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3,4-Anhydro-1,2-*O*-isopropylidene-β-D-tagatopyranose and 4,5-anhydro-1,2-*O*-isopropylidene-β-D-fructopyranose

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Dedicated to Professor Aleksander Zamojski on the occasion of his 70th birthday.

Abstract

3,4-Anhydro-1,2-*O*-isopropylidene-β-D-tagatopyranose (**8**) and 4,5-anhydro-1,2-*O*-isopropylidene-β-D-fructopyranose (**10**) have been prepared by treatment of 3,5-di-*O*-acetyl-1,2-*O*-isopropylidene-4-*O*-toluene-*p*-sulfonyl-β-D-fructopyranose with methanolic sodium methoxide. The structures of **8** and **10** were assigned by ^{1}H and ^{13}C NMR spectroscopy and that of **10** by X-ray crystallography; both exist in half-chair conformations. Compounds **8** and **10** interconvert in aqueous sodium hydroxide, giving a ratio of 1:2 at equilibrium. The monoacetates of **8** and **10** (5-*O*-acetyl-3,4-anhydro-1,2-*O*-isopropylidene-β-D-tagatopyranose and 3-*O*-acetyl-4,5-anhydro-1,2-*O*-isopropylidene-β-D-fructopyranose) undergo stereospecific epoxide ring opening in 80% acetic acid to give mainly the axial monoacetates 5-*O*-acetyl-1,2-*O*-isopropylidene-β-D-fructopyranose and 4-*O*-acetyl-1,2-*O*-isopropylidene-β-D-tagatopyranose, respectively.

Keywords: Anhydroketose; Epoxide migration; Stereospecific ring opening

1. Introduction

The base-catalysed rearrangement of oxiranes (epoxides) bearing a vicinal hydroxyl group [1,2], known as epoxide migration [3], has been studied extensively by ourselves [4,5] and by others [3,6–8]. The rearrangement has been used for the synthesis of sugars and polyols by chain extension [9,10]. In continuation of our work on methyl anhydropentopyranosides [11,12], we wished to examine the preparation and equilibration of the ketose-derived epoxides 3,4-anhydro-1,2-*O*-isopropylidene-β-D-tagatopyranose (**8**) and 4,5-anhydro-1,2-*O*-isopropylidene-β-D-fructopyranose (**10**). The preparation of the anhydrotagatose **8** has previously been described by Ohle and Schultz [13] and much later by Rao et al. [14]. Treatment of the sulfonate **2** with an excess of hot methanolic sodium methoxide afforded a crystalline epoxide, which was assigned the anhydrotagatose structure **8**. Such vigorous conditions are known to cause epoxide migration in epoxides containing a vicinal trans-hydroxyl group. The epoxide isolated by Ohle might therefore be the anhydrofructose

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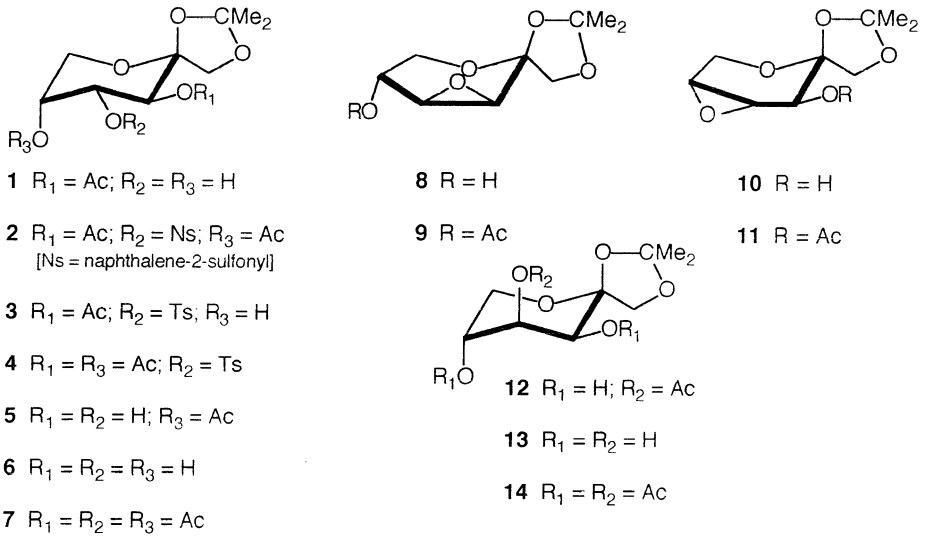


Scheme 1.

