The organocatalytic [3+2] cycloaddition of azomethine ylides and α,β-unsaturated aldehydes as a convenient tool for the enantioselective synthesis of pyrrolizidines and indolizidines†‡

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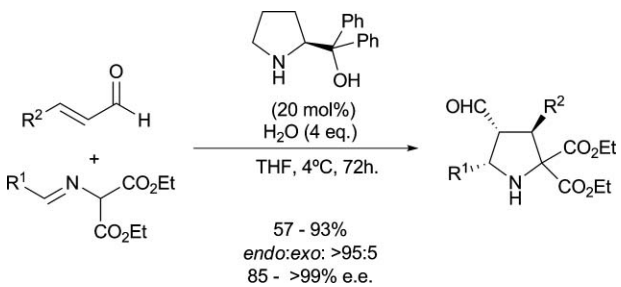
We have developed a simple and straightforward procedure for the enantioselective preparation of densely substituted bicyclic and tricyclic nitrogen heterocycles using conveniently substituted enantiopure pyrrolidines as common synthetic intermediates, which are easily accessible by our recently developed organocatalytic enantioselective [3+2] cycloaddition of α,β-unsaturated aldehydes and azomethine ylides. The designed synthetic pathway makes use of a ring-closing metathesis reaction for building up the pyrrolizidine and indolizidine skeletons, while the access to the hexahydrocyclopenta[*a*]pyrrolizine structure has been carried out relying on a fully diastereoselective intramolecular Pauson–Khand reaction.

Introduction

Asymmetric organocatalysis has emerged as a very powerful methodological approach for the enantioselective preparation of chiral compounds, and nowadays constitutes a very interesting alternative to the standard metal-catalyzed reactions.[1] Additional benefits of this methodology are associated to the compatibility of the catalyst and the intermediates participating in the catalytic cycle towards the presence of water (which turns into a more operationally simple experimental protocol), and to the fact that most of the organocatalysts usually employed are robust and air stable reagents. As a result of this, the last few years have witnessed an impressive growth of this particular field of research, with the development of a huge number of new methodologies which allow many different reactions to be carried out that were until that moment exclusively available under metal-centered Lewis acid catalysis.

However, despite the important advances in asymmetric organocatalysis, several issues still remain unsolved. In particular, the application of organocatalytic reactions to carry out key transformations in the context of the syntheses of complex molecules or natural products still remains rather unexplored,[2] although recent reports show a remarkable tendency to incorporate this methodology as a general instrument of the synthetic organic chemist's toolbox.[3] For this reason, we consider that the development of synthetic procedures for the preparation of basic organic skeletons using some of the organocatalytic reactions already developed in the literature as key steps, and especially the application of asymmetric organocatalysis to the stereocontrolled construction of heterocyclic structures containing multiple substituents in a simple and modular way is an area of particular interest which would also contribute to the progress of the field.

As a consequence of this, and in the context of our ongoing programs directed towards the enantioselective synthesis of nitrogen heterocycles,[4] we became interested in carrying out the asymmetric synthesis of pyrrolizidines and indolizidines containing multiple substituents as test molecules for us to check the applicability of our recently developed methodology for the organocatalytic enantioselective [3+2] cycloaddition reaction between azomethine ylides and α,β-unsaturated aldehydes (Scheme 1).[5]



Scheme 1 The organocatalytic enantioselective [3+2] cycloaddition reaction of azomethine ylides with enals developed in our group.

In this paper, we wish to report an efficient and very straightforward procedure for the enantioselective preparation of densely substituted indolizidines and pyrrolizidines starting from these pyrrolidine cycloadducts using simple and high-yielding transformations. In addition, we have also developed a protocol for the stereocontrolled synthesis of a more complex tricyclic compound with a hexahydrocyclopenta[*a*]pyrrolizine ring system containing multiple stereogenic centres using the same starting materials by using a fully diastereoselective intramolecular Pauson–Khand reaction as key step. The pyrrolizidine and indolizidine bicyclic frameworks constitute the basic structural features in a variety of

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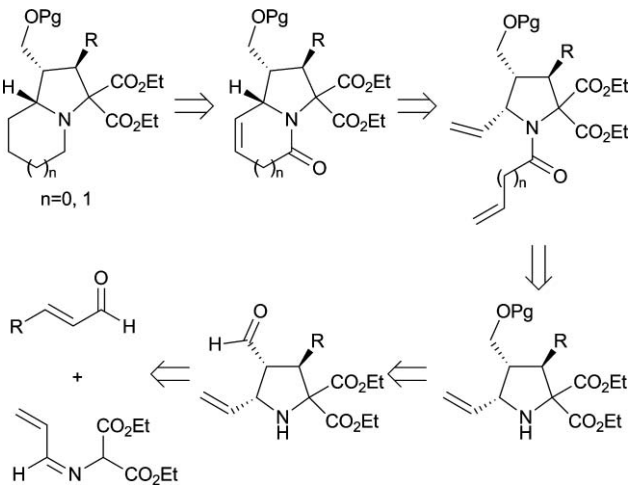
naturally occurring compounds[6] and the cyclopenta[*a*]pyrrolizine skeleton can be found in the structure of the myrmicarin family of natural products.[7]

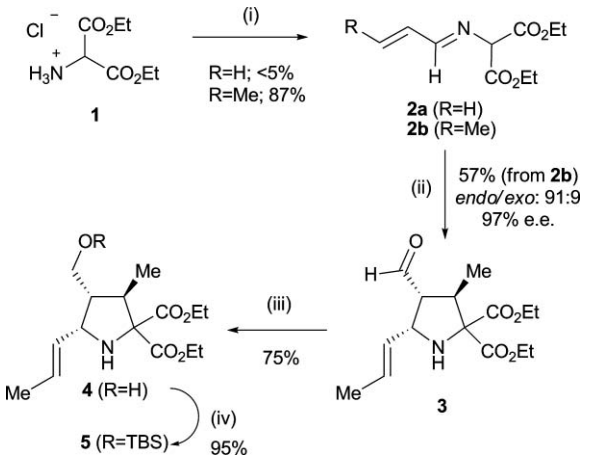
Results and discussion

The access to pyrrolizidines and indolizidines was planned according to the retrosynthetic approach shown in Scheme 2, in which a ring-closing metathesis reaction was proposed for the building-up of the bicyclic structure using a conveniently *N*-substituted pyrrolidine which incorporates an alkenyl substituent at the 5-position as a precursor. This compound should be easily prepared by means of our [3+2] cycloaddition protocol, using an α,β-unsaturated aldehyde as the dipolarophile, and the imine derived from diethyl aminomalonate and acrolein as the dipole precursor.



