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NHC-mediated cross-coupling of sugar-derived cyclic nitrones with enals: general and efficient synthesis of polyhydroxylated pyrrolizidines and indolizidines†

Wen-Yuan Xu,[a,c] Ren Iwaki,[b] Yue-Mei Jia,[a] Wei Zhang,[a] Atsushi Kato*[b] and Chu-Yi Yu*[a]

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A general and efficient method for the synthesis of polyhydroxylated pyrrolizidines and indolizidines has been developed based on the NHC-catalyzed cross-coupling of sugar-derived cyclic nitrones with enals, which afforded the key intermediates, γ-hydroxyl amino esters, in good to excellent yields. Thus, a variety of polyhydroxylated pyrrolizidines and indolizidines have been synthesized and assayed against various glycosidases, which showed that aryl or alkyl substituents at C-7 of pyrrolizidines or at C-8 of indolizidines reduced the potency of the glycosidase inhibition of these bicyclic iminosugars.

Introduction

Naturally-occurring polyhydroxylated pyrrolizidine and indolizidine alkaloids, the bicyclic iminosugars, and their derivatives[1] have attracted significant attentions due to their important bioactivities and potential clinical applications in treating diseases such as diabetes, lysosomal storage disorders and viral infections.[2] Important representatives of the naturally-occurring bicyclic iminosugars include casuarine (**1**) from *Casuarina equisetifolia*[3] (an inhibitor of α-glucosidase), hyacinthacine A_2 (**2**) from *Muscari armeniacum*[4] (an inhibitor of amyloglucosidase and lactase), castanospermine (**3**) from *Castanospermum australe*[5] (an inhibitor of α-glucosidases) and swainsonine (**4**) from *Swainsona canescens*[6] (an inhibitor of α-mannosidases) (Fig. 1).

Since a number of enantiomers[7] of the naturally-occurring iminosugars are found to be even more potent inhibitors of the same enzymes as themselves,[8] and/or inhibitors of different glycosidases,[9] the bicyclic iminosugars together with their enantiomers and analogues have attracted considerable attention.[10] Many efforts have thus been made on the synthesis of both the natural bicyclic iminosugars and the synthetic analogues including the enantiomers of the natural products.[11] However, there is still a lack of efficient methods for the synthesis of this kind of compounds, especially the diversity-oriented ones which are badly needed for the study of structure–activity relationships. More efforts are still required into the development of general and efficient methods for the synthesis of bicyclic iminosugars.

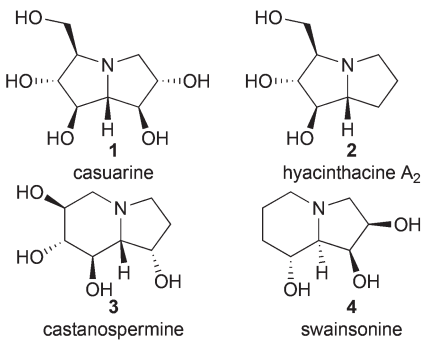


Fig. 1 Selected natural bicyclic polyhydroxylated alkaloids.

Among the numerous methods developed for the synthesis of polyhydroxylated alkaloids, those employing cyclic nitrones as key intermediates could be one of the most efficient strategies for the construction of this kind of compounds. This is because nitrones, with the ability to participate in a variety of synthetically useful reactions such as 1,3-dipolar cycloaddition, nucleophilic additions and cross-coupling reactions,[12] have proved to be powerful building blocks for the construction of numerous nitrogen-containing compounds, natural and/or synthetic.[13] In particular, sugar-derived cyclic nitrones[14] (Fig. 2) have already been shown to be powerful synthons for the synthesis of polyhydroxylated alkaloids, including polyhydroxylated pyrrolizidines and indolizidines.[15] Therefore, we are interested in developing novel and efficient methods for

[a]*Beijing National Laboratory for Molecular Science (BNLMS), CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100191, China. E-mail: yucy@iccas.ac.cn*
[b]*Department of Hospital Pharmacy, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan*
[c]*University of Chinese Academy of Sciences, Beijing 100049, China*
†Electronic supplementary information (ESI) available. See DOI: 10.1039/c3ob40696b

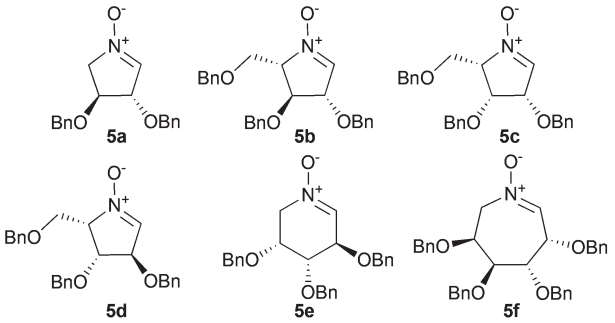


Fig. 2 Nitrones used in this study.

the synthesis of bicyclic iminosugars using sugar-derived cyclic nitrones as key intermediates.

To further exploit the potential applications of sugar-derived cyclic nitrones in the synthesis of iminosugars, we have recently been interested in the NHCs-catalysed coupling reactions of cyclic nitrones with enals, because the predictable products, γ-hydroxyl amino esters, could be versatile precursors of bicyclic iminosugars.

In the past decades, *N*-heterocyclic carbenes[16] (NHCs) have been extensively studied as versatile ligands in transition metal catalysis[17] and organocatalysts themselves.[18] An important application of NHCs is that they can react with enals to generate homoenolates, which are unique three-carbon synthons for unconventional C–C bond formation. Considerable excellent work has appeared focusing on the reactivity of NHC-mediated homoenolates,[19] but few examples have been used in natural product synthesis.[20] In 2008, Scheidt *et al.* reported the first use of NHCs in the cross-coupling reaction of nitrones with α,β-unsaturated aldehydes to afford γ-hydroxyl amino ester products.[21]

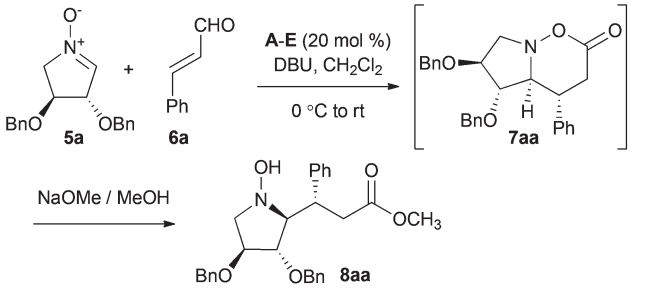
In the context of our continuing interests in iminosugars[22] and their derivatives,[23] herein we report a new method for the general and efficient synthesis of polyhydroxylated pyrrolizidines and indolizidines based on the NHC-catalyzed cross-coupling of sugar-derived cyclic nitrones with enals.

Results and discussion

Optimization of the reaction conditions

Nitrone **5a** and cinnamaldehyde **6a** were employed as the substrates for the investigation of optimal conditions of the coupling reactions, while a variety of different diazolium and triazolium salts have been explored as catalysts (Table 1). Under similar conditions, thiazolium salt **A** and diazolium salt **B** were found to be ineffective in catalysing the coupling reactions (Table 1, entry 1–2), while diazolium salt **C** was effective in catalysing the reaction which afforded the desired coupling product, γ-hydroxyl amino ester (**8aa**), in moderate yield (56%, Table 1, entry 3). Triazolium salt **D** showed similar efficiency as catalyst and the reaction took shorter time to finish, yielding the desired product in better yield with better diastereoselectivity (dr > 95 : 5) (Table 1, entry 4). Diazolium salt **E** can also effect the reaction but gave much poorer yield (Table 1, entry 5). Therefore, triazolium salt **D** was chosen as the catalyst for the coupling reactions.

Table 1 Optimization of reaction conditions[a]



Entry	Cat.	Time/h	Conv. (%)	Yield[b] (%)	dr[d]
1	**A**[c]	24	0	0	—
2	**B**[c]	24	0	0	—
3	**C**	24	99	56	>95 : 5
4	**D**	8	99	93	>95 : 5
5	**E**	24	30	20	>95 : 5

[a] 2 : 1 ratio of **5a** to **6a**; 20 mol% base. [b] Isolated yield. [c] Under different temperatures (−10 °C, 0 °C, 25 °C) and solvents (CH_2Cl_2, THF, EtOH), no reactions occurred. [d] dr determined by ^{1}H NMR spectroscopy.

It is worth noting that the coupling reaction of nitrone **5a** and cinnamaldehyde **6a** initially formed an intermediate, the six-membered-ring cyclic γ-hydroxylamine lactone **7aa**, which was isolable and found to be stable enough during purification on silica gel chromatography, and could be stored for months at below 0 °C. However, since lactone **7aa** can be easily transformed into the desired final product, *i.e.* γ-hydroxyl amino esters **8**, we decided not to separate the intermediate **7aa** in the latter study. Thus, γ-hydroxyl amino ester **8aa** was obtained in "one-pot" reaction when the reaction was immediately quenched with NaOMe–MeOH after the consumption of enals.

Scope of the substrates

To investigate the scope of the substrates, a variety of cyclic nitrones and enals were attempted in the coupling reactions under the optimal reaction conditions (Table 2). Although the (*Z*)-enals should have similar reactivities according to the reported homoenolate addition mechanism of this kind of reactions,[19a,24] only the readily available (*E*)-enals were used in our study. It was found that enals substituted with alkenyls or electron-rich aryls (*i.e.* **6a–d**) were good substrates for the coupling reaction with cyclic nitrones, while enals substituted with alkyls or electron-deficient aryls were poor substrates for the reactions, possibly due to the relatively poor nucleophilicity of the homoenolates formed from the addition of these substrates and NHC.

