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Higher glycosamino acid precursors: C_7 and C_8 aminodialdoses via regio- and stereoselective [3+2] cycloaddition of vinyl trimethylsilane to *C*-glycosyl nitrones

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Abstract—Protected C_7 and C_8 aminodialdoses were prepared stereoselectively from readily available C_5 and C_6 monosaccharide *N*-benzyl nitrones, by regio- and diastereoselective 1,3-dipolar cycloaddition reactions with vinyl trimethylsilane, followed by acetyl chloride-mediated cleavage of the 5-(trimethylsilyl)isoxazolidine formed. The cycloaddition reaction took place in moderate to good global yields (67–74%); estimation of diastereoselectivities from isolated yields showed total *endo* preference for the reaction of the D-*galacto* configured nitrone and high *endo* preference for the D-*ribo* analogue, but *exo* preference for the D-*xylo* configured substrate. Attack on the *re* face of the nitrone was predominant in all cases. The absolute configuration of one of the protected 3-(α-D-*galacto*-pentopyranos-5-yl)isoxazolidine products was assigned by X-ray crystallographic analysis, allowing correlation of the configuration at the new stereogenic centre in the corresponding aminodialdose. For non-crystalline isoxazolidines, configurations were assigned on the basis of NOESY experiments and/or chemical correlation. Combined yields of aminodialdoses coming from isoxazolidines having identical configuration at C(3) sometimes reached high values (up to 90%). These compounds are precursors of higher-chain glycosamino acids. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Higher-carbon (C_7–C_9) amino deoxy sugars—some of which participate as important components of natural products—are substances of high biological interest. A particular class of amino sugar derivatives are the glycosamino acids,[1] among which the sialic acids constitute a very important group of biomolecules.[2] A review on recent advances in the synthesis of sialic acid derivatives and mimetics has been published recently.[3] Diverse synthetic routes have been applied to obtain other natural and unnatural higher-carbon amino sugars. Thus, a synthesis of di-*N*-acetyl-legionaminic acid, a 5,7-diamino-3,5,7,9-tetradeoxynon-2-ulosonic acid, and eight of its stereoisomers by way of condensation of oxalacetic acid with four 2,4-diacetamido-2,4,6-trideoxyhexoses, has been described.[4] β-Amino acids also having an aryl group at the β position can be obtained enantioselectively by addition of ketene silyl acetals to *C*-aryl *N*-benzyl nitrones.[5] Simple amino sugars have been prepared by opening of the isoxazolidine ring of the cycloadducts obtained in the reaction of *C*-glycosyl nitrones with conveniently substituted olefins.[6,7] Complete regioselectivity and high stereoselectivity has been observed,[8] as expected from the preliminary studies,[9,10] in the reaction of vinyl trimethylsilane as the dipolarophile, with various nitrones derived from aromatic and aliphatic aldehydes as the 1,3-dipole; the 5-(trimethylsilyl)isoxazolidine resulting from the similar reaction of an *aldehydo*-tetrose nitrone, as treated with acetyl chloride, afforded the corresponding 3-acetamido-2,3-dideoxy-*aldehydo*-hexose derivative.[11] To our knowledge, this methodology has not been employed for preparing amino sugars having a carbon chain of more than six carbon atoms, and we planned to apply it, starting from easily available, protected α-D-*galacto*-hexodialdo-1,5-pyranose, and α-D-*xylo*- and α-D-*ribo*-pentodialdo-1,4-furanose nitrones, to the stereoselective synthesis of C_7 and C_8 3-aminodialdoses, which could be considered intermedi-

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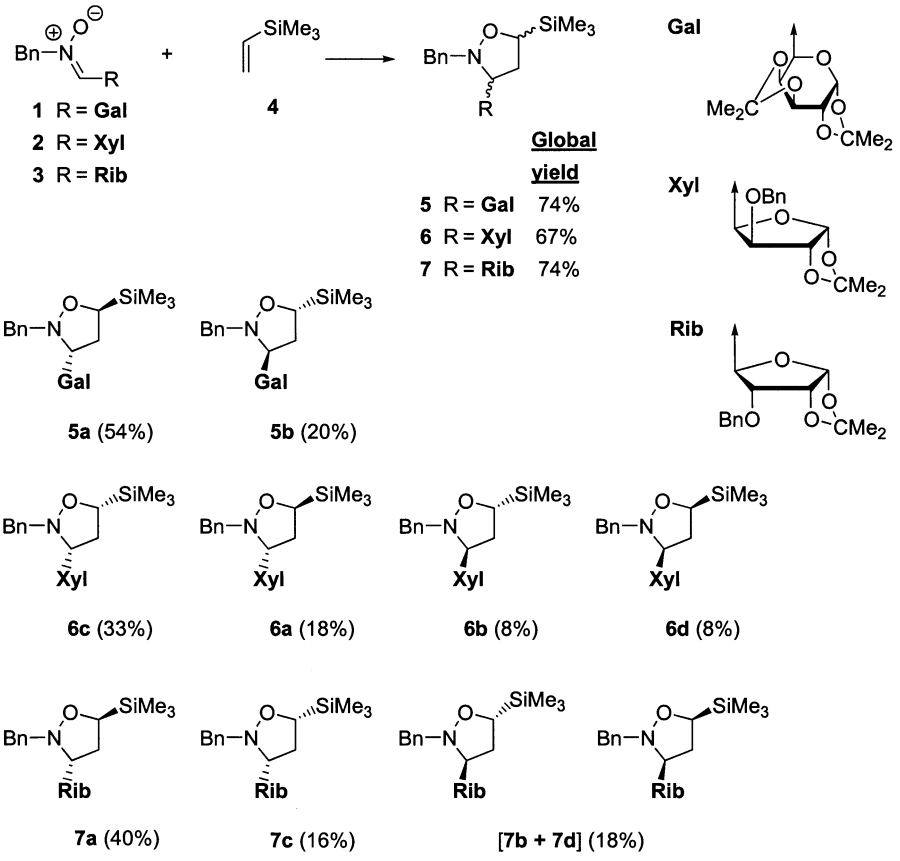


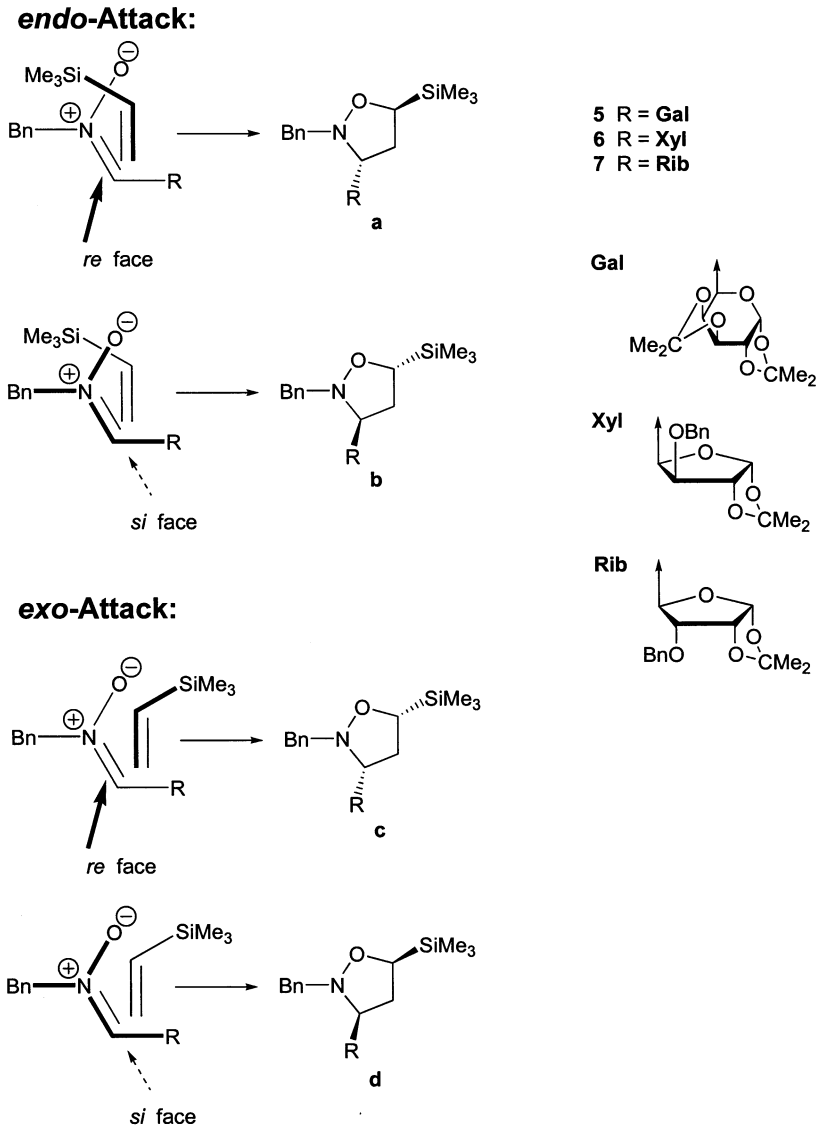
Scheme 1. Isoxazolidine derivatives: configurational structures and yields.

ate precursors of β-amino glycuronic acids. We report here the results of these reactions, including a study of the *endo*/*exo* diastereoselectivity and the diastereofacial selectivity of the [3+2] cycloaddition, necessary for accurate determination of the absolute configuration of the new stereogenic centre created in the elongated carbon chain of the aminodialdoses obtained.

2. Results

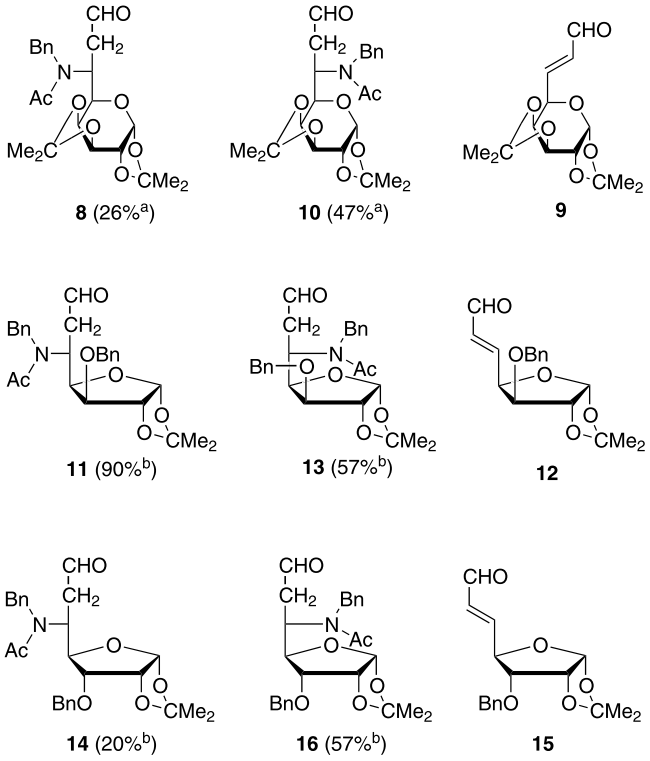
Reaction of (*Z*)-*N*-benzyl *C*-glycosylnitrones **1**–**3**, easily prepared[12] from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, and 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylo- and α-D-ribofuranose, respectively, with a large excess of vinyl trimethylsilane **4** in toluene at 80°C, afforded diastereomeric mixtures of the 2-benzyl-3-(glycopyranos-5-yl or glycofuranos-4-yl)-5-(trimethylsilyl)isoxazolidines **5**–**7** regioselectively (Scheme 1). The diastereomers could be separated by column chromatography, followed by TLC for certain fractions, the global yields of pure isomers reaching 67–74%. Only two diastereomeric compounds, **5a** and **5b**, were obtained from **1**; the former was the major product and could be isolated in 54% yield as a crystalline compound, X-ray diffraction analysis of which established its (2*R*,3*R*,5*S*) absolute configuration. The diastereomer **5b** was isolated in 20% yield. In this case, the results indicate an exclusive, or almost exclusive, *endo* approach of the reagents (Scheme 2), as well as a preference for attack on the *re* face of the sugar nitrone, since no other diastereomeric cycloadduct could be isolated or detected. For the reaction of the α-D-*xylo* configured nitrone **2** with **4**, a mixture of four diastereomers (**6a**–**6d**) was obtained; the major product was **6c** (33% isolated yield), followed by **6a** (18%), **6b** (8%, as calculated from the ^{1}H NMR spectrum of the 2:1 **6b**/**6d** mixture obtained after column and TL chromatographies), and **6d** (8%, as the sum of pure fraction yield, from TLC, and that corresponding to the mixture with **6b**, cited above). In turn, the α-D-*ribo* configured nitrone **3** led in the reaction with vinylsilane **4** to a diastereomeric mixture (**7a**–**7d**), column chromatography of which gave rise to two main fractions. The former fraction was subjected to preparative TLC, which afforded three products: pure **7c** (16%), pure **7a** (40%), and a 4:1 diastereomeric mixture (from the ^{1}H NMR spectrum) (9%) of **7b** and **7d**. The latter fraction from the column consisted of a 2:1 mixture of the same diastereomers **7b** and **7d** (9%).