Scheme 2

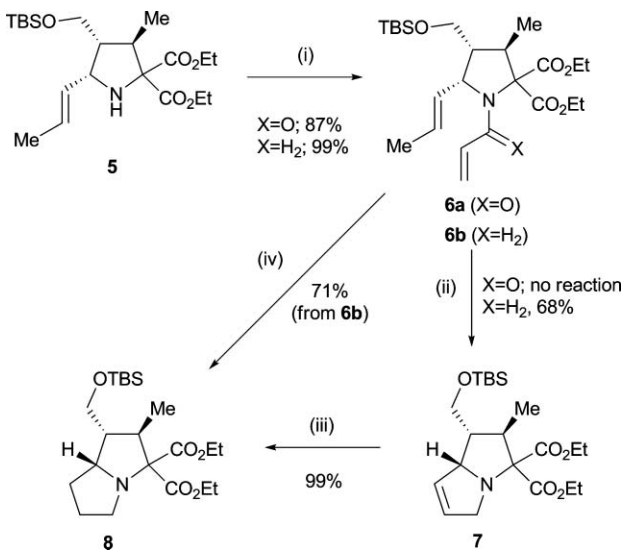
We started our work (Scheme 3) with the preparation of the diethyl aminomalonate-derived imine **2a** by condensation of the commercially available hydrochloride salt **1** with acrolein. However, after several attempts using different reaction conditions, we were not able to obtain **2a** in any case, probably because



Scheme 3 *Reagents and conditions*: (i) RCH=CHCHO, Et_3N, CH_2Cl_2, r.t. 72 h. (ii) (*S*)-α,α-diphenylprolinol (20 mol%), H_2O (4 eq.), THF, 4 °C, 72 h. (iii) $NaBH_4$, MeOH, 0 °C, 30 min. (iv) TBSCl, imidazole, DMAP (cat.), DMF, r.t., 8 h.

of the inherent instability of the product which is believed to undergo fast self-condensation. For this reason, we decided to use imine **2b** derived from crotonaldehyde as the starting material, which had already been successfully employed by us during our preliminary studies in the [3+2] cycloaddition reaction, and presuming that the presence of the additional methyl group at the unsaturated centre would not have a strongly negative effect in the ring-closing metathesis reaction proposed for the construction of the bicyclic framework. With imine **2b** in hand, we carried out the cycloaddition reaction with crotonaldehyde using (*S*)-α,α-diphenylprolinol as catalyst under the optimized conditions, obtaining pyrrolidine **3** in a moderate 57% yield but with excellent *endo*-selectivity and as a highly enantiopure material. We also carried out the reaction at higher scale (1 g of **2b**) obtaining cycloadduct **3** in exactly the same yield (57%). Reduction of the formyl group and subsequent *O*-protection as a TBS ether was carried out under standard conditions, furnishing smoothly compound **5** in excellent overall yield.

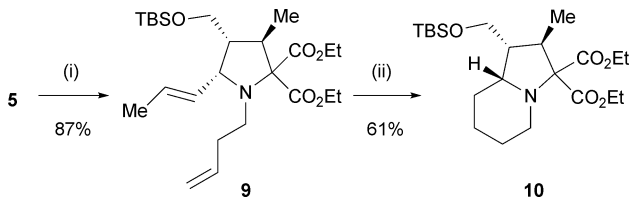
Next (Scheme 4), we proceeded to carry out the *N*-acylation of pyrrolidine **5** with acryloyl chloride and the obtained product **6a** was subjected to ring-closing metathesis reaction under different reaction conditions, which included the use of both first and second generation Grubbs catalysts and carrying out the reaction in boiling solvents. Disappointingly, no reaction was observed and the starting material was recovered unchanged in all cases. We attributed this lack of reactivity towards the metathesis reaction to the low reactivity of the α,β-unsaturated amide moiety and, for this reason, we decided to modify the synthetic route by installing an *N*-allyl substituent at the pyrrolidine precursor. Reaction of **5** with allyl iodide occurred smoothly, furnishing derivative **6b** which, upon treatment with second generation Grubbs catalyst in CH_2Cl_2 at r.t., furnished in a short reaction time the desired bicyclic product **7** in good yield.



Scheme 4 *Reagents and conditions*: (i) CH_2=CHCOCl or CH_2=$CHCH_2I$, K_2CO_3, CH_3CN, reflux, 3–4 h. (ii) 2nd Generation Grubbs cat. (5 mol%), CH_2Cl_2, r.t., 2 h. (iii) H_2 (1 atm), Pd/C (cat.), MeOH, r.t., 3 h. (iv) 1. 2nd Generation Grubbs cat. (5 mol%), CH_2Cl_2, r.t., 2 h. 2. H_2 (1 atm), Pd/C (cat.), MeOH, r.t., 2 h.

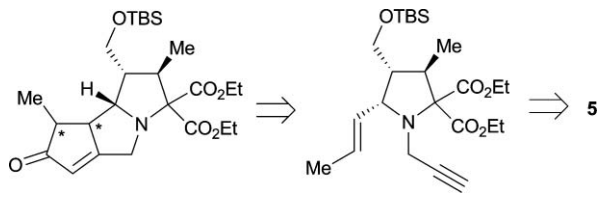
Finally, the target pyrrolizidine **8** was obtained in almost quantitative yield after catalytic hydrogenation. It has to be pointed out that the ^{1}H NMR analysis of the crude of the metathesis reaction indicated the presence of other regioisomeric pyrrolizidine byproducts which presumably had to be formed after C=C double bond migration. This could be avoided by carrying out the metathesis/hydrogenation sequence in a one-pot manner, obtaining **7** directly from **6b** in much better overall yield.

