614. *Aspects of Stereochemistry. Part XIX.[1] Isopropylidene Derivatives of Some Polyhydric Alcohols. Observations on the Hydrolytic Behaviour and Migration of Cyclic Ketals*

By N. Baggett, K. W. Buck, A. B. Foster, R. Jefferis, B. H. Rees, and
J. M. Webber

A correlation between the steric environment and the n.m.r. signals for the Me protons of the ketal groups in a series of O-isopropylidene carbohydrate derivatives is utilised in following the course of graded acidic hydrolysis of the acetone groups. Evidence is presented which indicates that ketal migration does not occur to a significant extent under hydrolysing conditions.

Acetonation of xylitol under various conditions of catalysis affords mixtures of two di-O-isopropylidene derivatives. The pure isomers have been isolated and shown to be the 1,2:4,5- and 1,2:3,4-diketals.

AN important method in the structural determination of cyclic acetals and ketals of polyhydric alcohols is graded acidic hydrolysis.[2] Subsequent interpretations of structure are valid only if migrations have not occurred, and this proviso is frequently stated. Whilst cyclic ketal migrations apparently have not been described, cyclic acetal migrations are known [3] although they may be due to unusual molecular situations. We now report an

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[1] Part XVIII, J. S. Brimacombe, M. E. Evans, A. B. Foster, and J. M. Webber, *J.*, 1964, 2735.
[2] S. A. Barker and E. J. Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[3] R. E. Reeves, *J. Amer. Chem. Soc.*, 1949, **71**, 2868; C. E. Ballou, *ibid.*, 1960, **82**, 2585; J. W. van Cleve, Abs. Papers Amer. Chem. Soc. Meeting, Atlantic City, September 1962, p. 8D; T. G. Bonner, E. J. Bourne, and D. Lewis, *J.*, 1963, 3375.

application of n.m.r. spectroscopy to isopropylidene derivatives of certain polyhydric alcohols in order to gain information on migration and structure.
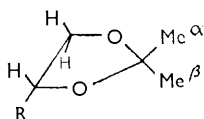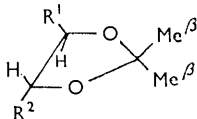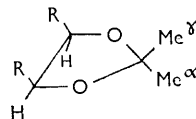
(I)   α (terminal)   (II)   αT (threo)   (III)   αC (erythro)

In n.m.r. spectroscopy the signals for the Me protons of isopropylidene groups are unsplit and occur in the region τ 8·0—9·0 [unless otherwise stated, the τ values subsequently recorded are for methanol–water (3 : 1) containing 0·6% of t-butyl alcohol as internal reference (τ 8·96)]. An α-ketal (I) (Barker and Bourne's terminology [4]) has its Me groups in different environments, and thus the Me$^{\alpha}$ and Me$^{\beta}$ groups are, respectively, *cis* to H/H and H/R at positions 4 and 5 in the 1,3-dioxolan ring. Because of its closer proximity to the group R, Me$^{\beta}$ is (usually) more effectively deshielded than Me$^{\alpha}$, and this causes the signal for the Me$^{\beta}$ protons to appear at lower field.[5] For example, 1,2-O-isopropylidene-glycerol (I; R = $CH_2 \cdot OH$) had equal signals at 8·84 and 8·79 which may be assigned to Me$^{\alpha}$ and Me$^{\beta}$ groups, respectively. Also in this category are 1,2:3,4-di-O-isopropylidene-erythritol (8·85, 8·78) and its L-threitol analogue [6] (8·86, 8·81), 1,2:4,5-di-O-isopropylidene-ribitol [7] (8·84, 8·76), and 1,2:5,6-di-O-isopropylidene-D-mannitol (V) (8·85, 8·82).

The αT-ketal (*threo*) (II) contains two Me$^{\beta}$ groups, and a single sharp signal will result if $R^1 = R^2$ as in 3,4-O-isopropylidene-D-mannitol (8·83). Where $R^1 \neq R^2$ the signal will depend on the degree of difference between R^1 and R^2; thus, 3,4-O-isopropylidene-L-rhamnitol had a single sharp signal at 8·81, and in this case (for the D-form) $R^1 = CH(OH) \cdot Me$ and $R^2 = CH(OH) \cdot CH_2 \cdot OH$. 1,2:3,4:5,6-Tri-O-isopropylidene-D-mannitol, which has two Me$^{\alpha}$ and four Me$^{\beta}$ groups, had signals of relative strength 1 : 2 at 8·87 and 8·83, with the latter signal having a shoulder to lower field thus reflecting the two slightly different types of Me$^{\beta}$ groups in the terminal and central ketal rings. More distinct differences were observed with 1,2:3,4-di-O-isopropylidene-L-rhamnitol which had incompletely resolved signals at 8·86 and 8·84 with shoulders to higher and lower field; these signals did not overlap with the doublet (8·96, J ca. 6 c./sec.) for the terminal Me group.

