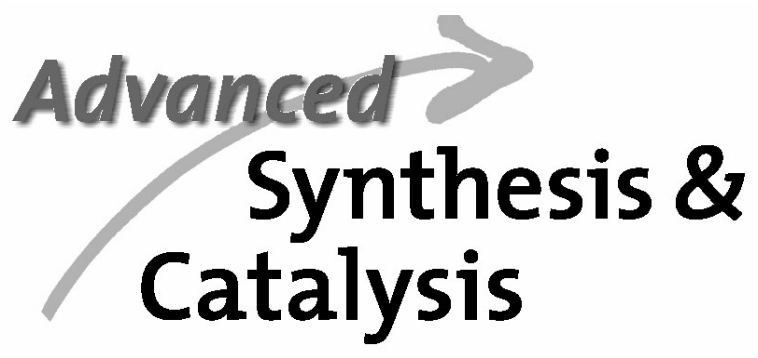



Supporting Information

# Supporting information

## Screening-optimization of catalysts[1]

Screening of catalysts

A range of known epoxidation catalysts was selected for a screening, with 3,4-dihydro-2*H*-pyran as a model substrate for glycals (Table 1). Catalysts tested included (a) W-based catalysts ($Na_2WO_4.2H_2O$, $Q_2WO_4$, $Q_2W_2O_{11}$, $Q_3PW_4O_{24}$ and $Q_4[\gamma\text{-}SiW_{10}(H_2O)_2O_{34}]$; Q = quaternary ammonium), (b) Mo-based catalysts ($Mo(CO)_6$, $Q_3PMo_{12}O_{40}$) and (c) a selection of metal alkoxides ($Mo(O^iPr)_5$, $Ti(O^iPr)_4$, $VO(O^iPr)_3$, $Zr(OEt)_4$).

**Table 1. Epoxidation-methanolysis of 3,4-dihydro-2*H*-pyran with different homogeneous catalysts.[a]**

| Entry | Catalyst | Time (h) | Yield (%)[b] |
|---|---|---|---|
| 1 | $Na_2WO_4.2H_2O$ | 24 | 77 |
| 2 | $Q_2WO_4$ | 5 | 73 |
| 3 | $Q_2W_2O_{11}$ | 5,25 | 7 |
| 4 | $Q_3PW_4O_{24}$ | 24 | 85 |
| 5 | $Q_4[\gamma\text{-}SiW_{10}(H_2O)_2O_{34}]$ | 3 | 11 |
| 6 | $Mo(CO)_6$ | 24 | 30 |
| 7 | $Q_3PMo_{12}O_{40}$ | 5 | 7 |
| 8 | $Mo(O^iPr)_5$ | 24 | / |
| 9 | $Ti(O^iPr)_4$ | 2,25 | 70 |
| 10 | $VO(O^iPr)_3$ | 6 | 60 |
| 11 | $Zr(OEt)_4$ | 6 | / |

[a]Conditions: 3,4-dihydro-*2H*-pyran: 0,2 M in MeOH, catalyst: 0.04 eq. (calculated per metal atom), $H_2O_2$: 2 eq. against DHP. [b]Yields are calculated based on GC data in which *cis* and *trans* opened epoxides are combined as desired product.

It is clear that the molybdenum catalysts (entries 6-8) show low performance. The Venturello complex (entry 4) and $Ti(O^iPr)_4$ (entry 9) stand out respectively among the W-based catalysts (entries 1-5) and the metal alkoxides (entries 8-11). Although titanium is commonly used for epoxidations, e.g. in the Sharpless epoxidation, the results with the Ti-catalyst are quite remarkable, as $Ti(O^iPr)_4$ is generally used with $^tBuOOH$, rather than with aqueous hydrogen peroxide. For both catalysts a short optimization procedure was set up to find the best reaction conditions.

Optimization of reaction conditions for $PW_4O_{24}^{3-}$ and $Ti(O^iPr)_4$

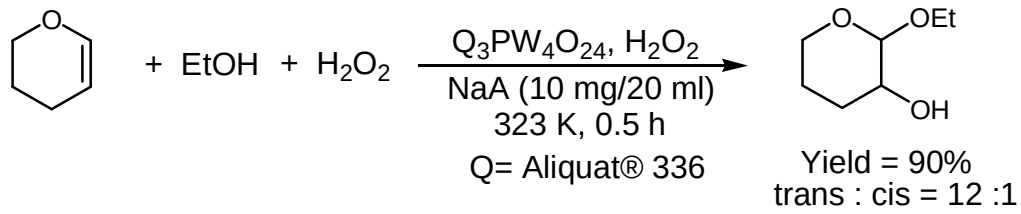
For reactions with the Venturello compound, it was found that **addition of a base, such as an alkaline zeolite is necessary in order to suppress acid-catalyzed alcohol addition** on the double bond. Therefore 10 mg of NaA zeolite was added per 20 ml of reaction mixture in all further tests. A temperature of 323 K was applied for all reactions. Other parameters considered were the nature of the quaternary ammonium salt and the composition of the solvent/nucleophile mixture. It is clear that the Venturello compound works in a range of alcoholic solvents. The highest activity and selectivity are achieved in ethanol (entries 12 and 13) while the catalyst activity is much higher in a 1:1 mixture of methanol and 1,4-dioxane than in pure methanol (compare entry 12 with 17). If a higher ratio of dioxane:MeOH is used (entry 18) the selectivity drops because of more diol formation. This is presumably due to the fact that dioxane enhances the nucleophilicity of both methanol and water present in the reaction.[2] The use of acetonitrile as co-solvent (entry 16) led to high conversion of starting enol ether, but the desired products were not formed. Attempts to incorporate more complex alcohols as nucleophiles in 1,4-dioxane were less successful. In the case of 4-pentene-1-ol (entry 20) a significant amount of the 5-hydroxy-1,2-epoxypentane epoxide was detected, indicating that the reactivity of the enol ether and terminal olefin were not sufficiently differentiated. A similar result was obtained with citronellol (entry 21). The secondary alcohol group of exo-norborneol (entry 22) showed to be too hindered as diol was formed as the major product. Finally, the influence of the quaternary ammonium species used as counter ion in the Venturello compound was assessed by comparing the use of tetrabutyl ammonium and Aliquat® 336 ions in ethanol (entries 13 and 14). The results indicate that Aliquat® 336 affords similar yield but improved stereoselectivity in the epoxide opening. Optimal reaction conditions are summarized in Scheme 1.

**Table 2: Optimization of reaction conditions for Venturello-complex catalyzed reactions.**

| Entry | $Q^+$ | Solvent | Nucleophile | Time (h) | Yield (%) | *trans : cis* |
|---|---|---|---|---|---|---|
| 12 | 1 $(Bu)_4N^+$ | MeOH | - | 24 | 81 | 17.5 : 1 |
| 13 | 1 | EtOH | - | 0.5 | 85 | 9 : 1 |
| 14 | 2 (Aliquat® 336) | EtOH | - | 0.5 | 88 | 12 : 1 |
| 15 | 1 | n-PrOH | - | 0.25 | 81 | 8 : 1 |
| 16 | 1 | MeCN | EtOH[a] | 1 | 0[b] | / |
| 17 | 1 | 1,4-dioxane | MeOH[c] | 3 | 78 | 8 : 1 |
| 18 | 1 | 1,4-dioxane | MeOH[d] | 0.5 | 70 | 8 : 1 |
| 19 | 1 | 1,4-dioxane | EtOH[c] | 0.5 | 45 | 5 : 1 |
| 20 | 1 | 1,4-dioxane | 4-pentene-1-ol[e] | 0.5 | 47 | 9 : 1 |
| 21 | 1 | 1,4-dioxane | Citronellol[a] | 1.5 | 16 | 4 : 1 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 22 | 1 | | 1,4-dioxane | Exo-norborneol[a] | 1.5 | 10 | 4 : 1 |

General conditions: DHP: 0,2 M in solvent, $Q_3PW_4O_{24}$: 0,01 eq. (calculated on compound), NaA: 10 mg/20 ml, $H_2O_2$: 2 eq., 323K, [a]Equimolar amounts of nucleophile and substrate (0.2 M), [b]Conversion was 97% but no desired products were obtained, [c]dioxane : alcohol = 1:1, [d]dioxane : MeOH = 4:1, [e]dioxane : 1,4-pentene-1-ol = 7:3.