Once the synthetic pathway was fully optimized, we faced the synthesis of the closely related indolizidine derivative **10** starting from **5** (Scheme 5). Therefore, **5** was treated with homoallyl bromide in the same reaction conditions and the obtained *N*-homoallylated derivative **9** furnished the target compound **10** after the corresponding ring-closing metathesis/hydrogenation sequence in excellent yield. It also has to be mentioned that both final compounds, pyrrolizidine **8** and indolizidine **10**, were obtained as single diastereoisomers, which indicated that all the transformations performed in their synthesis from **5** proceeded with no epimerization at any of the stereogenic centres present at the starting material. This is of particular relevance, especially considering that the stereogenic centre present at the junction of both cycles can easily epimerize during the metathesis/hydrogenation sequence if it is involved in the C=C bond migration side reaction observed in the metathesis reaction when we isolated synthetic intermediate **7**.



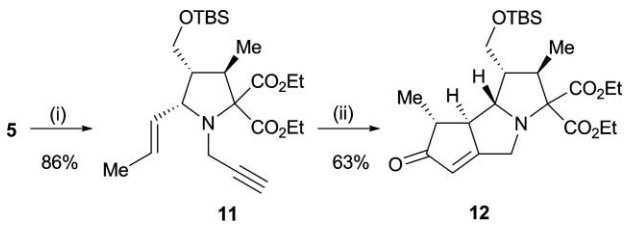
Scheme 5 *Reagents and conditions*: (i) CH_2=$CHCH_2CH_2Br$, K_2CO_3, KI (cat.), CH_3CN, reflux, 96 h. (ii) 1. 2nd Generation Grubbs cat. (5 mol%), CH_2Cl_2, r.t., 1 h. 2. H_2 (1 atm), Pd/C (cat.), MeOH, r.t., 10 h.

With an efficient synthetic protocol for the enantioselective synthesis of target pyrrolizidine and indolizidine heterocycles in hand, we faced next the possibility of building up the more complex cyclopenta[*a*]pyrrolizine tricyclic structure according to the retrosynthetic plan depicted in Scheme 6. Our proposal was essentially based on an intramolecular Pauson–Khand reaction with a conveniently substituted *N*-propargyl pyrrolidine, easily accessible from pyrrolidine cycloadduct **5**. This Pauson–Khand reaction implies the formation of two new stereogenic centres and, consequently, special attention has to be paid to employ the most appropriate reaction conditions which would enable achieving the highest possible diastereocontrol.



Scheme 6

Treating cycloadduct **5** with propargyl bromide under the conditions already employed before cleanly furnished derivative **11** (Scheme 7) and next, this compound was subjected to Pauson–Khand reaction with one equivalent of $Co_2(CO)_8$ using standard conditions (CH_2Cl_2 as solvent and at r.t.). After 1 h, complete consumption of the starting material was observed and, after elaboration with NMO for the oxidative cleavage of the organocobalt reaction intermediate and chromatographic purification, we were able to isolate hexahydrocyclopenta[*a*]pyrrolizine compound **12** in good yield and, more importantly, as a single diastereoisomer as NMR analysis of the crude reaction mixture indicated. This points towards the chiral information present at the structure of the precursor **11** being able to control very efficiently the stereochemical outcome of the intramolecular Pauson–Khand reaction. The configuration of the two newly generated stereogenic centres was established by the corresponding NOE difference experiment.



Scheme 7 *Reagents and conditions*: (i) Propargyl bromide, K_2CO_3, KI (cat.), CH_3CN, reflux, 9 h. (ii) 1. $Co_2(CO)_8$, CH_2Cl_2, r.t., 1 h. 2. NMO, CH_3CN, r.t., 2 h.

Conclusions

To sum up, we have demonstrated that our recently reported protocol for carrying out the organocatalytic enantioselective [3+2] cycloaddition between α,β-unsaturated aldehydes and azomethine ylides can be a reliable tool for the asymmetric synthesis of valuable nitrogen heterocycles such as pyrrolizidines, indolizidines and hexahydrocyclopenta[*a*]pyrrolizines containing multiple substituents. Our approach relies mainly on the preparation of a 2-alkenyl substituted pyrrolidine cycloadduct in which a conveniently functionalized side chain containing a C–C double or triple bond is subsequently introduced by a simple *N*-alkylation procedure. The bicyclic heterocycles (pyrrolizidines and indolizidines) can be built up by applying a ring-closing metathesis reaction and the access to the more complex hexahydro-2*H*-cyclopenta[*a*]pyrrolizin-9-one ring system can be achieved by intramolecular Pauson–Khand reaction. In the later case, two new stereogenic centres are formed in a fully diastereoselective way, demonstrating the ability of the preexisting stereogenic centres to control the stereochemical outcome of this reaction in a very efficient way.

Experimental section

General information

NMR spectra were recorded at 20–25 °C, running at 300 MHz for ^{1}H and 75 MHz for ^{13}C in $CDCl_3$ solution and resonances are reported in ppm relative to tetramethylsilane unless otherwise stated. The following abbreviations were used to designate

chemical shift multiplicities: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet, br = broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Assignments of individual signals were carried out using COSY, HMQC, DEPT and NOESY experiments. IR spectra were obtained by depositing a film on a KBr plate. Mass spectra were recorded under electron impact (EI) or chemical ionization (CI) at 70 eV. Optical rotations were recorded in solution in a 1 dm length cell using a Na lamp in the solvent and concentration indicated in each case, and values are given in 10^{-1} deg cm^2 g^{-1}. TLC was carried out with 0.2 mm thick silica gel plates (Merck Kiesegel F_{254}) and visualization was accomplished by UV light or by spraying with phosphomolybdic acid. Flash column chromatography on silica gel was performed with Merck Kiesegel 60 (230–400 mesh). All solvents used in reactions were dried and purified according to standard procedures. All other reagents were used as purchased. All air- or moisture-sensitive reactions were performed under argon. The glassware was oven dried (140 °C) overnight and purged with argon prior to use. Enantiomeric excesses (e.e.) were determined by HPLC under conditions specified in each case.

