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Synthesis of hybrids of D-glucose and D-galactose with 1-deoxynojirimycin analogues using ring-closing metathesis

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Abstract

Four hybrids of azasugars with D-glucose and D-galactose have been synthesized from 3-nitro-2,3-unsaturated-*O*-glycosides. All the hybrid molecules showed moderate activity against β-galactosidase, the one derived from D-glucose and 1,4-dideoxygulonojirimycin **18**, and **26**, which is a hybrid of D-glucose and 1,4-dideoxymannohomonojrimycin, showed selectivity toward α-glucosidase and β-galactosidase, respectively.

Keywords: RCM; Diastereoselective hydroxylation; Stereoselective nucleophilic addition

1. Introduction

Carbohydrate processing enzymes viz. glycosidases and glycosyl transferases are involved in the biosynthesis of glycoconjugates, which play important roles[1] in many cellular functions such as cell–cell adhesion, cell differentiation, recognition of microorganisms, etc. via carbohydrate–carbohydrate and carbohydrate–protein interactions. These cellular functions and related diseases could be controlled[2] by inhibiting the carbohydrate processing enzymes. As a result, development of glycosidase inhibitors has become[3] an active area of research and a number of useful inhibitors have been developed and marketed against diseases such as type II diabetes,[4] influenza,[5] and Gaucher's disease.[6] In addition, efforts in developing glycosidase inhibitors against cancer,[7] HIV,[8] and other diseases have also been reported. Among many glycosidase inhibitors, azasugars such as nojirimycin, 1-deoxynojirimycin, and their analogues have received a large attention.[9]

Further, hybrid molecules, which are generally made up of either natural products or a combination of a natural product and synthetic compounds are known to have altered or improved properties.[10] In view of this, we have recently reported[11] the synthesis of new hybrid molecules made up of 1-deoxynojirimycin analogues and D-glucose and D-galactose and reported their glycosidase inhibitory properties. In these hybrid molecules, the anomeric carbon was a part of the bicyclic system and thus was not free. In designing glycosidase inhibitors the mimicking of charge and geometry of the transition states involved in the mechanism of glycosidase inhibition have been addressed seriously.[3] It could thus be of interest to study the glycosidase inhibitory properties of hybrid molecules made up of 1-deoxynojirmycin analogues and D-glucose and D-galactose with an alkoxy group being present at the anomeric carbon. Recently, Jenkins and co-workers[12] reported the syntheses of aza-heteroannulated sugars, which are hybrids of D-glucose and azepanes akin to 1-deoxyhomonojirimycin analogues,[12a] and hybrids of D-glucose and pyrrolidine derivatives bearing a methoxy group at the anomeric carbons.[12b] In view of the importance of 1-deoxynojirmycin[9] and our own interest in the chemistry of aliphatic nitro compounds especially that of carbohydrate based,[11,13] we hereby report the synthesis and biological evaluation of four new hybrid molecules made up of D-glucose and D-galactose, and 1-deoxynojirmycin analogues.

A general retrosynthetic analysis for the synthesis of these new hybrid molecules is presented in Scheme 1, which

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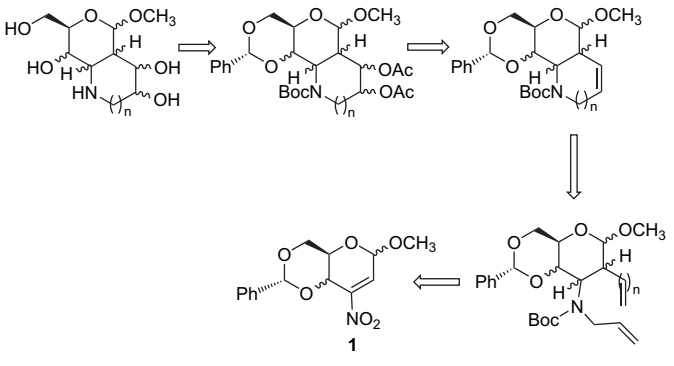
indicates the importance of 3-nitro-2,3-unsaturated glycosides and ring-closing metathesis in our synthetic endeavors. The synthesis begins with the elaboration of methyl 4,6-*O*-benzylidine-2,3-dideoxy-3-nitro-α and β-D-*erythro*-hex-2-enopyranosides **1**.[14]



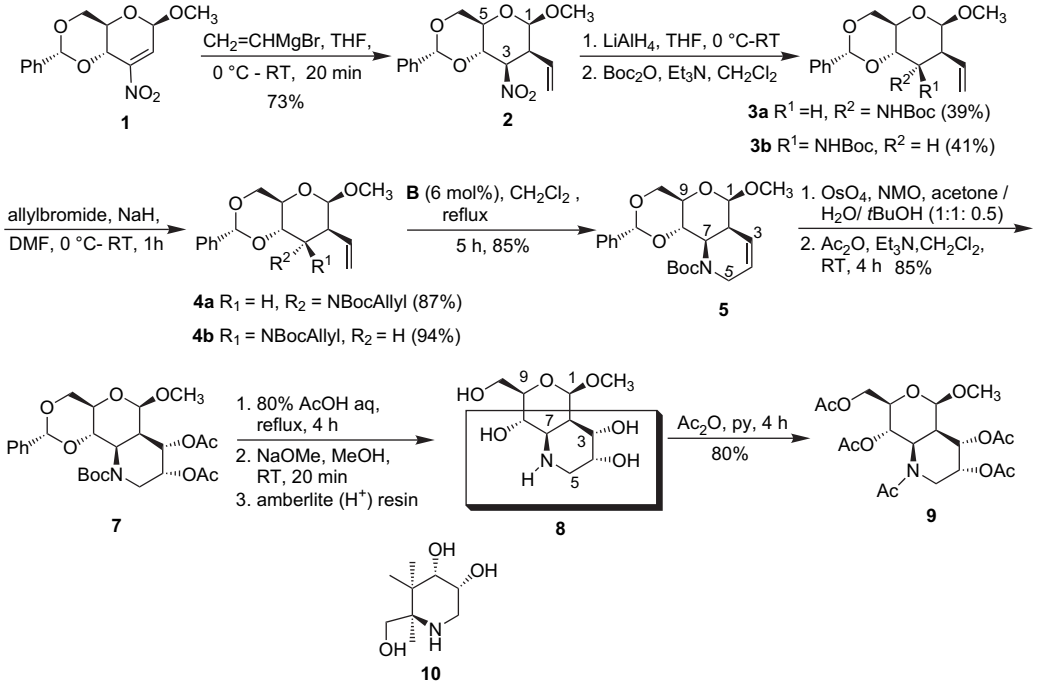
Scheme 1.

2. Results and discussions

Treatment of 3-nitrosugar derivative **1**[14] (Scheme 2) with vinyl magnesium bromide gave **2** as a single product in 73% yield as confirmed from its ^{1}H NMR and COSY spectral data[15] and the stereochemistry of **2** was confirmed by NOE interaction experiments. Thus, irradiation of H-1 enhances the peaks corresponding to H-2, H-3, and H-5 while no NOE correlation was observed between H-2 and H-4. Further, the values of $J_{1,2}$=1.96 Hz and $J_{2,3}$=5.36 Hz revealed that a cis (axial–equatorial) relationship exists between these hydrogens. It is clear that attack of the nucleophile takes place from the same side of the methoxy group, most likely because of the formation of the five membered transition state (Fig. 1).

This result is opposite to that of the literature report,[16] where attack of the Gilman reagent on 3-nitro-2,3-unsaturated glycosides occurs from the side opposite to the anomeric $-OCH_3$ group mainly on the basis of steric factors. On the other hand, in the present case it appears that the polarized species CH_2=CHMgBr coordinates with the $-OCH_3$ group as shown in Figure 2 leading to the observed product. Reduction of **2** with $LiAlH_4$ followed by protection of the free amine as NHBoc group gave a 1:1 mixture of two isomers **3a** and **3b** in 80% yield, which could be readily separated by column chromatography. Clearly, epimerization of **2** had occurred even under mild conditions (−10 °C to room temperature). The structures of **3a** and **3b** were confirmed by ^{1}H NMR spectroscopic analysis, COSY, and NOE interaction experiments. Thus, NOE interactions were observed between H-3 and H-1 in **3b** with $J_{3,4}$=9.76 Hz indicating that H-3 and H-4 are diaxially oriented, which was not the case with **3a**. Both the isomers **3a** and **3b** underwent smooth allylation with allyl bromide in the presence of NaH to give dienes **4a** and **4b** in 87% and 94% yields, respectively.

Ring-closing metathesis of diene **4b** by using the second generation Grubbs catalyst **B**[17] gave the expected bicyclic compound **5** in 85% yield. However, compound **4a** failed to undergo metathesis reaction under varying conditions, most probably because of the trans diaxial orientation of the two diene moieties. We, therefore, proceeded further with compound **5** whose dihydroxylation with OsO_4/*N*-methylmorpholine *N*-oxide (NMO) gave diol **6** in 85% yield and its acetylation gave the diacetate **7** in 86% yield. The cis dihydroxy groups were found to have α-geometry as revealed by ^{1}H NMR and NOE spectroscopic analyses[15] of the corresponding



Scheme 2.

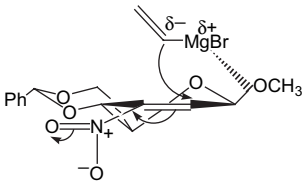


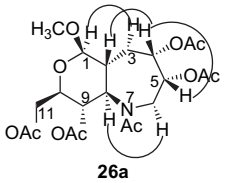
Figure 1. Chelation controlled nucleophilic attack on 3-nitro 2,3-unsaturated glucoside **1**.

pentaacetate **9**, obtained later. Compound **9** showed NOE correlation between H-1, H-2, H-7, and H-9; and H-3, H-4, H-5$_\beta$, and H-8.[15] Removal of benzylidene and *N*-Boc protecting group of diacetate **7** by heating it in 80% aq AcOH for 2 h[18] followed by deacetylation under Zamplen condition gave the desired tetrahydroxy compound **8**, which represents a hybrid of D-glucose and 1,4-dideoxymannonojirimycin **10** and was characterized as the corresponding acetyl derivative **9**.