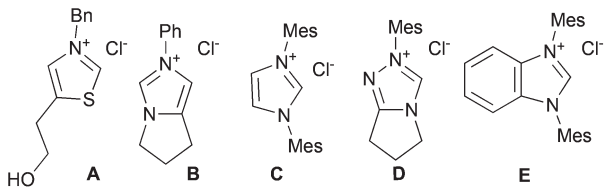
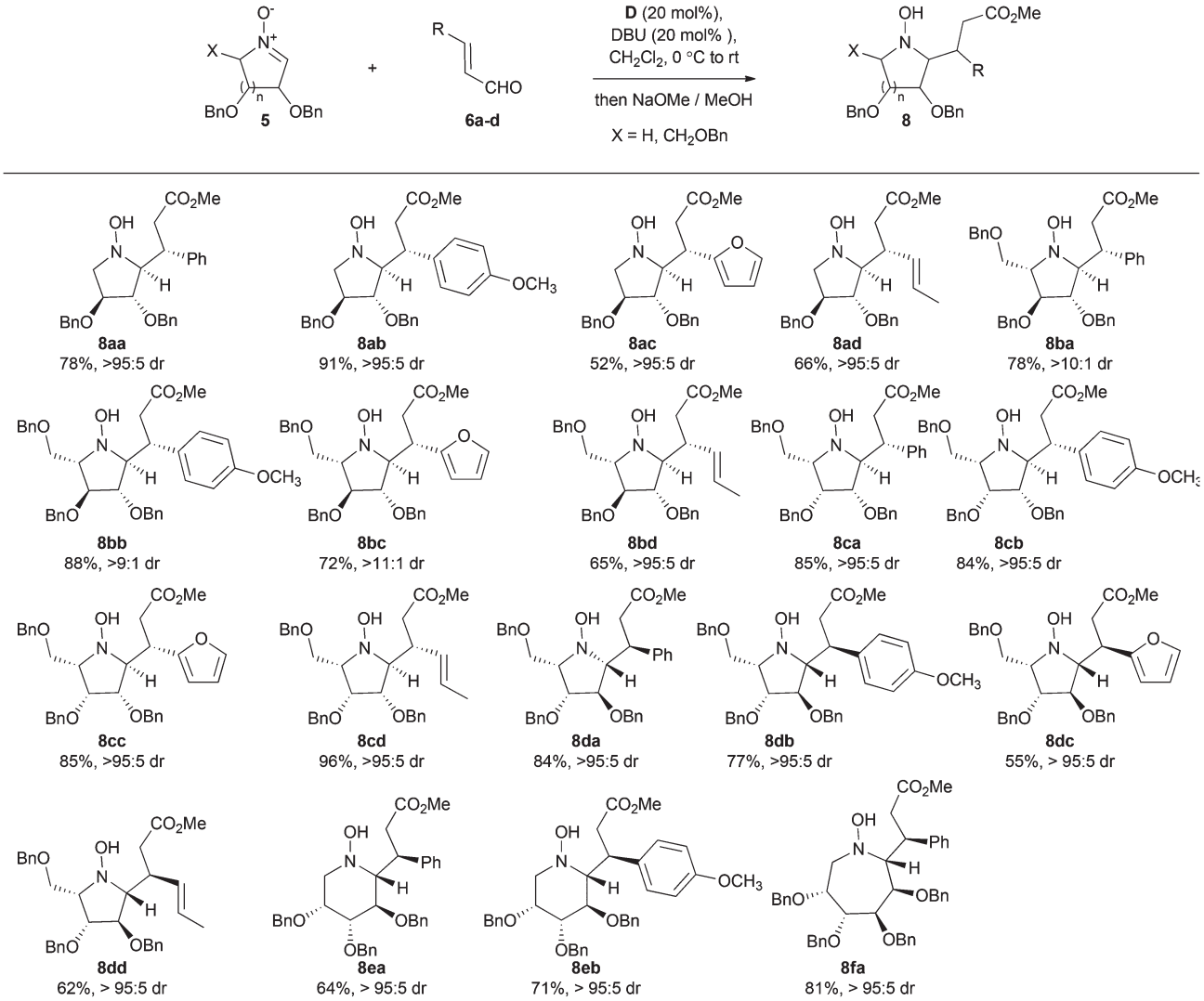


Table 2 Scope of the substrates[a,b]



[a] General conditions: **5** (2.0 equiv.), **6** (1.0 equiv.), **D** (20 mol%), DBU (20 mol%). Given are isolated yields. Diastereomeric ratio determined after separation. [b] R: **6a** = Ph, **6b** = 4-MeOPh; **6c** = 2-furyl; **6d** = 1-propenyl.

Under the optimized reaction conditions, a variety of cyclic nitrones (*i.e.* **5a–5f**) were used in the coupling reactions with various enals (**6a–d**). It was found that all the cyclic nitrones (*i.e.* **5a–5f**) were good substrates for the NHC-catalysed coupling reactions, which produced the desired products in good to excellent yields. For most of the reactions, products with 1,7,7α-*cis* configuration were isolated as single products.

The relative configuration of the coupling products **7aa** can be explained by the relative topicity of the transition state of the reaction proposed in Fig. 3. The benzyloxy group at C-2 of nitrone shields the *Re* face of the C=N bond of the nitrone. Therefore, the homoenolate, formed during the catalytic cycle, approaches the nitrone from the less hindered *Si* face. The intermolecular H-bridge between nitrone and the hydroxyl group of the homoenolate may preorganize the two substrates

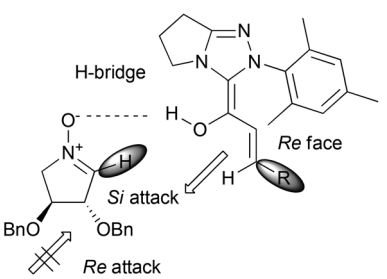


Fig. 3 Postulated transition-state model for the *cis* selectivity.

in such a way that the homoenolate approaches nitrone with its *Re* face, thus lead to the all *cis*-configuration of the two newly formed stereogenic centers and benzyloxy group at C-2 of nitrones.[16a,25]

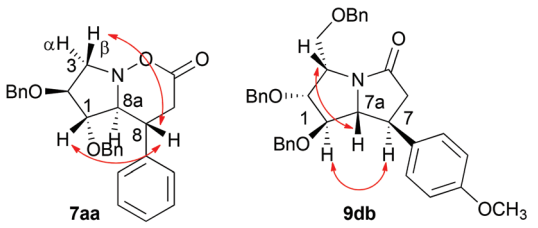


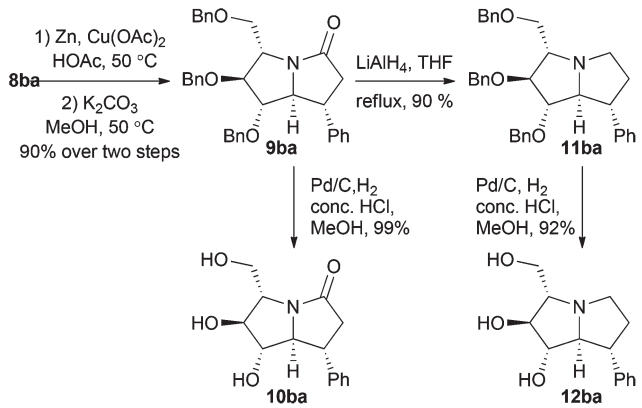
Fig. 4 NOE interactions in **7aa** and **9db**.

The relative configurations of the two newly introduced stereocenters were assigned on the basis of NOESY experiments of **9db**. The observed interactions of H-1–H-7 indicate a *cis* configuration between H-1 and H-7. The *cis* configuration between H-7α and H-3 was assigned through the interactions between H-7α–H-3, thus a 1,7,7α-*cis* configuration was assigned with respect to the benzyloxy groups already present in the molecule. The *cis* configuration could be further confirmed on the basis of the NOESY experiment of the intermediate lactone (*i.e.* **7aa**) (Fig. 4).

Synthesis of bicyclic iminosugars

With the γ-hydroxyl amino esters in hand, a few steps of simple transformations would lead to the synthesis of the target compounds, *i.e.* polyhydroxylated pyrrolizidines and indolizidines. Taken the synthesis of (7*R*)-phenylhyacinthacine A_2 as an example, reduction of **8ba** by Zn–Cu(OAc)$_2$–AcOH[26] or Fe–Cu(OAc)$_2$–AcOH gave the corresponding γ-amino ester, which was immediately treated with K_2CO_3/MeOH to afford lactam **9ba**. Direct hydrogenolysis of **9ba** gave polyhydroxylated lactam **10ba**. Reduction of lactam **9ba** by $LiAlH_4$ gave the corresponding tertiary amine **11ba**, which was further hydrogenated to afford (7*R*)-7-phenylhyacinthacine A_2 (*i.e.* **12ba**) in excellent yield (Scheme 1).

Thus, a number of polyhydroxylated pyrrolizidines and indolizidines have been prepared by this methodology. However, when the 2-furyl substituted lactams (*i.e.* **9**) were subjected to debenzylation by catalytic hydrogenation or BCl_3, a mixture of complicated products were obtained (Fig. 5, overall yields from enals **6**).



Scheme 1 Synthesis of (7*R*)-7-phenylhyacinthacine A_2.

Evaluation of glycosidase inhibitions of the synthesized bicyclic iminosugars

All the synthesized bicyclic iminosugars were assayed as potential inhibitors of a range of glycosidase (as shown in ESI†).

The best inhibition was observed in lactams **10eb** and **10fa** (IC_{50} 57 μM and 58 μM, respectively, against β-glucuronidase from *E. coli*). Most of the lactams had no inhibition against glycosidases. Only few lactams had moderate inhibition; for example, lactam **10bb** had moderate inhibition (IC_{50} 480 μM against β-glucosidase and IC_{50} 259 μM against β-galactosidase, both from bovine liver). Besides, the bicyclic azepane lactam **10fa** had inhibitions against various glycosidases. The bulk of the pyrrolizidines were less potent than original natural products. Therefore, the aryl and alkyl substituents at C-7 of pyrrolizidines or at C-8 of indolizidines had caused loss of glycosidase inhibitory activity.[27] The biological study results observed herein might be valuable for further structure–activity studies on polyhydroxylated pyrrolizidines and indolizidines.

Conclusions

In summary, a general and efficient method for the synthesis of polyhydroxylated pyrrolizidines and indolizidines has been

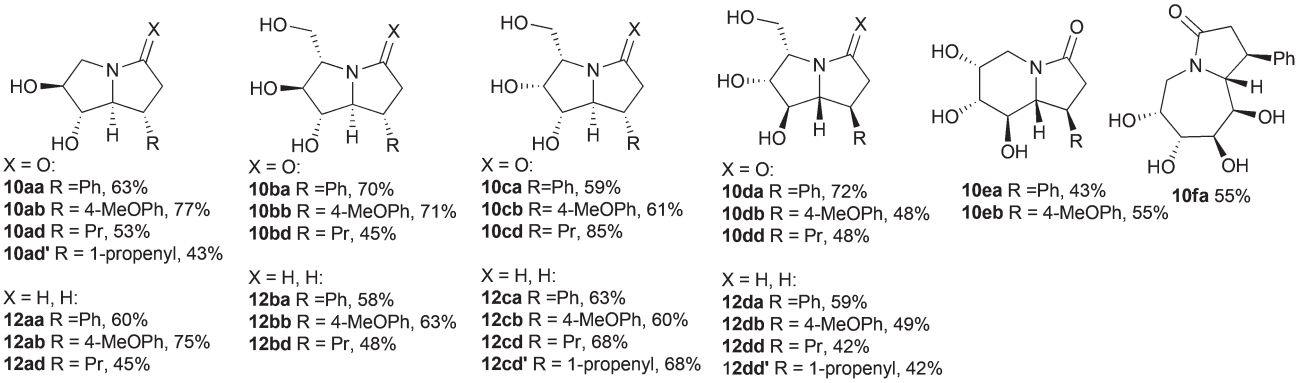


Fig. 5 Synthesized polyhydroxylated pyrrolizidines and indolizidines.

developed based on the NHC-catalyzed cross-coupling of sugar-derived cyclic nitrones with enals, which afforded the key intermediates, γ-hydroxyl amino esters, in good to excellent yields. Thus, a variety of polyhydroxylated pyrrolizidines and indolizidines have been synthesized starting from the γ-hydroxyl amino esters *via* a few steps of simple transformations in good to excellent yields. The resulting polyhydroxylated pyrrolizidines and indolizidines were assayed against various glycosidases, which showed that most of the polyhydroxylated lactams have no inhibition, while several synthesized pyrrolizidines and indolizidines only had moderated inhibition. This indicated that the aryl or alkyl substitutions at C-7 of pyrrolizidines or C-8 of indolizidines reduced the inhibitory activity of glycosidases. These results might be valuable for further structure–activity studies of substituted iminosugars and for design and synthesis of more potent and selective glycosidase inhibitors. The application of this methodology in the synthesis of naturally-occurring iminosugars, including bicyclic iminosugars and nortropane iminosugars, was under way and will be reported in due course.