Diethyl 2-butenylideneaminomalonate (2b)

Et_3N (1.32 mL, 9.45 mmol) and crotonaldehyde (0.78 mL, 9.45 mmol) were added to a stirred suspension of diethyl aminomalonate hydrochloride **1** (2.00 g, 9.45 mmol) in CH_2Cl_2 (20 mL) at 0 °C. Na_2SO_4 was added and the suspension was stirred for 72 h at r.t., after which the crude reaction mixture was filtered and the solvent was removed under reduced pressure. Et_2O (20 mL) was added over the resulting slurry and this ethereal phase was washed with water (3 × 10 mL), after which it was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. Imine **2b** (2.06 g, 8.22 mmol) was obtained as a yellowish oil and was used in the following step without further purification. Yield: 87%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (m, 6H, CH_3CH$_2$O), 1.62 (d, 3H, J = 4.6 Hz, CH_3CH=CH), 3.10 (s, 1H, CH(CO$_2$Et)$_2$), 4.22 (m, 4H, CH$_3$CH_2O), 5.37 (t, 1H, J = 6.6 Hz, CHCH=CH), 5.60 (m, 1H, CH=CHCH$_3$), 8.60 (d, J = 3.0 Hz, 1H, CH=N). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 14.0 (*C*H$_3$CH$_2$O), 15.8 (*C*H$_3$CH=CH), 62.0, 64.0 (CH$_3$*C*H$_2$O), 75.1 (*C*H(CO$_2$Et)$_2$), 128.0 (*C*H=CH), 130.2 (CH=*C*H)), 169.1 (CH=N), 171.4, 171.9 (CO$_2$Et).

Diethyl (3*R*,4*R*,5*R*)-4-formyl-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (3)

Crotonaldehyde (0.28 mL, 3.39 mmol) was added over a solution of (*S*)-α,α-diphenylprolinol (0.18 g, 0.68 mmol) in THF (3 mL) at r.t. and, after stirring for 30 min at this temperature, the reaction was cooled to 4 °C, and imine **2b** (1.00 g, 4.41 mmol) and H_2O (0.24 mL, 13.56 mmol) were added at once. After stirring for 72 h, the solvent was removed under reduced pressure and the crude reaction mixture was subjected directly to flash column chromatography purification (hexane–AcOEt 8 : 2), affording pyrrolidine **3** (0.58 g, 1.93 mmol) as a colorless oil. Yield: 57%. IR: ν_{max}(film)/cm^{-1}: 1630 (C=O), 1725 (C=O), 3329 (NH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.10 (d, 3H, J = 6.8 Hz, CH_3CH), 1.26 (t, 6H, J = 7.1 Hz, CH_3CH$_2$O), 1.64 (d, 3H, J = 6.8 Hz, CH_3CH=CH), 2.81 (m, 2H, CH$_3$CH+OH), 3.14 (m, 1H, CHCHO), 4.27 (m, 4H, CH$_3$CH_2O), 4.34 (m, 1H, CHN), 5.33 (m, 1H, CH=CH), 5.97 (m, 1H, CH=CH), 9.58 (d, 1H, J = 2.7 Hz, CHO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (*C*H$_3$CH), 14.1, 15.0 (*C*H$_3$CH$_2$O), 17.6 (*C*H$_3$CH=CH), 38.9 (*C*HCH$_3$), 60.3 (CHN), 60.8 (*C*HCHO), 61.6, 61.7 (CH$_3$*C*H$_2$O), 74.7 (*C*(CO$_2$Et)$_2$), 128.9 (*C*H=CH), 129.6 (CH=*C*H), 170.2, 171.3 (CO$_2$Et), 201.7 (CHO). MS (EI) [*m*/*z* (rel. abundance)]: 297 (M$^+$, 4), 224 (100), 178 (9), 150 (16), 122 (12), 107 (8), 95 (8), 80 (11), 55 (7). HRMS: *m*/*z* calculated for [$C_{15}H_{23}NO_5$]$^+$ is 297.1576; found: 297.1574.

The synthesis of **3** (0.77 g, 2.60 mmol, 57% Yield) was also carried out at higher scale according to the same experimental procedure using crotonaldehyde (0.73 mL, 8.82 mmol), (*S*)-α,α-diphenylprolinol (0.22 g, 0.88 mmol) imine **2b** (1.00 g, 4.41 mmol) and H_2O (317 μL, 17.64 mmol) in THF (20 mL)

Diethyl (3*R*,4*R*,5*R*)-4-hydroxymethyl-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (4)

$NaBH_4$ (0.05 g, 1.21 mmol) was added at once over a cooled (0 °C) solution of **3** (0.30 g, 1.01 mmol) in MeOH (10 mL) and the mixture was stirred for 30 min at this temperature, after which a saturated NH_4Cl aqueous solution (10 mL) and CH_2Cl_2 (10 mL) were added. After stirring the biphasic mixture for further 30 min, the layers were separated and brine (10 mL) was added to the aqueous phase, which was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **4** (0.24 g, 0.78 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 6 : 4). Chiral HPLC analysis indicated that **4** was obtained with a 97% e.e. (Chiralcel OD column, 1.00 mL min^{-1}, hexane–*i*PrOH 95 : 5. Major isomer: t_R = 9.18 min; minor isomer: t_R = 11.06 min). Yield: 75%. $[\alpha]_D^{20}$ = +6.0 (c = 1.0, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1724 (C=O), 3353 (OH + NH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.11 (d, 3H, J = 6.9 Hz, CH_3CH), 1.26 (m, 6H, CH_3CH$_2$O), 1.69 (d, 3H, J = 6.1 Hz, CH_3CH=CH), 1.87 (s br, 1H, OH/NH), 2.10 (m, 1H, CH$_3$CH), 2.74 (m, 2H, CHCH$_2$OH+OH/NH), 3.67 (m, 2H, CH_2OH), 4.11 (m, 1H, CHN), 4.20 (m, 4H, CH$_3$CH_2O), 5.50 (m, 1H, CH=CH), 5.68 (m, 1H, CH=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (*C*H$_3$CH), 14.2, 15.5 (*C*H$_3$CH$_2$O), 17.8 (*C*H$_3$CH=CH), 40.1 (*C*HCH$_3$), 51.0 (*C*HCH$_2$OH), 61.0 (CHN), 61.5, 61.6 (CH$_3$*C*H$_2$O), 61.9 (CH$_2$OH), 74.9 (*C*(CO$_2$Et)$_2$), 128.1 (*C*H=CH), 130.7 (CH=*C*H), 171.0, 171.7 (CO$_2$Et). MS (EI) [*m*/*z* (rel. abundance)]: 299 (M$^+$, 2), 253 (4), 226 (100), 194 (7), 180 (14), 154 (11), 134 (14), 120 (10), 95 (9), 55 (6). Anal. Calculated for $C_{15}H_{25}NO_5$: C, 60.18; H, 8.42; N, 4.68. Found: C, 60.23; H, 8.47; N, 4.59.