Similarly, the isomeric 3-nitroglucal derivative[14] **11** (Scheme 3), having the anomeric −OCH$_3$ group in α orientation, was also transformed into a bicyclic compound **18**, a hybrid of D-glucose and 1,4-dideoxygulonojirimycin **19**. Interestingly, the direction of the addition of vinyl magnesium bromide was again dependent on the geometry of the −OCH$_3$ group at the anomeric carbon. Thus, adduct **12** was obtained as a single product in 75% yield whose structure was confirmed by ^{1}H NMR spectral data and NOE experiments.

Thus, NOE interactions between H-4 and H-2 in **12**, and the values of $J_{1,2}$=3.16 Hz and $J_{2,3}$=10.52 Hz revealed a (equatorial−axial) relationship between H-1 and H-2 and trans diaxial relationship between H-2 and H-3. Reduction of **12** followed by protection of free amine as −NHBoc gave two isomers **13a** and **13b** in 1:1.3 ratio. The isomer **13b** underwent smooth allylation with allyl bromide in the presence of NaH to give diene **14** in 87% yield whereas the isomer **13a** failed to undergo allylation. Diene **14** was then converted to the desired hybrid bicyclic molecule **18**, which was characterized as its pentaacetate **18a**, by following the same reaction sequence as described in Scheme 1. Details of the experiments leading to **18** are given in Supplementary data.

A hybrid molecule containing higher homologue of the 1-deoxynojirimycin was prepared from 3-nitroglucal **1** (Scheme 4) as well as from the corresponding 3-nitrogalactal derivative **27** (Scheme 5). Treatment of **1** (Scheme 4) with allyl magnesium chloride gave a single product **20** in 69% yield. Surprisingly, addition of the Grignard reagent takes place from the direction opposite to the anomeric methoxy group,[19] in contrast to the direction of the addition of vinyl magnesium bromide to **1** as observed earlier (vide supra). It is likely that the relatively bulkier allyl group allows the nucleophile to attack from the side opposite to the OCH$_3$ group. Reduction of **20** with LiAlH$_4$ followed by protection of the free amine as NHBoc gave a 1:1 mixture of two isomers **21a** and **21b** in 78% yield that could be readily separated by column chromatography. The structures of compounds **21a** and **21b** were confirmed by ^{1}H NMR spectroscopic analysis, COSY, and NOE interaction experiments.[15]



26a

Figure 2. NOEs observed in compound **26a**.

The NHBoc group in **21a** is axially oriented and attempted N-allylation failed under a variety of conditions possibly because of the steric hindrance. However, compound **21b** underwent smooth allylation with allyl bromide in the presence of NaH at 0 °C to room temperature over 1 h to give compound **22** in 95% yield. Ring-closing metathesis of diene **22** by using the first generation Grubbs' catalyst **A**[17] produced the expected bicyclic compound **23** in 91% yield. Dihydroxylation of **23** was carried out with OsO$_4$/*N*-methylmorpholine *N*-oxide (NMO) to form diol **24** in 89% yield, which was converted into the diacetate **25** by acetylation using Ac$_2$O/Et$_3$N. The cis dihydroxy groups in **24** were found to have α-geometry as revealed by ^{1}H NMR and NOESY spectroscopic analyses of the corresponding pentaacetate **26a**. For compound **26a**, in its NOESY spectrum, strong crosspeaks were observed between H1−H3α, H3β−H2, H2−H4, and H4−H5, which confirmed the structure assigned to it as shown in Figure 2. Compound **26** represents a hybrid of D-glucose and 1,4-dideoxymannohomonojirimycin (**26b**).

Similarly, 3-nitrogalactal derivative[14] **27** (Scheme 5) was also transformed into a bicyclic compound **34**, which is a hybrid of D-galactose and 1,4-dideoxygulohomonojirimycin **35a** by following the same reaction sequence as shown in Scheme 4. Spectroscopic details of all the compounds are given in Supplementary data.

The hybrid azasugars **8**, **18**, **26**, and **34** were evaluated for inhibition activity toward a few commercially available glycosidases[20] at millimolar concentration (Table 1). All the hybrid molecules **8**, **18**, **26**, and **34** showed reasonable inhibition against β-galactosidase (entry 4). However, compound **18** showed specific inhibition of α-glucosidase (entry 1) whereas **26** inhibited β-galactosidase (entry 4).

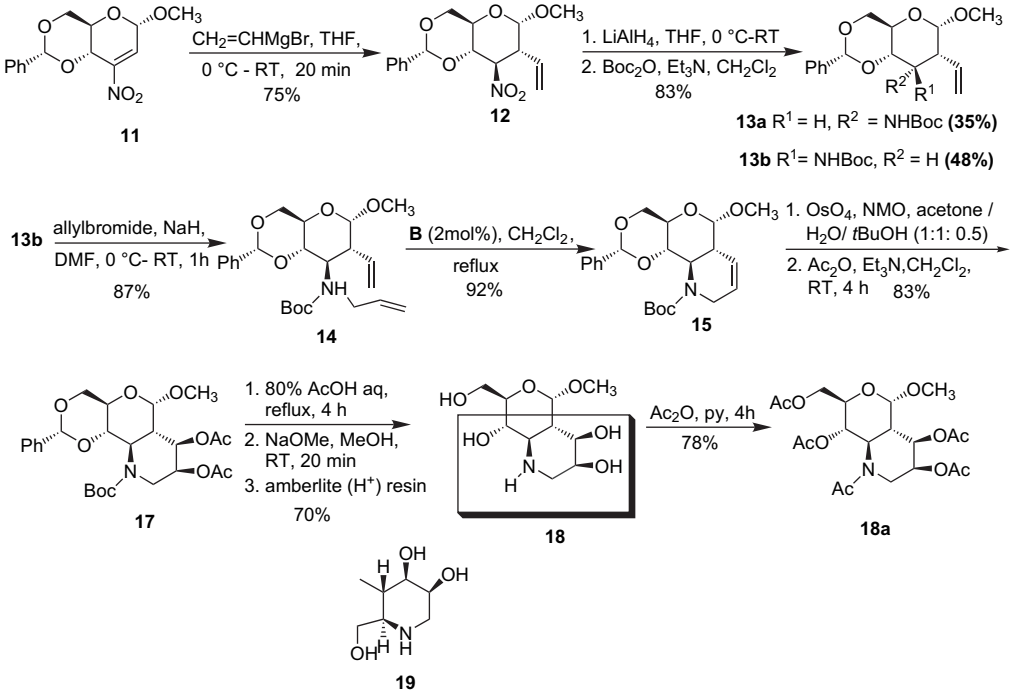
3. Conclusion

We have synthesized four novel hybrids of D-glucose as well as D-galactose and 1-deoxynojirimycin analogues starting from 3-nitro-2,3-unsaturated glycosides, which act as moderate glycosidase inhibitors. It is likely that structural variations of these hybrid molecules could lead to better/altered glycosidase inhibitions.

4. Experimental

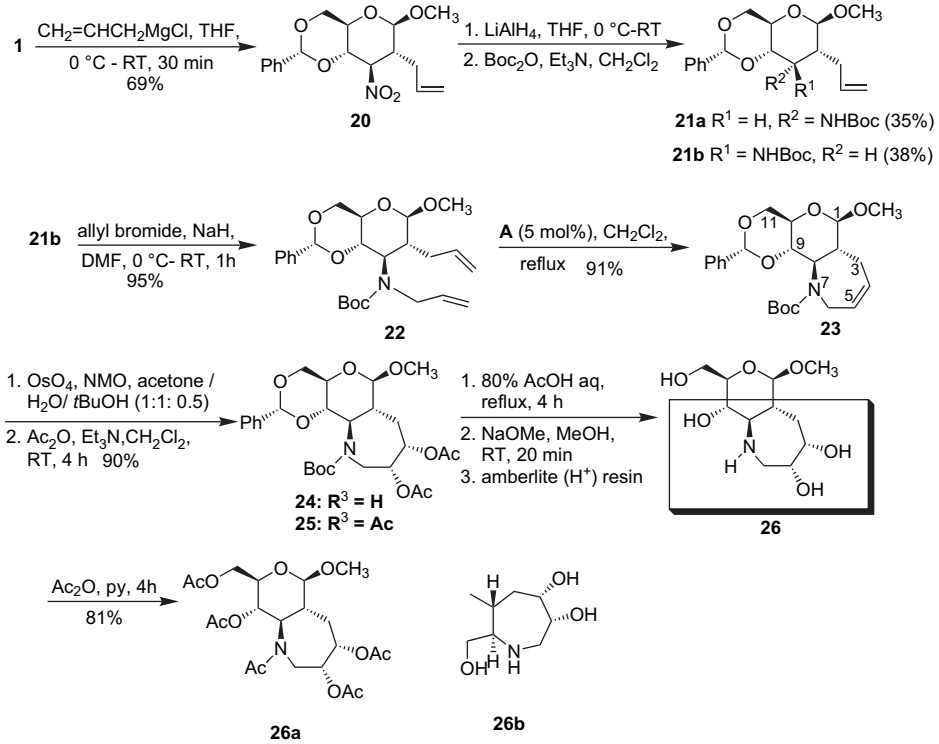
4.1. General

The ^{1}H NMR, NOE, and ^{13}C NMR spectra were recorded on JEOL-JNM 400 MHz and 100 MHz spectrometers,

