DOI: 10.1002/ejoc.201001102

Synthesis of Fused Oxa-Aza Spiro Sugars from D-Glucose-Derived δ-Lactone as Glycosidase Inhibitors

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Keywords: Glycosylation / Metathesis / Dihydroxylation / Spiro compounds / Azasugars / Enzyme inhibitors

Four conformationally constrained fused oxa-aza spiro sugars have been synthesized from perbenzylated D-gluconolactone involving *C*-glycosylation of ketoses by using Me_3SiCN, ring-closing metathesis, and diastereoselective dihydroxylation as key steps. Two of the four spiro sugars were found to be highly selective but moderate inhibitors of α-mannosidase.

Introduction

In recent years an increasing interest in the design and synthesis of inhibitors of carbohydrate-processing enzymes[1] (i.e., glycosidases and glycotransferases) has been witnessed. As glycosidases are essential for normal cellular development, glycosidase inhibitors have potential therapeutic applications in a number of carbohydrate-mediated diseases such as cancer,[2] diabetes,[3] lysosomal storage disorders,[4] viral infection including influenza,[5] and HIV.[6] In the last few years a large number of glycosidase inhibitors has been designed and synthesized and tested for their activity against several glycosidases. As a result, glycosidase inhibitors such as Tamiflu, Zanamivir, Miglitol, Miglustat, Acarbose, Voglibose, and so on[7] have been approved as drugs to treat various carbohydrate-mediated diseases.

Polyhydroxylated derivatives of nitrogen-containing heterocycles, such as piperidines, pyrrolidines, indolizidines, pyrrolizidines, calystegines, and azepanes, are probably the most fascinating class of active compounds towards glycosidases so far. For example, *N*-butyl-1-deoxynojirimycin (**1**, Zavesca) and *N*-hydroxyethyl-1-deoxynojirimycin (**2**, Miglitol; Figure 1) have both been approved as medicines.[8] Besides these, isofagomine[9] (**3**) is the most potent β-glucosidase inhibitor found so far; swainsonine[10] (**4**) is a potent α-mannosidase inhibitor, alexine[11] (**5**) is also an effective thioglucosidase inhibitor, castanospermine (**6**) and its stereoisomers also have potential therapeutic applications.[12]

As part of our ongoing program of developing novel carbohydrate molecules[13] as glycosidase inhibitors and also our recent study on spiroaminal frameworks[14] as glycosidase inhibitors, we became interested in synthesizing

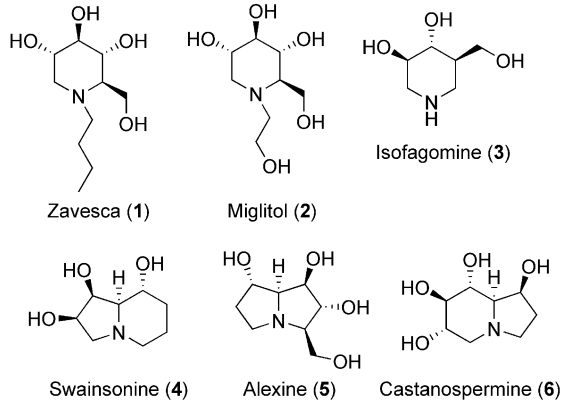

Figure 1. Some of the most important polyhydroxylated alkaloids.

structurally interesting and conformationally constrained novel fused oxa-aza spiro sugars viz. **17**, **25**, **31**, and **32** as glycosidase inhibitors. These spiro sugars were derived by carrying out spiroannulation at the anomeric center of monosaccharides. We can also consider these oxa-aza spiro sugars as "sugar-tethered azasugars" or "sugar-templated azasugars" (piperidine and azepane) or "spiro carbon linked oxa-aza disaccharides". Due to the conformational rigidity of the spiro system, these spiro sugars should hold the hydroxy substituents in precisely defined arrangements and hence should have potential for specific interactions. Herein, we report the synthesis of four novel fused oxa-aza spiro sugars and their enzyme inhibition activity towards glycosidases. The key steps in their synthesis involved *C*-glycosylation of ketoses, which were derived from vinyl or allyl Grignard addition reactions of D-gluconolactone (**7**), ring-closing metathesis reactions, and diastereoselective dihydroxylations by using RuO_4 or OsO_4.

Results and Discussion

As outlined in Scheme 1, target molecules **17** and **25** could be obtained from global deprotection of benzylated

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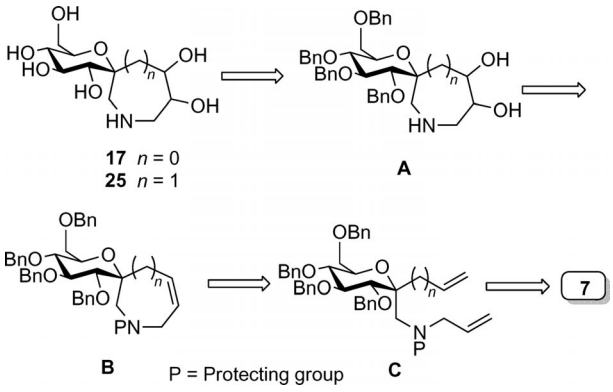
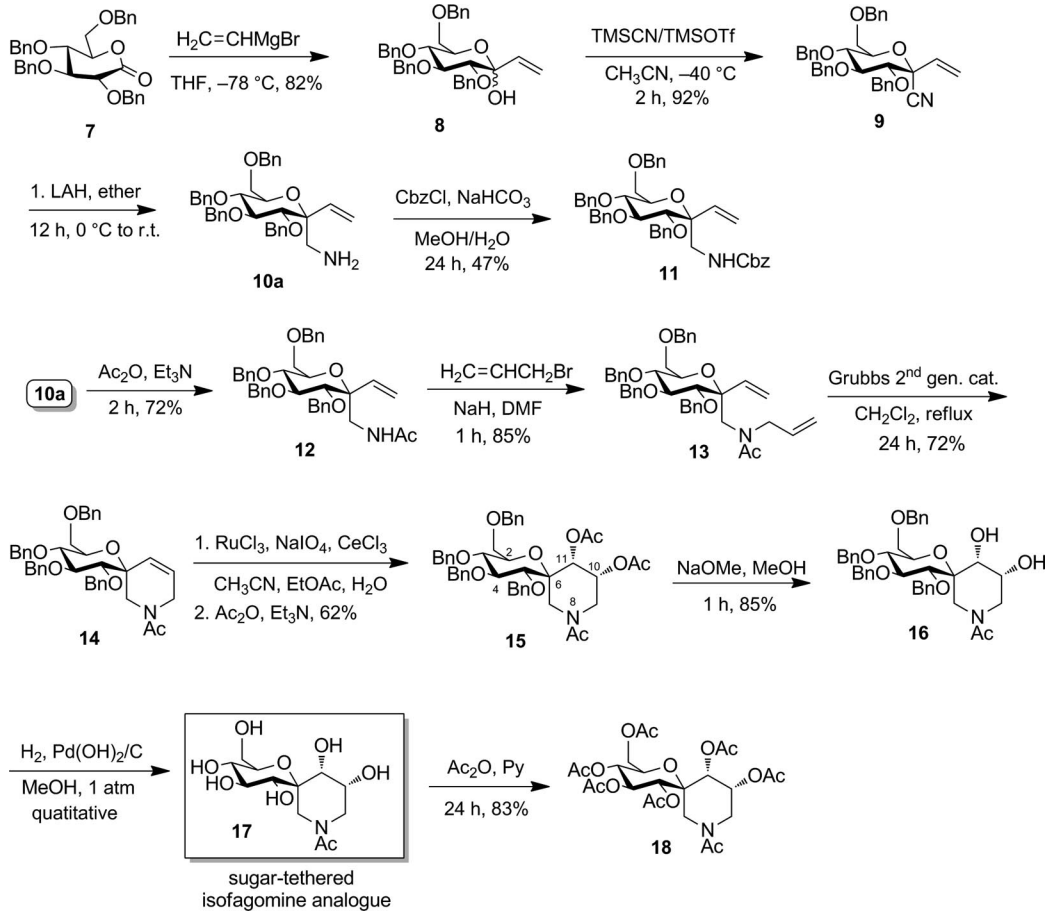
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201001102.

spiro sugar **A**, which could be easily prepared from diastereoselective dihydroxylation of olefin **B**, assembled, in turn, from diene **C** using ring-closing metathesis. Metathesis precursor diene **C** could be prepared from perbenzylated D-gluconolactone **7** through a few sequential reactions such as vinyl or allyl Grignard addition, followed by *C*-glycosylation, and functional-group manipulations of the resulting glycosyl cyanide.



Scheme 1. Retrosynthetic analysis of spiro sugars **17** and **25**.

As depicted in Scheme 2, synthesis of one of the target molecules viz. glucose-tethered isofagomine analogue **17** began with the Grignard reaction of D-glucono-1,5-lactone **7** using vinylmagnesium bromide,[15] followed by *C*-glycosylation of the so-obtained 1-*C*-vinylated hexapyranose **8** using Me_3SiCN in the presence of Me_3SiOTf to afford glycosyl cyanide[16] **9** in 92% yield. Reduction of the cyanide[17] group by using $LiAlH_4$ in Et_2O gave primary amine **10a**. Our initial attempts to protect the primary amine with $(Boc)_2O$ in the presence of Et_3N were unsuccessful, and protection as a Cbz carbamate afforded **11** in only 47% yield. However, the easily removable nature of the Cbz group through hydrogenolysis encouraged us to continue the synthesis with Cbz as the N-protecting group. Due to the rotameric nature of the carbamate, the NMR spectra of all the intermediates of the sequence were highly complex and difficult to analyze. To overcome this problem we chose the acetyl group as the N-protecting group. Thus, acetylation of amine **10a** gave amide **12** in good yield, which upon treatment with allyl bromide in the presence of NaH afforded ring-closing metathesis (RCM) precursor diene **13** in 85% yield. RCM reaction of diene **13** with the Grubbs first-generation catalyst did not give desired cyclic adduct **14**. Further, RCM of diene **13** with the Grubbs second-generation catalyst[18] (5 mol-%) in dichloromethane under refluxing conditions afforded desired spiro olefin **14** in 72% yield. The structure of spiro olefin **14** was confirmed through spectral analysis. Appearance of four internal characteristic olefinic protons in its ^1H NMR spectrum at δ =



Scheme 2. Synthesis of "glucose-templated isofagomine analogue" **17**.

