Carbohydrate Research 345 (2010) 1142–1148

Contents lists available at ScienceDirect

Carbohydrate Research

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

Synthesis of 1,4-dideoxy-1,4-iminoheptitol and 1,5-dideoxy-1,5-iminooctitols from D-xylose

Amit Kumar, Mohammed Abrar Alam, Shikha Rani, Yashwant D. Vankar *

Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India

ARTICLE INFO

Article history:
Received 11 March 2010
Received in revised form 5 April 2010
Accepted 18 April 2010
Available online 21 April 2010

Keywords:
Iminosugars
Lactol
Wittig olefination
Ring closing metathesis
Dihydroxylation
D-Xylose

ABSTRACT

The synthesis of iminosugars from inexpensive D-xylose in high yields has been developed. The key step in this synthesis involves Wittig olefination or chelation-controlled attack of Grignard reagents on lactol and ring-closing metathesis using first or second generation Grubbs' catalysts.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

Polyhydroxylated pyrrolidine and piperidine alkaloids, both natural and synthetic, have attracted considerable attention due to their ability to inhibit glycosidases.[1] Some inhibitors of glycosidases have been identified as important chemotherapeutic agents with application in the treatment of influenza,[2] cancer,[3] AIDS,[4] and diabetes.[5] 1,4-Dideoxy-1,4-iminoalditols,[1b] and 1,5-dideoxy-1,5-iminoalditols[1b] are an important class of glycosidase inhibitors, which are protonated at physiological pH and thus they mimic a glycopyranosyl cation. Polyhydroxylated pyrrolidines and piperidines connected to a polyhydroxy chain through C–C bonds (iminoalditols) are considered as acyclic imino-*C*-disaccharide[6] analogues, and they act as glycosidase inhibitors. A large number of iminoalditols have been found to be inhibitors of glycosidases. Thus, for example, 1,4-dideoxy-1,4-imino-D-mannitol[7] **1** (Fig. 1), an iminohexitol, is an inhibitor of α-mannosidases. Iminoheptitols such as 1,4-imino-L-*glycero*-D-*ido* (**2**) and 1,4-imino-L-*glycero*-D-*gluco*-heptitols (**3**)[8] are good and specific inhibitors of α- and β-glucosidases. Recently, Fleet et al.[9] reported that 1,4-imino-D-*glycero*-L-*talo*-heptitol (**4**) is a specific inhibitor of naringinase. Similarly, iminooctitols such as 1,4,7-trideoxy1,4-imino-D-*glycero*-L-*manno*-octitol (**5**)[10] and 1,5-dideoxy-1,5-imino-D-*erthyro*-D-*talo*-octitols (**6**)[11] show moderate glycosidase inhibition.

It has been observed that slight changes such as stereochemistry,[12] ring size,[13] and hydroxyl group location[14] in these sugar analogues produce considerable differences in inhibitory activity. As part of an ongoing research project in our laboratory toward the synthesis of natural and unnatural hybrid azasugars,[15] we became interested in developing new routes to iminoalditol analogues with a view to assess their glycosidase inhibitory activity vis-à-vis the structural features. Our synthetic strategy relies on the Wittig olefination or chelation-controlled nucleophilic addition followed by the ring-closing metathesis (RCM) to form five- or six-membered rings.

2. Results and discussion

A general retrosynthetic analysis is presented in Scheme 1. 1,4-Dideoxy-1,4-iminoheptitol **16** and 1,5-dideoxy-1,5-iminooctitols

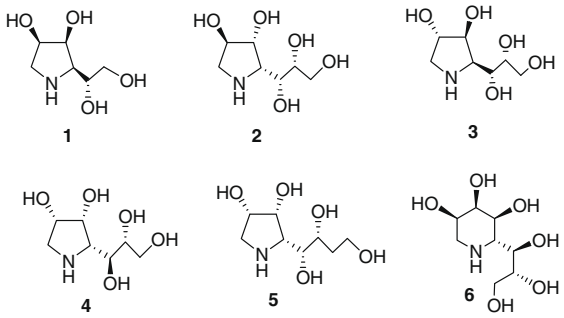
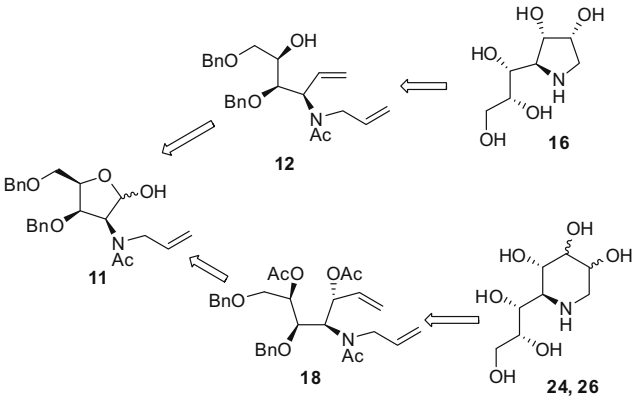


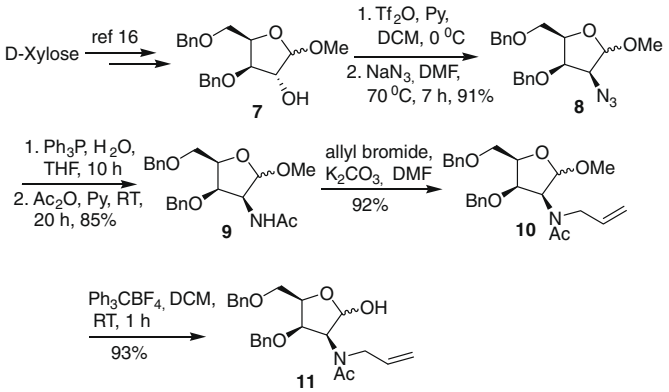
Figure 1. Structures of some selected iminoalditols.

* Corresponding author. Fax: +91 512 259 0007.
E-mail address: vankar@iitk.ac.in (Y.D. Vankar).

0008-6215/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2010.04.016



Scheme 1. Retrosynthetic analysis.



Scheme 2. Synthesis of common precursor lactol **11**.

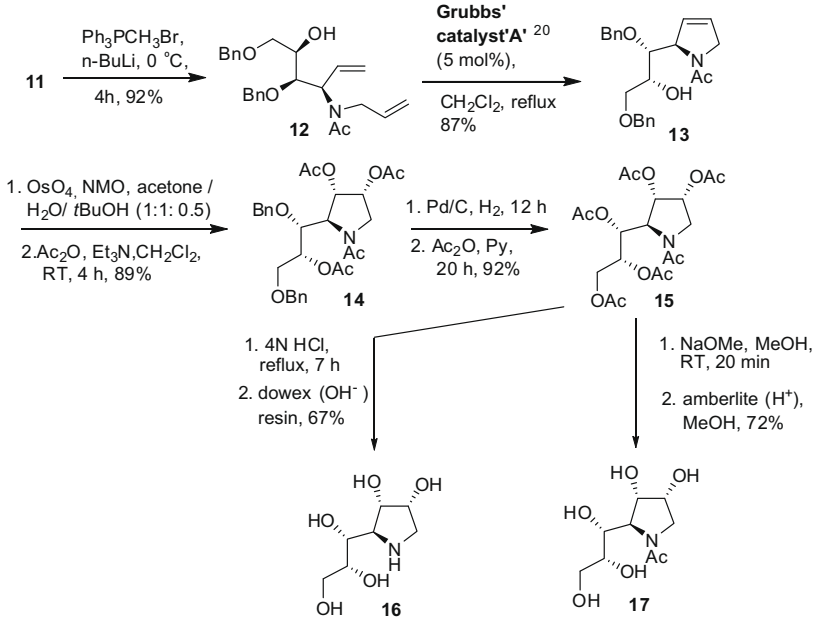
24 and **26** could be synthesized by the ring-closing metathesis (RCM) of respective dienes. Compounds **12** and **18** could be obtained from lactol **11**, which is easily derived from D-xylose as shown in Scheme 2.

