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Carbohydrate Research 334 (2001) 81–89

CARBOHYDRATE RESEARCH

# Preparation of 1,2-*O*-isopropylidene derivatives of α-D-galactoseptanose, β-L-altroseptanose, and 3-*O*-methyl-α-D-guloseptanose☆

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Received 10 April 2001; accepted 26 June 2001

**Abstract**

Displacement of the tosyloxy group in 5-*O*-benzyl-1,2-*O*-isopropylidene-4-*O*-(*p*-toluenesulfonyl)-α-D-glucoseptanose has yielded derivatives of 1,2-*O*-isopropylidene-α-D-galactoseptanose. Acid catalysed acetonation then gave 1,2:3,4-di-*O*-isopropylidene-α-D-galactoseptanose or 1,2;4,5-di-*O*-isopropylidene-α-D-galactoseptanose using lower acid concentrations. Reduction of the ketone derived from 1,2:3,4-*O*-isopropylidene-α-D-septanose gave 1,2;3,4-di-*O*-isopropylidene-β-L-altroseptanose. Reaction of 3,4-anhydro-5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-galactoseptanose with sodium methoxide gave 5-*O*-benzyl-1,2-*O*-isopropylidene-4-*O*-methyl-α-D-glucoseptanose and 5-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-guloseptanose. Solution-state conformations of these compounds have been deduced from their $^1$H NMR spectra. © 2001 Published by Elsevier Science Ltd.

*Keywords:* Septanose compounds; Acetals; Conformations

## 1. Introduction

Inversion of configuration at C-4 of D-glucose gives rise to D-galactose. We describe here the conversion of a derivative of 1,2-*O*-isopropylidene-α-D-glucoseptanose into a derivative of 1,2-*O*-isopropylidene-α-D-galactoseptanose and the preparation of other D-galactoseptanose compounds from this product. Inversion of configuration at C-4 and C-5 gave L-altro derivatives, and inversion at C-3 and C-4 gave D-gulo derivatives.

## 2. Results and discussion

The benzyl ether (**1b**) of 1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose (**1a**) was chosen as the starting material for the preparation of D-galactoseptanose compounds. Crystalline **1b** was obtained in 90% yield by benzylation of **1a** using sodium hydride in DMF, followed by benzyl chloride. Hydrolysis of **1b** using an aqueous hydrochloric acid–dioxane mixture gave 5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucoseptanose (**2a**) in 47% yield, based on a 41% recovery of starting material. As this procedure involved recycling of recovered starting material several times in order to avoid hydrolysis of **2a** to 5-*O*-benzyl-D-glucose, the use of an acidified solution of **1b** in ethanol was examined. Although no advantage was found using this procedure, it is of some interest that two additional byproducts,

☆ Septanose carbohydrates, Part 6. For Part 5, see Ref. 1.

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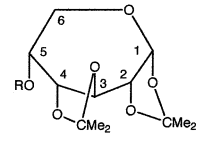
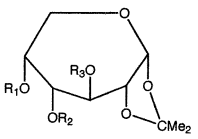
0008-6215/01/$ - see front matter © 2001 Published by Elsevier Science Ltd.

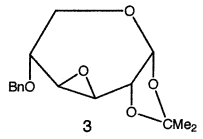
PII: S0008-6215(01)00179-3



(1a) R = H
(1b) R = -$CH_2C_6H_5$
(1c) R = Ac



| | R1 | R2 | R3 |
|---|---|---|---|
| (2a) | Bn | H | H |
| (2b) | Bn | Ts | H |
| (2c) | Bn | H | Ts |
| (2d) | Bn | Ts | Ts |
| (2e) | Bn | Ts | Bz |
| (2f) | Ac | Ac | Ac |
| (2g) | Bn | Me | H |
| (2h) | Bn | Me | Ac |



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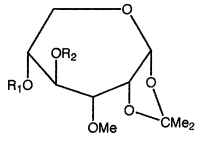
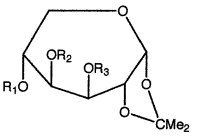
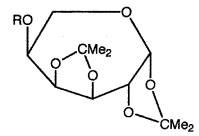


| | R1 | R2 |
|---|---|---|
| (5a) | Bn | H |
| (5b) | Bn | Ac |
| (5c) | Ac | Ac |



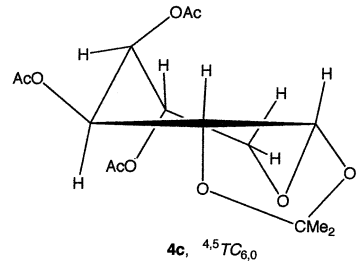
| | R1 | R2 | R3 |
|---|---|---|---|
| (4a) | Bn | H | H |
| (4b) | H | H | H |
| (4c) | Ac | Ac | Ac |
| (4d) | H | $CMe_2$ | |
| (4e) | Ac | $CMe_2$ | |
| (4f) | $CMe_2$ | H | |
| (4g) | $CMe_2$ | Ac | |



