615. *Aspects of Stereochemistry. Part XX.*[1] *Reaction of 3-O-Methyl-D-glucitol with Acetone and Benzaldehyde*[2]

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Acetonation of 3-*O*-methyl-D-glucitol gives, in addition to the expected 1,2:5,6-di-*O*-isopropylidene derivative, a small amount of the 2,4:5,6-compound. On benzylidenation, 3-*O*-methyl-D-glucitol affords, in addition to 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol, two 2,4:5,6-di-*O*-benzylidene derivatives which differ only in the arrangement of the substituents at the acetal carbon atom in the 5,6-*O*-benzylidene group. Evidence supporting these structural assignments is presented.

Acid-catalysed acetonation of 3-*O*-methyl-D-glucitol gives the expected[3] 1,2:5,6-di-*O*-isopropylidene derivative (I) in good yield.[4] However, when light petroleum (b. p. 40—60°) was used for recrystallisation of the crude product, a second di-*O*-isopropylidene derivative {*B*, m. p. 136°, $[\alpha]_D$ +13·5° in chloroform, cf. m. p. 56°, $[\alpha]_D$ −21° in chloroform for the pure 1,2:5,6-di-*O*-isopropylidene derivative (*A*)} of low solubility was detected. Fractionation on silica gel of the crude product from an acetonation catalysed by sulphuric acid revealed the presence of *ca.* 10% of isomer *B*. The substantial difference in structure of isomers *A* and *B* indicated by the optical rotations was confirmed by the absorption patterns in the hydroxyl stretching region of the infrared for *ca.* 0·005M-solutions of isomers

[1] Part XIX, preceding Paper.
[2] Preliminary report of some of these results: N. Baggett, K. W. Buck, A. B. Foster, M. H. Randall, and J. M. Webber, *Proc. Chem. Soc.*, 1964, 118.
[3] J. A. Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[4] M. A. Bukhari, A. B. Foster, J. Lehmann, M. H. Randall, and J. M. Webber, *J.*, 1963, 4167.

A and *B* in carbon tetrachloride. Under these conditions intermolecular hydrogen bonding is precluded and the relevant absorptions may be assigned to free and intramolecularly bonded hydroxyl groups.[5,6] Thus, 1,2:5,6-di-*O*-isopropylidene-3-*O*-methyl-D-glucitol (*A*) had a single band at 3566 cm.$^{-1}$ (ε 50) for bonded secondary hydroxyl groups (cf. absorption at *ca.* 3629 cm.$^{-1}$ for free secondary hydroxyl groups) whereas isomer *B* had absorptions at 3648 (ε 27), 3612 (ε 44, Δν 36), and *ca.* 3546 cm.$^{-1}$ (ε 7, Δν 102). The absorption at 3648 cm.$^{-1}$ is characteristic of free primary hydroxyl groups, and the position and intensities of the first two absorptions are characteristic of the grouping CH(OR)·CH_2·OH [cf. 1,2-*O*-isopropylideneglycerol,[7] which has bands at 3647 (ε 25) and 3608 cm.$^{-1}$ (ε 49, Δν 39)].

