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Chapter 3

Stereoselectivity in the Lewis acid mediated reduction of ketofuranosides

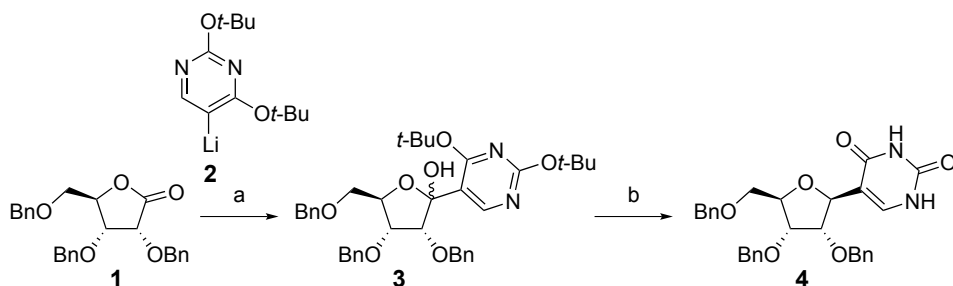
3.1 Introduction

C-glycosides are carbohydrates of which the aglycon is attached to the anomeric center through a carbon atom. Examples of naturally occurring C-glycosides are pseudouridine,¹⁻⁴ a C-nucleoside and the C-aryl glycoside dapagliflozin.⁵ These structures are close mimics of naturally occurring *O*- and *N*-glycosides, but are metabolically more stable, by virtue of the

stable carbon-carbon bond that connects the aglycon to the carbohydrate ring.¹⁻² As a result, many of these C-glycosides have appealing biological properties, ranging from antibiotic and antiviral activity to anticancer activity.^{1-3,6-7} For example, the C-glycoside analogue of the naturally occurring O-glycoside phlorizin, dapagliflozin, is currently being used for the treatment of type 2 diabetes.⁵

A commonly used method to synthesize C-glycosides entails the reaction of a glycosyl lactone with an alkyl or aryl nucleophile to give an intermediate glycosyl hemi-ketal that can be reduced under Lewis acidic conditions to provide the target compounds.^{1-2,8-15} In this process a new stereogenic center is created and control over the stereochemical course of the reaction is required to enable a productive and effective overall transformation. Several examples of this strategy have been reported in literature.^{1-2,8-15} Of note is the reduction of perbenzylated ribofuranose ketosides to provide the beta-linked products in a highly stereoselective fashion.¹⁵⁻¹⁶ Scheme 3.1 depicts a synthesis of pseudouridine that builds on the stereoselective reduction of perbenzylated riboketosides.¹⁷ Reaction of perbenzylated ribonolactone **1** with lithiated pyrimidine **2** gave the intermediate hemi-ketal **3** that was reduced with triethylsilane (TES) using $\text{BF}_3 \cdot \text{OEt}_2$ as the Lewis acid. After complete removal of the *tert*-butyl protecting groups with trifluoroacetic acid (TFA) the desired 1,2-*trans* compound **4** was obtained as a single anomer. The stereoselectivity in the reduction is striking because the nucleophile comes in *cis* with respect to the substituent at C2.

Scheme 3.1 The diastereoselective synthesis of protected pseudouridine.

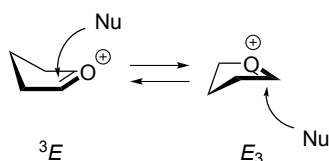


Reagents and conditions: (a) **2**, THF, -78 °C to -55 °C, 58%; (b) i) TES, $\text{BF}_3 \cdot \text{OEt}_2$, DCM, -78 °C to -10 °C; ii) TFA, -5 °C, 68% over 2 steps.

An explanation for the striking stereoselectivity can be found in the nature of the reactive intermediate in the reaction: the furanosyl oxocarbenium ion. In Chapter 2, a method to establish the relative stability of completely decorated furanosyl oxocarbenium ions is described. A complete survey of the energy landscape of the entire conformational space for the four possible pentoses (ribose, arabinose, xylose and lyxose) provided a clear

picture how the three ring substituents on the furanosyl oxocarbenium ion affect the stability, and therefore the reactivity in addition reactions. Given the enhanced stability of tertiary cations over their secondary counterparts it is likely that ketofuranosyl oxocarbenium ions are involved in the reduction of the C-furanosides described above. To investigate how the substituent at the anomeric center of ketofuranoses influences the stability of the corresponding oxocarbenium ions and the nucleophilic additions to these, this Chapter describes the reduction of the methyl and phenyl C-furanoses of all four possible pentoses (Figure 3.1). The conformational energy landscape of the intermediate oxocarbenium ions has been mapped to correlate the experimental outcome of the reduction reactions.

Chapter 2



This Chapter

R = alkyl or aryl

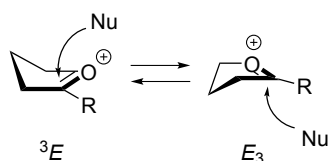
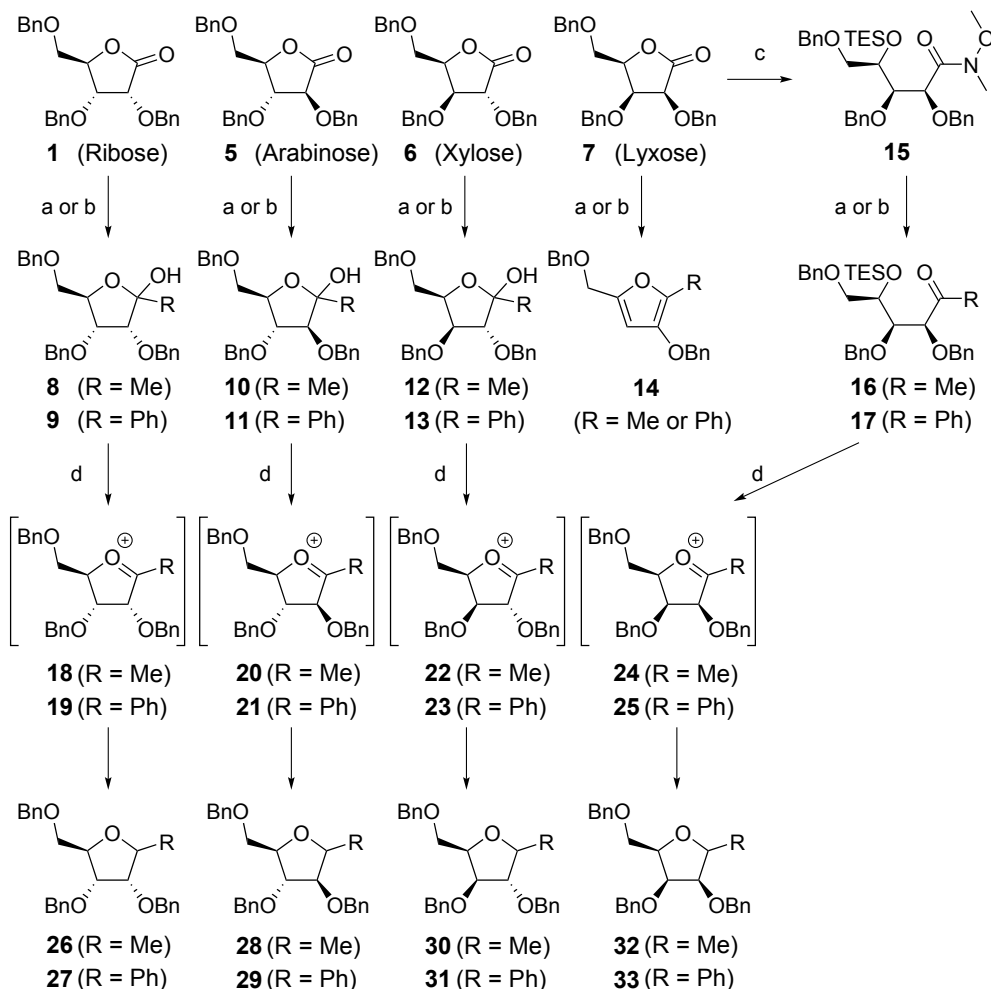


Figure 3.1 In chapter 2 furanosyl oxocarbenium ions were studied, this chapter investigates on ketofuranosyl oxocarbenium ions.