The αC-ketal (*erythro*) (III) has Me$^{\alpha}$ and Me$^{\gamma}$ groups, and since the latter group is *cis* to non-protonic substituents at positions 4 and 5 in the 1,3-dioxolan ring its signal should appear at lower field than that for Me$^{\beta}$. Thus, 1,2:4,5-di-O-isopropylidene-D-mannitol [8] (IV), which has two Me$^{\alpha}$, Me$^{\beta}$, and Me$^{\gamma}$ groups, had signals at 8·84, 8·81, and 8·70; the signals at 8·84 and 8·81 were not completely resolved but their combined area was three times that of the signal at 8·70. Other examples of Me$^{\gamma}$ groups are provided by 1,2- and 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose. The former compound (Me$^{\alpha}$ and Me$^{\gamma}$ groups) had equal signals at 8·87 and 8·72, and the latter at 8·87, 8·83, 8·77, and 8·72, corresponding to two Me$^{\alpha}$, Me$^{\beta}$, and Me$^{\gamma}$ groups.

Hydrolysis of isopropylidene derivatives can be followed conveniently by observing the pattern change of the Me proton signals. The hydrolyses subsequently described were effected at 25—26° with a methanol–water (3 : 1) mixture containing 0·6% of t-butyl alcohol and 1·6% of toluene-*p*-sulphonic acid. In this solution the Me proton signal pattern for 1,2:3,4:5,6-tri-O-isopropylidene-D-mannitol ($t_{\frac{1}{2}}$ hydrolysis for α-ketal *ca.* 65 min.; 10% solution) simplified to a single sharp signal at 8·83 for the 3,4-O-isopropylidene

[4] S. A. Barker and E. J. Bourne, *J.*, 1952, 905.
[5] N. Baggett, K. W. Buck, A. B. Foster, M. H. Randall, and J. M. Webber, *Proc. Chem. Soc.*, 1964, 118, and references cited therein.
[6] A. B. Foster, A. H. Olavesen, and J. M. Webber, *J.*, 1961, 5095.
[7] K. W. Buck, A. B. Foster, B. H. Rees, J. M. Webber, and F. E. Hardy, *Chem. and Ind.*, 1964, 1623.
[8] (a) L. A. Boggs, Abs. Papers Amer. Chem. Soc. Meeting, Atlantic City, September 1959, p. 6D; (b) A. B. Foster, J. Lehmann, and J. M. Webber, unpublished preparation.

derivative which therafter diminished slowly. This established reaction [9] exemplifies the more ready hydrolysis of α- than of αT-ketals.[2] Likewise, the complex pattern for

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\begin{array}{cccc}
\text{(V)} & \text{(IV)} & \text{(VI)} & \text{(VII)}
\end{array}
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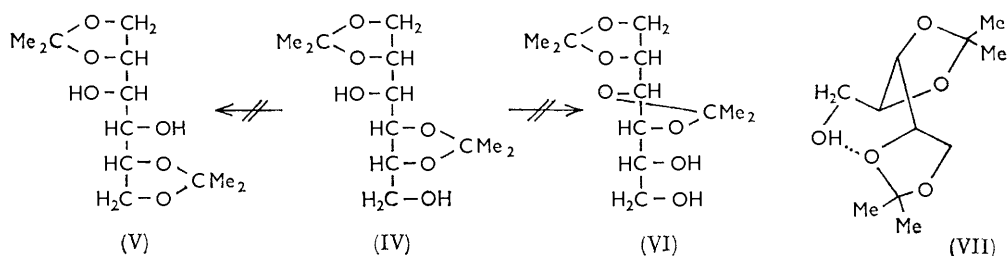
1,2:3,4-di-O-isopropylidene-L-rhamnitol simplified to a single signal (8·83) for the 3,4-O-isopropylidene derivative.[10] Similar results were obtained with 1,2:3,4-di-O-isopropylidene-5-O-toluene-p-sulphonyl-L-rhamnitol and 5-acetamido-5,6-dideoxy-1,2:3,4-di-O-isopropylidene-D-gulitol.[11]

