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PAPER

Asymmetric synthesis of 1-deoxyazasugars from chiral aziridines†

Alok Singh,[a] Bongchan Kim,[b] Won Koo Lee*[b] and Hyun-Joon Ha*[a]

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A general and facile synthesis of enantiopure 1-deoxyazasugars was achieved from stereoselective dihydroxylation of a common synthetic intermediate, piperidine ring fused oxazolidin-2-one, originating from a commercially available starting substrate, chiral aziridine-2-carboxylate, in high yields.

Introduction

Azasugars as structural analogs of true sugars whose ring oxygen atom is replaced by nitrogen attract great attention due to their occurrence in nature and their interesting biological activities. Many polyhydroxylated piperidine alkaloids have been revealed from diverse natural sources including many different microorganisms and plants.[1] Among them nojirimycin, the closest analog of pyranose from a structural point of view, was isolated in 1966.[2] However, the hydroxyl group at C-1 causes some difficulties in isolation and handling. Its deoxy-analogs without a hydroxyl group at C-1, called deoxynojirimycins, were isolated and characterized from natural sources.[3] On the basis of their structural similarity to sugar many azasugars have biological activities in carbohydrate-related metabolic pathways including glycosidase and glycotransferase and have possible therapeutic applications as antidiabetic, anticancer and antibacterial agents.[4] Many of them are derivatives of deoxynojirimycins with diverse stereochemistry of the hydroxyl groups along the carbons of the piperidine ring, with representative examples such as miglitol,[5] miglustat[6] and OGT.[7] Though there is a rich literature dealing with asymmetric synthesis of deoxynojirimycins,[8,9] an easy and facile access to their synthesis is still needed, with full control of all hydroxy configurations.

In this report, we describe the synthesis of six different stereoisomers of deoxynojirimycins including L-1-deoxyidonojirimycin (L-Ido-DNJ, **1a**), L-1-deoxygalactonojirimycin (L-Galacto-DNJ, **1b**), L-1-deoxygulonojirimycin (L-Gulo-DNJ, **1c**), L-1-deoxynojirimycin (L-DJN, **1d**), L-1-deoxyaltronojirimycin (L-Altro-DNJ, **1e**) and L-1-deoxymannojirimycin (L-Manno-DNJ, **1f**) from (2*S*)-aziridine-2-carboxylate (Fig. 1). In the same manner all six D-deoxyazasugars were also synthesized from (2*R*)-aziridine-2-carboxylate.

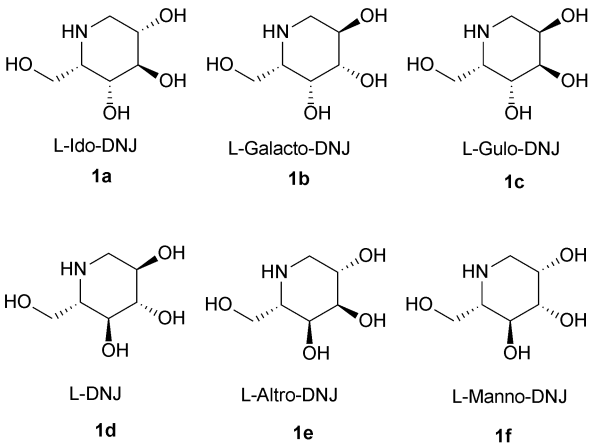


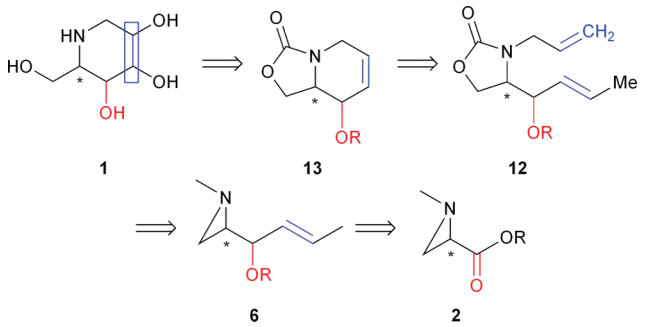
Fig. 1 Some stereoisomers of deoxynojirimycins.

For the last several years we have shown that the enantiopure aziridine-2-carboxylate serves as a starting substrate for the asymmetric synthesis of many nitrogen-containing cyclic and acyclic compounds based on the functional group-transformation of the carboxylate group and aziridine ring opening in a regio- and stereoselective manner.[10] Based on the same synthetic strategy, we prepared all six isomers of DNJ starting from the enantiopure aziridine-2-carboxylate.

The synthetic plan for deoxynojirimycins (**1**) with complete control of four stereocenters in the piperidine ring was based on the stereoselective dihydroxylation of the common synthetic intermediate **13**. Its piperidine ring was formed by ring-closing metathesis (RCM) between the alkenyl pendent at C-4 and the *N*-allyl group present at the ring nitrogen of 3,4-dialkenyl oxazolidin-2-one (**12**). The stereochemistry of the hydroxymethyl group at C-2 of the piperidine ring can be pre-determined by the selection of the starting aziridine-2-carboxylate (**2**) with the star mark in Scheme 1. Thereby, all six isomers (**1a–1f**) starting from the same chiral aziridine-2-carboxylate had the same stereochemistry at C-2 of the piperidine ring. These isomers (**1a–1f**) were classified into two different groups, **1a–1c** and **1d–1f**, by the stereochemistry at the

[a]*Department of Chemistry and Protein Research Centre for Bio-Industry, Hankuk University of Foreign Studies, Yongin, 449-719, Korea. E-mail: hjha@hufs.ac.kr; Fax: +82-31-3304566; Tel: +82-31-3304369*
[b]*Department of Chemistry, Sogang University, Seoul 121-742, Korea. E-mail: wonkoo@sogang.ac.kr; Fax: +82-2-7010967; Tel: +82-2-7058449*

† Electronic supplementary information (ESI) available: Electronic supplementary information (ESI) available: Spectral data for D-deoxyazasugars and actual ^{1}H and ^{13}C-NMR spectra for all compounds. See DOI: 10.1039/c0ob00730g



Scheme 1 Retrosynthetic analysis of DNJs starting from the enantiopure aziridine-2-carboxylate bearing the chirality denoted as star mark.

C-3 hydroxy group, with the red color showing its origination from the hydroxyl group of compound **6**. The absolute configuration of C-3 is controlled by the stereoselective reduction of the carbonyl functional group at 2-acylaziridine, the alkylated product of aziridine-2-carboxylate (**2**), in either an *erythro* or *threo* selective way. In this manner we were able to elaborate all six L-DNJ isomers starting from (2*S*)-aziridine-2-carboxylate as shown in Scheme 1.

Results and discussion

The aziridine-2-yl propynyl ketone (**4**) was prepared from alkynylation of the corresponding Weinreb amide prepared from ethyl (2*S*)-aziridine-2-carboxylate in 95% yield over two steps.[11] This ketone was selectively reduced by non-chelating bulky reducing agent L-Selectride® to provide *threo* alcohol (**5a**) exclusively. The reduction of the same ketone by $NaBH_4$ with $ZnCl_2$ yielded chelation-controlled product *erythro* (**5b**) isomer selectively.[11a] Each of the alkynyl alcohols was converted to olefin **6a** and **6b** by reduction with $LiAlH_4$ in 94 and 93% yield respectively (Scheme 2).

The hydroxy groups were protected by TBS to **7a** and **7b**, which survived throughout the following reactions. The aziridine rings of **7a** and **7b** were opened by an oxygen nucleophile, acetate, to yield **8a** and **8b**. The acetyl groups in **8a** and **8b** were hydrolyzed by KOH in EtOH to give 1,2-hydroxyamines (**9a** and **9b**) in quantitative yield. These were cyclized[12] to oxazolidin-2-ones, **10a** and **10b** with CDI and DBU in CH_2Cl_2. The α-methylbenzyl groups in **10a** and **10b** were removed by Na in liquid NH_3 at −78 °C to afford **11a** and **11b** in 94 and 93% yields respectively. Allylation of the ring nitrogen proceeded with allyl iodide in the presence of NaH as a base to afford **12a** and **12b** which were ready for RCM. The piperidine ring fused oxazolidin-2-ones were formed from **12a** and **12b** in the presence of 10 mol% of 1st generation of Grubbs' catalyst, benzylidene-bis(tricyclohexylphosphine)dichlororuthenium, to yield **13a** and **13b** in quantitative yield respectively.[13] These bicycles (**13a** and **13b**) were common intermediates for the preparation of DNJs by introducing two hydroxyl groups to the olefin at C-4 and C-5 of the piperidine ring in a stereoselective manner. All of the reactions mentioned above for the formation of **13a** and **13b** from chiral aziridine-2-carboxylates proceeded in more than 93% yield (Scheme 2).