3.2 Results and discussion

The synthesis of the furanosyl lactols used in this study and the Lewis acid mediated reductions are depicted in Scheme 3.2. The ribose, arabinose and xylose derived perbenzylated methyl- and phenyl ketofuranose starting materials were prepared from the perbenzylated lactones. Ribonolactone **1**, arabinolactone **5** and xylonolactone **6** were reacted with methyl lithium or phenyl lithium to yield the methyl- and phenyl ketofuranoses that were directly used in the reduction step. Subjecting perbenzylated lyxonolactone **7** to methyl- or phenyl lithium did not yield the desired ketofuranoses but instead furan **14** was isolated as a result of a double β -elimination sequence. Because furan formation could not be suppressed it was decided to generate the lyxose oxocarbenium ions *in situ* in the projected reduction reactions from their linear precursors **16** and **17**. These were synthesized from Weinreb amide **15** that was generated from lactone **7** using *N,O*-dimethylhydroxylamine and trimethylaluminium. Reaction of the Weinreb amide **15** with methyl- or phenyl lithium delivered the open chain ketones of which the alcohol functions were capped as triethyl silyl ether.

Scheme 3.2 Synthesis of the perbenzylated ribo-, arabino, and xylofuranosyl hemi-ketals, the lyxose configured ketones and their ensuing reduction reactions.



Reagents and conditions: (a) MeLi, THF, -78 °C, **8**: 77%, **10**: 86%, **12**: 93%, **16**: 72%; (b) PhLi, THF, -78 °C, **9**: 48%, **11**: 70%, **13**: 91%, **17**: 60%; (c) i) *N,O*-dimethylhydroxylamine HCl, AlMe₃, THF, 0 °C; ii) TES-Cl, imidazole, THF, 0 °C, 73% over 2 steps; (d) TES, BF₃·OEt₂, DCM, -78 °C (see Table 3.1).

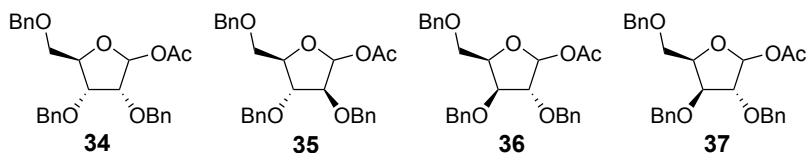


Figure 3.2 Reference aldose furanosyl donors from Chapter 2.

Table 3.1 Results of the Lewis acid mediated reduction.

Reaction conditions a

R = H

[D]TES, TMSOTf

DCM, -78 °C

Reaction conditions b

R = Me or Ph

TES, BF₃·OEt₂

DCM, -78 °C

Furanosyl donor	Product			1,2- <i>trans</i> : 1,2- <i>cis</i> ^[a,b]	Yield ^[c]
Ribose					
R = H: 34		R = D: 38	R = D:	2:>98	50%
R = Me: 8		R = Me: 26	R = Me:	>98:2	64%
R = Ph: 9		R = Ph: 27	R = Ph:	>98:2	78%
Arabinose					
R = H: 35		R = D: 39	R = D:	2:>98	62%
R = Me: 10		R = Me: 28	R = Me:	>98:2	83%
R = Ph: 11		R = Ph: 29	R = Ph:	85:15	65%
Xylose					
R = H: 36		R = D: 40	R = D:	15:85	40%
R = Me: 12		R = Me: 30	R = Me:	85:15	87%
R = Ph: 13		R = Ph: 31	R = Ph:	75:25	79%
Lyxose					
R = H: 37		R = D: 41	R = D:	2:>98	100%
R = Me: 16		R = Me: 32	R = Me:	>98:2	44%
R = Ph: 17		R = Ph: 33	R = Ph:	>98:2	60%

^[a]Ratio determined by ¹H NMR spectroscopy, stereochemistry was identified using ²J coupling-constants measured from HSQC-HECADE NMR spectra. ^[b]Addition of [D]TES to aldoses affords the *cis* product (reaction conditions **a**) while addition of TES in ketoses (reaction conditions **b**) gives the *trans* product (*cis* addition). ^[c]Yield of isolated furanosides after column chromatography.

The six ketofuranoses **8-13** and two linear chain lyxose-derived ketones **16** and **17** were subjected to a Lewis acid mediated reduction protocol using triethylsilane as reducing agent and boron trifluoride diethyletherate as Lewis acid in dichloromethane at -78 °C. The results of these reactions are summarized in Table 3.1, in combination with the results obtained in the experiments of the corresponding aldoses (in which furanosyl acetates were treated with [D]TES and TMSOTf, see Chapter 2). As can be seen in all cases preferentially the 1,2-*trans* C-furanosides were formed, corresponding to an attack of the hydride *cis* with respect to the substituent at C2. These results closely resemble those obtained for the aldoses **34-37**. In the case of ribose and lyxose, the reactions were completely stereoselective and the products were obtained as a single diastereomer, independent of the substituent on the anomeric position. In the arabinose series, both the

aldose **35** and methyl ketofuranose **10** yielded a single product, where the reduction of phenyl ketofuranose **11** proceeded with diminished stereopreference. The *xylo*-aldofuranose **36** and *xylo*-methyl ketofuranose **12** reacted with a similar preference for the 1,2-*cis* products,⁹ where the phenyl ketofuranose **13** again displayed the least stereoselectivity.

To account for the stereoselectivity observed in the reduction of the ketofuranoses and assess the influence of the substituent on the anomeric position on the intermediate oxocarbenium ions, the energy landscapes of the permethylated ketofuranosyl oxocarbenium ions **43-44**, **46-47**, **49-50**, and **52-53** (Figure 3.3) were calculated. To this extent the free energy surface (FES) mapping method was used, introduced by Rhoad et al.¹⁸ and adapted to interrogate the aldofuranosyl oxocarbenium ions as described in Chapter 2. In this method, the energy associated with the complete conformational space is calculated, and mapped on a spherical graph, the pseudorotational circle (see Chapter 2, figure 2.2b).¹⁹ Each conformation is described here by a phase angle (P), that defines the shape of the ring and the puckering amplitude (τ_m), that indicates how far out of the median plane the outlying atoms are positioned. The energy of 81 fixed ring conformers were calculated with Gaussian 03,²⁰ by employing the B3LYP density functional and the 6-311G** basis set, and these were corrected for the solvent (CH_2Cl_2) using the polarizable continuum model (PCM) function. Because rotation of the C4-C5 bond significantly influences the stability of the furanosyl oxocarbenium ions as described in Chapter 2, the FES of the oxocarbenium ions was scanned for the three individual *gg*, *gt* and *tg* C4-C5 rotamers (Chapter 2, figure 2.2c). Thus for each furanosyl oxocarbenium ion 243 (3x81) conformers were optimized and the associated energies determined.

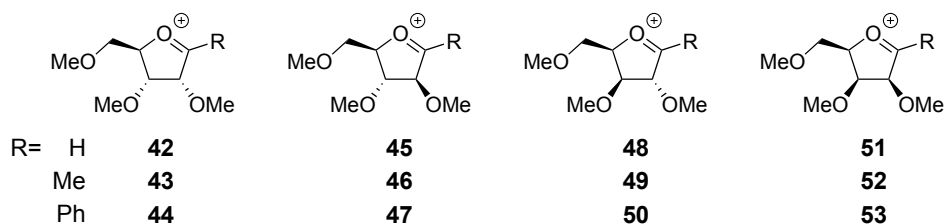


Figure 3.3 The investigated furanosyl oxocarbenium ions.

Ribose

In Figure 3.4, the oxocarbenium ion FES maps for the ribofuranosyl (**42**), methyl ribofuranosyl (**43**) and phenyl ribofuranosyl (**44**) oxocarbenium ions are graphed vertically over the different rows. In the columns, the *gg*, *gt*, *tg* and the global lowest FES maps are displayed from left to right. The global FES map is a combination of the absolute lowest energies of the *gg*, *gt* and *tg* in a single picture. From these maps it becomes clear that the ribofuranosyl E_3 oxocarbenium ion is highly preferred, independent of the nature of the anomeric substituent.²¹ In the E_3 oxocarbenium ions the C2 and C3 methyloxy groups adopt a pseudoequatorial and pseudoaxial position respectively, maximizing the stabilizing effect on the oxocarbenium ion. In all oxocarbenium ions the C4-C5 *gg* rotamer is more stable than its *gt* counterpart, which in turn is preferred over the *tg* conformer. Small differences can be observed for the maps of the different anomeric substituents. The energy maps of the methyl furanosyl oxocarbenium ion conformers are somewhat steeper than the map of its unsubstituted ribofuranosyl oxocarbenium ion congener. The phenyl ribofuranosyl oxocarbenium ion maps on the other hand show a decreased energy difference between the 3E *gg* and E_3 *gg* conformer. The energy difference is large enough (~ 2.7 kcal mol⁻¹) to account for the selectivity in the reaction.

