Synthesis of Some C-5 Branched Hexopyranoses

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The stereoselectivity of diazomethane and dimethylsulfonium methylide additions to the C-5 aldehyde group in 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose or the C-5 ketone function of 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranos-5-ulose and 1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-phenyl-α-D-*xylo*-pentofuranos-5-ulose have been investigated. Reactions with the aldehyde and the methyl ketone gave predominantly the *gluco*-epoxide while the *ido*-epoxide was the predominant product from the phenyl ketone. During the reactions the following pyranoses were isolated and characterized: 1,6-anhydro-3-*O*, 5-*C*-dimethyl-β-L-idopyranose, 1,6-anhydro-3-*O*-methyl-5-*C*-phenyl-β-L-idopyranose, 3-*O*, 5-*C*-dimethyl-D-glucopyranose and 1,6-anhydro-3-*O*, 5-*C*-dimethyl-β-D-glucopyranose.

Monosaccharides with methyl, hydroxymethyl and formyl branching have been isolated from plant sources. For instance apiose (3-*C*-hydroxymethyl-D-*glycero*-tetrulose) has been isolated from parsley,[1] hamamelose (2-*C*-hydroxymethyl-D-ribose) from witch hazel,[1] the alditol 2-*C*-methyl-D-erythritol from *Convolvulus glomeratus*[2] and 2-*C*-methyl-D-erythronic acid from cacti.[3] The interest in branched carbohydrates was greatest when they were constituents of antibiotics such as olivomycin (2,6-dideoxy-3-*C*-methyl-L-*arabino*-hexose),[1] streptomycin (5-deoxy-3-*C*-formyl-L-lyxose)[1] and lancamycin (2,6-dideoxy-3-*C*, 3-*O*-dimethyl-L-*xylo*-hexose).[1] The synthesis of such branched carbohydrates, which includes formation of chiral centres, has, to a great extent, been based upon appropriate oxo derivatives. The stereoselectivities obtained from different reactions have varied.[4] For 4-uloses stereoselectivity of Grignard addition depends on the orientation of the C-3 oxygen function. In pyranose rings equatorial oxygen functions at C-3 result preferentially in equatorial attack at C-4, while the presence of axial C-3 functions gives the opposite orientation of the attack. 4,6-*O*-Benzylidene derivatives of a number of 2- and 3-uloses have been examined with respect to the stereoselectivity of Grignard reactions. While 3-uloses show a strong preference for equatorial attack by methyl nucleophiles, reactions with the 2-uloses are less selective.[4]

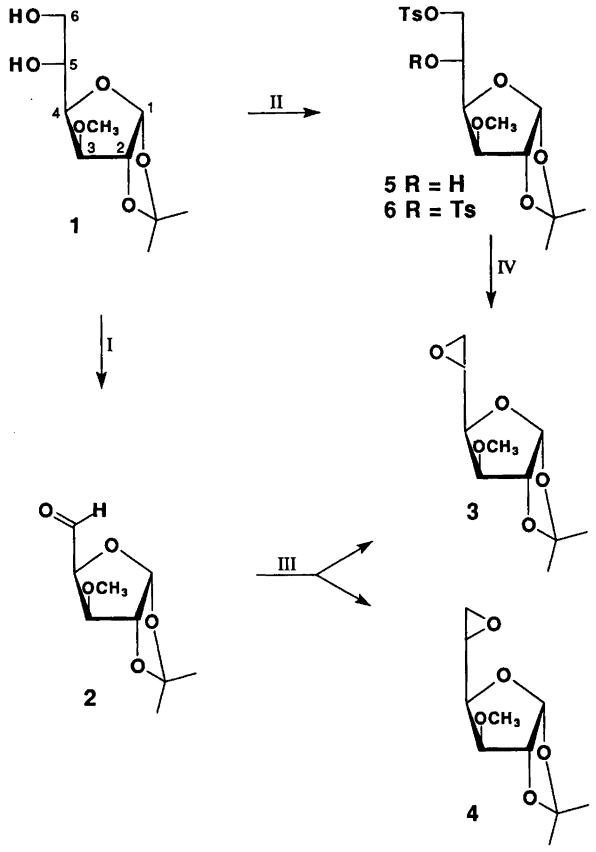
During investigations on the stereoselectivity of additions of diazomethane to some exocyclic ketones with chiral α-carbon atoms, we have synthesized a number of carbohydrates with C-5 branching.

Results and discussion

The starting point for the reactions was 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**1**)[5] which is readily obtained from D-glucose. Oxidation of **1** with sodium periodate gave 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose (**2**).[6] We have previously investigated the stereoselectivity of Grignard additions to this compound and we have been able to show that it is possible to influence the ratio of the products due to chelation and non-chelation mechanisms by utilizing pentaoxapentadecane as a competing chelator.[7] 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose lacking the 3-*O*-methyl group has also been studied. This compound exists as a dimer whose structure has been proved to change on going from chloroform to methanol as the solvent.[8]

Although additions to the oxo group in aldehydes will not produce a branching point, it is of general interest to investigate the stereoselectivity of the reactions and to characterize new products. Addition of diazomethane in diethyl ether to **2** gave the two diastereomeric epoxides **3**:**4** in the ratio 75:25. This ratio changed slightly to 83:17 in a reaction medium containing 40 % methanol. Similar solvent effects have been shown previously.[9]

It is well known that addition of diazomethane to ketones also leads to formation of ketones with an additional carbon atom in the chain instead of a branch.[10] This was also observed in our reactions in varying amounts. The diastereomeric epoxides were separated by TLC. The NMR spectra of these products were very similar and direct identification from the spectra of the two products was not possible. Tosylation of **1** gave both the monotosylate **5** and the ditosylate **6** which were separated. The point of tosylation in **5** was inferred from the ^{1}H NMR shift of H_5 which appeared at 4.25 ppm. This is close to the value of the corresponding proton in **1** (4.02 ppm). The other monotosylate was also observed in minor amounts and the shift of H_5 here was 5.11 ppm. Treatment of **5** with sodium methoxide in methanol gave **3** in high yield. This is a normal S_N2



