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A Divergent and Stereoselective Approach for the Syntheses of Some Polyhydroxylated Indolizidine and Pyrrolizidine Iminosugars

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A common, divergent, and efficient approach to the syntheses of (+)-steviamine (**9**), (–)-1-deoxy-8a-*epi*-castanospermine (**10**), (+)-trihydroxyindolizidine (**11**), (+)-3,7a-di-*epi*-hyacinthacine A1 (**12**), and (–)-2-*epi*-lentiginosine (**4**) was achieved by starting from D-ribose-derived intermediate **13**. The key steps involved in these syntheses are a highly diasteroselective Grignard addition to a ribosylimine, a one-pot stereoselective intramolecular reductive amination, a selectve deprotection of a silyl ether, and a ring-closing metathesis (RCM) reaction.

Introduction

Iminosugars (azasugars or iminocyclitols) are small molecules of both synthetic and natural origin that mimic carbohydrates in biological systems. Structurally, they are the nitrogen analogues of monosaccharides, in which the oxygen atom in the ring is replaced by a nitrogen atom. Iminosugars are important in their ability to inhibit glycoprocessing enzymes,[1] which play an important role in several metabolic processes.[2] The polyhydroxylated indolizidines and pyrrolizidines (see Figure 1) belong to a class of iminosugars that are known for their interesting therapeutic applications.[3]

The natural product (–)-steviamine (**1**) is the first example of this new class of indolizidine alkaloids that inhibits the α-galactosaminidase (GalNAcase) enzyme[4] and may be used for the treatment of Schindler/Kanzaki disease.[5] Interestingly, the synthetic compound (+)-steviamine (**9**) was found to inhibit the α-rhamnosidase enzyme.[4] Inhibitiors of this enzyme are potential therapeutic agents for the treatment of bacillary dysentery, cancer,[6a] tuberculosis, and leprosy.[6b]

(+)-Castanospermine (**2**) and its congeners play a pivotal role in inhibiting the progression of multiple sclerosis,[7] cancer,[8] and diabetes.[9] (+)-Hyacinthacine A1 (**5**),[10] (–)-swainsonine (**3**), and its isomers[11] are known for their glycosidase inhibitory activity. (–)-Swainsonine (**3**) has also been screened for the treatment of life-threatening diseases such as HIV, cancer, and immunological disorders.[12]

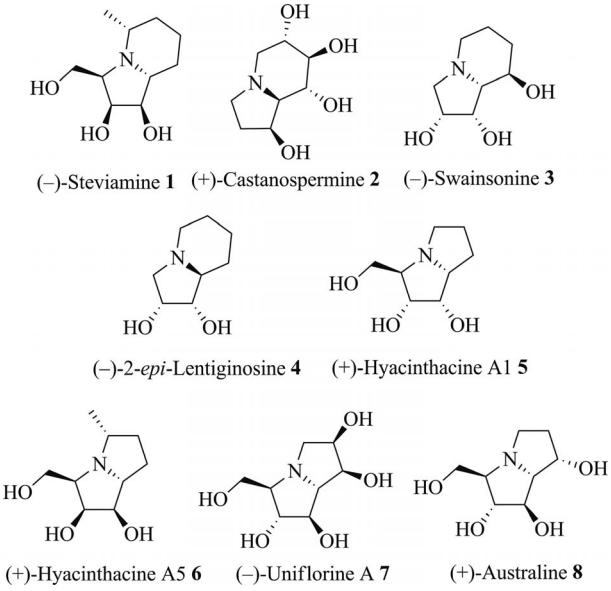

Figure 1. Some naturally occurring polyhydroxylated indolizidine and pyrrolizidine alkaloids.

(–)-2-*epi*-Lentiginosine (**4**) is a potent inhibitor of α-mannosidase and has an IC_{50} value of 4.6 μM.[13] The synthetic compound (–)-trihyroxyindolizidine (**11**) was found to be a selective inhibitor of rat intestinal sucrase.[14] Because of the interesting biological activities of these iminosugars, numerous synthetic approaches have been developed, thus far, that use different strategies.[15,16] Herein, we present a divergent and highly stereoselective approach for the syntheses of various polyhydroxylated indolizidine and pyrrolizidine iminosugars (see Figure 2). A divergent approach to synthesize small molecules is a challenging task for the synthetic chemists. This approach provides a number of diverse molecules in a few short steps, which is a great help for a drug discovery program.

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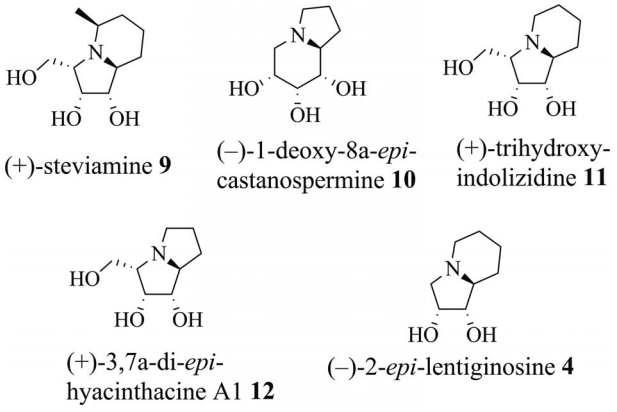
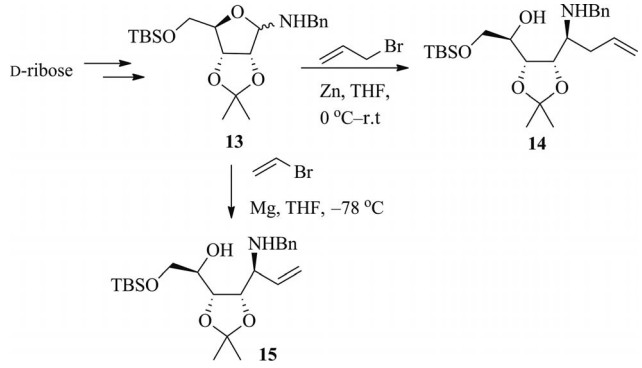


Figure 2. Iminosugars synthesized from **14**.

In the course of developing synthetic approaches towards these biologically active compounds,[17] we recently communicated a flexible and highly stereoselective method for the syntheses of *erythro* isomers **14**[18] and **15**[19] (see Scheme 1) through a Grignard addition to *N*-glycosylamine **13**. In this publication, we present some logical functional group manipulations of **14** and **15** to construct different indolizidine and pyrrolizidine rings (see Figure 2).

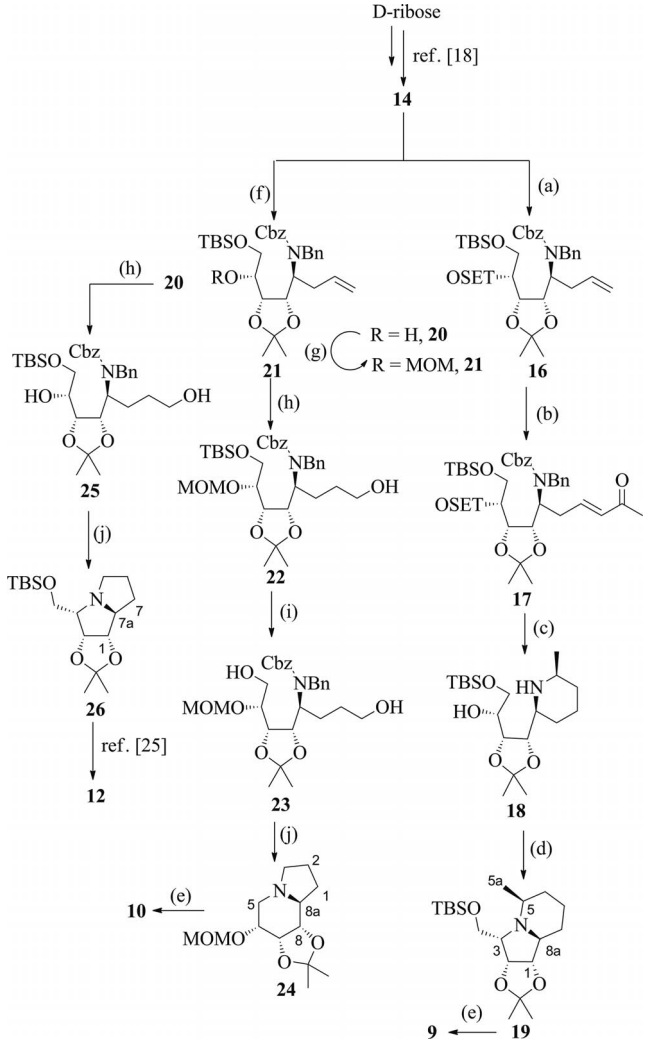


Scheme 1. Synthesis of key intermediates **14** and **15** from D-ribose (TBS = *tert*-butyldimethylsilyl).

Results and Discussion

We envisaged the syntheses of steviamine (**9**), 1-deoxy-8a-*epi*-castanospermine (**10**), indolizidine **11**, 3,7a-di-*epi*-hyacinthacine A1 (**12**), and 2-*epi*-lentiginosine (**4**) to start from intermediate **14** and an alternative synthesis of **12** to start from key intermediate **15**.