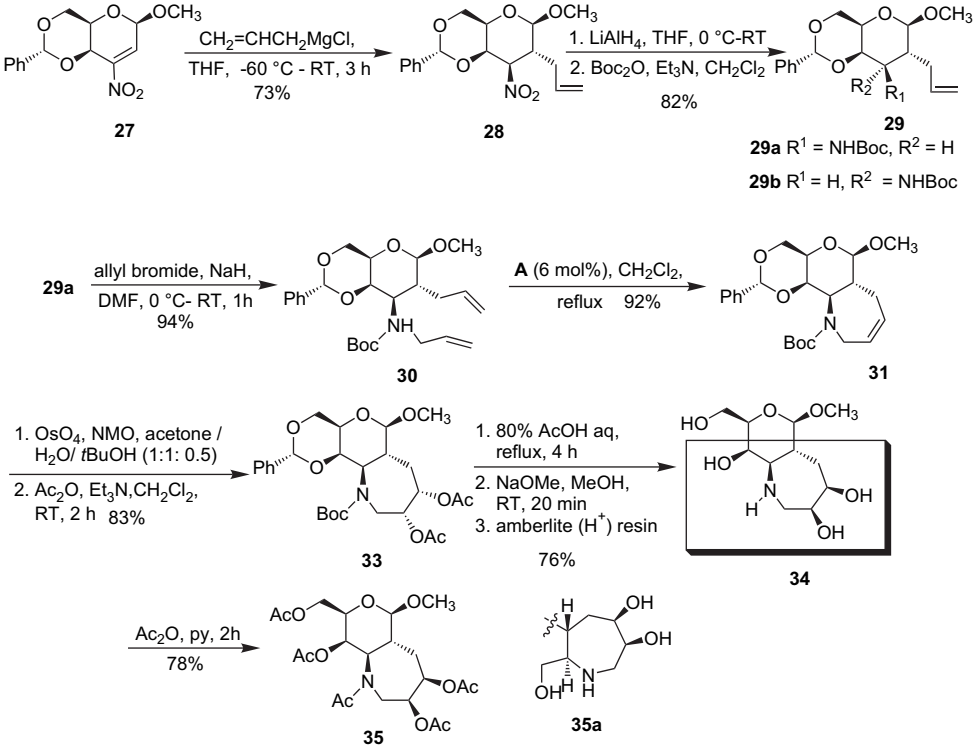


Scheme 3.

respectively. The chemical shift values are reported in parts per million 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 ethyl acetate as eluent. The separation of isomers was performed on Chromatotron using plates coated with silica gel PF_{254} (E-Merck, Germany). Rotation values were recorded on Autopol II automatic polarimeter at the wavelength of sodium D-line (589 nm) at 25 °C. Elemental analyses were carried out on a Thermoquest CE-instruments EA-1110 C, H, N, S analyzer. Melting points were determined using a Fischer–John melting point apparatus. The mass



Scheme 4.



Scheme 5.

spectra were recorded on a Micromass Quattro II Triple Quadrupole Mass Spectrometer.

4.1.1. General procedure (A): vinylation and allylation of 3-nitro-2,3-glycals

To a stirred solution of a 3-nitro-glycal derivative **1** or **11** (1 mmol) in THF (4 mL) at −10 °C was added dropwise vinyl magnesium bromide (1.5 mmol) or allyl magnesium chloride (2 mmol). The reaction was slowly brought to room temperature for 1 h and after completion of reaction (TLC monitoring), the reaction mixture was quenched with saturated aq NH_4Cl and extracted with ethyl acetate (2×50 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated to obtain a crude product, which was purified by column chromatography.

4.1.2. General procedure (B): reduction of the nitro group using lithium aluminum hydride

To a suspension of $LiAlH_4$ (76 mg, 2 mmol) in THF at 0 °C was added dropwise a solution of a nitro compound (1 mmol) in THF (5 mL). The reaction mixture was slowly brought to room temperature and stirred for 0.5−1.5 h. The reaction mixture was cooled to 0 °C, treated with EtOAc (2 mL) and water (3 mL), and neutralized with 1 N NaOH and stirred for 1 h. The resulting white precipitate was removed by filtration through a Celite pad and the filtrate was extracted with ethyl acetate (3×20 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude amine, which was dissolved in dichloromethane (5 mL) and treated with Et_3N (0.18 mL, 1.3 mmol) and $(Boc)_2O$ (216 mg, 1.2 mmol) at room temperature and then the mixture was stirred for 3 h. The reaction mixture was extracted with dichloromethane (3×20 mL) and organic layer was washed with water and brine. Usual work up gave a crude product, which was purified by column chromatography gave the two separable isomers in equal ratio.

Table 1
IC_{50} (mM) values for compounds **8**, **18**, **26** and **34**[a]

Entry	Enzyme	8	18	26	34
1	α-Glucosidase (rice)	NI	3.3	NI	NI
2	β-Glucosidase (almonds)	NI	NI	NI	NI
3	α-Galactosidase (coffee beans)	NI	NI	NI	NI
4	β-Galactosidase (bovine liver)	4.68	8.5	4.68	8.5

[a] Inhibition studies were carried out at millimolar concentration, optimal pH of the enzymes, and 37 °C. NI− no inhibition at 5 mM concentration of the inhibitor.

4.1.3. General procedure (C): N-allylation of Boc protected amine

To a stirred solution of Boc protected amine (1 mmol) in dry DMF at 0 °C were added allyl bromide (144 mg, 1.22 mmol) and NaH (72 mg, 3.06 mmol). The reaction mixture was stirred for 1 h at 0 °C and after completion of reaction (TLC monitoring) it was quenched with saturated aq NH_4Cl and extracted with diethyl ether (3×20 mL). The extract was washed with water and brine, and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a crude product, which was purified by column chromatography to give diene.

4.1.4. General procedure (D): for ring-closing metathesis of diene

To a stirred solution of a diene (0.928 mmol) in dry CH_2Cl_2 (15 mL) at room temperature was added Grubbs' catalyst **A** or **B** (42 mg, 0.055 mmol). The reaction mixture was stirred at same temperature for 4–6 h and after completion of reaction (TLC monitoring), the solvent was evaporated and the crude product was purified by column chromatography to give cyclized product.

4.1.5. General procedure (E): dihydroxylation using OsO_4/NMO

To a stirred solution of an olefin (0.54 mmol) in acetone/water/*tert*-butanol (1:1:0.4) at room temperature were added $NMO\cdot H_2O$ (0.67 mmol) and OsO_4 (0.002 equiv). The reaction mixture was stirred for 12–14 h (monitored by TLC) and it was treated with $Na_2S_2O_5$ (228 mg, 0.67 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 work up gave a crude product, which was purified by column chromatography.

4.1.6. General procedure (F): acetylation of diol

A stirred solution of a diol (l mmol) in dry CH_2Cl_2 (5 mL) was treated with Et_3N (0.34 mg, 2.5 mmol), acetic anhydride (275 mg, 2.7 mmol), and catalytic amount of DMAP. The reaction mixture was stirred for 3 h and after completion of reaction (TLC monitoring) it was extracted with ethyl acetate (2×10 mL). The organic phase was washed with 1 N HCl, water, and finally with brine. Usual work up gave a crude product, which was purified by column chromatography to give diacetate.

4.1.7. General procedure (G): for benzylidene, N-Boc, and acetyl group deprotection

A solution of a diacetate (1 mmol) in 80% aq AcOH (10 mL) was kept for 4 h at 80–90 °C. After cooling, the mixture was evaporated and the evaporation was repeated azeotropically with ethanol, toluene, and ethanol. Deacetylation of this crude compound was done under Zamplen condition (NaOMe in MeOH) at room temperature, which was filtered through Amberlite (H^+) ion exchange resin for the enzyme inhibition studies.

4.1.8. General procedure (H): for acetylation

Acetylation of the tetrahydroxy compound was done using pyridine and acetic anhydride (1:1, 2 mL) at room temperature for 10 h. Usual work up followed by column chromatography gave the pure pentaacetate.

*4.1.8.1. (2R,4aR,6R,7S,8R,8aS)-6-Methoxy-8-nitro-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxine (**2**).* Methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-glucopyranoside was vinylated using the general procedure (A) and purified over silica gel column chromatography. Yield: 73% (colorless solid, mp 197–198 °C). $[\alpha]_D^{28}$ −98.7 (*c* 2.3, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1557, 1642 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.35 (m, 5H, Ar–H), 5.89 (ddd, 1H, *J*=17.0, 10.2, 3.1 Hz, $-CH{=}CH_2$), 5.56 (s, 1H, Ph–C*H*), 5.33–5.15 (br dd, 2H, *J*=17.0, 10.2 Hz, $-CH{=}CH_2$), 4.82 (dd, 1H, *J*=10.5, 5.3 Hz, H-3), 4.65 (d, 1H, *J*=2.0 Hz, H-1), 4.44 (dd, 1H, *J*=10.5, 4.6 Hz, H-6e), 4.34 (t, 1H, *J*=10.7 Hz, H-4), 3.95 (t, 1H, *J*=10.2 Hz, H-6a), 3.54 (s, 3H, OMe), 3.52–3.49 (m, 1H, H-5), 3.32–3.29 (m, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 129.2, 128.2, 127.8, 125.9, 122.6, 102.5, 101.7, 86.0, 74.1, 68.6, 67.3, 57.5, 49.9. ESMS: *m/z* 344 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{19}NO_6$ (321.12): C, 59.81; H, 5.96; N, 4.36. Found: C, 60.10; H, 5.98; N, 4.39.

*4.1.8.2. tert-Butyl(2R,4aR,6R,7S,8S,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**3a**).* Nitro olefins **2** were reduced to amino olefins **3a** and **3b** using the general procedure (B) and purified over silica gel column chromatography. Yield: 39% (colorless solid, mp 212–214 °C). $[\alpha]_D^{28}$ −31.7 (*c* 0.85, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1527, 1680 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48–7.34 (m, 5H, Ar–H), 6.10–6.01 (m, 1H, $-CH{=}CH_2$), 5.58 (s, 1H, Ph–C*H*), 5.34 (dd, 1H, *J*=18.5, 10.0 Hz, $-CH{=}CH_2$), 5.32–5.21 (m, 1H, $-CH{=}CH_2$), 4.89 (br s, 1H, NH), 4.77 (d, 1H, *J*=2.2 Hz, H-1), 4.39 (dd, 1H, *J*=10.0, 4.36 Hz, H-6e), 3.98 (br s, 1H, H-3), 3.89 (dd, 1H, *J*=4.1, 9.5 Hz, H-4), 3.78 (t, 1H, *J*=10.0 Hz, H-6a), 3.71 (dd, 1H, *J*=9.5, 4.1 Hz, H-5), 3.51 (s, 3H, OMe), 3.32–3.24 (m, 1H, H-2), 1.41 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 134.1, 132.8, 129.8, 128.3, 126.1, 119.3, 101.9, 101.1, 74.7, 69.4, 65.3, 57.2, 52.1, 48.0, 29.7, 28.3. MSES: *m/z* 414 $[M+Na]^+$. Anal. Calcd for $C_{21}H_{29}NO_6$ (391.20): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.34; H, 7.50; N, 3.62.

