

## Study of Stereoselectivity in Organometallic Additions to 1,2-*O*-Isopropylidene-*O*- $\alpha$ -D-xylopentodialdo-1,4-furanose

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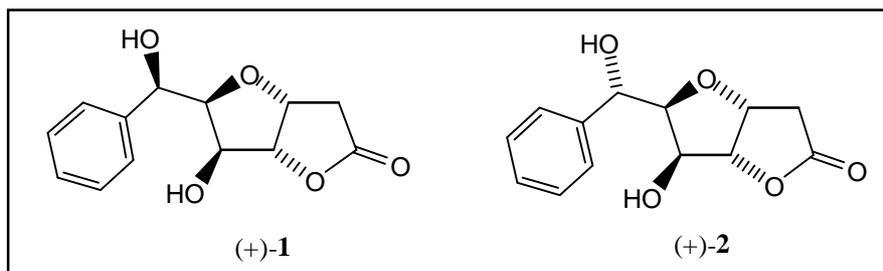
**Abstract:** Diastereofacial selectivity of the addition of organometallic reagents to 1,2-*O*-isopropylidene-*O*- $\alpha$ -D-xylopentodialdo-1,4-furanoses (**6**) was studied.

**Keywords:** Organometallic reagents, stereoselectivity, addition to carbonyl.

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### Introduction

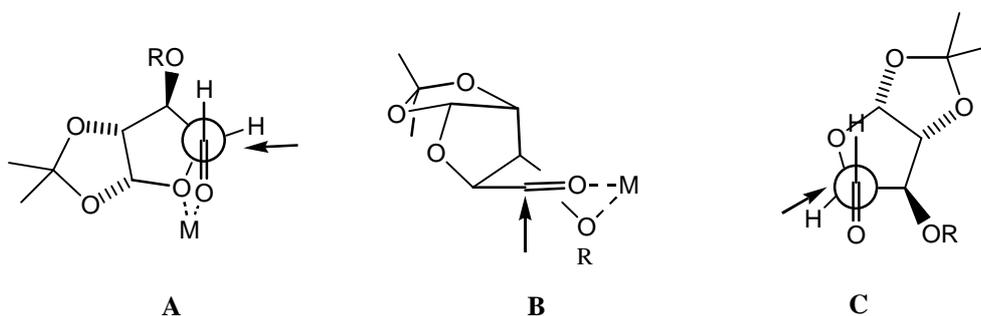
Goniofufurone (+)-**1** and 7-*epi*-goniofufurone (+)-**2** were recently isolated from the stem bark of Thai *Goniothalamus giganteus* Hook f., Thomas (Annonaceae) and shown to exhibit cytotoxic activity in tests with several human tumor cell lines [1,2]. We have developed a total synthesis of both diastereomers (+)-**1** and (+)-**2** starting from D-glucose [3]. The key steps are the phenyl magnesium bromide addition to 1,2-*O*-isopropylidene- $\alpha$ -D-xylopentodialdo-1,4-furanose and palladium(II)-catalyzed oxycarbonylation of the corresponding 1-phenyl-5-hexene-1,2,3,4-tetrols. Whilst the Pd(II)-catalyzed formal *O*-cyclization and carbon monoxide addition yielded the required bicyclic skeletons with high *regio*-preference and excellent *threo*-selectivity (concerning the newly formed stereocentre at C-3) [4,5], Grignard addition of phenyl magnesium bromide to **6a** in tetrahydrofuran led to two diastereomeric alcohols **7a** and **8a** in a 1:3 ratio favouring formation of the *L-ido* diastereomer **8a**, possessing the correct stereochemistry for less cytotoxic 7-*epi*-goniofufurone (+)-**2** (Scheme 1).



**Scheme 1.** Goniofufurone (+)-1 and 7-*epi*-goniofufurone (+)-2.

## Results and Discussion

In connection with the above-mentioned synthesis, we were interested in obtaining a more reliable access to alcohol **7** while at the same time improving the ratio of this component to **8**, therefore we decided to investigate the diastereoselectivity of additions of organometallic reagents to aldehydes **6** in a more detail. The design of addition of C-nucleophiles to aldehydes **6** could be based on models of either chelation-control: 1,2- (**A**) versus 1,3- (**B**) asymmetric induction or non-chelation-control (Felkin-Anh model **C**), leading to alcohols **8** (*L-ido*) (model **A**) or **7** (*D-gluco*) (models **B**, **C**) (Scheme 2).

