with benzoyl chloride in pyridine at room temperature, but on being treated with benzoic acid–trifluoroacetic anhydride for 2 hr. at 60°, it afforded the 3-*O*-benzoyl derivative (IX) in good yield, the 2 : 4-methylene bridge (βC) remaining intact. This relative resistance to benzoylation is interesting. It is true that the 3-hydroxyl group is axial with respect to the acetal ring and that axial hydroxyl groups in *cyclo*hexane derivatives are difficult to esterify; [14] but this difficulty is usually attributed to steric hindrance by a pair of β-hydrogen atoms and this effect cannot be operative in a cyclic acetal since the β-positions are occupied by the ring oxygens.[15] Nevertheless, several compounds similar to (V), such as 2 : 4-*O*-benzylidene-xylitol [16] and 2 : 4-*O*-methylene-D-glucitol,[17] resist complete benzoylation, whereas the 2 : 4-*O*-methylene derivatives of ribitol [2] and D-talitol,[5] in which the 3-hydroxyl groups are

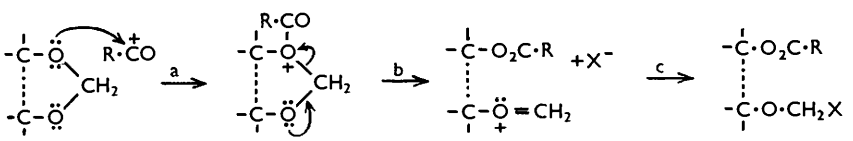
[6] Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942.
[7] Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, 1954, **76**, 3206.
[8] Randles, Tatlow, and Tedder, *J.*, 1954, 436.
[9] Bourne, Stacey, Tatlow, and Worrall, *ibid.*, p. 2006; Bourne, Tatlow, and Worrall, *J.*, 1957, **315**.
[10] Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367.
[11] Ness, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 2215.
[12] Cf. also Müller, *Ber.*, 1932, **65**, 1055.
[13] Cf. Haworth, Hirst, and Teece, *J.*, 1930, 1405; 1931, 2858.
[14] Eliel, *Experientia*, 1953, **9**, 91.
[15] Cf. Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 2.
[16] Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1946, **68**, 1769.
[17] Bourne and Wiggins, *J.*, 1944, 517.

equatorial, apparently do not. However, 2 : 4-*O*-methylenexylitol, in which the 3-hydroxyl group is axial, as in (V), can be fully benzoylated easily in high yield.[3] Clearly the ease of benzoylation of the 3-hydroxyl groups in these compounds is not determined solely by their axial or equatorial arrangements and other substituents on the acetal rings must play a part. Models reveal that if three large groups are present in positions 1, 5, and 6 of 2 : 4-*O*-methylene-D-glucitol access of reagents to position 3 is hindered. During benzoylation of 2 : 4-*O*-benzylidenexylitol, the benzylidene and 1 : 5-di-*O*-benzoyl groups together act in a similar way, but in the methylene analogue the two ester groups alone do not provide an adequate shield. Models also show that approach to the equatorial 3-position during benzoylation of the 2 : 4-*O*-methylene derivatives of ribitol and D-talitol is not blocked by ester groups introduced preferentially at the other positions. That compound (V) can be acetylated easily in pyridine at room temperature is probably due to the difference in size of the acetyl and benzoyl groups.

Reaction of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol with a nine-fold excess of an equimolecular mixture of benzoic acid and trifluoroacetic anhydride for 12 hr. at 25° (these conditions were chosen arbitrarily) afforded, after treatment with water, a 64% yield of a tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol identical with that prepared by Bourne and Wiggins [17] by Schotten–Baumann benzoylation of 2 : 4-*O*-methylene-D-glucitol. It seemed reasonable to assume that benzoic acid had reacted in the same way as acetic acid during fission of the βT-acetal ring and also that it was the 3-hydroxyl group which was resistant in the direct benzoylation of 2 : 4-*O*-methylene-D-glucitol; on both arguments the product was 1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (X). This was confirmed by acetylation when the product obtained was different from the 5-*O*-acetyl-1 : 3 : 6-tri-*O*-benzoyl derivative (IX) described above and must have been therefore 3-*O*-acetyl-1 : 5 : 6-tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (XI). The alkaline conditions used by Bourne and Wiggins [17] in the preparation of their compound (X) suggest that migration of benzoyl groups was extremely unlikely during its subsequent acetylation.