The synthetic intermediate **13a** bearing two stereocenters originating from the chirality of aziridine-2-carboxylate and the stereoselective reduction of a ketone was utilized as a substrate to introduce two more hydroxyl groups at the olefin in the piperidine ring. For the preparation of *anti*- and *syn* diols at C-4 and C-5 of the piperidine ring two different methods were applied *i.e.* epoxidation followed by regioselective hydrolytic epoxide ring opening and the direct dihydroxylation reaction, respectively. Epoxidation of **13a** with oxone®[14] in acetone provided **14a** in 71% yield which was reacted further with acetone in the presence of $BF_3{\cdot}Et_2O$ as Lewis acid to yield diol bound as acetal at C-4 and C-5 of the piperidine ring (**15a**). Hydrolytic cleavage of the oxazolidin-2-one ring was accomplished by LiOH in EtOH with concomitant cleavage of the TBS protecting group to provide the corresponding amino alcohol. Finally the acetonide was cleaved with HCl in methanol followed by treatment with an ion-exchange resin (Amberlite IRA-410 OH^- form) afforded pure L-Ido-DNJ (**1a**)[15] in 96% yield over two steps. The epoxidation reaction of **16b** with MCPBA after removal of the TBS group from **13a** afforded epoxyalcohol **17b**, from which L-Galacto-DNJ (**1b**) was obtained by following the known procedure.[16] Direct dihydroxylation[17] of the synthetic intermediate **13a** with OsO_4 yielded **18c** in quantitative yield with the right configurations of all hydroxyl groups at C-2 to C-5 for L-Gulo-DNJ (**1c**). The same hydrolytic reaction with LiOH in EtOH yielded L-Gulo-DNJ (**1c**) in 95% yield (Scheme 3).

The same sequential reactions used to introduce the two hydroxyl groups to **1a**, **1b** and **1c** were applied to the similar olefinic piperidine intermediate **13b** to prepare another set of DNJ isomers including L-DNJ (**1d**), L-Altro-DNJ (**1e**) and L-Manno-DNJ (**1f**).

Direct epoxidation reaction of **13b** with Oxone® and epoxidation with MCPBA after removal of the TBS protecting group as **16e** yielded **14d** and **17e** in 68% and 77% yields, respectively. Cleavage of epoxides from **14d** and **17e** to diols followed by hydrolytic removal of oxazoldin-2-one ring and global deprotection yielded L-DNJ (**1d**) and L-Altro-DNJ (**1e**) respectively. The direct dihydroxylation of **13b** yielded **18f** which was converted to L-Manno-DNJ (**1f**) as in the previous case for **1c** in high yield (Scheme 4).

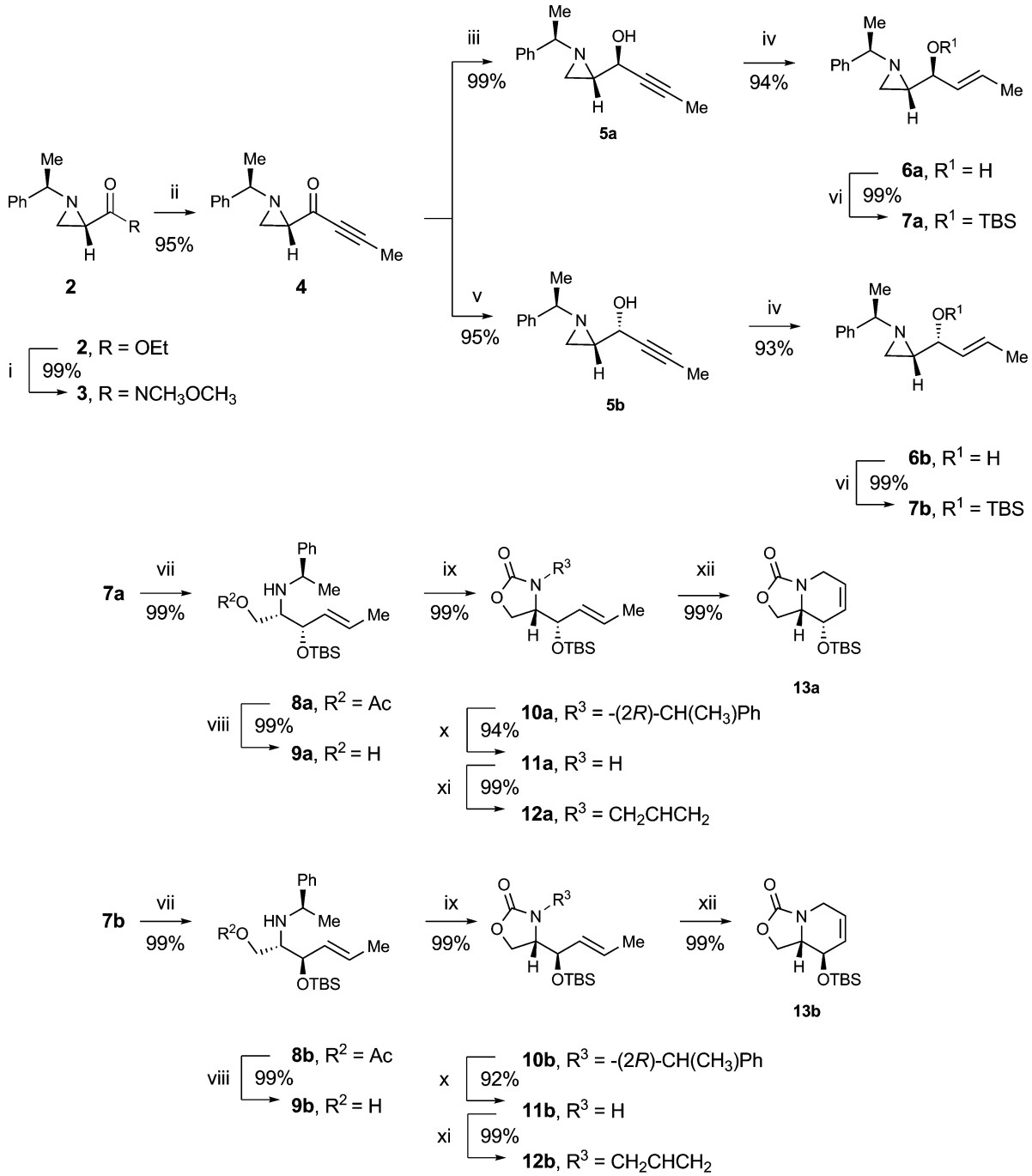
Conclusions

We would like to draw the conclusion that the general and facile synthesis of enantiopure deoxynojirimycins was achieved from stereoselective dihydroxylation of a common synthetic intermediate, piperidine ring fused oxazolidin-2-one **13**, originating from a commercially available starting substrate, chiral aziridine-2-carboxylate, with full control of all the configurations and in high yields. On the basis of this synthetic strategy we have synthesized all six D-enantiomers of 1-deoxynojirimycin starting from (2*R*)-aziridine-2-carboxylate instead of (2*S*)-aziridine-2-carboxylate which is described fully in the ESI† of this paper.

Experimental

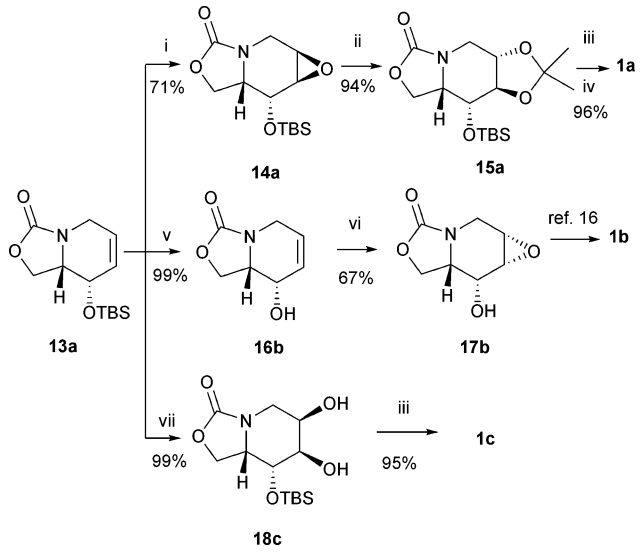
General

All non-aqueous reactions were run in flame-dried glassware under a positive pressure of nitrogen with exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds. Anhydrous solvents were obtained using standard drying techniques. Unless stated otherwise, commercial grade reagents were used without further