Opening of the isoxazolidine ring of compounds **5**–**7** was effected by treatment with acetyl chloride, a method used[6] to transform other 5-(trimethylsilyl)-isoxazolidines into 3-aminoaldehydes minimising the β-elimination to the respective α,β-unsaturated aldehyde, which had been observed when fluoride was used



Scheme 2. Reagent orientations in the cycloaddition reaction of **1**–**3** with **4**, and configurations of the products.

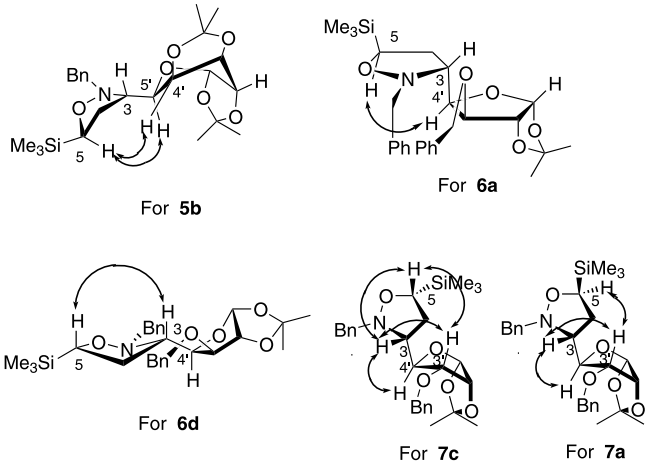
as the promotor.[8] Thus, treatment of **5**–**7**, at 0°C under argon, with acetyl chloride and subsequent quenching with an excess of aqueous sodium hydrogen carbonate led to the respective 3-aminoaldehydes. However, the corresponding α,β-unsaturated aldehyde was also isolated in variable yields (even as the major product in some cases). The reaction involves the immolation of a stereogenic centre, and hence only two epimeric 3-aminoaldehydes are to be expected from each set of diastereomeric isoxazolidines **5**, **6**, or **7**. From the crystalline compound **5a**, the protected 6-amino-octodialdose **8** (21%, corresponding to 26% from converted substrate) and its β-elimination product **9** (49% from converted substrate) were obtained. When compound **5b** was subjected to the same reaction, the products were **9** (8% from converted substrate) and **10**, the 6-epimer of **8**, in 30% yield (47% from converted substrate). Separate treatment of isoxazolidines **6c** and **6a** under the same conditions led to the same 5-amino-heptodialdose **11** (45%, corresponding to 71% from converted **6c**; 11%, that is 19% from converted **6a**), indicating identical 3*R* configuration in the substrates, and α,β-unsaturated aldehyde **12** (11%, corresponding to 17% from converted **6c**; 45% from converted **6a**). Under the same conditions, the 2:1 **6b**/**6d** mixture gave rise to the epimer **13** (30%, corresponding to 57% from converted substrate), and the same enone **12** (19%; 35% from converted substrate), but none (NMR spectra) of the other saturated epimer **11**. These facts demonstrate that **6b** and **6d** have the same 3*S* configuration. The isoxazolidines **7** showed analogous behaviour to that of their isomers **6**. Thus, in separate experiments, **7c** and **7a** were allowed to react with acetyl chloride under the above conditions to afford the same aminodialdose **14** (13 and 7%, respectively)—a proof of the same 3*R* configuration for both substrates—and the β-elimination product **15** (36 and 38%, respectively). Conversely, a **7b**/**7d** mixture led to a single aminodialdose **16** (46%, corresponding to 57% form converted substrate), epimer of **14** (showing that both **7b** and **7d** have the 3*S* configuration) and the same enone **15** (35%; 42% from converted substrate).



[a]Yield from converted substrate; [b]combined yield from converted substrates.

3. Discussion

Assignment of absolute configuration to C(3) and C(5) of the diastereomeric isoxazolidines **5**–**7** was made mainly on the basis of ^{1}H NMR data, including 1D NOESY experiments. For **5a**, X-ray diffraction analysis established its (2*R*,3*R*,5*S*) absolute configuration, as mentioned above. For the diastereomer **5b**, the *S* configuration was assigned to C(3), since opening of the isoxazolidine ring led, as explained above, to **10**, the 6-epimer of **8** formed from **5a**; that is, the difference in configuration of C(6) for **8** and **10** is a direct consequence of the different configuration at C(3) of the isoxazolidine ring in the precursors. The ^{1}H NMR spectrum of **5a** in deuterochloroform or in dimethylsulphoxide-d_6, at room temperature, showed the signals of one of the diastereotopic C(4) methylene protons and C(5)H split, indicating the existence of two conformers in slow equilibrium; the split signals collapsed on heating at 120°C in dimethylsulphoxide-d_6, as expected. The C(3)H/C(5′)H coupling constant values observed for **5a** (10.2 Hz) and **5b** (8.7 Hz) enabled deduction of the preferred (in solution) *anti* relationship between these isoxazolidine and sugar protons around the C(3)–C(5′) bond. Assignment of the *R* configuration to C(5) of **5b** was deduced from 1D NOESY experiments, which showed C(5)H/C(4′)H and, to a somewhat lesser extent, C(5)H/C(5′)H contacts and absence of contact between C(3)H and C(5)H. This supports the assignment of the 3,5-*trans* relationship (see Scheme 3), consistent with the steric hindrance that might appear between the bulky 1,2:3,4-diprotected sugar moiety and the trimethylsilyl group in a 3,5-*cis* disubstituted isoxazolidine ring.



Scheme 3. NOE (1D NOESY) contacts for **5b**, **6a**, **6d**, **7c**, and **7a**.

The *anti* relationship between the isoxazolidine C(3)H and the sugar C(4′)H, in the preferred conformation in chloroform, was also deduced from the corresponding coupling constant values observed (8.8–10.2 Hz) in the ^{1}H NMR spectra of all the diastereomeric isoxazolidines **6** obtained from the D-*xylo* configured nitrone **2**. Molecular models show that, in this conformation, a C(5)H/C(4′)H contact is possible for the 3*R*,5*S* configured structure **6a** if the isoxazolidine ring adopts an *envelope* conformation having the methylene carbon atom out of the plane, resulting in stabilisation by

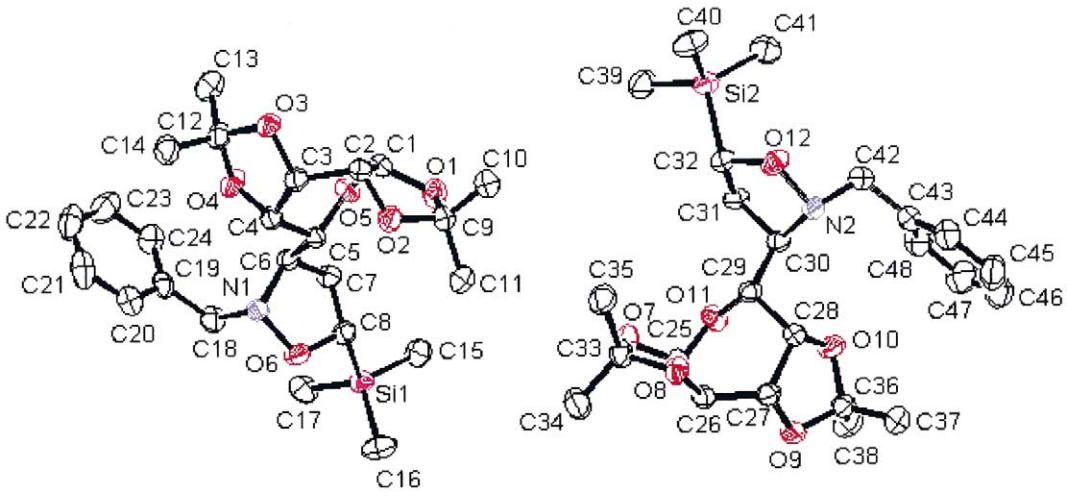


Figure 1. An ORTEP view of the unit cell for **5a**. On the left, the molecule *A*; on the right, the molecule *A′*.

Table 1. Selected bond distances (Å) and torsion angles (°) for **5a**

Bond lengths			Torsion angles		
Si1–C8	1.8884(48)	C1–O5–C5–C4	65.96(46)	H2–C2–C1–H1	−23.76(60)
Si2–C32	1.8907(37)	C25–O11–C29–C28	65.95(46)	H26–C26–C25–H25	−24.04(61)
O5–C5	1.4347(47)	C5–O5–C1–O1	86.59(45)	H3–C3–C2–H2	−74.97(53)
O11–C29	1.4193(55)	C29–O11–C25–O7	87.14(47)	H26–C26–C27–H27	−74.96(53)
O5–C1	1.3970(59)	C5–O5–C1–C2	−29.56(54)	H3–C3–C4–H4	−0.51(59)
O11–C25	1.4031(53)	C29–O11–C25–C26	−31.11(55)	H28–C28–C27–H27	−0.56(58)
C5–C4	1.5198(69)	C3–C2–C1–O5	−22.76(59)	H5–C5–C4–H4	−51.05(54)
C28–C29	1.5104(60)	C27–C26–C25–O11	−19.85(61)	H28–C28–C29–H29	−51.68(53)
C3–C4	1.5331(66)	C4–C3–C2–C1	36.63(56)	H6–C6–C5–H5	177.02(37)
C28–C27	1.5380(54)	C25–C26–C27–C28	33.74(57)	H29–C29–C30–H30	176.76(37)
C3–C2	1.5100(71)	C6–C5–C4–C3	−163.89(36)	H6–C6–C7–H7A	−34.91(56)
C26–C27	1.5083(71)	C27–C28–C29–C30	−165.47(36)	H6–C6–C7–H7B	87.46(50)
C2–C1	1.5117(76)	N1–O6–C8–Si1	−137.15(29)	H31A–C31–C30–H30	−35.07(56)
C26–C25	1.5080(72)	N2–O12–C32–Si2	−136.93(28)	H31B–C31–C30–H30	87.37(50)
O6–N1	1.4630(46)	N1–O6–C8–C7	−10.70(46)		
O12–N2	1.4674(47)	N2–O12–C32–C31	−10.78(44)		
N1–C6	1.4779(48)	O6–N1–C6–C5	−92.06(36)		
N2–C30	1.4582(58)	O12–N2–C30–C29	−92.36(37)		
C6–C7	1.5347(68)	O6–N1–C6–C7	29.39(40)		
C31–C30	1.5256(60)	O12–N2–C30–C31	30.22(41)		
C7–C8	1.5145(54)	C18–N1–C6–C5	153.53(38)		
C31–C32	1.5209(67)	C42–N2–C30–C29	152.75(37)		
O6–C8	1.4491(62)	C8–O6–N1–C6	−11.89(42)		
C12–C32	1.4526(65)	C32–O12–N2–C30	−12.20(42)		

stacking of the phenyl rings of the *N*-benzyl and *O*-benzyl groups. Such aromatic–aromatic interactions are known to be involved in the stabilisation of protein structures.[13] For the facial diastereomer **6b**, the two phenyl groups are too far from each other to interact. Hence, the product exhibiting such C(5)H/C(4′)H contact experimentally (1D NOESY) must have the structure **6a** (Scheme 3). For the major product, the 3*R*,5*R* configuration was assigned (**6c**), since it is the 5-epimer of **6a**, as mentioned above. The structure **6d** allows a C(3)H/C(5)H contact (Scheme 3), and is assigned to the product that experimentally showed a NOE effect between these protons. The remaining structural possibility (**6b**) was assigned to the other product.

Unlike the foregoing isoxazolidines, the C(3)H and C(4′)H of compounds **7** have a *gauche* disposition around the C(3)-C(4′) bond, since the corresponding coupling constant values are in the range 2.8–3.9 Hz. This may be explained taking into account that steric hindrance between the sugar and the isoxazolidine moieties decreases in these ribose derivatives **7** in such conformation, in comparison with the xylose derivatives **6** in the same conformation, as molecular models show. For the diastereomer showing C(5)H/C(3′)H, C(3)H/C(3′)H, C(3)H/C(4′)H, and C(3)H/C(5)H contacts (1D NOESY), the 3*R*,5*R* structure (**7c**), which might be stabilised similarly to **6a** (see above), was assigned (Scheme 3). The other product leading to the same aminodialdose **14** must therefore have the epimeric 3*R*,5*S* structure (**7a**), as was corroborated by the lack of C(3)H/C(5)H contact. The two remaining

Table 2. Puckering coordinates, amplitudes and phase magnitudes, and asymmetry parameters for **5a**

Ring	Q (Å)	φ (°)	θ (°)	ΔC_2	ΔC_s	Sequence
A pyranose	0.62(1)	−48(1)	79(1)	(C1) = 0.086	(O5–C5) = 0.088	O5–C1–C2–C3–C4–C5
A′ pyranose	0.60(1)	−43(1)	78(1)	(C25) = 0.086	(O11–C29) = 0.079	O11–C25–C26–C27–C28–C29
A dioxolane	0.316(4)	−97(1)	–	(O1) = 0.024	–	O1–C9–O2–C2–C1
A dioxolane	0.277(5)	−36(1)	–	(C3) = 0.051	–	O4–C4–C3–O3–C12
A′ dioxolane	0.317(4)	−94(1)	–	(O7) = 0.051	–	O7–C33–O8–C26–C25
A′ dioxolane	0.285(5)	35(1)	–	(C28) = 0.050	–	O9–C36–O10–C28–C27
A isoxazolidine	0.342(5)	89(1)	–	(O6) = 0.024	–	N1–C6–C7–C8–O6
A' isoxazolidine	0.346(4)	−127(1)	–	(O12) = 0.004	–	N2–C30–C31–C32–O12

diastereomers **7b** and **7d** have the 3*S* configuration and differ from each other only in the configuration at C(5), as both gave rise to the same heptodialdose **16**. However, accurate assignment of structure **7b** or **7d** to the major or the minor component of the mixed chromatographic fraction was not possible.