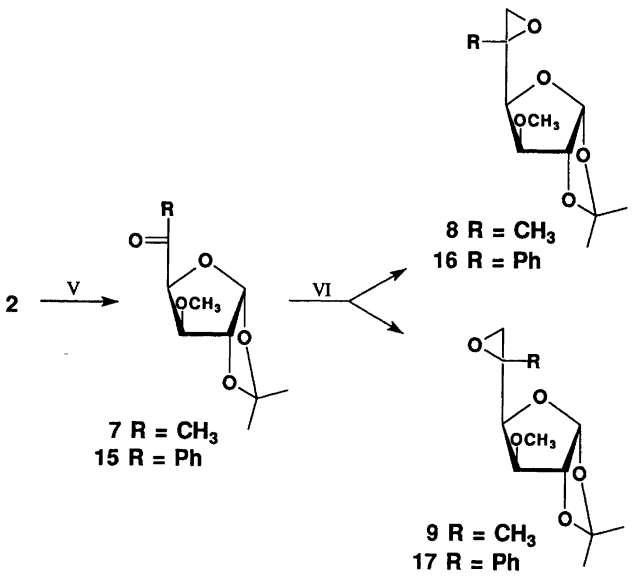
Scheme 1. Reaction conditions: I, $NaIO_4/H_2O$; II, *p*-TosCl/$CHCl_3$; III, (a) Me_2SCH_2/DMSO, (b) CH_2N_2/Et_2O; IV, Na/MeOH.

reaction which does not influence the stereochemistry at C_5. Consequently, this reaction proves that the predominant product of the diazomethane addition reaction to **1** was the D-*gluco*-isomer **3** and strongly implies that **4** was the L-idofuranose (Scheme 1).

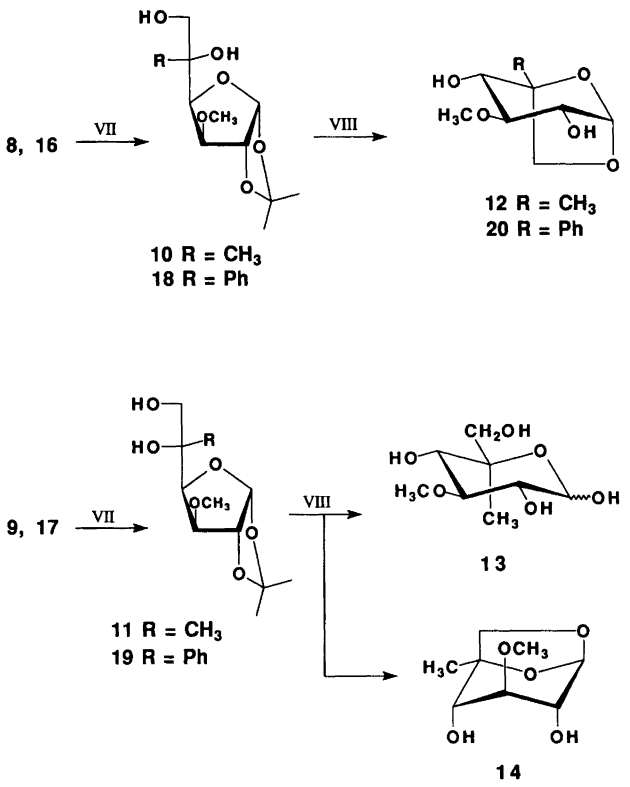
It is a well established technique to use sulfur ylides to produce epoxides by addition reactions.[11] Addition of dimethylsulfonium methylide to the aldehyde **2** gave an even higher excess of **3**, the ratio being **3**:**4** = 86:14. The isolated yield of **3** in this reaction was 43 %. In contrast with aldehydes, addition of carbon nucleophiles to carbohydrate ketones will create branched carbohydrates. The methyl ketone 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranos-5-ulose (**7**) was produced by a Grignard reaction followed by ruthenium tetraoxide oxidation (Scheme 2). Addition of diazomethane in diethyl ether to **7** gave a mixture of epoxides **8** and **9** in a ratio of 40:60. Addition of diazomethane in a diethyl ether:methanol solution (2:1) reversed the ratio of **8**:**9** to 55:45. The two epoxides were separated on an SiO_2 column, isolated in a total yield of 60 %, and their structures were determined after subsequent base-catalysed opening of the epoxide ring and acid-catalysed removal of the 1,2-*O*-isopropylidene group (Scheme 3). The minor product epoxide yielded **12** via **10** while the predominant product yielded a mixture of **13** and **14** via **11**. Consequently, the ratio of the epoxides **8**:**9** was 40:60. The structures of the key compounds **12**, **13** and **14** were verified by ^1H NMR spectroscopy. Acid treatment of 5-*C*-methyl-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose (**10**) led spontaneously to the formation of 1,6-anhydro-3-*O*,5-*C*-dimethyl-β-L-idopyranose (**12**). In this structure both the C-5 methyl group and the three oxygen functions at C-2, C-3 and C-4 are in equatorial positions and the conformation is $^4C_1$(L).[12] The vicinal coupling constants agree with the structure. An additional proof of the 1,6-anhydro structure is provided by the presence of a ^4J coupling of 1.4 Hz between H-4 and H-6(*exo*) indicating a rigid structure where the bonds joining the two mentioned protons form a planar W-structure.

The hydrolysis of 1,2-*O*-isopropylidene-3-*O*,5-*C*-dimethyl-α-D-glucofuranose (**11**) also gave a 1,6-anhydro compound **14**, but in about equal amounts to the monocyclic sugar **13**. The reason for this different behaviour is quite obvious. In the structure of 1,6-anhydro-3-*O*, 5-*C*-dimethyl-β-D-glucopyranose (**14**), although the C-5 methyl group is equatorially oriented, the three oxygen functions at C-2, C-3 and C-4 are all in axial positions. In the ^1H NMR spectrum of **14**, all the vicinal couplings are very small and furthermore there is no long-distance coupling as in the case of **12**. This is due to the absence of the W-structure. The conformation of **14** is $^1C_4$(D).