*4.1.8.3. tert-Butyl(2R,4aR,6R,7S,8R,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**3b**).* The procedure followed was identical with that described for the preparation of **3a** to give compound **3b**. Yield: 41% (colorless solid, mp 205–207 °C). $[\alpha]_D^{28}$ −53.3 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1530, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.48–7.34 (m, 10H, Ar–H both rotamer), 5.84–5.98 (m, 2H, $-CH{=}CH_2$, both rotamer), 5.52 (s, 1H, Ph–C*H*, for minor), 5.48 (s, 1H, Ph–C*H*, for major), 5.42–5.21 (m, 4H, $-CH{=}CH_2$, both rotamer), 4.65 (d, 1H, *J*=1.96 Hz, H-1 major), 4.60 (d, 1H, *J*=2.2 Hz, H-1 minor), 4.32 (dd, 1H, *J*=10.4 Hz, H-6e), 4.13–4.05 (m, 1H, H-2 minor), 3.88–3.69 (t, 2H, *J*=10.5 Hz, H-4, H-6a), 3.57–3.54 (m, 2H, H-5, H-3), 3.54 (s, 3H, OMe), 3.51 (s, 3H, OMe minor), 3.39 (t, 1H, *J*=9.7 Hz, H-3, minor), 3.10–3.07 (m, 1H, H-2), 1.43 (s, 9H, *tert*-butyl, major), 1.42 (s, 9H, *tert*-butyl, minor). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2, 137.0, 136.3, 134.4, 130.8, 130.5, 130.1, 129–128 (m, aromatic), 126.0, 122.1, 121.8, 121.5, 103.5, 103.3, 102.9, 102.7, 83.7, 80.7, 79.5, 77.5, 77.3, 75.9, 69.8, 68.5, 65.1, 62.6, 61.0, 57.0, 54.1, 52.0, 49.5, 47.6, 28.2, 27.6, 27.6. MSES: *m/z* 414 $[M+Na]^+$. Anal. Calcd for $C_{21}H_{29}NO_6$ (391.20): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.36; H, 7.50; N, 3.60.

*4.1.8.4. tert-Butylallyl((2R,4aR,6R,7S,8S,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-yl)carbamate (**4a**).* Amino olefin **3a** was N-allylated using the general procedure (C) to give **4a** (87%) as a colorless oil. Yield: 85% (colorless oil). $[\alpha]_D^{28}$ −58.4 (*c* 0.65, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1695, 1560 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.53−7.32 (m, 5H, Ar−H), 5.96−5.81 (m, 2H, −C*H*=CH_2), 5.53 (s, 1H, Ph−C*H*), 5.15−4.86 (m, 4H, 2×−CH=CH_2), 4.59 (br s, 1H), 4.35 (br s, 1H), 3.84−3.79 (m, 2H), 3.66 (s, 1H), 3.49 (s, 3H, OMe), 3.08−3.06 (m, 2H, allylic), 1.40 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 137.9−125.9 (m, aromatic), 119.0, 117.2, 102.8, 101.6, 101.2, 81.8, 80.1, 74.8, 70.6, 64.3, 56.5, 56.2, 41.9, 28.2, 28.1, 22.5. MSES: *m/z* 454 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{33}NO_6$ (431.23): C, 66.80; H, 7.71; N, 3.24. Found: C, 66.98; H, 7.50; N, 3.20.

*4.1.8.5. tert-Butylallyl((2R,4aR,6R,7S,8R,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-yl)carbamate (**4b**).* Amino olefin **3b** was N-allylated using the general procedure (C) to give **4b** (94%) as colorless oil. Yield: 90%. $[\alpha]_D^{28}$ −100.0 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1695, 1560 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.49−7.34 (m, 10H, Ar−H both rotamer), 6.00−5.96 (m, 2H, −C*H*=CH_2), 5.74−5.71 (m, 1H, −C*H*=CH_2, minor rotamer), 5.49 (s, 1H, Ph−C*H*), 5.29−5.13 (dd, 4H, *J*=17.0, 10.2 Hz, 2×−CH=CH_2), 5.04−4.88 (dd, 4H, *J*=17.8, 9.0 Hz, 2×−CH=CH_2, minor rotamer), 4.66 (br s, 1H), 4.55 (s, 1H, minor rotamer), 4.35−4.28 (m, 3H), 3.87 (m, 4H, both rotamer), 3.68 (br s, 1H, minor rotamer), 3.52 (m, 1H and OMe, both rotamer), 3.11−3.09 (m, 2H, allylic), 1.44−1.42 (s, 9H, *tert*-butyl, both rotamer). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 137.9−125.9 (m, Aromatic, both rotamer), 117.9, 116.9, 115.3, 104.9, 104.5, 100.8, 80.1, 79.8, 68.8, 68.0, 57.0, 56.7, 55.6, 44.4, 43.1, 31.1, 30.8, 28.2. MSES: *m/z* 454 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{33}NO_6$ (431.23): C, 66.80; H, 7.71; N, 3.24. Found: C, 66.90; H, 7.50; N, 3.25.

*4.1.8.6. 9-Methoxy-3-phenyl-1,4a,4b,8a,9,10a-hexahydro-6H-2,4,10-trioxa-5-aza-phenanthrene-5-carboxylic acid tert-butyl ester (**5**).* Diene **4b** was subjected to ring-closing metathesis following the general procedure (D) and purified over silica gel column chromatography. Yield: 85% (colorless oil). $[\alpha]_D^{28}$ −52.3 (*c* 0.65, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685, 1654 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.46−7.30 (m, 10H, Ar−H, both rotamer), 6.05 (br t, 2H, *J*=9.76 Hz, H-3 both rotamer), 5.86 (br dd, 1H, *J*=8.0, 10.7 Hz, H-4, rotamer-1), 5.79 (br dd, 1H, *J*=8.0, 10.7 Hz, H-4, rotamer-2), 5.49−5.47 (2×s, 2H, Ph−C*H*, rotamer-1 and -2), 4.74 (dd, 1H, *J*=4.8, 9.7 Hz, H-10e, rotamer-1), 4.60 (d, 2H, *J*=2.6 Hz, H-1, both rotamer), 4.47 (dd, 1H, *J*=10.0, 5.4 Hz, H-10e, rotamer-2), 4.33−4.29 (m, 3H, H-8, both rotamer and H-10a), 4.21 (dd, 2H, H-5′, both rotamer), 3.75−3.66 (m, 3H, H-9, both rotamer and H-7), 3.55 (s, 3H, OMe, rotamer-1), 3.50 (s, 3H, OMe, rotamer-2), 3.45 (dd, 1H, *J*=11.2, 5.1 Hz, H-5), 2.95 (br m, 1H, H-5, both rotamer), 1.46 (s, 9H, *tert*-butyl, rotamer-1), 1.37 (s, 9H, *tert*-butyl, rotamer-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2, 137.2, 128.1−125.3 (m, aromatic), 122.1, 121.6, 102.7, 102.6, 101.7, 101.1, 80.0, 74.1, 68.7, 68.2, 67.9, 57.2, 51.8, 50.3, 41.1, 40.6, 40.4, 40.3, 28.2. MSES: *m/z* 426 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{29}NO_6$ (403.20): C, 65.49; H, 7.24; N, 3.47. Found: C, 65.50; H, 7.50; N, 3.50.

*4.1.8.7. (7R,8S,8aR)-Diacetoxy-9-methoxy-3-phenyl-octahydro-2,4,10-trioxa-5-aza-phenanthrene-5-carboxylic acid tert-butyl ester (**7**).* Diol was acetylated using the general procedure (F) to give **7** (85%) as colorless solid, mp 220−222 °C. $[\alpha]_D^{28}$ −6.7 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.31−7.45 (m, 10H, Ar−H, both rotamer), 5.60 (dd, 2H, *J*=11.7, 3.4 Hz, H-3, both rotamer), 5.49 (s, 1H, Ph−C*H*, major), 5.44 (s, 1H, Ph−C*H*, minor), 5.21 (br s, 1H, H-4, minor), 5.09 (br s, 1H, H-4, major), 4.87 (dd, 1H, *J*=10.7, 5.1 Hz, H-10e, minor), 4.83 (s, 2H, H-1, both rotamer), 4.59 (dd, 1H, *J*=10.8, 5.3 Hz, H-10e, major), 4.31−4.37 (m, 3H, H-8, both rotamer and H-7), 4.23 (dd, 1H, *J*=15.4, 1.9 Hz, H-5′, major), 3.88−3.78 (m, 4H, H-9 and H-10, both rotamer), 3.53 (m. 2H, H-2, both rotamer), 3.44 (s, 3H, OMe, minor), 3.41(s, 3H, OMe, major), 3.19 (br d, 1H, *J*=15.1 Hz, H-2, major), 3.08 (br d, 1H, *J*=14.8 Hz, H-2, minor), 2.11−1.99 (4×s, 12H, OCOCH_3, both rotamer), 1.43 (s, 9H, *tert*-butyl, major), 1.36 (s, 9H, *tert*-butyl, minor). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.9, 169.8, 155.1, 154.9, 136.9, 129.0−128.9 (m, aromatic), 126.1, 126.0, 104.2, 104.1, 101.9, 101.5, 80.6, 80.5, 72.7, 72.6, 69.1, 68.9, 68.7, 68.6, 67.5, 65.3, 65.2, 57.6, 57.5, 53.9, 52.4, 41.8, 40.8, 39.9, 39.7, 31.1, 29.6, 28.2, 28.0, 20.9, 14.1. MSES: *m/z* 544 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{35}NO_{10}$ (521.23): C, 59.87; H, 6.76; N, 2.69. Found: C, 60.00; H, 6.80; N, 2.70.