Thus, alcohol **7** (Scheme 2), obtained[16] in two steps from D-xylose, on reaction with trifluoromethanesulfonic anhydride and pyridine gave the corresponding 2-*O*-triflate derivative, which was not isolated. The crude product, on reaction with NaN_3 in DMF at 70 °C, smoothly afforded the azido derivative **8** in 91% yield.

Reduction of the azido derivative **8** was achieved by treatment with Ph_3P in H_2O and THF to afford the corresponding amine, which was contaminated with phosphorus byproducts. The crude amine was acetylated under standard conditions using acetic anhydride and pyridine to give compound **9**, whose N-allylation with allyl bromide in the presence of K_2CO_3 led to monoallylated compound **10** in 92% yield.

Deprotection of the anomeric acetal **10** under usual conditions,[17] however, was not clean and led to several products from which the desired product could not be isolated. The problem was, however, circumvented by developing[18] an alternative method for the deprotection of anomeric acetals by the use of triphenylcarbenium tetrafluroborate, which gave the desired lactol **11** in excellent yield. The diene **12** (Scheme 3) was prepared from **11** under standard Wittig conditions[19] and the product underwent ring-closing metathesis with the first generation Grubbs' catalyst **A**[20] (5 mol %) to give the expected cyclic compound **13** in 87% yield. The olefin **13** was subjected to OsO_4 mediated catalytic *syn*-dihydroxylation and the corresponding diol was characterized as its triacetate **14** as a single diastereomer. Stereoselective dihydroxylation was expected due to the stereodirecting effect of the C-5 substituent in **13**.[21] The cis dihydroxy groups were found to have α-geometry as revealed by ^1H NMR spectroscopy and NOE spectral analysis of the corresponding monoacetate **17**, obtained later. Compound **17** showed NOE correlations between H-2 and H-5α; as well as H-5β, H-4, and H-3 as shown in Figure 2. Hydrogenolysis of **14** with 10% palladium hydroxide on activated carbon followed by acetylation gave pentaacetate **15** in 92% yield. This compound was deacetylated[22] with 4 N hydrochloric acid at 80 °C to give, after purification over a column of Dowex 50 resin, 1,4-dideoxy-1,4-imino-L-*glycero*-L-*gluco*-heptitol **16** (67%) as a syrup. Compound **15** upon deacetylation using NaOMe in MeOH gave the desired N-acetylated derivate **17**.

For the synthesis of 1,5-dideoxy-1,5-iminooctitols **24** and **26** (Scheme 4), lactol **11** was subjected to Grignard reaction with vinyl



Scheme 3. Synthesis of iminoheptitol **16**.

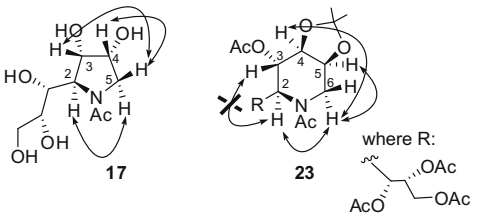


Figure 2. NOE correlations in **17** and **23**.

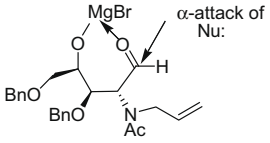


Figure 3. Chelation model.

magnesium bromide in THF to give the corresponding diol, which was acetylated using acetic anhydride in pyridine to give the diacetate **18** and its epimer **19** in 20:1 ratio (Scheme 4). The high diastereoselectivity was presumably due to the chelation-controlled[23] nucleophilic attack as shown in Figure 3. The stereochemistry was confirmed by ^{1}H NMR, COSY, and NOE spectral analysis of the corresponding pentaacetates **23** and **25**, obtained later.

Ring-closing metathesis of diene **18** with second generation Grubbs' catalyst **B**[20] (**3** mol %) gave the expected cyclic compound **20** in 88% yield. Dihydroxylation of **20** using a catalytic amount of OsO_4 and 2 equiv of NMO in acetone–water–*t*-butanol (2:2:1) at room temperature for 12 h afforded a mixture of diastereomers, which was separated at later stage. Thus, the crude diol, on treatment with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid[24] in acetone, formed the corresponding acetonides **21** and **22** in 1:1 ratio, which were separated by column chromatography. Hydrogenolysis of **21** with 10% palladium hydroxide on activated carbon followed by acetylation gave the pentaacetate **23** in 89% yield. The configuration and stereochemistry of the new chiral center was confirmed by ^{1}H NMR, COSY, and NOE experiments. Thus, compound **23** showed significant NOE interactions (Fig. 2) between H-2, H-4, H-5, and H-6α. Finally, global deprotection with aq HCl under refluxing conditions[22] afforded 1,5-dideoxy-1,5-imino-D-*threo*-L-*galacto*-octitol **24**. Similarly, other isomer **22** was converted to the desired product, 1,5-dideoxy-1,5-imino-D-*threo*-L-*allo*-octitol **26,** by the same sequence of reactions as described above.

3. Enzyme inhibition studies

All of the prepared iminoalditols **16**, **17**, **24**, and **26** were evaluated for glycosidase inhibition activity against a few commercially available glycosidases at millimolar concentrations (Table 1). These compounds showed poor inhibition against β-glucosidase (entry 2). However, compound **24** showed specific inhibition of α-galactosidase (entry 3) but again with poor inhibition.

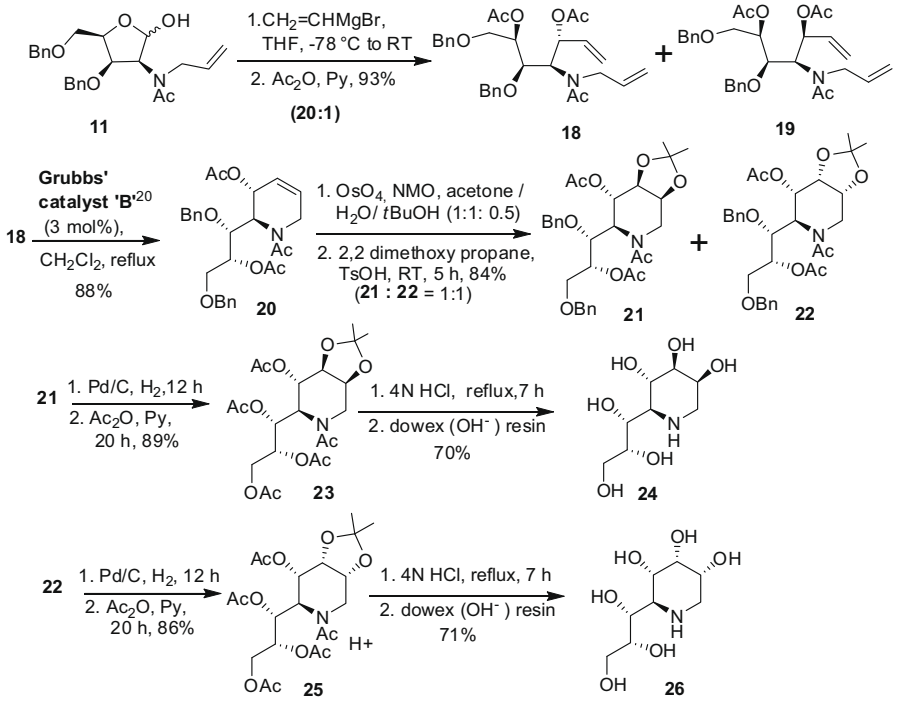
4. Conclusions

In conclusion, this paper describes short and efficient routes for the synthesis of 1,4-dideoxy-1,4-iminoalditols, and 1,5-dideoxy-1,5-iminoalditols from commercially available D-xylose. These compounds were found to be rather poor inhibitors of glycosidases. However, it is likely that structural variations of these iminooctitols could lead to better/altered glycosidase inhibition.

5. Experimental section

5.1. General methods and materials

The ^{1}H NMR, NOE, and ^{13}C spectra were recorded on a JEOL-JNM 400 MHz spectrometer. The chemical shift values are reported in



Scheme 4. Synthesis of the iminooctitols **24** and **26**.

