Carbohydrate Research 351 (2012) 7–16

Contents lists available at SciVerse ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Synthesis and biological activities of novel isoxazoline-linked pseudodisaccharide derivatives

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ARTICLE INFO

Article history:
Received 14 September 2011
Received in revised form 25 November 2011
Accepted 27 November 2011
Available online 4 December 2011

Keywords:
Pseudodisaccharide
1,3-Dipolar cycloaddition
Nitrile oxide
Isoxazoline
HIV-RT inhibition

ABSTRACT

A series of novel isoxazoline linked pseudodisaccharide derivatives were regiospecifically synthesized by 1,3-dipolar cycloaddition of α-allyl-*C*-glycopyranosides and sugar-derived nitrile oxides with good yields. The structures of the compounds were characterized by NMR spectroscopy and MS spectrometry and confirmed by the X-ray crystallographic analysis of compound ((5*S*)-3-(2,3-*O*-isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α- *C*-D-galactopyranoside. Their biological activities against glycosidases (α-amylase, α-glucosidase, and β-glucosidase) and HIV-RT, and antitumor activity were preliminarily evaluated. Some of them exhibited potent inhibitory activity to HIV-RT.

1. Introduction

It is well known that carbohydrates play crucial roles in a wide variety of biological systems,[1,2] and considerable attention has been paid to the design and synthesis of carbohydrate analogues for developing therapeutic potentials in the treatment of the diseases related to the carbohydrate metabolism, such as diabetes, human immunodeficiency virus (HIV) infection, metastatic cancer, and lysosomal storage diseases.[3–6] For example, the non-oxygen linked disaccharide analogues, in which the interglycosidic oxygen in the naturally occurring *O*-disaccharide is replaced by other atoms (e.g., carbon,[7] nitrogen,[8] and sulfur[9,10]), have been extensively studied due to their promising bioactivities and very good enzymatic stability. Furthermore, the heterocycle-linked disaccharide analogues which constructed a novel nucleoside-like pseudodisaccharide bearing two sugar moieties on the heterocycle have recently been synthesized,[11–17] and were found to be of good antitumor and/or anti HIV-RT activities.[15–17] As the further study on the synthesis and biological activity of such new pseudodisaccharide analogues, we would like to report herein a convenient synthesis of novel isoxazoline linked pseudodisaccharide analogues via 1,3-dipolar cycloaddition[18] of sugar-derived nitrile oxides to α-allyl-*C*-glycosides and the evaluation of their inhibitory activities against glycosidase and HIV-RT, and antitumor activity.

2. Results and discussion

2.1. The synthesis of isoxazoline linked pseudodisaccharide derivatives

The 3-(2,3,4,6-tetra-*O*-benzyl-α-D-glycopyranosyl)-1-propene (**1**–**3**) were readily prepared from the corresponding methyl D-glycopyranosides following the reported procedures.[19,20] The sugar-derived nitrile oxides (**4a**–**c**) were synthesized from the corresponding sugar oxime according to the literatures[15,21,22], and were used *in situ* to the 1,3-dipolar cycloaddition with the α-allyl-*C*-glycoside (**1**–**3**) based on our previous study.[15] Thus, taken the reaction of **1** and **4a** as the example (Scheme 1), the solution of the sugar oxime (1.0 mmol) and *N*-chlorosuccinimide (NCS) (1.0 mmol) in 1,2-dichloroethane (DCE) was refluxed for 20 min. to form the intermediate of chlorated sugar oxime. Then cooled to room temperature, to the solution the benzylated α-allyl-*C*-glucoside (**1**) (1.2 mmol) was added, and a solution of DMAP (1.0 mmol) in DCE was added dropwise within 2 h under refluxing to generate the sugar-derived nitrile oxide **4a**, and then the reaction mixture was refluxed for 1 h to complete the cycloaddition. In order to minimize the formation of the N-oxide dimer of the nitrile oxide under the basic condition[15], the solution of DMAP was slowly added dropwise to control the generation of the nitrile oxide **4a** for keeping the dipolarophile (**1**) excess. After common workup and silica gel column chromatography, the mixture of two diastereoisomers of the isoxazoline linked pseudodisaccharides (**5a** and **6a**) was

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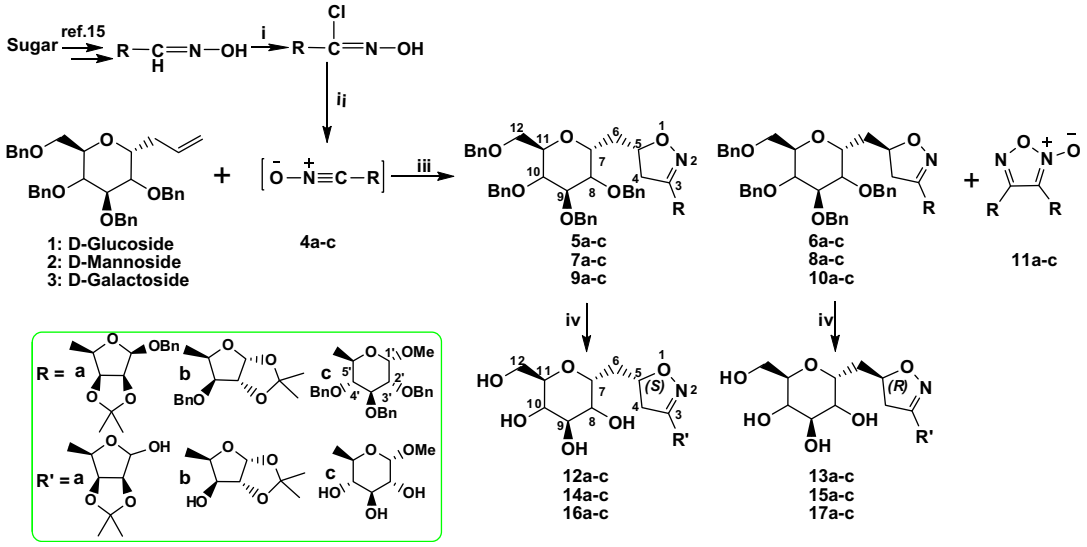
doi:10.1016/j.carres.2011.11.025



Scheme 1. Reagents and conditions: (i) DCE, NCS, reflux, 20 min; (ii) DMAP, DCE; (iii) DCE, DMAP, reflux, 3 h; (iv) MeOH, HCl, $Pd(OH)_2/C$, H_2, 2 h.

obtained in total yield of 90%, accompanied with the trace byproduct of nitrile oxide dimer (**11a**) and the recovery of benzylated α-allyl-*C*-glucoside (**1**) (8%). The diastereoisomeric mixture was separated by silica gel column chromatography again to afford the less polar isomer **5a** (49%) and the more polar isomer **6a** (41%), respectively. Similarly, the 1,3-dipolar cycloaddition of **1** to **4b**–**c**, and **2**–**3** to **4a**–**c** were carried out following the procedure (as shown in Scheme 1) and afforded the corresponding cycloadducts as the less polar products **5**, **7**, **9** and the more polar diastereoisomers **6**, **8**, **10** in good yields (listed in Table 1) and the nitrile oxide dimers **11a**–**c**,[15] respectively.

Subsequently, the cycloadducts **5–10** were debenzylated by catalytic hydrogenation with $Pd(OH)_2/C$ in MeOH–HCl (c_{HCl} = 0.3%) solution at room temperature, and the corresponding isoxazoline linked pseudodisaccharides **12**–**17** were produced in high yields of 74–95%, respectively.

2.2. The structures of compounds 5–10 and 12–17

The structures of compounds **5**–**10** and **12**–**17** were characterized by the analyses of ^1H NMR and ^{13}C NMR spectra, ^1H–^{13}C correlation, HRMS(ESI), optical rotations, and the X-ray crystallographic structure of compound **16a**. Theoretically, the 1,3-dipolar cycloaddition of nitrile oxide to alkene should form four stereoisomers of 3,4-disubstituted (*syn*) and 3,5-disubstituted (*anti*) isoxazolines. However, observed in their ^1H NMR spectra (the table of data can be found in supporting information), the typical 3,5-disubstituted isoxazoline signals,[23,24] such as the ^3J values of 7–11 Hz for 5-H/4-$H_{a,b}$ and the germinal coupling ^1J of ca. 17–18 Hz for 4-H_a/4-H_b, were found, which indicated that the 1,3-dipolar cycloaddition underwent in *anti*-form and regiospecifically produced the 3,5-disubstituted isoxazolines. This regioselectivity was in accordance with the previously reported results based on the nitrile oxide cycloaddition with terminal alkenes and alkynes.[25] The X-ray crystallographic structure of compound **16a** (Fig. 1)[26] suggested the configuration of C-5 to be of *S* form. Accordingly, its diastereoisomer **17a** should possess the *R* form at C-5. Furthermore, as shown in Table 2, each diastereoisomers of **5**, **7**, **9**, **12**, **14**, **16** and **6**, **8**, **10**, **13**, **15**, **17** exhibited similar NMR signals in H-5 and C-5 and optical rotations, respectively. For instance, the signals of H-5 in the less polar diastereoisomers **5**, **7**, **9** and **12**, **14**, **16** appeared in more downfield than those in the more polar diastereoisomers **6**, **8**, **10** and **13**, **15**, **17**. In contrast, the absorptions of C-5 in **5**, **7**, **9** and **12**, **14**, **16** were in more upfield than those in **6**, **8**, **10** and **13**, **15**, **17**. In addition, all of **5**, **7**, **9** and **12**, **14**, **16** had more positive optical rotations than their diastereoisomers **6**, **8**, **10** and **13**, **15**, **17**. Consequently, according to the consistencies of the spectral data, the polarities and the optical rotations of each diastereoisomers and the crystallographical structure of **16a**, the configurations of C-5 in **5**, **7**, **9** and **12**, **14**, **16**, and their diastereoisomers **6**, **8**, **10** and **13**, **15**, **17** were tentatively assigned as *S* and *R*, respectively.

2.3. Biological activities

The inhibitions against HIV-1 reverse transcriptase (HIV-RT) and glycosidase, and the antitumor activity of some of compounds **12**–**17** were preliminarily evaluated. The HIV-RT inhibitory activities of compounds **14**, **15**, **16a** and **17a** were measured using colorimetric reverse transcriptase assay by comparison with AZT.[27] As shown in Table 3, compounds **14b**, **15b**, **16a,** and **17a** exhibited very good HIV-RT inhibitory activity with the IC_{50} values of 7.17, 9.61, 4.31, and 4.64 μM, respectively, better than that of the positive control AZT. The glycosidase inhibitory activities of **12a**, **13a**, **14a**, **14b**, **15a**, **15b**, **16c,** and **17c** were determined with hydrolytic reactions of α-amylase, α-glucosidase, and β-glucosidase using acarbose as a control, respectively. However, the compounds showed a

Table 1
The yields of 1,3-dipolar cycloaddition reactions

α-Allyl-*C*-glycosides	**1**	**1**	**1**	**2**	**2**	**2**	**3**	**3**	**3**
Nitrile oxides	**4a**	**4b**	**4c**	**4a**	**4b**	**4c**	**4a**	**4b**	**4c**
Adducts	**5a**	**5b**	**5c**	**7a**	**7b**	**7c**	**9a**	**9b**	**9c**
	6a	**6b**	**6c**	**8a**	**8b**	**8c**	**10a**	**10b**	**10c**
Yields (%)	49	46	40	49	42	46	47	57	43
	41	31	30	29	35	38	30	19	36
Ratio of isomers	1.2:1	1.5:1	1.3:1	1.7:1	1.2:1	1.2:1	1.6:1	3.0:1	1.2:1
Total yield (%)	90	77	70	78	77	84	77	76	79

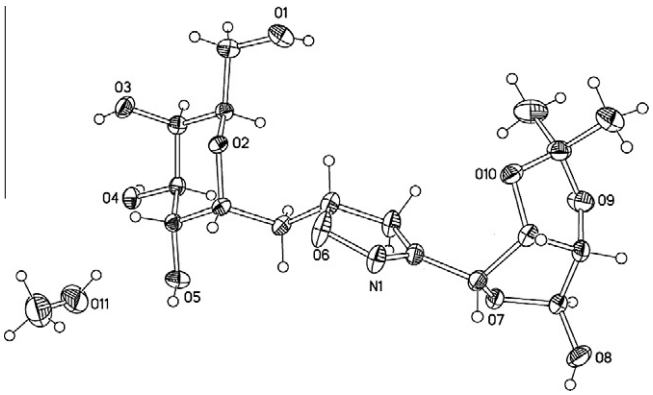


Figure 1. The X-ray crystallographic structure of compound **16a**.

selectively moderate inhibition to β-glucosidase, such as the inhibition of **14b**, and **15b** were 20% and 24% at the concentration of 2.7 μmol/mL, respectively. The cytotoxicities of the compounds **12–17** against breast cancer cell line were examined by the modified Mosmann protocol,[28] and only a few of them was found to be of a slight cytotoxicity, such as **13c** (13%), **15c** (13%), and **16c** (27%) at the concentration of 10 mmol/L.