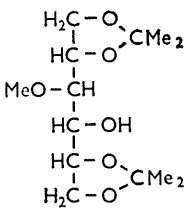
The presence of a free primary hydroxyl group in isomer *B* limits the structure to two reasonable possibilities involving 2,4:5,6- and 1,2:4,5-distributions of the cyclic ketals; the former has βC- and α-ketals (using Barker and Bourne's terminology [8]), and the latter α- and αC-ketals. Apparently, no example has been recorded of the formation of isolated αC- or βC-isopropylidene derivatives by direct reaction of acyclic polyhydric alcohols with acetone, although simple *erythro*-vicinal [9] and 1,3-diols [10] can be acetonated, and αC-isopropylidene derivatives of polyhydric alcohols can be obtained indirectly.[1] That isomer *B* was a 2,4:5,6-di-*O*-isopropylidene derivative of 3-*O*-methyl-D-glucitol was established by applying the reaction sequence methylation, acidic hydrolysis, periodate oxidation, borohydride reduction, and *p*-phenylazobenzoylation. Although the intermediate stages gave syrups, the final product was crystalline and identical with 1,3-di-*O*-methyl-2,4-di-*O*-*p*-phenylazobenzoyl-L-threitol (III). The authentic di-ester (III) was prepared by conversion of 1,3-*O*-benzylidene-L-threitol [11] into the crystalline 2,4-di-*O*-methyl ether followed by acidic hydrolysis and *p*-phenylazobenzoylation. The formation of 1,3-di-*O*-methyl-L-threitol from isomer *B* in the above reaction sequence requires the presence of a free hydroxyl group at position 1, and, for other than a 2,4:5,6-distribution of the ketal groups, the formation of seven-membered or larger rings. Thus, isomer *B* may be confidently assigned the structure (II). 2,4:5,6-Di-*O*-isopropylidene-3-*O*-methyl-D-glucitol is the first example of a six-membered isopropylidene derivative formed from an acyclic polyhydric alcohol although such compounds are formed from certain cyclic polyhydric alcohols.[12] The compound described by Valentin and Tomkuljak as 1,3-*O*-isopropylidene-2,4,5-tri-*O*-benzoylxylitol [13] is, in fact, a 2,3-*O*-isopropylidene derivative.[1]

The formation of a six-membered isopropylidene compound when other alternatives are precluded is exemplified by the ready conversion of 1,3,5,6-tetra-*O*-methyl-D-glucitol into the 2,4-*O*-isopropylidene derivative on acetonation catalysed by copper sulphate and sulphuric acid. 1,3,5,6-Tetra-*O*-methyl-D-glucitol is readily obtained by methylation of 2,4-*O*-benzylidene-D-glucitol followed by acidic hydrolysis.

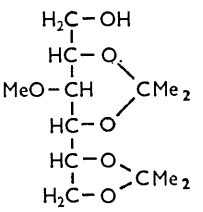
In seeking compounds for comparison with 2,4:5,6-di-*O*-isopropylidene-3-*O*-methyl-D-glucitol the reaction of 3-*O*-methyl-D-glucitol with benzaldehyde was examined since the expected [3] product was the 2,4:5,6-di-*O*-benzylidene derivative. When the reaction was catalysed with zinc chloride a crude product was obtained which, fortuitously, was fractionated readily to give two di-*O*-benzylidene derivatives, *C* (m. p. 143—144°, $[\alpha]_D$ +26·5° in chloroform) and *D* (m. p. 112—116°, $[\alpha]_D$ +25° in chloroform). The pattern of

[5] L. P. Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[6] A. B. Foster, A. H. Haines, and M. Stacey, *Tetrahedron*, 1961, **16**, 177.
[7] J. S. Brimacombe, A. B. Foster, and A. H. Haines, *J.*, 1960, 2582.
[8] S. A. Barker and E. J. Bourne, *J.*, 1952, 905.
[9] P. H. Hermans, *Z. phys. Chem.*, 1924, **113**, 337.
[10] W. E. Conrad, B. D. Gesner, L. A. Levasseur, R. F. Murphy, and H. M. Conrad, *J. Org. Chem.*, 1961, **26**, 3571.
[11] A. B. Foster, A. H. Haines, J. Homer, J. Lehmann, and L. F. Thomas, *J.*, 1961, 5005.
[12] A. N. Anikeeva and S. N. Danilov, *Zhur. obshchei Khim.*, 1962, **32**, 2498; J. K. N. Jones, *Canad. J. Chem.*, 1956, **34**, 840; see also preceding Paper (Part XIX).
[13] F. Valentin and D. Tomkuljak, *Chem. Zvesti*, 1949, **3**, 146.