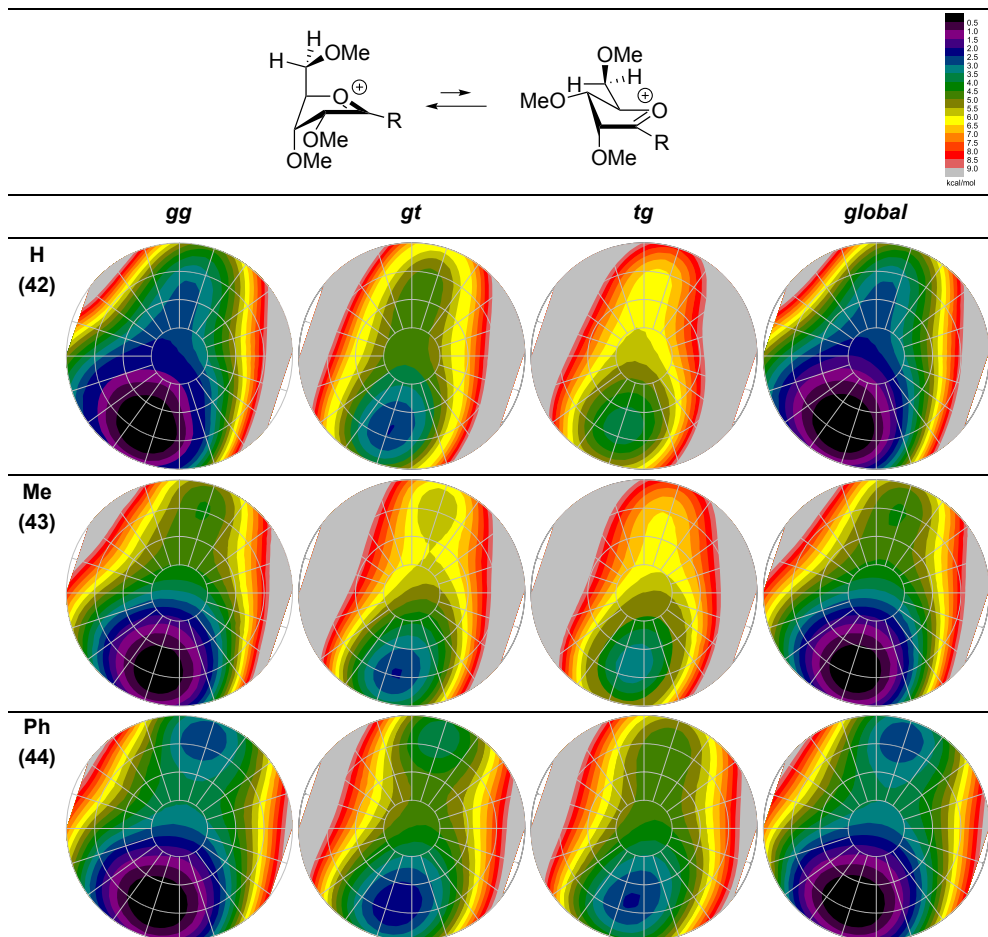


Figure 3.4 The *gg*, *gt*, *tg* and global FES maps of the ribofuranosyl oxocarbenium ions, mapped for the aldose (42), methyl ketose (43) and phenyl ketose (44).

A closer look at the structures associated with the energies in the FES maps of the methyl ketofuranose, shows that the methyl substituent is placed in an eclipsed conformation with respect to the plane of the oxocarbenium ion $[C=O^+]$ function (Figure 3.5a). This is surprising because the hyperconjugative stabilization of the carbocation would be most effective if the anomeric methyl group would position a proton perpendicular to the $C=O^+$ plane. To investigate this unexpected conformational finding, the energy associated with rotation of the methyl substituent around the C1-methyl bond was profiled. As can be seen in Figure 3.5c the eclipsed conformation is most stable where the perpendicular structure ($\phi = 90^\circ$) is $0.4 \text{ kcal mol}^{-1}$ higher in energy. This parallels the energy profile for the position of a methyl substituent next to an (uncharged) carbonyl group²² so apparently steric factors overrule the electronic preferences also in the furanosyl oxocarbenium ion case at hand. Indeed, if the methyl group would have provided a significant stabilization to

the oxocarbenium ion, the overall difference in energy between the different furanose ring conformers would be expected to be somewhat smaller, resulting in a more shallow FES. An analogous analysis for the phenyl ketofuranose reveals that the phenyl substituent is positioned parallel to the $C=O^+$ plane (Figure 3.5b) to allow for effective conjugative stabilization of the positive charge. In the E_3 conformation, this planar constellation does lead to an unfavorable 1,3-allyl interaction between the phenyl ring and the substituent on C2 (Figure 3.5d). This allyl strain can destabilize the E_3 conformer, thereby decreasing the energy difference with the 3E conformers, leading to flattening of the FES map for the phenyl keto furanosides.

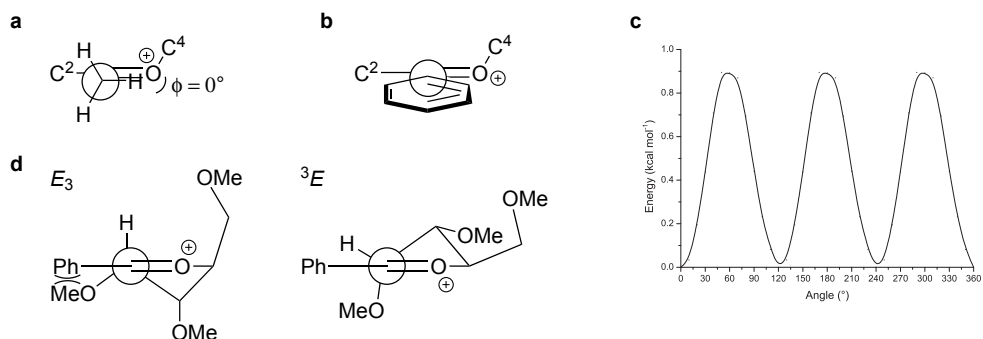


Figure 3.5 Conformation of the anomeric substituents relative to the oxocarbenium ion for a) methyl and b) phenyl. c) Rotation energy profile of the anomeric methyl substituent for the ribofuranosyl oxocarbenium ion. d) Steric interaction for phenyl substituted oxocarbenium ions, the figure reveals an unfavorable 1,3-allyl strain in the E_3 conformer.

The oxocarbenium ion FES maps for the non-substituted ($R = H$), the methyl- and phenyl substituted ribofuranosyl oxocarbenium ions show that a single envelope is preferred for all three furanoses, *i.e.* the 3E conformer. Inside attack of the nucleophile (TES) on this oxocarbenium ion conformer, leads to the formation of 1,2-*cis* products, providing an explanation for the stereoselectivity observed in the reaction of **34**, **8** and **9**.

Arabinose

The FES maps of the arabinofuranosyl oxocarbenium ions **46** and **47** are displayed next to those of arabinofuranosyl oxocarbenium ion **45** in Figure 3.6. From the global FES maps it becomes clear that the arabinosyl oxocarbenium ions preferentially take up an 3E conformation. The individual C4-C5 rotamer maps reveal that the *gg* conformers are the most stable. As with the arabino-aldose, the conformational preference of the arabinoketose oxocarbenium ions is less profound than the preference of the corresponding ribo-oxocarbenium ions. This can be accounted for by the fact that the C2 and C3 substituents cannot simultaneously adopt a most favorable orientation in either of

the envelope structures. In line with the FES maps for the different ribofuranosyl oxocarbenium ions, the FES maps for the methyl substituted arabinofuranose are somewhat steeper than the aldose while the maps for the phenyl substituted arabinofuranose are somewhat less steep. The global FES maps of the arabinofuranosyl oxocarbenium ions do not show a distinct two conformer model, instead they show a gradual increase in energy for the conformers around the ${}^3E - E_3$ axis (from 18° to 198°). From the flattened phenyl ketose oxocarbenium ion FES, one can expect an erosion of stereoselectivity in reactions involving this species. This is confirmed in the experiments: the *arabino* aldose and methyl ketofuranose both provide a single product upon reduction, where arabino phenyl ketofuranose gives an anomeric mixture with the major 1,2-*trans* product originating from a 3E oxocarbenium ion.