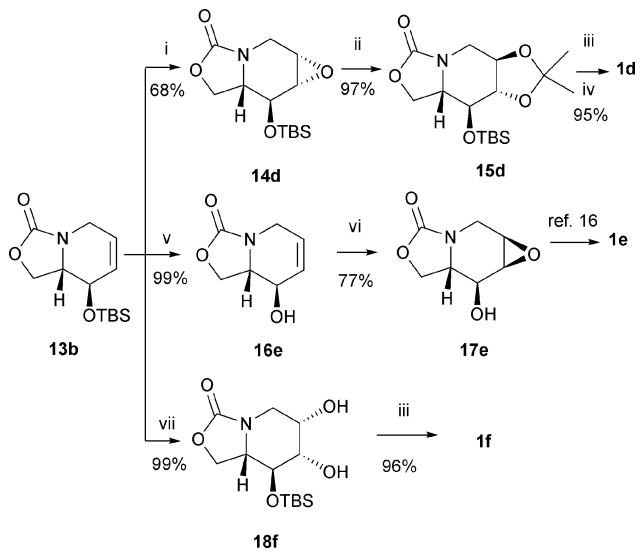


Scheme 2 *Reagents and conditions*: (i) isopropylmagnesium chloride, *N*,*O*-dimethyl hydroxyl-amine hydrochloride, THF, 0 °C, 1 h; (ii) 1-propynylmagnesium bromide, THF, −78 °C, 1 h, then at rt, 1 h; (iii) L-Selectride®, THF, −78 °C, 0.5 h; (iv) $LiAlH_4$, THF, reflux, 8 h; (v) $ZnCl_2$, MeOH, −78 °C, 0.5 h then $NaBH_4$, −78 °C, 1 h; (vi) TBSCl, DMAP, TEA, CH_2Cl_2, 17 h; (vii) AcOH, CH_2Cl_2, 15 h; viii) KOH, EtOH, 30 min; (ix) CDI, DBU, CH_2Cl_2, 0 °C then at rt, 24 h; (x) Na, liq. NH_3, THF, −78 °C, 30 min; (xi) allyl iodide, NaH, 1,2-dichlorethane, 0 °C then reflux, 10 h; (xii) benzylidene-bis(tricyclohexylphosphine)dichlororuthenium (1st generation of Grubbs' catalyst), CH_2Cl_2, 24 h.

purification. Both (2*R*)- and (2*S*)-1-[(*R*)-α-methylbenzyl]-2-aziridinecarboxylate ethyl esters were purchased from Imagene Co. Ltd. Their methyl esters were also purchased from Aldrich. Reactions were monitored by analytical thin-layer chromatography (TLC) performed on pre-coated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance, ninhydrin, phosphomolybdic acid or iodine. Flash chromatography was performed on 230–400 mesh silica gel with the indicated solvent systems. Melting points are uncorrected. Routine nuclear magnetic resonance spectra were recorded either on Varian Gemini 200 (200 MHz) or Varian Gemini 400 (400 MHz) spectrometers. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ 7.27



Scheme 3 *Reagents and Conditions*: (i) Oxone®, $NaHCO_3$, acetone, water, 30 min; (ii) $BF_3{\cdot}Et_2O$, acetone, CH_2Cl_2, 0 °C, 2 h; (iii) LiOH, 30% aq. EtOH, reflux, 4 h; (iv) HCl, MeOH, reflux, 4 h; (v) TBAF, THF, 0 °C, 1 h; (vi) MCPBA, NaH_2PO_4, CH_2Cl_2, 0 °C then rt, 3 days; (vii) OsO_4, NMO, CH_3CN, H_2O, 0 °C then rt, 3 h.



Scheme 4 *Reagents and Conditions*: (i) Oxone®, $NaHCO_3$, acetone, water, 30 min; (ii) $BF_3{\cdot}Et_2O$, acetone, CH_2Cl_2, 0 °C, 2 h; (iii) LiOH, 30% aq. EtOH, reflux, 4 h; (iv) HCl, MeOH, reflux, 4 h; (v) TBAF, THF, 0 °C, 1 h; (vi) MCPBA, NaH_2PO_4, CH_2Cl_2, 0 °C then rt, 3 days; (vii) OsO_4, NMO, CH_3CN, H_2O, 0 °C then rt, 3 h.

ppm; CD_3OD δ 3.31 ppm; D_2O δ 4.79 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, and br = broad), coupling constant in Hz, and integration. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of the solvent resonance as the internal standard ($CDCl_3$, δ 77.00 ppm; CD_3OD δ 49.15). All spectra were obtained with complete proton decoupling. Optical rotations were determined at 589 nm at 20 °C. Data are reported as follows: $[\alpha]_D$, concentration (c in g/100 mL), and solvent. Elemental analyses were performed using a Carlo Erba EA 1180 elemental analyzer. High resolution mass spectra were recorded on a 4.7 Tesla IonSpec ESI-FTMS or a Micromass Q-TOF Ultima Global Mass Spectrometer

(*S*)-*N*-methoxy-*N*-methyl 1-[(*R*)-1-phenylethyl]aziridine-2-carboxamide (3). To a stirred solution of **2** (2.46 g, 11.20 mmol) in anhydrous THF (33 mL) at 0 °C, under an inert atmosphere of N_2, were added *N*,*O*-dimethyl hydroxyl-amine hydrochloride (1.64 g, 16.8 mmol) and isopropylmagnesium chloride (2 M in THF, 16.80 mL, 33.6 mmol). After stirring at 0 °C for 1 h and warming to room temperature the mixture was quenched with aqueous NH_4Cl (10 mL). The reaction mixture was extracted with ethyl acetate (3 × 50 mL) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 50 : 50, v/v) to give **3** (2.61 g, 99% yield) as yellow oil: $[\alpha]_D^{20}$ = +20.48 (c = 0.649, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ 7.45–7.18 (m, 5H), 3.14 (s, 3H), 3.12 (s, 3H), 2.57 (d, J = 6.4 Hz, 1H), 2.56 (q, J = 6.4 Hz, 1H), 2.42 (dd, J = 3.1, 1.2 Hz, 1H), 1.76 (dd, J = 6.4, 1.3 Hz, 1H), 1.48 (d, J = 6.6 Hz, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 23.78, 32.36, 34.10, 35.05, 61.02, 70.53, 126.81, 127.11, 128.53, 144.28, 169.92; HRMS (ESI) calculated for $[C_{13}H_{18}N_2O_2+Na]^+$: 257.1266, Found 257.1268.

1-{(*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl}but-2-yn-1-one (4). To a stirred solution of **3** (1.77 g, 7.55 mmol) in anhydrous THF (7.5 mL) at −78 °C, under an inert atmosphere of N_2, was added 1-propynyl magnesium bromide (0.5 M in THF, 22.7 mL, 11.38 mmol). The reaction mixture was then stirred for 1 h at −78 °C and warmed to room temperature and stirred for an additional 1 h before being quenched with water. The reaction mixture was extracted with ethyl acetate (3 × 25 mL) and combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 70 : 30, v/v) to give **4** (1.53 g, 95% yield) as yellow oil: $[\alpha]_D^{20}$ = −148.11 (c = 1.078, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ 7.39–7.17 (m, 5H), 2.62 (q, J = 6.6 Hz, 1H), 2.43 (dd, J = 3.0, 1.2 Hz, 1H), 2.25 (dd, J = 6.5, 3.0 Hz, 1H), 1.99 (s, 3H), 1.86 (dd, J = 6.5, 1.3 Hz, 1H), 1.45 (d, J = 6.6 Hz, 3H); ^{13}C NMR (50 MHz; CDCl3) δ 4.24, 23.63, 36.15, 45.31, 69.48, 78.54, 92.16, 126.36, 127.08, 128.63, 143.66, 185.65; HRMS (ESI) calculated for $[C_{14}H_{15}NO+Na]^+$: 236.1052, Found 236.1051.

(*S*)-1-{(*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl}but-2-yn-1-ol (5a). To a stirred solution of **4** (1.53 g, 7.18 mmol) in anhydrous THF (20.0 mL) at −78 °C, under an inert atmosphere of N_2, was added L-Selectride (1 M in THF, 10.8 mL, 10.8 mmol). The reaction mixture was then stirred for 30 min at −78 °C. After the solution was warmed to room temperature, 10.0 mL of aqueous 10% aqueous NaOH solution was added. The reaction mixture was extracted with ethyl acetate (3 × 25 mL) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 70 : 30, v/v) to give **5a** (1.54 g, 99% yield) as brown solid: mp = 95 °C; $[\alpha]_D^{20}$ = +121.73 (c = 0.588, $CHCl_3$); ^1H NMR (200 MHz; $CDCl_3$) δ 7.41–7.23 (m, 5H), 4.04–3.91 (m, 1H), 2.57 (q, J = 6.6 Hz, 1H), 2.43 (d, J = 6.5 Hz, 1H), 1.96 (d, J = 3.4 Hz, 1H),

1.81 (ddd, J = 7.8, 6.4, 4.2 Hz, 1H), 1.63 (d, J = 2.1 Hz, 3H), 1.49 (d, J = 6.4 Hz, 1H), 1.44 (d, J = 6.6 Hz, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 3.57, 22.79, 31.00, 42.97, 61.93, 69.34, 78.40, 81.07, 127.15, 127.37, 128.48, 144.11; HRMS (ESI) calculated for $[C_{14}H_{17}NO+H]^+$: 216.1388, Found 216.1387.

