Synthetic Studies Towards Oligonucleotide Derivatives and Conjugates

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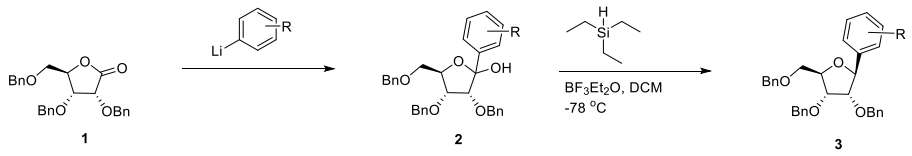
5 Reductions of furanose derived hemiketals, stereoselectivity in *C*-glycoside synthesis

5.1 Introduction

C-nucleosides are important naturally occurring compounds, which occur as modified nucleotides in RNA[1] and as nucleoside antibiotics[2,3,4]. In the field of nucleic acid research a lot of attention is directed to the design and synthesis of *C*-nucleosides[5,6,7] as fluorescent reporter molecules[8,9,10], as apolar deoxynucleosides to study DNA hydrogen bonding and translation[11,12], as artificial DNA lesions[13] and size expanded analogues called xRNA[8] and xDNA[14,15] with the aim of extending nucleic acid function. Among the synthetic methods to obtain *C*-nucleosides a two-step procedure entailing the reaction of tribenzyl ribonolactone **1** with an organolithium or organomagnesium compound and subsequent reduction of the resulting hemi-ketal **2** with triethyl silane and BF_3•Et_2O, seems to be most attractive (Scheme 5.1).[16,17] The stereochemical outcome of the procedure is defined in the reduction step and in general, an excess of the β-configured[18] *C*-nucleoside **3** is obtained.

Scheme 5.1: Synthesis of D-ribose-C-glycosides by organolithium addition followed by a silane reduction.

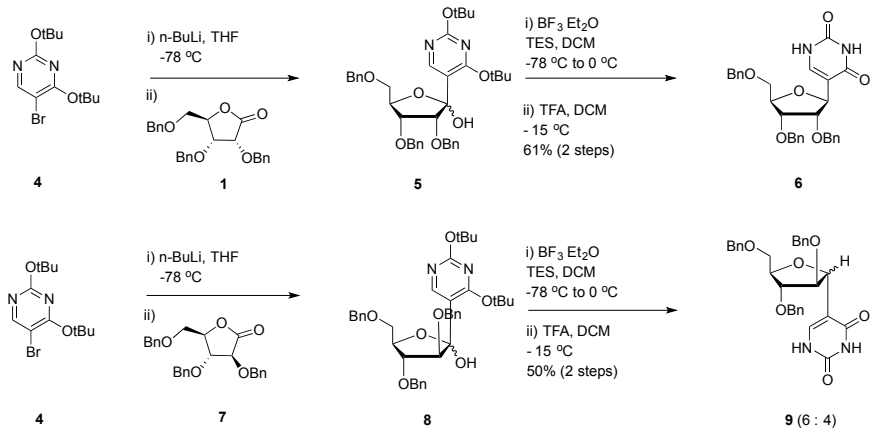


In contrast to the D-ribose derived C-nucleosides, a literature survey revealed that examples on the synthesis of corresponding D-arabinose C-glycosides are relatively scarce.[19,20,21]
As part of a program (see Chapter 4) to construct tRNA anticodon stem-loops, the naturally occurring *C*-nucleoside pseudouridine is of interest. This modified nucleoside is commonly found in different types of RNA and several syntheses have been described. [22,23,24]
This chapter describes the application of the methodology outlined in Scheme 5.1 to the synthesis of pseudouridine and its D-arabinose stereoisomer (Scheme 5.2, **6**, **9**). The method involves addition of organolitium compound to a protected furanose 1,4-lactone followed by stereoselective Lewis acid promoted reduction of the resulting ketofuranose with triethylsilane. Additionally a set of alkyl and (hetero)aromatic containing *C*-ribosides and *C*-arabinosides was prepared to investigate the stereochemical outcome of the reduction step leading to these *C*-furanosides.

Results and Discussion

The synthesis of pseudouridine started with the lithiation of known[25] bromide **4**, followed by the addition of benzyl protected lactone **1** yielding hemiketal **5** (Scheme 5.2). Reduction of the hemiketal using BF_3•Et_2O and triethylsilane at -78 °C followed by gradual warming to 0 °C led to the formation of the desired fully protected nucleoside and was accompanied by partial loss of the *tert*-butyl protective groups. Subsequent treatment with TFA in DCM at -15 °C led to complete removal of the *tert*-butyl groups to give the desired benzyl protected nucleoside **6** as a single stereoisomer. Contrary, the arabinose *C*-nucleoside **9**, synthesized by the same sequence of reactions and under the same conditions, gave a mixture of stereoisomers with a modest preference for the α product (60%).

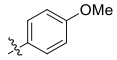
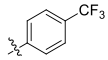
Scheme 5.2: Synthesis of 2',3',5'-tri-*O*-Benzyl-pseudouridine and its D-arabinose derivative.



Intrigued by the distinct stereochemical outcomes of the reductions of ribose and arabinose derived hemiketals the synthesis of a variety of arabinose (**15**) and ribose C-glycosides (**17**), featuring alkyl, vinyl, (substituted) phenyl and hetero aromatic residues at the anomeric centre was undertaken (Table 5.3). The required hemi-ketal precursors were prepared by treatment of the corresponding benzylated lactones (**1** and **7** respectively) with an appropriate organometallic reagent.

Reduction of benzyl protected arabino ketose **14a** gave the α-methyl arabinose *C*-glycoside **15a** in 90% yield. It is of interest to note that literature data on the stereochemical outcome of this reduction is inconsistent.[26,27] Synthesis of the methyl ribose derivative **17a** by the same sequence of events gave the β-anomer in 90% yield.

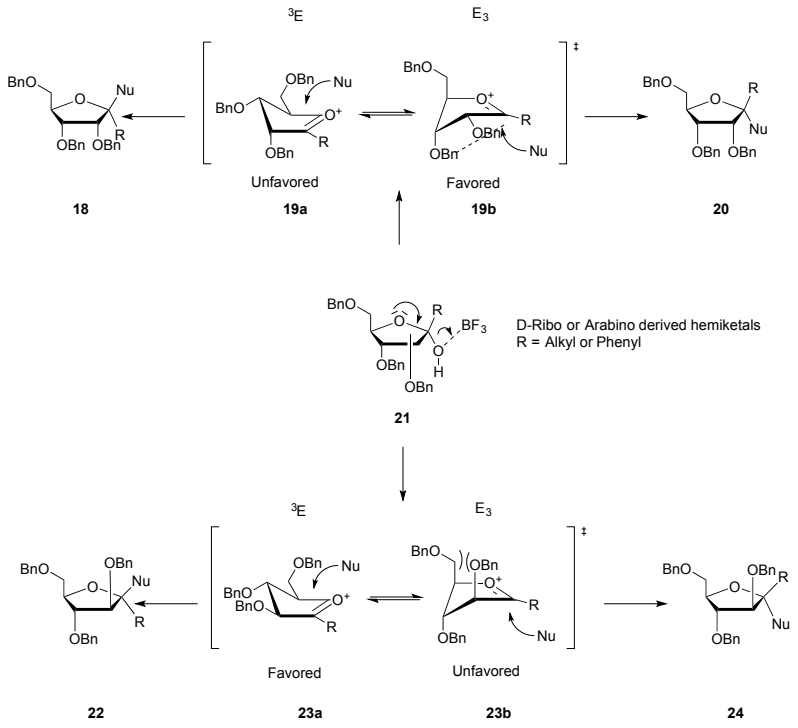
Table 5.3: Synthesis of D-arabinose and D-ribose *C*-glycosides.

	Arabinose		Ribose	
R	**α : β (%)**	**Yield**	**α : β**	**Yield**
Methyl (15a, 17a)	**α**	**90%**	**β**	**90%**
 **(15b, 17b)**	**85 : 15**	**72%**	**β**	**quant**
 **(15c, 17c)**	**80: 20**	**65%**	**β**	**78%**
 **(15d, 17d)**	**75 : 25**	**63%**	**β**	**65%**
 **(15e, 17e)**	**75 : 25**	**85%**	**β**	**70%**
 **(15f, 17f)**	**75 : 25**	**80%**	**β**	**50%**
Vinyl (15g, 17g)	**α**	**43%**	**β**	**33%**

The differently substituted phenyl hemi-ketals (**14c-f** and **16c-f**) were less reactive than **14a** and **16a**, and the reduction of these hemi-ketals required longer reaction times. Where the reduction of the ribo hemi-ketals (**16**) proceeded with excellent stereoselectivity the reduction of the arabino-phenyl hemi-ketals (**14**) proceeded with somewhat diminished selectivity. Likewise the furanyl substituted ketoses (**14b** and **16b**) produced the corresponding C-glycosides (**15b** and **17b**) in good yields and good to excellent selectivity. Reduction of the vinyl-substituted compounds (**14g** and **16g**) proceeded sluggishly and the yields were low. However, in each case a single vinyl C-furanoside was obtained, as indicated by ^{1}H-NMR of the crude reaction mixture. NOE-measurements proved the formation of the α-glycoside for arabinose (**15g**) and β-glycoside for ribose (**17g**).