*4.1.8.8. (3R,4S,4aR,5R,7R,8S,8aR)-7-(Acetoxymethyl)-1-acetyl-5-methoxyoctahydro-1H-pyrano[4,3-b]pyridine-3,4,8-triyl triacetate (**9**).* Diacetate was converted to pentaacetate using the general procedure (G) followed by general procedure (H) to give **9** (80%) as colorless solid, mp 186−188 °C. $[\alpha]_D^{28}$ −7.3 (*c* 0.85, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1743, 1653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.56 (dd, 1H, *J*=11.7, 3.2 Hz, H-3), 5.30 (br s, 1H, H-4), 5.16−5.12 (m, 2H, H-8, and H-7), 4.58 (s, 1H, H-1), 4.24 (d, 2H, *J*=3.4 Hz, H-10a and H-10e), 3.83 (dd, 1H, *J*=15.6, 2.7 Hz, H-5′), 3.76 (br s, 1H, H-9), 3.45 (s, 3H, OMe, minor), 3.44 (3H, OMe, major), 2.65 (br d, 1H, *J*=11.7 Hz, H-2), 2.11−1.99 (m, 16H, −OCOCH_3, −NCOCH_3, and H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7−169.6(m), 103.5, 73.3, 67.7, 67.6, 65.0, 64.9, 62.9, 62.4, 57.6, 51.5, 44.4, 39.2, 21.5, 20.9, 20.8. MSES: *m/z* 482 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{29}NO_{11}$ (459.44): C, 52.28; H, 6.36; N, 3.05. Found: C, 52.35; H, 6.40; N, 3.10.

*4.1.8.9. (2R,4aR,6S,7R,8R,8aS)-6-Methoxy-8-nitro-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxine (**12**).* This compound was prepared in 75% yield from **11** by using the same procedure as described for **2**. Yield: 75% (colorless solid,

mp 176–178 °C). $[\alpha]_D^{28}$ +63.2 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1557, 1642 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, 2H, *J*=3.4 Hz, Ar–H), 7.35 (d, 3H, *J*=3.1 Hz, Ar–H), 5.67–5.76 (ddd, 1H, *J*=17.1, 7.3, 2.4 Hz, –C*H*=CH_2), 5.57 (s, 1H, Ph–C*H*), 5.25 (dd, 2H, *J*=9.2, 2.6 Hz, –CH=CH_2), 4.98 (t, 1H, *J*=10.5 Hz, H-3), 4.7 (d, 1H, *J*=3.1 Hz, H-1), 4.3 (dd, 1H, *J*=4.3, 10.0 Hz, H-6e), 4.19 (t, 1H, *J*=9.7 Hz, H-4), 3.96 (ddd, 1H, *J*=10.0, 9.6, 4.6 Hz, H-5), 3.86 (t, 1H, *J*=10.2 Hz, H-6a), 3.39 (s, 3H, OMe), 3.01 (ddd, 1H, *J*=11.9, 3.2, 3.1 Hz, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 130.9, 129.2, 128.2, 126.0, 121.3, 101.3, 100.2, 86.6, 78.3, 68.9, 62.9, 62.2, 55.4, 50.4. MSES: *m/z* 344 $[M+Na]^+$. Anal. Calcd for $C_{16}H_{19}NO_6$ (321.12): C, 59.81; H, 5.96; N, 4.36. Found: C, 60.20; H, 5.97; N, 4.20.

*4.1.8.10. tert-Butyl(2R,4aR,6S,7R,8S,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**13a**).* This compound was obtained in 35% yield by following the general procedure (B): colorless solid, mp 198–200 °C. $[\alpha]_D^{28}$ +17.6 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1530, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49–7.35 (m, 5H, Ar–H), 5.81 (ddd, 1H, *J*=16.8, 10.0, 3.2 Hz, –C*H*=CH_2), 5.53 (s, 1H, Ph–C*H*), 5.17 (dd, 2H, *J*=10.0, 8.2 Hz, –CH=CH_2), 4.60 (d, 1H, *J*=3.4 Hz, H-1), 4.27 (dd, 1H, *J*=4.8, 10.2 Hz, H-6e), 3.92–3.87 (m, 2H, H-4 and H-5), 3.7 (t, 2H, *J*=10.4 Hz, H-3 and H-6a), 3.37 (s, 3H, OMe), 1.45–1.43 (m, 1H, H-2), 1.39 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.5, 137.4, 134.8, 128.9, 128.1, 126.1, 118.8, 101.7, 101.4, 79.7, 76.6, 69.1, 63.9, 55.0, 51.2, 29.6, 28.2. MSES: *m/z* 414 $[M+Na]^+$. Anal. Calcd for $C_{21}H_{29}NO_6$ (391.20): C, 64.40; H, 7.47; N, 3.58. Found: C, 64.30; H, 7.50; N, 3.62.

*4.1.8.11. tert-Butyl(2R,4aR,6S,7R,8R,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**13b**).* Yield: 48% (colorless solid, mp 186–188 °C). $[\alpha]_D^{28}$ +5.80 (*c* 1.55, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1530, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.49–7.34 (m, 10H, Ar–H, both rotamer), 5.79–5.76 (m, 1H, –C*H*=CH_2, minor rotamers), 5.74–5.67 (m, 1H, –C*H*=CH_2), 5.49 (s, 1H, Ph–C*H*), 5.39–5.13 (m, 4H, –CH=CH_2, both rotamer), 4.69–4.67 (m, 2H, minor rotamers), 4.66–4.62 (m, 1H), 4.50–4.47 (m, 2H, both rotamers), 4.35–4.28 (m, 2H, both rotamer), 3.87–3.70 (m, 4H, both rotamer), 3.52 (s, 6H, OMe, both rotamers), 3.09–3.06 (m, 1H, allylic, minor rotamer), 2.63–2.60 (m, 2H, allylic), 1.44–1.42 (s, 9H, *tert*-butyl, both rotamers). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9–125.9 (m, aromatic, both rotamers), 118.9, 101.7, 101.4, 68.8, 63.9, 55.0, 51.0, 30.8, 28.2. MSES: *m/z* 414 $[M+Na]^+$. Anal. Calcd for $C_{21}H_{29}NO_6$ (391.20): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.32; H, 7.50; N, 3.56.

*4.1.8.12. tert-Butylallyl((2R,4aR,6S,7R,8R,8aS)-6-methoxy-2-phenyl-7-vinylhexahydropyrano[3,2-d][1,3]dioxin-8-yl)carbamate (**14**).* Amino olefin **13a** was N-allylated using the general procedure (C) to give **14b** (87%) as a colorless oil. $[\alpha]_D^{28}$ +12.1 (*c* 1.4, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1695, 1562 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.49–7.34 (m, 10H, Ar–H, both rotamer), 5.81–5.67 (m, 3H, –C*H*=H_2, both rotamers), 5.41 (s, 1H, Ph–C*H*, both rotamers), 5.21–4.93 (m, 6H, 2×–CH=CH_2, both rotamers), 4.68 (br t, 1H, *J*=8.1 Hz, minor rotamers), 4.62–60 (m, 2H), 4.27–4.22 (m, 2H), 3.91–3.68 (m, 6H, both rotamers), 3.55–3.47 (m, 1H), 3.48(s, OMe both rotamers), 2.63–2.51 (m, 2H, allylic), 1.44–1.42 (s, 9H, *tert*-butyl, both rotamer). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 137.9–125.9 (m, aromatic, both rotamers), 118.9, 116.9, 114.3, 101.6, 101.1, 80.1, 79.8, 68.8, 68.0, 57.0, 56.7, 55.6, 49.6, 47.4, 44.1, 28.7, 28.2. MSES: *m/z* 454 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{33}NO_6$ (431.23): C, 66.80; H, 7.71; N, 3.24. Found: C, 66.92; H, 7.50; N, 3.21.

*4.1.8.13. 9-Methoxy-3-phenyl-1,4a,4b,8a,9,10a-hexahydro-6H-2,4,10-trioxa-5-aza-phenanthrene-5-carboxylic acid tert-butyl ester (**15**).* Diene underwent RCM using the general procedure (D) and purified over silica gel column chromatography. Yield: 92%. $[\alpha]_D^{28}$ +36.0 (*c* 0.25, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685, 1654 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.51–7.34 (m, 5H, Ar–H), 5.79 (tt, 1H, *J*=5.6, 2.6 Hz, H-3), 5.7 (s, 1H, Ph–C*H*), 5.6 (br d, 1H, *J*=10.0 Hz, H-4), 4.83 (br s, 1H, H-5′), 4.76 (d, 1H, *J*=3.9 Hz, H-1), 4.43 (br d, 1H, *J*=16.6 Hz, H-5), 4.30 (dd, 1H, *J*=16.0, 10.7 Hz, H-10e), 3.85–3.78 (m, 2H, H-8 and H-9), 3.63 (br d, 1H, *J*=4.1, 7.0 Hz, H-10a), 3.57 (br s, 1H, H-7), 3.38 (s, 3H, OMe), 2.87–2.80 (m, 1H, H-2), 1.47 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 137.5, 128.8, 128.2, 126.8, 126.0, 124.7, 101.3, 100.2, 80.1, 78.2, 69.1, 65.1, 56.4, 55.1, 47.1, 41.1, 28.5. MSES: *m/z* 426 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{29}NO_6$ (403.20): C, 65.49; H, 7.24; N, 3.47. Found: C, 65.50; H, 7.50; N, 3.50.