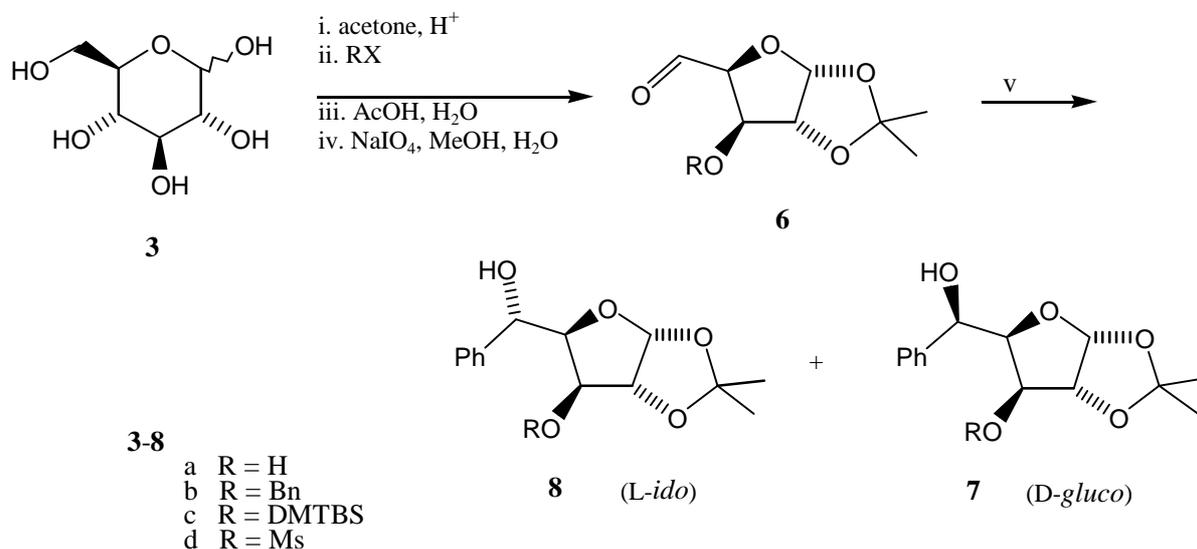


**Scheme 2.** Chelation models for 1,2- (**A**) and 1,3- (**B**) asymmetric induction, Felkin-Anh model (**C**).

We have prepared 3-*O*-*R*-substituted aldehydes **6a-d** from D-glucose (Scheme 3) with diverse protecting groups ( $R = H$  [6,7], Bn [6,8], TBDMS, Ms) in order to examine the effects of changes in the nature of the alkoxy group on the selectivity of the reaction. Treatment of aldehydes **6** with phenyl magnesium bromide in THF (see Table 1, Entry 1) or diethylether (Entries 2-4) gave in all cases the *L-ido* diastereomer **8** as a major product as a result of 1,2-chelation-control. The highest degree of selectivity found for **6b** is in accordance with the literature [6, 9-12], whilst aldehydes **6c** and **6d** with silyl (known for its non-chelation nature) and mesyl group (with opposite effect) gave about equal amounts of both diastereomers **7** and **8**.

Generally, addition of polyethers to the reaction mixture to suppress chelation usually causes a reversal in the stereoselectivity, yielding a Cram's product [13]. Addition of 18-C-6 and dibenzo-18-

C-6 crown-ether to the reaction of aldehyde **6b** with phenylmagnesium bromide inhibits chelation leading to a decrease of selectivity from 14:1 to 1:1.2 (comparison of entries 5 and 6).



**Scheme 3.** Reagents and conditions: (i)-(iv) see lit. [6-8], (v) PhM, solvent and reaction conditions see Table 1.

**Table 1.** Addition of Organometallic Reagents to Aldehyde.

Entry	Substrate	PhM	Conditions	Yield (%) <sup>b</sup>	L <i>ido</i> /D <i>gluco</i> <sup>a</sup>
1	6a	PhMgBr	THF	69	3.1
2	6b	PhMgBr	Et <sub>2</sub> O	70	14.1
3	6c	PhMgBr	Et <sub>2</sub> O	84	2.1 <sup>c</sup>
4	6d	PhMgBr	Et <sub>2</sub> O	78	1.6.1 <sup>c</sup>
5	6b	PhMgBr	Et <sub>2</sub> O, 18-C-6	89	1.1.2
6	6b	PhMgBr	Et <sub>2</sub> O, 18-C-6	86	1.1.2
7	6a	PhCeCl <sub>2</sub>	Et <sub>2</sub> O/ THF	68	1.1.6
8	6b	PhTi(O <sup>i</sup> Pr) <sub>3</sub>	Et <sub>2</sub> O	30	1.14

<sup>a</sup>Assignments of reaction ratios are based on the <sup>1</sup>H-NMR spectra of crude reaction mixtures.

<sup>b</sup>The yields refer to pure isolated products.

<sup>c</sup>Probable assignments, may eventually be reversed.

The reversal of diastereofacial selectivity was also achieved by use of phenylceriumdichloride [14, 15] (Entry 7), indicating the probability that model **B** was operating in this case.

Turning from chelation- to non-chelation-control, we reacted **6b** with phenyltitanium-tris-*O*-isopropoxide [16, 17], which is known to have only weakly Lewis acid properties [18, 19]. Obviously, phenyltitanium-tris-*O*-isopropoxide is incapable of effective chelation, so that carbonyl group in **6** is free to rotate. The fact that diastereoselectivity is nevertheless observed may be related to Anh's model of 1,2-asymmetric induction in addition reactions of chiral aldehydes having electronegative substituents at the  $\alpha$ -position. Accordingly, the most reactive conformation is the one having the alkoxy group positioned in such a way that the  $\sigma_{C-OR}$  orbital overlaps with the  $\pi_{C=O}$  orbital, providing a low lying LUMO. Antiperiplanar attack at an angle larger than  $90^\circ$  (Burgi-Dunitz trajectory) according to model **C** results in the Felkin-Anh-product.

Analogously to methyltitanium-tris-*O*-isopropoxide addition to aldehyde **6b** [20] we have carried out the reaction of **6b** with phenyltitanium-tris-*O*-isopropoxide. Indeed, the *D-gluco* diastereomer **7b** was preferentially formed (Entry 8).

The prepared compounds were identified by elemental analyses, optical rotations,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$ , and IR spectra (see Experimental). The absolute configuration at the newly formed stereocentre, and hence the configuration of alcohols **7b** and **8b**, was established by comparison of  $^1\text{H-}$ ,  $^{13}\text{C-NMR}$  data, and specific rotations with those described in the literature [6, 9-12]. The structures of **7a/ 8a** were established by total synthesis of (+)-**1**, (+)-**2** [3]. Assignment of the absolute configuration at C-5 in **7c,d/ 8c,d** was not deemed of interest in view of low degree of selectivity observed.

## Conclusions

One of two key steps of the total syntheses of (+)-goniofufurone **1** [3] resp. (7)-*epi*-goniofufurone **2** [3] may be optimized by the use of phenyltitanium-tris-*O*-isopropoxide (Entry 8) in place of phenylmagnesium bromide in the addition to 3-*O*-benzylated aldehyde **6b** (Entry 2).