Having established that the reduction of arabinose derived hemiketals (**14a–g**) produces C-glycosides with a high alpha selectivity[28] while the corresponding ribose derived hemiketals (**16a–g**) all yield beta C-glycosides, the question arises how these stereoselectivities can be explained. Under the applied conditions, the reduction of stable tertiary oxocarbenium ions derived from furanose hemiketal is likely to proceed via a S_N1 mechanism. The group of Woerpel devised a model that explains the stereoselectivity of nucleophilic attack on secondary five-membered-ring oxocarbenium ions.[29,30,31] In their studies, it was established by a systematic survey of alkyl and alkoxy substituents at varying positions that a C-3 alkoxy substituent is of prime importance by participating in the formation of a preferred ground state conformer (Scheme 5.4, **19b**, R = H) bearing the C-3 alkoxy substituent in a pseudo-axial position. Next, the incoming nucleophile is believed to approach from inside of the envelope. The preference for this trajectory is governed by the formation of a product in which the substituents are aligned staggered. This chain of events; formation of an oxocarbenium-ion with a C-3 pseudo-axially oriented alkoxy group followed by inside attack was found to account for the high (> 95%) stereoselectivities in the ribofuranose series observed. Although in these studies secondary oxocarbenium ions were studied, using allyl-trimethylsilane as the incoming nucleophile, this model can also be applied to the tertiary oxocarbenium ion reductions. For instance when translated to a hemi-ketal in the ribose configuration, it is expected that electrostatic interaction between the 3-*O*-benzyl oxygen and the positive charge at the anomeric center results in formation of the more stable E_3-conformed oxocarbenium-ion (**19b**). Subsequent attack of the nucleophile from the inside[31] of the envelope yields β-C-glycoside (**20**, Nu=H) (Scheme 5.4).

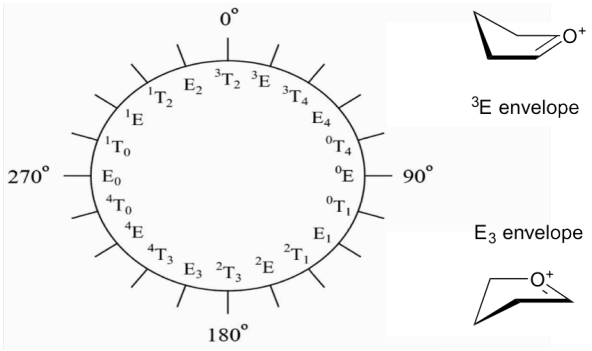
Scheme 5.4: Formation of tertiary oxocarbenium-ions and their conformational preferences.



Inside attack on the ^{3}E-conformer (**23a**) of the intermediate oxocarbenium ion of arabinose configuration, in which all substituents are placed in equatorial position, predicts the formation of alpha configured arabino C-glycosides **22** (**Nu=H**). Although the C-3 substituent resides in the favorable pseudo-axial orientation, the syn-butanol interaction between the 2-alkoxy and 4-alkoxymethyl substituent makes the E_3 conformer (**23b**) less favorable than the ^{3}E-conformation (Scheme 5.5).[30] To further investigate the conformational preferences of either ribose or arabinose derived oxocarbenium-ions quantum mechanical calculations were executed.

Recently, Rhoad *et al.*[32] reported a method to compute the potential energy surface (PES) of mono- and dioxygen-substituted furanosyl oxocarbenium-ions. In this method the structures of 81 different oxocarbenium-ion conformers defined by locking the dihedral angle between C1-C2-C3-C4 and C2-C1-O-C4 are optimized and the corresponding energies are calculated to determine the energetically most preferred conformer[33] (Figure 5.1). Here, this procedure is applied to arabinose- and ribose-derived tertiary oxocarbenium ions substituted at C-1 with either methyl or phenyl group.

Figure 5.1: Furanose oxocarbenium-ion conformers and corresponding ring dihedral angles depicted as the pseudo-rotational wheel.



To take into account the orientation of C4 methoxymethyl substituent three different conformers were evaluated for each of 81 oxocarbenium-ion conformations (Figure 5.2 A, B and C). The potential energy surfaces thus derived are depicted Figure 5.3 for all four studied oxocarbenium ions (A-D).

Figure 5.2: Different orientations of the 5-OMe group along the C-5, C-4 bond: A gauche, gauche; B trans, gauche ; C gauche, trans.

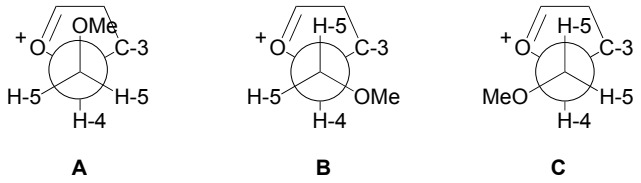
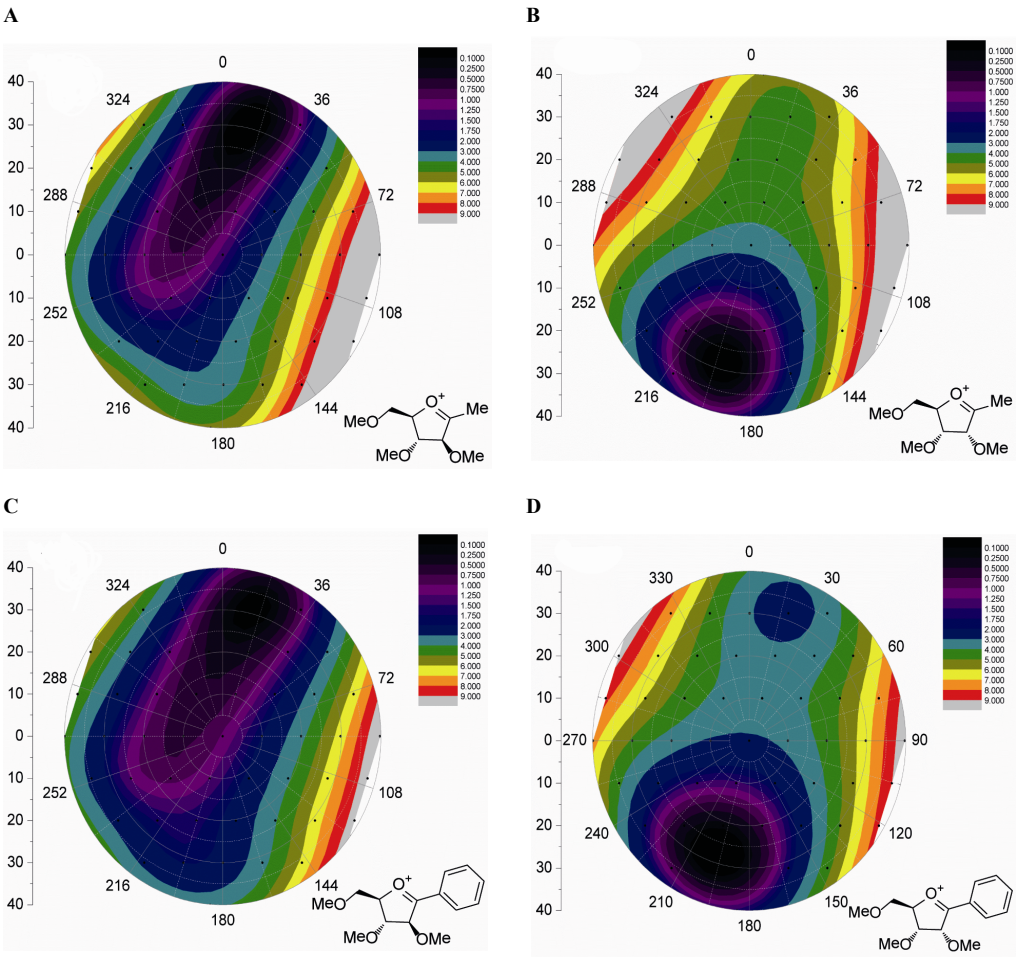


Figure 5.3: Potential energy surfaces of the 1-*C*-methyl-2,3,5-tri-*O*-methyl-D-arabinose (A) and ribose (B) oxocarbenium-ions, C and D depict the 1-*C*-phenyl-2,3,5-tri-*O*-methyl-D-arabinose and ribose oxocarbenium-ions respectively.

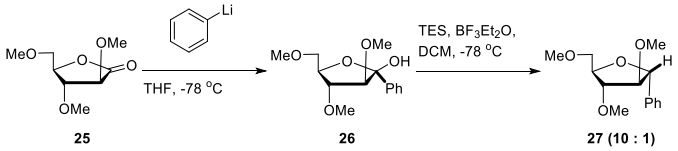


The potential energy surfaces of ribose-derived oxocarbenium ions (Figure 5.3 **B** and **D**) clearly depict the preference for the E_3-conformer whereas the arabinose derivatives have a preference for the ^{3}E-conformer (**A** and **C**). The conformational preferences of both ribose derived oxocarbenium-ions appear to be stronger than those of the arabinose counterparts as can be seen by the more confined "well" that represents the energy minimum of the energy surface. Although the preferential conformers of the arabinose oxocarbenium-ions are less defined, there is still about a 1 – 1.5 Kcal mol^{-1} difference in favor of the ^{3}E-conformer. It is proposed that this might be a result of steric factors between the C-2 and C-1 substituents being aligned in the same plane in the ^{3}E-conformer. Particularly for the phenyl substituted conformer in which case conjugation forces both the sugar and the phenyl ring in the same plane, leading to what can be seen as allylic strain. Nonetheless, inside attack of the nucleophile on these lowest energy conformers leads in all studied cases to the products with the experimentally observed stereochemistry. That is, arabinose derived hemiketals produce

predominantly alpha C-glycosides and the corresponding ribose derived hemiketals yield exclusively beta C-glycosides.

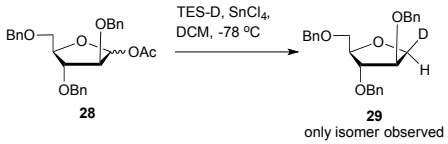
To speed up the computation the calculations were done on tri-O-methyl substituted furanosides, while the syntheses were performed with the synthetically useful tri-O-benzyl protected sugars. To allow for more direct comparison of the *in silico* results with the experimental outcome the synthesis and the reduction of methyl protected arabinose derived hemiketal **26** was undertaken (Scheme 5.6). In line with the computational data, the reduction of **26** led to the predominant formation of alpha isomer of **27** (α/β 10:1).

Scheme 5.5: Synthesis of 1-*C*-phenyl-2,3,5-tri-*O*-methyl-D-Arabinose.