10. Rao et al. [14] treated the crystalline epoxide with potassium hydrogen fluoride in refluxing methoxyethanol. The products were as expected from ring opening of the anhydrofructose **10** and the authors suggested that epoxide migration in **8** took place under the influence of KHF_2. This interpretation is contrary to our experience and gave us a further incentive to re-examine Ohle's '3,4-anhydro-1,2 - *O* - isopropylidene - β - D - tagatopyranose' and to explore its chemistry in greater detail.

2. Results and discussion

Reaction of 3-*O*-acetyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**1**) [13,15–17] with 1.1 equivalents of toluene-*p*-sulfonyl chloride in pyridine gave mainly the expected equatorial 4-sulfonate (**3**) as a syrup (Scheme 1). In the ^1H NMR spectrum, the H-4 signal (δ 4.93, $J_{4,3}$ 10.1, $J_{4,5}$ 3.3 Hz) was deshielded relative to its position in the spectrum of **1**. Acetylation of the crude syrup with acetic anhydride in pyridine afforded the crystalline 3,5-diacetate **4** (44% overall), whose structure was confirmed by ^1H and ^{13}C NMR. Compound **4** was treated with methanolic sodium methoxide (2 equivalents) at room temperature and the reaction monitored by thin-layer chromatography (TLC). Formation of the dihydroxysulfonate was followed by conversion into an epoxide of low R_f value, which was itself slowly converted into an epoxide of higher R_f value. Chromatography on silica gel yielded first a crystalline epoxide, mp 81–82 °C, in 29% yield, clearly identical to the epoxide isolated by the earlier workers [13,14], followed by an isomeric syrupy epoxide (44%). The latter epoxide, being formed first, was expected to be 3,4-anhydro-1,2-*O*-isopropylidene-β-D-tagatopyranose (**8**) and this was evident from its ^1H and ^{13}C NMR spectra; the signals for H-3 and H-4 were shielded relative to H-5 and H-6 and those for C-3 and C-4 were shielded relative to C-5 and C-6. Correspondingly, the crystalline epoxide that was formed as the secondary product gave shielded signals derived from a 4,5-anhydro ring.

Conclusive proof that the crystalline epoxide was 4,5-anhydro-1,2-*O*-isopropylidene-β-D-fructopyranose (**10**) was obtained by X-ray crystallography, shown in Fig. 1. The pyranose ring is in a half-chair conformation, $^2H_0$, in which the anomeric O-2 is axial with C-1 equatorial, known to be a very favourable arrangement [18]. The puckering parameters according to Cremer and Pople [19] are $Q = 0.475$ Å, $\Theta = 132.4°$, and $\Phi = 212.66°$ (the shape of the isopropylidene ring is described by the puckering parameters $Q_2 = 0.269$ Å and $\Phi_2 = 212.49°$). The hydroxyl proton H-3A (attached to O-3) was located in the penultimate difference Fourier map and seen to be involved in an intramolecular hydrogen bond to

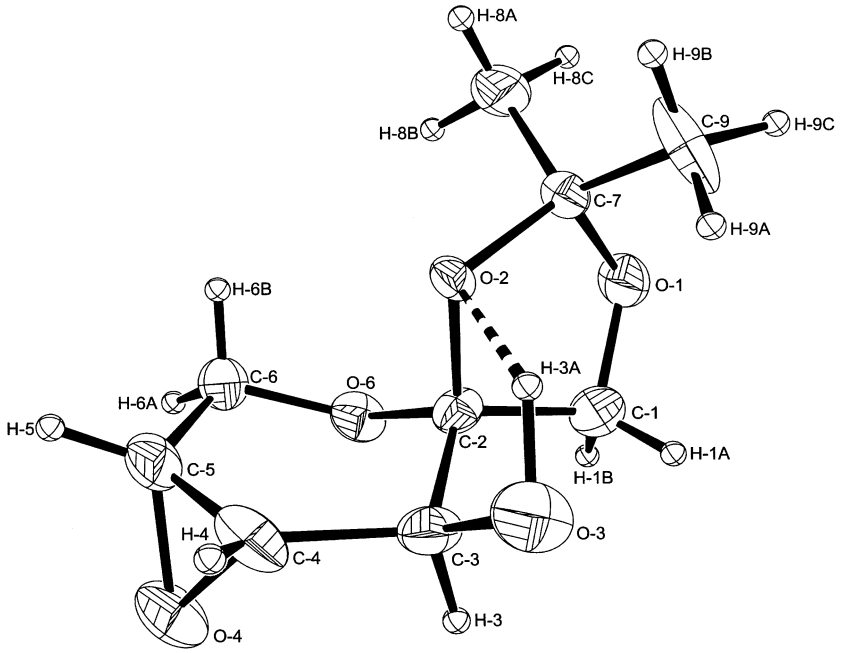


Fig. 1. ORTEX plot of **10**. Thermal ellipsoids are represented at the 30% probability level.