In contrast, the product not having anhydro structure, 3-*O*, 5-*C*-dimethyl-α-D-glucopyranose (**13**) showed large vicinal couplings ($J_{2,3}$ and $J_{3,4}$ = 9.3 Hz) indicating axial protons at C-2, C-3 and C-4. Thus, this compound is in the $^4C_1$(D) conformation with the C-5 methyl group axially oriented. The anomeric ratio as determined by ^1H NMR spectroscopy in D_2O was α:β = 15:85. Owing to the presence of the axial C-5 methyl group, the β-anomer is even more predominant than for D-glucopyranose (α:β = 38:62).



Scheme 2. Reaction conditions: V, (a) RMgI/Et_2O, (b) RuO_4; VI, CH_2N_2/Et_2O.



Scheme 3. Reaction conditions: VII, 0.5 M NaOH; VIII, 0.8–2 % H_2SO_4.

Starting with **2** the phenyl ketone **15** was made in the same manner as **7**. When **15** was reacted with diazomethane in diethyl ether the two epoxides **16** and **17** were formed in the ratio **16**:**17** = 89:11. The structure of **16** was proved by the same sequence of base- and acid-hydrolysis as previously described for **8**. ^1H and ^{13}C NMR data for **18** were clearly seen from the spectra of the mixture of **18** and **19**. Purification was performed in the last step and this yielded 1,6-anhydro-3-*O*-methyl-5-*C*-phenyl-β-L-idopyranose (**20**) derived from **18**. The characteristic long-distance coupling between H-4 and H-6(*exo*) for **20** was observed (^4J = 0.9 Hz). The reactions with **15** gave an excess of the *ido*-epimer which is the opposite of the reactions with **2** and **7**. The diazomethane additions were performed in diethyl ether with varying amounts of methanol. Homologation, which is a competing reaction to epoxide formation, was favoured with increasing methanol concentration. As has been suggested previously[9] homologation and formation of the *gluco*-epoxide may share a common intermediate.

Experimental

All chemicals were of *pro analysi* grade and the solvents were dried. Diazomethane was prepared from *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide.[13] Dimethylsulfonium methylide was made according to Corey and Chaykovsky.[11] ^1H NMR spectra were recorded at 400 MHz on a Bruker WM-400 instrument and ^{13}C spectra at 25.1 MHz on a Jeol FX-100 instrument in $CDCl_3$ solutions unless otherwise stated. Optical rotations were measured with a Perkin Elmer 241 polarimeter. Mass spectroscopy was performed on an AEI MS902 double focussing spectrometer using the direct inlet probe and electron impact at 70 eV. Both thin layer chromatography (TLC) and preparative layer chromatography (PLC) were performed on Merck *fertigplatten* (Silica gel G60 F_{254}, 0.25 mm). Medium-pressure chromatography was run on 30 cm columns using Merck Silica gel 60, 400 mesh and 4 atm pressure provided by a Duramat pump. For gas chromatography a Varian 3400 instrument with split–splitless injector, FID and equipped with a Vista 402 data system were used. Hydrogen was used as the carrier gas and the columns were BP-1 (cross-linked methyl silicon) and SP-2100 (methyl silicon oil) both 25 m × 0.33 mm, 0.25 μm. 1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose (**2**) was made from 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**1**)[5] [CAS reg. No. 43138-65-4] according to the general procedure by Guthrie.[6]

Reaction of **2** *with dimethylsulfonium methylide in DMSO/THF.* A solution of **2** (0.2 g, 0.99 mmol) in THF (10 ml) under N_2 was added dropwise to a suspension of dimethylsulfonium methylide (1.5 ml, 1.2 mmol). After the reaction mixture had been stirred at 0 °C for 20 min and subsequently at room temperature for 1.75 h, H_2O (50 ml) was added and the reaction mixture extracted with Et_2O (3 × 100 ml). Work-up yielded a light syrup (0.2 g, 0.93 mmol, 93 %) which contained **3** and **4** in the ratio 86:14. PLC of a part of the mixture (80 mg) using $CHCl_3$ as the eluent gave pure (R_f = 0.64) 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**3**) (40 mg, 43 %) as an oil. ^1H NMR: δ 5.92 (H-1, d, $J_{1,2}$ = 3.7 Hz), 4.62 (H-2, d, $J_{2,3}$ = 0 Hz), 3.85 (H-3, d, $J_{3,4}$ = 3.0 Hz), 3.73 (H-4, dd, $J_{4,5}$ = 7.1 Hz), 3.24 (H-5, ddd, $J_{5,6a(cis)}$ = 2.5 Hz, $J_{5,6b(trans)}$ = 4.0 Hz), 2.92 (H-6b, dd, J_{gem} = 5.0 Hz), 2.78 (H-6a, dd), 3.50 (OCH_3, s), 1.47 [CH_3, isopropyl (*endo*), s], 1.32 (CH_3, isopropyl (*exo*), s]. ^{13}C NMR: δ 105.2 (C-1, d), 82.0 (C-2, d), 84.3 (C-3, d), 81.5 (C_4, d), 47.9 (C-5, d), 46.6 (C-6, t), 111.8 (ketal C, s), 58.2 (OCH_3, q) 26.1 and 16.6 (2 × CH_3, isopropyl, q). Fractions with R_f = 0.5 contained 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose (**4**) (8.5 mg, 9 %). ^1H NMR: 5.97 (H-1, d, $J_{1,2}$ = 3.7 Hz), 4.62 (H-2, d, $J_{2,3}$ = 0 Hz), 3.79 (H-3, d, $J_{3,4}$ = 3.5 Hz), 3.85 (H-4, dd, $J_{4,5}$ = 5.7 Hz), 3.23 (H-5, ddd, $J_{5,6a(cis)}$ = 2.7 Hz, $J_{5,6b(trans)}$ = 4.4 Hz), 2.69 (H-6a, dd, J_{gem} = 4.8 Hz), 2.85 (H-6b, dd), 3.45 (OCH_3, s), 1.47 [CH_3, isopropyl (*endo*), s], 1.33 [CH_3, isopropyl (*exo*), s]. ^{13}C NMR: 105.4 (C-1, d), 81.9 (C-2, d), 85.7 (C-3, d), 81.9 (C-4, d), 49.0 (C-5, d), 43.3 (C-6, t), 111.8 (ketal C, s), 58.2 (OCH_3, q), 26.4 and 27.0 (2 × CH_3, isopropyl, q).