*4.1.8.14. (7S,8R,8aS)-Diacetoxy-9-methoxy-3-phenyl-octahydro-2,4,10-trioxa-5-aza-phenanthrene-5-carboxylic acid tert-butyl ester (**17**).* Diol was acetylated using the general procedure (F) to give **17** (83%) as colorless solid, mp 208–210 °C. $[\alpha]_D^{28}$ +36.42 (*c* 0.85, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48–7.34 (m, 5H, Ar–H), 5.66 (s, 1H, Ph–C*H*), 5.20 (br s, 1H, H-4), 5.15 (dd, 1H, *J*=11.8, 3.2 Hz, H-3), 4.98–4.94 (m, 1H, H-8), 4.67 (d, 1H, *J*=3.8 Hz, H-1), 4.47 (br d, 1H, *J*=12.1 Hz, H-5′), 4.31 (dd, 1H, *J*=11.0, 5.3 Hz, H-10e), 3.80 (d, 2H, *J*=6.8 Hz, H-8 and H-10a), 3.39 (t, 1H, *J*=10.7 Hz, H-7), 3.31 (s, 3H, OMe), 2.90 (br d, 1H, *J*=15.6 Hz, H-5), 2.57 (ddd, 1H, *J*=11.3, 3.9, 3.6 Hz, H-2), 2.09 (s, 3H, $OCOCH_3$), 2.01 (s, 3H, $OCOCH_3$), 1.47 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.6, 154.4, 137.3, 128.7, 128.1, 125.9, 101.2, 97.4, 80.0, 71.2, 69.0, 67.9, 63.9, 57.4, 55.1, 48.4, 41.3, 28.3, 20.9, 20.6. MSES: *m/z* 544 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{35}NO_{10}$ (521.23): C, 59.87; H, 6.76; N, 2.69. Found: C, 60.03; H, 6.80; N, 2.75.

*4.1.8.15. (3S,4R,4aS,5S,7R,8S,8aR)-7-(Acetoxymethyl)-1-acetyl-5-methoxyoctahydro-1H-pyrano[4,3-b]pyridine-3,4,8-triyl triacetate (**18a**).* Diacetate was converted to pentaacetate using

the general procedure (G) followed by the general procedure (H) to give **18a** (78%) as colorless solid, mp 174–176 °C. $[\alpha]_D^{28}$ +40.0 (*c* 0.06, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1742, 1654 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): 5.33 (br d, 1H, *J*=2.2 Hz, rotamer-1), 5.21 (br d, 1H, *J*=2.2 Hz, rotamer-2), 5.00 (br dd, 1H, *J*=11.4, 2.9 Hz, rotamer-1), 4.88 (br dd, 1H, *J*=11.4, 2.9 Hz, rotamer-2), 4.88 (t, 1H, *J*=10.0 Hz), 4.71 (dd, 1H, *J*=3.6, 12.7 Hz), 4.33 (dd, 1H, *J*=4.8, 12.4 Hz), 4.18–4.16 (m, 2H), 4.09 (dd, 1H, *J*=12.2, 2.2 Hz), 3.95–3.91 (m, 2H, both rotamer), 3.85 (dd, 1H, *J*=3.6.9 Hz), 3.33 (s, 3H, OMe, minor), 3.31 (s, 3H, OMe, major), 3.07 (dd, 1H, *J*=12.7, 2.7 Hz,), 2.98 (t, 1H, *J*=10 Hz), 2.81 (dd, 1H, *J*=14.6 Hz), 2.63 (ddd, 1H, *J*=14.1, 3.6, 3.2 Hz), 2.18–1.99 (m, 30H, both rotamer). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.2, 170.8, 169.9, 169.7, 169.5, 97.1, 96.6, 70.4, 69.2, 68.4, 68.0, 67.5, 67.3, 63.2, 62.6, 55.9, 55.4, 55.1, 47.6, 43.3, 40.4, 29.7, 29.3, 20.9, 20.8, 20.7, 20.5. MSES: *m/z* 482 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{29}NO_{11}$ (459.44): C, 52.28; H, 6.36; N, 3.05. Found: C, 52.35; H, 6.40; N, 3.10.

*4.1.8.16. (2R,4aR,6R,7R,8R,8aS)-7-Allyl-6-methoxy-8-nitro-2-phenylhexahydropyrano[3,2-d][1,3]dioxine (**20**).* Methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-glucopyranoside was allylated using the general procedure (A) and purified over silica gel column chromatography. Yield: 73% (colorless solid, mp 65–67 °C). $[\alpha]_D^{28}$ −38.7 (*c* 4.75, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1556, 1642 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.43–7.34 (m, 5H, Ar–H), 5.84 (ddd, 1H, *J*=7.3, 11.6, 16.8 Hz, $-CH{=}CH_2$), 5.57 (s, 1H, Ph–C*H*), 5.20 (dd, 2H, *J*=11.2, 5.1 Hz, $-CH{=}CH_2$), 4.73 (t, 1H, *J*=10.0 Hz, H-3), 4.34 (m, 2H, H-1 and H-6e), 4.13 (t, 1H, *J*=9.5 Hz, H-4), 3.85 (t, 1H, *J*=10.4 Hz, H-6a), 3.54 (s, 3H, OMe), 3.42 (m, 1H, H-5), 2.36 (m, 2H, allylic), 2.09 (m, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 131.4, 129.2, 128.1, 126.0, 120.1, 116.5, 102.7, 101.5, 86.9, 85.0, 68.7, 66.4, 57.3, 44.4, 30.9. MSES: *m/z* 358 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{21}NO_6$ (335.14): C, 60.89; H, 6.31; N, 4.18. Found: C, 60.95; H, 6.50; N, 4.30.

*4.1.8.17. tert-Butyl(2R,4aR,6R,7R,8S,8aS)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**21a**).* Nitro olefins **20** were reduced to amino olefins **21a** and **21b** using the general procedure (B) and purified over silica gel column chromatography. Yield: 35% (colorless solid, mp 125–127 °C). $[\alpha]_D^{28}$ −26.6 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1527, 1680 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.43–7.34 (m, 5H, Ar–H), 5.90–5.85 (m, 1H, $-CH{=}CH_2$), 5.49 (s, 1H, Ph–C*H*), 5.12 (br s, 2H, $-CH{=}CH_2$), 4.35–4.28 (m, 3H, H-1, H-6e, and NH), 3.81 (br s, 1H, H-4), 3.71 (t, 1H, *J*=10.0 Hz, H-6a), 3.45 (s, 3H, OMe), 3.38 (m, 2H, H-5, H-3), 2.40 (m, 2H, allylic), 1.71–1.68 (m, 1H, H-2), 1.42 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 155.6, 137.3, 134.5, 128.7, 128.0, 126.0, 117.5, 104.5, 101.2, 80.8, 79.5, 68.7, 67.6, 57.0, 52.2, 46.3, 30.9, 28.2. MSES: *m/z* 428 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{31}NO_6$ (405.22): C, 65.17, H, 7.71; N, 3.45. Found: C, 65.27; H, 7.70; N, 3.50.

*4.1.8.18. tert-Butyl(2R,4aR,6R,7R,8R,8aS)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**21b**).* Yield: 43% (colorless solid, mp 121–123 °C). $[\alpha]_D^{28}$ −23.6 (*c* 0.90, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 3338, 1680, 1527 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.54–7.34 (m, 5H, Ar–H), 5.94–5.80 (ddd, 1H, *J*=17.3, 15.8, 7.3 Hz, $-CH{=}CH_2$), 5.55 (s, 1H, Ph–C*H*), 5.20 (dd, 2H, *J*=17.0, 15.8 Hz, $-CH{=}CH_2$), 4.36 (d, 1H, *J*=9.0 Hz, H-1), 4.33 (dd, 1H, *J*=10.5, 4.8 Hz, H-6e), 3.85 (t, 1H, *J*=10.2 Hz, H-6a), 3.75 (t, 1H, *J*=9.5 Hz, H-4), 3.54 (s, 3H, OMe), 3.39 (ddd, 1H, *J*=14.4, 9.5, 4.8 Hz, H-5), 3.09 (t, 1H, *J*=10.0 Hz, H-3), 2.26–2.47 (m, 2H, allylic), 2.04–1.98 (m, 1H, H-2), 1.46 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 153.8, 137.1, 134.4, 129.0–127.5 (m, aromatic), 126.0, 125.7, 118.4, 104.5, 101.4, 83.6, 73.2, 68.9, 67.3, 61.2, 57.0, 43.8, 42.2, 30.3, 27.6. MSES: *m/z* 428 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{31}NO_6$ (405.22): C, 65.17; H, 7.71; N, 3.45. Found: C, 65.33; H, 7.74; N, 3.51.

*4.1.8.19. tert-Butylallyl((2R,4aR,6R,7R,8R,8aS)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-yl)carbamate (**22**).* Amino olefin was N-allylated using the general procedure (C) and purified over silica column chromatography. Yield: 95% (colorless oil). $[\alpha]_D^{26}$ −42.2 (*c* 0.90, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): *δ* 7.49–7.34 (m, 10H, Ar–H, both rotamers), 5.96–5.81 (m, 2H, $-CH{=}CH_2$), 5.38 (s, 1H, Ph–C*H*), 5.20–5.05 (m, 4H, 2×$-CH{=}CH_2$), 4.57 (br s, 1H, minor rotamer), 4.35–4.28 (m, 2H), 4.06 (br dd, 1H, *J*=16.1, 10.2 Hz, minor rotamer), 3.85 (br d, 1H, *J*=10.9 Hz, minor rotamer), 3.76 (t, 1H, *J*=10.3 Hz), 3.60–3.35 (m, 5H and OMe), 2.32–2.21 (m, 2H, allylic), 1.91–1.86 (m, 1H), 1.44, 1.42 (2×s, 9H, *tert*-butyl, both rotamers). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 155.9, 137.9–125.9 (m, aromatic, both rotamer), 117.9, 116.9, 115.3, 104.9, 104.5, 100.8, 80.1, 79.8, 68.8, 68.0, 57.0, 56.7, 55.6, 44.4, 43.1, 31.1, 30.8, 28.2. MSES: *m/z* 468 $[M+Na]^+$. Anal. Calcd for $C_{25}H_{35}NO_6$ (445.25): C, 67.39; H, 7.92; N, 3.14. Found: C, 67.40; H, 7.95; N, 3.50.