When 1,2:5,6-di-O-isopropylidene-D-mannitol (V) was hydrolysed, smooth and complete conversion into D-mannitol was observed ($t_{\frac{1}{2}}$ hydrolysis *ca.* 17 min.; 10% solution). Since no 3,4-O-isopropylidene derivative was formed, migration of ketal groups or recondensation with acetone did not occur. Migration of a cyclic ketal group from the 1,2- to the 3,4-position would require a 2,3-ketal (αC) as an intermediate, and, because of adverse non-bonded interactions,[12] such an intermediate would be unlikely to be formed and the absence of migration is not surprising. A similar situation occurs with 1,2:3,4-di-O-isopropylidene-erythritol since, after hydrolysis of the first isopropylidene group, the only possibility for migration is 1,2-(α) ⟶ 2,3-ketal (αC); smooth hydrolysis to erythritol was observed ($t_{\frac{1}{2}}$ hydrolysis *ca.* 45 min.; 16% solution). However, for the L-threitol analogue, hydrolysis of one ketal group leaves the possibility of the migration 1,2-(α) ⟶ 2,3-ketal (αT). Hydrolysis of 1,2:3,4-di-O-isopropylidene-L-threitol occurred more rapidly ($t_{\frac{1}{2}}$ hydrolysis *ca.* 26 min.; 16% solution) than with the erythritol compound, and there was a weak residual Me proton signal at 8·81 which was undoubtedly due to 2,3-O-isopropylidene-L-threitol (two equivalent Me^{β} groups) and corresponded to *ca.* 6% of the original material. Thus, even if none of the mono-O-isopropylidene compound was initially present as a contaminant, migration must have occurred only to a very limited extent.

A more likely case for ketal migration was 1,2:4,5-di-O-isopropylidene-D-mannitol (IV) the 4,5-ketal group of which is αC and which can be readily obtained by reduction of 2,3:5,6-di-O-isopropylidene-D-mannose with sodium borohydride. Indirect methods are necessary to prepare αC-ketals; there is no case reported of the condensation of an acyclic polyhydric alcohol with acetone to give such a product. The αC-ketal in compound (IV) is so located that migration is possible to the 5,6- (α) and/or to the 3,4-position (αT). 1,2:4,5-Di-O-isopropylidene-D-mannitol (IV) was smoothly and completely hydrolysed to D-mannitol ($t_{\frac{1}{2}}$ hydrolysis *ca.* 35 min.; 10% solution) with no significant change in the relative proportions of the three signals for Me protons, and hence hydrolysis of the α- (1,2-) and αC-ketal (4,5-) groups occurred at similar rates without migration. Migration of the 4,5-ketal to the 3,4-position (αT), (IV) ⟶ (VI), and/or to the 5,6-position (α), (IV) ⟶ (V), would have been indicated by disappearance of the signal at 8·70 for the Me^{γ} group, and the former migration would have given a product which has been shown to be stable under the hydrolysis conditions employed. The above examples establish the essential absence of ketal migrations under hydrolysing conditions and validates the proviso made in graded hydrolysis studies.

[9] L. F. Wiggins, *J.*, 1946, 13.
[10] M. A. Bukhari, A. B. Foster, J. Lehmann, and J. M. Webber, *J.*, 1963, 2287.
[11] A. B. Foster, T. D. Inch, and J. M. Webber, unpublished results.
[12] J. A. Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.