Diethyl (3*R*,4*R*,5*R*)-4-(*tert*-butyldimethylsilyloxymethyl)-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (5)

Imidazole (0.14 g, 2.06 mmol) and TBSCl (0.31 mL, 2.06 mmol) were sequentially added over a solution of **4** (0.21 g, 0.69 mmol) and DMAP (4 mg, 0.03 mmol) in dry DMF (10 mL) at r.t. After stirring at this temperature for 8 h, water (10 mL) was added and the mixture was extracted with Et_2O (3 × 15 mL). The combined organic layers were collected, washed sequentially

with a saturated $NaHCO_3$ solution (1 × 15 mL), brine (1 × 15 mL) and water (1 × 15 mL), dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **5** (0.27 g, 0.66 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 9 : 1). Yield: 95%. $[\alpha]_D^{20} = +20.7$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1735 (C=O), 2937 (NH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01 (s, 3H, $(CH_3)_2Si$), 0.02 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.09 (d, 3H, $J = 7.0$ Hz, CH_3CH), 1.25 (t, 6H, $J = 7.1$ Hz, CH_3CH$_2$O), 1.63 (d, 3H, $J = 6.0$ Hz, CH_3CH=CH), 2.11 (m, 1H, CH$_3$CH), 2.63 (m, 1H, CHCH$_2$OTBS), 2.76 (s, 1H, NH), 3.54 (d, 2H, $J = 6.2$ Hz, CH$_2$OTBS), 3.99 (d, 1H, $J = 7.8$ Hz, CHN), 4.27 (m, 4H, CH$_3$CH_2O), 5.46 (m, 2H, CH=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.6, −5.5 ($(CH_3)_2Si$), 13.9, 14.1 (CH_3CH_2O), 15.1 (CH_3CH), 17.7 (CH_3CH=CH), 18.1 ($(CH_3)_3C$), 25.8 ($(CH_3)_3C$), 40.6 ($CHCH_3$), 50.7 ($CHCH_2OTBS$), 61.3, 61.4 (CH_3CH_2O), 61.5 (CHN), 62.0 (CH_2OTBS), 75.0 ($C(CO_2Et)_2$), 126.6 (CH=CH), 131.1 (CH=CH), 171.2, 171.9 (CO_2Et). MS (CI) [m/z (rel. abundance)]: 414 (M^++H, 100), 398 (24), 356 (17), 340 (52), 328 (9), 282 (6), 208 (6), 103 (3). HRMS: m/z calculated for $[C_{21}H_{40}NO_5Si]^+$ (M^++H) is 414.2676; found: 414.2660.

Diethyl (3*R*,4*R*,5*R*)-1-acryloyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (6a)

A solution of **5** (0.30 g, 0.72 mmol) in dry CH_3CN (5 mL) was added over a suspension of K_2CO_3 (0.16 g, 1.15 mmol) in the same solvent (10 mL) and the mixture was refluxed for 2 h, after which acryloyl chloride (0.21 mL, 2.51 mmol) was added at once. Refluxing was maintained for further 2 h and next the reaction was cooled down to r.t. and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **6a** (0.29 g, 0.63 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 1 : 1). Yield: 87%. $[\alpha]_D^{20} = +26.9$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1735, 1658 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 6H, $(CH_3)_2Si$), 0.89 (s, 9H, $(CH_3)_3C$), 1.15 (d, 3H, $J = 6.7$ Hz, CH_3CH), 1.27 (m, 6H, CH_3CH$_2$O), 1.71 (d, 3H, $J = 6.3$ Hz, CH_3CH=CH), 2.30 (m, 1H, CHCH$_2$OSi), 2.50 (m, 1H, CH$_3$CH), 3.55 (m, 2H, CH$_2$OSi), 4.25 (m, 4H, CH$_3$CH_2O), 4.64 (m, 1H, CHN), 5.36-6.73 (m, 5H, CH$_3$CH=CH+CH_2=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −3.7 ($(CH_3)_2Si$), 13.0, 13.9 (CH_3CH_2O), 14.1 (CH_3CH), 17.8 (CH_3CH=CH), 17.9 ($(CH_3)_3C$), 25.6 ($(CH_3)_3C$), 41.5 ($CHCH_3$), 49.5 ($CHCH_2OSi$), 60.6 (CH_2OSi), 61.5, 61.6 (CH_3CH_2O), 62.6 (CHN), 74.7 ($C(CO_2Et)_2$), 127.2 (CH$_3$CH=CH), 128.1 (CH$_3$CH=CH), 128.7 (CH_2=CH), 129.6 (CH$_2$=CH), 165.2 (CON), 166.9, 168.2 (CO_2Et). MS (CI) [m/z (rel. abundance)]: 468 (M^++H, 100), 452 (14), 410 (42), 394 (19), 354 (20), 280 (12), 226 (7). HRMS: m/z calculated for $[C_{18}H_{43}NO_5Si]^+$ (M^++H) is 468.2781; found: 468.2805.

Diethyl (3*R*,4*R*,5*R*)-1-allyl-4-(*tert*-butyldimethylsilyloxymethyl)-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (6b)