## Experimental

### General

Solvents and reagents were purified and dried according to standard procedures. TLC analyses were carried out with Si60F<sub>254</sub>-coated aluminium sheets (E.Merck) using ethylacetate/ i-hexane mixtures; detection by UV at 254 nm, phosphomolybdic acid (10% in ethanol) or sulfuric acid (40% in water). Silica gel 32-63  $\mu\text{m}$  (Woelm) was used for flash chromatography, eluents as above. Melting points were determined on a Kofler hot block and are uncorrected. The optical rotations were measured on a POLAR L- $\mu\text{P}$  (IBZ Messtechnik) polarimeter at 589 nm. IR spectra were recorded on a PU 9800 FTIR spectrometer (Philips Analytical) in film or KBr discs (0.5 mg of sample and 300 mg of KBr).  $^1\text{H-NMR}$  and  $^{13}\text{C NMR}$  spectra were obtained on a Varian model VXR 300 spectrometer (at 300.3 MHz and 75.12 MHz, respectively). In the NMR experiments deuteriochloroform solutions with

tetramethylsilane as internal standard were measured; evaluation of  $^1\text{H}$ -NMR spectra was according to 1<sup>st</sup> order interpretation; and multiplicity of  $^{13}\text{C}$ -NMR signals was deduced from broad-decoupled or DEPT spectra. The ratios of diastereomers **7** and **8** were established by comparison of the integrals of H-1 signals in  $^1\text{H}$  NMR experiments performed on crude reaction mixtures.

### 3-*O*-[(<sup>t</sup>Butyl)-dimethylsilyl]-1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucofuranose 4c

To a stirred solution of bisacetonide glucose (**4a**, 4 g, 15 mmol) and triethylamine (2.4 mL, 17 mmol, 1.1 equiv) in dry dimethylformamide (20 mL), kept at 0-5 °C, a solution of (<sup>t</sup>butyl)-dimethylsilylchloride (2.562 g, 17 mmol, 1.1 equiv) in dry dimethylformamide (30 mL) was added dropwise over 30 min. The mixture was stirred at room temperature for another 30 h, then poured on ice/ water (100 mL) and extracted with chloroform (3 x 50 mL). The organic solutes were combined, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated (rotary evaporator). The residue was treated with *isohexane* and insoluble starting **4a** (1 g) filtered off. The crude product after solvent removal was purified by flash chromatography (silica gel 80 g, eluent ethylacetate - *isohexane* 1:1). Yield 4.15 g (74%),  $R_f=0.68$  (AcOEt - *i*-hexane 1:1),  $[\alpha]_D^{23}=-17.2$  (c=0.43,  $\text{CHCl}_3$ ).

### Spectral Data

$^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 5.80 (d, 1H, H-1,  $J_{1,2}=3.5$  Hz), 4.28 (d, 1H, H-2,  $J_{1,2}=3.5$  Hz), 4.16 (m, 2H, H-3, H-5), 4.04 (dd, 1H, H-4,  $J_{3,4}=6.1$  Hz,  $J_{4,5}=8.4$  Hz), 3.96 (dd, 1H, H-6, B of ABX,  $J_{A,B}=8.3$  Hz,  $J_{B,X}=2.7$  Hz), 3.88 (dd, 1H, H-6, A of ABX,  $J_{A,B}=8.3$  Hz,  $J_{A,X}=5.9$  Hz), 0.85 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 0.07, 0.08 (all s, 3H, Si(CH<sub>3</sub>)<sub>2</sub>).

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 111.7 (s, C(CH<sub>3</sub>)<sub>2</sub>), 108.8 (s, C(CH<sub>3</sub>)<sub>2</sub>), 105.2 (d, C-1), 85.6, 82.2, 75.4, 72.1 (all d, C-2, C-3, C-4, C-5), 67.7 (t, C-6), 29.9, 26.7, 26.3, 25.2 (all q, C(CH<sub>3</sub>)<sub>2</sub>), 25.6 (q, SiC(CH<sub>3</sub>)<sub>3</sub>), 18.0 (s, SiC(CH<sub>3</sub>)<sub>3</sub>), -5.3, -5.1 (all q, Si(CH<sub>3</sub>)<sub>2</sub>).

IR (thin film)  $\text{cm}^{-1}$ : 2988 w, 2955 s, 2934 s, 2893 w, 2859 w, 1381 m, 1372 s, 1255 s, 1217 s, 1132 s, 1078 s, 1022 s, 855 s, 779 m.

For  $\text{C}_{18}\text{H}_{34}\text{O}_6\text{Si}$  (Mr = 374.55) Calcd.: 57.72 % C, 9.15 % H; Found: 57.51 % C, 9.18 % H.

### 3-*O*-[(<sup>t</sup>Butyl)-dimethylsilyl]-1,2-*O*-isopropylidene- $\alpha$ -D-glucofuranose 5c

The glucofuranose bisacetonide (**4c**, 2.9 g, 7.7 mmol), dissolved in aq. acetic acid (75%, 30 mL), was stirred at room temperature for 48 h (TLC-monitoring). Removal of solvents *in vacuo* (20 mbar) leaves a yellow oil, which was dried in desiccator (NaOH, 20 mbar) for 2 days and purified by chromatography on silica gel 100g (eluent AcOEt - *i*-hexane 1:1). The furanose monoacetonide **5c** was obtained as a colourless oil; yield 1.9 g (76%),  $R_f=0.3$  (AcOEt - *i*-hexane 1:1),  $[\alpha]_D^{23}=-24.3$  (c= 0.77,  $\text{CHCl}_3$ ).

## Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 5.82 (d, 1H, H-1,  $J_{1,2}=3.6$  Hz), 4.34 (d, 1H, H-2,  $J_{1,2}=3.7$  Hz), 4.29 (d, 1H, H-3,  $J_{3,4}=2.7$  Hz), 4.03 (dd, 1H, H-4,  $J_{3,4}=2.7$  Hz,  $J_{4,5}=8.2$  Hz), 3.87 (ddd, 1H, H-5, dX of ABX,  $J_{A,X}=5.3$  Hz,  $J_{B,X}=3.2$  Hz,  $J_{4,5}=8.2$  Hz), 3.81 (dd, 1H, H-6, B of ABX,  $J_{A,B}=11.5$  Hz,  $J_{B,X}=3.2$  Hz), 3.73 (dd, 1H, H-6, A of ABX,  $J_{A,B}=11.5$  Hz,  $J_{A,X}=5.3$  Hz), 1.27, 1.46 (all s, 3H,  $\text{C}(\text{CH}_3)_3$ ), 0.88 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 0.14, 0.12 (all s, 3H,  $\text{Si}(\text{CH}_3)_2$ ).

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 118.8 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 104.9 (d, C-1), 85.3, 80.8, 75.6, 64.4 (all d, C-2, C-3, C-4, C-5), 68.6 (t, C-6), 26.2, 26.7 (all q,  $\text{C}(\underline{\text{C}}\text{H}_3)_2$ ), 25.6 (q,  $\text{SiC}(\underline{\text{C}}\text{H}_3)_3$ ), 18.0 (s,  $\text{SiC}(\underline{\text{C}}\text{H}_3)_3$ ), -5.1, -4.9 (all q,  $\text{Si}(\underline{\text{C}}\text{H}_3)_2$ ).

IR (thin film)  $\text{cm}^{-1}$ : 3436 br s (OH), 2955 s, 2932 s, 2888 s, 2859 s, 1383 m, 1375 m, 1217 s, 1134 s, 1082 s, 1018 s, 835 s, 779 m.

For  $\text{C}_{15}\text{H}_{30}\text{O}_6\text{Si}$  ( $M_r = 334.49$ ) Calcd.: 53.86 % C, 9.04 % H; Found: 53.97 % C, 8.95 % H.

1,2:5,6-di-*O*-Isopropylidene-3-*O*-mesyl- $\alpha$ -D-glucofuranose 4d

Prepared from bisacetone D-glucose (**4a**, 4 g, 15 mmol), mesylchloride (1.40 mL, 18 mmol, 1.2 equiv.) and pyridine (20 mL) under Ar atmosphere according to lit. [21]. Yield 3.771 g (74%), m.p.= 78 – 80 °C,  $R_f = 0.54$  (AcOEt - *i*-hexane 1:1),  $[\alpha]_D^{24} = -47.5$  (c=0.53,  $\text{CHCl}_3$ ), which was used without further purification {Lit. [21]: m.p.=80 – 82 °C,  $[\alpha]_D^{24} = -49$  -1 (c=1.0,  $\text{CHCl}_3$ )}

## Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 5.88 (d, 1H, H-1,  $J_{1,2}=3.6$  Hz), 4.91 (d, 1H, H-3,  $J_{3,4}=2.8$  Hz), 4.72 (d, 1H, H-2,  $J_{1,2}=3.6$  Hz), 4.11 (m, 3H, H-4, H-5, H-6), 3.94 (dd, 1H, H-6, A of ABX,  $J_{A,B}=8.9$  Hz,  $J_{A,X}=4.3$  Hz), 3.03 (s, 3H,  $\text{SO}_2\text{CH}_3$ ), 1.44, 1.36, 1.26, 1.25 (all s, 3H, CH<sub>3</sub>).

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 112.7, 109.6 (all s,  $\text{C}(\text{CH}_3)_2$ ), 105.2 (d, C-1), 83.7, 82.7, 79.8, 72.1 (all d, C-2, C-3, C-4, C-5), 67.6 (t, C-6), 38.0 (q,  $\text{SO}_2\text{CH}_3$ ), 26.9, 26.6, 26.2, 25.2 (all s, CH<sub>3</sub>).

For  $\text{C}_{13}\text{H}_{22}\text{O}_8\text{S}$  ( $M_r=338.38$ ).

1,2-*O*-Isopropylidene-3-*O*-mesyl- $\alpha$ -D-glucofuranose 5d

Following the procedure described for preparation of **5c**; the bisacetone (**4d**, 3.5 g, 10.3 mmol) was stirred in aq. acetic acid (75%, 30 mL) at room temperature for 24 h (TLC - monitoring). The monoacetone **5d** was obtained as a yellow, but analytically pure oil; yield 2.93 g (95%),  $R_f=0.3$  (AcOEt - *i*-hexane 1:1),  $[\alpha]_D^{23} = -21$  (c=0.42,  $\text{CHCl}_3$ ). {Lit. [22]:  $[\alpha]_D = -20.6$  (c=1.0,  $\text{CHCl}_3$ )}

## Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 5.93 (d, 1H, H-1,  $J_{1,2}=3.7$  Hz), 5.10 (d, 1H, H-3,  $J_{3,4}=2.5$  Hz), 4.76 (d, 1H, H-2,  $J_{1,2}=3.7$  Hz), 4.22 (dd, 1H, H-4,  $J_{3,4}=2.5$  Hz), 3.86 (bd, 2H, H-6, AB of ABX,  $J_{A,B}=9.4$  Hz), 3.73 (m, 1H, H-5, X of ABX), 3.14 (s, 3H,  $\text{SO}_2\text{CH}_3$ ), 1.49, 1.39 (all s, 3H,  $\text{CH}_3$ ).

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 112.7 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 105.0 (d, C-1), 83.3, 82.0, 78.4, 68.2 (all d, C-2, C-3, C-4, C-5), 63.9 (t, C-6), 38.1 (q,  $\text{SO}_2\underline{\text{C}}\text{H}_3$ ), 26.4, 26.1 (all s,  $\text{CH}_3$ ).