O-2 [O-2···H-3A 1.92(11) Å; O-2–H-3A–O-3 125(9)°]. The H–H dihedral angles are shown in Table 1, together with the coupling constants from the ^{1}H NMR spectrum. The very low coupling between the epoxide protons and those on C-3 and C-6 is to be expected from earlier work on methyl 3,4-anhydro-β-arabinosides [12,20] and *cis*-2-*tert*-butyl-4,5-epoxytetrahydropyran [21].

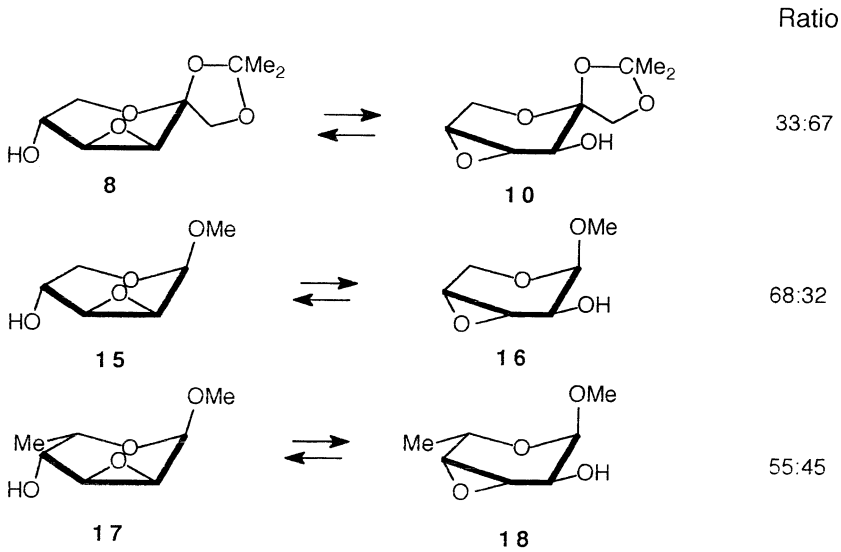
The interconversion of **8** and **10** in aqueous sodium hydroxide by epoxide migration was studied polarimetrically and by GLC (Scheme 2). At equilibrium the anhydrofructose **10** was favoured by 2:1. The equilibration was also conducted on a preparative scale, starting from **10**. Both epoxides were isolated from the mixture, after chromatography, in a 2:1 ratio. There is an interesting comparison with the analogous methyl 2,3-anhydro-β-D-lyxopyranoside (**15**) and 3,4-anhydro-β-D-arabinopyranoside (**16**) [11][1], together with methyl 2,3-anhydro-6-deoxy-α-L-gulopyranoside (**17**) and methyl 3,4-anhydro-6-deoxy-α-L-galactopyranoside (**18**) [22][1]. In both of these examples there is a preference for the 2,3-epoxide at equilibrium (Scheme 2). In the anhydroketose series the analogous 3,4-epoxide is disfavoured and this may be due to a greater freedom for O-2 and C-1 to become fully axial and equatorial, respectively, in **10**.

It is well known that the ring opening of an epoxide can be directed by a neighbouring *trans*-acetoxy group [4,5,11,23,24]. It was of interest to study the reaction of the acetates of **8** and **10** (**9** and **11**) with 80% acetic acid. The reaction product from **9** was 5-*O*-acetyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**5**), the axial monoacetate, as would be expected if the acetoxonium ion **19** is an intermediate [11,25–27] (Scheme 3). The location of the acetyl group on O-5 was apparent from the deshielded signal for H-5 in the ^{1}H NMR spectrum. O-Deacetylation afforded the known 1,2-*O*-isopropylidene-β-D-fructopyranose (**6**) [28]. Similarly, **11** gave the axial monoacetate **12** by participation of the 3-*O*-acetyl group; **12** was converted by deacetyla-

