# Formation of 3,6-Anhydro-4,5-*O*-isopropylidene-D-allose Dimethyl Acetal in the Methanolysis of 1,2:5,6-Di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose. Synthesis of 3,6-Anhydro-D-allose

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The acid-catalysed methanolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose yields principally methyl 3-*O*-*p*-tolylsulphonyl-α- and -β-D-glucopyranosides, together with a minor amount of 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (VI). Under the same conditions, 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose yields 3,6-anhydro-5-*O*-methyl-D-allose dimethyl acetal in good yield.

3,6-Anhydro-D-allose (IV) and 3,6-anhydro-5-*O*-methyl-D-allose (V) have been prepared by hydrolysis of the above derivatives and have been found to exist in aqueous solution in *aldehydo*, aldehydrol (*i.e.* hydrated aldehyde), and dimeric forms.

3,6-ANHYDRO-HEXOSES were first extensively investigated by Haworth and his co-workers.[1-3] These compounds undergo remarkable isomerizations, *e.g.* methyl 3,6-anhydro-α-D-glucopyranoside is smoothly converted [1] into methyl 3,6-anhydro-α-D-glucofuranoside on treatment with dilute aqueous sulphuric acid; retention of configuration at C-1 is apparently complete and is still without adequate explanation. Treatment of methyl 3,6-anhydro-2,4-di-*O*-methyl-α-D-glucopyranoside with acid [1] causes isomerization to the β-pyranoside, and a similar reaction occurs in the galactose series.[2] These products might be expected to be less stable than the starting materials.

There are four types of 3,6-anhydro-hexoses in which (i) either a furanose or pyranose ring system can be fused to the 3,6-anhydro-ring,[4] *e.g.* 3,6-anhydro-D-glucose (I); (ii) fusion of a furanose ring only is possible, *e.g.* 3,6-anhydro-D-idose (II); (iii) fusion of a pyranose ring only is possible without undue strain, *e.g.* 3,6-anhydro-D-galactose (III); and (iv) fusion of neither a pyranose nor a furanose ring is possible without undue strain, *e.g.* 3,6-anhydro-D-allose (IV). Only compounds of types (i), (ii), and (iii) have been described. 3,6-Anhydro-D-glucose exists in solution as an equilibrium mixture of the furanose forms but the anomeric configuration of the crystalline form remains unknown; methanolysis of methyl 3,6-anhydro-α-D-glucopyranoside gives a mixture of the α- and β-furanosides, the pyranose forms being strained. 3,6-Anhydro-D-galactose has been postulated to exist as an equilibrium mixture of pyranose and *aldehydo* forms; methanolysis of methyl 3,6-anhydro-α-D-galactopyranoside gives mainly 3,6-anhydro-D-galactose dimethyl acetal.[2] 3,6-Anhydro-D- and L-idose have been prepared [5] but have not been studied. Of the anhydrides of type (iv), 3,6-anhydro-D-

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[1] W. N. Haworth, L. N. Owen, and F. Smith, *J. Chem. Soc.*, 1941, 88.

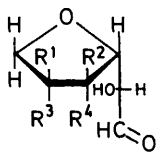
[2] W. N. Haworth, J. Jackson, and F. Smith, *J. Chem. Soc.*, 1940, 620.

[3] A. B. Foster, W. G. Overend, M. Stacey, and G. Vaughan, *J. Chem. Soc.*, 1954, 3367.

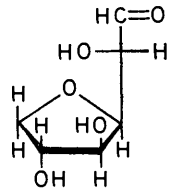
[4] A. B. Foster, *J. Chem. Soc.*, 1957, 2833.

[5] J. G. Buchanan and J. Conn, *J. Chem. Soc.*, 1965, 201.

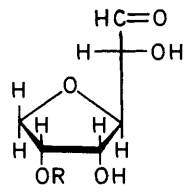
allose was hitherto unknown and 3,6-anhydro-D-altrose has been identified [5] (but not isolated) as a product of the acid hydrolysis of methyl 2,3-anhydro-α-D-mannopyranoside. We now report the synthesis of 3,6-anhydro-D-allose and of some related compounds.