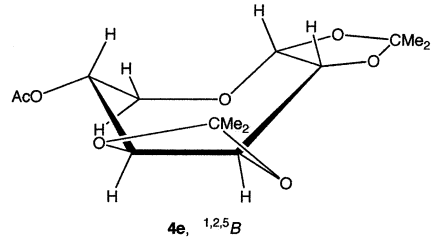
(6a) R = H
(6b) R = Ac

the α and β isomers of ethyl 5-*O*-benzyl-D-glucofuranoside steadily increased in concentration, notwithstanding the significant percentage of water in the hydrolysis mixture. Tosylation of **2a** gave a mixture of products that afforded the 4-*O*-tosyl derivative (**2b**) in 49% yield. A small amount of the isomeric monotosylate (**2c**) as well as the ditosylate (**2d**) (15%) was also isolated. The identity of the major monotosylate as **2b** followed from the chemical shifts of H-3 and H-4. In the $^1$H NMR spectrum of 1,2-*O*-isopropylidene-α-D-glucoseptanose, H-3 comes into resonance at higher frequency than H-4.[2] For **2b**, H-4 appears at higher frequency than H-3, and for the benzoate derivative of **2b**, compound **2e**, H-3 comes into resonance at significantly higher frequency than H-4 (see Table 1). Confirmation of the structure of **2b** is provided by the structures of products formed by ring opening of an epoxide (see below) derived from **2b**. The relatively high yield of monotosylate **2b** may be accounted for by the close proximity of the C-4 hydroxyl group to the oxygen function on C-5. In an earlier study, it was noted that the more reactive hydroxyl group towards tosylation of a diol was strongly intramolecularly hydrogen bonded.[3] From later studies,[4] it was concluded that polar interactions provide a more satisfactory explanation of the enhanced reactivity. The phenomenon has been reviewed.[5]

*1,2-O-Isopropylidene-α-D-galactoseptanose* (**4d**).—Treatment of **2b** with sodium benzoate in DMF at 100 °C gave a mixture of products. Chromatography of these products over silicic acid gave as the first eluted compound, crystalline epoxide **3**, which showed no carbonyl or hydroxyl group absorptions in the infrared spectrum. The $^1$H NMR spectrum of **3** confirmed the epoxide structure, the low frequencies of H-3 and H-4 being typical of hydrogen atoms attached to oxirane rings,[6] and this product is formulated as 3,4-anhydro-5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-galactoseptanose (**3**) with the configuration at C-3 and C-4 following from the mode of formation and from the structures of ring opening products (see below). A syrupy material eluted after **3** showed carbonyl absorption in the infrared spectrum, and the $^1$H NMR spectrum indicated a mixture of the 3-*O*-benzoyl and 4-*O*-benzoyl derivatives of 5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-galactoseptanose (**4a**). Saponification of this mixture gave the crystalline diol **4a** which yielded **4b** on hydrogenolysis. Acetylation of **4b** yielded a liquid triacetate **4c**. Proton coupling constants



**4c**, $^{4,5}TC_{6,0}$



**4e**, $^{1,2,5}B$

Table 1
$^1$H NMR chemical shifts ($\delta$, ppm)

| Compound | Solvent | H-1 | H-2 | H-3 | H-4 | H-5 | H-6a | H-6b | $PhCH_2$ | $CMe_2$ | Other |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1b** | $CDCl_3$ | 5.047 | 4.211 | 4.679 | 3.824 | 3.872 | 4.199 | 3.406 | 4.825, 4.730 | 1.614, 1.505 | |
| | | | | | | | | | | 1.481, 1.403 | |
| **2b** | $CDCl_3$ | 5.010 | 4.008 | 4.495 | 4.529 | 3.820 | 4.069 | 3.364 | 4.598, 4.569 | 1.541, 1.359 | 2.433 (Ts) |
| **2c** | $CDCl_3$ | 4.978 | 4.126 | 5.083 | 3.715 | 3.745 | 4.177 | 3.353 | 4.742, 4.628 | 1.206, 1.163 | 2.418 (Ts) |
| **2d** | $CDCl_3$ | 5.045 | 4.036 | 5.387 | 4.580 | 3.925 | 4.064 | 3.394 | 4.640, 4.546 | 1.389, 1.158 | 2.431, 2.419 (Ts) |
| **2e** | $CDCl_3$ | 5.155 | 4.383 | 6.136 | 4.841 | 3.915 | 4.116 | 3.462 | 4.830, 4.636 | 1.553, 1.336 | 2.301 (Ts) |
| **2h** | $CDCl_3$ | 5.038 | 4.287 | 5.732 | 3.261 | 3.759 | 4.144 | 3.348 | 4.855, 4.676 | 1.560, 1.363 | 3.382 (OMe), 2.128 (OAc) |
| **3** | $C_6D_6$ | 4.553 | 4.107 | 3.227 | 2.934 | 3.158 | 3.670 | 3.348 | 4.549, 4.407 | 1.526, 1.226 | |
| **4c** | $CDCl_3$ | 5.231 | 4.287 | 5.509 | 5.363 | 4.862 | 4.018 | 3.730 | | 1.574, 1.371 | 2.156, 2.114, 2.079 (3×OAc) |
| **4e** | $CDCl_3$ | 5.302 | 4.268 | 4.440 | 4.370 | 5.026 | 3.911 | 3.519 | | 1.555, 1.490, 1.375, 1.356 | 2.088 (OAc) |
| **4g** | $CDCl_3$ | 5.35 | 4.05 | 5.71 | 4.1 to | 4.3 | 3.92 | 3.72 | | 1.54, 1.43, 1.38, 1.34 | 2.12 (OAc) |
| **5b** | $CDCl_3$ | 5.367 | 4.453 | 3.388 | 5.554 | 3.518 | 3.751 | 3.562 | 4.615, 4.517 | 1.637, 1.346 | 3.422(OMe), 2.022 (OAc) |
| **5b** | $C_6D_6$ | 5.216 | 4.263 | 3.405 | 6.131 | 3.634 | 4.009 | 3.701 | 4.464, 4.384 | 1.421, 1.130 | 3.259 (OMe), 1.900 (OAc) |
| **5c** | $CDCl_3$ | 5.388 | 4.472 | 3.455 | 5.577 | 4.984 | 3.763 | 3.458 | | 1.643, 1.353 | 3.441 (OMe), 2.051, 2.005 (OAc) |
| **5c** | $C_6D_6$ | 5.160 | 4.220 | 3.358 | 6.097 | 5.395 | 4.017 | 3.629 | | 1.425, 1.112 | 3.203 (OMe), 1.899, 1.724 (OAc) |
| **6b** | $C_6D_6$ | 5.31 | 4.69 | 4.53 | 4.16 | 5.38 | 3.73 | 3.42 | | 1.58, 1.42, 1.24, 1.18 | 1.64 (OAc) |