For the synthesis of steviamine (**9**, see Figure 2), the amino functionality in **14** was converted to N(Bn)Cbz derivative **16** (Cbz = benzyloxycarbonyl) by using our earlier procedure.[18] The ozonolysis of the terminal olefin in **16** afforded an aldehyde. The crude aldehyde was subjected to a Wittig olefination by treating with $Ph_3P{=}CHCOCH_3$ in toluene and heating the reaction mixture at reflux to afford the (*E*) isomer of α,β-unsaturated ketone **17** (see Scheme 2). Next, we successfully carried out a one-pot stereoselective intramolecular reductive amination[20] and selective deprotection of the triethylsilyl (TES) group[21] by using 10% Pd/C and ammonium formate in methanol at reflux to give piperidine derivative **18**.[22] The secondary alcohol in **18** was treated with MsCl and pyridine to give a mesylated compound, which then underwent an intramolecular S_N2 reaction to afford indolizidine **19** in 70% yield.[23] The synthesis of steviamine (**9**) was achieved by treatment of compound **19** with aqueous HCl in methanol, which was followed by



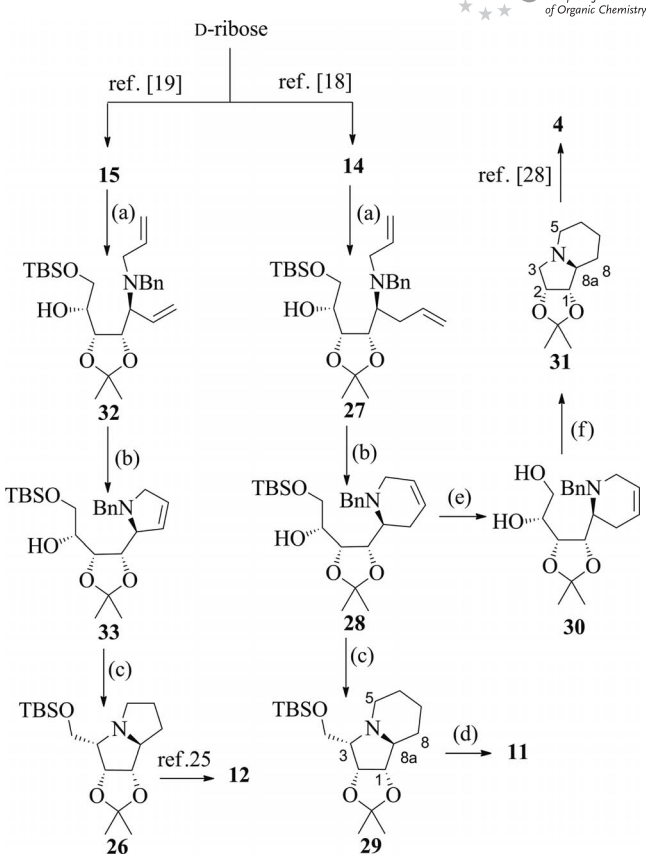
Scheme 2. Synthesis of compounds **9**, **10**, and **12** starting from **14**. Reagents and conditions: (a) see ref.[18]; (b) (i) O_3, CH_2Cl_2, –78 °C and then Me_2S, 0 °C, 2 h; (ii) $Ph_3P{=}CHCOCH_3$, toluene, reflux, 85% (over two steps); (c) $HCOONH_4$, 10% Pd/C, MeOH, reflux, 3 h, 80%; (d) pyridine, MsCl, room temp., 3 h, 70%; (e) HCl (6 M), MeOH, r.t. for **9** and reflux for **10**, 12 h, 90% for **9** and 90% for **10**; (f) CbzCl, $NaHCO_3$, MeOH, 0 °C to r.t., 2 h, 90%; (g) MOMCl (MOM = methoxymethyl), *N*,*N*-diisopropylethylamine (DIPEA), 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 0 °C to r.t., 95%; (h) $BH_3{\cdot}Me_2S$, tetrahydrofuran (THF), 0 °C to r.t., 2 h, then NaOH, H_2O_2, 0 °C, 2 h, 86% for **22** and 80% for **25**; (i) Bu_4NF, THF, r.t., 10 min, 95%; (j) (i) MsCl, NEt_3, CH_2Cl_2, DMAP, 0 °C, 15 min, (ii) 10% Pd/C, H_2, MeOH, 12 h, 90% for **24** and 86% for **26** (over two steps).

purification by ion-exchange chromatography. The analytical data of compound **9** was in good accordance with the reported values.[4]

1-Deoxy-8a-*epi*-castanospermine (**10**) is a synthetically known analogue of castanospermine (**2**).[24] To synthesize compound **10**, compound **14** was treated with CbzCl and $NaHCO_3$ in MeOH to furnish carbamate **20** in 90% yield. Masking of the secondary alcohol in **20** as a MOM ether by using MOMCl and DIPEA in CH_2Cl_2 afforded **21** in 95% yield. Hydroboration/oxidation of the terminal olefin in **21** was carried out by treatment with $BH_3{\cdot}Me_2S$ in THF and then treatment with $NaOH/H_2O_2$ to provide the desired primary alcohol **22** in 86% yield. Cleavage of the silyl ether in **22** by using Bu_4NF afforded diol **23** in a good yield. Mesylation of the diol functionality in **23** by treatment with MsCl, NEt_3, and DMAP in CH_2Cl_2 provided the dimesyl product, which upon hydrogenolysis with 10% Pd/C in methanol gave indolizidine derivative **24** in 90% yield. Finally, the removal of the isopropylidene acetal and MOM ether group in **24** was accomplished by adding aqueous HCl in methanol and heating at reflux. Purification of the resultant salt by an ion-exchange resin afforded the desired final product **10** in 90% yield. The spectral and physical data for **10** were in good agreement with the reported values.[24] Compound **20** was treated with $BH_3{\cdot}Me_2S$ in THF, which was followed by treatment with $NaOH/H_2O_2$ to afford diol **25** in 80% yield. Mesylation of diol **25** with MsCl and pyridine gave the dimesyl derivative, which was immediately subjected to hydrogenolysis with H_2 in presence of 10% Pd/C in methanol to give the desired pyrrolizidine **26** in 86% yield. The conversion of pyrrolidine **26** into 3,7a-di-*epi*-hyacinthacine A1 (**12**) is reported in the literature.[25]

Our next goal was to synthesize compounds **11**, **12**, and **4** under ring-closing metathesis (RCM)[26] conditions (see Scheme 3). To obtain the diene precursors for the preparation of the pyrrolizidine and indolizidine rings, the amino group in **14** and **15** underwent a chemoselective allylation by using allyl bromide and K_2CO_3 in CH_3CN and heating at reflux to furnish diene precursors **27** and **32** in 75 and 70% yield, respectively. Diene **27** and **32** were then subjected to an olefin metathesis by using 10 mol-% of the first-generation Grubbs catalyst in CH_2Cl_2 and heating at reflux to afford **28** and **33** in 80 and 85% yield, respectively. Hydrogenolysis of **28** and **33** by using 10% Pd/C in MeOH and then mesylation with MsCl in pyridine gave compounds **29** and **26**, respectively, in good yields. Finally, compound **29** was globally deprotected by treatment with aqueous HCl. Filtration of the resultant reaction mixture through ion-exchange chromatography gave indolizidine **11**. The spectral and physical data for **11** were in good agreement with the reported values.[14]

To synthesize (–)-2-*epi*-lentiginosine (**4**, see Scheme 3), compound **28** was treated with Bu_4NF in THF to afford diol **30** in 85% yield. The oxidative cleavage of diol **30** by using silica-supported sodium periodate[27] in CH_2Cl_2/H_2O (4:1) gave an aldehyde, which upon hydrogenation with catalytic 10% Pd/C in MeOH afforded bicyclic indolizidine **31** in 55% yield. The spectral and physical data of compound **31** were in good agreement with the reported values.[28] The conversion of the compound **31** into (–)-2-*epi*-lentiginosine (**4**) is reported in the literature.[28]



Scheme 3. Syntheses of compounds **4** and **11** from **14** and compound **12** from **15**. Reagents and conditions: (a) allyl bromide, K_2CO_3, CH_3CN, reflux, 12 h, 75% for **27**, 70% for **32**; (b) 10 mol-% Grubbs first-generation catalyst, CH_2Cl_2, reflux, 12 h, 80% for **28**, 85% for **33**; (c) (i) 10% Pd/C, H_2, MeOH, cat. $NaHCO_3$, 12 h; (ii) MsCl, pyridine, r.t., 2 h, 74% for **29**, 68% for **26** (over two steps); (d) HCl (6 M), r.t., 12 h, 85%; (e) Bu_4NF, THF, r.t., 1 h, 85%; (f) (i) $SiO_2/NaIO_4$, CH_2Cl_2/H_2O (4:1), 0 °C, 30 min; (ii) 10% Pd/C, H_2, MeOH, 12 h, 55% (over two steps).

Conclusions

We have successfully demonstrated our aforementioned strategy for the syntheses of different bicyclic iminosugars (see Figure 2) by using inexpensive and readily available D-ribose as the starting material. The key features of this strategy are its high diastereoselectivity, the stereocontrolled nucleophilic Grignard addition to a *N*-glycosylamine, a one-pot stereoselective intramolecular reductive amination, a selective silyl ether deprotection, a selective mesylation, a cyclization, and a RCM. This strategy provides the desired products in good yields and is also useful for building a library of compounds with improved therapeutic activities.

Experimental Section

General Methods: The moisture- and oxygen-sensitive reactions were carried out under nitrogen in flame- or oven-dried glassware

with magnetic stirring. Standard techniques were used to purify the solvents and reagents prior to use. Solutions were dried with Na_2SO_4 and then concentrated under reduced pressure. TLC was performed with Merck Kiesel gel 60, F254 plates (layer thickness 0.25 mm). Column chromatography was performed with silica gel (60–120 and 100–200 mesh), and ethyl acetate and hexane were used as the eluents. Melting points were determined with a Fisher Johns melting point apparatus. IR spectra were recorded with a Perkin–Elmer RX-1 FTIR system. The ^{1}H NMR (300 and 500 MHz) and ^{13}C NMR (75 and 100 MHz) spectroscopic data were recorded with Bruker Avance-300 and Varian-400 instruments. Chemical shifts were reported in ppm with respect to TMS as the internal standard. ^{1}H NMR spectroscopic data are reported as chemical shifts in ppm, which is followed by multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m)], number of proton(s), and coupling constants (*J*, in Hz). Optical rotations were measured with a JASCO digital polarimeter. Accurate mass measurements were performed with a Q STAR mass spectrometer (Applied Biosystems, USA).