In summary, we have regiospecifically synthesized a series of novel isoxazoline linked pseudodisaccharide analogues by 1,3-dipolar cycloaddition of α-allyl-*C*-glycosides and sugar-derived nitrile oxides, and followed by deprotection with Pd $(OH)_2$/C catalytic hydrogenation. The structures of the compounds were elucidated by NMR and MS spectral analyses with the aid of X-ray crystallographical structure of compound **16a**. Their biological activities against glycosidases (α-amylase, α-glucosidase, and β-glucosidase) and HIV-RT, and antitumor were preliminarily evaluated, and some of them exhibited potent inhibitory activity to HIV-RT. The further study of the synthesis and biological activities of novel heterocycle linked pseudodisaccharide analogues is underway.

3. Experimental

3.1. General methods

Melting points were measured on an SGW®X-4 micro melting point apparatus and are uncorrected. Optical rotations were determined on an SGW®-1 automatic polarimeter. ^{1}H NMR, ^{13}C NMR spectra were measured on a RT-NMR Bruker AVANCE 400 (400 MHz) spectrometer using tetramethylsilane (Me_4Si) as the internal standard. High-resolution mass spectra (HRMS) were carried out on a FTICR-MS (Ionspec 7.0 T) mass spectrometer in the electrospray-ionization (ESI) mode. X-ray crystallographic measurements were made on a Bruker SMART CCD diffractometer. The optical densities for examining the inhibitory activities against glycosidase and HIV-RT and anti-tumor activity were measured on a TU-1901 UV–vis spectrophotometer and a Bio-Rad Model 3550 microplate spectrophotometer, respectively. Thin-layer chromatography (TLC) was performed on precoated plates (Qingdao GF_{254}) with detection by UV light or with phosphomolybdic acid in EtOH–H_2O followed by heating. Column chromatography was performed using SiO_2 (Qingdao 300–400 mesh).

Table 3
Anti-HIV-RT activity

Compounds	IC_{50} (μM) (a colorimetric reverse transcriptase assay)	Compounds	IC_{50} (μM) (a colorimetric reverse transcriptase assay)
14a	>50	**14c**	>50
15a	>50	**15c**	>50
14b	7.17 ± 1.82	**16a**	4.31 ± 1.64
15b	9.61 ± 2.54	**17a**	4.64 ± 0.63
AZT	21.41 ± 1.93		

3.2. General procedure for the synthesis of compounds 5–10

A solution of sugar aldehyde oxime (293 mg, 1.0 mmol) and *N*-chlorosuccinimide (NCS) (134 mg, 1.0 mmol) in $ClCH_2CH_2Cl$ (10 mL) was refluxed for 20 min under N_2 atmosphere, and cooled to room temperature. To the solution α-allyl-*C*-glucoside **1** (678 mg, 1.2 mmol) was added and heated to reflux, then a solution of DMAP (122 mg, 1.0 mmol) in $ClCH_2CH_2Cl$ (10 mL) was added dropwise within 2 h, and the mixture was refluxed for another 1 h. The solution was concentrated under reduced pressure, the residue was submitted on a silica gel column chromatography using petroleum ether/ethyl acetate (v/v = 6:1) as the eluent to obtain the recovered α-allyl-*C*-glucoside (**1**, 8%) and the corresponding adducts mixture of **5a** and **6a** (90%, based on **1**) and the dimer (**11a**) of the sugar nitrile oxide (**4a**). Then the mixture of **5a** and **6a** was separated by silica gel column chromatography using cyclohexane/ethyl acetate (v/v = 10:1) as the eluent to obtain the less polar isomer **5a** (49%, based on **1**) and the more polar isomer **6a** (41%, based on **1**). Following the above procedure, the 1,3-dipolar cycloadditions of the α-allyl-*C*-glycosides (**1**–**3**) and the sugar nitrile oxides (**4a–c**) were carried out and afforded the corresponding cycloadducts of the less polar products **5**, **7**, **9** and the more polar **6**, **8**, **10**, and the dimers (**11a–c**) of the sugar nitrile oxides (**4a**–**c**).

3.2.1. ((5S)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (5a)

Colorless syrup; $[\alpha]_D^{25}$ +82.1 (*c* 1.0, $CHCl_3$); R_f = 0.34 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.94 (m, 1H, 6-H), 2.08 (m, 1H, 6-H), 2.86 (dd, 1H, *J* = 17.3 Hz, *J* = 6.8 Hz, CH_2, 4-H), 3.28 (dd, 1H, *J* = 17.0 Hz, *J* = 10.1 Hz, CH_2, 4-H), 3.59–3.76 (m, 6H, 8-H, 7-H, 10-

Table 2
The chemical shifts of H-5 and C-5 and the optical rotations of the adducts **5**–**10** and the deprotected products **12**–**17**

Compounds	**5a**	**6a**	**5b**	**6b**	**5c**	**6c**	**7a**	**8a**	**7b**	**8b**	**7c**	**8c**
H-5 (ppm)	4.77	4.76	4.70	4.70	4.62	4.59	4.84	4.83	4.73	4.67	4.63	4.58
C-5 (ppm)	78.1	78.3	78.0	78.3	78.0	78.1	76.3	76.6	76.8	76.9	76.6	76.7
$[\alpha]_D^{25}$	82.1	9.00	46.5	−21.1	113	16.5	47.6	−11.8	32.3	−30.5	88.3	−4.60
Compounds	**9a**	**10a**	**9b**	**10b**	**9c**	**10c**	**12a**	**13a**	**12b**	**13b**	**12c**	**13c**
H-5 (ppm)	4.79	4.78	4.75	4.69	4.63	4.58	4.80	4.76	4.80	4.75	4.80	4.78
C-5 (ppm)	77.5	78.4	76.8	76.9	76.0	76.2	77.7	79.1	77.7	79.1	77.8	79.6
$[\alpha]_D^{25}$	68.7	6.80	59.7	−22.4	77.1	6.00	69.9	−41.3	90.3	−25.7	108	38.7
Compounds	**14a**	**15a**	**14b**	**15b**	**14c**	**15c**	**16a**	**17a**	**16b**	**17b**	**16c**	**17c**
H-5 (ppm)	4.76	4.74	4.82	4.75	4.79	4.78	4.75	4.74	4.75	4.70	4.82	4.79
C-5 (ppm)	76.7	78.6	77.8	79.2	78.5	79.0	78.0	79.8	78.0	79.7	78.2	79.2
$[\alpha]_D^{25}$	80.0	−49.2	33.3	−37.7	84.4	18.6	66.9	−29.9	68.0	−36.3	108	47.0

H, 9-H, 12-H, 12-H), 4.36 (m, 1H, 11-H), 4.48 (d, 1H, J = 3.9 Hz, 2′-H), 4.38–4.69 (m, 7H, CH_2Ph), 4.76–4.93 (m, 3H, CH_2Ph), 4.77 (m, 1H, 5-H), 4.78 (d, 1H, J = 3.7 Hz, 3′-H), 4.89 (d, 1H, J = 5.4 Hz, 4′-H), 5.14 (s, 1H, 1′-H), 7.12–7.31 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.9 (CH_3), 26.4 (CH_3), 30.6 (6-C), 41.4 (4-C), 69.6 (12-C), 69.7 (CH_2Ph), 71.6 (11-C), 72.3 (CH_2Ph), 73.6 (CH_2Ph), 74.1 (CH_2Ph), 75.4 (CH_2Ph), 75.8 (4-C), 76.3 (7-C), 78.2 (10-C), 78.5 (5-C), 79.9 (8-C), 82.1 (9-C), 82.5 (3′-C), 85.5 (2′-C), 105.8 (1′-C), 113.4 (C, 13-C), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.4 (Ar), 128.50 (Ar), 128.5 (Ar), 128.8 (Ar), 128.9 (Ar), 128.9 (Ar), 137.5 (Ar), 138.5 (Ar), 138.6 (Ar), 138.7 (Ar), 139.1 (Ar), 156.9 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3978.

3.2.2. ((5*R*)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (6a)

White solid, mp: 122–123 °C; $[\alpha]_D^{25}$ +9.00 (c 1.0, $CHCl_3$); R_f = 0.30 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.22 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.96 (m, 1H, 6-H), 2.26 (m, 1H, 6-H), 2.92 (dd, 1H, J = 17.0 Hz, J = 8.4 Hz, CH_2, 4-H), 3.20 (dd, 1H, J = 17.1 Hz, J = 10.3 Hz, CH_2, 4-H), 3.65–3.71 (m, 6H, 8-H, 7-H, 10-H, 9-H, 12-H, 12-H), 4.22 (m, 1H, 11-H), 4.43–4.49 (m, 3H, CH_2Ph), 4.61–4.71 (m, 5H, CH_2Ph), 4.63 (d, 1H, J = 3.5 Hz, 2′-H), 4.75–4.82 (m, 2H, CH_2Ph), 4.76 (m, 1H, 5-H), 4.79 (d, 1H, J = 3.1 Hz, 3′-H), 4.90 (d, 1H, J = 3.2 Hz, 4′-H), 5.16 (s, 1H, 1′-H), 7.12–7.35 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.8 (CH_3), 26.3 (CH_3), 30.8 (6-C), 40.9 (4-C), 69.3 (12-C), 69.5 (11-C), 71.9 (CH_2Ph), 72.1 (CH_2Ph), 73.5 (CH_2Ph), 73.9 (CH_2Ph), 75.3 (CH_2Ph), 75.8 (4′-C), 76.3 (7-C), 78.4 (5-C), 79.2 (10-C), 80.06 (8-C), 82.1 (9-C), 82.6(3′-C), 85.4 (2′-C), 105.7 (1′-C), 113.3 (C, 13-C), 128.0 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.7 (Ar), 128.8 (Ar), 128.9 (Ar), 137.4 (Ar), 138.4 (Ar), 138.5 (Ar), 138.6 (Ar), 139.1 (Ar), 156.7 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3976.

3.2.3. ((5*S*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (5b)

Colorless syrup; $[\alpha]_D^{25}$ +46.5 (c 1.0, $CHCl_3$); R_f = 0.32 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.36 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 1.96 (m, 1H, 6-H), 2.13 (m, 1H, 6-H), 2.87 (dd, 1H, J = 17.2 Hz, J = 7.5 Hz, CH_2, 4-H), 3.25 (dd, 1H, J = 17.3 Hz, J = 10.2 Hz, CH_2, 4-H), 3.67–3.88 (m, 6H, 8-H, 7-H, 10-H, 9-H, 12-H, 12-H), 4.19 (d, 1H, J = 3.4 Hz, 2′-H), 4.39 (d, 1H, J = 3.6 Hz, 3′-H), 4.47 (m, 1H, 11-H), 4.54–4.58 (m, 2H, CH_2Ph), 4.61–4.70 (m, 6H, 5-H, CH_2Ph), 4.78 (d, 1H, J = 3.3 Hz, 2′-H), 4.85–4.99 (m, 2H, CH_2Ph), 5.29 (d, 1H, J = 3.6 Hz, 4′-H), 6.05 (d, 1H, J = 3.2 Hz, 1′-H), 7.04–7.37 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.8 (CH_3), 27.4 (CH_3), 30.9 (6-C), 41.7 (4-C), 69.6 (12-C), 74.4 (11-C), 72.4 (CH_2Ph), 72.8 (CH_2Ph), 73.2 (CH_2Ph), 74.0 (CH_2Ph), 75.5 (CH_2Ph), 75.7 (7-C), 76.8 (4′-C), 77.7 (10-C), 78.0 (5-C), 80.0 (2′-C), 82.6 (3′-C), 82.8 (8-C), 85.2 (9-C), 105.7 (1′-C), 112.6 (C, 13-C), 127.9 (Ar), 128.0 (Ar), 128.2 (Ar), 128.2 (Ar), 128.3 (Ar), 128.5 (Ar), 128.74] (Ar), 128.53] (Ar), 128.7 (Ar), 129.0 (Ar), 137.4 (Ar), 138.5 (Ar), 138.5 (Ar), 138.7 (Ar), 139.1 (Ar), 157.7 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3989.