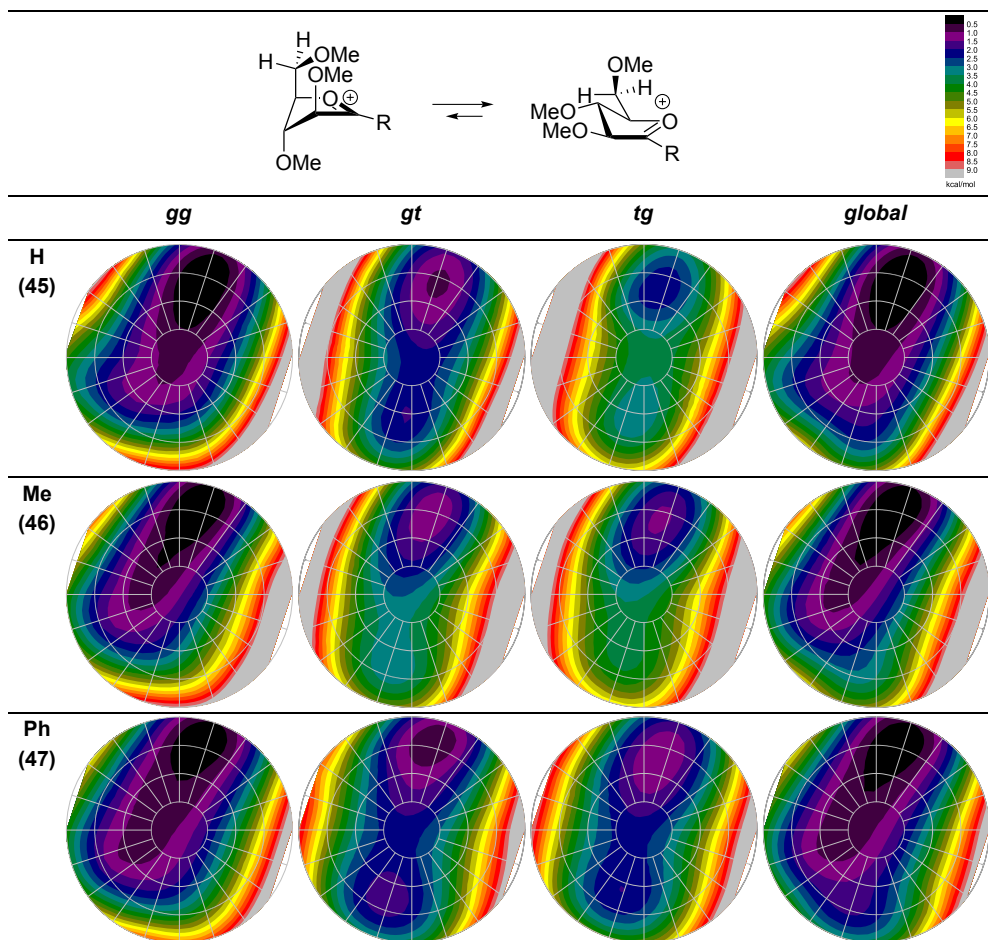


Figure 3.6 The *gg*, *gt*, *tg* and global FES maps of the arabinofuranosyl oxocarbenium ions, mapped for the aldose (45), methyl ketose (46) and phenyl ketose (47).

Xylose

The reductions of the xylofuranosides proceed with the least selectivity of the studied furanoses. The global xylofuranose oxocarbenium ion FES maps (Figure 3.7) show two energy minima, accounting for the formation of two anomers in the experiments. The major oxocarbenium ion conformer in the ketofuranoses is the *gg* E_3 envelope, where the minor 3E conformer places the C5 methoxy group in a *gt* position. In the aldose, the lowest energy conformation proved to be the 4T_3 , a structure that slightly deviates from the 3E - E_3 axis. This conformation optimally positions the C5-OMe over the furanosyl ring providing most stabilization. In the ketoxylofuranosyl FES maps, this effect is not observed. In line with the ribo- and arabino-case, the energy difference between the E_3 and 3E oxocarbenium ions for the methyl ketofuranose is somewhat larger than the difference observed in the aldofuranose and somewhat diminished for the phenyl furanosyl oxocarbenium ion. The larger energy difference between the E_3 and 3E methyl xylofuranosyl oxocarbenium ions is not reflected in the experimental results. Over the methyl ketofuranose, the phenyl ketose shows increased preference towards the 3E envelope, while still maintaining the E_3 as the major conformer but decreasing the energy difference between the two envelopes. The more shallow FES map for the phenyl xylofuranosyl oxocarbenium ion is reflected in the diminished stereoselectivity observed in the reduction of phenyl ketoside **13**.

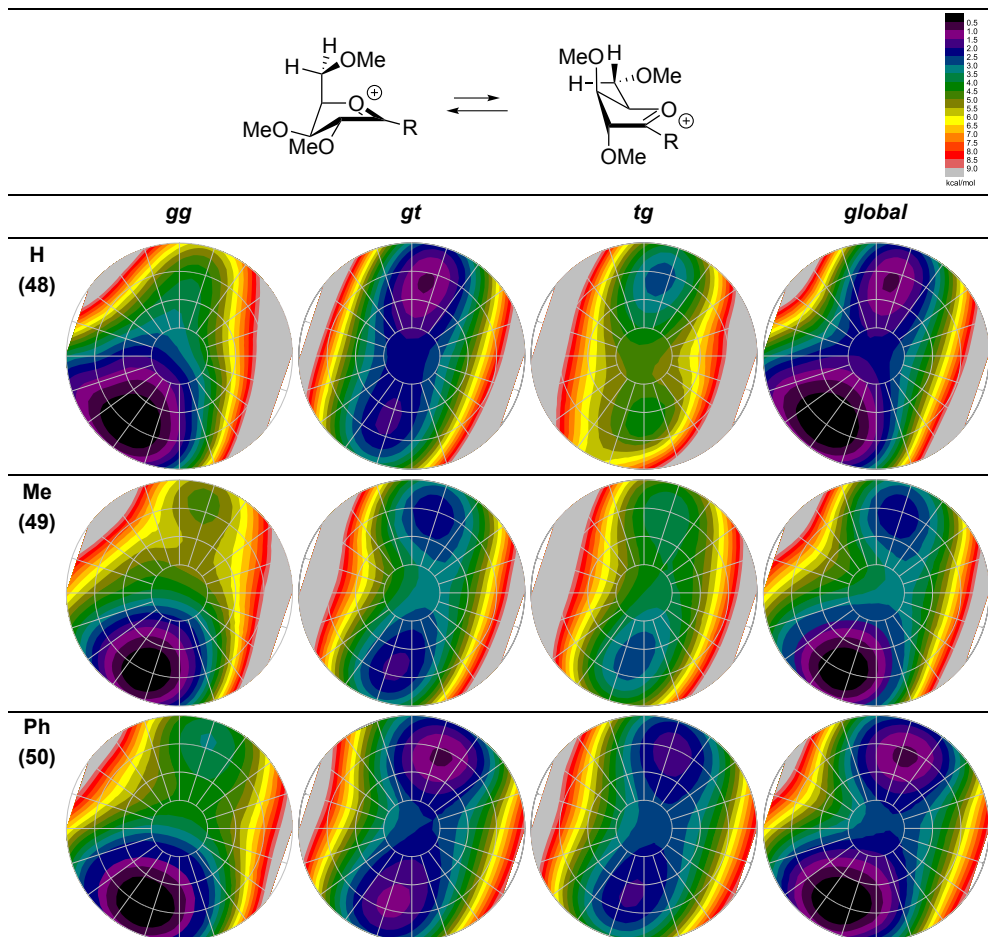


Figure 3.7 The *gg*, *gt*, *tg* and *global* FES maps of the xylofuranosyl oxocarbenium ions, mapped for the aldose (48), methyl ketose (49) and phenyl ketose (50).

Lyxose

In Figure 3.8, the FES maps for the lyxofuranosyl oxocarbenium ions are mapped for the aldose (51), methyl ketose (52) and phenyl ketose (53). Chapter 2 described the strong preference for the 3E lyxofuranosyl oxocarbenium ion envelope and the associated remarkable stereoselectivity in additions on this intermediate (*cis* with respect to *all* ring substituents). This strong conformational preference is maintained in the ketofuranosyl oxocarbenium ions as shown in the *global* FES maps. In the 3E oxocarbenium ion, lyxofuranose places the C2 substituent in the preferred pseudoequatorial position and the C3 substituent in a pseudoaxial position to allow stabilization of the positive charge at the anomeric position. The individual C4-C5 rotamer FES maps show a pseudoequatorial C5 *gt*, avoiding a sterically and electronically unfavorable interaction with the axial C3

substituent. Inside attack on the lyxofuranosyl 3E oxocarbenium ion leads to the all-*cis* addition product in both the aldose and ketoses.