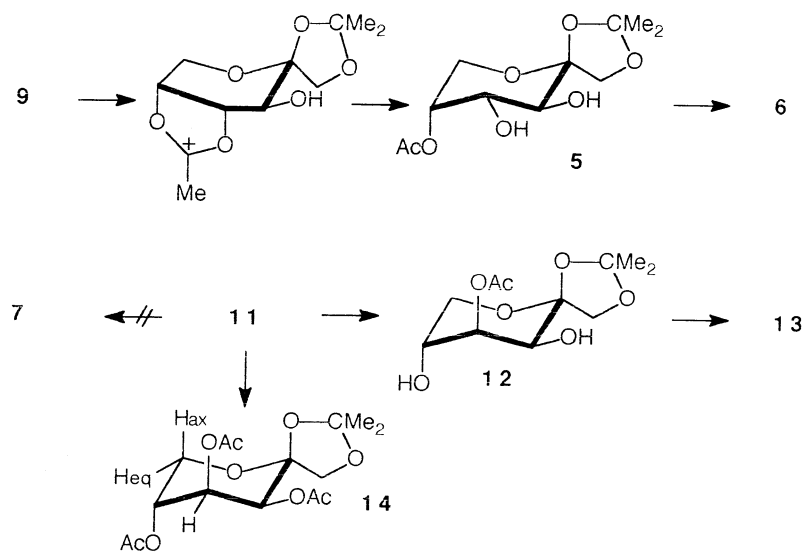
Table 1
Selected C–H torsion angles (°) and H–H coupling constants (Hz) for **10**

Bonds	Angles	^3J
H-3–C-3–C-4–H-4	105.36	≈0
H-4–C-4–C-5–H-5	0.14	3.9
H-5–C-5–C-6–H-6A	71.12	≈0
H-5–C-5–C-6–H-6B	46.35	≈0

[1] The original papers [11,22] describe the enantiomers of **15**–**18** but we show these forms for direct comparison with **8** and **10**.



Scheme 2.



Scheme 3.

tion and removal of the isopropylidene group into D-tagatose, identified by comparison with an authentic sample.

Ohle and Schultz [13] claimed to have converted the acetate of their crystalline anhydroketose, by treatment with acetic anhydride, acetic acid and a little pyridine, into 3,4,5-tri-*O*-acetyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**7**) [15]. Since we have now shown that the crystalline anhydroketose is the 4,5-anhydrofructose **10** and not the 3,4-anhydrotagatose **8**, we have reinvestigated the reaction. The crystalline product, isolated after recrystallisation in 39% yield, has now been shown to be 3,4,5-tri-*O*-acetyl-1,2-*O*-isopropylidene-β-D-tagatopyranose (**14**). Although it has a similar melting point and specific rotation to the fructose derivative **7** [15], it was converted into tagatose by alkaline methanolysis, followed by acidic hydrolysis. The ^{1}H NMR spectrum of **14** was as expected of the β-D-tagato configuration. Using H,H-COSY all of the signals were assigned; in particular there is long-range coupling (^4J) between H-4 and H-6_{eq}, which are in a 'W' relationship. The spectrum differed from that of authentic **7**, whose spectrum agreed with that already published

[17]. The formation of a product of *tagato* configuration is to be expected from some of our earlier work [29] on the treatment of acetoxy epoxides with acetic acid and acetic anhydride.

3. Experimental

General methods.—^{1}H NMR spectra were recorded at 400 MHz (Jeol EX400) and at 100 MHz (Jeol JNM); ^{13}C NMR spectra at 100 MHz (Jeol EX400). Optical rotations were measured with a Thorn–Bendix TBL-NPL polarimeter type 143D and a cell of 1 cm path length. Adsorption chromatography was conducted on silica gel (E. Merck) Kieselgel 60–70 230 mesh ASTM and TLC with Kieselgel 60F 254 as adsorbent. On TLC, sugar derivatives were visualised by ethanolic H_2SO_4, followed by heating; toluenesulfonates by alcoholic diphenylamine, followed by exposure to UV light [30]; epoxides by sodium iodide and methyl red, followed by heating [23]. GLC was carried out using a Perkin–Elmer F11 gas chromatograph with a 3% SE 30 column (1 m), employing an inlet pressure of 20 psi and a column temperature of 100–110 °C.