3.1. X-Ray structure analysis of crystalline compound 5a

The unit cell consists of two molecules of **5a** in slightly different conformations. A perspective view of the unit cell, showing the absolute configuration together with the atomic labelling scheme, is shown in Fig. 1. Bond lengths and torsion angles are shown in Table 1. One of the pyranose rings (that of molecule *A*, on the left of Fig. 1) shows the anomeric effect [O(5)–C(5) = 1.435(5) and O(5)–C(1) = 1.397(6) Å], while the other pyranose ring (that of molecule *A′*, on the right of Fig. 1) does not show this effect [O(11)–C(25) = 1.403(5) and O(11)–C(29) = 1.419(6) Å]. The geometry observed for the pyranose, dioxolane, and isoxazolidine rings is shown in Table 2; the two pyranose rings show conformations midway between $B_{2,5}$ ($\varphi = -60°$, $\theta = 90°$) and $^{O}S_{5}$ ($\varphi = -30°$, $\theta = 68°$), instead of that explicitly corresponding to any of these forms.[14] One of the two dioxolane rings of molecule *A* is in a conformation intermediate between *T* and *E*, and the other in *E* conformation. The two dioxolane rings of *A′* show *T* and *E* conformations, respectively. The isoxazolidine ring shows *T* conformation for both molecules *A* and *A′*. The dihedral angles between the pyranose and dioxolane rings are 76.0 and 79.3° for *A*, and 76.8 and 78.8° for *A′*. The crystal cohesion is governed by van der Waals forces. There are two intramolecular short contacts: C5···O2 = 3.060(6) Å, C5–H5···O2 = 106.4(3)°, and C29···O8 = 3.066(5) Å, C29–H29···O8 = 106.9(3)°.

4. Conclusion

The isolated yields of each diastereomer of the isoxazolidines **5**–**7** were used as data for an estimation of the *endo*/*exo* cycloaddition and facial diastereoselectivities. For the substrates **1** and **3**, the *re*/*si* diastereofacial selectivity reached ratios of 2.7:1 and ~2.0:1, respectively, while the *endo*/*exo* diastereoselectivity is total for **1** and ~3.3:1 for **3**. The *xylo* configured nitrone **2** showed a *re*/*si* diastereofacial selectivity of 3.0:1, but an inverted *exo*/*endo* diastereoselectivity of ~1.57:1. This may be attributed to the lower steric hindrance between the bulky trimethylsilyl group and the sugar moiety that exists in the transition state for cycloaddition from the *exo* approach in comparison with the same approach for the *ribo* configured nitrone **3**.

Isolated yields of aminodialdoses in the ring opening of the compounds **5**–**7** by reaction with acetyl chloride were low to moderate. Despite this, the combined yields of aminodialdose from substrates **6** and **7** having the same configuration at C(3) were higher: from **6c** and **6a**, 90% of **11**; from (**6b**+**6d**), 57% of **13**; from **7c** and **7a**, 20% of **14**; from (**7b**+**7d**), 57% of **16** were obtained. Thus, only from substrates **6** was the combined yield of the D-*glycero* configured aminodialdose **11** much higher than that of the epimer **13**; from the other substrates, **5** and **7**, the major aminodialdose has the L-*glycero* configuration (**10** and **16**).

In conclusion, the diastereoselective pathway described here for obtaining new higher-chain aminodialdoses from readily available sugar nitrones may be considered suitable enough for that objective, since the final products are obtained as stereochemically pure compounds, thereby overcoming the limitation of the low to moderate yields achieved. Moreover, the aminodialdoses obtained are direct precursors of higher-chain glycosamino acids.

5. Experimental

5.1. General

Hexane and ether were distilled from sodium prior to use. TLC was performed on silica gel plates (DC-Alufolien F_{254}, E. Merck, or Alugram Sil G/UV_{254}, Macherey–Nagel), and preparative TLC on Kieselgel 60 F_{254} 7739, E. Merck; detection of compounds was accomplished with UV light (254 nm) and by charring with H_2SO_4. Silica gel 60 (E. Merck, 0.040–0.063 mm) was used for column chromatography. Solutions were concentrated under diminished pressure at <40°. Melting points were determined on a Gallenkamp MFB-595 apparatus and are uncorrected. A Perkin–Elmer 241 MC polarimeter was used for measurement of optical rotations. IR spectra (neat or on a KBr disc) were obtained on a FTIR Bomem Michelson MB-120 spectrophotometer. ^{1}H NMR spectra (300 and 500 MHz) and ^{13}C NMR spectra (75.4 and 125.7 MHz) were recorded with a Bruker AMX-300 or an AMX-500

spectrometers; chemical shifts (δ) are expressed in ppm from TMS; coupling constants (J), in Hz. Assignments were confirmed by decoupling, homonuclear 2D COSY correlated spectra, heteronuclear 2D correlated (HETCOR) spectra, and 1D NOESY spectra. CI mass spectra were measured with a Micromass AutoSpecQ instrument, using methane as reagent gas and a resolution of 1000 (10% valley definition). HREIMS (70 eV) and HRCIMS (150 eV) experiments were performed with the same instrument, with a resolution of 10,000 (5% valley definition), or a VG AutoSpec spectrometer (HRCIMS, 70 eV, resolution of 8,500, 10% valley definition).

5.2. Reaction of (*Z*)-*N*-benzyl-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-ylidene)amine *N*-oxide, 1 with vinyl-trimethylsilane, 4: preparation of (2*R*,3*R*,5*S*)-2-benzyl-3-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5-yl)-5-(trimethylsilyl)isoxazolidine, 5a and (3*S*,5*R*)-2-benzyl-3-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5-yl)-5-(trimethylsilyl)-isoxazolidine, 5b

To a solution of nitrone **1**[12] (0.80 g, 2.20 mmol) in toluene (31 mL), cooled in an ice bath, dipolarophile **4** (7.7 mL, 5.0 g, 50 mmol) was added under an argon atmosphere and the mixture was heated at 80°C. Monitoring of the reaction (TLC, 6:1 and 1:1 hexane:ethyl acetate) indicated a complete conversion after 24 h. The solution was then concentrated to give a crude residue formed by the diastereomeric isoxazolidines **5** (0.98 g, 96%), which was subjected to column chromatography (10:1 hexane:ethyl acetate). First eluted **5a**, isolated as a solid (0.55 g, 54%); mp 54–56°C; crystallographic analysis evidenced its (2*R*,3*R*,5*S*) absolute configuration; R_f 0.45 (6:1 hexane:ethyl acetate); $[\alpha]_D^{25}=+3.7$ (c 1.8, CH_2Cl_2); IR (KBr) ν_{max} 1381 (CMe_2), 1252 ($_\delta$C–H of $SiCH_3$), and 752 cm^{-1} ($_\nu$Si–C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.20 (m, 5H, Ph), 5.50 (d, 1H, $J_{1',2'}=4.9$, H-1′), 4.54 (dd, 1H, $J_{2',3'}=2.1$, $J_{3',4'}=8.0$, H-3′), 4.47 (dd, 1H, $J_{4',5'}=1.5$, H-4′), 4.25 (dd, 1H, H-2′), 4.01, 3.95 (each d, each 1H, $J_{gem}=13.1$, CH_2Ph), 3.62 (dd, 1H, $J_{3,5'}=10.2$, H-5′), 3.44 (ddd, 1H, $J_{3,4a}=5.0$, $J_{3,4b}=7.4$, H-3), 3.44 (dd, 1H, $J_{4a,5}=1.0$, $J_{4b,5}=11.8$ for conformer I, $J_{4b,5}=13.1$ for conformer II, H-5), 2.35 (ddd, 1H, $J_{4a,4b}=12.3$, H-4a), 1.99 (ddd, 1H, $J_{4b,5}=11.5$ for conformer I, $J_{4b,5}=13.1$ for conformer II, H-4b), 1.46, 1.38, 1.29, 1.27 (each s, each 3H, $2CMe_2$), and 0.07 (s, 9H, $SiMe_3$); ^1H NMR (300 MHz, DMSO-d_6) δ 7.37–7.20 (m, 5H, Ph), 5.43 (d, 1H, $J_{1',2'}=4.9$, H-1′), 4.58 (dd, 1H, $J_{2',3'}=2.2$, $J_{3',4'}=8.0$, H-3′), 4.32 (dd, 1H, $J_{4',5'}=1.4$, H-4′), 4.30 (dd, 1H, H-2′), 3.93, 3.79 (each d, each 1H, $J_{gem}=13.6$, CH_2Ph), 3.45 (dd, 1H, $J_{3,5'}=9.5$, H-5′), 3.29–3.22 (m, 2H, H-3 and H-5), 2.20 (ddd, 1H, $J_{4a,4b}=12.1$, $J_{3,4a}=6.3$, $J_{4a,5}\approx 0$, H-4a), 1.99 (ddd, 1H, $J_{4a,4b}=12.4$, $J_{4b,5}=8.5$ or 7.9, $J_{3,4b}=7.9$ or 8.5, H-4b), 1.39, 1.29, 1.26, 1.23 (each s, each 3H, $2CMe_2$), and 0.01 (s, 9H, $SiMe_3$); ^1H NMR (300 MHz, DMSO-d_6, 120°C) δ 7.31–7.23 (m, 5H, Ph), 5.44 (d, 1H, $J_{1',2'}=4.9$, H-1′), 4.56 (dd, 1H, $J_{2',3'}=2.2$, $J_{3',4'}=7.9$, H-3′), 4.35 (dd, 1H, $J_{4',5'}=1.7$, H-4′), 4.26 (dd, 1H, H-2′), 3.99, 3.86 (each d, each 1H, $J_{gem}=13.7$, CH_2Ph), 3.56 (dd, 1H, $J_{3,5'}=9.5$, H-5′), 3.36 (dd, 1H, $J_{4a,5}=5.9$, $J_{4b,5}=12.9$, H-5), 3.29 (ddd, 1H, $J_{3,4a}=1.7$, $J_{3,4b}=8.2$, H-3), 2.30 (ddd, 1H, $J_{4a,4b}=12.2$, H-4a), 2.02 (ddd, 1H, H-4b), 1.43, 1.34, 1.30, 1.27 (each s, each 3H, $2CMe_2$), and 0.04 (s, 9H, $SiMe_3$); ^{13}C NMR (127.8 MHz, $CDCl_3$) δ 129.9, 129.0, 128.5, 128.1, 127.9, 126.9 (Ph), 108.5, 108.2 ($2CMe_2$), 96.3 (C-1′), 71.6 (C-2′), 70.5 (C-3′), 70.5 (C-4′), 69.9 (C-5), 67.6 (C-5′), 63.0 (C-3), 63.0 (CH_2Ph), 33.8 (C-4), 26.0, 25.7, 24.8, 23.9 ($2CMe_2$), and −3.7 ($SiMe_3$); CIMS: m/z 464 (41, $[M+H]^+$); 448 (27, $[M-Me]^+$); 348 (100, $[M-Me_3Si-CO-CH_2]^+$). Anal. calcd for $C_{24}H_{37}NO_6Si$: C, 62.20; H, 8.00; N, 3.02. Found: C, 62.59; H, 8.08; N, 3.36%.

Second eluted **5b** (0.202 g, 20%); oil; R_f 0.31 (6:1 hexane:ethyl acetate); $[\alpha]_D^{25}=-85$ (c 1.33, CH_2Cl_2); IR (KBr) ν_{max} 1381 (CMe_2), 1250 ($_\delta$C–H of $SiCH_3$), and 700 cm^{-1} ($_\nu$Si–C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.21 (m, 5H, Ph), 5.56 (d, 1H, $J_{1',2'}=5.0$, H-1′), 4.60 (dd, 1H, $J_{2',3'}=2.5$, $J_{3',4'}=7.8$, H-3′), 4.42 (d, 1H, $J_{gem}=13.9$, CH^aPh), 4.31 (dd, 1H, H-2′), 4.26 (dd, 1H, $J_{4',5'}=1.9$, H-4′), 3.88 (d, 1H, $J_{gem}=13.1$, CH^bPh), 3.82 (dd, 1H, $J_{3,5'}=8.7$, H-5′), 3.02 (br m, 1H, H-3), 3.51 (dd, 1H, $J_{4a,5}=8.9$, $J_{4b,5}=9.5$, H-5), 2.15 (m, 2H, 2H-4), [1.54, 1.45 (each s, each 3H), and 1.34 (s, 6H) $2CMe_2$], and 0.02 (s, 9H, $SiMe_3$); NOE contacts (1D NOESY): H-5, H-4′, H-5′; H-5′, H-5; H-3, CH_2Ph; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 130.2 (2C of Ph), 127.8 (3C of Ph), 126.6 (the other C of Ph), 109.2, 108.6 ($2CMe_2$), 96.2 (C-1′), 72.3 (C-4′), 70.8 (C-3′), 70.2 (C-2′ and C-5′), 68.7 (C-5), 63.7 (C-3), 62.5 (CH_2Ph), 34.4 (C-4), 26.0, 25.9, 24.9, 24.5 ($2CMe_2$), and −4.0 ($SiMe_3$); CIMS: m/z 464 (24, $[M+H]^+$); 448 (16, $[M-Me]^+$); 348 (100, $[M-Me_3Si-CO-CH_2]^+$). HRCIMS: m/z 463.2397 (calcd for $C_{24}H_{37}NO_6Si$: 463.2390), 464.2446 (calcd for $C_{24}H_{37}NO_6Si+H$: 464.2468).