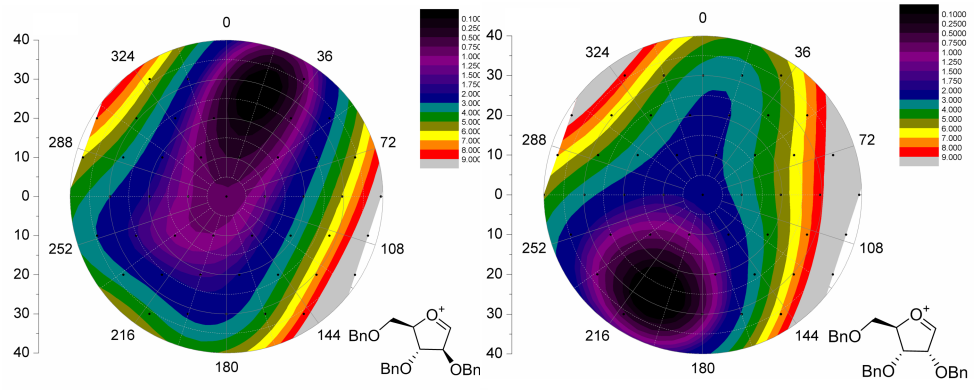
Further support for the mechanistic model described here is provided by the work of the group of Boons[34] and others[35–38]. Here, glycosylation reactions of D- and L-arabinose using ring constrained donors by means of cyclic 3,5-protective groups led to 1,2 cis addition of the acceptor alcohols leading to β-products. For instance, by locking a L-arabinose donor in the ^{3}E conformation by application of the 5,3-di-tert-butyl silylidene protecting group selective beta *O*-glycosylation reactions were achieved.[34] These results are in agreement with the model advanced in this work. The finding, that O-glycosylations with a tri-*O*-benzyl protected L-arabinose donor at the same temperature (-55 °C) significantly decreased the stereoselectivity; points to additional factors governing the stereoselectivity of glycosylation reactions. These are not accounted for by the presented mechanistic rationale at its current stage of development. Nevertheless, the predictive power of the current model was tested on secondary 2,3,5-tri-*O*-benzyl D-arabinose derived oxocarbenium-ions that are expected to exhibit beta selectivity. To achieve this, donor **28** was synthesized and reduced under the similar conditions as described above for the ketofuranose reductions (Scheme 5.6).

Scheme 5.6: The reduction of arabinose donor **28** with deuterated triethylsilane.



Reduction at -78 °C of 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-D-arabinose **28** under influence of $SnCl_4$ and TES-D as reducing agent gave stereoselectively the expected deuterated, β isomer **29**. This indicates that secondary arabinose oxocarbenium ions also favor the ^{3}E conformer. Next, this preference was confirmed by calculating the potential energy surfaces for the secondary 2,3,5-tri-*O*-methyl-D-arabinose and ribose oxocarbenium ions. (Figure 5.4, **A** and **B**)

Figure 5.4: Potential energy surface of the 2,3,5-tri-*O*-methyl-D-arabinose (**A**) and ribose (**B**) oxocarbenium-ions.



A similar trend was observed as found for the tertiary furanosyl oxocarbenium ions. Ribose exhibited a strong preference for the E_3 conformer while a more shallow PES was found for arabinose. Nonetheless, a preference of about 1 Kcal for the ^3E conformer was calculated. It can, therefore be concluded, that secondary arabinose derived oxocarbenium-ions should also react in a beta selective manner, provided that the right conditions are applied.[39]

Conclusion

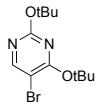
In conclusion the naturally occurring nucleoside pseudouridine was synthesized in a stereoselective fashion by the addition of the lithiated pyrimidine base to ribonolactone followed by Lewis acid mediated triethylsilane reduction. The synthesis of the corresponding D-arabinose derivative of pseudouridine proceeded with poor stereochemical selectivity. To explain these stereochemical outcomes alkyl and phenyl based D-arabinose hemiketals were reduced at -78 ^oC, yielding predominantly alpha *C*-glycosides, while the corresponding D-ribose hemiketals gave exclusively beta *C*-glycosides. The mechanistic explanation for these results was found with the aid of the model of the group of Woerpel. Thus, the preferred conformation of the lewis acid mediated formation of furanose oxocarbenium-ions is governed by the pseudo-axial positioning of the C-3 benzyloxy substituent. In the envelope type conformers, the stabilizing effect of the oxygen lone pairs on the secondary oxocarbenium ion is found to have the strongest control over the oxocarbenium-ion conformer. However, in its absence, steric 1,3 di-axial interactions can play an important role in determining the preferred conformer. In either case, the preferred oxocarbenium-ion conformer is subsequently attacked by the incoming nucleophile from the inside face of the envelope. The observed stereochemistry in the products is a direct result of both oxocarbenium-ion conformation and inside attack preferences. When applied to the reduction of D-ribose derived tertiary oxocarbenium-ions, the electrostatic interaction between the oxygen of the 3-*O*-benzyl substituent and the positive charge on C-1 drives towards the formation of the E_3 oxocarbenium-ion conformer. Inside attack leads to the beta *C*-glycoside as observed. D-arabinose derived tertiary oxocarbenium-ions favor a ^3E ground state conformer. This is proposed to be the result of a destabilizing 1,3-diaxial interaction between the C-2 and C-4 substituents in the otherwise preferred E_3 conformer. Subsequent inside attack on the

arabinose ^{3}E leads to alpha *C*-glycosides. This explanation of the stereo chemical outcome was confirmed by potential energy surface calculations revealing that the preference for the E_3 conformer for D-ribose is significantly greater (2 Kcal mol^{-1}) than the ^{3}E conformer for D-arabinose (1 Kcal mol^{-1}).
In addition, reduction of acetyl-α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose with $SnCl_4$ and TES-D gave the expected β-isomer of the deuterated sugar. The latter result suggests that the mechanistic model advanced here may be applicable to the aldofuranose derived oxocarbenium ions as well.

Experimental section

General methods and materials

Chemicals were purchased from Acros Organics and Sigma Aldrich and used as received. THF (Biosolve) and Dichloromethane (Biosolve, amylene stabilized) were treated with and stored on activated 4 Å molecular sieves. Compounds used in reactions requiring anhydrous conditions were co-evaporated with toluene three times. 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 (+/- 150 °C).
^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AV-400 instrument. Chemical shifts (δ) of ^{1}H and ^{13}C spectra are relative to tetramethylsilane. HRMS spectra were recorded by direct injection (2 µL of a µM solution in H_2O or MeCN and 0.1% formic acid) on a Thermo Finnigan LTQ Orbitrap equipped with a electro spray ion source in positive mode. IR spectra were recorded on a Shimadzu FT-IR 8300 and are reported in cm^{-1}.

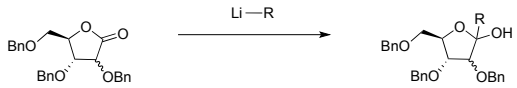


5-Bromo-2,4-di-tert-butoxy-pyrimidine (4)[25]

To a stirred solution of 5-bromo-2,4-dichloropyrimidine (0.56 g, 2.5 mmol) in dry THF (12.5 mL) was added a solution of KOtBu (6.25 mmol, 1.25 eq) in THF (25 mL). After two hours TLC showed complete conversion of the starting material into a less polar compound. The reaction mixture was quenched with H_2O (12.5 mL) and extracted with EtOAc (3 x 12.5 mL). The combined organic layers were washed with brine (12.5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was taken up in toluene and purified by silicagel column chromatography (Petroleum ether : EtOAc, 95 : 5) yielding the title pyrimidine as a colourless oil which solidified upon cooling (0.68 g, 2.23 mmol, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.25 (s, 1H); 1.65 (s, 9H); 1.60 (s, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 165.5; 162.7; 158.7; 99.3; 83.0; 80.5; 28.1.

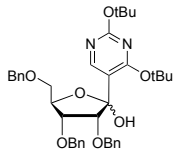
General procedure for organo-lithium formation and addition to 2,3,5-tri-O-benzyl-sugar-1,4-lactones



To a stirred and cooled (-78 °C) solution of bromide (1.1 mmol, 1.1 eq) in anhydrous THF (4 mL) was added a solution of n-BuLi in hexanes (0.68 mL, 1 M, 1.1 mmol, 1 eq). The metal halogen exchange was allowed to proceed for 20 minutes at -78 ^{0}C followed by the dropwise (30 minutes) addition of the respective sugar lactone (1 mmol) in anhydrous THF (4 mL). Upon completion (typically 2 – 4 hours) as indicated by TLC analysis the reaction mixture was quenched by the addition of a saturated aqueous solution of NH_4Cl (4 mL) at -78 ^{0}C. The reaction mixture was allowed to warm to room temperature, diluted with EtOAc (20 mL) and washed with H_2O (2 x 10 mL), brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Rapid silicagel purification allowed removal of any unreacted components and yielded complex mixtures of α- and β-hemiacetals and occasionally the keto-isomer. All intermediate lactols were assessed by ^{1}H-NMR and used without further identification.

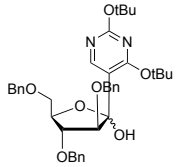
Procedure for the preparation of vinyl lithium

To tetravinyl stannane (1 mL, 5.47 mmol) was added dropwise (30 mins) a solution of n-butyl lithium (1.6 M in hexanes, 6.8 mL, 11 mmol, 2 eq) under vigorous stirring. Pentane (10 mL) was added and the supernatant was removed. The white residue was taken up in anhydrous THF (11 mL) yielding a solution (1 M) of vinyl lithium.



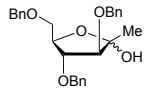
1-*C*-(5'-(2',3'-di-tert-butoxy)-pyrimidine)-2,3,5-tri-*O*-benzyl-D-ribofurano-1,4-lactol (5)

The title compound was prepared as described in the general procedure on a 8 mmol scale (2450 mg, corresponding bromide). After column chromatography (EtOAc : Toluene, 5 : 95 → 15 : 85) the title ketose was isolated (2.98 g) as a colorless oil.



