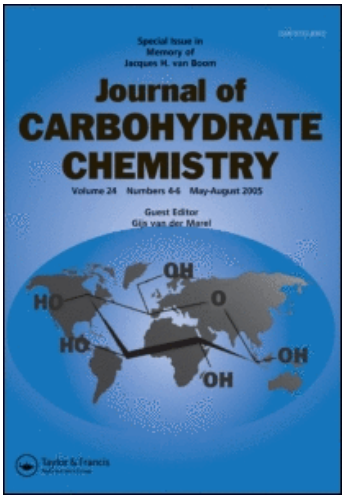

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ANOMERIZATION OF METHYL GLYCOSIDES BY ACID-CATALYSED METHANOLYSIS: TRAPPING OF INTERMEDIATES

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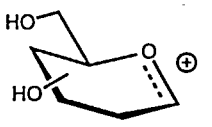
ABSTRACT

Intermediate oxocarbenium ions or other intermediates produced during acid catalyzed anomerization of some methyl glycosides were trapped by reduction with 4-methylmorpholine borane. The glycosylium ion intermediate formed on anomerization of methyl 4-*O*-methyl-α-D-glucopyranoside gave, as expected, only a mixture of the α- and β-D-glucopyranosides, as this reaction is slow compared to the degradation of the reducing agent. The more reactive methyl 2-deoxy-4-*O*-methyl-α-D-*arabino*-hexopyranoside gave two reduction products, namely, 1,5-anhydro-2-deoxy-4-*O*-methyl-D-*arabino*-hexitol and 2-deoxy-1,4-di-*O*-methyl-D-*arabino*-hexitol, indicating alternative reaction pathways, involving either *exo* or *endo* C–O cleavage. The aldofuranosides, when necessary methylated on O-5 in order to avoid formation of pyranosides, gave 1-*O*-methylalditols, indicating protonation of the ring oxygen, followed by *endo* C–O cleavage. The methyl 2-deoxy-5-*O*-methyl-α-D-*arabino*-hexofuranosides, however, gave a mixture of the 1,5-di-*O*-methylalditol and the 5-*O*-methyl-1,4-anhydroalditol. The methyl fructosides and 1-deoxyfructosides, both furanosidic and pyranosidic, gave mixtures of 2,5- and 2,6-anhydrohexitols, indicating that the anomerization of these glycosides also proceeds *via exo* C–O cleavage.

INTRODUCTION

Synthesis of alkyl glycosides by acid-catalyzed alcoholysis (Fischer synthesis), anomerization of glycosides on such treatment, and acid-catalyzed hydrolysis of alkyl

glycosides are closely related reactions. It is generally accepted that hydrolysis and anomerization of alkyl aldopyranosides proceed via a glycopyranosylium ion (e. g. 1) or a glycopyranosylium ion-like transition states. In addition to the arguments given by Capon,[1] e.g., the positive entropy of activation, this is supported by the positive volume of activation,[2] and by detailed kinetic studies by De Bruyne's group (compare e.g., Ref. 3).



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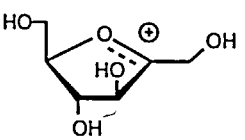
From the ^{18}O kinetic isotope effect on acid hydrolysis of isopropyl α-L-[1-^{18}O]-arabinofuranoside it was assumed that the hydrolysis proceeds *via* an acyclic 1-*O*-isopropyl-L-arabinitol-1-*C*-ylium ion.[4] The entropy of activation[1] and volume of activation[2] on acid hydrolysis of alkyl aldofuranosides are also low, in contradistinction to the values observed for the corresponding pyranosides. Lönnberg *et al.*[5] studied the acid-catalyzed hydrolyses of alkyl β-D-xylofuranosides, and their results indicate that the hydrolysis of xylofuranosides with an electron repellent aglycon group [$CH(CH_3)_2$, CH_2CH_3, or CH_3] proceeds mainly via *endo* C–O cleavage. Studies by Capon and Thacker[6] and by Lönnberg's group[7] further indicate that non-cyclic alkyl acetals are intermediates during anomerization of alkyl furanosides, and that the α- and β-furanosides are formed by nuclephilic attack of the hydroxyl group at C-4 on the protonated acetal.