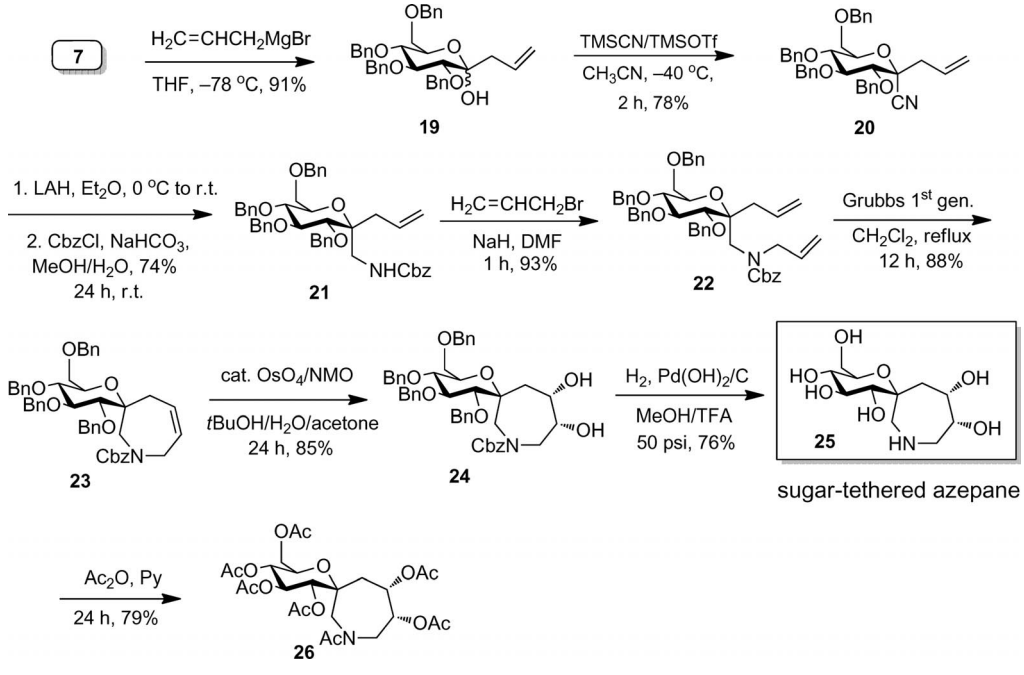
6.02–5.91 ppm indicated the formation of olefin **14** as a rotameric mixture (2:1 ratio).

Initial attempts at osmium tetroxide mediated dihydroxylation of conformationally constrained spiro olefin **14** failed under various experimental conditions and the starting material was recovered completely.[19] Epoxidation of olefin **14** using *m*-chloroperbenzoic acid[20a] and H_2O_2 in the presence of formic acid[20b] was also unsuccessful. To overcome this problem we chose a highly reactive bimetallic oxidizing system[21] ($RuCl_3/CeCl_3{\cdot}7H_2O/NaIO_4$) for the *cis*-dihydroxylation of olefin **14**. Thus, the reaction of olefin **14** with $RuCl_3$ (0.25 mol-%) in the presence of $CeCl_3{\cdot}7H_2O/NaIO_4$ in an EtOAc/CH_3CN/H_2O mixed solvent system at 0 °C followed by acetylation of the obtained α-diol gave acetate **15** in 62% overall yield.

The formation of product **15** was confirmed through spectral analysis. Thus, the ^1H NMR spectrum of compound **15** showed characteristic peaks of H-10 and H-11 as a broad singlet at δ = 5.31 ppm and a doublet at δ = 5.20 ppm (J = 3.85 Hz), respectively. Further, the formation of the α-diol was confirmed through nOe experiments (vide infra). Deacetylation of compound **15** was carried out by using a catalytic amount of sodium methoxide in MeOH, followed by debenzylation of diol **16** by using $Pd(OH)_2$ in MeOH in the presence of H_2 (1 atm) at room temperature to afford the deprotected "glucose-templated isofagomine analogue" **17** in quantitative yield. Deacetylation of compound **17** under various conditions was unsuccessful. The structure of free hydroxy compound **17** was confirmed through acetate derivative **18**, which was prepared by acetylation using Ac_2O/Py.

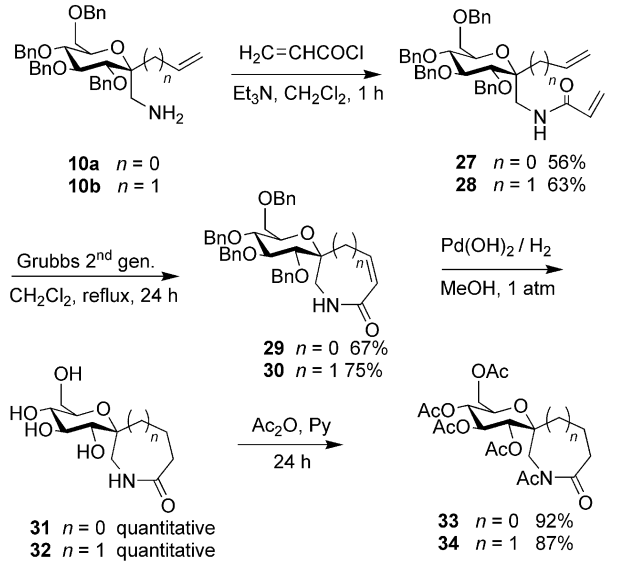
After the successful synthesis of spiro sugar **17**, our synthetic plan focused on the construction of sugar-tethered polyhydroxylated azepane **25** (Scheme 3). For this purpose, we chose 1-*C*-allylated glycosyl cyanide **20** as a starting material, which can be easily prepared in good yield using allylmagnesium chloride[22] addition to D-glucose-based lactone **7** followed by *C*-glycosylation of resulting 1-*C*-allylated hexapyranose[23] **19** with Me_3SiCN in the presence of Me_3SiOTf. Glycosyl cyanide **20** was converted into *C*-glycosylamine, followed by protection of the primary amine with CbzCl in the presence of $NaHCO_3$ to afford carbamate **21** in 74% yield. In this case, Cbz protection gave a good yield compared to amine **10a** (Scheme 2). The metathesis precursor was prepared by *N*-allylation of carbamate **21** using allyl bromide, and the RCM of diene **22** with Grubbs first-generation catalyst smoothly proceeded to provide desired olefin **23** in 88% yield. The structure of spiro olefin **23** was confirmed through ^1H and ^{13}C NMR spectroscopy and was found to exist as a 1:1 ratio of rotamers. Osmium tetroxide catalyzed dihydroxylation of olefin **23** successfully gave diol **24**. Global debenzylation of the α-diol using $Pd(OH)_2$ in MeOH in the presence of H_2 at 50 psi furnished the fully deprotected "glucose-templated polyhydroxylated azepane" **25** in 76% yield. Its structure was confirmed through spectral analysis, also of its acetylated derivative **26**.

Further, we also planned to synthesize glucose-tethered spirolactams **31** and **32** (Scheme 4). For the construction of these spiro sugars, we utilized intermediate *C*-glycosylamines **10a** and **10b**. Acroylation reaction of amines **10a** and **10b** with acryloyl chloride furnished dienes **27** and **28** in 56 and 63% yield, respectively. RCM reaction of dienes **27** and **28** using the Grubbs second-generation catalyst (5 mol-%) gave unsaturated spirolactams **29** and **30** in moderate yields. The ^1H NMR spectrum of compound **29** showed the internal olefinic protons at δ = 6.21 and 6.0 ppm as doublets with J = 9.9 Hz, and the NH proton



Scheme 3. Synthesis of "glucose-templated azepane analogue" **25**.

appeared at δ = 5.67 ppm as a broad singlet. Similarly, we also confirmed the structure of olefin **30**. Finally, debenzylation and saturation of the double bond of olefins **29** and **30** was achieved by hydrogenolysis [20% $Pd(OH)_2/H_2$, MeOH, 1 atm, r.t.]. The structures of polyhydroxy "sugar-templated spirolactams" **31** and **32** were confirmed through their ^1H, ^{13}C, and DEPT-135 NMR spectral analysis and also by spectral analysis of the corresponding acetyl derivatives **33** and **34**.



Scheme 4. Synthesis of "glucose-templated spirolactams" **31** and **32**.

The ^1H NMR, 2D COSY and nOe experiments unambiguously supported the structure of the newly generated α-diol configurations in spiro sugars **17** and **25**. To determine the diol configuration, initially we examined the conformation of the pyranose ring in these spiro sugars. For this purpose, we chose spiro piperidine **15** and spiro azepane **26** because of their well-resolved ^1H NMR splitting pattern as model systems. The large coupling constants (i.e., >9.0 Hz) for $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ (Figure 2) along with the positive nOe observations between H-2/H-4 or H-3/H-5 establish the $^4C_1$ chair conformation[24] of the pyranose ring in spiro sugars **15**, **26**, **33**, and **34**. On the basis of the inspection of molecular models and nOe experiments, the piperidine ring in spiro sugar **15** is also more likely in the rigid chair conformation (Figure 2). Thus, in spiro sugar **15** irradiation of the H-11 proton at δ = 5.20 ppm enhanced the H-5 proton signal at δ = 3.59 ppm, the H-9b proton signal at δ = 3.36 ppm, and the H-7b proton signal at δ = 2.97 ppm, clearly indicating that H-11, H-9b, and H-7b are axial protons. Further, upon irradiation of the signal for H-11, enhancement of the signals for three protons (H-5, H-7b, and H-9b) could only be possible when the –OAc group at C-11 is in the equatorial position, and also these enhancements are possible only in the particular rigid chair conformation of piperidine, which was apparent through the inspection of the molecular model. These observations revealed that the diol in the spiro sugar is an α-diol. In the case of spiro azepane **26**, we utilized the diastereotopic methylene (C-12) protons for the assignment of the diol configuration. Thus, irradiation of the H-5 proton signal at δ = 5.01 ppm enhanced only one of the two methylene protons (H-12a) at δ = 1.77 ppm, which was only possible in a particular rigid chair-like conformation in which H-12a should be β-oriented and also only one methylene proton, H-12a, enhancement clearly indicates the rigidity of such spiro systems. Further, irradiation of the H-12a proton signal at δ = 1.77 ppm enhanced the vicinal H-11 proton signal at δ = 5.24 ppm in 7% nOe, but irradiation of the H-12b proton signal at δ = 2.26 ppm did not show any enhancement in the vicinal H-11 proton signal. These observations clearly indicate that the H-12a and H-11 protons are *cis* to each other and that the –OAc group at C-11 is in α orientation. This suggests that the diol obtained had the α orientation of the –OH groups. The remaining nOe observations are shown in Figure 2.