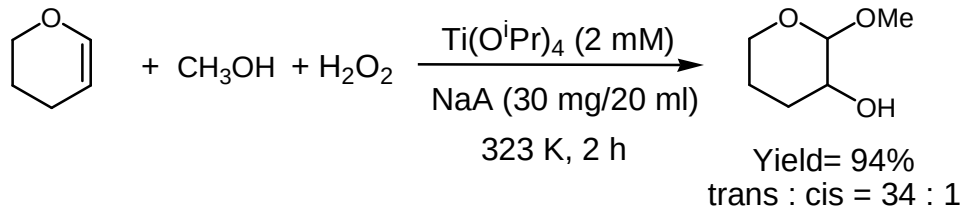

**Scheme 1: Optimized conditions for Venturello-compound.**

For $Ti(O^iPr)_4$ a thorough investigation of catalyst concentration, base, solvent/nucleophile system and temperature was performed, and a selection of the data is presented in Table 3. For optimal catalyst solubility, the $Ti(O^iPr)_4$ concentration was set at 2 mM. Among the different bases tested in methanol (entries 24-26), zeolite 4A (entry 26) gave the optimum combination of high reaction rate, selectivity and stereoselectivity. The use of triethylamine (entry 25) led to almost complete *trans* selectivity in the products, but with rather low yield. The solvent choice is limited due to the poor solubility of $Ti(O^iPr)_4$ in alcohols other than methanol, with consequent poor conversion and selectivity in ethanol and propanol (entries 26-28). Addition of dioxane as co-solvent (entry 29) resulted in drastic lowering of the activity and selectivity. The reaction rate can be increased by performing the reaction at 323 K; addition of a larger amount of NaA at this temperature (30 mg/20 ml, entries 31 *vs*. 32) resulted in a high yield with a significantly improved selectivity for the *trans* product. These investigations led to the proposed optimized reaction conditions of Scheme 2.

**Table 3. Overview of optimized parameters for titaniumisopropoxide.**

| Entry | Conc. (mM) | Base | Solvent | Nucleophile | Temp (K) | Time (h) | Yield (%) | *trans:cis* |
|---|---|---|---|---|---|---|---|---|
| 23 | **2** | **-** | MeOH | - | 303 | 6 | 73 | 10 : 1 |
| 24 | 2 | **$CaCO_3$** | MeOH | - | 303 | 3 | 88 | 11 : 1 |
| 25 | 2 | **$Et_3N$** | MeOH | - | 303 | 24 | 37 | 115 : 1 |
| 26 | 2 | **NaA (4A)** | **MeOH** | **-** | **303** | 3 | 94 | 20 : 1 |
| 27 | 2 | NaA | **EtOH** | - | 303 | 2 | 33 | 2,5 : 1 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 28 | 2 | NaA | **n-PrOH** | - | 303 | 2 | 23 | 3 : 1 |
| 29 | 2 | NaA | **1,4-dioxane** | **MeOH** | 303 | 65 | 81 | 5,5 : 1 |
| 30 | 2 | NaA | MeOH | - | **313** | 2 | 87 | 20,5 : 1 |
| 31 | 2 | NaA | MeOH | - | **323** | 1 | 86 | 19 : 1 |
| 32 | 2 | NaA (30 mg) | MeOH | - | **323** | 2 | 94 | 34 : 1 |




**Scheme 2. Optimized reaction conditions for reactions with Ti isopropoxide.**

**Experimental information for screening/optimization procedure**

Catalysts

$NaWO_4.H_2O$ and the metal alkoxides were commercially obtained. The Mimoun compound[3] and the silicotungsten compound ($Q_4[\gamma\text{-}SiW_{10}(H_2O)_2O_{34}]^{4-}$)[4] were prepared as described in literature reports.

**$Q_2WO_4$**

To a solution of 2,25 g (6,83 mmol) $Na_2WO_4.2H_2O$ in a little water is added a solution of 0,466 g (1,37 mmol) $((C_4H_9)_4N^+)HSO_4$ in 10 ml $CHCl_3$. After stirring for 1 h the organic layer is separated, dried with $MgSO_4$, filtered and concentrated under reduced pressure. 0,324 g of tetrabutylammoniumtungstate is obtained as an opal syrup.

**Venturello compound**

Tetrabutyl ammonium

10 g of $H_2WO_4$ is added to 7 ml of a 35 wt% aqueous solution of $H_2O_2$. The yellow mixture is stirred for 1 h on 50°C after which the mixture is poured over a filter to remove insoluble $WO_3$ particles. Once the solution is cooled down, 70 µl $H_3PO_4$ is added. After stirring for 1 h on 30°C, 1,08 g $(Bu)_4NHSO_4$ in 10 ml $CH_2Cl_2$ is added carefully. After stirring vigorously for 2 h the organic layer is separated washed with H2O (1x), dried with MgSO4, filtered and concentrated under reduced pressure.. 1,1 g (60%) of a colourless, easy to pulverize solid is obtained.

Aliquat as quaternary ammonium

10 g of $H_2WO_4$ is added to 28 ml of a 35 wt% aqueous solution of $H_2O_2$. The yellow mixture is stirred for 1,5 h on 60°C after which the mixture is poured over a filter to remove insoluble $WO_3$ particles. The filtrate is allowed to cool down and 1,2 ml $H_3PO_4$ is added. Bidistilled $H_2O$ is added to the mixture till the weight is 120 g. After 30 min stirring on RT a solution of 8,56 g Aliquat 336 in 180 ml $CH_2Cl_2$ is added drop wise over 15 min. The resulting mixture is stirred vigorously for 1 h after which the organic phase is separated, washed once with $H_2O$, dried with $MgSO_4$ and concentrated *in vacuo*. 11 g (70%) of the compound was obtained.

**Synthesis of glycal substrates**

**3,4,6-tri-*O*-benzyl-D-glucal (2)[5]**

To a solution of 3,4,6-tri-*O*-acetyl-D-glucal (2.72 g, 10 mmol) in benzene (20 ml), a 50% aqueous solution of NaOH (20 ml), t-BuOH (0.5 ml) and $(Bu)_4NHSO_4$ (0.64 g) were added. After heating to 50 °C, a mixture of benzylchloride (7 ml) and benzene (5 ml) was added in 0.4 ml portions every 10 min over a time span of 4.75 h. Thereafter the mixture is stirred for an additional 30 min at 50 °C after which TLC indicates consumption of the starting material and formation of a single product. After cooling, the organic layer is separated, washed with water (2 x) and dried over $MgSO_4$. After filtration the solvent is evaporated and the obtained crystals are washed with cold pentane. The crude product is purified by column chromatography on silica gel (ethyl acetate/petroleum ether 0:1 to 1:9) to afford glucal **2** (1.93 g, 48 %) as white crystals. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.36-7.16 (m, 15H, aromatic), 6.42 (dd, 1H, H-1), 4.84 (dd, 1H, H-2), 4.67-4.49 (m, 6H, $CH_2Ph$), 4.20 (m, 1H, H-3), 4.06 (m, 1H, H-5), 3.86 (t, 1H, H-4), 3.80 and 3.77 (m, 2H, H6 and H6'); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 144.7 (C-1), 99.9 (C-2), 76.6 (C-3), 74.5 (C-4), 75.7 (C-5), 68.7 (C-6), 73.6, 73.5, 70.4 (3 x $CH_2Ph$). The spectroscopic data were in agreement with the reported data[5].