Capon[1] assumes that the acid hydrolysis of fructofuranosides proceeds via a fructofuranosylium ion (2), and this is supported by kinetic studies on alkyl D-fructofuranosides performed by Lönnberg and Gylén.[8] The entropy of activation observed was positive. According to Szejtli,[9] the entropy of activation on acid hydrolysis of methyl β-D-fructopyranoside is also positive.



2

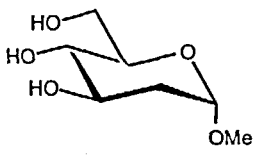
When acid-sensitive glycosides, such as 2-deoxypyranosides, 3,6-anhydrohexopyranosides, and ketofuranosides, are hydrolyzed with acid in the presence of 4-methylmorpholine borane, the reducing agent survives long enough to completely reduce the released sugar to the corresponding alditol.[10] The reducing agent was, however,

degraded before significant parts of more resistant glycosidic linkages were hydrolyzed. We therefore assumed that when the acid-catalyzed anomerization of an alkyl glycoside in the corresponding alcohol was performed in the presence of 4-morpholine borane, part of the oxocarbenium ions or other intermediates would be reduced and thus trapped, provided that the reaction was fast enough compared to the degradation of the reducing agent. We now report such studies on some methyl glycopyranosides and methyl glycofuranosides.

RESULTS AND DISCUSSION

The methyl glycosides were either known substances or were prepared by standard methods, as described in the experimental part. In order to preclude equilibration between furanosides and pyranosides, the aldosides were protected, either as pyranosides by methylation at O-4, or as furanosides by methylation at O-5. All methyl glycosides were subjected to the same treatment, namely, an aqueous solution of the glycoside (5 μmol) was freeze-dried and the amorphous product was dissolved in anhydrous M methanolic hydrogen chloride (3 mL) containing 4-methylmorpholine borane (50 μmol). After 3 days at ambient temperature (~22 °C), the product was isolated, acetylated, and analyzed by electron impact GC-MS (EI GC-MS). The various components were identified by comparison with authentic substances, published spectra, or by interpretation using established principles.[11] Some substances were also identified from their NMR spectra.

Methyl aldopyranosides. Methyl 4-*O*-methyl-α-D-glucopyranoside[12] was, as expected, too unreactive and gave only a mixture of α- and β-glucosides (8:2) under the conditions outlined above. 2-Deoxyhexopyranosides are considerably more reactive. The entropy of activation on acid hydrolysis of methyl α-D-glucopyranoside[1] (70 $J \cdot K^{-1} \cdot mol^{-1}$) and methyl 2-deoxy-α-D-*arabino*-hexopyranoside[13] (96 $J \cdot K^{-1} \cdot mol^{-1}$) are, however, of the same order of magnitude, which may indicate that they react by similar mechanisms, whereas most aldofuranosides have much lower entropies of activation. Methyl 2-deoxy-4-*O*-methyl-α-D-*arabino*-hexopyranoside (**3**) was therefore prepared and anomerized under reducing conditions.



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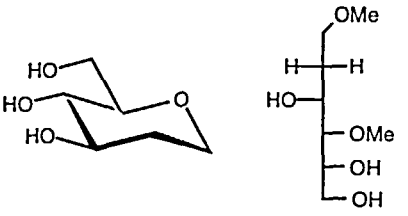
In addition to a mixture of the α- and β-glycosides (90 %, 9:1), 1,5-anhydro-2-deoxy-4-*O*-methyl-D-*arabino*-hexitol (**4**, 7 %) and 2-deoxy-1,4-di-*O*-methyl-D-*arabino*-hexitol (**5**, 3 %) were obtained. The result therefore indicates that **3** reacts by alternative pathways, involving either *exo*- or *endo*-cyclic C–O cleavage.



