Chapter 4

Chiral Pyrroline-Based Ugi-Three-Component Reactions Are Under Kinetic Control

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4.1 Introduction

The Ugi reaction is one of the most widely used multicomponent reactions and has found extensive application in the generation of structural diversity in diverse compound libraries.[1-3] In the classic Ugi four-component reaction, an aldehyde, an amine, a carboxylic acid, and an isocyanide are combined to form a diamide motif. In this event, the aldehyde

is condensed with the amine to generate an imine (**3**, Figure 4.1a). This species is protonated by the carboxylic acid component to provide an iminium ion (**4**), which is attacked by the isocyanide to generate a nitrilium ion (**5**). This cation is intercepted by the carboxylate to form an intermediate imidate (**6**). Mumm rearrangement of this imidate leads to the final Ugi product (**7**).[4] In the closely related Ugi-three-component reaction, preformed imines are made to react with an isocyanide and a carboxylic acid. As a result of an Ugi multicomponent reaction, a new chiral center is formed between the two newly created amide functions and it is often assumed that the stereoselectivity in the reaction is determined by the irreversible Mumm rearrangement, which terminates the series of preceding equilibria.[1-5]

Chiral carbohydrate-derived azidoaldehydes (exemplified by pentose derived 4-azido-aldehyde **8**) have been explored to generate cyclic imines as a starting point for an ensuing Ugi three-component reaction process (see Figure 4.1b-c).[6-9] During the course of these investigations it was observed that some of these reactions proceeded with excellent stereoselectivity while others provided diastereomeric products with little or no selectivity.[10-16] For example, the D-lyxo configured pyrroline (**12**) gave after Ugi reaction with a variety of isocyanides and carboxylates exclusively the all-*cis* pyrrolidines, whereas the D-arabino configured pyrroline (**13**) provided the 1,2-*cis*- and 1,2-*trans*-products in almost equal amounts.[9,17] The stereochemical course of these reactions is obviously guided by the configuration of the starting imine, but is not easily explained by considering the Mumm rearrangement as the stereoselectivity determining step. Would this be true, then formation of the thermodynamically more stable product would be expected. This chapter describes experimental and computational studies on the Ugi three-component reaction of all four possible 4-deoxy-4-azido-D-pentose derived pyrrolines **12**-**15**. The results indicate that the stereoselectivity of these Ugi multicomponent reactions is based on kinetic control and is determined at the stage of attack of the isocyanide at the iminium ion.

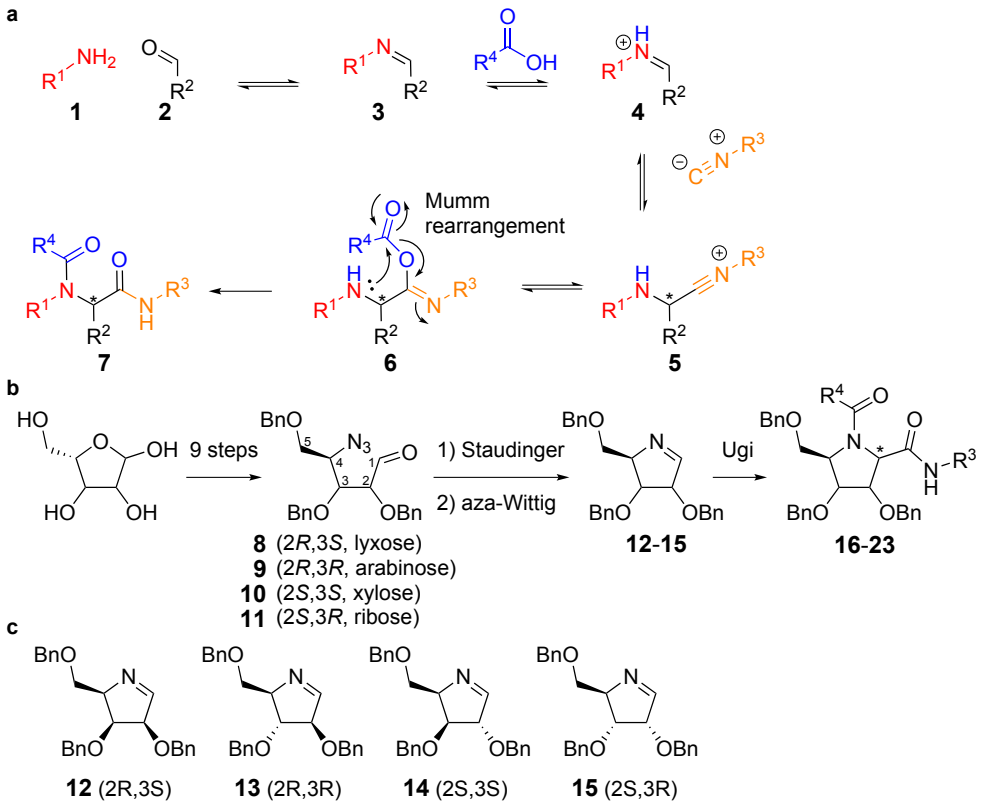
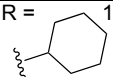
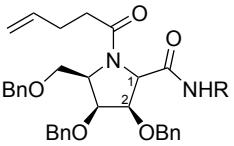
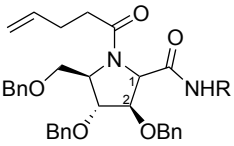
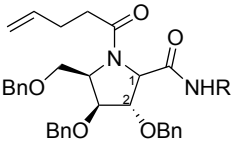
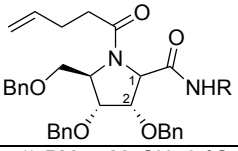


Figure 4.1 a) The Ugi multi-component reaction. b) The Ugi reaction on a preformed pyrroline, generated from a D-pentose derived 4-azido aldehyde, through a Staudinger-aza-Wittig reaction. c) the four investigated pentofuranosyl imines.

4.2 Results and discussion

The four diastereomeric pentose-derived azidoaldehydes used in this study, **8** (D-lyxo), **9** (D-arabino), **10** (D-xylo), and **11** (D-ribo), and corresponding imines (**12**-**15**) are depicted in Figure 4.1. Table 4.1 shows the results of the Ugi reaction of these imines with either *tert*-butyl isocyanide or cyclohexyl isocyanide and pent-4-enoic acid. To fully establish the stereochemistry of the newly formed stereocenters in products **16**-**23**, the pentenoyl groups, which give rise to rotameric product mixtures, were removed by iodine mediated hydrolysis (Table 4.2). The structures of the resulting products (**24**-**31**) were unambiguously established with ^{1}H and ^{13}C NMR spectroscopy.

Table 4.1 Products of the Ugi reaction on D-pentose derived pyrrolines **12**-**15**.[a]

azido-aldehyde	imine	Ugi product	R =  1,2-*cis*:1,2-*trans*[b] yield[c]	R =  1,2-*cis*:1,2-*trans*[b] yield[c]
8	**12**		>98:2 (**16a**) (**16b**) 55%	>98:2 (**17a**) (**17b**) 60%
9	**13**		58:42 (**18a**) (**18b**) 50%	54:46 (**19a**) (**19b**) 61%
10	**14**		43:57 (**20a**) (**20b**) 39%	45:55 (**21a**) (**21b**) 37%
11	**15**		>98:2 (**22a**) (**22b**) 49%	>98:2 (**23a**) (**23a**) 51%

[a]Reaction conditions: 1) PMe_3, MeOH, 0 °C 2) pent-4-enoic acid, RNC, MeOH, 0 °C. [b]Product ratios are determined by ^{1}H NMR at 393K to allow free rotation around the newly formed tertiary amide bond. Stereochemistry was assessed using NOESY NMR spectra of the individual deacylated products. [c]Yield of isolated furanosides after column chromatography.[18]

Table 4.2 Iodine mediated hydrolysis of the 4-pentenoyl group.

	Lyxose		Arabinose		Xylose		Ribose	
R=	*t*Bu (**16a**)	Cy (**17a**)	*t*Bu (**18a**,**18b**)	Cy (**19a**,**19b**)	*t*Bu (**20a**,**20b**)	Cy (**21a**,**21b**)	*t*Bu (**22a**)	Cy (**23a**)
cis	(**24**) 78%	(**25**) 71%	(**26a**) 52%	(**27a**) 85%	(**28a**) 75%	(**29a**) 51%	(**30**) 44%	(**31**) 29%
trans			(**26b**) 60%	(**27b**) 80%	(**28b**) 89%	(**29b**) 60%		

Reaction conditions: I_2, THF, H_2O.

The Ugi three-component reaction on lyxo-configured imine **12** proceeded with excellent 1,2-*cis* stereoselectivity to provide the all-*cis*-linked pyrrolidines **16a** and **17a**, in line with previous observations. A similar stereochemical outcome is observed for the ribo-configured imine **15**, with only the 1,2-*cis* pyrrolidines **22a** and **23a** formed. In contrast, Ugi three-component reaction on the arabino- and xylo-configured imines (**13** and **14**) proceeded with virtually no stereoselectivity. The stereochemical outcome of the Ugi

reaction cannot be rationalized through appreciation of the steric interactions in products **16**-**23**. For example, unfavorable 1,2-*cis* interactions would already be manifest in the imidate intermediates (**6**), thereby eliminating the Mumm rearrangement as the step governing the stereochemical outcome of the reaction. Rather, the parallels between the stereochemical course of *C*-allylation reactions on furanosyl oxocarbenium ions as reported by Woerpel and co-workers[19-20] and those described in Chapter 2 and the stereochemical outcome of the Ugi three-component reactions described here, become apparent. Woerpel and coworkers proposed a model to account for the stereoselectivity observed in *C*-allylation reactions of furanosides based on the conformational preferences of the intermediate oxocarbenium ions. They reasoned that the orientational preferences of the ring substituents dictate the relative stabilities of the oxocarbenium ion envelope conformers and this was confirmed by calculations in Chapter 2. Alkoxy substituents at C2 and C3 preferentially take up an equatorial and axial position, respectively (as in **33a**, see Figure 4.2). The C4 alkyl substituent does not have a strong preference for either orientation but can play an important role in combination with the other ring substituents through mutual steric interactions (see Chapter 2). Nucleophiles would then approach the intermediate envelope oxocarbenium ions preferentially from the "inside" (the side of the envelope *syn* to the carbon atom which lies out of the envelope plane) to avoid developing eclipsing interactions with the neighboring ring substituent. A final contributing factor is the steric interaction between the substituents and the incoming nucleophile. When these conformational preferences are translated to the iminium ions at hand it becomes clear that the D-lyxo iminium ion preferentially adopts an ^{3}E-conformation (**35a** Figure 4.2), allowing the C2 and C3 substituents to take up a preferred orientation. Inside attack on this iminium ion leads to the all cis-product. In the same vein, the D-ribo iminium ion prefers the E_3-envelope and inside attack on this conformer accounts for the formation of the 1,2-*cis* products. For the D-arabino and the D-xylo iminium ions the substituent preferences are conflicting, resulting in a mixture of iminium ion conformers of comparable stability and thereby leading to a mixture of diastereomeric products.

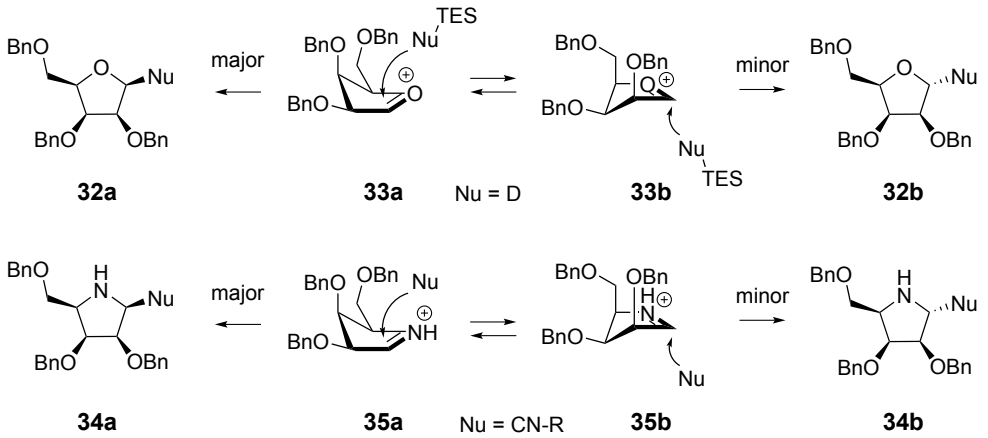


Figure 4.2 D-Lyxose oxocarbenium conformers **33a** and **33b** attacked by [D]triethylsilane and D-lyxo configured iminium ion conformers **35a** and **35b** attacked by an isocyanide.

To gain more insight into the course of the Ugi reactions on pentose derived pyrrolines, a quantum mechanical DFT study[21-22] was performed, in which the relative energies of the intermediates through which the reaction passes were calculated for all four diastereomeric imines, starting from either envelope conformer. The calculations were performed at the B3LYP/6-31G* level with inclusion of the solvent (methanol) through a Polarized Continuum Model and employed methyl substituted imines, methyl isocyanide, and acetic acid as reaction partners.[23] Energies of the individual reactants were added to the energies of the protonated imines and the nitrilium species in order to compare relative energies. In addition, transition states were calculated for the attack of the isocyanide on the protonated imines.

Figure 4.3 (top) shows the reaction pathway energy diagram of the D-lyxo configured imine **12** starting at the protonated imine (**36**). The pathway shows two exothermic steps, one, the formation of the imidate (**39**) from the nitrilium ion (**38**) and, the other, the Mumm rearrangement, proceeding through a cyclic intermediate[24] (**40**) that is higher in energy than the preceding imidate.[25] The large drop in energy in going from the nitrilium ion to the imidate indicates that the addition of the carboxylate to the nitrilium ion is essentially nonreversible. Therefore the stereochemistry of the Ugi reaction is determined before this event. The calculations provide support for the two conformer hypothesis, described above. Two low energy envelope conformations were found for the D-lyxo iminium ion (**36a** and **36b**), of which the ^{3}E-envelope ion (**36a**) is the one lower in energy. This conformer places the C2 and C3 substituents in favorable positions while steric interactions between the C2 and C4 substituent are minimal in this structure. Notably, the difference in energies between the conformers is larger in the two transition states (**37a**

and **37b**) in which the isocyanide attacks the iminium ions than in the starting envelope conformers **36a** and **36b**. This contrasts the perception that steric interactions between the axially oriented C3 substituent and the incoming nucleophile make transition state **37a** less favorable. A close inspection of transition state **37a** for the attack on the methyl isocyanide on the ^3E iminium ion reveals that the C3 substituent actually approaches the incoming nucleophile. A possible explanation for this approach is the electrostatic stabilization of the positive charge that develops on the isocyanide carbon atom by the C3 oxygen substituent while the addition progresses.[26-27] Figure 4.3 (middle) depicts the course of the addition and shows the $^3E \rightarrow {}^3T_2^{\ddagger} \rightarrow E_2$ reaction trajectory in which the stabilizing interaction of the C3-substituent and the incoming nucleophile becomes clear. The calculated difference in energy between the two transition states ($\Delta\Delta E^{\ddagger}$ = 2.5 kcal mol^{-1}; 1,2-*cis*:1,2-*trans*, **37a**:**37b** = 98:2) corroborates the observed stereoselectivity in the Ugi reaction of imine **12** (experimental 1,2-*cis*:1,2-*trans* = >98:2).

The Free Energy Surface (FES) maps, introduced in Chapter 2, for D-lyxo configured imine **36** (Figure 4.3 bottom) corroborates the finding of two low energy conformers **36a** and **36b**. The energy difference between these ^3E and E_3 envelopes obtained with the initial conformer search (Scheme 4.3 top) and the FES maps (Figure 4.3 bottom) is consistent (1.8 vs 1.9 kcal mol^{-1}). In both envelopes, the *gt* rotamer is lowest in energy as steric repulsions are avoided that are present in the *gg* rotamer (description of the rotamers can be found in Chapter 2).

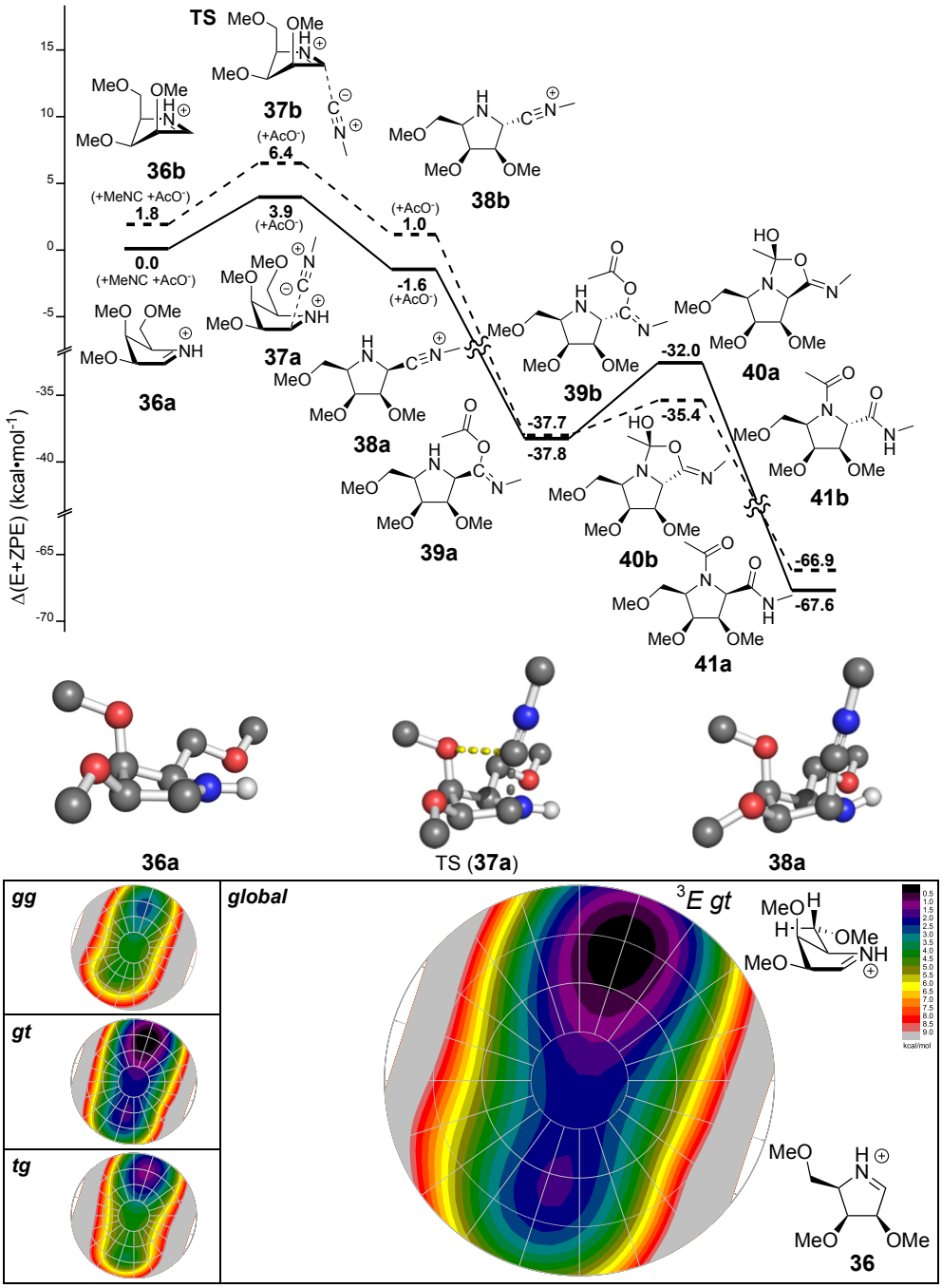


Figure 4.3 Top: Energy diagram of the Ugi reaction on the D-lyxo configured imine starting at the iminium ion. Energies are given relative to the combined energy of the ^3E iminium ion **36a** and its reaction partners. Middle: Optimized structures of the D-lyxo ^3E iminium ion (**36a**), the transition state (**37a**) of the attack of the isocyanide on this ion and the resulting nitrilium ion (**38a**). Bottom: FES map of D-lyxo configured iminium ion **36**.

The other three imine stereoisomers show similar energy diagrams (see Figure 4.6-4.6 top), indicating that the reaction pathways of the Ugi reactions of these imines are comparable to the one described for the D-lyxo imine.[28] The relative energies of the iminium ion envelope conformers, the transition states of the corresponding isocyanide additions, and the resulting nitrilium ions are summarized in Table 4.3. Although the overall reaction pathways are similar there are important differences to note. For both the D-arabino and D-xylo configured iminium ions, the energy difference between the transition states of the isocyanide additions is smaller than the difference in energy between the starting envelope conformers. Also here the stabilizing interaction of the axially oriented C3-substituent with the nucleophile becomes apparent. For example, while the D-xylo configured E_3 iminium ion is favored over its ^3E counterpart by 1 kcal mol^{-1}, the transition state originating from the latter ion is slightly lower in energy than the transition state derived from the former. The D-ribo Ugi reaction energy profile parallels that of its D-lyxo congener. The difference in energy between the two isocyanide addition transition states is larger than the energy difference between the parent iminium ion envelopes leading to the selective formation of the 1,2-*cis*-nitrilium ion and subsequently the 1,2-*cis*-Ugi product. The calculated energy differences between the transition states nicely match the experimental stereoselectivities for the four diastereomeric imines as summarized in Table 4.3. Finally, the calculations confirm that the relative stabilities of the Ugi products cannot account for the observed selectivities.