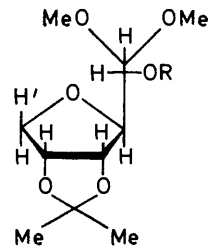
(I) $R^3 = R^4 = OH, R^1 = R^2 = H$
(III) $R^2 = R^3 = OH, R^1 = R^4 = H$



(II)



(IV) R = H
(V) R = Me



(VI) R = H
(VII) R = Ac

In previous work [6] aimed at the preparation of D-allose an anomeric mixture of methyl 2,4,6-tri-*O*-acetyl-3-*O*-*p*-tolylsulphonyl-D-glucopyranosides was obtained by methanolysis [7] and subsequent acetylation of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose. On pouring the acetylation mixture into aqueous sodium hydrogen carbonate solution an unexpectedly small quantity (65—70% yield) of products was precipitated. Examination of the water-soluble material by n.m.r. spectroscopy revealed the presence of methoxy-, acetate, and isopropylidene groups, but not of a sulphonate group. Saponification of this material with sodium methoxide gave a compound shown to be 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (VI). The same compound was obtained more conveniently, after neutralization of the methanolysis mixture, by chromatography on alumina or silicic acid, and was characterized as the crystalline *p*-phenylazobenzoate. The acetate (VII), benzoate, *p*-nitrobenzoate, and toluene-*p*-sulphonate did not crystallize.

The structure of the product (VI) was established by n.m.r. spectroscopy. No single spectrum showed signals for all the protons clearly but a comparison of the spectra in two solvents with that of the acetate (VII) and that of the 5-*O*-methyl derivative (see later) allowed the assignment of a signal to every proton and the determination of all coupling constants. The spectrum of (VI) in [$^2H_6$]benzene (Figure 1) showed the presence of one hydroxy-, one isopropylidene, and two methoxy-groups. Since both of the latter were removed by hydrolysis with acid, they must represent a dimethyl acetal group; compound (VI) is therefore a derivative of an aldehyde which cannot cyclize to a furanoside or pyranoside. Such aldehydes form dimethyl acetals on heating with methanolic acid. Acetylation converted (VI) into a compound (VII) which showed the signal of only one acetyl group in its n.m.r. spectrum. Since the isopropylidene and the acetyl groups account for only three potential hydroxy-groups of the hexose derivative, (VI) must be an anhydro-compound, but not an oxiran because the anhydride ring is not opened by acid.

The signal of the anomeric proton must be a doublet, and in these spectra there is only one doublet, which is assigned to H-1. The only signal with the same splitting as H-1 is a triplet, at δ 3·79 p.p.m. in the spectrum of (VI) and at δ 5·35 in the spectrum of its acetate (Figure 1). This signal is therefore that of H-2, and its shift to lower field on acetylation indicates that the acetoxy-group is on C-2. The signal for the methylene group at C-6 is readily recognized in the spectrum of the acetate as the AB part of an ABX spectrum, and a septet in the spectrum of (VI) at δ 4·64 p.p.m. must be the signal of H-5, since no other proton should show such multiplicity. The clearly distinguishable pair of doublets at δ 4·98 and 4·86 p.p.m., respectively, must be the signal of H-4, since its splittings do not match those of H-2.

Formation of a similar anhydro-derivative from 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose (see later) indicates that O-5 is not

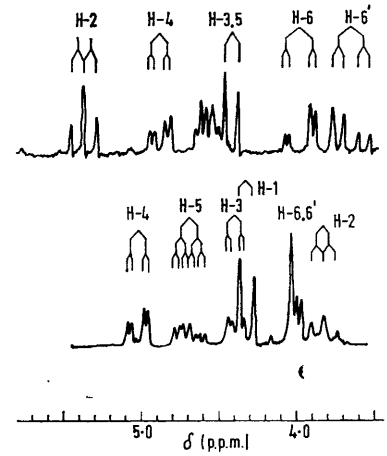



FIGURE 1 Partial n.m.r. spectra of 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (VI) (lower curve) and its 2-acetate (VII) (upper curve) in [$^2H_6$]benzene

involved in the anhydro-ring. The only conceivable structure which accounts for an acid-stable anhydro-ring, the non-formation of furanosides and pyranosides, and the stability of an isopropylidene acetal that persists in substantial amount in acidified methanol