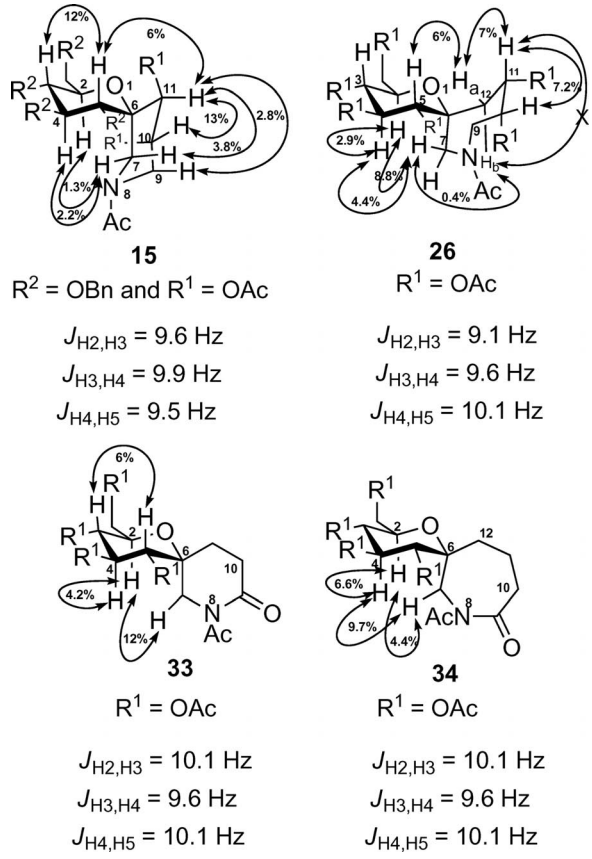


Figure 2. nOe observations and homonuclear proton coupling constants of compounds **15**, **26**, **33**, and **34**.

The inhibitory activities of spiro compounds **17**, **25**, **31**, and **32** were tested against five commercially available enzymes,[25] and the results are summarized in Table 1. These spiro compounds did not show any significant inhibition against α-glucosidase from yeast and α-galactosidase from coffee beans. However, spiro sugars **17** and **25** showed highly selective but moderate inhibition towards α-mannosidase from jack beans and were inactive towards other gly-

cosidases (Table 1). Thus, compounds **17** and **25** showed inhibitions against α-mannosidase at a concentration of 0.4 and 0.5 mM, respectively. Spirolactam **31** also showed moderate inhibition against α-mannosidase as well as β-galactosidase at 1.2 and 2.9 mM concentrations, respectively. Likewise, spiro sugar **32** also showed inhibition against β-glucosidase along with α-mannosidase and β-galactosidase, but activity was considerably reduced toward β-glucosidase. Thus, spirolactams **31** and **32** were nonselective glycosidase inhibitors towards glycosidases. Even though the inhibition was moderate to poor, this present inhibition activity study on such oxa-aza spiro sugars suggests that structural variations of these spiro sugars could promote better and specific glycosidase inhibition. We are currently investigating this possibility and we will report our results in due course.

Table 1. IC_{50} [mM] values of spiro compounds **17**, **25**, **31**, and **32**.[a]

Enzyme	17	25	31	32
α-Glucosidase (yeast)	NI	NI	NI	NI
β-Glucosidase (almonds)	NI	NI	NI	20.3
α-Mannosidase (Jack beans)	0.4	0.5	1.2	2.7
α-Galactosidase (coffee beans)	NI	NI	NI	NI
β-Galactosidase (bovine)	NI	NI	2.9	3.3

[a] NI: no inhibition at 3 mM concentration; inhibition studies were carried out optimal pH of the enzymes at 37 °C.

Conclusions

In summary, we have synthesized a new class of glucose-templated oxa-aza spiro sugars from glucose-derived *δ*-lactone. The synthesis of these novel fused spiro sugars involved *C*-glycosylation of ketoses, a RCM reaction, and diastereoselective dihydroxylation as the key steps. Further, spiro sugars **17** and **25** showed highly specific but moderate inhibition towards α-mannosidase. To the best of our knowledge this is the first report on such conformationally constrained oxa-aza spiro sugars as glycosidase inhibitors. Further work to extend the scope of the present study is in progress.

Experimental Section

General: Infrared spectra were recorded with a Bruker FTIR Vector 22 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a JEOL LA-400 (400 and 100 MHz, respectively) spectrometer or JEOL ECX-500 spectrometer (500 and 125 MHz, respectively) in solutions of $CDCl_3$ using tetramethylsilane as the internal standard. Mass spectra were recorded with a Waters HAB 213 Q TOF Premier Micromass spectrometer. Optical rotations were recorded with an Autopol II automatic polarimeter at the wavelength of the sodium D line (589 nm) at 25 °C. Column chromatography was performed on silica gel (100–200 mesh) and thin-layer chromatography (TLC) was performed on silica gel plates made by using grade G silica gel obtained from s.d. fine-chem Ltd., Mumbai, or on Merck silica gel precoated on aluminum plates. Melting points were determined using a Fischer-John melting point apparatus. All solvents and common reagents were purified by established procedures.

General Procedure A

Deprotection of Benzyl Groups: To a solution of a benzyl-protected spiro sugar (0.1 mmol) in MeOH (2 mL) was added 20% $Pd(OH)_2$/C (50 mg). The reaction mixture was stirred under 1 atm H_2 pressure for 3–4 d at room temperature. The catalyst was filtered off through Celite and concentrated in vacuo to obtain polyhydroxylated spiro sugars.

General Procedure B

Acetylation of Hydroxy Spiro Sugars: A mixture of a polyhydroxy spiro sugar derivative (20 mg) in acetic anhydride (0.5 mL) and pyridine (0.5 mL) and a catalytic amount of DMAP was stirred for 24 h at room temperature. The reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL), washed with water (5 mL) and brine (3 mL), dried with $MgSO_4$, concentrated in vacuo, and purified by silica gel chromatography to give the pure acetylated spiro sugars.

General Procedure C

Acryloylation of Glycosyl Amines: To a stirred solution of amine **10a** or **10b** (1.35 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C was added dropwise Et_3N (0.224 mL, 1.62 mmol) followed by acryloyl chloride (0.128 mL, 1.62 mmol). The reaction mixture was stirred for 1 h, and after completion of the reaction (TLC monitoring), it was extracted with CH_2Cl_2 (2 × 40 mL). Usual workup gave a crude product that was purified by column chromatography to give diene **27** or **28**.

Benzyl [(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)-2-vinyltetrahydro-2*H*-pyran-2-yl]methylcarbamate (11): To a suspension of $LiAlH_4$ (118.5 mg, 0.312 mmol) in dry ether (8 mL) was added glycosyl cyanide **9** (600 mg, 0.104 mmol, 8–10 mL of Et_2O) dropwise, and the mixture was stirred for 30 min at 0–5 °C under a nitrogen atmosphere. The reaction mixture was stirred overnight at room temperature. After completion of the reaction, the reaction mixture was cooled to 0 °C, and the excess amount of $LiAlH_4$ was quenched with EtOAc and 30% NaOH (5–6 mL). It was then filtered through Celite and washed thoroughly with diethyl ether (3 × 20 mL). The filtrate was dried (Na_2SO_4) and concentrated under reduced pressure. Liquid crude product **10a** (587 mg, 1.01 mmol) was dissolved in MeOH/H_2O (9:1) and CbzCl (0.12 mL, 1.52 mmol) was added at 0 °C followed by $NaHCO_3$ (127.7 mg, 1.52 mmol). The reaction mixture was stirred for 24 h at room temperature. After completion of the reaction, methanol was evaporated under reduced pressure and worked up by ethyl acetate, dried with Na_2SO_4, and purified by silica gel column chromatography to afford product **11**. Yield: 47% (two steps, 349 mg, liquid). R_f = 0.50 (hexane/ethyl acetate, 4:1). $[a]_D^{28}$ = +25.71 (c = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3435, 3030, 2924, 1724, 1515, 1497, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.18 (m, 25 H, Ar-H), 5.91 (dd, J = 11.0, 17.5 Hz, 1 H, -C*H*=CH_2), 5.45 (d, J = 17.5 Hz, 1 H, -CH=CH_aH_b), 5.21 (d, J = 10.9 Hz, 1 H, -CH=CH_aH_b), 5.09–5.05 (m, 3 H), 4.90–4.81 (m, 4 H), 4.69–4.50 (m, 4 H), 3.88 (t, J = 9.3 Hz, 1 H), 3.73–3.56 (m, 6 H), 3.46 (d, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.6, 138.3, 138.0, 136.6, 128.4–127.4 (m, Ar-C), 126.9, 116.2, 84.3, 83.7, 78.5, 78.3, 75.6, 75.4, 74.9, 73.7, 72.7, 69.2, 66.6, 38.7 ppm. HRMS: calcd. for $C_{45}H_{47}NO_7$ $[M + Na]^+$ 714.3431; found 714.3434.

***N*-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)-2-vinyltetrahydro-2*H*-pyran-2-yl]methyl}acetamide (12):** A procedure similar to that described for the synthesis of **11** was employed for the reduction of glycosyl cyanide **9** (1.2 g) Crude primary amine (1.25 gm) **10a** was dissolved in CH_2Cl_2 (12.0 mL) and cooled to 0 °C. Acetic anhydride (0.3 mL, 3.25 mmol), Et_3N (0.45 mL, 3.25 mmol), and a catalytic amount of DMAP were

added to the solution, and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL), washed with water (50 mL) and brine (30 mL), dried with Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography to afford pure acetylated derivative **12** as a liquid. Yield: 72% (two steps, 933 mg). R_f = 0.50 (hexane/ethyl acetate, 1:1). $[\alpha]_D^{28}$ = +25.0 (c = 0.8, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3320, 3030, 2923, 1738, 1660, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.19 (m, 20 H, Ar-H), 5.92 (dd, J = 11.0, 17.5 Hz, 1 H, -C*H*=CH_2), 5.59 (br. s, 1 H, -N*H*Ac) 5.43 (dd, J = 1.7, 17.5 Hz, 1 H, -CH=CH_aH_b), 5.22 (dd, J = 1.3, 10.9 Hz, 1 H, -CH=CH_aH_b), 4.86–4.81 (m, 4 H, 2 PhCH_2), 4.62 (d, J = 10.9 Hz, 1 H, PhC*H*) ppm. 4.59–4.51 (m, 3 H, 3 PhC*H*), 3.88 (t, 1 H, J = 9.3 Hz), 3.72–3.61 (m, 5 H), 3.50 (t, 1 H, J = 9.6 Hz) 3.46 (d, 1 H, J = 9.6 Hz), 1.80 (s, 3 H, COCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 138.6, 138.2, 138.1, 138.0, 137.9, 128.4–127.4 (m, Ar-C), 116.0, 84.4, 83.8, 78.6, 77.9, 75.8, 75.6, 74.9, 73.4, 72.7, 69.6, 37.4, 22.9 ppm. HRMS: calcd. for $C_{39}H_{43}NO_6$ [M + H]$^+$ 622.3169; found 622.3166.