(*R*)-1-{((*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl)}but-2-yn-1-ol (5b). To the solution of **4** (1.00 g, 4.60 mmol) in MeOH (30.0 mL) at −78 °C was added $ZnCl_2$ (0.348 g, 6.97 mmol). The solution was stirred for 30 min, and $NaBH_4$ (0.940 g, 6.90 mmol) was added at −78 °C. The mixture was stirred for an additional 1 h at −78 °C before being quenched with water (30.0 mL). The reaction mixture was extracted with methylene chloride (3 × 30 mL) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 70 : 30, v/v) to give **5b** (0.95 g, 95% yield) as brown solid: mp = 89 °C; $[\alpha]_D^{20}$ = +60.34 (*c* 0.434, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.36–7.19 (m, 5H), 4.28–4.19 (m, 1H), 2.61 (q, J = 6.6 Hz, 1H), 2.60 (d, J = 6.5 Hz, 1H), 2.09 (d, J = 3.4 Hz, 1H), 1.82 (ddd, J = 7.2, 6.4, 3.7 Hz, 1H), 1.75 (d, J = 2.2 Hz, 3H), 1.50 (d, J = 6.4 Hz, 1H), 1.43 (d, J = 6.6 Hz, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 3.58, 22.87, 30.59, 42.30, 60.57, 69.20, 77.93, 81.25, 126.76, 127.16, 128.37, 143.97; HRMS (ESI) calculated for $[C_{14}H_{17}NO+H]^+$: 216.1388, Found 216.1384.

(*S*,*E*)-1-{(*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl}but-2-en-1-ol (6a). To a stirred solution of **5a** (1.54 g, 7.17 mmol) in anhydrous THF (21.3 mL) at 0 °C, under an inert atmosphere of N_2, was added $LiAlH_4$. After stirring for 30 min at 0 °C, the solution was warmed to room temperature. Then the reaction mixture was refluxed for 8 h, then quenched with saturated aqueous $KHSO_4$ solution. The reaction mixture was extracted with ethyl acetate (3 × 25 mL) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 70 : 30, v/v) to give **6a** (1.45 g, 94% yield) as white solid : mp = 46 °C; $[\alpha]_D^{20}$ = + 94.77 (*c* 0.673, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.41–7.23 (m, 5H), 5.54 (dq, J = 15.4, 6.5 Hz, 1H), 5.08 (ddq, J = 15.3, 8.4, 1.6 Hz, 1H), 3.75–3.57 (m, 1H), 2.51 (q, J = 6.6 Hz, 1H), 1.95 (d, J = 5.6 Hz, 1H), 1.91 (d, J = 3.4 Hz, 1H), 1.58 (dd, J = 6.5, 4.4 Hz, 1H), 1.52 (d, J = 6.5 Hz, 3H), 1.49 (d, J = 6.5 Hz, 1H), 1.45 (d, J = 6.6 Hz, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 17.62, 22.54, 31.23, 42.77, 69.46, 71.75, 126.72, 126.97, 127.35, 128.47, 131.44, 144.31; HRMS (ESI) calculated for $[C_{14}H_{19}NO+Na]^+$: 240.1365, Found 240.1361.

(*R*,*E*)-1-{(*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl}but-2-en-1-ol (6b). The same procedure as for **6a** yielded **6b** from **5b** in 93% yield. mp = 58 °C; $[\alpha]_D^{20}$ = + 29.47 (*c* 0.424, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.36–7.23 (m, 5H), 5.63 (dq, J = 15.4, 6.5 Hz, 1H), 5.24 (ddq, J = 15.0, 7.3, 1.6 Hz, 1H), 3.95 (dd, J = 7.3, 3.8 Hz, 1H), 2.61 (q, J = 6.4 Hz, 1H), 2.60 (d, J = 6.4 Hz, 1H), 1.98 (d, J = 3.6 Hz, 1H), 1.61 (d, J = 6.5 Hz, 3H), 1.60 (d, J = 6.4 Hz, 1H), 1.42 (d, J = 6.6 Hz, 3H), 1.40 (d, J = 6.4 Hz, 1H); ^{13}C NMR (50 MHz; $CDCl_3$) δ 17.67, 23.05, 29.97, 41.96, 69.16, 70.07, 126.64, 127.03, 127.91, 128.28, 130.84, 144.19; HRMS (ESI) calculated for $C_{14}H_{19}NO$ $[M+Na]^+$: 240.1364, Found 240.1360.

(*S*)-2-[(*S*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]-1-[(*R*)-1-phenylethyl)aziridine] (7a). To a solution of *t*-butyldimethylsilyl chloride (2.01 g, 13.34 mmol) in anhydrous CH_2Cl_2 (25.0 mL), under an inert atmosphere of N_2, was added DMAP (0.82 g, 6.66 mmol) and TEA (3.70 mL, 26.67 mmol). The mixture was stirred for 5 min and then treated with **6a** (1.45 g, 6.67 mmol) in 12.5 mL of CH_2Cl_2. The mixture was stirred for 17 h at room temperature and was treated with 12.5 mL of saturated aqueous $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were washed with 10 mL of brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 95 : 5, v/v) to give **7a** (2.21 g, 99% yield) as colorless oil: $[\alpha]_D^{20}$ = +13.74 (*c* 0.742, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.40–7.17 (m, 5H), 5.50 (dq, J = 15.4, 6.5 Hz, 1H), 5.30 (ddq, J = 15.2, 7.6, 1.6 Hz, 1H), 3.71 (t, J = 6.2 Hz, 1H), 2.42 (q, J = 6.6 Hz, 1H), 1.71 (d, J = 3.5 Hz, 1H), 1.61 (d, J = 6.2 Hz, 3H), 1.60 (d, J = 6.6 Hz, 1H), 1.41 (d, J = 6.6 Hz, 3H), 1.33 (d, J = 6.6 Hz, 1H), 0.73 (s, 9H), –0.10 (s, 3H), –0.16 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.78, –4.50, 17.57, 18.11, 22.66, 25.84, 30.63, 44.63, 70.09, 75.23, 125.65, 126.93, 127.24, 128.16, 131.69, 144.15; HRMS (ESI) calculated for $[C_{20}H_{33}NOSi+Na]^+$: 354.2229, Found 354.2223.

(*S*)-2-[(*R*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]-1-[(*R*)-1-phenylethyl)aziridine] (7b). The same procedure as for **7a** yielded **7b** from **6b** in quantitative yield. $[\alpha]_D^{20}$ = +46.90 (*c* 0.714, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.32–7.21 (m, 5H), 5.40 (dq, J = 15.2, 6.5 Hz, 1H), 4.90 (ddq, J = 15.3, 7.8, 1.6 Hz, 1H), 3.46 (t, J = 6.4 Hz, 1H), 2.39 (q, J = 6.6 Hz, 1H), 1.83 (d, J = 3.0 Hz, 1H), 1.53 (dd, J = 6.3, 3.3 Hz, 1H), 1.49 (d, J = 2.6 Hz, 1H), 1.42 (d, J = 6.5 Hz, 3H), 1.38 (d, J = 6.6 Hz, 3H), 0.84 (s, 9H), –0.01 (s, 3H), –0.04 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.57, –4.51, 17.43, 18.12, 22.34, 25.83, 33.43, 44.04, 70.07, 75.68, 124.98, 126.99, 127.37, 127.97, 132.44, 143.84; HRMS (ESI) calculated for $[C_{20}H_{33}NOSi+Na]^+$: 354.2229, Found 354.2232.

(2*S*,3*S*,*E*)-3-(*t*-butyldimethylsilyloxy)-2-[(*R*)-1-phenylethylamino]hex-4-enyl acetate (8a). To a solution of **7a** (1.25 g, 3.77 mmol) in anhydrous CH_2Cl_2 (15.0 mL) under an inert atmosphere of N_2 was added AcOH (1.50 mL, 26.39 mmol). The mixture was stirred for 15 h and then quenched with 20 mL saturated aqueous $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with 10 mL of brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 90 : 10, v/v) to give **8a** (1.48 g, 99% yield) as colorless oil: $[\alpha]_D^{20}$ = +54.14 (*c* 0.731, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.35–7.16 (m, 5H), 5.68–5.52 (m, 1H), 5.52–5.28 (m, 1H), 4.14 (dd, J = 11.2, 5.2 Hz, 1H), 4.06 (dd, J = 11.1, 5.0 Hz, 1H), 4.03 (d, J = 5.1 Hz, 1H), 3.90 (dd, J = 11.2, 6.2 Hz, 1H), 2.56 (q, J = 5.2 Hz, 1H), 2.05 (s, 3H), 1.78 (bs, 1H), 1.65 (d, J = 5.6 Hz, 3H), 1.32 (d, J = 6.6 Hz, 3H), 0.87 (s, 9H), –0.02 (s, 3H), –0.04 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –5.31, –4.43, 17.35, 17.82, 20.56, 24.98, 25.61, 55.62, 58.39, 63.32, 73.75, 126.47, 126.54, 126.58, 127.98, 131.40, 145.39, 170.23; HRMS (ESI) calculated for $[C_{22}H_{37}NO_3Si+H]^+$: 392.2621, Found 392.2628.