5.3. Reaction of (*Z*)-*N*-benzyl-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranos-5-ylidene)amine *N*-oxide, 2 with vinyl-trimethylsilane, 4: preparation of the 2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidines (3*R*,5*R*)-6c, (3*R*,5*S*)-6a, (3*S*,5*R*)-6b, and (3*S*,5*S*)-6d

To a solution of nitrone **2**[12] (1.26 g, 3.30 mmol) in toluene (46 mL), cooled in an ice bath, dipolarophile **4** (11.5 mL, 7.46 g, 74.4 mmol) was added under an argon atmosphere and the mixture was heated at 80°C until monitoring of the reaction (TLC, 6:1 and 1:1 hexane:ethyl acetate) indicated complete conversion (24 h). The solution was then concentrated to give a crude residue formed by the diastereomeric isoxazolidines **6** (1.56 g, 98%), which was subjected to column chromatography (8:1 hexane:ethyl acetate). First eluted **6c**, isolated as an oil (0.503 g, 33%); R_f 0.46 (6:1 hexane:ethyl acetate); $[\alpha]_D^{22}=+8.4$ (c 0.7, CH_2Cl_2); IR (KBr) ν_{max} 1377 (CMe_2), 1254 ($_\delta$C–H of $SiCH_3$), and 735 cm^{-1} ($_\nu$Si–C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.21 (m, 10H, 2Ph), 5.88 (d, 1H, $J_{1',2'}=3.8$, H-1′), 4.55 (d, 1H, $J_{2',3'}\approx 0$, H-2′), 4.54, 4.37 (each d, each 1H, $J_{gem}=11.7$, O-CH_2Ph), 4.11 (d, 1H, $J_{3',4'}=3.0$, H-3′), 4.01 (dd, 1H, $J_{3,4'}=10.2$, H-4′), 3.97, 3.59 (each d, each 1H, $J_{gem}=13.2$, N-CH_2Ph), 3.81 (dd, 1H, $J_{4a,5}=8.4$, $J_{4b,5}=10.8$, H-5), 3.69 (ddd, 1H, $J_{3,4a}=8.1$, $J_{3,4b}=3.8$, H-3), 2.64

(ddd, 1H, $J_{4a,4b}=12.5$, H-4a), 2.22 (ddd, 1H, H-4b), 1.44, 1.28 (each s, each 3H, CMe_2), and 0.07 (s, 9H, $SiMe_3$); NOE contacts (1D NOESY): H-3, N-C*H*H-Ph; H-5, N-CH_2Ph, H-4a; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.6, 137.5, 129.3, 128.3, 128.1, 127.6, 127.3, 127.0 (2Ph), 111.5 (*C*Me_2), 104.7 (C-1′), 82.4 (C-4′), 82.1 (C-3′), 82.0 (C-2′), 71.7 (O-*C*H_2Ph), 66.4 (C-5), 62.7 (C-3), 58.8 (N-*C*H_2Ph), 35.1 (C-4), 26.5, 26.1 (C*Me*$_2$), and −3.8 (Si*Me*$_3$); CIMS: m/z 484 (33, $[M+H]^+$); 468 (37, $[M-Me]^+$); 368 (100, $[M-Me_3Si-CO-CH_2]^+$); HRCIMS: m/z 483.2444 (calcd for $C_{27}H_{37}NO_5Si$: 483.2441).

Second eluted **6a** (0.253 g, 16%); oil; R_f 0.35 (6:1 hexane:ethyl acetate); $[\alpha]_D^{23}=+1.0$ (c 0.3, CH_2Cl_2); IR (KBr) ν_{max} 1377 (CMe_2), 1256 ($_\delta$C–H of $SiCH_3$), and 735 cm^{-1} ($_\nu$Si–C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.23 (m, 10H, 2Ph), 5.90 (d, 1H, $J_{1',2'}=3.9$, H-1′), 4.59 (d, 1H, $J_{2',3'}\approx 0$, H-2′), 4.59, 4.39 (each d, each 1H, $J_{gem}=11.6$, O-CH_2Ph), 4.18 (dd, 1H, $J_{3,4'}=9.9$, $J_{3',4'}=3.1$, H-4′), 4.12 (d, 1H, H-3′), 3.86, 3.80 (each d, each 1H, $J_{gem}=13.3$, N-CH_2Ph), 3.70 (dd, 1H, $J_{3,4a}\approx 0$, $J_{3,4b}=7.4$, H-3), 3.58 (dd, 1H, $J_{4a,5}=5.4$, $J_{4b,5}=13.5$, H-5), 2.48 (ddd, 1H, $J_{4a,4b}=12.3$, $J_{3,4a}=0.6$, H-4a), 2.08 (ddd, 1H, H-4b), 1.50, 1.30 (each s, each 3H, CMe_2), and 0.06 (s, 9H, $SiMe_3$); NOE contacts (1D NOESY): H-3, N-CH_2Ph; H-5, H-4′, H-4a; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.7, 137.5, 129.4, 128.5, 128.2, 127.7, 127.5, 127.0 (2Ph), 111.6 (*C*Me_2), 104.9 (C-1′), 82.0, 82.0 (C-2′/C-3′), 80.2 (C-4′), 71.7 (O-*C*H_2Ph), 70.2 (C-5), 63.3 (N-*C*H_2Ph), 62.3 (C-3), 34.0 (C-4), 26.7, 26.2 (C*Me*$_2$), and −3.5 (Si*Me*$_3$); CIMS: m/z 484 (20, $[M+H]^+$); 468 (28, $[M-Me]^+$); 368 (100, $[M-Me_3Si-CO-CH_2]^+$); HRCIMS: m/z 483.2430 (calcd for $C_{27}H_{37}NO_5Si$: 483.2441).

Third eluted a mixture of **6a** and (**6b**+**6d**) (0.123 g, 8.0%), which was subjected to preparative TLC (6:1 hexane:ethyl acetate, two elutions), to afford three fractions: that of $R_f=0.65$ was identified as **6a** (0.025 g, 1.6%); the fraction of $R_f=0.39$ (0.020 g, 1.3%) was a 2:1 mixture (**6b**+**6d**), similar to the last eluted product from the column (see below); the fraction of $R_f=0.26$ was pure **6d** (0.053 g, 3.5%): oil; $[\alpha]_D^{20}=-74.6$ (c 1.4, CH_2Cl_2); IR (KBr) ν_{max} 1381 (CMe_2), 1248 ($_\delta$C–H of $SiCH_3$), and 739 cm^{-1} ($_\nu$Si–C); HRCIMS: m/z 483.2452 (calcd for $C_{27}H_{37}NO_5Si$: 483.2441); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.24 (m, 10H, 2Ph), 5.97 (d, 1H, $J_{1',2'}=3.9$, H-1′), 4.72, 4.43 (each d, each 1H, $J_{gem}=11.9$, O-CH_2Ph), 4.63 (d, 1H, $J_{2',3'}\approx 0$, H-2′), 4.13 (dd, 1H, $J_{3,4'}=8.8$, $J_{3',4'}=3.4$, H-4′), 3.96, 3.86 (each d, each 1H, $J_{gem}=13.5$, N-CH_2Ph), 3.84 (d, 1H, H-3′), 3.58 (dd, 1H, $J_{4a,5}=6.1$, $J_{4b,5}=11.9$, H-5), 3.35 (ddd, 1H, $J_{3,4a}=7.3$, $J_{3,4b}=7.3$, H-3), 2.20 (ddd, 1H, $J_{4a,4b}=11.9$, H-4a), 1.49 (overlapped m, 1H, H-4b), 1.48, 1.33 (each s, each 3H, CMe_2), and −0.002 (s, 9H, $SiMe_3$); NOE contacts (1D NOESY): H-3, N-CH_2Ph, H-5, H-4a; H-5, N-C*H*H–Ph, H-3, H-4a; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 138.1, 137.0, 129.6, 128.4, 128.2, 128.1, 127.9, 126.7 (2Ph), 111.5 (*C*Me_2), 105.2 (C-1′), 82.8 (C-4′)), 82.0 (C-3′), 81.6 (C-2′), 71.4 (O-*C*H_2Ph), 66.2 (C-5), 65.5 (C-3), 60.7 (N-*C*H_2Ph), 35.2 (C-4), 26.6, 26.3 (C*Me*$_2$), and −3.7 (Si*Me*$_3$).

Last eluted a 2:1 mixture (**6b**+**6d**) (0.177 g, 11.5%); oil; $R_f=0.23$ (6:1 hexane:ethyl acetate); IR (KBr) ν_{max} 1379 (CMe_2), 1252 ($_\delta$C–H of $SiCH_3$), and 733 cm^{-1} ($_\nu$Si–C); CIMS: m/z 484 (11, $[M+H]^+$); 468 (15, $[M-Me]^+$); 368 (100, $[M-Me_3Si-CO-CH_2]^+$); HRCIMS: m/z 483.2436 (calcd for $C_{27}H_{37}NO_5Si$: 483.2441); for the major component **6b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.24 (m, 10H, 2Ph), 6.01 (d, 1H, $J_{1',2'}=3.9$, H-1′), 4.73, 4.42 (each d, each 1H, $J_{gem}=11.8$, O-CH_2Ph), 4.63 (d, 1H, $J_{2',3'}\approx 0$, H-2′), 4.26 (dd, 1H, $J_{3,4'}=9.0$, $J_{3',4'}=3.1$, H-4′), 3.92, 3.84 (each d, each 1H, $J_{gem}=14.0$, N-CH_2Ph), 3.90 (d, 1H, H-3′), 3.46 (dd, 1H, $J_{4a,5}=10.0$, $J_{4b,5}=8.5$, H-5), 3.09 (ddd, 1H, $J_{3,4a}=2.1$, $J_{3,4b}=6.9$, H-3), 1.97 (ddd, 1H, $J_{4a,4b}=11.8$, H-4a), 1.74 (ddd, 1H, H-4b), 1.34 (s, 6H, CMe_2), and 0.006 (s, 9H, $SiMe_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.9, 137.0, 130.0, 128.5, 128.2, 128.1, 127.9, 127.8 (2Ph), 111.6 (*C*Me_2), 105.4 (C-1′), 82.8 (C-4′)), 82.1 (C-3′), 81.2 (C-2′), 71.6 (O-*C*H_2Ph), 68.9 (C-5), 63.7 (C-3), 60.7 (N-*C*H_2Ph), 35.0 (C-4), 26.6 (C*Me*$_2$), and −3.9 (Si*Me*$_3$); the minor component had ^{1}H and ^{13}C NMR spectra, respectively, identical to those of **6d**.

5.4. Reaction of (*Z*)-*N*-benzyl-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-ribofuranos-5-ylidene)amine *N*-oxide, 3 with vinyl-trimethylsilane, 4: preparation of the 2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidines (3*R*,5*R*)-7c, (3*R*,5*S*)-7a, (3*S*,5*R*)-7b, and (3*S*,5*S*)-7d

To a solution of nitrone **3**[12] (0.522 g, 1.36 mmol) in toluene (19 mL), cooled in an ice bath, dipolarophile **4** (4.76 mL, 3.08 g, 30.7 mmol) was added under an argon atmosphere, and the mixture was heated at 80°C for 20 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate). The solution was concentrated to give a crude residue formed by the diastereomeric isoxazolidines **7** (0.658 g, 100%), which was subjected to column chromatography (6:1 hexane:ethyl acetate). First eluted a mixture of products (0.471 g), which were separated by preparative TLC (same eluent, three runs) in three fractions: **7c** (0.103 g, 16%), **7a** (0.263 g, 40%), and a 4:1 mixture (^{1}H NMR) of isomers (**7b**+**7d**) (0.059 g, 9%). From the column, second eluted a 2:1 mixture of the same isomers (**7b**+**7d**) (0.058 g, ∼9%), and last eluted (pure ethyl acetate as the eluent) a residual mixture (0.094 g).