Reaction of **2** *with diazomethane.* A 0.5 molar solution of CH_2N_2 in Et_2O (9 ml) was added dropwise to a solution of **2** (250 mg, 1.2 mmol) in dry Et_2O (5 ml). When the reaction was complete (no more evolution of N_2), the solvent was

evaporated off under reduced pressure to yield a pale yellow syrup (259 mg, 1.2 mmol), **3**:**4** = 75:25 (GLC).

1,2-O-Isopropylidene-3-O-methyl-6-O-tosyl-α-D-glucofuranose (**5**). Under stirring at 0 °C an ice-cold solution of *p*-TosCl (5.5 g, 28.9 mmol) in $CHCl_3$ (10 ml) was added to a suspension of **1** (5.5 g, 23.5 mmol) in dry pyridine (10 ml). After an additional 48 h of stirring, crushed ice was added and the mixture was extracted with $CHCl_3$ (3 × 50 ml). Work-up yielded a yellow syrup (7.89 g). $CHCl_3$ (15 ml) was added and the mixture was stored at −20 °C for 24 h. Crystallized ditosylate **6**, m.p. 118–118.5 °C, was removed by filtration. MS: Calcd. for $C_{24}H_{30}O_{10}S_2$ = 542.1280. Obs. 542.1268. ^{1}H NMR: δ 5.76 (H-1, d, $J_{1,2}$ = 3.64 Hz), 4.53 (H-2, d, $J_{2,3}$ = 0 Hz), 3.78 (H-3, d, $J_{3,4}$ = 3.12 Hz), 4.27 (H-4, dd, $J_{4,5}$ = 7.34 Hz), 5.07 (H-5, m), 4.04 and 4.33 (H-6a and H-6b, resp., 2 × dd, J_{gem} = 11.29 Hz, $J_{5,6a}$ = 6.24 Hz, $J_{5,6b}$ = 2.07 Hz), 3.33 (3 H, OCH_3, s), 1.30 [3 H, CH_3, isopropyl (*exo*), s], 1.44 [3 H, CH_3, isopropyl (*endo*), s], 7.79 and 7.65 (2 × 2 H, H-2′, H-6′, d, J = 8.1 Hz), 7.34 and 7.29 (2 × 2 H, H-3′, H-5′, d), 2.42 (3 H, CH_3, tos). ^{13}C NMR: δ 105.1 (C-1, d), 80.6 (C-2, d), 82.5 (C-3, d), 78.0 (C-4, d), 68.5 (C-5, d), 74.7 (C-6, t), 112.2 (ketal C, s), 57.5 (OCH_3, q), 26.2 and 26.8 (2 × CH_3, isopropyl, q), 21.6 (2 × CH_3, tos, q), 144.9 and 144.7 (2 C-1′, s), 129.7, 128.0 (2 C-2′, s and 2 C-3′, s), 132.3 and 133.7 (2 C-4′, s).

The syrup was applied to a SiO_2 column (2.5 × 25 cm) and eluted with CH_2Cl_2. Fractions containing the monotosylate **5** as the major product were combined and evaporated to give an oil (5.1 g). ^{1}H NMR: δ 5.71 (H-1, d, $J_{1,2}$ = 3.5 Hz), 4.43 (H-2, d, $J_{2,3}$ = 0 Hz), 3.75 (H-3, d, $J_{3,4}$ = 3.0 Hz), 4.12 (H-4, dd, $J_{4,5}$ = 7.9 Hz), 4.25 (H-5, m), 4.01 and 4.09 (2 H-6, dd, J_{gem} = 8.2 Hz), 3.35 (3 H, OCH_3, s), 1.31 [3 H, CH_3, isopropyl (*exo*), s], 1.47 [3 H, CH_3, isopropyl (*endo*), s], 7.68 (2 H, H-2′, H-6′, d, J = 8.1 Hz), 7.26 (2 H, H-3′, H-5′, d), 2.42 (3 H, CH_3, tos). ^{13}C NMR: δ 105.0 (C-1, d), 81.4 (C-2, d), 84.0 (C-3, d), 79.0 (C-4, d), 67.2 (C-5, d), 72.2 (C-6, t), 111.7 (ketal C, s), 57.7 (OCH_3, q), 26.1 and 26.6 (2 × CH_3, isopropyl, q), 21.4 (CH_3, tos, q), 144.7 (C′-1, s), 129.7, 127.8 (C′-2, s, C′3, s) and 132.7 (C′-4, s).

5,6-Anhydro-1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose (**3**) *from* **5**. A solution of sodium methoxide prepared from Na (0.03 g, 1.3 mmol) and dry MeOH (1.5 ml) was added with stirring to a suspension of **5** (0.34 g, 0.9 mmol) in dry $CHCl_3$ (3 ml). Stirring was continued for 15 min, H_2O (10 ml) was added and the water layer was extracted with $CHCl_3$ (2 × 50 ml). Work-up yielded **3** (183 mg, 0.84 mmol, 93 %) as a colourless liquid. NMR spectra were identical with those of **3** obtained above.