(2*S*,3*R*,*E*)-3-(*t*-butyldimethylsilyloxy)-2-[(*R*)-1-phenylethylamino]hex-4-enyl acetate (8b). The same procedure as for **8a** yielded **8b** from **7b** in quantitative yield. $[\alpha]_D^{20} = +30.22$ (*c* 0.695, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.36–7.20 (m, 5H), 5.61 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.32 (ddq, *J* = 15.0, 7.4, 1.6 Hz, 1H), 4.19 (dd, *J* = 11.3, 4.6 Hz, 1H), 4.06 (dd, *J* = 8.0, 4.2 Hz, 1H), 4.02 (d, *J* = 4.0 Hz, 1H), 3.89 (q, *J* = 6.6 Hz, 1H), 2.53 (dd, *J* = 10.4, 4.2 Hz, 1H), 2.06 (s, 3H), 1.71 (dd, *J* = 6.3, 1.4 Hz, 3H), 1.64 (bs, 1H), 1.31 (d, *J* = 6.6 Hz, 3H), 0.83 (s, 9H), 0.02 (s, 3H), –0.04 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.96, –4.15, 17.67, 18.10, 20.99, 24.92, 25.83, 55.42, 58.32, 63.15, 74.29, 126.68, 126.83, 128.15, 128.32, 131.73, 145.43, 170.90; HRMS (ESI) calculated for $[C_{22}H_{37}NO_3Si+H]^+$: 392.2621, Found 392.2621.

(2*S*,3*S*,*E*)-3-(*t*-butyldimethylsilyloxy)-2-[(*R*)-1-phenylethylamino]hex-4-en-1-ol (9a). To a solution of **8a** (5.78 g, 14.76 mmol) in 45.0 mL of EtOH at room temperature was added KOH (4.14 g, 73.81 mmol). The mixture was stirred for 30 min at room temperature and then quenched with 40.0 mL of water. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with 30 mL of brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 80 : 20, v/v) to give **9a** as colorless oil (5.14 g, 99% yield): $[\alpha]_D^{20} = +19.84$ (*c* = 0.695, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.28–7.13 (m, 5H), 5.61 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.30 (ddq, *J* = 15.2, 7.6, 1.6 Hz, 1H), 4.01 (t, *J* = 7.5 Hz, 1H), 3.85 (q, *J* = 6.6 Hz, 1H), 3.57 (dd, *J* = 10.7, 4.6 Hz, 1H), 3.36 (dd, *J* = 10.7, 2.8 Hz, 1H), 2.34 (ddd, *J* = 7.3, 4.5, 2.8 Hz, 1H), 1.65 (dd, *J* = 6.4, 1.5 Hz, 3H), 1.34 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 9H), 0.02 (s, 3H), –0.019 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –5.20, –4.30, 17.35, 17.79, 24.74, 25.63, 55.13, 58.97, 60.15, 74.10, 126.23, 126.58, 127.68, 128.09, 131.46, 145.10; HRMS (ESI) calculated for $[C_{20}H_{35}NO_2Si+H]^+$: 350.2515, Found 350.2511.

(2*S*,3*R*,*E*)-3-(*t*-butyldimethylsilyloxy)-2-[(*R*)-1-phenylethylamino]hex-4-en-1-ol (9b). The same procedure as for **9a** yielded **9b** from **8b** in quantitative yield. $[\alpha]_D^{20} = -15.8$ (*c* = 0.818, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.38 – 7.20 (m, 5H), 5.59 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.29 (ddq, *J* = 15.2, 7.6, 1.6 Hz, 1H), 4.08 (t, *J* = 6.4 Hz, 1H), 3.88 (q, *J* = 6.6 Hz, 1H), 3.62 (s, 1H), 3.60 (s, 1H), 2.38 (dd, *J* = 9.2, 4.2 Hz, 1H), 1.68 (dd, *J* = 6.3, 0.8 Hz, 3H), 1.33 (d, *J* = 6.6 Hz, 3H), 0.84 (s, 9H), 0.03 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –5.12, –4.29, 17.45, 17.88, 24.43, 25.67, 54.92, 59.22, 59.72, 75.20, 126.40, 126.77, 127.47, 128.20, 131.97, 145.44; HRMS (ESI) calculated for $[C_{20}H_{35}NO_2Si+H]^+$: 350.2515, Found 350.2518.

(*S*)-4-[(*S*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]-3-[(*R*)-1-phenylethyl]oxazolidin-2-one (10a). To a solution of **9a** (1.29 g, 3.68 mmol) in anhydrous CH_2Cl_2 (11.30 mL) at 0 °C, under an inert atmosphere of N_2 was added CDI (0.89 g, 5.51 mmol) and DBU (1.92 mL, 12.87 mmol). The reaction mixture was then stirred for 1 h at 0 °C and warmed to room temperature and stirred for an additional 24 h before being quenched with water. The reaction mixture was extracted with CH_2Cl_2 (3 × 25 mL) and combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 90 : 10, v/v) to give **10a** (1.37 g, 99% yield) as colorless oil: $[\alpha]_D^{20} = -36.30$ (*c* = 0.482, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.42–7.33 (m, 5H), 5.73 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.46 (ddq, *J* = 15.2, 7.6, 1.6 Hz, 1H), 5.18 (q, *J* = 7.2 Hz, 1H), 4.26 (dd, *J* = 9.0, 3.6 Hz, 1H), 4.16–4.26 (m, 1H), 4.0 (t, *J* = 8.8 Hz, 1H), 3.36 (ddd, *J* = 12.8, 8.7, 3.7 Hz, 1H), 1.73 (ddd, *J* = 6.4, 2.7, 1.3 Hz, 3H), 1.66 (d, *J* = 7.2 Hz, 3H), 0.78 (s, 9H), 0.07 (s, 3H), –0.018 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –5.42, –4.99, 17.70, 17.74, 18.72, 25.42, 52.77, 57.86, 62.96, 71.37, 126.07, 127.06, 127.84, 128.57, 129.82, 139.10, 158.32; HRMS (ESI) calculated for $[C_{21}H_{33}NO_3Si+Na]^+$: 398.2127, Found 398.2121.

(*S*)-4-[(*R*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]-3-[(*R*)-1-phenylethyl]oxazolidin-2-one (10b). The same procedure as for **10a** yielded **10b** from **9b** in quantitative yield. mp = 67 °C; $[\alpha]_D^{20} = -12.17$ (*c* = 0.419, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 7.39–7.24 (m, 5H), 5.54 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.19 (ddq, *J* = 15.0, 7.4, 1.6 Hz, 1H), 5.21–5.12 (m, 1H), 4.27 (dd, *J* = 8.3, 4.1 Hz, 1H), 4.17 (d, *J* = 6.8 Hz, 1H), 4.00 (t, *J* = 9.0 Hz, 1H), 3.42–3.23 (m, 1H), 1.68 (dd, *J* = 6.8 Hz, 3H), 1.59 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.91, –3.50, 17.64, 17.98, 18.60, 25.74, 53.14, 59.63, 62.90, 74.11, 127.30, 127.76, 128.60, 129.41, 129.61, 139.65, 158.91; HRMS (ESI) calculated for $[C_{21}H_{33}NO_3Si+Na]^+$: 398.2128, Found 398.2127.

(*S*)-4-[(*S*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]oxazolidin-2-one (11a). To a stirred solution of **10a** (3.0 g, 7.98 mmol) in anhydrous THF (25.0 mL) at –78 °C, was added freshly cut sodium metal (0.754 g, 27.95 mmol), and 25.0 mL of liquid ammonia. Blue color started appearing slowly and in 5 min the reaction mixture became blue in color. The reaction mixture was stirred at –78 °C for 30 min. As soon as all the starting material was consumed the mixture was quenched with 15 mL of water. The reaction mixture was extracted with ethyl acetate (3 × 100 mL) and combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 70 : 30, v/v) to give **11a** (2.03 g, 94% yield) as white solid: mp = 55 °C; $[\alpha]_D^{20} = +24.20$ (*c* = 0.537, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 5.75 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.30 (ddq, *J* = 15.2, 7.6, 1.6 Hz, 1H), 5.35–5.26 (bs, 1H), 4.33 (t, *J* = 8.8 Hz, 1H), 4.10 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.96 (t, *J* = 7.2 Hz, 1H), 3.71 (ddd, *J* = 13.5, 7.7, 5.1 Hz, 1H), 1.72 (dd, *J* = 6.5, 1.6 Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.85, –4.06, 17.81, 18.04, 25.78, 57.08, 66.41, 75.51, 128.86, 130.28, 159.90; HRMS (ESI) calculated for $[C_{13}H_{25}NO_3Si+Na]^+$: 294.1501, Found 294.1511.