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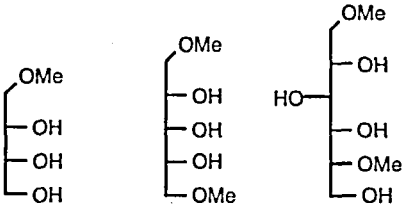
Methyl aldofuranosides. D-Erythrose on treatment with methanolic sulfuric acid yielded a mixture of α-furanoside, β-furanoside and dimethyl acetal in the proportions 22:65:13, in analogy with the results by Hockett and Manyard Jr.[14] When this mixture was subjected to methanolysis under reducing conditions, 1-*O*-methyl-D-erythritol (**6**) was obtained as the single product. Methyl 5-*O*-methyl-β-D-ribofuranoside[15] gave, under the same conditions, a mixture of the α- and β-furanosides (43 %, 1:3) and 1,5-di-*O*-methyl-D-ribitol (**7**, 57 %). Analogously, a mixture of methyl 5-*O*-methyl-α- and β-D-glucofuranoside (1:3) prepared from 5-*O*-methyl-D-glucose[16] gave the α- and β-glycosides (77 %, 1:2) and 1,5-di-*O*-methyl-D-glucitol (**8**, 23 %).



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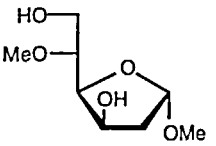
Thus the three adofuranosides gave exclusively non-cyclic reduction products, in agreement with the assumption of *endo* C–O cleavage.

The entropy of activation for hydrolysis of alkyl furanosides is generally negative, e.g., -42 $J \cdot K^{-1} \cdot mol^{-1}$ for methyl α-D-glucofuranoside,[17] but is positive (15 $J \cdot K^{-1} \cdot mol^{-1}$) for methyl-2-deoxy-α-D-*arabino*-hexofuranoside.[17] Methyl 2-deoxy-5-*O*-methyl-α-D-*arabino*-hexofuranoside (**9**) also deviated from the other aldofuranosides, and gave a mixture of 1,4-anhydro-2-deoxy-5-*O*-methyl-D-*arabino*-hexitol (**10**, 47 %) and 1,5-di-*O*-methyl-D-*arabino*-hexitol (**11**, 53 %).



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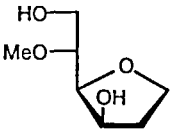

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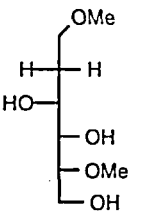
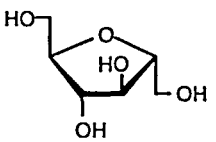


11

Methyl ketosides. The entropies of activation on acid hydrolysis of alkyl D-fructofuranosides is positive, e.g., 54 $J \cdot K^{-1} \cdot mol^{-1}$ for methyl β-D-fructofuranoside,[8] and it is suggested that protonation of the glycosidic oxygen, followed by heterolysis to a D-fructofuranosylium ion, is the rate determining step. The same conclusion has been drawn for methyl β-D-fructopyranoside,[9] but without reference to the original publication. The entropy of activation on hydrolysis of methyl β-D-fructopyranoside is positive, 85 $J \cdot K^{-1} \cdot mol^{-1}$ (calculated from the data given in Ref. 18.). Acid catalyzed methanolysis of methyl α-D-fructofuranoside[19] under reducing conditions gave a mixture of 2,5-anhydro-D-mannitol (**12**, 49 %), 2,5-anhydro-D-glucitol (**13**, 40 %) and 1,5-anhydro-D-mannitol (**14**, 11 %) No methyl fructosides were obtained. The results indicate that the equilibrium between the different fructosides is rapidly established, and that the equilibrium between the two furanosides, as well as that between the two pyranosides, proceeds via fructosylium ions. The acetates of **12** and **13** gave similar mass spectra, but the acetate of **13** was identified as the *manno* derivative from its retention time by comparison with an authentic sample. The 1,5-anhydro derivative (**14**) was identified as the *manno* derivative from its ^{13}C NMR spctrum.[20] On similar treatment, methyl β-D-fructopyranoside [21] also gave **12**, **13**, and **14**, but in different proportions, 33:23:44.