A solution of **5** (0.29 g, 0.70 mmol) in dry CH_3CN (5 mL) was added over a suspension of K_2CO_3 (0.31 g, 2.24 mmol) in the same solvent (10 mL) and the mixture was refluxed for 2 h, after which allyl iodide (0.26 mL, 2.80 mmol) was added at once. Refluxing was maintained for further 90 min, and next the reaction was cooled down to r.t. and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **6b** (0.31 g, 0.69 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 9.5 : 0.5). Yield: 99%. $[\alpha]_D^{20} = +1.5$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1740 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.00 (s, 3H, $(CH_3)_2Si$), 0.01 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.06 (d, 3H, $J = 6.9$ Hz, CH_3CH), 1.26 (m, 6H, CH_3CH$_2$O), 1.63 (dd, 3H, $J = 0.9$, 6.1 Hz, CH_3CH=CH), 2.25 (m, 1H, CHCH$_2$OTBS), 2.64 (m, 1H, CH$_3$CH), 3.50 (m, 5H, CHN+CH$_2$OTBS+CH$_2$N), 4.20 (m, 4H, CH$_3$CH_2O), 4.90 (m, 2H, CH_2=CH), 5.33 (m, 1H, CH$_3$CH=CH), 5.43 (m, 1H, CH$_3$CH=CH), 5.78 (m, 1H, CH$_2$=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.6, −5.5 ($(CH_3)_2Si$), 14.1, 14.3 (CH_3CH_2O), 14.8 (CH_3CH), 17.7 (CH_3CH=CH), 18.1 ($(CH_3)_3C$), 25.9 ($(CH_3)_3C$), 42.2 ($CHCH_3$), 48.7 ($CHCH_2OTBS$), 53.3 (CH_2N), 60.7, 61.0 (CH_3CH_2O), 62.4 (CH_2OTBS), 68.1 (CHN), 78.8 ($C(CO_2Et)_2$), 114.3 (CH_2=CH), 127.0 (CH$_3$CH=CH), 131.5 (CH$_3$CH=CH), 138.1 (CH$_2$=CH), 170.4, 170.7 (CO_2Et). MS (CI) [m/z (rel. abundance)]: 453 (M^++H, 11), 438 (11), 381 (25), 380 (100). HRMS: m/z calculated for $[C_{24}H_{43}NO_5Si]^+$ (M^++H) is 453.2911; found: 453.2920.

Diethyl (1*R*,2*R*,7a*R*)-1-(*tert*-butyldimethylsilyloxymethyl)-2-methyl-1,2,5,7a-tetrahydropyrrolizine-3,3-dicarboxylate (7)

A solution of **6b** (0.12 g, 0.26 mmol) in dry CH_2Cl_2 (25 mL) and second generation Grubbs catalyst (11 mg, 0.01 mmol) was stirred at r.t. for 90 min. Next, the mixture was filtered and the solvent was removed under reduced pressure. Compound **7** (0.07 g, 0.18 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 8 : 2). Yield: 68%. $[\alpha]_D^{20} = +48.3$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1737 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.02 (s, 6H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.05 (d, 3H, $J = 6.1$ Hz, CH_3CH), 1.27 (m, 6H, CH_3CH$_2$O), 2.12 (m, 2H, CH$_3$CH+CHCH$_2$OTMS), 3.29 (dd, 1H, $J = 5.8$, 14.3 Hz, CH_AH$_B$N), 3.46 (dd, 1H, $J = 4.7$, 14.3 Hz, CH_AH$_B$OTBS), 3.59 (dd, 1H, $J = 4.7$, 14.3 Hz, CH$_A$H$_B$OTBS), 3.84 (dd, 1H, $J = 1.8$, 14.3 Hz, CH$_A$H$_B$N), 4.23 (m, 4H, CH$_3$CH_2O), 4.71 (m, 1H, CHN), 5.69 (m, 1H, CH=CH), 5.80 (m, 1H, CH=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.55, −5.47 ($(CH_3)_2Si$), 13.9, 14.2 (CH_3CH_2O), 14.9 (CH_3CH), 18.1 ($(CH_3)_3C$)), 25.8 ($(CH_3)_3C$)), 40.1 ($CHCH_3$), 50.4 ($CHCH_2OTBS$), 58.7 (CH_2N), 61.2, 61.3 (CH_3CH_2O), 63.4 (CH_2OTBS), 72.7 (CHN), 81.4 ($C(CO_2Et)_2$), 126.9 (CH=CH), 128.4 (CH=CH), 168.6, 169.6 (CO_2Et). MS (CI) [m/z (rel. abundance)]: 412 (M^++H, 100), 396 (22), 354 (12), 338 (61), 280 (5), 225 (25), 206 (4), 168 (4). HRMS: m/z calculated for $[C_{21}H_{38}NO_5Si]^+$ (M^++H) is 412.2519; found: 412.2524.

Diethyl (1*R*,2*R*,7a*R*)-1-(*tert*-butyldimethylsilyloxymethyl)-2-methyltetrahydro-1*H*-pyrrolizine-3,3(2*H*)-dicarboxylate (8)

A solution of **7** (0.07 g, 0.18 mmol) in MeOH (10 mL) was stirred in the presence of Pd/C (10 mg) under a H_2 atmosphere

(balloon) at r.t. for 2 h. Next, the mixture was filtered and the solvent was removed under reduced pressure. Compound **9** (0.07 g, 0.18 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 8 : 2). Yield: 99%. $[\alpha]_D^{20} = +1.6$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1733 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.03 (s, 6H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.00 (d, 3H, $J = 6.7$ Hz, CH_3CH), 1.26 (m, 6H, CH_3CH$_2$O), 1.57 (m, 1H, CH_AH$_B$CHN), 1.78 (m, 3H, CH_2CH$_2$N+CH$_A$$H_B$CHN), 2.07 (m, 1H, C$HCH_2$OTBS), 2.40 (m, 2H, CH$_3CH$+C$H_AH_B$N), 3.07 (m, 1H, CH$_A$$H_B$N), 3.60 (dd, 1H, $J = 7.8$, 10.3 Hz, CH_AH$_B$OTBS), 3.70 (dd, 1H, $J = 5.0$, 10.3 Hz, CH$_A$$H_B$OTBS), 3.89 (m, 1H, CHN), 4.26 (m, 4H, CH$_3$CH_2O). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.6, −5.5 ($(CH_3)_2Si$), 13.9, 14.2 (*C*H$_3$CH$_2$O), 14.5 (*C*H$_3$CH), 18.1 ((*C*H$_3$)$_3$C)), 25.8 ((CH$_3$)$_3$*C*)), 25.9 (*C*H$_2$CH$_2$N), 27.0 (*C*H$_2$CHN), 38.8 (CH$_3$*C*H), 47.3 (*C*HCH$_2$OTBS), 51.2 (CH$_2$N), 61.0, 61.2 (CH$_3$*C*H$_2$O), 62.2 (CH$_2$OTBS), 65.8 (CHN), 80.5 (*C*(CO$_2$Et)$_2$), 168.6, 170.1 (CO$_2$Et). MS (CI) [*m*/*z* (rel. abundance)]: 414 (M$^+$+H, 68), 398 (22), 356 (14), 340 (100), 282 (3), 208 (2). HRMS: *m*/*z* calculated for $[C_{21}H_{40}NO_5Si]^+$ (M$^+$+H) is 414.2676; found: 414.2665.