1-*C*-(5'-(2',3'-di-tert-butoxy)-pyrimidine)-2,3,5-tri-*O*-benzyl-D-arabinofurano-1,4-lactol (8)

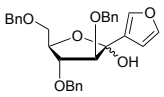
The title compound was prepared as described in the general procedure on a 1 mmol scale (300 mg, corresponding bromide). After column chromatography (EtOAc : Toluene, 5 : 95 → 2 : 8) the title ketose was isolated (336 mg) as a colorless oil.



1-*C*-Methyl-2,3,5-tri-*O*-benzyl-D-arabinofurano1,4-lactol (14a)

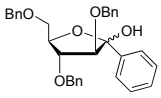
To a stirred and cooled solution (-78 °C) of MeLi (3.13 mL, 1.6 M in Et_2O, 5 mmol) in anhydrous

THF (10 mL) was added dropwise (30 minutes) a solution of 2,3,5,-tri-*O*-benzyl-D-arabino-1,4-lactone (2.3 g, 5.5 mmol, 1.1 eq) in anhydrous THF (14 mL). After 2 hrs the reaction was quenched by the addition of saturated aqueous NH_4Cl (4 mL), diluted with EtOAc (75 mL) and allowed to warm to room temperature. The organic layer was washed H_2O (2 x 21 mL), brine (21 mL), dried on $MgSO_4$ and concentrated under reduced pressure. Rapid silicagel purification allowed removal of any unreacted components and yielded complex mixtures of α- and β-hemiacetals as a colorless oil (2.0 g).



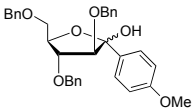
1-*C*-(3'-furanyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranolactol (14b)

The title compound was prepared as described in the general procedure on a 1 mmol scale. After column chromatography (EtOAc : Petroleum ether, 1 : 9 – 2 : 8) the title ketose was isolated (300 mg) as a colorless oil.



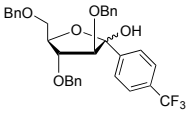
1-*C*-Phenyl-2,3,5-Tri-*O*-benzyl-D-arabinofuranolactol (14c)

The title compound was prepared as described in the general procedure. After column chromatography (Et_2O : Petroleum ether, 3 : 7) the title lactone was isolated (347 mg) as a pale yellow oil.



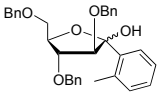
1-*C*-(*p*-methoxy)-Phenyl-2,3,5,-Tri-*O*-benzyl-D-arabinofuranolactol (14d)

The title compound was prepared as described in the general procedure. After column chromatography (Et_2O : Petroleum ether, 2 : 8 – 4 : 6) the title lactone was isolated (467 mg) as a pale yellow oil.



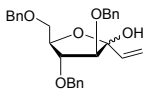
1-*C*-(*p*-trifluoromethyl)-Phenyl-2,3,5,-Tri-*O*-benzyl-D-arabinofuranolactol (14e)

The title compound was prepared as described in the general procedure on a 0.5 mmol scale (lactone). After column chromatography (Et_2O : Petroleum ether, 2 : 7) the title lactone was isolated (230 mg) as a pale yellow oil.



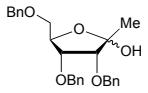
1-*C*-*o*-Toluoyl-2,3,5-tri-*O*-benzyl-D-arabinofuranolactol (14f)

The title compound was prepared as described in the general procedure. After column chromatography (EtOAc : Petroleum ether, 7.5 : 92.5 – 15 : 85) the title lactone was isolated (440 mg) as a colorless oil.



1-*C*-Vinyl-2,3,5-tri-*O*-benzyl-D-arabinofuranolactol (14g)

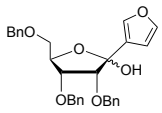
To a stirred and cooled (-78 °C) of 2,3,5-tri-*O*-benzyl-D-arabino-1,4-lactone (418 mg, 1 mmol) in anhydrous THF (4 mL) was added dropwise a solution of vinyl lithium (1.5 mL, 1 M (as previously described), 1.5 eq). After two hours a second addition of vinyl lithium (0.5 mL, 1 M, 0.5 eq) was made and the reaction mixture was stirred for an additional 3 hours. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL). The reaction mixture was diluted with EtOAc (25 mL) and washed with saturated aqueous NH_4Cl (3 x 10 mL), H_2O (10 mL), brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Rapid silica gel purification (EtOAc : Petroleum ether, 2 : 8) allowed removal of some unreacted lactone yielding a complex mixture of α- and β-hemiacetals and the keto-isomer as a colorless oil (430 mg).



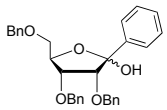
1-*C*-Methyl-2,3,5-tri-*O*-benzyl-D-ribofuranolactol (16a)

To a stirred and cooled solution (-78 °C) of 2,3,5,-tri-*O*-benzyl-D-ribono-1,4-lactone (0,9 mmol, 0,38 g) in anhydrous THF (3 mL) was added dropwise (20 minutes) a solution of methyl lithium in hexanes (0,69 mL, 1.6 M, 1.1 mmol). After 2 hrs an additional 0.2 mmol of MeLi were added. The reaction was quenched by the addition of saturated aqueous NH_4Cl (1 mL), diluted with EtOAc (20 mL) and allowed to warm to room temperature. The organic layer was washed H_2O (2 x 7 mL), brine (7 mL), dried on $MgSO_4$ and concentrated under reduced pressure. Rapid silicagel purification allowed removal of any unreacted components and yielded complex mixtures of α- and β-hemiacetals as a colorless oil (0.31 g).

1-*C*-(3'-furanyl)-2,3,5-tri-*O*-benzyl-D-ribofuranolactol (16b)

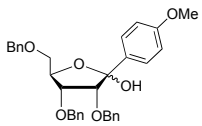


The title compound was prepared as described in the general procedure. After column chromatography (EtOAc : Petroleum ether, 1 : 9) the title ketose was isolated (188 mg) as a colorless oil.



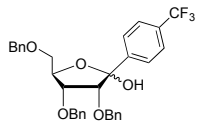
1-*C*-Phenyl-2,3,5-tri-*O*-benzyl-D-ribofuranolactol (16c)

The title compound was prepared as described in the general procedure. After column chromatography (Et_2O : Petroleum ether, 2 : 8 - 3 : 7) the title lactone was isolated (218 mg) as a pale yellow oil.



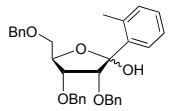
1-*C*-(*p*-methoxy)-Phenyl-2,3,5,-tri-*O*-benzyl-D-ribofuranolactol (16d)

The title compound was prepared as described in the general procedure. After column chromatography (Et_2O : Petroleum ether, 3 : 7 – 1 : 1) the title lactone was isolated (360 mg) as a pale yellow oil.



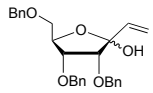
1-*C*-(*p*-trifluoromethyl)-Phenyl-2,3,5,-tri-*O*-benzyl-D-ribofuranolactol (16e)

The title compound was prepared as described in the general procedure. After column chromatography (Et_2O : Petroleum ether, 2 : 8) the title lactone was isolated (394 mg) as a pale yellow oil.



1-*C*-*o*-Toluoyl-2,3,5-tri-*O*-benzyl-D-ribofuranolactol (16f)

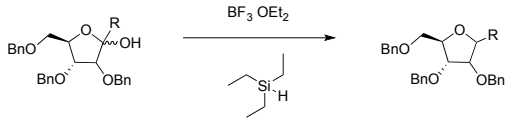
The title compound was prepared as described in the general procedure on a 1 mmol scale. After column chromatography (EtOAc : Petroleum ether, 1 : 9 – 3 : 7) the title lactone was isolated (375 mg) as a colorless oil.



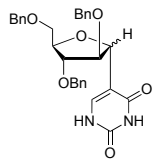
1-*C*-Vinyl-2,3,5-tri-*O*-benzyl-D-ribofuranolactol (16g)

To a stirred and cooled (-78 °C) of 2,3,5-tri-*O*-benzyl-D-arabino-1,4-lactone (418 mg, 1 mmol) in anhydrous THF (4 mL) was added dropwise a solution of vinyl lithium (2 mL, 1 M (as previously described), 2 eq). The reaction mixture was stirred for 5 hours. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL). The reaction mixture was diluted with EtOAc (25 mL) and washed with saturated aqueous NH_4Cl (3 x 10 mL), H_2O (10 mL), brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Rapid silica gel purification (EtOAc : Petroleum ether, 15 : 85) allowed removal of some unreacted lactone yielding a complex mixture of α- and β-hemiacetals and the keto-isomer as a colorless oil (367 mg).

General Procedure for the triethylsilane/$BF_3{\cdot}Et_2O$ reduction of 2,3,5-tri-*O*-benzyl-D-arabino- and ribofuranosyl ketoses towards their corresponding C-glycosides



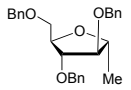
To a stirred and cooled (-78 °C) solution of 2,3,5-tri-*O*-Benzyl-keto-furanose (0.2 mmol) in anhydrous DCM (3 mL) was added triethylsilane (42 µL, 0.27 mmol, 1.35 eq) and $BF_3.Et_2O$ (34 µL, 0.27 mmol, 1.35 eq). The reaction mixture was stirred at -78 °C using a cryostate until TLC analysis revealed complete or near complete conversion (aliphatic ketoses reacted within 1 – 2 hours whereas the aromatic substituted sugars required several hours). The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ (3 mL). The reaction mixture was dilluted with EtOAc (25 mL) and washed with saturated aqueous $NaHCO_3$ (2 x 10 mL), H_2O (10 mL), Brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Crude reaction mixtures were analysed by ^{1}H-NMR prior to silicagel column chromatography to determine the α/β ratio.