The hydrolytic behaviour of six-membered cyclic ketals was next investigated. Whilst six-membered cyclic ketals may be formed from certain cyclic polyhydric alcohols [13] (an additional example is 2,4-O-methylene-D-glucitol which affords a 1,3:5,6-di-O-iso-propylidene derivative [8b]) there is no substantiated published example of the formation of a six-membered cyclic ketal with an acyclic polyhydric alcohol (*i.e.*, a compound containing three or more contiguous hydroxyl groups) although a case has recently been encountered; [14] 3-O-methyl-D-glucitol gives a small amount of the 2,4:5,6-di-O-iso-propylidene derivative in addition to the predicted 1,2:5,6-compound.[15] As shown below, xylitol condenses with acetone to give the 1,2:4,5- and 1,2:3,4-di-O-isopropylidene derivatives and not a 1,3:4,5-compound as reported by Valentin and Tomkuljak.[16] Further illustrating the point, acetone condenses with glycerol to give 1,2- but no detectable amount of 1,3-O-isopropylidene derivative. Six-membered isopropylidene derivatives can be obtained indirectly. Thus, 2-O-benzylglycerol [17] was readily acetonated, and the benzyl ether group removed from the product by hydrogenolysis over palladised charcoal to yield 1,3-O-isopropylideneglycerol which was characterised as the *p*-phenylazobenzoate. 1,3-O-Isopropylideneglycerol and its 2-O-benzyl ether each had single Me proton signals (8·78 and 8·79, respectively) which suggests that the molecules are conformationally unstable in aqueous methanol (cf. *cis*-2-phenyl-1,3-dioxan derivatives [18]). It is of interest that, in carbon tetrachloride, 2-O-benzyl-1,3-O-isopropylideneglycerol showed two Me proton signals (8·70, 8·79). 3-O-Benzyl-1,2-O-isopropylideneglycerol had signals at 8·85 and 8·82 (cf. 1,2-O-isopropylideneglycerol, 8·88, 8·84).

On acidic hydrolysis (10% solutions) 2-O-benzyl-1,3-O-isopropylideneglycerol and 3-O-benzyl-1,2-O-isopropylideneglycerol had $t_{\frac{1}{2}}$ hydrolyses of *ca.* 1·0 and *ca.* 15 min., respectively; the sensitivity of the former compound to acid was most noticeable. Similar results were observed with 1,3- and 1,2-O-isopropylideneglycerol ($t_{\frac{1}{2}}$ hydrolyses *ca.* 1·0 and *ca.* 7 min., respectively). In the hydrolysis of 1,3-O-isopropylideneglycerol, after disappearance of the Me proton signal at 8·78, weak signals at 8·88 and 8·84 were detectable corresponding to *ca.* 5% of the original material and clearly due to 1,2-O-isopropylideneglycerol. Some of this material was probably impurity originally present, so that ketal ring contraction occurred to a negligible extent if at all.

The observation that acetonation of ribitol gave a mixture of di-O-isopropylidene derivatives [7,19] prompted an investigation of the corresponding reaction of xylitol. Catalysis of the acetone–xylitol reaction with sulphuric acid–copper sulphate [20] gave a product containing components *A* and *B* in the ratio *ca.* 1:3 (determined by gas chromatography). Similar products, but in different ratios (*ca.* 1:2·3 and *ca.* 1:11, respectively), were formed when sulphuric acid [16] and zinc chloride were separately used as catalysts. Isomer *B* could be crystallised from these mixtures, and its m. p. (36°) and that (60—61°) of its benzoate indicate probable identity with the 1,2,3,4-di-O-iso-propylidenexylitol (m. p. 33—34°) and the derived benzoate (m. p. 60—61°) described by Hudson and his co-workers [20] who clearly established the presence of the primary hydroxyl function but did not detect the second isomer.

Fractionation of the di-O-isopropylidenexylitol mixture by preparative gas chromatography gave isomer *A* which had Me proton signals of equal intensity at 8·81 and 8·73. This symmetrical signal pattern, which is closely similar to that for 1,2,4,5-di-O-isopropylideneribitol, is indicative of equal numbers of Me$^{\alpha}$ and Me$^{\beta}$ groups, *i.e.*, a 1,2,4,5-distribution of the ketal groups. Confirmation was provided when the benzoate of

[13] *E.g.*, J. K. N. Jones, *Canad. J. Chem.*, 1956, **34**, 840; A. N. Anikeeva and S. N. Danilov *Zhur. obshchei Khim.*, 1962, **32**, 2498; J. G. Buchanan and R. M. Saunders, *J.*, 1964, 1796.
[14] Part XX, A. B. Foster, M. H. Randall, and J. M. Webber, following Paper.
[15] A. B. Foster, J. Lehmann, M. H. Randall, and J. M. Webber, *J.*, 1963, 4167.
[16] F. Valentin and D. Tomkuljak, *Chem. Zvesti*, 1949, **3**, 146.
[17] A. J. E. Porck and B. M. Craig, *Canad. J. Chem.*, 1955, **33**, 1286.
[18] N. Baggett, B. Dobinson, A. B. Foster, J. Homer, and L. F. Thomas, *Chem. and Ind.*, 1961, 106.
[19] M. A. Bukhari, A. B. Foster, J. Lehmann, J. M. Webber, and J. H. Westwood, *J.*, 1963, 2291.
[20] R. M. Hann, A. T. Ness, and C. S. Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 73.

isomer A was found to be identical with 3-O-benzoyl-1,2:4,5-di-O-isopropylidenexylitol obtained [7] by application of a benzoate exchange reaction to 1,2:4,5-di-O-isopropylidene-3-O-p-bromobenzenesulphonylribitol.