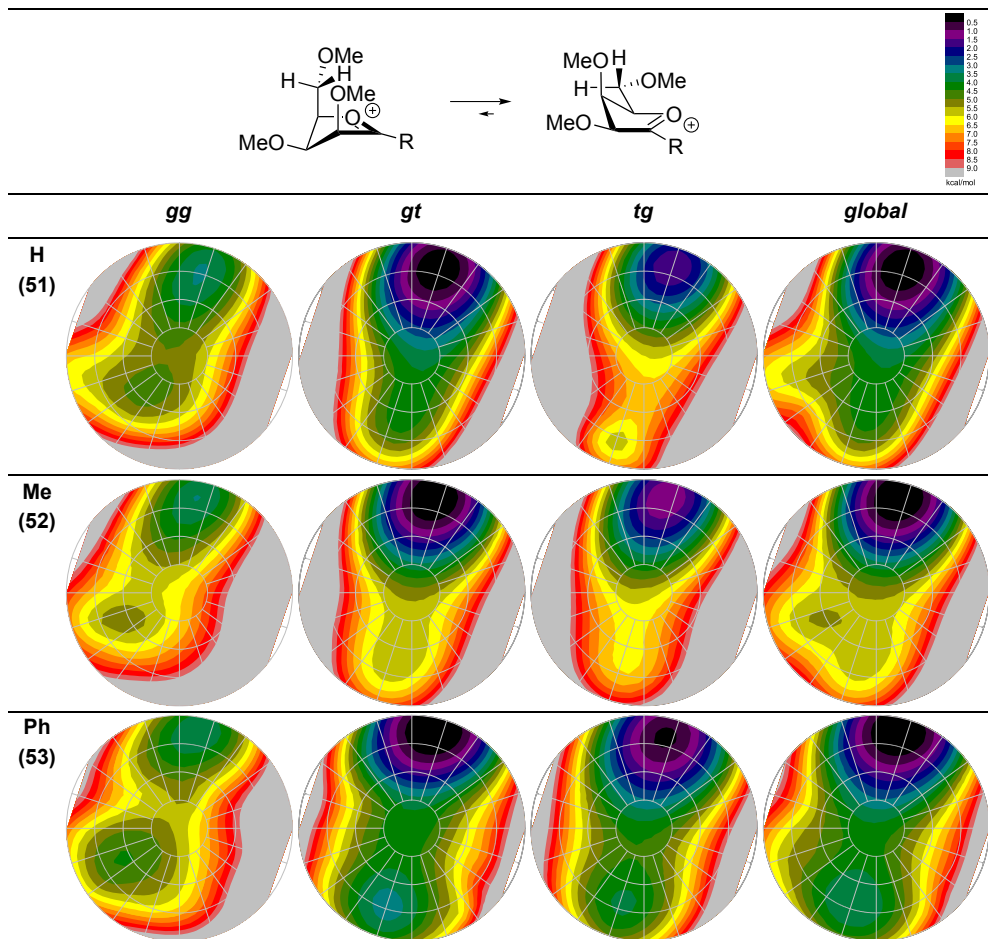


Figure 3.8 The *gg*, *gt*, *tg* and global FES maps of the lyxofuranosyl oxocarbenium ions, mapped for the aldose (51), methyl ketose (52) and phenyl ketose (53).

3.3 Conclusion

Overall it can be concluded that the nature of the anomeric substituent on the studied furanosides has a small effect on the stereoselectivity of the studied reduction reactions. The detailed calculations show that the energy differences between the various oxocarbenium ion conformers are mostly maintained, independent of the nature of the anomeric appendage. Small changes are observed for the methyl/phenyl ketoses with respect to the aldoses. The anomeric methyl substituent makes the preference for one of the two envelopes stronger, where the phenyl substituent leads to smaller energy

differences. This latter effect can be partially attributed to the destabilizing 1,3-allyl strain between the anomeric phenyl ring positioned parallel to the $C=O^+$ plane and the pseudoequatorial C2 substituent. Also the general conjugative stabilization of the oxocarbenium by the phenyl ring can lead to diminished relative energies for the different oxocarbenium ion conformers. The differences in energy between the different oxocarbenium ions provide a reliable prediction for the stereoselectivity of reactions on these intermediates using the inside attack model. Notably, substitution reactions at the anomeric center of all furanosides proceed with great stereoselectivity to provide the 1,2-*cis* addition products, independent of the substitution pattern on the carbohydrate ring and the anomeric center.

Experimental section

Calculations. In all calculations, methyl ethers were used because of their reduced calculation costs over benzyl ethers. All calculations were performed with DFT *ab initio* calculations with the B3LYP model. The starting conformer for the Free Energy Surface (FES) was optimized by starting from a conformer distribution search option included in the Spartan 04²³ program in gas phase at 6-31G* as basis set. All generated geometries were optimized with Gaussian 03²⁰ at 6-311G**, their zero-point energy (ZPE) corrections calculated, and further optimized with incorporated polarizable continuum model (PCM) to correct for solvation in dichloromethane. The geometry with the lowest, ZPE corrected, solvated free energy was selected as the starting point for the FES. Two dihedral angles of the five-membered ring were constrained, namely C4-O4-C1-C2 (τ_o , θ_3) and C1-C2-C3-C4 (τ_z , θ_o), with angles from -40° up to 40° over 9 steps (10° per step) giving a total of 81 conformers and dictating the entire pseudo rotational space within a maximum amplitude (τ_m) of 40° . All other internal coordinates were unconstrained. The geometries were optimized, their ZPE calculated and corrected for solvation with Gaussian 03 at 6-311G** as above. The FES was visualized as polar contour plot through the Origin 8.5 graphing software by putting the phase angle (P) as θ , the amplitude (τ_m) at r and the energy, corrected for ZPE and optimized in solvent, at the Z-axis. To interrogate all rotamers of the C5 substituent, the starting conformer was modified by rotating the O4-C4-C5-O5 dihedral to each of the three staggered configurations (gauche-gauche = -65° , gauche-trans = 65° , trans-gauche = 175°) and then generating the FES through the above mentioned method generating a total of 243 optimized geometries. These three FESs were graphed individually and in a combined plot by comparing the corrected free energies, and for each point selecting the geometry of lowest energy from the three entities.

Synthesis

General. The Lewis acid mediated reductions of arabinofuranosyl and ribofuranosyl ketoses have been published earlier by van Delft.¹⁷ Chemicals were purchased from Acros Organics and Sigma Aldrich and used as received. All non-commercially available starting materials were synthesized in Chapter 2. THF (Biosolve) was distilled over $LiAlH_4$ and dichloromethane (Biosolve, amylene stabilized) was distilled over P_2O_5 before being treated and stored over activated 4 Å molecular sieves. All reactions were performed at ambient temperature under an argon atmosphere unless stated otherwise. Reactions were monitored by TLC on Kieselgel 60 F254 (Merck). Compounds were visualized by using UV light (254 nm) or applying a solution of $(NH_4)_6Mo_7O_{24} \cdot 4 H_2O$ 25 g/L, $(NH_4)_4Ce(SO_4)_4 \cdot 2 H_2O$ 10 g/L, 10% H_2SO_4 in H_2O followed by charring ($\pm 150^\circ C$). 1H - and ^{13}C -NMR spectra were recorded on a Bruker AV-400 instrument. Chemical shifts (δ) of 1H and ^{13}C spectra are relative to

tetramethylsilane. NMR peak assignments were made using COSY and HSQC experiments, where applicable NOESY and HSQC-HECADE²⁴ experiments were used to determine the stereochemical configuration.

2,3,5-Tri-O-benzyl-D-xylo-1,4-lactone (6). 2,3,5-Tri-O-benzyl-D-xylofuranose (6.9 g, 16.4 mmol) was dissolved in DMSO (25 ml, 345 mmol). Ac₂O (16 ml, 172 mmol) was added and the reaction was stirred at room temperature for 44 hours after which TLC analysis indicated full conversion. The reaction mixture was quenched with ice water, extracted with Et₂O, the organic layer washed with H₂O and brine, dried over MgSO₄, filtered and concentrated.