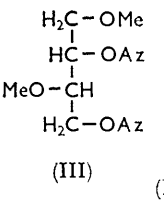
benzyl proton signals in the n.m.r. spectrum of the crude product (see following Paper) indicated it to be essentially an equimolar mixture of isomers *C* and *D*. The combined yield of isomers *C* and *D* was not high, and further examination of the reaction mixture gave 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol the structure of which was established when methylation gave a product identical with 2,4-*O*-benzylidene-1,3,5,6-tetra-*O*-methyl-D-glucitol obtained by methylation of 2,4-*O*-benzylidene-D-glucitol.[14] The conditions of reaction between 3-*O*-methyl-D-glucitol and benzaldehyde could be modified to give substantial amounts of the mono-*O*-benzylidene derivative.



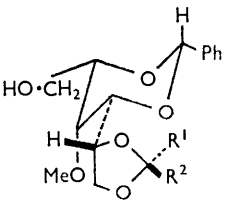
(I)



(II)



(III)



(IV) $R^1 = H, R^2 = Ph$ (Isomer *C*)

(V) $R^1 = Ph, R^2 = H$ (Isomer *D*)

(Az = $CO \cdot C_6H_4 \cdot N{:}NPh$)

The similar optical rotations of isomers *C* and *D* suggested structural similarity, and that each isomer contained a free primary hydroxyl group was established when reduction of the respective, crystalline, toluene-*p*-sulphonates with lithium aluminium hydride gave deoxy-derivatives.[15] The location of the free hydroxyl group at position 1 in each case was proved by the formation of 1,3-di-*O*-methyl-2,4-di-*O*-*p*-phenylazobenzoyl-L-threitol (III) when isomers *C* and *D* were separately subjected to the methylation and degradation sequence described above for 2,4:5,6-di-*O*-isopropylidene-3-*O*-methyl-D-glucitol; isomer *C* gave a crystalline di-*O*-methyl derivative. Thus, isomers *C* and *D* are 2,4,5,6-di-*O*-benzylidene-3-*O*-methyl-D-glucitol derivatives. Consideration of the thermodynamic stability of the various possible structures [3] leads to only one reasonable distribution of the benzylidene groups, involving the 2,4:5,6-positions with the two possible orientations of the substituents at the 5,6-acetal carbon atom. Confirmation of this view was provided by graded acidic hydrolysis of isomer *D* using toluene-*p*-sulphonic acid in aqueous dioxan at *ca.* 30°, which afforded 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol.

The n.m.r. spectroscopic data cited in the following Paper and the arguments based thereon permit the assignment of structures (IV) and (V), respectively, to isomers *C* and *D*.

Rice and Johnson [16] characterised 3-*O*-methyl-D-glucitol as a di-*O*-benzylidene derivative whose physical constants (m. p. 130—131°, $[\alpha]_D$ +25° in chloroform) indicate it to be a mixture of isomers *C* and *D*.

The close structural similarity between the 2,4:5,6-di-*O*-isopropylidene and 2,4:5,6-di-*O*-benzylidene derivatives, *C* and *D*, of 3-*O*-methyl-D-glucitol, and the product of copper sulphate-catalysed acetonation of 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol (presumably the 5,6-*O*-isopropylidene derivative) is emphasised by the data in the Table which concerns

Infrared spectral data * for some cyclic acetals and ketals of 3-*O*-methyl-D-glucitol

	$\nu_{max.}$ ($cm.^{-1}$) (ε)		
Derivative	Free OH	Bonded OH	
2,4:5,6-Di-*O*-isopropylidene	3648(27)	3612(44)	3546(7)
2,4:5,6-Di-*O*-benzylidene (*C*)	3642(58)	3610(72)	3540(8)
2,4:5,6-Di-*O*-benzylidene (*D*)	3642(45)	3610(62)	3540(8)
2,4-*O*-Benzylidene-5,6-*O*-isopropylidene	3643(49)	3612(64)	3546(11)

* Determined on *ca.* 0·005M-solutions in carbon tetrachloride.