The infrared spectrum of a $\not> 0\cdot005$M-solution of isomer B in carbon tetrachloride (conditions where intermolecular hydrogen bonding is precluded and absorptions in the hydroxyl stretching region may be assigned to free and intramolecularly bonded hydroxyl groups [21]) showed bands at 3634 (ε 14, free primary OH), 3601 (ε 49, $\Delta\nu$ 33, bonded OH involved in a five-membered ring; [21] cf. 2-methoxyethanol, $\Delta\nu$ 31), and 3500 cm.$^{-1}$ (ε 10, $\Delta\nu$ 134, bonded OH involved in a seven-membered ring, cf. 4-methoxybutanol, $\Delta\nu$ 180). The first two absorptions are characteristic [22] of the grouping CH(OR)·CH$_2$·OH and the last absorption is consistent with a 1,2:3,4-distribution of the ketal groups since such a molecule could adopt a conformation (VII) where the hydrogen bond C(5)·OH $\cdots$ O(2) could form. In the alternative structure involving six-membered ketal rings, an " O "-inside, *cis*-decalin-type, ring system with an equatorial CH$_2$·OH group would occur [12] in which a hydrogen bond C(5)·OH $\cdots$ O(2) would not be possible.

Isomer B had signals for Me protons at 8·78 and 8·73 in the ratio 1 : 3, a pattern consistent with one Me$^\alpha$ and three Me$^\beta$ groups, *i.e.*, a 1,2:3,4-distribution of the ketal rings. Two signals of comparable intensity would be expected for a 1,3:2,4-diketal, corresponding to the axial and equatorial isopropylidene methyl groups (cf. methyl 4,6-O-isopropylidene-2,3-di-O-methyl-α-D-galactopyranoside which has a *cis*-decalin-type ring system and had Me proton signals at 8·71 and 8·80). Isomer B underwent relatively slow acidic hydrolysis in the solvent system noted above ($t_{\frac{1}{2}}$ hydrolysis *ca.* 60 min. for α-ketal; 10% solution), and the initial pattern of Me proton signals changed to a single signal at 8·73 consistent with selective hydrolysis of an α-ketal leaving an αT-group. Graded acidic hydrolysis of isomer B using Valentin and Tomkuljak's conditions [16] gave a mono-O-isopropylidene derivative isolated as the tri-O-benzoate (m. p. 103—105°) in 28% yield (cf. m. p. 103—104° recorded by the Czech workers). The tri-O-benzoate had a single, unsymmetrical Me proton signal at 8·57 (CCl$_4$), consistent with the presence of two, slightly different, Me$^\beta$ groups, *i.e.*, a 2,3-location of the ketal residue.

Valentin and Tomkuljak [16] recorded that the di-O-isopropylidenexylitol formed by sulphuric-acid catalysis failed to undergo tritylation and hence did not contain a primary hydroxyl group. In our hands, tritylation of isomer B alone, or in admixture with isomer A, could be effected and the parent alcohol regenerated by catalytic hydrogenolysis of the crystalline trityl derivative. The presence of a primary hydroxyl group is therefore further confirmed, and the 1,2:3,5-distribution of the cyclic ketal groups in di-O-isopropylidenexylitol assigned by the Czech workers [16] is erroneous. It should be noted that the evidence, other than that of the tritylation experiment, adduced by the Czech workers accords with a 1,2:3,4-distribution of the ketal rings, and there can be little doubt that isomer B is 1,2:3,4-di-O-isopropylidene-DL-xylitol.