[6] R. Ahluwahlia, S. J. Angyal, and M. H. Randall, *Carbohydrate Res.*, 1967, **4**, 478.
[7] S. Peat and L. F. Wiggins, *J. Chem. Soc.*, 1938, 1092.

containing only 2% of acetone, is (VI). This structure contains two *cis*-fused five-membered rings, a particularly stable arrangement. Such a structure would be formed if the tosyloxy-group were displaced by back-side attack of O-6. If the displacement were not accompanied by inversion on C-3, the product would be a derivative of 3,6-anhydro-D-glucose; however, hydrolysis of (VI) gave a sugar different from 3,6-anhydro-D-glucose. None of the coupling constants is incompatible with structure (VI). The coupling constants also support the assigned configuration of C-2; the epimer, 3,6-anhydro-D-altrose, would have $J_{1.2}$ *ca.* 9 and $J_{2.3}$ *ca.* 3 Hz in a zig-zag form of the carbon chain with the dimethyl acetal group so rotated as to avoid a 1,3-parallel interaction with O-3.

Sulphonyloxy-groups are normally stable under acidic conditions but a few instances are known where primary tosyloxy-groups are displaced internally with concomitant formation of a ring.[8,9] Similar internal displacement of a secondary tosyloxy-group is rarer and we are aware of only two described cases.[8,10] In all of these instances displacement occurs with inversion and results in the formation of a tetrahydrofuran ring. The formation of a derivative of 3,6-anhydro-D-allose from 3-*O*-*p*-tolylsulphonyl-D-glucose is therefore in accordance with previous experience. The reaction is analogous to the formation of 3,6-anhydro-hexoses from 2,3-anhydro-hexoses on acid hydrolysis;[5] here, also, the oxygen atom on C-6 displaces a substituent on C-3 (but not on C-2) with inversion.

Displacement of the 3-sulphonate group by O-6 with concomitant inversion of configuration is sterically impossible in the glucopyranose series. Although such displacement is sterically possible in the glucofuranose series, the transition state would be highly strained; in fact, the reaction does not occur. Vargha [11] found that on boiling with sodium hydroxide solution—conditions which facilitate [12] elimination with ring formation much more than does acid—1,2-*O*-isopropylidene-3-O-*p*-tolylsulphonyl-α-D-glucofuranose gave 1,2-*O*-isopropylidene-α-D-glucofuranose as the only product. We found that sodium hydrogen carbonate will give this product in aqueous solution, though not in *NN*-dimethylformamide. Even forcing conditions, such as boiling the disodio-derivative in 1,2-dimethoxyethane, did not cause internal elimination of the tosyl group.

Thus the displacement of the sulphonate group must involve an acyclic form (as it does also in the corresponding conversion of 2,3-anhydro-D-mannose into 3,6-anhydro-D-altrose [5]). It is assumed that methanolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose first gives a mixture of methyl furanosides in equilibrium with substantial amounts of the acyclic forms, and that this is followed by gradual conversion into the more stable pyranosides. Once the pyranosides have been formed, displacement of the sulphonate group becomes extremely slow because the proportion of acyclic forms in equilibrium is very small.

Support for this view was obtained by methanolysis of 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose,[11] a sugar which cannot form pyranoside derivatives. After 28 h complete desulphonylation had occurred, and syrupy 3,6-anhydro-5-*O*-methyl-D-allose dimethyl acetal (characterized as the 2,4-bis-*p*-nitrobenzoate) was formed. The structure of this compound was established on the basis of n.m.r. data and by acid hydrolysis, which yielded 3,6-anhydro-5-*O*-methyl-D-allose (V). The n.m.r. spectrum of the 2,4-bis-*p*-nitrobenzoate in [$^2H_6$]acetone is similar to that of (VII) but now both the triplet of H-2 (at δ 5·80 p.p.m.) and the pair of doublets of H-4 (at δ 5·51) appear at low field, owing to the presence of the two acyl groups, on O-2 and O-4.