(*S*)-4-[(*R*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]oxazolidin-2-one (11b). The same procedure as for **11a** yielded **11b** from **10b** in 92% yield. mp = 144 °C; $[\alpha]_D^{20} = -57.42$ (*c* = 0.368, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 5.74 (dq, *J* = 15.4, 6.5 Hz, 1H), 5.51 (bs, 1H), 5.32 (ddq, *J* = 15.0, 7.4, 1.6 Hz, 1H), 4.39 (t, *J* = 8.6 Hz, 1H), 4.28 (dd, *J* = 8.8, 4.8 Hz, 1H), 3.97 (t, *J* = 6.9 Hz, 1H), 3.72 (dt, *J* = 10.7, 5.6 Hz, 1H), 1.73 (dd, *J* = 6.4, 1.5 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –5.06, –4.33, 17.54, 17.82, 25.60, 56.86, 66.14, 74.50, 129.27, 129.48, 160.31; HRMS (ESI) calculated for $[C_{13}H_{25}NO_3Si+Na]^+$: 294.1501, Found 294.1508.

(*S*)-3-allyl-4-[(*S*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]oxazolidin-2-one (12a). To a solution of **11a** (2.03 g, 7.49 mmol) in anhydrous ethylene dichloride (24.0 mL) at 0 °C, under an inert atmosphere of N_2, was added NaH (1.08 g, 44.94 mmol). The reaction mixture was then stirred for 1 h at 0 °C. Allyl iodide (2.39 mL, 26.22 mmol) was added to the mixture at 0 °C and warmed to room temperature. The reaction mixture was heated to reflux for 10 h and cooled to the room temperature, quenched with aqueous NH_4Cl solution (10 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 100 mL) and combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 90 : 10, v/v) to give **12a** (2.30 g, 99% yield) as colorless oil: $[\alpha]_D^{20}$ = −104.54 (*c* = 0.621, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 5.89–5.64 (m, 2H), 5.45–5.18 (m, 3H), 4.32–4.12 (m, 4H), 3.77 (td, *J* = 11.0, 5.8 Hz, 1H), 3.60 (dd, *J* = 15.4, 7.8 Hz, 1H), 1.69 (d, *J* = 6.5 Hz, 3H), 0.85 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (50 MHz; $CDCl_3$) δ −4.90, −4.30, 17.94, 18.11, 25.79, 45.75, 58.10, 63.55, 72.11, 118.82, 127.50, 130.31, 132.37, 158.35; HRMS (ESI) calculated for $[C_{16}H_{29}NO_3Si+Na]^+$: 334.1814, Found 334.1810.

(*S*)-3-allyl-4-[(*R*,*E*)-1-(*t*-butyldimethylsilyloxy)but-2-enyl]oxazolidin-2-one (12b). The same procedure as for **12a** yielded **12b** from **11b** in quantitative yield. $[\alpha]_D^{20}$ = + 5.16 (*c* = 0.542, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 5.89–5.65 (m, 2H), 5.39–5.16 (m, 3H), 4.33–4.14 (m, 4H), 3.72 (dq, *J* = 8.8, 2.4 Hz, 1H), 3.58 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.71 (dd, *J* = 6.5, 0.8 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C-NMR (50 MHz; $CDCl_3$) δ −4.86, −3.86, 17.87, 18.03, 25.76, 45.01, 58.94, 62.97, 71.59, 118.42, 129.23, 129.64, 132.30, 158.53; HRMS (ESI) calculated for $[C_{16}H_{29}NO_3Si$ +Na]$^+$: 334.1814, Found 334.1811.

(8*S*,8a*S*)-8-(*t*-butyldimethylsilyloxy)-8,8a-dihydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (13a). Grubbs' catalyst benzylidene-bis(tricyclohexylphosphine)dichlororuthenium (10 mol%, 0.610 g, 0.74 mmol) was added to a solution of **12a** (2.31 g, 7.43 mol) in CH_2Cl_2 (304 mL) and the mixture was stirred for 24 h at room temperature. After evaporation, the residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 80 : 20, v/v) to give **13a** (1.98 g, 99% yield) as brown solid: mp = 49 °C; $[\alpha]_D^{20}$ = +224.49 (*c* = 0.514, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 6.08–5.86 (m, 2H), 4.44 (dd, *J* = 8.3, 4.7 Hz, 1H), 4.35 (t, *J* = 8.3 Hz, 1H), 4.22 (td, *J* = 18.9, 2.3 Hz, 1H), 4.06 (dd, *J* = 5.6, 2.5 Hz, 1H), 3.81 (ddq, *J* = 7.7, 4.6, 2.5 Hz, 1H), 3.70 (td, *J* = 19.0, 1.9 Hz, 1H), 0.88 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ −5.24, −4.08, 17.52, 25.23, 40.49, 54.87, 62.77, 63.94, 125.95, 127.16, 157.54; HRMS (ESI) calculated for $[C_{13}H_{23}NO_3Si+Na]^+$: 292.1345, Found 292.1341.

(8*R*,8a*S*)-8-(*t*-butyldimethylsilyloxy)-8,8a-dihydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (13b). The same procedure as for **13a** yielded **13b** from **12b** in quantitative yield. mp = 93 °C; $[\alpha]_D^{20}$ = −25.58 (*c* = 0.514, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 5.72 (s, 2H), 4.51 (dd, *J* = 8.9, 8.0 Hz, 1H), 4.22 (dd, *J* = 9.0, 4.3 Hz, 1H), 4.17 (dd, *J* = 3.4, 2.5 Hz, 1H), 4.15–4.03 (m, 1H), 3.65 (dd, *J* = 18.3, 2.8 Hz, 1H), 3.51 (ddd, *J* = 7.8, 7.8, 4.3 Hz, 1H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ −4.85, −4.37, 17.67, 25.46, 40.64, 56.18, 67.01, 68.16, 123.67, 130.27, 156.97; HRMS (ESI) calculated for $[C_{13}H_{23}NO_3Si+Na]^+$: 292.1345, Found 292.1349.

(1a*R*,6a*S*,7*R*,7a*S*)-7-(*t*-butyldimethylsilyloxy)tetrahydro-1a*H*-oxazolo[3,4-*a*]oxireno[2,3-*d*]pyridin-4(2*H*)-one (14a). To a suspension of the **13a** (1.0 g, 3.71 mmol) and sodium hydrogen carbonate (4.67 g, 55.67 mmol) in acetone (100 mL) and water (50 mL) was added oxone (11.41 g, 18.55 mmol) over 10 min and the suspension was stirred for 30 min at room temperature when TLC indicated complete consumption of the starting material. The organic phase was extracted into ethyl acetate (3 × 50 mL) and combined organic extracts were washed with 10% aqueous sodium bissulfite (50 mL) and water 25 mL, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 40 : 60, v/v) to give **14a** (0.75 g, 71% yield) as white solid : mp = 165 °C; $[\alpha]_D^{20}$ = +34.44 (*c* = 0.409, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 4.36 (t, *J* = 9.3 Hz, 1H), 4.20 (t, *J* = 3.0 Hz, 1H), 4.18–4.09 (m, 1H), 4.01–3.84 (m, 3H), 3.70 (dd, *J* = 12.4, 5.9 Hz, 1H), 3.10 (t, *J* = 11.6 Hz, 1H), 0.91 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (50 MHz; CD_3OD) δ −5.17, −4.20, 18.63, 26.07, 42.14, 54.35, 64.19, 64.76, 71.96, 72.48, 160.20; HRMS (ESI) calculated for $[C_{13}H_{23}NO_4Si+H]^+$: 286.1475, Found 286.1472.

(3a*S*,8a*S*,9*R*,9a*R*)-9-(*t*-butyldimethylsilyloxy)-2,2-dimethyltetrahydro-3a*H*-[1,3]dioxolo[4,5-*d*]oxazolo[3,4-*a*]pyridin-6(4*H*)-one (15a). Suspension of **14a** (0.75 g, 2.63 mmol) in CH_2Cl_2 (28.0 mL) and acetone (12.0 mL) at 0 °C, was added $BF_3{\cdot}Et_2O$ (1.67 mL, 13.18 mmol). The reaction mixture was stirred for 2 h at 0 °C, when TLC indicated complete consumption of the starting material. The reaction mixture was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 80 : 20, v/v) to give **15a** (0.859 g, 94% yield) as white solid : mp = 88 °C; $[\alpha]_D^{20}$ = +42.8 (*c* = 0.676, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 4.47 (td, *J* = 6.9, 2.5 Hz, 1H), 4.32 (t, *J* = 10.0 Hz, 1H), 4.07–3.90 (m, 3H), 3.61 (d, *J* = 14.0 Hz, 1H), 3.60 (d, *J* = 13.4 Hz, 1H), 3.39 (dd, *J* = 13.4, 3.4 Hz, 1H), 1.39 (s, 3H), 1.25 (s, 3H), 0.78 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ −5.24, −4.42, 17.59, 23.84, 25.41, 26.62, 41.90, 51.02, 64.68, 69.69, 70.14, 74.35, 108.75, 159.78; HRMS (ESI) calculated for $[C_{16}H_{29}NO_5Si+H]^+$: 344.1893, Found 344.1898.