[14] S. J. Angyal and J. V. Lawler, *J. Amer. Chem. Soc.*, 1944, **66**, 837.
[15] R. S. Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 107.
[16] F. A. H. Rice and A. R. Johnson, *J. Amer. Chem. Soc.*, 1959, **81**, 4419.

the infrared absorptions in the hydroxyl stretching region for *ca.* 0·005M-solutions in carbon tetrachloride. The absorptions at 3642—3648 cm.$^{-1}$ may be assigned to free primary hydroxyl groups. The $\Delta\nu$ values (31—36) of the absorptions at 3610—3612 cm.$^{-1}$ indicate [6] intramolecular hydrogen bonds involving five-membered rings, *i.e.*, the system C(1)·OH · · · O(2). Likewise, the $\Delta\nu$ values (97—102) of the weak absorptions at *ca.* 3540 cm.$^{-1}$ reflect hydrogen bonds involving six-membered rings, *i.e.*, the system C(1)·OH · · · O(3)Me. A related pattern of hydrogen bonding is shown by 1,3-*O*-benzylidene-L-threitol which has been discussed in detail elsewhere.[17]

Experimental

Thin-layer chromatography was performed on silica gel and detection effected separately with iodine vapour and vanillin–sulphuric acid.[18] Where specified, organic solvents were dried with $MgSO_4$. Light petroleum refers to the fraction of b. p. 60—80° unless stated otherwise. Optical rotations at 5461 Å were determined on 1- or 2-cm. layers using a Bendix-Ericsson type 143A polarimeter.

Reaction of 3-O-*Methyl*-D-*glucitol with Acetone*.—A mixture of 3-*O*-methyl-D-glucitol (8·4 g., $[\alpha]_D$ +7·7° in H_2O, prepared by the reduction of 3-*O*-methyl-D-glucose [19] with sodium borohydride), acetone (200 ml.), and conc. sulphuric acid (3 ml.) was shaken overnight at room temperature, neutralised with potassium carbonate, filtered, and concentrated. The residue was repeatedly extracted with chloroform, and the combined extracts were washed with water, dried, and evaporated. Crystallisation of the product from light petroleum (b. p. 40—60°) yielded a mixture of *di*-O-*isopropylidene derivatives* (8·6 g., 72%), m. p. 57—58°, $[\alpha]_D$ −18° (*c* 1·1 in $CHCl_3$) (Found: C, 56·4; H, 8·7. $C_{13}H_{24}O_6$ requires C, 56·5; H, 8·7%). Examination of the product by thin-layer chromatography using benzene–methanol (9 : 1) revealed components with R_F *ca.* 0·5 and 0·25.

A solution of the foregoing mixture (3 g.) in the minimum volume of ether was added to a column (46 × 4 cm.) of silica gel (Davison), and the column was eluted with the same solvent. Fraction 1 (900 ml.) contained 1,2:5,6-di-*O*-isopropylidene-3-*O*-methyl-D-glucitol (2·68 g.), m. p. 56° [from light petroleum (b. p. 40—60°)], $[\alpha]_D$ −21° (*c* 2·7 in $CHCl_3$). It is probable that the previously described [4] 1,2:5,6-di-*O*-isopropylidene derivative was slightly impure, but it gave a pure methanesulphonate identical with that (m. p. 117—118°, $[\alpha]_D$ +13° in $CHCl_3$) prepared from the above product in the usual manner. Fraction 2 (200 ml.) contained a negligible amount of material, and fraction 3 (*ca.* 1 l.) contained 2,4:5,6-*di*-O-*isopropylidene*-3-O-*methyl*-D-*glucitol* (0·3 g.), m. p. 136° (from light petroleum), $[\alpha]_D$ +13·5° (*c* 1·6 in $CHCl_3$) (Found: C, 56·3; H, 8·35%).