3.2.4. ((5*R*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (6b)

Colorless syrup; $[\alpha]_D^{25}$ −21.8 (c 1.0, $CHCl_3$); R_f = 0.29 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.87 (m, 1H, 6-H), 2.19 (m, 1H, 6-H), 2.77 (dd, 1H, J = 17.2 Hz, J = 8.9 Hz, CH_2, 4-H), 3.16 (dd, 1H, J = 17.3 Hz, J = 10.3 Hz, CH_2, 4-H), 3.64 (m, 3H, 8-H, 7-H, 10-H), 3.81 (m, 3H, 9-H, 12-H, 12-H), 4.09 (m, 1H, 11-H), 4.13 (d, 1H, J = 3.4 Hz, 3′-H), 4.42–4.62 (m, 8H, CH_2Ph), 4.70 (m, 1H, 5-H), 4.78 (d, 1H, J = 3.3 Hz, 2′-H), 4.76–4.89 (m, 2H, CH_2Ph), 5.10 (d, 1H, J = 3.3 Hz, 4′-H), 6.01 (d, 1H, J = 3.6 Hz, 1′-H), 7.04–7.37 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.7 (CH_3), 27.3 (CH_3), 31.4 (6-C), 41.5 (4-C), 69.3 (12-C), 72.1 (11-C), 72.2 (CH_2Ph), 72.6 (CH_2Ph), 73.5 (CH_2Ph), 73.9 (CH_2Ph), 75.3 (CH_2Ph), 75.7 (7-C), 77.1 (4′-C), 77.1 (10-C), 78.4 (5-C), 79.1 (2′-C), 80.0 (3′-C), 82.7 (8-C), 85.0 (9-C), 105.6 (1′-C), 112.6 (C, 13-C), 127.9 (Ar), 128.0 (Ar), 128.2 (Ar), 128.2 (Ar), 128.3 (Ar), 128.5 (Ar), 128.7 (Ar), 128.5 (Ar), 128.7 (Ar), 129.0 (Ar), 137.4 (Ar), 138.4 (Ar), 138. (Ar), 138.7 (Ar), 139.1 (Ar), 157.4 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3986.

3.2.5. ((5S)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (5c)

White solid, mp: 118–119 °C; $[\alpha]_D^{25}$ +113 (c 1.0, $CHCl_3$); R_f = 0.45 (silica gel, cyclohexane/dichlormethane/diethyl ether v/v = 3:8:0.5); ^{1}H NMR ($CDCl_3$): δ 1.82 (m, 1H, 6-H), 2.02 (m, 1H, 6-H), 2.51 (dd, 2H, J = 7.8 Hz, J = 2.1 Hz, CH_2, 4-H), 3.35 (s, 3H, OCH_3), 3.46 (t, 1H, J = 9.6 Hz, CH), 3.51 (dd, 1H, J = 9.6 Hz, J = 3.4 Hz, CH), 3.56 (d, 2H, J = 9.6 Hz, CH), 3.64 (m, 2H, CH_2, 12-H), 3.67 (m, 1H, CH, 9-H), 3.72 (m, 1H, CH, 2′-H), 4.05 (t, 1H, J = 9.2 Hz, 3′-H), 4.33 (m, 1H, CH, 11-H), 4.48–4.66 (m, 6H, CH_2Ph), 4.55 (d, 1H, J = 3.4 Hz, 5′-H), 4.62 (m, 1H, 5-H), 4.63 (d, 1H, J = 3.9 Hz, 1′-H), 4.77 (m, 5H, CH_2Ph), 4.84 (d, 1H, J = 10.8 Hz, CH_2Ph), 4.89 (d, 1H, J = 11.0 Hz, CH_2Ph), 4.99 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.12–7.35 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 31.0 (6-C), 39.4 (4-C), 56.0 (OCH_3), 66.9 (CH_2Ph), 69.7 (12-C), 71.3 (11-C), 72.2 (7-C), 73.3 (CH_2Ph), 73.8 (CH_2Ph), 74.0 (5′-C), 74.8 (CH_2Ph), 75.4 (CH_2Ph), 75.7 (CH_2Ph), 76.3 (CH_2Ph), 78.0 (5-C), 78.4 (10-C), 78.6 (4′-C), 79.8 (2′-C), 80.2 (8-C), 82.3 (9-C), 82.3 (3′-C), 98.6 (1′-C), 128.1 (Ar), 128.1 (Ar), 128.3 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.5 (Ar), 128.8 (Ar), 128.9 (Ar), 128.9 (Ar), 138.4 (Ar), 138.4 (Ar), 138.6 (Ar), 138.6 (Ar), 139.1 (Ar), 156.9 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4879.

3.2.6. ((5*R*)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-glucopyranoside (6c)

Colorless syrup; $[\alpha]_D^{25}$ +16.5 (c 1.0, $CHCl_3$); R_f = 0.40 (silica gel, cyclohexane/ dichlormethane/diethyl ether v/v = 3:8:0.5); ^{1}H NMR ($CDCl_3$): δ 1.90 (m, 1H, 6-H), 2.16 (m, 1H, 6-H), 2.65 (dd, 1H, J = 17.0 Hz, J = 9.0 Hz, CH_2, 4-H), 3.01 (dd, 1H, J = 16.7 Hz, J = 10.4 Hz, CH_2, 4-H), 3.36 (s, 3H, OCH_3), 3.50–3.68 (m, 8H, CH), 4.04 (m, 2H, CH, 3′-H, 11-H), 4.48–4.66 (m, 6H, CH_2Ph), 4.57 (d, 1H, J = 3.4 Hz, 5′-H), 4.58 (d, 1H, J = 3.9 Hz, 1′-H), 4.59 (m, 1H, 5-H), 4.77 (m, 5H, CH_2Ph), 4.82 (d, 1H, J = 10.8 Hz, CH_2Ph), 4.87 (d, 1H, J = 11.0 Hz, CH_2Ph), 4.96 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.12–7.45 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 30.3 (6-C), 39.2 (4-C), 56.0 (OCH_3), 67.2 (CH_2Ph), 69.6 (12-C), 71.8 (11-C), 72.2 (7-C), 73.7 (CH_2Ph), 73.8 (CH_2Ph), 73.9 (5′-C), 75.1 (CH_2Ph), 75.4 (CH_2Ph), 75.8 (CH_2Ph), 76.3 (CH_2Ph), 78.1 (5-C), 79.3 (10-C), 79.8 (4′-C), 80.2 (2′-C), 80.2 (8-C), 82.2 (9-C), 82.7 (3′-C), 98.7 (1′-C), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.4 (Ar), 128.9 (Ar), 129.0 (Ar), 129.3 (Ar), 129.3 (Ar), 129.3 (Ar), 138.6 (Ar), 138.6 (Ar), 138.6 (Ar), 139.1 (Ar), 139.2 (Ar), 157.0 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4867.

3.2.7. ((5*S*)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (7a)

Colorless syrup; $[\alpha]_D^{25}$ +47.7 (c 1.0, $CHCl_3$); R_f = 0.38 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.32 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.86 (m, 1H, 6-H), 2.00 (m, 1H, 6-H),

2.92 (dd, 1H, J = 17.4 Hz, J = 7.1 Hz, CH_2, 4-H), 3.55 (dd, 1H, J = 17.4 Hz, J = 10.3 Hz, CH_2, 4-H), 3.72–3.92 (m, 6H, 8-H, 7-H, 10-H, 9-H, 12-H, 12-H), 4.32 (m, 1H, 11-H), 4.52–4.67 (m, 7H, CH_2Ph), 4.66 (d, 1H, J = 3.6 Hz, 2′-H), 4.70–4.80 (m, 3H, CH_2Ph), 4.84 (m, 1H, 5-H), 4.85 (t, 1H, J = 3.8 Hz, 3′-H), 4.95 (d, 1H, J = 3.6 Hz, 4′-H), 5.22 (s, 1H, 1′-H), 7.20–7.44 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.6 (CH_3), 26.4 (CH_3), 36.1 (6-C), 41.7 (4-C), 69.5 (12-C), 69.8 (CH_2Ph), 70.6 (11-C), 72.0 (CH_2Ph), 72.5 (CH_2Ph), 73.9 (CH_2Ph), 74.1 (CH_2Ph), 74.4 (4′-C), 75.4 (7-C), 76.3 (10-C), 76.7 (5-C), 77.2 (8-C), 78.6 (9-C), 82.1 (3′-C), 85.5 (2′-C), 105.9 (1′-C), 113.4 (C, 13-C), 127.9 (Ar), 128.1 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.8 (Ar), 128.8 (Ar), 128.9 (Ar), 137.5 (Ar), 138.6 (Ar), 138.7 (Ar), 138.7 (Ar), 138.9 (Ar), 157.0 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NNaO_{10}$ ([M+Na]$^+$), 878.3880, found: 878.3877

3.2.8. ((5*R*)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (8a)

Colorless syrup; $[\alpha]_D^{25}$ −11.8 (c 1.0, $CHCl_3$); R_f = 0.36 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.90 (m, 1H, 6-H), 2.16 (m, 1H, 6-H), 3.01 (dd, 1H, J = 17.1 Hz, J = 7.9 Hz, CH_2, 4-H), 3.21 (dd, 1H, J = 17.0 Hz, J = 10.2 Hz, CH_2, 4-H), 3.59–4.02 (m, 6H, 8-H, 7-H, 10-H, 9-H, 12-H, 12-H), 4.16 (m, 1H, 11-H), 4.52–4.64 (m, 8H, CH_2Ph), 4.67 (d, 1H, J = 3.6 Hz, 2′-H), 4.73 (m, 2H, CH_2Ph), 4.83 (m, 1H, 5-H), 4.84 (t, 1H, J = 3.6 Hz, 3′-H), 4.98 (d, 1H, J = 3.6 Hz, 4′-H), 5.22 (s, 1H, 1′-H), 7.26–7.41 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.8 (CH_3), 26.3 (CH_3), 35.2 (6-C), 40.6 (4-C), 69.3 (12-C), 69.5 (CH_2Ph), 72.0 (11-C), 72.8 (CH_2Ph), 73.7 (CH_2Ph), 74.3 (CH_2Ph), 74.3 (CH_2Ph), 75.2 (4′-C), 76.3 (7-C), 76.6 (10-C), 76.6 (5-C), 76.7 (8-C), 78.5 (9-C), 82.3 (3′-C), 85.4 (2′-C), 105.8 (1′-C), 113.3 (C, 13-C), 128.0 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.8 (Ar), 128.9 (Ar), 129.0 (Ar), 137.4 (Ar), 138.6 (Ar), 138.7 (Ar), 138.7 (Ar), 138.9 (Ar), 157.1 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NNaO_{10}$ ([M+Na]$^+$), 878.3880, found: 878.3884.

3.2.9. ((5*S*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (7b)

Colorless syrup; $[\alpha]_D^{25}$ +32.4 (c 1.0, $CHCl_3$); R_f = 0.40 (silica gel, cyclohexane/ dichlormethane/ diethyl ether v/v = 3:8:0.5); ^{1}H NMR ($CDCl_3$): δ 1.32 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.69 (m, 1H, 6-H), 1.91 (m, 1H, 6-H), 2.76 (dd, 1H, J = 17.6 Hz, J = 7.5 Hz, CH_2, 4-H), 3.18 (dd, 1H, J = 17.5 Hz, J = 7.2 Hz, CH_2, 4-H), 3.59 (m, 1H, 8-H), 3.74 (m, 3H, 7-H, 12-H, 10-H), 3.81 (m, 2H, 9-H, 12-H), 4.12 (d, 1H, J = 3.4 Hz, 3′-H), 4.20 (m, 1H, 11-H), 4.49 (d, 1H, J = 3.6 Hz, 2′-H), 4.46–4.66 (m, 10H, CH_2Ph), 4.73 (m, 1H, 5-H), 5.12 (d, 1H, J = 3.4 Hz, 4′-H), 5.97 (d, 1H, J = 3.4 Hz, 1′-H), 7.18–7.35 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.7 (CH_3), 27.3 (CH_3), 36.4 (6-C), 44.9 (4-C), 69.6 (12-C), 70.1 (11-C), 72.0 (CH_2Ph), 72.5 (CH_2Ph), 72.9 (CH_2Ph), 73.8 (CH_2Ph), 73.9 (CH_2Ph), 74.4 (7-C), 75.2 (4′-C), 76.7 (10-C), 76.8 (2′-C), 76.8 (5-C), 78.1 (3′-C), 82.8 (8-C), 85.2 (9-C), 105.7 (1′-C), 112.6 (C, 13-C), 127.9 (Ar), 128.1 (Ar), 128.3 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.7 (Ar), 129.0 (Ar), 137.4 (Ar), 138.6 (Ar), 138.6 (Ar), 138.7 (Ar), 138.9 (Ar), 157.7 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3985.