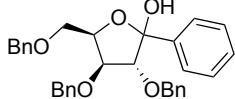
The residue was purified by silica gel column chromatography (7.5%-12.5% EtOAc/petroleum ether) to provide the title compound (6.5 g, 15.5 mmol, 95 % yield) as a white solid which was recrystallized from MeOH to provide an analytical sample. *R*_f = 0.80 (25/75 EtOAc/petroleum ether). ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.17 (m, 15H, CH_{Ar} Bn), 5.04 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.69 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.65 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.60 – 4.48 (m, 5H, C-4, C-2, 3xCHH Bn), 4.36 (t, *J* = 7.1 Hz, 1H, C-2), 3.76 (dd, *J* = 10.9, 2.8 Hz, 1H, C-5a), 3.70 (dd, *J* = 10.9, 3.2 Hz, 1H, C-5b). ¹³C NMR (101 MHz, CDCl₃) δ 173.4 (C=O), 137.7, 137.4, 137.2 (C_q Bn), 128.6, 128.6, 128.5, 128.4, 128.2, 128.2, 127.8, 127.8, 127.7 (CH_{Ar} Bn), 79.5 (C-3), 77.4 (C-2, C-4), 73.7, 72.8, 72.7 (3xCH₂ Bn), 67.2 (C-5). [α]_D²⁰ = 91.9° (c = 1, CHCl₃). IR (neat): 608, 625, 646, 671, 698, 743, 799, 835, 864, 912, 930, 972, 993, 1024, 1070, 1088, 1105, 1128, 1188, 1213, 1242, 1285, 1344, 1377, 1393, 1454, 1466, 1497, 1732, 1769, 2872, 2909. HR-MS: [M+H]⁺ Calculated for C₂₆H₂₆O₅: 419.18530; found 419.18545.

2,3,5-tri-O-benzyl-1-methyl-D-xylofuranose (12). 2,3,5-Tri-O-benzyl-D-xylo-1,4-lactone (**6**, 252 mg, 0.60 mmol), three times coevaporated with toluene, was dissolved in anhydrous THF (2.5 ml) and cooled to -78 °C. Methyl lithium (0.41 ml, 0.66 mmol, 1.6 M in Et₂O) was added slowly. After 3 hours TLC analysis indicated full conversion. The reaction was quenched by addition of NH₄Cl (2.5 ml, sat. aq.), and the mixture was allowed to warm to room temperature. The suspension was extracted 3 times with EtOAc and the combined organic layers washed with brine, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (20%-30% EtOAc/pentane) to provide the title compound (243 mg, 0.56 mmol, 93 % yield) as colorless oil which was used directly in the next step. *R*_f = 0.55 (25/75 EtOAc/pentane).

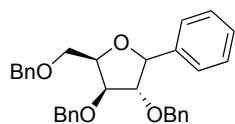
2,3,5-Tri-O-benzyl-1-deoxy-α/β-1-methyl-D-xylofuranose (30). 2,3,5-tri-O-benzyl-1-methyl-D-xylofuranose (**12**, 242 mg, 0.56 mmol) three times coevaporated with toluene, was dissolved in anhydrous DCM (7.2 ml) and cooled to -78 °C. Triethylsilane (116 μl, 0.73 mmol) was added before drop wise addition of BF₃·OEt₂ (92 μl, 0.73 mmol). The reaction was stirred for 6 days at -78 °C after which TLC analysis indicated near full conversion, the reaction was quenched with NaHCO₃ (8 ml, sat. aq.), warmed to room temperature and the suspension extracted with EtOAc (3x). The combined organic layers were washed with H₂O and brine, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (8%-12% EtOAc/pentane) to provide an anomeric mixture (α/β = 15:85) of the title compound (203 mg, 0.49 mmol, 87 % yield) as a colorless oil. *R*_f = 0.80 (20/80 EtOAc/Petroleum ether). β-Anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.21 (m, 15H, CH_{Ar} Bn), 4.63 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.56 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.54 – 4.43 (m, 4H, 4xCHH Bn), 4.18 (ddd, *J* = 6.5, 5.3, 4.1 Hz, 1H, C-4), 3.99 – 3.91 (m, 2H, C-1, C-3), 3.81 – 3.76 (m, 1H, C-5a), 3.73 (dd, *J* = 10.0, 6.5 Hz, 1H, C-5b), 3.65 (dd, *J* = 4.1, 1.3 Hz, 1H, C-2), 1.35 (d, *J* = 6.5 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 138.3, 138.1, 137.9 (3xC_q Bn), 128.6, 128.5, 128.5, 128.4, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6 (CH_{Ar} Bn), 88.7 (C-2), 83.5 (C-3), 80.1 (C-4), 79.9 (C-1), 73.6, 71.8, 71.8 (3xCH₂ Bn), 68.6 (C-5), 19.9 (CH₃). α-Anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.21 (m, 15H, CH_{Ar} Bn), 4.62 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.57 – 4.44 (m, 5H, 5xCHH Bn), 4.40 – 4.34 (m, 1H, C-4), 4.32 – 4.25 (m, 1H, C-1), 4.04 (dd, *J* = 4.3, 1.3 Hz, 1H, C-3), 3.78 (dd, *J* = 9.9, 5.3 Hz, 1H, C-2), 3.73 – 3.64 (m, 2H, C-5), 1.27 (d, *J* = 7.0 Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 138.2, 138.1 (3xC_q Bn), 128.6, 128.4, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6 (CH_{Ar} Bn), 82.7 (C-2), 82.1 (C-3), 78.5 (C-4), 76.2 (C-1), 73.5,

72.4, 72.0 (3xCH₂ Bn), 68.7 (C-5), 14.6 (CH₃). IR (neat): 606, 640, 673, 696, 733, 799, 849, 910, 930, 970, 993, 1026, 1069, 1088, 1190, 1206, 1312, 1344, 1393, 1454, 1497, 1771, 2862, 2913. HR-MS: [M+H]⁺ Calculated for C₂₇H₃₀O₄: 419.22169; found: 419.22142.

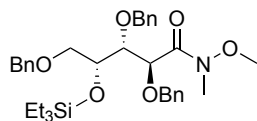
2,3,5-tri-*O*-benzyl-1-phenyl-D-xylofuranose (13). Bromobenzene (76 μ l, 0.70 mmol) was dissolved in THF (1.5 ml) and cooled to -78 °C. *n*-Butyl lithium (0.45 ml, 0.70 mmol, 1.6 M in hexanes) was added slowly and the mixture was stirred for 30 minutes. Three times with toluene coevaporated 2,3,5-Tri-*O*-benzyl-D-xylono-1,4-lactone (**6**, 230 mg, 0.55 mmol) in anhydrous THF (1.5 ml) was added drop wise. After 2 hours TLC analysis indicated full conversion, the reaction was quenched with NH₄Cl (3 ml, sat. aq.), and the suspension extracted with EtOAc. The organic layer was washed with H₂O and brine, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (10%-14% EtOAc/pentane) to provide the title compound (250 mg, 0.50 mmol, 91 % yield) as a colorless oil which was used directly in the next step. *R*_f = 0.55 (20/80 EtOAc/pentane).