(*R*)-1-{(4*R*,5*S*)-5-[(*S*)-1-(Benzylamino)allyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-(*tert*-butyldimethylsilyloxy)ethanol (15): To a solution of *N*-glycosylamine **13** (2 g, 4.75 mmol) in dry THF (10 mL) was added dropwise vinylmagnesium bromide (1.0 M solution in THF, 23.7 mL) at –78 °C under nitrogen. The reaction mixture was warmed to room temp., and after stirring at r.t. for 2 h, the mixture was quenched with a saturated solution of NH_4Cl. The resulting solution was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The resulting crude material was purified by silica gel column chromatography (10% ethyl acetate in hexane) to give compound **15** (1.54 g, 72% yield) as a syrup. $[\alpha]_D^{26}$ = –12.6 (*c* = 1.3, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2931, 2857, 1459, 1379, 1214, 1068, 916, 836, 750, 667 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 5 H, Ph), 5.69 (m, 1 H, -C*H*=CH_2), 5.36 (d, *J* = 10.1 Hz, 1 H, -CH=C*H*$_2$), 5.18 (d, *J* = 17.2 Hz, 1 H, -CH=C*H*$_2$), 4.16 (dd, *J* = 5.5, 9.6 Hz, 1 H, 5-H), 3.91 (dd, *J* = 5.5, 9.6 Hz, 1 H, 4-H), 3.85 (dd, *J* = 2.0, 10.5 Hz, 1 H, C*H*$_2$OTBS), 3.82 (d, *J* = 12.1 Hz, 1 H, NC*H*$_2$Ph), 3.72 (dd, *J* = 2.0, 10.5 Hz, 1 H, -C*H*$_2$OTBS), 3.60 (d, *J* = 12.1 Hz, 1 H, NC*H*$_2$Ph), 3.60 [m, 1 H, -C*H*(OH)CH_2OTBS], 3.32 (t, *J* = 9.6 Hz, 1 H, -NC*H*CH=CH_2), 1.35 (s, 3 H, C*H*$_3$), 1.28 (s, 3 H, C*H*$_3$), 0.92 (s, 9 H, *t*BuSi), 0.09 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.1 (-*C*H=CH_2), 136.3 (C_q-Ph), 128.8, 128.6, 127.5 (Ph), 118.6 (-CH=*C*H$_2$), 108.5 [$(CH_3)_2C(O)_2$], 79.2 (C-5), 77.2 (C-4), 69.4 (-*C*H$_2$OTBS), 65.0 [-*C*H(OH)CH_2OTBS], 60.7 (N*C*HCH=CH_2), 50.6 (-N*C*H$_2$Ph), 27.8 (-*C*H$_3$), 26.0 [-SiC(*C*H$_3$)$_3$], 25.6 (-*C*H$_3$), 18.5 [-Si*C*(CH$_3$)$_3$], –5.2 (-Si*C*H$_3$), –5.3 (-Si*C*H$_3$) ppm. MS (ESI): *m*/*z* = 422 [M + H]$^+$. HRMS (ESI): calcd. for $C_{23}H_{40}NO_4Si$ [M + H]$^+$ 422.27102; found 422.2711.

Benzyl Benzyl[(*S*,*E*)-1-{(4*S*,5*S*)-5-[(*R*)-3,3-diethyl-8,8,9,9-tetramethyl-4,7-dioxa-3,8-disiladecan-5-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}-5-oxohex-3-enyl]carbamate (17): Through a solution of terminal olefin **16** (1.0 g, 1.46 mmol) in CH_2Cl_2 (15 mL) at –78 °C was passed ozone gas for 20 min (until the solution changed to light blue). The reaction mixture was treated with dimethyl sulfide (0.52 mL, 7.3 mmol) at –78 °C and then stirred for another 30 min. The reaction mixture was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were washed with brine and dried with the anhydrous Na_2SO_4. The organic layers were concentrated under reduced pressure to obtain the crude aldehyde, which was used in the next step without purification. To the solution of the crude aldehyde in dry toluene (10 mL) was added Ph_3P=CHCOCH$_3$ (0.69 g, 2.19 mmol) at r.t., and the reaction mixture was heated at reflux for 2 h. The solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (8% ethyl acetate in hexane) to yield the (*E*) isomer of α,β-unsaturated ketone **17** (0.9 g, 85% yield) as a thick colorless syrup. $[\alpha]_D^{26}$ = –8.6 (*c* = 0.23, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2985, 2932, 1697 (N*CO*OCH$_2$Ph), 1497, 1370, 1251, 1067, 985, 836, 748, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer): δ = 7.45–7.10 (m, 10 H, 2 Ph), 6.65 (m, 1 H, -C*H*=CHCOCH$_3$), 5.70 (d, *J* = 15.8 Hz, 1 H, -CH=C*H*COCH$_3$), 5.41–4.79 (m, 2 H, NCOOC*H*$_2$Ph), 4.77–4.48 (m, 2 H, -NC*H*$_2$Ph), 4.36–4.15 (m, 3 H, 5-H and -C*H*$_2$OTBS), 4.08–3.52 (m, 3 H, 4-H, -C*H*OTES, and NC*H*CH_2CH=CH), 2.62–2.32 (m, 2 H, -C*H*$_2$CH=CH), 2.09 (s, 3 H, COC*H*$_3$), 1.44 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 1.02–0.88 [m, 9 H, Si(CH_2CH_3)$_3$], 0.89 (s, 9 H, *t*BuSi), 0.75–0.50 [m, 6 H, Si(CH_2)$_3$], 0.10–0.01 (m, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major rotamer): δ = 198.5 (*C*OCH$_3$), 156.7 (N*C*OOPh), 146.1 (-*C*H=CHCOCH$_3$), 139.5 (C_q-Ph), 136.4 (C_q-Ph), 132.8 (-CH=*C*HCOCH$_3$), 128.4, 128.2, 128.0, 127.7, 127.3, 126.7 (Ph), 107.7 [$(CH_3)_2C(O)_2$], 79.5 (C-5), 76.8 (C-4), 72.1 (-*C*H$_2$OTBS), 67.1 (-*C*HOTES), 64.7 (NCOO*C*H$_2$Ph), 55.7 (N*C*HCH$_2$CH=CH), 46.7 (N*C*H$_2$Ph), 33.2 (*C*H$_2$CH=CH), 26.1 (CO*C*H$_3$), 25.9 (CH_3), 24.4 (CH_3), 18.2 [Si*C*(CH$_3$)$_3$], 6.8 [Si(CH_2CH$_3$)$_3$], 4.9 [Si(*C*H$_2$CH$_3$)$_3$], –5.5 (Si*C*H$_3$) ppm. MS (ESI): *m*/*z* = 748 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{40}H_{63}NO_7NaSi_2$ [M + H]$^+$ 748.40353; found 748.40426.

(*R*)-2-(*tert*-Butyldimethylsilyloxy)-1-{(4*R*,5*S*)-2,2-dimethyl-5-[(2*S*,6*S*)-6-methylpiperidin-2-yl]-1,3-dioxolan-4-yl}ethanol (18): To a solution of α,β-unsaturated ketone **17** (0.50 g, 0.68 mmol) in MeOH (10 mL) were added 10% Pd/C (10 mg) and ammonium formate (0.17 g, 2.72 mmol), and the resulting solution was heated at reflux for 3 h. After completion of the reaction, the mixture was filtered through a pad of Celite, which was then washed with MeOH (2 × 10 mL). The filtrate was concentrated by using a rotary evaporator, and purification of the crude residue by silica gel column chromatography (30% ethyl acetate in hexane) afforded **18** (0.2 g, 80% yield) as a thick colorless syrup. $[\alpha]_D^{26}$ = +35.8 (*c* = 0.66, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3437, 2924, 1450, 1379, 1215, 1066, 868, 769, 667 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.98 (dd, *J* = 4.9, 10.3 Hz, 1 H, 5-H), 3.79–3.71 (m, 2 H, -C*H*$_2$OTBS), 3.59 (dd, *J* = 4.9, 10.3 Hz, 1 H, 4-H), 3.52 [m, 1 H, -C*H*(OH)CH_2OTBS], 2.82 (ddd, *J* = 1.9, 10.3 Hz, 1 H, NC*H*CH_2CH_2-), 2.60 [m, 1 H, NC*H*(CH$_3$)], 1.91–1.76 [m, 2 H, NCH(CH$_3$)C*H*$_2$- and NCHC*H*$_2$-], 1.62 (m, 1 H, NCHCH$_2$C*H*$_2$-), 1.40 [m, 1 H, NCH(CH$_3$)C*H*$_2$-], 1.27 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.05 (m, 1 H, NCHCH$_2$C*H*$_2$-), 1.01 (d, *J* = 6.4 Hz, 3 H, 10-H), 0.96–0.86 (m, 1 H, NCHC*H*$_2$-), 0.83 (s, 9 H, *t*BuSi), 0.01 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 107.7 [$(CH_3)_2C(O)_2$], 80.5 (C-5), 77.3 (C-4), 69.9 [-*C*H(OH)CH_2OTBS], 65.3 (*C*H$_2$OTBS), 56.1 [N*C*H(CH$_3$)CH$_2$-], 51.7 (N*C*HCH$_2$CH$_2$-), 34.4 [NCH(CH$_3$)*C*H$_2$-], 29.5 (NCH*C*H$_2$CH$_2$-), 27.9 (NCHCH$_2$*C*H$_2$-), 26.0 [SiC(*C*H$_3$)$_3$], 25.3 (CH_3), 24.0 (CH_3), 22.5 [NCH(*C*H$_3$)], 18.6 [Si*C*(CH$_3$)$_3$], –5.2 ($SiCH_3$) ppm. MS (ESI): *m*/*z* = 374 [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{40}NO_4Si$ [M + H]$^+$ 374.27177; found 374.27211.