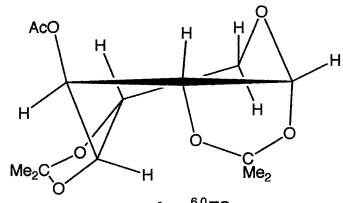
for 1,2-*O*-isopropylidene-α-D-glucoseptanose triacetate (**2f**), except for those involving H-4, are similar to those of **4c**, indicating similar conformations for these two compounds, probably the twist-chair conformation, $^{4,5}TC_{6,0}$.[2] Four-bond spin coupling between H-4 and H-6a (a W configuration) is consistent with this conformation.

*1,2:3.4-Di*-O-*isopropylidene*-α-D-*galactoseptanose* (**4d**).—Treatment of **4a** with acidified acetone and 2,2-dimethoxypropane yielded a liquid compound, which on hydrogenolysis gave the crystalline alcohol **4d**. In order to eliminate the possibility of a change of configuration at C-1 during the acetonation of **4a**, **4d** was hydrolysed to give a 1,2-*O*-isopropylidene compound whose triacetate was identified as **4c**, thereby confirming the alpha configuration of **4d**. Proton spin-coupling constants obtained for the acetate **4e** derived from **4d** are markedly different from those of the gluco analog,[2] indicating a different conformation. Earlier calculations by Hendrickson[7] showed that it is not possible to fuse two five-membered rings cis–anti–cis to a seven-membered ring in a chair or twist-conformation without considerable distortion. If the seven-membered ring is in a boat or twist-boat conformation, such a fusion of five-membered rings can take place without undue strain.

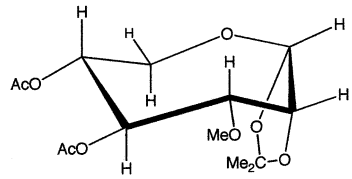
*Conformation of* **4e**.—Of the 28 boat, twist-boat conformations that are involved in the boat–twist-boat pseudorotational continuum for the septanose ring,[8] three conformations, $^{1,2,5}B$, $^{1,2}TB_{3,4}$, and $_{3,4,0}B$, appear to be most likely for **4e**. Of these, conformation $^{1,2,5}B$ corresponds to the lowest-energy boat conformation of oxepan, boat-2, deduced by Bocian and Strauss.[9] However, none of the mentioned conformations account well for the observed proton coupling constants listed in Table 2; in particular, the value of $J_{3,4}$, is far too large for a dihedral angle of 34° in conformation $^{1,2,5}B$.[9] It may be that the molecule is undergoing pseudolibration over the three mentioned conformations in solution. In the solid state, the septanose ring of **4e** has been described[10] as a boat, $^{1,2,5}B$, flattened in the region of C-3 and C-4. If the solution-state conformation is similar to that observed in the solid state, this flattening in the C-3–C-4 region would account for the large magnitude of $J_{3,4}$.

*3*-O-*Acetyl*-*1,2:4,5-di*-O-*isopropylidene*-α-D-*galactoseptanose* (**4g**).—Treatment of **4b** with acetone containing 0.02% sulfuric acid by volume gave a mixture of two products, one of which was identified as **4d** by gas chromatography. The major product was identified by acetylation and analysis of the $^1$H NMR spectrum as 1,2:4,5-di-*O*-isopropylidene-α-D-galactoseptanose (**4f**) derived acetate **4g**. Increasing the reaction time resulted in an increase in the ratio of **4d** to **4f**. Isomer **4f** is therefore the kinetically controlled product, and **4d** the product of thermodynamic control. Similar results were reported for the gluco and ido analogs.[2,11]

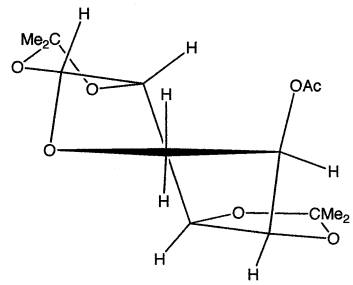
A probable conformation of **4g** in solution has been deduced by examination of the proton-spin coupling constants. Various boat and twist-boat conformations are excluded by the values of $J_{2,3}$ and $J_{3,4}$. Of the two twist-chair conformations, $^{6,0}TC_{4,5}$ and $^{3,4}TC_{5,6}$ formed by twisting around C-1–C-2 of the chair conformation, $^5C_{1,2}$, conformation, $^{3,4}TC_{5,6}$, with an expected dihedral angle of 32° for H-2–H-3 does not account for the value of 3.0 Hz for $J_{2,3}$. Conformation $^{6,0}TC_{4,5}$ appears to account for the observed coupling constants.