**3,4,6-tri-*O*-methyl-D-glucal (3)[6]**

To a solution of 3,4,6-tri-*O*-acetyl-D-glucal (2.8 g, 10.3 mmol) in freshly distilled THF (10 ml) was added powdered NaOH (2.5 g, 62.5 mmol), followed by TBAI (380 mg, 0.27 mmol) and MeI (2.88 ml, 46.35 mmol). The mixture was stirred at room temperature. More THF was added when reaction mixture turned into a paste. On completion (3 h) the reaction mixture was poured into water and extracted with DCM. The combined organic layers were washed with water and dried over $Na_2SO_4$. After filtration, the solvent was evaporated and the crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1:9) to afford the methylated glucal **3** (550 mg, 28 %) as a pale yellow oil. $^1$H NMR ($CDCl_3$, 400 MHz): d 6.38 (dd, *J* = 1.3, 6.2, 1H, H-1), 4.82 (dd, *J* = 2.8, 6.2 Hz, 1H, H-2), 3.96 (ddd, *J* = 3.1, 5.2, 8.3 Hz, 1H, H-5), 3.88 (ddd, *J*=1.4, 2.8, 6.0 Hz, 1H, H-3), 3.71-3.60 (m, 2H, H-6 and H-6'), 3.54 (s, 3H, OMe), 3.46 (dd, *J* = 6.0, 8.4 Hz, 1H, H-4), 3.41 (s, 3H, OMe), 3.40 (s, 3H, OMe). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 144.78 (C-1), 99.79 (C-2), 76.98, 76.54, 76.14 (C-3, C-4 and C-5), 71.07 (C-6), 59.43,

59.39, 55.91 (3 x OMe). The spectroscopic data were in agreement with the reported data[7].

**3,4,6-tri-*O*-*tert*-Butyldimethylsilyl-D-glucal (4)[8]**

To a solution of D-glucal (2 g, 13.7 mmol) and imidazole (6.15 g, 90.4 mmol) in DMF (105 ml), *tert*-butyldimethylsilyl chloride (6.81 g in 22.5 ml DMF, 45.2 mmol) was added drop wise. After stirring at room temperature overnight, the reaction mixture was diluted with water. The aqueous layer was extracted with diethyl ether. The combined organic phase were washed with water, dried over $MgSO_4$, filtered and evaporated. Chromatography on silica gel (ethyl acetate/petroleum ether 1:99 to 1:9) afforded glucal **4** (4.0 g, 60%) as a colourless oil; $^1$H NMR ($CDCl_3$, 300 MHz): δ 6.32 (dd, *J* = 6.2 Hz, H-1), 4.69 (ddd, *J* = 1.2, 4.4, 6.2 Hz, 1H, H-2), 3.99 (m, 1H, H-5), 3.96-3.92 (m, 1H, H-6), 3.91-3.87 (m, 1H, H-4), 3.82-3.78 (m, 1H, H-3), 3.76 (dd, *J* = 3.3, 10.9 Hz, 1H, H-6'), 0.90 (s, 9H, $^t$Bu), 0.88 (s, 18H, $^t$Bu), 0.10 (s, 6H, C*H*$_3$-Si), 0.08 (s, 6H, C*H*$_3$-Si), 0.06 (s, 3H, C*H*$_3$-Si), 0.05 (s, 3H, C*H*$_3$-Si); $^{13}$C NMR ($CDCl_3$, 75.5 MHz): δ 143.23 (C-1), 101.60 (C-2), 80.34, 70.46, 66.98, 62.00, 26.22 (*Me*$_3$CSi), 26.09 (*Me*$_3$CSi), 18.6 (Me$_3$*C*Si), 18.2 (Me$_3$*C*Si), -4.07 (*C*H$_3$-Si), -4.16 (*C*H$_3$-Si), -4.47 (*C*H$_3$-Si), -5.01 (*C*H$_3$-Si). The spectroscopic data were in agreement with the reported data[8].

**6-*O*-*tert*-Butyldiphenylsilyl-D-glucal (5)[8]**

To a solution of D-glucal (2.11 g, 14.44 mmol) and imidazole (1.965 g, 28.87 mmol) in dry DMF (30 ml) at 0°C, *tert*-butyldiphenylsilyl chloride (4.0 ml, 17.02 mmol) in 3 ml DMF was added drop wise. The reaction was stirred for 4 h at 0°C and 2 h at room temperature. It was then diluted with water and the aqueous phase was extracted with diethyl ether. The combined organic layers were washed with water and dried over $MgSO_4$. After filtration, the solvent was evaporated and the crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 2:8 to 1:1) to afford the silylated glucal **5** (3.5 g, 63%) as a colourless oil; $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.70-7.67 (m, 4H, Ph), 7.44-7.35 (m, 6H, Ph), 6.30 (dd, 1H, *J* = 1.8 and 6.2 Hz, H-1), 4.71 (dd, 1H, *J* = 2.2 and 6.2 Hz, H-2), 4.26 (br s, 1H, OH), 4.00 (s, 2H), 3.97 (s, 2H), 2.88 (br s, 1H, OH), 2.28 (m, 1H), 1.06 (s, 9H, *Me*$_3$C-Si); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 144.4 (C-1), 135.6, 133.0, 129.8, 127.7 (aromatic), 102.3 (C-2), 77.1, 71.5, 69.7, 63.6, 26.7 (*Me*$_3$C-Si), 19.2 (*Me*$_3$C-Si). The spectroscopic data were in agreement with the reported data[8].

**3,4-di-*O*-benzyl-D-glucal (6)[8,9]**

To a solution of silylated glucal **5** (2.5 g, 6.5 mmol) in dry THF (14.9 ml) at 0 °C, NaH (0.546 g, 13.65 mmol) is added portion wise. The solution is stirred for 2 h at 0 °C after which n-$Bu_4NI$ (0.480 g, 1.3 mmol) is added, followed by drop wise addition of BnBr (1.7 ml, 4.3 mmol in 4.1 ml THF). The ice bath was removed and the mixture allowed to stir overnight. The reaction was then diluted with water and extracted with diethyl ether (3 x). The combined organic phases are washed two times with water, one time with brine and dried over $MgSO_4$. After filtration the solvent was evaporated and the crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1:99 - 5:95) to afford 6-*O*-TPDPS-3,4-di-*O*-benzyl-D-glucal (1.95 g, 53%) as a pale yellow oil.

To a solution of 6-*O*-TPDPS-3,4-di-*O*-benzyl-D-glucal (1.95 g, 3.46 mmol) in dry THF (30 ml) at -20 °C (MeOH and ice), TBAF (5.2 ml of 1 M THF solution, 5.2 mmol) was added drop wise. After 1.5 h the ice bath was removed. The reaction was stirred for another 4 h after which the solvent was evaporated. The crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1:9 - 1:1) to afford benzylated glucal **6** (1.1 g, 97%, from glucal 32%) as a colourless oil. $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.25 (m, 10H, 2 x Ph), 6.39 (dd, *J* = 1.3, 6.1 Hz, 1H, H-1), 4.89-4.87 (m, 1H, H-2), 4.87-4.84 and, 4.74-4.54 (m, 4H, 2 x C*H*$_2$Ph), 4.25-4.215 (m, 1H, H-5), 3.96-3.91 (m, 1H, H-3), 3.87-3.84 (m, 2H, H-6, H-6'), 3.80 (dd, *J* = 6.2, 8.5 Hz, 1H, H-4), 1.95 (br s, 1H, OH). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 144.8 (C-1), 138.4, 138.3, 128.7, 128.6, 128.2, 128.1, 128.0 (aromatic), 100.4 (C-2), 77.6 (C-5), 75.8, 74.8, 74.0, 70.8 (2 x *C*$H_2$Ph, C-3, C-4), 62.0 (C-6).

**3,4-di-*O*-benzyl-D-xylal (8)[6,10]**

(i) tetra-*O*-acetyl-D-xylose: A mixture of NaAc (17 g) and freshly distilled acetic anhydride (95 ml) was heated to 115 °C. The heating is removed and D-xylose (20 g) was added in small portions to avoid that the temperature exceeds 90 °C. After addition the mixture was heated once more to 115 °C and stirred for 3 h after which TLC showed consumption of starting material and formation of a single product. The mixture is cooled down and a mixture of water (400 ml, ice cold) and DCM (200 ml) was added and the resulting solution was stirred overnight. The layers were separated and the aqueous layer was extracted three times with DCM. The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2 x), water (1 x) and dried over $MgSO_4$. After

filtration the solvent was evaporated and the obtained crystals were decolourized with active carbon to yield 38 g of acetylated xylose.