*4.1.8.20. 6-Methoxy-2-phenyl-4,4a,6,6a,7,10,11a,11b-octahydro-1,3,5-trioxa-11-aza-cyclohepta[a]naphthalene-11-carboxylic acid tert-butyl ester (**23**).* Diene underwent RCM using the general procedure (D) and purified over silica gel column chromatography. Yield: 91%. $[\alpha]_D^{26}$ −26.6 (*c* 1.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1691, 1654 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): *δ* 7.49–7.34 (m, 10H, Ar–H, both rotamers), 5.70 (m, 4H, H-5, H-4, both rotamer), 5.50 (2×s, 2H, Ph–C*H*, both rotamer), 4.55 (br t, 1H, *J*=14.8 Hz, H-6′, rotamer-1), 4.37–4.31 (m, 5H, H-11e, H-1, both rotamers, and H-6), 4.18 (m, 2H, both rotamers), 3.84 (t, 2H, *J*=10.2 Hz, H-11a), 3.56 (2×s, 6H, OMe), 3.45–3.34 (m, 4H, H-10 and H-8, both rotamers), 2.54 (m, 2H, H-6, both rotamers), 2.17–2.03 (m, 2H, H-3, H-3′), 1.60–1.58 (m, 2H, H-2, both rotamers), 1.42 (s, 9H, *tert*-butyl, minor-1), 1.33 (s, 9H, *tert*-butyl, major). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 155.6, 137.4, 130.1–126.2 (m, aromatic), 104.9,

104.8, 101.7, 101.2, 80.0, 79.8, 78.3, 69.1, 69.0, 68.9, 68.8, 60.0, 58.6, 57.2, 57.1, 46.2, 40.3, 39.5, 28.3, 28.2, 28.1, 27.8. MSES: *m/z* 418 $[M+H]^+$. Anal. Calcd for $C_{23}H_{31}NO_6$ (417.22): C, 66.10; H, 7.58; N, 3.35. Found: C, 66.50; H, 7.48; N, 3.34.

*4.1.8.21. (8R,9S)-Diacetoxy-6-methoxy-2-phenyldecahydro-1,3,5-trioxa-11-aza-cyclohepta[a]naphthalene-11-carboxylic acid tert-butyl ester (**25**).* Diol was acetylated using the general procedure (F) to give **25** (90%) as colorless solid, mp 95–97 °C. $[\alpha]_D^{26}$ −60.0 (*c* 0.60, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1745, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.49–7.34 (m, 10H, Ar–H, both rotamers), 5.49 (s, 1H, Ph–C*H*, rotamer-1), 5.45 (s, 1H, Ph–C*H*, rotamer-2), 5.42–5.40 (m, 1H, H-4, rotamer-1), 5.33 (br s, 1H, H-4, rotamer-2), 4.84 (tt, 1H, *J*=7.3, 3.4 Hz, H-5, rotamer-1), 4.75 (tt, 1H, *J*=7.3, 3.4 Hz, H-5, rotamer-2), 4.34–4.29 (m, 5H, H-11e, H-1, both rotamers and H-6′, rotamer-1), 4.05 (t, 1H, *J*=10.2 Hz, H-11a, rotamer-1), 3.86–3.81 (m, 3H, H-11a, both rotamer, H-8), 3.68 (br d, 1H, *J*=12.6 Hz, H-6), 3.56–3.52 (m, 2H, H-9), 3.47 (2×s, 3H, OMe), 3.40–3.34 (m, 1H, H-10), 3.25–3.19 (m, 2H, H-6, both rotamers), 2.27 (m, 4H, H-3 and H-3′, both rotamers), 2.14, 2.01 (2×s, 6H, $OCOCH_3$, rotamer-1), 2.10, 1.99 (2×s, 6H, $NHCOCH_3$, rotamer-2), 1.48 (s, 9H, *tert*-butyl, rotamer-1), 1.27 (s, 9H, *tert*-butyl, rotamer-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.4, 169.1, 155.3, 137.1, 129.0–127.9 (m, aromatic), 126.4, 125.9, 104.6, 104.5, 101.9, 100.7, 80.7, 80.6, 79.2, 79.0, 72.0, 71.7, 68.8, 68.6, 67.3, 66.9, 58.6, 57.4, 57.1, 57.0, 41.1, 40.2, 39.6, 39.4, 28.0, 27.8, 26.9, 21.0, 20.7. MSES: *m/z* 536 $[M+H]^+$. Anal. Calcd for $C_{27}H_{37}NO_{10}$ (535.24): C, 60.55; H, 6.96; N, 2.62. Found: C, 60.50; H, 7.00; N, 2.65.

*4.1.8.22. (3R,4S,5aR,6R,8R,9S,9aR)-8-(Acetoxymethyl)-1-acetyl-6-methoxydecahydropyrano-[4,3-b]azepine-3,4,9-triyl triacetate (**26a**).* Diacetate was converted to pentaacetate using the general procedure (G) followed by the general procedure (H) to give **26a** (81%) as colorless solid, mp 78–80 °C. $[\alpha]_D^{26}$ −10.5 (*c* 0.85, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1743, 1653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 5.39 (t, 1H, *J*=4.4 Hz, H-4, minor), 5.34 (t, 1H, H-4, *J*=4.4 Hz, major), 4.94 (t, 1H, *J*=9.8 Hz, H-9, minor), 4.80 (t, 1H, *J*=9.8 Hz, H-9, major), 4.73–4.70 (m, 1H, H-5, major), 4.63 (t, 1H, *J*=10.2 Hz, H-8), 4.37 (dd, 1H, *J*=12.2, 5.1 Hz, H-11e), 4.29 (d, 1H, *J*=8.2 Hz, H-1), 4.17–4.11 (m, 2H, H-11a, major and minor), 4.00–3.95 (m, 1H, H-6′, minor), 3.90 (ddd, 1H, *J*=6.8, 4.6, 1.9 Hz, H-10), 3.75–3.73 (m, 1H, H-10, minor), 3.52–3.50 (m, 1H, H-6′), 3.49 (s, 3H, OMe), 3.37 (dd, 1H, *J*=15.3, 2.6 Hz, H-6), 3.10 (dd, 1H, *J*=15.3, 2.6 Hz, H-6, minor), 2.23–1.96 (m, 31H, $OCOCH_3$, $NCOCH_3$ and *H*-3), 1.48–1.43 (m, 1H, H-3′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2–170.0 (m), 104.0, 73.1, 72.1, 68.7, 67.0, 62.7, 57.0, 56.3, 42.8, 38.7, 26.0, 21.7, 21.0, 20.8, 20.6. MSES: *m/z* 474 $[M+H]^+$. Anal. Calcd for $C_{21}H_{31}NO_{11}$ (473.19): C, 53.27; H, 6.60; N, 2.96. Found: C, 53.20; H, 6.50; N, 3.00.

*4.1.8.23. (2R,4aR,6R,7R,8R,8aR)-7-Allyl-6-methoxy-8-nitro-2-phenylhexahydropyrano[3,2-d][1,3]dioxine (**28**).* Methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-galactopyranoside was allylated using the general procedure (A) and purified over silica gel column chromatography. Yield: 73% (colorless solid, mp 71–72 °C). $[\alpha]_D^{23}$ +40.0 (*c* 0.60, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1556, 1642 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, 2H, *J*=3.6 Hz, Ar–H), 7.33 (d, 3H, *J*=4.2 Hz, Ar–H), 5.72–5.78 (ddd, *J*=17.5, 9.3 Hz, 1H, –CH=CH_2), 5.55 (s, 1H, Ph–C*H*), 5.10 (dd, 2H, *J*=17.5, 10.0 Hz, –CH=CH_2), 4.62 (dd, 1H, *J*=12.2, 3.6 Hz), 4.54 (br d, 1H, *J*=3.6 Hz, H-4), 4.39 (d, 1H, *J*=12.4 Hz, H6e), 4.26 (d, 1H, *J*=8.7 Hz, H-1), 4.14 (d, 1H, *J*=12.4 Hz, H6a), 3.54 (s, 3H, OMe), 3.47 (br s, 1H, H-5), 2.86–2.84 (m, 1H, H-2), 2.55–2.51 (m, 1H, allylic), 2.25–2.30 (m, 1H, allylic). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 132.5, 128.9, 128.0, 126.0, 119.5, 102.4, 100.5, 85.1, 72.6, 69.0, 66.6, 56.8, 37.0, 30.8. MSES: *m/z* 358 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{21}NO_6$ (335.14): C, 60.89; H, 6.31; N, 4.18. Found: C, 60.95; H, 6.50; N, 4.30.

*4.1.8.24. tert-Butyl(2R,4aR,6R,7R,8R,8aR)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**29a**).* Compound **29a** was prepared in 52% yield from compound **28** following the procedure used for the preparation of **3a** (colorless solid, mp 83–85 °C). $[\alpha]_D^{23}$ +73.3 (*c* 0.30, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1530, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, 2H, *J*=3.6 Hz, Ar–H), 7.34 (s, 3H, Ar–H), 5.83–5.92 (ddd, *J*=15.8, 7.56 Hz, 1H, –C*H*=CH_2), 5.52 (s, 1H, Ph–C*H*), 5.07 (s, 1H, NH), 4.98 (dd, 2H, *J*=30.0, 10.7 Hz, –CH=CH_2), 4.29 (br d, 1H, *J*=12.4 Hz, H6e), 4.20 (d, 1H, *J*=8.56 Hz, H-1), 4.03 (br d, 1H, *J*=12.2 Hz, H6a), 3.94 (br s, 1H, H-4), 3.86 (br t, 1H, *J*=10.0 Hz, H-3), 3.52 (s, 3H, OMe), 3.38 (br s, 1H, H-5), 2.23–2.33 (m, 2H, allylic), 1.95–1.91 (m, 1H, H-2), 1.41 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 137.9, 134.8, 129.2, 128.2, 126.5, 117.2, 104.3, 101.3, 79.7, 74.1, 69.5, 67.1, 56.8, 51.1, 40.8, 40.5, 28.4. MSES: *m/z* 428 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{31}NO_6$ (405.22): C, 65.17; H, 7.71; N, 3.45. Found: C, 65.37; H, 7.75; N, 3.50.