**4g**, $^{6,0}TC_{4,5}$




**5c**, $^5C_{1,2}$




**6b**, $^{1,2}TB_{3,4}$

*1,2:3,4-Di*-O-*isopropylidene*-β-L-*altrosep*-*tanose* (**6a**).—Oxidation of **4d** with ruthenium tetroxide gave a ketone that was reduced with sodium borohydride to give a

Table 2
$^1$H NMR coupling constants (*J*, Hz)

| Compound | Solvent | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5}$ | $J_{5,6a}$ | $J_{5,6b}$ | $J_{6a,6b}$ | $J_{CH2}$ | Other |
|---|---|---|---|---|---|---|---|---|---|---|
| **1b** | $CDCl_3$ | 3.94 | 7.16 | 9.60 | 2.17 | 1.65 | 1.60 | 13.79 | 11.59 | |
| **2b** | $CDCl_3$ | 3.93 | 6.71 | 9.61 | 1.92 | 3.08 | 1.87 | 13.83 | 11.98 | |
| **2c** | $CDCl_3$ | 4.00 | 7.56 | 9.26 | 2.23 | 2.99 | 1.85 | 13.93 | 11.78 | |
| **2d** | $CDCl_3$ | 4.14 | 6.72 | 8.86 | 2.03 | 4.29 | 1.93 | 13.50 | 12.01 | |
| **2e** | $CDCl_3$ | 4.00 | 7.46 | 9.63 | 1.90 | 3.48 | 1.87 | 13.65 | 12.21 | |
| **2h** | $CDCl_3$ | 3.95 | 7.72 | 9.30 | 1.75 | 3.28 | 1.96 | 13.40 | 12.35 | |
| **3** | $C_6D_6$ | 3.65 | 1.94 | 4.37 | 5.60 | 8.82 | 5.21 | 12.04 | 12.10 | $J_{2,4}$ 0.56 |
| **4c** | $CDCl_3$ | 3.75 | 7.45 | 0.88 | 6.01 | 2.22 | 2.28 | 14.17 | | $J_{4,6a}$ 1.15 |
| **4e** | $CDCl_3$ | 4.93 | 8.20 | 7.61 | 9.97 | 6.28 | 10.66 | 11.35 | | |
| **4g** | $CDCl_3$ | 3.8 | 3.0 | 1.5 | ND | 5.6 | 8.8 | 11.6 | | |
| **5b** | $CDCl_3$ | 5.13 | 1.33 | 10.18 | 9.01 | 10.86 | 4.09 | 12.60 | 11.80 | |
| **5b** | $C_6D_6$ | 5.10 | 1.23 | 10.28 | 9.03 | 11.00 | 4.25 | 12.74 | 11.97 | |
| **5c** | $CDCl_3$ | 5.11 | 1.33 | 10.16 | 9.44 | 10.86 | 4.42 | 12.65 | | |
| **5c** | $C_6D_6$ | 5.07 | 1.25 | 10.24 | 9.36 | 10.97 | 4.49 | 12.56 | | |
| **6b** | $C_6D_6$ | 4.7 | 6.3 | 8.0 | 2.2 | 4.3 | 1.8 | 13.5 | | |

mixture of two products, separable by silicic acid column chromatography, giving **4d** and a new, crystalline product, **6a**. Identification of the new product as the altro isomer was confirmed by treatment with aqueous acid, followed by sodium borohydride. Acetylation gave a hexitol hexaacetate that had the same GLC retention time as hexa-*O*-acetylaltritol. Acetylation of **6a** gave the liquid acetate, **6b** whose $^1$H NMR spectrum was readily analysed (data in Tables 1 and 2).

The solution-state conformation of **6b** is probably similar to that of **4e** as the spin coupling constants, except for those involving H-5, are similar to those of **4e**. We note that the value of $J_{6a,6b}$, 13.5 Hz, is consistent with O-5 being antiperiplanar to one of the geminal hydrogen atoms,[12] as expected for the $^{1,2}TB_{3,4}$ conformation.

*4,5-Di*-O-*acetyl-1,2*-O-*isopropylidene-3*-O-*methyl*-α-D-*guloseptanose* (**5c**).—Refluxing a solution of epoxide **3** with sodium methoxide in methanol gave two products in approximately equal amounts. Separation of these products was effected by column chromatography. The second product that eluted, **2g**, was identified by analysis of the $^1$H NMR spectrum of the derived acetate and by comparison of the coupling constants and chemical shifts with those of **2e** as 3-*O*-acetyl-5-*O*-benzyl-1,2-*O*-isopropylidene-4-*O*-methyl-α-D-glucoseptanose (**2h**). This confirmed the galacto configuration of **3**. The first eluted product was identified as 5-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-guloseptanose (**5a**) by analysis of the $^1$H NMR spectrum of the derived acetate **5b**. Hydrogenolysis of **5a**, followed by acetylation, gave the crystalline diacetate **5c** whose structure has been confirmed by X-ray diffraction.[13] A one-step conversion of **2b** into **2g** and **5a** involves treatment of **2b** with sodium methoxide in methanol.