Experimental

Material and methods

All reagents were used as received from commercial sources without further purification or prepared as described in the literature. Dichloromethane was distilled from calcium hydride. NaOMe was prepared from sodium and methanol before use. Methanol was dried over 4 Å molecular sieves. Tetrahydrofuran was distilled from sodium and benzophenone immediately before use. Analytical TLC was performed with 0.20 mm silica gel 60F plates with 254 nm fluorescent indicator. TLC plates were visualized by ultraviolet light or by treatment with a spray of Pancaldi reagent ($(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O) or a 0.5% solution of $KMnO_4$ in acetone. Chromatographic purification of products was carried out by chromatography on silica gel (200–300 mesh). Acidic ion exchange chromatography was performed on Amberlite IR-120 (H^+) or Dowex 50WX8-400 H^+ form. Melting points were determined using an electrothermal melting point apparatus. Melting points are uncorrected. Infrared spectra were recorded on a JASCOFT/IR-480 plus Fourier transform spectrometer. NMR spectra were measured in $CDCl_3$ (with TMS as internal standard) or D_2O on a Broker AV300 or AV600 magnetic resonance spectrometer (^1H at 300 MHz or 600 MHz, ^{13}C at 75 MHz). High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific LTQ/FT mass spectrometer or a GCT mass spectrometer. Polarimetry was carried out using an Optical Activity AA-10R polarimeter and the measurements were made at the sodium D-line with a 0.5 dm path length cell. Concentrations (*c*) are given in gram per 100 mL.

General procedure for cross-coupling of cyclic nitrones with α,β-unsaturated aldehydes and subsequent *in situ* methanolysis

To an oven-dried flask containing a magnetic stirring bar was added catalyst **D** (27 mg, 0.10 mmol) and nitrone **5** (1.0 mmol). The mixture was dissolved in CH_2Cl_2 (10 mL, 0.1 M) and cooled to 0 °C. To the flask was sequentially added the enal (0.50 mmol) and DBU (15 μL, 0.10 mmol) *via* syringe under Ar atmosphere. The reaction mixture was stirred overnight at room temperature and 0.50 mL NaOMe (1.0 M in MeOH) was added *via* syringe. After 30 min the reaction was diluted with diethyl ether and filtered through a pad of Celite. The reaction mixture was concentrated and purified by flash column chromatography on silica gel (EtOAc–petroleum ether = 1/5) to afford the γ-hydroxyl amino ester product as **8** a yellow or colourless syrup.

(4*R*,4*aS*,5*S*,6*S*)-5,6-Bis(benzyloxy)-4-phenylhexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazin-2-one (7aa)

According to general procedure without addition of NaOMe, prepared from enal **6a** (0.25 mL, 2.00 mmol) and nitrone **5a** (1.21 g, 4.00 mmol) to afford **7aa** (0.69 g, 81%) as colourless oil; $[\alpha]_D^{20}$ +10.6 (*c* 2.65 in CH_2Cl_2); ν_{max}/cm^{-1} 3062, 3031, 2922, 2860, 1756, 1621, 1496, 1454, 1097, 740, 699; δ_H ($CDCl_3$, 300 MHz) 7.42–7.29 (m, 13 H), 7.11–7.07 (m, 2H), 4.64 (d, J = 11.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.33 (s, 2H), 4.17–4.13 (m, 2H), 4.02 (dd, J_1 = 2.7 Hz, J_2 = 9.0 Hz, 1H), 3.89 (s, 1H), 3.44 (dt, J_1 = 8.7 Hz, J_2 = 11.7 Hz, 1H), 3.25 (dd, J_1 = 4.2 Hz, J_2 = 12.6 Hz, 1H), 2.92 (dd, J_1 = 12.0 Hz, J_2 = 15.9 Hz, 1H), 2.77 (dd, J_1 = 8.5 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 175.6, 140.1, 137.5, 137.2, 129.0, 128.6, 128.5, 128.0, 127.96, 127.92, 127.7, 127.4, 85.6, 83.0, 72.6, 71.6, 71.2, 46.9, 46.7, 41.9; HRMS (ESI) calcd for $C_{27}H_{28}NO_4^+$ $[M + H]^+$ 430.2013, found 430.2009.

(*R*)-Methyl 3-((2*S*,3*S*,4*S*)-3,4-bis(benzyloxy)-1-hydroxypyrrolidin-2-yl)-3-phenylpropanoate (8aa)

According to general procedure, prepared from enal **6a** (0.85 mL, 6.75 mmol) and nitrone **5a** (4.0 g, 13.45 mmol) to afford **8aa** (2.45 g, 78%) as colourless oil; $[\alpha]_D^{20}$ +10.4 (*c* 3.45 in CH_2Cl_2); ν_{max}/cm^{-1} 3446, 3030, 2918, 2857, 1735, 1496, 1454, 1094, 739, 699; δ_H ($CDCl_3$, 300 MHz) 7.26–7.07 (m, 13H), 6.81–6.78 (m, 2H), 5.62 (s, br, 1H), 4.42 (d, J = 12.0 Hz, 1H), 4.30 (d, J = 12.0 Hz, 1H), 4.01 (d, J = 11.1 Hz, 1H), 3.90 (d, J = 11.1 Hz, 1H), 3.75–3.69 (m, 2H), 3.59 (d, J = 6.0 Hz, 1H), 3.49 (s, 3H), 3.27 (d, J = 10.8 Hz, 1H), 3.03 (t, J = 5.7 Hz, 1H), 2.93 (q, J = 5.4 Hz, 2H), 2.59 (dd, J_1 = 6.3 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.3, 141.0, 138.0, 137.5, 128.5, 128.4, 128.2, 128.1, 127.7, 127.6, 126.7, 83.5, 79.3, 76.7, 71.3, 70.9, 59.8, 51.8, 41.0, 34.9; HRMS (ESI) calcd for $C_{28}H_{32}NO_5^+$ $[M + H]^+$ 462.2281, found 462.2273.

(*R*)-Methyl 3-(2*S*,3*S*,4*S*)-3,4-bis(benzyloxy)-1-hydroxypyrrolidin-2-yl)-3-(4-methoxyphenyl)propanoate (8ab)

According to general procedure, prepared from enal **6b** (0.69 g, 4.28 mmol) and nitrone **5a** (2.58 g, 8.68 mmol) to afford **8ab** (1.92 g, 91%) as colourless oil; $[\alpha]_D^{20}$ +6.7 (*c* 1.50 in CH_2Cl_2); ν_{max}/cm^{-1} 3447, 3030, 2947, 2905, 1735, 1513, 1455, 1113, 739, 699; δ_H ($CDCl_3$, 300 MHz) 7.28–7.23 (m, 5H), 7.16–7.14 (m, 3H), 7.06 (d, J = 8.7 Hz, 2H), 6.86–6.83 (m, 2H), 6.73 (d, J = 8.7 Hz, 2H), 5.47 (s, br, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.33 (d, J = 12.0 Hz, 1H), 4.08 (d, J = 11.4 Hz, 1H), 3.97 (d, J =

11.4 Hz, 1H), 3.77 (d, J = 5.1 Hz, 1H), 3.67–3.66 (m, 4H), 3.58 (d, J = 5.7 Hz, 1H), 3.52 (s, 3H), 3.29 (d, J = 10.8 Hz, 1H), 3.01–2.91 (m, 2H), 2.89–2.81 (m, 1H), 2.57 (dd, J_1 = 6.6 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.4, 158.4, 138.0, 137.6, 133.0, 129.0, 128.5, 128.3, 127.84, 127.80, 127.79, 127.71, 113.9, 83.7, 79.3, 77.4, 71.4, 71.0, 59.9, 55.2, 51.9, 40.4, 35.4; HRMS (ESI) calcd for $C_{29}H_{34}NO_6^+$ $[M + H]^+$ 492.2386, found 492.2371.

(*S*)-Methyl 3-((2*S*,3*S*,4*S*)-3,4-bis(benzyloxy)-1-hydroxypyrrolidin-2-yl)-3-(furan-2-yl)propanoate (8ac)

According to general procedure, prepared from enal **6c** (0.58 g, 4.80 mmol) and nitrone **5a** (2.89 g, 9.70 mmol) to afford **8ac** (1.12 g, 51%) as colourless oil; $[\alpha]_D^{20}$ +14.9 (*c* 2.15 in CH_2Cl_2); ν_{max}/cm^{-1} 3446, 3031, 2949, 2861, 1736, 1454, 1365, 1094, 731, 698; δ_H ($CDCl_3$, 300 MHz) 7.36–7.25 (m, 9H), 7.11–7.08 (m, 2H), 6.27 (q, J = 1.8 Hz, 1H), 6.10 (d, J = 3.0 Hz, 1H), 5.66 (s, br, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 4.23–4.14 (m, 2H), 3.92–3.84 (m, 2H), 3.74 (d, J = 5.4 Hz, 1H), 3.64 (s, 3H), 3.39 (d, J = 10.5 Hz, 1H), 3.20 (t, J = 5.4 Hz, 1H), 3.04 (dd, J_1 = 5.4 Hz, J_2 = 10.5 Hz, 1H), 2.90 (dd, J_1 = 7.7 Hz, J_2 = 16.2 Hz, 1H), 2.66 (dd, J_1 = 6.3 Hz, J_2 = 16.2 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.1, 154.9, 141.7, 138.0, 137.7, 128.5, 128.3, 127.84, 127.77, 110.3, 106.1, 83.4, 79.3, 75.3, 71.6, 70.9, 59.8, 52.0, 35.2, 33.5; HRMS (ESI) calcd for $C_{26}H_{30}NO_6^+$ $[M + H]^+$ 452.2073, found 452.2069.

(*R*,*E*)-Methyl 3-((2*S*,3*S*,4*S*)-3,4-bis(benzyloxy)-1-hydroxypyrrolidin-2-yl)hex-4-enoate (8ad)

According to general procedure, prepared from enal **6d** (0.50 mL, 4.50 mmol) and nitrone **5a** (2.69 g, 9.0 mmol) to afford **8ad** (1.28 g, 66%) as colourless oil; $[\alpha]_D^{20}$ −5.5 (*c* 3.30 in CH_2Cl_2); ν_{max}/cm^{-1} 3438, 3030, 2916, 2861, 1736, 1454, 1103, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.36–7.27 (m, 10H), 5.85 (s, br, 1H), 5.52–5.35 (m, 2H), 4.56–4.38 (m, 4H), 3.90 (d, J = 5.8 Hz, 1H), 3.68 (d, J = 6.6 Hz, 1H), 3.62 (s, 3H), 3.38 (d, J = 10.7 Hz, 1H), 3.08–3.00 (m, 2H), 2.90–2.86 (m, 1H), 2.59 (dd, J_1 = 6.9 Hz, J_2 = 15.3 Hz, 1H), 2.31 (dd, J_1 = 7.2 Hz, J_2 = 15.6 Hz, 1H), 1.63 (d, J = 5.7 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 174.4, 137.9, 137.7, 130.6, 128.5, 128.4, 127.9, 127.9, 127.8, 126.8, 83.4, 79.4, 75.5, 71.6, 71.0, 60.4, 51.7, 39.4, 35.7, 18.1; HRMS (ESI) calcd for $C_{26}H_{32}NO_5^+$ $[M + H]^+$ 546.2855, found 546.2842.