(3a*R*,4*S*,6*S*,9a*S*,9b*S*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2,6-trimethyloctahydro[1,3]dioxolo[4,5-*a*]indolizidine (19): To a stirred solution of compound **18** (0.1 g, 0.26 mmol) in pyridine (5 mL) was added dropwise MsCl (0.03 mL, 0.40 mmol), and the reaction mixture was stirred at r.t. for 12 h. The solvent was evaporated under reduced pressure, and the resulting crude material was purified by column chromatography (20% ethyl acetate in hexane) to give bicyclic indolizidine **19** (0.068 g, 70% yield). $[\alpha]_D^{26}$ = +16.9 (*c* = 1.88, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2920, 2851, 1464, 1214, 743, 667 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.69 (dd, *J* = 5.4, 7.3 Hz, 1 H, 1-H), 4.20 (dd, *J* = 5.4, 7.3 Hz, 1 H, 2-H), 3.89 (m, 1 H,

-CH_2OTBS), 3.75–3.63 (m, 2 H, -CH_2OTBS and 3-H), 2.88 (m, 1 H, 8a-H), 2.62 (m, 1 H, 5-H), 2.00 (m, 1 H, 6-H_a), 1.72 (m, 1 H, 6-H_b), 1.66–1.51 (m, 2 H, 8-H_a and 8-H_b), 1.45 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.29–1.0 (m, 2 H, 7-H_a and 7-H_b), 1.17 (d, J = 5.8 Hz, 3 H, 5a-H), 0.90 (s, 9 H, *t*BuSi), 0.06 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 113.6 [$(CH_3)_2C(O)_2$], 84.3 (C-1), 77.9 (C-2), 63.1 (C-8a), 61.4 (C-3), 58.1 (-CH_2OTBS), 52.6 (C-5), 34.4 (C-7), 30.3 (C-8), 25.9 [SiC(CH_3)$_3$ and CH_3], 24.5 (CH_3), 23.9 (C-7), 20.7 (C-5a), 18.2 [SiC(CH_3)$_3$], –5.5 (SiCH_3) ppm. MS (ESI): m/z = 356 [M + H]$^+$. HRMS (ESI): calcd. for $C_{19}H_{38}NO_3Si$ [M + H]$^+$ 356.26203; found 356.26155.

(1*S*,2*R*,3*S*,5*R*,8a*S*)-Octahydro-3-(hydroxymethyl)-5-methylindolizidine-1,2-diol (9): Aqueous HCl (6 M solution, 1 mL) was added to compound **19** (0.05 g, 014 mmol) in MeOH (2 mL) at room temp. The reaction mixture was stirred for 12 h and then concentrated in vacuo. The residue was dissolved in a small amount of distilled water, and the resulting solution was neutralized with aqueous NaOH (2 M solution). The crude product was purified by an acid resin column [DOWEX 50WX8, 100–200 mesh, distilled water and then NH_4OH (1 M solution)] to give **9** (0.025 g, 90% yield) as a yellow oil. $[\alpha]_D^{26}$ = –32.4 (c = 1.0, MeOH); ref.[4] $[\alpha]_D^{22}$ = –34.0 (c = 1.0, MeOH). IR (neat): $\tilde{\nu}_{max}$ = 3316, 2943, 2831, 1449, 1219 cm^{-1}. ^{1}H NMR (300 MHz, D_2O): δ = 4.27 (t, J = 7.2 Hz, 1 H, 1-H), 3.98–3.80 (m, 2 H, -CH_2OTBS), 3.73 (t, J = 6.6 Hz, 1 H, 2-H), 3.48 (m, 1 H, 3-H), 2.82 (m, 1 H, 5-H), 2.65 (m, 1 H, 8a-H), 1.92 (m, 1 H, 8-H_a), 1.79–1.60 (m, 2 H, 6-H_a and 7-H_a), 1.40–1.14 (m, 3 H, 6-H_b, 8-H_b, and 7-H_b), 1.09 (d, J = 6.0 Hz, 3 H, 5a-H) ppm. ^{13}C NMR (75 MHz, D_2O): δ = 73.2 (C-1), 68.5 (C-2), 66.2 (C-3), 60.7 (-CH_2OTBS), 56.0 (C-5), 52.4 (C-8a), 32.5 (C-6), 28.4 (C-8), 22.9 (C-7), 18.5 (C-5a) ppm. MS (ESI): m/z = 202 [M + H]$^+$. HRMS (ESI): calcd. for $C_{10}H_{20}NO_3$ [M + H]$^+$ 202.14479; found 202.14377.

Benzyl Benzyl[(*S*)-1-{(4*S*,5*R*)-5-[(*R*)-2-(*tert*-butyldimethylsilyloxy)-1-hydroxyethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}but-3-enyl]carbamate (20): To a stirred suspension of *N*-benzyl compound **14** (1.0 g, 2.30 mmol) in MeOH (10 mL) were added $NaHCO_3$ (0.77 g, 9.20 mmol) and CbzCl (0.39 mL, 2.76 mmol) at 0 °C. The reaction mixture was warmed to r.t., was stirred for 2 h, and then was filtered through a pad of Celite. The filtrate was concentrated in vacuo. The residue was purified by column chromatography (5% ethyl acetate in hexane) to afford **20** (1.18 g, 90% yield) as a thick colorless liquid. $[\alpha]_D^{26}$ = +2.1 (c = 0.59, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3483, 2930, 1692 (NCOOCH_2Ph), 1456, 1369, 1213, 1059, 910, 834, 751, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer): δ = 7.49–7.01 (m, 10 H, 2 Ph), 5.84–5.48 (m, 1 H, -CH=CH_2), 5.25–4.74 (m, 5 H, -CH=CH_2, NCOOCH_2Ph, and 5-H), 4.69–4.40 (m, 2 H, -NCH_2Ph), 4.27 (m, 1 H, 4-H), 3.98–3.52 [m, 4 H, -CH_2OTBS, -CH(OH)CH$_2$OTBS, and NCHCH$_2$CH=CH$_2$], 2.75 (br. s, 1 H, OH), 2.50–2.10 (m, 2 H, NCHCH_2CH=CH$_2$), 1.37 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.90 (s, 9 H, *t*BuSi), 0.07 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.1 (NCOOPh), 139.5 (C_q-Ph), 135.1 (-CH=CH$_2$), 127.9, 127.7, 127.1, 126.5 (Ph), 116.7 (-CH=CH$_2$), 108.1 [$(CH_3)_2C(O)_2$], 79.6 (C-5), 69.1 (C-4), 67.1 [NCOOCH$_2$Ph and -CH(OH)CH$_2$OTBS], 64.6 (-CH$_2$OTBS), 54.7 (NCHCH$_2$), 46.8 (NCH$_2$Ph), 33.6 (CH$_2$CH=CH$_2$), 26.8 (CH_3), 25.8 [SiC(CH_3)$_3$], 24.6 (CH_3), 18.2 [SiC(CH_3)$_3$], –5.4 ($SiCH_3$), –5.4 ($SiCH_3$) ppm. MS (ESI): m/z = 570 [M + H]$^+$. HRMS (ESI): calcd. for $C_{32}H_{48}NO_6Si$ [M + H]$^+$ 570.32699; found 570.32454.

Benzyl Benzyl[(*S*)-1-{(4*S*,5*S*)-2,2-dimethyl-5-[(*R*)-8,8,9,9-tetramethyl-2,4,7-trioxa-8-siladecan-5-yl]-1,3-dioxolan-4-yl}but-3-enyl]carbamate (21): To the solution of alcohol **20** (0.80 g, 1.40 mmol) in dichloromethane (10 mL) were added *N*,*N*-diisopropylethylamine (1.51 mL, 8.40 mmol), MOMCl (0.34 mL, 4.20 mmol), and a catalytic amount of DMAP at 0 °C. The resulting mixture was warmed to r.t. and then stirred overnight. After completion of reaction, water and brine solution were added to the reaction mixture. The organic layer was separated, dried with anhydrous $NaSO_4$, and then concentrated in vacuo. The residue was purified by silica gel column chromatography (3% ethyl acetate and hexane) to give MOM ether **21** (0.82 g, 95% yield) as a thick, syrupy liquid. $[\alpha]_D^{26}$ = –20.1 (c = 0.12, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2929, 2855, 1697 (NCOOCH_2Ph), 1458, 1369, 1214, 1102, 770, 667 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, major rotamer): δ = 7.47–7.05 (m, 10 H, 2 Ph), 5.72 (m, 1 H, -CH=CH$_2$), 5.06 (s, 2 H, NCOOCH_2Ph), 5.01–4.74 (m, 6 H, -CH=CH_2, -NCH_2Ph, and -OCH_2OCH$_3$), 4.48–4.20 (m, 3 H, and 5-H, 4-H, and CH_2OTBS), 4.10–3.62 (m, 2 H, and NCHCH$_2$CH=CH$_2$), 3.45 (s, 3 H, OCH$_2$OCH_3), 3.22 (s, 1 H, -CHOMOM), 2.50–2.01 (m, 2 H, -CH_2CH=CH$_2$), 1.42 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.90 (s, 9 H, *t*BuSi), 0.07 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major rotamer): δ = 157.0 (NCOOCH$_2$Ph), 139.7 (C_q-Ph), 136.4 (-CH=CH$_2$), 135.2 (C_q-Ph), 128.5, 128.3, 128.2, 127.6, 127.1, 126.5 (Ph), 116.9 (-CH=CH$_2$), 108.0 [$(CH_3)_2C(O)_2$], 96.9 (OCH$_2$OCH$_3$), 79.6 (C-5), 77.4 (C-4), 74.8 (-CHOMOM), 67.6 (NCOOCH$_2$Ph), 62.7 (-CH$_2$OTBS), 55.9 (OCH$_2$OCH$_3$), 55.4 (NCHCH$_2$CH=CH$_2$), 46.8 (NCH$_2$Ph), 33.6 (-CH$_2$CH=CH$_2$), 26.1 (CH_3), 25.8 [SiC(CH_3)$_3$], 24.3 (CH_3), 18.3 [SiC(CH_3)$_3$], –5.5 ($SiCH_3$) ppm. MS (ESI): m/z = 614 [M + H]$^+$. HRMS (ESI): calcd. for $C_{34}H_{52}NO_7Si$ [M + H]$^+$ 614.35361; found 614.35076.