***N*-Allyl-*N*-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)-2-vinyltetrahydro-2*H*-pyran-2-yl]methyl}acetamide (13):** To a stirred solution of acetyl-protected amine **12** (500 mg, 0.828 mmol) in dry DMF (10.0 mL) at 0 °C was added allyl bromide (0.1 mL, 1.24 mmol) and NaH (60 mg, 1.24 mmol). The reaction mixture was stirred for 1 h at 0 °C and after completion of the reaction (TLC monitoring), the reaction mixture was quenched with saturated aq. NH_4Cl and extracted with diethyl ether (3 × 40 mL). The extract was washed with water and brine and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave a crude product, which was purified by column chromatography to give diene **13**. Yield: 85% (452 mg), colorless liquid, R_f = 0.50 (hexane/ethyl acetate, 7:3). $[\alpha]_D^{28}$ = +23.07 (c = 0.65, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3064, 2923, 1727, 1651, 1495, 1422 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, mixture of rotamers 3:1 ratio): δ = 7.40–7.18 (m, 40 H, Ar-H, both rotamers), 6.24–6.18 (m, 1 H, major), 5.96–5.90 (m, 1 H, minor) 5.69–5.63 (m, 2 H, both rotamers), 5.50 (dd, 1 H, J = 1.7, 17.2 Hz, minor), 5.45 (dd, 1 H, J = 2.0, 17.1 Hz, major), 5.18 (dd, 1 H, J = 1.7, 11.0 Hz, minor), 5.14–5.01 (m, 5 H, both rotamers), 4.94 (d, 1 H, J = 11.0 Hz, PhC*H*, minor). 4.88–4.82 (m, 6 H, 6 PhC*H*, both rotamers), 4.79 (d, 1 H, J = 11.3 Hz, PhC*H*, major), 4.75–4.71 (m, 3 H, 3 PhC*H*, both rotamers), 4.65–4.60 (m, 2 H, 2 PhC*H*, minor), 4.62 (d, 1 H, J = 12.2 Hz, PhC*H*, major), 4.55 (d, 1 H, J = 11.7 Hz, PhC*H*, major), 4.53–4.50 (m, 1 H, PhC*H*, minor), 4.19 (dd, 1 H, J = 5.1, 18.2 Hz, major), 3.91–3.55 (m, 15 H, both rotamers), 3.49 (t, 1 H, J = 9.6 Hz, major) 3.40–3.31 (m, 3 H, both rotamers), 2.03 (s, 6 H, COCH_3, both rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.7, 138.9, 138.7, 138.4, 138.4, 138.1, 137.9, 137.7, 136.3, 135.3, 133.2, 132.9, 128.4–127.5 (m, Ar-C), 116.3, 115.7, 113.9, 85.3, 84.9, 83.3, 83.2, 81.7, 81.6, 78.7, 78.6, 75.5, 75.3, 75.2, 73.5, 73.4, 72.6, 72.5, 69.8, 69.4, 50.3, 46.8, 39.5, 21.7, 21.3 ppm. HRMS: calcd. for $C_{42}H_{47}NO_6$ [M + H]$^+$ 662.3482; found 622.3488.

1-[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-1-oxa-8-azaspiro[5.5]undec-10-en-8-yl]ethanone (14): To a stirred solution of compound **13** (320 mg, 0.496 mmol) in dry CH_2Cl_2 (8.0 mL) at room temperature was added the Grubbs 2nd generation catalyst (5 mol-%, 21 mg). The mixture was heated at reflux in CH_2Cl_2 and stirred overnight under a nitrogen atmosphere. After completion of the reaction, the solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography to obtain compound **14**. Yield: 72% (220 mg), liquid, R_f = 0.4 (hexane/ethyl acetate, 2:3). $[\alpha]_D^{28}$ = +41.58 (c = 0.95, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3031, 2921, 1726, 1643, 1452, 1271 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, mixture of rotamers 2:1 ratio): δ = 7.33–7.13 (m, 40 H, Ar-H, both rotamers), 6.01 (dt, J = 3.1, 9.9 Hz, 1 H, -CH=C*H*CH_2, minor), 5.92 (dt, J = 3.4, 9.9 Hz, 1 H, -CH=C*H*CH_2, major), 5.73 (d, J = 9.9 Hz, 1 H, -C*H*=$CHCH_2$, major), 5.63 (d, J = 10.3 Hz, 1 H, -C*H*=$CHCH_2$, minor), 4.88–4.84 (m, 6 H, both rotamers), 4.80 (d, J = 10.6, Hz, 1 H, major), 4.79 (d, J = 11.3 Hz, 1 H, major), 4.70 (d, J = 10.6 Hz, 1 H, minor), 4.65–4.59 (m, 5 H, both rotamers), 4.54 (d, J = 10.6 Hz, 1 H, minor), 4.51 (d, J = 11.3 Hz, 1 H, major), 4.41 (d, 1 H, J = 12.0 Hz, major), 4.36(m, 1 H, minor), 4.06–4.03 (m, 1 H, major), 3.99–3.97 (m, 1 H, major), 3.91 (t, 1 H, J = 9.2 major), 3.87–3.60 (m, 11 H, both rotamers), 3.56–3.47 (m, 4 H, both rotamers), 2.10 (s, 3 H, COCH_3, minor), 1.99 (s, 3 H, COCH_3, major) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.6, 169.4, 138.6, 138.3, 138.1, 137.9, 137.8, 137.6, 130.7, 129.7, 129.1, 128.4–127.5 (m, Ar-C), 84.2, 84.0, 83.3, 83.1, 78.3, 78.2, 75.6, 75.3, 75.2, 74.8, 73.8, 73.5, 73.1, 73.1, 68.9, 68.8, 45.4, 44.8, 41.2, 38.8, 21.5, 21.3 ppm. HRMS: calcd. for $C_{40}H_{43}NO_6$ [M + H]$^+$ 634.3169; found 634.3168.

(2*R*,3*R*,4*S*,5*R*,6*R*,10*R*,11*R*)-8-Acetyl-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-1-oxa-8-azaspiro[5.5]undecane-10,11-diyl Diacetate (15): A mixture of $NaIO_4$ (60.5 mg, 0.283 mmol) and $CeCl_3{\cdot}7H_2O$ (6.2 mg, 0.0189 mmol) in H_2O (1 mL) was stirred at room temperature for a few minutes. The reaction mixture was cooled to 0 °C and EtOAc (1.5 mL), CH_3CN (3.0 mL), and $RuCl_3{\cdot}H_2O$ (5.2 mg, 0.005 mmol) were added successively. After the mixture was stirred for 2.0 min, a solution of **14** (120 mg, 0.189 mmol) in EtOAc (1.5 mL) was added, and the resulting heterogeneous mixture was stirred until the reaction was complete (TLC monitoring). The reaction mixture was diluted with EtOAc (25 mL). The organic layer was washed with aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified with SiO_2 (hexanes/EtOAc). Acetylation of the diol was carried out conventionally using acetic anhydride and Et_3N to give spiro sugar **15**. Yield: 62% (two steps, 88.2 mg), colorless liquid. R_f = 0.30 (hexane/ethyl acetate, 1:4). $[\alpha]_D^{28}$ = +10.0 (c = 0.25, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 2922, 2853, 1742, 1649, 1452, 1370 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 20 H, Ar-H), 5.31 (br. s, 1 H, H-10), 5.20 (d, J = 3.8 Hz, 1 H, H-11), 4.98 (d, J = 14.9 Hz, 1 H, H-7a), 4.93 (d, J = 10.7 Hz, 1 H, PhC*H*), 4.90 (d, J = 10.3 Hz, 1 H, PhC*H*), 4.83 (d, J = 10.7 Hz, 1 H, PhC*H*), 4.81 (d, J = 11.4 Hz, 1 H, PhC*H*), 4.79 (d, J = 12.2 Hz, 1 H, PhC*H*), 4.71 (d, J = 11.0 Hz, 1 H, PhC*H*), 4.47 (d, J = 11.4 Hz, 1 H, PhC*H*), 4.41 (d, J = 10.3 Hz, 1 H, PhC*H*), 4.10–4.08 (m, 1 H, H-2), 3.96 (dd, J = 2.7, 11.8 Hz, 1 H, -C*H*OBn), 3.92 (t, J = 9.6 Hz, 1 H, H-4), 3.92–3.89 (m, 1 H, H-9a), 3.75 (t, J = 9.9 Hz, 1 H, H-3), 3.59 (d, J = 9.5 Hz, 1 H, H-5), 3.60–3.58 (m, 1 H, -C*H*OBn), 3.36 (d, J = 14.9 Hz, 1 H, H-9b), 2.97 (d, J = 14.9 Hz, 1 H, H-7b), 2.07 (s, 3 H, COCH_3), 2.02 (s, 3 H, COCH_3), 1.97 (s, 3 H, COCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 170.5, 170.0, 138.9, 138.5, 138.3, 138.0, 128.6–127.2 (m, Ar-C), 83.5, 78.5, 78.3, 77.5, 75.9, 75.8, 74.9, 73.9, 73.7, 69.6, 67.2, 48.8, 40.4, 21.3, 20.9, 20.8 ppm. HRMS: calcd. for $C_{44}H_{49}NO_{10}$ [M + H]$^+$ 752.3435; found 752.3434.