Compound **7c**: oil; R_f 0.42 (6:1 hexane:ethyl acetate); $[\alpha]_D^{23}=+153$ (c 1.52, CH_2Cl_2); IR (KBr) ν_{max} 1377 (CMe_2), 1254 ($_\delta$C–H of $SiCH_3$), and 735 cm^{-1} ($_\nu$Si–C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.28 (m, 10H, 2Ph), 5.69 (d, 1H, $J_{1',2'}=3.7$, H-1′), 4.71, 4.54 (each d, each 1H, $J_{gem}=11.3$, O-CH_2Ph), 4.55 (dd, 1H, $J_{2',3'}=4.6$, H-2′), 4.22 (dd, 1H, $J_{3',4'}=7.8$, $J_{3,4'}=3.2$, H-4′), 4.06 (dd, 1H, H-3′), 4.06, 3.79 (each d, each 1H, $J_{gem}=13.2$, N-CH_2Ph), 3.65 (dd, 1H, $J_{4a,5}=5.3$, $J_{4b,5}=12.7$, H-5), 3.35 (ddd, 1H, $J_{3,4a}=J_{3,4b}=8.2$, H-3), 2.30 (ddd, 1H, $J_{4a,4b}=12.7$, H-4a), 2.14 (ddd, 1H, H-4b), 1.58, 1.36 (each s, each 3H, CMe_2), and 0.059 (s, 9H, $SiMe_3$); NOE contacts (1D NOESY): H-3, H-4′, H-3′, N-CH_2-Ph, H-5; H-5, H-3′, N-C*H*HPh, H-3, H-4a; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 138.0, 137.9, 129.6, 128.1, 128.0,

127.9, 127.5, 126.9 (2Ph), 112.8 (CMe$_2$), 104.1 (C-1′), 80.7 (C-4′), 78.6 (C-2′), 78.5 (C-3′), 71.8 (O-CH$_2$Ph), 67.1 (C-5), 66.7 (C-3), 61.9 (N-CH$_2$Ph), 34.9 (C-4), 26.9, 26.8 (CMe_2), and −3.7 (SiMe_3); HRCIMS: m/z 483.2437 (calcd for $C_{27}H_{36}NO_5Si$: 483.2441).

Compound **7a**: oil; R_f 0.33 (6:1 hexane:ethyl acetate); $[\alpha]_D^{23}=+101$ (c 1.8, CH_2Cl_2); IR (KBr) ν_{max} 1377 (CMe$_2$), 1252 ($_\delta$C–H of SiCH$_3$), and 737 cm^{-1} ($_\nu$Si–C); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.36–7.26 (m, 10H, 2Ph), 5.69 (d, 1H, $J_{1',2'}=3.7$, H-1′), 4.77, 4.53 (each d, each 1H, $J_{gem}=11.4$, O-CH_2Ph), 4.59 (dd, 1H, $J_{2',3'}=4.1$, H-2′), 4.23 (dd, 1H, $J_{3',4'}=8.6$, $J_{3,4'}=2.8$, H-4′), 4.15, 3.93 (each d, each 1H, $J_{gem}=14.0$, N-CH_2Ph), 4.11 (dd, 1H, H-3′), 3.48 (dd, 1H, $J_{4a,5}=7.0$, $J_{4b,5}=11.7$, H-5), 3.17 (ddd, 1H, $J_{3,4a}=4.2$, $J_{3,4b}=10.3$, H-3), 2.33 (ddd, 1H, $J_{4a,4b}=11.6$, H-4a), 1.92 (ddd, 1H, H-4b), 1.57, 1.37 (each s, each 3H, CMe$_2$), and 0.02 (s, 9H, SiMe$_3$); NOE contacts (1D NOESY): H-3, H-4′, H-3′, N-CH_2-Ph; H-5, H-3′, N-CHHPh, H-4a; ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 137.5, 129.7, 128.2, 127.9, 127.8, 126.7 (2Ph), 112.8 (CMe$_2$), 103.7 (C-1′), 79.2 (C-4′), 78.6 (C-3′), 77.6 (C-2′), 71.9 (O-CH$_2$Ph), 69.5 (C-5), 63.7 (C-3), 62.2 (N-CH$_2$Ph), 33.6 (C-4), 26.7, 26.6 (CMe_2), and −3.9 (SiMe_3); HRCIMS: m/z 483.2429 (calcd for $C_{27}H_{36}NO_5Si$: 483.2441).

Isomer mixture (**7b**+**7d**): oil; $R_f=0.22$ (6:1 hexane:ethyl acetate); IR (KBr) ν_{max} 1377 (CMe$_2$), 1254 ($_\delta$C–H of SiCH$_3$), and 741 cm^{-1} ($_\nu$Si–C); HRCIMS: m/z 483.2438 (calcd for $C_{27}H_{36}NO_5Si$: 483.2441); the NMR spectra showed signals for two isomers in a 4:1 ratio; for the major component: ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.33–7.24 (m, 10H, 2Ph), 5.83 (d, 1H, $J_{1',2'}=3.9$, H-1′), 4.52, 4.14 (each d, each 1H, $J_{gem}=11.4$, O-CH_2Ph), 4.51 (dd, 1H, $J_{2',3'}=4.4$, H-2′), 4.00 (dd, 1H, $J_{3,4'}=3.9$, $J_{3',4'}=8.9$, H-4′), 3.92, 3.84 (each d, each 1H, $J_{gem}=13.1$, N-CH_2Ph), 3.72 (dd, 1H, $J_{4a,5}=6.4$, $J_{4b,5}=9.5$, H-5), 3.64 (dd, 1H, H-3′), 3.15 (ddd, 1H, $J_{3,4a}=2.5$, $J_{3,4b}=9.0$, H-3), 2.33 (ddd, 1H, $J_{4a,4b}=12.0$, H-4a), 2.10 (ddd, 1H, H-4b), 1.57, 1.35 (each s, each 3H, CMe$_2$), and 0.04 (s, 9H, SiMe$_3$); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 137.3, 137.2, 130.0, 128.1, 128.0, 127.9, 127.8, 127.7 (2Ph), 112.5 (CMe$_2$), 104.3 (C-1′), 80.7 (C-4′)), 79.1 (C-3′), 76.5 (C-2′), 71.6 (O-H$_2$Ph), 70.4 (C-5), 63.5 (N-H$_2$Ph), 63.3 (C-3), 34.8 (C-4), 26.6, 26.5 (CMe_2), and −3.8 (SiMe_3); for the minor component: ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.33–7.24 (m, 10H, 2Ph), 5.81 (d, overlapped with the signal for the respective proton of the major component, 1H, $J_{1',2'}\approx4.1$, H-1′), 4.54, 4.12 (each d, each 1H, $J_{gem}=11.3$, O-H_2Ph), 4.51 (dd, 1H, $J_{2',3'}=4.1$, H-2′), 3.94 (dd, 1H, $J_{3,4'}=3.8$, $J_{3',4'}=8.7$, H-4′), 3.92, 3.84 (each d, each 1H, $J_{gem}=13.1$, N-H_2Ph), 3.71 (dd, 1H, $J_{4a,5}=6.6$, $J_{4b,5}=12.2$, H-5), 3.63 (dd, 1H, H-3′), 3.26 (ddd, 1H, $J_{3,4a}=8.3$, $J_{3,4b}=6.7$, H-3), 2.44 (ddd, 1H, $J_{4a,4b}=11.8$, H-4a), 2.24 (ddd, 1H, H-4b), 1.56, 1.27 (each s, each 3H, CMe$_2$), and 0.06 (s, 9H, SiMe$_3$); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 137.5, 137.3, 130.0, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7 (2Ph), 112.2 (CMe$_2$), 104.1 (C-1′), 79.9 (C-4′)), 79.4 (C-3′), 76.5 (C-2′), 71.5 (O-CH$_2$Ph), 67.4 (C-5), 64.9 (N-CH$_2$Ph), 61.1 (C-3), 35.1 (C-4), 29.5, 26.6 (CMe_2), and −3.7 (SiMe_3).

5.5. Reaction of (2*R*,3*R*,5*S*)-2-benzyl-3-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5-yl)-5-(trimethylsilyl)isoxazolidine, 5a with acetyl chloride: preparation of 6-(*N*-benzyl)acetamido-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-octodialdo-1,5-pyranose, 8 and (*E*)-6,7-didehydro-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-octodialdo-1,5-pyranose, 9

A suspension of **5a** (0.19 g, 0.41 mmol) and sodium hydrogen carbonate (0.115 g) in freshly distilled tetrahydrofuran (5 mL) was cooled at 0°C and treated with acetyl chloride (0.43 mL, 0.61 mmol) under argon. The mixture was maintained at 0°C for 3 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×25 mL), and the combined ethereal layers were dried (MgSO$_4$) and concentrated to give a crude product, purification of which was achieved by column chromatography (6:1→1:1 gradient, hexane:ethyl acetate), to afford unreacted **5a** (36 mg, indicating 81% of conversion), compound **8** (37 mg, 21%, corresponding to 26% yield from converted substrate), and compound **9** (46 mg, 39%, corresponding to ∼49% from converted substrate). Compound **8**: syrup; R_f 0.67 (1:1 hexane:ethyl acetate); $[\alpha]_D^{23}=-10$ (c 0.68, CH_2Cl_2); IR (KBr) ν_{max} 1717 (aldehyde C=O), 1653 (amide C=O), and 1383 cm^{-1} (CMe$_2$); HREIMS: m/z 433.2091 (calcd for $C_{23}H_{31}NO_7$: 433.2101), 418.1849 (calcd for $C_{23}H_{31}NO_7$–CH$_3$: 418.1866); major amide conformer (62.5%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.39 (dd, 1H, $J_{CHO,7a}=2.3$, $J_{CHO,7b}=2.0$, CHO), 7.35–7.14 (m, 5H, Ph), 5.48 (d, 1H, $J_{1,2}=5.2$, H-1), 4.71, 4.55 (each d, each 1H, $J_{gem}=16.6$, CH_2Ph), 4.30–4.25 (overlapped signal, 1H, H-6), 4.51 (dd, 1H, $J_{2,3}=2.3$, $J_{3,4}=8.1$, H-3), 4.29 (dd, 1H, $J_{1,2}=4.8$, $J_{2,3}=2.3$, H-2), 4.23 (dd, 1H, $J_{3,4}=7.9$, $J_{4,5}=1.7$, H-4), 4.60–4.50 (overlapped, H-5), 2.98 (ddd, 1H, $J_{7a,7b}=17.0$, $J_{6,7a}=5.6$, $J_{7a,CHO}=2.5$, H-7a), 2.67 (ddd, 1H, $J_{7a,7b}=17.0$, $J_{6,7b}=5.7$, $J_{7b,CHO}=1.6$, H-7b), 2.16 (s, 3H, Me–C=O), [1.55 (s, 3H), 1.45 (s, 6H), and 1.32 (s, 3H) 2CMe$_2$]; ^{13}C NMR (125.7 MHz, CDCl$_3$) δ 200.4 (CHO), 171.7 (N-OCH$_3$), 136.7, 128.9, 128.6, 127.9, 127.4, 127.3 (Ph), 109.4, 109.1 (2CMe$_2$), 96.7 (C-1), 71.1 (C-3), 70.9 (C-4), 70.7 (C-2), 69.0 (C-5), 54.2 (C-6), 54.2 (CH_2Ph), 44.6 (C-7), 29.7, 26.0 (each double intensity, 2CMe_2), and 23.1 (*Me*–CO–N); minor amide conformer (37.5%): ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.33 (br s, 1H, CHO), 7.35–7.14 (m, 5H, Ph), 5.49 (d, 1H, $J_{1,2}=5.1$, H-1), 5.05, 4.06 (each d, each 1H, $J_{gem}=15.7$, CH_2Ph), 4.65 (m, 1H, H-6), 4.50 (dd, 1H, $J_{2,3}=2.4$, $J_{3,4}=7.9$, H-3), 4.29 (dd, 1H, $J_{1,2}=4.8$, $J_{2,3}=2.3$, H-2), 4.01 (dd, 1H, $J_{3,4}=8.0$, $J_{4,5}=1.5$, H-4), 3.86 (dd, 1H, $J_{4,5}=1.2$, $J_{5,6}=10.2$, H-5), 2.92 (dd, 1H, $J_{7a,7b}=18.1$, $J_{6,7a}=4.1$, H-7a), 2.60 (dd, 1H, $J_{7a,7b}=18.1$, $J_{6,7b}=9.0$, H-7b), 2.49 (s, 3H, Me–C=O), 1.42, 1.41, 1.34, and 1.32 (each s, each 3H, 2CMe$_2$); ^{13}C NMR (125.7 MHz, CDCl$_3$) δ 199.3 (CHO), 172.9 (N-COCH$_3$), 138.5, 128.9, 128.6, 127.9, 127.4, 127.3 (Ph), 109.5, 108.7 (2CMe$_2$), 96.7 (C-1), 71.0 (C-3), 70.7 (C-2), 70.1 (C-4), 67.8 (C-5), 52.5 (C-6), 45.3 (CH_2Ph), 44.9 (C-7), 25.1, 24.8, 24.5, 24.3 (2CMe_2), and 21.9 (*Me*–CO–N). Compound **9**: syrup;

R_f 0.33 (1:1 hexane:ethyl acetate); $[\alpha]_D^{25} = -48$ (*c* 2.0, CH_2Cl_2); IR (KBr) ν_{max} 1684 (α,β-unsaturated HC=O), 1385 (CMe_2), 1090, and 1071 cm^{-1} (*trans* H–C=C–H); ^1H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, 1H, $J_{CHO,7}$ = 7.9, CHO), 6.78 (dd, 1H, $J_{5,6}$ = 4.4, $J_{6,7}$ = 15.8, H-6), 6.38 (ddd, 1H, $J_{5,7}$ = 1.7, $J_{6,7a}$ = 15.7, $J_{CHO,7}$ = 7.9, H-7), 5.60 (d, 1H, $J_{1,2}$ = 5.0, H-1), 4.67 (dd, 1H, $J_{2,3}$ = 2.5, $J_{3,4}$ = 7.8, H-3), 4.56 (dd, 1H, $J_{4,5}$ = 1.9, $J_{5,6}$ = 4.1, H-5), 4.37 (dd, 1H, $J_{1,2}$ = 5.0, $J_{2,3}$ = 2.6, H-2), 4.33 (dd, 1H,$J_{3,4}$ = 7.8, $J_{4,5}$ = 2.1, H-4), 1.52, 1.42, 1.35, and 1.33 (each s, each 3H, $2CMe_2$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 193.1 (CHO), 151.3 (C-6), 132.6 (C-7), 109.7, 108.7 ($2CMe_2$), 96.2 (C-1), 72.5 (C-4), 70.7 (C-3), 70.2 (C-2), 67.5 (C-5), 25.9, 25.7, 24.6, and 24.3 ($2CMe_2$); HRCIMS: *m*/*z* 285.1350 (calcd for $C_{14}H_{20}O_6$+H: 285.1338), 283.1175 (calcd for $C_{14}H_{20}O_6$-H: 283.1181), 269.1039 (calcd for $C_{14}H_{20}O_6$–CH_3: 269.1025).