Benzyl Benzyl[(*S*)-1-{(4*S*,5*S*)-2,2-dimethyl-5-[(*R*)-8,8,9,9-tetramethyl-2,4,7-trioxa-8-siladecan-5-yl]-1,3-dioxolan-4-yl}-4-hydroxybutyl]carbamate (22): To a solution of olefin **21** (0.70 g, 1.14 mmol) in dry THF was added BH_3·Me_2S (0.16 mL, 1.71 mmol) dropwise at 0 °C, and the stirring was continued for 2 h at room temp. The resulting solution was quenched by the addition of NaOH (10% aqueous solution, 3 mL) and then by H_2O_2 (30% solution, 2 mL) at 0 °C, and the resulting mixture was stirred for another 2 h. Water (10 mL) was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate (20 mL). The organic layer was washed with brine, and the solvent was evaporated on a rotary evaporator. The crude product was purified by silica gel column chromatography (15% ethyl acetate in hexane) to afford **22** (0.62 g, 86% yield) as a syrup. $[\alpha]_D^{26}$ = –31.8 (c = 1.33, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3457, 2935, 2856, 1695 (NCOOCH_2Ph), 1256, 1102, 835, 699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, major rotamer): δ = 7.44–7.07 (m, 10 H, 2 Ph), 5.12 (s, 2 H, NCOOCH_2Ph), 4.73–4.43 (m, 3 H, OCH_2OCH$_3$ and 5-H), 4.33 (s, 2 H, -NCH_2Ph), 4.03 (m, 1 H, 4-H) 3.86–3.33 (m, 5 H, -CH_2OTBS, -CH_2OH, and -CHOMOM) 3.45 (s, 3 H, -OCH_3), 3.24 (m, 1 H, NCHCH$_2$-), 1.72–1.20 [m, 4 H, -(CH_2)$_2$CH$_2$OH], 1.39 (s, 3 H, CH_3), 1.19 (s, 3 H, CH_3), 0.86 (s, 9 H, *t*BuSi), 0.06–0.01 (m, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major rotamer): δ = 157.2 (NCOOCH$_2$Ph), 139.8 (C_q-Ph), 136.2 (C_q-Ph), 128.4, 128.3, 128.1, 127.9, 127.4, 126.8, 126.6 (Ph), 108.0 [$(CH_3)_2C(O)_2$], 96.8 (OCH$_2$OCH$_3$), 79.9 (C-5), 77.2 (C-4), 74.9 (-CHOMOM), 67.1 (NCOOCH$_2$Ph), 62.7 (-CH$_2$OH), 62.3 (-CH$_2$OTBS), 55.9 (OCH$_2$OCH$_3$), 55.6 (NCHCH$_2$-), 46.6 (-NCH$_2$Ph), 28.7 (NCHCH$_2$-), 26.1 (CH_3), 25.8 [SiC(CH_3)$_3$], 25.2 (NCHCH$_2$$CH_2$-), 24.5 ($CH_3$), 18.2 [Si$C$($CH_3$)$_3$], –5.5 ($SiCH_3$) ppm. MS (ESI): m/z = 632 [M + H]$^+$. HRMS (ESI): calcd. for $C_{34}H_{54}NO_8Si$ [M + H]$^+$ 632.36400; found 632.36132.

Benzyl Benzyl[(*S*)-4-hydroxy-1-{(4*S*,5*S*)-5-[(*R*)-2-hydroxy-1-(methoxymethoxy)ethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}butyl]carbamate (23): To a stirred solution of **22** (0.5 g, 0.79 mmol) in THF (5 mL) was added Bu_4NF (1.0 M solution in THF, 0.79 mL) at room temp.

The reaction mixture was stirred for 1 h and then was concentrated. The resulting crude compound was purified by column chromatography (60% ethyl acetate in hexane) to provide diol **23** (0.39 g, 95% yield) as a thick colorless liquid. $[\alpha]_D^{26}$ = –1.77 (*c* = 0.33, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3447, 2927, 1691 (N*CO*OCH$_2$Ph), 1454, 1211, 1112, 1067, 700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, major rotamer): δ = 7.51–7.15 (m, 10 H, 2 Ph), 5.16 (s, 2 H, NCOOC*H*$_2$Ph), 4.80–4.51 (m, 4 H, -NC*H*$_2$Ph and -OC*H*$_2$OCH$_3$), 4.29 (dd, *J* = 3.0, 6.7 Hz, 1 H, 5-H), 4.03 (dd, *J* = 3.0, 6.7 Hz, 1 H, 4-H), 3.91 (m, 1 H, -C*H*OMOM), 3.73 (m, 1 H, -C*H*$_2$OH), 3.68–3.47 [m, 3 H, -CH(MOM)C*H*$_2$OH and -C*H*$_2$OH], 3.44 (s, 3 H, OCH$_2$OC*H*$_3$), 3.35 (m, 1 H, NC*H*CH$_2$-), 1.80–1.20 [m, 4 H, -(C*H*$_2$)$_2$CH$_2$OH], 1.42 (s, 3 H, CH$_3$), 1.22 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, major rotamer): δ = 157.4 (N*C*OOCH$_2$Ph), 139.8 (C$_q$-Ph), 136.2 (C$_q$-Ph), 128.7, 128.4, 128.0, 127.4, 126.9 (Ph), 108.4 [(CH$_3$)$_2$*C*(O)$_2$], 97.3 (O*C*H$_2$OCH$_3$), 80.7 (C-5), 79.6 (C-4), 76.2 (-*C*HOMOM), 67.6 (NCOO*C*H$_2$Ph), 64.3 [-*C*H(MOM)CH$_2$OH], 62.4 (-*C*H$_2$OH), 55.9 (OCH$_2$O*C*H$_3$), 55.2 (N*C*HCH$_2$-), 46.5 (N*C*H$_2$Ph), 29.0 (NCH*C*H$_2$-), 26.2 (CH$_3$), 25.4 (NCHCH$_2$*C*H$_2$-), 24.4 (CH$_3$) ppm. MS (ESI): *m*/*z* = 540 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{28}H_{39}NO_8Na$ [M + Na]$^+$ 540.25853; found 540.25679.

(3a*R*,4*R*,9a*S*,9b*S*)-4-(Methoxymethoxy)-2,2-dimethyloctahydro-[1,3]dioxolo[4,5-*g*]indolizidine (24): To a solution of diol **23** (0.3 g, 0.58 mol) in dry CH_2Cl_2 (4 mL) were added NEt_3 (0.20 mL, 1.45 mmol), MsCl (0.06 mL, 0.87 mmol), and a catalytic amount of DMAP at 0 °C. The reaction mixture was stirred for 15 min at 0 °C. The organic layer was washed with brine, separated, and concentrated in vacuo. The crude dimesylated product was subjected to hydrogenation by using 10% Pd/C (30 mg) in MeOH (5 mL), as the reaction mixture was stirred for 12 h. The mixture was filtered through a pad of Celite, which was then washed with MeOH (2 × 10 mL). The filtrate was concentrated, and the crude residue was purified by silica gel column chromatography (80% ethyl acetate in hexane) to give bicyclic indolizidine **24** (0.145 g, 90% yield) as a colorless liquid. $[\alpha]_D^{26}$ = +20.05 (*c* = 0.71, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2932, 2822, 1217, 1041, 755 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.78 (s, 2 H, OC*H*$_2$OCH$_3$), 4.42 (dd, *J* = 4.5, 8.3 Hz, 1 H, 8-H), 4.04 (ddd, *J* = 5.3, 10.2 Hz, 1 H, 6-H), 3.87 (dd, *J* = 4.5, 8.3 Hz, 1 H, 7-H), 3.42 (s, 3 H, OCH$_2$OC*H*$_3$), 3.10 (dd, *J* = 5.3, 10.2 Hz, 1 H, 5-H$_a$), 3.05 (ddd, *J* = 2.6, 10.2 Hz, 1 H, 3-H$_a$), 2.39–2.00 (m, 4 H, 8a-H, 5-H$_b$, 1-H$_a$, and 2-H$_a$), 1.93–1.67 (m, 2 H, 3-H$_b$ and 2-H$_b$), 1.46 (m, 1 H, 1-H$_b$), 1.55 (s, 3 H, CH$_3$), 1.40 (s, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.6 [(CH$_3$)$_2$*C*(O)$_2$], 96.2 (O*C*H$_2$OCH$_3$), 79.0 (C-7), 74.6 (C-8), 73.0 (C-6), 64.8 (OCH$_2$O*C*H$_3$), 55.5 (C-8a), 53.4 (C-3), 51.7 (C-5), 28.5 (C-1), 28.3 (CH$_3$), 26.3 (CH$_3$), 21.5 (C-2) ppm. MS (ESI): *m*/*z* = 258 [M + H]$^+$. HRMS (ESI): calcd. for $C_{13}H_{24}NO_4$ [M + H]$^+$ 258.17109; found 258.16998.