X-ray crystallography.—A crystal of **10** (approximate dimensions $0.20 \times 0.22 \times 0.30$ mm) was used for data collection. Crystallographic measurements were made at 293(2) K on a CAD4 automatic four-circle diffractometer in the range $2.06 < \theta < 21.91°$. Data (728 reflections) were corrected for Lorentz and polarization but not for absorption. Despite several recrystallisation attempts, it was not possible to grow larger crystals. This was unfortunate given the weak diffracting ability of the sample selected.

Crystal data: $C_9H_{14}O_5$, $M = 202.20$, monoclinic, $a = 9.002(3)$, $b = 5.553(1)$, $c = 10.590(4)$ Å, $\beta = 111.28(3)°$, $U = 493.3(3)$ Å^3, space group $P2_1$, $Z = 2$, $D_c = 1.361$ g cm^{-3}, μ (Mo K_α) $= 0.111$ mm^{-1}, $F(000) = 216$.

In the final least-squares cycles all atoms were allowed to vibrate anisotropically. Hydrogen atoms were included at calculated positions where relevant, except for H-3A, which was located and refined at a distance of 1.08 Å from O-3. H-3A is involved in intramolecular hydrogen-bonding to O-4. [H-3A…O-2 1.92(11) Å, O-3–H-3A–O-2 125(9)°.]

The solution of the structure (SHELX86) [31] and refinement (SHELX93) [32] converged to a conventional [i.e., based on 487 with $F_o > 4\sigma(F_o)$], $R_1 = 0.0911$ and $wR_2 = 0.2041$. Goodness-of-fit = 0.934. The maximum and minimum residual densities were 0.352 and -0.525 e Å^{-3}, respectively. The asymmetric unit (shown in Fig. 1), along with the labelling scheme used, was produced using ORTEX [33]. Final fractional atomic coordinates and isotropic thermal parameters, bond distances and angles and tables of anisotropic temperature factors are available as supplementary data (see Section 4).

3,5-Di-O-*Acetyl-1,2*-O-*isopropylidene-4*-O-*toluene*-p-*sulfonyl-β*-D-*fructopyranose* (**4**).—The acetate (**1**) [15] (8.61 g) in pyridine (25 mL) was stirred at room temperature (rt) and toluene-*p*-sulfonyl chloride (6.9 g, 1.1 equiv) was added. The mixture was left overnight at rt and the product isolated using CH_2Cl_2 to yield a crude syrup (11.34 g). TLC showed a major spot corresponding to a monosulfonate (**3**) (R_f 0.64), together with a small amount of disulfonate (R_f 0.75). ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.80 (d, 2 H, J 7.7 Hz, Ar), 7.35 (d, 2 H, Ar) 5.40 (d, 1 H, $J_{3,4}$ 10.1 Hz, H-3), 4.93 (dd, 1 H, $J_{4,5}$ 3.3 Hz, H-4), 4.16 (m, 1 H, H-5), 3.33 (1 H, br s, OH, D_2O-exchangeable), 2.43 (s, 3 H, Ts), 1.80 (s, 3 H, Ac), 1.45, 1.37 (2 s, ea 3 H, Me_2C).

The above syrup was acetylated with an excess of Ac_2O in pyridine. Isolation using CH_2Cl_2 and crystallisation from EtOH gave the diacetate **4** (6.67 g, 37% from **1**), mp 113–114 °C. Recrystallised from EtOH **4** had mp 114–116 °C, $[\alpha]_D$ $-121°$ (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2 H, J 8.3 Hz, Ar), 7.34 (d, 2 H, Ar), 5.34 (d, 1 H, $J_{3,4}$ 10.3 Hz, H-3), 5.23 (m, 1 H, H-5), 5.01 (dd, 1 H, $J_{4,5}$ 3.9 Hz, H-4), 4.00 (d, 1 H, $J_{6a,6b}$ 13.2 Hz, H-6a), 3.94 and 3.90 (ABq, 2H, $J_{1a,1b}$ 9.3 Hz, H-1a, H-1b), 3.77 (dd, 1 H, $J_{6b,5}$ 2.0 Hz, H-6b) 2.43 (s, 3 H, Ts), 2.04 and 1.93 (2 s, ea 3 H, 2 × Ac), 1.45 and 1.39 (2 s, ea 3 H, Me_2C). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9 and 169.4 (2 × Me*C*O), 144.8 and 133.5 (Ar quaternary), 129.3 and 127.6 (Ar methine),

112.1 (Me_2C),104.2 (C-2), 75.3 (C-4), 71.5 (C-1), 69.4 (C-5), 66.3 (C-3), 61.8 (C-6), 25.7 and 25.6 (Me_2C), 21.3 *Me*Ar). Anal. Calcd for $C_{20}H_{26}O_{10}S$: C, 52.39; H,5.72; S, 6.99. Found: C 52.47; H,5.69; S, 6.87.