3.2.10. ((5*R*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (8b)

Colorless syrup; $[\alpha]_D^{25}$ −30.5 (c 1.0, $CHCl_3$); R_f = 0.50 (silica gel, cyclohexane/dichlormethane/diethyl ether v/v = 3:8:0.5); ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.63 (m, 1H, 6-H), 2.09 (m, 1H, 6-H), 2.78 (dd, 1H, J = 17.3 Hz, J = 8.7 Hz, CH_2, 4-H), 3.12 (dd, 1H, J = 17.4 Hz, J = 10.4 Hz, CH_2, 4-H), 3.55 (m, 1H, 8-H), 3.72 (m, 3H, 7-H, 12-H, 10-H), 3.82 (m, 2H, 9-H, 12-H), 4.01 (m, 1H, 11-H), 4.12 (d, 1H, J = 3.5 Hz, 3′-H), 4.46 (d, 1H, J = 2.1 Hz, 2′-H), 4.49–4.64 (m, 10H, CH_2Ph), 4.67 (m, 1H, 5-H), 5.10 (d, 1H, J = 3.4 Hz, 4′-H), 5.98 (d, 1H, J = 3.6 Hz, 1′-H), 7.19–7.29 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.7 (CH_3), 27.3 (CH_3), 35.6 (6-C), 41.2 (4-C), 69.3 (12-C), 69.7 (11-C), 71.9 (CH_2Ph), 72.7 (CH_2Ph), 72.8 (CH_2Ph), 73.7 (CH_2Ph), 73.8 (CH_2Ph), 74.2 (7-C), 75.2 (4′-C), 76.5 (10-C), 76.7 (2′ -C), 76.9 (5-C), 78.3 (3′-C), 82.7 (8-C), 85.2 (9-C), 105.6 (1′-C), 112.6 (C, 13-C), 127.9 (Ar), 128.0 (Ar), 128.1 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.7 (Ar), 128.8 (Ar), 128.8 (Ar), 129.0 (Ar), 137.4 (Ar), 138.6 (Ar), 138.6 (Ar), 138.7 (Ar), 138.8 (Ar), 157.4 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NO_{10}$ ([M]$^+$), 855.3982, found: 855.3988.

3.2.11. ((5*S*)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (7c)

White solid, mp: 69–70 °C; $[\alpha]_D^{25}$ +88.4 (c 1.0, $CHCl_3$); R_f = 0.35 (silica gel, cyclohexane/ dichlormethane/ diethyl ether v/v = 3:4:0.5); ^{1}H NMR ($CDCl_3$): δ 1.63 (m, 1H, 6-H), 1.93 (m, 1H, 6-H), 2.53 (d, 2H, J = 3.1 Hz, CH_2, 4-H), 3.37 (s, 3H, OCH_3), 3.45 (t, 1H, J = 9.6 Hz, CH), 3.51 (dd, 1H, J = 9.6 Hz, J = 3.5 Hz, CH), 3.58 (m, 1H, 7-H), 3.71 (m, 3H, CH_2, 12-H, 10-H), 3.77 (m, 2H, CH, 9-H, 2′-H), 4.03 (t, 1H, J = 9.3 Hz, 3′-H), 4.16 (m, 1H, CH, 11-H), 4.46–4.66 (m, 10H, CH_2Ph), 4.48 (d, 1H, J = 3.3 Hz, 5′-H), 4.53 (d, 1H, J = 3.9 Hz, 1′-H), 4.63 (m, 1H, 5-H), 4.77 (m, 2H, CH_2Ph), 4.84 (d, 1H, J = 10.8 Hz, CH_2Ph), 4.98 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.19–7.36 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 36.4 (6-C), 39.6 (4-C), 55.9 (OCH_3), 66.8 (CH_2Ph), 69.5 (12-C), 70.0 (11-C), 71.9 (7-C), 72.5 (CH_2Ph), 73.8 (CH_2Ph), 73.8 (5′-C), 74.4 (CH_2Ph), 74.7 (CH_2Ph), 75.3 (CH_2Ph), 76.2 (CH_2Ph), 76.6 (5-C), 76.6 (10-C), 78.4 (4′-C), 78.5 (2′-C), 78.5 (8-C), 80.1 (9-C), 82.2 (3′-C), 98.6 (1′-C), 127.9 (Ar), 128.0 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.4 (Ar), 128.4 (Ar), 128.4 (Ar), 128.7 (Ar), 128.9 (Ar), 138.3 (Ar), 138.5 (Ar), 138.7 (Ar), 138.8 (Ar), 139.0 (Ar), 156.8 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4864.

3.2.12. ((5*R*)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-mannopyranoside (8c)

Colorless syrup; $[\alpha]_D^{25}$ −4.60 (c 1.0, $CHCl_3$); R_f = 0.42 (silica gel, cyclohexane/dichlormethane/diethyl ether v/v = 3:4:0.5); ^{1}H NMR ($CDCl_3$): δ 1.63 (m, 2H, 6-H), 2.53 (dd, 1H, J = 19.6 Hz, J = 9.4 Hz, CH_2, 4-H), 2.96 (dd, 1H, J = 19.6 Hz, J = 10.4 Hz, CH_2, 4-H), 3.37 (s, 3H, OCH_3), 3.53 (m, 3H, CH, 10-H, 8-H, 7-H), 3.65 (m, 1H, 4′-H), 3.72 (m, 2H, CH_2, 12-H), 3.77 (t, 1H, J = 9.3 Hz, 9-H), 3.86 (m, 1H, CH, 2′-H), 3.98 (m, 1H, CH, 3′-H), 4.22 (m, 1H, CH, 11-H), 4.45–4.67 (m, 10H, CH_2Ph), 4.48 (d, 1H, J = 3.3 Hz, 5′-H), 4.56 (d, 1H, J = 3.9 Hz, 1′-H), 4.58 (m, 1H, 5-H), 4.75 (m, 2H, CH_2Ph), 4.82 (d, 2H, J = 10.8 Hz, CH_2Ph), 4.99 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.18–7.52 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 35.1 (6-C), 39.0 (4-C), 55.9 (OCH_3), 67.1 (CH_2Ph), 69.4 (12-C), 69.4 (11-C), 72.0 (7-C), 72.8 (CH_2Ph), 73.6 (CH_2Ph), 73.8 (5′-C), 74.2 (CH_2Ph), 74.8 (CH_2Ph), 76.3 (CH_2Ph), 76.5 (CH_2Ph), 76.7 (5-C), 78.6 (10-C), 78.7 (4′-C), 79.4 (2′-C), 80.1 (8-C), 80.1 (9-C), 82.3 (3′-C), 98.7 (1′-C), 128.0 (Ar), 128.0 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.4 (Ar), 128.4 (Ar), 128.5 (Ar), 128.8 (Ar), 128.9 (Ar), 138.5 (Ar), 138.6 (Ar), 138.7 (Ar), 138.8 (Ar), 139.1 (Ar), 157.1 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4868.

3.2.13. ((5*S*)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (9a)

Colorless syrup; $[\alpha]_D^{25}$ +68.7 (c 1.0, $CHCl_3$); R_f = 0.30 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.26 (s, 3H, CH_3), 1.42(s, 3H, CH_3), 1.86 (m, 2H, 6-H), 2.82 (dd, 1H,

J = 17.4 Hz, J = 7.3 Hz, CH_2, 4-H), 3.28 (dd, 1H, J = 17.2 Hz, J = 10.3 Hz, CH_2, 4-H), 3.71 (m, 3H, CH, 8-H, 7-H, 10-H), 3.94 (m, 2H, 9-H, 12-H), 4.09 (m, 1H, 12-H), 4. 25 (m, 1H, 11-H), 4.45–4.75 (m, 10H, CH_2Ph), 4.67 (d, 1H, J = 3.6 Hz, 2′-H), 4.79 (m, 1H, 5-H), 4.80 (t, 1H, J = 3.8 Hz, 4′-H), 4.90 (d, 1H, J = 3.6 Hz, 3′-H), 5.15 (s, 1H, 1′-H), 7.19–7.31 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.9 (CH_3), 26.4 (CH_3), 34.4 (6-C), 41.7 (4-C), 67.8 (12-C), 68.3 (CH_2Ph), 69.5 (11-C), 73.2 (CH_2Ph), 73.5 (CH_2Ph), 73.5 (CH_2Ph), 73.7 (CH_2Ph), 73.9 (4′-C), 74.6 (7-C), 76.3 (10-C), 77.5 (5-C), 77.6 (8-C), 78.6 (9-C), 82.1 (3′-C), 85.52 (2′-C), 105.8 (1′-C), 113.3 (C, 13-C), 128.0 (Ar), 128.0 (Ar), 128.2 (Ar), 128.2 (Ar), 128.3 (Ar), 128.4 (Ar), 128.5 (Ar), 128.8 (Ar), 128.9 (Ar), 128.9 (Ar), 137.5 (Ar), 138.6 (Ar), 138.9 (Ar), 138.9 (Ar), 138.9 (Ar), 157.1 (C=N); HRMS(ESI): calcd for $C_{52}H_{58}NO_{10}$ ([M+H]$^+$), 856.4061, found: 856.4057

3.2.14. ((5*R*)-3-(Benzyl 2,3-*O*-isopropylidene-4-*C*-5-deoxy-D-lyxofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (10a)

Colorless syrup; $[\alpha]_D^{25}$ +6.80 (c 1.0, $CHCl_3$); R_f = 0.29 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.21 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.80 (m, 1H, 6-H), 2.18 (m, 1H, 6-H), 2.89 (dd, 1H, J = 16.9 Hz, J = 8.1 Hz, CH_2, 4-H), 3.10 (dd, 1H, J = 16.9 Hz, J = 10.1 Hz, CH_2, 4-H), 3.65 (m, 1H, 7-H), 3.73 (dd, 1H, 8-H), 3.81 (m, 2H, 10-H, 12-H), 4.01 (m, 2H, 9-H, 12-H), 4.12 (m, 1H, 11-H), 4.45–4.78 (m, 10H, CH_2Ph), 4.62 (d, 1H, J = 3.1 Hz, 2′-H), 4.78 (m, 1H, 5-H), 4.79 (t, 1H, J = 3.8 Hz, 3′-H), 4.90 (d, 1H, J = 3.6 Hz, 4′-H), 5.15 (s, 1H, 1′-H), 7.21–7.34 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 24.7 (CH_3), 26.2 (CH_3), 32.5 (6-C), 40.6 (4-C), 67.9 (12-C), 69.5 (CH_2Ph), 72.1 (11-C), 72.3 (CH_2Ph), 72.9 (CH_2Ph), 73.4 (CH_2Ph), 73.7 (CH_2Ph), 74.7 (4′-C), 76.2 (7-C), 76.7 (10-C), 78.4 (5-C), 78.9 (8-C), 79.6 (9-C), 82.2 (3′-C), 85.4 (2′-C), 105.7 (1′-C), 113.2 (C, 13-C), 128.0 (Ar), 128.1 (Ar), 128.3 (Ar), 128.3 (Ar), 128.5 (Ar), 128.7 (Ar), 128.7 (Ar), 128.8 (Ar), 128.8 (Ar), 128.9 (Ar), 137.4 (Ar), 138.5 (Ar), 138.7 (Ar), 138.7 (Ar), 138.9 (Ar), 156.9 (C=N); HRMS(ESI): calcd for $C_{52}H_{58}NO_{10}$ ([M+H]$^+$), 856.4061, found: 856.4056.

3.2.15. ((5*S*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (9b)

Colorless syrup; $[\alpha]_D^{25}$ +59.8 (c 1.0, $CHCl_3$); R_f = 0.28 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.80 (m, 2H, 6-H), 2.77 (dd, 1H, J = 17.6 Hz, J = 7.3 Hz, CH_2, 4-H), 3.18 (dd, 1H, J = 17.5 Hz, J = 10.4 Hz, CH_2, 4-H), 3.65 (s, 1H, 8-H, 10-H), 3.70 (dd, 1H, J = 10.8 Hz, J = 3.6 Hz, 12-H), 3.95 (m, 2H, 7-H, 9-H), 4.08 (m, 1H, 12-H), 4.10 (d, 1H, J = 3.4 Hz, 3′-H), 4.23 (m, 1H, 11-H), 4.46 (d, 1H, J = 3.6 Hz, 2′-H), 4.45–4.73 (m, 10H, CH_2Ph), 4.75 (m, 1H, 5-H), 5.11 (d, 1H, J = 3.3 Hz, 4′-H), 5.97 (d, 1H, J = 3.4 Hz, 1′-H), 7.19–7.30 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.8 (CH_3), 27.3 (CH_3), 34.7 (6-C), 41.9 (4-C), 67.7 (12-C), 67.9 (11-C), 72.8 (CH_2Ph), 73.1 (CH_2Ph), 73.1 (CH_2Ph), 73.5 (CH_2Ph), 73.5 (CH_2Ph), 73.8 (7-C), 74.5 (4′-C), 76.1 (10-C), 76.8 (5-C), 77.4 (2′-C), 78.3 (3′-C), 82.8 (8-C), 85.1 (9-C), 105.7 (1′-C), 112.6 (C, 13-C), 128.0 (Ar), 128.0 (Ar), 128.0 (Ar), 128.2 (Ar), 128.2 (Ar), 128.5 (Ar), 128.8 (Ar), 128.8 (Ar), 128.8 (Ar), 129.1 (Ar), 137.4 (Ar), 138.5 (Ar), 138.9 (Ar), 138.9 (Ar), 139.0 (Ar), 157.7 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NNaO_{10}$ ([M+Na]$^+$), 878.3880, found: 878.3875.