Benzylidenation of 3-O-*Methyl*-D-*glucitol*.—A mixture of 3-*O*-methyl-D-glucitol (3·45 g.), benzaldehyde (10 ml.), and zinc chloride (3 g.; dried at 120° for 6 hr.) was shaken at room temperature overnight and poured into a well-stirred mixture of water and light petroleum. Insoluble material was collected, washed with light petroleum, and dissolved in chloroform. The solution was washed with aqueous sodium hydrogen carbonate and water, dried, and concentrated, to give a mixture of di-*O*-benzylidene-3-*O*-methyl-D-glucitol derivatives (1·35 g., 20·5%). A solution of this product in hot benzene (*ca.* 20 ml.) was filtered, treated with an equal volume of boiling light petroleum, and stored at 0° for 2 hr. The resultant precipitate (0·54 g.) was recrystallised from benzene–light petroleum, to give 2,4:5,6-*di*-O-*benzylidene*-3-O-*methyl*-D-*glucitol*-C (0·28 g., 4·3%), m. p. 143—144°, $[\alpha]_D$ +26·5° (*c* 0·98 in $CHCl_3$) (Found: C, 68·0; H, 6·7. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5%).

Storage of the mother-liquors at 0° overnight gave a second fraction (0·5 g.) which, after recrystallisation from benzene–light petroleum, gave 2,4:5,6-*di*-O-*benzylidene*-3-O-*methyl*-D-*glucitol*-D (0·37 g., 5·6%), m. p. 112—116°, $[\alpha]_D$ +25° (*c* 2·16 in $CHCl_3$) (Found: C, 67·7; H, 6·7%).

The isomers *C* and *D* could also be separated by fractional crystallisation from benzene, and they showed distinct differences in the infrared spectra in the region 650—800 cm.$^{-1}$: *C* had bands at *ca.* 685, 737, and 743, and *D* at *ca.* 662, 700, 733, 758, and 766.

[17] S. A. Barker, A. B. Foster, A. H. Haines, J. Lehmann, J. M. Webber, and G. Zweifel, *J.*, 1963, 4161.
[18] "Chromatography," E. Merck AG, Darmstadt, 2nd edn., p. 30.
[19] W. L. Glen, G. S. Myers, and G. A. Grant, *J.*, 1951, 2568.

Conversion of 2,4:5,6-*Di*-O-*benzylidene*-3-O-*methyl*-D-*glucitol*-C *and* -D *into* 1,3-*Di*-O-*methyl*-2,4-*di*-O-p-*phenylazobenzoyl*-L-*threitol*.—To a solution of isomer *D* (1·7 g.; m. p. 109—112°) in dimethylformamide (15 ml.) was added methyl iodide (4 ml.) and silver oxide (4 g.; gradually during 3 hr.). After shaking overnight, the mixture was filtered, and the solid was washed well with chloroform. The combined filtrate and washings were washed with water (5 × 100 ml.), dried, and concentrated. A solution of the resultant oil (1·6 g.) in benzene was added to a column (1 × 40 cm.) of neutral alumina. Elution with benzene–ether (1 : 1) gave syrupy 2,4:5,6-di-*O*-benzylidene-1,3-di-*O*-methyl-D-glucitol-*D* (1·59 g., 91%) which appeared homogeneous on examination by thin-layer chromatography using benzene–ether (1 : 1) (R_F *ca.* 0·8; cf. *ca.* 0·4 for starting material).

A solution of the foregoing product (1·59 g.) in acetone (*ca.* 2 ml.) was hydrolysed with 0·05M-sulphuric acid at 100° for 5 hr. The cooled solution was extracted with light petroleum, de-acidified with Amberlite IRA-400 (OH^- form), and concentrated, to yield syrupy 1,3-di-*O*-methyl-D-glucitol (0·67 g., 75%). A solution of this product, sodium hydrogen carbonate (0·3 g.), and sodium metaperiodate (1·4 g.) in water (75 ml.) was stored for 3 hr. at room temperature and extracted continuously with chloroform overnight. Concentration of the extract afforded syrupy 1,3-di-*O*-methyl-L-threitol (0·44 g., 91%). Treatment of the diol (0·25 g.) with pyridine (4 ml.) and *p*-phenylazobenzoyl chloride (1 g.) at 100° for 4 hr., then at 37° overnight, followed by isolation of the product by the standard procedure,[20] gave 1,3-*di*-O-*methyl*-2,4-O-p-*phenylazobenzoyl*-L-*threitol* (0·67 g., 71%), m. p. 112·5—113° (from ethanol), $[\alpha]_{5461}$ +226° (*c* 0·2 in $CHCl_3$) (Found: C, 67·7; H, 5·1; N, 9·95. $C_{32}H_{30}N_4O_6$ requires C, 67·8; H, 5·3; N, 9·9%).