In contrast to its behaviour on methanolysis in the presence of an acid, 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-*p*-tolylsulphonyl-D-glucofuranose does not form an anhydro-sugar on treatment with a hot ethanolic solution of sodium hydroxide because the sugar cannot change into an acyclic form. The base merely removes the *p*-tolylsulphonyl group.[11]

Methanolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose may therefore be rationalized as follows: methanolysis results in rapid removal of the isopropylidene groups with concurrent formation of furanosides and acyclic forms. Sulphonate displacement then proceeds through the acyclic form to give the 3,6-anhydro-ring, and subsequent formation of the dioxolan ring gives the stable system of two *cis*-fused five-membered rings which exists in 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal. Our experimental data do not distinguish between an isopropylidene migration and removal as acetone dimethyl acetal, followed by formation of a new acetal ring in the 4,5-position.

The graded acidic hydrolysis of 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (VI) was conveniently followed by n.m.r. spectroscopy: in 0·1N-hydrochloric acid at 25° the isopropylidene resonances at δ 1·45 and 1·32 p.p.m. disappeared in 1 h, being replaced by a singlet for acetone at δ 2·17. The signals of the dimethyl acetal group at δ 3·40 and 3·44 p.p.m. were still present; they, in turn, disappeared after 3·5 h at 55°, being replaced by the signal of methanol at δ 3·30. Work-up then gave 3,6-anhydro-D-allose (IV) as a syrup.

It is well known that in aqueous solution the *aldehydo*-forms of sugars are in equilibrium with the hydrated (' aldehydrol ') forms but the position of the equilibrium is not well established. Anet found that in aqueous solutions of 2,3,4,5,6-penta-*O*-methyl- [13] and 2,3,4,5-

[8] J. Defaye and J. Hildesheim, *Tetrahedron Letters*, 1968, 313; for a review, see J. Defaye, *Adv. Carbohydrate Chem. Biochem.*, 1970, **25**, 203.
[9] S. S. Brown and G. M. Timmis, *J. Chem. Soc.*, 1961, 3656.
[10] P. A. J. Gorin, *Canad. J. Chem.*, 1963, **41**, 2417.
[11] L. von Vargha, *Ber.*, 1936, **69**, 2098.
[12] D. H. Ball and F. W. Parrish, *Adv. Carbohydrate Chem. Biochem.*, 1969, **24**, 167.
[13] E. F. L. J. Anet, personal communication.

tetra-*O*-methyl-D-glucose [14] at 30° the proportion of *aldehydo*- to aldehydrol forms was about 1 : 1. Horton and his co-workers [15] observed that 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose exists in aqueous solution entirely as the aldehydrol. The aldehydrol form of fully acetylated *aldehydo*-aldoses, according to Horton and Wander,[16] is favoured overwhelmingly over the free aldehyde form. However, the extent of hydration of aldehydes depends on the electron-attracting properties of substituents on the α-carbon atom; an acetoxy-group in that position would favour hydration more than a methoxy-group. It was of interest therefore to study the hydration of 3,6-anhydro-D-allose, in which the hydroxy-group on C-2 is free. The free hydroxy-group, however, introduces an added complication since it is well established that α-hydroxy-aldehydes readily dimerize in solution.[17]

The n.m.r. spectrum of 3,6-anhydro-D-allose (IV) in deuterium oxide (Figure 2) shows, *inter alia*, a singlet

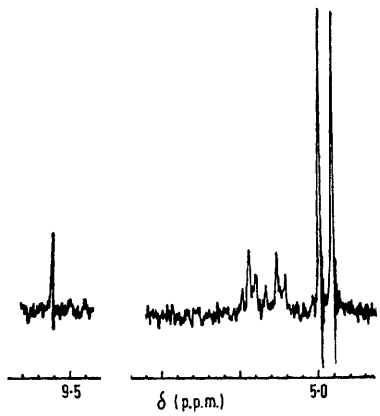



FIGURE 2 The signals of the anomeric proton in the n.m.r. spectrum of 3,6-anhydro-D-allose (IV) in deuterium oxide

at δ 9·65 (free aldehyde), complex multiplets at 5·21—5·53 (dimers), and a doublet at 4·96 p.p.m. ($J_{1,2}$ 5·0 Hz) (aldehydrol). The chemical shifts assigned to the free aldehyde and aldehydrol forms are in accord with reported data; [14,15] the pattern of the dimers is similar to that observed in the n.m.r. spectrum of DL-glyceraldehyde [18] and glycolaldehyde.[19] At 43°, with 0·14 g of aldehyde dissolved in 0·3 ml of deuterium oxide, integration showed 3·6% aldehyde, 50% dimers, and 46% aldehydrol (total integral 1H). Heating the sample increased the amount of free aldehyde at the expense of the other forms, and dilution diminished the proportion of the dimeric forms, as expected. Anet has already noted [14] the increase in the proportion of the *aldehydo-form* with increasing temperature.