For  $\text{C}_{10}\text{H}_{18}\text{O}_8\text{S}$  ( $M_r=298.31$ ).

1,2-*O*-Isopropylidene-3-*O*-R- $\alpha$ -D-xylopentodialdo-1,4-furanose 6a-d

Prepared from monoacetone glucoses **4a-d** by modified procedures of Inch [6] and Lichtenthaler [7]. To a cooled solution (0 °C) of **4** in water/methanol (1:2) was added in one portion  $\text{NaIO}_4$  and stirring was continued at 0-20 °C for 2 h (TLC - monitoring). The solid precipitate ( $\text{NaIO}_3$ ) was filtered off and the solvent was removed on a rotavapory (20 mbar, 25 °C), the residue was partitioned between chloroform (3 x 50 mL) and water (15 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated at reduced pressure to a colourless oil, which was additionally dried in a desiccator ( $\text{P}_2\text{O}_5$ , 0.01 mbar) for 2 h. The crude products of diol - cleavage were used in the next reactions without another purification.

1,2-*O*-Isopropylidene- $\alpha$ -D-xylopentodialdo-1,4-furanose 4a

Prepared from **5a** (1 g, 4.54 mmol) and  $\text{NaIO}_4$  (1.1 g, 5.14 mmol) in water/methanol (1:2, 20 mL). Yield 580 mg (68%),  $R_f=0.6$  (AcOEt).

## Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.40 (bs, 1H, H-5), 5.98 (bs, 1H, H-1), 3.97-4.55 (m, 3H, H-2, H-3, H-4), 1.47, 1.31 (all s, 3H,  $\text{CH}_3$ ).

For  $\text{C}_8\text{H}_{12}\text{O}_5$  ( $M_r=188.18$ ).

3-*O*-Benzyl-1,2-*O*-isopropylidene- $\alpha$ -D-xylopentodialdo-1,4-furanose 4b

Prepared from **5b** (1.0 g, 3 mmol),  $\text{NaIO}_4$  (1.28 g, 6 mmol, 2 equiv) in water/methanol (1:2, 15 mL). Yield 803 mg (96%),  $R_f=0.6$  (AcOEt- *i*-hexane 1:1).

## Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 9.68 (s, 1H, H-5), 7.26-7.35 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.12 (s, 1H, H-1,  $J_{1,2}=3.5$  Hz), 4.63 (m, 4H, H-2, H-4,  $\text{CH}_2$ ), 4.32 (d, 1H, H-3,  $J_{3,4}=3.1$  Hz), 1.46, 1.40 (all s, 3H,  $\text{CH}_3$ ).

For  $\text{C}_{15}\text{H}_{18}\text{O}_5$  ( $M_r=278.31$ ).

3-*O*-[(<sup>t</sup>Butyl)-dimethylsilyl]-1,2-*O*-Isopropylidene- $\alpha$ -D-xylopentodialdo-1,4-furanose 6c

From **5c** (1.69 g, 5.0 mmol), NaIO<sub>4</sub> (2.13 g, 10 mmol, 2 equiv) in water/methanol (1:2, 30 mL). Yield 1.305 g (86%), R<sub>f</sub>=0.68 (AcOEt).

For C<sub>14</sub>H<sub>26</sub>O<sub>5</sub>Si (M<sub>r</sub>=302.44).

1,2-*O*-Isopropylidene-3-*O*-mesyl- $\alpha$ -D-xylopentodialdo-1,4-furanose 6d

From **5d** (3.28 g, 11 mmol), NaIO<sub>4</sub> (4.705 g, 22 mmol, 2 equiv.) in water/methanol (1:2, 30 mL). Yield 2.41 g (82%), R<sub>f</sub>=0.27 (AcOEt - *i*-hexane 1:1).

For C<sub>9</sub>H<sub>14</sub>O<sub>7</sub>S (M<sub>r</sub>=266.27).

1,2-*O*-Isopropylidene-3-*O*-R-5-*C*-phenyl- $\beta$ -L-ido- 8a-d and  $\alpha$ -D-glucopentofuranose 7a-d

Prepared from aldehydes **6a-d** according to lit. [4,6]. The crude aldehydes **6a-d** were dissolved in dry ether and added dropwise to a solution of phenylmagnesium bromide in ether, prepared from bromobenzene and magnesium at -10 °C during 2 h. The mixtures were stirred at 0 °C for 4 h, and at r.t. for 24 h, then quenched with cold, saturated aqueous ammonium chloride and extracted with ether. After drying (Na<sub>2</sub>SO<sub>4</sub>) and solvent removal a yellow oils were obtained, whose were purified by flash chromatography on silica gel.

3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*C*-phenyl- $\beta$ -L-ido- 8b and  $\alpha$ -D-glucopentofuranose 7b

Prepared from aldehyde **6b** (1.113 g, 4 mmol), bromobenzene (1.05 mL, 10 mmol, 2.5 equiv) and magnesium (0.243 g, 10 mmol) in ether (35 mL). Yield 1.285 g (90%) of the mixture of diastereomers **8b** and **7b** (14:1) was purified by chromatography (silica gel, 40 g, AcOEt - *i*-hexane 1:2); fraction 1 compound **7b** (*D*-gluco), 90 mg (6.3 %), yellow oil, R<sub>f</sub>=0.35 (AcOEt - *i*-hexane 1:2), [ $\alpha$ ]<sub>D</sub><sup>23</sup> = -74 (c=1.0, CHCl<sub>3</sub>). {Lit. [12]: [ $\alpha$ ]<sub>D</sub><sup>24</sup> = -77 (c=4.02, CHCl<sub>3</sub>), lit. [9]: [ $\alpha$ ]<sub>D</sub><sup>25</sup> = -93 (CHCl<sub>3</sub>), lit. [6]: [ $\alpha$ ]<sub>D</sub><sup>23</sup> = -76 (c=1.0, CHCl<sub>3</sub>)}; fraction 2 compound **7b** (*L*-ido); 580 mg (41 %), colourless oil, R<sub>f</sub>=0.26 (AcOEt - *i*-hexane 1:2), [ $\alpha$ ]<sub>D</sub><sup>22</sup> = -32.1 (c=0.76, CHCl<sub>3</sub>), {lit. [12]: [ $\alpha$ ]<sub>D</sub><sup>23</sup> = -33.5 (c = 2.0, CHCl<sub>3</sub>)}. In addition, 330 mg (23 %) of an intermediate fraction containig both **7b** and **8b** was collected.