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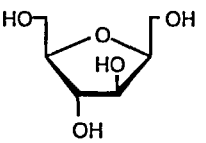

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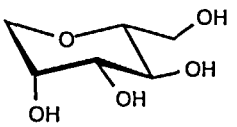

14

A mixture of 1-deoxy-α and β-D-fructofuranosides (32.5 %) and 1-deoxy-β-D-fructopyranoside (67.5 %), prepared by Fischer synthesis from 1-deoxy-D-fructose,[22] gave similar results, namely, a mixture of 2,5-anhydro-1-deoxy-D-mannitol, 2,5-anhydro-1-deoxy-D-glucitol, and 2,6-anhydro-1-deoxy-D-mannitol, in the relative proportions 63:21:16.

In a separate experiment, methyl β-D-glucofuranoside was treated under similar conditions as described above for the other glycosides, the only difference being that the reaction was performed in M ethanolic hydrogen chloride. The main products were the methyl α- and β-D-glucopyranosides. Only traces of furanosides and of 1-*O*-ethyl-D-glucitol were observed. The results therefore indicate that the reduction of intermediates is slow under these conditions, not only compared to the transglycosidation and anomerization of the furanosides but also to the much slower transformation of the furanosides into pyranosides.

CONCLUSION

It seems reasonable to assume that the equilibrium between furanosides and pyranosides during a Fischer synthesis proceeds *via* a non-cyclic intermediate, possibly an oxocarbenium ion or a closely related species. The anomeriszation of alkyl aldofuranosides proceeds, as discussed above, *via* a dialkyl acetal, which gives a mixture of the anomeric furanosides much faster than it gives a 1-*O*-alkyl alditol-1-ylium ion. The formation of 1-*O*-alkylalditols during anomerization of alkyl aldofuranosides under reducing conditions may either be due to reduction of an 1-*O*-alkyl alditol-1-ylium ion, or to nucelophilic attack of the hydride upon the O-4 protonated glycoside. The reduction under the conditions used is, however, slow compared to the anomerization

The results indicate that glycosylium ions are the most important intermediates during anomerization of alkyl ketosides, both furanosides and pyranosides.

The present study gives no information on the mechanism for anomerization of alkyl aldopyranosides, but according to other evidence, the main route involves glycopyranosylium ions.

The methyl 2-deoxy-D-*arabino*-hexofuranosides and the corresponding pyranosides occupy an intermediate position and give both cyclic and non-cyclic reduction products.

EXPERIMENTAL

General methods. All glycosides were freeze-dried and kept under argon before use. Methanol was distilled over Mg/I_2[23] and kept over 3 Å molecular sieves. Glassware was dried for 10 h at 110 °C. The flasks used in the anomerization reactions were cooled in a desiccator. Concentrations were performed under reduced pressure below 40 °C. TLC was performed on 0.25 mm precoated silica-gel plates (MERCK, silica-gel $60F_{254}$) and

detection by UV and/or by spraying the plates with 8% aq. H_2SO_4 solution, followed by heating at 250 °C. For column chromatography MERCK silica-gel K 60 (0.040-0.063 mm) was used. ^1H and ^{13}C NMR spectra was recorded on a JEOL JNM-GSX 270 instrument and chemical shifts were measured relative to TMS (δ 0.0 ppm) or acetone (δ 31.0 ppm, $\underline{C}H_3$; δ 2.2 ppm, $C\underline{H}_3$) as internal standards. FAB-MS, in the negative mode, was performed on a JEOL SX 102 instrument, using a triethanolamine or *m*-nitrobenzylalcohol matrix. EI GC-MS was conducted on an HP 5890-HP 5970 instrument, using an HP-5MS fused-silica capillary column and helium as carrier gas. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

