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THE ACETONATION OF D-TALOSE

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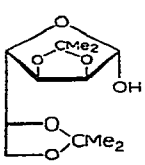
ABSTRACT

The acetonation of α-D-talopyranose in the presence of anhydrous copper(II) sulphate and sulphuric acid has been re-examined, and the major products have been shown to be 2,3:5,6-di-*O*-isopropylidene-α-D-talofuranose (**1**, 28%) and 1,2:5,6-di-*O*-isopropylidene-β-D-talofuranose (**2**, 10%). These structures were allocated primarily on the basis of mass spectrometry and nuclear magnetic resonance spectroscopy. Oxidation of diacetal **1** with acetic anhydride in methyl sulphoxide gave 2,3:5,6-di-*O*-isopropylidene-D-talono-1,4-lactone (**4**). 1,2:5,6-Di-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-β-D-talofuranose (**3**) was obtained on sulphonylation of diacetal **2**.

INTRODUCTION AND DISCUSSION

Bimolecular nucleophilic displacement of *endo*-sulphonyloxy groups attached to trioxabicyclo[3.3.0]octane ring systems has afforded stereospecific syntheses of a number of 3-amino-3-deoxy[1,2] and 3-deoxy-3-fluoro sugars[3,4] which are often difficult to prepare by other methods. Such displacements have been reported with 1,2:5,6-di-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-allofuranose[1,3] and 1,2:5,6-di-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-gulofuranose[2,4]. With a view to extending these studies, we sought to prepare 1,2:5,6-di-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-β-D-talofuranose (**3**) which contains an *endo*-sulphonyloxy group that should, by analogy, undergo ready displacement.



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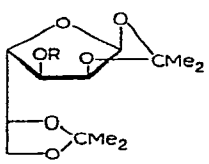
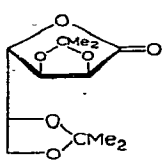


2 R = H
3 R = $SO_2 \cdot C_6H_4Me$



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Acetonation of D-talose, in the presence of anhydrous copper(II) sulphate and concentrated sulphuric acid, was reported[5] to yield a mixture of 2,3:5,6-di-*O*-isopropylidene-D-talofuranose (**1**) and 1,2:5,6-di-*O*-isopropylidene-β-D-talofuranose (**2**).

Diacetal **1** was not isolated, and its presence was indicated by the isolation of 2,3:5,6-di-*O*-isopropylidene-D-talono-1,4-lactone (**4**) following oxidation of the products of acetonation with alkaline permanganate. The structure of diacetal **2** was founded on its recovery after oxidation, which implied the absence of a free, primary hydroxyl group. Clearly, a more definitive allocation of structure is required in this case, and it was thought that modern spectroscopic methods might be applied advantageously to this problem.

Although new preparations of D-talose have been reported[6,7] recently, hydroxylation of D-galactal[8] with perbenzoic acid appeared to be most amenable to large-scale work. This procedure gives a mixture of D-talose and D-galactose that is separated by extraction of D-talose into boiling methanol, in which D-galactose is relatively insoluble. In our hands, complete separation of the two hexoses was not achieved by the extraction procedure, although the methanol-soluble material was enriched in D-talose. Chromatographically pure D-talose was obtained either by peracetylation of the hexose mixture, followed by fractional crystallisation of the derived penta-*O*-acetyl-α-D-talopyranose and deacetylation, or, more efficiently, by using the counter-current extraction procedure described in the Experimental section.

Acetonation[5] of α-D-talopyranose was shown (t.l.c.) to give two major products and a small proportion of a third component. Chromatography on silica gel afforded the major components, which were designated as *A* and *B* in order of their elution from the column. Compound *A* (28%) was further purified by distillation, and compound *B* (10%) was obtained in crystalline form. Elemental analyses showed that they were both diacetals, and this was also clearly indicated[9] by the presence of a prominent peak at *m/e* 245 (M − 15) in their mass spectra (see Figs. 1 and 2).

Mass spectrometry provides[9] an elegant means of distinguishing between di-*O*-isopropylidenealdohexopyranoses and their furanose counterparts. The most characteristic fragmentation process of di-*O*-isopropylidenealdohexofuranoses is scission of the C-4–C-5 bond, which gives rise[9] to an ion of *m/e* 101. Peaks at *m/e* 101 were present in the mass spectra of both *A* and *B* (Figs. 1 and 2), which are thus identified as talofuranose diacetals. Although the mass spectra of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose are closely similar, the 2,3:5,6-diacetal has a more intense peak at *m/e* 243 (M − 17), due[9] to the attachment of the hydroxyl group to C-1 rather than to C-3. This difference was also apparent* in the spectra of diacetals *A* and *B*, which were tentatively assigned the 2,3:5,6- and 1,2:5,6-arrangements, respectively, on this basis.