*4.1.8.25. tert-Butyl(2R,4aR,6R,7R,8S,8aR)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-ylcarbamate (**29b**).* Yield: 30%, colorless oil. $[\alpha]_D^{23}$ +13.3 (*c* 0.15, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1530, 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.49–7.34 (m, 10H, Ar–H, both rotamer), 5.85–5.76 (m, 1H, –C*H*=CH_2), 5.55 (s, 1H, Ph–C*H*), 5.09–5.00 (m, 2H, –CH=CH_2), 4.67 (br s, 1H, minor rotamer), 4.42–4.07 (m, 6H), 3.75–3.31 (m, 5H and OMe, both rotamer), 2.29–2.28 (m, 1H, allylic, minor rotamer), 1.89–1.78 (m, 2H, allylic), 1.44–1.42 (s, 9H, *tert*-butyl, both rotamer). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.8, 137.1, 134.4, 129.2, 128.4, 128.2, 127.5, 126.0, 125.7, 118.4, 118.0, 104.5, 101.4, 83.6, 68.3, 67.3, 61.2, 57.0, 43.8, 42.2, 30.3, 27.6, 27.3. MSES: *m/z* 428 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{31}NO_6$ (405.22): C, 65.17; H, 7.71; N, 3.45. Found: C, 65.29; H, 7.70; N, 3.52.

*4.1.8.26. tert-Butylallyl((2R,4aR,6R,7R,8R,8aR)-7-allyl-6-methoxy-2-phenylhexahydropyrano[3,2-d][1,3]dioxin-8-yl)carbamate (**30**).* Amino olefin was N-allylated using the general procedure (C) and purified over silica gel column chromatography. Yield: 94% (colorless oil). $[\alpha]_D^{23}$ +64.0 (*c* 1.5, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.34 (m, 5H, Ar–H), 5.70–5.64 (m, 2H, –C*H*=CH_2), 5.45 (s, 1H, Ph–C*H*), 4.98–4.82 (m, 4H, 2×–CH=CH_2), 4.29–4.19 (m, 3H), 3.93 (br s, 2H), 3.73–3.67 (m, 2H, H-3 and H-4), 3.45 (s, 3H, OMe), 3.31 (s, 1H, H-5), 2.24–2.22 (m, 2H, allylic), 2.06–2.00 (m, 1H, H-2), 1.37 (s, 9H, *tert*-butyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 137.9–125.9 (m, aromatic), 117.3, 115.1, 104.8, 100.8, 80.2, 79.8, 69.6, 67.0, 56.7, 55.3, 47.4, 37.9, 30.8, 28.3. MSES: *m/z* 468 $[M+Na]^+$. Anal. Calcd for $C_{25}H_{35}NO_6$ (445.25): C, 67.39; H, 7.92; N, 3.14. Found: C, 67.41; H, 7.92; N, 3.52.

*4.1.8.27. 6-Methoxy-2-phenyl-4,4a,6,6a,7,10,11a,11b-octahydro-1,3,5-trioxa-11-aza-cyclohepta[a]naphthalene-11-carboxylic acid tert-butyl ester (**31**).* Diene underwent RCM using the general procedure (D) and purified over silica gel column chromatography. Yield: 92%. $[\alpha]_D^{23}$ +76.0 (*c* 1.25, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685, 1654 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.47 (d, 2H, *J*=5.12 Hz, Ar–H), 7.33 (d, 3H, *J*=6.0 Hz, Ar–H, major and minor), 5.63 (br d, 2H, *J*=5.1 Hz, H-5, H-4), 5.54 (s, 1H, Ph–C*H*, major), 5.52 (s, 1H, Ph–C*H*, minor), 4.31 (br d, 2H, *J*=12.2 Hz, H-8 and H-6′), 4.22 (d, 1H, *J*=8.2 Hz, H-1), 4.31 (br s, 1H, H-9), 4.09–4.00 (m, 2H, H-11, H-11′), 3.82 (br d, 2H, *J*=16.3 Hz, H-6, major and minor), 3.50 (s, 3H, OMe, major), 3.47 (s, 3H, OMe, minor), 3.40 (br s, 1H, H-10), 2.63–2.55 (m, 2H, H-3, H-3′, major and minor), 1.95–1.92 (m, 1H, H-2), 1.46 (s, 9H, *tert*-butyl, minor), 1.42 (s, 9H, *tert*-butyl, major). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 154.8, 138.1, 137.8, 129.2–128.5 (m, aromatic), 126.1, 126.0, 104.9, 104.8, 100.7, 100.6, 79.9, 75.5, 75.2, 69.6, 68.7, 60.7, 59.4, 56.5, 56.4, 42.9, 42.3, 39.2, 39.0, 29.0–28.3 (m). MSES: *m/z* 440 $[M+Na]^+$. Anal. Calcd for $C_{23}H_{31}NO_6$ (417.22): C, 66.10; H, 7.58; N, 3.35. Found: C, 66.40; H, 7.48; N, 3.34.

*4.1.8.28. (8R,9S)-Diacetoxy-6-methoxy-2-phenyldecahydro-1,3,5-trioxa-11-aza-cyclohepta[a]naphthalene-11-carboxylic acid tert-butyl ester (**33**).* Diol was acetylated using the general procedure (F) to give **33** (83%) as colorless solid, mp 121–123 °C. $[\alpha]_D^{23}$ +71.0 (*c* 1.25, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 7.52–7.33 (m, 5H, Ar–H, major and minor), 5.56 (s, 1H, Ph–C*H*, major), 5.54 (s, 1H, Ph–C*H*, minor), 5.53 (br s, 1H, H-4), 4.76 (dt, 1H, *J*=10.5, 7.1 Hz, H-5, major), 4.72 (dt, 1H, *J*=10.5, 7.1 Hz, H-5, minor), 4.35 (d, 1H, *J*=8.2 Hz, H-1, minor), 4.32 (dd, 1H, *J*=12.2, 1.2 Hz, H-11′), 4.20 (d, 1H, *J*=8.3 Hz, H-1, major), 4.17 (br d, 1H, *J*=1.7 Hz, H-9), 4.11 (d, 1H, *J*=6.3 Hz, H-11, minor), 4.06 (dd, 1H, *J*=12.4, 1.9 Hz, H-11, major), 3.87 (dd, 1H, *J*=12.7, 2.7 Hz, H-8), 3.58–3.50 (m, 2H, H-6, H-6′), 3.50–3.48 (m, 1H, H-10, major and minor), 3.48 (s, 3H, OMe), 2.72–2.68 (m, 1H, H-2), 2.33 (dd, 1H, *J*=14.6, 5.8 Hz, H-3′), 2.09, 2.00 (2s, 6H, $OCOCH_3$, major), 2.08, 1.98 (2s, 6H, $OCOCH_3$, minor), 1.49 (s, 9H, *tert*-butyl, minor), 1.48 (s, 9H, *tert*-butyl, major), 1.28–1.23 (m, 1H, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 169.3, 155.4, 138.0, 128.7, 128.0, 126.1, 104.6, 100.58, 100.50, 81.2, 74.2,72.2, 67.6, 67.3, 67.2, 59.2, 56.4, 43.1, 33.1, 28.2, 27.1, 21.1, 20.8. MSES: 536 $[M+H]^+$. Anal. Calcd for $C_{27}H_{37}NO_{10}$ (535.24): C, 60.55; H, 6.96; N, 2.62. Found: C, 60.50; H, 7.00; N, 2.65.

*4.1.8.29. (3R,4S,5aR,6R,8R,9R,9aR)-8-(Acetoxymethyl)-1-acetyl-6-methoxydecahydropyrano[4,3-b]azepine-3,4,9-triyl triacetate (**35**).* Diacetate was converted to pentaacetate using the general procedure (G) followed by the general procedure (H) to give **35** (78%) as colorless solid, mp 88–90 °C. $[\alpha]_D^{26}$ +10.5 (*c* 0.85, CH_2Cl_2). IR (CH_2Cl_2) ν_{max}: 1743, 1653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.32 (br s, 1H, H-8), 5.27 (br s, 1H, H-4), 4.59 (br d, 1H, *J*=10.5 Hz, H-5), 4.19 (dd, 1H, *J*=13.6, 2.4 Hz, H-8), 4.14 (d, 1H, *J*=8.3 Hz, H-1), 4.08 (qt, 1H, *J*=9.5, 4.9 Hz, H-11′), 3.88 (t, 1H, *J*=6.6 Hz, H-11), 3.47–3.40 (m, 2H, H-10 and H-6), 3.46 (s, 3H, OMe), 3.32 (br d, 1H, *J*=13.9 Hz, H-6′), 2.43–2.35 (m, 1H, H-2), 2.27 (dd, 1H, *J*=14.8, 5.6 Hz, H-3), 1.97–2.14 (m, 15H, 4×$OCOCH_3$, $NCOCH_3$), 1.22–1.20 (m, 1H, H-3′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9–169.6 (m), 104.4, 73.1, 71.9, 67.3, 67.1, 61.8, 57.4, 57.0, 43.7, 33.6, 29.6, 27.5, 21.9–20.7 (m). MSES: *m/z* 474 $[M+H]^+$. Anal. Calcd for $C_{21}H_{31}NO_{11}$ (473.19): C, 53.27; H, 6.60; N, 2.96. Found: C, 53.30; H, 6.40; N, 2.90.

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Supplementary data

^1H and ^{13}C NMR spectra of compounds reported in this article can be found in the online version. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.01.005.

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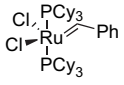
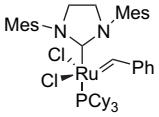


A

Grubbs' 1st Generation catalyst



B

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20. All the enzymes (α-galactosidase, β-galactosidase, α-glucosidase, and β-glucosidase) and the corresponding substrate were purchased from Sigma Chemicals Co. The inhibition potencies of the sugar–azasugar hybrids **8**, **18**, **26**, and **34** were evaluated using α-glycosidases. The IC_{50} values obtained are summarized in Table 1.