Methyl 3,6-Di-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (15). Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside[24] (380 mg, 1.07 mmol), was dissolved in freshly distilled THF (15 mL) containing $NaBH_3CN$ (400 mg, 6.37 mmol). The mixture was cooled on an ice-bath and a saturated solution of HCl in ether was added until evolution of gas ceased.[25] The solution was filtered through Celite and after standard work-up, chromatography of the residue (toluene/ethyl acetate, 4:1) gave the title compound as a syrup in 60 % yield. ^1H NMR ($CDCl_3$) δ 7.4-7.1 (m, 10 H, aromatic), 4.85 (d, 1 H, $J_{1,2a}$ 2.4 Hz, $J_{1,2e}$ small, H-1), 4.60 (m, 4 H, $PhC\underline{H}_2$), 3.74 (s, 3 H, $OC\underline{H}_3$), 3.83-3.64 (m, 5 H, H-3–H-6), 2.26 (m, 1 H, $J_{2a,2e}$ 13 Hz, $J_{2e,3}$ 5 Hz, H-2e), 1.65 (m, 1 H, $J_{2a,3}$ 11 Hz, H-2a). ^{13}C NMR ($CDCl_3$) δ 138.4, 138.1, 128.5, 128.3, 127.7, 127.6, 126.9 (aromatic carbons), 98.6 (C-1), 73.5 ($Ph\underline{C}$), 71.6, 71.4, 70.4, 69.9, (C-3, C-4, C-5, C-6), 54.7 ($O\underline{C}H_3$), 34.6 (C-2). The absence of a signal at ~ δ 62 demonstrates that the 6-position is substituted.

Anal. Calcd for $C_{21}H_{26}O_5$: C, 70.4; H, 7.31. Found: C, 70.2; H, 7.24.

Methyl 2-Deoxy-4-*O*-methyl-α-D-*arabino*-hexopyranoside (4). A solution of methyl 3,6-di-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (200 mg, 0.56 mmol) and CH_3I (91 mg, 40 μL, 0.64 mmol) in DMF (5 mL), was added dropwise to DMF (5 mL) containing NaH (50 mg, 1.25 mmol). The mixture was stirred for 10 h and after standard work-up the product was purified by column chromatography (toluene/ethyl acetate, 12:1) to give crude methyl 3,6-di-*O*-benzyl-4-*O*-methyl-2-deoxy-α-D-*arabino*-hexopyranoside in 91 % yield. This compound was dissolved in toluene/ethyl acetate (1:1) and hydrogenolyzed over Pd(C) and for 20 h. After conventional work-up, the crude product was obtained in quantitative yield and purified by column chromatography (toluene/ethyl acetate, 1:3). Crystallization from ethyl acetate/hexane gave **4**, mp 82-85 °C, $[\alpha]_D^{25}$ +128 ° (*c* 0.3, $CHCl_3$). ^1H NMR (CD_3OD) δ 4.78 (d, 1 H, $J_{1,2a}$ 3.3 Hz, H-1), 4.00 (m, 1 H, $J_{2e,3}$ 5 Hz, $J_{2a,3}$ 11 Hz, $J_{3,4}$ 8.8 Hz, H-3), 3.7-3.5 (m, 4 H, H-4 - H-6), 3.60 (s, 3 H, $OC\underline{H}_3$), 3.30 (s, 3 H, $OC\underline{H}_3$), 2.14 (m, 1 H, $J_{2a,2e}$ 12.8 Hz, H-2e), 1.67 (m, 1 H, H-2a). ^{13}C NMR (CD_3OD) δ 99.7 (C-1), 82.7, 73.0, 70.0, 62.4 (C-3, C-4, C-5,

C-6), 60.9, 54.9 (O<u>C</u>H$_3$), 39.1 (C-2). The EI MS of acetylated **4** gave, *inter alia,* ions *m/z* 203 (M - CH_2OAc) and *m/z* 185 (M - OCH_3 - AcOH), demonstrating free hydroxyl groups in the 3- and 6-positions of **4**.

Anal. Calcd for $C_8H_{16}O_5$: C, 50.0; H, 8.39. Found: C, 49.8; H, 8.27. FABMS Calcd for (M-1): 191.0920. Found: 191.0919.