Table 1
IC_{50} (mM) values for compounds **16**, **17**, **24** and **26**[a]

Entry	Enzyme	16	17	24	26
1	α-Glucosidase (rice)	NI[b]	6.2	NI	NI
2	β-Glucosidase (almonds)	4.2	5.7	NI	8.7
3	α-Galactosidase (coffee beans)	6.7	NI	3.2	7.3
4	β-Galactosidase (bovine liver)	NI	NI	NI	NI
5	α-Mannosidase (jack beans)	NI	NI	NI	NI

[a] Inhibition studies were carried out at millimolar concentration, optimal pH of the enzymes, and 37 °C.
[b] NI: no inhibition at 3 mM concentration of the inhibitor.

parts per million (ppm) using $CDCl_3$ as internal reference. All reactions were carried out using freshly distilled and dry solvents. Column chromatography was performed over silica gel (100–200 mesh) using hexane and EtOAc as eluent. The separation of isomers was performed on chromatotron using plates coated with Silica Gel PF254 (E-Merck, Germany). Rotation values were recorded on an Autopol II automatic polarimeter at the wavelength of sodium D-line (589 nm) at 25 °C. Melting points were determined using a Fischer-John melting point apparatus.

5.2. General procedure for inhibition assay

The enzymes α-galactosidase (coffee beans), α-glucosidases (rice and yeast), β-galactosidase (bovine liver), β-glucosidase (almond), and all the corresponding substrates were purchased from Sigma Chemical Co. Inhibition studies of the iminoalditols **16**, **17**, **24**, and **26** were determined by measuring the residual hydrolytic activities of the glycosidases.

The substrate concentration (2 mM) was prepared in 0.025 M citrate buffer with pH 4.0, and test compounds were preincubated with the enzymes for 1 h at 37 °C. The enzyme reaction was initiated by the addition of 100 μL substrate and the controls were run simultaneously in the absence of the test compound. The reaction was terminated at the end of 10 min by the addition of 0.05 M borate buffer (pH 9.8) and the absorbance of the liberated *p*-nitrophenol was measured at 405 nm using a Schimadzu spectrophotometer UV-160A. One unit of glycosidase activity is defined as the amount of enzymes that hydrolyzed 1 μM of *p*-nitrophenyl pyranoside per min at 25 °C.[25]

5.2.1. (3*S*,4*R*,5*R*)-3-Azido-4-(benzyloxy)-5-(benzyloxymethyl)-2-methoxytetrahydrofuran (8)

To a solution of compound **7** (5.0 g, 14.53 mmol) in CH_2Cl_2 were added pyridine (2.9 mL, 29.0 mmol) and triflic anhydride (2.69 mL, 15.9 mmol) at 0 °C after which it was stirred at room temperature for 20 min. When TLC revealed no starting material, the solution was diluted with water, washed with saturated $NaHCO_3$ (2 × 50 mL), CH_2Cl_2 (2 × 50 mL), brine solution (2 × 50 mL), and then dried over Na_2SO_4. Removal of the solvent gave crude triflate, which was dissolved in 40 mL of dry DMF, and sodium azide (2.83 g, 3 equiv, 43.5 mmol) was added to the solution. The reaction mixture was heated to 70 °C for 7 h and after completion of the reaction (TLC monitoring) it was cooled and extracted with diethyl ether (3 × 30 mL). The extract was washed with water, brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a crude product which was purified by column chromatography to give azido compound **8** in 91% (4.9 g, oil) yield in two steps. R_f = 0.41 (hexane–EtOAc 9:1), $[\alpha]_D^{28}$ +33.6 (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2870, 2106, 1584, 1496 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.27 (m, 10H, Ar-H), 4.87 (d, 1H, *J* = 12.6 Hz, –O*CH*$_2$Ph), 4.84 (d, 1H, *J* = 4.8 Hz, H-1), 4.73 (d, 1H, *J* = 12.2 Hz, –O*CH*$_2$Ph), 4.63–4.56 (2d, 2H, *J* = 12.2 Hz, –O*CH*$_2$Ph), 4.15–4.12 (ddd, 1H, *J* = 8.5, 5.8, 4.1 Hz, H-4), 4.04 (t, 1H, *J* = 5.8 Hz, H-3), 3.82 (dd, 1H, *J* = 5.6, 4.4 Hz, H-2), 3.68 (dd, 1H, *J* = 12.9, 8.5 Hz, H-5), 3.47 (s, 3H, OMe), 3.30 (dd, 1H, *J* = 13.6, 4.3 Hz, H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 137.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 101.7, 79.0, 78.8, 74.8, 73.6, 72.6, 55.7, 52.6. MSES: *m/z* 392 $[M+Na]^+$.

5.2.2. *N*-((3*S*,4*R*,5*R*)-4-(Benzyloxy)-5-(benzyloxymethyl)-2-methoxytetrahydrofuran-3-yl)acetamide (9)

To a solution of compound **8** (4.5 g, 12.2 mmol) in dry THF (30 mL) at room temperature were added triphenylphosphine (4.8 g, 18.3 mmol) and water (288 mg, 36.6 mmol). The mixture was stirred for 10 h, diluted with EtOAc, washed with brine, dried over Na_2SO_4, and then concentrated to give crude amine. The crude amine was dissolved in CH_2Cl_2 (25 mL) and treated with pyridine (3.0 mL), Ac_2O (3.0 mL), and a catalytic amount of DMAP at room temperature, and the mixture was stirred for 20 h. The reaction mixture was extracted with CH_2Cl_2 (3 × 25 mL) and the organic layer washed with water and brine. Evaporation of the solvent followed by purification using SiO_2 column chromatography gave **9**. Yield: 85% (4.1 g, overall yield for two steps), (colorless solid, mp 121–123 °C), R_f = 0.48 (hexane–EtOAc 3:2), $[\alpha]_D^{28}$ +110.4 (*c* 1.05, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3292, 3089, 2909, 1649, 1559, 1047 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.29 (m, 10H, Ar-H), 7.03 (d, 1H, *J* = 8.2 Hz, H-1), 4.75 (s, 1H, *NH*-Ac), 4.60 (d, 1H, *J* = 10.7 Hz, –O*CH*$_2$Ph), 4.55–4.48 (m, 3H, –O*CH*$_2$Ph), 4.45 (2d, 2H, *J* = 3.6 Hz, H-3, H-2), 4.43 (br d, 1H, *J* = 7.8 Hz, H-4), 3.81 (dd, 1H, *J* = 10.4, 3.1 Hz, H-5), 3.71 (dd, 1H, *J* = 10.7, 1.4 Hz, H-5′), 3.32 (s, 3H, OMe), 1.33 (s, 3H, NH-*Ac*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.5, 137.3, 128.4–127.6 (m, aromatic), 106.9, 77.3, 77.2, 74.1, 72.5, 68.2, 54.8, 52.7, 22.3. MSES: *m/z* 408 $[M+Na]^+$.

5.2.3. *N*-Allyl-*N*-((3*S*,4*R*,5*R*)-4-(benzyloxy)-5-(benzyloxymethyl)-2-methoxytetrahydrofuran-3-yl)acetamide (10)

To the reaction mixture of **9** (4.0 g, 10.2 mmol) and allyl bromide (1.3 mL, 15.3 mmol) in 20 mL dry DMF was added K_2CO_3 (4.14 g, 30.3 mmol) and stirred at room temperature for 4 h. After usual work up with diethyl ether and column chromatographic purification compound **10** was obtained. Yield: 92% (4.1 g, colorless oil). R_f = 0.50 (hexane–EtOAc 7:3), $[\alpha]_D^{28}$ +82.6 (*c* 7.9, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3089, 2909, 1659, 1605, 1047 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers): δ 7.35–7.21 (m, 10H, Ar-H), 5.83–5.75 (m, 1H, –*CH*=CH_2), 5.21 (dd, 2H, *J* = 12.0, 6.08 Hz, –CH=*CH*$_2$), 5.03 (d, 1H, *J* = 1.4 Hz, H-1), 4.62 (d, 1H, *J* = 11.9 Hz, –O*CH*$_2$Ph), 4.52–4.46 (m, 3H, –O*CH*$_2$Ph), 4.40 (d, 1H, *J* = 11.6 Hz, allylic), 4.35–4.30 (m, 2H, H-4, H-3), 4.21 (m, 1H), 4.15 (m, 1H), 3.96–3.91 (dd, 1H, *J* = 10.7, 1.4 Hz, H-5′), 3.79–3.70 (m, 3H, H-5, H-2, allylic), 3.32 (s, 3H, OMe), 2.01 (s, 3H, NH-*Ac*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 137.9, 134.6, 134.4, 128.5–127.6 (m, aromatic), 115.6, 114.4, 79.8, 78.8, 78.7, 74.4, 74.2, 73.4, 68.0, 67.5, 63.1, 55.7, 55.5, 49.5, 49.5, 48.0, 21.5. MSES: *m/z* 448 $[M+Na]^+$.