6-Deoxy-1,2-O-isopropylidene-3-O-methyl-α-D-hexofuranos-5-ulose (**7**). A Grignard reagent was prepared from CH_3I (23.4 ml, 0.38 mol) in dry Et_2O (100 ml) and Mg (8.2 g, 0.34 mol) in dry Et_2O (200 ml). The mixture was cooled to 4 °C, and a solution of **2** (41 g, 0.2 mol) in dry Et_2O (100 ml) was added dropwise with stirring. After an additional hour of stirring at 20 °C, the reaction mixture was neutralized with sat. NH_4Cl, acidified with 1 M HCl and extracted with Et_2O (3 × 200 ml). Work-up yielded a mixture of 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose and 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-idofuranose (40.5 g, 0.19 mmol, 92 %) in the ratio 37:63. To a vigorously stirred mixture of RuO_2 (3.35 g, 25.2 mmol) and K_2CO_3 (14.3 g, 100 mmol) in CH_2Cl_2 (500 ml), was added dropwise a solution of $NaIO_4$ (110 g, 0.51 mol) in H_2O (500 ml). After an additional 0.5 h of stirring, the above mixture of alcohols (40 g, 0.18 mol) in $CHCl_3$ (130 ml) was added, and the reaction mixture was stirred for 48 h. Excess oxidation agent was removed by addition of 2-propanol (4 ml) and the precipitate was filtered. The crude product was extracted with $CHCl_3$ (3 × 40 ml) and work-up yielded **7** (33 g, 0.15 mol, 85 %) as a yellow syrup. ^{1}H NMR: δ 6.05 (H-1, d, $J_{1,2}$ = 3.6 Hz), 4.59 (H-2, d, $J_{2,3}$ = 0 Hz), 4.03 (H-3, d, $J_{3,4}$ = 3.7 Hz), 4.58 (H-4, d), 2.23 (3 H, C5-Me, s), 3.36 (3 H, OCH_3, s), 1.49 [3 H, CH_3, isopropyl (*endo*), s], 1.34 [3 H, CH_3, isopropyl (*exo*), s]. ^{13}C NMR: δ 105.6 (C-1, d), 80.9 (C-2, d), 85.6 (C-3, d), 85.1 (C-4, d), 206.2 (C-5, s), 112.0 (ketal C, S), 57.9 (OCH_3, q), 27.9 (C-6, q), 26.6 and 26.1 (2 × CH_3, isopropyl, q).

Addition of diazomethane to 6-deoxy-1,2-O-isopropylidene-3-O-methyl-α-D-xylo-hexofuranos-5-ulose (**7**). A 0.44 molar solution of CH_2N_2 in Et_2O (65 ml, 28.4 mmol) was added dropwise to stirred **6** (2.84 g, 13.1 mmol) in Et_2O (30 ml). An additional 24 h of stirring and evaporation of the solvent under reduced pressure gave a dark yellow liquid (3.0 g). TLC showed four spots and the major one (60 %, R_f = 0.75 in Et_2O) was shown (GLC) to be a mixture of the epimeric epoxides **8** and **9**, (**8**:**9** = 40:60). When the addition reaction was performed in a solvent consisting of 25 % MeOH and 75 % Et_2O, the ratio **8**:**9** was 55:45 (GLC). The reaction mixture was applied to a column (SiO_2) and eluted with Et_2O. The combined fractions containing **8** and **9** were applied to another column (SiO_2) and eluted with hexane: Et_2O = 70:30 and 65 fractions (50 ml) were collected. Fractions 42–46 (94.3 mg, 3 %) contained 5,6-anhydro-3-*O*,5-*C*-dimethyl-1,2-*O*-isopropylidene-β-L-idofuranose (**8**). Calcd. for $C_{11}H_{18}O_5$: 230.1154. Obs. $M^{\cdot+}$ = 230.1146. *m/z* (%): 230 (0.1), 215 (5), 145 (10), 144 (17), 141 (12), 87 (22), 86 (31), 85 (91), 83 (25), 59 (70), 56 (73), 57 (21), 43 (100). ^{1}H NMR: 5.89 (H-1, d, $J_{1,2}$ = 3.4 Hz), 4.52 (H-2, d, $J_{2,3}$ = 0 Hz), 3.74 (H-3, d, $J_{3,4}$ = 3.9 Hz), 2.53 [H-6a (*cis* CH_3), d, J_{gem} = 5.1 Hz], 2.79 [H-6b (*trans* CH_3), d], 3.42 (3 H, OCH_3, s), 1.46 [3 H, CH_3, isopropyl (*endo*), s], 1.38 [3 H, CH_3, isopropyl (*exo*), s], 1.38 (3 H, C5-Me, s). ^{13}C NMR: δ 105.1 (C-1, d), 82.1 (C-4, d), 82.3 (C-2, d), 85.8 (C-3, d), 55.1 (C-5, s), 49.7 [C-5 (epoxide), t], 111.6 (ketal C, s), 57.7 (OCH_3, q), 18.4 (C5-Me, q), 26.3 and 26.8 (2 × CH_3, isopropyl, q). Fractions 19–27 (0.26 g, 8.6 %) contained 5,6-anhydro-5-*C*-methyl-1,2-*O*-isopropylidene-D-glucofuranose (**9**). MS: Calcd. for $C_{11}H_{18}O_5$: 230.1154. Obs. $M^{\cdot+}$ 230.1146. *m/z* (%): 230 (0.4), 215 (7),

145 (14), 144 (23), 87 (25), 85 (37), 85 (86), 83 (26.2), 59 (79), 58 (72), 43 (100). ^{1}H NMR: δ 5.88 (H-1, d, $J_{1,2}$ = 3.4 Hz), 4.58 (H-2, d, $J_{2,3}$ = 0 Hz), 3.77 (H-3, $J_{3,4}$ = 3.4 Hz), 4.24 (H-4, d), 2.75 [H6a (*cis* CH_3), d, J_{gem} = 4.9 Hz], 3.03 [H 6b (*trans* CH_3), d], 3.43 (3 H, OCH_3, s), 1.49 [3 H, CH_3, isopropyl (*endo*), s], 1.32 [3 H, CH_3, isopropyl (*exo*), s], 1.38 [3 H, CH_3 (C5-Me), s]. ^{13}C NMR: δ 105.1 (C-1, d), 80.0 (C-4, d) 81.4 (C-2, d), 84.9 (C-3, d), 55.5 (C-5, s), 51.6 [C-6 (epoxide), t], 111.8 (ketal C, s), 18.8 (C5-Me, q), 26.6 and 26.9 (2 × CH_3, isopropyl, q), 57.8 (OCH_3, q).