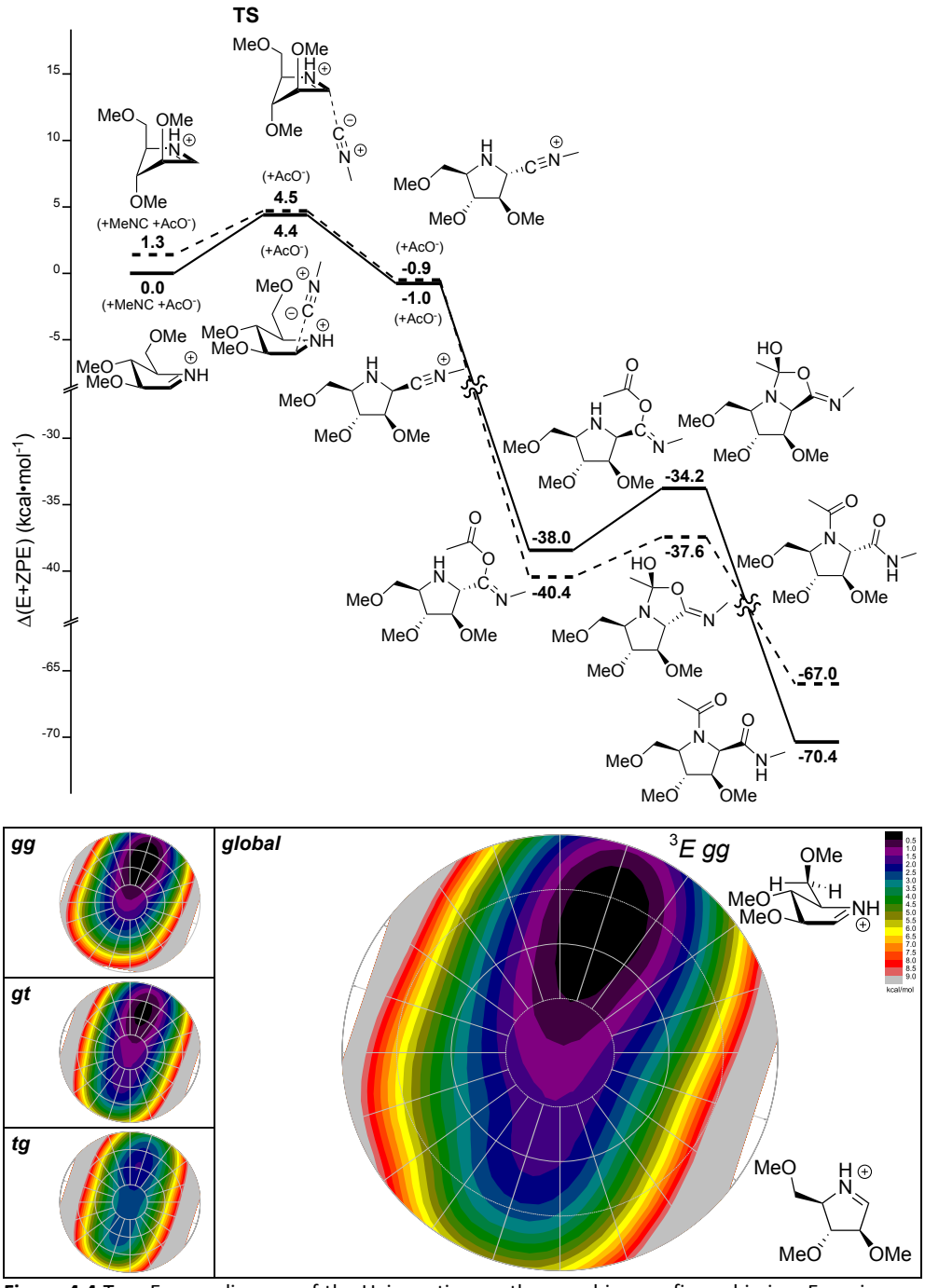


Figure 4.4 Top: Energy diagram of the Ugi reaction on the D-arabino configured imine. Energies are given relative to the combined energy of the ^{3}E iminium ion and its reaction partners. Bottom: FES map of D-arabino configured iminium ion.

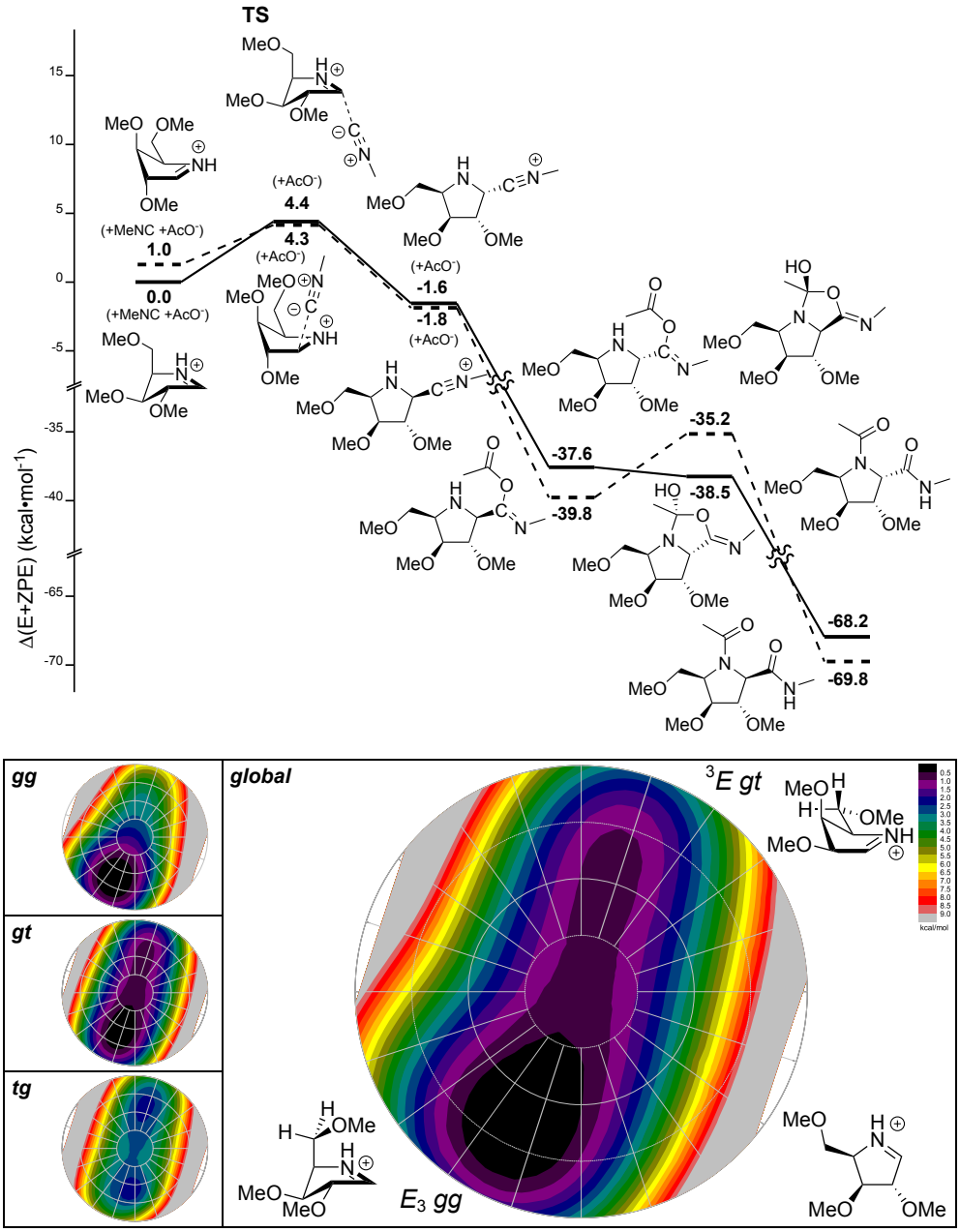


Figure 4.5 Top: Energy diagram of the Ugi reaction on the D-xylo configured imine. Energies are given relative to the combined energy of the E_3 iminium ion and its reaction partners. Bottom: FES map of D-xylo configured iminium ion.

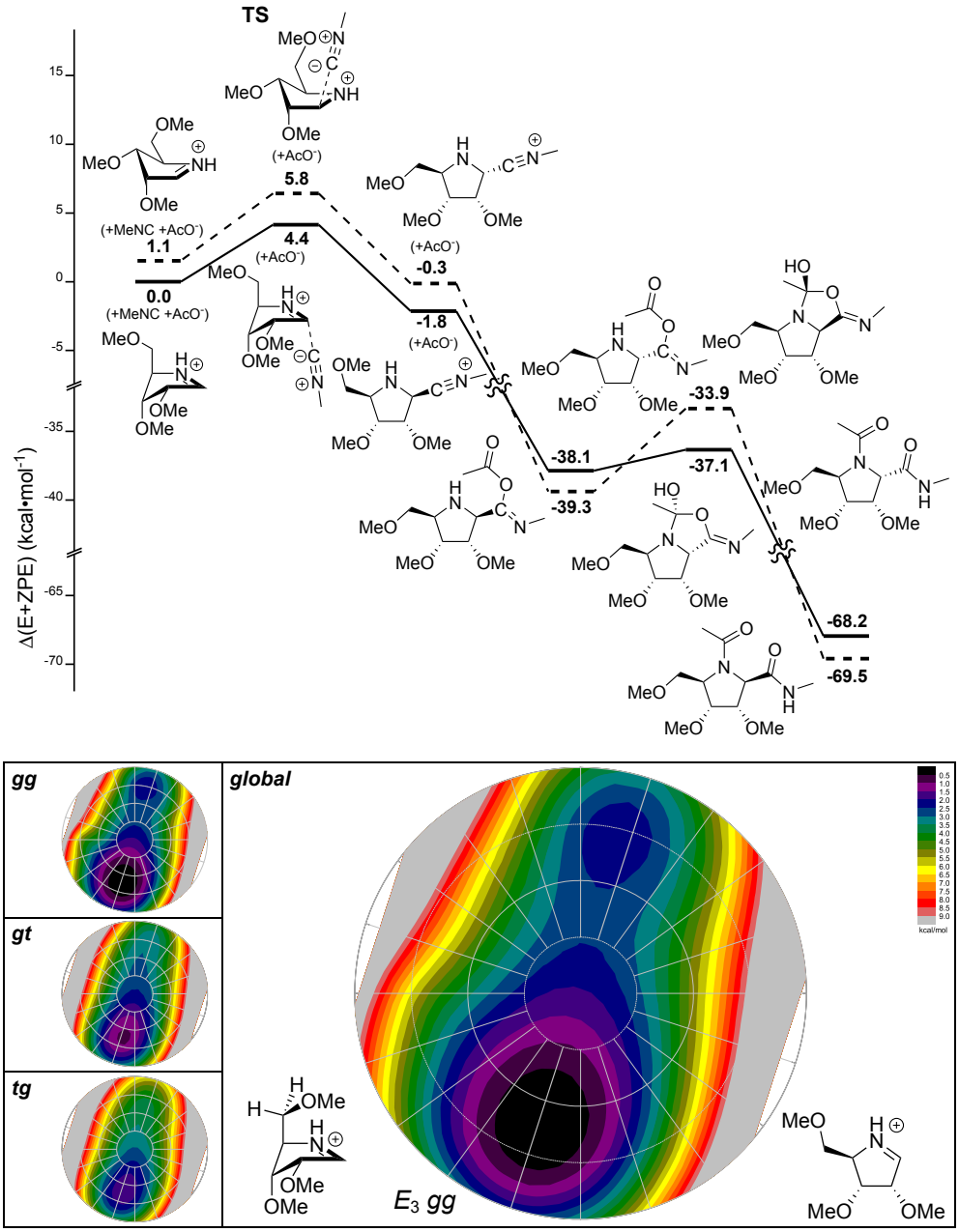


Figure 4.6 Top: Energy diagram of the Ugi reaction on the D-ribo configured imine. Energies are given relative to the combined energy of the E_3 iminium ion and its reaction partners. Bottom: FES map of D-ribo configured iminium ion.

Table 4.3 Relative energies of iminium ion conformers, transition states, nitrilium ions and theoretical product ratios.

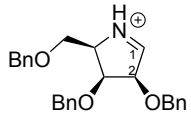
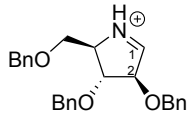
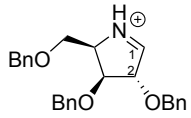
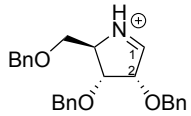
starting iminium ions	products	iminium ions (kcal mol^{-1})	TSs (kcal mol^{-1})	nitrilium ions (kcal mol^{-1})
Lyxo	1,2-*cis* (**16a**)	E_3: 0.0	E_3: 3.9	-1.6
	1,2-*trans* (**16b**)	^3E: 1.8	^3E: 5.4	1.0
			$\Delta\Delta E^{\ddagger}$ = 2.5	(**16a**:**16b** = 98:2)
Arabino	1,2-*cis* (**18a**)	^3E: 0.0	^3E: 4.4	-1.0
	1,2-*trans* (**18b**)	E_3: 1.3	E_3: 4.5	-0.9
			$\Delta\Delta E^{\ddagger}$ = -0.1	(**18a**:**18b** = 55:45)
Xylo	1,2-*cis* (**20a**)	E_3: 0.0	E_3: 4.4	-1.6
	1,2-*trans* (**20b**)	^3E: 1.0	^3E: 4.3	-1.8
			$\Delta\Delta E^{\ddagger}$ = 0.1	(**20a**:**20b** = 45:55)
Ribo	1,2-*cis* (**22a**)	E_3: 0.0	E_3: 4.4	-1.8
	1,2-*trans* (**22b**)	^3E: 1.1	^3E: 5.8	-0.3
			$\Delta\Delta E^{\ddagger}$ = 1.4	(**22a**:**22b** = 91:9)

Figure 4.6-4.6 bottom give the FES maps for the D-arabino, D-xylo and D-ribo configured iminium ions, respectively. The maps support the energy differences of the envelope conformers of these isomers that were found by the initial conformer search, starting from the ^3E and E_3 envelopes. The largest deviation is seen for the D-ribose configured iminium ion, where the energy difference has increased from 1.1 kcal mol^{-1} in the initial conformer search to 2.3 kcal mol^{-1} in the FES map. This may be accounted for by the more thorough interrogation of the conformer space and/or the use of a larger basis set in the FES map method (6-31G* vs 6-311G**). The energy differences between the two envelopes were found to increase in the transition states. Therefore this energy difference may well explain why the Ugi reaction for the ribo configured imine gave only a single product. When the iminium ion FES maps are compared with the aldoses FES maps described in Chapter 2, it becomes clear that stabilizing stereoelectronic interactions play a smaller role. The arabino iminium ion and the aldose oxocarbenium ion FES map are comparable but the iminium ion has a greater preference for ^3E because the E_3 conformer is less stabilized by stereoelectronically interactions. The xylo iminium ion FES map shows that the iminium ion preferentially takes up an E_3 envelope and that the iminium ion FES map is more shallow than the oxocarbenium ion map, indicating that the iminium ions are

overall more stable and the relative differences smaller. The conformer preference of the ribo iminium ion for the E_3 envelope has decreased in comparison with the ribosyl oxocarbenium ion, suggesting that the iminium ions in methanol requires less stabilizing interactions.

4.3 Conclusion

The experimental results supported by the calculational data reported here show that the diastereoselectivity of the Ugi three-component reaction using pentose derived pyrrolines is determined in the transition state of the isocyanide addition step to the iminium ion and that these reactions therefore proceed under kinetic control. This stands in contrast to the classic mechanistic view that the Ugi reaction proceeds through a series of equilibrium reactions before ending with the irreversible Mumm rearrangement in the thermodynamically favored product. For the pyrrolines studied here, the conformation of the iminium ion intermediates, in combination with the stabilizing effect of an axially positioned C3 ether on the developing positive charge in the incoming nucleophile, is the deciding factor in the stereochemical course of the isocyanide addition reaction. It might well be that the kinetic scenario described here is not only valid for the pyrrolines used in this study but also of importance for many other Ugi reactions and other multicomponent reaction featuring isocyanides. The results therefore may help in the development of predictive models for diastereoselective Ugi-type multicomponent reactions, which would have considerable impact in library design for drug discovery and development.

Experimental section

Calculations. For all calculations, the benzyl ethers were replaced by methyl ethers and methyl isocyanide and acetic acid were used as reaction partners. To find the lowest energy conformation of the starting iminium ions, the intermediate nitrilium ions, the imidate intermediates, the bicyclic Mumm rearrangement intermediates and the final products the following calculations were performed. First, the conformer distribution option included in the Spartan '04 program[29] was used to find a set of initial gas-phase geometries. For the iminium ions, the nitrilium ions (both 1,2-*cis* and 1,2-*trans*) and the final products (both 1,2-*cis* and 1,2-*trans*) the conformer distribution search was performed using DFT calculations at the B3LYP/6-31G* level. For the imidates, both the *E*- and *Z*-amides of the 1,2-*cis* and 1,2-*trans* epimers were evaluated using semi-empirical calculations at the AM1 level. Also for the bicyclic intermediates of the Mumm rearrangements, all isomers (1,2-*cis*/1,2-*trans*, E/Z amide configuration and R/S alcohol configuration) were subjected to the conformer distribution search using semi-empirical calculations at the AM1 level. After the semi empirical AM1 calculations a DFT calculation at the B3LYP/6-31G* level was done on the set of isomers. Next, the geometry of a selected set of the lowest energy conformers was optimized in Gaussian 03[30] at the B3LYP/6-31G* level and zero point energy corrections for these were calculated. For the iminium ions two conformers were optimized, for the nitrilium ions 6-8 geometries were optimized, for the imidates 18-20 structures were optimized, for the bicyclic Mumm rearrangement intermediates 24-27 structures were optimized and for the final products 6-7 structures were optimized. In the case where calculations for the iminium ion conformers converged to a single envelope, a

partial structural optimization with geometrical constraints was done to find the energy of the alternative envelope. Finally, the solvent (methanol) effect was incorporated using the polarizable continuum model (PCM) and after inclusion of the unscaled gas-phase zero-point energies, the energies of the conformers were determined. The energies of all reaction components were added up to establish the total energy.

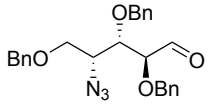
The transition states for the addition of the isocyanide to the different iminium ions were found through the Berny optimization algorithm, which was started after placing the methyl isocyanide in the vicinity (1.75-1.85 Å) of the electrophilic iminium ion. The found structures were checked for the absence of imaginary frequencies and the presence of only one imaginary frequency for the transition states. Intrinsic reaction coordinate (IRC) calculations were performed to verify that each transition state indeed connected the reactants and products.

FES maps were calculated according to the procedure described in Chapter 2.

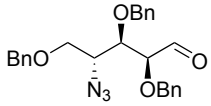
Synthesis

General. All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. Methanol used in the SAWU-3CR was distilled from magnesium (5 g/L)/molecular iodine (0.5 g/L) and stored on activated 3Å molecular sieves under argon. Reactions were performed at room temperature unless stated otherwise and were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with 20% sulfuric acid in EtOH or with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (25 g/l) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/l) in 10% sulfuric acid (aq.) followed by charring at ~150 °C. Flash column chromatography was performed on silica gel (40-63µm). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 750 or Bruker AV 400 in $CDCl_3$, CD_3OD, CD_3CN or C_6D_6. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^{1}H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C NMR spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments. Where applicable NOESY and HMBC experiments were used to further elucidate the structure.

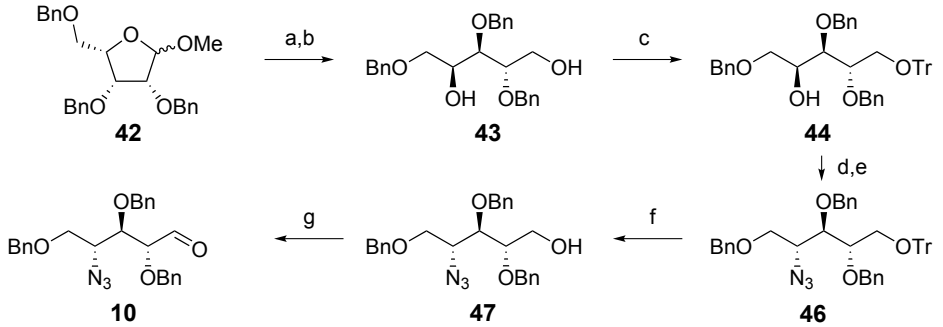
2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-lyxose (8). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-lyxose (**8**) was prepared as described by Bonger *et al*.[9]



2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-arabinose (9). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-arabinose (**9**) was prepared as described by Bonger *et al*.[9]

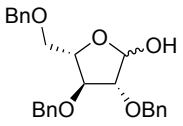


Scheme 4.1 Synthesis of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylose (**10**).

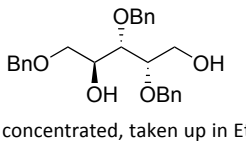


Reagents and conditions: (a) $NaBH_4$, EtOH, 85%; (b) TrCl, Et_3N, DMAP, DCM, 88%; (c) MsCl, pyridine, 4 °C, 96%; (d) NaN_3, 15-crown-5, Bu_4NHSO_4, DMF, 100 °C, 90%; (e) *p*-TsOH, $CHCl_3$, MeOH, 85%; (f) Dess-Martin periodinane, DCM, 4 °C, 66%.

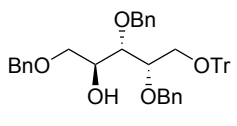
2,3,5-Tri-*O*-benzyl-L-arabinofuranose (42) 2,3,5-Tri-*O*-benzyl-L-arabinofuranose (**42**) was synthesized as its enantiomer (compound **5**) described in Chapter 2.



2,3,5-Tri-*O*-benzyl-L-arabinitol (43). To a cooled solution (0 °C) of 2,3,5-Tri-*O*-benzyl-L-arabinofuranose (**42**, 20 g, 48 mmol) in EtOH (500 ml) was added sodium borohydride (4.2 g, 111 mmol). After stirring for 5 hours at room temperature, TLC analysis showed complete conversion of the starting material into a lower running product. The pH of the reaction mixture was adjusted to pH 4-5 by the addition of acetic acid and the resulting mixture was concentrated, taken up in EtOAc and washed consecutively with 1 M HCl (aq.), $NaHCO_3$ (sat. aq.), and brine. The organic layer was dried (anhydrous $MgSO_4$), filtered and concentrated. The residue was purified by silica gel column chromatography (30-60% EtOAc/PE) yielding the title compound (17 g, 41 mmol, 85 % yield) as a turbid syrup. R_f = 0.6 (1/1; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.18 (m, 15H, C*H*$_{Ar}$), 4.61 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.57 (d, *J* = 12.2 Hz, 2H, 2xC*H*H Bn), 4.53 (d, *J* = 11.1 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.47 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 3.99 (q, *J* = 5.1 Hz, 1H, C-4), 3.79 – 3.66 (m, 4H, C-1, C-2, C-3), 3.65 – 3.57 (m, 2H, C-5), 3.07 (bs, 1H, OH), 2.89 (bs, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 137.9 (3xC_q Bn), 128.4, 128.4, 128.1, 128.1, 127.9, 127.8, 127.8 (*C*H$_{Ar}$ Bn), 79.5 (*C*-2), 78.4 (*C*-3), 73.7, 73.4, 72.8 (3x *C*H$_2$ Bn), 71.1 (*C*-5), 70.5 (*C*-4), 61.3 (*C*-1). $[\alpha]^{20}_D$: -2.7° (c = 1, $CHCl_3$). IR (neat): 698, 737, 1003, 1028, 1072, 1092, 1209, 1321, 1352, 1396, 1454, 1715, 2338, 2868, 3030, 3310, 3372, 3447, 3482. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21658.