Alcohol **8b** (*L*-ido)

## Spectral Data

<sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 7.31- 7.48 (m, 10H, C<sub>6</sub>H<sub>5</sub>), 6.03 (d, 1H, J<sub>1,2</sub>=3.8 Hz, H-1), 5.07 (d, 1H, J<sub>4,5</sub>=7.6 Hz, H-5), 4.61 (d, 1H, J<sub>1,2</sub>=3.8 Hz, H-2), 4.56 (d, 1H, J=11.5 Hz, CH<sub>2</sub>), 4.34 (dd, 1H, J<sub>3,4</sub>=3.2 Hz, J<sub>4,5</sub>=7.6 Hz, H-4), 4.32 (d, 1H, J=11.7 Hz, CH<sub>2</sub>), 3.64 (d, 1H, J<sub>3,4</sub>=3.1Hz, H-3), 1.50 , 1.32 (all s, 3H, C(CH<sub>3</sub>)<sub>2</sub>).

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 139.7, 137.0 (all s, *i*- $\text{C}_6\text{H}_5$ ), 128.5, 128.3, 128.1, 128.0, 127.7, 127.1 (all d,  $\text{C}_6\text{H}_5$ ), 111.9 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 105.2 (d, C-1), 71.8 (t,  $\text{CH}_2$ ), 72.4, 82.2, 82.2, 84.5 (all d, C-2, C-3, C-4, C-5), 26.3, 26.8 (all q,  $\text{C}(\underline{\text{C}}\text{H}_3)_2$ ).

IR (thin film)/  $\text{cm}^{-1}$ : 3453 m (OH), 2979 m, 2932 m, 2892 m, 1497 m, 1455 s, 1375 s, 1217 s, 1076 s, 1022 s, 760 s, 700 s.

For  $\text{C}_{21}\text{H}_{24}\text{O}_5$  ( $M_r=356.42$ ) Calcd.: 70.77 %C, 6.97 %H; Found: 71.09 %C, 6.91 %H.

### Alcohol **7b** (*D*-gluco)

#### Spectral Data

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 7.34- 7.43 (m, 10H,  $\text{C}_6\text{H}_5$ ), 6.12 (d, 1H,  $J_{1,2}=3.8$  Hz, H-1), 5.23 (d, 1H,  $J_{4,5}=6.1$  Hz, H-5), 4.72 (d, 1H,  $J=11.6$  Hz,  $\text{CH}_2$ ), 4.70 (d, 1H,  $J_{1,2}=3.9$  Hz, H-2), 4.51 (d, 1H,  $J=11.4$  Hz,  $\text{CH}_2$ ), 4.45 (dd, 1H,  $J_{3,4}=3.3$  Hz,  $J_{4,5}=6.1$  Hz, H-4), 4.10 (d, 1H,  $J_{3,4}=3.2$  Hz, H-3), 1.55, 1.38 (all s, 3H,  $\text{C}(\text{CH}_3)_2$ ).

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 141.8, 137.6 (all s, *i*- $\text{C}_6\text{H}_5$ ), 129.9, 129.7, 128.9, 128.8, 127.7, 127.2 (all d,  $\text{C}_6\text{H}_5$ ), 113.1 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 106.2 (d, C-1), 73.4 (t,  $\text{CH}_2$ ), 73.4, 82.8, 83.5, 83.9 (all d, C-2, C-3, C-4, C-5), 27.3, 27.8 (all q,  $\text{C}(\underline{\text{C}}\text{H}_3)_2$ ).

IR (thin film)/  $\text{cm}^{-1}$ : 3450 m (OH), 2980 m, 2930 m, 1497 m, 1455 s, 1456 s, 1376 s, 1220 s, 1070 s, 1024 s, 760 s, 700 s.

For  $\text{C}_{21}\text{H}_{24}\text{O}_5$  ( $M_r=356.42$ ) Calcd.: 70.77 %C, 6.97 %H; Found: 71.12 %C, 6.93 %H.

### 3-*O*-[(<sup>t</sup>Butyl)-dimethylsilyl]-1,2-*O*-isopropylidene-5-*C*-phenyl- $\beta$ -*L*-ido- **8c** and $\alpha$ -*D*-glucopentofuranose **7c**

Prepared from **6c** (1.305 g, 4.3 mmol), bromobenzene (1.37 mL, 13 mmol, 3 equiv) and magnesium (0.316 g, 13 mmol) in ether (40 mL). Yield 1.382 g (84 %), yellow oil,  $R_f=0.26$  (AcOEt - *i*-hexane 1:3). The product consists of a 2:1 mixture of *L*-ido/*D*-gluco diastereomers **8c**/**7c** by  $^1\text{H}$ -NMR. The NMR data are given from this mixture and probable assignments may eventually be reversed.