1-[(2*R*,3*R*,4*S*,5*R*,6*S*,10*R*,11*R*)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-10,11-dihydroxy-1-oxa-8-azaspiro[5.5]undecan-8-yl]ethanone (16): To a solution of compound **15** (80 mg, 0.106 mmol) in dry MeOH (1.5 mL) at 0 °C was added a catalytic amount of NaOMe. The mixture was stirred for 1 h at room temperature and after completion of the reaction (TLC monitoring) MeOH was evaporated. The product was extracted with EtOAc (3 × 20 mL), and the organic layer was washed with water and brine. Evaporation of the solvent followed by purification by using SiO_2 column chromatography gave diol **16**. Yield: 85% (60.4 mg), colorless li-

quid. R_f = 0.20 (hexane/ethyl acetate, 1:9). $[\alpha]_D^{28}$ = +31.25 (c = 0.4, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3453, 2921, 2852, 1642, 1452 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.18 (m, 20 H, Ar-H), 5.05 (d, J = 14.9 Hz, 1 H), 4.94 (d, J = 11.4 Hz, 1 H, PhC*H*), 4.88–4.79 (m, 3 H, 3 PhC*H*), 4.69 (d, J = 11.1 Hz, 1 H, PhC*H*), 4.52–4.47 (m, 2 H, 2 PhC*H*), 4.38 (d, J = 12.0 Hz, 1 H, PhC*H*), 4.15–4.12 (m, 1 H), 4.08 (d, J = 9.7 Hz, 1 H), 3.94–3.88 (m, 3 H), 3.63 (d, J = 2.6 Hz, 1 H), 3.56–3.54 (m, 1 H), 3.47 (dd, J = 6.6, 10.3 Hz, 1 H), 3.38 (t, J = 9.7 Hz, 1 H), 3.15 (d, J = 14.0 Hz, 1 H), 2.76 (d, J = 14.6 Hz, 1 H), 1.98 (s, 3 H, COC*H*$_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 138.3, 137.9, 137.8, 128.4–127.2 (m, Ar-C), 83.1, 80.5, 78.9, 77.8, 75.6, 74.9, 72.9, 72.3, 69.9, 69.6, 68.7, 51.9, 40.3, 21.2 ppm. HRMS: calcd. for $C_{40}H_{45}NO_8$ $[M + H]^+$ 668.3223; found 668.3223.

1-[(2*R*,3*S*,4*S*,5*R*,6*S*,10*R*,11*R*)-3,4,5,10,11-Pentahydroxy-2-(hydroxymethyl)-1-oxa-8-azaspiro(5.5)undecan-8-yl]ethanone (17): General procedure A was employed to obtain compound **17**. Yield: quantitative (30 mg), liquid. R_f = 0.30 (MeOH/ethyl acetate, 1:4). $[\alpha]_D^{28}$ = –15.0 (c = 0.4, MeOH). ^1H NMR (500 MHz, D_2O): δ = 3.91–3.89 (m, 2 H), 3.81 (d, J = 3.4 Hz, 1 H), 3.72 (d, J = 9.7 Hz, 1 H), 3.61–3.55 (m, 3 H), 3.50 (t, J = 9.7 Hz, 1 H), 3.26–3.22 (m, 3 H), 2.75 (d, J = 14.9 Hz, 1 H), 2.03 (s, 3 H, COC*H*$_3$) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 173.8, 80.6, 74.5, 73.3, 69.8, 69.3, 67.8, 60.6, 51.6, 40.1, 20.5 ppm. HRMS: calcd. for $C_{12}H_{21}NO_8$ $[M + H]^+$ 308.1345; found 308.1344.

(2*R*,3*R*,4*S*,5*R*,6*S*,10*R*,11*R*)-2-(Acetoxymethyl)-8-acetyl-1-oxa-8-azaspiro[5.5]undeca-ne-3,4,5,10,11-pentayl Pentaacetate (18): Compound **18** was prepared by general procedure B. Yield: 83% (30 mg), oil. R_f = 0.20 (hexane/ethyl acetate, 1:9). $[\alpha]_D^{28}$ = +30.0 (c = 0.55, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 2923, 2853, 1753, 1650, 1370, 1235 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.34 (t, J = 10.3 Hz, 1 H, H-4), 5.28 (br. s, 1 H, H-10), 5.25 (d, J = 10.3 Hz, 1 H, H-5), 5.21 (d, J = 14.9 Hz, 1 H, H-7a), 5.03 (t, J = 10.3 Hz, 1 H, H-3), 4.72 (d, J = 3.4 Hz, 1 H, H-11), 4.34–4.31 (m, 1 H, H-2), 4.19 (dd, J = 2.3, 12.3 Hz, 1 H, C*H*OAc), 4.01 (dd, J = 4.8, 12.3 Hz, 1 H, C*H*OAc), 3.95 (d, J = 15.1 Hz, 1 H, H-9a), 3.38 (d, J = 15.2 Hz, 1 H, H-9b), 2.74 (d, J = 14.6 Hz, 1 H, H-7b), 2.11 (s, 3 H, COC*H*$_3$), 2.07 (s, 3 H, COC*H*$_3$), 2.04 (s, 3 H, COC*H*$_3$), 2.03 (s, 3 H, COC*H*$_3$), 2.02 (s, 6 H, 2 COC*H*$_3$), 1.97 (s, 3 H, COC*H*$_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 170.5, 170.4, 170.2, 169.9, 169.8, 169.1, 76.8, 71.1, 70.6, 68.8, 68.7, 68.7, 66.8, 62.8, 49.0, 40.7, 21.3, 20.9, 20.8, 20.7–20.6 (m, COC*H*$_3$) ppm. HRMS: calcd. for $C_{24}H_{33}NO_{14}$ $[M + H]^+$ 560.1979; found 560.1978.

Benzyl [(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl]methylcarbamate (21): To a suspension of $LiAlH_4$ (166.4 mg, 4.38 mmol) in dry ether (10 mL) was added dropwise glycosyl cyanide **20** (860 mg, 1.46 mmol, 12 mL of Et_2O), and the mixture was stirred for 30 min at 0–5 °C under a nitrogen atmosphere. The reaction mixture was stirred overnight at room temperature. After completion of the reaction, the reaction mixture was cooled to 0 °C, and the excess amount of $LiAlH_4$ was quenched with EtOAc and 30% NaOH (5–6 mL). The reaction mixture was then filtered through Celite and washed thoroughly with diethyl ether (3 × 30 mL). The filtrate was dried (Na_2SO_4) and concentrated under reduced pressure. Liquid crude product **10b** (871 mg, 1.467 mmol) was dissolved in MeOH/H_2O (9:1) and CbzCl (0.3 mL, 2.20 mmol) was added at 0 °C followed by $NaHCO_3$ (185.2 mg, 2.20 mmol). The reaction mixture was stirred for 24 h at room temperature. After completion of the reaction, methanol was evaporated under reduced pressure and worked up with ethyl acetate, dried with Na_2SO_4, and the crude product was purified by silica gel column chromatography to afford product **21**. Yield: 74% (785 mg), colorless liquid. R_f = 0.50 (hexane/ethyl acetate, 7:3). $[\alpha]_D^{28}$ = +40.76 (c = 0.65, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3431, 3031, 2920, 2856, 1724, 1640, 1514, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.18 (m, 25 H, Ar-*H*), 5.90–5.87 (m, 1 H, C*H*=CH$_2$), 5.15–5.11 (m, 2 H, -*NH*, CH=C*H*$_a$H$_b$), 5.09 (s, 2 H, PhC*H*$_2$), 5.03 (d, J = 17.4 Hz, 1 H, CH=CH$_a$*H*$_b$), 4.88 (d, J = 11.0 Hz, 1 H, PhC*H*), 4.87 (d, J = 10.5 Hz, 1 H, PhC*H*), 4.82–4.78 (m, 2 H, 2 PhC*H*), 4.66 (d, J = 11.0 Hz, 1 H, PhC*H*), 4.60–4.56 (m, 2 H, 2 PhC*H*), 4.53 (d, J = 11.9 Hz, 1 H, PhC*H*), 3.87 (t, J = 9.1 Hz, 1 H), 3.68–3.55 (m, 6 H), 3.48 (t, J = 9.1 Hz, 1 H, PhC*H*), 2.56 (dd, J = 4.6, 14.7 Hz, 1 H, C*H*$_a$H$_b$CH=CH$_2$), 2.35 (dd, J = 8.9, 14.4 Hz, 1 H, CH$_a$*H*$_b$CH=CH$_2$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.8, 138.4, 138.3, 138.1, 136.7, 133.5, 128.7–127.1 (m, Ar-C), 84.4, 81.3, 78.9, 78.2, 75.7, 75.2, 75.1, 73.5, 73.0, 69.4, 66.8, 40.9, 39.7 ppm. HRMS: calcd. for $C_{46}H_{49}NO_7$ $[M + H]^+$ 728.3587; found 728.3587.

Benzylallyl {[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl]methyl}carbamate (22): A procedure similar to that described for the synthesis of **13** was employed. Yield: 93% (883 mg, from 900 mg, 1.237 mmol of **21**), colorless liquid. R_f = 0.50 (hexane/ethyl acetate, 4:1). $[\alpha]_D^{28}$ = +43.75 (c = 1.2, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3031, 2918, 2859, 1701, 1454 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, mixture of rotamers 1:1 ratio): δ = 7.36–7.17 (m, 50 H, Ar-*H*), 5.94–5.92 (m, 2 H), 5.74–5.72 (m, 2 H), 5.24–5.03 (m, 10 H), 4.92–4.51 (m, 18 H), 4.37–4.17 (m, 4 H), 3.91–3.43 (m, 16 H), 2.57–2.48 (m, 3 H), 2.36–2.31 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.3, 156.7, 138.7, 138.5, 138.0, 136.9, 136.8, 134.4, 134.3, 133.7, 133.5, 128.6–127.1 (m, Ar-C), 118.4, 116.6, 83.8, 81.6, 81.4, 80.5, 80.3, 79.0, 75.7, 75.4, 74.9, 73.5, 72.8, 69.7, 69.6, 67.4, 49.6, 42.8, 41.8, 38.4 ppm. HRMS: calcd. for $C_{49}H_{53}NO_7$ $[M + H]^+$ 768.3900; found 768.3900.