The spectrum of 3,6-anhydro-5-*O*-methyl-D-allose (V), formed by acid hydrolysis of the dimethyl acetal, was practically indistinguishable from that of 3,6-anhydro-D-allose. Again, heating the solution increased the proportion of the *aldehydo*-form.

## EXPERIMENTAL

The n.m.r. spectra were measured with a Varian A-60 spectrometer (tetramethylsilane as internal reference).

*Methanolysis of* 1,2:5,6-*Di*-O-*isopropylidene*-3-O-p-*tolylsulphonyl*-α-D-*glucofuranose*.[7]—The title compound (15 g) and methanolic 1% (w/v) sulphuric acid (200 ml) were heated under reflux for 24·5 h. After neutralization of the cooled mixture with solid sodium hydrogen carbonate the inorganic salts were filtered off and the slighly yellow solution was concentrated to an oil. The oil was dissolved in water (100 ml) and the solution was extracted successively with hexane (3 × 33 ml), ether (4 × 33 ml), and dichloromethane (4 × 33 ml). These fractions were examined by t.l.c. (silicic acid; ethyl acetate as eluant, iodine vapour for detection). The hexane extract (0·23 g) was composed of fast-moving material and was discarded. The ether extracts (1·25 g) were composed of three components, the one with lowest mobility being the methyl 3-*O*-*p*-tolylsulphonyl-α- and β-D-glucopyranosides (identified by comparison with authentic material). The component with intermediate mobility was later shown to be 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal. The third component was not identified but was different from the component isolated from the hexane extract. In the dichloromethane extract (3·8 g) only the slowest-moving components were detectable. The ether extract was fractionated on CC7 Mallinckrodt silicic acid (100—200 mesh) (ethyl acetate as eluant). The faster-moving eomponent was discarded and the following component was obtained as a homogeneous syrup. Distillation at 110° and 0·05 mmHg (bath temp.) yielded 3,6-*anhydro*-4,5-O-*isopropylidene*-D-*allose dimethyl acetal* (VI) (0·9 g), $[\alpha]_D^{25}$ −18·1° (*c* 1·2 in $CHCl_3$) (Found: C, 53·25; H, 8·3. $C_{11}H_{20}O_6$ requires C, 53·2; H, 8·1%), δ ($CDCl_3$) 1·34 and 1·50 (3H each, s, $Me_2C$=), 2·75 (s, OH), 3·43 and 3·49 (3H each, s, 2 × OMe), 3·67 (t, *J* 5·1 Hz, sharpened on exchange with $D_2O$, H-2), 3·92—4·11 (3H, m), 4·33 (d, $J_{1,2}$ 5·4 Hz, H-1), and 4·83 (2H, m); δ ($C_6D_6$) (Figure 1) 1·28 and 1·53 (3H each, s, $Me_2C$=), 3·79br (s, OH), 3·17 and 3·20 (3H each, s, 2 × OMe), 3·79 (t, *J* 5·2 Hz, sharpened on exchange with $D_2O$, H-2), 4·27 (d, $J_{1,2}$ 5·4 Hz, H-1), 4·64 (seven-line m, H-5), and 4·98 p.p.m. (pair of d, $J_{3,4}$ 1·6, $J_{4,5}$ 6·4 Hz, H-4).