(ii) 3,4-di-*O*-acetyl-D-xylal: acetylated xylose (15 g) was dissolved in glacial acetic acid (4 ml) and acetic anhydride (4 ml). After 10 min of stirring the mixture was cooled to 0 °C and 33 % HBr in acetic acid (26.8 ml) was added drop wise. The reaction was allowed to stir at room temperature for 2.5 h This crude acetobromoxylose solution was added dropwise to a mixture of NaAc.$3H_2O$ (12.72 g), acetone (80 ml), water (21.5 ml), glacial acetic acid (21.5 ml) and zinc dust (67 g) at 0 °C. During the addition the temperature of the mixture was kept under 8 °C. The reaction mixture was stirred 1 h more at 0 °C and 1.5 h at room temperature. After completion the mixture was filtered on Celite® and the zinc washed with 1 : 1 mixture of acetic acid and water. Ice water was added to the filtrate. The aqueous phase was extracted with chloroform (6 x). The combined organic layers were washed with saturated $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1 : 9) 5.8 g of the title component is obtained as a colourless oil.

(iii) 3,4-di-*O*-benzyl-D-xylal: Following the procedure for the preparation of methylated glucal **3** (replacing MeI by BnBr), xylal **8** was obtained from 3,4-di-*O*-acetyl-D-xylal in 60% yield as a pale yellow oil. $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.26 (m, 10H, 2 x Ph), 6.55 (d, *J* = 6.2 Hz, 1H, H-1), 4.93 (ddd, *J* = 1.4, 4.5, 6.1 Hz, 1H, H-2), 4.68-4.51 (m, 4H, 2 x C*H*$_2$Ph), 4.11 (ddd, *J* = 1.5, 4.2, 11.6 Hz, 1H, H-5), 3.97 (dd, *J* = 2.1, 11.7 Hz, 1H, H-5'), 3.88-3.84 (m, 1H, H-3), 3.70-3.66 (m, 1H, H-4); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 146.9 (C-1), 138.7, 138.2, 128.69, 128.6, 128.1, 128.0, 127.9 (aromatic), 99.2 (C-2), 73.1 (C-4), 71.5, 70.3 (2 x *C*$H_2$Ph), 69.5 (C-3), 64.3 (C-5). The spectroscopic data were in agreement with the reported data[5].

**3,4,6-tri-*O*-acetyl-D-galactal (9)[11]**

(i) penta-*O*-acetyl-D-galactose: acetic anhydride (175 ml) was added to a flask with D-galactose (25 g) and NaAc (12.5 g). The mixture is heated gently and after 0.5 h the white paste changes into a white solution. Further heating gives a colourless solution (1 h), later changing into a brown solution (2 h). Thereafter the solution is stirred another 2.5 h under reflux till TLC shows the consumption of the starting material and the formation of a single product.

The mixture is cooled, poured into a beaker with ice and kept in the fridge (4 °C) overnight. The obtained crystals are filtered, washed with water and ethanol and dried under vacuum. Water and ethyl acetate are added to the oily residue. The layers are separated and the organic layer is washed with water. The organic layer is dried with $MgSO_4$, filtered and concentrated. The obtained oil is recrystallized in ethanol. Combined with the first crystals, 23.5 g (43%) of D-galactose pentaacetate is obtained.

(ii) 2,3,4,6-tetra-*O*-acetyl-1-bromo-D-galactose: acetylated galactose (20 g) is dissolved in DCM (40 ml). With stirring 33% HBr in acetic acid (37 ml) is added in small portions. After 2 h TLC showed complete consumption of the starting material. The reaction mixture is concentrated under vacuum. To the obtained oil, toluene (150 ml) is added and the mixture is concentrated again under vacuum. This is repeated with toluene (150 ml) and two times diethyl ether (150 ml). An orange/brown oil is obtained.

(iii) 3,4,6-tri-*O*-acetyl-D-galactal: The orange/brown oil obtained in step (ii) is quickly dissolved in 50 % aqueous acetic acid (245 ml) and zinc dust (47 g) is added. The mixture is vigorously stirred on 0 °C for 5 h. After reaction the mixture is filtered on Celite® and water and DCM are added to the filtrate. The layers are separated and the water layer is extracted once with DCM. The combined organic layers are washed with ice water (2x), cold saturated $NaHCO_3$ (3x), ice water (2x) and brine (1x). Thereafter the organic layer is dried with $MgSO_4$, filtered and concentrated under vacuum and the crude product is purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1:9 to 1:4) and 8.2 g of the title component was obtained as a colourless oil. $^1$H NMR (400 MHz) ($CDCl_3$): δ 6.47 (dd, 1H, H-1), 5.56 (t, 1H, H-3), 5.43 (t, 1H, H-4), 4.73 (m, 1H, H-2), 4.31 (m, 1H, H-5) 4.29-4.19 (m, 2H, H-6 and H-6'); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 170.0 (3 x C=O),145.3 (C-1), 98.8 (C-2), 63.8 (C-3), 63.8 (C-4), 72.8 (C-5), 61.8 (C-6), 20.7-20.5 (3 x -$CH_3$).

**3,4,6-tri-*O*-benzyl-D-galactal**

Following the procedure for the preparation of benzylated glucal **2**, galactal **10** was obtained from 3,4,6-tri-*O*-acetyl-D-galactal in 54 % yield as white crystals; mp 54 °C (lit., 52-54 °C); $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.38-7.20 (m, 15H, 3 x Ph), 6.36 (dd, 1H, *J* = 1.5 and 6.2 Hz, H-1), 4.88-4.83 (m, 2H, H-2 and C*H*$_2$Ph), 4.67-4.39 (m, 5H, C*H*$_2$Ph), 4.21-4.16 (m, 2H, H-3 and H-5), 3.95-3.94 (m, 1H, H-4), 3.80-3.76 (m, 1H, H-6), 3.68-3.64 (m, 1H, H-6'); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 144.1 (C-1), 138.5, 138.4, 138.0, 128.3, 128.2, 128.1, 127.8, 127.7, 127.5, 127.4 (3 x Ph), 99.9 (C-2), 75.7 (C-3), 73.4, 73.3 (2 x *C*H$_2$Ph),

71.4 (C-4), 70.9 (*C*$H_2$Ph), 70.8 (C-5), 68.4 (C-6). The spectroscopic data were in agreement with the reported data[5].

**NMR data epoxidation-alcoholysis reactions**

(Product numbering refers to entries in tables 1 and 3.)

**Methyl 3,4,6-tri-*O*-acetyl-b-D-glucopyranoside (1)[12]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 5.15-5.00 (m, 2H, H-3 and H-4), 4.41 (dd, 1H, H-2), 4.28 (d, *J*= 7.76 Hz, 1H, H-1), 4.20-4.09 (m, 2H, H-6 and H-6'), 3.70 (m, 1H, H-5), 3.58 (s, 3H, -OMe), 2.10, 2.05, 2.03 (3s, 9H, 3x -OCOC$\underline{H}_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 171-170 (3 x C=O), 103.7 (C-1), 74.5 (C-5), 71.7 (C-3), 68.4 (C-2), 67.3 (C-4), 62.0 (C-6), 57.3 (-OMe), 20.9-20.4 (3 x -OCO$\underline{C}$H$_3$).

**Methyl 3,4,6-tri-*O*-benzyl-b-D-glucopyranoside (2)[13, 14]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.38-7.09 (m, 15H, aromatic), 4.93-4.80 and 4.65-4.51 (m, 6H, $CH_2$Ph), 4.18 (d, *J*= 7.17 Hz, 1H, H-1), 3.74-3.42 (m, 6H, H-2, H-3, H-4, H-5, H-6 and H-6'), 3.55 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 103.5 (C-1), 84.3 (C-3), 77.4 (C-4), 75.0 ($CH_2$Ph), 74.9 (C-5), 74.8 ($CH_2$Ph), 74.4 (C-2), 73.3 ($CH_2$Ph), 68.6 (C-6), 57.0 (-OMe).