(2*R*,3*R*,4*S*,5*R*,6*R*)-Benzyl-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-1-oxa-8-azaspiro[5.6]dodec-10-ene-8-carboxylate (23): To a stirred solution of compound **22** (485 mg, 0.632 mmol) in dry CH_2Cl_2 (10 mL) at room temperature was added the Grubbs 1st generation catalyst (5 mol-%, 26 mg). The mixture was heated at reflux in CH_2Cl_2 and stirred overnight under a nitrogen atmosphere. After completion of the reaction, the solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography to obtain compound **23**. Yield: 88% (411 mg), liquid. R_f = 0.2 (hexane/ethyl acetate, 4:1). $[\alpha]_D^{28}$ = +33.33 (c = 0.3, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3030, 2922, 2851, 1702, 1604, 1453, 1419 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, mixture of rotamers 1:1 ratio): δ = 7.33–7.12 (m, 50 H, Ar-*H*), 5.69–5.61 (m, 4 H), 5.29–5.03 (m, 4 H), 4.92 (d, J = 11.0 Hz, 1 H), 4.87 (d, J = 11.1 Hz, 1 H), 4.85–4.73 (m, 6 H), 4.69 (d, J = 11.1 Hz, 1 H), 4.67 (d, J = 11.1 Hz, 1 H), 4.62 (d, J = 12.2 Hz, 1 H), 4.56 (d, J = 11.0 Hz, 1 H), 4.55–4.38 (m, 5 H), 4.28 (d, J = 15.6 Hz, 1 H), 4.27 (d, J = 14.9 Hz, 1 H), 4.12–4.09 (m, 1 H), 4.07 (d, J = 15.3 Hz, 1 H), 3.84 (dd, J = 3.8, 17.2 Hz, 1 H), 3.78–3.56 (m, 10 H), 3.41–3.39 (m, 2 H), 3.33 (dd, J = 3.4, 11.1 Hz, 1 H), 2.24 (dd, J = 1.1, 11.1 Hz, 1 H) 2.58–2.53 (m, 2 H), 2.44–2.41 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.4, 156.2, 138.7–138.3 (m, Ar-C), 137.1, 136.6, 128.6–127.5 (m, Ar-C), 127.2, 126.6, 126.1, 86.6, 86.2, 83.8, 83.7, 80.7, 79.5, 78.9, 78.7, 75.7, 75.6, 75.5, 74.9, 74.8, 73.5, 73.4, 72.9, 69.1, 68.6, 67.6, 67.1, 48.3, 46.7, 45.6, 44.3, 38.3, 37.8 ppm. HRMS: calcd. for $C_{47}H_{49}NO_7$ $[M + H]^+$ 740.3587; found 740.3584.

(2*R*,3*R*,4*S*,5*R*,6*R*,10*R*,11*S*)-Benzyl-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-10,11-dihydroxy-1-oxa-8-azaspiro[5.6]dodecane-8-carboxylate (24): To a stirred solution of compound **23** (330 mg, 0.446 mmol) in acetone/water/*t*BuOH (2:2:1) at room temperature was added NMO·H_2O (78.4 mg, 0.669 mmol) and OsO_4 (25 mg/

mL solution in *t*BuOH, 0.02 mL, 0.002 mmol). The reaction mixture was stirred for 24 h and then treated with $Na_2S_2O_5$ (127.1 mg, 0.669 mmol). The reaction mixture was stirred for another 1 h and extracted with EtOAc (3 × 40 mL). The organic layer was washed with 1 N HCl, water, and finally with brine. Usual workup thereafter gave a crude product, which was purified by column chromatography to give diol **24** as a major product. Yield: 86% (297 mg), oil. R_f = 0.3 (hexane/ethyl acetate, 1:1). $[\alpha]_D^{28}$ = +26.67 (*c* = 0.45, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3442, 3031, 2923, 1700, 1453, 1422 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, mixture of rotamers 1:1 ratio): δ = 7.33–7.14 (m, 50 H, Ar-*H*), 5.10 (d, *J* = 12.3 Hz, 1 H), 5.06 (s, 2 H), 4.97 (d, *J* = 12.3 Hz, 1 H), 4.92 (d, *J* = 10.9 Hz, 1 H), 4.88 (d, *J* = 11.2 Hz, 1 H), 4.86 (d, *J* = 10.8 Hz, 1 H), 4.83–4.77 (m, 5 H), 4.68 (d, *J* = 11.2 Hz, 2 H), 4.59 (d, *J* = 12.0 Hz, 1 H), 4.58 (d, *J* = 10.9 Hz, 1 H), 4.52 (d, *J* = 12.3 Hz, 1 H), 4.51 (d, *J* = 10.3 Hz, 1 H), 4.45–4.40 (m, 3 H), 4.22–4.11 (m, 5 H), 3.97 (d, *J* = 15.2 Hz, 1 H), 3.87 (dd, *J* = 4.8, 14.6 Hz, 1 H), 3.78 (dd, *J* = 2.8, 10.9 Hz, 1 H), 3.75–3.58 (m, 7 H), 3.50 (d, *J* = 9.7 Hz, 1 H), 3.39 (dd, *J* = 4.0, 10.9 Hz, 1 H), 3.34–3.30 (m, 3 H), 3.21 (dd, *J* = 6.9, 14.6 Hz, 1 H), 3.15 (d, *J* = 15.2 Hz, 1 H), 2.77 (dd, *J* = 10.6, 17.15 Hz, 1 H), 2.61–2.04 (m, 4 H), 1.61 (d, *J* = 13.7 Hz, 1 H, -OH), 1.52 (d, *J* = 14.3 Hz, 1 H, -OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.3, 155.9, 138.5–138.1 (m, Ar-C), 136.8, 136.2, 128.6–127.7 (m, Ar-C), 86.0, 85.8, 83.8, 83.6, 78.7, 78.6, 78.3, 78.2, 76.1, 75.6, 75.0, 74.8, 73.5, 73.4, 72.4, 72.1, 69.7, 69.6, 69.2, 69.0, 67.9, 67.4, 67.1, 66.6, 51.1, 50.5, 47.9, 47.0, 41.6, 41.4 ppm. HRMS: calcd. for $C_{47}H_{51}NO_9$ $[M + H]^+$ 774.3642; found 774.3641.

(2*R*,3*S*,4*S*,5*R*,6*R*,10*R*,11*S*)-2-(Hydroxymethyl)-1-oxa-8-azaspiro[5.6]-dodecane-3,4,5,10,11-pentaol (25): The benzyl-protected spiro sugar (75 mg, 0.269 mmol) was dissolved in MeOH (10 mL) and 20% $Pd(OH)_2$/C (50 mg) and trifluoroacetic acid (0.5 mL) were added. The reaction mixture was stirred under 50 psi H_2 pressure for 3–4 d at room temperature. The catalyst was filtered off through Celite, concentrated, and the filtrate was passed through Dowex (50X) basic resin column to obtain polyhydroxylated spiro azepane **25**. Yield: 76% (21 mg), liquid. $[\alpha]_D^{28}$ = –60.0 (*c* = 0.3, MeOH). ^1H NMR (500 MHz, D_2O): δ = 4.09 (br. d, *J* = 9.1 Hz, 1 H), 3.87 (br. s, 1 H), 3.71–3.69 (m, 1 H), 3.58–3.51 (m, *J* = 2H Hz), 3.42 (td, *J* = 3.0, 9.5 Hz, 1 H), 3.27–3.17 (m, 2 H), 3.14 (dd, *J* = 2.7, 9.5 Hz, 1 H), 3.01–2.98 (m, 1 H), 2.83–2.78 (m, 2 H), 2.57–2.52 (m, 1 H) 1.38 (d, *J* = 14.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 77.2, 76.9, 73.7, 73.1, 72.9, 70.1, 67.7, 61.1, 51.6, 47.9, 39.4 ppm. HRMS: calcd. for $C_{11}H_{21}NO_7$ $[M + H]^+$ 280.1396; found 280.1398.

(2*R*,3*R*,4*S*,5*R*,6*R*,10*R*,11*S*)-2-(Acetoxymethyl)-8-acetyl-1-oxa-8-azaspiro[5.6]dodecane-3,4,5,10,11-pentayl pentaacetate (26): Compound **26** was prepared by general procedure B: Yield: 79% (32 mg), light yellow oil. R_f = 0.20 (hexane/ethyl acetate, 1:9). $[\alpha]_D^{28}$ = +16.0 (*c* = 0.5, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 2923, 2852, 1746, 1656, 1370 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.49 (br. s, 1 H, H-10), 5.33 (t, *J* = 10.1 Hz, 1 H, H-4), 5.25–5.23 (m, 1 H, H-11), 5.00 (d, *J* = 10.0 Hz, 1 H, H-5), 4.99 (t, *J* = 9.6 Hz, 1 H, H-3), 4.85 (d, *J* = 15.1 Hz, 1 H, H-7a), 4.38–4.36 (m, 1 H, H-2), 4.15 (dd, *J* = 5.0, 12.3 Hz, 1 H, C*H*OAc), 4.02 (dd, *J* = 5.9, 15.1 Hz, 1 H, H-9a), 3.97 (dd, *J* = 2.2, 12.3 Hz, 1 H, C*H*OAc), 3.26 (dd, *J* = 5.5, 15.1 Hz, 1 H, H-9b), 3.06 (d, *J* = 15.1 Hz, 1 H, H-7b), 2.28–2.23 (m, 1 H, H-7a), 1.77 (d, *J* = 14.2 Hz, 1 H, H-7a), 2.15 (s, 3 H, COC*H*$_3$), 2.09 (s, 3 H, COC*H*$_3$), 2.08 (s, 3 H, COC*H*$_3$), 2.06 (s, 3 H, COC*H*$_3$), 2.01 (s, 3 H, COC*H*$_3$), 1.99 (s, 3 H, COC*H*$_3$), 1.97 (s, 3 H, COC*H*$_3$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 170.8, 170.2, 169.9, 169.8, 169.7, 169.5, 75.9, 74.8, 71.6, 69.9, 69.5, 68.8, 67.9, 50.4, 45.1, 38.8, 22.1, 21.0–20.7 (m, 6 COC*H*$_3$) ppm. HRMS: calcd. for $C_{25}H_{35}NO_{14}$ $[M + H]^+$ 574.2136; found 574.2136.

***N*-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)-2-vinyltetrahydro-2*H*-pyran-2-yl]methyl}acrylamide (27):** Compound **27** was prepared by general procedure C. Yield: 56% (520 mg), liquid. R_f = 0.30 (hexane/ethyl acetate, 3:2). $[\alpha]_D^{28}$ = +35.0 (*c* = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3418, 2917, 1661, 1626, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.19 (m, 20 H, Ar-*H*), 6.17–6.13 (m, 2 H), 5.90–5.97 (m, 2 H), 5.48–5.42 (m, 2 H), 5.21 (dd, *J* = 0.9, 10.7 Hz, 1 H), 4.93–4.82 (m, 4 H, 2 PhC*H*$_2$), 4.65–4.49 (m, 4 H, 2 PhC*H*$_2$), 3.90 (t, *J* = 9.2 Hz, 1 H), 3.83–3.57 (m, 6 H), 3.50 (t, *J* = 9.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.0, 138.7, 138.6, 138.4, 138.2, 138.0, 130.9, 128.6–127.6 (m, Ar-C), 126.0, 116.2, 81.2, 80.7, 78.1, 76.1, 74.4, 74.2, 73.5, 72.8, 71.7, 70.1, 37.2 ppm. HRMS: calcd. for $C_{40}H_{43}NO_6$ $[M + H]^+$ 634.3169; found 634.3165.