*1,2-*O*-Isopropylidene-3-*O*,5-*C*-dimethyl-*β*-*L*-idofuranose* (**10**). Compound **10** was made by adding 0.5 M NaOH (5 ml) to **8** (46 mg, 0.2 mmol). After being stirred at 60 °C for 6 h, the reaction mixture was neutralized with 1 M HCl/sat. NH_4Cl and extracted with $CHCl_3$ (3 × 30 ml). Work-up gave **10** (48 mg, 0.19 mmol) as a colourless liquid: $[\alpha]_D$ = −39.6° ($CHCl_3$, *c* = 2.4); MS: Calcd. for $C_{11}H_{19}O_6$ (*M*−1): 247.1182. Obs. (*M*−1) 247.1181. *m/z* (%): 233 (2.4), 217 (24), 185 (5), 173 (10), 159 (19), 142 (8), 114 (13), 113 (51), 101 (52), 85 (67), 59 (75), 58 (66), 43 (100). ^{1}H NMR: δ 6.00 (H-1, d, $J_{1,2}$ = 3.9 Hz), 4.58 (H-2, d, $J_{2,3}$ = 0 Hz), 4.04 (H-3, d, $J_{3,4}$ = 3.4 Hz), 3.92 (3 H, OCH_3, s), 1.30 [3 H, CH_3 (C5-Me), s], 1.50 [3 H, CH_3, isopropyl (*endo*), s], 1.33 [3 H, CH_3, isopropyl (*exo*), s]. ^{13}C NMR: δ 104.9 (C-1, d), 81.0 (C-2, d), 86.1 (C-3, d), 80.6 (C-4, d), 72.8 (C-5, s), 68.1 (C-6, t), 111.7 (ketal C, s), 57.5 (OCH_3, q), 22.4 (C5-Me, q), 26.7 and 26.1 (2 × CH_3, isopropyl, q).

*1,2-*O*-Isopropylidene-3-*O*,5-C-dimethyl-α-*D*-glucofuranose* (**11**). Compound **11** was made by adding 0.5 M NaOH (12 ml) to **9** (0.13 g, 0.57 mmol). After 3 h of stirring at 60 °C, the reaction mixture was neutralized with 1 M HCl/sat. NH_4Cl and extracted with $CHCl_3$ (3 × 75 ml). Work-up gave **11** (0.13 g, 0.53 mmol, 92 %) as a colourless liquid: $[\alpha]_D$ = −45.0° ($CHCl_3$, *c* = 2.86); MS: Calcd. for $C_{11}H_{19}O_3$ (*M*−1) = 247.1182. Obs. ($M^{\cdot}$+ −1) = 247.1181. *m/z* (%): 233 (2), 217 (17), 185 (3), 173 (7), 159 (6), 142 (9), 114 (13), 113 (47), 101 (48), 85 (69), 59 (79), 58 (60), 43 (100). ^{1}H NMR: δ 5.9 (H-1, d, $J_{1,2}$ = 3.9 Hz), 4.58 (H-2, d), 3.97 (H-3, $J_{3,4}$ = 3.4 Hz), 3.90 (H-4, d), 3.52 and 3.59 (H-6a and H-6b, J_{gem} = 7.8 Hz), 3.43 (3 H, OCH_3, s), 1.28 [3 H, CH_3 (C5-Me), s], 1.49 [3 H, CH_3, isopropyl (*endo*), s], 1.33 [3 H, CH_3, isopropyl (*exo*), s], ^{13}C NMR: δ 103.9 (C-1, d), 80.8 (C-4, d), 85.2 (C-3, d), 82.0 (C-2, d), 73.3 (C-5, s), 68.3 (C-6, t) 111.2 ketal C, s), 56.9 (OCH_3, q), 21.8 (C5-Me, q), 26.3 and 25.8 (2 × CH_3, isopropyl, q).

*1,6-Anhydro-3-*O*,5-C-dimethyl-β-*L*-idopyranose* (**12**). Compound **12** was made by hydrolysing **10** (40 mg, 0.16 mmol) with 2 % H_2SO_4 (5 ml). After being stirred for 4 h at 95 °C, the reaction mixture was neutralized with $BaCO_3$, filtered and extracted with $CHCl_3$ (2 × 10 ml). Work-up yielded **12** (31 mg, 14.9 mmol, 92.6 %) as white crystals. Recrystallization from $CHCl_3$ yielded colourless needles, m.p. 138.5–139 °C. R_f (TLC) = 0.58 in acetone. ^{1}H NMR: δ 5.25 (H-1, d, $J_{1,2}$ = 1.9 Hz), 3.56 (H-2, dt, $J_{2,3}$ = 8.4 Hz), 3.25 (H-3, t, $J_{3,4}$ = 8.4 Hz), 3.52 (H-4, dd, $J_{4,6b}$ = 1.4 Hz), 3.38 [H-6b (*exo*), dd, J_{gem} = 8.1 Hz], 4.02 [H-6a (*endo*), d], 2.68 (H-OH-4, d, *J* = 3.3 Hz), 2.26 (H-OH-2, d, *J* = 9.3 Hz), 1.42 (3 H, CH_3, C5-Me, s), 3.56 (3 H, OCH_3, s). ^{13}C NMR: δ 102.0 (C-1, d), 86.2 (C-3, d), 80.8 (C-5, s), 75.4 (C-2, d), 75.2 (C-4, d), 69.9 (C-6, t), 60.1 (OCH_3, q), 18.5 (C5-Me, q). MS: Calcd. for $C_7H_{10}O_4$ (*M*−$HOCH_3$): 158.0573. Obs. (*M*−32) = 158.0573. *m/z* (%): 158 (2), 131 (4), 117 (63), 101 (4), 85 (5), 75 (5), 74 (100), 73 (12), 71 (16), 43 (42).