(6*R*,7*R*,8*S*,8a*S*)-Octahydroindolizine-6,7,8-triol (10): To the stirred suspension of compound **24** (0.1 g, 0.39 mmol) in MeOH (2 mL) was added aqueous HCl (6 M solution, 2 mL), and the reaction mixture was stirred and heated at reflux for 12 h. The solvent was evaporated on a rotary evaporator. Distilled water (1 mL) was added to the crude residue, and the resulting solution was neutralized with aqueous NaOH (2 M solution). The solution was concentrated in vacuo. The residue was purified by an acid resin column [DOWEX 50WX8, 100–200 mesh, distilled water and then NH_4OH (1 M solution)] to give **10** (0.06 g, 90% yield) as a white solid. M.p. 165–167 °C; ref.[24] m.p. 166–168 °C. $[\alpha]_D^{26}$ = –36.1 (*c* = 1.0, H_2O); ref.[24] $[\alpha]_D^{22}$ = –36.3 (*c* = 1.0, H_2O). IR (neat): $\tilde{\nu}_{max}$ = 3415, 2922, 2853, 1459, 1388, 1046, 770 cm^{-1}. ^{1}H NMR (500 MHz, D_2O): δ = 3.99 (br. s, 1 H, 7-H), 3.82 (br. d, *J* = 8.9 Hz, 1 H, 6-H), 3.50 (d, *J* = 10 Hz, 1 H, 8-H), 3.16 (m, 1 H, 3-H$_a$), 3.03 (m, 1 H, 5-H$_a$), 2.75 (m, 1 H, 8a-H), 2.61 (m, 1 H, 5-H$_b$), 2.54 (m, 1 H, 3-H$_b$), 2.03 (m, 1 H, 1-H$_a$), 1.89–1.70 (m, 2 H, 2-H$_a$ and 1-H$_b$), 1.47 (m, 1 H, 2-H$_b$) ppm. ^{13}C NMR (75 MHz, D_2O): δ = 74.0 (C-8), 73.7 (C-7), 70.0 (C-6), 64.8 (C-8a), 55.7 (C-5), 52.6 (C-3), 29.3 (C-1), 23.3 (C-2) ppm. MS (ESI): *m*/*z* = 174 [M + H]$^+$. HRMS (ESI): calcd. for $C_8H_{16}NO_3$ [M + H]$^+$ 174.11285; found 174.11247.

Benzyl Benzyl[(*S*)-1-{(4*S*,5*R*)-5-[(*R*)-2-(*tert*-butyldimethylsilyloxy)-1-hydroxyethyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-4-hydroxybutyl]-carbamate (25): Compound **25** was prepared using the procedure developed for the preparation of compound **22**. The crude product was purified by silica gel chromatography (17% ethyl acetate in hexane) to yield **25** (80% yield). $[\alpha]_D^{26}$ = –18.14 (*c* = 2.76, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3445, 2929, 2857, 1681 (N*CO*OCH$_2$Ph), 1460, 1374, 1254, 1058, 836, 775, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, major rotamer): δ = 7.49–7.01 (m, 10 H, 2 Ph), 5.28–4.91 (m, 3 H, NCOOC*H*$_2$Ph and OH), 4.65 (s, 2 H, C*H*$_2$Ph), 4.30 (m, 1 H, 5-H), 3.96 (m, 1 H, 4-H), 3.81–3.56 (m, 4 H, -C*H*$_2$OH, and -C*H*$_2$OTBS), 3.55–3.29 [m, 2 H, -C*H*(OH)CH$_2$OTBS and NC*H*CH$_2$-], 1.84–1.38 [m, 4 H, -(C*H*$_2$)$_2$CH$_2$OH], 1.36 (s, 3 H, CH$_3$), 1.10 (s, 3 H, CH$_3$), 0.90 (s, 9 H, *t*BuSi), 0.08 (s, 6 H, SiMe$_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.3 (N*C*OOCH$_2$Ph), 139.5 (C$_q$-Ph), 136.2 (C$_q$-Ph), 128.2, 128.0, 127.9, 127.8, 127.1, 126.5 (Ph), 108.0 [(CH$_3$)$_2$*C*(O)$_2$], 80.0 (C-5), 76.1 (C-4), 69.0 (-NCOO*C*H$_2$Ph), 67.3 [-*C*H(OH)-CH$_2$OTBS], 64.1 (-*C*H$_2$OTBS), 61.3 (-*C*H$_2$OH), 53.7 (N*C*HCH$_2$-), 46.5 (-N*C*H$_2$Ph), 28.3 (-*C*H$_2$CH$_2$OH), 27.0 (CH$_3$), 25.8 [SiC-(*C*H$_3$)$_3$], 24.6 (CH$_3$), 23.9 (NCH*C*H$_2$-), 18.2 [Si*C*(CH$_3$)$_3$], –5.5 (SiCH$_3$), –5.4 (SiCH$_3$) ppm. MS (ESI): *m*/*z* = 588 [M + H]$^+$. HRMS (ESI): calcd. for $C_{32}H_{50}NO_7Si$ [M + H]$^+$ 588.33435; found 588.33511.

(3a*R*,4*S*,8a*S*,8b*S*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2-dimethylhexahydro-3a*H*-[1,3]dioxolo[4,5-*a*]pyrrolizidine (26): Compound **26** was prepared using the procedure developed for the preparation of compound **24**. The crude product was purified by column chromatography (20% ethyl acetate in hexane) to give compound **26** as a yellow oil (86% yield). $[\alpha]_D^{26}$ = +26.90 (*c* = 1.44, $CHCl_3$); ref.[25] $[\alpha]_D^{25}$ = +29.7 (*c* = 0.209, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2932, 2858, 1464, 1378, 1078, 1254, 837 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.74 (dd, *J* = 5.0, 5.8 Hz, 1 H, 2-H), 4.50 (d, *J* = 5.8 Hz, 1 H, 1-H), 3.93 (dd, *J* = 7.1, 9.9 Hz, 1 H, -C*H*$_2$OTBS), 3.67 (dd, *J* = 5.8, 9.9 Hz, 1 H, -C*H*$_2$OTBS), 3.43 (dd, *J* = 2.2, 11.9 Hz, 1 H, 5-H$_a$), 3.02–2.86 (m, 2 H, 3-H and 7a-H), 2.72 (dd, *J* = 5.7, 11.9 Hz, 1 H, 5-H$_b$), 1.95–1.80 (m, 2 H, 7-H$_a$ and 6-H$_a$), 1.68 (m, 1 H, 7-H$_b$), 1.51 (s, 3 H, CH$_3$), 1.36 (m, 1 H, 6-H$_b$), 1.28 (s, 3 H, CH$_3$), 0.89 (s, 9 H, *t*BuSi), 0.07 (s, 6 H, SiMe$_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.9 [(CH$_3$)$_2$-*C*(O)$_2$], 83.1 (C-1), 81.7 (C-2), 72.2 (-*C*H$_2$OTBS), 68.5 (C-3), 63.0 (C-7a), 53.1 (C-5), 28.2 (C-7), 26.5 (CH$_3$), 25.9 [SiC(*C*H$_3$)$_3$], 24.7 (CH$_3$), 24.1 (C-6), 18.3 [Si*C*(CH$_3$)$_3$], –5.4 (SiCH$_3$), –5.3 (SiCH$_3$) ppm. MS (ESI): *m*/*z* = 328 [M + H]$^+$. HRMS (ESI): calcd. for $C_{17}H_{34}NO_3Si$ [M + H]$^+$ 328.22964; found 328.23025.

(*R*)-1-[(4*R*,5*S*)-5-{(*S*)-1-[Allyl(benzyl)amino]but-3-enyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(*tert*-butyldimethylsilyloxy)ethanol (27): To amino compound **14** (1.5 g, 3.44 mmol) in acetonitrile (15 mL) were added allyl bromide (0.58 mL, 6.89 mmol) and K_2CO_3 (1.42 g, 10.3 mmol) at 0 °C. The reaction mixture was warmed to r.t. and then heated at reflux for 12 h. The resulting mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuo. The crude residue was dissolved in water, and the resulting solution was extracted with ethyl acetate (2 × 50 mL). The combined organic extracts were concentrated in vacuo. Purification of the crude residue by column chromatography (5% ethyl acetate in hexane) afforded **27** (1.23 g, 75% yield) as yellow oil. $[\alpha]_D^{26}$ = +25.6 (*c* =