1-*C*-(5'-(2',3'-di-tert-butoxy)-pyrimidine)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (9)

The title compound was synthesized using conditions as described in the general procedure (250 mg, 0.39 mmol), allowing the reaction mixture to warm from -78 °C to r.t. The reaction mixture was cooled to -15 °C and TFA (3 mL) was added. The reaction mixture was stirred for 30 minutes, poured on ice water and extracted with DCM. The organic layer was saturated aqueous $NaHCO_3$, H_2O (3x) and Brine, dried (Na_2SO_4) and concentrated under reduced pressure. Silicagel column chromatography (EtOAc : Petroleum ether) yielded the title C-glycoside as a mixture of anomers (α/β, 1 : 0.9) (185 mg, 0.36 mmol, 92%)

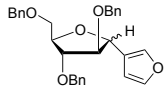
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 9.89 (s, 0.9H), 9.79 (s, 0.9H), 9.74 (s, 1H), 7.40 (d, *J* = 5.2 Hz, 1H), 7.37 – 7.17 (m, 26H), 7.14 – 7.08 (m, 3.8H), 5.07 (s, 1H), 5.02 (d, *J* = 2.8 Hz, 0.9H), 4.73 (d, *J* = 12.1 Hz, 1H), 4.61 – 4.56 (m, 2H), 4.56 – 4.47 (m, 3.8H), 4.47 – 4.36 (m, 3.8H), 4.36 – 4.29 (m, 1.9H), 4.23 (d, *J* = 3.9 Hz, 0.9H), 4.19 (s, 1H), 4.15 (td, *J* = 6.1, 3.0 Hz, 0.9H), 3.97 (s, 1H), 3.90 (d, *J* = 2.7 Hz, 0.9H), 3.68 – 3.59 (m, 1.9H), 3.59 – 3.50 (m, 1.9H), 3.19 – 3.08 (m, 0.9H). IR (neat): 3066, 2926, 2362, 2342, 1715, 1669, 1496, 1454, 1271, 1206, 1095, 1028, 737, 698. HRMS: calculated for $[C_{30}H_{30}N_2O_6 + H]^+$: 515,21766; found : $[M + H]^+$: 515.21786.



1-*C*-α-(Methyl)-2,3,5-tri-*O*-Benzyl-D-arabinofuranose (15a)

The title compound was synthesized following the general procedures (162 mg, 0.37 mmol). Silicagel column chromatography (EtOAc : Petroleum ether) yielded the title C-glycoside as a colorless oil (140 mg, 0.33 mmol, 90%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.17 (m, 15H), 4.62 – 4.46 (m, 6H), 4.22 (dd, *J* = 5.7, 4.0 Hz, 1H), 4.17 – 4.09 (m, 1H), 4.02 (t, *J* = 3.7 Hz, 1H), 3.76 (dd, *J* = 5.0, 3.3 Hz, 1H), 3.58 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.53 (dd, *J* = 10.0, 5.7 Hz, 1H), 1.31 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 138.1, 137.9, 128.4, 128.4, 128.4, 128.3, 128.3, 127.8, 127.7, 127.7, 127.6, 89.2, 85.4, 81.0, 78.2, 73.3, 71.9, 71.9, 70.4, 19.2. IR (neat): 2864, 1722, 1092, 1028, 734, 696. HRMS: calculated for $[C_{27}H_{30}O_4 + H]^+$: 419.22169; found $[M + H]^+$: 419.22165.

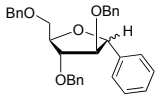


1-*C*-α/β-(3'-furanosyl)-2,3,5-tri-*O*-Benzyl-D-arabinofuranose (15b)

The title compound was synthesized following the general procedures (146 mg, 0.3 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 1 : 9 – 12.5 : 87.5) yielded the title *C*-glycoside as a colorless oil (100 mg, 0.22 mmol, 72%)

^{1}H-NMR 400 MHz ($CDCl_3$) δ 7.48 (s, 0.25H), 7.44 – 7.37 (m, 3H), 7.37 – 7.21 (m, 17.25H), 7.17 – 7.09 (m, 0.5H), 6.48 (d, 0.25H), 6.44 (d, 1H), 5.00 (d, *J* = 3.7 Hz, 0.25H), 4.95 (d, *J* = 5.4 Hz, 1H), 4.64 – 4.44 (m, 7.25H), 4.36 – 4.30 (m, 0.25H), 4.27 (dd, *J* = 5.1 Hz, 1H), 4.19 – 4.11 (m, 2H), 4.05 – 4.01 (m, 0.25H), 3.95 – 3.91 (m, 0.25H), 3.70 (dd, *J* = 9.9, 5.8 Hz, 0.25H), 3.63 (d, *J* = 5.3 Hz, 2.25H). ^{13}C-NMR (101 MHz, CDCl3) δ 143.4, 142.6, 141.1, 140.2, 138.1, 137.8, 137.6, 128.4, 128.4, 128.4, 128.3, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 124.7, 110.9, 109.0, 88.8,

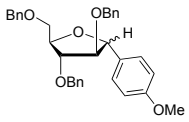
85.0, 84.4, 83.9, 82.2, 81.3, 76.7, 76.1, 73.4, 73.3, 72.1, 72.2, 71.7, 71.5, 70.4, 70.2. HRMS: calculated for $[C_{30}H_{30}O_5 + Na]^+$: 493.19855; found $[M + Na]^+$: 493.19795. IR (neat): 2864, 1497, 1455, 1072, 1026, 735, 696.



1-*C*-α/β-(Phenyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (15c)

The title compound was synthesized following the general procedures (275 mg, 0.55 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 25 : 75) yielded the title C-glycoside as a colorless oil (173 mg, 0.36 mmol, 65%).

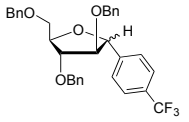
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 2.36H), 7.36 – 7.23 (m, 12.2H), 7.22- 7.16 (m, 3.8H), 6.91 – 6.85 (m, 0.32H), 5.10 (d, *J* = 3.7 Hz, 0.16H), 4.98 (d, *J* = 6.1 Hz, 1H), 4.65 – 4.45 (m, 4.3H), 4.45 – 4.37 (m, 3H), 4.24 (dt, *J* = 6.3, 3.1 Hz, 0.16H), 4.21 (t, *J* = 4.1 Hz, 1H), 4.13 (dd, *J* = 6.1, 4.0 Hz, 1H), 4.09 – 3.93 (m, 0.72H), 3.79 (dd, *J* = 9.9, 5.9 Hz, 0.16H), 3.72 – 3.60 (m, 2.16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 138.2, 138.1, 137.8, 137.7, 137.7, 137.6, 136.6, 128.4, 128.3, 128.3, 128.1, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 127.4, 126.3, 90.1, 85.0, 84.9, 84.0, 83.8, 83.1, 82.4, 81.8, 73.3, 73.3, 72.2, 71.8, 71.6, 71.4, 70.4, 70.2. IR (neat): 2858, 1496, 1454, 1093, 1028, 734. HRMS: calculated for $[C_{32}H_{32}O_4 + Na]^+$: 503.21928; found $[M + Na]^+$: 503.21863.



1-*C*-α/β-(*p*-Methoxy-phenyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (15d)

The title compound was synthesized following the general procedures (254 mg, 0.5 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 1 : 9 – 3 : 7) yielded the title *C*-glycoside as a colorless oil (161 mg, 0.32 mmol, 63%).

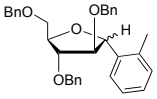
1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.13 (m, 21H), 6.93 (dd, *J* = 6.6, 2.9 Hz, 0.74H), 6.86 (dd, *J* = 8.7, 1.5 Hz, 2.74H), 5.03 (d, *J* = 3.7 Hz, 0.37H), 4.91 (d, *J* = 6.3 Hz, 1H), 4.65 – 4.34 (m, 8.6H), 4.20 (t, *J* = 4.3 Hz, 1.37H), 4.11 (m, 1H), 4.03 (m, 1H), 3.90 (d, *J* = 3.7 Hz, 0.37H), 3.79 – 3.75 (m, 4.5H), 3.69 - 3.67 (m, 0.37H), 3.64 (dd, *J* = 5.5, 1.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 159.1, 138.2, 138.1, 137.8, 137.7, 132.4, 128.6, 128.3, 128.3, 128.2, 128.1, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 113.7, 113.2, 90.0, 85.0, 84.8, 84.0, 83.4, 82.8, 82.1, 81.4, 77.3, 77.0, 76.7, 73.3, 71.8, 71.6, 71.4, 70.4, 70.2, 55.1. IR (neat): 2860, 1613, 1514, 1454, 1247, 1093, 1028, 830, 735, 697. HRMS: calculated for $[C_{33}H_{34}O_5 + NH_4]^+$: 528.27445; $[C_{33}H_{34}O_5 + Na]^+$: 533.22985; found $[M + NH_4]^+$: 528.27488; $[M + Na]^+$: 533.22926.



1-*C*-α/β-(*p*-Trifluoromethyl-phenyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (15e)

The title compound was synthesized following the general procedures (314 mg, 0.49 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 2 : 8) yielded the title C-glycoside as a colorless oil (230 mg, 0.43 mmol, 85%).

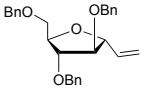
1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.3 Hz, 2.6H), 7.51 – 7.43 (m, 3H), 7.37 – 7.23 (m, 14.5H), 7.22 – 7.11 (m, 4H), 6.81 (d, *J* = 1.8 Hz, 0.3H), 6.79 (d, *J* = 2.3 Hz, 0.3H), 5.14 (d, *J* = 3.7 Hz, 0.3H), 5.04 (d, *J* = 5.6 Hz, 1H), 4.66 – 4.55 (m, 2.9H), 4.55 – 4.42 (m, 6.2H), 4.28 (td, *J* = 6.3, 2.7 Hz, 0.3H), 4.20 (t, *J* = 3.7 Hz, 1H), 4.15 (d, *J* = 12.2 Hz, 0.3H), 4.08 – 4.03 (m, 1.3H), 4.01 – 3.95 (m, 0.3H), 3.78 (dd, *J* = 9.8, 5.9 Hz, 0.3H), 3.71 – 3.61 (m, 2.3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.58, 141.00, 138.11, 137.96, 137.55, 137.38, 137.25, 129.67 (q, *J* = 32.3 Hz), 128.45, 128.37, 128.33, 128.16, 127.84, 127.71, 127.68, 127.63, 127.42, 125.2 (q, *J* = 4 Hz), 124.6 (q, *J* = 4 Hz), 89.91, 84.78, 84.39, 83.84, 83.15, 82.79, 82.56, 82.34, 73.37, 73.28, 72.24, 71.84, 71.53, 71.48, 70.27, 70.13. IR (neat): 1327, 1114, 1095, 1066, 1016, 735, 695. HRMS: calculated for $[C_{33}H_{31}F_3O_4 + H]^+$: 549.22472; $[C_{33}H_{31}F_3O_4 + Na]^+$: 571.20667; found $[M + H]^+$: 549.22472; $[M + Na]^+$: 571.20653.