2-O-*Acetyl*-3,6-*anhydro*-4,5-O-*isopropylidene*-D-*allose Dimethyl Acetal* (VII).—3,6-Anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (0·2 g) and 1 : 1 pyridine–acetic anhydride (3 ml) were stored for 3 days at 0°. The mixture was then concentrated *in vacuo* to an oil, which was homogeneous on t.l.c. [silica gel; benzene–ether (1 : 1)]. The oil was distilled to yield the *acetylated acetal* (0·18 g), b.p. 150° at 0·1 mmHg (bath temp.), $[\alpha]_D^{25}$ −27·2° (*c* 1·7 in $CHCl_3$) (Found: C, 53·6; H, 7·6. $C_{13}O_7H_{22}$ requires C, 53·8; H, 7·6%), δ ($CDCl_3$) 1·33 and 1·50 (3H each, s, $Me_2C$=), 2·10 (3H, s, Ac), 3·40 and 3·42 (3H each, s, 2 × OMe), 3·9 (m), 4·25 (poorly resolved d), 4·41 (d, $J_{1,2}$ 5·0 Hz, H-1), 4·75 (m), 5·08 (t, *J* 5·0 Hz, H-2); δ ($C_6D_6$) (Figure 1) 1·24 and 1·49 (3H each, s, $Me_2C$=), 1·73 (3H, s, Ac), 3·10 and 3·19 (3H each, s, 2 × OMe), 3·63 (pair of d,

[14] E. F. L. J. Anet, *Carbohydrate Res.*, 1968, **8**, 164.
[15] D. Horton, M. Nakadate, and J. M. J. Tronchet, *Carbohydrate Res.*, 1968, **7**, 56.
[16] D. Horton and J. D. Wander, *Carbohydrate Res.*, 1971, **16**, 477.
[17] D. Gardiner, *Carbohydrate Res.*, 1966, **2**, 234.
[18] M. H. Randall, unpublished data.
[19] G. C. S. Collins and W. O. George, *J. Chem. Soc.* (*B*), 1971, 1352.

$J_{6.6'}$ −10·5, $J_{5.6'}$ 4·2 Hz, H-6'), 3·95 (pair of d, $J_{5.6}$ 2·0 Hz, H-6), 4·40 (d, $J_{1.2}$ 5·0 Hz, H-1), 4·86 (pair of d, $J_{3.4}$ 1·8, $J_{4.5}$ 6·3 Hz, H-4), and 5·35 p.p.m. (t, $J$ 5·0 Hz, H-2).

3,6-*Anhydro*-4,5-O-*isopropylidene*-2-O-p-*phenylazobenzoyl*-D-*allose Dimethyl Acetal*.—3,6-Anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (0·19 g) was dissolved in a small volume of pyridine and *p*-phenylazobenzoyl chloride (0·3 g) was added. After 36 h the mixture was heated at 100° for 2 h. The excess of *p*-phenylazobenzoyl chloride was destroyed with a small volume of water and the mixture was poured into dilute sodium hydrogen carbonate solution and extracted with chloroform (3 × 20 ml). The extract was washed with dilute hydrochloric acid until the washings remained acid, then with dilute sodium hydrogen carbonate, and finally with water. The dried ($Na_2SO_4$) chloroform extract was concentrated to an oil (0·44 g), which was passed through a small column of CC7 Mallinckrodt silicic acid (100—200 mesh) (chloroform as eluant). A homogeneous fraction (0·32 g) was obtained which was crystallized twice from ethanol to yield the *acetal* (0·12 g), m.p. 76°, $[\alpha]_D^{25}$ 8·3° (*c* 0·35 in $CHCl_3$) (Found: C, 63·25; H, 6·05; N, 6·0. $C_{24}H_{28}N_2O_7$ requires C, 63·15; H, 6·15; N, 6·15%).

3,6-*Anhydro*-D-*allose*.—A solution of 3,6-anhydro-4,5-*O*-isopropylidene-D-allose dimethyl acetal (0·55 g) in 0·1N-hydrochloric acid (5 ml) was heated for 3·5 h at 55°. The solution was cooled and neutralized with IRA 400 resin ($HCO_3^-$ form). The resin was filtered off and the solution was concentrated to yield 3,6-*anhydro*-D-*allose* (IV) (0·3 g), $[\alpha]_D^{25}$ −33·2° (*c* 3·8 in $H_2O$), δ ($D_2O$) (0·14 g in 0·3 ml; 43°, acetone as internal standard at δ 2·17) 3·3—4·3 (complex m), 4·52 (s, DOH), 4·96 (d, $J_{1.2}$ 5·0 Hz, H-1 of aldehydrol), 5·21—5·53 (m, H-1 of dimeric forms), and 9·65 p.p.m. (s, H-1 of *aldehydo*-form). Integration of these signals showed the presence of 3·6% free aldehyde, 50% dimeric forms, and 46% hydrated form.