3,4,6-Tri-*O*-benzyl-2-deoxy-D-*arabino*-hexose Diethyl Dithioacetal (16). Methyl 3,4,6-tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside[26] (1.7 g, 3.8 mmol) was dissolved in concentrated HCl (8.5 mL), ethanethiol (10 mL) was added and the mixture kept at ambient temperature for 24 h. After usual work-up the product was purified by column chromatography (toluene/ethyl acetate, 10:1) giving the title compound as a syrup in 7 % yield. ^{1}H NMR ($CDCl_3$) δ ~ 7.28 (15 H, aromatic), 4.53 (6 H, Ph-C<u>H</u>$_2$), 4.06 (m, 1 H, $J_{3,4}$ 3.7 Hz, H-3), 3.87 (m, 1 H, $J_{5,6}$ 3.7 Hz, H-5), 3.73 (dd, 1 H, $J_{1,2}$ 4.8 Hz, $J_{1,2'}$ 9.89 Hz, H-1), 3.59 (dd, 1H, $J_{4,5}$ 8.1 Hz, H-4), 3.55 (d, 2 H, H-6), 2.43 (4 H, S-C<u>H</u>$_2$), 2.00 (m, 2H, $J_{2,2'}$ 14.3 Hz, $J_{2,3}$ 9.2 Hz, $J_{2',3}$ 3.7 Hz, H-2), 1.19 (6 H, CH_2-C<u>H</u>$_3$). ^{13}C NMR ($CDCl_3$) δ 138.2,137.8, 137.5, 128.5, 128.3,128,3, 128.2, 127.9, 127.9 127.6 (aromatic carbons), 76.5, 76.5, 73.5 (Ph-<u>C</u>), 73.2 , 73.1, 71.1, 71.0, (C-3, C-4, C-5, C-6), 48.0 (C-1), 36.6 (C-2), 24.3, 23.2 (S-C<u>H</u>$_2$), 14.4, 14.3 (CH_2-C<u>H</u>$_3$). FABMS Calcd for (M+Na): 563.2266. Found: 563.2280.

3,4,6-Tri-*O*-benzyl-2-deoxy-5-*O*-methyl-D-*arabino*-hexose Dimethyl Acetal (17). A solution of 3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hexose diethyl thioacetal (242 mg, 450 μmol) and CH_3I (230 μg, 1.6 mmol, 100 μL) in DMF (25 mL) was added dropwise to DMF (25 mL) containing NaH (22 mg, 740 μmol), the mixture was stirred for 2 h, and then worked up. The crude 2-deoxy-3,4,6-tri-*O*-benzyl-5-*O*-methyl-D-*arabino*-hexose diethyl dithioacetal (226 mg, 410 μmol) was added to a solution of *N*-iodosuccinimide (221 mg, 980 μmol) in methanol (50 mL). The mixture was stirred for 5 min and the reaction quenched by adding M aqueous $Na_2S_2O_3$. After work-up the crude 3,4,6-tri-*O*-benzyl-2-deoxy-5-*O*-methyl-D-*arabino*-hexose dimethyl acetal was purified by column chromatograthy (light petroleum/ethyl acetate, 10:1), giving the title compound as a syrup in 59 % yield. ^{13}C NMR ($CDCl_3$) δ 138.7, 138.5, 138.2, 128.3, 128.2, 128.0, 127.9, 127.8, 127.5 (aromatic carbons), 102.0 (C-1), 80.5, 80.1, 76.1 (Ph-<u>C</u>), 74.1, 73.4, 73.1 (C-3, C-4, C-5), 68.8 (C-6), 57.5 (O-C<u>H</u>$_3$), 52.9 (O-C<u>H</u>$_3$), 52.4 (O-C<u>H</u>$_3$), 34.6 (C-2). FABMS Calcd for (M+Na): 517.2566. Found: 517.2528.