(*R*)-Methyl 3-((2*S*,3*S*,4*S*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-phenylpropanoate (8ba)

According to general procedure, prepared from enal **6a** (0.60 mL, 4.77 mmol) and nitrone **5b** (4.00 g, 9.58 mmol) to afford **8ba** (2.18 g, 78%) as colourless oil; $[\alpha]_D^{20}$ +15.4 (*c* 1.95 in CH_2Cl_2); ν_{max}/cm^{-1} 3435, 3030, 2886, 1736, 1453, 1098, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.16 (m, 18H), 6.88–6.85 (m, 2H), 5.57 (s, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.52–4.39 (m, 3H), 4.07 (t, J = 11.1 Hz, 2H), 3.99–3.96 (m, 1H), 3.89 (dd, J_1 = 3.6 Hz, J_2 = 8.4 Hz, 1H), 3.80–3.73 (m, 2H), 3.63–3.52 (m, 5H), 3.40 (t, J = 6.0 Hz, 1H), 2.97 (dd, J_1 = 8.4 Hz, J_2 = 15.9 Hz, 1H), 2.62 (dd, J_1 = 6.0 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.3, 141.2, 138.3, 138.1, 137.7, 128.5, 128.3, 128.2, 128.1, 127.7, 127.69, 127.6, 127.5, 126.7, 83.8, 82.7, 74.3, 73.3, 71.3, 71.2, 68.2, 66.1, 51.7, 41.5, 35.2; HRMS (ESI) calcd for $C_{11}H_{20}NO_3^+$ $[M + H]^+$ 582.2850, found 582.2839.

(*R*)-Methyl 3-((2*S*,3*S*,4*S*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(4-methoxyphenyl)-propanoate (8bb)

According to general procedure, prepared from enal **6b** (0.71 g, 4.41 mmol) and nitrone **5b** (3.66 g, 8.77 mmol) to afford **8bb** (2.21 g, 88%) as colourless oil; $[\alpha]_D^{20}$ +17.1 (*c* 2.10 in CH_2Cl_2); ν_{max}/cm^{-1} 3445, 3031, 2909, 1736, 1513, 1454, 1249, 1113, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.20 (m, 13H), 7.10 (d, J = 8.7 Hz, 2H), 6.92–6.89 (m, 2H), 6.79 (d, J = 8.7 Hz, 2H), 5.63 (s, br, 1H), 4.61–4.60 (m, 1H), 4.52–4.40 (m, 3H), 4.10 (q, J = 11.4 Hz, 2H), 3.97 (s, 1H), 3.89 (dd, J_1 = 3.0 Hz, J_2 = 7.8 Hz, 1H), 3.79–3.77 (m, 1H), 3.71–3.66 (m, 4H), 3.58–3.52 (m, 5H), 3.37 (t, J = 6.0 Hz, 1H), 2.94 (dd, J_1 = 8.1 Hz, J_2 = 15.9 Hz, 1H), 2.60 (dd, J_1 = 6.6 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.2, 158.3, 138.3, 138.1, 137.7, 133.1, 129.0, 128.3, 128.1, 128.0, 127.7, 127.66, 127.60, 127.5, 113.8, 83.9, 82.7, 74.3, 73.3, 71.3, 71.2, 68.2, 66.2, 55.1, 51.7, 40.8, 35.5; HRMS (ESI) calcd for $C_{37}H_{42}NO_7^+$ $[M + H]^+$ 612.2961, found 612.2955.

(*S*)-Methyl 3-((2*S*,3*S*,4*S*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(furan-2-yl)propanoate (8bc)

According to general procedure, prepared from enal **6c** (0.55 g, 4.50 mmol) and nitrone **5b** (3.75 g, 9.0 mmol) to afford **8bc** (1.69 g, 72%) as colourless oil; $[\alpha]_D^{20}$ +1.3 (*c* 1.50 in CH_2Cl_2); ν_{max}/cm^{-1} 3436, 3031, 2919, 2866, 1736, 1454, 1109, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.34–7.21 (m, 14H), 7.06–7.02 (m, 2H), 6.26–6.25 (m, 1H), 6.06 (d, J = 3.0 Hz, 1H), 5.54 (s, br, 1H), 4.65–4.40 (m, 4H), 4.20–4.11 (m, 2H), 3.96–3.93 (m, 2H), 3.87–3.78 (m, 2H), 3.66–3.56 (m, 5H), 3.49 (t, J = 5.7 Hz, 1H), 2.89 (dd, J_1 = 7.8 Hz, J_2 = 16.2 Hz, 1H), 2.64 (dd, J_1 = 6.0 Hz, J_2 = 16.2 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.2, 155.0, 141.6, 138.4, 138.2, 137.9, 128.41, 128.40, 128.3, 128.1, 127.9, 127.7, 127.68, 127.62, 110.3, 106.1, 83.4, 82.5, 73.4, 72.3, 71.5, 71.2, 68.0, 65.9, 52.0, 35.7, 33.4; HRMS (ESI) calcd for $C_{34}H_{38}NO_7^+$ $[M + H]^+$ 572.2648, found 572.2643.

(*R*,*E*)-Methyl 3-((2*S*,3*S*,4*S*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)hex-4-enoate (8bd)

According to general procedure, prepared from enal **6d** (0.50 mL, 4.53 mmol) and nitrone **5b** (3.78 g, 9.05 mmol) to afford **8bd** (1.60 g, 65%) as colourless oil; $[\alpha]_D^{20}$ +11.4 (*c* 0.35 in CH_2Cl_2); ν_{max}/cm^{-1} 3421, 3030, 2917, 2861, 1736, 1454, 1363, 1109, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.36–7.21 (m, 15H), 5.52–5.33 (m, 2H), 4.67 (s, 1H), 4.62–4.52 (m, 3H), 4.48–4.32 (m, 3H), 3.98–3.95 (m, 1H), 3.91 (d, J = 4.8 Hz, 1H), 3.74 (dd, J_1 = 2.1 Hz, J_2 = 6.9 Hz, 1H), 3.64–3.57 (m, 5H), 3.19–3.15 (m, 1H), 3.07–2.98 (m, 1H), 2.56 (dd, J_1 = 7.5 Hz, J_2 = 15.3 Hz, 1H), 2.28 (dd, J_1 = 6.6 Hz, J_2 = 15.6 Hz, 1H), 1.63 (d, J = 5.7 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.5, 138.4, 138.2, 138.0, 130.8, 128.6, 128.42, 128.37, 128.1, 127.72, 127.65, 127.0, 126.6, 83.5, 83.0, 73.4, 72.5, 71.6, 71.3, 68.3, 66.3, 65.4, 51.6, 39.8, 35.6, 18.1;

HRMS (ESI) calcd for $C_{33}H_{40}NO_6^+$ $[M + H]^+$ 546.2856, found 546.2848.

(*R*)-Methyl 3-((2*S*,3*S*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-phenylpropanoate (8ca)

According to general procedure, prepared from enal **6a** (0.75 mL, 5.96 mmol) and nitrone **5c** (5.00 g, 12.00 mmol) to afford **8ca** (2.96 g, 85%) as colourless oil; $[\alpha]_D^{20}$ −26.0 (*c* 1.00 in CH_2Cl_2); ν_{max}/cm^{-1} 3419, 3036, 2920, 2866, 1736, 1454, 1093, 737, 699; δ_H ($CDCl_3$, 300 MHz) 7.32–7.08 (m, 20H), 5.55 (s, br, 1H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.52–4.42 (m, 3H), 4.16 (d, *J* = 11.7 Hz, 1H), 3.94 (d, *J* = 3.9 Hz, 1H), 3.89–3.87 (m, 2H), 3.65–3.61 (m, 1H), 3.53 (s, 3H), 3.48–3.44 (m, 2H), 2.98–2.90 (m, 2H), 2.79 (dd, J_1 = 7.8 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 173.2, 140.4, 138.2, 138.1, 138.0, 128.8, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 126.9, 81.1, 77.4, 76.9, 73.4, 72.5, 67.0, 65.8, 51.6, 42.2, 37.6; HRMS (ESI) calcd for $C_{36}H_{40}NO_6^+$ $[M + H]^+$ 582.2856, found 582.2839.

(*R*)-Methyl 3-((2*S*,3*S*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(4-methoxyphenyl)-propanoate (8cb)

According to general procedure, prepared from enal **6b** (1.02 g, 6.30 mmol) and nitrone **5c** (5.27 g, 12.63 mmol) to afford **8cb** (3.21 g, 84%) as colourless oil; $[\alpha]_D^{20}$ −8.5 (*c* 1.65 in CH_2Cl_2); ν_{max}/cm^{-1} 3404, 3030, 2926, 1735, 1512, 1454, 1111, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.34–7.23 (m, 15H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 8.4 Hz, 2H), 5.58 (s, br, 1H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.59 (m, 1H), 4.54 (d, *J* = 3.9 Hz, 1H), 4.50–4.47 (m, 2H), 4.21 (d, *J* = 12.0 Hz, 1H), 3.95 (t, *J* = 3.9 Hz, 1H), 3.89–3.87 (m, 2H), 3.73 (s, 3H), 3.63–3.59 (m, 1H), 3.54 (s, 3H), 3.46–3.35 (m, 2H), 2.95–2.89 (m, 2H), 2.88–2.79 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 173.2, 158.4, 138.2, 138.15, 138.0, 129.8, 128.51, 128.46, 128.43, 128.42, 128.0, 127.92, 127.9, 127.84, 127.82, 127.7, 113.7, 81.4, 73.5, 73.4, 72.6, 67.0, 65.8, 55.2, 51.6, 41.5, 38.0; HRMS (ESI) calcd for $C_{37}H_{42}NO_7^+$ $[M + H]^+$ 612.2961, found 612.2951.

(*S*)-Methyl 3-((2*S*,3*S*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(furan-2-yl)propanoate (8cc)

According to general procedure, prepared from enal **6c** (0.57 g, 4.68 mmol) and nitrone **5c** (3.91 g, 9.37 mmol) to afford **8cc** (2.26 g, 84%) as colourless oil; $[\alpha]_D^{20}$ −5.2 (*c* 1.55 in CH_2Cl_2); ν_{max}/cm^{-1} 3419, 3030, 2924, 2868, 1736, 1454, 1099, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.30–7.21 (m, 16H), 6.24–6.23 (m, 1H), 6.01 (d, *J* = 3.0 Hz, 1H), 5.58 (s, br, 1H), 4.69–4.61 (m, 3H), 4.50–4.44 (m, 4H), 4.25 (d, *J* = 11.4 Hz, 1H), 3.96–3.90 (m, 3H), 3.69–3.61 (m, 2H), 3.59 (s, 3H), 3.26–3.23 (m, 1H), 2.78–2.75 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 173.0, 154.6, 141.5, 138.3, 138.2, 138.1, 128.4, 128.37, 128.0, 127.8, 127.7, 110.4, 106.7, 80.3, 75.3, 73.5, 73.2, 72.7, 66.8, 65.8, 51.8, 36.4, 35.3; HRMS (ESI) calcd for $C_{34}H_{38}NO_7^+$ $[M + H]^+$ 572.2648, found 572.2640.