(8*S*,8a*S*)-8-hydroxy-8,8a-dihydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (16b). To a solution of **13a** (0.45 g, 1.78 mmol) in anhydrous THF (6.9 mL) at 0 °C, under an inert atmosphere of N_2, was added TBAF (3.56 mL, 3.56 mmol, 1 M in THF). The reaction mixture was then stirred for 1 h at 0 °C then warmed to room temperature and quenched with saturated aqueous NH_4Cl solution (5.0 mL). The reaction mixture was extracted with ethyl acetate (3 × 20 mL) and combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CHCl_3$–MeOH = 90 : 10, v/v) to give **16b** (0.24 g, 99%) as white solid: mp = 105 °C; $[\alpha]_D^{20}$ = +296.14 (*c* = 0.315, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 6.09–5.86 (m, 2H), 4.53 (dd, *J* = 8.4, 3.0 Hz, 1H), 4.50 (dd, *J* = 16.6, 8.5 Hz, 1H), 4.21–3.99 (m, 1H), 4.07 (t, *J* = 2.7 Hz, 1H), 3.94 (ddd, *J* = 8.5, 5.7, 2.7 Hz,

1H), 3.73 (td, J = 19.0, 1.9 Hz, 1H); ^{13}C NMR (50 MHz; CD_3OD) δ 41.80, 56.44, 62.71, 65.63, 127.21, 128.22, 159.82; HRMS (ESI) calculated for $[C_7H_9NO_3+H]^+$: 156.0661, Found 156.0656.

(1a*S*,6a*S*,7*R*,7a*R*) - 7 - hydroxytetrahydro - 1a*H* - oxazolo[3,4-*a*]oxireno[2,3-*d*]pyridin-4(2*H*)-one (17b). MCPBA (2.7 g, 12.07 mmol) was added to a suspension of **14b** (0.39 g, 2.51 mmol) and NaH_2PO_4 (2.08 g, 17.34 mmol) in CH_2Cl_2 (32.0 mL) at 0 °C. After stirring at room temperature for 3 days, the insoluble materials were filtered off and filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (EtOAc–MeOH = 80 : 20, v/v) to give **17b** (0.28 g, 67%) as white solid : mp = 97 °C; $[\alpha]_D^{20}$ = +52.86 (c = 0.087, MeOH); ^{1}H NMR (400 MHz; CD_3OD) δ 4.52 (dd, J = 8.6, 5.4 Hz, 1H), 4.31 (t, J = 8.8 Hz, 1H), 4.01 (d, J = 14.7 Hz, 1H), 3.97 (t, J = 4.7 Hz, 1H), 3.80 (dq, J = 9.3, 4.3 Hz, 1H), 3.46 (dd, J = 5.2, 3.8 Hz, 1H), 3.41 (td, J = 3.8, 1.2 Hz, 1H), 3.37 (dd, J = 14.7, 1.34 Hz, 1H); ^{13}C NMR (100 MHz; CD_3OD) δ 40.43, 52.52, 53.05, 56.10, 62.13, 64.14, 160.00; HRMS (ESI) calculated for $[C_7H_9NO_4+H]^+$: 172.0614, Found 172.0610.

(6*R*,7*R*,8*R*,8a*S*)-8-(*t*-butyldimethylsilyloxy)-6,7-dihydroxy-tetrahydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (18c). To a solution of **13a** (0.50 g, 1.86 mmol) in CH_3CN–H_2O = 9 : 1 ratio (9.0 mL of CH_3CN, 1.0 mL of H_2O) (45.0 mL) at 0 °C, was added NMO (0.43 g, 3.71 mmol) and OsO_4 (4% in water, 0.63 mL, 2.47 mmol). The reaction mixture was then stirred for 10 min at 0 °C and warmed to room temperature and stirred for an additional 3 h before being quenched with saturated aqueous Na_2SO_3. The reaction mixture was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (*n*-hexane–EtOAc = 30 : 60, v/v) to give **18c** (0.56 g, 99% yield) as white solid : mp = 178 °C; $[\alpha]_D^{20}$ = +44.23 (c = 0.391, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 4.34 (t, J = 9.2 Hz, 1H), 4.25–4.09 (m, 1H), 4.17 (dd, J = 8.8, 3.1 Hz, 1H), 3.95 (dd, J = 5.8, 2.6 Hz, 1H), 3.89 (dd, J = 4.1, 1.4 Hz, 1H), 3.86 (dd, J = 4.1, 1.6 Hz, 1H), 3.67 (dd, J = 12.5, 5.7 Hz, 1H), 3.09 (t, J = 11.7 Hz, 1H), 0.91 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (50 MHz; CD_3OD) δ –5.14, –4.18, 18.57, 26.08, 42.08, 54.22, 64.10, 64.67, 71.84, 72.35, 160.03; HRMS (ESI) calculated for $[C_{13}H_{25}NO_5Si+H]^+$: 304.1580, Found 304.1582.

(1a*S*,6a*S*,7*S*,7a*S*)-7-(*t*-butyldimethylsilyloxy)tetrahydro-1a*H*-oxazolo[3,4-*a*]oxireno[2,3-*d*]pyridin-4(2*H*)-one (14d). The same procedure as for **14a** yielded **14d** from **13b** in 68% yield. mp = 112 °C; $[\alpha]_D^{20}$ = +14.24 (c = 0.612, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 4.44 (t, J = 8.4 Hz, 1H), 4.14 (dd, J = 8.7, 5.0 Hz, 1H), 3.89 (dd, J = 4.6, 2.3 Hz, 1H), 3.74 (dd, J = 14.1, 2.5 Hz, 1H), 3.73 (t, J = 8.8 Hz, 1H), 3.55 (ddd, J = 13.2, 8.2, 5.0 Hz, 1H), 3.34 (dd, J = 9.0, 2.9 Hz, 1H), 3.07 (dd, J = 14.0, 1.7 Hz, 1H), 0.85 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (50 MHz; CD_3OD) δ –4.80, –3.46, 19.06, 26.42, 46.55, 59.96, 67.78, 70.31, 73.47, 75.29, 159.92; HRMS (ESI) calculated for $[C_{13}H_{23}NO_4Si+H]^+$: 286.1475, Found 286.1471.

(3a*R*,8a*S*,9*S*,9a*S*)-9-(*t*-butyldimethylsilyloxy)-2,2-dimethyltetrahydro-3a*H*-[1,3]dioxolo[4,5-*d*]oxazolo[3,4-*a*]pyridin-6(4*H*)-one (15d). The same procedure as for **15a** yielded **15d** from **14d** in 97% yield. mp = 72 °C; $[\alpha]_D^{20}$ = +20.08 (c = 0.457, $CHCl_3$); ^{1}H NMR (200 MHz; $CDCl_3$) δ 4.43 (t, J = 8.4 Hz, 1H), 4.37–4.23 (m, 2H), 4.13 (dd, J = 9.0, 4.2 Hz, 1H), 3.90 (t, J = 7.2 Hz, 1H), 3.83 (dd, J = 7.7, 4.5 Hz, 1H), 3.73 (dd, J = 9.7, 3.0 Hz, 1H), 2.96 (dd, J = 13.0, 7.6 Hz, 1H), 1.56 (s, 3H), 1.37 (s, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (50 MHz; $CDCl_3$) δ –4.43, –4.01, 18.21, 25.78, 25.94, 28.38, 42.12, 53.27, 66.96, 70.50, 71.36, 76.32, 110.43, 156.82; HRMS (ESI) calculated for $[C_{16}H_{29}NO_5Si+H]^+$: 344.1893, Found 344.1899.

(8*R*,8a*S*)-8-hydroxy-8,8a-dihydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (16e). The same procedure as for **16b** yielded **16e** from **13b** in quantitative yield. mp = 99 °C; $[\alpha]_D^{20}$ = +26.02 (c = 0.365, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 5.89 (s, 2H), 4.69 (t, J = 8.5 Hz, 1H), 4.45 (dd, J = 8.9, 4.6 Hz, 1H), 4.28–3.98 (m, 2H), 3.74 (dd, J = 18.1, 2.9 Hz, 1H), 3.64 (ddd, J = 11.7, 8.2, 4.6 Hz, 1H); ^{13}C NMR (50 MHz; CD_3OD) δ 41.67, 57.66, 68.24, 68.99, 124.79, 131.38, 159.35; HRMS (ESI) calculated for $[C_7H_9NO_3+H]^+$: 156.0661, Found 156.0668.