5.2.4. *N*-Allyl-*N*-((3*S*,4*R*,5*R*)-4-(benzyloxy)-5-(benzyloxymethyl)-2-hydroxyl tetrahydrofuran-3-yl) acetamide (11)

To a solution of compound **10** (3.8 g, 8.79 mmol) in dry CH_2Cl_2 (20 mL) at room temperature was added triphenylcarbenium tetrafluroborate (2.9 g, 8.79 mmol). The mixture was stirred for 1 h and after completion of reaction (TLC monitoring) it was quenched with $NaHCO_3$ and extracted with dichloromethane (3 × 20 mL) and the organic layer washed with water and brine. Evaporation of the solvent followed by purification using SiO_2 column chromatography gave lactol **11**. Yield: 93% (3.4 g, colorless oil). R_f = 0.52 (hexane–EtOAc 2:3), $[\alpha]_D^{28}$ +18.5 (*c* 1.9, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3349, 2923, 2827, 1649, 1495 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of diastereomers): δ 7.33–7.21 (m, 20H, Ar-H), 7.20 (d, 2H, *J* = 2.96 Hz, H-1), 5.81–5.75 (m, 2H, –*CH*=CH_2), 5.54 (br s, 1H), 5.20–5.24 (m, 3H, –CH=*CH*$_2$), 4.59–4.44 (m, 10H,

4 × –O*CH*$_2$Ph), 4.01 (br d, 1H, *J* = 19.2 Hz), 3.71 (m, 3H), 1.97 (s, 6H, NH-*Ac*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 137.6, 137.3, 137.2, 133.3, 132.7, 128.5–127.5 (m, aromatic), 116.8, 116.7, 116.0, 100.0, 99.3, 95.7, 95.5, 81.6, 79.1, 78.9, 78.2, 77.9, 77.8, 77.3, 76.6, 75.8, 74.2, 73.2, 72.9, 72.5, 72.4, 72.1, 52.6, 49.2, 48.1, 47.8, 47.6, 21.7, 21.6, 21.3. MSES: *m/z* 434 [M+Na]$^+$.

5.2.5. *N*-Allyl-*N*-((3*S*,4*R*,5*R*)-4,6-bis(benzyloxy)-5-hydroxyhex-1-en-3-yl)acetamide (12)

To a stirred solution of 2.5 g (7.1 mmol) of methyltriphenylphosphonium bromide in 15 mL of dry THF at 0 °C under argon was added dropwise 1.1 mL (7.1 mmol) of 2.0 M butyllithium in hexane during 2 min. A color change from yellow to red occurred. The mixture was stirred for 15 min at 0 °C and a solution of 1.5 g (3.59 mmol) of the preceding lactol in 5 mL of dry THF was added in dropwise fashion. Solid began to form in the resulting cream colored suspension. The mixture was stirred for 4 h and the reaction was quenched by the addition of 2 mL of water. The dark brown mixture was extracted several times with ether, and the combined organic layers were washed with 10 mL of saturated aqueous NaCl, and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by purification using column chromatography gave diene **12**. Yield: 92% (1.30 g, oil). R_f = 0.48 (hexane–EtOAc 3:2), $[\alpha]_D^{28}$ −15.3 (*c* 1.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2923, 2827, 1659, 1497 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (m, 10H, Ar-H), 5.94–5.86 (m, 1H, H-2), 5.78–5.75 (m, 1H, –C*H*=CH$_2$), 5.46–5.37 (dd, 2H, *J* = 24.6, 16.3 Hz, H-1), 5.18–5.06 (dd, 2H, *J* = 29.6, 16.3 Hz, –CH=C*H*$_2$), 4.74 (d, 1H, *J* = 11.2 Hz, –O*CH*$_2$Ph), 4.65–4.55 (2d, 2H, *J* = 11.2 Hz, –O*CH*$_2$Ph), 4.43 (d, 1H, *J* = 11.2 Hz, –O*CH*$_2$Ph), 4.16–3.96 (m, 4H), 3.54 (d, 1H, *J* = 14.1 Hz), 3.43–3.35 (m, 2H), 2.07 (s, 3H, NH-*Ac*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 138.0, 137.2, 134.9, 133.7, 128.3–127.7 (m, aromatic), 120.3, 117.4, 78.1, 74.9, 74.4, 73.4, 73.3, 71.4, 70.8, 69.5, 61.6, 51.4, 46.3, 29.6, 22.4. MSES: *m/z* 432[M+Na]$^+$.

5.2.6. 1-((*R*)-2-((1*R*,2*R*)-1,3-Bis(benzyloxy)-2-hydroxypropyl)-2H-pyrrol-1(5*H*)-yl)ethanone (13)

To a stirred solution of diene **12** (600 mg, 1.46 mmol) in dry CH_2Cl_2 (100 mL), the first generation Grubbs' catalyst (60 mg, 0.050 mmol) was added. The reaction mixture was heated to reflux under nitrogen for 14 h, then cooled, before all the solvent was evaporated under vacuum and the crude product was purified by column chromatography to give cyclized product **13**. Yield: 87% (495 mg, oil). R_f = 0.52 (hexane–EtOAc 1:1), $[\alpha]_D^{28}$ +26.9 (*c* 1.3, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2922, 2852, 1725, 1679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (m, 10H, Ar-H), 6.04 (dd, 1H, *J* = 4.2, 2.2 Hz, H-2), 5.83 (d, 1H, *J* = 6.3 Hz, H-3), 4.91 (br s, 1H, H-5), 4.72–4.46 (m, 5H, 2 × –O*CH*$_2$Ph, H-1′), 4.19 (br d, 1H, *J* = 14.4 Hz, H-4), 4.08 (dd, 1H, *J* = 14.2, 2.1 Hz, H-1), 3.97 (dd, 1H, *J* = 7.3, 2.9 Hz, H-6), 3.88–3.86 (m, 1H, H-7), 3.58 (d, 1H, *J* = 6.0 Hz, H-1), 1.90 (s, 3H, NH-*Ac*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 138.3, 137.9, 128.9–127.6 (m, aromatic), 125.0, 124.6, 79.4, 74.9, 73.4, 71.8, 70.6, 69.2, 66.1, 64.9, 55.1, 54.6, 22.5. HRMS calcd for $C_{23}H_{27}NO_4$ [M+H]$^+$ 382.2013, found 382.1911.