2,3,5-Tri-*O*-benzyl-1-deoxy- α/β -1-phenyl-D-xylofuranose (31). 2,3,5-tri-*O*-benzyl-1-phenyl-D-xylofuranose (**13**, 238 mg, 0.48 mmol), three times coevaporated with toluene, was dissolved in anhydrous DCM (6.9 ml) and cooled to -78 °C. Triethylsilane (103 μ l, 0.65 mmol) was added followed by drop wise addition of BF₃·OEt₂ (82 μ l, 0.65 mmol). After 3 days of stirring at this temperature, TLC analysis indicated full conversion. The reaction was quenched with NaHCO₃ (7 ml, sat. aq.), allowed to warm to room temperature and the suspension extracted with EtOAc (3x). The combined organic layers were washed with H₂O and brine, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (6-8% EtOAc/pentane) to provide an anomeric mixture (α/β = 25:75) of the title compound (183 mg, 0.38 mmol, 79% yield) as a colorless oil. *R*_f = 0.76 (20/80 EtOAc/petroleum ether). β -Anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.49 – 7.11 (m, 20H, CH_{Ar} Ph, CH_{Ar} Bn), 4.85 (d, *J* = 4.0 Hz, 1H, C-1), 4.67 – 4.39 (m, 6H, 6xCHH Bn), 4.40 – 4.35 (m, 1H, C-4), 4.09 – 4.05 (m, 1H, C-3), 3.99 (dd, *J* = 4.1, 1.4 Hz, 1H, C-2), 3.92 (dd, *J* = 10.0, 5.3 Hz, 1H, C-5a), 3.87 (dd, *J* = 9.9, 6.2 Hz, 1H, C-5b). ¹³C NMR (101 MHz, CDCl₃) δ 140.7 (C_q Ph), 138.3, 138.0, 137.7 (C_q Bn), 128.5, 128.5, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.5, 126.7 (CH_{Ar} Ph, CH_{Ar} Bn), 89.6 (C-2), 86.1 (C-1), 83.3 (C-3), 80.7 (C-4), 73.6, 72.0, 71.5 (3xCH₂ Bn), 68.4 (C-5). α -Anomer: ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.13 (m, 18H, CH_{Ar} Ph, CH_{Ar} Bn), 6.93 – 6.86 (m, 2H, CH_{Ar} Ph), 5.21 (d, *J* = 3.5 Hz, 1H, C-1), 4.67 – 4.60 (m, 1H, C-4), 4.59 – 4.39 (m, 4H, 4xCHH Bn), 4.13 (dd, *J* = 4.0, 1.2 Hz, 1H, C-2), 4.10 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.04 – 4.00 (m, 1H, CHH Bn), 3.96 – 3.93 (m, 1H, C-3), 3.84 – 3.75 (m, 2H, C-5). ¹³C NMR (101 MHz, CDCl₃) δ 140.7 (C_q Ph), 138.4, 138.0, 137.8 (C_q Bn), 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.6, 127.5, 127.5 (CH_{Ar} Ph, CH_{Ar} Bn), 83.2 (C-3), 82.8 (C-2), 82.5 (C-1), 73.5, 72.5, 72.1 (3xCH₂ Bn), 68.6 (C-5). IR (neat): 604, 646, 694, 731, 887, 908, 951, 986, 1003, 1026, 1067, 1206, 1252, 1308, 1358, 1452, 1495, 2860, 2918, 3028. HR-MS: [M+H]⁺ Calculated for C₃₂H₃₂O₄: 481.23734; found: 481.23748.

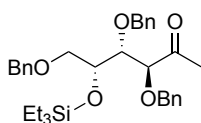


2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-D-lyxonic *N,O*-dimethyl hydroxylamide (15). *N,O*-dimethylhydroxylamine-HCl (506 mg, 5.2 mmol), three times coevaporated with toluene, was dissolved in anhydrous THF (8 ml) and cooled to 0 °C. AlMe₃ (2M in toluene, 2.4 ml, 4.8 mmol) was added slowly and stirred for 30 minutes. 2,3,5-Tri-*O*-benzyl-D-lyxono-1,4-lactone (**7**, 1.0 g, 2.40 mmol) in anhydrous THF (8 ml) was slowly added, stirred for 5 minutes and allowed to warm to room temperature. After 1.5 hours, TLC analysis indicated full conversion. The reaction was quenched using EtOAc and the mixture washed with potassium sodium tartrate (sat. aq.), the aqueous layer was extracted with EtOAc and the combined organic layers washed with brine, dried over MgSO₄, filtered and concentrated. The crude 2,3,5-tri-*O*-benzyl-D-lyxonic *N,O*-dimethyl hydroxylamide, three times coevaporated with toluene, was put under argon, dissolved in



anhydrous THF (12 ml) and cooled to 0 °C. Imidazole (245 mg, 3.6 mmol) was added followed by drop wise addition of triethylchlorosilane (1.0 ml, 6.0 mmol) and the mixture stirred for 5 minutes at 0 °C after which the mixture was allowed to warm to room temperature. After overnight stirring, TLC analysis indicated full conversion and the reaction was quenched with NaHCO₃ (sat. aq.). The suspension was extracted with Et₂O and the combined organic layers were washed with brine, the combined aqueous layers were extracted with Et₂O and the combined organic layers dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (14%-16% EtOAc/pentane) to provide the title compound (1.0 g, 1.8 mmol, 73%) as a colorless oil. R_f = 0.60 (20/80 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.17 (m, 15H, CH_{Ar} Bn), 4.88 (d, J = 8.8 Hz, 1H, C-2), 4.56 – 4.43 (m, 5H, CHH Bn), 4.40 (d, J = 11.9 Hz, 1H, 5xCHH Bn), 4.25 – 4.18 (m, 1H, C-4), 3.95 (dd, J = 8.8, 2.2 Hz, 1H, C-3), 3.61 – 3.46 (m, 5H, CH₃N, C-5), 3.13 (s, 3H, CH₃O), 0.92 (t, J = 7.9 Hz, 9H, 3xCH₃ TES), 0.67 – 0.49 (m, 6H, 3xCH₂ TES). ¹³C NMR (101 MHz, CDCl₃) δ 172.3 (C=O), 138.7, 138.2, 137.7 (C_q Bn), 128.4, 128.3, 128.2, 127.8, 127.8, 127.6, 127.5 (CH_{Ar} Bn), 80.0 (C-3), 74.9, 73.3 (2xCH₂ Bn), 72.7 (C-2), 71.8 (CH₂ Bn), 71.6 (C-5), 70.8 (C-4), 61.7 (NCH₃), 32.1 (OCH₃), 7.1 (CH₃ TES), 5.4 (CH₂ TES). IR (neat): 613, 694, 731, 787, 956, 999, 1076, 1090, 1142, 1238, 1454, 1663, 2874, 2951. $[\alpha]^{20}_D$: -3.1 (c = 1, CHCl₃). HRMS: [M+H]⁺ Calculated for C₃₄H₄₇NO₆Si: 594.32454; found: 594.32451.

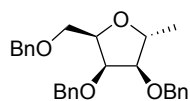
2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-1-methyl-D-lyxose (16). 2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-D-lyxonic *N,O*-



dimethyl hydroxylamide (**15**, 416 mg, 0.7 mmol), three times coevaporated with toluene, was dissolved in anhydrous THF (4 ml) and cooled to -78 °C. Methyl lithium (0.70 ml, 1.12 mmol, 1.6 M in Et₂O) was added drop wise. After 5 hours of stirring at this temperature, TLC analysis indicated complete conversion. The reaction was quenched with NH₄Cl (sat. aq.), the suspension extracted with Et₂O, the organic layer

washed with water, the combined aqueous layers extracted with Et₂O, the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (4%-5% EtOAc/pentane) yielding the title compound (278 mg, 0.51 mmol, 72% yield) as a colorless oil. R_f = 0.7 (10/90 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.23 (m, 15H, CH_{Ar} Bn), 4.64 (d, J = 11.7 Hz, 1H, CHH Bn), 4.60 (d, J = 11.7 Hz, 1H, CHH Bn), 4.55 (d, J = 11.9 Hz, 1H, CHH Bn), 4.51 (d, J = 12.4 Hz, 1H, CHH Bn), 4.48 (d, J = 12.1 Hz, 1H, CHH Bn), 4.44 (d, J = 12.0 Hz, 1H, CHH Bn), 4.11 – 4.07 (m, 1H, C-4), 4.07 (d, J = 3.7 Hz, 1H, C-2), 3.94 (dd, J = 5.6, 3.7 Hz, 1H, C-3), 3.68 (dd, J = 10.3, 3.7 Hz, 1H, C-5a), 3.64 (dd, J = 10.3, 5.6 Hz, 1H, C-5b), 2.17 (s, 3H, COCH₃), 0.89 (t, J = 7.9 Hz, 9H, CH₃ TES), 0.61 – 0.48 (m, 6H, CH₂ TES). ¹³C NMR (101 MHz, CDCl₃) δ 210.0 (C=O), 138.3, 138.3, 137.7 (C_q Bn), 128.5, 128.4, 127.9, 127.8, 127.7, 127.6 (CH_{Ar} Bn), 84.6 (C-2), 81.8 (C-3), 73.6, 73.3, 72.9 (3xCH₂ Bn), 72.6 (C-4), 72.3 (C-5), 27.9 (C=OCH₃), 7.0 (CH₃ TES), 4.9 (CH₂ TES). IR (neat): 606, 694, 731, 783, 908, 980, 1003, 1026, 1074, 1088, 1207, 1283, 1350, 1414, 1454, 1715, 2874, 2911, 2951. $[\alpha]^{20}_D$: 0.8 (c = 1, CHCl₃). HRMS: [M+H]⁺ Calculated for C₃₃H₄₄O₅Si: 549.30308; found: 549.30337.