1,2:4,5-Di-O-isopropylidenexylitol (A) had no band for free hydroxyl groups but absorptions at 3597 [ε 41, $\Delta\nu$ 32 (calculated on the basis of absorption at 3629 cm.$^{-1}$ for free secondary OH [23]), bonded secondary hydroxyl group involved in a five-membered ring], and 3557 cm.$^{-1}$ (ε 23, $\Delta\nu$ 72). The latter absorption must also be due to a hydrogen bond involving a five-membered ring since the alternative, six-membered ring is precluded on steric grounds (cf. 1,2-O-isopropylideneglycerol [22]). The large $\Delta\nu$ is indicative of an unusual molecular situation. Although $\Delta\nu$ values for intramolecular hydrogen bonds forming five-membered rings can vary within the range 30—170, values greater than 45 are usually associated with diols of cyclic compounds or with acyclic diols where abnormal steric interactions occur.[21]

[21] A. B. Foster, A. H. Haines, and M. Stacey, *Tetrahedron*, 1961, **16**, 177.
[22] J. S. Brimacombe, A. B. Foster, and A. H. Haines, *J.*, 1960, 2582.
[23] A. R. H. Cole and P. R. Jefferies, *J.*, 1956, 4391.

EXPERIMENTAL

Physical Methods.—Gas chromatography was performed on a Pye Argon instrument with β-ionisation detection, a polyethyleneglycol adipate column, and a gas pressure of *ca.* 8 lb. per sq. in.

N.m.r. spectra were obtained with a Varian A60 instrument using 5—20% solutions in methanol–water (3 : 1) containing 0·6% of t-butyl alcohol as internal reference; all signals are recorded on the τ scale.

Dilute-solution infrared spectra were determined on 2- or 3-cm. layers of *ca.* 0·005M-solutions in carbon tetrachloride, using fused quartz cells and a Unicam S.P. 100 spectrometer equipped with a grating (3000 lines per in.).[21]

Isopropylidenation of Xylitol.—(*a*) A mixture of xylitol (40 g.; m. p. 93—95°), anhydrous copper sulphate (85 g.), conc. sulphuric acid (0·9 ml.), and dry acetone (770 ml.) was shaken at room temperature for 48 hr. The filtered solution was shaken for 1 hr. with calcium hydroxide (35 g.), insoluble material was removed, and the filtrate was concentrated. Distillation of the residue gave a mixture of di-*O*-isopropylidenexylitols (48 g., 73%), b. p. 102°/0·3 mm. In other experiments the neutralisation was more conveniently effected with ammonia. Analysis of the mixture by gas chromatography at 175° revealed components *A* and *B* with retention times of 11 and 20 min. and in the ratio *ca.* 1 : 3 (deduced from peak areas).

(*b*) A mixture[16] of xylitol (10 g.) and acetone (200 ml.) containing conc. sulphuric acid (2 ml.) was shaken at room temperature for 17 hr., and then worked up essentially as in (*a*) to give a product (11 g., 70%), b. p. 102—104°/0·4 mm., containing components *A* and *B* in the ratio *ca.* 1 : 2·3; Valentin and Tomkuljak[16] record b. p. 99—100°/0·5 mm. and the mono-*O*-isopropylidene derivative described by these workers was not encountered.

(*c*) Acetone was shaken with an excess of zinc chloride for 2 hr., and to the filtered solution (200 ml.) xylitol (16 g.) was added and the mixture was shaken at room temperature for 16 hr. Aqueous sodium hydroxide (400 ml., 20%) was then added dropwise and the mixture was extracted with chloroform (5 × 200 ml.). The combined extracts were washed with water, dried (MgSO$_4$), and concentrated. Distillation of the residue gave the product (13 g., 52%), b. p. 103°/0·3 mm., which contained components *A* and *B* in the ratio *ca.* 1 : 11 and which partially crystallised on storage. Repeated recrystallisation from hexane gave the component *B*, m. p. 36° (lit.,[20] m. p. 33—34° for 1,2:3,4-di-*O*-isopropylidenexylitol). The products described in (*a*) and (*b*) partially crystallised when seeded with the above compound.

The isomer mixture from (*a*) was fractionated using a Wilkens Autoprep 600 instrument with a column of Carbowax 20M at 240°. Component *A*, obtained first, gave, by the usual method, a benzoate, m. p. 114—116°, which was identical with authentic 3-*O*-benzoyl-1,2:4,5-di-*O*-isopropylidenexylitol obtained by a different route[7] (Found: C, 64·3; H, 7·0. Calc. for C$_{18}$H$_{24}$O$_6$: C, 64·3; H, 7·2%).