3.2.16. ((5*R*)-3-(1,2-*O*-Isopropylidene-3-benzyl-4-*C*-5-deoxy-D-xylofuranosidyl)isoxazoline-5- yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (10b)

Colorless syrup; $[\alpha]_D^{25}$ −22.3 (c 1.0, $CHCl_3$); R_f = 0.26 (silica gel, cyclohexane/ethyl acetate v/v = 3:1); ^{1}H NMR ($CDCl_3$): δ 1.32 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.71 (m, 1H, 6-H), 2.13 (m, 1H, 6-H), 2.74 (dd, 1H, J = 17.4 Hz, J = 9.1 Hz, CH_2, 4-H), 3.06 (dd, 1H, J = 17.3 Hz, J = 10.4 Hz, CH_2, 4-H), 3.64 (dd, 1H, J = 10.1 Hz, J = 5.5 Hz, 8-H), 3.71 (m, 2H, J = 10.8 Hz, J = 3.6 Hz, 10-H, 7-H), 3.79 (m, 1H, 12-H), 3.98 (m, 3H, 9-H, 12-H, 11-H), 4.10 (d, 1H, J = 3.4 Hz, 3′-H), 4.48 (d, 1H, J = 3.5 Hz, 2′-H), 4.38–4.72 (m, 10H, CH_2Ph), 4.69 (m, 1H, 5-H), 5.09 (d, 1H, J = 3.3 Hz, 4′-H), 5.98 (d, 1H, J = 3.6 Hz, 1′-H), 7.18–7.32 (m, 25H, Ar); ^{13}C NMR ($CDCl_3$): δ 26.7 (CH_3), 27.3 (CH_3), 33.1 (6-C), 41.2 (4-C), 67.8 (12-C), 68.9 (11-C), 72.7 (CH_2Ph), 72.8 (CH_2Ph), 73.3 (CH_2Ph), 73.3 (CH_2Ph), 73.7 (CH_2Ph), 73.7 (7-C), 74.6 (4′-C), 76.5 (10-C), 76.9 (5-C), 77.4 (2′-C), 78.8 (3′-C), 82.6 (8-C), 85.0 (9-C), 105.6 (1′-C), 112.6 (C, 13-C), 127.3 (Ar), 128.0 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.5 (Ar), 128.7 (Ar), 128.8 (Ar), 129.0 (Ar), 137.4 (Ar), 138.5 (Ar), 138.7 (Ar), 138.9 (Ar), 138.9 (Ar), 157.4 (C=N); HRMS(ESI): calcd for $C_{52}H_{57}NNaO_{10}$ ([M+Na]$^+$), 878.3880, found: 878.3876

3.2.17. ((5*S*)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (9c)

Colorless syrup; $[\alpha]_D^{25}$ +77.1 (c 1.0, $CHCl_3$); R_f = 0.45 (silica gel, cyclohexane/dichlormethane/diethyl ether v/v = 3:10:0.5); ^{1}H NMR ($CDCl_3$): δ 1.75 (m, 2H, 6-H), 2.53 (d, 2H, J = 8.8 Hz, CH_2, 4-H), 3.35 (s, 3H, OCH_3), 3.46 (t, 1H, J = 9.6 Hz, CH), 3.50 (dd, 1H, J = 9.6 Hz, J = 3.4 Hz, CH), 3.68 (m, 3H, CH, CH_2, 4′-H, 7-H, 12-H), 3.90 (m, 2H, CH, CH_2, 12-H, 9-H), 4.04 (m, 2H, CH, 2′-H, 11-H), 4.05 (t, 1H, J = 9.2 Hz, 3′-H), 4.20 (m, 1H, CH, 11-H), 4.42–4.67 (m, 10H, CH_2Ph), 4.50 (d, 1H, J = 3.5 Hz, 5′-H), 4.55 (d, 1H, J = 3.3 Hz, 1′-H), 4.63 (m, 1H, 5-H), 4.79 (d, 1H, J = 11.1 Hz, CH_2Ph), 4.84 (d, 1H, J = 12.1 Hz, CH_2Ph), 4.86 (d, 1H, J = 11.0 Hz, CH_2Ph), 4.98 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.20–7.39 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 27.3 (6-C), 39.6 (4-C), 55.9 (OCH_3), 66.9 (CH_2Ph), 67.6 (12-C), 68.0 (11-C), 70.9 (7-C), 73.0 (CH_2Ph), 73.4 (CH_2Ph), 73.8 (5′-C), 73.8 (CH_2Ph), 73.8 (CH_2Ph), 74.4 (CH_2Ph), 74.7 (CH_2Ph), 76.0 (5-C), 76.3 (10-C), 78.5 (4′-C), 78.5 (2′-C), 80.1 (8-C), 82.2 (9-C), 82.2 (3′-C), 98.6 (1′-C), 127.9 (Ar), 128.1 (Ar), 128.2 (Ar), 128.4 (Ar), 128.4 (Ar), 128.5 (Ar), 128.5 (Ar), 128.7 (Ar), 128.9 (Ar), 129.1 (Ar), 138.2 (Ar), 138.4 (Ar), 138.8 (Ar), 138.8 (Ar), 139.0 (Ar), 156.9 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4863.

3.2.18. ((5*R*)-3-(Methyl 2,3,4-tri-*O*-benzyl-5-*C*-6-deoxy-α-D-glucopyranosidyl)isoxazoline-5-yl) methyl 2,3,4,6-tetra-*O*-benzyl-α-*C*-D-galactopyranoside (10c)

Colorless syrup; $[\alpha]_D^{25}$ +6.00 (c 1.0, $CHCl_3$); R_f = 0.50 (silica gel, cyclohexane/ dichlormethane/ diethyl ether v/v = 3:10:0.5); ^{1}H NMR ($CDCl_3$): δ 1.68 (m, 1H, 6-H), 2.15 (m, 1H, 6-H), 2.43 (dd, 1H, J = 16.9 Hz, J = 9.5 Hz, CH_2, 4-H), 2.92 (dd, 1H, J = 16.9 Hz, J = 9.5 Hz, CH_2, 4-H), 3.37 (s, 3H, OCH_3), 3.49 (m, 2H, CH, 10-H, 8-H), 3.60 (dd, 1H, J = 10.1 Hz, J = 4.7 Hz, CH, 4′-H), 3.65 (dd, 1H, J = 7.2 Hz, J = 2.2 Hz, CH, 7-H), 3.74 (m, 2H, CH_2, 12-H), 3.97 (dd, 2H, J = 10.7 Hz, J = 4.1 Hz, CH, 2′-H, 9-H), 4.02 (m, 2H, CH, 3′-H, 11-H), 4.40–4.74 (m, 11H, CH_2Ph), 4.48 (d, 1H, J = 3.5 Hz, 5′-H), 4.58 (m, 1H, 5-H), 4.59 (d, 1H, J = 3.4 Hz, 1′-H), 4.75 (d, 1H, J = 11.1 Hz, CH_2Ph), 4.82 (d, 1H, J = 10.8 Hz, CH_2Ph), 4.97 (d, 1H, J = 10.8 Hz, CH_2Ph), 7.20–7.39 (m, 35H, Ar); ^{13}C NMR ($CDCl_3$): δ 27.3 (6-C), 39.1 (4-C), 55.9 (OCH_3), 67.0 (CH_2Ph), 68.0 (12-C), 69.2 (11-C), 72.6 (7-C), 73.3 (CH_2Ph), 73.6 (CH_2Ph), 73.6 (5′-C), 73.8 (CH_2Ph), 73.8 (CH_2Ph), 74.7 (CH_2Ph), 74.9 (CH_2Ph), 76.2 (5-C), 76.7 (10-C), 79.2 (4′-C), 79.4 (2′-C), 80.0 (8-C), 82.1 (9-C), 82.1 (3′-C), 98.6 (1′-C), 127.9 (Ar), 128.0 (Ar), 128.1 (Ar), 128.2 (Ar), 128.3 (Ar), 128.3 (Ar), 128.5 (Ar), 128.7 (Ar), 128.8 (Ar), 128.9 (Ar), 138.4 (Ar), 138.5 (Ar), 138.6 (Ar), 138.9 (Ar), 139.1 (Ar), 156.9 (C=N); HRMS(ESI): calcd for $C_{65}H_{69}NO_{11}$ ([M]$^+$), 1039.4871, found: 1039.4866.

3.3. General procedure for the synthesis of compounds 12–17

To a solution of the cycloadduct (**5a**) (171 mg, 0.2 mmol) in MeOH (6 mL) was added a catalytic amount of $Pd(OH)_2/C$. The mixture was stirred under H_2 atmosphere for 2 h. The catalyst was filtered off, and the solvent was removed by evaporation. The residue was applied on silica gel column chromatography with the eluent of MeOH/ethyl acetate (v/v = 1:9) to afford the corresponding debenzylated product **12a** (64 mg, 79%). Under the same condition, the debenzylation of the cycloadducts **5**–**10** was carried out to afford the corresponding debenzylated products **12**–**17**.

3.3.1. ((5*S*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-glucopyranoside (12a)

White solid, mp: 90–91 °C; Yield: 79%; $[\alpha]_D^{25}$ +69.9 (*c* 1.0, H_2O); ^1H NMR (CD_3OD): δ 1.29 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.90 (m, 2H, 6-H), 2.87 (dd, 1H, *J* = 17.3 Hz, *J* = 6.2 Hz, CH_2, 4-H), 3.30 (m, 3H, 4-H, 2CH), 3.45 (m, 2H, CH), 3.58 (m, 2H, CH), 3.79 (dd, 1H, *J* = 11.7 Hz, *J* = 2.2 Hz, CH), 4.12 (m, 1H, CH), 4.60 (d, 1H, *J* = 5.4 Hz, 2′-H), 4.80 (m, 1H, 5-H), 4.94 (m, 2H, 3′-H, 4′-H), 5.44 (s, 1H, 1′-H); ^{13}C NMR (CD_3OD): δ 23.8 (CH_3), 25.3 (CH_3), 29.9 (CH_2, 6-C), 41.0 (CH_2, 4-C), 62.1 (CH_2, 12-C), 71.2 (CH, 8-C), 71.5 (CH, 10-C), 73.1 (CH, 4′-C), 73.8 (CH, 7-C), 74.1 (CH, 9-C), 76.1 (CH, 5-C), 77.7 (CH, 11-C), 81.8 (CH, 3′-C), 86.1 (CH, 2′-C), 101.3 (CH, 1′-C), 113.1 (C, 13-C), 157.6 (C═N); HRMS(ESI): calcd for $C_{17}H_{28}NO_{10}$ ($[M+H]^+$), 406.1713, found: 406.1708.

3.3.2. ((5*R*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-glucopyranoside (13a)

White solid, mp: 84–86 °C; Yield: 80%; $[\alpha]_D^{25}$ −41.4 (*c* 1.0, H_2O); ^1H NMR (CD_3OD): δ 1.32 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.88 (m, 1H, 6-H), 2.14 (m, 1H, 6-H), 2.95 (dd, 1H, *J* = 17.2 Hz, *J* = 7.9 Hz, CH_2, 4-H), 3.19 (dd, 1H, *J* = 17.1 Hz, *J* = 10.1 Hz, CH_2, 4-H), 3.26 (m, 1H, CH), 3.52 (m, 2H, CH), 3.60 (m, 2H, CH), 3.79 (dd, 1H, *J* = 11.7 Hz, *J* = 2.2 Hz, CH), 4.01 (m, 1H, CH), 4.59 (d, 1H, *J* = 6.4 Hz, 2′-H), 4.76 (m, 1H, 5-H), 4.88 (t, 1H, *J* = 6.4 Hz, 3′-H), 4.94 (d, 1H, *J* = 3.7 Hz, 4′-H), 5.31 (s, 1H, 1′-H); ^{13}C NMR (CD_3OD): δ 23.6 (CH_3), 25.3 (CH_3), 30.2 (CH_2, 6-C), 40.4 (CH_2, 4-C), 62.0 (CH_2, 12-C), 71.2 (CH, 8-C), 71.7 (CH, 10-C), 73.5 (CH, 4′-C), 74.1 (CH, 7-C), 74.2 (CH, 9-C), 76.0 (CH, 5-C), 79.1 (CH, 11-C), 82.2 (CH, 3′-C), 86.1 (CH, 2′-C), 101.4 (CH, 1′-C), 113.0 (C, 13-C), 157.7 (C═N); HRMS(ESI): calcd for $C_{17}H_{28}NO_{10}$ ($[M+H]^+$), 406.1713, found: 406.1710.