When isomer *C* was submitted to the above reaction sequence it afforded, initially, 2,4:5,6-*di*-O-*benzylidene*-1,3-*di*-O-*methyl*-D-*glucitol*-C (65%), m. p. 97° (from light petroleum), $[\alpha]_D$ +35° (*c* 2·1 in $CHCl_3$) (Found: C, 68·3; H, 6·7. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·8%), and finally a di-*O*-*p*-phenylazobenzoate, m. p. 112° alone or in admixture with the product described above, $[\alpha]_{5461}$ +225° (*c* 0·2 in $CHCl_3$); the infrared spectra (KBr discs) of the two esters were indistinguishable.

When 2,4:5,6-di-*O*-isopropylidene-3-*O*-methyl-D-glucitol was subjected to the above sequence of reactions it also gave 1,3-di-*O*-methyl-2,4-di-*O*-*p*-phenylazobenzoyl-L-threitol, m. p. 113—113·5° and mixed m. p. 112·5—113° with the above esters, $[\alpha]_{5461}$ +229° (*c* 0·19 in $CHCl_3$); the infrared spectrum (KBr disc) was also indistinguishable from those of the above esters.

Authentic 1,3-*Di*-O-*methyl*-2,4-*di*-O-p-*phenylazobenzoyl*-L-*threitol*.—A solution of 1,3-*O*-benzylidene-L-threitol[11] (1 g., m. p. 133°) in dimethylformamide (20 ml.) was treated with methyl iodide (7 ml.) and silver oxide (12 g.) as described above, to give 1,3-O-*benzylidene*-2,4-*di*-O-*methyl*-L-*threitol* (0·66 g., 58%), m. p. 65° (from light petroleum), $[\alpha]_D$ +53° (*c* 1·3 in $CHCl_3$) (Found: C, 65·8; H, 7·45. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%).

The foregoing dimethyl ether (0·22 g.) was hydrolysed with 0·05M-sulphuric acid (20 ml.) at 100° for 4 hr. The cooled hydrolysate was extracted with light petroleum (3 × 75 ml.), neutralised with sodium hydrogen carbonate, and continuously extracted with chloroform overnight. Concentration of the dried extract gave syrupy 1,3-di-*O*-methyl-L-threitol (0·12 g., 86%) which was *p*-phenylazobenzoylated as described above, to give 1,3-di-*O*-methyl-2,4-di-*O*-*p*-phenylazobenzoyl-L-threitol (0·32 g., 74%), m. p. 112—113° (from ethanol), $[\alpha]_{5461}$ +230° (*c* 0·2 in $CHCl_3$). The di-ester was identical with the di-esters described above.

Conversion of the Isomeric 2,4:5,6-*Di*-O-*benzylidene*-3-O-*methyl*-D-*glucitol Derivatives into* 1-*Deoxy-derivatives*.—A solution of isomer *D* (0·5 g.; m. p. 109—112°) and toluene-*p*-sulphonyl chloride (0·36 g.) in pyridine (4 ml.) was stored overnight at room temperature. A small amount of water was added to the mixture which was then poured into aqueous sodium hydrogen carbonate. The precipitate was collected and washed with water. Its solution in chloroform was then washed with aqueous sodium hydrogen carbonate and water, and dried. Concentration of the solution and crystallisation of the residue (0·64 g.) from ethanol gave 2,4:5,6-*di*-O-*benzylidene*-1-O-*toluene*-p-*sulphonyl*-D-*glucitol*-D (0·37 g., 52·9%), m. p. 117—119°, $[\alpha]_D$ +22° (*c* 1·1 in $CHCl_3$) (Found: C, 63·6; H, 5·8; S, 5·9. $C_{28}H_{30}O_8S$ requires C, 63·9; H, 5·7; S, 6·1%).