Pyrrolizidine **8** (0.54 g, 1.30 mmol, 71% yield) was also prepared directly from **6b** (0.83 g, 1.84 mmol) following the same procedure as described for **7** and subsequently carrying out the hydrogenation of the crude reaction mixture as described.

Diethyl (3*R*,4*R*,5*R*)-1-(1-but-3-enyl)-4-(*tert*-butyldimethylsilyloxymethyl)-3-methyl-5-((*E*)-1-propenyl)pyrrolidine-2,2-dicarboxylate (9)

A solution of **5** (0.39 g, 0.94 mmol) in dry CH_3CN (5 mL) was added over a suspension of K_2CO_3 (0.26 g, 1.88 mmol) and KI (8 mg, 0.05 mmol) in the same solvent (10 mL) and the mixture was refluxed for 2 h, after which 4-bromo-1-butene (0.38 mL, 3.76 mmol) was added at once. Refluxing was maintained for a further 96 h, and next the reaction was cooled down to r.t. and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **9** (0.29 g, 0.62 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 9.5 : 0.5). Yield: 67%. $[\alpha]_D^{20} = +34.5$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1729 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01 (s, 3H, $(CH_3)_2Si$), 0.02 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.04 (d, 3H, $J = 6.9$ Hz, CH_3CH), 1.25 (m, 6H, CH_3CH$_2$O), 1.65 (d, 3H, $J = 5.5$ Hz, CH_3CH=CH), 2.15 (m, 2H, CH_2CH$_2$N), 2.28 (m, 1H, CHCH$_2$OSi), 2.60 (m, 1H, CH$_3$CH), 2.75 (m, 1H, CH_AH$_B$N), 2.97 (m, 1H, CH$_A$$H_B$N), 3.50 (m, 2H, C$H_2$OTBS), 3.63 (m, 1H, CHN), 4.20 (m, 4H, CH$_3$CH_2O), 4.93 (m, 2H, CH_2=CH), 5.48 (m, 2H, CH=CHCH$_3$), 5.72 (m, 1H, CH$_2$=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.6, −5.5 ($(CH_3)_2Si$), 14.0, 14.3 (*C*H$_3$CH$_2$O), 14.6 (*C*H$_3$CH), 17.6 (*C*H$_3$CH=CH), 18.2 ((*C*H$_3$)$_3$C), 25.8 ((CH$_3$)$_3$*C*), 35.1 (*C*H$_2$CH$_2$N), 41.7 (CH$_3$*C*H), 48.6 (*C*HCH$_2$OTBS), 51.6 (CH$_2$N), 60.9, 61.6 (CH$_3$*C*H$_2$O), 62.1 (CH$_2$OTBS), 69.0 (CHN), 79.6 (*C*(CO$_2$Et)$_2$), 114.8 (*C*H$_2$=CH), 126.0 (CH$_3$*C*H=CH), 132.9 (CH$_3$CH=*C*H), 137.2 (CH$_2$=*C*H), 170.4, 170.6 (CO$_2$Et). MS (CI) [*m*/*z* (rel. abundance)]: 468 (M$^+$+H, 25), 466 (6), 452 (10), 426 (100), 410 (6), 394 (34). HRMS: *m*/*z* calculated for $[C_{25}H_{45}NO_5Si]^+$ (M$^+$+H) is 468.3156; found: 468.3145.

Diethyl (1*R*,2*R*,8a*R*)-1-(*tert*-butyldimethylsilyloxymethyl)-2-methylhexahydroindolizine-3,3(5*H*)-dicarboxylate (10)

A solution of **9** (0.11 g, 0.23 mmol) in dry CH_2Cl_2 (25 mL) and second generation Grubbs catalyst (9.7 mg, 0.01 mmol) was stirred at r.t. for 60 min. The mixture was filtered and the solvent was removed under reduced pressure. The crude mixture was dissolved in MeOH (10 mL) and the reaction was stirred in the presence of Pd/C (10 mg) under a H_2 atmosphere (balloon) at r.t. for 10 h. Next, the mixture was filtered and the solvent was removed under reduced pressure. Compound **10** (0.06 g, 0.14 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 9.5 : 0.5). Yield: 61%. $[\alpha]_D^{20} = +35.9$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1727 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01 (s, 3H, $(CH_3)_2Si$), 0.02 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.22 (m, 9H, CH_3CH+CH_3CH$_2$O), 1.51 (m, 2H, CH_2CH$_2$N), 1.76 (m, 2H, CH_2CH$_2$CH$_2$N), 2.10 (m, 3H, CH_2CHN+CHCH$_2$OTBS), 2.88 (m, 1H, CH$_3$CH), 3.35 (m, 1H, CHN), 3.46 (dd, 1H, $J = 7.0$, 9.8 Hz, CH_AH$_B$OTBS), 3.69 (dd, 1H, $J = 6.8$, 9.8 Hz, CH$_A$$H_B$OTBS), 4.20 (m, 4H, CH$_3CH_2$O). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.5, −5.4 ($(CH_3)_2Si$), 14.0, 14.4 (*C*H$_3$CH$_2$O), 15.9 (*C*H$_3$CH), 18.2 ((*C*H$_3$)$_3$C), 24.9 (*C*H$_2$CH$_2$CH$_2$N), 25.7 (*C*H$_2$CH$_2$N), 25.9 ((CH$_3$)$_3$*C*), 27.3 (*C*H$_2$CHN), 44.4 (*C*HCH$_3$), 48.3 (*C*HCH$_2$OTBS), 48.7 (CH$_2$N), 60.1, 60.8 (CH$_3$*C*H$_2$O), 62.4 (CHN), 64.4 (CH$_2$OTBS), 78.1 (*C*(CO$_2$Et)$_2$), 167.4, 170.5 (CO$_2$Et). MS (EI) [*m*/*z* (rel. abundance)]: 427 (M$^+$, 1), 412 (1), 368 (1), 354 (100), 342 (1), 298 (1), 268 (6), 222 (3), 148 (5), 134 (4), 73 (6). Anal. Calculated for $C_{22}H_{41}NO_5Si$ is C, 61.79; H, 9.66; N, 3.28; found: C, 61.86; H, 9.36; N, 3.48.