Prolonged treatment of the di-*O*-methylene compound (I) with acetic acid and trifluoracetic anhydride (24 hr. at 25°) did not result in much scission of the βC-ring since the mono-*O*-methylene product (V) was obtained as before, in only slightly diminished yield (92%). This conforms with earlier observations that βC-rings are, in general, far more stable than βT-rings. Nevertheless, it is remarkable that only the βT-ring of the acetal (I) should break and, further, that it should do so entirely in the one direction, and we advance the following explanation.

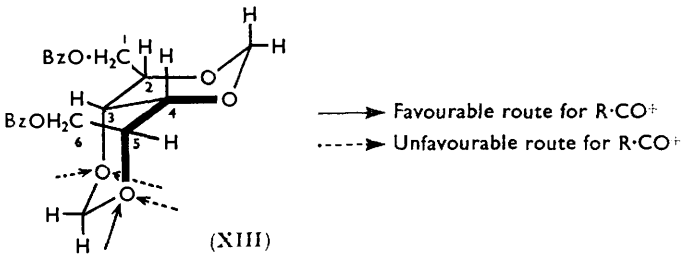
The βT-ring will presumably first form an oxonium complex with the $R{\cdot}CO^+$ ions which occur in acetolysis [cf. (a)]. Scission can then occur (b) in a manner similar to that suggested by Ingold [18] for the hydrolysis of simple acetals. The positive charge on the intermediate will be distributed between an oxonium and a carbonium cation, and will be neutralized (c) by the addition of X^- to give the final product. For example, with acetic



anhydride, acetic acid, and concentrated sulphuric acid, $R{\cdot}CO^+$ will be Ac^+, and X^- will be AcO^-. With an equimolecular mixture of a carboxylic acid and trifluoroacetic anhydride, the ions will be $R{\cdot}CO^+$ and $CF_3{\cdot}CO_2^-$. The unstable syrup formed initially in the reaction of the acetal (I) with acetic acid and trifluoroacetic anhydride was very probably 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-3-*O*-trifluoroacetoxymethyl-D-glucitol (XII), the trifluoroacetoxymethyl group of which would be extremely unstable.

[18] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953. p. 334.

The most favoured conformation (XIII) of the acetal (I) is analogous to that of *cis*-decalin and with the oxygens " inwards " (other conformations involve greater steric interactions). It is clear from Mills's arguments [15] that the 2 : 4-*O*-methylene ring (βC) should be relatively stable as it has the large CH_2·OBz group in an equatorial position, and that the 3 : 5-ring (βT) should be relatively unstable as the $-CH_2$·OBz group is axial here. The reason for the attack of R·CO^+ on the βT-ring at position 5, and not at 3, becomes apparent also, in the following manner: Oxonium ions are pyramidal [19] with bond angles of about 110° and so theoretically the R·CO^+ ion can bond with oxygen atoms at positions 3 and 5 in the normal equatorial or axial directions (see XIII). The two axial directions can be ruled out for the usual conformational reasons and the equatorial direction on the oxygen at 3 also, as there would be a considerable non-bonded interaction between the R·CO group and the CH_2·OBz group joined to position 2, in a similar manner to the well-known axial–axial 1 : 3-interaction of *cyclo*hexane conformational analysis. The only unhindered position left is the equatorial direction at the 5-oxygen, which would lead, after removal of the trifluoroacetoxymethyl group, to the formation of compound (V) or (X), only. This is also borne out by the use of atomic models, when it is possible to form an oxonium complex at oxygen 5 but not at oxygen 3. The possibility that a significant amount of ring scission had occurred by utilisation of the 3-oxygen atom, to give the 3-*O*-acetyl-5-*O*-trifluoroacetoxymethyl derivative, which by methanolysis afforded initially the 3-acetate and then, by migration, the 5-acetate (V), is therefore remote; moreover acyl groups which are prone to migrate have not been observed to do so during methanolysis.[20,21]



(XIII)