5.2.7. (2*S*,3*S*,4*R*)-2-((1*R*,2*R*)-2-Acetoxy-1,3-bis(benzyloxy)propyl)-1-acetylpyrrolidine-3,4-diyl diacetate (14)

To a stirred solution of an olefin **13** (450 mg, 1.18 mmol) in acetone–water–*t*-butanol (1:1:0.4) at room temperature were added NMO·H_2O (151 mg, 1.29 mmol) and OsO_4 (576 μL, 0.002 equiv). The reaction mixture was stirred for 14 h and it was treated with $Na_2S_2O_5$ (430 mg, 1.18 mmol). The reaction mixture was further stirred for 1 h and extracted with EtOAc (2 × 30 mL). The organic layer was washed with 1 N HCl, water, and finally with brine. Usual workup gave a crude product, which was dissolved in CH_2Cl_2 (7 mL) and treated with pyridine (1 mL), Ac_2O (1 mL), and a catalytic amount of DMAP at room temperature and the mixture was stirred for 4 h. The reaction mixture was extracted with CH_2Cl_2 (2 × 15 mL) and the organic layer was washed with water and brine. Evaporation of the solvent followed by purification using SiO_2 column chromatography gave triacetate **14**. Yield: 89% (530 mg, overall yield for two steps), colorless solid, mp 141–143 °C, R_f = 0.40 (hexane–EtOAc 2:3), $[\alpha]_D^{28}$ +27.2 (*c* 1.1, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2922, 1744, 1653 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (m, 10H, Ar-H), 5.59 (d, 1H, *J* = 8.0 Hz, H-3), 5.49–5.44 (dt, 1H, *J* = 7.8, 4.6 Hz, H-2), 5.27–5.23 (q, 1H, *J* = 10.9, 5.6 Hz, H-5), 4.76 (d, 1H, *J* = 11.9 Hz, –O*CH*$_2$Ph), 4.54 (br s, 2H, –O*CH*$_2$Ph), 4.38 (d, 1H, *J* = 11.9 Hz, –O*CH*$_2$Ph), 4.22 (br d, 1H, *J* = 5.6 Hz, H-4), 4.11 (s, 1H, H-7), 3.71–3.62 (m, 2H, H-6, H-7′), 3.41 (t, 1H, *J* = 9.5 Hz, H-1), 3.14 (t, 1H, *J* = 9.2 Hz, H-1′), 2.10–1.91 (3s, 9H, –OCO*CH*$_3$), 1.75 (s, 3H, –NHCO*CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3–169.5 (m), 137.8, 137.6, 128.8–127.7 (m, aromatic), 75.6, 74.9, 73.2, 72.4, 71.7, 70.6, 97.9, 63.5, 48.7, 22.2–20.5 (m). HRMS calcd for $C_{29}H_{36}NO_9$: [M+H]$^+$ 542.2392, found: 542.2391.

5.2.8. (1*R*,2*R*)-1-((2*R*,3*S*,4*R*)-3,4-Diacetoxy-1-acetylpyrrolidin-2-yl)propane-1,2,3-triyl triacetate (15)

To a stirred solution of triacetate **14** (300 mg, 0.55 mmol) in ethanol (4 mL) was added 10% Pd/C (150 mg). The mixture was stirred under hydrogen atmosphere at room temperature for 12 h. After completion of the reaction, the mixture was filtered through a Celite pad, washed with EtOH, and the filtrate was concentrated under vacuo to give the corresponding diol. Acetylation of the crude diol was done using pyridine and acetic anhydride (1:1, 2 mL) at room temperature for 20 h. Usual workup followed by column chromatography gave the pure pentaacetate **15**. Yield: 92% (225 mg, overall yield over two steps), (oil), R_f = 0.52 (hexane–EtOAc 1:4), $[\alpha]_D^{28}$ +16.2 (*c* 1.6, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1744, 1653 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.56 (m, 2H, H-3, H-5), 5.30 (m, 2H, H-2, H-6), 4.21 (br s, 1H, H-4), 4.17 (d, 1H, *J* = 4.6 Hz, H-7), 4.05 (dd, 1H, *J* = 11.7, 8.0, Hz, H-7), 3.73 (dd, 1H, *J* = 9.5, 7.8 Hz, H-1′), 3.37 (dd, 1H, *J* = 9.0, 8.5 Hz, H-1), 2.14–1.98 (m, 18 H, 5 × OCO*CH*$_3$ and –NHCO*CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4–169.4 (m), 71.3, 70.2, 70.1, 69.4, 62.5, 61.7, 48.7, 22.2–20.4 (m). HRMS calcd for $C_{19}H_{28}NO_{11}$ [M+H]$^+$ 446.1657, found 446.1648.

5.2.9. (1*R*,2*R*)-1-((2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl) propane-1,2,3-triol (16)

A solution of **15** (100 mg, 0.22 mmol) and 4 M hydrochloric acid (2 mL) was stirred for 7 h at 80 °C and then evaporated. The residue was purified by chromatography on a column of DOWEX basic resin and concentrated under reduced pressure to get 1,4-dideoxy-1,4-iminoheptitol **16**. Yield: 67% (30 mg), light brownish solid. $[\alpha]_D^{28}$ −17.5 (*c* 0.8, MeOH). ^{1}H NMR (400 MHz, D_2O): δ 4.32 (dd, 1H, *J* = 8.2, 4.1 Hz, H-3), 4.24 (br d, 1H, *J* = 1.7 Hz, H-2), 3.94 (t, 1H, *J* = 4.1 Hz, H-5), 3.75 (q, 1H, *J* = 6.3, 4.3 Hz, H-6), 3.59–3.57 (br d, 1H, *J* = 2.2 Hz, H-4), 3.56–3.54 (d, 1H, *J* = 4.8 Hz, H-7), 3.51 (dd, 1H, *J* = 11.7, 6.6 Hz, H-7′), 3.34 (dd, 1H, *J* = 12.9, 3.9 Hz, H-1), 3.22 (dd, 1H, *J* = 12.6, 1.4 Hz, H-1′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 73.9, 72.9, 72.3, 70.0, 65.3, 64.9, 52.3. HRMS calcd for $C_7H_{16}NO_5$ [M+H]$^+$ 194.1028, found 194.1024.

5.2.10. 1-((2*R*,3*S*,4*R*)-3,4-Dihydroxy-2-((1*R*,2*R*)-1,2,3-trihydroxypropyl)pyrrolidin-1-yl)ethanone (17)

Deacetylation of the pentaacetate **15** was done using NaOMe in MeOH at room temperature. The crude product was filtered through Amberlite (H^+) ion exchange resin for the enzyme inhibition studies. Yield: 72%. $[\alpha]_D^{28}$ +27.5 (*c* 0.9, MeOH). ^{1}H NMR (400 MHz, D_2O) (mixture of rotamers): δ 4.35 (dd, 1H, *J* = 8.7, 3.6 Hz, H-2), 4.27 (dd, 1H, *J* = 7.5, 3.4 Hz, H-3), 4.09 (t, 1H,

J = 4.1 Hz, H-3, minor rotamer), 4.00 (m, 1H, H-2, minor rotamer), 3.80 (dd, 1H, J = 8.0, 4.8 Hz, H-4), 3.75 (dd, 1H, J = 8.5, 3.6 Hz, H-5), 3.65 (dd, 1H, J = 10.7, 4.4 Hz, H-1), 3.60–3.52 (m, 3H, H-6, 2 × H-7), 3.39 (dd, 1H, J = 11.2, 5.6 Hz, H-1′). ^{13}C NMR (100 MHz, D_2O): δ 176.6, 74.0, 73.3, 72.4, 71.6, 69.2, 67.5, 65.1, 54.7, 53.7, 53.2, 24.1. HRMS calcd for $C_9H_{18}NO_6$ $[M+H]^+$ 236.1129, found 236.1053.

5.2.11. (2*R*,3*R*,4*S*,5*R*)-4-(*N*-Allylacetamido)-1,3-bis(benzyloxy) hept-6-ene-2,5-diyl diacetate (18)

To a stirred solution of lactol **11** (1.50 g, 3.59 mmol) in dry THF (20 mL) was added dropwise vinyl magnesium bromide (2.87 mL, 21.54 mmol, 1.0 M solution in THF) at −78 °C, and the reaction mixture was stirred at 0 °C for 3 h. The reaction was quenched with saturated NH_4Cl solution and the aqueous phase of the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to get oil. Acetylation of the diol was done using pyridine and acetic anhydride (1:1, 4 mL) at room temperature for 10 h. Usual workup followed by column chromatography afforded first diene **18** (89%, 1.67 g) and second its epimer **19** (4%, 80 mg) as colorless oils. Data for **18**: $[\alpha]_D^{28}$ +19.1 (*c* 1.1, CH_2Cl_2). R_f = 0.50 (hexane–EtOAc 7:3). IR (CH_2Cl_2) ν_{max}: 2803, 1734, 1659, 1632 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.24 (m, 10H, Ar-H), 6.01 (br m, 1H, –C*H*=CH_2), 5.70–5.66 (m, 1H, H-2), 5.57 (br t, 1H), 5.49 (d, 1H, J = 16.8 Hz), 5.29–5.15 (m, 4H, H-1, –CH=CH_2), 5.08 (d, 1H, J = 17.8 Hz), 4.70 (d, 1H, J = 10.9 Hz, –OCH_2Ph), 4.57–4.51 (2d, 3H, J = 11.2 Hz, –OCH_2Ph), 4.30 (br d, 1H, J = 8.0 Hz), 4.15 (br d, 1H, J = 10.2 Hz), 3.91 (t, 1H, J = 8.7 Hz), 3.85 (d, 1H, J = 11.9 Hz), 3.66 (dd, 1H, J = 11.2, 1.9 Hz), 2.06 (s, 6H, OCOCH_3), 1.93 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3–169.4 (m) 144.3, 138.5, 138.1, 133.9, 133.5, 128.3–126.7, 120.9, 112.4, 76.3, 75.4, 73.9, 72.3, 71.5, 68.6, 68.2, 22.9, 21.1, 15.0. HRMS calcd for $C_{30}H_{37}NNaO_7$ $[M+Na]^+$ 546.2463, found 546.2469.