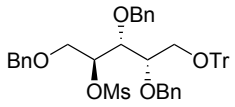


2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-arabinitol (44). 2,3,5-Tri-*O*-benzyl-L-arabinitol (**43**, 17 g, 41 mmol) was dissolved in DCM (300 ml). To this solution was added Et_3N (12 ml, 85 mmol), triphenylmethyl chloride (16 g, 57 mmol) and DMAP (0.60 g, 4.7 mmol). The reaction mixture was stirred overnight after which the reaction was quenched by addition of MeOH (3.5 ml). The mixture was concentrated under reduced pressure, the residue taken up in EtOAc and washed with 0.1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried using anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (50% Ether/PE) yielding 2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-arabinitol (25 g, 37 mmol, 88 %



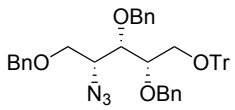
yield). R_f = 0.7 (1/3; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.38 (d, *J* = 6.9 Hz, 6H, CH_{Ar} Tr), 7.31 – 7.14 (m, 22H, CH_{Ar} Bn, CH_{Ar} Tr), 7.07 – 7.02 (m, 2H, CH_{Ar}), 4.68 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.55 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.48 – 4.38 (m, 4H, C*H*H Bn), 3.99 – 3.92 (m, 2H, C-2, C-4), 3.78 (dd, *J* = 7.3, 3.1 Hz, 1H, C-3), 3.56 (dd, *J* = 9.8, 3.6 Hz, 1H, C-5a), 3.52 (dd, *J* = 10.0, 5.3 Hz, 1H-C-5b), 3.48 (dd, *J* = 9.8, 6.0 Hz, 1H, C-1a), 3.34 (dd, *J* = 9.7, 5.8 Hz, 1H, C-1b).2.80 (d, *J* = 5.4 Hz, 1H, O*H*), ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (3xC_q Tr), 138.1, 138.0 (3xC_q), 128.6, 128.4, 128.3, 128.3, 128.1, 128.1, 127.8, 127.8, 127.6, 127.5, 127.0 (*C*H$_{Ar}$ Tr, *C*H$_{Ar}$ Bn), 87.0 (*C*$_q$ Tr), 78.1 (*C*-2), 77.9 (*C*-3), 73.8, 73.3, 73.1 (3x*C*H$_2$ Bn), 71.2 (*C*-5), 70.1 (*C*-4), 63.1 (*C*-1). $[\alpha]^{20}_D$: -1.7° (c = 1, $CHCl_3$). IR (neat): 619, 633, 648, 696, 746, 899, 988, 1001, 1028, 1070, 1153, 1182, 1215, 1321, 1393, 1449, 1491, 1599, 2320, 2868, 3030, 3061. HR-MS: [M+Na$^+$] Calculated for $C_{45}H_{44}O_5$: 687.30810; found: 687.30799.

2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (45). 2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-arabinitol (**44**, 21 g, 32 mmol) was coevaporated twice with toluene, dissolved in pyridine (70 ml) and cooled to 0 °C. Methanesulfonyl chloride (6.4 ml, 82 mmol) was added and the solution stirred for 22 hours at 4 °C. The reaction mixture was quenched by addition of methanol (15 ml) and then concentrated under reduced pressure. The residue was taken up in EtOAc and subsequently washed with 0.1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (70% Toluene/PE - 5% EtOAc/Toluene) yielding 2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (23 g, 32 mmol, 96 % yield) as a slightly yellow highly viscous oil.



R_f = 0.6 (1/9; EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.1 Hz, 6H, CH_{Ar} Tr), 7.32 – 7.18 (m, 22H, CH_{Ar} Bn, CH_{Ar} Tr), 7.17 – 7.11 (m, 2H, CH_{Ar}), 4.95 (ddd, *J* = 7.6, 3.9, 3.0 Hz, 1H, C-4), 4.62 (d, *J* = 11.3 Hz, 1H, C*H*H Bn-3), 4.58 (d, *J* = 11.4 Hz, 1H, C*H*H Bn-2), 4.51 (d, *J* = 11.3 Hz, 1H, C*H*H Bn-3), 4.51 (d, *J* = 11.3 Hz, 1H, C*H*H Bn-2), 4.41 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-5), 4.37 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-5), 4.07 (t, *J* = 3.9 Hz, 1H, C-3), 3.81 (dd, *J* = 11.3, 3.0 Hz, 1H, C-5a), 3.74 – 3.66 (m, 2H, C-2, C-5b), 3.35 (dd, *J* = 10.1, 5.2 Hz, 1H), 3.29 (dd, *J* = 10.1, 5.7 Hz, 1H), 2.86 (s, 3H, CH_3 Ms). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (3xC_q Tr), 138.1, 137.7, 137.7 (3xC_q Bn), 128.7, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.8, 127.8, 127.2 (*C*H$_{Ar}$ Tr, *C*H$_{Ar}$), 87.3 (*C*$_q$ Tr), 82.5 (*C*-4), 79.4 (*C*-3), 78.6 (*C*-2), 74.8 (*C*H$_2$ Bn-3), 73.3 (*C*H$_2$ Bn-2, *C*H$_2$ Bn-5), 69.1 (*C*-5), 63.1 (*C*-1), 38.5 (*C*H$_3$ Ms). $[\alpha]^{20}_D$: -7.5° (c = 1, $CHCl_3$). IR (neat): 633, 696, 745, 810, 845, 912, 968, 1001, 1028, 1074, 1090, 1155, 1175, 1217, 1356, 1449, 1491, 2876, 2934, 3030. HR-MS: [M+Na$^+$] Calculated for $C_{46}H_{46}O_7S$: 765.28565; found: 765.28558.

2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (46). 2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (**45**, 23 g, 32 mmol) was coevaporated twice with toluene and dissolved in DMF (200 ml). Sodium azide (13 g, 200 mmol), 15-crown-5 (1.3 ml, 6.7 mmol) and tetrabutylammonium hydrogen sulfate (2.3 g, 6.7 mmol). The resulting suspension was stirred at 100 °C for 5 days until TLC showed complete conversion into a higher running product. The reaction mixture was concentrated under reduced pressure, taken up in EtOAc and subsequently washed with water. The aqueous layer was extracted with EtOAc and the combined organic layers washed with water, $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (2%-10% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (20 g, 28 mmol, 90 % yield).



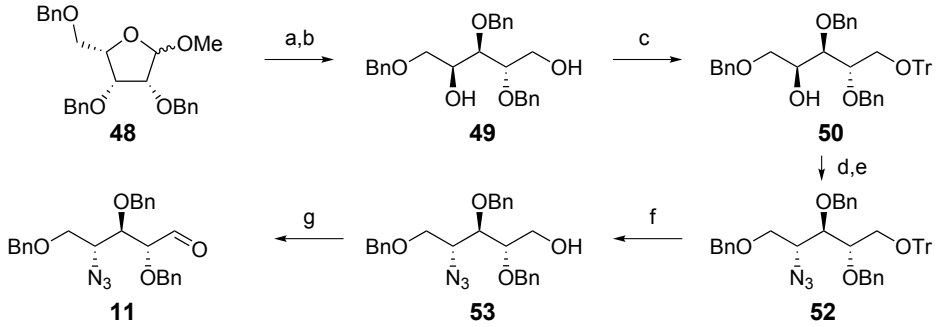
R_f = 0.7 (1/9; EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.0 Hz, 6H, CH_{Ar} Tr), 7.31 – 7.14 (m, 24H, 15xCH_{Ar} Bn, 9xCH_{Ar} Tr), 4.71 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.61 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.46 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.39 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.35 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 3.96 (dd, *J* = 5.7, 4.4 Hz, 1H, C-3), 3.76 (q, *J* = 4.6 Hz, 1H, C-2), 3.58 – 3.53 (m, 1H, C-4), 3.54 – 3.38 (m, 3H, C-5, C-1a), 3.22 (dd, *J* = 10.3, 4.6 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (3xC_q Tr), 138.2, 138.1, 137.8 (3xC_q Bn), 128.7, 128.6, 128.4, 128.4, 128.3, 128.1, 127.9, 127.7, 127.6, 127.1 (*C*H$_{Ar}$), 86.9 (*C*$_q$ Tr), 79.2 (*C*-2), 78.3 (*C*-3), 75.0 (*C*H$_2$ Bn), 73.1 (*C*H$_2$ Bn), 72.8 (*C*H$_2$ Bn), 69.4 (*C*-5), 62.6 (*C*-1), 61.3 (*C*-4). $[\alpha]^{20}_D$: 6.6° (c = 1, $CHCl_3$). IR (neat):

633 696, 746, 804, 918, 970, 1001, 1028, 1092, 1173, 1217, 1342, 1358, 1396, 1449, 1491, 2874, 2924, 3030, 3061. HR-MS: [M+Na$^+$] Calculated for $C_{45}H_{44}N_3O_4$: 712.31458; found: 712.31442.

2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylitol (47). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (**46**, 19 g, 28 mmol) was dissolved in chloroform (125 ml) and MeOH (125 ml) and a catalytic amount of *p*-toluenesulfonic acid monohydrate (250 mg, 1.3 mmol) was added. The reaction mixture was stirred for 3 hours after which it was diluted with DCM and washed with $NaHCO_3$ (sat. aq.) and brine. The solution was then dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (20%-30% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylitol (11 g, 24 mmol, 85 % yield) as a colorless liquid. R_f = 0.35 (1/9; EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.19 (m, 15H, CH_{Ar} Bn), 4.71 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.57 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.54 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.45 (d, *J* = 12 Hz, 1H, C*H*H Bn), 4.59 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 3.81 – 3.72 (m, 2H, C-1, C-3), 3.71 – 3.61 (m, 3H, C-4, C-2, C-1), 3.61 – 3.51 (m, 2H, C-5), 2.27 (bs, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 137.8, 137.6 (3xC_q Bn), 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 126.9 (*C*H$_{Ar}$ Bn), 79.8 (*C*-2), 78.1 (*C*-3), 74.6, 73.3, 72.9 (3x*C*H$_2$ Bn), 69.5 (*C*-5), 61.3 (*C*-1), 60.8 (*C*-4). $[\alpha]^{20}_D$: -7.1° (c = 1, $CHCl_3$). IR (neat): 696, 735, 820, 847, 881, 910, 957, 993, 1028, 1059, 1088, 1101, 1207, 1269, 1319, 1342, 1358, 1393, 1454, 1497, 1535, 1722, 2097, 2326, 2868, 2926, 3030, 3063, 3503. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{29}N_3O_4$: 448.22308; found: 448.22323.

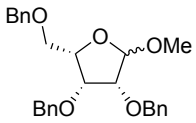
2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylose (10). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylitol (**47**, 224 mg, 0.50 mmol) was dissolved in DCM (10 ml) and cooled to 0 °C. Dess-Martin periodinane (318 mg, 0.75 mmol) was added and the reaction mixture stirred overnight at 0-4 °C. A mixture of 10% $NaHCO_3$ (aq.)/1M $Na_2S_2O_3$ (aq. 1/1 v/v, 25 ml) was added and the solution stirred vigorously for 30 minutes. The organic layer was separated and washed with $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (5-13% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylose (147 mg, 0.33 mmol, 66 % yield) which was used immediately in the SAWU reaction. R_f = 0.6 (1/9; EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H, C-1), 7.37 – 7.19 (m, 15H, CH_{Ar} Bn), 4.71 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.58 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.55 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.48 – 4.37 (m, 3H, 3xC*H*H Bn), 3.94 – 3.84 (m, 2H, C-2, C-3), 3.86 – 3.81 (m, 1H, C-4), 3.55 – 3.47 (m, 2H, C-5). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2 (*C*-1), 137.3, 136.9, 136.6 (C_q Bn), 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7 (*C*H$_{Ar}$ Bn), 81.3 (*C*-2), 78.3 (*C*-3), 73.9, 73.2, 73.1 (3x*C*H$_2$ Bn), 68.8 (*C*-5), 60.5 (*C*-4). $[\alpha]^{20}_D$: -7.5° (c = 1, $CHCl_3$). IR (neat): 696, 735, 822, 849, 912, 1003, 1026, 1070, 1090, 1207, 1267, 1314, 1348, 1362, 1396, 1454, 1728, 2099, 2866, 2924, 3030. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{27}N_3O_4$: 446.20743; found: 446.20745.

Scheme 4.2 Synthesis of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribose (**11**).

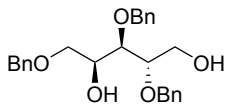


Reagents and conditions: (a) H_2SO_4, AcOH, H_2O, 100 °C; (b) $NaBH_4$, EtOH, 48% (2 steps); (c) TrCl, Et_3N, DMAP, DCM, 44%; (d) MsCl, pyridine, 4 °C, 75%; (e) NaN_3, 15-crown-5, Bu_4NHSO_4, DMF, 100 °C, 76%; (f) *p*-TsOH, $CHCl_3$, MeOH, 84%; (g) Dess-Martin periodinane, DCM, 4 °C, 84%.

2,3,5-Tri-*O*-benzyl-1-*O*-methyl-L-lyxofuranose (48). 2,3,5-Tri-*O*-benzyl-1-*O*-methyl-L-lyxofuranose (**48**) was prepared as its enantiomer (compound **10**) described in Chapter 2.



2,3,5-Tri-*O*-benzyl-L-lyxitol (49). To a solution of acetic acid (290 ml) and aq. 3 M sulphuric acid (77 ml, 232 mmol) was added 2,3,5-Tri-*O*-benzyl-1-*O*-methyl-L-lyxofuranose (**48**, 21.4 g, 39 mmol, 80% pure). The mixture was heated to 100 °C for 1 hour and then cooled to ambient temperature. The solution was neutralized with $NaHCO_3$ (sat. aq.) and then extracted with DCM (3x). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The product was purified by flash chromatography (40-100% Ether/PE) yielding the hydrolyzed product. To a cooled solution (0 °C) of the hydrolyzed furanose in EtOH (310 ml) was added sodium borohydride (2.3 g, 61 mmol). After 5h of stirring at room temperature, the pH of the reaction mixture was adjusted to pH 4-5 by the addition of acetic acid. The resulting mixture was then concentrated, taken up in EtOAc and washed consecutively with 1 M HCl (aq.), $NaHCO_3$ (sat. aq.), and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by silica gel column chromatography (20-40% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-L-lyxitol (5.3 g, 12.6 mmol, 48 % yield) as a highly viscous syrup consisting of a mixture of products resulting from the reduction of the furanose and pyranose isomers of L-lyxofuranose (55% of the desired furanose product). R_f = 0.6 (40/60; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 15H, CH_{Ar} Bn), 4.75 – 4.40 (m, 6H, 3xCH_2 Bn), 4.00 (dt, *J* = 6.0, 2.1 Hz, 1H, C-4), 3.88 – 3.65 (m, 4H, C-1, C-2, C-3), 3.52 (dd, *J* = 9.4, 6.1 Hz, 1H, C-5a), 3.45 (dd, *J* = 9.5, 6.1 Hz, 1H, C-5b), 2.81 (s, 1H, O*H*), 2.57 (s, 1H, O*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.9, 137.9 (3xC_q Bn), 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.9, 127.8 (*C*H_{Ar} Bn), 79.6 (*C*-2), 77.0 (*C*-3), 74.3, 73.4, 72.4 (3x*C*H_2 Bn), 71.3 (*C*-5), 69.7 (*C*-4), 60.5 (*C*-1). $[\alpha]^{20}_D$: 16° (c = 1, $CHCl_3$). IR (neat): 608, 698, 737, 912, 1028, 1063, 1094, 1209, 1244, 1327, 1391, 1454, 1732, 2872, 3030, 3333, 3366, 3456. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{30}O_5$: 423.21660; found: 423.21658. Spectroscopic data matched literature data.[31]



2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-lyxitol (50). 2,3,5-Tri-*O*-benzyl-L-lyxitol (**49**, 5.3 g, 12.6 mmol) was dissolved in DCM (126 ml). To this solution was added Et_3N (7.1 ml, 51 mmol), triphenylmethyl chloride (10.6 g, 38 mmol) and DMAP (0.50 g, 3.8 mmol). The reaction mixture was stirred for 6 days after which the reaction was quenched with MeOH (8 ml) and the mixture was concentrated under reduced pressure. The residue was taken up in EtOAc and washed with 1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15-25% Ether/PE) yielding 2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-lyxitol (3.7 g, 5.6 mmol, 44 % yield). R_f = 0.4 (25/75; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 6.5 Hz, 6H, CH_{Ar} Tr), 7.36 (m, 2H, CH_{Ar}), 7.33 – 7.14 (m, 20H, CH_{Ar} Bn, CH_{Ar} Tr), 7.01 – 6.96 (m, 2H, CH_{Ar} Tr), 4.73 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.47 – 4.39 (m, 2H, 2xC*H*H Bn), 4.36 (d, *J* = 11.0 Hz, 1H, C*H*H Bn), 4.12 (m, 1H, C-4), 3.92 (dd, *J* = 7.1, 2.2 Hz, 1H, C-3), 3.83 (m, 1H, C-2), 3.58 – 3.47 (m, 3H, C-1a, C-5), 3.29 (dd, *J* = 10.3, 4.6 Hz, 1H, C-1b), 2.76 (d, *J* = 6.9 Hz, 1H, OH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (3xC_q Tr), 138.1, 138.1, 137.8 (3xC_q Bn), 128.7, 128.4, 128.4, 128.2, 127.9, 127.8, 127.7, 127.6, 127.0 (CH_{Ar} Bn, CH_{Ar} Tr), 86.7 (*C*$_q$ Tr), 78.5 (*C*-2), 77.0 (*C*-3), 73.7, 73.3, 72.9 (3xCH_2 Bn), 71.2 (*C*-5), 69.5 (*C*-4), 62.7 (*C*-1). $[\alpha]^{20}_D$: 18.6° (c = 1, $CHCl_3$). IR (neat): 633, 696, 746, 901, 1001, 1028, 1051, 1072, 1090, 1155, 1215, 1327, 1393, 1449, 1491, 2868, 2924, 3030, 3061. HR-MS: [M+Na$^+$] Calculated for $C_{45}H_{44}O_5$: 687.30810; found: 687.30789.

2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-lyxitol (51). 2,3,5-Tri-*O*-benzyl-1-*O*-trityl-L-lyxitol (**50**, 3.7 g, 5.6 mmol) was dissolved in pyridine (15 ml) and cooled to 0 °C. Methanesulfonyl chloride (1.1 ml, 14 mmol) was added and the solution stirred overnight at 4 °C. TLC analysis of the reaction showed complete conversion into a higher running spot. The reaction mixture was quenched by addition of methanol (4 ml) and then concentrated under reduced pressure. The residue was taken up in EtOAc and washed with 1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (70% Toluene/PE - 3% EtOAc/Toluene) yielding 2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-lyxitol (3.8 g, 4.2 mmol, 75 % yield) as a highly viscous syrup. R_f = 0.75 (10/90; EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 6H, CH_{Ar} Tr), 7.38 – 7.10 (m, 22H, CH_{Ar} Tr, CH_{Ar} Bn), 7.02 (dd, *J* = 6.6, 2.9 Hz, 2H, CH_{Ar} Tr), 5.24 (ddd, *J* = 7.0, 3.9, 3.7 Hz, 1H, C-4), 4.69 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.63 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.54 – 4.46 (m, 2H, 2xC*H*H Bn), 4.45 – 4.35 (m, 2H, C*H*H Bn), 4.08 (dd, *J* = 7.0, 3.7 Hz, 1H, C-3), 3.80 (ddd, *J* = 7.0, 4.1, 3.2 Hz, 1H, C-2), 3.74 (dd, *J* = 10.8, 7.0 Hz, 1H, C-5a), 3.65 (dd, *J* = 10.4, 3.2 Hz, 1H, C-1a), 3.58 (dd, *J* = 10.8, 3.9 Hz, 1H, C-5b), 3.27 (dd, *J* = 10.4, 4.1 Hz, 1H, C-1b), 2.87 (s, 3H, CH_3 Ms). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (*C*$_q$ Tr), 138.2, 137.7, 137.5 (*C*$_q$ Bn), 128.8, 128.6, 128.4, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7, 127.1 (*C*H$_{Ar}$), 87.0 (*C*$_q$ Tr), 80.8 (*C*-4), 77.8 (*C*-2), 77.0 (*C*-3), 74.5, 73.4, 72.3 (3x*C*H$_2$ Bn), 69.8 (*C*-5), 61.7 (*C*-1), 38.7 (*C*H$_3$ Ms). $[\alpha]^{20}_D$: 6.6° (c = 1, $CHCl_3$). IR (neat): 633, 696, 746, 804, 918, 970, 1001, 1028, 1092, 1173, 1217, 1342, 1358, 1396, 1449, 1491, 2874, 2924, 3030, 3061. HR-MS: [M+Na$^+$] Calculated for $C_{46}H_{46}O_7S$: 765.28565; found: 765.28570.