The solution-state conformation of **5c** may be deduced from the NMR data. The large magnitudes of $J_{3,4}$, $J_{4,5}$, and $J_{5,6a}$ require these pairs of hydrogens to be antiperiplanar. The chair conformation $^5C_{1,2}$ satisfies this requirement. Twisting around the C-1–C-2 bond gives the twist-chair conformations, $^{3,4}TC_{5,6}$ and $^{6,0}TC_{4,5}$, thereby relieving eclipsing around C-1–C-2. Either of these twist-chair conformations would account for the observed NMR parameters, including the unusually high frequency of absorption of H-4, the result of close proximity of H-4 and O-1 or O-2.[14] The former conformation is expected to be favoured by the anomeric effect.

## 3. Experimental

*General methods.*—See Ref. 11. For the data presented in Tables 1 and 2 the methylene hydrogens of benzyl ether groups were analysed as AB systems, H-5, H-6a, and H-6b were analysed as ABX systems,[15] except for **5b** for which the program GNMR (Cherwell Scientific) was used iteratively for H-4, H-5, H-6a, and H-6b as a four-spin system. Data for aromatic hydrogens are not reported.

*5*-O-*Benzyl-1,2:3,4-di*-O-*isopropylidene*-α-D-*glucoseptanose* (**1b**).—Sodium hydride (5 g. 1:1 emulsion with mineral oil, washed with anhyd ether) was added to a solution of **1a** (8.02 g, 30.8 mmol) in DMF (40 mL), and the suspension was stirred for 1.5 h. Benzyl chloride (4 mL, 34.8 mmol) was added whilst cooling, and the solution was stirred for a further 2 h. Water was added in small portions in order to destroy excess sodium hydride. After adding water (400 mL), the mixture was kept at rt until crystallisation was complete. Crude **1b** (10.6 g) was collected by filtration and recrystallised from an EtOH–water mixture to give **1b** (9.8 g, 91%) as white needles: mp 130–131 °C; $[\alpha]_D^{23}$ −47.1° (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 65.30; H, 7.65.

*5*-O-*Benzyl-1,2*-O-*isopropylidene*-α-D-*glucoseptanose* (**2a**).—A solution of **1b** (13.9 g, 39.7 mmol) in dioxane (100 mL) and HCl (2 M, 50 mL) was left at 40 °C for 24 h. Partial evaporation of the neutralised (2 M aq NaOH) reaction mixture followed by dilution with water to ca. 300 mL resulted in crystallisation of **1b,** which was collected and washed with water. Chloroform (3 × 50 mL) extracts of the aq filtrates were washed with water (50 mL), dried and evaporated to give crude **2a** (2.70 g). The recovered **1b** was treated as

above (dioxane, 80 mL, aq 2 M HCl, 40 mL) to give crude **2a** (1.54 g) and recovered **1b**, which yielded a further 1.34 g of crude **2a** after similar treatment; total yield of crude **2a**, 5.58 g and recovered **1b** (5.64 g). Recrystallisation of crude **2a** from benzene gave 3.05 g of **2a** with a further 0.44 g obtained by adding light petroleum to the filtrate, giving a total yield of 3.49 g of **2a** (47% based on unrecovered **1b**). A sample was recrystallized from benzene–light petroleum to needles, mp 120–122 °C; $[\alpha]_D^{23}$ −19.3° (*c* 0.21, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 62.05; H, 6.96.