5.2.12. (2*R*,3*R*,4*S*,5*S*)-4-(*N*-Allylacetamido)-1,3-bis(benzyloxy) hept-6-ene-2,5-diyl diacetate (19)

$[\alpha]_D^{28}$ +22.1 (*c* 0.8, CH_2Cl_2). R_f = 0.49 (hexane–EtOAc 7:3). IR (CH_2Cl_2) ν_{max}: 2903, 1744, 1659, 1642 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.25 (m, 10H, Ar-H), 5.95 (m, 1H, –C*H*=CH_2), 5.72 (m, 1H, H-2), 5.57 (t, 1H, J = 5.6 Hz), 5.17–5.03 (m, 5H, H-4, H-1, –CH=CH_2), 4.27 (d, 1H, J = 11.2 Hz, –OCH_2Ph), 4.57–4.51 (m, 4H, 3 × –OCH_2Ph), 4.35 (br d, 1H, J = 7.0 Hz), 4.19–4.17 (m, 1H), 3.96–3.82 (m, 2H), 3.65 (d, 1H, J = 11.4 Hz), 2.06 (s, 6H, 2 × –OCOCH_3), 1.95 (s, 3H, NHCOCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3–169.4 (m) 144.3, 138.5, 138.1, 133.9, 133.5, 128.3–126.7 (m, aromatic), 120.9, 112.4, 76.3, 75.4, 73.9, 72.3, 71.5, 68.6, 68.2, 22.9, 21.1, 15.0. HRMS calcd for $C_{30}H_{37}NNaO_7$ $[M+Na]^+$ 546.2648, found 546.2469.

5.2.13. (2*R*,3*R*)-2-((1*S*,2*R*)-2-Acetoxy-1,3-bis(benzyloxy)propyl)-1-acetyl-1,2,3,6-tetrahydropyridin-3-yl acetate (20)

Compound **20** (890 mg) was obtained from **18** (1.0 g, 1.91 mmol) using the procedure which was used to obtain **13**. Yield: 88%, colorless syrup, R_f = 0.40 (hexane–EtOAc 2:3). $[\alpha]_D^{28}$ −74.8 (*c* 3.7, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2922, 2852, 1725, 1679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.34–7.30 (m, 20H, Ar-H, both rotamers), 5.95–5.90 (ddd, 2H, J = 5.8, 3.8, 2.2 Hz, H-2, both rotamers), 5.81 (br dd, 2H, J = 5.8, 3.8, 2.2 Hz, H-2, both rotamers), 5.41 (dd, 2H, J = 11.2, 5.6 Hz, H-4, both rotamers), 5.17 (d, 1H, J = 9.7 Hz, rotamer-II), 4.99–4.93 (m, 2H, H-1′, both rotamers), 4.67 (2d, 2H, J = 11.2 Hz, –OCH_2Ph, both rotamers), 4.55–4.47 (m, 8H, –OCH_2Ph, both rotamers), 4.29 (d, 1H, J = 9.5 Hz, rotamer-II), 4.10 (br d, 1H, J = 19.7 Hz, rotamer-II), 3.88 (dd, 2H, J = 10.2, 2.2 Hz, both rotamers), 3.69–3.58 (m, 4H), 3.20 (dd, 1H, J = 14.0 Hz, rotamer-II), 2.08–1.98 (m, 18 H, 6 × –COCH_3). 13C NMR (100 MHz, $CDCl_3$): δ 170.3–169.5 (m), 137.7, 137.3, 136.9, 130.9, 128.7–127.8 (m, aromatic), 122.5, 121.1, 74.9, 74.3, 73.4, 71.1, 70.7, 76.1, 66.3, 65.6, 56.8, 49.7, 42.7, 38.5, 21.8–20.8 (m). HRMS calcd for $C_{28}H_{33}NNaO_7$ $[M+Na]^+$ 518.2155, found 518.2150.

5.2.14. (3a*S*,6*R*,7*R*,7a*S*)-6-((1*R*,2*R*)-2-Acetoxy-1,3-bis(benzyloxy)-propyl)-5-acetyl-2,2-dimethylhexa-hydro-[1,3]dioxolo[4,5-*c*]-pyridin-7-yl acetate (21)

To a stirred solution of an olefin **20** (1.61 mmol) in acetone–water–*t*-butanol (1:1:0.4) at room temperature were added $NMO{\cdot}H_2O$ (188 mg, 1.61 mmol) and OsO_4 (710 μL, 0.002 equiv). The reaction mixture was stirred for 12–14 h (monitored by TLC) and it was treated with $Na_2S_2O_5$ (296 mg, 1.77 mmol). The reaction mixture was further stirred for 1 h and extracted with EtOAc (2 × 20 mL). The organic layer was washed with 1 N HCl, water, and finally with brine. Usual workup gave the crude diol which was dissolved in CH_2Cl_2 (5 mL) and then treated with 2,2-dimethoxypropane (1.0 mL, 8.05 mmol) and catalytic amount of *p*-toluenesulfonic acid at room temperature. The reaction mixture was stirred for 5 h and progress of the reaction was monitored by TLC. Evaporation of the solvent gave a residue, which was purified by column chromatography to give two separable diastereomers **21** and **22**. Data for **21**: Yield: 41% (375 mg), colorless solid, mp 114–116 °C; R_f = 0.42 (hexane–EtOAc, 3:2), $[\alpha]_D^{28}$ +66.6 (*c* 0.2, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2922, 2852, 1735, 1679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.36–7.24 (m, 20H, Ar-H, for both), 5.60 (t, 1H, J = 5.1 Hz, major rotamer), 5.40 (m, 1H, H-3, minor rotamer), 5.20 (q, 1H, J = 5.6, 1.9 Hz, H-6), 4.85 (t, 1H, J = 5.1 Hz, H-2), 4.75 (t, 1H, J = 5.1 Hz, H-2, minor rotamer), 4.68–4.47 (m, 6H, both rotamers), 4.33 (dd, 1H, 1H, J = 7.5, 4.1 Hz), 4.25–4.19 (m, 4H, both rotamers), 3.93 (br d, 1H, J = 8.5 Hz, minor rotamer), 3.71–3.60 (m, 5H), 3.21 (d, 1H, 1H, J = 12.1 Hz, minor rotamer), 2.95 (d, 1H, J = 12.1 Hz, minor rotamer), 2.09–1.92 (m, 18H, 6 × –COCH_3), 1.38 (2s, 6H, –CH_3, both rotamers), 1.27 (2s, 6H, –CH_3, both rotamers). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3–169.9 (m), 138.7, 137.8, 129.4–127.0 (m, aromatic), 110.1, 109.4, 81.4, 79.4, 78.8, 75.4, 73.3, 72.8, 72.4, 71.7, 69.3, 68.7, 67.3, 51.7, 50.7, 45.7, 29.6, 27.0, 25.8, 25.7, 24.3, 24.0, 22.6, 21.7–21.0 (m). HRMS calcd for $C_{31}H_{40}NO_9$ $[M+H]^+$ 570.2703, found 570.2631.