**Methyl 3,4-di-*O*-benzyl-b-D-glucopyranoside (3)[15]**

$^1$H NMR (400 MHz) ($CDCl_3$) δ ppm 4.22 (d, *J* = 7.71 Hz, 1H, H-1), 3.54 (s, 3H, OMe).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 103.8 (C-1), 84.3 (C-3), 75.4, 75.1 and 75.05 (C-2, C-3, C-4 and C-5), 61.9 (C-6), 57.3 (OMe).

**Methyl 3,4,6-tri-*O*-methyl-b-D-glucopyranoside or 1,3,4,6-tetra-*O*-methyl-b-D-glucopyranoside (4a)[13]:**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.14 (d, *J*= 7.71 Hz, 1H, H-1), 3.65, 3.542, 3.537, 3.41 (4 x s, 12H, 4 x -OMe).

$^{13}$C NMR (75,5 MHz) ($CDCl_3$): δ 103.6 (C-1), 86.0 (C-3), 79.4 (C-5), 75.0 (C-2), 74.0 (C-4), 71.2 (C-6), 60.7, 60.3, 59.3 and 57.1 (4 x -OMe).

**Methyl 3,4,6-tri-*O*-methyl-a-D-mannopyranoside or 1,3,4,6-tetra-*O*-methyl-a-D-mannopyranoside (4b)[13]**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.76 (d, *J*= 1.71 Hz, 1H, H-1), 3.37 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 100.4 (C-1), 56.2 (-OMe).

**Methyl 6-*O*-TBDPS-b-D-glucopyranoside (5a)[16]**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.18 (d, *J* = 7.70 Hz, 1H, H-1), 3.49 (s, 3H, -OMe).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 103.4 (C-1), 76.4 (C-3), 74.8 (C-5), 73.6 (C-2), 72.1 (C-4), 64.8 (C-6), 56.9 (-OMe), 26.8 ($(\underline{C}H_3)_3C$-), 19.2 ($(CH_3)_3\underline{C}$-).

**Methyl 6-*O*-TBDPS-a-D-mannopyranoside (5b)[17]**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ ppm 4.68 (d, *J*= 1.24 Hz, 1H, H-1), 3.31 (s, 3H, -OMe).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 100.6 (C-1), 65.2 (C-6), 56.60 (OMe).

**Methyl 3,4,6-tri-*O*-TBDMS-b-D-glucopyranoside (6a)[18]**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.43 (d, *J*= 4.76 Hz, 1H, H-1), 3.45 (s, 3H, -OMe).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 103.0 (C-1), 78.1 (C-3), 74.3, 72.8 and 70.6 (C-2, C-4 and C-5), 63.23 (C-6), 56.41 (-OMe).

**Methyl 3,4,6-tri-*O*-TBDMS-a-D-mannopyranoside (6b)[18]**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.73 (d, *J*=1.29 Hz, 1H, H-1), 3.32 (s, 3H, -OMe).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 99.5 (C-1).

**Methyl 3,4,6-tri-*O*-acetyl-b-D-galactopyranoside (7a)[19]**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 5.39 (d, 1H, H-4), 4.93 (dd, 1H, H-2), 4.29 (d, 1H, *J*=7.72 Hz, H-1), 4.22-3.77 (m, 4H, H-3, H-5, H-6 and H-6'), 3.60 (s, 3H, -OMe), 2.13, 2.06 (2s, 9H, 3x -OCOC$\underline{H}_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 170.5-170.0 (3 x C=O), 104.0 (C-1), 72.5 (C-3), 70.6 (C-5), 69.1 (C-2), 67.1 (C-4), 61.3 (C-6), 57.3 (-OMe), 20.9-20.3 (3 x -OCO$\underline{C}H_3$).

**Methyl 3,4,6-tri-*O*-acetyl-a-D-galactopyranoside (7b)[20]**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.88 (d, *J*= 3.84 Hz, 1H, H-1), 3.47 (s, 3H, OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 99.5 (C-1), 61.8 (C-6), 55.6 (OMe).

**Methyl 3,4,6-tri-*O*-benzyl-b-D-galactopyranoside (8a)[21]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.34-7.09 (m, 15H, aromatic), 4.88 (d, 1H, H-4), 4.75-4.55 (m, 6H, $CH_2Ph$), 4.56 (d, 1H, H-2), 4.18 (d, 1H, *J*= 7.65 Hz, H-1), 3.93 (t, 2H, H-3 and H-5), 3.70-3.55 (m, 2H, H-6 and H-6'), 3.52 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 104.0 (C-1), 81.9 (C-3), 74.4 ($CH_2Ph$), 73.5 (C-5), 73.4 ($CH_2Ph$), 72.7 (C-4), 72.2 ($CH_2Ph$), 71.1 (C-2), 68.6 (C-6), 56.8 (-OMe).

**Methyl 3,4,6-tri-*O*-benzyl-a-D-galactopyranoside (8b)[21]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.84 (d, *J*= 4.09 Hz, 1H, H-1), 3.40 (s, 3H, OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 99.5 (C-1), 79.4 (C-3), 73.9 (C-5), 68.9 (C-6), 55.3 (-OMe).

**Methyl 3,4-di-*O*-benzyl-b-D-xylopyranoside (9a)[22]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.23 (d, *J*= 6.15 Hz, 1H, H-1), 3.50 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 103.9 (C-1), 56.7 (-OMe).

**Methyl 3,4-di-*O*-benzyl-a-D-lyxopyranoside (9b)**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.82 (d, *J*= 2.13 Hz, 1H, H-1), 3.45 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 101.0 (C-1), 55.5 (-OMe).

**Methyl 2,3,4,6-tetra-*O*-acetyl-a-D-mannopyranoside (10a)[23]**

$^1$H NMR (400 MHz, $CDCl_3$): δ ppm 5.34 (dd, *J* = 9.99, 3.30 Hz, 1H, H-3), 5.31-5.26 (dd, 1H, H-4), 5.24 (dd, *J* = 3.32, 1.79 Hz, 1H, H-2), 4.71 (d, *J* = 1.75 Hz, 1H, H-1), 4.28 (dd, *J* = 12.21, 5.41 Hz, 1H, H-6), 4.13 (dd, *J* = 12.21, 2.49 Hz, 1H, H-6'), 3.97 (ddd, *J* = 9.50, 5.46, 2.49 Hz, 1H, H-5), 3.41 (s, 3H, -OMe), 2.15, 2.10, 2.04, 1.99 (4 x s, -OCOC$\underline{H}_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ ppm 170.6, 170.0, 169.82, 169.7 (4 x -O$\underline{C}$O$CH_3$), 98.6 (C-1), 69.5 (C-2), 69.1 (C-3), 68.4 (C-5), 66.2 (C-4), 62.5 (C-6), 55.3 (OMe), 20.8, 20.7, 20.63, 20.61 (4 x -OCO$\underline{C}H_3$).

**Methyl 2,3,4,6-tetra-*O*-acetyl b-D-glucopyranoside (10b)[23]**

$^1$H NMR (300 MHz, $CDCl_3$): δ ppm 5.24-5.05 (m, 2H, H-3, H-4), 4.98 (dd, *J* = 9.46, 7.91 Hz, 1H, H-2), 4.44 (d, *J* = 7.90 Hz, 1H, H-1), 4.31-4.24 (m, 1H, H-6), 4.19-4.08 (m, 1H, H-6'), 3.51 (s, 3H, -OMe), 2.09, 2.05, 2.02, 2.00 (4xs, OCOC$\underline{H}_3$).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ ppm 170.61, 170.56, 170.2, 169.3 (4 x O<u>C</u>O$CH_3$), 101.6 (C-1), 72.9 (C-3), 71.8 (C-5), 71.3 (C-2), 68.5 (C-4), 61.9 (C-2), 56.9 (-OMe), 20.8, 20.65, 20.66, 20.5 (4 x OCO<u>C</u>$H_3$).