*Hydrolysis of* **1b** *using acidified aq EtOH.*—To a solution of **1b** (6.00 g, 17.1 mmol) in EtOH (200 mL) at 30 °C was added aq HCl (0.2 M, 100 mL). The reaction mixture was kept at 30 °C for 70 h. Samples examined using TLC (silica gel, EtOAc eluent) showed four spots, **1b** ($R_f$ 0.73), **2a** ($R_f$ 0.54), ethyl glycosides ($R_f$ 0.47) and 5-*O*-benzyl-D-glucose ($R_f$ 0.23). The intensities of spots due to **1b** and **2a** were approximately equal after 70 h, and the intensity of spot $R_f$ 0.47 steadily increased during the reaction time. After neutralising the reaction mixture with Amberlite IRA-400 ($HCO_3^-$), the filtered mixture was evaporated until the residue contained a large number of needle crystals which were collected, washed with 1:4 EtOH–water and air dried to give **1b** (1.18 g), mp 128–129 °C. Chloroform (4 × 30 mL) extracts of the evaporated filtrate (ca. 100 mL) were filtered through a short bed of silicic acid, evaporated, and a benzene solution of the residue evaporated. Seeding a solution of the residue in a small volume of light petroleum gave needle crystals of **2a** (1.12 g, 21%), mp 119–121 °C. Chromatography of the filtrate using silica gel and ether gave **1b** (0.18 g), **2a** (0.48 g, 9%), a mixture of **2a** and ethyl glycosides (0.47 g) and ethyl glycosides (0.22 g, 4.3%). Acetylation of the glycosides fraction using acetic anhydride and pyridine with the usual workup gave a colourless liquid product: $^1$H NMR ($CHCl_3$): $\delta$ 5.505 (ddd, $J_{2,3}$ 2.84, $J_{3,4}$ 5.01, $J_{1,3}$ 0.48 Hz, H-3α), 5.314 (dd, $J_{2,3}$ 1.12, $J_{3,4}$ 4.75 Hz, H-3β), 5.221 (dt, $J_{1,2}$ 4.65, $J_{1,4}$ 0.60 Hz, H-1α), 5.227 (dd, $J_{1,2}$ 0.46, $J_{2,3}$ 1.12 Hz, H-2β). 4.950 (d, H-1β). 4.933 (dd, H-2α), 4.779 (dd, $J_{5,6a}$ 2.39, $J_{6a,6b}$ 12.20 Hz, H-6aβ), 4.706 (d, $J_{AB}$ 11.25 Hz, $PhCH_AH_B$–O–), 4.688 ($J_{CD}$ 11.45 Hz, $PhCH_CH_D$–O–), 4.609 (dd, $J_{5,6a}$ 2.54, $J_{6a,6b}$ 12.10 Hz, H-6aα), 4.461 (d, $H_B$), 4.435 (d, $H_D$), 4.395 (dd, $J_{4,5}$ 9.12 Hz, H-4β), 4.363 (dd, $J_{4,5}$ 8.12 Hz, H-4α), 4.167 (dd, $J_{5,6b}$ 4.90 Hz, H-6bα), 4.150 (dd, $J_{5,6b}$ 4.04 Hz, H-6bβ), 3.957 (ddd, H-5β), 3.854 (ddd, H-5α), 3.735 (dq, 1 H, $J_{CH_2}$ 9.79, $J_{CH_2,Me}$ 7.08 Hz, O–$CH_2$–Me), 3.731 (dq, 1 H, $J_{CH_2}$ 9.79, $J_{CH_2,Me}$ 7.08 Hz, O–$CH_2$–Me) 3.507 (dq, 1 H, O–$CH_2$–Me), 3.487 (dq, 1 H, O–$CH_2$–Me), 2.103 (s, 3 H, OAc), 2.100 (s, 6 H, OAc), 2.068 (s, 3 H, OAc), 1.970 (s, 3 H, OAc), 1.964 (s, 3 H, OAc), 1.201 (tr, 3 H, $CH_3$), 1.170 (tr, 3 H, –$CH_3$) (assignments by spin-decoupling). Ratio of anomers, α:β = 1:1.

*Treatment of 5-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucoseptanose* (**2a**) *with* p-*toluenesulfonyl chloride.*—A solution of **2a** (4.65 g, 15 mmol) and *p*-toluenesulfonyl chloride (4.00 g, 21 mmol) in pyridine (30 mL) was kept for 50 h at 25 °C. After the addition of water (1 mL), the reaction mixture was kept for 1 h at 25 °C then shaken with $CHCl_3$ (30 mL) and water (100 mL). The aqueous solution was extracted with $CHCl_3$ (30 mL), and the combined $CHCl_3$ solutions were washed with 1.5 M aq $H_2SO_4$, followed by satd aq $NaHCO_3$, filtered through a short bed of silica gel (E. Merck 7734), and evaporated. A benzene solution of the products gave needle crystals (3.55 g) that were recrystallised from MeOH to give 5-*O*-benzyl-1,2-*O*-isopropylidene-4-*O*-(*p*-toluenesulfonyl)-α-D-glucoseptanose (**2b**) (3.40 g, 49%): mp 141–143 °C; $[\alpha]_D^{23}$ −48.5° (*c* 0.7, $CHCl_3$). Anal. Calcd for $C_{23}H_{28}O_8S$: C, 59.47; H, 6.08. Found: C, 59.44; H, 6.31.

Chromatography of the products in the benzene filtrates over silica gel (E. Merck 7736, 80 g) using 1:6 $Et_2O$–benzene as eluent and 20 mL fractions, gave 5-*O*-benzyl-1,2-*O*-isopropylidene-3,4-di-*O*-(*p*-toluenesulfonyl)-α-D-glucoseptanose (**2d**, 1.41 g, 15%) in fractions 10–16. Recrystallisation of the ditosylate from a mixture of MeOH and EtOAc gave colourless needles (1.35 g): mp 149–151 °C; $[\alpha]_D^{20}$ +30.9° (*c* 1.26, $CHCl_3$). Anal. Calcd for $C_{30}H_{34}O_{10}S_2$: C, 58.24; H, 5.54. Found: C, 58,50; H, 5.57. TLC of fractions 29–38 showed only one spot. Crystallisation of this

product (0.45 g) from MeOH gave needles (0.18 g, 2.5%), recrystallised from EtOH to give 5-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-(*p*-toluenesulfonyl)-α-D-glucoseptanose (**2c**): mp 120–121 °C; $[\alpha]_D^{20}$ +31.4° (*c* 1.55, $CHCl_3$). Anal. Calcd for $C_{23}H_{28}O_8S$: C, 59.47; H, 6.08. Found: C, 59.56; H, 6.27. Fractions 20–28 (0.49 g) contained **2b** and **2c** by TLC.