(*R*,*E*)-Methyl 3-((2*S*,3*S*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)hex-4-enoate (8cd)

According to general procedure, prepared from enal **6d** (0.58 mL, 5.35 mmol) and nitrone **5c** (4.39 g, 10.50 mmol) to afford **8cd** (2.75 g, 96%) as colourless oil; $[\alpha]_D^{20}$ −52.0 (*c* 1.15 in CH_2Cl_2); ν_{max}/cm^{-1} 3343, 2927, 1654, 1453, 1122, 703; δ_H ($CDCl_3$, 300 MHz) 7.30–7.27 (m, 15H), 5.60–5.58 (m, 1H), 5.23–5.21 (m, 1H), 4.77–4.71 (m, 1H), 4.66–4.59 (m, 3H), 4.53–4.46 (m, 2H), 4.40–4.36 (m, 1H), 4.08–4.05 (m, 1H), 3.92 (d, *J* = 6.3 Hz, 2H), 3.65–3.62 (m, 1H), 3.60 (s, 3H), 3.24–3.17 (m, 1H), 3.39–3.33 (m, 1H), 2.77–2.73 (m, 1H), 2.60–2.39 (m, 2H), 1.55–1.53 (m, 3H); δ_C ($CDCl_3$, 75 MHz) 173.3, 138.2, 138.1, 138.0, 129.5, 128.49, 128.45, 128.1, 127.9, 127.8, 127.7, 80.9, 77.6, 76.3, 73.5, 73.4, 72.7, 67.5, 65.9, 51.4, 40.8, 37.6, 18.0; HRMS (ESI) calcd for $C_{36}H_{40}NO_4^+$ $[M + H]^+$ 550.2957, found 550.2947.

(*S*)-Methyl-((2*R*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-phenylpropanoate (8da)

According to general procedure, prepared from enal **6a** (0.55 mL, 4.37 mmol) and nitrone **5d** (3.63 g, 8.62 mmol) to afford **8da** (2.14 g, 84%) as colourless oil; $[\alpha]_D^{20}$ +17.4 (*c* 2.30 in CH_2Cl_2); ν_{max}/cm^{-1} 3452, 3027, 2910, 2863, 1735, 1453, 1169, 1095, 738, 699; δ_H ($CDCl_3$, 300 MHz) 7.34–7.16 (m, 18H), 6.81–6.78 (m, 2H), 5.46 (s, br, 1H), 4.54–4.49 (m, 4H), 3.88–3.82 (m, 3H), 3.79–3.75 (m, 2H), 3.69–3.63 (m, 1H), 3.56 (s, 3H), 3.52 (d, *J* = 4.8 Hz, 1H), 3.44–3.38 (m, 1H), 3.22 (t, *J* = 3.4 Hz, 1H), 2.89 (dd, J_1 = 6.0 Hz, J_2 = 15.9 Hz, 1H), 2.59 (dd, J_1 = 5.7 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.6, 140.9, 138.4, 138.3, 137.5, 128.5, 128.37, 128.36, 128.2, 128.1, 127.8, 127.7, 127.6, 127.58, 127.4, 126.7, 81.7, 79.0, 77.9, 73.4, 71.8, 71.1, 67.9, 67.2, 51.7, 40.8, 34.4; HRMS (ESI) calcd for $C_{36}H_{40}NO_6^+$ $[M + H]^+$ 582.2856, found 582.2844.

(*S*)-Methyl 3-((2*R*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(4-methoxyphenyl)-propanoate (8db)

According to general procedure, prepared from enal **6b** (1.16 g, 7.16 mmol) and nitrone **5d** (6.00 g, 14.3 mmol) to afford **8db** (3.39 g, 77%) as colourless oil; $[\alpha]_D^{20}$ +97.1 (*c* 0.35 in CH_2Cl_2); ν_{max}/cm^{-1} 3454, 3031, 2918, 2863, 1735, 1611, 1513, 1454, 1250, 1095, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.33–7.25 (m, 15H), 7.13 (d, *J* = 8.7 Hz, 2H), 6.87–6.84 (m, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 5.49 (s, br, 1H), 4.55–4.46 (m, 4H), 3.96 (d, *J* = 11.1 Hz, 1H), 3.87–3.83 (m, 2H), 3.80–3.77 (m, 2H), 3.73 (s, 3H), 3.68 (dd, J_1 = 4.2 Hz, J_2 = 8.7 Hz, 1H), 3.57 (s, 3H), 3.52 (d, *J* = 4.8 Hz, 1H), 3.44–3.38 (m, 1H), 3.19 (t, *J* = 4.8 Hz, 1H), 2.86 (dd, J_1 = 9.0 Hz, J_2 = 15.6 Hz, 1H), 2.56 (dd, J_1 = 5.7 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.6, 158.5, 138.4, 138.3, 137.6, 132.8, 129.1, 128.4, 128.2, 127.8, 127.7, 127.5, 114.0, 81.8, 79.0, 77.9, 73.5, 71.9, 71.2, 68.2, 67.3, 55.3, 51.7, 40.2, 34.9; HRMS (ESI) calcd for $C_{37}H_{42}NO_7$ $[M + H]^+$ 612.2961, found 612.2955.

(*R*)-Methyl 3-((2*R*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)-3-(furan-2-yl)propanoate (8dc)

According to general procedure, prepared from enal **6c** (0.70 g, 5.75 mmol) and nitrone **5d** (4.80 g, 11.5 mmol) to afford **8dc** (1.82 g, 55%) as colourless oil; $[\alpha]_D^{20}$ +21.1 (*c* 1.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3448, 3030, 2949, 2864, 1735, 1454, 1094, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.31–7.23 (m, 14H), 7.07–7.05 (m, 2H), 6.29–6.27 (m, 1H), 6.10 (d, *J* = 3.3 Hz, 1H), 5.35 (s, br, 1H), 4.59–4.46 (m, 4H), 4.08 (s, 2H), 3.94–3.87 (m, 2H), 3.79 (t, *J* = 9.0 Hz, 1H), 3.68 (dd, J_1 = 4.5 Hz, J_2 = 9.0 Hz, 1H), 3.62 (d, *J* = 4.8 Hz, 1H), 3.60 (s, 3H), 3.46–3.40 (m, 1H), 3.32 (t, *J* = 4.5 Hz, 1H), 2.83 (dd, J_1 = 8.7 Hz, J_2 = 16.2 Hz, 1H), 2.57 (dd, J_1 = 6.0 Hz, J_2 = 16.2 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.3, 155.0, 141.6, 138.4, 138.36, 137.8, 128.45, 128.42, 128.3, 127.8, 127.75, 127.68, 127.64, 127.5, 110.3, 106.1, 81.9, 79.2, 75.7, 73.5, 71.9, 71.4, 67.9, 67.3, 51.9, 35.4, 33.3; HRMS (ESI) calcd for $C_{34}H_{38}NO_7^+$ $[M + H]^+$ 572.2648, found 572.2640.

(*S*,*E*)-Methyl 3-((2*R*,3*R*,4*R*,5*S*)-3,4-bis(benzyloxy)-5-((benzyloxy)-methyl)-1-hydroxypyrrolidin-2-yl)hex-4-enoate (8dd)

According to general procedure, prepared from enal **6d** (0.80 mL, 7.24 mmol) and nitrone **5d** (6.00 g, 14.30 mmol) to afford **8dd** (2.43 g, 62%) as colourless oil; $[\alpha]_D^{20}$ +40.0 (*c* 1.05 in CH_2Cl_2); ν_{max}/cm^{-1} 3449, 3031, 2949, 2866, 1736, 1454, 1109, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.33–7.23 (m, 15H), 5.52–5.45 (m, 1H), 5.40–5.34 (m, 1H), 5.33 (s, br, 1H), 4.56–4.47 (m, 4H), 4.40–4.27 (m, 2H), 3.91 (d, *J* = 5.4 Hz, 1H), 3.83–3.77 (m, 1H), 3.69 (dd, J_1 = 4.5 Hz, J_2 = 9.0 Hz, 1H), 3.58 (s, 3H), 3.54 (d, *J* = 5.4 Hz, 1H), 3.41–3.35 (m, 1H), 3.12–3.06 (m, 1H), 2.97 (t, *J* = 5.1 Hz, 1H), 2.51 (dd, J_1 = 7.8 Hz, J_2 = 15.6 Hz, 1H), 2.27–2.16 (m, 1H), 1.63 (d, *J* = 6.0 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 174.8, 138.5, 138.4, 137.9, 130.8, 128.5, 128.48, 128.46, 127.90, 127.88, 127.7, 127.6, 127.5, 82.0, 79.1, 75.9, 73.6, 71.9, 71.5, 68.4, 67.5, 51.7, 39.3, 35.4, 18.2; HRMS (ESI) calcd for $C_{33}H_{40}NO_6^+$ $[M + H]^+$ 546.2856, found 546.2842.

(*S*)-Methyl 3-phenyl-3-((2*R*,3*R*,4*R*,5*R*)-3,4,5-tris(benzyloxy)-1-hydroxypiperidin-2-yl)propanoate (8ea)

According to general procedure, prepared from enal **6a** (0.50 mL, 3.97 mmol) and nitrone **5e** (3.60 g, 8.60 mmol) to afford **8ea** (1.50 g, 64%) as colourless oil; $[\alpha]_D^{20}$ +24.0 (*c* 0.25 in CH_2Cl_2); ν_{max}/cm^{-1} 3439, 3030, 2923, 2860, 1735, 1453, 1119, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.35–7.19 (m, 18H), 6.83–6.82 (m, 2H), 5.41 (s, br, 1H), 4.69–4.46 (m, 4H), 3.90–3.77 (m, 5H), 3.66 (dd, J_1 = 4.2 Hz, J_2 = 8.7 Hz, 1H), 3.59 (s, 3H), 3.53 (d, *J* = 4.5 Hz, 1H), 3.43–3.37 (m, 1H), 3.22 (t, *J* = 5.1 Hz, 1H), 2.88 (dd, J_1 = 9.0 Hz, J_2 = 15.9 Hz, 1H), 2.59 (dd, J_1 = 5.1 Hz, J_2 = 15.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.7, 141.0, 138.5, 138.4, 137.6, 128.6, 128.48, 128.47, 128.3, 128.2, 127.9, 127.8, 127.72, 127.69, 127.6, 126.8, 81.9, 79.2, 78.0, 73.6, 72.0, 71.2, 68.0, 67.3, 51.8, 41.0, 34.7; HRMS (ESI) calcd for $C_{36}H_{40}NO_6^+$ $[M + H]^+$ 582.2856, found 582.2842.