**n-Propyl 3,4,6-tri-*O*-acetyl-b-D-glucopyranoside (11)[24]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 5.19-4.98 (m, 2H, H-3 and H-4), 4.36 (d, 1H, *J*= 7.80 Hz, H-1), 4.28 (dd, 1H, H-2), 2.08, 2.03 (2s, 9H, 3x -OCOC<u>H</u>$_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 170.7, 170.6, 169.6 (3 x C=O), 102.8 (C-1), 74.4 (C-5), 72.1 (C-3), 72.0 (-O<u>C</u>$H_2CH_2CH_3$), 71.7 (C-4), 68.5 (C-2), 62.1 (C-6), 22.7 (-$OCH_2$<u>C</u>$H_2CH_3$), 20.7, 20.6 and 20.5 (3 x -OCO<u>C</u>$H_3$), 10.71 (-O $CH_2CH_2$<u>C</u>$H_3$).

**Methyl 3,4,6-tri-*O*-benzyl-b-D-glucopyranoside (12a)[13, 14]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.38-7.09 (m, 15H, aromatic), 4.93-4.80 and 4.65-4.51 (m, 6H, $CH_2$Ph), 4.18 (d, 1H, *J*= 7.21 Hz, H-1), 3.74-3.42 (m, 6H, H-2, H-3, H-4, H-5, H-6 and H-6'), 3.55 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 103.6 (C-1), 84.4 (C-3), 77.5 (C-4), 74.99 ($CH_2$Ph), 74.97 (C-5), 74.8 ($CH_2$Ph), 74.5 (C-2), 73.3 ($CH_2$Ph), 68.7 (C-6), 57.0 (-OMe).

**Methyl 3,4,6-tri-*O*-benzyl-a-D-mannopyranoside (12b)[13, 25]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.68 (d, *J*=1.79 Hz, 1H, H-1), 3.36 (s, 3H, -OMe).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 99.3 (C-1), 83.1 (C-3), 77.4 (C-4), 68.4 (C-6), 55.0 ($OCH_3$).

**Ethyl 3,4,6-tri-*O*-benzyl-b-D-glucopyranoside (13a)[26]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.38-7.09 (m, 15H, aromatic), 4.95-4.58 and 4.57-4.49 (m, 6H, $CH_2$Ph), 4.26 (d, 1H, *J*= 7.25 Hz, H-1), 4.04-3.43 (m, 6H, H-2, H-3, H-4, H-5, H-6 and H-6'), 3.55 (s, 2H, -OC<u>H</u>$_2CH_3$), 1.26 (t, 3H, -$OCH_2$C<u>H</u>$_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 102.4 (C-1), 84.4 (C-3), 77.4 (C-4), 74.95 ($CH_2$Ph), 74.9 (C-5), 74.8 ($CH_2$Ph), 74.4 (C-2), 73.3 ($CH_2$Ph), 68.7 (C-6), 65.3 (-O<u>C</u>$H_2CH_3$), 15.0 (-$OCH_2$<u>C</u>$H_3$).

**Ethyl 3,4,6-tri-*O*-benzyl-a-D-mannopyranoside (13b)**

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.0 (C-1), 83.3 (C-3), 77.3 (C-4), 63.3 (-O<u>C</u>$H_2CH_3$), 14.0 (-$OCH_2$<u>C</u>$H_3$).

**n-Propyl 3,4,6-tri-*O*-benzyl-b-D-glucopyranoside (14a)**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.42-7.1 (m, 15H, aromatic), 4.95-4.80 and 4.60-4.40 (m, 6H, $CH_2Ph$), 4.25 (d, 1H, *J*= 7.04 Hz, 1H, H-1), 3.95-3.41 (m, 6H, H-2, H-3, H-4, H-5, H-6 en H-6').

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 102.6 (C-1), 84.4 (C-3), 77.5 (C-4), 74.97 (C-5), 74.95 ($CH_2Ph$), 74.9 ($CH_2Ph$), 74.6 (C-2), 73.3 ($CH_2Ph$), 71.5 (-O<u>C</u>$H_2CH_2CH_3$), 68.8 (C-6), 22.7 (-O $CH_2$<u>C</u>$H_2CH_3$), 10.3 (-$OCH_2CH_2$<u>C</u>$H_3$).

**n-Propyl 3,4,6-tri-*O*-benzyl-a-D-mannopyranoside (14b)**

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.2 (C-1).

**n-Propyl 3,4,6-tri-*O*-benzyl-a-D-glucopyranoside (14c)[27]**

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 96.8 (C-1).

**Ethyl 3,4-di-*O*-benzyl-b-D-glucopyranoside (15a)**

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.39-7.26 (m, 6H, Ph), 4.96-4.83 and 4.65 (4 x d, 4H, 2 x $CH_2Ph$), 4.30 (d, *J*=7.73 Hz, 1H, H-1), 3.94 (dd, *J* = 9.62, 7.09 Hz, 1H, OC<u>H</u>$_2CH_3$) 3.86 (dd, *J*= 11.93, 2.74 Hz, 1H, H-6), 3.71 (dd, *J* = 11.93, 4.53 Hz, 1H, H-6'), 3.64-3.56 (m, 3H, H-3, H-4, -OC<u>H</u>$_2CH_3$), 3.52-3.47 (dd, *J*= 9.23, 7.72 Hz, 1H, H-2), 3.38 (ddd, *J* = 9.30, 4.53, 2.70 Hz, 1H, H-5), 1.26 (t, 3H, -$OCH_2$C<u>H</u>$_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 138.6, 138.0, 128.4, 128.0, 127.9, 127.85 and 127.7 (aromatic), 102.6 (C-1), 84.3 (C-3), 77.3 (C-4), 75.4 (C-5), 75.1 and 75.0 (<u>C</u>$H_2Ph$), 74.7 (C-2), 65.6 (-O<u>C</u>$H_2CH_3$), 62.0 (C-6), 15.1 (-$OCH_2$<u>C</u>$H_3$).

**Ethyl 3,4-di-*O*-benzyl-a-D-mannopyranoside (15b)**

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 98.9 (C-1).

**Ethyl 3,4,6-tri-*O*-methyl-b-D-glucopyranoside (16a)[28]**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.22 (d, *J*=7.75 Hz, 1H, H-1), 3.96 (dd, *J* = 9.58, 7.09 Hz, 1H, -OC<u>H</u>$_2CH_3$), 3.65, 3.54 and 3.40 (3 x s, 9H, -OMe), 3.65-3.55 (m, 3H, H-6, H-6' and -

$OC\underline{H_2}CH_3$), 3.40-3.35 (m, 1H, H-2), 3.35-3.28 (m, 1H, H-5), 3.24-3.15 (2H, H-3 and H-4), 1.25 (t, 3H, $-OCH_2C\underline{H_3}$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 102.4 (C-1), 86.0 (C-3 or C-4), 79.4 (C-3 or C-4), 75.0 (C-5), 74.0 (C-2), 71.3 (C-6), 65.3 ($-O\underline{C}H_2CH_3$), 60.6, 60.3 and 59.3 (3 x OMe), 15.1 ($-OCH_2\underline{C}H_3$).

**Ethyl 3,4,6-tri-*O*-methyl-**a**-D-mannopyranoside (16b)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.87 (d, *J*= 2.16 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.9 (C-1).

**Ethyl 3,4,6-tri-*O*-methyl-**a**-D-glucopyranoside (16c)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.86 (d, *J*= 4.29 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.0 (C-1).

**Ethyl 6-*O*-TBDPS-**b**-D-glucopyranoside (17a)**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.26 (d, *J* = 7.70 Hz, 1H, H-1).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 102.1 (C-1), 76.5, 75.0, 73.6 and 72.0 (C-2, C-3, C-4 and C-5), 64.8 (C-6), 61.5 ($-O\underline{C}H_2CH_3$), 26.8 ($(\underline{C}H_3)_3C$-), 19.2 ($(CH_3)_3\underline{C}$-), 15.2 ($-OCH_2\underline{C}H_3$).

**Ethyl 6-*O*-TBDPS-**a**- D-mannopyranoside (17b)**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.78 (d, *J*=1.32 Hz, 1H, H-1).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 99.2, 71.8, 70.9, 70.6 and 70.3 (C-2, C-3, C4 and C-5), 65.2 (C-6), 63.0 ($-O\underline{C}H_2CH_3$), 26.8 ($(\underline{C}H_3)_3C$-), 19.2 ($(CH_3)_3\underline{C}$-), 14.9 ($-OCH_2\underline{C}H_3$).