1-*C*-α/β-(*o*-Toluoyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (15f)

The title compound was synthesized following the general procedures (255 mg, 0.5 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 25 : 75) yielded the title C-glycoside as a colorless oil (194 mg, 0.4 mmol, 80%).

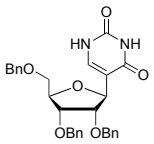
1H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 0.25H), 7.52 (dd, *J* = 7.2, 2.0 Hz, 1.25H), 7.36 – 7.08 (m, 22H), 6.88 – 6.78 (m, 0.25H), 5.23 (d, *J* = 5.9 Hz, 1.25H), 4.66 – 4.49 (m, 5.5H), 4.49 – 4.44 (m, 1H), 4.44 – 4.35 (m, 2H), 4.22 (t, *J* = 3.8 Hz, 1.25H), 4.13 (dd, *J* = 6.0, 3.7 Hz, 1H), 4.06 – 3.98 (m, .075H), 3.91 (d, *J* = 12.3 Hz, 0.25H), 3.82 (dd, *J* = 10.0, 6.0 Hz, 0.25H), 3.74 – 3.62 (m, 2.5H), 2.32 (s, 3H), 2.18 (s, 0.75H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 138.3, 138.2, 137.9, 137.8, 137.7, 137.6, 135.4, 134.8, 134.1, 130.2, 129.5, 128.4, 128.3, 128.3, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.1, 126.3, 126.1, 125.6, 89.8, 85.8, 84.7, 82.1, 82.0, 81.8, 81.1, 80.3, 73.4, 73.3, 72.2, 71.8, 71.6, 71.4, 70.5, 70.4, 19.4. IR (neat): 2925, 2861, 1496, 1455, 1073, 1028, 734, 697. HRMS: calculated for $[C_{33}H_{34}O_4 + Na]^+$: 517.23493; found $[M + Na]^+$: 517.23426.



1-*C*-α-(Vinyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (15g)

The title compound was synthesized following the general procedures (135 mg, 0.3 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 5 : 95 – 15 - 85) yielded the title C-glycoside as a colorless oil (56 mg, 0.13 mmol, 43%) contaminated with approximately 10% of **14g** as determined by ^1H-NMR.

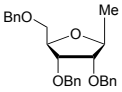
1H NMR (400 MHz, $CDCl_3$) δ 7.72 (m, 1H), 7.53 (m, 1H), 7.36 – 7.25 (m, 14H), 5.95 (ddd, *J* = 17.2, 10.4, 7.0 Hz, 1H), 5.35 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.20 (dd, *J* = 10.4, 1.3 Hz, 1H), 4.61 – 4.48 (m, 6H), 4.45 (m, 1H), 4.25 – 4.19 (m, 1H), 4.11 – 4.07 (m, 1H), 3.95 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.59 (dd, *J* = 5.5, 2.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 138.0, 137.7, 136.6, 128.4, 128.4, 128.3, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 117.2, 88.1, 84.9, 83.5, 81.3, 73.4, 72.0, 71.9, 70.2. HRMS: calculated for $[C_{28}H_{30}O_4 + H]^+$: 431.22169; found $[M + H]^+$: 431.22178.



2',3',5'-Tri-*O*-benzyl-pseudouridine (6)

The title compound was reduced using conditions as described in the general procedure (2840 mg, 4.4 mmol), allowing the reaction mixture to warm from -78 °C to r.t. The reaction mixture was cooled to -15 °C and TFA (15 mL) was added. The reaction mixture was stirred for 30 minutes, poured on ice water (50 mL) and extracted with DCM (100 mL). The aqueous layer was discarded and the organic layer was washed with saturated aqueous $NaHCO_3$ (30 mL), H_2O (3x 30 mL) and Brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Silicagel column chromatography (Acetone : DCM 5 : 95 → 15 : 85) yielded the title C-glycoside as a colorless oil (1.29 g, 2.5 mmol, 70%)

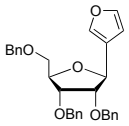
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 9.27 (s, 1H), 7.60 (d, *J* = 5.8 Hz, 1H), 7.43 (d, *J* = 6.8 Hz, 2H), 7.35 – 7.15 (m, 13H), 5.04 (s, 1H), 4.95 – 4.61 (m, 2H), 4.57 – 4.36 (m, 3H), 4.33 – 4.17 (m, 2H), 4.05 (d, *J* = 4.6 Hz, 1H), 3.95 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.85 (dd, *J* = 10.7, 2.2 Hz, 1H), 3.62 (dd, *J* = 10.8, 3.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 151.9, 139.0, 138.1, 138.0, 137.7, 128.4, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 112.9, 79.3, 78.4, 78.2, 75.5, 73.2, 71.8, 71.1, 68.5. HRMS: calculated for $[C_{30}H_{30}N_2O_6 + H]^+$: 515.21766; found $[M + H]^+$: 515.21771.



1-*C*-β-Methyl-2,3,5-tri-*O*-benzyl-D-ribofuranose (17a)

The title compound was synthesized following the general procedures (150 mg, 0.35 mmol). Silicagel column chromatography (EtOAc : Petroleum ether 1 : 9) yielded the title C-glycoside as a colorless oil (140 mg, 0.32 mmol, 90%)

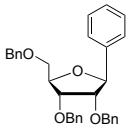
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 15H), 4.62 – 4.45 (m, 6H), 4.16 (q, *J* = 4.4 Hz, 1H), 4.10 (p, *J* = 6.3 Hz, 1H), 3.87 (dd, *J* = 5.3, 4.3 Hz, 1H), 3.50 – 3.41 (m, 3H), 1.25 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 137.9, 137.9, 128.3, 128.2, 128.2, 128.0, 127.8, 127.6, 127.5, 127.5, 82.5, 81.5, 77.4, 76.8, 73.3, 72.0, 71.6, 70.5, 19.0. IR (neat): 2872, 1721, 1454, 1097, 1027, 736, 697. HRMS: calculated for $[C_{27}H_{30}O_4 + Na]^+$: 441.20363; found $[M + Na]^+$: 441.20330.



1-*C*-β-(3'-Furanosyl)-2,3,5-tri-*O*-benzyl-D-ribofuranose (17b)

The title compound was synthesized following the general procedures (185 mg, 0.38 mmol). Silicagel column chromatography (EtOAc : Petroleum ether, 1 : 9 → 12.5 : 87.5) yielded the title C-glycoside as a colorless oil (180 mg, 0.38 mmol, quant).

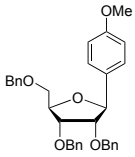
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.37 (m, 1H), 7.36 – 7.20 (m, 16H), 6.39 – 6.23 (m, 1H), 4.97 (d, *J* = 6.7 Hz, 1H), 4.65 – 4.45 (m, 6H), 4.28 (q, *J* = 4.0 Hz, 1H), 4.05 – 3.95 (m, 1H), 3.84 (dd, *J* = 6.7, 5.2 Hz, 1H), 3.66 – 3.51 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 143.2, 140.2, 138.1, 137.9, 137.7, 128.4, 128.3, 128.1, 127.8, 127.8, 127.6, 124.8, 108.5, 82.2, 81.6, 77.4, 75.7, 73.4, 72.2, 71.9, 70.4. IR (neat): 2886, 2362, 1497, 1454, 1151, 1091, 1050, 1018, 876, 748, 729, 696. HRMS: calculated for $[C_{30}H_{30}O_5 + Na]^+$: 493.19855; found $[M + Na]^+$: 493.19820.



1-*C*-β-phenyl-2,3,5-tri-*O*-benzyl-D-ribofuranose (17c)

The title compound was synthesized following the general procedures (0.2 g, 0.4 mmol). Silicagel column chromatography (EtO_2 : Petroleum ether 2 : 8) yielded the title C-glycoside as a colorless oil (150 mg, 0.31 mmol, 78%).

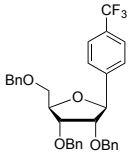
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 6.7 Hz, 2H), 7.34 – 7.19 (m, 15H), 7.19 – 7.11 (m, 3H), 5.03 (d, *J* = 6.6 Hz, 1H), 4.63 – 4.50 (m, 4H), 4.46 (d, *J* = 1.8 Hz, 2H), 4.35 (q, *J* = 4.0 Hz, 1H), 4.01 (t, *J* = 4.6 Hz, 1H), 3.85 – 3.77 (m, 1H), 3.64 (dd, *J* = 10.4, 4.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 138.1, 137.9, 137.7, 128.9, 128.2, 128.2, 128.2, 127.6, 127.6, 127.6, 127.5, 127.5, 126.2, 125.2, 83.6, 82.5, 81.6, 77.4, 73.3, 72.1, 71.8, 70.3. IR (neat): 2870, 2358, 1496, 1454, 1367, 1144, 1106, 1051, 1010, 730, 696. HRMS: calculated for $[C_{32}H_{32}O_4 + Na]^+$: 503.21928; found $[M + Na]^+$: 503.21884



1-*C*-β-(*p*-Methoxyphenyl)-2,3,5-tri-*O*-benzyl-D-ribofuranose (17d)

The title compound was synthesized following the general procedures (175 mg, 0.33 mmol). Silicagel column chromatography (EtO_2 : Petroleum ether 3 : 7) yielded the title C-glycoside as a colorless oil (110 mg, 0.21 mmol, 65%)

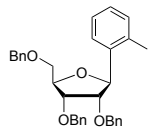
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 16H), 7.17 (dd, *J* = 6.7, 2.8 Hz, 2H), 6.88 – 6.77 (m, 2H), 4.97 (d, *J* = 6.8 Hz, 1H), 4.68 – 4.50 (m, 4H), 4.46 (s, 2H), 4.32 (q, *J* = 4.0 Hz, 1H), 4.04 – 3.96 (m, 1H), 3.79 (s, 4H), 3.68 – 3.59 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 138.1, 137.9, 137.8, 132.4, 128.3, 128.2, 128.0, 127.7, 127.7, 127.60, 127.5, 113.7, 83.5, 82.3, 81.6, 77.5, 77.3, 77.0, 76.7, 73.4, 72.1, 71.8, 70.5, 55.2. IR (neat): 2903, 2358, 1615, 1516, 1454, 1253, 1145, 1105, 1052, 1027, 834, 814, 735, 698. HRMS: calculated for $[C_{33}H_{34}O_5 + Na]^+$: 533.22985; found $[M + Na]^+$: 533.22948.