Another effect occurred when a 10 : 1 molar ratio of acetic acid to trifluoroacetic anhydride was used in reaction with the diacetal (I) for 12 hr. at 25°: this gave 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol [4] (II) in 90% yield. The following explanation is advanced. Here an equilibrium (3), additional to (1) and (2), becomes important. In (1) the equilibrium position is almost 100% to the right and in (3) about 80%, in the presence of excess of acetic acid.[9] The 10 : 1 mixture therefore consists essentially of a mixture of acetic acid and acetic anhydride in the presence of a strong acid, trifluoroacetic. This is the same as the Hudson acetolysis mixture save that the concentrated sulphuric acid is replaced by trifluoroacetic, and it reacts in the same way. It affords a useful experimental confirmation of the correctness of equation (3).

$$AcOH + CF_3{\cdot}CO{\cdot}OAc \rightleftharpoons Ac_2O + CF_3{\cdot}CO_2H \quad . . . . . (3)$$

It seems from the above results that mixtures of carboxylic acids and trifluoroacetic anhydride are likely to have wide application for the cleavage of cyclic acetals under mild conditions and often with a high degree of specificity. An important advantage over the usual methods of acetolysis is that trifluoroacetoxy-groups in the products can be removed with methanol alone, without detriment to other groups, whereas the removal of acetoxy-groups requires more drastic conditions, resulting in low overall yields.

[19] Walsh, *J.*, 1953, 2296; Ferriso and Hornig, *J. Chem. Phys.*, 1955, **23**, 1464.
[20] Bourne, Huggard, and Tatlow, *J.*, 1953, 735.
[21] Bourne, Stacey, Tatlow, and Tatlow, *J.*, 1951, 826.

Experimental

1 : 6-*Di*-O-*benzoyl*-2 : 4-3 : 5-*di*-O-*methylene*-D-*glucitol*.—Prepared by the method of Hann, Wolfe, and Hudson,[4] this compound had m. p. 159—160° and $[\alpha]_D^{14}$ +17·7° (*c* 2·31 in $CHCl_3$). These authors gave m. p. 158—159° and $[\alpha]_D$ +18·7° (in $CHCl_3$).

5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) A solution of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (0·50 g.) in trifluoroacetic anhydride (1·50 ml., 9 mol.) and glacial acetic acid (0·62 ml., 9 mol.) was kept at 25° for 3 hr. (constant rotation). Volatile material was then removed *in vacuo* and the residual syrup was co-distilled once with dry carbon tetrachloride. The product, presumably 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-3-*O*-trifluoroacetoxymethyl-D-glucitol, was a syrup, which decomposed very rapidly with evolution of formaldehyde. No attempt was made to purify this compound and it was refluxed *in situ* with dry methanol (15 ml.) for 1 hr. Evaporation of the methanol left a white wax which gave, on crystallization from ethanol, 5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·54 g.), m. p. 149—150°, $[\alpha]_D^{17}$ +4·2° (*c* 4·35 in $CHCl_3$) (Found: C, 62·1; H, 5·7%; N-alkali uptake, 6·89 ml./g. $C_{23}H_{24}O_9$ requires C, 62·2; H, 5·4%; N-alkali uptake, 6·76 ml./g.). Even after 24 hr. at 25° a 92% yield of this same product was obtained.

(*b*) The reaction mixture was prepared as in (*a*) but, after being kept at 25° for 3 hr., it was poured into sodium hydrogen carbonate solution. The solution was extracted with chloroform, and the extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue, recrystallized from ethanol, gave 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·50 g.), m. p. 149—150°, alone and on admixture with the product obtained in (*a*).

2 : 4-O-*Methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·20 g.) was dissolved in dry methanol (10 ml.) in which a small piece of sodium had been dissolved, and the solution was kept at room temperature for 14 hr. Evaporation of the methanol left a white solid, which, on recrystallization from ethanol, gave 2 : 4-*O*-methylene-D-glucitol (0·08 g.), m. p. and mixed m. p. 163—164°, $[\alpha]_D^{21}$ −9·9° (*c* 1·00 in H_2O) (Found: C, 43·4; H, 7·3. Calc. for $C_7H_{14}O_6$: C, 43·3; H, 7·3%). Ness *et al.*[3] gave m. p. 163—164° and $[\alpha]_D$ −9·8° (in H_2O).