5.6. Reaction of (3*S*,5*R*)-2-benzyl-3-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5-yl)-5-(trimethylsilyl)isoxazolidine, 5b with acetyl chloride: preparation of 6-(*N*-benzyl)acetamido-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-L-*glycero*-α-D-*galacto*-octodialdo-1,5-pyranose, 10 and (*E*)-6,7-didehydro-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-octodialdo-1,5-pyranose, 9

A suspension of **5b** (0.094 g, 0.20 mmol) and sodium hydrogen carbonate (0.058 g) in freshly distilled tetrahydrofuran (2.5 mL) was cooled at 0°C and treated with acetyl chloride (0.21 mL, 0.30 mmol) under argon. The mixture was maintained at 0°C for 45 min (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×15 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.075 mg), purification of which was achieved by column chromatography (6:1→1:1 gradient, hexane:ethyl acetate), to afford unreacted **5b** (34 mg, indicating 64% conversion), compound **10** (26 mg, 30%, corresponding to 47% yield from converted substrate), and compound **9** (3 mg, ~5%, corresponding to ~8% from converted substrate). Compound **10**: syrup; R_f 0.29 (1:1 hexane:ethyl acetate); $[\alpha]_D^{26} = -38$ (*c* 1.3, CH_2Cl_2); IR (KBr) ν_{max} 1734 (aldehyde C=O), 1653 (amide C=O), and 1381 cm^{-1} (CMe_2); HRCIMS: *m*/*z* 434.2179 (calcd for $C_{23}H_{31}NO_7$+H: 434.2179); major amide conformer (62.5%): ^1H NMR (500 MHz, $CDCl_3$) δ 9.37 (br s, 1H, CHO), 7.35–7.12 (m, 5H, Ph), 5.48 (d, 1H, $J_{1,2}$ = 5.0, H-1), 4.68, 4.48 (each d, each 1H, J_{gem} = 17.0, CH_2Ph), 4.62 (m, 1H, H-5), 4.57 (dd, 1H, $J_{2,3}$ = 2.3, $J_{3,4}$ = 7.9, H-3), 4.33 (dd, 1H, $J_{1,2}$ = 4.9, $J_{2,3}$ = 2.3, H-2), 4.32 (m, 1H, H-6), 4.18 (dd, 1H, $J_{3,4}$ = 7.9, $J_{4,5}$ = 1.4, H-4), 2.89 (br m, 1H, H-7a), 2.67 (ddd, 1H, $J_{7a,7b}$ = 16.8, $J_{6,7b}$ = 5.2, $J_{7b,CHO}$ = 2.4, H-7b), 2.08 (s, 3H, Me–C=O), 1.51, 1.42, 1.32, and 1.28 (each s, each 3H, $2CMe_2$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 200.4 (CHO), 173.2 (N-*C*OCH$_3$), 137.3, 128.7, 128.4, 127.5, 127.1, 126.8 (Ph), 109.4, 108.9 ($2CMe_2$), 96.3 (C-1), 71.0 (C-3), 70.9 (C-4), 70.4 (C-2), 67.2 (C-5), 67.2 (C-6), 52.0 (*C*H$_2$Ph), 43.6 (C-7), 25.9, 25.7, 24.9, 24.3 ($2CMe_2$), and 22.9 (*Me*–CO–N); minor amide conformer (37.5%): ^1H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1H, CHO), 7.32–7.10 (m, 5H, Ph), 5.51 (d, 1H, $J_{1,2}$ = 5.2, H-1), 5.39, 3.62 (each d, each 1H, J_{gem} = 16.2, CH_2Ph), 4.79 (ddd, 1H, $J_{5,6} \approx 10.5$, $J_{6,7a}$ = 10.5, $J_{6,7b}$ = 2.9, H-6), 4.63 (dd, 1H, $J_{2,3}$ = 2.3, $J_{3,4}$ = 7.8, H-3), 4.33 (dd, 1H, $J_{1,2}$ = 5.1, $J_{2,3}$ = 2.4, H-2), 4.11 (dd, 1H, $J_{3,4}$ = 7.9, $J_{4,5}$ = 1.7, H-4), 3.84 (d, 1H, $J_{4,5} \approx 0$, $J_{5,6}$ = 9.6, H-5), 2.59 (dd, 1H, $J_{7a,7b}$ = 17.7, $J_{6,7a}$ = 10.6, $J_{7a,CHO} \approx 0$, H-7a), 2.38 (dd, 1H, $J_{7a,7b}$ = 17.8, $J_{6,7b}$ = 3.2, $J_{7b,CHO} \approx 0$, H-7b), 2.35 (s, 3H, Me–C=O), 1.59, 1.46, 1.34, and 1.25 (each s, each 3H, $2CMe_2$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 198.2 (CHO), 172.2 (N-*C*OCH$_3$), 138.8, 128.7, 128.4, 127.5, 127.1, 126.8 (Ph), 109.7, 108.5 ($2CMe_2$), 96.4 (C-1), 71.1 (C-3), 70.7 (C-4), 70.1 (C-2), 66.0 (C-5), 52.0 (C-6), 44.5 (*C*H$_2$Ph), 42.7 (C-7), 29.6, 26.0, 25.9, 24.6 ($2CMe_2$), and 22.9 (*Me*–CO–N). The ^1H NMR of **10** at 120°C (300 MHz, DMSO-d_6) showed collapsed signals: δ 9.35 (s, 1H, CHO), 7.35–7.21 (m, 5H, Ph), 5.48 (d, 1H, $J_{1,2}$ = 5.0, H-1), 4.61 (dd, 1H, $J_{2,3}$ = 2.4, $J_{3,4}$ = 8.0, H-3), 4.32 (dd, 1H, $J_{1,2}$ = 5.1, $J_{2,3}$ = 2.4, H-2), 4.27 (dd, 1H, $J_{3,4}$ = 7.9, $J_{4,5}$ = 1.8, H-4), 2.72 (ddd, 1H, $J_{7a,7b}$ = 17.3, $J_{6,7a}$ = 8.7, $J_{7a,CHO}$ = 2.1, H-7a), 2.60 (dd, 1H, $J_{7a,7b}$ = 17.3, $J_{6,7b}$ = 4.4, $J_{7b,CHO}$ = 1.6, H-7b), 2.07 (s, 3H, Me–C=O), 1.49, 1.41 (each s, each 3H), and 1.31 (s, 6H), $2CMe_2$. Compound **9** was identified with that obtained from **5a** (identical ^1H and ^{13}C NMR spectra, respectively).

5.7. Reaction of (3*R*,5*R*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine, 6c with acetyl chloride: preparation of 5-(*N*-benzyl)acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*xylo*-heptodialdo-1,4-furanose, 11 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-heptodialdo-1,4-furanose, 12

A suspension of **6c** (0.386 g, 0.80 mmol) and sodium hydrogen carbonate (0.223 g) in freshly distilled tetrahydrofuran (9.3 mL) was cooled at 0°C and treated with acetyl chloride (0.85 mL, 1.20 mmol) under argon. The mixture was maintained at 0°C for 4.5 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×25 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.426 g), fractionation of which was achieved by column chromatography (6:1 hexane:ethyl acetate); first eluted unreacted **6c** (0.139 g, indicating 64% conversion). Second eluted compound **12** (0.027 g, 11%, corresponding to 17% yield from converted substrate), identified (NMR spectra) with the α,β-unsaturated aldehyde obtained from **6a** (see next paragraph). Third eluted compound **11** (0.164 g, 45%, corresponding to 71% yield from converted substrate). Last eluted a residual fraction (0.076 g) using pure ethyl acetate as the eluent. Compound **11** was an oil; R_f 0.50 (1:1 hexane:ethyl acetate); $[\alpha]_D^{22} = -29$ (*c* 0.53, CH_2Cl_2); IR (KBr) ν_{max} 1723 (aldehyde C=O), 1640 (amide C=O), and 1410 cm^{-1} (CMe_2); CIMS: *m*/*z* 454 (88, $[M+H]^+$); 150 (75 $[PhCH_2NHCOCH_3+H]^+$);

107 (168, $[PhCH_2NH_2]^+$); 91 $[C_7H_7]^+$); 59 (100 $[CH_3COCH_3+H]^+$); HRCIMS: m/z 454.2233 (calcd for $C_{26}H_{31}NO_6$+H: 454.2230); major amide conformer (57%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.52 (dd, 1H, $J_{CHO,6a}=1.6$, $J_{CHO,6b}=2.9$, CHO), 7.38–7.05 (m, 10H, 2Ph), 5.86 (d, 1H, $J_{1,2}=3.5$, H-1), 5.10 (br m, 1H, H-5), 4.66, 4.43 [or 4.59, 4.37] (each d, each 1H, $J_{gem}=11.6$ [for both], O-CH_2Ph), 4.58 (overlapped dd, 1H, $J_{3,4}=3.3$, $J_{4,5}=5.5$, H-4), 4.55 (d, 1H, $J_{2,3}\approx 0$, H-2), 4.49 (d, 1H, $J_{gem}=17.5$, one of the *geminal* N-CH_2Ph; the signal of the other is overlapped), 3.90 (d, 1H, H-3), 3.00 (ddd, 1H, $J_{6a,6b}=16.8$, $J_{5,6a}=4.6$, H-6a), 2.68 (ddd, 1H, $J_{5,6b}=8.1$, H-6b), 2.05 (s, 3H, Me–C=O), 1.27, and 1.26 (each s, each 3H, CMe_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 194.8 (CHO), 166.2 (N-*C*OCH$_3$), 131.4, 131.2, 123.1, 122.9, 122.8, 122.7, 122.4, 122.3, 122.1, 120.5 (2Ph), 105.9 (*C*Me$_2$), 99.0 (C-1), 75.9 (C-3), 75.6 (C-2), 75.4 (C-4), 66.0 (O-*C*H$_2$Ph), 45.7 (N-*C*H$_2$Ph), 44.7 (C-5), 39.0 (C-6), 20.5, 20.3 (C*Me*$_2$), and 16.8 (*Me*–CO–N); minor amide conformer (43%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.44 (br s, 1H, CHO), 7.38–7.05 (m, 10H, 2Ph), 5.85 (d, 1H, $J_{1,2}=3.6$, H-1), 4.80 (br m, 1H, H-5), 4.59, 4.37 [or 4.66, 4.43] (each d, each 1H, $J_{gem}=11.6$ [for both], O-CH_2Ph), 4.49 (d, 1H, $J_{2,3}\approx 0$, H-2), 4.49 (d, 1H, $J_{gem}=17.5$, one of the *geminal* N-CH_2Ph; the signal of the other is overlapped), 4.17 (dd, 1H, $J_{4,5}=6.8$, H-4), 3.49 (d, 1H, $J_{3,4}=3.1$, H-3), 2.93 (dd, 1H, $J_{6a,6b}=18.0$, $J_{5,6a}=4.2$, $J_{CHO,6a}\approx 0$, H-6a), 2.77 (ddd, 1H, $J_{5,6b}=8.8$, $J_{CHO,6b}=1.2$, H-6b), 2.20 (s, 3H, Me–C=O), 1.40, and 1.27 (each s, each 3H, CMe_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 193.4 (CHO), 166.3 (N-*C*OCH$_3$), 131.1, 130.7, 123.1, 122.8, 122.6, 122.4, 122.3, 122.1, 121.8, 121.7, 121.4, 120.5 (2Ph), 105.9 (*C*Me$_2$), 98.9 (C-1), 76.8 (C-3), 75.7 (C-2), 74.2 (C-4), 66.0 (O-*C*H$_2$Ph), 45.7 (N-*C*H$_2$Ph), 45.4 (C-5), 39.1 (C-6), 20.9, 20.8 (C*Me*$_2$), and 16.2 (*Me*–CO–N). The NMR spectra at 110 or 90°C in DMSO-d_6 showed collapsed signals: ^{1}H NMR at 110°C (300 MHz) δ 9.49 (dd, 1H, $J_{CHO,6a}=2.0$, $J_{CHO,6b}=2.0$, CHO), 7.36–7.20 (m, 10H, 2Ph), 5.80 (d, 1H, $J_{1,2}=3.8$, H-1), 4.76 (dd, 1H, $J_{5,6a}=5.4$, $J_{5,6b}=7.3$, H-5), 4.64, 4.46 (each d, each 1H, $J_{gem}=11.6$, O-CH_2Ph), 4.63 (overlapped, 1H,, H-4), 4.63, 4.42 (each d, each 1H, $J_{gem}=16.2$, N-CH_2Ph), 2.83 (ddd, 1H, $J_{6a,6b}=16.7$, $J_{5,6a}=5.4$, H-6a), 2.68 (ddd, 1H, $J_{5,6b}=7.7$, H-6b), 2.03 (s, 3H, Me–C=O), 1.30, and 1.24 (each s, each 3H, CMe_2); the following signals are best observed at 90°C: 4.63 (d, 1H, $J_{2,3}\approx 0$, H-2), 3.75 (br s, 1H, H-3); ^{13}C NMR at 90°C (75.5 MHz, DMSO-d_6) δ 199.9 (CHO), 170.7 (N-*C*OCH$_3$), 137.1, 127.9, 127.8, 127.4, 126.6 (Ph), 110.6 (*C*Me$_2$), 104.0 (C-1), 81.2 (C-3), 81.0 (C-4), 70.8 (C-2), 50.8 (C-5), 50.8 (O-*C*H$_2$Ph), 44.4 (N-*C*H$_2$Ph), 44.4 (C-6), 26.2, 25.9 (C*Me*$_2$), and 21.6 (*Me*–CO–N).