1-*C*-β-(4'-Trifluoromethyl-phenyl)-2,3,5-tri-*O*-benzyl-D-ribofuranose (17e)

The title compound was synthesized following the general procedures (0.28 g, 0.5 mmol). Silicagel column chromatography (EtO_2 : Petroleum ether 2 : 8) yielded the title C-glycoside as a colorless oil (192 mg, 0.35 mmol, 70%).

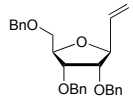
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.45 (m, 5H), 7.34 – 7.25 (m, 10H), 7.25 – 7.20 (m, 3H), 7.17 – 7.13 (m, 2H), 5.04 (d, *J* = 7.1 Hz, 1H), 4.63 – 4.48 (m, 5H), 4.45 – 4.33 (m, 2H), 4.02 (dd, *J* = 4.9, 3.7 Hz, 1H), 3.78 (dd, *J* = 7.0, 5.1 Hz, 1H), 3.66 (dd, *J* = 10.4, 4.0 Hz, 1H), 3.60 (dd, *J* = 10.4, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 137.9, 137.7, 137.4, 129.6 (q, *J* = 32 Hz), 128.3, 128.2, 128.0, 127.8, 127.7, 127.7, 127.5, 126.4, 126.1, 125.5 (q, *J* = 4 Hz), 83.8, 82.1, 81.6, 77.3, 73.4, 72.3, 71.9, 70.3. IR (neat): 1224, 1116, 1092, 1065, 1013, 836, 727, 696. HRMS: calculated for $[C_{33}H_{31}F_3O_4 + Na]^+$: 571.20667; found $[M + Na]^+$: 571.20676.



1-*C*-β-(2-Toluoyl)-2,3,5-tri-*O*-benzyl-D-ribofuranose (17f)

The title compound was synthesized following the general procedures (150 mg, 0.3 mmol). Silicagel column chromatography (Et_2O : Petroleum ether, 20 : 80) yielded the title C-glycoside as a colorless oil (75 mg, 0.15 mmol, 50%).

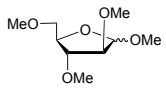
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.49 (m, 1H), 7.31 - 7.26 (m, 9H), 7.26 – 7.22 (m, 3H), 7.20 – 7.15 (m, 2H), 7.15 – 7.08 (m, 3H), 5.29 (d, *J* = 6.1 Hz, 1H), 4.68 – 4.50 (m, 5H), 4.46 (d, *J* = 11.9 Hz, 1H), 4.34 (dd, *J* = 8.0 Hz, *J* = 3.9 Hz, 1H), 4.07 (t, *J* = 5.0 Hz, 1H), 3.91 – 3.85 (m, 1H), 3.73 (dd, *J* = 10.5, 3.9 Hz, 1H), 3.65 (dd, *J* = 10.5, 3.9 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 138.2, 138.0, 137.9, 135.7, 130.1, 128.3, 128.2, 128.0, 127.7, 127.6, 127.6, 127.4, 126.0, 125.9, 83.5, 81.3, 79.8, 77.6, 73.4, 72.3, 72.1, 70.2, 19.5. IR (neat): 2854, 1723, 1496, 1454, 1120, 1028, 873, 736, 697. HRMS: calculated for $[C_{33}H_{34}O_4 + Na]^+$: 517.23493; found $[M + Na]^+$: 517.23464.



1-*C*-β-Vinyl-2,3,5-tri-*O*-benzyl-D-ribofuranose (17g)

The title compound was synthesized following the general procedures (186 mg, 0.42 mmol). Silicagel column chromatography (EtO_2 : Petroleum ether 12 : 88) yielded the title C-glycoside as a colorless oil (60 mg, 0.14 mmol, 33%) contaminated with approximately 10% of the ethyl glycoside as determined by ^{1}H-NMR.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 16H), 5.84 (ddd, *J* = 17.1, 10.4, 6.8 Hz, 1H), 5.43 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.22 (d, *J* = 10.5 Hz, 1H), 4.58 (m, 6H), 4.54 – 4.46 (m, 1H), 4.25 (q, *J* = 4.3 Hz, 1H), 3.95 – 3.91 (m, 1H), 3.79 – 3.70 (m, 1H), 3.57 – 3.52 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 137.9, 137.9, 136.7, 128.4, 128.1, 127.9, 127.8, 127.6, 117.7, 82.1, 81.4, 81.3, 77.5, 73.4, 72.1, 71.9, 70.4. IR (neat): 2922, 1497, 1455, 1090, 1027, 928, 735, 697. HRMS: calculated for $[C_{28}H_{30}O_4 + NH_4]^+$: 448.24824; $[C_{28}H_{30}O_4 + Na]^+$: 453.20363; found $[M + NH_4]^+$: 448.24837; $[M + Na]^+$: 453.20314.

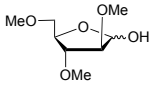


Methyl-α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose

D-Arabinose (1.75 g, 12 mmol) was suspended in MeOH (45 mL). A cold (0 °C) solution of AcCl (0.8 mL) in MeOH (5 mL) was added dropwise. The reaction mixture was stirred overnight during which the suspension had become a clear solution. Ag(II)O (2.7 g, 11.6 mmol) was added and the mixture was filtered over celite after 5 minutes of additional stirring. The filtrate was diluted with dry toluene (10 mL) and concentrated. The reaction crude was taken up in DMF (41 mL) and sodium hydride (1.2 g, 49 mmol, 6 eq based on crude yield) was added at 0 °C. After 15 minutes MeI (1.2 g, 49 mmol, 6 eq based on crude yield) and the reaction mixture was stirred overnight at room temperature. Quenching by methanol followed by concentration yielded a syrup which was taken up in EtOAc (50 mL) which was washed with water (3x 15 mL). Due to the solubility of the product in water the aqueous layers were repeatedly extracted with $CHCl_3$ (6x 30 mL) before drying ($MgSO_4$) and concentrating the combined organic layers. Silicagel column chromatography (Et_2O : Petroleum ether, 25 : 75) yielded the title sugar as a 9 : 1 mixture of anomers (1.3 g, 6.4 mmol, 57% over two steps).

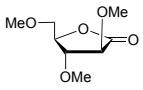
Major isomer:

^{1}H NMR (400 MHz, Chloroform-d) δ 4.92 (s, 1H), 4.11 (dd, J = 6.0, 3.8 Hz, 1H), 3.72 – 3.68 (m, 1H), 3.62 – 3.48 (m, 3H), 3.44 – 3.34 (m, 12H). ^{13}C NMR (101 MHz, CDCl3) δ 106.7, 89.3, 85.8, 80.9, 72.8, 59.3, 58.0, 57.5, 54.9. IR (neat): 2913, 2828, 1728, 1456, 1189, 1108, 1050, 1011, 940. HRMS: calculated for $[C_9H_{18}O_5 + Na]^+$: 229.10464; found $[M + Na]^+$: 229.10490.



α/β-2,3,5-Tri-*O*-methyl-D-arabinofuranose

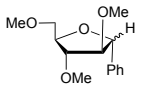
Methyl-α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose (1.3 g, 6.4 mmol) was taken up in 1,4-dioxane : aqueous 4 N HCl (37.5 mL, 1 : 1 v/v) and refluxed for 4 hrs. The reaction mixture was cooled to r.t. and diluted with EtOAc (75 mL). The organic layer was washed with sat aq $NaHCO_3$ (2 x 10 mL), Brine (10 mL) and dried (Na_2SO_4). Both aqueous layers were repeatedly extracted with $CHCl_3$ (4 x 50 mL), combined, dried (Na_2SO_4) and concentrated. Silicagel column chromatography (EtOAc : Petroleum ether, 25 : 75 → 1 : 1) yielded the title sugar as a mixture of anomers (700 mg).



2,3,5-Tri-*O*-methyl-D-arabinofurano-1,4-lactone (25)

α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose (700 mg, 3.6 mmol) was taken up in DMSO (5.4 mL) and Ac_2O (3.6 mL) was added. The reaction mixture was stirred over night at r.t. prior to quenching with ice water (10 mL). The reaction mixture was extracted with EtOAc (5 x 30 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Silicagel column chromatography (EtOAc : Petroleum ether, 1 : 9) yielded the title lactone as an oil (270 mg, 1.43 mmol, 40%).

^{1}H NMR (400 MHz, Chloroform-d) δ 4.20 (ddd, J = 7.4, 4.6, 3.0 Hz, 1H), 4.06 – 4.00 (m, 1H), 3.96 – 3.89 (m, 1H), 3.64 – 3.56 (m, 4H), 3.53 (dd, J = 11.4, 4.7 Hz, 1H), 3.42 (s, 3H), 3.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 81.3, 80.4, 78.9, 70.7, 59.2, 58.4, 58.1. IR (neat): 2934, 1785, 1660, 1596, 1456, 1401, 1326, 1190, 1048, 979, 953, 872. HRMS: calculated for $[C_8H_{14}O_5 + H]^+$: 191.09140; found $[M + H]^+$: 191.09165.