3.3.3. ((5*S*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-glucopyranoside (12b)

White solid, mp: 78–80 °C; Yield: 80%; $[\alpha]_D^{25}$ +90.3 (*c* 1.0, H_2O); ^1H NMR (CD_3OD): δ 1.33 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.98 (m, 2H, 6-H), 2.87 (dd, 1H, *J* = 17.5 Hz, *J* = 7.2 Hz, CH_2, 4-H), 3.30 (m, 2H, CH, 4-H, 10-H), 3.46 (m, 2H, 9-H, 12-H), 3.63 (m, 2H, 7-H, 12-H), 3.81 (dd, 1H, *J* = 9.8 Hz, *J* = 1.9 Hz, 8-H), 4.10 (m, 1H, 11-H), 4.27 (d, 1H, *J* = 2.8 Hz, 3′-H), 4.56 (d, 1H, *J* = 3.5 Hz, 2′-H), 4.80 (m, 1H, 5-H), 4.94 (d, 1H, *J* = 2.8 Hz, 4′-H), 5.99 (d, 1H, *J* = 3.5 Hz, 1′-H); ^{13}C NMR (CD_3OD): δ 25.4 (CH_3), 26.2 (CH_3), 30.0 (CH_2, 6-C), 41.0 (CH_2, 4-C), 62.1 (CH_2, 12-C), 71.2 (CH, 8-C), 71.5 (CH, 9-C), 73.1 (CH, 7-C), 73.9 (CH, 10-C), 74.0 (CH, 4′-C), 76.8 (CH, 3′-C), 77.3 (CH, 11-C), 77.7 (CH, 5-C), 85.6 (CH, 2′-C), 105.4 (CH, 1′-C), 112.1 (C, 13-C), 158.1 (C═N); HRMS(ESI): calcd for $C_{17}H_{28}NO_{10}$ ($[M+H]^+$), 406.1713, found: 406.1709.

3.3.4. ((5*R*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-glucopyranoside (13b)

White solid, mp: 67–69 °C; Yield: 90%; $[\alpha]_D^{25}$ −25.7 (*c* 1.0, H_2O); ^1H NMR (CD_3OD): δ 1.33 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.98 (m, 2H, 6-H), 2.87 (dd, 1H, *J* = 17.5 Hz, *J* = 7.2 Hz, CH_2, 4-H), 3.30 (m, 2H, CH, 4-H, 10-H), 3.46 (m, 2H, 9-H, 12-H), 3.63 (m, 2H, 7-H, 12-H), 3.81 (dd, 1H, *J* = 9.8 Hz, *J* = 1.9 Hz, 8-H), 4.10 (m, 1H, 11-H), 4.27 (d, 1H, *J* = 2.8 Hz, 3′-H), 4.56 (d, 1H, *J* = 3.5 Hz, 2′-H), 4.75 (m, 1H, 5-H), 4.94 (d, 1H, *J* = 2.8 Hz, 4′-H), 5.99 (d, 1H, *J* = 3.5 Hz, 1′-H); ^{13}C NMR (CD_3OD): δ 25.4 (CH_3), 26.1 (CH_3), 30.1 (CH_2, 6-C), 40.4 (CH_2, 4-C), 62.0 (CH_2, 12-C), 71.2 (CH, 8-C), 71.7 (CH, 9-C), 73.5 (CH, 7-C), 74.1 (CH, 10-C), 74.1 (CH, 4′-C), 76.9 (CH, 3′-C), 77.4 (CH, 11-C), 79.1 (CH, 5-C), 85.6 (CH, 2′-C), 105.4 (CH, 1′-C), 112.1 (C, 13-C), 158.0 (C═N); HRMS(ESI): calcd for $C_{17}H_{28}NO_{10}$ ($[M+H]^+$), 406.1713, found: 406.1716.

3.3.5. ((5*S*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D-glucopyranoside (12c)

White solid, mp: 103–105 °C; Yield: 80%; $[\alpha]_D^{25}$ +108 (*c* 1.0, H_2O); ^1H NMR (D_2O): δ 1.95 (m, 2H, 6-H), 2.84 (dd, 1H, *J* = 17.2 Hz, *J* = 7.1 Hz, CH_2, 4-H), 3.26 (dd, 1H, CH_2, *J* = 16.7 Hz, *J* = 7.3 Hz, 4-H), 3.30 (s, 3H, OCH_3), 3.43 (m, 2H, 10-H, 9-H), 3.52 (m, 2H, 7-H, 12-H), 3.57 (m, 2H, 11-H, 12-H), 3.67 (dd, 1H, *J* = 9.3 Hz, *J* = 3.2 Hz, 2′-H), 3.73 (m, 1H, 8-H), 3.76 (d, 1H, *J* = 1.9 Hz, 3′-H), 4.00 (d, 1H, *J* = 10.5 Hz, 4′-H), 4.32 (d, 1H, *J* = 10.5 Hz, 5′-H), 4.73 (d, 1H, *J* = 3.5 Hz, 1′-H), 4.78 (m, 1H, 5-H); ^{13}C NMR (D_2O): δ 33.3 (CH_2, 6-C), 39.2 (CH_2, 4-C), 55.9 (OCH_3), 61.7 (CH_2, 12-C), 67.4 (CH, 8-C), 67.8 (CH, 4′-C), 71.1 (CH, 2′-C), 71.4 (CH, 5′-C), 71.5 (9-CH), 72.0 (CH, 7-C), 73.2 (CH, 3′-C), 74.5 (CH, 10-C), 75.6 (CH, 11-C), 77.8 (CH, 5-C), 100.3 (CH, 1′-C), 159.6 (C═N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ($[M+Na]^+$), 432.1482, found: 432.1479.

3.3.6. ((5*R*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D- glucopyranoside (13c)

White solid, mp: 140 °C (decomposed); Yield: 86%; $[\alpha]_D^{25}$ +38.7 (*c* 1.0, H_2O); ^1H NMR (D_2O): δ 1.93 (m, 1H, 6-H), 2.16 (m, 1H, 6-H), 2.92 (dd, 1H, *J* = 17.2 Hz, *J* = 8.4 Hz, CH_2, 4-H), 3.18 (dd, 1H, CH_2, *J* = 17.0 Hz, *J* = 10.3 Hz, 4-H), 3.34 (s, 3H, OCH_3), 3.46–3.53 (m, 5H, 10-H, 8-H, 7-H, 4′-H, 12-H), 3.63 (m, 3H, 12-H, 9-H, 2′-H), 3.81 (d, 1H, *J* = 10.0 Hz, 3′-H), 4.10 (d, 1H, *J* = 10.5 Hz, 11-H), 4.33 (d, 1H, *J* = 9.9 Hz, 5′-H), 4.71 (d, 1H, *J* = 3.5 Hz, 1′-H), 4.80 (m, 1H, 5-H); ^{13}C NMR (D_2O): δ 29.8 (CH_2, 6-C), 37.9 (CH_2, 4-C), 54.9 (OCH_3), 61.9 (CH_2, 12-C), 67.8 (CH, 8-C), 71.2 (CH, 4′-C), 71.6 (CH, 2′-C), 71.8 (CH, 5′-C), 72.3 (9-CH), 73.5 (CH, 7-C), 73.6 (CH, 3′-C), 74.0 (CH, 10-C), 74.2 (CH, 11-C), 79.6 (CH, 5-C), 100.6 (CH, 1′-C), 158.1 (C═N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ($[M+Na]^+$), 432.1482, found: 432.1478.

3.3.7. ((5*S*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-mannopyranoside (14a)

White solid, mp: 116–117 °C; Yield: 93%; $[\alpha]_D^{25}$ +80.0 (*c* 1.0, H_2O); ^1H NMR (CD_3OD): δ 1.25 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.70 (m, 1H, 6-H), 1.97 (m, 1H, 6-H), 2.78 (dd, 1H, *J* = 17.5 Hz, *J* = 5.9 Hz, CH_2, 4-H), 3.21 (dd, 1H, *J* = 17.5 Hz, *J* = 10.0 Hz, CH_2, 4-H), 3.45 (m, 1H, CH), 3.54 (t, 1H, *J* = 9.2 Hz, CH), 3.64 (m, 2H, CH), 3.74 (m, 2H, CH), 4.00 (d, 1H, *J* = 9.2 Hz, CH), 4.69 (d, 1H, *J* = 5.4 Hz, 2′-H), 4.76 (m, 1H, 5-H), 4.97 (d, 1H, *J* = 3.8 Hz, 4′-H), 5.09 (t, 1H, *J* = 5.4 Hz, 3′-H, 4′-H), 5.38 (s, 1H, 1′-H); ^{13}C NMR (CD_3OD): δ 24.1 (CH_3), 25.3 (CH_3), 33.0 (CH_2, 6-C), 41.1 (CH_2, 4-C), 61.6 (CH_2, 12-C), 67.7 (CH, 8-C), 71.1 (CH, 10-C), 72.0 (CH, 4′-C), 74.4 (CH, 7-C), 75.6 (CH, 9-C), 76.7 (CH, 5-C), 78.2 (CH, 11-C), 80.8 (CH, 3′-C), 85.3 (CH, 2′-C), 100.5 (CH, 1′-C), 114.1 (C, 13-C), 158.5 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ($[M]^+$), 405.1635, found: 405.1631.

3.3.8. ((5*R*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-mannopyranoside (15a)

White solid, mp: 72–74 °C; Yield: 76%; $[\alpha]_D^{25}$ −49.2 (*c* 1.0, H_2O); ^1H NMR (D_2O): δ 1.29 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.73 (m, 1H, 6-H), 2.18 (m, 1H, 6-H), 2.98 (dd, 1H, *J* = 17.3 Hz, *J* = 7.7 Hz, CH_2, 4-H), 3.20 (dd, 1H, *J* = 17.2 Hz, *J* = 10.1 Hz, CH_2, 4-H), 3.49 (m, 1H, CH), 3.62 (t, 1H, *J* = 8.2 Hz, CH), 3.68 (dd, 1H, *J* = 8.3 Hz, *J* = 2.9 Hz, CH),

3.72 (t, 1H, J = 5.6 Hz, CH), 3.74 (s, 1H, CH), 3.79 (dd, 1H, J = 11.7 Hz, J = 2.7 Hz, CH), 3.96 (m, 1H, CH), 4.59 (d, 1H, J = 5.7 Hz, 2′-H), 4.74 (m, 1H, 5-H), 4.90 (t, 1H, J = 5.6 Hz, 3′-H), 4.94 (d, 1H, J = 3.7 Hz, 4′-H), 5.32 (s, 1H, 1′-H); ^{13}C NMR (D_2O): δ 23.6 (CH_3), 25.3 (CH_3), 33.7 (CH_2, 6-C), 40.3 (CH_2, 4-C), 61.9 (CH_2, 12-C), 68.4 (CH, 8-C), 71.6 (CH, 10-C), 71.7 (CH, 4′-C), 74.4 (CH, 7-C), 75.5 (CH, 9-C), 75.9 (CH, 5-C), 78.6 (CH, 11-C), 82.2 (CH, 3′-C), 86.1 (CH, 2′-C), 101.4 (CH, 1′-C), 113.0 (C, 13-C), 157.8 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1637.

3.3.9. ((5*S*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-mannopyranoside (14b)

White solid, mp: 102–105 °C; Yield: 80%; $[\alpha]_D^{25}$ +33.3 (c 1.0, H_2O); ^{1}H NMR (CD_3OD): δ 1.33 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.80 (m, 1H, 6-H), 2.00 (m, 1H, 6-H), 2.85 (dd, 1H, J = 17.5 Hz, J = 6.9 Hz, CH_2, 4-H), 3.32 (m, 1H, CH_2, 4-H), 3.49 (m, 1H, 10-H), 3.65 (m, 2H, 9-H, 12-H), 3.78 (m, 3H, 7-H, 12-H), 4.10 (d, 1H, J = 10.2 Hz, 11-H), 4.26 (d, 1H, J = 2.4 Hz, 3′-H), 4.56 (d, 1H, J = 3.3 Hz, 2′-H), 4.82 (m, 1H, 5-H), 4.95 (d, 1H, J = 2.4 Hz, 4′-H), 5.99 (d, 1H, J = 3.3 Hz, 1′-H); ^{13}C NMR (CD_3OD): δ 25.3 (CH_3), 26.1 (CH_3), 34.4 (CH_2, 6-C), 41.0 (CH_2, 4-C), 62.0 (CH_2, 12-C), 68.4 (CH, 8-C), 71.6 (CH, 9-C), 72.0 (CH, 7-C), 74.5 (CH, 10-C), 75.4 (CH, 4′-C), 76.8 (CH, 3′-C), 77.3 (CH, 11-C), 77.8 (CH, 5-C), 85.6 (CH, 2′-C), 105.4 (CH, 1′-C), 112.1 (C, 13-C), 158.1 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1631.