(*S*)-Methyl 3-(4-methoxyphenyl)-3-((2*R*,3*R*,4*R*,5*R*)-3,4,5-tris(benzyloxy)-1-hydroxypiperidin-2-yl)propanoate (8eb)

According to general procedure, prepared from enal **6b** (0.50 g, 3.08 mmol) and nitrone **5e** (2.59 g, 6.20 mmol) to afford **8eb** (1.34 g, 71%) as colourless oil; $[\alpha]_D^{20}$ +32.0 (*c* 0.50 in CH_2Cl_2); ν_{max}/cm^{-1} 3446, 3031, 2919, 1667, 1514, 1456, 1123; δ_H ($CDCl_3$, 300 MHz) 7.34–7.12 (m, 15H), 6.86–6.80 (m, 4H), 5.28 (s, br, 1H), 4.53–4.50 (m, 4H), 3.95 (d, *J* = 11.1 Hz, 1H), 3.86–3.82 (m, 3H), 3.79–3.75 (m, 4H), 3.66 (dd, J_1 = 4.2 Hz, J_2 = 8.7 Hz, 1H), 3.58 (m, 3H), 3.51 (d, *J* = 4.8 Hz, 1H), 3.40 (d, *J* = 4.5 Hz, 1H), 3.17 (t, *J* = 4.8 Hz, 1H), 2.85 (dd, J_1 = 9.0 Hz, J_2 = 15.9 Hz, 1H), 2.56 (dd, J_1 = 5.4 Hz, J_2 = 15.6 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.7, 158.5, 138.5, 138.4, 137.7, 133.0, 129.1, 128.5, 128.4, 128.3, 127.8, 127.73, 127.70, 127.5, 114.0, 82.0, 79.1, 77.9, 73.6, 71.9, 71.3, 68.1, 67.4, 55.3, 51.8, 40.3, 35.0; HRMS (ESI) calcd for $C_{37}H_{42}NO_7^+$ $[M + H]^+$ 612.2961, found 612.2955.

(4*S*,4*aR*,5*R*,6*R*,7*R*,8*R*)-5,6,7,8-Tetrakis(benzyloxy)-4-phenyloctahydro-2*H*-[1,2]oxazino[2,3-*a*]azepin-2-one (7fa)

According to general procedure, prepared from enal **6a** (0.35 mL, 2.78 mmol) and nitrone **5f** (2.99 g, 5.56 mmol) to afford **7fa** (1.50 g, 81%) as colourless oil; $[\alpha]_D^{20}$ +7.3 (*c* 3.0 in CH_2Cl_2); ν_{max}/cm^{-1} 3062, 3029, 2922, 1761, 1495, 1454, 1101, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.36–7.20 (m, 20H), 7.04–7.03 (m, 5H), 4.76–4.58 (m, 4H), 4.49–4.42 (m, 1H), 4.31–4.29 (m, 3H), 3.95–3.75 (m, 5H), 3.68 (m, 1H), 3.40 (d, *J* = 14.5 Hz, 1H), 3.26 (m, 1H), 3.07 (dd, J_1 = 9.6 Hz, J_2 = 14.7 Hz, 1H), 2.49 (dd, J_1 = 2.7 Hz, J_2 = 14.7 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.9, 143.2, 138.8 138.42, 138.40, 137.4, 128.8, 128.5, 128.38, 128.36, 127.95, 127.92, 127.90, 127.8, 127.74, 127.70, 127.6, 127.1, 78.2, 77.4, 76.0, 73.7, 73.4, 72.5, 72.3, 71.5, 52.4, 42.3, 36.0; HRMS (ESI) calcd for $C_{43}H_{44}NO_5^+$ $[M + H]^+$ 670.3159, found 670.3159.

General procedure for reduction of γ-hydroxyl amino esters 8 and subsequent cyclization to lactams 9

Activated Zn (0.65 g, 10 mmol) and $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol) were added to HOAc (15 mL), and the suspension was stirred for five minutes at room temperature. Hydroxylamine **8** (1 mmol) in HOAc (5 mL) was added to the suspension, and then stirred at 50 °C until TLC indicated that the starting material disappeared. The mixture was filtered through Celite, concentrated under reduced pressure, and then redissolved in dichloromethane. The solution was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated again. The residue was redissolved in MeOH, K_2CO_3 (0.18 g, 1.30 mmol) was added. The mixture was stirred at 55 °C until TLC showed the intermediate disappeared. The reaction mixture was concentrated and purified by silica gel chromatography (EtOAc–petroleum ether) to give compound **9** as colourless oil.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9aa)

Following general procedure, starting from **8aa** (1.44 g, 3.10 mmol) to give **9aa** (1.10 g, 86%) as colourless oil; $[\alpha]_D^{20}$ +120.0 (*c* 0.75 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2918, 1696, 1454, 1110, 739, 699; δ_H ($CDCl_3$, 300 MHz) 7.31–7.11 (m, 15H), 4.37 (d, *J* = 11.7 Hz, 1H), 4.31–4.25 (m, 2H), 4.21–4.12 (m, 2H), 4.04 (d, *J* = 11.4 Hz, 1H), 3.84–3.78 (m, 1H), 3.68 (dd, J_1 = 4.2 Hz, J_2 = 12.3 Hz, 1H), 3.41–3.31 (m, 2H), 3.08 (dd, J_1 = 9.0 Hz, J_2 = 17.1 Hz, 1H), 2.62 (dd, J_1 = 2.7 Hz, J_2 = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.4, 140.1, 137.6, 137.3, 128.8, 128.47, 128.41, 128.0, 127.9, 127.8, 127.4, 84.6, 81.8, 72.3, 71.6, 68.5, 46.4, 40.5, 40.3; HRMS (ESI) calcd for $C_{27}H_{28}NO_3^+$ $[M + H]^+$ 414.2069, found 414.2062.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-1-(4-methoxyphenyl)-tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9ab)

Following general procedure, starting from **8ab** (0.89 g, 1.81 mmol) to give **9ab** (0.68 g, 85%) as colourless oil; $[\alpha]_D^{20}$ +124.0 (*c* 1.00 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2932, 1695, 1514, 1454, 1250, 1111, 832, 740, 699; δ_H ($CDCl_3$, 300 MHz) 7.31–7.13 (m, 10H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 4.35 (t, *J* = 11.4 Hz, 2H), 4.26 (d, *J* = 11.7 Hz, 1H), 4.17–4.10 (m, 3H), 3.77–3.71 (m, 4H), 3.67 (d, *J* = 4.2 Hz, 1H), 3.40–3.32 (m, 2H), 3.05 (dd, J_1 = 9.0 Hz, J_2 = 16.9 Hz, 1H), 2.55 (dd, J_1 = 2.7 Hz, J_2 = 16.9 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.3, 158.6, 137.6, 137.3, 132.1, 128.9, 128.4, 128.3, 127.8, 127.77, 127.74, 127.72, 114.0, 84.7, 81.7, 72.2, 71.5, 68.7, 55.1, 46.3, 40.6, 39.9; HRMS (ESI) calcd for $C_{28}H_{30}NO_4^+$ $[M + H]^+$ 444.2175, found 444.2168.

(1*S*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-1-(furan-2-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9ac)

Following general procedure, starting from **8ac** (0.74 g, 1.65 mmol) to give **9ac** (0.50 g, 75%) as colourless oil; $[\alpha]_D^{20}$ +74.8 (*c* 2.30 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2875, 1700, 1454, 1111, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.35–7.23 (m, 11H), 6.26 (q, *J* = 1.5 Hz, 1H), 6.11 (d, *J* = 3.3 Hz, 1H), 4.47–4.41 (m, 2H), 4.38–4.29 (m, 2H), 4.16 (q, *J* = 2.1 Hz, 1H), 4.08 (t, *J* = 7.2 Hz, 1H), 3.88–3.81 (m, 1H), 3.65 (dd, J_1 = 4.8 Hz, J_2 = 12.0 Hz, 1H), 3.42–3.34 (m, 2H), 2.96 (dd, J_1 = 8.7 Hz, J_2 = 16.8 Hz, 1H), 2.59 (dd, J_1 = 3.3 Hz, J_2 = 16.8 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 173.9, 153.6, 142.0, 137.7, 137.4, 128.4, 128.36, 127.9, 127.8, 127.75, 110.4, 107.2, 84.5, 82.5, 72.6, 71.7, 67.7, 46.3, 38.1, 34.8; HRMS (ESI) calcd for $C_{25}H_{25}NO_4Na^+$ $[M + Na]^+$ 426.1681, found 426.1675.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-1-((*E*)-prop-1-en-1-yl)-tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9ad)

Following general procedure, starting from **8ad** (0.56 g, 1.33 mmol) to give **9ad** (0.40 g, 80%) as colourless oil; $[\alpha]_D^{20}$ +15.5 (*c* 3.10 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2917, 1698, 1453, 1416, 1110, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.37–7.29 (m, 10H), 5.53–5.30 (m, 2H), 4.58–4.43 (m, 4H), 4.18–4.15 (m, 1H), 3.97–3.91 (m, 2H), 3.78 (dd, J_1 = 3.0 Hz, J_2 = 12.3 Hz, 1H), 3.28 (dd, J_1 = 6.0 Hz, J_2 = 12.3 Hz, 1H), 3.16–3.06 (m, 1H), 2.86–2.78 (m, 1H), 2.16 (dd, J_1 = 1.6 Hz, J_2 = 16.5 Hz, 1H), 1.58 (d, *J* = 6.0 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 174.4, 137.7, 137.4, 129.6, 128.5, 128.4, 127.9, 127.8, 127.7, 127.5, 84.3, 81.7, 72.0, 71.5, 68.3, 46.3, 40.1, 39.0, 17.8; HRMS (ESI) calcd for $C_{24}H_{28}NO_3^+$ $[M + H]^+$ 378.2069, found 378.2057.

(1*R*,5*S*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9ba)

Following general procedure, starting from **8ba** (1.06 g, 1.83 mmol) to give **9ba** (0.89 g, 90%) as colourless oil; $[\alpha]_D^{20}$ +44.0 (*c* 3.00 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2866, 1695, 1412, 1113, 741, 699; δ_H ($CDCl_3$, 300 MHz) 7.32–7.24 (m, 14H), 7.18–7.14 (m, 4H), 7.07–7.04 (m, 2H), 4.58–4.33 (m, 4H), 4.29–4.18 (m, 3H), 4.08 (q, *J* = 4.5 Hz, 1H), 3.89 (d, *J* = 11.1 Hz, 1H), 3.80–3.67 (m, 2H), 3.56 (dd, J_1 = 4.2 Hz, J_2 = 9.6 Hz, 1H), 3.38 (dd, J_1 = 5.4 Hz, J_2 = 8.1 Hz, 1H), 3.07 (dd, J_1 = 9.0 Hz, J_2 = 17.1 Hz, 1H), 2.60 (dd, J_1 = 2.7 Hz, J_2 = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.0, 140.1, 137.9, 137.7, 137.6, 128.8, 128.4, 128.36, 128.32, 128.0, 127.9, 127.8, 127.7, 127.4, 87.7, 83.0, 73.3, 72.3, 72.2, 69.0, 67.4, 58.9, 40.26, 40.24; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 534.2639, found 534.2623.