(1a*R*,6a*S*,7*S*,7a*R*)-7-hydroxytetrahydro-1a*H*-oxazolo[3,4-a]-oxireno[2,3-*d*]pyridin-4(2*H*)-one (17e). The same procedure as for **17b** yielded **17e** from **16e** in 77% yield. mp = 122 °C; $[\alpha]_D^{20}$ = –47.99 (c = 0.012, MeOH); ^{1}H NMR (400 MHz; CD_3OD) δ 4.43 (t, J = 8.5 Hz, 1H), 4.27 (dd, J = 8.9, 4.7 Hz, 1H), 3.88 (t, J = 4.6 Hz, 1H), 3.86 (dd, J = 15.0, 3.5 Hz, 1H), 3.70 (ddd, J = 13.4, 8.4, 4.7 Hz, 1H), 3.51 (t, J = 3.8 Hz, 1H), 3.46 (t, J = 13.5 Hz, 1H), 3.37 (t, J = 12.1 Hz, 1H); ^{13}C NMR (100 MHz; CD_3OD) δ 39.86, 53.69, 54.54, 57.01, 67.68, 70.31, 159.42; HRMS (ESI) calculated for $[C_7H_9NO_4+H]^+$: 172.0614, Found 172.0619.

(6*S*,7*S*,8*S*,8a*S*)-8-(*t*-butyldimethylsilyloxy)-6,7-dihydroxy-tetrahydro-1*H*-oxazolo[3,4-*a*]pyridin-3(5*H*)-one (18f). The same procedure as for **18c** yielded **18f** from **13b** in quantitative yield. mp = 118 °C; $[\alpha]_D^{20}$ = +29.25 (c = 0.411, MeOH); ^{1}H NMR (200 MHz; CD_3OD) δ 4.47 (t, J = 8.4 Hz, 1H), 4.18 (dd, J = 8.7, 5.0 Hz, 1H), 3.93 (dd, J = 4.2, 2.1 Hz, 1H), 3.77 (t, J = 9.0 Hz, 1H), 3.76 (dd, J = 11.6, 2.4 Hz, 1H), 3.59 (ddd, J = 13.2, 8.2, 5.0 Hz, 1H), 3.42 (dd, J = 9.0, 2.9 Hz, 1H), 3.11 (dd, J = 14.0, 1.7 Hz, 1H), 0.89 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (50 MHz; CD_3OD) δ –4.79, –3.45, 19.06, 26.44, 46.55, 59.95, 67.77, 70.29, 73.47, 75.27, 159.90; HRMS (ESI) calculated for $[C_{13}H_{25}NO_5Si+H]^+$: 304.1580, Found 304.1587.

L - 1 - deoxyidonojirimycin (L - Ido - DNJ, (2*S*,3*R*,4*R*,5*S*) - 2-(hydroxymethyl)piperidine-3,4,5-triol), (1a). To a solution of **15a** (0.20 g, 0.58 mmol) in 20 mL of aq. 30% EtOH at room temperature was added LiOH (0.70 g, 2.91 mmol). The reaction mixture was heated to reflux for 4 h and cooled to room temperature. The insoluble materials were filtered off and the filtrate was evaporated. The residue was dissolved in 20 mL of MeOH. Concentrated hydrochloric acid (2.0 mL) was added to the solution at room temperature. The reaction mixture was heated to reflux for 4 h and cooled to the room temperature and the solvent was evaporated. After evaporation of the reaction mixture, the residue was treated with basic ion-exchange resin (Amberlite IRA-410 OH^- form) using water as eluent to yield **1a** (0.90 g, 96% yield) as white solid: mp = 137 °C, $[\alpha]_D^{20}$ = +8.9 (c = 0.726, H_2O); ^{1}H NMR (400 MHz; D_2O) δ 4.34 (ddq, J = 11.3, 4.8, 3.0 Hz, 1H), 4.30 (d, J = 4.5 Hz, 1H), 4.17 (t, J = 3.8 Hz, 1H), 4.01 (dd, J = 12.3, 4.8 Hz, 1H), 3.91 (dd, J = 12.3, 8.8 Hz, 1H), 3.66 (dd, J = 7.2, 5.0 Hz, 1H), 3.44 (dd, J = 12.2, 4.9 Hz, 1H), 3.22 (t, J = 11.8 Hz, 1H); ^{13}C NMR (50 MHz; D_2O) δ 46.90, 57.45, 59.46, 65.01, 65.29, 71.51;

HRMS (ESI) calculated for $[C_6H_{13}NO_4+H]^+$: 164.0923, Found 164.0929.

L-1-deoxygulonojirimycin (L-Gulo-DNJ, (2*S*,3*R*,4*R*,5*R*)-2-(hydroxymethyl)piperidine-3,4,5-triol (1c). To a solution of **18c** (0.5 g, 1.65 mmol) in 20 mL of aq. 30% EtOH at room temperature was added LiOH (0.19 g, 8.24 mmol). The reaction mixture was heated to reflux for 4 h and cooled to the room temperature. The insoluble materials were filtered off and the filtrate was evaporated. After evaporation of the reaction mixture, the residue was treated with basic ion-exchange resin (Amberlite IRA-410 OH^- form) using water as eluent to yield **1c** (0.29 g, 95%) as pale yellow oil: $[\alpha]_D^{20}$ = +14.83 (*c* = 0.817, H_2O); ^1H NMR (400 MHz; D_2O) δ 4.25 (dq, *J* = 11.4, 4.8, 2.9 Hz, 1H), 4.12 (dd, *J* = 4.6, 1.4 Hz, 1H), 4.05 (t, *J* = 3.6 Hz, 1H), 3.89 (dd, *J* = 12.3, 4.8 Hz, 1H), 3.81 (dd, *J* = 12.1, 9.0 Hz, 1H), 3.53 (ddq, *J* = 8.5, 4.6, 1.4 Hz, 1H), 3.30 (dd, *J* = 12.1, 5.0 Hz, 1H), 3.12 (t, *J* = 11.8 Hz, 1H); ^{13}C NMR (50 MHz; D_2O) δ 47.0, 59.48, 63.58, 67.37, 72.01, 73.44; HRMS (ESI) calculated for $[C_6H_{13}NO_4+H]^+$: 164.0923, Found 164.0921.

L-1-deoxynojirimycin (L-DJN, (2*S*,3*S*,4*S*,5*R*)-2-(hydroxymethyl)piperidine-3,4,5-triol) (1d). The same procedure as for **1a** yielded **1d** from **15d** in 95% yield. mp = 194 °C, $[\alpha]_D^{20}$ = –40.15 (*c* = 0.522, H_2O); ^1H NMR (400 MHz, D_2O) δ 3.70 (s, 1H), 3.43 (d, *J* = 12.5 Hz, 1H), 3.34 (dd, *J* = 10.7, 5.7 Hz, 1H), 3.30 (t, *J* = 10.0 Hz, 1H), 3.18 (dd, *J* = 9.6, 2.4 Hz, 1H), 2.82 (d, *J* = 13.7 Hz, 1H), 2.63 (d, *J* = 13.7 Hz, 1H), 2.49 (ddd, *J* = 7.9, 5.6, 2.9 Hz 1H); ^{13}C NMR (50 MHz,D_2O) δ 52.40, 62.95, 64.96, 70.50, 70.79, 77.0; HRMS (ESI) calculated for $C_6H_{13}NO_4$ $[M+H]^+$: 164.0923, Found 164.0918.

L-1-deoxymannojirimycin (L-Man-DNJ, (2*S*,3*S*,4*S*,5*S*)-2-(hydroxymethyl)piperidine-3,4,5-triol) (1f). The same procedure as for **1c** yielded **1f** from **18f** in 96% yield. mp = 183 °C, $[\alpha]_D^{20}$ = +40.42 (*c* = 0.728, H_2O); ^1H NMR (400 MHz; D_2O) δ 4.23 (ddd, *J* = 4.3, 2.9, 1.4 Hz, 1H), 3.98 (dd, *J* = 12.6, 3.3 Hz, 1H), 3.85 (t, *J* = 10.0 Hz, 1H), 3.86 (dd, *J* = 12.6, 6.8 Hz, 1H), 3.68 (dd, *J* = 9.6, 3.1 Hz, 1H), 3.40 (dd, *J* = 13.6, 3.1 Hz, 1H), 3.23 (dd, *J* = 13.6, 1.4 Hz, 1H), 3.15 (dq, *J* = 10.3, 3.3 Hz, 1H); ^{13}C NMR (50 MHz; D_2O) δ 51.0, 61.99, 63.70, 69.53, 70.10, 76.26; HRMS (ESI) calculated for $[C_6H_{13}NO_4+H]^+$: 164.0923, Found 164.0928.

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