*4,5-Anhydro-1,2-*O*-isopropylidene-β-*D*-fructopyranose* (**10**) *and 3,4-anhydro-1,2-*O*-isopropylidene-β-*D*-tagatopyranose* (**8**).—The sulfonate **4** (24 g), in MeOH (150 mL), was treated with a solution of NaOMe [from Na (2.46 g)] in MeOH (210 mL) at rt for 28 h. TLC throughout the period indicated the rapid conversion into a monotosyl diol, followed by the formation of an epoxide of low R_f value, which was slowly converted into another epoxide of higher R_f value. Solid CO_2 was then added and the mixture evaporated to dryness. The residue was extracted with hot benzene and the filtered extract evaporated to yield a syrup, which was chromatographed on silica gel. Toluene–EtOAc (9:1) eluted first the anhydrofructose (**10**) (3.08 g, 29%), mp 78–79 °C, $[\alpha]_D$ −86° (*c* 1.0, $CHCl_3$) (lit. [13] mp 81–82 °C, $[\alpha]_D$ −80.7°, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (d, 1 H, $J_{6a,6b}$ 13.3 Hz, H-6a), 4.03 and 4.01 (ABq, 2 H, $J_{1a,1b}$ 9.0 Hz, H-1a, H-1b), 4.03 (d, 1 H, H-6b), 3.70 (d, 1 H, $J_{3,OH}$ 11.7 Hz, H-3), 3.28 (d, 1 H, $J_{4,5}$ 3.9 Hz, H-4), 3.20 (d, 1 H, H-5), 2.30 (d, 1 H, $J_{OH,3}$ 11.7 Hz, OH-3), 1.54 and 1.44 (2 s, ea. 3 H, Me_2C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.5 (Me_2C), 101.4 (C-2), 72.6 (C-1), 63.3 (C-3), 58.6 (C-6), 53.9 (C-5), 49.5 (C-4), 26.6 and 26.0 (Me_2C); Anal. Calcd for $C_9H_{14}O_5$: C, 53.46; H, 6.98. Found: C, 53.48; H,7.01.

Further elution yielded, after evaporation, the syrupy anhydrotagatose (**8**) (4.70 g, 44%), $[\alpha]_D$ −22° (*c* 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08 (ABq, 2 H, H-1a, H-1b), ~4.02 (bd, 1 H, H-5), 4.00 (d, 1 H, $J_{6a,6b}$ 12.1 Hz, H-6a), 3.56 (d, 1 H, H-6b), 3.37 (bs, 1 H, H-4), 3.29 (d, 1 H, $J_{3,4}$ 3.9 Hz, H-3), 2.24 (d, 1 H, *J* 8.6 Hz, OH-5), 1.49 (s, 6 H, Me_2C); ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.0 (Me_2C), 100.1 (C-2), 73.3 (C-1), 62.9 (C-5), 62.1 (C-6), 53.9 (C-3), 51.8 (C-4), 26.2 and 25.5 (Me_2C); Anal. Found: C, 53.60; H, 7.06.

*3-*O*-Acetyl-4,5-anhydro-1,2-*O*-isopropylidene-β-*D*-fructopyranose* (**11**).—The anhydrofructose (**10**) (100 mg) was treated for 20 h with Ac_2O (0.5 mL) in pyridine (1 mL). Isolation using $CHCl_3$ gave the acetate (**11**), (75 mg, 62%), mp 80–81 °C, $[\alpha]_D$ −87.8° (*c* 3.4, $CHCl_3$); (lit.: mp 80–81 °C, $[\alpha]_D$ −28.6°); ^{1}H NMR (100 MHz, $CDCl_3$): δ 4.84 (s, 1 H, H-3), 3.70–4.20 (4 H, m, H-4, H-5, CH_2), 3.16 (s, 2 H, CH_2), 2.10 (s, 3 H, Ac), 1.46 and 1.38 (2 s, ea 3 H, Me_2C). Anal. Calcd. for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.56; H, 6.90.