(1*R*,5*S*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9bb)

Following general procedure, starting from **8bb** (0.65 g, 1.07 mmol) to give **9bb** (0.50 g, 82%) as colourless oil; $[\alpha]_D^{20}$ +46.7 (*c* 1.20 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2864, 1694, 1454, 1251, 1114, 739, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.16 (m, 13H), 7.16–7.05 (m, 4H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.59–4.52 (m, 2H), 4.46 (d, *J* = 11.1 Hz, 1H), 4.36 (d, *J* = 11.7 Hz, 1H), 4.30–4.20 (m, 3H), 4.07 (q, *J* = 4.5 Hz, 1H), 3.98 (d, *J* = 11.4 Hz, 1H), 3.75–3.67 (m, 5H), 3.57 (dd, J_1 = 3.9 Hz, J_2 = 9.6 Hz, 1H), 3.39 (dd, J_1 = 5.1 Hz, J_2 = 8.1 Hz, 1H), 3.08 (dd, J_1 = 9.0 Hz, J_2 = 16.8 Hz, 1H), 2.56 (dd, J_1 = 5.4 Hz, J_2 = 16.8 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 174.0, 158.8, 138.0, 137.8, 137.7, 132.2, 129.0, 128.45, 128.40, 128.36, 128.0, 127.8, 114.2, 87.9, 83.0, 73.3, 72.3, 72.2, 69.0, 67.7, 58.9, 55.3, 40.6, 39.7; HRMS (ESI) calcd for $C_{36}H_{38}NO_5^+$ $[M + H]^+$ 564.2750, found 564.2743.

(1*S*,5*S*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(furan-2-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9bc)

Following general procedure, starting from **8bc** (0.58 g, 1.00 mmol) to give **9bc** (0.45 g, 85%) as colourless oil; $[\alpha]_D^{20}$ +56.7 (*c* 1.2 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2864, 1698, 1454, 1363, 1115, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.35–7.19 (m, 16H), 6.30 (t, *J* = 2.4 Hz, 1H), 6.16 (d, *J* = 3.0 Hz, 1H), 4.67–4.45 (m, 4H), 4.39 (d, *J* = 11.4 Hz, 1H), 4.30 (t, *J* = 4.8 Hz, 1H), 4.24–4.14 (m, 2H), 4.04 (q, *J* = 4.5 Hz, 1H), 3.86–3.80 (m, 1H), 3.69 (dd, J_1 = 5.4 Hz, J_2 = 9.9 Hz, 1H), 3.55 (dd, J_1 = 3.6 Hz, J_2 = 9.9 Hz, 1H), 3.46 (dd, J_1 = 5.4 Hz, J_2 = 8.1 Hz, 1H), 2.97 (dd, J_1 = 9.0 Hz, J_2 = 16.8 Hz, 1H), 2.60 (dd, J_1 = 3.3 Hz, J_2 = 16.8 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 173.6, 153.6, 142.2, 138.1, 137.9, 128.48, 128.45, 128.42, 128.0, 127.9, 127.8, 110.6, 107.3, 87.8, 83.8, 73.4, 72.8, 72.4, 69.2, 66.9, 59.0, 38.2, 34.7; HRMS (ESI) calcd for $C_{33}H_{34}NO_5^+$ $[M + H]^+$ 524.2437, found 524.2428.

(1*R*,5*S*,6*S*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-((*E*)-prop-1-en-1-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9bd)

Following general procedure, starting from **8bd** (1.00 g, 1.83 mmol) to give **9bd** (0.75 g, 82%) as colourless oil; $[\alpha]_D^{20}$ +32.9 (*c* 0.85 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2919, 2862, 1687, 1453, 1110, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.33–7.24 (m, 15H), 5.54–5.35 (m, 2H), 4.60–4.45 (m, 6H), 4.31 (t, *J* = 4.2 Hz, 1H), 4.11–4.05 (m, 1H), 4.06–4.01 (m, 1H), 3.99–3.91 (m, 1H), 3.66–3.54 (m, 2H), 3.11–3.06 (m, 1H), 2.84–2.76 (m, 1H), 2.19 (dd, J_1 = 3.0 Hz, J_2 = 16.5 Hz, 1H), 1.63 (d, *J* = 5.7 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 174.2, 138.1, 137.9, 137.8, 129.3, 128.5, 128.0, 127.9, 127.8, 127.77, 127.71, 87.7, 82.9, 73.4, 72.3, 72.2, 69.1, 67.3, 59.0, 39.7, 38.5, 18.0; HRMS (ESI) calcd for $C_{32}H_{35}NO_4Na^+$ $[M + Na]^+$ 520.2464, found 520.2458.

(1*R*,5*S*,6*R*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9ca)

Following general procedure, starting from **8ca** (0.72 g, 1.27 mmol) to give **9ca** (0.50 g, 76%) as colourless oil; $[\alpha]_D^{20}$ +47.8 (*c* 1.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3029, 2924, 2873, 1696, 1454, 1142, 737, 699; δ_H ($CDCl_3$, 300 MHz) 7.23–7.15 (m, 16H), 7.04–6.99 (m, 4H), 4.77–4.45 (m, 4H), 4.43–4.38 (m, 1H), 4.04–3.88 (m, 4H), 3.78 (d, *J* = 11.1 Hz, 1H), 3.71–3.61 (m, 2H), 3.06 (dd, J_1 = 8.4 Hz, J_2 = 16.5 Hz, 1H), 2.91 (dd, J_1 = 4.2 Hz, J_2 = 8.1 Hz, 1H), 2.46 (d, *J* = 16.8 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 175.6, 140.6, 138.23, 138.16, 137.5, 128.9, 128.45, 128.42, 128.40, 128.0, 127.9, 127.8, 127.7, 127.68, 127.5, 79.2, 79.13, 73.9, 73.3, 72.4, 67.0, 66.3, 57.0, 41.5, 41.2; HRMS (ESI) calcd for $C_{35}H_{36}NO_4^+$ $[M + H]^+$ 534.2644, found 534.2633.

(1*R*,5*S*,6*R*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9cb)

Following general procedure, starting from **8cb** (1.50 g, 2.46 mmol) to give **9cb** (1.13 g, 81%) as colourless oil; $[\alpha]_D^{20}$ +37.3 (*c* 0.75 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2930, 2870, 1694, 1513, 1454, 1251, 1115, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.31–7.21 (m, 13H), 7.14–7.11 (m, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.55–4.53 (m, 4H), 4.43 (t, *J* = 7.2 Hz, 1H), 4.17 (d, *J* = 11.4 Hz, 1H), 4.11–3.91 (m, 4H), 3.79–3.74 (m, 4H), 3.64 (t, *J* = 4.5 Hz, 1H), 3.10 (dd, J_1 = 8.4 Hz, J_2 = 16.5 Hz, 1H), 3.02 (dd, J_1 = 4.2 Hz, J_2 = 7.8 Hz, 1H), 2.47 (d, *J* = 16.8 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 175.6, 158.8, 138.2, 138.1, 137.5, 132.5, 128.7, 128.38, 128.36, 127.88, 127.85, 127.7, 127.65, 127.61, 114.1, 79.1, 78.9, 73.7, 72.3, 67.2, 66.3, 56.8, 55.3, 41.6, 40.5; HRMS (ESI) calcd for $C_{34}H_{38}NO_5^+$ $[M + H]^+$ 564.2744, found 564.2744.

(1*S*,5*S*,6*R*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(furan-2-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9cc)

Following general procedure, starting from **8cc** (0.54 g, 0.94 mmol) to give **9cc** (0.40 g, 81%) as colourless oil; $[\alpha]_D^{20}$ +40.0 (*c* 0.50 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2927, 2872, 1699, 1455, 1139, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.35–7.20 (m, 16H), 6.29–6.28 (m, 1H), 6.10 (d, *J* = 3.3 Hz, 1H), 4.69 (m, 2H), 4.54 (m, 2H), 4.38–4.32 (m, 2H), 4.20 (d, *J* = 8.4 Hz, 1H), 4.02–3.95 (m, 2H), 4.18–4.08 (m, 1H), 3.76 (t, *J* = 8.7 Hz, 2H), 3.16 (dd, J_1 = 4.5 Hz, J_2 = 7.5 Hz, 1H), 3.03 (dd, J_1 = 8.4 Hz, J_2 = 16.2 Hz, 1H), 2.50 (dd, J_1 = 1.5 Hz, J_2 = 13.5 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 175.2, 154.3, 142.1, 138.3, 138.2, 137.7, 128.5, 128.47, 128.43, 128.06, 127.99, 127.91, 127.8, 127.7, 110.5, 107.2, 79.4, 73.9, 73.3, 72.9, 66.9, 66.5, 57.0, 39.6, 35.8; HRMS (ESI) calcd for $C_{33}H_{34}NO_5^+$ $[M + H]^+$ 524.2437, found 524.2435.

(1*R*,5*S*,6*R*,7*S*,7*aS*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-((*E*)-prop-1-en-1-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9cd)

Following general procedure, starting from **8cd** (0.88 g, 1.62 mmol) to give **9cd** (0.72 g, 90%) as colourless oil; $[\alpha]_D^{20}$ +8.0 (*c* 1.5 in CH_2Cl_2); ν_{max}/cm^{-1} 3062, 3030, 2918, 2874, 1697, 1453, 1139, 738, 698; δ_H ($CDCl_3$, 300 MHz) 7.31–7.25 (m, 15H), 5.56–5.44 (m, 1H), 5.28–5.20 (m, 1H), 4.71–4.62 (m, 2H), 4.56–4.52 (m, 3H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.23–4.11 (m, 3H), 3.96–3.91 (m, 1H), 3.79–3.73 (m, 1H), 3.68 (dd, J_1 = 4.2 Hz, J_2 = 7.5 Hz, 1H), 3.08–3.01 (m, 1H), 2.84 (dd, J_1 = 7.8 Hz, J_2 = 16.2 Hz, 1H), 2.16 (d, *J* = 16.2 Hz, 2H), 1.60 (d, *J* = 6.0 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 175.4, 138.2, 138.1, 137.6, 128.6, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 79.3, 78.0, 73.8, 73.2, 72.2, 66.4, 66.2, 56.6, 40.3, 38.4, 17.9; HRMS (ESI) calcd for $C_{32}H_{36}NO_4^+$ $[M + H]^+$ 498.2644, found 498.2640.

(1*S*,5*S*,6*R*,7*R*,7*aR*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9da)

Following general procedure, starting from **8da** (1.52 g, 2.61 mmol) to give **9da** (1.19 g, 86%) as colourless oil; $[\alpha]_D^{20}$ −45.2 (*c* 1.55 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2870, 1692, 1454, 1109, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.02 (m, 20H), 4.57–4.45 (m, 4H), 4.38 (d, *J* = 8.4 Hz, 1H), 4.24–4.14 (m, 2H), 4.10–4.02 (m, 2H), 3.95–3.91 (m, 1H), 3.75 (d, *J* = 6.4 Hz, 1H), 3.66 (t, *J* = 7.8 Hz, 1H), 3.49 (t, *J* = 7.8 Hz, 1H), 3.05 (dd, J_1 = 8.7 Hz, J_2 = 16.8 Hz, 1H), 2.59 (d, *J* = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 172.7, 140.2, 138.3, 138.0, 137.7, 128.3, 128.2, 127.9, 127.7, 127.68, 127.66, 127.4, 127.1, 85.8, 79.1, 73.2, 73.1, 72.6, 66.2, 64.0, 55.3, 41.9, 40.6; HRMS (ESI) calcd for $C_{35}H_{36}NO_4^+$ $[M + H]^+$ 534.2644, found 534.2643.