5.2.15. (3a*R*,6*R*,7*R*,7a*R*)-6-((1*R*,2*R*)-2-Acetoxy-1,3-bis(benzyloxy)-propyl)-5-acetyl-2,2-dimethylhexa hydro-[1,3]dioxolo[4,5-*c*] pyridin-7-yl acetate (22)

Data for **22**: Yield: 43% (395 mg), colorless liquid. R_f = 0.40 (hexane–EtOAc 3:2), $[\alpha]_D^{28}$ −5.2 (*c* 1.2, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 2922, 2852, 1735, 1679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.41–7.30 (m, 20H, Ar-H, for both), 5.68–5.63 (m, 2H, for both), 4.99–4.93 (m, 2H), 4.84 (d, 1H, J = 11.0 Hz), 4.66–4.46 (m, 5H), 4.27 (m, 2H), 4.13 (m, 1H), 3.77–3.51 (m, 3H), 2.93 (dd, 1H, J = 14.4, 10.4 Hz), 2.09–1.97 (m, 18H, 6 × –COCH_3), 1.38 (s, 3H, –CH_3, major rotamers), 1.37 (s, 3H, –CH_3, minor rotamers), 1.32 (2s, 6H, –CH_3, both rotamers). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3–169.4 (m), 137.9, 137.7, 128.4–127.7 (m, aromatic), 110.0, 109.8, 75.2, 74.3, 73.9, 73.6, 72.6, 70.5, 69.3, 68.4, 67.6, 67.0, 66.7, 57.2, 50.3, 43.9, 38.4, 29.6, 28.0, 26.1, 26.0, 24.1, 21.9, 21.8, 20.8, 20.6. HRMS calcd for $C_{31}H_{39}NNaO_9$ $[M+Na]^+$ 592.2523, found 592.2540.

5.2.16. (1*R*,2*R*)-1-((3a*S*,6*S*,7*S*,7a*S*)-7-Acetoxy-5-acetyl-2,2-dimethyl-hexahydro-[1,3]dioxolo[4,5-*c*]pyridin-6-yl)propane-1,2,3-triyl triacetate (23)

This compound was prepared in 89% yield from **21** by using the same procedure as described for **15**. Yield: 89% (overall yield in two

steps). R_f = 0.52 (hexane–EtOAc 2:3), $[\alpha]_D^{28}$ +36.6 (c 0.75, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1743, 1657 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.54 (dd, 1H, J = 5.6, 3.9 Hz, H-3), 5.35 (dd, 1H, J = 5.6, 3.9 Hz, H-3), 5.22 (dd, 1H, J = 9.5, 5.6 Hz, H-4), 5.01–4.98 (ddd, 1H, J = 8.0, 5.8, 1.9 Hz, H-7), 4.32–4.26 (m, 2H, H-2, H-6), 4.23 (dd, 1H, J = 11.6, 5.6 Hz, H-8), 3.91 (dd, 1H, J = 10.2, 6.3 Hz, H-8′), 3.81 (d, 1H, J = 15.3 Hz, H-1), 3.51 (d, 1H, J = 15.3 Hz, H-1′), 2.19–2.13 (2s, 6H, 2 × –COCH_3), 2.07–2.00 (3s, 9H, 3 × –COCH_3), 1.37 (s, 3H, –CH_3), 1.28 (s, 3H, –CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6–169.5 (m), 110.4, 72.4, 71.5, 68.5, 68.2, 66.2, 62.4, 48.2, 44.9, 25.3, 24.0, 21.8, 21.0, 20.6. HRMS calcd for $C_{21}H_{31}NNaO_{11}$ $[M+Na]^+$ 496.1795, found 496.1792.

5.2.17. (2*S*,3*S*,4*S*,5*S*)-2-((1*R*,2*R*)-1,2,3-Trihydroxypropyl) piperidine-3,4,5-triol (24)

This compound was prepared in 70% yield from **23** by using the same procedure as described for **16**. Yield: 70% (50 mg), colorless solid, mp 121–123 °C. $[\alpha]_D^{28}$ −20.0 (*c* 0.1, H_2O). ^1H NMR (400 MHz, D_2O): δ 4.21–4.4.07 (m, 2H), 3.90–3.88 (m, 2H), 3.68–3.49 (m, 4H), 3.16–3.09 (m, 1H), 2.98–2.86 (m, 1H). ^{13}C NMR (100 MHz, D_2O): δ 73.5, 72.2, 70.5, 69.5, 68.8, 66.0, 63.5, 58.4, 58.4, 56.5, 43.9. HRMS calcd for $C_8H_{18}NO_6$ $[M+H]^+$ 224.1134, found 224.1135.

5.2.18. (1*R*,2*R*)-1-((3a*R*,6*S*,7*S*,7a*R*)-7-Acetoxy-5-acetyl-2,2-dimethyl-hexahydro-[1,3]dioxolo[4,5-*c*]-pyridin-6-yl)propane-1,2,3-triyl triacetate (25)

Compound **25** (210 mg) was obtained from **22** (300 mg, 0.52 mmol) using the procedure as was used to obtain **23**. Yield: 86% (overall yield in two steps). R_f = 0.48 (hexane–EtOAc 2:3), $[\alpha]_D^{28}$ −15.2 (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1743, 1657 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.81 (dd, 1H, J = 9.7, 2.2 Hz, H-6), 5.23 (t, 1H, J = 2.9 Hz, H-4), 5.14–5.12 (ddd, 1H, J = 8.0, 6.6, 2.2 Hz, H-7), 4.93 (br d, 1H, J = 9.8 Hz, H-5), 4.29–4.20 (m, 2H, H-8, H-2), 4.09 (dd, 1H, J = 4.9, 3.4 Hz, H-3), 3.88–3.82 (m, 2H, H-8′, H-1′), 3.01–2.95 (dd, 1H, J = 14.6, 10.4 Hz, H-1), 2.23 (s, 3H, –COCH_3), 2.08–2.02 (4 × s, 12H, 4 × –COCH_3), 1.54 (s, 3H, –CH_3), 1.34 (s, 3H, –CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5–169.2 (m), 110.4, 74.4, 69.3, 68.4, 67.9, 67.4, 66.9, 62.1, 49.5, 44.1, 28.0, 25.9, 21.1, 20.8, 20.6, 20.5. HRMS calcd for $C_{21}H_{32}NO_{11}$ $[M+H]^+$ 474.1972, found 474.1970.

5.2.19. (2*S*,3*S*,4*R*,5*R*)-2-((1*R*,2*R*)-1,2,3-Trihydroxypropyl) piperidine-3,4,5-triol (26)

Compound **26** (33 mg) was obtained from **25** (100 mg, 0.21 mmol) using the procedure as was used to obtain **24**. Yield: 71%, colorless solid, mp 132–133 °C. $[\alpha]_D^{28}$ −13.1 (*c* 0.3, H_20). ^1H NMR (400 MHz, D_2O): δ 4.13 (s, 1H), 4.08 (d, 1H, J = 2.4 Hz), 4.02–3.97 (m, 2H), 3.68–3.50 (m, 3H), 3.34 (dd, 1H, J = 13.4, 2.9 Hz), 3.28–3.20 (m, 1H), 3.06 (d, 1H, J = 13.4 Hz). ^{13}C NMR (100 MHz, D_2O): δ 74.2, 72.5, 67.6, 67.4, 67.2, 63.8, 61.1, 49.3. HRMS calcd for $C_8H_{18}NO_6$ $[M+H]^+$ 224.1129, found 224.1035.

Acknowledgments

We thank the Department of Science and Technology, New Delhi, for financial support to Y.D.V. in the form of Ramanna Fellowship (Grant No. SR/S1/RFOC-04/2006). A.K. thanks Council of Scientific and Industrial Research for senior research fellowships.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2010.04.016.