Diethyl (3*R*,4*R*,5*R*)-4-(*tert*-butyldimethylsilyloxymethyl)-3-methyl-5-((*E*)-1-propenyl)-1-(1-prop-2-ynyl)pyrrolidine-2,2-dicarboxylate (11)

A solution of **5** (0.36 g, 0.87 mmol) in dry CH_3CN (10 mL) was added over a suspension of K_2CO_3 (0.24 g, 1.74 mmol) and KI (7 mg, 0.04 mmol) in the same solvent (20 mL) and the mixture was refluxed for 2 h, after which propargyl bromide (0.39 mL, 3.48 mmol) was added at once. Refluxing was maintained for a further 7 h, and next the reaction was cooled down to r.t. and water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Compound **11** (0.34 g, 0.74 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 9 : 1). Yield: 86%. $[\alpha]_D^{20} = +25.8$ ($c = 1.0$, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1730 (C=O), 3303 (C–H$_{alkyne}$) ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.01 (s, 3H, $(CH_3)_2Si$), 0.02 (s, 3H, $(CH_3)_2Si$), 0.87 (s, 9H, $(CH_3)_3C$), 1.18 (d, 3H, $J = 6.4$ Hz, CH_3CH), 1.27 (m, 6H, CH_3CH$_2$O), 1.68 (dd, 3H, $J = 1.3$, 6.4 Hz, CH_3CH=CH), 2.08 (t, 1H, $J = 2.4$ Hz, *H*CCCH$_2$), 2.35 (m, 2H, CH$_3$CH+CHCH$_2$OTBS), 3.70 (m, 5H, CHCH=CH+CH$_2$OTBS+CH$_2$N), 4.27 (m, 4H, CH$_3$CH_2O), 5.30 (m, 1H, CH=CH), 5.64 (m, 1H, CH=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.6, −5.5 ($(CH_3)_2Si$), 14.0, 14.1 (*C*H$_3$CH$_2$O), 14.3 (*C*H$_3$CH), 17.7 (*C*H$_3$CH=CH), 18.2 ((*C*H$_3$)$_3$C), 25.8 ((CH$_3$)$_3$*C*), 36.7 (CH$_2$N), 42.8 (*C*HCH$_3$), 48.4 (*C*HCH$_2$OTBS), 60.7, 61.0 (CH$_3$*C*H$_2$O), 62.5 (CH$_2$OTBS), 64.9 (CHN), 71.2 (H*C*C), 76.7

($C(CO_2Et)_2$), 80.5 (HC*C*), 128.5 (*C*H=CH), 129.8 (CH=*C*H), 168.4, 170.5 (CO_2Et). MS (CI) [*m*/*z* (rel. abundance)]: 452 (M^++H, 100), 436 (17), 412 (12), 394 (13), 378 (100), 320 (8), 286 (92), 265 (47), 246 (5), 189 (7). HRMS: *m*/*z* calculated for $[C_{24}H_{42}NO_5Si]^+$ (M^++H) is 452.2832; found: 452.2822.

Diethyl (1*R*,2*R*,8*R*,8a*R*,8b*R*)-1-(*tert*-butyldimethylsilyloxymethyl)-2,8-dimethyl-7-oxo-1,5,7,8,8a,8b-hexahydro-2*H*-cyclopenta[*a*]pyrrolizine-3,3-dicarboxylate (12)

$Co_2(CO)_8$ (0.13 g, 0.37 mmol) was added over a solution of **11** (0.14 g, 0.31 mmol) in dry CH_2Cl_2 (10 mL) at r.t. and the mixture was stirred at this temperature for 1 h. Next, the solvent was removed under reduced pressure and the crude mixture was dissolved in MeCN (10 mL). NMO (0.36 g, 3.10 mmol) was added and the reaction was stirred for further 2 h, after which the solvent was again removed under reduced pressure. Compound **12** (0.09 g, 0.20 mmol) was obtained as a colorless oil after flash column chromatography purification (hexane–EtOAc 7 : 3). Yield: 63%. $[\alpha]_D^{20} = +50.2$ (c = 1.0, CH_2Cl_2). IR: ν_{max}(film)/cm^{-1}: 1715, 1731 (C=O) ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 6H, $(CH_3)_2Si$), 0.86 (s, 9H, $(CH_3)_3C$), 1.07 (d, 3H, J = 7.0 Hz, CH_3CH), 1.26 (m, 9H, CH_3CH$_2$O+CH_3CHCO), 2.15 (m, 2H, C*H*CH$_2$OTBS+CH$_3$C*H*CO), 2.65 (m, 1H, C*H*CHCO), 2.76 (m, 1H, CH$_3$C*H*), 3.55 (dd, 1H, J = 7.8, 10.1 Hz, CHN), 3.70 (m, 3H, CH_AH$_B$N+CH$_2$OTBS), 3.91 (d, 1H, J = 16.0 Hz, CH$_A$$H_B$N), 4.24 (m, 4H, CH$_3CH_2$O), 5.97 (s, 1H, CH=C). ^{13}C NMR (75 MHz, $CDCl_3$): δ −5.5, −5.3 ($(CH_3)_2Si$), 13.8, 14.0 (*C*H$_3$CH$_2$O), 14.2 (*C*H$_3$CHCO), 15.5 (*C*H$_3$CH), 18.2 ((*C*H$_3$)$_3$C), 25.8 ((CH$_3$)$_3$*C*), 42.6 (*C*HCH$_3$), 46.5 (*C*HCH$_2$OTBS), 47.2 (*C*HCO), 48.6 (CH$_2$N), 52.8 (*C*HCHCH$_2$OTBS), 61.2, 61.5 (CH$_3$*C*H$_2$O), 62.3 (CH$_2$OTBS), 70.9 (CHN), 77.8 ($C(CO_2Et)_2$), 124.2 (*C*H=C), 168.9, 169.6 (CO_2Et), 183.8 (CH=*C*CO), 212 (C=O). MS (CI) [*m*/*z* (rel. abundance)]: 480 (M^++H, 100), 478 (35), 468 (8), 464 (15), 422 (9), 406 (60), 372 (32), 332 (3). HRMS: *m*/*z* calculated for $[C_{25}H_{42}NO_6Si]^+$ (M^++H) is 480.2781; found: 480.2783.

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