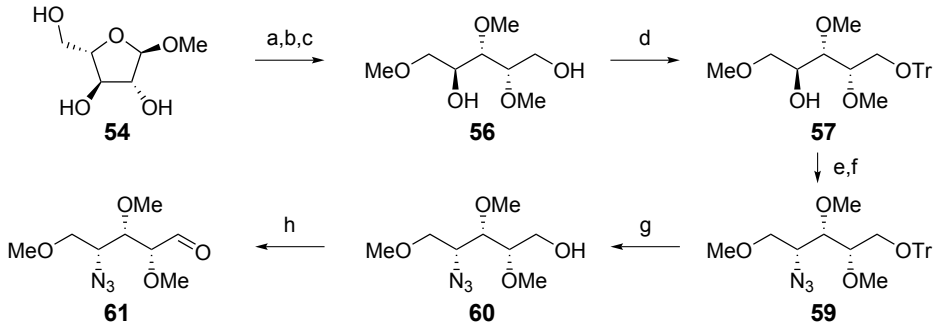
2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-ribitol (52). 2,3,5-Tri-*O*-benzyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-lyxitol (**51**, 3.8 g, 5.1 mmol) was coevaporated twice with toluene and then dissolved in DMF (40 ml). Sodium azide (2.1 g, 33 mmol), 15-crown-5 (0.2 ml, 1.1 mmol) and tetrabutylammonium hydrogen sulphate (0.37 g, 1.1 mmol) were added and the resulting suspension was stirred at 100 °C for 2 days. The mixture was diluted with EtOAc and washed with water. The aqueous layer was extracted with EtOAc and subsequently the layers were combined and washed with water, $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (5-6% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-ribitol (2.7 g, 3.9 mmol, 76 % yield). R_f = 0.85 (5/95; EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 6H, CH_{Ar} Tr), 7.34

– 7.16 (m, 22H, CH_{Ar} Bn, CH_{Ar} Tr), 7.05 – 6.99 (m, 2H, CH_{Ar} Bn), 4.71 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.56 (d, *J* = 10.9 Hz, 1H, C*H*H Bn), 4.50 – 4.37 (m, 4H, 4xC*H*H Bn), 4.00 – 3.95 (m, 1H, C-4), 3.90 (dd, *J* = 6.6, 4.2 Hz, 1H, C-3), 3.74 – 3.68 (m, 1H, C-2), 3.63 (d, *J* = 5.6 Hz, 2H, C-5), 3.53 (dd, *J* = 10.3, 3.0 Hz, 1H, C-1a), 3.28 (dd, *J* = 10.3, 4.7 Hz, 1H, C-1b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (C_q Tr), 138.1, 138.0, 137.8 (3xC_q Bn), 128.8, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.7, 127.7, 127.1 (CH_{Ar}), 86.7 (C_q Tr), 78.5 (*C*-3), 78.3 (*C*-2), 74.0, 73.3, 72.5 (3xCH_2 Bn), 69.9 (*C*-5), 62.6 (*C*-1), 62.5 (*C*-4). $[\alpha]^{20}_D$: 11.3° (c = 1, $CHCl_3$). IR (neat): 633, 696, 746, 899, 1001, 1018, 1028, 1076, 1090, 1153, 1215, 1265, 1325, 1366, 1391, 1449, 1491, 2095, 2868, 2924, 3030, 3061. HR-MS: [M+Na^+] Calculated for $C_{45}H_{43}N_3O_4$: 712.31458; found: 712.31438.

2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribitol (53). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-1-*O*-trityl-D-ribitol (**52**, 2.6 g, 3.8 mmol) was dissolved in chloroform (20 ml) and MeOH (20 ml) and a catalytic amount of *p*-toluenesulfonic acid monohydrate (0.05 g, 0.28 mmol) was added. The reaction mixture was stirred for 6h after which it was diluted with DCM and washed with $NaHCO_3$ (sat. aq.) and brine. The solution was then dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (15%-20% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribitol (1,4 g, 3.2 mmol, 84 % yield). R_f = 0.15 (5/95; EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 15H, CH_{Ar}), 4.68 – 4.58 (m, 2H, 2xC*H*H Bn), 4.56 (d, *J* = 11.5 Hz, 1H, C*H*H Bn), 4.47 (d, *J* = 11.5 Hz, 2H, 2xC*H*H Bn), 4.43 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 3.93 – 3.88 (m, 1H, C-4), 3.81 – 3.68 (m, 3H, C-1, C-3), 3.67 – 3.56 (m, 3H, C-2, C-5), 2.30 (bs, 1H, O*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6 (C_q Bn), 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.7, 127.7 (CH_{Ar}), 78.6 (*C*-2), 78.1 (*C*-3), 74.1, 73.3, 71.9 (3xCH_2 Bn), 69.7 (*C*-5), 62.3 (*C*-4), 60.4 (*C*-1). $[\alpha]^{20}_D$: -11.5° (c = 1, $CHCl_3$). IR (neat): 604, 696, 735, 822, 849, 880, 910, 1001, 1028, 1069, 1092, 1207, 1267, 1315, 1366, 1391, 1454, 1497, 1726, 2095, 2868, 2914, 3030. HR-MS: [M+H^+] Calculated for $C_{26}H_{29}N_3O_4$: 448.22308; found: 448.22316.

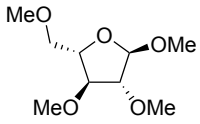
2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribose (11). 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribitol (**53**, 224 mg, 0.5 mmol) was dissolved in DCM (10 ml) and cooled to 0 °C. Dess-Martin periodinane (424 mg, 1.0 mmol) was added and the reaction mixture stirred overnight at 0-4 °C. The reaction mixture was quenched by addition of a mixture of 10% $NaHCO_3$ (aq.)/1M $Na_2S_2O_3$ (aq. 1/1 v/v, 25 ml) and stirred for 30 minutes. The organic layer was separated and washed with $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (13% EtOAc/PE) yielding 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribose (188 mg, 0.42 mmol, 84 % yield). R_f = 0.6 (10/90; EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 1.1 Hz, 1H, C-1), 7.37 – 7.26 (m, 14H, CH_{Ar} Bn), 7.22 – 7.18 (m, 2H, CH_{Ar} Bn), 4.75 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.58 – 4.52 (m, 2H, 2xC*H*H Bn), 4.49 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.45 (d, *J* = 11.4 Hz, 1H, C*H*H Bn), 4.06 (dd, *J* = 2.2, 1.1 Hz, 1H, C-2), 3.89 – 3.81 (m, 2H, C-3, C-4), 3.79 (dd, *J* = 10.0, 2.4 Hz, 1H, C-5a), 3.64 (dd, *J* = 10.1, 5.6 Hz, 1H, C-5b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2 (*C*-1), 137.7, 137.1, 137.0 (C_q Bn), 128.5, 128.4, 128.1, 128.0, 127.8, 127.7 (C_q Bn), 82.2 (*C*-2), 79.7 (*C*-3), 73.3, 73.3, 73.0 (3xCH_2 Bn), 69.5 (*C*-5), 60.1 (*C*-4). $[\alpha]^{20}_D$: 13.7° (c = 1, $CHCl_3$). IR (neat): 698, 735, 750, 1028, 1088, 1105, 1260, 1271, 1317, 1364, 1454, 1730, 2100, 2860, 2938. HR-MS: [M+NH_4^+] Calculated for $C_{26}H_{27}N_3O_4$: 463.23398; found: 463.23415.

Scheme 4.3 Synthesis of 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylose (**61**)

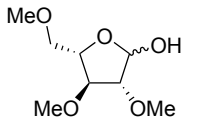


Reagents and conditions: (a) NaH, MeI, DMF, 80%; (b) HCl, H_2O, 1,4-dioxane, 100 °C, 70%; (c) $NaBH_4$, EtOH, 95%; (d) TrCl, Et_3N, DMAP, DCM, 90%; (e) MsCl, pyridine, 4 °C, 96%; (f) NaN_3, 15-crown-5, Bu_4NHSO_4, DMF, 100 °C, 80%; (g) *p*-TsOH, chloroform, MeOH, 90%, (h) Dess-Martin periodinane, DCM, 4 °C, 88%.

1,2,3,5-Tetra-*O*-methyl-α-L-arabinofuranose (54). Methyl-α-L-arabinofuranose was synthesized as described in *Org. Lett.* **2013**, *15*, 3026-3029, 10.1021/ol4012053. Methyl-α-L-arabinofuranose (10.4 g, 63 mmol) was dissolved in DMF (320 ml) and cooled to 0 °C. Sodium hydride (15 g, 380 mmol) was added and the reaction stirred for 5 minutes before dropwise addition of iodomethane (24 ml, 380 mmol). The reaction mixture was then slowly allowed to warm to room temperature and stirred overnight. After overnight stirring, TLC analysis indicated complete conversion. The reaction was quenched with cold water and extracted with DCM. The combined organic layers were washed with 1M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (3-20% EtOAc/PE) yielding 1,2,3,5-Tetra-*O*-methyl-α-L-arabinofuranose (11 g, 51 mmol, 80 % yield). R_f = 0.4 (25/75; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (s, 1H, C-1), 4.14 – 4.08 (m, 1H, C-4), 3.70 (d, *J* = 1.7 Hz, 1H, C-2), 3.62 – 3.51 (m, 3H, C-3, C-5), 3.42 (s, 3H, O*CH*$_3$), 3.42 (s, 3H, O*CH*$_3$), 3.41 (s, 3H, O*CH*$_3$), 3.40 (s, 3H, O*CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 106.8 (*C*-1), 89.5 (*C*-2), 86.0 (*C*-3), 81.0 (*C*-4), 73.0 (*C*-5), 59.5, 58.2, 57.6, 55.0 (4xO*C*H$_3$). $[\alpha]^{20}_D$: -191.8° (c = 1, $CHCl_3$). IR (neat): 941, 1011, 1057, 1105, 1188, 1315, 1367, 1452, 2828, 2911, 2930, 2988. HR-MS: [M+NH_4^+] Calculated for $C_9H_{18}O_5$: 224.14925; found: 224.14939.



2,3,5-Tri-*O*-methyl-L-arabinofuranose (55). 1,2,3,5-Tetra-*O*-methyl-α-L-arabinofuranose (**54**, 8.3 g, 40 mmol) in 1,4-dioxane (140 ml) and 4M aq. HCl (140 ml) was refluxed for 4 hours. The mixture was cooled to rt, neutralized with Et_3N and concentrated under reduced pressure. The crude product was purified by flash chromatography (100% Ether) yielding 2,3,5-Tri-*O*-methyl-L-arabinofuranose (5.4 g, 28 mmol, 70 % yield). R_f = 0.25 (50/50; EtOAc/PE). α-Anomer ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (d, *J* = 6.0 Hz, 1H, C-1), 4.34 – 4.28 (m, 1H, C-4), 3.74 (d, *J* = 2.0 Hz, 1H, C-2), 3.71 (s, 1H, O*H*), 3.61 (dd, *J* = 4.4, 1.8 Hz, 1H, C-3), 3.51 (d, *J* = 5.7 Hz, 2H, C-5), 3.43 (s, 3H, O*CH*$_3$), 3.42 (s, 3H, O*CH*$_3$), 3.40 (s, 3H, O*CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 100.5 (*C*-1), 88.6 (*C*-2), 85.3 (*C*-3), 81.3 (*C*-4), 73.0 (*C*-5), 59.3, 57.9, 57.5 (3xO*C*H$_3$). β-Anomer ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (dd, *J* = 9.3, 4.4 Hz, 1H, C-1), 4.11 (d, *J* = 9.3 Hz, 1H, O*H*), 4.01 (q, *J* = 4.3 Hz, 1H, C-4), 3.84 (t, *J* = 4.9 Hz, 1H, C-3), 3.75 (m, 1H, C-2), 3.55 – 3.52 (m, 2H, C-5), 3.47 (s, 3H, O*CH*$_3$), 3.44 (s, 3H, O*CH*$_3$), 3.42 (s, 3H, O*CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 95.9 (*C*-1), 86.2 (*C*-2), 83.8 (*C*-3), 80.4 (*C*-4), 73.7 (*C*-5), 59.3, 58.0, 57.8 (3xO*C*H$_3$). IR (neat): 924, 974, 1057, 1094, 1111, 1190, 1346, 1452, 1638, 2830, 2901, 2932, 2984, 3364, 3397. HR-MS: [M+H^+] Calculated for $C_8H_{16}O_5$: 193.10705; found: 193.10684.



2,3,5-Tri-*O*-methyl-L-arabinitol (56). To a cooled solution (0 °C) of 2,3,5-Tri-*O*-methyl-L-arabinofuranose (**55**, 5.3 g, 28 mmol) in EtOH (130 ml) was added sodium borohydride (2.4 g, 64 mmol). After 4 hours at room temperature, TLC analysis showed complete conversion of the starting material into a lower running product and the pH of the reaction mixture was adjusted to pH 4-5 by the addition of acetic acid. The resulting mixture was concentrated and consecutively purified by flash chromatography (75% EtOAc/PE - 20% MeOH/EtOAc) yielding 2,3,5-Tri-*O*-methyl-L-arabinitol (5.1 g, 26 mmol, 95 % yield). R_f = 0.10 (75/25; EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (ddd, *J* = 7.2, 5.1, 4.0 Hz, 1H, C-4), 3.84 (dd, *J* = 11.7, 5.2 Hz, 1H, C-1a), 3.79 (dd, *J* = 11.7, 4.9 Hz, 1H, C-1b), 3.60 – 3.53 (m, 3H, C-5, C-2), 3.51 (s, 3H, 2-OCH_3), 3.47 (s, 3H, 3-OCH_3), 3.41 (s, 3H, 5-OCH_3), 3.40 (dd, *J* = 7.3, 3.4 Hz, 1H, C-3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 81.1 (*C*-2), 80.7 (*C*-3), 73.5 (*C*-5), 70.0 (*C*-4), 61.2 (*C*-1), 59.8 (3-OCH_3), 59.1 (5-OCH_3), 58.7 (2-OCH_3). $[\alpha]^{20}_D$: -1.6° (c = 1, $CHCl_3$). IR (neat): 989, 1043, 1096, 1234, 1454, 1641, 1715, 2830, 2934, 3321. HR-MS: [M+H$^+$] Calculated for $C_8H_{18}O_5$: 195.12270; found: 195.12286.

2,3,5-Tri-*O*-methyl-1-*O*-trityl-L-arabinitol (57). 2,3,5-Tri-*O*-methyl-L-arabinitol (**56**, 5.1 g, 26 mmol) was dissolved in DCM (180 ml). To this solution was added Et_3N (8 ml, 57 mmol), triphenylmethyl chloride (10.6 g, 38 mmol) and DMAP (0.3 g, 2.8 mmol). The reaction mixture was stirred overnight after which the reaction was quenched by addition of MeOH (2.5 ml). The mixture was concentrated under reduced pressure, the residue taken up in EtOAc and washed with 0.1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The combined aqueous layers were combined and extracted with EtOAc. The combined organic layers were then dried using anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-80% Ether/PE) yielding 2,3,5-Tri-*O*-methyl-1-*O*-trityl-L-arabinitol (11 g, 25 mmol, 96 % yield). R_f = 0.75 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.8 Hz, 6H, CH_{Ar} Tr), 7.30 (t, *J* = 7.5 Hz, 6H, CH_{Ar} Tr), 7.24 (d, *J* = 8.3 Hz, 3H, CH_{Ar} Tr), 3.91 – 3.83 (m, 1H, C-4), 3.63 (ddd, *J* = 6.1, 6.0, 1.9 Hz, 1H, C-2), 3.56 – 3.43 (m, 3H, C-1a, C-5), 3.44 (s, 3H, 2-OCH_3), 3.39 (s, 3H, 5-OCH_3), 3.35 (dd, *J* = 7.4, 1.9 Hz, 1H, C-3), 3.26 (s, 3H, 3-OCH_3), 3.23 (dd, *J* = 9.6, 6.5 Hz, 1H, C-1b), 2.75 (d, *J* = 3.5 Hz, 1H, O*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1 (C_q Tr), 128.8, 128.0, 127.2 (3xCH_{Ar}), 87.2 (C_q Tr), 80.2 (*C*-3), 80.0 (*C*-2), 73.7 (*C*-5), 69.8 (*C*-4), 62.6 (*C*-1), 60.1 (3-OCH_3), 59.4 (2-OCH_3), 59.2 (5-OCH_3). $[\alpha]^{20}_D$: 9.8° (c = 1, $CHCl_3$). IR (neat): 633, 650, 704, 746, 843, 880, 899, 932, 993, 1001, 1032, 1076, 1088, 1186, 1219, 1321, 1366, 1449, 1491, 1597, 2828, 2893, 2930, 2978. HR-MS: [M+Na$^+$] Calculated for $C_{27}H_{32}O_5$: 459.21420; found: 459.21393.

2,3,5-Tri-*O*-methyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (58). 2,3,5-Tri-*O*-methyl-1-*O*-trityl-L-arabinitol (**57**, 13 g, 30 mmol) was coevaporated twice with toluene, dissolved in pyridine (66 ml) and cooled to 0 °C. Methanesulfonyl chloride (6 ml, 78 mmol) was added and the solution stirred for 18 hours while allowing the solution to slowly warm to room temperature. The reaction mixture was quenched by addition of methanol (15 ml) and then concentrated under reduced pressure. The residue was taken up in EtOAc and washed with 0.1 M HCl (aq.), $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (15-50% EtOAc/PE) yielding 2,3,5-Tri-*O*-methyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (15 g, 29 mmol, 90 % yield). R_f = 0.80 (70/30 EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.5 Hz, 6H, CH_{Ar} Tr), 7.31 (t, *J* = 7.5 Hz, 6H, CH_{Ar} Tr), 7.25 (d, *J* = 6.6 Hz, 3H, CH_{Ar} Tr), 4.91 (ddd, *J* = 6.2, 6.2, 2.5 Hz, 1H, C-4), 3.75 (dd, *J* = 11.4, 2.5 Hz, 1H, C-5a), 3.68 – 3.61 (m, 2H, C-3, C-5b), 3.48 – 3.39 (m, 2H, C-1a, C-2), 3.36 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.25 – 3.16 (m, 1H, C-1b), 3.07 (s, 3H, CH_3 Ms). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (C_q Tr), 128.8, 128.0, 127.3 (3xCH_{Ar} Tr), 87.4 (C_q Tr), 80.9 (*C*-4), 80.1 (*C*-3), 79.1 (*C*-2), 71.4 (*C*-5), 61.6 (*C*-1), 61.2, 59.0, 59.0 (3xOCH_3), 38.8 (*C*H$_3$ MS). $[\alpha]^{20}_D$: -0.4° (c = 1, $CHCl_3$). IR (neat): 708, 748, 766, 918, 968, 1001, 1032, 1090, 1144, 1153, 1175, 1219, 1354, 1449, 1491, 2832, 2886, 2932, 3055. HR-MS: [M+Na$^+$] Calculated for $C_{28}H_{34}O_7S$: 537.19175; found: 537.19154.

2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (59). 2,3,5-Tri-*O*-methyl-4-*O*-methanesulfonyl-1-*O*-trityl-L-arabinitol (**58**, 16 g, 30 mmol) was dissolved in DMF (150 ml). Sodium azide (13 g, 200 mmol), 15-crown-5 (1.3 ml, 6.5 mmol) and tetrabutylammonium hydrogen sulfate (2.2 g, 6.5 mmol). The resulting suspension was stirred at 100 °C for 4 days. The reaction mixture was concentrated under reduced pressure, then taken up in EtOAc and washed with water. The aqueous layer was extracted with EtOAc and the combined organic layers washed with water, $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure yielding the crude product. The residue was purified by flash chromatography (5% EtOAc/PE) yielding 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (11 g, 24 mmol, 80 % yield). R_f = 0.80 (70/30 EtOAc/PE). R_f = 0.75 (30/70 EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 6H, CH_{Ar} Tr), 7.34 – 7.27 (m, 6H, CH_{Ar}), 7.27 – 7.21 (m, 3H, CH_{Ar}), 3.62 (ddd, *J* = 6.7, 5.4, 4.1 Hz, 1H, C-4), 3.56 (dd, *J* = 10.1, 4.0 Hz, 1H, C-5a), 3.54 -3.51 (m, 1H, C-3), 3.47 (dd, *J* = 10.0, 6.8 Hz, 1H, C-5b), 3.45 (s, 3H, OCH_3), 3.38 (s, 3H, OCH_3), 3.37 (s, 3H, OCH_3), 3.36 – 3.31 (m, 2H, C-1a, C-2), 3.28 – 3.18 (m, 1H, C-1b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9 (C_q Tr), 128.7, 128.0, 127.2 (3xCH_{Ar} Tr), 87.1 (C_q Tr), 80.8, 80.7 (*C*-2, *C*-3), 72.2 (*C*-5), 61.8 (*C*-4), 61.7 (*C*-1), 61.0, 59.2, 58.7 (3xOCH_3). $[\alpha]^{20}_D$: 7.3° (c = 1, $CHCl_3$). IR (neat): 633, 704, 746, 764, 899, 926, 1001, 1032, 1076, 1111, 1198, 1221, 1267, 1449, 1491, 2093, 2828, 2893, 2928, 2980. HR-MS: [M+Na^+] Calculated for $C_{27}H_{31}N_3O_4$: 484.22068; found: 484.22021.

2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylitol (60). 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-1-*O*-trityl-D-xylitol (**59**, 11 g, 24 mmol) was dissolved in chloroform (75 ml) and MeOH (75 ml) and a catalytic amount of *p*-toluenesulfonic acid monohydrate (250 mg, 1.3 mmol) was added. The reaction mixture was stirred for 3 hours after which the mixture was neutralized with Et_3N and concentrated under reduced pressure. The crude product was purified by flash chromatography (15-80% EtOAc/PE) yielding 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylitol (4.8 g, 22 mmol, 90 % yield). R_f = 0.10 (70/30 EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (dd, *J* = 11.9, 4.1 Hz, 1H, C-1a), 3.72 – 3.66 (m, 2H, C-1b, C-4), 3.66 – 3.57 (m, 2H, C-5), 3.54 (s, 3H, 3-OCH_3), 3.48 (s, 3H, 2-OCH_3), 3.47 – 3.42 (m, 2H, C-2, C-3), 3.41 (s, 3H, 5-OCH_3), 2.18 (s, 1H, O*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 81.3 (*C*-2), 81.0 (*C*-3), 72.0 (*C*-5), 61.2 (*C*-4), 61.0 (*C*-1), 60.8 (3-OCH_3), 59.2 (5-OCH_3), 58.6 (2-OCH_3). $[\alpha]^{20}_D$: -9.0° (c = 1, $CHCl_3$). IR (neat): 677, 735, 941, 914, 989, 1055, 1078, 1096, 1196, 1269, 1323, 1462, 2093, 2832, 2897, 2932, 2980, 3354, 3402. HR-MS: [M+H^+] Calculated for $C_8H_{17}N_3O_4$: 220.12918; found: 220.12921.