Lithium aluminium hydride (0·3 g.) was added to a solution of the foregoing toluene-*p*-sulphonate (0·3 g.) in ether (30 ml.), and the stirred mixture was boiled under reflux for 12 hr.

[20] N. Baggett, A. B. Foster, A. H. Haines, and M. Stacey, *J.*, 1960, 3528.

Excess of reductant in the cooled mixture was destroyed with ethyl acetate, and the alcoholates with water. Insoluble material was collected and washed well with ether, and the combined filtrate and washings were washed with water. Concentration of the dried solution and elution of the residue (0·22 g.) from a column (22 × 1 cm.) of neutral alumina with benzene–ether (1 : 1; 200 ml.) gave 2,4:5,6-*di*-O-*benzylidene*-1-*deoxy*-3-O-*methyl*-D-*glucitol*-D (50 mg.), m. p. 80—82° (from light petroleum), $[\alpha]_{5461}$ +52° (*c* 0·3 in $CHCl_3$) (Found: C, 70·8; H, 6·6. $C_{21}H_{24}O_5$ requires C, 70·8; H, 6·8%).

Using essentially the above methods, 2,4:5,6-di-*O*-benzylidene-3-*O*-methyl-D-glucitol-*C* (m. p. 139—140°) was converted into the *toluene*-p-*sulphonate*-C (55%), m. p. 99—100° (from ethanol), $[\alpha]_D$ +34° (*c* 1·18 in $CHCl_3$) (Found: C, 64·1; H, 6·0; S, 6·1%), and thence into 2,4:5,6-*di*-O-*benzylidene*-1-*deoxy*-3-O-*methyl*-D-*glucitol*-C (14%), m. p. 111° (from light petroleum), $[\alpha]_{5461}$ +23° (*c* 0·11 in $CHCl_3$) (Found: C, 70·5; H, 6·7%).

2,4-O-*Benzylidene*-3-O-*methyl*-D-*glucitol*.—(*a*) A mixture of 3-*O*-methyl-D-glucitol (4·23 g.), benzaldehyde (10 ml.), and zinc chloride (5 g.) was shaken at room temperature for 36 hr., and poured into a well stirred mixture of water and light petroleum. The precipitated di-*O*-benzylidene derivatives (3·16 g.) were removed, and the aqueous layer of the filtrate was continuously extracted with chloroform for 4 days. Concentration of the extract and recrystallisation of the residue from chloroform gave 2,4-O-*benzylidene*-3-O-*methyl*-D-*glucitol* (0·39 g.), m. p. 165—166°, $[\alpha]_D$ +17° (*c* 1·4 in MeOH) (Found: C, 59·4; H, 7·2. $C_{14}H_{20}O_6$ requires C, 59·2; H, 7·0%).

(*b*) A mixture of 3-*O*-methyl-D-glucitol (2 g.), benzaldehyde (3 ml.), zinc chloride (2·5 g.), and conc. hydrochloric acid (2 ml.) was shaken at room temperature for 24 hr. and then poured into dilute ammonia. The mixture was extracted with chloroform (3 × 100 ml.) to remove di-*O*-benzylidene derivatives and other, unidentified material, and then continuously extracted with the same solvent for 3 days. Concentration of the extract gave 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol (2·1 g., 75%), m. p. 167°, after three recrystallisations from chloroform.

2,4-O-*Benzylidene*-1,3,5,6-*tetra*-O-*methyl*-D-*glucitol*.—A mixture of 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol (0·1 g.), dimethylformamide (3 ml.), methyl iodide (2 ml.), and silver oxide (3 g.) was shaken overnight at room temperature. After dilution with dimethylformamide the mixture was filtered and the insoluble material washed well with chloroform. The combined filtrate and washings were washed with water (5 × 100 ml.), dried, and concentrated. Recrystallisation of the residue from light petroleum gave the tetra-*O*-methyl ether (70 mg., 58%), m. p. 84°. The product was identical (mixed m. p. and infrared spectra) with that obtained by methylation of 2,4-*O*-benzylidene-D-glucitol.[14]