These assignments were supported by n.m.r. spectroscopy (deuteriochloroform) of the diacetals by comparison of the H-1 couplings. The H-1 signals in both spectra were shifted well downfield, and, for diacetal *A*, H-1 appeared as a doublet (*J* 9 Hz) centred at τ 4.59, which collapsed to a singlet upon the addition of deuterium oxide. This treatment also removed a doublet (*J* 9 Hz) centred at τ 5.64, which can be

*This is seen more clearly from the original mass spectra, where peak amplifications of fourteen- and fifty-fold are recorded, than from Figs. 1 and 2.

ascribed to the hydroxylic proton. The n.m.r. data are readily reconciled with structure **1**, where strong coupling is observed initially between the hydroxylic proton[10] and H-1. Exchange of the hydroxylic proton for deuterium removed this coupling. The resulting appearance of H-1 as a singlet ($J < 0.5$ Hz) signified a *trans*-arrange-

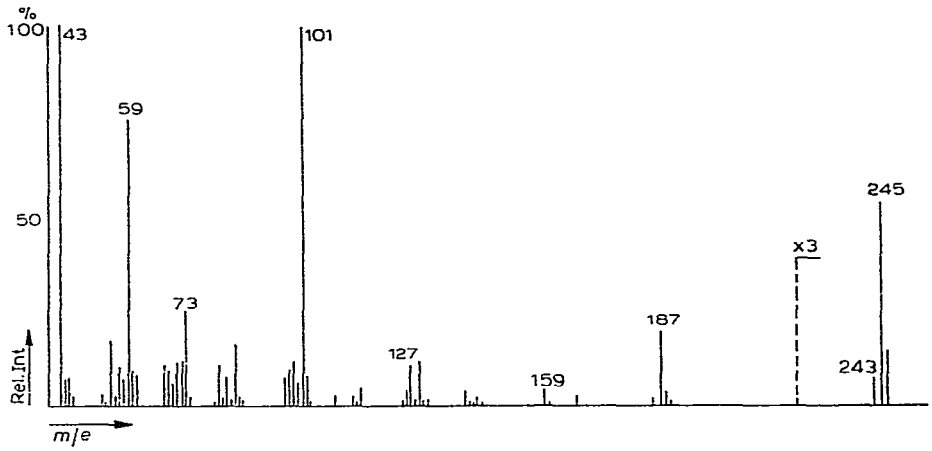

Fig. 1. Mass spectrum of diacetal *A* (2,3:5,6-di-*O*-isopropylidene-α-D-talofuranose).

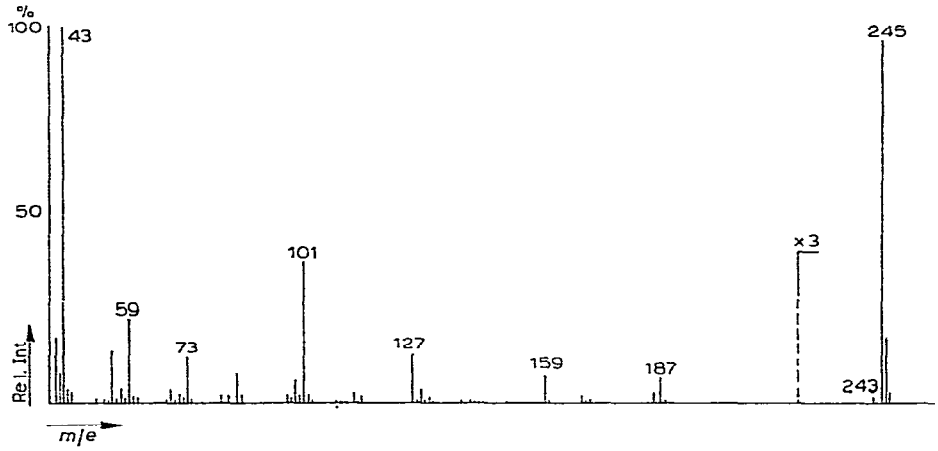

Fig. 2. Mass spectrum of diacetal *B* (1,2:5,6-di-*O*-isopropylidene-β-D-talofuranose).

ment[11] of the protons at C-1 and C-2. The H-1 signal for diacetal *B* was observed as a doublet (J 4 Hz), centred at τ 4.16, which was unaffected by the addition of deuterium oxide. The size of the H-1–H-2 coupling is compatible[11] with a *cis*-arrangement of these protons, as required by structure **2**. The combined spectroscopic evidence supports the structures 2,3:5,6-di-*O*-isopropylidene-α-D-talofuranose (**1**) for *A* and 1,2:5,6-di-*O*-isopropylidene-β-D-talofuranose (**2**) for *B*.