Acetylation and hydrolysis of 3,4-anhydro-1,2-O-isopropylidene-β-D-tagatopyranose (**8**).—The anhydro compound **8** (370 mg) was acetylated using Ac_2O in pyridine and the product isolated using $CHCl_3$. The crude syrupy 5-acetate (**9**) (410 mg, 92%) showed ^{1}H NMR (100 MHz, $CDCl_3$); δ 2.10 (s, 3 H, Ac), 1.46 (s, 6 H, Me_2C). The syrup (370 mg) was treated with 80% HOAc at rt for 3 days. After evaporation of the solution, the crude product was chromatographed on silica gel (15 g). Toluene–EtOAc (1:1) eluted 5-*O*-acetyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**5**), which crystallised from EtOAc–light petroleum (340 mg, 86%), mp 103–104 °C, $[\alpha]_D$ −153.7° (*c* 1.06, $CHCl_3$); ^{1}H NMR (100 MHz, $CDCl_3$); δ 5.15 (m, 1 H, $J_{4,5} \approx J_{5,6a} \approx J_{5,6b} \approx 2$ Hz, H-5), 2.13 (s, 3 H, Ac), 1.49 and 1.45 (2 s, ea. 3 H, Me_2C). The acetate **5** (190 mg) was treated with methanolic NaOMe (6 mL) [from Na (20 mg)] for 1 h at rt. After deionisation using Zeo–Karb 225 (NH_4^+) resin the evaporated residue was recrystallised from EtOAc to give 1,2-*O*-isopropylidene-β-D-fructopyranose (**6**) (130 mg, 81%), mp 120–122 °C, indistinguishable from an authentic sample prepared by deacetylation of **1** (lit. [28] mp 121–122 °C).

*Hydrolysis of 3-*O*-acetyl-4,5-anhydro-1,2-*O*-isopropylidene-β-*D*-fructopyranose* (**11**).—The acetate **11** (500 mg) was treated with 80% HOAc (10 mL) at rt for 3 days. TLC indicated that the product was largely a single monoacetate. After evaporation, the crude product was chromatographed on silica gel (10 g), eluting with toluene–EtOAc (1:1). 4-*O*-Acetyl-1,2-*O*-isopropylidene-β-D-tagatopyranose (**12**) was isolated as a syrup (290 mg, 54%); ^{1}H NMR (100 MHz, $CDCl_3$) δ 5.04 (dd, $J_{3,4}$ 3.0, $J_{4,5}$ 2.6 Hz, H-4), 2.06 (s, 3 H, Ac), 1.44 and 1.36 (2 s, ea. 3 H, Me_2C); Anal. Calcd. for $C_{11}H_{18}O_7$: C, 50.38; H, 6.92.

Found: C, 50.37; H, 6.73. Deacetylation of the acetate **12** (270 mg) with methanolic NaOMe and deionisation and evaporation as for **6** above gave syrupy 1,2-*O*-isopropylidene-β-D-tagatopyranose (**13**) (135 mg, 60%). The acetal (135 mg) was treated with 0.05 M H_2SO_4 (2 mL) at 40 °C for 3 h, neutralised with $BaCO_3$ and filtered through Celite. After evaporation the syrup was crystallised from EtOH to give D-tagatose, mp 113 °C, indistinguishable from an authentic sample. GLC analysis of the pertrimethylsilyl ether of the product showed a single peak (retention time 7.1 min), identical to that of the perTMS ether of authentic tagatose (1 m column of 3% SE 30, at 110 °C, carrier gas pressure 20 psi).

*Equilibration studies of 3,4-anhydro-1,2-*O*-isopropylidene-β-*D*-tagatopyranose* (**8**) *and 4,5-anhydro-1,2-*O*-isopropylidene-β-*D*-fructopyranose* (**10**)

Polarimetric studies. Each anhydrocompound was dissolved in 0.05 M NaOH (*c* 1.0) at 25 °C and the changes in optical rotation with time were measured. The 3,4-anhydrotagatose **8** {$[\alpha]_D$ −20° (H_2O)} showed $[\alpha]_D$ −28° after 5 min and −51° (constant) after 12 h. The 4,5-anhydrofructose **10** {$[\alpha]_D$ −66° (H_2O)} showed −59° after 5 min and −51° (constant). after 12 h. The ratio at equilibrium is therefore 2:1 in favour of **10**.