Component *B*, obtained second, gave a benzoate m. p. 60—61° (lit.,[20] m. p. 60—61° for 1-*O*-benzoyl-2,3:4,5-di-*O*-isopropylidenexylitol).

Tritylation Experiments.—The di-*O*-isopropylidenexylitol mixture (14 g.), prepared as described in (*a*), was treated with a mixture of trityl chloride (20 g.) and pyridine (100 ml.) at *ca.* 100° for 2 hr. Solvent was then removed by distillation under reduced pressure, and a solution of the residue in chloroform was washed quickly with ice-cold 2N-hydrochloric acid, aqueous cadmium chloride, aqueous sodium hydrogen carbonate, and water. Concentration of the dried (MgSO$_4$) solution and recrystallisation of the residue from ethanol gave slightly impure 1,2:3,4-di-*O*-isopropylidene-5-*O*-trityl-DL-xylitol (15 g., 60%), m. p. 73—75°. Hydrogenolysis of the product over 5% palladised charcoal gave 1,2:3,4-di-*O*-isopropylidene-DL-xylitol contaminated with *ca.* 5% of the 1,2:4,5-isomer, as established by gas chromatography. The pure *trityl compound*, prepared by the above method from crystalline 1,2:3,4-di-*O*-isopropylidene-DL-xylitol, had m. p. 73—75° (Found: C, 75·6; H, 7·3. C$_{30}$H$_{34}$O$_5$ requires C, 75·9; H, 7·2%).

1,3-O-Isopropylideneglycerol.—2-*O*-Benzylglycerol[17] (2·11 g.) was shaken overnight with a mixture of acetone (40 ml.), anhydrous copper sulphate (4 g.), and conc. sulphuric acid (0·04 ml.). The mixture was neutralised by pouring into excess of conc. ammonia. The filtered mixture was concentrated and the residue distilled to give 2-O-*benzyl*-1,3-O-*isopropylideneglycerol* (1·98 g., 77%), b. p. 140—160° (bath)/0·4 mm. (Found: C, 70·3; H, 8·0. C$_{13}$H$_{18}$O$_3$ requires C, 70·2; H, 8·2%).

A solution of the foregoing benzyl ether (1·0 g.) in ethanol (30 ml.) was shaken at room temperature in an atmosphere of hydrogen at a slight overpressure in the presence of 5% palladised charcoal (2 g.). When uptake of hydrogen had ceased, the mixture was filtered and concentrated under diminished pressure. Distillation of the residue gave slightly impure 1,3-*O*-isopropylideneglycerol (0·26 g., 42%), b. p. *ca.* 130° (bath)/33 mm. The product was converted into the p-*phenylazobenzoate*, m. p. 145—147·5° (from ethanol) in the usual way [24] (cf. m. p. 80—81° for the *p*-phenylazobenzoate of 1,2-*O*-isopropylideneglycerol [24]) (Found: C, 67·2; H, 6·2. $C_{19}H_{20}N_2O_4$ requires C, 67·0; H, 5·9%).

Methyl 4,6-O-*Isopropylidene*-2,3-*di*-O-*methyl*-α-D-*galactopyranoside*.—A mixture of methyl 2,3-di-*O*-methyl α-D-galactopyranoside [25] (1·02 g.), anhydrous copper sulphate (2 g.), conc. sulphuric acid (0·1 ml.), and acetone (50 ml.) was shaken overnight at room temperature. The mixture was poured into excess of aqueous ammonia and the filtered solution was concentrated to remove most of the acetone. The residual solution was extracted with chloroform (3 × 25 ml.), and the combined extracts were washed with water, dried (MgSO₄), and evaporated. Distillation of the residue gave a product, b. p. 120—140° (bath)/0·1 mm., which solidified on storage. Recrystallisation from light petroleum (b. p. 60—80°) gave the galactopyranoside (0·94 g., 78%), m. p. 132—134°, $[\alpha]_D$ +199° (*c* 1·1 in $CHCl_3$) (Found: C, 54·95; H, 8·5. Calc. for $C_{12}H_{22}O_6$: C, 54·95; H, 8·45%) (lit.,[13] m. p. 130°, $[\alpha]_D$ +189° in $CHCl_3$ for the same product prepared in a different manner).

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM 15.

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[25] D. J. Bell and G. D. Greville, *J.*, 1955, 1136.