*3-O-Benzoyl-5-O-benzyl-1,2-O-isopropylidene-4-O-(p-toluenesulfonyl)-α-D-glucoseptanose* (**2e**).—Benzoylation of **2b** (147 mg, 0.32 mmol) using BzCl in pyridine and standard workup gave needle crystals of **2e** (89 mg, 49%) from EtOH: mp 129–131 °C, $[\alpha]_D^{20}$ −45.6° (*c* 1.12, $CHCl_3$). Anal. Calcd for $C_{30}H_{32}O_9S$: C, 63.37; H, 5.67. Found: C, 63.24; H, 5.83.

*Treatment of* **2b** *with sodium benzoate*.—A stirred mixture of **2b** (1.20 g, 2.58 mmol), sodium benzoate (1.2 g, 8.3 mmol) and DMF (30 mL) was kept at 100–105 °C for 3 h. After the addition of water (200 mL), the cooled reaction mixture was extracted with benzene (3 × 50 mL), and each extract was shaken with water (100 mL), dried and evaporated to give a total of 1.13 g of liquid products that were warmed with aq NaOH (2 M, 5 mL) and sufficient MeOH to give a homogeneous solution. After 1 h, MeOH was removed by evaporation, and the mixture was extracted with $CHCl_3$ (3 × 20 mL). The extracts were washed with water (20 mL), dried, and evaporated to give 0.78 g of products that crystallised from benzene–light petroleum to give needles of 5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-galactoseptanose (**4a**) (0.55 g, 69%). Recrystallisation from $CHCl_3$–benzene gave needles of **4a**: mp 143–145 °C; $[\alpha]_D^{24}$ −57.9 ° (*c* 1.25, $CHCl_3$). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.82; H, 7.12.

Chromatography of the benzene–light petroleum filtrates over silicic acid using 1:1 ether–light petroleum as eluent gave 3,4-anhydro-5-*O*-benzyl-1.2-*O*-isopropylidene-α-D-galactoseptanose (**3**) (0.17 g) as the first-eluted material and a further 0.03 g of **4a** (total yield of **4a**, 72%). Recrystallisation of **3** from $CHCl_3$–benzene gave white needles: mp 75–76 °C; $[\alpha]_D^{20}$ −43.0° (*c* 0.8, $CHCl_3$). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.94; H, 7.21.

*1,2-O-Isopropylidene-α-D-galactoseptanose* (**4b**).—A solution of **4a** (0.175 g, 0.56 mmol) in MeOH (5 mL) was stirred with hydrogen and 5% Pd–C at rt and pressure. After uptake of hydrogen uptake had ceased, the solution was filtered through Celite and evaporated to give 0.132 g of a liquid which crystallised on addition of a few drops of EtOAc. Recrystallisation from EtOAc–acetone gave colourless prisms of **4b** (100 mg, 81%): mp 178–180 °C; $[\alpha]_D^{20}$ −14.8° (*c* 0.8, water). Anal. Calcd for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found: C, 49.36; H, 7.33. Acetylation of **4b** (0.100 g) using pyridine and $Ac_2O$ with the usual workup gave a colourless liquid product, **4c** (0.173 g): $[\alpha]_D^{21}$ −8.6° (*c* 1.33, $CHCl_3$).

*1,2:3,4-Di-O-isopropylidene-α-D-galactoseptanose* (**4d**).—A mixture of **4a** (0.29 g, 0.94 mmol), anhyd $CuSO_4$ (0.44 g), 2,2-dimethoxypropane (5 mL), and acetone containing 2% v/v $H_2SO_4$ (0.1 mL) was stirred at 22 °C for 16 h. The filtered reaction mixture was neutralised using ammonia gas. It was then shaken with water (20 mL) and $CHCl_3$ (20 mL), and the $CHCl_3$ extract was evaporated to give a pale-yellow liquid (0.34 g). Hydrogenolysis of this product as above gave a colourless liquid (0.26 g) which crystallised as prisms (0.145 g, 60%) from benzene–light petroleum. Recrystallisation from benzene–light petroleum gave prisms of **4d**: mp 102–103 °C; $[\alpha]_D^{20}$ +18.9° (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.52; H, 7.59.

Acetylation of **4d** using $Ac_2O$ and pyridine with usual workup gave needle crystals of **4e** from light petroleum: mp 103–104 °C; $[\alpha]_D^{20}$ +27.6° (*c* 1.55, $CHCl_3$). Analysis by X-ray diffraction.[7]

*Proof of α-configuration in* **4d**.—A solution of **4d** (5 mg) in HCl (0.2 M, 0.06 mL) was kept for 70 h at 30 °C. Evaporation of the neutralised reaction mixture, followed by acetylation and GLC analysis, revealed only one peak with the same retention time as **4c**.

*3-O-Acetyl-1,2:4,5-di-O-isopropylidene-α-D-galactoseptanose* (**4g**).—To a solution of **4b** (200 mg, 0.91 mmol) in acetone (50 mL) was added concd $H_2SO_4$ (10 μL). After 1 h, the neutralised (aq $NH_3$) mixture was evaporated, and the residue was shaken with water and

$CHCl_3$ ($3 \times 10$ mL). Chromatography of the liquid products (0.080 g) left on evaporation of the $CHCl_3$ extracts over silicic acid gave 1,2:4,5-di-*O*-isopropylidene-α-D-galactoseptanose (**4f**, 61.1 mg, 92% based on unrecovered **4b**); $R_f$ 0.2, silica, 1:1 ether–light petroleum) eluted with 1:1 ether–light petroleum and **4d** (6.4 mg; $R_f$ 0.1). Evaporation of the aqueous solution gave **4b** (0.144 g). Acetylation of **4f** using $Ac_2O$ and pyridine and the usual workup gave crystalline **4g** (65 mg), which crystallised from light petroleum to give white needles: mp 118–121 °C; $[\alpha]_D^{23}$ −65.3° (*c* 0.45, $CHCl_3$). Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.34. Found: C, 55.66; H, 7.33.