Methyl 2-Deoxy-5-*O*-methyl-α-D-*arabino*-hexofuranoside (10). 3,4,6-Tri-*O*-benzyl-2-deoxy-5-*O*-methyl-D-*arabino*-hexose dimethyl acetal (120 mg, 2.4 μmol) was dissolved in methanol containing 10 % acetic acid and hydrogenolyzed over Pd (C) and for 20 h. The crude product was purified by column chromatography (chloroform/methanol, 30:1) giving the title compound as a syrup in 22 % yield. ^{1}H NMR (D_2O) δ 5.28 (dd, 1 H, $J_{1,2e}$ 5.9 Hz, $J_{1,2a}$ 5.5 Hz, H-1), 4.51 (m, 1 H, $J_{3,4}$ 3.3 Hz, H-

3), 4.04 (dd, 1 H, $J_{6,6'}$ 12.8 Hz, H-6), 3.99 (dd, 1 H, $J_{4,5}$ 8.4 Hz, H-4), 3.70 (dd, 1 H, $J_{6',6}$ 12,8 Hz, H-6'), 3.60 (m, 1 H, $J_{5,6}$ 2.9 Hz, $J_{5,6'}$ 4.0 Hz, H-5), 3.84 (s, 3 H, O-C$\underline{H}_3$), 3.41 (s, 3 H, O-C$\underline{H}_3$), 2.32 (dd dd, 1 H, $J_{2a,3}$ 1.5 Hz, $J_{2a,2e}$ 15.0 Hz, H-2a), 2.15 (dd dd, 1 H, $J_{2e,3}$ 4.4 Hz, $J_{2e,2a}$ 15.0 Hz, H-2e). ^{13}C NMR (D_2O) δ 105.4, (C-1), 79.7 (C-4), 79.0 (C-3), 71.4 (C-5), 60.2, (C-6), 57.7 (O-$\underline{C}H_3$), 55.9 (O-$\underline{C}H_3$), 42.3, (C-2). FAB-MS. Calcd for (M-1): 191.0920. Found: 191.0930. The amorphous product showed $[\alpha]_D^{25}$ +120 ° (*c* 0.05, EtOH), indicating that it was the α-glycoside. Lit. value for methyl α-D-*arabino*-hexofuranoside is $[\alpha]_D^{25}$ +117 ° (*c* 0.99, EtOH).[27]

Methyl 5-*O*-Methyl-α/β-D-glucofuranoside (18). 5-*O*-Methyl-D-glucose[16] (50 mg, 260 μmol) was dissolved in M methanolic HCl and stirred for 1 h at ambient temperature. Neutralization with AG 2 -X 8 ion exchange resin (OH^-) and concentration gave the title product in quantitative yield. The ^{13}C NMR spectrum showed, *inter alia*, signals for C-1 carbons at δ 109.5 (β), 103.5 (α), and their relative intensities gave the α/β ratio 1:3.

Methyl 1-Deoxy-D-fructosides (19). 1-Deoxy D-fructose[22] (50 mg, 280 μmol) was methanolyzed as above, giving a mixture of the two furanosides (33 %) and the β-pyranoside (67 %) in quantitative yield. The components were identified by EI GC–MS of the acetylated product, but the two furanosides were not further characterized.

Anomerization reactions. The glycoside (5 μmol) was dissolved in 1 mL of water and freeze-dried. The freeze-dried glycoside was kept under argon before being dissolved in anhydrous M methanolic hydrogen chloride (3 mL). The solution was added to a flask containing 4-morpholine borane (50 μmol). The flask was sealed with a rubber septum and the atmosphere exchanged into argon. After 3 days at room temperature, 300 μL was removed by a syringe and filtered through a mixed bed of Dowex 50W-X8 (H^+) and AG 2-X 8 (OH^-). The solution was concentrated, acetylated, and investigated by EI GC–MS. The different components were identified by comparison with authentic substances or published spectra, or by interpretation, using established principles. The relative amounts of the components were estimated from the intensities the of the peaks in the ion stream chromatograms. The only 1,5- (2,6-) anhydrohexitol formed during the reaction with the fructosides was identified as the mannitol derivative from its ^{13}C NMR spectrum.[20] The only 2,6- anhydroalditol obtained from the 1-deoxyfructosides was assumed to be the *manno* derivative by analogy.

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