***N*-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl]methyl}acrylamide (28):** Compound **28** was prepared by general procedure C. Yield: 63% (550 mg), solid. R_f = 0.30 (hexane/ethyl acetate, 3:2). $[\alpha]_D^{28}$ = +50.0 (*c* = 0.55, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3318, 3030, 2917, 2864, 1663, 1628, 1453 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.19 (m, 20 H, Ar-*H*), 6.15–6.10 (m, 2 H, -NH, -C*H*=CH$_2$), 5.91–5.84 (m, 1 H, -C*H*=CH$_2$), 5.72 (dd, *J* = 10.2, 16.8 Hz, 1 H, -CH=C*H*$_a$H$_b$), 5.42 (dd, *J* = 1.2, 10.2 Hz, 1 H, -CH=CH$_a$*H*$_b$), 5.12 (br. d, *J* = 10.2 Hz, 1 H, -CH=C*H*$_a$H$_b$), 5.03 (br. d, *J* = 17.0 Hz, 1 H, -CH=CH$_a$*H*$_b$), 4.88 (2 d, *J* = 11.2 Hz, 2 H, PhC*H*$_2$), 4.81 (2 d, *J* = 11.0 Hz, 2 H PhC*H*$_2$), 4.65 (d, *J* = 11.2 Hz, 1 H, PhC*H*), 4.59–4.51 (m, 3 H, 3 PhC*H*), 3.88 (t, *J* = 9.2 Hz, 1 H), 3.81–3.52 (m, 6 H), 3.39 (t, *J* = 9.5 Hz, 1 H), 2.50 (dd, *J* = 5.1, 14.6 Hz, 1 H, -C*H*$_a$H$_b$CH=CH$_2$), 2.35 (dd, *J* = 9.0, 14.6 Hz, 1 H, -CH$_a$*H*$_b$-CH=CH$_2$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 140.1, 140.0, 139.9, 139.7, 135.0, 132.8, 130.3–129.2 (m, Ar-C), 127.9, 120.7, 86.4, 83.2, 80.8, 79.6, 77.6, 77.1, 76.9, 75.4, 74.8, 71.5, 41.8, 41.3 ppm. HRMS: calcd. for $C_{41}H_{45}NO_6$ $[M + H]^+$ 648.3325; found 648.3322.

(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-1-oxa-8-azaspiro[5.5]undec-10-en-9-one (29): To a stirred solution of compound **27** (180 mg, 0.284 mmol) in dry CH_2Cl_2 (3–4 mL) at room temperature was added the Grubbs 2nd generation catalyst (12 mg, 0.014 mmol). The mixture was heated at reflux for 24 h, and after completion of the reaction, the solvent was evaporated and the residue was purified by column chromatography. Yield: 67% (115 mg), liquid. R_f = 0.20 (hexane/ethyl acetate, 2:3). $[\alpha]_D^{28}$ = +24.0 (*c* = 0.5, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3383, 3030, 2922, 2852, 1685, 1619, 1453 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.13 (m, 20 H, Ar-*H*), 6.22 (d, *J* = 9.9 Hz, 1 H, -C*H*=CH-), 6.0 (d, *J* = 9.9 Hz, 1 H, -CH=C*H*-), 5.67 (br. s, 1 H, -N*H*), 4.83 (m, 2 H, PhC*H*$_2$), 4.79 (d, *J* = 10.7 Hz, 1 H, PhC*H*), 4.76 (d, *J* = 11.1 Hz, 1 H, PhC*H*), 4.64 (d, *J* = 10.7 Hz, 1 H, PhC*H*), 4.59 (d, *J* = 12.3 Hz, 1 H, PhC*H*), 4.53 (d, *J* = 10.3 Hz, 1 H, PhC*H*), 4.49 (d, *J* = 12.2 Hz, 1 H, PhC*H*), 3.84 (d, *J* = 13.8 Hz, 1 H), 3.72–3.58 (m, 7 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.6, 143.1, 138.2, 138.0, 137.9, 137.5, 128.7–127.8 (m, Ar-C), 127.1, 83.1, 82.8, 78.1, 75.7, 75.6, 75.1, 73.7, 73.5, 72.7, 68.8, 41.3 ppm. HRMS: calcd. for $C_{38}H_{39}NO_6$ $[M + H]^+$ 606.2856; found 606.2859.

(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-1-oxa-8-azaspiro[5.6]dodec-10-en-9-one (30): A procedure similar to that described for the synthesis of **29** was employed. Yield: 75% (350 mg, from 488 mg, 0.754 mmol of **28**), liquid. R_f = 0.30 (hexane/ethyl acetate, 1:1). $[\alpha]_D^{28}$ = +29.28 (*c* = 0.7, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 3290, 2923, 2854, 2852, 1669, 1621, 1454 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.13 (m, 20 H, Ar-*H*), 6.24–6.19 (m, 1 H, C*H*=CH-), 5.99 (br. s, 1 H, -N*H*), 5.94 (d, *J* = 12.0 Hz, 1 H,

-CH=C*H*-), 4.92 (d, *J* = 11.1 Hz, 1 H, PhC*H*), 4.91 (d, *J* = 10.8 Hz, 1 H, PhC*H*), 4.89–4.78 (m, 2 H, PhCH_2), 4.66–4.59 (m, 2 H, PhCH_2), 4.57 (d, *J* = 10.5 Hz, 1 H, PhC*H*), 4.50 (d, *J* = 12.3 Hz, 1 H, PhC*H*), 3.77 (t, *J* = 9.2 Hz, 1 H), 3.73–3.64 (m, 3 H), 3.55 (dd, *J* = 5.4, 15.1 Hz, 1 H), 3.45–3.43 (m, 2 H), 3.36 (dd, *J* = 6.8, 15.2 Hz, 1 H), 2.65 (ddd, *J* = 1.4, 5.1, 16.6 Hz, 1 H, -C$H_a$$H_b$CH=CH-), 2.35 (dd, *J* = 5.7, 16.6 Hz, 1 H, -C$H_a$$H_b$CH=CH-) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.21, 138.3, 138.2, 138.1, 138.0, 137.9, 128.6–127.7 (m, Ar-C), 125.6, 84.5, 84.4, 81.3, 78.5, 75.8, 75.7, 75.1, 73.6, 73.3, 68.8, 42.7, 40.2 ppm. HRMS: calcd. for $C_{39}H_{41}NO_6$ $[M + H]^+$ 620.3012; found 620.3012.

(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-Trihydroxy-2-(hydroxymethyl)-1-oxa-8-aza-spiro[5.5]undec-an-9-one (31): Compound **31** was prepared by general procedure A. Yield: quantitative (24 mg), liquid. R_f = 0.40 (MeOH/ethyl acetate, 1:4). $[\alpha]_D^{28}$ = +31.82 (*c* = 1.1, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.70 (d, *J* = 12.6 Hz, 1 H), 3.58 (dd, *J* = 4.9, 12.6 Hz, 1 H), 3.48 (d, *J* = 14.5 Hz, 1 H), 3.42 (t, *J* = 9.9 Hz, 1 H), 3.36–3.15 (m, 4 H), 2.49–2.42 (m, 1 H), 2.29–2.09 (m, 2 H), 1.63–1.55 (m, 1 H) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 175.6, 74.9, 73.7, 73.5, 73.3, 70.2, 60.9, 39.2, 29.2, 26.2 ppm. HRMS: calcd. for $C_{10}H_{17}NO_6$ $[M + H]^+$ 248.1134; found 248.1137.

(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-Trihydroxy-2-(hydroxymethyl)-1-oxa-8-aza-spiro[5.6]dodec-an-9-one (32): Compound **32** was prepared by general procedure A. Yield: quantitative (25 mg), liquid. R_f = 0.40 (MeOH/ethyl acetate, 1:4). $[\alpha]_D^{28}$ = +39.4 (*c* = 0.9, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.72 (dd, *J* = 2.2, 12.3 Hz, 1 H), 3.61 (dd, *J* = 4.8, 12.6 Hz, 1 H), 3.56 (t, *J* = 9.1 Hz, 1 H), 3.47 (d, *J* = 16.0 Hz, 1 H), 3.37 (d, *J* = 14.9 Hz, 1 H), 3.28 (d, *J* = 10.0 Hz, 1 H), 3.24–3.21 (m, 1 H), 3.18 (d, *J* = 9.4 Hz, 1 H), 2.56 (td, *J* = 2.5, 14.3 Hz, 1 H), 2.23 (dd, *J* = 4.3, 14.3 Hz, 1 H), 2.03 (td, *J* = 5.1, 13.7 Hz, 1 H), 1.75–1.62 (m, 3 H) ppm. ^{13}C NMR (125 MHz, D_2O): δ = 181.9, 77.5, 74.4, 73.9, 73.1, 70.0, 60.8, 40.8, 39.4, 34.6, 17.0. HRMS: calcd. for $C_{11}H_{19}NO_6$ $[M + H]^+$ 262.1291; found 262.1292.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-(Acetoxymethyl)-8-acetyl-9-oxo-1-oxa-8-aza-spiro[5.5]undecane-3,4,5-triyl Triacetate (33): Compound **33** was prepared by general procedure B: Yield: 92%, liquid. R_f = 0.7 (hexane/ethyl acetate, 3:7). $[\alpha]_D^{28}$ = +49.0 (*c* = 1.0, CH_2Cl_2). IR (neat): ṽ = 2925, 2853, 1755, 1711, 1444 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.33 (t, *J* = 9.6 Hz, 1 H, H-4), 5.11 (d, *J* = 10.1 Hz, 1 H, H-5), 5.00 (t, *J* = 10.1 Hz, 1 H, H-3), 4.90 (d, *J* = 15.1 Hz, 1 H, H-7a), 4.12 (dd, *J* = 5.9, 12.3 Hz, 1 H, C$H_a$$H_b$OAc), 3.93 (dd, *J* = 1.8, 12.3 Hz, 1 H, CH$_a$$H_b$OAc), 3.74–3.71 (m, 1 H, H-2), 3.34 (d, *J* = 14.7 Hz, 1 H, H-7b), 2.70–2.63 (m, 1 H), 2.54 (s, 3 H, COCH_3), 2.52–2.46 (m, 1 H), 2.04 (s, 3 H, COCH_3), 2.03 (s, 3 H, COCH_3), 2.00 (s, 3 H, COCH_3), 2.00–1.97 (m, 1 H), 1.97 (s, 3 H, COCH_3), 1.91–1.88 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.9, 172.3, 170.5, 170.1, 169.6, 169.4, 74.6, 73.1, 71.5, 70.0, 68.9, 62.6, 40.8, 31.3, 30.8, 27.2, 20.8, 20.7, 20.6 ppm. HRMS: calcd. for $C_{20}H_{27}NO_{11}$ $[M + H]^+$ 458.1662; found 458.1663.