GLC studies. The mixture of epoxides was isolated by deionisation and evaporation and subjected to GLC using a 1 m column of SE 30 with inlet pressure of 20 psi and a column temperature of 100°. The retention times were 1.5 and 2.5 min for **8** and **10**, respectively, and the ratio of **8**:**10** was 1:2.

Equilibration and isolation of epoxides. The anhydrofructose **10** (300 mg) was treated with 0.05 M NaOH (2 mL) and the reaction followed by TLC. After 12 h there was no further change, the mixture was neutralised with diluted HCl, evaporated and the syrupy residue subjected to chromatography on silica gel. Toluene–EtOAc (9:1) eluted the anhydrofructose **10** (180 mg); further elution with toluene–EtOAc (1:1) eluted the syrupy anhydrotagatose **8** (100 mg).

*3,4,5-Tri-*O*-acetyl-1,2-*O*-isopropylidene-β-*D*-tagatopyranose* (**14**).—The acetoxyepoxide **11** (500 mg) was dissolved in a mixture of Ac_2O (2.0 mL), glacial HOAc (4.0 mL) and three drops of dry pyridine and the mixture was heated at 100 °C for 7 h and left for 40 h at rt. The mixture was evaporated to a syrup and extracted from water with $CHCl_3$. TLC of the evaporated $CHCl_3$ solution showed that the major product corresponded to a triacetate, together with more polar material. The syrup was therefore treated with Ac_2O in pyridine and the product isolated using $CHCl_3$. Crystallised from EtOH, 3,4,5-tri-*O*-acetyl-1,2-*O*-isopropylidene-β-D-tagatopyranose (**14**) (277 mg, 39%), had mp 95–96 °C, $[\alpha]_D$ −124° (*c* 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (td, 1 H, $J_{4,5}$ 3.8 Hz, H-4), 5.16 (d, 1 H, $J_{3,4}$ 3.35 Hz, H-3), 4.86 (m, 1 H, H-5), 4.29 (dd, 1 H, $J_{6ax,6eq}$ 13.1, $J_{6ax,5}$ 1.8 Hz, H-6_{ax}), 3.97 (d, 1 H, $J_{1a,1b} \approx 9$ Hz, H-1a), 3.90 (d, 1 H, H-1b), 3.71 (dt, 1 H, $J_{6eq,5} \approx J_{6eq,4} \approx 1.5$ Hz, H-6_{eq}), 2.14, 2.11, and 2.05 (3 s, ea. 3 H, 3 × Ac), 1.50 and 1.40 (2 s, ea. 3 H, Me_2C); Anal. Calcd for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40. Found: C, 51.95; H, 6.38.

*3,4,5-Tri-*O*-acetyl-1,2-*O*-isopropylidene-β-*D*-fructopyranose* (**7**) *[15].*—^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (d, 1 H, $J_{3,4}$ 10.5 Hz, H-3), 5.34 (m, 1 H, H-5), 5.29 (dd, 1 H, $J_{4,3}$ 3.1 Hz, H-4), 4.10 (bd, $J_{6a,6b}$ 13.3 Hz, H-6a), 3.98 (d, 1 H, $J_{1a,1b}$ 9.4 Hz, H-1a), 3.93 (d, 1 H, H-1b), 3.76 (dd, 1 H, $J_{6b,5}$ 1.2 Hz, H-6b), 2.14, 2.09, and 1.99 (3 s, ea. 3 H, 3 × Ac), 1.47 and 1.41 (2 s, ea. 3 H, Me_2C).

*O-Deacetylation of 3,4,5-tri-*O*-acetyl-1,2-*O*-isopropylidene-β-*D*-tagatopyranose, followed by acid hydrolysis*.—The triacetate **14** (500 mg) was treated with methanolic NaOMe [15 mL, Na (50 mg)] until deacetylation was complete (TLC). The solution was deionised using Zeo–Karb 225 (NH_4^+) resin and evaporated to give **13** as a syrup. The acetal **13** (200 mg) was treated with 0.05 M H_2SO_4 (5 mL) at 40 °C for 3 h, neutralised ($BaCO_3$), filtered (Celite) and evaporated to give D-tagatose (50 mg), mp 113 °C, indistinguishable from an authentic sample.

4. Supplementary material

Full crystallographic details, excluding structure features, have been deposited with

the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Tel.: +44-1223-336408; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) quoting CCDC 135058.

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