**Ethyl 3,4,6-tri-*O*-TBDMS-**b**-D-glucopyranoside (18a)**

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 4.53 (d, *J* = 4.58 Hz, 1H, H-1), 4.08 (dd, *J* = 10.17, 6.74 Hz, 1H), 3.89 (m, 2H), 3.79-3.76 (m, 2H), 3.71 (dd, *J* = 10.15, 5.67 Hz, 1H), 3.61-3.55 (m, 1H, H-5), 3.49 (dd, *J* = 9.44, 7.06 Hz, 1H), 1.20 (t, 3H, $-OCH_2C\underline{H_3}$), 0.95-0.86 (27H, 3 x $^{t}$Bu), 0.13-0.10 (12H, 4 x $C\underline{H_3}Si$), 0.05 (6H, 2x $C\underline{H_3}Si$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 101.5 (C-1), 78.5 (C-3), 74.1, 72.6 and 70.5 (C-2, C-4 and C-5), 64.5 ($-O\underline{C}H_2CH_3$), 63.3 (C-6), 26.5-25.5 (9C, 9 x $\underline{C}H_3$) 18.3, 18.25 and 18.0 (3 x $Me_3\underline{C}Si$), 15.1 ($-OCH_2\underline{C}H_3$), -3.8, -4.1, -4.2, -4.6, -5.2 and -5.4 (6 x $\underline{C}H_3Si$).

**Ethyl 3,4,6-tri-*O*-TBDMS-**a**-D-mannopyranoside (18b)**

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.79 (d, *J* = 2.93 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 96.1 (C-1).

**Ethyl 3,4,6-tri-*O*-TBDMS-**a**-D-glucoyranoside (18c)**

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.42 (d, *J* = 6.40 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 102.4 (C-1).

**n-Propyl 3,4,6-tri-*O*-acetyl-**b**-D-galactopyranoside (19a)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 5.00-4.91 (m, 2H, H-3 en H-4), 4.35 (d, 1H, *J*= 7.76 Hz, H-1), 4.22-4.07 and 3.96-3.68 (m, 4H, H-2, H-5, H-6 en H-6'), 2.13, 2.05 (2s, 9H, 3x -OCOC$\underline{H}_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 170.4, 170.3 and 170.1 (3 x C=O), 103.1 (C-1), 72.5 (C-3), 72.0 (-O$\underline{C}H_2CH_2CH_3$), 70.6 (C-5), 69.0 (C-2), 67.1 (C-4), 61.3 (C-6), 22.7 (-O $CH_2\underline{C}H_2CH_3$), 20.7, 20.6 and 20.5 (3 x -OCO$\underline{C}H_3$), 10.2 (-O $CH_2CH_2\underline{C}H_3$).

**n-Propyl 3,4,6-tri-*O*-acetyl-**a**-D-galactopyranoside (19b)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.92 (d, *J*= 3.44 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.5 (C-1), 70.8 (C-3), 70.4 (-O$\underline{C}H_2CH_2CH_3$), 68.2 (C-5), 67.0 (C-2), 66.6 (C-4), 61.8 (C-6), 22.6 (-O $CH_2\underline{C}H_2CH_3$), 20.7-20.5 (3 x -OCO$\underline{C}H_3$), 10.5 (-O $CH_2CH_2\underline{C}H_3$).

**Ethyl 3,4,6-tri-*O*-benzyl-**b**-D-galactopyranoside (20a)[29]**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 7.4-7.2 (m, 15H, aromatic), 4.95 (d, 1H, H-4), 4.90-4.40 (m, 6H, $CH_2Ph$), 4.24 (d, 1H, *J*= 7.67 Hz, H-1), 4.02-3.90 and 3.82-3.40 (m, 5H, H-2, H-3, H-5, H-6 en H-6'), 3.61 (s, 2H, -OC$\underline{H}_2CH_3$), 1.23 (t, 3H, -$OCH_2C\underline{H}_3$).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 102.9 (C-1), 81.4 (C-3), 74.4 ($CH_2Ph$), 73.6 (C-5), 73.4 ($CH_2Ph$), 72.8 (C-4), 72.3 ($CH_2Ph$), 71.2 (C-2), 68.6 (C-6), 65.1 (-O$\underline{C}H_2CH_3$), 15.0 (-$OCH_2\underline{C}H_3$).

**Ethyl 3,4,6-tri-*O*-benzyl-**a**-D-galactopyranoside (20b)[26b]**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ 4.95 (d, *J*= 3.98 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.3 (C-1), 79.7 (C-3), 74.6 ($CH_2Ph$), 74.0 (C-5), 73.4 ($CH_2Ph$), 72.4 ($CH_2Ph$), 69.5 (C-4), 68.9 (C-2), 68.8 (C-6), 63.5 (O<u>C</u>$H_2CH_3$), 14.96 (-$OCH_2$<u>C</u>$H_3$).

**n-Propyl 3,4,6-tri-*O*-benzyl-**b**-D-galactopyranoside (21a)**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.23 (d, *J*= 7.66 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 103.3 (C-1), 82.0 (C-3), 74.5 ($CH_2Ph$), 73.8 (C-5), 73.6 ($CH_2Ph$), 73.5 ($CH_2Ph$), 73.1 (C-4), 72.5 (-O<u>C</u>$H_2CH_2CH_3$), 71.5 (C-2), 68.8 (C-6), 22.8 (-$OCH_2$<u>C</u>$H_2CH_3$), 10.4 (-O $CH_2CH_2$<u>C</u>$H_3$).

**n-Propyl 3,4,6-tri-*O*-benzyl-**a**-D-talopyranoside (21b)**

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 97.5 (C-1).

**n-Propyl 3,4,6-tri-*O*-benzyl-**a**-D-galactopyranoside (21c)**

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 98.6 (C-1).

**Ethyl 3,4-di-*O*-benzyl-**b**-D-xylopyranoside (22a)**

$^1$H NMR (300 MHz, $CDCl_3$): δ 7.40-7.27 (10H, 2xPh), 4.73-4.59 (4H, 2 x C<u>H$_2$</u>Ph), 4.29 (d, *J* = 6.56 Hz, 1H, H-1), 3.97 (dd, *J* = 11.70, 4.57 Hz, 1H, H-5), 3.88 (dd, *J* = 9.66, 7.10 Hz, 1H, -OC<u>H$_2$</u>$CH_3$), 3.65-3.45 (m, 4H, H-2, H-3, H-4 and -OC<u>H$_2$</u>$CH_3$), 3.28 (dd, *J* = 11.71, 8.85 Hz, 1H, H-5'), 1.24 (t, 3H, -$OCH_2$C<u>H$_3$</u>).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 138.7, 138.6 and 128.7-127.6 (12C, aromatic), 102.7 (C-1), 82.00 (C-3), 77.1 (C-4), 74.4 and 73.03 (2 x $CH_2Ph$), 73.0 (C-2), 65.1 (-O<u>C</u>$H_2CH_3$), 63.1 (C-5), 15.2 (-$OCH_2$<u>C</u>$H_3$).

**Ethyl 3,4-di-*O*-benzyl-**b**-D-lyxopyranoside (22b)**

$^1$H NMR (300 MHz, $CDCl_3$): δ 4.95 (d, *J* = 1.66 Hz, 1H, H-1).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ 99.8 (C-1).