(2*R*,3*R*,4*S*,5*R*,6*R*)-2-(Acetoxymethyl)-8-acetyl-9-oxo-1-oxa-8-aza-spiro[5.6]dodecane-3,4,5-triyl Triacetate (34): Compound **34** was prepared by general procedure B: Yield: 87%, liquid. R_f = 0.75 (hexane/ethyl acetate, 3:7). $[\alpha]_D^{28}$ = +66.0 (*c* = 0.75, CH_2Cl_2). IR (neat): ṽ = 2924, 2851, 1754, 1710, 1434 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.41 (t, *J* = 9.6 Hz, 1 H, H-4), 5.18 (d, *J* = 16.0 Hz, 1 H, H-7a), 5.00 (d, *J* = 10.0 Hz, 1 H, H-5), 4.92 (t, *J* = 10.1 Hz, 1 H, H-3), 4.12 (dd, *J* = 6.4, 11.9 Hz, 1 H, C$H_a$$H_b$OAc), 3.84 (d, *J* = 11.9 Hz, 1 H, CH$_a$$H_b$OAc), 3.77–3.74 (m, 1 H, H-2), 3.32 (d, *J* = 16.0 Hz, 1 H, H-7b), 2.70–2.59 (m, 2 H), 2.53 (s, 3 H, COCH_3), 2.06 (s, 3 H, COCH_3), 2.05 (s, 3 H, COCH_3), 2.01 (s, 3 H, COCH_3), 1.97 (s, 3 H, COCH_3), 1.94–1.64 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5, 173.9, 170.8, 170.1, 169.7, 169.5, 76.0, 74.5, 71.7, 70.2, 68.8, 62.9, 41.9, 40.1, 38.7, 27.5, 20.9, 20.8, 20.7, 18.1 ppm. HRMS: calcd. for $C_{21}H_{29}NO_{11}$ $[M + H]^+$ 472.1819; found 472.1817.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all new compounds, and DEPT-135, 2D-COSY, and nOe spectra of some selected compounds.

Acknowledgments

We thank the Council of Scientific and Industrial Research, New Delhi for financial support [Grant No. 01(2298)/09/EMR-II]. A.P.J.P. and P.G. thank University Grant Commission, New Delhi, for Senior Research Fellowship and Y.S.R. thanks the Council of Scientific and Industrial Research, New Delhi, for a Senior Research Fellowship.

[1] For some recent accounts on glycosidases and their inhibitors, see: a) P. Compain, O. R. Martin, *Iminosugars*, Wiley, England, 2**007**; b) B. G. Winchester, *Tetrahedron: Asymmetry* **2009**, *20*, 645–651; c) B. G. Davis, *Tetrahedron: Asymmetry* **2009**, *20*, 652–671; d) P. Compain, V. Chagnault, O. R. Martin, *Tetrahedron: Asymmetry* **2009**, *20*, 672–711; e) V. H. Lillelund, H. H. Jensen, X. Liang, M. Bols, *Chem. Rev.* **2002**, *102*, 515–553; f) K. Afarinkia, A. Bahar, *Tetrahedron: Asymmetry* **2005**, *16*, 1239–1287; g) D. L. Zechel, S. G. Withers, *Acc. Chem. Res.* **2000**, *33*, 11–18; h) T. D. Heightman, A. T. Vasella, *Angew. Chem. Int. Ed.* **1999**, *38*, 750–770; i) G. M. Gloster, G. J. Davies, *Org. Biomol. Chem.* **2010**, *8*, 305–320; j) A. E. Stuetz, *Iminosugars as Glycosidase Inhibitors: Nojirimycin and Beyond*, Wiley-VCH, Weinheim, Germany, **1999**; k) Y. Ichikawa, Y. Igarashi, M. Ichikawa, Y. Suhara, *J. Am. Chem. Soc.* **1998**, *120*, 3007–3018.

[2] a) T. Tsuruoka, H. Fukuyasu, M. Ishii, T. Usui, S. Shibahara, S. Inouye, *J. Antibiot.* **1996**, *49*, 155–161; b) P. E. Gross, M. A. Baker, J. P. Carver, J. W. Dennis, *Clin. Cancer Res.* **1995**, *1*, 935–944.

[3] a) P. S. Johnston, H. E. Lebovitz, R. F. Coniff, D. C. Simonson, P. Raskin, C. L. Munera, *J. Clin. Endocrinol. Metab.* **1998**, *83*, 1515–1522; b) P. B. Anzeveno, L. J. Creemer, J. K. Daniel, C.-H. R. King, P. S. Liu, *J. Org. Chem.* **1989**, *54*, 2539–2542; c) J. A. Balfour, D. McTavish, *Drugs* **1993**, *46*, 1025–1054.

[4] T. D. Butters, R. A. Dwek, F. M. Platt, *Chem. Rev.* **2000**, *100*, 4683–4696 and references cited therein.

[5] C. U. Kim, W. Lew, M. A. Williams, H. Liu, L. Zhang, S. Swaminathan, N. Bischofberger, M. S. Chen, D. B. Mendel, C. Y. Tai, W. G. Laver, R. C. Stevens, *J. Am. Chem. Soc.* **1997**, *119*, 681–690.

[6] L. Ratner, N. V. Heyden, D. Dedera, *Virology* **1991**, *181*, 180–192 and references cited therein.

[7] a) A. M. S. Mayer, M. Guzman, R. Peksa, M. Hall, M. J. Fay, P. B. Jacobson, A. M. Romanic, S. P. Gunasekera, *Diab. Res. Clin. Prac.* **2007**, *78*, 30–33; b) S. Alfasano, P. Pampin, J. Estrada, J. C. R. Rey, P. Giraldo, J. Sancho, M. Pocovi, *Blood Cells Mol. Dis.* **2005**, *35*, 268–276; c) S. Yamagishi, T. Matsui, S. Ueda, K. Fukami, S. Okuda, *Curr. Drug Met.* **2009**, *10*, 159–163.

[8] T. D. Butters, R. A. Dwek, F. M. Platt, *Curr. Top. Med. Chem.* **2003**, *3*, 561–574.

[9] T. M. Jespersen, W. Dong, M. R. Sierks, T. Skrydstrup, I. Lundt, M. Bols, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1778–1779.

[10] A. E. Nerm, *Tetrahedron* **2000**, *56*, 8579–8629.

[11] H. Yoda, H. Katoh, K. Takabe, *Tetrahedron Lett.* **2000**, *41*, 7661–7665.

[12] K. Burgess, I. Henderson, *Tetrahedron* **1992**, *48*, 4045–4066.

[13] a) B. Gopal Reddy, Y. D. Vankar, *Angew. Chem. Int. Ed.* **2005**, *44*, 2001–2004; b) K. Jayakanthan, Y. D. Vankar, *Tetrahedron*

Lett. **2006**, *47*, 8667–8671; c) K. Jayakanthan, Y. D. Vankar, *Org. Lett.* **2005**, *7*, 5441–5444; d) V. R. Doddi, Y. D. Vankar, *Eur. J. Org. Chem.* **2007**, 5583–5589; e) M. A. Alam, A. Kumar, Y. D. Vankar, *Eur. J. Org. Chem.* **2008**, 4972–4980; f) M. A. Alam, Y. D. Vankar, *Tetrahedron Lett.* **2008**, *49*, 5534–5536; g) V. R. Doddi, H. P. Kokatla, A. P. John Pal, R. K. Basak, Y. D. Vankar, *Eur. J. Org. Chem.* **2008**, 5731–5739; h) A. Kumar, G. K. Rawal, Y. D. Vankar, *Tetrahedron* **2008**, *64*, 2379–2390; i) P. Gupta, Y. D. Vankar, *Eur. J. Org. Chem.* **2009**, 1925–1933; j) N. Kumari, B. G. Reddy, Y. D. Vankar, *Eur. J. Org. Chem.* **2009**, 160–169.

[14] A. P. John Pal, Y. D. Vankar, *Tetrahedron Lett.* **2010**, *51*, 2519–2524.

[15] a) X. Li, H. Ohtake, H. Takahashi, S. Ikegami, *Tetrahedron* **2001**, *57*, 4297–4309; b) P. A. V. van Hooft, M. A. Leeuwenburgh, H. S. Overkleeft, G. A. van der Marel, C. A. A. van Boeckel, J. H. van Boom, *Tetrahedron Lett.* **1998**, *39*, 6061–6064.

[16] T. Yamanoi, Y. Nara, S. Matsuda, Y. Oda, A. Yoshida, K. Katsuraya, M. Watanabe, *Synlett* **2007**, 785–789.

[17] E. N. Shaitanova, I. I. Gerus, M. Yu. Belik, V. P. Kukhar, *Tetrahedron: Asymmetry* **2007**, *18*, 192–198.

[18] U. K. Pandit, H. S. Overkleeft, B. C. Borer, H. Bieraugel, *Eur. J. Org. Chem.* **1999**, 959–968.

[19] a) P. Dupau, R. Epple, A. A. Thomas, V. V. Fokin, K. B. Sharpless, *Adv. Synth. Catal.* **2002**, *344*, 421–433; b) M. Schroder, *Chem. Rev.* **1980**, *80*, 187–213.

[20] a) S. D. Markad, N. S. Karanjule, T. Sharma, S. B. Sabharwal, V. Puranik, D. D. Dhavale, *Org. Biomol. Chem.* **2006**, *4*, 2549–2555; b) V. R. Doddi, A. Kumar, Y. D. Vankar, *Tetrahedron* **2008**, *64*, 9117–9122.

[21] a) B. Plietker, M. Niggemann, *J. Org. Chem.* **2005**, *70*, 2402–2405; b) P. Tiwari, A. K. Misra, *J. Org. Chem.* **2006**, *71*, 2911–2913.

[22] a) M. D. Lewis, J. K. Cha, Y. Kishi, *J. Am. Chem. Soc.* **1982**, *104*, 4976–4978; b) E. Brenna, C. Fuganti, P. Grasselli, S. Serra, S. Zambotti, *Chem. Eur. J.* **2002**, *8*, 1872–1878.

[23] Y. Oda, T. Yamanoi, *Synthesis* **2007**, 3021–3031.

[24] K. Zhang, F. Schweizer, *Synlett* **2005**, 3111–3115.

[25] Y.-T. Li, S.-C. Li, *Methods in Enzymology* (Ed.: V. Ginsberg), Academic Press, New York, **1972**, p. 702.

Received: August 5, 2010
Published Online: November 17, 2010