1,2-O-*Isopropylidene*-3-O-p-*tolylsulphonyl*-α-D-*glucofuranose*.—A solution of 1,2:5,6-di-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose (16·3 g) in 60% acetic acid (160 ml) was heated at 60—65° for 4·5 h. The mixture was concentrated to dryness under reduced pressure and the residue extracted with chloroform (4 × 50 ml), which was washed with water (3 × 25 ml), dried ($Na_2SO_4$), and concentrated to an oil (15·4 g). T.l.c. (ethyl acetate as irrigant) showed traces of starting material. The mixture was fractionated on CC7 Mallinckrodt silicic acid (100—200 mesh) [elution with benzene–ether (3 : 7)]. 1,2-*O*-Isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose [11] (12·7 g) was obtained as a syrup, δ ($CDCl_3$) 1·23 and 1·43 (3H each, s, $Me_2C$=), 2·43 (3H, s, ArMe), 2·6—4·0 (5H, m), 4·16 (pair of d, $J_{3.4}$ 1·3, $J_{4.5}$ 4·5 Hz, H-4), 4·57 (d, $J_{1.2}$ 1·8 Hz, H-2), 5·00 (d, H-3), 5·87 (d, H-1), and 7·3—8·0 p.p.m. (4H, 2d, ArH).

*Attempted Intramolecular Displacement Reactions with* 1,2-O-*Isopropylidene*-3-O-p-*tolylsulphonyl*-α-D-*glucofuranose*.—(*a*) The title compound (0·19 g), water (10 ml), and sodium hydrogen carbonate (0·2 g) were boiled together for 42 h. T.l.c. [silicic acid; benzene–ether (1 : 1)] then showed the complete absence of starting material. The mixture was evaporated and the remaining solid extracted with hot acetone (3 × 20 ml). Concentration of the extracts yielded a solid, which was recrystallized from ethanol–light petroleum to give 1,2-*O*-isopropylidene-α-D-glucofuranose (0·08 g), m.p. and mixed m.p. 160°.

(*b*) The title compound (0·08 g), *NN*-dimethylformamide (10 ml), and sodium hydrogen carbonate (0·08 g) were heated at 100° for 60 h. T.l.c. then showed only starting material.

(*c*) The title compound (0·5 g) was dissolved in 1,2-dimethoxyethane (75 ml) and a few pieces of sodium were added. After storage overnight the excess of sodium was removed and the mixture was refluxed for 12 h, poured into water, and extracted continuously with chloroform; concentration of the extracts gave an oil, indistinguishable from starting material by n.m.r. spectroscopy.

1,2-O-*Isopropylidene*-5-O-*methyl*-3-O-p-*tolylsulphonyl*-α-D-*glucofuranose*.[11]—A solution of 1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose (9·5 g) in pyridine (100 ml) was cooled to 0°, and benzoyl chloride (3·57 ml) was added. After 3 days at 0°, water was added, and the mixture was acidified with dilute hydrochloric acid. It was then extracted with chloroform (5 × 25 ml); the extract was washed with sodium hydrogen carbonate followed by water, dried ($Na_2SO_4$), and concentrated to an oil (12·5 g). This oil was heated for 20 h with *NN*-dimethylformamide (30 ml), methyl iodide (45 ml), and silver oxide (25 g). Chloroform was then added and the solution filtered; concentration of the filtrate yielded an oil which was dissolved in anhydrous methanol (100 ml), and a trace of sodium was added. After 25° for 17 h, water (200 ml) was added and the mixture was extracted with chloroform (4 × 50 ml). The chloroform solution was washed with water (2 × 25 ml), dried ($Na_2SO_4$), and concentrated to an oil (14·5 g); t.l.c. [benzene–ether (4 : 1)] revealed the presence of two main components corresponding to 1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose and a monomethyl derivative. Fractionation of the mixture [CC7 100—200 mesh Mallinckrodt silicic acid; benzene–ether (4 : 1)] gave 1,2-*O*-isopropylidene-5-*O*-methyl-3-*O*-*p*-tolylsulphonyl-α-D-glucofuranose (5·75 g), $[\alpha]_D^{25}$ −23·5° (*c* 1·85 in $CHCl_3$), δ ($CDCl_3$) 1·27 and 1·47 (3H each, s, $Me_2C$=), 2·47 (3H, s, ArMe), 3·13 (3H, s, OMe), 3·15—4·2 (4H, m), 4·33 (pair of d, $J_{3.4}$ 1·25, $J_{4.5}$ 4·25 Hz, H-4), 4·73 (d, $J_{1.2}$ 1·9 Hz, H-2), 5·00 (d, H-3), 5·90 (d, H-1), and 7·3—7·9 p.p.m. (4H, 2d, ArH).