3.3.10. ((5*R*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-mannopyranoside (15b)

White solid, mp: 72–74 °C; Yield: 74%; $[\alpha]_D^{25}$ −37.7 (c 1.0, H_2O); ^{1}H NMR (D_2O): δ 1.28 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.73 (m, 1H, 6-H), 2.16 (m, 1H, 6-H), 2.88 (dd, 1H, J = 17.5 Hz, J = 7.8 Hz, CH_2, 4-H), 3.21 (dd, 1H, J = 17.5 Hz, J = 10.4 Hz, CH_2, 4-H), 3.50 (m, 1H, 10-H), 3.57 (t, 1H, J = 9.3 Hz, 9-H), 3.64 (dd, 1H, J = 12.2 Hz, J = 5.6 Hz, 12-H), 3.75 (m, 3H, 7-H, 12-H), 3.96 (d, 1H, J = 5.7 Hz, 11-H), 4.38 (S, 1H, 3′-H), 4.68 (S, 1H, 2′-H), 4.75(m, 1H, 5-H), 4.99 (S, 1H, 4′-H), 6.03 (d, 1H, J = 3.0 Hz, 1′-H); ^{13}C NMR (D_2O): δ 25.5 (CH_3), 26.1 (CH_3), 32.7 (CH_2, 6-C), 40.6 (CH_2, 4-C), 61.6 (CH_2, 12-C), 67.7 (CH, 8-C), 71.1 (CH, 9-C), 71.7 (CH, 7-C), 74.5 (CH, 10-C), 75.5 (CH, 4′-C), 75.9 (CH, 3′-C), 77.8 (CH, 11-C), 79.2 (CH, 5-C), 84.8 (CH, 2′-C), 105.0 (CH, 1′-C), 113.4 (C, 13-C), 158.3 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1632.

3.3.11. ((5*S*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D- mannopyranoside (14c)

White solid, mp: 115–118 °C; Yield: 80%; $[\alpha]_D^{25}$ +84.4 (c 1.0, H_2O); ^{1}H NMR (CD_3OD): δ 1.72 (m, 1H, 6-H), 2.00 (m, 1H, 6-H), 2.79 (dd, 1H, J = 17.8 Hz, J = 6.8 Hz, CH_2, 4-H), 3.19 (dd, 1H, CH_2, J = 17.6 Hz, J = 7.3 Hz, 4-H), 3.30 (s, 3H, OCH_3), 3.43 (m, 2H, 10-H, 9-H), 3.52 (m, 2H, 7-H, 12-H), 3.57 (m, 2H, 11-H, 12-H), 3.67 (dd, 1H, J = 9.3 Hz, J = 3.2 Hz, 2′-H), 3.73 (m, 1H, 8-H), 3.76 (d, 1H, J = 1.9 Hz, 3′-H), 4.00 (d, 1H, J = 10.5 Hz, 4′-H), 4.32 (d, 1H, J = 10.5 Hz, 5′-H), 4.73 (d, 1H, J = 3.5 Hz, 1′-H), 4.76 (m, 1H, 5-H); ^{13}C NMR (CD_3OD): δ 33.3 (CH_2, 6-C), 39.2 (CH_2, 4-C), 55.9 (OCH_3), 61.7 (CH_2, 12-C), 67.4 (CH, 8-C), 67.8 (CH, 4′-C), 71.1 (CH, 2′-C), 71.4 (CH, 5′-C), 71.5 (9-CH), 72.0 (CH, 7-C), 73.2 (CH, 3′-C), 74.5 (CH, 10-C), 75.6 (CH, 11-C), 78.5 (CH, 5-C), 100.3 (CH, 1′-C), 159.6 (C═N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ([M+Na]$^+$), 432.1482, found: 432.1479.

3.3.12. ((5*R*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D- mannopyranoside (15c)

White solid, mp: 137 °C (decomposed); Yield: 87%; $[\alpha]_D^{25}$ +18.6 (c 1.0, H_2O); ^{1}H NMR (CD_3OD): δ 1.82 (m, 1H, 6-H), 2.24 (m, 1H, 6-H), 2.98 (dd, 1H, J = 17.2 Hz, J = 8.3 Hz, CH_2, 4-H), 3.19 (dd, 1H, CH_2, J = 17.2 Hz, J = 6.6 Hz, 4-H), 3.43 (s, 3H, OCH_3), (m, 2H, 10-H, 9-H), 3.52 (m, 2H, 7-H, 12-H), 3.56 (m, 1H, 12-H), 3.68 (m, 2H, 11-H, 2′-H), 3.81 (m, 2H, 8-H, 3′-H), 4.09 (m, 1H, 4′-H), 4.36 (d, 1H, J = 10.5 Hz, 5′-H), 4.73 (d, 1H, J = 3.5 Hz, 1′-H), 4.83 (m, 1H, 5-H); ^{13}C NMR (CD_3OD): δ 33.3 (CH_2, 6-C), 37.8 (CH_2, 4-C), 54.9 (OCH_3), 61.5 (CH_2, 12-C), 67.8 (CH, 8-C), 68.2 (CH, 4′-C), 71.5 (CH, 2′-C), 71.8 (CH, 5′-C), 71.8 (9-CH), 72.2 (CH, 7-C), 73.6 (CH, 3′-C), 74.7 (CH, 10-C), 75.3 (CH, 11-C), 79.0 (CH, 5-C), 100.6 (CH, 1′-C), 158.1 (C═N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ([M+Na]$^+$), 432.1482, found: 432.1485.

3.3.13. ((5*S*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-galactopyranoside (16a)

White solid, mp: 88–90 °C; Yield: 85%; $[\alpha]_D^{25}$ +101 (c 1.0, H_2O); ^{1}H NMR (D_2O): δ 1.23 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.81 (m, 2H, 6-H), 2.76 (dd, 1H, J = 17.5 Hz, J = 5.8 Hz, CH_2, 4-H), 3.22 (dd, 1H, J = 17.4 Hz, J = 10.2 Hz, CH_2, 4-H), 3. 62 (m, 4H, CH), 3.86 (m, 2H, CH), 4.11 (m, 1H, CH), 4.67 (d, 1H, J = 4.5 Hz, 2′-H), 4.75 (m, 1H, 5-H), 4.96 (d, 1H, J = 3.8 Hz, 4′-H), 5.03 (t, 1H, J = 4.5 Hz, 3′-H), 5.37 (s, 1H, 1′-H); ^{13}C NMR (D_2O): δ 24.1 (CH_3), 25.2 (CH_3), 29.2 (CH_2, 6-C), 41.2 (CH_2, 4-C), 61.5 (CH_2, 12-C), 68.1 (CH, 8-C), 69.5 (CH, 10-C), 70.0 (CH, 4′-C), 72.4 (CH, 7-C), 72.7 (CH, 9-C), 76.8 (CH, 11-C), 78.0 (CH, 5-C), 80.7 (CH, 3′-C), 85.2 (CH, 2′-C), 100.4 (CH, 1′-C), 114.2 (C, 13-C), 158.5 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1639.

3.3.14. ((5*R*)-3-(2,3-*O*-Isopropylidene-5-deoxy-D-lyxofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-galactopyranoside (17a)

White solid, mp: 93–95 °C; Yield: 87%; $[\alpha]_D^{25}$ −29.9 (c 1.0, H_2O); ^{1}H NMR (D_2O): δ 1.23 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.76 (m, 1H, 6-H), 2.10 (m, 1H, 6-H), 2.85 (dd, 1H, J = 17.4 Hz, J = 7.9 Hz, CH_2, 4-H), 3.17 (dd, 1H, J = 17.4 Hz, J = 10.1 Hz, CH_2, 4-H), 3.59 (m, 2H, CH), 3.65 (dd, 1H, J = 9.8 Hz, J = 2.8 Hz, CH), 3.74 (t, 1H, J = 9.8 Hz, CH), 4.01 (m, 1H, CH), 4.67 (d, 1H, J = 4.2 Hz, 2′-H), 4.75 (m, 1H, 5-H), 4.98 (d, 1H, J = 3.4 Hz, 4′-H), 5.02 (t, 1H, J = 4.2 Hz, 3′-H), 5.37 (s, 1H, 1′-H); ^{13}C NMR (D_2O): δ 24.0 (CH_3), 25.2 (CH_3), 29.3 (CH_2, 6-C), 40.7 (CH_2, 4-C), 61.3 (CH_2, 12-C), 68.3 (CH, 8-C), 69.3 (CH, 10-C), 70.1 (CH, 4′-C), 72.5 (CH, 7-C), 73.5 (CH, 9-C), 76.5 (CH, 11-C), 79.8 (CH, 5-C), 80.9 (CH, 3′-C), 85.3 (CH, 2′-C), 100.6 (CH, 1′-C), 114.1 (C, 13-C), 158.3 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1630.

3.3.15. ((5*S*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α- *C*-D-galactopyranoside (16b)

White solid, mp: 108–110 °C; Yield: 95%; $[\alpha]_D^{25}$ +68.0 (c 1.0, H_2O); ^{1}H NMR (D_2O): δ 1.25 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.83 (m, 2H, 6-H), 2.76 (dd, 1H, J = 17.5 Hz, J = 6.5 Hz, CH_2, 4-H), 3.18 (dd, 1H, CH_2, J = 17.6 Hz, J = 10.1 Hz, 4-H), 3.60 (m, 3H, 10-H, 9-H, 12-H), 3.66 (m, 1H, 7-H), 3.85 (m, 2H, 8-H, 12-H), 4.09 (m, 1H, 11-H), 4.35 (d, 1H, J = 2.0 Hz, 3′-H), 4.65 (d, 1H, J = 3.3 Hz, 2′-H), 4.74 (m, 1H, 5-H), 4.97 (s, 1H, 4′-H), 5.99 (d, 1H, J = 3.2 Hz, 1′-H); ^{13}C NMR (D_2O): δ 25.5 (CH_3), 26.0 (CH_3), 29.3 (CH_2, 6-C), 41.1 (CH_2, 4-C), 61.5 (CH_2, 12-C), 68.2 (CH, 8-C), 69.4 (CH, 9-C), 70.0 (CH, 7-C), 72.5 (CH, 10-C), 72.6 (CH, 4′-C), 75.3 (CH, 3′-C), 77.8 (CH, 11-C), 78.0 (CH, 5-C), 84.8 (CH, 2′-C), 105.0 (CH, 1′-C), 113.4 (C, 13-C), 158.5 (C═N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1641.

3.3.16. ((5*R*)-3-(1,2-*O*-Isopropylidene-5-deoxy-D-xylofuranose-4-yl)isoxazoline-5-yl) methyl α-*C*-D-galactopyranoside (17b)

White solid, mp: 95–97 °C; Yield: 94%; $[\alpha]_D^{25}$ −36.3 (c 1.0, H_2O); ^{1}H NMR (D_2O): δ 1.24 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.74 (m, 1H, 6-H), 2.08 (m, 1H, 6-H), 2.85 (dd, 1H, J = 17.5 Hz, J = 8.0 Hz, CH_2, 4-H), 3.14 (dd, 1H, CH_2, J = 17.6 Hz, J = 10.3 Hz, 4-H), 3.57 (m, 2H, 10-H, 9-H), 3.64 (dd, 1H, J = 9.2 Hz, J = 2.3 Hz, 12-H), 3.73 (m, 1H, 7-H), 3.85 (m, 2H, 8-H, 12-H), 4.03 (m, 1H, 11-H), 4.34 (d, 1H, J = 1.7 Hz, 3′-H), 4.64 (d, 1H, J = 3.3 Hz, 2′-H), 4.76 (m, 1H, 5-H), 4.95 (s, 1H, 4′-H), 5.98 (d, 1H, J = 3.2 Hz, 1′-H); ^{13}C NMR (D_2O): δ

25.5 (CH_3), 26.0 (CH_3), 29.2 (CH_2, 6-C), 40.6 (CH_2, 4-C), 61.3 (CH_2, 12-C), 68.3 (CH, 8-C), 69.3 (CH, 9-C), 70.1 (CH, 7-C), 72.5 (CH, 10-C), 73.5 (CH, 4′-C), 75.4 (CH, 3′-C), 77.8 (CH, 11-C), 79.7 (CH, 5-C), 84.8 (CH, 2′-C), 105.0 (CH, 1′-C), 113.4 (C, 13-C), 158.3 (C=N); HRMS(ESI): calcd for $C_{17}H_{27}NO_{10}$ ([M]$^+$), 405.1635, found: 405.1641.

3.3.17. ((5*S*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D-galactopyranoside (16c)

White solid, mp: 102–103 °C; Yield: 90%; $[\alpha]_D^{25}$ +108 (*c* 1.0, H_2O); ^{1}H NMR (CD_3OD): δ 1.94 (m, 2H, 6-H), 2.85 (dd, 1H, *J* = 17.2 Hz, *J* = 7.3 Hz, CH_2, 4-H), 3.27 (dd, 1H, CH_2, *J* = 17.2 Hz, *J* = 10.2 Hz, 4-H), 3.43 (s, 3H, OCH_3), 3.49 (dd, 1H, *J* = 9.3 Hz, *J* = 3.7 Hz, 10-H), 3.68–3.74 (m, 5H, CH, 8-H, 4′-H, 7-H, 12-H), 3.83 (m, 1H, 2′-H), 3.94 (m, 2H, 9-H, 3′-H), 4.23 (m, 1H, 11-H), 4.35 (d, 1H, *J* = 10.0 Hz, 5′-H), 4.73 (d, 1H, *J* = 3.5 Hz, 1′-H), 4.78 (m, 1H, 5-H); ^{13}C NMR (CD_3OD): δ 30.7 (CH_2, 6-C), 38.7 (CH_2, 4-C), 54.9 (OCH_3), 61.4 (CH_2, 12-C), 67.7 (CH, 8-C), 68.9 (CH, 4′-C), 69.3 (CH, 2′-C), 70.8 (CH, 5′-C), 71.9 (9-CH,), 72.0 (CH, 7-C), 72.2 (CH, 3′-C), 73.2 (CH, 10-C), 73.6 (CH, 11-C), 78.2 (CH, 5-C), 100.6 (CH, 1′-C), 158.3 (C=N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ([M+Na]$^+$), 432.1482, found: 432.1478.