*1,2:3,4-Di-O-isopropylidene-β-L-altroseptanose* (**6a**).—To a solution of **4d** (180 mg, 0.69 mmol) in EtOH-free $CHCl_3$ (4 mL) was added a mixture of $K_2CO_3$ (0.40 g), sodium metaperiodate (0.50 g) and ruthenium dioxide (Engelhard, 50 mg) in water (4 mL) and the mixture was stirred vigorously for 1 h. After addition of 2-propanol (0.5 mL) and stirring for 10 min, water (16 mL) was added. Separation of the $CHCl_3$ layer, followed by two further extractions with $CHCl_3$ and evaporation of the combined dried extracts, gave a colourless liquid ketone (0.175 g). A solution of the crude ketone in EtOH (10 mL) was added dropwise over 15 min to a stirred solution of $NaBH_4$ (0.3 g) in EtOH (5 mL). After stirring the reaction mixture for 0.75 h, acetone (2 mL) was added to destroy excess borohydride. After evaporating the reaction mixture, the residue was shaken with water and $CHCl_3$. Evaporation of the $CHCl_3$ extracts gave a mixture of 1:1.4 **4d** and **6a** (0.175 g), by GLC analysis (160 °C, retention times 6.3 and 5.3 min, respectively). Chromatography of the products over silicic acid (6 g) using 1:1 ether–light petroleum, gave fractions containing mainly **6a** that were combined to give crude **6a** (70 mg). Crystallisation from a benzene–light petroleum mixture gave needles (49 mg, 27%) that were recrystallised from benzene–light petroleum to give **6a**: mp 101–102 °C; $[\alpha]_D^{24}$ +38.7° (*c* 0.6, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.75. Found: C, 55.20; H, 7.64.

*5-O-Acetyl-1,2:3,4-di-O-isopropylidene-β-L-altroseptanose* (**6b**).—Acetylation of **6b** using $Ac_2O$ and pyridine with the usual workup and chromatography over silicic acid, followed by short-path distillation at 0.25 mm Hg and 105–110 °C bath, gave **6b** as a colourless liquid; $[\alpha]_D^{24}$ +23.9° (*c* 1.2, $CHCl_3$). Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.34. Found: C, 55.28; H, 7.65.

*Treatment of epoxide* **3** *with sodium methoxide*.—A solution of **3** (787 mg, 2.69 mmol) in 3 M sodium methoxide in MeOH (12 mL) in a tightly stoppered r.b. flask was kept at 90 °C for 48 h. After evaporation, an aqueous solution of the reaction products was extracted with $CHCl_3$. TLC (silica gel, ether) showed two spots of approximately equal intensity $R_f$ 0.35 and 0.20. Chromatography of the extract over silicic acid (10 g) using 1:2 $Et_2O$–light petroleum gave **5a** ($R_f$ 0.35, 288 mg, 33%) followed by **2g** ($R_f$ 0.20, 200 mg, 23%). Acetylation of **2g** using $Ac_2O$ and pyridine with the usual workup gave crystals of **2h**. Recrystallisation from benzene–light petroleum gave **2h** as needles: mp 87–88 °C; $[\alpha]_D^{22}$ −28.5° (*c* 1.75, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C, 62.43; H, 7.02. Acetylation of **5a** gave crystals of **5b** that yielded needles from benzene–light petroleum: mp 105–106 °C; $[\alpha]_D^{22}$ −2.0° (*c* 1.75, $CHCl_3$). Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C. 62.15; H, 7.07.

A solution of **5a** (0.25 g, 0.77 mmol) in MeOH (20 mL) was stirred with 10% Pd–C (Aldrich) under hydrogen for 1 h, after which time no further uptake of hydrogen occurred. Acetylation ($Ac_2O$–pyridine) of the residue left upon filtration and evaporation of the reaction product with usual workup gave a crystalline product which yielded colourless prisms of **5c** (0.17 g, 69%) from benzene–light petroleum: mp 114–116 °C; $[\alpha]_D^{22}$ +35.0° (*c* 1.45, $CHCl_3$). Analysis by X-ray diffraction.[10]

*Treatment of* **2b** *with sodium methoxide*.—After a solution of **2b** (1.86 g, 4.0 mmol) in 3 M NaOMe (20 mL) had been kept at 22 °C for 3.5 h, the mixture was kept at 70 °C for 60 h. TLC (silica, 1:1 EtOAc–light petroleum) showed only **2g** and **5a** at $R_f$ 0.10 and 0.23, respectively. The residue left upon evaporation of the reaction mixture was shaken with $CHCl_3$ and water, and the $CHCl_3$ extracts were chromatographed over silicic acid using 1:1 EtOAc–light petroleum and monitored by TLC to give **5a** (0.89 g, 68%) and **2g** (0.34 g,

26%), identified by acetylation and $^1$H NMR spectra of the derived acetates.

## Acknowledgements

We are grateful to Dr E. Challen for carbon and hydrogen analyses.

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