2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylose (61). 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylitol (**60**, 110 mg, 0.50 mmol) was dissolved in DCM (10 ml) and cooled to 0 °C. Dess-Martin periodinane (424 mg, 1.0 mmol) was added and the reaction mixture stirred overnight at 0-4 °C. A mixture of 10% $NaHCO_3$ (aq.)/1M $Na_2S_2O_3$ (aq. 1/1 v/v, 25 ml) was added and the solution stirred vigorously for 30 minutes. The organic layer was separated and washed with $NaHCO_3$ (sat. aq.) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (20-30% EtOAc/PE) yielding 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylose (96 mg, 0.44 mmol, 88 % yield) which was used immediately in the SAWU reaction. R_f = 0.50 (40/60 EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (d, *J* = 1.0 Hz, 1H, C-1), 3.84 – 3.80 (m, 1H, C-4), 3.79 (dd, *J* = 4.2, 1.1 Hz, 1H, C-2), 3.73 (dd, *J* = 4.9, 4.3 Hz, 1H, C-3), 3.62 (dd, *J* = 10.1, 4.7 Hz, 1H, C-5a), 3.56 (dd, *J* = 10.2, 6.5 Hz, 1H, C-5b), 3.53 (s, 3H, OCH_3), 3.50 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1 (*C*-1), 84.2 (*C*-2), 81.1 (*C*-3), 71.6 (*C*-5), 60.7 (*C*-4), 60.2, 59.3, 59.2 (3xOCH_3). $[\alpha]^{20}_D$: 47.1° (c = 1, $CHCl_3$). IR (neat): 851, 916, 954, 1002, 1029, 1092, 1196, 1269, 1315, 1339, 1458, 1730, 2097, 2833, 2897, 2933, 2987. HR-MS: [M+H^+] Calculated for $C_8H_{15}N_3O_4$: 218.11353; found: 218.11350.

2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-lyxose (12). Trimethylphospine (1M in toluene, 0.80 ml, 0.80 mmol) was added to a cooled (0 °C), with toluene coevaporated solution of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-lyxose (**8**, 179 mg, 0.40 mmol) in anhydrous MeOH (2 ml). The reaction mixture was stirred for 1 hour at 0 °C. Subsequently, the mixture was concentrated before coevaporation with toluene (3x under high vacuum) yielding the crude cyclic imine. R_f = 0.25 (25/75 EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 2.4 Hz, 1H, C-1), 7.41 – 7.05 (m, 15H, CH_{Ar} Bn), 4.70 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.69 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.65 – 4.53 (m, 4H, 4xC*H*H Bn), 4.37 (d, *J* = 4.9 Hz, 1H, C-2), 4.27 – 4.17 (m, 1H, C-3), 4.01 – 3.85 (m, 3H, C-4, C-5). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3 (*C*-1), 138.2, 138.2, 137.5 (3xC_q Bn), 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6 (*C*H_{Ar} Bn), 85.9 (*C*-2), 78.0 (*C*-3), 73.8 (*C*H_2 Bn), 73.6 (*C*-4), 73.5, 73.0 (2x*C*H_2 Bn), 68.8 (*C*-5). IR (neat): 698, 737, 1028, 1096, 1207, 1362, 1454, 1684, 2866, 2926, 3028. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{27}NO_3$: 402.20637; found: 402.20640. Spectroscopic data matched literature data.[9]

2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-arabinose (13). Trimethylphospine (1M in toluene, 0.87 ml, 0.87 mmol) was added to a cooled (0 °C) and, with toluene, coevaporated solution of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-arabinose (**9**, 193 mg, 0.43 mmol) in anhydrous MeOH (2.2 ml). The reaction mixture was stirred for 1 hour at 0 °C. Subsequently, the mixture was concentrated before coevaporation with toluene (3x under high vacuum) yielding the crude cyclic imine. R_f = 0.30 (10/90 EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 2.3 Hz, 1H, C-1), 7.39 – 7.26 (m, 15H, CH_{Ar} Bn), 4.64 – 4.51 (m, 7H, C-2, 6xC*H*H Bn), 4.19 – 4.14 (m, 1H, C-4), 4.11 (t, *J* = 3.8 Hz, 1H, C-3), 3.76 (dd, *J* = 9.8, 4.6 Hz, 1H, C-5a), 3.55 (dd, *J* = 9.8, 6.3 Hz, 1H, C-5b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0 (*C*-1), 138.1, 137.9, 137.5 (3xC_q Bn), 128.6, 128.4, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6 (*C*H_{Ar} Bn), 90.7 (*C*-2), 84.4 (*C*-3), 76.8 (*C*-4), 73.3, 72.3, 72.0 (3x*C*H_2 Bn), 71.0 (*C*-5). IR (neat): 608, 696, 735, 847, 910, 959, 1003, 1028, 1074, 1096, 1206, 1250, 1267, 1312, 1341, 1362, 1454, 1497, 2860, 3030, 3063. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{27}NO_3$: 402.20637; found: 402.20595. Spectroscopic data matched literature data.[9]

2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-xylose (14). Trimethylphospine (1M in toluene, 0.66 ml, 0.66 mmol) was added to a cooled (0 °C) and, with toluene, coevaporated solution of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-xylose (**10**, 147 mg, 0.33 mmol) in anhydrous MeOH (1.7 ml). The reaction mixture was stirred for 1 hour at 0 °C. Subsequently, the mixture was concentrated before coevaporation with toluene (3x under high vacuum) yielding the crude cyclic imine. R_f = 0.30 (25/75 EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 1.5 Hz, 1H, C-1), 7.39 – 7.18 (m, 15H), 4.68 – 4.45 (m, 7H, C-2, 6xC*H*H Bn), 4.39 – 4.31 (m, 1H, C-4), 4.17 (dd, *J* = 6.4, 4.7 Hz, 1H, C-3), 3.80 – 3.72 (m, 2H, C-5). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (*C*-1), 138.5, 138.0, 137.7 (3xC_q Bn), 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5 (*C*H_{Ar} Bn), 88.5 (*C*-2), 83.1 (*C*-3), 73.4, 72.7 (2x*C*H_2 Bn), 72.6 (*C*-4), 72.5 (*C*H_2 Bn), 67.9 (*C*-5). IR (neat): 696, 735, 1003, 1028, 1076, 1098, 1206, 1364, 1454, 1498, 2859, 2922. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{27}NO_3$: 402.20637; found: 402.20596.

2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-ribose (15). Trimethylphospine (1M in toluene, 0.84 ml, 0.84 mmol) was added to a cooled (0 °C) and, with toluene, coevaporated solution of 2,3,5-Tri-*O*-benzyl-4-deoxy-4-azido-D-ribose (**11**, 0.19 g, 0.42 mmol) in anhydrous MeOH (2.1 ml). The reaction mixture was stirred for 1 hour at 0 °C. Subsequently, the mixture was concentrated before coevaporation with toluene (3x under high vacuum) yielding the crude cyclic imine. R_f = 0.30 (25/75 EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 1.6 Hz, 1H, C-1), 7.37 – 7.12 (m, 15H, CH_{Ar} Bn), 4.69 (d, *J* = 11.7 Hz, 1H, C*H*H Bn), 4.66 – 4.39 (m, 6H, C-2, 5xC*H*H Bn), 4.39 – 4.35 (m, 1H, C-4), 4.02 (dd, *J* = 6.0, 2.0 Hz, 1H, C-3), 3.67 (dd, *J* = 9.7, 3.6 Hz, 1H, C-5a), 3.57 (dd, *J* = 9.7, 4.2 Hz, 1H, C-5b). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (*C*-1), 137.8, 137.7, 137.5 (C_q Bn), 128.3, 128.2, 127.9, 127.9, 127.8, 127.6, 127.5, 127.3 (*C*H_{Ar} Bn), 83.5 (*C*-2), 77.4 (*C*-4), 76.5 (*C*-3), 73.1, 72.7, 71.7 (3x*C*H_2 Bn), 69.5 (*C*-5). IR (neat): 696, 735, 912,

1001, 1026, 1098, 1175, 1207, 1260, 1310, 1362, 1684, 1744, 2860, 3030, 3063. HR-MS: [M+NH_4^+] Calculated for $C_{26}H_{27}NO_3$: 402.20637; found: 402.20614.

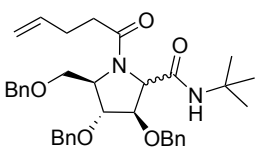
2,3,5-Tri-*O*-methyl-4-deoxy-4-amino-D-xylofuranose (62). Trimethylphospine (1M in toluene, 0.88 ml, 0.88 mmol) was added to a cooled (0 °C) and, with toluene, coevaporated solution of 2,3,5-Tri-*O*-methyl-4-deoxy-4-azido-D-xylose (**61**, 96 mg, 0.44 mmol) in anhydrous MeOH (2.2 ml). The reaction mixture was stirred for 1 hour at 0 °C. Subsequently, the mixture was concentrated before coevaporation with toluene (3x under high vacuum) yielding the crude cyclic imine. R_f = 0.20 (50/50 EtOAc/PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 1.3 Hz, 1H, C-1), 4.37 (d, *J* = 4.4 Hz, 1H, C-2), 4.34 – 4.26 (m, 1H, C-4), 3.86 (dd, *J* = 6.5, 4.7 Hz, 1H, C-3), 3.64 (dd, *J* = 10.0, 4.4 Hz, 1H, C-5a), 3.59 (dd, *J* = 10.2, 4.8 Hz, 1H, C-5b), 3.49 (s, 3H, CH_3 Me), 3.44 (s, 3H, CH_3 Me), 3.36 (s, 3H, CH_3 Me). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6 (*C*-1), 89.9 (*C*-2), 84.9 (*C*-3), 72.2 (*C*-4), 70.0 (*C*-5), 59.2, 58.5, 57.8 (3xO*C*H_3). IR (neat): 322, 338, 390, 419, 492, 530, 632, 862, 948, 1104, 1195, 1226, 1299, 1456, 1646, 1950, 2006, 2102, 2334, 2362, 2831, 2926, 3300. HR-MS: [M+H^+] Calculated for $C_8H_{15}NO_3$: 174.11247; found: 174.11256.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (16a).** Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-lyxose (**12**, 0.20 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (82 µl, 0.8 mmol) and *tert*-butyl isocyanide (28 µl, 0.25 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (20-40% EtOAc/toluene) yielding the title compound as a single stereoisomer in 55% yield (64 mg, 0.11 mmol). R_f = 0.35 (40/60 EtOAc/toluene). 5:4 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.22 (m, 15H, CH_{Ar}), 5.96 (s, 1H, N*H*), 5.89 – 5.68 (m, 1H, =C*H*), 5.07 – 4.86 (m, 2H, =CH_2), 4.76 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.72 – 4.61 (m, 1H, C*H*H Bn), 4.59 – 4.47 (m, 4H, C-2, 3xC*H*H Bn), 4.47 – 4.38 (m, 2H, C-3, C*H*H Bn), 4.37 – 4.28 (m, 1H, C-5), 4.17 – 4.09 (m, 1H, C-6a), 3.89 – 3.79 (m, 2H, C-4, C-6b), 2.92 – 2.76 (m, 1H, C*H*HCH pentenyl), 2.46 – 2.24 (m, 3H, C*H*HCH pentenyl, CH_2CO pentenyl), 1.20 (s, 9H, 3xCH_3 *t*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8 (N*C*=O pentenyl), 167.0 (NH*C*(O)-2), 138.4, 137.9, 137.8 (*C*$_q$ Bn), 137.4 (=*C*H pentenyl), 128.6, 128.5, 128.3, 128.3, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5 (*C*H$_{Ar}$ Bn), 115.2 (=*C*H$_2$ pentenyl), 78.8 (*C*-4), 76.8 (*C*-3), 74.9, 73.8, 72.4 (3x*C*H$_2$ Bn), 69.8 (*C*-6), 65.0 (*C*-2), 58.9 (*C*-5), 50.9 (*C*$_q$ *t*-butyl), 33.4 (*C*H$_2$CH pentenyl), 29.0 (*C*H$_2$CO pentenyl), 28.6 (*C*H$_3$ *t*-butyl). $[\alpha]^{20}_D$: 10.8° (c = 1, $CHCl_3$). IR (neat): 604, 615, 656, 696, 735, 822, 843, 912, 955, 1003, 1026, 1059, 1098, 1142, 1177, 1213, 1250, 1285, 1308, 1364, 1395, 1404, 1454, 1497, 1524, 1658, 2870, 2926, 2965, 3030, 3063, 3329. HR-MS: [M+H^+] Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33214. Spectroscopic data matched literature data.[9]

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (17a).** Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-lyxose (**12,** 0.20 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (82 µl, 0.80 mmol) and cyclohexyl isocyanide (31 µl, 0.25 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (20-50% EtOAc/toluene) yielding the title compound as a single stereoisomer in 60% yield (73 mg, 0.12 mmol). R_f = 0.25 (40/60 EtOAc/toluene). 1:1

Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 15H, CH_{Ar} Bn), 6.08 (d, *J* = 7.8 Hz, 1H, N*H*), 5.86 – 5.71 (m, 1H, =C*H* pentenyl), 5.07 – 4.89 (m, 2H, =CH_2 pentenyl), 4.72 – 4.61 (m, 3H, C-2, 2xC*H*H Bn-3), 4.60 – 4.41 (m, 4H, C-3, 2xC*H*H Bn-4, 2xC*H*H Bn-3), 4.40 – 4.31 (m, 1H, C-5), 4.21 – 4.11 (m, 1H, C-6a), 3.91 – 3.78 (m, 2H, C-4, C-6b), 3.76 – 3.66 (m, 1H, C*H* Cy), 2.43 – 2.25 (m, 4H, CH_2CH pentenyl, CH_2CO pentenyl), 1.78 – 1.38 (m, 6H, 3xCH_2 Cy), 1.24 – 0.52 (m, 4H, 2xCH_2 Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7 (N*C*=O pentenyl), 166.8 (NH*C*(O)-1), 138.3, 137.9, 137.8 (3xC_q Tr), 137.4 (=*C*H pentenyl), 128.6, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.6 (*C*H_{Ar} Bn), 115.2 (=CH_2 pentenyl), 78.9 (*C*-4), 76.8 (*C*-3), 74.9 (*C*H_2 Bn-3), 73.7 (*C*H_2 Bn-6), 72.4 (*C*H_2 Bn-4), 69.6 (*C*-6), 64.5 (*C*-2), 58.7 (*C*-5), 47.7 (*C*H Cy), 33.4 (*C*H_2CH pentenyl), 32.6, 32.5 (2x*C*H Cy), 29.0 (*C*H_2CO), 25.5, 24.8, 24.6 (3x*C*H_2 Cy). $[\alpha]^{20}_{D}$: 8.2° (c = 1, $CHCl_3$). IR (neat): 627, 696, 735, 820, 845, 891, 912, 959, 1003, 1028, 1067, 1101, 1144, 1211, 1256, 1275, 1308, 1352, 1406, 1452, 1497, 1526, 1655, 2853, 2928, 3030, 3063, 3292. HR-MS: [M+H$^+$] Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34803. Spectroscopic data matched literature data.[9]

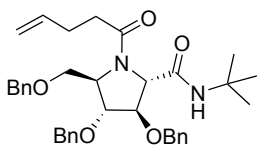
***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco/D-manno-hexonamide (18).**



Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-arabinose (**13**, 0.22 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (89 µl, 0.87 mmol) and *tert*-butyl isocyanide (31 µl, 0.27 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (5-15% EtOAc/toluene; 2,3-*trans*-isomer **18b**: 5% EtOAc/toluene, 2,3-*cis*-isomer **18a** 5-15% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 58:42 in 50% combined yield (64 mg, 0.11 mmol) as a light yellow oil.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (18a).** R_f = 0.40 (25/75 EtOAc/toluene). 5:1 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.12 (m, 15H, CH_{Ar}), 5.83 (m, 1H, =*C*H pentenyl), 5.09 – 4.96 (m, 2H, =CH_2 pentenyl), 4.92 (d, *J* = 11.2 Hz, 1H, C*H*H Bn), 4.64 (d, *J* = 11.6 Hz, 1H, C*H*H Bn), 4.59 – 4.39 (m, 5H, C-2, 4xC*H*H Bn), 4.27 – 4.14 (m, 3H, C-3, C-4, C-6a), 3.95 – 3.88 (m, 1H, C-5), 3.48 (dd, *J* = 9.7, 2.4 Hz, 1H, C-6b), 2.46 – 2.33 (m, 3H, CH_2CH pentenyl, C*H*HCO pentenyl), 2.32 – 2.23 (m, 1H, C*H*HCO pentenyl), 1.30 (s, 9H, 3xCH_3 *t*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (N*C*=O pentenyl), 168.2 (NH*C*(O)-1), 137.8, 137.7, 137.5 (3xC_q Bn), 137.1 (=*C*H pentenyl), 128.6, 128.6, 128.4, 128.1, 128.1, 127.9, 127.9 (*C*H_{Ar}), 115.5 (=CH_2 pentenyl), 82.3 (*C*-3), 79.6 (*C*-4), 73.3, 72.8, 72.7 (*C*H_2 Bn), 65.8 (*C*-6), 64.4 (*C*-2), 60.5 (*C*-5), 51.3 (C_q *t*-butyl), 33.5 (*C*H_2CO pentenyl), 28.7 (*C*H_2CH pentenyl), 28.7 (3x*C*H_3 *t*-butyl). $[\alpha]^{20}_{D}$: -29.7° (c = 1, $CHCl_3$). IR (neat): 608, 696, 735, 820, 845, 912, 1001, 1026, 1074, 1094, 1206, 1225, 1248, 1287, 1304, 1329, 1364, 1393, 1454, 1497, 1541, 1661, 1866, 2918, 2963, 3030, 3065, 3327. HR-MS: [M+H$^+$] Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33233. Spectroscopic data matched literature data.[9]

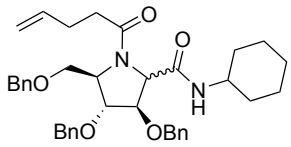
***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (18b).** R_f =



0.45 (25/75 EtOAc/toluene). 7:2 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.19 (m, 15H, CH_{Ar}), 5.95 (s, 1H, N*H*), 5.88 – 5.70 (m, 1H, =*C*H pentenyl), 5.07 – 4.90 (m, 2H, =CH_2 pentenyl), 4.70 – 4.54 (m, 3H, C-5, 2xC*H*H Bn), 4.54 – 4.41 (m, 4H, 4xC*H*H Bn), 4.26 (s, 1H, C-2), 4.22 (s, 1H, C-3), 4.15 (s, 1H, C-4), 3.97 (dd, *J* = 8.8, 4.4 Hz, 1H, C-6), 3.48 (dd, *J* = 10.5, 9.0 Hz, 1H, C-6), 2.42 – 2.32 (m, 2H, CH_2CH pentenyl), 2.32 – 2.22 (m, 2H, CH_2CO pentenyl), 1.08 (s, 9H, 3xCH_3 *t*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0 (N*C*=O pentenyl), 169.1 (NH*C*(O)-1), 138.4, 137.1 (2xC_q Bn), 137.0 (=*C*H pentenyl), 136.9 (C_q Bn), 128.6, 128.5, 128.3, 128.0, 127.7, 127.7, 127.7 (*C*H_{Ar}), 115.7 (=CH_2 pentenyl), 86.1 (*C*-4), 81.0 (*C*-3), 73.2, 71.8, 71.6 (3x*C*H_2 Bn), 69.8 (*C*-2), 66.6 (*C*-6), 63.9 (*C*-5), 51.4 (C_q *t*-butyl), 34.0 (*C*H_2CO pentenyl), 28.8 (*C*H_2CH

pentenyl), 28.2 (3x*C*H$_3$ *t*-butyl). $[\alpha]^{20}_D$: -26.7° (c = 1, $CHCl_3$). IR (neat): 698, 735, 800, 912, 1001, 1028, 1076, 1096, 1206, 1225, 1254, 1281, 1298, 1314, 1364, 1400, 1454, 1497, 1528, 1655, 1678, 2857, 1868, 2922, 2961, 3030, 3065. HR-MS: $[M+H^+]$ Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33243. Spectroscopic data matched literature data.[9]

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco/D-manno-hexonamide (19).**

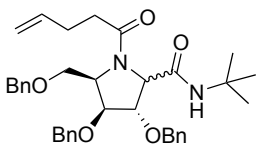


Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-arabinose (**13,** 0.22 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (89 µl, 0.87 mmol) and cyclohexyl isocyanide (34 µl, 0.27 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (5-15% EtOAc/toluene; 2,3-*trans*-isomer **19b**: 5-6% EtOAc/toluene, 2,3-*cis*-isomer **19a** 6-15% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 54:46 in 61% combined yield (81 mg, 0.13 mmol) as a light yellow oil.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (19a).** R_f = 0.35 (25/75 EtOAc/toluene). 7:1 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 1H, N*H*), 7.40 – 7.16 (m, 15H, CH_{Ar}), 5.88 – 5.72 (m, 1H, =C*H* pentenyl), 5.08 – 4.90 (m, 3H, =CH_2 pentenyl, C*H*H Bn-3), 4.69 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-4), 4.61 – 4.42 (m, 4H, C-2, C*H*H Bn-3, C*H*H Bn-4, C*H*H Bn-6), 4.38 (d, *J* = 12.3 Hz, 1H, C*H*H Bn-6), 4.28 (dd, *J* = 9.7, 3.6 Hz, 1H, C-6a), 4.23 – 4.18 (m, 2H, C-3, C-4), 3.88 – 3.82 (m, 1H, C-5), 3.80 – 3.64 (m, 1H, C*H* Cy), 3.47 (dd, *J* = 9.8, 1.7 Hz, 1H, C-6b), 2.44 – 2.31 (m, 3H, C*H*HCH pentenyl, CH_2CO pentenyl), 2.29 – 2.18 (m, 1H, C*H*HCH pentenyl), 1.84 – 1.71 (m, 2H, CH_2 Cy), 1.66 – 1.49 (m, 3H, CH_2 Cy, C*H*H Cy), 1.33 – 1.19 (m, 2H, CH_2 Cy), 1.01 – 0.72 (m, 3H, CH_2 Cy, C*H*H Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4 (N*C*=O pentenyl), 168.0 (NH*C*(O)-1), 137.9, 137.6, 137.3 (3xC_q Bn), 137.1 (=*C*H pentenyl), 128.7, 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 127.9 (*C*H_{Ar}), 115.6 (=*C*H_2 pentenyl), 81.9 (*C*-3), 79.2 (*C*-4), 73.2, 73.1, 72.9 (3x*C*H_2 Bn), 66.0 (*C*-6), 63.4 (*C*-2), 60.2 (*C*-5), 48.5 (*C*H Cy), 33.4 (*C*H_2CH pentenyl), 33.0, 32.8 (2x*C*H_2 Cy), 28.7 (*C*H_2CO), 25.3, 25.2, 25.1 (3x*C*H_2 Cy). $[\alpha]^{20}_D$: -23.8° (c = 1, $CHCl_3$). IR (neat): 696, 735, 912, 1001, 1026, 1074, 1098, 1206, 1256, 1306, 1329, 1364, 1404, 1452, 1537, 1657, 2853, 2928, 3318. HR-MS: $[M+H^+]$ Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34813. Spectroscopic data matched literature data.[9]