#### Spectral Data for alcohol **8c** (*L*-ido)

$^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 7.26- 7.36 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.01 (d, 1H,  $J_{1,2}=3.6$  Hz, H-1), 4.95 (d, 1H,  $J_{4,5}=5.8$  Hz, H-5), 4.38 (m, 2H,  $J_{1,2}=3.5$  Hz,  $J_{3,4}=3.2$  Hz, H-2, H-4), 4.12 (d, 1H,  $J_{3,4}=2.9$  Hz, H-3), 1.48, 1.31 (all s, 3H,  $\text{C}(\text{CH}_3)_2$ ), 0.94 (s, 9H,  $\text{Si}(\text{CH}_3)_3$ ), 0.10, -0.04 (all s,  $\text{Si}(\text{CH}_3)_2$ ).

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 139.8 (s, *i*- $\text{C}_6\text{H}_5$ ), 128.4, 128.1, 127.3 (all d,  $\text{C}_6\text{H}_5$ ), 111.9 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 104.8 (d, C-1), 72.4, 76.9, 83.9, 85.7 (all d, C-2, C-3, C-4, C-5), 26.4, 26.9 (all q,  $\text{C}(\underline{\text{C}}\text{H}_3)_2$ ), 25.7 (q,  $\text{C}(\underline{\text{C}}\text{H}_3)_3$ ), 17.9 (s,  $\underline{\text{C}}(\text{CH}_3)_3$ ), -4.4, -5.2 (all q,  $\text{Si}(\text{CH}_3)_2$ ).

Spectral Data for alcohol **7c** (*D*-gluco)

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.26- 7.38 (m, 5H,  $\text{C}_6\text{H}_5$ ), 5.94 (d, 1H,  $J_{1,2}=3.8$  Hz, H-1), 4.98 (m, 1H, H-5), 4.35 (m, 3H, H-2, H-3, H-4), 1.46, 1.30 (all s, 3H,  $\text{C}(\text{CH}_3)_2$ ), 0.94 (s, 9H,  $\text{SiC}(\text{CH}_3)_3$ ), 0.16, 0.10 (all s,  $\text{Si}(\text{CH}_3)_2$ ).

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 141.7 (s, *i*- $\text{C}_6\text{H}_5$ ), 128.4, 127.8, 126.5 (all d,  $\text{C}_6\text{H}_5$ ), 111.6 (s,  $\text{C}(\text{CH}_3)_2$ ), 105.0 (d, C-1), 72.1, 76.3, 83.0, 85.3 (all d, C-2, C-3, C-4, C-5), 26.4, 26.9 (all q,  $\text{C}(\text{CH}_3)_2$ ) 25.7 (q,  $\text{C}(\text{CH}_3)_3$ ), 17.9 (s,  $\text{C}(\text{CH}_3)_3$ ), -4.6, -5.1 (all q,  $\text{Si}(\text{CH}_3)_2$ ).

IR (thin film)/  $\text{cm}^{-1}$ : 3439 br m (OH), 2955 s, 2932 s, 1383 w, 1375 w, 1254 m, 1219 m, 1165 m, 1132 m, 1078 s, 844 s, 835 s, 777 m, 764 m.

For  $\text{C}_{20}\text{H}_{32}\text{O}_5\text{Si}$  ( $M_r=356.42$ ) Calcd.: 63.12 %C, 8.48 %H; Found: 63.39 %C, 8.46 %H.

1,2-*O*-Isopropylidene-3-*O*-mesyl-5-*C*-phenyl- $\beta$ -*L*-ido- **8d** and  $\alpha$ -*D*-gluco-pentofuranose **7d**

From **6d** (1.602 g, 6 mmol), bromobenzene (1.9 mL, 18 mmol, 3 equiv) and magnesium (437 mg, 18 mmol) in ether (45 mL). Yield 1.612 g (78 %) as a yellow oil,  $R_f=0.28$  (AcOEt - *i*-hexane 1:1). The product consists of a 1.6:1 mixture of *L*-ido/*D*-gluco diastereomers **8d/7d**. The NMR data are given from this mixture and probable assignments may eventually be reversed.

Spectral Data for alcohol **8d** (*L*-ido)

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 133.7 (s, *i*- $\text{C}_6\text{H}_5$ ), 129.0, 128.6, 127.3 (all d,  $\text{C}_6\text{H}_5$ ), 112.7 (s,  $\text{C}(\text{CH}_3)_2$ ), 104.6 (d, C-1), 72.2, 81.7, 82.7, 83.6 (all d, C-2, C-3, C-4, C-5), 26.6, 26.3 (all q,  $\text{C}(\text{CH}_3)_2$ ) 37.9 (q,  $\text{SO}_2\text{CH}_3$ ).

Spectral Data for alcohol **7d** (*D*-gluco)

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 138.4 (s, *i*- $\text{C}_6\text{H}_5$ ), 129.3, 128.9, 127.5 (all d,  $\text{C}_6\text{H}_5$ ), 111.9 (s,  $\text{C}(\text{CH}_3)_2$ ), 105.0 (d, C-1), 73.4, 75.3, 82.2, 85.1 (all s, C-2, C-3, C-4, C-5), 26.7, 26.1 (all q,  $\text{C}(\text{CH}_3)_2$ ) 37.9 (q,  $\text{SO}_2\text{CH}_3$ ).

IR (thin film)/  $\text{cm}^{-1}$ : 3486 br m (OH), 2990 m, 2936 m, 1363 s (SO), 1341 s, 1306 s, 1170 s (SO), 1163 w, 1152 s, 1088 s, 1024 s, 972 s, 957 s, 909 s, 845 s, 835 s.

For  $\text{C}_{15}\text{H}_{20}\text{O}_7\text{S}$  ( $M_r=344.39$ ) Calcd.: 52.31 %C, 5.85 %H; Found: 52.21 %C, 5.94 %H.