1.66, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2929, 2856, 1460, 1250, 1064, 778 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.16 (m, 5 H, Ph), 6.00 (m, 1 H, $NCH_2CH{=}CH_2$), 5.80 (m, 1 H, -$CH{=}CH_2$), 5.57 (br. s, 1 H, OH), 5.22–5.11 (m, 2 H, $NCH_2CH{=}CH_2$), 5.09–4.97 (m, 2 H, -$CH{=}CH_2$), 4.35 (dd, J = 6.1, 8.3 Hz, 1 H, 5-H), 4.15 (dd, J = 6.1, 9.4 Hz, 1 H, 4-H), 3.83 (d, J = 13.2 Hz, 1 H, -NCH_2Ph), 3.75 (dd, J = 2.2, 10.5 Hz, 1 H, -CH_2OTBS), 3.64 (dd, J = 4.5, 10.5 Hz, 1 H, -CH_2OTBS), 3.55 (d, J = 13.2 Hz, 1 H, -NCH_2Ph), 3.38 [m, 1 H, -CH(OH)CH_2OTBS], 3.32–3.14 (m, 2 H, $NCH_2CH{=}CH_2$ and $NCHCH_2$-), 3.08 (dd, J = 7.9, 13.9 Hz, 1 H, $NCH_2CH{=}CH_2$), 2.54–2.31 (m, 2 H, -$CH_2CH{=}CH_2$), 1.36 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 0.91 (s, 9 H, tBuSi), 0.08 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.0 (C_q-Ph), 137.4 ($NCH_2CH{=}CH_2$), 134.9 (-$CH_2CH{=}CH_2$), 129.8, 128.3, 127.4 (C-Ph), 119.0 ($NCH_2CH{=}CH_2$), 115.8 (-$CH_2CH{=}CH_2$), 107.7 [$(CH_3)_2C(O)_2$], 77.4 (C-5), 77.1 (C-4), 69.1 (-CH_2OTBS), 65.0 [-CH(OH)CH_2OTBS], 58.1 (NCH_2Ph), 54.7 ($NCH_2CH{=}CH_2$), 54.1 ($NCHCH_2$-), 31.2 ($CH_2CH{=}CH_2$), 27.6 (CH_3), 26.0 [SiC-$(CH_3)_3$], 25.2 (CH_3), 18.2 [Si$C(CH_3)_3$], –5.2 ($SiCH_3$), –5.1 ($SiCH_3$) ppm. MS (ESI): m/z = 476 $[M + H]^+$. HRMS (ESI): calcd. for $C_{27}H_{46}NO_4Si$ $[M + H]^+$ 476.31763; found 476.31906.

(*R*)-1-{(4*R*,5*S*)-5-[(*S*)-1-Benzyl-1,2,3,6-tetrahydropyridin-2-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-(*tert*-butyldimethylsilyloxy)-ethanol (28): To a solution of diene **27** (0.92 g, 1.93 mmol) in dry CH_2Cl_2 (250 mL) was added Grubbs' first-generation catalyst (0.16 g, 0.19 mmol), and the resulting purple solution turned to brown after 10 min. The reaction mixture was stirred and heated at reflux for another 12 h, and then the solvent was removed under reduced pressure. The resulting residue was purified by column chromatography (3% ethyl acetate in hexane) to give compound **28** (0.69 g, 80% yield) as a light brown oil. $[\alpha]_D^{26}$ = +12.9 (c = 1.18, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2927, 2854, 1458, 1249, 751, 666 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 5 H, Ph), 5.88 (br. d, J = 10.5 Hz, 1 H, $NCH_2CH{=}CH$-), 5.55 (br. d, J = 10.5 Hz, 1 H, $NCH_2CH{=}CH$-), 4.33 (dd, J = 5.6, 10.2 Hz, 1 H, 5-H), 4.19 (dd, J = 5.6, 9.4 Hz, 1 H, 4-H), 3.85 (dd, J = 2.2, 10.5 Hz, 1 H, -CH_2OTBS), 3.78 (d, J = 12.4 Hz, 1 H, CH_2Ph), 3.73 (m, 1 H, -CH_2OTBS), 3.71 (d, J = 12.4 Hz, 1 H, CH_2Ph), 3.63 [m, 1 H, -CH(OH)CH_2OTBS], 3.26 (m, 1 H, $NCH_2CH{=}CH$-), 3.14–3.05 (m, 2 H, $NCHCH_2CH{=}CH$- and $NCH_2CH{=}CH$-), 2.47–2.22 (m, 2 H, $NCHCH_2CH{=}CH$-), 1.36 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 0.93 (s, 9 H, tBuSi), 0.10 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8 (C_q-Ph), 129.5, 128.5, 127.5 (C-Ph), 124.5 ($NCHCH_2CH{=}CH$-), 122.7 ($NCHCH_2CH{=}CH$-), 107.8 [$(CH_3)_2C(O)_2$], 77.6 (C-5), 76.6 (C-4), 69.8 [-CH(OH)CH_2OTBS], 65.3 (-CH_2OTBS), 55.5 (-NCH_2Ph), 54.7 ($NCH_2CH{=}CH_2$-), 45.2 ($NCHCH_2CH{=}CH$-), 28.0 ($NCHCH_2CH{=}CH$-), 26.0 [SiC(CH_3)$_3$], 25.5 (CH_3), 21.1 (CH_3), 18.6 [Si$C(CH_3)_3$], –5.1 ($SiCH_3$) ppm. MS (ESI): m/z = 448 $[M + H]^+$. HRMS (ESI): calcd. for $C_{25}H_{42}NO_4Si$ $[M + H]^+$ 448.28610; found 448.28776.

(3a*R*,4*S*,9a*S*,9b*S*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-2,2-dimethyloctahydro-[1,3]dioxolo[4,5-*a*]indolizidine (29): To a solution of compound **28** (0.16 g, 0.35 mmol) in MeOH (3 mL) were added 10% Pd/C (20 mg) and $NaHCO_3$ (5 mg), and the reaction mixture was stirred under an atmosphere of H_2 for 12 h. The reaction mixture was filtered through a pad of Celite, which was then washed with MeOH (2 × 10 mL), and the filtrate was concentrated in vacuo. To a solution of the crude residue in pyridine (5 mL) was added MsCl (0.04 mL, 0.53 mmol) dropwise at room temp. The resulting mixture was stirred overnight, and the pyridine was evaporated in vacuo. The residue was purified by silica gel chromatography (20% ethyl acetate in hexane) to give the protected bicyclic indolizidine **29** (0.09 g, 74% yield) as a colored oil. $[\alpha]_D^{26}$ = +37.70 (c = 2.75, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2929, 2855, 1464, 1375, 1254, 1086, 839 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.62 (t, J = 6.0 Hz, 1 H, 1-H), 4.14 (dd, J = 1.1, 6.0 Hz, 1 H, 2-H), 3.80 (dd, J = 4.9, 10.5 Hz, 1 H, -CH_2OTBS), 3.67 (dd, J = 6.0, 10.5 Hz, 1 H, -CH_2OTBS), 3.24 (dd, J = 5.6, 11.3 Hz, 1 H, 5-H_a), 3.15 (m, 1 H, 3-H), 2.99 (dd, J = 1.8, 11.3 Hz, 1 H, 5-H_b), 2.80 (m, 1 H, 8a-H), 1.79 (m, 1 H, 8-H_a), 1.69–1.08 (m, 5 H, 6-H_a, 7-H_a, 8-H_b, 6-H_b, and 7-H_b), 1.44 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 0.89 (s, 9 H, tBuSi), 0.06 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.2 [$(CH_3)_2C(O)_2$], 83.4 (C-1), 79.4 (C-2), 63.8 (-CH_2OTBS), 62.0 (C-3), 61.7 (C-8a), 46.6 (C-5), 25.9 (CH_3), 25.8 [SiC(CH_3)$_3$], 25.0 (C-6), 24.4 (C-8), 24.2 (CH_3), 19.7 (C-7), 18.0 [Si$C(CH_3)_3$], –5.5 ($SiCH_3$) ppm. MS (ESI): m/z = 342 $[M + H]^+$. HRMS (ESI): calcd. for $C_{18}H_{36}NO_3Si$ $[M + H]^+$ 342.24536; found 342.24590.

(1*S*,2*R*,3*S*,8a*S*)-3-(Hydroxymethyl)-octahydroindolizidine-1,2-diol (11): To compound **29** (0.05 g, 0.14 mmol) in MeOH (2 mL) was added aqueous HCl (6 M solution, 1 mL), and the resulting solution was stirred at room temp for 12 h. The reaction mixture was concentrated in vacuo to obtain the crude product, which was dissolved in distilled water (1 mL). The resulting solution was neutralized with aqueous NaOH (2 M solution) and then was concentrated. Purification by an acid resin column [DOWEX 50WX8, 100–200 mesh, distilled water and then aqueous NH_4OH (2 M solution)] gave **11** (0.023 g, 85% yield) as a yellow oil. $[\alpha]_D^{26}$ = +7.1 (c = 1.0, H_2O); ref.[14] $[\alpha]_D^{22}$ = –8.7 (c = 1.2, H_2O). IR (neat): $\tilde{\nu}_{max}$ = 3315, 2943, 2831, 1449, 1019, 771 cm^{-1}. ^1H NMR (500 MHz, D_2O): δ = 4.34 (t, J = 6.2 Hz, 1 H, 1-H), 3.82 (t, J = 5.8 Hz, 1 H, 2-H), 3.78–3.65 (m, 2 H, -CH_2OH), 3.37 (m, 1 H, 5-H_a), 3.04–2.90 (m, 2 H, 5-H_b, 3-H), 2.80 (ddd, J = 3.7, 9.4 Hz, 1 H, 8a-H), 1.73 (m, 1 H, 8-H_a), 1.62 (m, 1 H, 6-H_a), 1.57–1.37 (m, 2 H, 7-H_a and 8-H_b), 1.35–1.13 (m, 2 H, 6-H_b and 7-H_b) ppm. ^{13}C NMR (75 MHz, D_2O): δ = 73.6 (C-1), 69.7 (C-2), 64.6 (-CH_2OH), 64.2 (C-2), 57.8 (C-8a), 48.0 (C-5), 24.6 (C-6), 20.9 (C-7), 20.7 (C-8) ppm. MS (ESI): m/z = 188 $[M + H]^+$. HRMS (ESI): calcd. for $C_9H_{18}NO_3$ $[M + H]^+$ 188.12798; found 188.12812.