**Ethyl 2,3,4,6-tetra-*O*-acetyl-**a**-D-mannopyranoside (23)[30]**

$^1$H NMR (400 MHz, $CDCl_3$)?: δ ppm 5.37 (dd, *J* = 10.00, 3.45 Hz, 1H, H-3), 5.31-5.24 (dd, 1H, H-4), 5.23 (dd, *J* = 3.41, 1.79 Hz, 1H, H-2), 4.82 (d, *J* = 1.66 Hz, 1H, H-1), 4.28 (dd, *J* = 12.21, 5.35 Hz, 1H, H-6), 4.11 (dd, *J* = 12.18, 2.49 Hz, 1H, H-6'), 4.00 (dddd, *J* = 9.93,

5.33, 2.46, 0.49 Hz, 1H, H-5), 3.75 (dd, *J* = 9.81, 7.10 Hz, 1H, -OC$\underline{H_2}$$CH_3$), 3.55 (dd, *J* = 9.81, 7.06 Hz, 1H, -OC$\underline{H_2}$$CH_3$), 2.15, 2.10, 2.04 and 1.99 (s, 4x3H, -OCOC$\underline{H_3}$), 1.25 (t, *J* = 7.08, 7.08 Hz, 3H, $OCH_2C\underline{H_3}$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ ppm 170.6, 170.0, 169.8, 168.7 (4x O$\underline{C}OCH_3$), 97.4 (C-1), 69.8 (C-2), 69.1 (C-3), 68.4 (C-5), 66.4 (C-4), 63.9 (O$\underline{C}H_2CH_3$), 62.6 (C-6), 20.9, 20.7, 20.6, 20.5 (4x OCO$\underline{C}H_3$), 14.9 ($OCH_2\underline{C}H_3$).

**1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzyl-**a/ß-**D-glucopyranose**[31]**:** (a/ß = 1,35/1)**:** Yellow Oil;

*a-acetyl:* $^1$H NMR (400 MHz, $CDCl_3$): d 7.32-7.14 (m, 15 H, aromatic protons), 6.29 (d, *J* = 3.64 Hz, 1 H, H-1), 5.04 (dd, *J*= 10.02 and 3.64 Hz, 1 H, H-2), 4.70-4.47 (m, 6 H, $PhCH_2$), , 4.98 (dd, *J* = 9.95 and 8.97 Hz, 1 H, H-3), 3.84-3.56 (3 H, H-4,H-5, H-6,6'), 2.10, 1.95 (2 x s, 6 H, 2 x -OCOC$\underline{H_3}$).

$^{13}$C NMR (100 MHz, $CDCl_3$): d 169.37, 169.02 (2 C=O), 138.50-127.60 (aromatic carbons), 90.0 (C-1), 79.9, 77.2, 75.35, 75.3, 73.6, 73.2, 71.9, 68.15 (C-6), 20.9 and 20.6 (-OCO$\underline{C}H_3$).

*b-acetyl:* $^1$H NMR (400 MHz, $CDCl_3$): d 7.32-7.14 (m, 15 H, aromatic protons), 5.60 (d, *J* = 8.4 Hz, 1H, H-1), 5.11 (dd, *J* = 9.24 and *J* = 8.20 Hz, 1 H, H-2), 4.85-4.70 (m, 6 H, $PhCH_2$), 3.84-3.56 (m, 4H, H-3, H-4,H-5, H-6,6'), 2.07, 1.93 (2 x s, 6 H, 2 x -$OCOCH_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): d 169.37, 169.82 (2 C=O), 138.50-127.60 (aromatic carbons), 92.2 (C-1), 82.7, 77.1, 75.8, 75.1, 75.0, 73.5, 72.2, 68.15 (C-6), 20.91 and 20.72 (2 x -OCO$\underline{C}H_3$).

## References


[1] P. Levecque, D. Gammon, H.H Kinfe, P. Jacobs, D. De Vos, B. Sels, *Org. Biomol. Chem*. **2007**, 1800.

[2] C., Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, Verl. Chemie Weinheim, **1990**.

[3] J. Prandi, H.B. Kagan, H. Mimoun, *Tetrahedron Lett.*, **1986**, *27*, No. 23, 2617-2620.

[4] K. Kamata, K. Yonehara, Y. Sumida, K. Yamaguchi, S. Hikichi, N. Mizuno, *Science*, **2003**, *300*, 964-966.

[5] M. Chmielewski, I. Fokt, J. Grodner, G. Grynkiewicz, W. Szeja, *J. Carbohydr. Chem*. **1989**, *8*, 5, 735.

[6] S.K. Madhusudan, G. Agnihotri, D.S., Negi, A.K. Misra, *Carbohydr. Res.* **2005**, *340*, 1373.

[7] L.V. Dunkerton, N.K. Adair, J.M. Euske, K.T. Brady, P.D. Robinson, *J. Org. Chem.*, **1988**, *53*, 845-850.

[8] J.P. Lellouche, S. Koeller, *J. Org. Chem.* **2001**, *66*, 693.

[9] a. I.D. Blackburne, P.M. Fredericks, R.D. Guthrie, *Aust. J. Chem*. **1976**, *29*, 381; b. desilylation with 1,5 eq TBAF in THF (10 ml/mmol).

[10] R. Parker, F. Prechtl, S. Haremza, F. Meyer, V. Vill, G. Gesekus, WO 2004/002979 A2.

[11] a. M.L. Wolfrom, A. Thompson, *Methods in Carbohydrate Chemistry II: Reactions with carbohydrates* **1962**, 211. b. H.W. Fletcher, *Methods in Carbohydrate Chemistry II: Reactions with Carbohydrates* **1962**, 226. c. E Fischer, *Ber. Dtsch Chem Ges.* **1914**, 47, 196.

[12] D. Horton, J. H. Lauterbach, *Carbohydr. Res.*, **1975**, *43*, 9-33.

[13] C.H. Marzabadi, C.D. Spilling, *J. Org. Chem*., **1993**, *58*, 3761.

[14] a. F. Nicotra, L. Panza, F. Ronchetti, G. Russo, L. Toma, *J. Chem. Soc. Perkin Trans. I* **1987**, 1319; b. C. Mayato, R. L. Dorta, T. Vázquez, *Tetrahedron: Assymmetry* **2004**, *15*, 2385.

[15] Y. Vera-Aroyo, P. Borrachero, F. Cabrera-Escribano, A. T. Carmona, M. Gómez-Guillén, *Tetrahedron: Assymmetry* **2004**, *15*, 429.

[16] A. Roën, J.I. Padrón, J. T. Vázquez, *J. Org. Chem.* **2003**, *68*, 4615.

[17] K. C. Nicolaou, J. I. Trjillo, K. Chibale, *Tetrahedron* **1997**, *53*, 8751.

[18] M.-K. Chung, M. Schlaf, *J. Am. Chem. Soc.* **2005**, *127*, 18085.

[19] L. Pouységu, B. De Jéso, J.-C. Lartigue, M. Prétaud, M. Ratier, *Chem. Pharm. Bull.* **2002**, *50*, 1114.

[20] P. M. Collins, W. G. Overend, B. A. Rayner, *Carbohydr. Res.*, **1973**, *31*, 1-16.

[21] D. K. Watt, D. J. Brasch, D. S. Larsen, L. D. Melton, J. Simpson, *Carbohydr. Res.* **1996**, *285*, 1.

[22] C. Demetzos, A. L. Skaltsounis, *J. Nat. Prod.* **1994**, *57*, 1234.

[23] A. Goti, F. Cardona, G. Soldaini, C. Crestini, C. Fiani, R. Saladino, *Adv. Synth. Catal.* **2006**, *348*, 476.

[24] B. Helferich, D. Arndt, *Chem. Ber.*, **1967**, *100*, 2117.

[25] J. Beignet, J. Tiernan, C. H. Woo, B. M. Kariuki, L. R. Cox, *J. Org. Chem.* **2004**, *69*, 6341.

[26] O. J. Plante, E. R. Palmacci, P. H. Seeberger, *Org. Lett.*, **2002**, *2*, 3841; b. J. Stanek, A. Sele, R. Jaques, A. Rossi, *Helv. Chim. Acta*, **1972**, *55*, 434.

[27] A. B., Charette, N. Turcotte, B. Cote, *J. Carbohydr. Chem.*, **1994**, *13*, 421.

[28] J. E. Walace, L. R. Schroeder, *J. Chem. Soc, Perkin Trans. 2: Phys. Org. Chem. (1972-1999)*, **1977**, *6*, 795.

[29] Z. Kaluza, W. Fudong, C. Belzecki, M. Chmielewski, *Tetrahedron Lett.*, **1989**, *30*, 5171.

[30] A. Banaszek, A. Zamojski, *Pol. J. Chem.*, **1979**, *53*, 2029.

[31] P. Tiwari, A.K. Misra, *J. Org. Chem.* **2006**, *71*, 2911.