*3-*O*, 5-C-Dimethyl-*D*-glucopyranose* (**13**). To a mixture of **10** and **11** (157 mg, 0.63 mmol, **10**:**11** = 53:47, GLC) was added 0.8 % H_2SO_4 (10 ml). After 13 h at 80 °C, neutralization with $BaCO_3$ and filtration, the filtrate was extracted with $CHCl_3$ (3 × 20 ml). Usual work-up yielded a colourless syrup (84 mg, 0.40 mmol, 63.5 %). PLC (acetone) gave three fractions: The first fraction was shown to be **12** (42 mg, R_f = 0.58), the second fraction (8.9 mg, R_f = 0.47) contained a compound only consistent with 1,6-anhydro-3-*O*,5-*C*-dimethyl-β-*D*-glucopyranose (**14**) and the third fraction contained **13** (26 mg, R_f = 0.24). The anomeric ratio, α:β was 15:85 (400 MHz ^{1}H NMR in D_2O). NMR data for the β-anomer: ^{1}H NMR (D_2O): δ 4.78 (H-1, d, $J_{1,2}$ = 7.8 Hz), 3.24 (H-2, dd, $J_{2,3}$ = 9.3 Hz), 3.32 (H-3, t, $J_{3,4}$ = 9.3 Hz), 3.65 (H-4, d), 3.58 and 3.54 [H-6a and H-6b, d, J_{gem} = 11.5 Hz], 1.23 [3 H, CH_3 (C5-Me), s], 3.72 (3 H, OCH_3, s), ^{13}C NMR (D_2O): δ 94.1 (C-1, d), 77.3 (C-2, d), 85.2 (C-3, d), 72.3 (C-4, d), 78.3 (C-5, s), 68.6 (C-6, t), 14.9 (C5-Me, q), 61.2 (OCH_3, q).

*1,6-Anhydro-3-*O*,5-C-dimethyl-β-*D*-glucopyranose* (**14**). To **11** was added 2 % H_2SO_4 (12 ml) and the mixture was stirred for 4 h at 95 °C. Neutralization with $BaCO_3$, filtration and evaporation of the solvent yielded a mixture of **13** and **14** (total 94.5 mg). PLC of the reaction mixture using acetone as the eluent yielded **13** (43.7 mg, R_f = 0.24) and **14** (39 mg, R_f = 0.47). Data for **14**: ^{1}H NMR: δ 5.45 (H-1, br s), 3.65 (H-2, br s), 3.46 (H-3, d, $J_{3,4}$ < 1 Hz), 3.53 (H-4, d), 4.19 [H-6a (*endo*), d, J_{gem} = 7.1 Hz], 3.43 [H-6b (*exo*), d], 3.45 (3 H, OCH_3, s), 2.65 (1 H, OH-4, s), 2.20 (1 H, OH-2, s), 1.47 (3 H, CH_3, C5-Me, s), ^{13}C NMR (CD_3OD): δ 103.8 (C-1, d), 71.3 (C-2, d), 85.0 (C-3, d), 71.1 (C-4, d), 81.1 (C-5, s), 67.9 (C-6, t), 57.9 (OCH_3, q), 18.6 (C5-Me, q).

*1,2-*O*-Isopropylidene-3-*O*-methyl-5-C-phenyl-α-*D*-xylo-pentofuranos-5-ulose* (**15**). A Grignard reaction was performed by dropwise addition of a solution of PhI (6.12 g, 3.4 ml, 29.9 mmol) in dry Et_2O (12 ml) to a suspension of Mg (0.34 g, 14 mmol) in dry Et_2O (5 ml). After the reaction mixture had been refluxed for 0.5 h, **2** (3.0 g, 14.9 mmol) in dry Et_2O (15 ml) was added dropwise. Stirring at room temperature was maintained for 18 h before acidification with 1 M HCl and extraction with $CHCl_3$ (3 × 50 ml). Work-up yielded a brown syrup (4.1 g, 14.6 mmol, 98.2 %) which was oxidized without further purification. To a

vigorously stirred mixture of RuO_2 (0.35 g, 2.63 mmol), K_2CO_3 (1.43 g, 0.01 mmol) and CH_2Cl_2 (50 ml) was added $NaIO_4$ (9 g, 42 mmol) in H_2O (50 ml). After addition of the previously mentioned Grignard product in $CHCl_3$ (10 ml), stirring was continued for an additional 48 h. In order to speed up the reaction, additional $NaIO_4$ (5 g, 23.4 mmol) and RuO_2 (0.2 g, 1.5 mmol) were added. When the reaction was complete, excess oxidant was reduced by addition of 2-propanol. Work-up yielded **15** (3.9 g, 14 mmol, 96 %) as a dark syrup. Crystallization from MeOH gave colourless crystals, m.p. 122–123 °C. ^{1}H NMR: δ 6.14 (H-1, d, $J_{1,2}$ = 3.9 Hz), 4.64 (H-2, d, $J_{2,3}$ = 0 Hz), 4.20 (H-3, d, $J_{3,4}$ = 3.9 Hz), 5.54 (H-4, d), 3.18 (3 H, OCH_3, s), 1.56 [3 H, CH_3, isopropyl(*endo*), s], 1.37 [3 H, CH_3, isopropyl(*exo*), s], 7.96 (2 H-*o*, d), 7.48 (2 H-*m*, t), 7.53 (1 H-*p*, t). ^{13}C NMR: δ 105.4 (C-1, d), 81.5 (C-2, d), 86.2 (C-3, d), 83.5 (C-4, d), 194.0 (C-5, s), 26.3 and 27.0 (2 × CH_3, isopropyl, q), 58.1 (OCH_3, q), 136.0 (C-1, s), 133.2 (C-4, d), 128.1 and 128.5 (C-2, C-3, C-5 and C-6, all d).