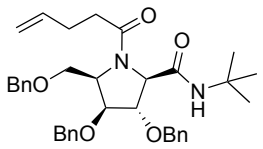
***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (19b).** R_f = 0.40 (25/75 EtOAc/toluene). 7:2 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.15 (m, 15H, CH_{Ar}), 6.01 (d, *J* = 8.1 Hz, 1H, N*H*), 5.91 – 5.70 (m, 1H, C*H* pentenyl), 5.10 – 4.91 (m, 2H, CH_2 pentenyl), 4.70 – 4.54 (m, 3H, C-5, C*H*H Bn-3, C*H*H Bn-6), 4.54 – 4.39 (m, 4H, C*H*H Bn-3, 2xC*H*H Bn-4, C*H*H Bn-6), 4.36 (s, 1H, C-2), 4.21 (s, 1H, C-4), 4.15 (s, 1H, C-3), 3.98 (dd, *J* = 8.8, 4.4 Hz, 1H, C-6a), 3.64 – 3.52 (m, 1H, C*H* Cy), 3.49 (dd, *J* = 10.5, 9.0 Hz, 1 H, C-6b), 2.41 – 2.31 (m, 3H, C*H*HCH pentenyl, CH_2CO pentenyl), 2.30 – 2.21 (m, 1H, C*H*HCH pentenyl), 1.83 – 0.49 (m, 10H, CH_2 Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0 (N*C*=O pentenyl), 168.8 (NH*C*(O)-1), 138.4, 137.1 (2xC_q Bn), 137.0 (=*C*H pentenyl), 136.9 (C_q Bn), 128.6, 128.6, 128.5, 128.5, 128.3, 128.1, 127.8, 127.7, 127.7 (*C*H_{Ar}), 115.7 (=*C*H_2 pentenyl), 86.0 (*C*-3), 80.9 (*C*-4), 73.2 (*C*H_2 Bn-6), 71.8 (*C*H_2 Bn-3), 71.6 (*C*H_2 Bn-4), 69.1 (*C*-2), 66.7 (*C*-6), 64.0 (*C*-5), 48.6 (*C*H Cy), 34.0 (*C*H_2CH pentenyl), 32.8, 32.0 (2x*C*H_2 Cy), 28.9 (*C*H_2CO pentenyl), 25.3, 24.8, 24.8 (3x*C*H_2 Cy). $[\alpha]^{20}_D$: -11.8° (c = 1, $CHCl_3$). IR (neat): 698, 737, 912, 1001, 1028, 1076, 1098, 1152, 1206, 1254, 1319, 1350, 1366, 1404, 1454, 1497, 1530, 1651, 2855, 2928, 3030, 3063. HR-MS: $[M+H^+]$ Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34821. Spectroscopic data matched literature data.[9]

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido/D-gulo-hexonamide (20).**



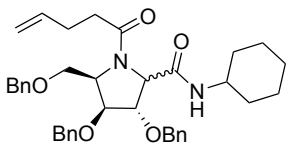
Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-xylose (**14**, 0.17 mmol) was dissolved in anhydrous MeOH (0.6 ml) and cooled to 0 °C. Next, pent-4-enoic acid (67 µl, 0.66 mmol) and *tert*-butyl isocyanide (23 µl, 0.21 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (6-20% EtOAc/toluene; 2,3-*trans*-isomer **20b**: 6-7% EtOAc/toluene, 2,3-*cis*-isomer **20a** 7-20% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 43:57 in 39% combined yield (38 mg, 0.06 mmol) as a light yellow oil.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (20a).** R_f = 0.40 (25/75 EtOAc/toluene). 5:4 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.16 (m, 15H, CH_{Ar}), 5.87 – 5.69 (m, 1H, =C*H* pentenyl), 5.28 (s, 1H, N*H*), 5.04 – 4.90 (m, 2H, =CH_2 pentenyl), 4.76 (d, *J* = 12.1 Hz, 1H, C*H*H Bn), 4.74 – 4.58 (m, 4H, C-3, 3xC*H*H Bn), 4.51 – 4.37 (m, 3H, 2xC*H*H Bn, C-4), 4.23 – 4.14 (m, 2H, C-1, C-5), 3.65 – 3.59 (m, 1H, C-6a), 3.53 (dd, *J* = 10.0, 3.2 Hz, 1H, C-6b), 2.42 – 2.23 (m, 3H, CH_2CO, C*H*HCH pentenyl), 2.21 – 2.14 (m, 1H, C*H*HCH pentenyl), 1.30 (s, 9H, 3xCH_3 *t*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5 (N*C*=O pentenyl), 168.4 (NH*C*(O)-1), 138.3, 138.2, 137.9 (3xC_q Bn), 137.5 (=*C*H pentenyl), 128.5, 128.5, 128.4, 128.4, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5 (*C*H_{Ar}), 115.2 (=CH_2 pentenyl), 81.2 (*C*-3), 80.2 (*C*-4), 73.7, 73.6, 73.5 (CH_2 Bn), 68.5 (*C*-6), 62.8 (*C*-2), 56.7 (*C*-5), 51.6 (C_q *t*-butyl), 33.0 (CH_2CH pentenyl), 29.2 (*C*H_2CO), 28.7 (3x*C*H_3 *t*-butyl). $[\alpha]^{20}_D$: 34.7° (c = 1, $CHCl_3$). IR (neat): 667, 698, 735, 802, 847, 912, 953, 1001, 1028, 1061, 1080, 1113, 1134, 1173, 1225, 1258, 1308, 1331, 1364, 1393, 1423, 1454, 1497, 1545, 1628, 1686, 1719, 1757, 2868, 2926, 2963, 3030, 3065, 3329. HR-MS: [M+H$^+$] Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33234.



***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (20b).** R_f = 0.50 (25/75 EtOAc/toluene). 3:2 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.20 (m, 15H, CH_{Ar}), 7.03 (s, 1H, N*H*), 5.88 – 5.68 (m, 1H, =C*H* pentenyl), 5.08 – 4.89 (m, 3H, =CH_2, C*H*H Bn), 4.81 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.73 – 4.39 (m, 6H, C-5, C-3, 4xC*H*H Bn), 4.11 (d, *J* = 4.5 Hz, 1H, C-3), 4.03 (dd, *J* = 6.9, 5.8 Hz, 1H, C-2), 3.95 (dd, *J* = 9.8, 4.9 Hz, 1H, C-6a), 3.69 (dd, *J* = 9.9, 2.2 Hz, 1H, C-6b), 2.46 – 2.17 (m, 4H, CH_2CH pentenyl, CH_2CO pentenyl), 1.14 (s, 9H, *t*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (N*C*=O pentenyl), 170.3 (NH*C*(O)-1), 137.8, 137.7, 137.6 (3xC_q Bn), 137.1 (=*C*H pentenyl), 128.5, 128.5, 128.0, 127.9, 127.9, 127.9, 127.6 (*C*H_{Ar}), 115.6 (=CH_2 pentenyl), 84.6 (*C*-3), 81.0 (*C*-4), 73.7, 72.9, 72.1 (3x*C*H_2 Bn), 67.5 (*C*-2), 66.7 (*C*-6), 58.2 (*C*-5), 51.1 (C_q *t*-butyl), 33.2 (*C*H_2CO pentenyl), 29.1 (*C*H_2CH pentenyl), 28.3 (3x*C*H_3 *t*-butyl). $[\alpha]^{20}_D$: 34.2° (c = 1, $CHCl_3$). IR (neat): 611, 631, 700, 735, 912, 1001, 1028, 1099, 1217, 1283, 1306, 1321, 1364, 1393, 1404, 1454, 1497, 1541, 1661, 1672, 2870, 2922, 2963, 3030, 3065, 3316. HR-MS: [M+H$^+$] Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33240.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido/D-gulo-hexonamide (21).**



Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-xylose (**14**, 0.17 mmol) was dissolved in anhydrous MeOH (0.55 ml) and cooled to 0 °C. Next, pent-4-enoic acid (67 µl, 0.66 mmol) and cyclohexyl isocyanide (26 µl, 0.21 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (6-20% EtOAc/toluene; 2,3-*trans*-

isomer **21b**: 6-7% EtOAc/toluene, 2,3-*cis*-isomer **21a** 7-20% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 45:55 in 37% combined yield (37 mg, 0.06 mmol) as a light yellow oil.

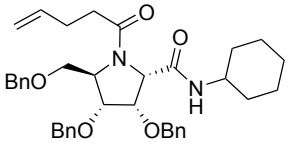
***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (21a).** R_f = 0.30 (25/75 EtOAc/toluene). 6:5 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.19 (m, 15H, CH_{Ar}), 5.84 – 5.70 (m, 1H, =C*H* pentenyl), 5.37 (d, *J* = 8.1 Hz, 1H, N*H*), 5.05 – 4.88 (m, 2H, =CH_2 pentenyl), 4.77 – 4.58 (m, 5H, C-3, 4xC*H*H Bn), 4.51 – 4.41 (m, 3H, C-4, 2xC*H*H Bn), 4.23 – 4.16 (m, 2H, C-2, C-5), 3.82 – 3.69 (m, 1H, C*H* Cy), 3.66 – 3.61 (m, 1H, C-6a), 3.54 (dd, *J* = 10.0, 3.2 Hz, 1H, C-6b), 2.38 – 2.27 (m, 3H, C*H*HCH pentenyl, CH_2CO pentenyl), 2.19 – 2.13 (m, 1H, C*H*HCH pentenyl), 2.01 – 0.70 (m, 10H, 5xCH_2 Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6 (N*C*=O pentenyl), 168.3 (NH*C*(O)-1), 138.7, 138.2, 138.0 (3xC_q Bn), 137.6 (=*C*H pentenyl), 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6 (CH_{Ar}), 115.2 (=CH_2 pentenyl), 81.2 (*C*-3), 80.0 (*C*-4), 73.7, 73.5, 73.4 (CH_2 Bn), 68.5 (*C*-6), 61.1 (*C*-2), 56.8 (*C*-5), 48.8 (*C*H Cy), 33.1 (CH_2 Cy), 33.1 (CH_2CH pentenyl), 33.0 (*C*HCO pentenyl), 29.2, 25.6, 25.0, 24.9 (CH_2 Cy). $[\alpha]^{20}_D$: 37.5° (c = 1, $CHCl_3$). IR (neat): 681, 696,735, 912, 1003, 1028, 1063, 1082, 1111, 1134, 1209, 1236, 1250, 1271, 1310, 1331, 1364, 1418, 1452, 1497, 1545, 1649, 2853, 2928, 3030, 3065, 3300. HR-MS: [M+H$^+$] Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34809.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (21b).** R_f = 0.40 (25/75 EtOAc/toluene). 4:3 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.17 (m, 16H, 15xCH_{Ar}, N*H*), 5.88 – 5.69 (m, 1H, =C*H* pentenyl), 5.07 – 4.90 (m, 2H, =CH_2), 4.80 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.69 – 4.43 (m, 6H, 5xC*H*H Bn, C-5), 4.43 – 4.38 (m, 1H, C-3), 4.20 (d, *J* = 4.1 Hz, 1H, C-2), 4.03 (dd, *J* = 7.1, 5.4 Hz, 1H, C-4), 3.99 (dd, *J* = 9.7, 5.0 Hz, 1H, C-6a), 3.70 (dd, *J* = 9.7, 2.1 Hz, 1H, C-6b), 3.60 – 3.47 (m, 1H, C*H* Cy), 2.41 – 2.25 (m, 3H, C*H*HCH pentenyl, CH_2CO pentenyl), 2.24 – 2.13 (m, 1H, C*H*HCH pentenyl), 1.88 – 0.44 (m, 10H, 5xCH_2 Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5 (N*C*=O pentenyl), 170.2 (NH*C*(O)-1), 137.6, 137.6 (3xC_q Bn), 137.2 (=*C*H pentenyl), 128.6, 128.5, 128.2, 128.0, 128.0, 127.9 (CH_{Ar}), 115.6 (=CH_2 pentenyl), 84.6 (*C*-3), 81.1 (*C*-4), 73.7, 72.9, 72.2 (3xCH_2 Bn), 67.0 (*C*-2), 66.6 (*C*-6), 58.3 (*C*-5), 48.4 (*C*HCy), 33.2 (CH_2 Cy), 32.7 (CH_2CH pentenyl), 32.2 (CH_2 Cy), 28.7 (CH_2CO pentenyl), 25.3, 25.1, 25.0 (3xCH_2 Cy). $[\alpha]^{20}_D$: 18.9° (c = 1, $CHCl_3$). IR (neat): 696, 737, 912, 1001, 1028, 1101, 1207, 1254, 1281, 1319, 1364, 1410, 1452, 1497, 1522, 1533, 1655, 1661, 2855, 2928, 3030, 3065, 3308. HR-MS: [M+H$^+$] Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34815.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-altro-hexonamide (22a).** Crude 2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-ribose (**15**, 0.21 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (86 µl, 0.84 mmol) and *tert*-butyl isocyanide (30 µl, 0.26 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (10-15% EtOAc/toluene) yielding the title compound as a single stereoisomer in 49% yield (60 mg, 0.10 mmol). R_f = 0.55 (25/75 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 13H, CH_{Ar} Bn), 7.19 – 7.14 (m, 2H, CH_{Ar} Bn), 6.76 (s, 1H, N*H*), 5.88 – 5.75 (m, 1H, =C*H* pentenyl), 5.05 – 4.92 (m, 2H, =CH_2 pentenyl), 4.76 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-3), 4.70 (d, *J* = 11.5 Hz, 1H, C*H*H Bn-4), 4.65 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-4), 4.61 (dd, *J* = 9.1, 4.4 Hz, 1H, C-3), 4.55 – 4.50 (m, 2H, C-5, C*H*H Bn-3), 4.44 (d, *J* = 9.1 Hz, 1H, C-2), 4.43 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-6), 4.38 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-6), 4.07 (d, *J* = 4.4 Hz, 1H, C-4), 3.66 (dd, *J* = 9.9, 4.9 Hz, 1H, C-6a), 3.53 (dd, *J* = 9.9, 2.6 Hz, 1H, C-6b), 2.40 – 2.31 (m, 4H, CH_2CH pentenyl, CH_2CO pentenyl), 1.06 (s, 9H, 3xCH_2 *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3 (N*C*=O pentenyl), 168.9 (NH*C*(O)-1), 137.9, 137.8, 137.4 (3xC_q Bn), 137.3 (=*C*H pentenyl), 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8,

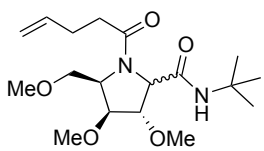
127.8, 127.5 (*C*H$_{Ar}$ Bn), 115.3 (=*C*H$_2$ pentenyl), 79.7 (*C*-4), 79.0 (*C*-3), 73.5 (*C*H$_2$ Bn-6), 73.1 (*C*H$_2$ Bn-4), 72.9 (*C*H$_2$ Bn-3), 67.8 (*C*-6), 65.7 (*C*-2), 62.9 (*C*-5), 51.0 (*C*$_q$ *tert*-butyl), 33.7 (*C*H$_2$CH pentenyl), 28.7 (*C*H$_2$CO pentenyl), 28.2 (3x*C*H$_3$ *tert*-butyl). $[\alpha]^{20}_D$: 14.4° (c = 1, $CHCl_3$). IR (neat): 698, 737, 912, 1001, 1028, 1043, 4069, 1103, 1223, 1277, 1306, 1364, 1406, 1454, 1497, 1535, 1657, 1676, 2866, 2924, 2963, 3030, 3063, 3348. HR-MS: [M+H$^+$] Calculated for $C_{36}H_{44}N_2O_5$: 585.33230; found: 585.33213.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-altro-hexonamide (23a).** Crude



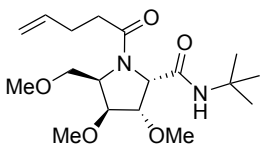
2,3,5-Tri-*O*-benzyl-4-deoxy-4-amino-D-ribose (**15**, 0.21 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (86 µl, 0.84 mmol) and cyclohexyl isocyanide (33 µl, 0.26 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (10-30% EtOAc/toluene) yielding the title compound as a single stereoisomer in 51% yield (65 mg, 0.11 mmol). R_f = 0.50 (25/75 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.21 (m, 13H, C*H*$_{Ar}$ Bn), 7.19 – 7.12 (m, 2H, C*H*$_{Ar}$ Bn), 6.85 (d, *J* = 8.0 Hz, 1H, N*H*), 5.87 – 5.71 (m, 1H, =C*H* pentenyl), 5.05 – 4.91 (m, 2H, =C*H*$_2$), 4.73 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.64 (s, 2H, C*H*$_2$ Bn-4), 4.62 (dd, *J* = 9.1, 4.4 Hz, 1H, C-3), 4.56 – 4.50 (m, 3H, C-2, C-5, C*H*H Bn-3), 4.42 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-6), 4.37 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-6), 4.04 (d, *J* = 4.4 Hz, 1H, C-4), 3.67 (dd, *J* = 9.9, 4.8 Hz, 1H, C-6a), 3.65 – 3.55 (m, 1H, C*H* Cy), 3.52 (dd, *J* = 9.9, 2.4 Hz, 1H, C-6), 2.39 – 2.29 (m, 4H, C*H*$_2$CH pentenyl, C*H*$_2$CO pentenyl), 1.65 (d, *J* = 12.2 Hz, 1H, C*H*HCH Cy), 1.59 – 1.38 (m, 3H, C*H*HCH Cy, C*H*HCCH Cy, C*H*HCH$_2$CH Cy), 1.24 – 1.07 (m, 2H, C*H*HCH$_2$CH Cy, C*H*HCH$_2$CH Cy), 0.95 – 0.80 (m, 2H, CH$_2$C*H*$_2$CH$_2$ Cy), 0.79 – 0.67 (m, 1H, C*H*HCH Cy), 0.67 – 0.52 (m, 1H, C*H*HCH Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2 (NC=O pentenyl), 168.7 (NH*C*(O)-1), 137.9, 137.7 (3x*C*$_q$ Bn), 137.2 (=*C*H pentenyl), 128.6, 128.5, 128.4, 128.2, 127.9, 127.8, 127.5 (*C*H$_{Ar}$ Bn), 115.3 (=*C*H$_2$ pentenyl), 79.5 (*C*-4), 78.7 (*C*-3), 73.4 (*C*H$_2$ Bn-6), 72.9 (*C*H$_2$ Bn-4), 72.7 (*C*H$_2$ Bn-3), 67.8 (*C*-6), 64.9 (*C*-5), 62.8 (*C*-2), 48.4 (*C*H Cy), 33.7 (*C*HCH$_2$ pentenyl), 32.6 (*C*H$_2$CH Cy), 32.1 (*C*H$_2$CH Cy), 28.7 (*C*H$_2$CO pentenyl), 25.4 (*C*H$_2$(CH$_2$)$_2$ Cy), 24.8 (*C*H$_2$CH$_2$CH Cy), 24.7 (*C*H$_2$CH$_2$CH Cy). $[\alpha]^{20}_D$: 11.9° (c = 1, $CHCl_3$). IR (neat): 698, 737, 912, 1003, 1028, 1103, 1190, 1209, 1258, 1273, 1321, 1358, 1408, 1452, 1497, 1535, 1657, 2855, 2928, 3030, 3063, 3308, 3339. HR-MS: [M+H$^+$] Calculated for $C_{38}H_{46}N_2O_5$: 611.34795; found: 611.34808.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-ido/D-gulo-hexonamide (63).**



Crude 2,3,5-Tri-*O*-methyl-4-deoxy-4-amino-D-xylofuranose (**62**, 0.22 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (90 µl, 0.88 mmol) and *tert*-butyl isocyanide (31 µl, 0.28 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (20-70% EtOAc/toluene; 2,3-*trans*-isomer **63b**: 20-30% EtOAc/toluene, 2,3-*cis*-isomer **63a** 30-70% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 44:56 in 46% combined yield (36 mg, 0.10 mmol).