3-*O*-Benzyl-1,2-*O*-isopropylidene-5-*C*-phenyl- $\alpha$ -*D*-gluco **7b** and  $\beta$ -*L*-ido-pentofuranose **8b**

To a freshly prepared solution of phenylmagnesium bromide [prepared from bromobenzene (0.8 mL, 7.6 mmol, 2.5 equiv) and magnesium (0.185 g, 7.6 mmol) in dry ether (15 mL) by standard procedure] a solution of 18-C-6 (2.009 g, 7.6 mmol, 2.5 equiv) and dibenzo 18-C-6 crown-ether (2.739 g, 7.6 mmol) in ether (10 mL) was added dropwise at room temperature. The mixture was additionally treated in ultrasound bath for 30 min. Then the aldehyde **6b** (865 mg, 3 mmol) was added at  $-10$  °C.

The mixture was stirred at 0 °C for 4 h, and at r.t. for 24 h, then quenched with saturated aqueous ammonium chloride (30 mL) and extracted with ether. After drying ( $\text{Na}_2\text{SO}_4$ ) and solvent removal a yellow oil was obtained; yield 950 mg (89 %) resp. 920 mg (86 %) as a 1.2:1 mixture of *D-gluco/L-ido* **7b/8b** diastereomers.

To a stirred solution of aldehyde **6b** (1.0 g, 3.59 mmol) in dry ether (20 mL) was added a solution of  $\text{PhTi}(\text{O}^i\text{Pr})_3$  (1.195 g, 3.95 mmol, 1.1 equiv) in ether (20 mL) at  $-30$  °C during 20 min. The mixture was stirred at  $-30$  °C for 4 h and at r.t. for 48 h, then quenched with saturated aq. ammonium chloride (20 mL), extracted with ether (3 x 20 mL), dried with  $\text{Na}_2\text{SO}_4$ . After removal of solvent a yellow oil was obtained. Yield 383 mg (30 %). The product consists of a 14:1 mixture of **7b/ 8b** diastereomers according to  $^1\text{H-NMR}$  data.

#### 1,2-*O*-Isopropylidene-5-*C*-phenyl- $\alpha$ -*D-gluco* **7a** and $\beta$ -*L-ido*pentofuranose **8a**

Anhydrous cerium chloride (740 mg, 3 mmol) prepared by heating of  $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$  (1.12 g, 3 mmol) at 130-140 °C for 5 h *in vacuo* [23], was suspended in tetrahydrofuran (10 mL) at room temperature. The suspension was sonicated for 1 h, then stirred for 2 h at r.t. A solution of phenyllithium (3 mL, 1M solution in ether) was added at  $-10$  °C and stirred for 45 min. A solution of crude **6a** (580 mg, 3 mmol) in ether (5 mL) at  $-5$  °C was added and stirring was continued at r.t. for 48 h, then quenched with saturated aqueous NaF (25 mL), extracted with ether (3 x 20 mL), dried with  $\text{Na}_2\text{SO}_4$ . After removal of solvent a yellow oil was obtained. Yield 544 mg (68 %). The product consists of a 1.6:1 mixture of *D-gluco/L-ido* diastereomers **7a/8a** according to  $^1\text{H-NMR}$  data.

#### Alcohol **8a** (*L-ido*)

##### Spectral Data

$^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$ : 7.31- 7.57 (m, 5H,  $\text{C}_6\text{H}_5$ ), 6.01 (d, 1H,  $J_{1,2}=3.7$  Hz, H-1), 4.98 (d, 1H,  $J_{4,5}=8.4$  Hz, H-5), 4.46 (dd, 1H,  $J_{1,2}=3.7$  Hz,  $J_{2,3}=0.8$  Hz, H-2), 4.24 (dd, 1H,  $J_{3,4}=2.8$  Hz,  $J_{4,5}=8.4$  Hz, H-4), 3.61 (bd, 1H,  $J_{3,4}=3.1$ Hz, H-3), 1.49 , 1.31 (all s, 3H,  $\text{C}(\text{CH}_3)_2$ ).

$^{13}\text{C-NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$ : 143.4 (s, *i*- $\text{C}_6\text{H}_5$ ), 130.2, 129.9, 129.2 (all d,  $\text{C}_6\text{H}_5$ ), 113.7 (s,  $\underline{\text{C}}(\text{CH}_3)_2$ ), 107.4 (d, C-1), 79.6, 76.6, 86.9, 87.8 (all d, C-2, C-3, C-4, C-5), 28.0, 27.4 (all q,  $\text{C}(\underline{\text{C}}\text{H}_3)_2$ ).

#### Alcohol **7a** (*D-gluco*)

##### Spectral Data

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.34- 7.43 (m, 10H,  $\text{C}_6\text{H}_5$ ), 6.12 (d, 1H,  $J_{1,2}=3.8$  Hz, H-1), 5.23 (d, 1H,  $J_{4,5}=6.1$  Hz, H-5), 4.72 (d, 1H,  $J=11.6$  Hz,  $\text{CH}_2$ ), 4.70 (d, 1H,  $J_{1,2}=3.9$  Hz, H-2), 4.51 (d, 1H,  $J=11.4$

Hz, CH<sub>2</sub>), 4.45 (dd, 1H, J<sub>3,4</sub>=3.3 Hz, J<sub>4,5</sub>=6.1 Hz, H-4), 4.10 (d, 1H, J<sub>3,4</sub>=3.2 Hz, H-3), 1.55, 1.38 (all s, 3H, C(CH<sub>3</sub>)<sub>2</sub>).

<sup>13</sup>C-NMR (CD<sub>3</sub>OD) δ: 144.6 (s, *i*-C<sub>6</sub>H<sub>5</sub>), 130.2, 129.6, 129.0 (all d, C<sub>6</sub>H<sub>5</sub>), 113.6 (s, C(CH<sub>3</sub>)<sub>2</sub>), 107.2 (d, C-1), 73.1, 76.5, 85.6, 87.4 (all d, C-2, C-3, C-4, C-5), 28.0, 27.4 (all q, C(CH<sub>3</sub>)<sub>2</sub>).

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*Sample Availability:* Available from the authors.