Acetylation of 5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—This compound (0·40 g.), acetylated with acetic anhydride in pyridine, gave, after recrystallization from aqueous ethanol, 3 : 5-*di*-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·37 g.), m. p. 185°, $[\alpha]_D^{17}$ +9·6° (*c* 1·42 in acetone) (Found: C, 61·8; H, 5·5%; N-alkali uptake, 8·12 ml./g. $C_{25}H_{26}O_{10}$ requires C, 61·7; H, 5·4%; N-alkali uptake, 8·23 ml./g.).

1 : 6-*Di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—Benzoyl chloride (0·89 ml., 2 mol.) was added dropwise to an ice-cold solution of 2 : 4-*O*-methylene-D-glucitol (0·75 g.) {prepared by the method of Ness *et al.*[3] this compound had m. p. 163—164° and $[\alpha]_D^{17}$ −10·1° (*c* 2·10 in H_2O)} in dry pyridine (100 ml.) and the solution was kept at 0° for 15 min., and at room temperature for 3 hr. more before being poured into water. The precipitated solid recrystallized from ethanol, to give the 1 : 6-*dibenzoate* (0·62 g.), m. p. 155—156°, $[\alpha]_D^{15}$ +15·0° (*c* 2·14 in $CHCl_3$) (Found: C, 62·4; H, 5·2; Bz, 52·0. $C_{21}H_{22}O_8$ requires C, 62·7; H, 5·5; Bz, 52·2%).

Acetylation of 1 : 6-*Di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—This compound (0·30 g.), acetylated with acetic anhydride in pyridine, gave 3 : 5-di-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·33 g.), m. p. 185° (from ethanol) alone and on admixture with the specimen obtained previously.

3-O-*Acetoxymethyl*-5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) Prepared by the method of Hann, Wolfe, and Hudson [4] this compound had m. p. 125°, $[\alpha]_D^{22}$ +1·9° (*c* 2·18 in $CHCl_3$) (Found: C, 60·5; H, 5·3%; N-alkali uptake, 7·83 ml./g. Calc. for $C_{26}H_{28}O_{11}$: C, 60·5; H, 5·5%; N-alkali uptake, 7·75 ml./g.). These authors gave m. p. 115—116° and $[\alpha]_D^{20}$ +9·3° (in $CHCl_3$). (*b*) 1 : 6-Di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (0·50 g.) was dissolved in warm trifluoroacetic anhydride (1·50 ml., 9 mol.) and acetic acid (6·21 ml., 90 mol.) and the solution was kept at 25° for 12 hr. Volatile material was then removed *in vacuo*, and the residual solid recrystallized from ethanol, to give 3-*O*-acetoxymethyl-5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·56 g.), m. p. 125° [alone and on admixture with the compound obtained as in (*a*)], $[\alpha]_D^{19}$ +2·4° (*c* 2·34 in $CHCl_3$) (Found: C, 60·6; H, 5·3%; N-alkali uptake, 7·51 ml./g.).

Hydrolysis of 3-O-*Acetoxymethyl*-5-O-*acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—The compound (1·50 g.) was dissolved in 2N-hydrochloric acid (2·0 ml.) and ethanol (5 ml.),

refluxed for 15 min., then cooled quickly. The precipitate was filtered off, washed with water, and recrystallized four times from ethanol, to give 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·38 g.), m. p. 147—149°, alone and on admixture with the compound obtained previously.

5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-3-O-*methyl*-2 : 4-O-*methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (1·40 g.) was refluxed with silver oxide (5·0 g.) in methyl iodide (30 ml.) for 36 hr. The methyl iodide was removed and the residue extracted exhaustively with boiling chloroform. Evaporation of the filtered extracts left a syrup, which, when crystallized three times from ethanol, gave the 3-*methyl ether* (0·78 g.), m. p. 141—142°, depressed on admixture with the starting material, $[\alpha]_D^{19}$ +4·4° (*c* 1·54 in $CHCl_3$) (Found: C, 63·2; H, 5·7; OMe, 7·1%; N-alkali uptake, 6·45 ml./g. $C_{24}H_{26}O_9$ requires C, 62·9; H, 5·7; OMe, 6·8%; N-alkali uptake, 6·55 ml./g.).