2,4-O-*Isopropylidene*-1,3,5,6-*tetra*-O-*methyl*-D-*glucitol*.—A mixture of 2,4-*O*-benzylidene-1,3,5,6-tetra-*O*-methyl-D-glucitol (0·3 g.), ethanol (2 ml.), and 0·05M-sulphuric acid (25 ml.) was kept at 100° for 3·5 hr. The cooled solution was extracted with light petroleum, neutralised with barium carbonate, and then continuously extracted with chloroform overnight. Concentration of the dried extract and distillation of the residue gave 1,3,5,6-tetra-*O*-methyl-D-glucitol (0·16 g., 74%), b. p. 130—140°/0·1 mm., which appeared homogeneous (R_F 0·2) on thin-layer chromatography using benzene–methanol (9 : 1).

A mixture of the foregoing diol (0·14 g.), acetone (25 ml.), anhydrous copper sulphate (1·5 g.), and conc. sulphuric acid (0·5 ml.) was shaken overnight at room temperature. The mixture was neutralised with potassium carbonate and the insoluble material collected and washed well with acetone. Concentration of the combined filtrate and washings gave a product which had $\nu_{max.}$ *ca.* 3500 (OH) and 1725 $cm.^{-1}$ (C=O). The product was eluted from a column (1·3 × 20 cm.) of neutral alumina with ether (150 ml.) after a preliminary washing with benzene (75 ml.), to give 2,4-O-*isopropylidene*-1,3,5,6-*tetra*-O-*methyl*-D-*glucitol* (85 mg.), b. p. 120—130°/0·1 mm. (Found: C, 56·5; H, 9·5. $C_{13}H_{26}O_6$ requires C, 56·1; H, 9·4%). The product had no infrared bands for OH or C=O and appeared homogeneous (R_F 0·6) in thin-layer chromatography using benzene–methanol (9 : 1).

Isopropylidenation of 2,4-O-*Benzylidene*-3-O-*methyl*-D-*glucitol*.—A mixture of the title compound (0·25 g.), acetone (30 ml.), and anhydrous copper sulphate (2 g.) was shaken overnight at room temperature. Insoluble material was collected and washed well with acetone, and the combined filtrate and washings were concentrated. Recrystallisation of the residue (0·24 g.) from light petroleum gave 2,4-O-*benzylidene*-5,6-O-*isopropylidene*-3-O-*methyl*-D-*glucitol* (0·12 g., 43%), m. p. 108°, $[\alpha]_{5461}$ +17·7° (*c* 1·2 in $CHCl_3$) (Found: C, 62·9; H, 7·7. $C_{17}H_{24}O_6$ requires C, 62·95; H, 7·5%).

Graded Acidic Hydrolysis of 2,4:5,6-*Di*-O-*benzylidene*-3-O-*methyl*-D-*glucitol* (m. p. 112—116°). —The title compound (49 mg.) was dissolved in a portion (1 ml.) of a mixture prepared from toluene-*p*-sulphonic acid (48 mg.), dioxan (4·5 ml.), and water (0·5 ml.), and the hydrolysis was followed at *ca.* 30° using a Varian A60 n.m.r. spectrometer. The solution had benzyl proton signals initially at τ 4·40 and 4·59, and finally a single signal at 4·63 after 18 hr. The mixture was poured into excess of aqueous sodium hydrogen carbonate and extracted with chloroform (3 × 50 ml.) and then overnight with the same solvent containing a trace of ammonia to prevent acetal hydrolysis. The latter extract was concentrated, and the residue (37 mg.) was recrystallised from chloroform, to yield 2,4-*O*-benzylidene-3-*O*-methyl-D-glucitol (12 mg.), m. p. 164° alone or in admixture with the authentic compound described above; the infrared spectra (KBr discs) of the two compounds were indistinguishable.

Infrared Spectra.—Spectra in the hydroxyl stretching region were determined essentially as previously described.[6]

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