(*R*)-1-{(4*R*,5*S*)-5-[(*S*)-1-Benzyl-1,2,3,6-tetrahydropyridin-2-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}ethane-1,2-diol (30): To a stirred solution of compound **28** (0.2 g, 0.447 mmol) in THF (2 mL) was added Bu_4NF (1.0 M solution in THF, 0.44 mL) at r.t., and the resulting mixture was stirred for 1 h. After evaporation of the solvent in vacuo, the crude product was purified by column chromatography (25% ethyl acetate in hexane) to afford diol **30** (0.127 g, 85% yield) as a yellow oil. $[\alpha]_D^{26}$ = +25.70 (c = 0.5, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3422, 2929, 2855, 1452, 1376, 1218, 1065, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 5 H, Ph), 5.91 (br. d, J = 10.2 Hz, 1 H, $NCH_2CH{=}CH$-), 5.58 (br. d, J = 10.2 Hz, 1 H, $NCH_2CH{=}CH$-), 4.42 (dd, J = 5.6, 9.8 Hz, 1 H, 5-H), 4.21 (dd, J = 5.6, 8.6 Hz, 1 H, 4-H), 3.88–3.67 [m, 5 H, -CH_2OH, -CH(OH)CH_2OH, and NCH_2Ph], 3.32 (m, 1 H, $NCH_2CH{=}CH$-), 3.14–3.05 (m, 2 H, $NCH_2CH{=}CH$- and $NCHCH{=}CH$-), 2.55–2.24 (m, 2 H, $NCHCH_2CH{=}CH$-), 1.40 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.4 (C_q-Ph), 129.3, 128.4, 127.5 (Ph), 124.4 ($NCH_2CH{=}CH$-), 122.2 ($NCH_2CH{=}CH$-), 107.9 [$(CH_3)_2C(O)_2$], 78.3 (C-5), 77.0 (C-4), 68.6 [-CH(OH)CH_2OH], 64.3 (-CH_2OH), 55.8 (-NCH_2Ph), 54.2 ($NCH_2CH{=}CH$-), 45.0 ($NCHCH_2CH{=}CH$-), 29.5 ($NCHCH_2CH{=}CH$-), 27.7 (CH_3), 25.2 (CH_3) ppm. MS (ESI): m/z = 334 $[M + H]^+$. HRMS (ESI): calcd. for $C_{19}H_{28}NO_4$ $[M + H]^+$ 334.20262; found 334.20128.

(3a*R*,9a*S*,9b*S*)-2,2-Dimethyloctahydro-[1,3]dioxolo[4,5-*a*]indolizidine (31): Silica-supported $NaIO_4$ (0.128 g, 0.60 mmol) was added to diol **30** (0.1 g, 0.30 mmol) in CH_2Cl_2/H_2O (2 mL/0.5 mL)

at 0 °C, and the resulting mixture was stirred for 30 min. The reaction mixture was then filtered through a pad of Celite, and the filtrate was concentrated in vacuo. The resulting crude aldehyde was then subjected to hydrogenation with 10% Pd/C (18 mg) in MeOH (2 mL) for 12 h. Again, the reaction mixture was filtered through a pad of Celite, which was then washed with MeOH (2 × 5 mL). The filtrate was concentrated in vacuo, and the residue was purified by column chromatography (80% ethyl acetate in hexane) to provide bicyclic indolizidine **31** (0.033 g, 55% yield) as a colorless oil. $[a]_D^{26}$ = –47.50 (*c* = 0.5, $CHCl_3$); ref.[28] $[a]_D^{25}$ = –49.7 (*c* = 0.49, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2929, 2856, 1462, 1254, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.65 (dd, *J* = 6.7, 11.8 Hz, 1 H, 2-H), 4.18 (t, *J* = 6.7 Hz, 1 H, 1-H), 3.36 (dd, *J* = 6.7, 9.8 Hz, 1 H, 3-H_a), 2.96 (br. d, *J* = 11.8 Hz, 1 H, 5-H_a), 2.31 (dd, *J* = 5.0, 9.8 Hz, 1 H, 3-H_b), 2.23–2.00 (m, 2 H, 5-H_b and 8a-H), 1.91 (m, 1 H, 8-H_a), 1.75 (m, 1 H, 7-H_a), 1.63–1.20 (m, 4 H, 6-H_a, 8-H_b, 7-H_b, and 6-H_b), 1.46 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 114.0 [$(CH_3)_2C(O)_2$], 84.1 (C-1), 77.2 (C-2), 68.8 (C-8a), 59.6 (C-3), 52.4 (C-5), 28.4 (C-6), 27.1 (CH_3), 25.0 (C-8), 24.3 (CH_3), 23.7 (C-7) ppm. MS (ESI): *m*/*z* = 220 $[M + Na]^+$. HRMS (ESI): calcd. for $C_{11}H_{19}NO_2Na$ $[M + Na]^+$ 220.1323; found 220.1325.

(*R*)-1-[(4*R*,5*S*)-5-{(*S*)-1-[Allyl(benzyl)amino]allyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(*tert*-butyldimethylsilyloxy)ethanol (32): By using the same procedure as described for **27**, compound **15** was used as the starting material to afford compound **32** (70% yield). $[a]_D^{26}$ = –20.0 (*c* = 0.10, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3075, 2931, 2856, 1250, 1065, 837, 777 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.16 (m, 5 H, Ph), 6.05 (br. s, 1 H, OH), 5.92–5.69 (m, 2 H, NCH_2CH=CH_2 and $NCHCH$=CH_2), 5.45 (dd, *J* = 1.7, 10.2 Hz, 1 H, $NCHCH$=CH_2), 5.23–5.11 (m, 3 H, $NCHCH$=CH_2 and NCH_2CH=CH_2), 4.39 (dd, *J* = 5.5, 9.5 Hz, 1 H, 5-H), 4.23 (dd, *J* = 5.5, 9.5 Hz, 1 H, 4-H), 3.91 (d, *J* = 12.8 Hz, 1 H, NCH_2Ph), 3.75 (dd, *J* = 2.1, 10.8 Hz, 1 H, -CH_2OTBS), 3.64 (dd, *J* = 4.5, 10.7 Hz, 1 H, -CH_2OTBS), 3.51 [dd, *J* = 2.1, 10.8 Hz, 1 H, -CH(OH)-CH_2OTBS], 3.37–3.27 (m, 2 H, NCHCH=CH_2 and NCH_2CH=CH_2), 3.24 (d, *J* = 12.8 Hz, 1 H, NCH_2Ph), 2.86 (dd, *J* = 9.0, 13.4 Hz, 1 H, NCH_2CH=CH_2), 1.29 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 0.92 (s, 9 H, *t*BuSi), 0.09 (s, 3 H, $SiMe_2$), 0.08 (s, 3 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.9 (C_q-Ph), 134.6 ($NCHCH$=CH_2), 131.6 (NCH_2CH=CH_2), 129.9, 128.5, 127.6 (Ph), 121.0 (NCH_2CH=CH_2), 119.6 ($NCHCH$=CH_2), 108.7 [$(CH_3)_2C(O)_2$], 77.5 (C-5), 76.2 (C-4), 69.0 [-CH(OH)CH_2OTBS], 65.0 (-CH_2OTBS), 61.8 (NCH_2Ph), 54.6 (NCH_2CH=CH_2), 53.4 ($NCHCH$=CH_2), 27.7 (CH_3), 26.0 [SiC(CH_3)$_3$], 25.6 (CH_3), 18.5 [SiC$(CH_3)_3$], –5.2 (SiCH_3), –5.1 (SiCH_3) ppm. MS (ESI): *m*/*z* = 462 $[M + H]^+$. HRMS (ESI): calcd. for $C_{26}H_{44}NO_4Si$ $[M + H]^+$ 462.30162; found 462.30341.

(*R*)-1-{(4*R*,5*S*)-5-[(*S*)-1-Benzyl-2,5-dihydro-1*H*-pyrrol-2-yl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-(*tert*-butyldimethylsilyloxy)ethanol (33): By using the same procedure as described for **28**, compound **32** was used as the starting material to afford compound **33** (85% yield). $[a]_D^{26}$ = –6.6 (*c* = 1.82, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 2988, 2931, 1455, 1253, 771 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.18 (m, 5 H, Ph), 6.01 (dd, *J* = 2.2, 5.3 Hz, 1 H, NCH_2CH=CH-), 5.86 (br. d, *J* = 5.3 Hz, 1 H, NCH_2CH=C*H*-), 4.18 (dd, *J* = 5.2, 9.0 Hz, 1 H, 5-H), 3.98–3.86 (m, 3 H, 4-H, -CH_2OTBS and NCH_2Ph), 3.83–3.70 [m, 3 H, -CH_2OTBS, -CH(OH)CH_2OTBS, and NCHCH=CH-], 3.46 (d, *J* = 12.8 Hz, 1 H, -NCH_2Ph), 3.43 (d, *J* = 12.8 Hz, 1 H, NCH_2CH=CH-), 3.29 (d, *J* = 12.8 Hz, 1 H, NCH_2CH=CH-), 1.45 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 0.93 (s, 9 H, *t*BuSi), 0.11 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.4 (C_q-Ph), 130.1 (NCH_2CH=CH-), 129.7, 128.4, 127.6, 127.4 (Ph and NCH_2CH=*C*H-), 108.8 [$(CH_3)_2C(O)_2$], 78.8 (C-4), 76.9 (C-5), 71.4 [-CH(OH)CH_2OTBS], 69.6 (-CH_2OTBS), 65.0 (NCH_2CH=CH-), 60.6 (NCH_2Ph), 56.5 (NCHCH=CH-), 28.3 (CH_3), 25.9 [SiC(CH_3)$_3$], 25.7 (CH_3), 18.4 [SiC$(CH_3)_3$], –5.3 (SiCH_3), –5.2 (SiCH_3) ppm. MS (ESI): *m*/*z* = 434 $[M + H]^+$. HRMS (ESI): calcd. for $C_{24}H_{40}O_4NSi$ $[M + H]^+$ 434.27094; found 434.27211.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra for all compounds synthesized.

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