2,3,5-Tri-*O*-benzyl-1-deoxy-α-1-methyl-D-lyxofuranose (32). 2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-1-methyl-D-

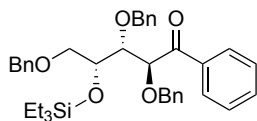


lyxose (**16**, 137 mg, 0.25 mmol), three times coevaporated with toluene, was dissolved in anhydrous DCM (3.1 ml) and cooled to -78 °C. Triethylsilane (52 μl, 0.33 mmol) was added before drop wise addition of BF₃·OEt₂ (82 μl, 0.65 mmol). After 1 week of stirring at this temperature TLC analysis showed partial conversion, with the remainder still

being the starting material. The reaction was quenched with NaHCO₃ (sat. aq.), allowed to warm to room temperature and extracted with Et₂O, the organic layer was washed with water and brine, the combined aqueous layers extracted with Et₂O, the combined organic layers dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (8-13% EtOAc/pentane) yielding the title compound (46 mg, 0.11 mmol, 44% yield) as a single diastereomer. R_f = 0.55 (20/80 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.24 (m, 15H, CH_{Ar} Bn), 4.72 (d, J = 11.8 Hz, 1H, CHH Bn), 4.64 – 4.56 (m, 3H, 3xCHH Bn), 4.50 (d, J = 11.9 Hz, 1H, CHH Bn), 4.47 (d, J = 12.0 Hz, 1H, CHH Bn), 4.27 – 4.21 (m, 1H, C-4), 4.19 – 4.11 (m, 1H, C-1), 4.08 (t, J = 4.2 Hz, 1H, C-4), 3.74 (dd, J = 9.8, 5.8 Hz, 1H, C-5a), 3.67 (dd, J = 9.7, 6.7 Hz, 1H, C-5b), 3.55

(dd, $J = 7.7, 4.2$ Hz, 1H, C-2), 1.24 (d, $J = 6.3$ Hz, 3H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 138.5, 138.3, 138.0 (C_q Bn), 128.5, 128.4, 128.4, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7 (CH_{Ar} Bn), 85.1 (C-2), 78.6 (C-4), 77.2 (C-3), 75.6 (C-1), 73.6, 73.5, 72.7 (CH₂ Bn), 69.1 (C-5), 19.4 (CH₃). $[\alpha]_D^{20} = 26.6^\circ$ ($c = 1.1$, CHCl₃). IR (neat): 696, 735, 810, 845, 914, 932, 1003, 1026, 1061, 1086, 1146, 1206, 1273, 1312, 1344, 1366, 1452, 1497, 1722, 2866, 2924, 2968. HR-MS: [M+H⁺] Calculated for C₂₇H₃₀O₄: 419.22169; found: 419.22149.

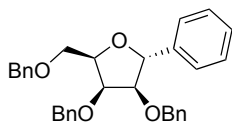
2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-1-phenyl-D-lyxose (17). Bromobenzene (76 μ l, 0.72 mmol) was dissolved in



anhydrous THF (1 ml) and cooled to -78°C . *n*-Butyl lithium (0.45 ml, 0.72 mmol, 1.6 M in hexanes) was added drop wise and the mixture was stirred at this temperature for 30 minutes. 2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-D-lyxonic *N*,*O*-dimethyl hydroxylamide (**15**, 342 mg, 0.58 mmol), three times coevaporated with toluene, in dry THF (4 ml) was added slowly and the reaction mixture

stirred for 18 hours. TLC analysis indicated full consumption of the starting material and the reaction was quenched with NH₄Cl (sat. aq.), the suspension was extracted with Et₂O, the organic layer was washed with water and brine, the combined aqueous layers were extracted with Et₂O, the combined organic layers dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (4%-7% EtOAc/pentane) to provide the title compound (210 mg, 0.34 mmol, 60% yield) as a colorless oil. $R_f = 0.80$ (10/90 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃) δ 8.06 – 7.98 (m, 2H, *m*-CH_{Ar} Ph), 7.53 – 7.45 (m, 1H, *p*-CH_{Ar} Ph), 7.39 – 7.33 (m, 2H, *o*-CH_{Ar} Ph), 7.32 – 7.21 (m, 10H, CH_{Ar} Bn), 7.16 – 7.09 (m, 3H, CH_{Ar} Bn), 6.95 – 6.89 (m, 2H, CH_{Ar} Bn), 5.14 (d, $J = 7.4$ Hz, 1H, C-2), 4.56 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.45 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.42 – 4.34 (m, 3H, 3xCHH Bn), 4.29 (d, $J = 11.4$ Hz, 1H, CHH Bn), 4.27 – 4.20 (m, 1H, C-4), 4.04 (dd, $J = 7.4, 3.1$ Hz, 1H, C-3), 3.59 – 3.50 (m, 2H, C-5), 0.91 (t, $J = 7.9$ Hz, 9H, CH₃ TES), 0.63 – 0.52 (m, 6H, CH₂ TES). ¹³C NMR (101 MHz, CDCl₃) δ 200.4 (C=O), 138.1, 137.8, 137.5, 137.1 (C_q Ph, C_q Bn), 133.2 (*p*-CH_{Ar} Ph), 129.0 (*m*-CH_{Ar} Ph), 128.4, 128.3, 128.1, 128.0, 127.8, 127.8, 127.6, 127.4 (CH_{Ar} Bn, *o*-CH_{Ar} Ph), 80.9 (C-3), 79.7 (C-2), 74.2, 73.2, 72.0 (CH₂ Bn), 71.7 (C-4), 71.5 (C-5), 7.1 (CH₃ TES), 5.2 (CH₂ TES). IR (neat): 652, 694, 735, 802, 824, 845, 812, 1001, 1026, 1070, 1090, 1177, 1207, 1248, 1269, 1315, 1362, 1395, 1452, 1688, 1722, 2874, 2951. $[\alpha]_D^{20}$: 3.2 ($c = 1$, CHCl₃). HRMS: [M+H⁺] Calculated for C₃₈H₄₆O₅Si: 611.31873; found: 611.31904.

2,3,5-Tri-*O*-benzyl-1-deoxy- α -1-phenyl-D-lyxofuranose (33). 2,3,5-Tri-*O*-benzyl-4-*O*-triethylsilyl-1-phenyl-D-



lyxose (**17**, 70 mg, 0.12 mmol), three times coevaporated with toluene, was dissolved in anhydrous DCM (1.4 ml) and cooled to -78°C . Triethylsilane (24 μ l, 0.15 mmol) was added before drop wise addition of BF₃·OEt₂ (38 μ l, 0.30 mmol). After 1 week of stirring at this temperature TLC analysis showed partial conversion, with the remainder still being the starting material. The reaction was

quenched NaHCO₃ (sat. aq.), the suspension was extracted with Et₂O, the organic layer was washed with water and brine, the combined aqueous layers were extracted with Et₂O, the combined organic layers were dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel column chromatography (8-10% EtOAc/pentane) yielding the title compound (43 mg, 0.09 mmol, 77 % yield) as a single diastereomer. $R_f = 0.60$ (10/90 EtOAc/pentane). ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.21 (m, 18H, CH_{Ar} Bn, CH_{Ar} Ph), 7.18 – 7.09 (m, 2H, 2xCH_{Ar} Ph), 5.05 (d, $J = 7.7$ Hz, 1H, C-2), 4.79 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.63 (d, $J = 11.7$ Hz, 1H, CHH Bn), 4.61 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.53 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.50 – 4.42 (m, 2H, C-4, CHH Bn), 4.40 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.17 (t, $J = 4.1$ Hz, 1H, C-3), 3.91 – 3.83 (m, 2H, C-2, C-5a), 3.78 (dd, $J = 9.8, 6.4$ Hz, 1H, C-5b). ¹³C NMR (101 MHz, CDCl₃) δ 141.1 (C_q Ph), 138.4, 138.3, 137.8 (C_q Bn), 128.5, 128.5, 128.5, 128.4, 127.8, 127.7, 127.6, 126.2 (CH_{Ar} Ph, CH_{Ar} Bn), 86.2 (C-2), 81.3 (C-1), 79.6 (C-4), 77.5 (C-3), 73.7, 73.6, 72.6 (CH₂ Bn), 69.2 (C-5). $[\alpha]_D^{20} = 25.8^\circ$ ($c = 1$, CHCl₃). IR (neat): 652, 694, 729, 752, 833, 887, 920, 961, 984, 1007, 1026, 1053, 1084, 1101, 1144, 1159, 1204, 1360, 1452, 1493, 2859, 2884, 2899, 2949, 3030. HR-MS: [M+H⁺] Calculated for C₃₂H₃₂O₄: 481.23734; found: 481.23746.

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