3.3.18. ((5*R*)-3-(Methyl-6-deoxy-α-D-glucopyranoside-5-yl)isoxazoline-5-yl) methyl α-*C*-D-galactopyranoside (17c)

White solid, mp: 161 °C, decomposed; Yield: 92%; $[\alpha]_D^{25}$ +47.0 (*c* 1.0, H_2O); ^{1}H NMR (CD_3OD): δ 1.92 (m, 1H, 6-H), 2.18 (m, 1H, 6-H), 2.96 (dd, 1H, *J* = 17.1 Hz, *J* = 8.4 Hz, CH_2, 4-H), 3.20 (dd, 1H, CH_2, *J* = 17.0 Hz, *J* = 10.3 Hz, 4-H), 3.45 (s, 3H, OCH_3), 3.49 (dd, 2H, *J* = 9.6 Hz, *J* = 3.7 Hz, 10-H, 8-H), 3.56–3.73 (m, 3H, CH, 4′-H, 7-H, 12-H), 3.83 (m, 2H, 2′-H, 12-H), 3.94 (m, 2H, 9-H, 3′-H), 4.23 (m, 1H, 11-H), 4.35 (d, 1H, *J* = 9.9 Hz, 5′-H), 4.73 (d, 1H, *J* = 3.7 Hz, 1′-H), 4.83 (m, 1H, 5-H); ^{13}C NMR (CD_3OD): δ 29.9 (CH_2, 6-C), 37.8 (CH_2, 4-C), 54.9 (OCH_3), 61.4 (CH_2, 12-C), 67.8 (CH, 8-C), 68.8 (CH, 4′-C), 69.3 (CH, 2′-C), 70.8 (CH, 5′-C), 71.7 (9-CH), 72.2 (CH, 7-C), 72.4 (CH, 3′-C), 73.4 (CH, 10-C), 73.6 (CH, 11-C), 79.2 (CH, 5-C), 100.6 (CH, 1′-C), 158.1 (C=N); HRMS(ESI): calcd for $C_{16}H_{27}NNaO_{11}$ ([M+Na]$^+$), 432.1482, found: 432.1476.

3.4. Biological activity assays

3.4.1. Inhibition of glycosidases

The inhibitory activity of the synthesized compounds against α-amylase, α-glucosidase, and β-glucosidase: The α-glucosidase (yeast) and β-glucosidase (almonds) were obtained from Fluka; α-amylase (*Bacillaceae*, 4000 U/mg) from Sanland-chen International Inc., Xiamen, China. Two substrates, *p*-nitrophenyl α-glucopyranoside (PNPG) and (−)-D-salicin, were purchased from Sigma Chemical Co. All other commercial reagents were used as received. Each enzyme assay was measured as follows.

The α-amylase assay was performed using 1% starch as substrate in phosphate buffer, pH 6.0, at 50 °C. The enzyme solution (0.1 mL, 5 mg of solid enzyme in 50 mL of pH 6.0 phosphate buffer), 0.1 mL of inhibitor (1 mg/mL) and 1 mL of buffer were incubated for 10 min, and then 1 mL of substrate was added. After 10 min, 2 mL of 3,5-dinitrosalicylic acid was added, and then the reaction was heated in boiling water for 5 min. The solution was finally diluted to 20 mL after cooling down. Absorbance readings were taken on a TU-1901 UV–vis spectrophotometer at 540 nm using distilled deionized water as a blank control and acarbose as a positive control.

The β-glucosidase assay was performed using (−)-D-salicin (2 mg/mL) as substrate in phosphate buffer, pH 4.8, at 35 °C. The enzyme solution (0.1 mL, 10 mg of solid enzyme in 10 mL of pH 4.8 acetate buffer), 0.1 mL of inhibitor (1 mg/mL), and 0.9 mL of buffer were incubated for 10 min, and then 0.8 mL of substrate was added. After 10 min, 2 mL of 3,5-dinitrosalicylic acid was added, and then the reaction mixture was heated in boiling water for 5 min. The solution was finally diluted to 20 mL after cooling down. Absorbance readings were taken on a TU-1901 UV–vis spectrophotometer at 540 nm using distilled deionized water as a blank control.

The α-glucosidase assay was performed using PNPG (1 mg/mL) as substrates in phosphate buffer, pH 6.8, at 37 °C. The enzyme solution (0.1 mL, 10 mg of solid enzyme in 10 mL of pH 6.8 phosphate buffer), 0.1 mL of inhibitor (1 mg/mL), 1.9 mL of buffer, and 0.05 mL glutathione (reduced, 1 mg/mL) were incubated for 10 min, and then 0.15 mL of substrate was added. The reaction was quenched with 10 mL of sodium carbonate (0.1 mol/L) after 10 min, and the solution was finally diluted to 20 mL after cooling down. Absorbance readings were taken on a TU-1901 UV–vis spectrophotometer at 400 nm using distilled deionized water as a blank control.

3.4.2. *In vitro* colorimetric reverse transcriptase assay

The HIV-RT inhibition assay was performed by using a colorimetric reverse transcriptase assay (Roche), and the procedure for assaying RT inhibition was performed as described in the kit protocol. Briefly, the reaction mixture consists of template/primer complex, 2′-deoxy-nucleotide-5′-triphosphates (dNTPs) and reverse transcriptase (RT) enzyme in the lysis buffer with or without inhibitors. After 1 h incubation at 37 °C the reaction mixture was transferred to streptavidine-coated microtiter plate (MTP). The biotins labeled dNTPs that are incorporated in the template due to activity of RT were bound to streptavidine. The unbound dNTPs were washed using wash buffer and antidigoxigenin-peroxidase (DIG-POD) was added in MTP. The DIG-labeled dNTPs incorporated in the template was bound to anti-DIG-POD antibody. The unbound anti-DIG-POD was washed and the peroxide substrate (ABST) was added to the MTP. A colored reaction product was produced during the cleavage of the substrate catalyses by a peroxide enzyme. The absorbance of the sample was determined at OD 405 nM using microtiter plate ELISA reader. The resulting color intensity is directly proportional to the actual RT activity. The percentage inhibitory activity of RT inhibitors was calculated by comparing to a sample that does not contain an inhibitor. The percentage inhibition was calculated by formula as given below: % Inhibition = 100 − [(OD 405 nm with inhibitor/OD 405 nm without inhibitor) × 100].

3.4.3. Antitumor activity

The cytotoxicity of the compounds against breast cancer cell line was examined by the modified Mosmann's protocol as follows: Briefly, cells (10^4 cells per well) were plated in 96-well culture plates and cultured overnight at 37 °C in a 5% CO_2 humidified incubator. Compounds were added to the wells at final concentrations of 1, 10, and 100 μmol/L. Control wells were prepared by addition of DMEM. Wells containing DMEM without cells were used as blanks. The plates were incubated at 37 °C in a 5% CO_2 incubator for 48 h. Upon completion of the incubation, stock MTT dye solution (10 μL, 5 mg/mL) was added to each well. After 4 h of incubation, the supernatant was removed and DMSO (100 μL) was added to dissolve the MTT. The optical density of each well was measured on a microplate spectrophotometer at a wavelength of 570 nm. The cytotoxicity effect was calculated according to the formula: (ODcontrol − ODtreated)/ODcontrol × 100%.

Acknowledgments

The financial supports from the 973 Program (2010CB534913), the National Natural Science Foundation of China (20972039, 21172051), the Natural Science Foundations of the Department

of Education of Hebei (2009309, Y2011119, and ZH2011110), the Natural Science Foundations of Hebei University (2009-175) and open research fund of the State Key Laboratory of Natural and Biomimetic Drugs, Peking University (20080205) are gratefully acknowledged.

Supplementary data

Supplementary data (^{1}H and ^{13}C NMR spectra for compounds **5**–**10** and **12**–**17**, table for the chemical shifts of H-4 and coupling constants of $J_{4a/4b}$ and $J_{4a,4b/5}$ of compounds and tables of glycosidase inhibitory activities and cytotoxicity) associated with this article can be found, in the online version, at doi:10.1016/j.carres.2011.11.025.

References

1. Varki, A. *Glycobiology* **1993**, *3*, 97–130.
2. Sears, P.; Wong, C. H. *Angew. Chem., Int. Edit.* **1999**, *38*, 2300–2324.
3. Witczak, Z. J.; Nieforth, K. A. *Carbohydr. Drug Des.* **1997**, 1–24.
4. Seeberger, P. H.; Werz, D. B. *Nat. Rev. Drug Disc.* **2005**, *4*, 751–763.
5. Doones, K. J.; Gamblin, D. P.; Davis, B. G. *Chem. Eur. J.* **2006**, *12*, 656–665.
6. Bertozzi, C. R.; Pratt, M. R. *Chem. Soc. Rev.* **2005**, *34*, 58–68.
7. Liu, L.; McKee, M.; Postema, M. H. D. *Curr. Org. Chem.* **2001**, *5*, 1133–1167.
8. Arjona, O.; Gómez, A. M.; López, J. C.; Plumet, J. *Chem. Rev.* **2007**, *107*, 1919–2036.
9. Manzano, V. E.; Uhrig, M. L.; Varela, O. *J. Org. Chem.* **2008**, *73*, 7224–7235.
10. Repetto, E.; Marino, C.; Uhrig, M. L.; Varela, O. *Eur. J. Org. Chem.* **2008**, 540–547.
11. Ernst, B.; Hart, G. W.; Sinaÿ, P. *Carbohydr. Chem. Biol.* **2000**, 493–583.
12. Dondoni, A.; Massi, A.; Sabbatini, S.; Bertolasi, V. *J. Org.Chem.* **2002**, *67*, 6979–6994.
13. Brandi, A.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem. Rev.* **2003**, *103*, 1213–1269.
14. Marra, A.; Vecchi, A.; Chiappe, C.; Melai, B.; Dondoni, A. *J. Org. Chem.* **2008**, *73*, 2458–2461.
15. Zhang, P. Z.; Li, X. L.; Chen, H.; Li, Y. N.; Wang, R. *Tetrahedron Lett.* **2007**, *48*, 7813–7816.
16. Li, X. L.; Wang, R.; Wang, Y. P.; Chen, H.; Li, Z. W.; Ba, C. L.; Zhang, J. C. *Tetrahedron* **2008**, *64*, 9911–9920.
17. Chen, H.; Zhang, H. Z.; Feng, J. N.; Li, X. L.; Jiao, L. L.; Qin, Z. B.; Yin, Q. M.; Zhang, J. C. *Eur. J. Org. Chem.* **2009**, 6100–6103.
18. For the cycloaddition of nitrile oxide in carbohydrate chemistry, please see: Gallos, J. K.; Koumbis, A. E. *Curr. Org. Chem.* **2003**, *7*, 397–426. and the papers of R. M. Paton.
19. Hosomi, A.; Sakata, Y.; Sukurai, H. *Carbohydr. Res.* **1987**, *171*, 223–232.
20. Bombard, S.; Maillet, M.; Capmau, M. L. *Carbohydr. Res.* **1995**, *275*, 433–440.
21. Gallos, J. K.; Koftis, T. V.; Koumbis, A. E.; Moutsos, V. I. *Synlett* **1999**, 1289–1291.
22. Gallos, J. K.; Koftis, T. V. *J. Chem. Soc., Perkin Trans. 1* **2001**, 415–423.
23. Gould, R. O.; McGhie, K. E.; Paton, R. M. *Carbohydr. Res.* **1999**, *322*, 1–13.
24. Paton, R. M.; Young, A. A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 629–635.
25. Mabrour, M.; Bougrin, K.; Benhida, R.; Loupy, A.; Soufiaoui, M. *Tetrahedron Lett.* **2007**, *48*, 443–447. and references therein.
26. CCDC ID: 814231 contains the supplementary crystallographic data of compound **16a** for this paper. The data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.
27. Reverse Transcriptase Assay, Colorimetric kit, Roche Diagnostics GmbH, Roche Applied Science, Sandhofer Strasse 116, D-68305 Mannheim, Germany.
28. Moody, C. J.; Warrellow, G. J. *Tetrahedron Lett.* **1987**, *28*, 6089–6092.