*5,6-Anhydro-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-phenyl-*α*-*D*-glucofuranose* (**17**) *and 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-phenyl-*β*-*L*-idofuranose* (**16**). To a solution of **15** (100 mg, 0.36 mmol) in Et_2O (5 ml), saturated with H_2O, was added dropwise a solution of CH_2N_2 (0.8 mmol) in Et_2O (4 ml). After 12 h at room temperature the reaction mixture was concentrated under reduced pressure to yield a thin, colourless syrup (103 mg). TLC of the reaction mixture showed seven spots of which the epimeric epoxides were the major components (60 %) and the isomeric benzyl ketone a minor component (10 %) (^{1}H NMR). The reaction mixture (67 mg) was applied to PLC plates and eluted with EtOAc : CH_2Cl_2 = 30 : 70. Fraction 3 (R_f = 0.63) and fraction 4 (R_f = 0.68) contained **17** and **16**, respectively. The ratio **17** : **16** was 11 : 89 (GLC and ^{1}H NMR). ^{1}H NMR (**17**): δ 5.95 (H-1, d, $J_{1,2}$ = 3.7 Hz), 4.23 (H-2, d, $J_{2,3}$ = 0 Hz), 3.81 (H-3, d, $J_{3,4}$ = 3.2 Hz), 4.61 (H-4, d), 2.85 [H-6b (*trans* Ph), d, J_{gem} = 7.0 Hz], 2.43 [H-6a (*cis* Ph), d], 3.45 (3 H, OCH_3, s), 1.55 [3 H, CH_3, isopropyl(*endo*), s], 1.32 [3 H, CH_3, isopropyl(*exo*), s], 7.20–7.50 (5 H, Ph, m). ^{1}H NMR (**16**): δ 5.99 (H-1, d, $J_{1,2}$ = 3.8 Hz), 4.58 (H-2, d, $J_{2,3}$ = 0 Hz), 3.59 (H-3, d, $J_{3,4}$ = 3.3 Hz), 4.87 (H-4, d), 3.28 [H-6b (*trans* Ph), d, J_{gem} = 7.2 Hz], 2.58 [H-6a (*cis* Ph), d], 3.26 (3 H, OCH_3, s), 1.55 [3 H, CH_3, isopropyl(*endo*), s], 1.34 [3 H, CH_3, isopropyl(*exo*), s], 7.20–7.50 (5 H, Ph, m). ^{13}C NMR (**16**): δ 104.9 (C-1, d), 81.7 (C-2, d), 84.3 (C-3, d), 78.6 (C-4, d), 58.1 (C-5, s), 50.1 (C-6, t), 57.8 (CH_3, q), 111.6 (ketal C, s), 26.1 and 26.9 (2 × CH_3, isopropyl, q), 126.4, 127.8, 128.3, 129.9 and 138.1 (Ph).

*1,2-*O*-Isopropylidene-3-*O*-methyl-5-*C*-phenyl-α-*D*-glucofuranose* (**19**) *and 1,2-*O*-isopropylidene-3-*O*-methyl-5-*C*-phenyl-β-*L*-idofuranose* (**18**). To a mixture of **17** and **16** (50 mg, 0.17 mmol, **17** : **16** = 11 : 89) was added 0.5 M NaOH (7 ml). After being stirred at 60 °C for 12 h, the reaction mixture was neutralized with 1 M HCl/sat. NH_4Cl and extracted with $CHCl_3$ (3 × 5 ml). Work-up yielded a mixture of **19** and **18** (49 mg, 0.16 mmol, 93 %, **19** : **18** = 11 : 89) as a colourless syrup. ^{1}H NMR (**18**): δ 6.05 (H-1, d, $J_{1,2}$ = 3.0 Hz), 4.43 (H-2, d, $J_{2,3}$ = 0 Hz), 3.43 (H-3, d, $J_{3,4}$ = 3.4 Hz), 4.56 (H-4, d), 4.00 and 3.88 (H-6a and H-6b, d, J_{gem} = 11.2 Hz), 3.07 (3 H, OCH_3, s), 1.53 [3 H, CH_3, isopropyl(*endo*), s], 1.32 [3 H, CH_3, isopropyl(*exo*), s], 7.20–7.50 (5 H, Ph, m), 3.75 and 2.28 (OH-6, OH-5). ^{13}C NMR (**18**): δ 105.4 (C-1, d), 81.7 (C-2, d), 86.2 (C-3, d), 80.7 (C-4, d), 75.7 (C-5, s), 69.4 (C-6, t), 57.7 (OCH_3, q), 26.1 and 26.8 (2 × CH_3, isopropyl, q), 125.1, 127.4, 128.4, 130.7 and 142.4 (Ph).

*1,6-Anhydro-3-*O*-methyl-5-*C*-phenyl-β-*L*-idopyranose* (**20**). Compound **20** was made by adding 0.8 % H_2SO_4 (15 ml) to a mixture of **19** and **18** (49 mg, 0.16 mmol, **19** : **18** = 11 : 89) in MeOH (15 ml). Stirring at 85 °C for 24 h, neutralization with $BaCO_3$ and work-up yielded a thin syrup (41 mg, 0.15 mmol, 96 %) consisting mainly of **20**. ^{1}H NMR: δ 5.48 (H-1, d, $J_{1,2}$ = 1.3 Hz), 3.74 (H-2, dd, $J_{2,3}$ = 6.8 Hz), 3.37 (H-3, dd, $J_{3,4}$ = 6.6 Hz), 3.65 (H-4, dd, $J_{4,6b(exo)}$ = 0.9 Hz), 4.58 [H-6a (*endo*), d, J_{gem} = 7.7 Hz], 3.79 [H-6b (*exo*), dd], 3.66 (3 H, OCH_3, s), 1.85 and 2.28 (OH-4, OH-2), 7.20–7.50 (5 H, Ph, m).

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