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-ido-hexonamide (63a).** R_f = 0.35



(75/25 EtOAc/toluene). 6:5 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 – 5.75 (m, 1H, =C*H* pentenyl), 5.53 (s, 1H, N*H*), 5.11 – 4.93 (m, 2H, =C*H*$_2$), 4.37 (dd, *J* = 9.0, 7.8 Hz, 1H, C-4), 4.32 – 4.19 (m, 2H, C-2, C-5), 4.02 (t, *J* = 8.6 Hz, 1H, C-3), 3.56 – 3.51 (m, 1H, C-6a), 3.49 (s, 3H, C*H*$_3$ Me-3), 3.47 (s, 3H, C*H*$_3$ Me-4), 3.45 – 3.39 (m, 1H, C-6b), 3.32 (s, 3H, C*H*$_3$ Me-6), 2.50 –

2.42 (m, 1H, C*H*HCH pentenyl), 2.42 – 2.33 (m, 2H, CH_2CO), 2.28 – 2.19 (m, 1H, C*H*HCH pentenyl), 1.35 (s, 9H, 3xCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8 (N*C*=O pentenyl), 168.3 (NH*C*(O)-1), 137.6 (=*C*H pentenyl), 115.3 (=*C*H_2 pentenyl), 82.3 (*C*-4), 82.0 (*C*-3), 71.1 (*C*-6), 61.4 (*C*-2), 59.5 (*C*H_3 Me-3), 59.4 (*C*H_3 Me-4), 59.1 (*C*H_3 Me-6), 56.5 (*C*-5), 51.8 (*C*$_q$ *tert*-butyl), 33.1 (*C*H_2CH pentenyl), 29.3 (*C*H_2CO), 28.8 (3x*C*H_3 *tert*-butyl). $[\alpha]^{20}_D$: 32.3° (c = 1, $CHCl_3$). IR (neat): 910, 1011, 1067, 1115, 1202, 1258, 1364, 1393, 1422, 1450, 1549, 1630, 1668, 2828, 2851, 2926, 2967, 3076, 3318. HR-MS: [M+H$^+$] Calculated for $C_{18}H_{32}N_2O_5$: 357.23840; found: 357.23835.

***N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-gulo-hexonamide (63b).** R_f = 0.60 (75/25 EtOAc/toluene). 2:1 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 – 5.75 (m, 1H, =C*H* pentenyl), 5.11 – 4.94 (m, 2H, =C*H*$_2$ pentenyl), 4.44 – 4.35 (m, 1H, C-5), 4.04 (t, *J* = 5.1 Hz, 1H, C-3), 3.99 (d, *J* = 4.6 Hz, 1H, C-2), 3.91 (dd, *J* = 9.7, 4.6 Hz, 1H, C-5), 3.72 (t, *J* = 7.3, 5.8 Hz, 1H, C-4), 3.55 (dd, *J* = 9.6, 1.8 Hz, 1H, C-6), 3.48 (s, 3H, C*H*$_3$ Me-3), 3.43 (s, 3H, C*H*$_3$ Me-4), 3.38 (s, 3H, C*H*$_3$ Me-6), 2.42 – 2.32 (m, 3H, C*H*HCH pentenyl, CH_2CO), 2.27 – 2.21 (m, 1H, C*H*HCH pentenyl), 1.33 (s, 9H, 3xC*H*$_3$ *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (N*C*=O pentenyl), 170.8 (NH*C*(O)-1), 137.2 (=*C*H pentenyl), 115.6 (=*C*H_2 pentenyl), 86.9 (*C*-3), 83.0 (*C*-4), 68.3 (*C*-6), 67.2 (*C*-2), 59.0 (*C*H_3 Me-6), 58.8 (*C*H_3 Me-4), 58.3 (*C*H_3 Me-3), 57.7 (*C*-5), 51.0 (*C*$_q$ *tert*-butyl), 33.1 (*C*H_2CH pentenyl), 28.7 (*C*H_2CO pentenyl), 28.6 (3x*C*H_3 *tert*-butyl). $[\alpha]^{20}_D$: 23.2° (c = 1, $CHCl_3$). IR (neat): 914, 995, 1057, 1111, 1198, 1225, 1285, 1321, 1364, 1393, 1454, 1545, 1663, 1676, 2835, 2926, 2963, 3310. HR-MS: [M+H$^+$] Calculated for $C_{18}H_{32}N_2O_5$: 357.23840; found: 357.23839.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-ido/D-gulo-hexonamide (64).** Crude 2,3,5-Tri-*O*-methyl-4-deoxy-4-amino-D-xylofuranose (**62**, 0.22 mmol) was dissolved in anhydrous MeOH (0.7 ml) and cooled to 0 °C. Next, pent-4-enoic acid (90 µl, 0.88 mmol) and cyclohexyl isocyanide (34 µl, 0.28 mmol) were successively added and the reaction mixture was stirred overnight at 0-4 °C. $NaHCO_3$ (sat. aq.) was added to the mixture before allowing it to warm to room temperature while stirring. Ethyl acetate was added to the mixture and the organic phase was washed with $NaHCO_3$ (sat. aq.) and brine. The organic phase was dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the product was isolated by silica gel chromatography (15-70% EtOAc/toluene; 2,3-*trans*-isomer **64b**: 15-30% EtOAc/toluene, 2,3-*cis*-isomer **64a** 40-70% EtOAc/toluene) yielding a separable 2,3-*cis*:2,3-*trans* mixture with a ratio of 46:54 in 53% combined yield (45 mg, 0.12 mmol).

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-ido-hexonamide (64a).** R_f = 0.35 (75/25 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 – 5.74 (m, 1H, =C*H* pentenyl), 5.70 (d, *J* = 8.1 Hz, 1H, N*H*), 5.09 – 4.94 (m, 2H, =C*H*$_2$ pentenyl), 4.40 – 4.22 (m, 3H, C-2, C-4, C-5), 4.05 (t, *J* = 8.6 Hz, 1H, C-3), 3.86 – 3.74 (m, 1H, C*H* Cy), 3.53 (dd, *J* = 10.2, 3.8 Hz, 1H, C-6a), 3.48 (s, 3H, C*H*$_3$ Me-3), 3.48 (s, 3H, C*H*$_3$ Me-4), 3.46 – 3.40 (m, 1H, C-6b), 3.32 (s, 3H, C*H*$_3$ Me-6), 2.52 – 2.43 (m, 1H, C*H*HCH pentenyl), 2.43 – 2.32 (m, 2H, CH_2CO pentenyl), 2.28 – 2.17 (m, 1H, C*H*HCH pentenyl), 1.99 – 1.87 (m, 2H, C*H*$_2$ Cy), 1.75 – 1.55 (m, 4H, 2xC*H*$_2$ Cy), 1.44 – 1.28 (m, 2H, C*H*$_2$ Cy), 1.23 – 1.05 (m, 2H, C*H*$_2$ Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2 (N*C*=O pentenyl), 168.3 (NH*C*(O)-1), 137.5 (=*C*H pentenyl), 115.4 (=*C*H_2 pentenyl), 82.5 (*C*-4), 82.0 (*C*-3), 70.9 (*C*-6), 61.0 (*C*-2), 59.6 (*C*H_3 Me-3), 59.4 (*C*H_3 Me-4), 59.2 (*C*H_3 Me-6), 56.6 (*C*-5), 48.8 (*C*H Cy), 33.2, 33.2, 33.0 (*C*H_2CH pentenyl, 2x*C*H_2 Cy), 29.2 (*C*H_2CO pentenyl), 25.7, 25.0, 24.9 (3x*C*H_2 Cy). $[\alpha]^{20}_D$: 25.9° (c = 1, $CHCl_3$). IR (neat): 912, 959, 1011, 1065, 1113, 1202, 1250, 1350, 1418, 1449, 1549, 1653, 2830, 2855, 2928, 2980, 3292. HR-MS: [M+H$^+$] Calculated for $C_{20}H_{34}N_2O_5$: 383.25405; found: 383.25446.

***N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-methyl-D-gulo-hexonamide (64b).** R_f = 0.55 (75/25 EtOAc/toluene). 3:1 Mixture of rotamers; major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.1 Hz, 1H, N*H*), 5.92 – 5.73 (m, 1H, =C*H*), 5.11 – 4.94 (m, 2H, =CH_2), 4.48 – 4.37 (m, 1H, C-5), 4.08 (d, *J* = 4.7 Hz, 1H, C-2), 4.02 (t, *J* = 5.2 Hz, 1H, C-3), 3.93 (dd, *J* = 9.7, 4.5 Hz, 1H, C-6), 3.78 – 3.69 (m, 2H, C-4, C*H* Cy), 3.55 (dd, *J* = 9.7, 1.8 Hz, 1H, C-6a), 3.48 (s, 3H, CH_3 Me-3), 3.43 (s, 3H, CH_3 Me-4), 3.40 (s, 3H, CH_3 Me-6), 2.51 – 2.28 (m, 3H, C*H*HCH pentenyl, CH_2CO), 2.28 – 2.16 (m, 1H, C*H*HCH pentenyl), 1.94 – 1.80 (m, 2H, CH_2 Cy), 1.78 – 1.50 (m, 3H, C*H*H Cy, CH_2 Cy), 1.43 – 1.28 (m, 3H, C*H*H Cy, CH_2 Cy), 1.22 – 1.00 (m, 2H, CH_2 Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5 (N*C*=O pentenyl), 170.6 (NH*C*(O)-1), 137.1 (=*C*H pentenyl), 115.6 (=*C*H_2 pentenyl), 87.0 (*C*-3), 83.1 (*C*-4), 68.3 (*C*-6), 66.6 (C-2), 58.9 (*C*H_3 Me-3), 58.9 (*C*H_3 Me-4), 58.4 (*C*H_3 Me-6), 57.6 (*C*-5), 48.3 (*C*H Cy), 33.2, 33.1, 33.0 (*C*H_2CH pentenyl, 2x*C*H_2 Cy), 28.7 (*C*H_2CO), 25.7, 25.1 (2x*C*H_2 Cy). $[\alpha]^{20}_D$: 21.4° (c = 1, $CHCl_3$). IR (neat): 912, 957, 980, 997, 1051, 1196, 1225, 1256, 1277, 1319, 1418, 1449, 1539, 1659, 1734, 2853, 2928, 2980, 3304. HR-MS: [M+H$^+$] Calculated for $C_{20}H_{34}N_2O_5$: 383.25405; found: 383.25444.

***N*-(*tert*-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (24).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (**16a**, 62 mg, 0.11 mmol) was dissolved in a mixture of THF (1.5 ml) and water (0.5 ml). Iodine (81 mg, 0.3 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (40-80% EtOAc/toluene) yielding the title compound in 78% yield (42 mg, 83 µmol). R_f = 0.15 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H, N*H* *tert*-butyl), 7.35 – 7.22 (m, 15H, CH_{Ar}), 4.76 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-3), 4.66 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-3), 4.64 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.55 (s, 2H, CH_2 Bn-6), 4.51 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.29 (dd, *J* = 6.2, 4.0 Hz, 1H, C-3), 3.98 (dd, *J* = 6.3, 4.0 Hz, 1H, C-4), 3.84 (d, *J* = 6.3 Hz, 1H, C-2), 3.79 (dd, *J* = 9.5, 4.4 Hz, 1H, C-6a), 3.73 – 3.67 (m, 1H, C-6b), 3.61 – 3.55 (m, 1H, C-5), 1.22 (s, 9H, 3x*C*H_3 *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2 (*C*-1), 138.6, 138.4, 138.3 (*C*$_q$ Bn), 128.5, 128.4, 128.2, 127.9, 127.8, 127.6, 127.6, 127.4 (*C*H$_{Ar}$ Bn), 79.8 (*C*-3), 79.7 (*C*-4), 73.8 (*C*H_2 Bn-3), 73.7 (*C*H_2 Bn-6), 72.9 (*C*H_2 Bn-4), 71.6 (*C*-6), 62.3 (*C*-2), 58.1 (*C*-5), 50.6 (*C*$_q$ *tert*-butyl), 28.7 (3x*C*H_3 *tert*-butyl). $[\alpha]^{20}_D$: 7.3° (c = 1, $CHCl_3$). IR (neat): 696, 737, 910, 949, 1026, 1057, 1099, 1109, 1144, 1215, 1275, 1364, 1393, 1454, 1497, 1531, 1663, 2868, 2924, 2965, 3030, 3063, 3321. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 503.29043; found: 503.29011.

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (25).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-galacto-hexonamide (**17a**, 75 mg, 0.12 mmol) was dissolved in a mixture of THF (1.7 ml) and water (0.5 ml). Iodine (93 mg, 0.37 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (40-80% EtOAc/toluene) yielding the title compound in 71% yield (46 mg, 86 µmol). R_f = 0.35 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.3 Hz, 1H, N*H* Cy), 7.38 – 7.20 (m, 15H, CH_{Ar} Bn), 4.71 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-3), 4.67 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-3), 4.62 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-4), 4.53 (s, 2H, 2x*CH*H Bn-6), 4.50 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-4), 4.41 (dd, *J* = 6.2, 3.9 Hz, 1H, C-3), 4.06 (d, *J* = 6.4 Hz, 1H, C-2), 4.04 (dd, *J* = 6.1, 3.9 Hz, 1H, C-4), 3.79 – 3.63 (m, 4H, C-5, C-6, C*H* Cy), 1.79 – 1.71 (m, 1H, C*H*HCH Cy), 1.67 – 1.42 (m, 4H, C*H*HCH Cy, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.36 – 1.01 (m, 4H, C*H*HCH Cy, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.00 – 0.90 (m, 1H, C*H*HCH Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4 (*C*-1), 138.4, 138.2, 138.0 (3x*C*$_q$ Bn), 128.5, 128.5, 128.3, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5 (*C*H$_{Ar}$ Bn), 79.7 (*C*-3), 79.4 (*C*-

4), 73.9 (*C*H$_2$ Bn-3), 73.6 (*C*H$_2$ Bn-6), 72.9 (*C*H$_2$ Bn-4), 71.0 (*C*-6), 61.5 (*C*-2), 58.2 (*C*-5), 47.9 (*C*H Cy), 32.7 (2x*C*H$_2$CH Cy), 25.6 (*C*H$_2$(CH$_2$)$_2$ Cy), 24.7, 24.7 (2x*C*H$_2$CH$_2$CH Cy). $[\alpha]^{20}_D$: 3.6° (c = 0.9, $CHCl_3$). IR (neat): 696, 735, 891, 912, 957, 1028, 1057, 1094, 1126, 1150, 1209, 1254, 1312, 1350, 1360, 1404, 1452, 1497, 1526, 1653, 1717, 2853, 2928, 3030, 3063, 3321. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30583. Spectroscopic data matched literature data.[9]

***N*-(*tert*-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (26a).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (**18a**, 49 mg, 84 µmol) was dissolved in a mixture of THF (1.2 ml) and water (0.4 ml). Iodine (64 mg, 0.25 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (14-25% EtOAc/toluene) yielding the title compound in 52% yield (22 mg, 44 µmol). R_f = 0.40 (40/60 EtOAc/toluene).[1]H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.20 (m, 15H, CH_{Ar}), 7.18 (s, 1H, N*H tert*-butyl), 4.60 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.53 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-6), 4.51 – 4.47 (m, 1H, C*H*H Bn-6), 4.46 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.45 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.39 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.23 (dd, *J* = 5.5, 1.4 Hz, 1H, C-3), 4.00 (d, *J* = 5.5 Hz, 1H, C-2), 3.85 – 3.80 (m, 1H, C-4), 3.57 – 3.43 (m, 3H, C-5, C-6), 1.30 (s, 9H, 3x*C*H$_3$ *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1 (*C*-1), 138.4, 138.2, 137.9 (3x*C*$_q$ Bn), 128.5, 128.5, 128.3, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7 (*C*H$_{Ar}$ Bn), 83.8 (*C*-4), 83.3 (*C*-3), 73.3 (*C*H$_2$ Bn-6), 73.0 (*C*H$_2$ Bn-3), 72.5 (*C*-6), 71.5 (*C*H$_2$ Bn-4), 65.3 (*C*-2), 62.6 (*C*-5), 50.6 (*C*$_q$ *tert*-butyl), 28.9 (3x*C*H$_3$ *tert*-butyl). $[\alpha]^{20}_D$: 2.0° (c = 1, $CHCl_3$). IR (neat): 696, 735, 910, 943, 1003, 1028, 1070, 1094, 1207, 1229, 1256, 1271, 1364, 1391, 1454, 1497, 1522, 1670, 1722, 2857, 2922, 2963, 3030, 3325. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 502.29043; found: 502.28966. Spectroscopic data matched literature data.[9]

***N*-(*tert*-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (26b).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (**18b**, 47 mg, 80 µmol) was dissolved in a mixture of THF (1.1 ml) and water (0.3 ml). Iodine (61 mg, 0.24 mmol) was added and the reaction stirred for 15 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (10% EtOAc/toluene) yielding the title compound in 60% yield (24 mg, 48 µmol). R_f = 0.65 (40/60 EtOAc/toluene). [1]H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H, N*H tert*-butyl), 7.38 – 7.21 (m, 15H, CH_{Ar} Bn), 4.76 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.61 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.55 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-4), 4.51 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-6), 4.47 (d, *J* = 12.1 Hz, 1H, C*H*H Bn-6), 4.43 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-4), 4.34 (t, *J* = 2.9 Hz, 1H, C-3), 3.88 (dd, *J* = 5.4, 3.1 Hz, 1H, C-4), 3.65 (d, *J* = 2.5 Hz, 1H, C-2), 3.57 (dd, *J* = 9.6, 4.3 Hz, 1H, C-6a), 3.53 (dd, *J* = 9.6, 5.7 Hz, 1H, C-6b), 3.26 – 3.20 (m, 1H, C-5), 1.32 (s, 9H, 3x*C*H$_3$ Bn). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3 (*C*-1), 138.4, 138.1, 138.0 (3x*C*$_q$ Bn), 128.6, 128.5, 128.4, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7 (*C*H$_{Ar}$ Bn), 87.5 (*C*-3), 85.1 (*C*-4), 73.4 (*C*H$_2$ Bn-6), 72.0 (*C*H$_2$ Bn-4), 71.8 (*C*H$_2$ Bn-3), 69.1 (*C*-6), 66.2 (*C*-2), 62.5 (*C*-5), 50.5 (*C*$_q$ *tert*-butyl), 28.8 (3x*C*H$_3$ *tert*-butyl). $[\alpha]^{20}_D$: -0.8° (c = 1, $CHCl_3$). IR (neat): 625, 637, 696, 735, 804, 824, 851, 908, 957, 1003, 1028, 1074, 1092, 1177, 1207, 1227, 1269, 1306, 1331, 1364, 1391, 1454, 1497, 1516, 1670, 2795, 2859, 2920, 2963, 3030, 3063, 3088, 3326. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 503.29043; found: 503.28954. Spectroscopic data matched literature data.[9]

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (27a).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gluco-hexonamide (**19a**, 62 mg, 0.10 mmol) was dissolved in a mixture of THF (1.4 ml) and water (0.4 ml). Iodine (77 mg, 0.3 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (30-40% EtOAc/toluene) yielding the title compound in 85% yield (46 mg, 87 µmol). R_f = 0.30 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.15 (m, 16H, N*H* Cy, CH_{Ar}), 4.59 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-3), 4.54 – 4.46 (m, 3H, C*H*H Bn-4, 2xC*H*H Bn-6), 4.44 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-3), 4.40 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.29 (dd, *J* = 5.5, 1.4 Hz, 1H, C-3), 4.13 (d, *J* = 5.6 Hz, 1H, C-2), 3.86 – 3.83 (m, 1H, C-4), 3.81 – 3.69 (m, 1H, C*H* Cy), 3.54 – 3.45 (m, 3H, C-5, C-6), 1.88 – 1.79 (m, 1H, C*H*HCH Cy), 1.79 – 1.70 (m, 1H, C*H*HCH Cy), 1.70 – 1.50 (m, 3H, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.43 – 1.27 (m, 2H, 2xC*H*HCH$_2$CH), 1.21 – 0.98 (m, 3H, 2xC*H*HCH Cy, C*H*H(CH$_2$)$_2$ Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8 (*C*-1), 138.3, 138.1, 137.9 (3xC_q Bn), 128.5, 128.5, 128.3, 127.9, 127.9, 127.8, 127.8, 127.8, 127.7 (CH_{Ar}), 83.5 (*C*-4), 83.1 (*C*-3), 73.3 (CH_2 Bn-6), 73.0 (CH_2 Bn-3), 72.2 (*C*-6), 71.5 (CH_2 Bn-4), 64.6 (*C*-2), 62.6 (*C*-5), 47.7 (C*H* Cy), 33.1, 33.0 (2xCH$_2$CH Cy), 25.7 (CH$_2$(CH$_2$)$_2$ Cy), 24.9, 24.8 (2xCH$_2$CH$_2$CH Cy). $[\alpha]^{20}_D$: 11.5° (c = 1, $CHCl_3$). IR (neat): 696, 733, 891, 908, 957, 1003, 1028, 1070, 1090, 1206, 1252, 1315, 1362, 1393, 1452, 1497, 1520, 1659, 2853, 2926, 3319, 3329. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30558.

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (27b).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-manno-hexonamide (**19b**, 26 mg, 42 µmol) was dissolved in a mixture of THF (0.6 ml) and water (0.2 ml). Iodine (32 mg, 0.13 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (10-16% EtOAc/toluene) yielding the title compound in 80% yield (18 mg, 34 µmol). R_f = 0.60 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.7 Hz, 1H, N*H* Cy), 7.43 – 7.15 (m, 15H, CH_{Ar}), 4.77 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.62 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.54 – 4.44 (m, 3H, C*H*H Bn-4, 2xC*H*H Bn-6), 4.41 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-4), 4.36 (t, *J* = 2.9 Hz, 1H, C-3), 3.88 (dd, *J* = 5.6, 3.2 Hz, 1H, C-4), 3.73 (d, *J* = 2.6 Hz, 1H, C-2), 3.77 – 3.65 (m, 1H, C*H* Cy), 3.58 (dd, *J* = 9.6, 4.2 Hz, 1H, C-6a), 3.53 (dd, *J* = 9.6, 5.6 Hz, 1H, C-6b), 3.24 – 3.18 (m, 1H, C-5), 1.91 – 1.84 (m, 1H, C*H*HCH Cy), 1.79 – 1.52 (m, 4H, C*H*HCH Cy, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.43 – 1.27 (m, 2H, 2xC*H*HCH$_2$CH Cy), 1.21 – 1.02 (m, 3H, 2xC*H*HCH Cy, C*H*H(CH$_2$)$_2$ Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (*C*-1), 138.3, 138.1, 138.0 (3xC_q Bn), 128.6, 128.5, 128.4, 128.2, 128.1, 127.9, 127.9, 127.8, 127.8 (CH_{Ar}), 87.3 (*C*-3), 85.0 (*C*-4), 73.4 (CH_2 Bn-6), 72.0 (CH_2 Bn-4), 71.7 (CH_2 Bn-3), 69.0 (*C*-6), 65.8 (*C*-2), 62.5 (*C*-5), 47.8 (C*H* Cy), 33.1 (2xCH$_2$CH Cy), 25.7 (CH$_2$(CH$_2$)$_2$ Cy), 25.0, 24.9 (2xCH$_2$CH$_2$CH Cy). $[\alpha]^{20}_D$: 2.2° (c = 1, $CHCl_3$). IR (neat): 613, 696, 735, 822, 847, 891, 908, 957, 1001, 1028, 1072, 1092, 1207, 1252, 1310, 1342, 1354, 1452, 1497, 1514, 1667, 1726, 2853, 2926, 3030, 3063, 3325. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30544.