Confirmation of the structure of diacetal **1** was afforded by its conversion into the known[5] 2,3:5,6-di-*O*-isopropylidene-D-talono-1,4-lactone (**4**) on oxidation with

acetic anhydride–methyl sulphoxide[12]. 1,2:5,6-Di-*O*-isopropylidene-β-D-talofuranose (**2**) gave a crystalline sulphonate (**3**) on treatment with toluene-*p*-sulphonyl chloride in pyridine.

Mills[13] predicted, from conformational principles, that the 2,3:5,6-diacetal **1** would preponderate at equilibrium on acetonation of D-talose, and our findings substantiate his arguments. The proportion of diacetal **2** found in this investigation is significantly less than that (~ 34%) obtained in a comparable experiment by Bosshard[5], whose material was of uncertain purity.

2,3:5,6-Di-*O*-isopropylidenealdohexoses are currently of interest, since they offer a means, by way of the chloro derivatives, of synthesising nucleosides containing these sugars[14].

EXPERIMENTAL

Thin-layer chromatography (t.l.c.) was performed on Kieselgel G, and detection was effected with the vanillin–sulphuric acid reagent[15]. Infrared spectra were obtained on a Perkin–Elmer 257 spectrometer, and n.m.r. spectra were obtained with a Perkin–Elmer R-10 spectrometer for *ca.* 10% solutions in deuteriochloroform with tetramethylsilane as internal reference. Mass spectra were measured with an A.E.I. MS9 spectrometer (ionising potential 58 ev), using a direct insertion technique.

Preparation of α-D-*talopyranose.* — A mixture of D-talose and D-galactose was prepared by hydroxylation of D-galactal as described in the literature[8]. The proportion of D-talose in the mixture was increased by a single extraction with boiling methanol, followed by filtration and evaporation. This mixture was used in the purification procedures described below. Repeated treatments with boiling methanol failed to give D-talose in chromatographically pure form.

(*a*) *Acetylation.* The mixture (2 g) in pyridine (48 ml) containing acetic anhydride (50 ml) was stirred for 17.5 h at room temperature, and t.l.c. (ethyl acetate–acetone, 1:1) then indicated that the reaction was complete. The solution was poured into ice–water (300 ml), the aqueous solution was extracted with chloroform (3 × 500 ml), and the combined extracts were washed with water (3 × 500 ml) and dried ($CaCl_2$). Removal of the solvent afforded a syrup which crystallised (0.58 g) from ethanol. Recrystallisation from chloroform–ethanol gave penta-*O*-acetyl-α-D-talopyranose (0.11 g), m.p. 106–107°; lit., m.p. 106.5–107° (ref. 16), m.p. 104–105° (ref. 7). Additional quantities (totalling 0.67 g) of the pentaacetate were obtained from the mother liquors by fractional crystallisation.

The pentaacetate (0.6 g) was deacetylated by using the Zemplén procedure, and, on complete reaction, the solution was stirred with a slight excess of Amberlite IR-120(H^+) resin until it was neutral. The filtered solution was concentrated, and the syrupy residue was crystallised from an equal quantity of methanol to give α-D-talopyranose (0.14 g), m.p. 129–130°; lit.[8], m.p. 133–134°. This material was shown to be pure by paper chromatography (ethyl acetate–pyridine–water, 40:11:6).

(*b*) *Countercurrent extraction.* D-Talose and D-galactose had R_F values of 0.13

and 0.07, respectively, in butyl alcohol saturated with water, and this solvent system was the most suitable of those examined for use with a Gallenkamp countercurrent apparatus. A typical run was conducted as follows.