5.8. Reaction of (3*R*,5*R*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine, 6a with acetyl chloride: preparation of 5-(*N*-benzyl)acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*xylo*-heptodialdo-1,4-furanose, 11 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-heptodialdo-1,4-furanose, 12

A suspension of **6a** (0.127 g, 0.26 mmol) and sodium hydrogen carbonate (0.072 g) in freshly distilled tetrahydrofuran (3 mL) was cooled at 0°C and treated with acetyl chloride (0.30 mL, 0.42 mmol) under argon. The mixture was maintained at 0°C for 1 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (4×25 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.100 g). Column chromatography of 0.094 g of this crude material, successively eluting with 3:1, 1:1, and 1:3 hexane:ethyl acetate, afforded unreacted **6a** (40 mg, indicating 57% of conversion), the α,β-unsaturated aldehyde **12** (19 mg, ~26%, corresponding to 45% yield from converted substrate), and a compound (12 mg, ~11%, corresponding to ~19% yield from converted substrate) that proved to be identical with **11** (respectively identical ^{1}H and ^{13}C NMR spectra). Compound **12** was an oil; R_f 0.52 (3:1 hexane:ethyl acetate); $[\alpha]_D^{23}=-34$ (*c* 0.89, CH_2Cl_2); IR (KBr) ν_{max} 1620 (α,β-unsaturated HC=O), 1383 (CMe_2), 1092, and 1026 cm^{-1} (*trans* H–C=C–H); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (d, 1H, $J_{CHO,6}=7.8$, CHO), 7.54–7.24 (m, 5H, Ph), 6.75 (dd, 1H, $J_{5,6}=15.8$, $J_{4,5}=5.1$, H-5), 6.38 (ddd, 1H, $J_{4,6}=1.6$, H-6), 6.02 (d, 1H, $J_{1,2}=3.8$, H-1), 4.89 (ddd, 1H, $J_{3,4}=3.4$, H-4), 4.68 (d, 1H, $J_{2,3}=0$, H-2), 4.67, 4.47 (each d, each 1H, $J_{gem}=12.1$, CH_2Ph), 4.04 (dd, 1H, H-3), 1.50, and 1.34 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 193.0 (CHO), 150.1 (C-6), 136.9 (*ipso*-C of Ph), 133.4 (C-5), 128.5, 128.2, 128.0 (Ph), 112.1, (*C*Me$_2$), 105.1 (C-1), 83.7 (C-3), 83.1 (C-2), 79.4 (C-4), 72.2 (*C*H$_2$Ph), 26.8, and 26.2 (C*Me*$_2$); HRCIMS: m/z 304.1338 (calcd for $C_{17}H_{20}O_5$: 304.1311), 289.1083 (calcd for $C_{17}H_{20}O_5$–CH_3: 289.1076).

5.9. Reaction of the 2:1 mixture of (3*S*,5*R*)- and (3*S*,5*S*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine, 6b and 6d with acetyl chloride: preparation of 5-(*N*-benzyl)acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-L-*glycero*-α-D-*xylo*-heptodialdo-1,4-furanose, 13 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-heptodialdo-1,4-furanose, 12

A suspension of the 2:1 mixture **6b**/**6d** (0.087 g, 0.18 mmol) and sodium hydrogen carbonate (0.050 g) in freshly distilled tetrahydrofuran (2 mL) was cooled at 0°C and treated with acetyl chloride (0.21 mL, 0.30 mmol) under argon. The mixture was maintained at 0°C for 3 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×20 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.080 g). A major part of this (0.072 g) was subjected to column chromatography (3:1 and 1:1 hexane:ethyl acetate, successively); first eluted a 4:1 mixture of unreacted starting material (0.046 g, indicating 53% of conversion) and the α,β-unsaturated aldehyde **12** (19%, corresponding to 35% yield from converted substrate); second eluted a unique 5-acetamido compound **13** (22 mg, 30%, corresponding to 57% yield from converted

substrate), different from **11** described in the above two paragraphs; **13** was an oil; R_f 0.32 (1:1 hexane:ethyl acetate); $[\alpha]_D^{20}=-35$ (c 0.85, CH_2Cl_2); IR (KBr) ν_{max} 1723 (aldehyde C=O), 1642 (amide C=O), and 1412 cm^{-1} (CMe_2); HRCIMS: m/z 454.2219 (calcd for $C_{26}H_{31}NO_6$+H: 454.2230); major amide conformer (56%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.24 (dd, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx 2.5$, CHO), 7.34–7.13 (m, 10H, 2Ph), 5.92 (d, 1H, $J_{1,2}=3.8$, H-1), 5.00, 4.03 (each d, each 1H, $J_{gem}=16.2$, O-CH_2Ph), 4.7–4.6 (overlapped m, 1H, H-5), 4.7–4.6 (overlapped m, 1H, H-4), 4.62 (overlapped d, 1H, $J_{2,3}\approx 0$, H-2), 4.62, 4.30 (each d, each 1H, $J_{gem}=11.6$, N-CH_2Ph), 3.79 (d, 1H, $J_{3,4}=2.8$, H-3), 2.74 (ddd, 1H, $J_{6a,6b}=16.3$, $J_{5,6a}=7.1$, H-6a), 2.21 (ddd, 1H, $J_{5,6b}=4.7$, H-6b), 2.10 (s, 3H, Me–C=O), 1.42, and 1.31 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 199.6 (CHO), 172.0 (N-COCH$_3$), 137.0, 136.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.5, 127.0, 126.9 (2Ph), 111.8 (CMe$_2$), 104.6 (C-1), 81.5 (C-4), 80.9 (C-3), 78.6 (C-2), 70.9 (O-CH$_2$Ph), 50.8 (C-5), 44.2 (N-CH$_2$Ph), 44.0 (C-6), 29.5, 26.6 (CMe_2), and 23.0 (*Me*–CO–N); minor amide conformer (44%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.01 (br s, 1H, CHO), 7.34–7.13 (m, 10H, 2Ph), 5.90 (d, 1H, $J_{1,2}=3.7$, H-1), 5.00, 4.03 (each d, each 1H, $J_{gem}=16.2$, O-CH_2Ph), 4.90 (ddd, 1H, $J_{5,6a}\approx J_{4,5}\approx 10.3$, $J_{5,6b}=2.9$, H-5), 4.71, 4.32 (each d, each 1H, $J_{gem}=12.1$, N-CH_2Ph), 4.66 (d, 1H, $J_{2,3}\approx 0$, H-2), 4.11 (dd, 1H, $J_{3,4}=3.1$, H-4), 3.70 (d, 1H, H-3), 2.48 (ddd, 1H, $J_{6a,6b}=17.7$, $J_{CHO,6a}=1.1$, H-6a), 2.41 (s, 3H, Me–C=O), 1.66 (dd, 1H, H-6b), 1.39, and 1.32 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.6 (CHO), 173.0 (N-COCH$_3$), 138.4, 136.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.5, 127.0, 126.7 (2Ph), 111.6 (CMe$_2$), 104.5 (C-1), 81.6 (C-2), 79.8 (C-3), 78.0 (C-4), 71.0 (O-CH$_2$Ph), 52.0 (N-CH$_2$Ph), 50.8 (C-5), 42.4 (C-6), 26.2, 26.0 (CMe_2), and 22.1 (*Me*–CO–N). The NMR spectra at 90°C in DMSO-d_6 showed collapsed signals: ^{1}H NMR (300 MHz) δ 9.34 (dd, 1H, $J_{CHO,6a}=1.6$, $J_{CHO,6b}=2.1$, CHO), 7.34–7.24 (m, 10H, 2Ph), 5.85 (d, 1H, $J_{1,2}=3.8$, H-1), 4.80 (dd, 1H, $J_{5,6a}\approx J_{4,5}=9.6$, $J_{5,6b}=3.9$, H-5), 4.74 (d, 1H, $J_{2,3}\approx 0$, H-2), 4.67, 4.45 (each d, each 1H, $J_{gem}=11.7$, O-CH_2Ph), 4.57, 4.35 (each d, each 1H, $J_{gem}=16.0$, N-CH_2Ph), 4.25 (m, 1H, H-4), 3.89 (d, 1H, $J_{3,4}=3.2$, H-3), 2.71 (overlapped with the water signal, 1H, H-6a), 2.68 (ddd, 1H, $J_{6a,6b}=16.8$, H-6b), 2.08 (s, 3H, Me–C=O), 1.32, and 1.27 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 184.5 (CHO), 172.5 (N-COCH$_3$), 142.6, 142.4, 133.3, 132.9, 132.8, 132.2 (2Ph), 125.0 (CMe$_2$), 109.1 (C-1), 86.2 (C-2), 85.4 (C-3), 82.8 (C-4), 75.6 (O-CH$_2$Ph), 55.5 (N-CH$_2$Ph), 55.5 (C-5), 47.2 (C-6), 30.9, 30.6 (CMe_2), and 26.5 (*Me*–CO–N).

5.10. Reaction of (3*R*,5*R*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine, 7c with acetyl chloride: preparation of 5-(*N*-benzyl)acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*ribo*-heptodialdo-1,4-furanose, 14 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-heptodialdo-1,4-furanose, 15

A suspension of **7c** (0.048 g, 0.10 mmol) and sodium hydrogen carbonate (0.028 g) in freshly distilled tetrahydrofuran (1.2 mL) was cooled at 0°C and treated with acetyl chloride (0.11 mL, 0.16 mmol) under argon. The mixture was maintained at 0°C for 2 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×10 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.028 g), purification of which was achieved by preparative TLC (1:1 hexane:ethyl acetate) to afford three fractions; that of R_f 0.69 was the α,β-unsaturated aldehyde **15** (0.011 g, 36%) identical with that obtained from **7a** (see below); a second fraction (0.010 g, R_f 0.51) showed no sugar proton signal in its ^{1}H NMR spectrum, and the third fraction was **14** (0.006 g, 13%); HRCIMS: m/z 454.2238 (calcd for $C_{26}H_{31}NO_6$+H: 454.2230); major amide conformer (68%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (br s, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx 0$, CHO), 7.43–7.11 (m, 10H, 2Ph), 5.65 (d, 1H, $J_{1,2}=3.7$, H-1), 5.36 (m, 1H, H-5), 4.77, 4.53 (each d, each 1H, $J_{gem}=11.5$, O-CH_2Ph), 4.52, 4.06 (each d, each 1H, $J_{gem}=16.8$, N-CH_2Ph), 4.49 (dd, 1H, $J_{2,3}=4.1$, H-2), 4.13 (dd, 1H, $J_{3,4}=8.9$, $J_{4,5}=6.3$, H-4), 3.29 (dd, 1H, H-3), 2.57 (dd, 1H, $J_{6a,6b}=17.0$, $J_{5,6a}=4.9$, H-6a), 2.48 (ddd, 1H, $J_{5,6b}=8.0$, $J_{6b,CHO}=2.3$, H-6b), 2.03 (s, 3H, Me–C=O), and 1.26 (s, 6H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 199.9 (CHO), 172.6 (N-COCH$_3$), 137.5, 137.4, 129.7, 128.8, 128.4, 128.3, 127.3, 127.1, 127.0, 126.8, 126.7, 125.9 (2Ph), 113.1 (CMe$_2$), 103.9 (C-1), 80.3 (C-3), 77.9 (C-4), 76.2 (C-2), 72.2 (O-CH$_2$Ph), 50.5 (C-5), 49.4 (N-CH$_2$Ph), 43.8 (C-6), 31.9 (*Me*–CO–N), 26.6, and 26.4 (CMe_2); minor amide conformer (32%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx 0$, CHO), 7.43–7.11 (m, 10H, 2Ph), 5.72 (d, 1H, $J_{1,2}=3.5$, H-1), 4.81, 4.57 (each d, each 1H, $J_{gem}=11.6$, O-CH_2Ph), 4.62 (m, 1H, H-5), 4.52, 4.06 (each d, each 1H, $J_{gem}=16.8$, N-CH_2Ph), 4.51 (overlapped, 1H, H-2), 4.15 (dd, 1H, $J_{3,4}=9.5$, $J_{4,5}=3.1$, H-4), 3.41 (dd, 1H, $J_{2,3}=4.2$, H-3), 2.74 (dd, 1H, $J_{6a,6b}=18.2$, $J_{5,6a}=9.7$, H-6a), 2.32 (m, 1H, H-6b), 1.93 (s, 3H, Me–C=O), 1.37, and 1.29 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 198.8 (CHO), 169.8 (N-COCH$_3$), 138.7, 138.2, 129.1, 128.7, 128.6, 128.5, 128.4, 128.2, 127.9, 125.9 (2Ph), 113.4 (CMe$_2$), 104.3 (C-1), 80.6 (C-4), 78.8 (C-3), 76.7 (C-2), 72.1 (O-CH$_2$Ph), 52.8 (C-5), 49.4 (N-CH$_2$Ph), 43.5 (C-6), 32.8 (*Me*–CO–N), 26.7, and 26.5 (CMe_2).