***N*-(*tert*-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (28a).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (**20a**, 28 mg, 47 µmol) was dissolved in a mixture of THF (0.7 ml) and water (0.2 ml). Iodine (36 mg, 0.14 mmol) was added and the reaction stirred for 15 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash

chromatography (10-25% EtOAc/toluene) yielding the title compound in 75% yield (18 mg, 35 µmol). R_f = 0.40 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 14H, CH_{Ar} Bn, N*H* *tert*-butyl), 7.20 – 7.15 (m, 2H, CH_{Ar} Bn), 4.62 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-3), 4.53 (s, 2H, 2xC*H*H Bn-6), 4.49 (d, *J* = 7.2 Hz, 1H, C*H*H Bn-3), 4.46 (d, *J* = 7.2 Hz, 1H, C*H*H Bn-4), 4.30 (d, *J* = 11.7 Hz, 1H, C*H*H Bn-4), 4.29 (dd, *J* = 5.4, 1.3 Hz, 1H, C-3), 4.01 (d, *J* = 5.1 Hz, 1H, C-2), 3.83 (dd, *J* = 3.5, 1.0 Hz, 1H, C-4), 3.71 – 3.61 (m, 2H, C-5, C-6a), 3.56 (dd, *J* = 9.2, 7.1 Hz, 1H, C-6b), 1.33 (s, 9H, 3xCH_3 *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4 (*C*-1), 138.3, 138.2, 138.0 (3xC_q Bn), 128.6, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7 (CH_{Ar} Bn), 82.8 (*C*-4), 82.5 (*C*-3), 73.5 (CH_2 Bn-6), 73.4 (CH_2 Bn-3), 71.9 (CH_2 Bn-4), 68.9 (*C*-6), 64.5 (*C*-2), 60.1 (*C*-5), 50.6 (C_q *tert*-butyl), 28.9 (3xCH_3 *tert*-butyl). $[\alpha]^{20}_D$: 5.8° (c = 1, $CHCl_3$). IR (neat): 847, 912, 1003, 1028, 1078, 1098, 1177, 1225, 1267, 1364, 1393, 1454, 1497, 1526, 1609, 1653, 1668, 2855, 2922, 2963, 3030, 3063, 3088, 3291, 3310. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 503.29043; found: 503.28988.

***N*-(tert-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (28b).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (**20b**, 33 mg, 56 µmol) was dissolved in a mixture of THF (0.8 ml) and water (0.2 ml). Iodine (43 mg, 0.17 mmol) was added and the reaction stirred for 15 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (10-15% EtOAc/toluene) yielding the title compound in 89% yield (25 mg, 50 µmol). R_f = 0.50 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H, N*H* *tert*-butyl), 7.38 – 7.17 (m, 15H, CH_{Ar}), 4.71 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.60 – 4.52 (m, 3H, C*H*H Bn-3, 2xC*H*H Bn-6), 4.50 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-4), 4.32 (s, 1H, C-3), 4.31 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-4), 3.88 (d, *J* = 4.1 Hz, 1H, C-4), 3.82 – 3.72 (m, 2H, C-5, C-6a), 3.71 (s, 1H, C-2), 3.60 (dd, *J* = 8.8, 7.2 Hz, 1H, C-5), 1.21 (s, 9H, 3xCH_3 *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7 (*C*-1), 138.5, 138.1, 138.1 (C_q Bn), 128.6, 128.5, 128.4, 127.8, 127.8, 127.7, 127.7, 127.7 (CH_{Ar}), 85.0 (*C*-3), 81.4 (*C*-4), 73.5 (CH_2 Bn-6), 71.6 (CH_2 Bn-4), 71.2 (CH_2 Bn-3), 70.9 (*C*-6), 66.0 (*C*-2), 60.7 (*C*-4), 50.3 (C_q *tert*-butyl), 28.6 (3xCH_3 *tert*-butyl). $[\alpha]^{20}_D$: 4.7° (c = 1, $CHCl_3$). IR (neat): 822, 849, 908, 937, 1003, 1028, 1074, 1090, 1177, 1207, 1227, 1267, 1308, 1364, 1391, 1454, 1497, 1522, 1607, 1667, 1724, 2859, 2920, 2963, 3030, 3063, 3304. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 503.29043; found: 503.28975.

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (29a).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-ido-hexonamide (**21a**, 20 mg, 33 µmol) was dissolved in a mixture of THF (0.5 ml) and water (0.1 ml). Iodine (25 mg, 0.10 mmol) was added and the reaction stirred for 15 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (15-25% EtOAc/toluene) yielding the title compound in 51% yield (9 mg, 16 µmol). R_f = 0.35 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.7 Hz, 1H, N*H* Cy), 7.38 – 7.23 (m, 13H, CH_{Ar} Bn), 7.21 – 7.15 (m, 2H, CH_{Ar}), 4.61 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.54 (s, 2H, 2xC*H*H Bn-6), 4.50 – 4.45 (m, 2H, C*H*H Bn-3, C*H*H Bn-4), 4.33 (dd, *J* = 5.1, 1.0 Hz, 1H, C-3), 4.30 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-4), 4.10 (d, *J* = 5.1 Hz, 1H, C-2), 3.83 (dd, *J* = 3.5, 1.5 Hz, 1H, C-4), 3.81 – 3.71 (m, 1H, C*H* Cy), 3.71 – 3.61 (m, 2H, C-5, C-6a), 3.56 (dd, *J* = 9.0, 7.2 Hz, 1H, C-6b), 1.91 – 1.51 (m, 5H, 2xC*H*HCH Cy, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.44 – 1.03 (m, 5H, 2xC*H*HCH Cy, 2xC*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3 (*C*-1), 138.3, 138.1, 138.0 (3xC_q Bn), 128.6, 128.5, 128.3, 128.0, 127.9, 127.8, 127.7 (CH_{Ar} Bn), 82.7 (*C*-4), 82.4 (*C*-3), 73.6 (CH_2 Bn-6), 73.3 (CH_2 Bn-3), 71.9 (CH_2 Bn-4), 69.1 (*C*-6), 64.2 (*C*-2), 60.3 (*C*-5), 47.8 (*C*H Cy), 33.4, 33.1 (2xCH_2CH Cy), 25.8 (CH_2(CH$_2$)$_2$ Cy), 25.1, 25.0 (2xCH_2CH$_2$CH Cy). $[\alpha]^{20}_D$: -4.1° (c = 1, $CHCl_3$). IR (neat): 841, 891,

912, 1028, 1078, 1099, 1209, 1254, 1314, 1350, 1364, 1452, 1497, 1528, 1653, 1722, 2795, 2853, 2926, 3007, 3030, 3061, 3088, 3200, 3296. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30566.

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (29b).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-gulo-hexonamide (**21b**, 27 mg, 44 µmol) was dissolved in a mixture of THF (0.6 ml) and water (0.2 ml). Iodine (33 mg, 0.13 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (15-25% EtOAc/toluene) yielding the title compound in 60% yield (14 mg, 26 µmol). R_f = 0.50 (40/60 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.5 Hz, 1H, N*H* Cy), 7.37 – 7.23 (m, 13H, CH_{Ar} Bn), 7.21 – 7.16 (m, 2H, CH_{Ar} Bn), 4.71 (d, *J* = 11.8 Hz, 1H, C*H*H Bn-3), 4.60 – 4.51 (m, 3H, C*H*H Bn-3, 2xC*H*H Bn-6), 4.45 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-4), 4.35 (s, 1H, C-3), 4.28 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-4), 3.88 (d, *J* = 4.2 Hz, 1H, C-4), 3.82 – 3.77 (m, 1H, C-5), 3.79 (s, 1H, C-2), 3.72 (dd, *J* = 9.1, 5.5 Hz, 1H, C-6a), 3.65 – 3.58 (m, 1H, C*H* Cy), 3.59 (dd, *J* = 8.9, 7.5 Hz, 1H, C-6b), 1.86 – 1.76 (m, 1H, C*H*HCH Cy), 1.69 – 1.59 (m, 1H, C*H*HCH$_2$CH Cy), 1.57 – 1.40 (m, 3H, C*H*HCH Cy, C*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.38 – 1.27 (m, 1H, C*H*HCH$_2$CH), 1.24 – 1.02 (m, 3H, C*H*HCH Cy, C*H*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 0.92 – 0.77 (m, 1H, C*H*HCH Cy). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4 (*C*-1), 138.5, 138.1, 138.0 (*C*$_q$ Bn), 128.6, 128.5, 128.3, 128.0, 127.9, 127.9 (*C*H$_{Ar}$ Bn), 84.9 (*C*-3), 81.3 (*C*-4), 73.5 (*C*H$_2$ Bn-6), 71.7 (*C*H$_2$ Bn-4), 71.3 (*C*H$_2$ Bn-3), 70.9 (*C*-6), 65.6 (*C*-2), 60.6 (*C*-5), 47.6 (*C*H Cy), 33.0, 32.6 (2x*C*H$_2$CH Cy), 25.7 (*C*H$_2$(CH$_2$)$_2$ Cy), 24.9, 24.8 (2x*C*H$_2$CH$_2$CH Cy). [α]$^{20}_D$: -3.5° (c = 1, $CHCl_3$). IR (neat): 822, 849, 891, 910, 845, 955, 1003, 1028, 1074, 1090, 1207, 1254, 1314, 1364, 1395, 1452, 1497, 1518, 1607, 1661, 1717, 1799, 1853, 2926, 3030, 3063, 3326. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30566.

***N*-(*tert*-butyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-O-benzyl-D-altro-hexonamide (30).** *N*-(*tert*-butyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-altro-hexonamide (**22a**, 62 mg, 0.11 mmol) was dissolved in a mixture of THF (1.5 ml) and water (0.4 ml). Iodine (80 mg, 0.32 mmol) was added and the reaction stirred for 30 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 5 ml) was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash chromatography (12-25% EtOAc/toluene) yielding the title compound in 44% yield (24 mg, 47 µmol). R_f = 0.45 (70/30 EtOAc/toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H, N*H* *tert*-butyl), 7.40 – 7.20 (m, 15H, CH_{Ar} Bn), 4.73 (d, *J* = 11.6 Hz, 1H, C*H*H Bn-3), 4.67 (d, *J* = 11.5 Hz, 1H, C*H*H Bn-3), 4.48 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-4), 4.46 (d, *J* = 11.9 Hz, 1H, C*H*H Bn-6), 4.43 – 4.39 (m, 1H, C*H*H Bn-6), 4.41 – 4.38 (m, 1H, C-3), 4.28 (d, *J* = 12.0 Hz, 1H, C*H*H Bn-4), 3.82 – 3.78 (m, 1H, C-4), 3.79 (d, *J* = 4.1 Hz, 1H, C-2), 3.63 (dd, *J* = 10.0, 3.0 Hz, 1H, C-6a), 3.54 (dd, *J* = 10.0, 3.3 Hz, 1H, C-6b), 3.46 (dt, *J* = 9.3, 3.1 Hz, 1H, C-5), 1.31 (s, 9H, 3xC*H*$_3$ *tert*-butyl). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2 (*C*-1), 138.8, 138.1, 138.0 (3x*C*$_q$ Bn), 128.5, 128.5, 128.5, 128.2, 128.2, 127.9, 127.9, 127.9, 127.8, 127.5 (*C*H$_{Ar}$ Bn), 80.4 (*C*-4), 78.2 (*C*-3), 74.0 (*C*H$_2$ Bn-3), 73.3 (*C*H$_2$ Bn-6), 72.2 (*C*H$_2$ Bn-4), 68.0 (*C*-6), 63.6 (*C*-2), 60.0 (*C*-5), 50.6 (*C*$_q$ *tert*-butyl), 28.9 (3x*C*H$_3$ *tert*-butyl). [α]$^{20}_D$: 12° (c = 0.5, $CHCl_3$). IR (neat): 698, 737, 910, 1028, 1047, 1074, 1115, 1177, 1217, 1281, 1312, 1364, 1393, 1454, 1497, 1533, 1609, 1661, 1721, 2862, 2870, 2926, 2967, 3030, 3063, 3088, 3310. HR-MS: [M+H$^+$] Calculated for $C_{31}H_{38}N_2O_4$: 503.29043; found: 503.29008.

***N*-(cyclohexyl)-2,5-dideoxy-2,5-imino-3,4,6-tri-*O*-benzyl-D-altro-hexonamide (31).** *N*-(cyclohexyl) [*N*-(pent-4-enoyl)-2,5-dideoxy-2,5-imino]-3,4,6-tri-*O*-benzyl-D-altro-hexonamide (**23a**, 95 mg, 0.16 mmol) was dissolved in a mixture of THF (2.5 ml) and water (0.3 ml). Iodine (118 mg, 0.47 mmol) was added and the reaction stirred for 15 minutes. A mixture of 1M $Na_2S_2O_3$ (aq.) and $NaHCO_3$ (sat. aq., 1/1 v/v, 10 ml)

was added and the mixture vigorously stirred for 5 minutes. The suspension was extracted with EtOAc and the combined organic layers washed with brine, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by preparative HPLC chromatography. This yielded the title compound in 29% yield (24 mg, 45 µmol). R_f = 0.4 (70/30 EtOAc/toluene). ^{1}H NMR (400 MHz, CD_3CN) δ 7.43 (d, *J* = 8.1 Hz, 1H, N*H* Cy), 7.37 – 7.21 (m, 15H, CH_{Ar} Bn), 4.65 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.62 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.60 (d, *J* = 11.3 Hz, 1H, C*H*H Bn), 4.50 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.45 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.44 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.37 (t, *J* = 4.1 Hz, 1H, C-3), 3.82 (dd, *J* = 9.2, 3.7 Hz, 1H, C-4), 3.80 (d, *J* = 4.7 Hz, 1H, C-2), 3.68 – 3.57 (m, 1H, C*H* Cy), 3.62 (dd, *J* = 10.1, 3.1 Hz, 1H, C-6a), 3.50 (dd, *J* = 10.1, 4.3 Hz, 1H, C-6b), 3.32 – 3.26 (m, 1H, C-5), 1.80 – 1.50 (m, 5H, 2x*CH*HCH Cy, 2x*CH*HCH$_2$CH Cy, C*H*H(CH$_2$)$_2$ Cy), 1.40 – 1.21 (m, 2H, 2x*CH*HCH$_2$CH Cy), 1.21 – 1.04 (m, 3H, 2x*CH*HCH Cy, C*H*H(CH$_2$)$_2$ Cy). ^{13}C NMR (101 MHz, CD_3CN) δ 170.7 (*C*-1), 140.1, 139.5 (3x C_q Bn), 129.3, 129.0, 128.8, 128.8, 128.6, 128.6, 128.5, 128.3 (CH_{Ar} Bn), 82.1 (*C*-4), 79.8 (*C*-3), 74.7, 73.6, 72.8 (3x*C*H$_2$ Bn), 69.8 (*C*-6), 63.7 (*C*-2), 60.9 (*C*-5), 48.5 (*C*H Cy), 33.7, 33.6 (2x*C*H$_2$CH Cy), 26.3 (*C*H$_2$(CH$_2$)$_2$ Cy), 25.6, 25.6 (2x*C*H$_2$CH$_2$CH Cy). $[\alpha]^{20}_D$: 23.3° (c = 0.2, CH_3CN). IR (neat): 602, 635, 696, 733, 800, 822, 847, 891, 912, 959, 1003, 1026, 1063, 1086, 1107, 1128, 1206, 1252, 1310, 1348, 1362, 1402, 1452, 1497, 1518, 1651, 2853, 2928, 3030, 3341. HR-MS: [M+H$^+$] Calculated for $C_{33}H_{40}N_2O_4$: 529.30608; found: 529.30593.

References and notes

[1] Domling, A.; Ugi, I. *Angew. Chem. Int. Ed.* **2000**, *39*, 3168-3210, 10.1002/1521-3773(20000915)39:18<3168::AID-ANIE3168>3.0.CO;2-U.

[2] Domling, A. *Chem. Rev.* **2006**, *106*, 17-89, 10.1021/cr0505728.

[3] Ruijter, E.; Scheffelaar, R.; Orru, R. V. A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6234-6246, 10.1002/anie.201006515.

[4] El Kaim, L.; Grimaud, L. *Tetrahedron* **2009**, *65*, 2153-2171, 10.1016/j.tet.2008.12.002.

[5] Ugi, I.; Meyr, R. *Chem. Ber.* **1961**, *94*, 2229-2233, 10.1002/cber.19610940844.

[6] Timmer, M. S. M.; Risseeuw, M. D. P.; Verdoes, M.; Filippov, D. V.; Plaisier, J. R.; van der Marel, G. A.; Overkleeft, H. S.; van Boom, J. H. *Tetrahedron Asymm.* **2005**, *16*, 177-185, 10.1016/j.tetasy.2004.11.079.

[7] Bonger, K. M.; Wennekes, T.; Filippov, D. V.; Lodder, G.; van der Marel, G. A.; Overkleeft, H. S. *Eur. J. Org. Chem.* **2008**, 3678-3688, 10.1002/ejoc.200800340.

[8] Wennekes, T.; Bonger, K. M.; Vogel, K.; van den Berg, R. J. B. H. N.; Strijland, A.; Donker-Koopman, W. E.; Aerts, J. M. F. G.; van der Marel, G. A.; Overkleeft, H. S. *Eur. J. Org. Chem.* **2012**, 6420-6454, 10.1002/ejoc.201200923.

[9] Bonger, K. M.; Wennekes, T.; de Lavoir, S. V. P.; Esposito, D.; den Berg, R. J. B. H. N.; Litjens, R. E. J. N.; van der Marel, G. A. *QSAR Comb. Sci.* **2006**, *25*, 491-503, 10.1002/qsar.200540198.

[10] Chapman, T. M.; Davies, I. G.; Gu, B.; Block, T. M.; Scopes, D. I. C.; Hay, P. A.; Courtney, S. M.; McNeill, L. A.; Schofield, C. J.; Davis, B. G. *J. Am. Chem. Soc.* **2005**, *127*, 506-507, 10.1021/ja0439241.

[11] Banfi, L.; Basso, A.; Guanti, G.; Riva, R. *Tetrahedron Lett.* **2004**, *45*, 6637-6640, 10.1016/j.tetlet.2004.07.015.

[12] Banfi, L.; Basso, A.; Guanti, G.; Merlo, S.; Repetto, C.; Riva, R. *Tetrahedron* **2008**, *64*, 1114-1134, 10.1016/j.tet.2007.10.058.

[13] Cerulli, V.; Banfi, L.; Basso, A.; Rocca, V.; Riva, R. *Org. Biomol. Chem.* **2012**, *10*, 1255-1274, 10.1039/c1ob06632c.

[14] Flanagan, D. M.; Joullie, M. M. *Synth. Commun.* **1989**, *19*, 1-12, 10.1080/00397918908050946.

[15] Bowers, M. M.; Carroll, P.; Joullie, M. M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 857-865, 10.1039/p19890000857.

[16] de Graaff, C.; Ruijter, E.; Orru, R. V. A. *Chem. Soc. Rev.* **2012**, *41*, 3969-4009, 10.1039/c2cs15361k.

[17] In this chapter carbohydrate numbering is used.

[18] Product ratios are determined by ^{1}H NMR at 393K to allow free rotation around the newly formed tertiary amide bond.

[19] Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Smith, D. M.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 10879-10884, 10.1021/ja0524043.

[20] Smith, D. M.; Tran, M. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 14149-14152, 10.1021/ja0375176.

[21] Maeda, S.; Komagawa, S.; Uchiyama, M.; Morokuma, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 644-649, 10.1002/anie.201005336.

[22] Cheron, N.; Ramozzi, R.; El Kaim, L.; Grimaud, L.; Fleurat-Lessard, P. *J. Org. Chem.* **2012**, *77*, 1361-1366, 10.1021/jo2021554.

[23] The stereoselectivity of the Ugi reaction of the per-*O*-methylated xylo derived imine was similar to that for the Ugi reaction of its per-*O*-benzylated counterpart.

[24] Several bicyclic intermediates can be formed in this reaction step, differing in the stereochemistry of the newly formed hemiaminal linkage and the stereochemistry of the double bond. The lowest energy intermediate is shown in the figure.

[25] Although the addition of the isocyanide to the imine can also be envisioned to proceed via an S_N2-like pathway in which the incoming isocyanide displaces an anomeric (covalent) acetate, this pathway is deemed to be less likely given the stabilities of the intermediate iminium ions and the polarity of the solvent.

[26] Chao, C. S.; Lin, C. Y.; Mulani, S.; Hung, W. C.; Mong, K. K. T. *Chem. Eur. J.* **2011**, *17*, 12193-12202, 10.1002/chem.201100732.

[27] The steric panelty can be estimated at 1.8 kcal mol^{-1} from corresponding *syn*-butanol interactions, while in the transition state the energy differences actually increase by 0.7 kcal mol^{-1} over the ground state conformers. A rough estimate for the stabilizing interaction could therefore be the sum of these two at 2.5 kcal mol^{-1}.

[28] When all iminium ions are compared it becomes clear that the ^{3}E Ara is the most stable conformer of the four isomers (ΔE; ^{3}E Lyxo = 1.00 kcal mol^{-1}, ^{3}E Ara = 0.00 kcal mol^{-1}, E_3 Xylo = 0.96 kcal mol^{-1}, E_3 Ribo = 0.99 kcal mol^{-1}).

[29] Spartan '04, Kong, J. *et al.*, Wavefunction Inc. **2004**.

[30] Gaussian 03 (Revision D.01), Frisch, M. J. *et al.*, Gaussian, Inc. **2004**.

[31] Naka, T.; Minakawa, N.; Abe, H.; Kaga, D.; Matsuda, A. *J. Am. Chem. Soc.* **2000**, *122*, 7233-7243, Doi 10.1021/Ja000541o.