3-O-*Methyl*-2 : 4-O-*methylene*-D-*glucitol*.—5-*O*-Acetyl-1 : 6-di-*O*-benzoyl-3-*O*-methyl-2 : 4-*O*-methylene-D-glucitol (0·40 g.) was kept in dry methanol (20 ml.), in which a small piece of sodium had been dissolved, at room temperature for 16 hr. Evaporation left a syrup which was sublimed at 150°/0·005 mm., to give a crystalline product. In a later experiment these crystals were used to seed the product from its solution in ethanol–ether, to give 3-O-*methyl*-2 : 4-O-*methylene*-D-*glucitol* (0·11 g.), m. p. 144°, depressed on admixture with the starting material, $[\alpha]_D^{21}$ −3·3° (*c* 2·70 in H_2O) (Found: C, 46·3; H, 7·4; OMe, 15·2. $C_8H_{16}O_6$ requires C, 46·2; H, 7·7; OMe, 14·9%).

Periodate oxidation by Reeves's method [22] showed that, after 20 min., 1 hr., and 17 hr., 1 mole of this compound had consumed 0·91, 0·97, and 1·04 moles of sodium periodate, respectively, and after 17 hr. had liberated 0·92 mole of formaldehyde, isolated as its dimedone derivative, m. p. and mixed m. p. 188°.

Benzoylation of 5-O-*Acetyl*-1 : 6-*di*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—(*a*) Attempted benzoylation with benzoyl chloride in pyridine was unsuccessful; the starting material was recovered in 80% yield together with a small amount of crystals with m. p. 141—142°, depressed on admixture with the starting material. (*b*) A solution of 5-*O*-acetyl-1 : 6-di-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·18 g.) and benzoic acid (0·074 g., 1·50 mol.) in trifluoroacetic anhydride (0·084 ml., 1·50 mol.) and trifluoroacetic acid (0·20 ml.) was kept at 60° for 2 hr., poured into aqueous sodium hydrogen carbonate, and extracted with chloroform. The extracts were dried ($MgSO_4$) and evaporated to a syrup, which was twice crystallized from aqueous ethanol, to give 5-O-*acetyl*-1 : 3 : 6-*tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol* (0·15 g.), m. p. 142—142·5°, alone and on admixture with the compound obtained as in (*a*), depressed on admixture with the starting material, $[\alpha]_D^{17}$ −18·8° (*c* 1·60 in $CHCl_3$) (Found: C, 65·7; H, 5·1%; N-alkali uptake, 7·37 ml./g. $C_{30}H_{28}O_{10}$ requires C, 65·7; H, 5·1%; N-alkali uptake, 7·30 ml./g.).

1 : 5 : 6-*Tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—A solution of 1 : 6-di-*O*-benzoyl-2 : 4-3 : 5-di-*O*-methylene-D-glucitol (1·00 g.) and benzoic acid (2·65 g., 9 mol.) in trifluoroacetic anhydride (3·00 ml., 9 mol.) was kept at 25° for 12 hr., poured into aqueous sodium hydrogen carbonate, and extracted with chloroform. Evaporation of the dried ($MgSO_4$) extracts left a solid, which recrystallized from aqueous ethanol to give the 1 : 5 : 6-tribenzoate (0·78 g.), m. p. 154—154·5°, alone and on admixture with the tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol obtained by Bourne and Wiggins,[17] $[\alpha]_D^{15}$ −9·3° (*c* 3·33 in $CHCl_3$) (Found: C, 66·5; H, 4·9; Bz, 62·7. Calc. for $C_{28}H_{26}O_9$: C, 66·4; H, 5·2; Bz, 62·25%). Bourne and Wiggins gave m. p. 154° and $[\alpha]_D$ −10·0° (in $CHCl_3$).

3-O-*Acetyl*-1 : 5 : 6-*tri*-O-*benzoyl*-2 : 4-O-*methylene*-D-*glucitol*.—1 : 5 : 6-Tri-*O*-benzoyl-2 : 4-*O*-methylene-D-glucitol (0·40 g.) with acetic anhydride in pyridine gave the 3-*acetate*, needles (from ethanol) (0·44 g.), m. p. 107° (depressed on admixture with the 5-acetate obtained previously), $[\alpha]_D^{17}$ −12·8° (*c* 4·91 in $CHCl_3$) (Found: C, 65·7; H, 4·9%; N-alkali uptake 7·27 ml./g. $C_{30}H_{28}O_{10}$ requires C, 65·7; H, 5·1%; N-alkali uptake 7·30 ml./g.).

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