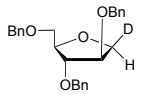
1-*C*-α/β-(Phenyl)-2,3,5-tri-*O*-methyl-D-arabinofuranose (26)

The title compound was synthesized following the general procedures for Grignard addition (105 mg, 0.55 mmol), followed by workup and subsequent treatment with triethylsilane and BF_3•EtO_2 of the reaction crude following general procedure. Silicagel column chromatography (Et_2O : Petroleum ether, 12.5 : 87.5) yielded the title C-glycoside as a mixture of α (> 90%) and β (< 10%) (80 mg, 0.32 mmol, 53% over two steps).

Alpha (major) isomer:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.37 – 7.30 (m, 2H), 7.30 – 7.24 (m, 1H), 4.88 (d, *J* = 5.5 Hz, 1H), 4.32 – 4.26 (m, 1H), 3.87 – 3.80 (m, 2H), 3.65 – 3.54 (m, 2H), 3.44 (s, 3H), 3.40 (s, 3H), 3.35 (s, 3H). ^{13}C NMR (101

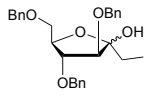
MHz, CDCl3) δ 140.4, 128.4, 127.7, 126.3, 92.1, 87.0, 83.8, 81.4, 73.0, 59.3, 58.1, 57.6. IR (neat): 2923, 2364, 2343, 1731, 1457, 1109. HRMS: calculated for $[C_{14}H_{20}O_4 + Na]^+$: 275.12538; found $[M + Na]^+$: 275.12543.



1-β-(Deutero)-2,3,5-tri-*O*-benzyl-D-arabinofuranose (29)

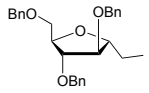
Acetyl-α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose (84 mg, 0.2 mmol) was taken up in DCM (3 mL) and treated with triethylsilane-D (42 µL, 0.27 mmol, 1.35 eq) and $SnCl_4$ (32 µL, 0.27 mmol, 1.35 eq) at -78 °C and stirred over night. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (3 mL), diluted with EtOAc (25 mL) and washed with sat. aq. $NaHCO_3$ (2 x 10 mL), water (10 mL), brine (10 mL) dried ($MgSO_4$) and concentrated under reduced pressure. Silicagel column chromatography (EtOAc : Petroleum ether, 15 : 85) yielded the title sugar as an oil (42 mg, 0.11 mmol, 55%).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.37 – 7.25 (m, 15H), 4.61 – 4.51 (m, 4H), 4.51 – 4.41 (m, 2H), 4.09 – 4.03 (m, 2H), 3.96 (dd, J = 3.9, 1.6 Hz, 1H), 3.92 (d, J = 4.5 Hz, 1H), 3.62 (dd, J = 10.0, 6.1 Hz, 1H), 3.57 (dd, J = 10.0, 5.7 Hz, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 138.2, 137.8, 128.5, 128.4, 127.8, 127.8, 127.8, 127.7, 127.6, 84.6, 83.2, 82.74, 73.4, 71.8, 71.3 (t, J = 22.2 Hz), 71.2, 70.4. IR (neat): 2920, 2852, 1497, 1454, 1071, 1028, 734, 695. HRMS: calculated for $[C_{26}H_{27}DO_4 + Na]^+$: 428.19426; found $[M + Na]^+$: 428.19335.



1-*C*-Ethyl-2,3,5-tri-*O*-benzyl-D-arabinofuranolactol[28]

To a stirred and cooled (0 ºC) of 1-*C*-vinyl-2,3,5,-tri-*O*-benzyl-D-arabinofuranolactol (89 mg, 0.2 mmol) in toluene (4 mL) was added Stryker's reagent (72.4 mg, 0.38 mmol, 1.9 eq) in toluene (7 mL). After two hours TLC analysis (EtOAc : Petroleum ether, 25 :75) showed disappearance of the starting material and formation of a less polar compound. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (10 mL). The reaction mixture was diluted with EtOAc (10 mL) and washed with saturated aqueous NH_4Cl (10 mL). The combined aqueous layers were extracted with EtOAc (20 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Rapid silica gel purification (EtOAc : Petroleum ether, 1 : 9) yielded a complex mixture of α- and β-hemiacetals as a colorless oil (50 mg).

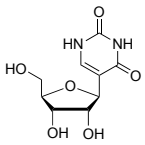


1-*C*-α-(Ethyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose[28]

The title compound was synthesized following the general procedures (50 mg, 0.1 mmol). Silicagel column chromatography (EtOAc : Pentane, 2 : 98 – 5 : 95) yielded the title C-glycoside as a colorless oil (40 mg, 92 µmol, 92%)

1H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.23 (m, 15H), 4.62 – 4.45 (m, 6H), 4.19 (dd, J = 5.9, 3.8 Hz, 1H), 4.02 (dd, J = 3.9, 2.8 Hz, 1H), 3.91 (ddd, J = 7.3, 6.1, 4.3 Hz, 1H), 3.81 (dd, J = 4.5, 2.8 Hz, 1H), 3.58 (dd, J = 10.0, 6.0 Hz, 2H), 1.73 – 1.61 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 138.2, 137.9, 128.4, 128.4, 127.8,

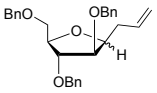
127.8, 127.7, 127.6, 87.5, 85.5, 83.8, 81.2, 73.4, 71.8, 71.7, 70.3, 26.30, 10.16. IR (neat): 2923, 1454, 1094, 1028, 736. HRMS: calculated for $[C_{28}H_{32}O_4 + Na]^+$: 455.21928; found $[M + Na]^+$: 455.21860.



Pseudouridine

To a stirred and cooled (-78 °C) of benzyl protected pseudouridine **9** (1 g, 1.9 mmol) in anhydrous DCM (22 mL) was added dropwise a solution of BCl_3 in DCM (1 M, 11 mL, 11 mmol, 5.6 eq). The reaction mixture was allowed to warm to 0 °C o.n. The reaction was quenched by the addition of anhydrous MeOH (2.25 mL), stirred for 5 minutes, concentrated under reduced pressure and co-evaporated with toluene (2x 5 mL). The reaction crude was crystallized from EtOH/MeOH (1 : 3, 200 mL) yielding the title compound as a white solid (0.5 g, 1.9 mmol, quant)

^{1}H NMR (400 MHz, Deuterium Oxide) δ 7.60 (s, 1H), 4.61 (d, *J* = 5.5 Hz, 1H), 4.22 (t, *J* = 5.4 Hz, 1H), 4.08 (t, *J* = 5.4 Hz, 1H), 3.95 (q, *J* = 4.9 Hz, 1H), 3.78 (dd, *J* = 12.5, 3.1 Hz, 1H), 3.66 (dd, *J* = 12.5, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, D_2O) δ 165.3, 152.8, 141.5, 110.4, 83.3, 79.1, 73.3, 70.8, 61.5. IR (neat): 3177, 2944, 1716, 1682, 1661, 1443, 1424, 1226, 1112, 1051, 1030, 867, 852. HRMS: calculated for $[C_9H_{12}N_2O_6 + Na]^+$: 267.05876; found $[M + Na]^+$: 267.05869.



1-*C*-α/β-(allyl)-2,3,5-tri-*O*-benzyl-D-arabinofuranose[39]

Acetyl-α/β-2,3,5-tri-*O*-methyl-D-arabinofuranose (84 mg, 0.2 mmol) was taken up in DCM (3 mL) and treated with allyltrimethylsilane (42 µL, 0.27 mmol, 1.35 eq) and $SnCl_4$ (32 µL, 0.27 mmol, 1.35 eq) at -78 °C and slowly warmed to -25 °C. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (2 mL), diluted with EtOAc (25 mL) and washed with sat. aq. $NaHCO_3$ (2 x 10 mL), water (10 mL), brine (10 mL) dried ($MgSO_4$) and concentrated under reduced pressure. Silicagel column chromatography (EtOAc : Petroleum ether, 5 : 95) yielded the title sugar as a mixture of anomers (85 : 15, β : α, 67 mg, 0.15 mmol, 75%).

Beta isomer:

^{1}H NMR (400 MHz, Chloroform-d) δ 7.46 – 7.16 (m, 15H), 5.80 (ddd, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.11 (dd, *J* = 17.2, 1.8 Hz, 1H), 5.07 – 4.98 (m, 1H), 4.62 – 4.44 (m, 5H), 4.36 (d, *J* = 11.9 Hz, 1H), 4.05 – 4.01 (m, 1H), 4.03 (dd, *J* = 7.0, 3.4 Hz, 1H), 3.92 (d, *J* = 2.7 Hz, 1H), 3.81 (d, *J* = 3.5 Hz, 1H), 3.63 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.51 (dd, *J* = 9.8, 6.9 Hz, 1H), 2.59 – 2.45 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 137.9, 137.8, 134.8, 128.4, 128.3, 128.3, 127.8, 127.7, 127.6, 127.6, 127.5, 116.9, 83.7, 82.7, 82.6, 80.9, 73.2, 71.3, 71.2, 70.6, 33.1. IR (neat): 2861, 1721, 1496, 1454, 1273, 1070, 1028, 738, 697. HRMS: calculated for $[C_{29}H_{32}O_4 + Na]^+$: 467.21928; found $[M + Na]^+$: 467.21888.

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(39) Arabinose donor **28** was also reacted at -78 ^{o}C with allyl trimethylsilane in a reaction similar to the one described for **29**. At -78 ^{o}C no product formation was observed. Instead, hydrolysis of the starting material was observed. These results indicate insufficient reactivity of allyl trimethylsilane under these conditions. Executing the reaction under gradual warming to -25 ^{o}C yielded a mixture of the C-alkylated product in a α : β ratio of 15 : 85. The β face attack of the allyl nucleophile indicates the expected formation of the ^{3}E oxocarbenium-ion conformer as observed in the other reactions in the D-arabinose series. Full experimental detail and compound characterisation is given in the experimental section.

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