References

1. (a) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1645–1680; (b)*Iminosugars as Glycosidase Inhibitors: Nojirimycin and Beyond*; Stutz, A. E., Ed.; Wiley-VCH: Weinheim, 1999.
2. (a) Chand, P.; Kotian, P. L.; Dehghani, A.; El-Kattan, Y.; Lin, T.-H.; Hutchison, T. L.; Sudhakar Babu, Y.; Bantia, S.; Elliott, A. J.; Montgomery, J. A. *J. Med. Chem.* **2001**, *44*, 4379–4392; (b) Kim, C. U.; Lew, W.; Williams, M. A.; Liu, H.; Zhang, L.; Swaminathan, S.; Bischofbergen, N.; Chen, M. S.; Mendel, D. B.; Tai, C. Y.; Laver, W. G.; Stevens, R. C. *J. Am. Chem. Soc.* **1997**, *119*, 681–690.
3. (a) Nishimura, Y.; Satoh, T.; Adachi, H.; Kondo, S.; Takeuchi, T.; Azetaka, M.; Fukuyasu, H.; Iizuka, Y. *J. Med. Chem.* **1997**, *40*, 2626–2633; (b) Zitzmann, N.; Mehta, A. S.; Carrouée, S.; Butters, T. D.; Platt, F. M.; McCauley, J.; Blumberg, B. S.; Dwek, R. A.; Block, T. M. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11878–11882.
4. (a) Westervelt, P.; Gendelman, H. E.; Patner, L. *Proc. Natl. Acad. Sci. U.S.A.* **1991**, *88*, 3097–3101; (b) Karlsson, G. B.; Butter, T. D.; Dwek, R. A.; Platt, F. M. *J. Biol. Chem.* **1993**, *268*, 570–576.
5. (a) Treadway, J. L.; Mendys, P.; Hoover, D. J. *Expert Opin. Invest. Drugs* **2001**, *10*, 439–454; (b) Jacob, G. S. *Curr. Opin. Struct. Biol.* **1995**, *5*, 605–611.
6. (a) Svensson, B.; Sierks, M. R. *Carbohydr. Res.* **1992**, *227*, 29–44; (b) Lee, S.-B.; Park, K.-H.; Robyt, J. F. *Carbohydr. Res.* **2001**, *331*, 13–18; (c) Aleshin, A. E.; Firsov, L. M.; Honzat, R. *J. Biol. Chem.* **1994**, *269*, 15631–15639; (d) McCarter, J. D.; Yeung, W.; Chow, J.; Dolphin, D.; Withers, S. G. *J. Am. Chem. Soc.* **1997**, *119*, 5792–5797.
7. (a) Fleet, G. W. J.; Shaw, A. N.; Evans, S. V.; Fellows, L. E. *J. Chem. Soc., Chem. Commun.* **1984**, 1240–1241; (b) Palamartczky, G.; Mitchell, M.; Smith, P. W.; Fleet, G. W. J.; Elbein, A. D. *Arch. Biochem. Biophys.* **1985**, *242*, 35–45.
8. Legler, G. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319–384.
9. Hakansson, A. E.; van Ameijde, J.; Guglielmini, L.; Horne, G.; Nash, R. J.; Evinson, E. L.; Katoc, A.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2007**, *18*, 282–289.
10. Carmona, A. T.; Fuentes, J.; Robina, I.; García, E. R.; Demange, R.; Vogel, P.; Winters, A. L. *J. Org. Chem.* **2003**, *68*, 3874–3883.
11. (a) Picasso, S.; Chen, Y.; Vogel, P. *Carbohydr. Lett.* **1994**, *1*, 1–8; (b) Chen, Y.; Vogel, P. *J. Org. Chem.* **1994**, *59*, 2487–2496.
12. (a) Nemr, A. E. *Tetrahedron* **2000**, *56*, 8579–8629; (b) Pyne, S. G. *Curr. Org. Synth.* **2005**, *2*, 39–57.
13. (a) Dhavale, D. D.; Markad, S. D.; Karanjule, N. S.; Reddy, J. P. *J. Org. Chem.* **2004**, *69*, 4760–4766; (b) Li, H.; Blériot, Y.; Chantereau, C.; Mallet, J. M.; Sollogoub, M.; Zhang, Y.; Rodríguez-García, E.; Vogel, P.; Jiménez-Barbero, J.; Sinaÿ, P. *Org. Biomol. Chem.* **2004**, *2*, 1492–1499; (c) Moutel, S.; Shipman, M.; Martin, O. R.; Ikeda, K.; Asano, N. *Tetrahedron: Asymmetry* **2005**, *16*, 487–491.
14. (a) Jespersen, T. M.; Dong, W.; Sierks, M. R.; Skrydstrup, T.; Lundt, I.; Bols, M. *Angew. Chem., Int. Ed.* **1994**, *33*, 1778–1779; (b) Goti, A.; Cardona, F.; Brandi, A.; Picasso, S.; Vogel, P. *Tetrahedron:Asymmetry* **1996**, *7*, 1659–1674.
15. (a) Reddy, B. G.; Vankar, Y. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 2001–2004; (b) Jayakanthan, K.; Vankar, Y. D. *Org. Lett.* **2005**, *7*, 5441–5444; (c) Jayakanthan, K.; Vankar, Y. D. *Tetrahedron Lett.* **2006**, *49*, 8667–8671; (d) Rawal, G. K.; Rani, S.; Kumar, A.; Vankar, Y. D. *Tetrahedron Lett.* **2006**, *47*, 9117–9120; (e) Ramana, D. V.; Vankar, Y. D. *Eur. J. Org. Chem.* **2007**, 5583–5589; (f) Kumar, A.; Rawal, G. K.; Vankar, Y. D. *Tetrahedron* **2008**, *64*, 2379–2390; (g) Ramana, D. V.; Hari Prasad, K.; John Pal, A. P.; Basak, R. K.; Vankar, Y. D. *Eur. J. Org. Chem.* **2008**, 5731–5739; (h) Kumari, N.; Reddy, B. G.; Vankar, Y. D. *Eur. J. Org. Chem.* **2009**, 160–169; (i) Ramana, D. V.; Vankar, Y. D. *Carbohydr. Res.* **2009**, *344*, 606–612; (j) Kumari, N.; Vankar, Y. D. *Org. Biomol. Chem.* **2009**, *7*, 2104–2109; (k) Suman Reddy, Y.; Kadigachalam, P.; Raman, D. V.; Vankar, Y. D. *Tetrahedron Lett.* **2009**, *50*, 5827–5830.
16. Jeong, L. S.; Moon, R. H.; Choi, Y. J.; Chun, M. W.; Kim, H. O. *J. Org. Chem.* **1998**, *63*, 4821–4825.
17. (a) Wong, A.; Munos, J. W.; Devasthali, V.; Johnson, K. A.; Liu, H.-W. *Org. Lett.* **2004**, *6*, 3625–3628; (b) Sharma, G. V. M.; Kumar, K. R. *Tetrahedron: Asymmetry* **2004**, *15*, 2323–2326.
18. Kumar, A.; Doddi, V. R.; Vankar, Y. D. *J. Org. Chem.* **2008**, *73*, 5993–5995.
19. (a) Postema, M. H. D.; Calimente, D.; Liu, L.; Behrmann, T. L. *J.Org. Chem.* **2000**, *65*, 6061; (b) Pearson, W. H.; Hines, J. V. *J. Org. Chem.* **2000**, *65*, 5785; (c) Freeman, F.; Robarge, K. D. *Carbohydr. Res.* **1986**, *154*, 270.
20. Grubbs, R. H.. In *Handbook of Metathesis*; Wiley-VCH: Weinheim, 2003; Vol. 2. .
21. Lindsay, K. B.; Pyne, S. G. *J. Org. Chem.* **2002**, *67*, 774–7780.
22. Ogawa, S.; Ohishi, Y.; Asada, M.; Tomoda, A.; Takahashi, A.; Ooki, Y.; Mori, M.; Itoh, M.; Korenaga, T. *Org. Biomol. Chem.* **2004**, *2*, 884–889.
23. Shing, T. K. M.; Elsley, D. A.; Gillhouley, J. G. *J. Chem. Soc., Chem. Commun.* **1989**, 1280–1282.
24. Ali, S. M.; Hoemann, M. Z.; Aube, J.; Mitscher, L. A.; Georg, G. I.; McCall, R.; Jayasinghe, L. R. *J. Med. Chem.* **1995**, *38*, 3821–3828.
25. Li, Y.-T.; Li, S.-C. In *Methods in Enzymology*; Ginsberg, V., Ed.; Academic Press, 1972; p 702.