5.11. Reaction of (3*R*,5*S*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine 7a with acetyl chloride: preparation of 5-(*N*-benzyl)acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*ribo*-heptodialdo-1,4-furanose, 14 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-heptodialdo-1,4-furanose, 15

A suspension of **7a** (0.171 g, 0.354 mmol) and sodium hydrogen carbonate (0.099 g) in freshly distilled tetrahydrofuran (4.2 mL) was cooled at 0°C and treated with acetyl chloride (0.38 mL, 0.54 mmol) under argon. The mixture was maintained at 0°C for 2 h (TLC

monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×15 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.120 g), purification of which was achieved by column chromatography (3:1 hexane:ethyl acetate). First eluted the α,β-unsaturated aldehyde **15** (0.041 g, 38%); oil, R_f 0.38 (3:1 hexane:ethyl acetate); $[\alpha]_D^{20}=+54.5$ (*c* 0.4, CH_2Cl_2); IR (KBr) ν_{max} 1690 (α,β-unsaturated HC=O), 1381 (CMe_2), 1092, and 1022 cm^{-1} (*trans* H–C=C–H); ^1H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, 1H, $J_{CHO,6}=7.8$, CHO), 7.36–7.34 (m, 5H, Ph), 6.68 (dd, 1H, $J_{5,6}=15.8$, $J_{4,5}=4.5$, H-5), 6.35 (ddd, 1H, $J_{4,6}=1.6$, H-6), 5.80 (d, 1H, $J_{1,2}=3.7$, H-1), 4.79, 4.55 (each d, each 1H, $J_{gem}=12.0$, CH_2Ph), 4.71 (dddd, 1H, $J_{3,4}=3.4$, $J_{2,4}=0.5$, H-4), 4.63 (ddd, 1H, $J_{2,3}=4.2$, H-2), 3.56 (dd, 1H, H-3), 1.62, and 1.38 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 192.9 (CHO), 151.7 (C-5), 136.8 (*ipso*-C of Ph), 132.0 (C-6), 128.4, 128.2, 128.1 (Ph), 113.3, (*C*Me$_2$), 103.9 (C-1), 81.8 (C-3), 77.2 (C-2), 76.6 (C-4), 72.5 (*C*H$_2$Ph), 26.6, and 26.3 (C*Me*$_2$); HRCIMS: *m*/*z* 304.1297 (calcd for $C_{17}H_{20}O_5$: 304.1311), 289.1077 (calcd for $C_{17}H_{20}O_5$–CH_3: 289.1076).

Second eluted was a mixture which was resolved by preparative TLC (1:1 hexane:ethyl acetate) in three fractions; that of R_f 0.43 (0.022 g) and that of $R_f\approx0$ (0.024 g) showed no sugar proton signal in their ^1H NMR spectra; the second fraction (R_f 0.13) was the amino sugar **14** (0.011 g, 7%); oil, identical (^1H NMR) with that obtained from **7c**.

5.12. Reaction of the mixture of (3*S*,5*R*)- and (3*S*,5*S*)-2-benzyl-3-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-5-(trimethylsilyl)isoxazolidine (7b+7d) with acetyl chloride: preparation of 5-(*N*-benzyl)-acetamido-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-L-*glycero*-α-D-*ribo*-heptodialdo-1,4-furanose 16 and (*E*)-5,6-didehydro-5,6-dideoxy-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-heptodialdo-1,4-furanose 15

A suspension of the mixture of **7b** and **7d** (0.095 g, 0.200 mmol) and sodium hydrogen carbonate (0.055 g) in freshly distilled tetrahydrofuran (2.4 mL) was cooled at 0°C and treated with acetyl chloride (0.22 mL, 0.31 mmol) under argon. The mixture was maintained at 0°C for 2 h (TLC monitoring, 6:1 and 1:1 hexane:ethyl acetate), and the reaction was quenched by adding saturated aqueous sodium hydrogen carbonate until neutral pH. The mixture was extracted with ether (3×15 mL), and the combined ethereal layers were dried ($MgSO_4$) and concentrated to give a crude product (0.082 g), purification of which was achieved by column chromatography (3:1 and 1:1 hexane:ethyl acetate). First eluted unreacted (**7b**+**7d**) (0.018 g, indicating 81% of conversion). Second eluted the α,β-unsaturated aldehyde **15** (0.021 g, ~35%, corresponding to 42% yield from converted substrate). Last eluted **16** (0.042 g, 46%, corresponding to 57% from converted substrate); oil, R_f 0.36 (1:1 hexane:ethyl acetate); $[\alpha]_D^{22}=+33$ (*c* 0.4, CH_2Cl_2); IR (KBr) ν_{max} 1723 (aldehyde C=O), 1642 (amide C=O), and 1410 cm^{-1} (CMe_2); HRCIMS: *m*/*z* 454.2230 (calcd for $C_{26}H_{31}NO_6$+H: 454.2230); first amide conformer (51%): ^1H NMR (300 MHz, $CDCl_3$) δ 9.49 (br s, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx0$, CHO), 7.52–7.10 (m, 10H, 2Ph), 5.46 (d, 1H, $J_{1,2}=3.6$, H-1), 4.97, 4.30 (each d, each 1H, $J_{gem}=15.8$, O-CH_2Ph), 4.70, 4.40 (each d, each 1H, $J_{gem}=10.9$, N-CH_2Ph), 4.69 (overlapped m, 1H, H-5), 4.46 (dd, 1H, $J_{2,3}=3.9$, H-2), 4.27 (overlapped, 1H, H-4), 3.59 (dd, 1H, $J_{3,4}=8.3$, H-3), 2.94 (dd, 1H, $J_{6a,6b}=17.7$, $J_{5,6a}=6.1$, H-6a), 2.65 (dd, 1H, $J_{5,6b}=6.5$, H-6b), 2.10 (s, 3H, Me–C=O), 1.51, and 1.47 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 199.1 (CHO), 171.0 (N-*C*OCH$_3$), 138.5, 136.5, 128.3, 128.2, 127.9, 127.2, 126.6 (2Ph), 113.0 (*C*Me$_2$), 103.4 (C-1), 79.4 (C-3), 78.8 (C-4), 77.0 (C-2), 71.8 (O-*C*H$_2$Ph), 51.3 (C-5), 45.5 (N-*C*H$_2$Ph), 44.0 (C-6), 21.9 (*Me*–CO–N), and 20.9 (C*Me*$_2$); second amide conformer (49%): ^1H NMR (300 MHz, $CDCl_3$) δ 9.22 (s, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx0$, CHO), 7.52–7.10 (m, 10H, 2Ph), 5.61 (d, 1H, $J_{1,2}=3.7$, H-1), 5.05 (m, 1H, H-5), 4.97, 4.30 (each d, each 1H, $J_{gem}=15.8$, O-CH_2Ph), 4.69, 4.40 (each d, each 1H, $J_{gem}=11.3$, N-CH_2Ph), 4.58 (dd, 1H, $J_{2,3}=3.9$, H-2), 4.05 (overlapped, 1H, H-4), 3.56 (dd, 1H, $J_{3,4}=8.3$, H-3), 2.89 (dd, 1H, $J_{6a,6b}=18.3$, $J_{5,6a}=8.3$, H-6a), 2.64 (dd, 1H, $J_{5,6b}=4.4$, H-6b), 2.34 (s, 3H, Me–C=O), 1.33, and 1.30 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 198.1 (CHO), 171.0 (N-*C*OCH$_3$), 137.3, 137.0, 128.6, 128.4, 128.3, 128.2, 127.1, 126.2 (2Ph), 112.9 (*C*Me$_2$), 103.4 (C-1), 79.4 (C-3), 78.1 (C-4), 76.7 (C-2), 71.8 (O-*C*H$_2$Ph), 52.5 (C-5), 45.5 (N-*C*H$_2$Ph), 44.4 (C-6), 22.4 (*Me*–CO–N), and 14.0 (C*Me*$_2$). The NMR spectra at 80°C in DMSO-d_6 showed collapsed signals: ^1H NMR (300 MHz) δ 9.43 (s, 1H, $J_{CHO,6a}\approx J_{CHO,6b}\approx0$, CHO), 7.35–7.18 (m, 10H, 2Ph), 5.60 (d, 1H, $J_{1,2}=3.6$, H-1), 4.70 (dd, 1H, $J_{2,3}=4.1$, H-2), 4.61, 4.44 (each d, each 1H, $J_{gem}=11.3$, O-CH_2Ph), 4.53 (overlapped m, 1H, H-5), 4.53 (br s, 1H, N-CH_2Ph), 4.03 (m, 1H, H-4), 3.71 (dd, 1H, $J_{3,4}=8.6$, H-3), 3.00 (overlapped with the water signal, 1H, H-6a), 2.80 (ddd, 1H, $J_{6a,6b}=17.3$, $J_{5,6b}=5.7$, H-6b), 2.07 (s, 3H, Me–C=O), 1.36, and 1.28 (each s, each 3H, CMe_2); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 205.7 (CHO), 176.2 (N-*C*OCH$_3$), 144.1, 143.4, 133.5, 133.3, 133.0, 132.9, 131.9, 131.4 (2Ph), 117.2 (*C*Me$_2$), 108.4 (C-1), 83.8 (C-3), 82.6 (C-4), 81.5 (C-2), 75.7 (O-*C*H$_2$Ph), 54.2 (C-5), 49.1 (N-*C*H$_2$Ph), 44.5 (C-6), 35.2 (*Me*–CO–N), 31.5 and 30.7 (C*Me*$_2$).

5.13. Crystallographic analysis of compound 5a[†]

Single crystals of the compound were in the form of colourless prisms with well shaped faces. The crystal

[†] Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 185112. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

used had approximate dimensions 0.32×0.32×0.60 mm and belonged to the triclinic system with systematic absences consistent with the space group $P1$. Unit-cell parameters and crystal orientation matrix, determined on a CAD4 Enraf–Nonius four-circle automated, graphite-monochromated, diffractometer from the least-squares treatment of the setting angles of 25 independent reflections within the range $3<\theta<13°$, were $a=5.823(2)$, $b=12.793(1)$, and $c=18.891(1)$ Å, $\alpha=103.11(1)$, $\beta=98.83(1)$, $\gamma=103.13(2)°$, $V=1303.2(5)$ Å^3, $D_{calcd}=1.182$ g cm^{-3} for $Z=1$, $F(000)=500$ and the absorption coefficient $\mu=0.126$ mm^{-1}. Intensity data were collected at room temperature in the $\omega/2\theta$ scan mode, using Mo Kα radiation ($\lambda=0.71069$ Å) up to $\theta=25°$ for a total of 5048 reflections ($-6<h<6$, $-15<k<14$, $0<l<22$). Three reference reflections (1–55, 1–62 and 1–34) were measured every hour to monitor crystal stability and were re-centred after every hundred measured reflections to monitor crystal orientation. No significant intensity changes were observed. Corrections were made for Lorentz-polarisation effects, but not for extinction and absorption. This last effect was not taken into account because the crystal absorption with Mo radiation was practically negligible. A total of 4694 reflections were considered observed [$I>2\sigma(I_0)$].

The structure was solved by direct methods using SIR97[15] to locate all non-hydrogen atoms, and refinement based on F^2 using SHELXL97.[16] All H-atoms were included fixed in the later refinement placed in geometrically calculated positions. The isotropic thermal parameters of each H-atom were fixed at 1.2 and 1.5 times the equivalent isotropic thermal parameters of the carrier atom. The final cycle of refinements led to a final agreement factor $R=0.05$, and $Rw(F^2)=0.13$ for $w=1/[\sigma^2(F_o^2)+(0.111.2P)^2+0.0741P]$ where $P=(F_o^2+2F_c^2)/3$ for 577 variables, $(\Delta/\sigma)_{max}=0.009$ and $S=1.04$. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography.[17] Maximum and minimum electron densities in the final difference map were 0.339 and −0.048 e Å^{-3}, respectively. The geometrical analysis was performed using PARST.[18]

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