The mixture (2 g) was dissolved in the lower phase of water saturated with butyl alcohol (60 ml), and the solution was distributed in the first six tubes of the countercurrent apparatus. Five hundred transfers were then carried out automatically by using an upper phase of butyl alcohol saturated with water, with shaking and settling times of 3 min each; the volumes of the upper and lower phases employed were 20 ml and 10 ml, respectively. Combination and evaporation of the appropriate fractions from the lower phase (as indicated by paper chromatography) gave a syrup which was crystallised from an equal volume of methanol at 0°. Two recrystallisations gave α-D-talopyranose (1.1 g), m.p. 128–129°, which was shown to be free from D-galactose by paper chromatography.

Acetonation of α-D-talopyranose. — Crystalline D-talose (1 g) in dry acetone (25 ml) containing conc. sulphuric acid (0.05–0.1 ml) and anhydrous copper sulphate (2.5 g) was shaken for 48 h at room temperature, after which time t.l.c. (ethyl acetate–chloroform, 2:1) showed the presence of two major components, together with a small proportion of a slower-moving component and unreacted hexose. Solid material was filtered off and washed thoroughly with acetone, and the filtrate was neutralised with a few drops of conc. ammonia and filtered. Removal of the solvent left a syrupy residue (*ca.* 1 g) which was chromatographed on silica gel (elution with ethyl acetate–hexane, 1:1) to give, in order of elution, 2,3:5,6-di-*O*-isopropylidene-α-D-talofuranose (**1**) (0.41 g, 28%), b.p. 150–160° (bath)/0.1–0.2 mm, $[\alpha]_D$ +2 ±1° (*c* 2, chloroform), ν_{max} 1375 (CMe_2) and 3400 cm^{-1} (OH) (Found: C, 55.8; H, 8.1. $C_{12}H_{20}O_6$ calc.: C, 55.4; H, 7.7%); and 1,2:5,6-di-*O*-isopropylidene-β-D-talofuranose (**2**) (0.14 g, 10%), m.p. 85–86° (from ether–light petroleum, b.p. 40–60°), $[\alpha]_D$ −25 ±1° (*c* 0.47, chloroform), ν_{max} 1375 (CMe_2) and 3465 cm^{-1} (OH) (Found: C, 55.2; H, 7.4. $C_{12}H_{20}O_6$ calc.: C, 55.4; H, 7.7%). Bosshard[5] reported $[\alpha]_D$ −25.2° (*c* 3.1, acetone) for a syrupy material of uncertain purity.

The n.m.r. spectra showed the following salient features: diacetal **1**, τ 4.59 (1-proton doublet, *J* 9 Hz, H-1); 5.64 (1-proton doublet, *J* 9 Hz OH); 8.53, 8.62, and 8.68 (12 protons, integrated ratio *ca.* 2:1:1, 2 CMe_2); addition of deuterium oxide resulted in the collapse of the H-1 doublet at τ 4.59 to a singlet and the disappearance of the doublet at τ 5.64; diacetal **2**, τ 4.16 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1); 8.43, 8.59, and 8.63 (12 protons, integrated ratio *ca.* 1:1:2, 2 Me_2C).

2,3:5,6-Di-O-isopropylidene-D-talono-1,4-lactone (**4**). — A solution of the diacetal **1** (0.11 g) in methyl sulphoxide (8 ml) and acetic anhydride (1 ml) was stirred for 19 h at room temperature, whereupon t.l.c. (ethyl acetate–hexane, 1:1) revealed the formation of a single product. Most of the solvent was evaporated off at low pressure (*ca.* 0.5 mm), the residue was dissolved in chloroform (25 ml), and the organic layer was washed with water (5 × 15 ml) and dried ($MgSO_4$). Removal of the solvent afforded a crystalline residue (0.1 g) which was recrystallised from light petroleum (b.p. 100–120°) to give the lactone **4**, m.p. 129–130°, $[\alpha]_D$ +19 ±2° (*c* 0.49, acetone),

ν_{max} 1770 (γ-lactone) and 1380 cm^{-1} (CMe_2); lit.[5], m.p. 129–130°, $[\alpha]_D$ +17 ±2° (*c* 1.85, acetone).

1,2:5,6-Di-O-isopropylidene-3-O-toluene-p-sulphonyl-β-D-talofuranose (**3**). — Treatment of the diacetal **2** with toluene-*p*-sulphonyl chloride in pyridine, in the usual way, gave the sulphonate **3** (73%), m.p. 136–137° (from aqueous ethanol), $[\alpha]_D$ −84.5° (*c* 0.6, chloroform) (Found: C, 54.75; H, 6.2; S, 7.9. $C_{19}H_{26}O_8S$ calc.: C, 55.1; H, 6.3; S, 7.7%).

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