*Methanolysis of* 1,2-O-*Isopropylidene*-5-O-*methyl*-3-O-p-*tolylsulphonyl*-α-D-*glucofuranose*.—The title compound (2·17 g) and methanolic 2% hydrogen chloride (60 ml) were heated under reflux for 28 h. After neutralization with sodium hydrogen carbonate the inorganic salts were filtered off and the filtrate was concentrated to an oil which was extracted with boiling acetone (3 × 25 ml). Concentration of these extracts yielded an oil (1·1 g) which, according to its n.m.r. spectrum ($D_2O$), contained no sulphonate and isopropylidene groups but three methoxy-groups. T.l.c. (silica gel; ethyl acetate) showed the presence of a major component, together with trace amounts of material with higher mobility. Fractionation on CC7 Mallinckrodt silicic acid (100—200 mesh) (30 g) (ethyl acetate as eluant) gave the major component, 3,6-anhydro-5-*O*-methyl-D-allose dimethyl acetal (0·9 g).

A sample (0·14 g) was treated with *p*-nitrobenzoyl chloride in pyridine at 25° for 24 h. The excess of chloride was destroyed with water and the mixture was poured into sodium hydrogen carbonate solution, whereupon a solid (0·3 g) separated out. Recrystallization from ethanol yielded 3,6-*anhydro*-5-O-*methyl*-2,4-*bis*-O-p-*nitrobenzoyl*-D-*allose dimethyl acetal* (0·22 g), m.p. 110°, $[\alpha]_D^{25}$ −44·1° (*c* 0·5 in $CHCl_3$) (Found: C, 53·4; H, 4·7; N, 5·3. $C_{23}H_{24}N_2O_{12}$ requires C, 53·1; H, 4·6; N, 5·4%), δ [$(CD_3)_2CO$]

3·34 (3H, s, OMe), 3·42 (6H, s, 2 × OMe), 3·58—4·34 (3H, m), 4·52 (pair of d, $J_{2,3}$ 5·0, $J_{3,4}$ 4·0 Hz, H-3), 4·74 (d, $J_{1,2}$ 5·4 Hz, H-1), 5·51 (pair of d, $J_{4,5}$ 5·2 Hz, H-4), 5·80 (t, outer signals show broadening, H-2), and 8·3 p.p.m. (8H, s, ArH).

3,6-*Anhydro*-5-O-*methyl*-D-*allose* (V).—A solution of 3,6-anhydro-5-*O*-methyl-D-allose dimethyl acetal (0·24 g) in 0·2N-sulphuric acid (5 ml) was heated at 60° for 2 h. The solution was cooled and then neutralized with IRA 400 resin ($HCO_3^-$ form). After separation from the resin the filtrate was concentrated *in vacuo* to yield an oil; t.l.c. [silica gel; ethyl acetate–acetone (1 : 1)] showed this to be mainly one compound, with no starting material remaining. A homogeneous sample of 3,6-anhydro-5-*O*-methyl-D-allose (0·14 g) was obtained by column chromatography under the foregoing conditions; δ ($D_2O$) 3·33 (s, OMe), 3·46—4·54 (m), 4·94 (d, $J_{1,2}$ 5·0 Hz, H-1 of aldehydrol), 5·17—5·54 (m, H-1 of dimeric forms), and 9·65 p.p.m. (s, H-1 of free aldehyde).

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