(1*S*,5*S*,6*R*,7*R*,7*aR*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9db)

Following general procedure, starting from **8db** (1.70 g, 2.79 mmol) to give **9db** (1.12 g, 71%) as colourless oil; $[\alpha]_D^{20}$ −41.9 (*c* 1.05 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2917, 2870, 1697, 1514, 1454, 1113, 832, 740, 699; δ_H ($CDCl_3$, 300 MHz) 7.30–7.16 (m, 15H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.54 (d, *J* = 8.7 Hz, 2H), 4.58–4.44 (m, 4H), 3.39 (d, *J* = 11.4 Hz, 1H), 4.24 (t, *J* = 7.5 Hz, 1H), 4.20–4.17 (m, 1H), 4.12–4.03 (m, 2H), 3.96–3.92 (m, 1H), 3.79–3.75 (m, 1H), 3.65 (s, 3H), 3.60 (d, *J* = 7.5 Hz, 1H), 3.54 (t, *J* = 7.5 Hz, 1H), 3.05 (dd, J_1 = 8.7 Hz, J_2 = 17.1 Hz, 1H), 2.53 (d, *J* = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 172.7, 158.5, 138.4, 138.1, 137.8, 132.4, 129.3, 128.34, 128.31, 128.2, 127.9, 127.67, 127.61, 127.4, 113.6, 85.8, 79.1, 73.2, 73.1, 72.5, 66.4, 64.2, 55.3, 55.2, 42.3, 39.9; HRMS (ESI) calcd for $C_{36}H_{40}NO_6^+$ $[M + H]^+$ 582.2856, found: 582.2844.

(1*R*,5*S*,6*R*,7*R*,7*aR*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-(furan-2-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9dc)

Following general procedure, starting from **8dc** (0.42 g, 0.74 mmol) to give **9dc** (0.35 g, 91%) as colourless oil; $[\alpha]_D^{20}$ −43.3 (*c* 0.60 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2921, 2866, 1696, 1454, 1415, 1112, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.37–7.17 (m, 16H), 6.12–6.08 (m, 2H), 4.69–4.55 (m, 3H), 4.52–4.42 (m, 3H), 4.24 (t, *J* = 7.2 Hz, 1H), 4.02–3.93 (m, 3H), 3.80–3.74 (m, 2H), 3.57 (t, *J* = 7.5 Hz, 1H), 2.98 (dd, J_1 = 8.4 Hz, J_2 = 16.8 Hz, 1H), 2.60 (d, *J* = 16.5 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 172.3, 153.8, 141.6, 138.5, 138.3, 137.9, 128.5, 128.3, 127.9, 127.8, 127.4, 110.5, 107.5, 85.6, 79.8, 73.3, 73.26, 73.1, 66.1, 64.3, 55.3, 40.2, 35.8; HRMS (ESI) calcd for $C_{33}H_{34}NO_5^+$ $[M + H]^+$ 524.2437, found 524.2435.

(1*S*,5*S*,6*R*,7*R*,7*aR*)-6,7-Bis(benzyloxy)-5-((benzyloxy)methyl)-1-((*E*)-prop-1-en-1-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (9dd)

Following general procedure, starting from **8dd** (1.24 g, 2.28 mmol) to give **9dd** (0.95 g, 84%) as colourless oil; $[\alpha]_D^{20}$ −25.6 (*c* 1.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3034, 2916, 1694, 153, 1123, 736, 696; δ_H ($CDCl_3$, 300 MHz) 7.33–7.22 (m, 15H), 5.49–5.30 (m, 2H), 4.75–4.70 (m, 1H), 4.66–4.62 (m, 1H), 4.60–4.55 (m, 2H), 4.51–4.46 (m, 2H), 4.30–4.17 (m, 3H), 3.89–3.81 (m, 2H), 3.67 (d, *J* = 9.6 Hz, 1H), 2.98–2.91 (m, 1H), 2.81 (dd, J_1 = 6.9 Hz, J_2 = 16.2 Hz, 1H), 2.11 (d, *J* = 16.2 Hz, 1H), 1.28 (d, *J* = 5.1 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 172.8, 138.4, 138.3, 138.1, 130.0, 128.4, 128.36, 128.3, 128.0, 127.7, 127.65, 127.58, 127.51, 127.5, 127.3, 85.2, 79.0, 73.5, 73.2, 72.2, 66.2, 64.0, 55.0, 42.2, 41.1, 17.5; HRMS (ESI) calcd for $C_{32}H_{35}NO_4Na^+$ $[M + Na]^+$ 520.2464, Found 520.2457.

(1*S*,6*R*,7*R*,8*R*,8*aR*)-6,7,8-Tris(benzyloxy)-1-phenylhexahydroindolizin-3(2*H*)-one (9ea)

Following general procedure, starting from **8ea** (1.16 g, 1.99 mmol) to give **9ea** (0.80 g, 75%) as colourless oil; $[\alpha]_D^{20}$ −70.0 (*c* 0.20 in CH_2Cl_2); ν_{max}/cm^{-1} 3355, 3030, 2924, 1690, 1453, 1100, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.37–7.11 (m, 18H), 7.08–7.03 (m, 2H), 4.54–4.40 (m, 4H), 4.38 (d, *J* = 11.1 Hz, 1H), 4.23 (t, *J* = 7.2 Hz, 1H), 4.18–4.13 (m, 1H), 4.10–4.02 (m, 1H), 3.96–3.92 (m, 1H), 3.78–3.75 (m, 1H), 3.70 (t, *J* = 8.1 Hz, 1H), 3.50 (t, *J* = 7.8 Hz, 1H), 3.08 (dd, J_1 = 8.7 Hz, J_2 = 17.1 Hz, 1H)), 2.61 (d, *J* = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 172.9, 140.4, 138.5, 138.2, 137.8, 128.5, 128.4, 128.0, 127.9, 127.8, 127.5, 127.3, 86.0, 79.3, 73.4, 73.2, 72.7, 66.5, 64.2, 55.5, 42.1, 40.8; HRMS (ESI) calcd for $C_{35}H_{36}NO_4$ $[M + H]^+$ 534.2644, found 534.2639.

(1*S*,6*R*,7*R*,8*R*,8*aR*)-6,7,8-Tris(benzyloxy)-1-(4-methoxyphenyl)-hexahydroindolizin-3(2*H*)-one (9eb)

Following general procedure, starting from **8eb** (0.46 g, 0.75 mmol) to give **9eb** (0.33 g, 78%) as colourless oil; $[\alpha]_D^{20}$ −52.0 (*c* 5.0 in CH_2Cl_2); ν_{max}/cm^{-1} 3031, 2924, 1686, 1513, 1454, 1251, 1104, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.33–7.15 (m, 15H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.55 (d, *J* = 8.7 Hz, 2H), 4.59–4.37 (m, 4H), 4.38 (d, *J* = 11.3 Hz, 1H), 4.25 (t, *J* = 7.4 Hz, 1H), 4.18 (dd, J_1 = 5.1 Hz, J_2 = 9.6 Hz, 1H), 4.12–4.05 (m, 2H), 3.97–3.93 (m, 1H), 3.77 (dd, J_1 = 1.9 Hz, J_2 = 9.6 Hz, 1H), 3.68 (s, 3H), 3.65–3.62 (m, 1H), 3.56–3.51 (m, 1H), 3.07 (dd, J_1 = 8.9 Hz, J_2 = 17.2 Hz, 1H), 2.54 (d, *J* = 17.0 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 172.9, 158.8, 138.6, 138.3, 137.9, 132.6, 129.5, 128.5, 128.48, 128.39, 128.1, 127.84, 127.80, 127.6, 113.8, 86.0, 79.4, 73.4, 73.3, 72.7, 66.7, 55.5, 55.4, 42.5, 40.1; HRMS (ESI) calcd for $C_{35}H_{38}NO_3^+$ $[M + H]^+$ 564.2750, found 564.2759.

(1*S*,6*R*,7*R*,8*R*,9*R*,9*aR*)-6,7,8,9-Tetrakis(benzyloxy)-1-phenylhexahydro-1*H*-pyrrolo[1,2-*a*]azepin-3(2*H*)-one (9fa)

Following general procedure, starting from **8fa** (0.60 g, 0.85 mmol) to give **9fa** (0.40 g, 72%) as colourless oil; $[\alpha]_D^{20}$ −45.0 (*c* 0.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2921, 2878, 1698, 1496, 1454, 1109, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.50–7.19 (m, 21H), 7.08–7.00 (m, 4H), 4.80 (d, *J* = 12.3 Hz, 1H), 4.73–4.63 (m, 3H), 4.64–4.57 (m, 2H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.24 (dd, J_1 = 6.9 Hz, J_2 = 14.1 Hz, 1H), 4.04–3.96 (m, 2H), 3.89–3.85 (m, 2H), 3.67 (d, *J* = 3.3 Hz, 1H), 3.04–2.91 (m, 2H), 2.65 (dd, J_1 = 6.0 Hz, J_2 = 16.8 Hz, 1H), 2.45 (dd, J_1 = 9.0 Hz, J_2 = 17.1 Hz, 1H); δ_C ($CDCl_3$, 75 MHz) 173.4, 140.8, 138.9, 138.8, 138.7, 137.7, 128.9, 128.6, 128.4, 128.3, 128.29, 128.1, 128.0, 127.8, 127.69, 27.66, 127.6, 127.5, 127.4, 127.2, 127.0, 79.7, 79.0, 75.7, 74.0, 73.7, 72.2, 71.8, 66.5, 42.2, 39.6, 38.8; HRMS (ESI) calcd for $C_{43}H_{43}NO_5Na^+$ $[M + Na]^+$ 676.3039, found 676.3029.

General procedure for the reduction of lactams 9 to 11

$LiAlH_4$ (104 mg, 3 mmol) was added to a solution of the lactam **9** (1 mmol) in THF (10 mL) at 0 °C. The reaction mixture was refluxed for 2 h, then quenched with water (30 μL), an aqueous 10% NaOH (20 μL), and water (60 μL) and stirred for 1 h at room temperature. Sodium sulphate was added and the mixture was stirred for 1 h and filtered through Celite, and the filtrate was concentrated under vacuum to give a residue, which was purified by silica gel chromatography (EtOAc–petroleum ether) to give an oil product.

General procedure for hydrogenation of 9 or 11 to bicyclic iminosugars 10 or 12

Conc. HCl (1.3 mL) and 10% Pd/C (13 mg) were added to a solution of compound **9** or **11** (0.25 mmol) in methanol (13 mL). The mixture was then stirred at room temperature under an atmosphere of H_2 overnight. After completion of the reaction, the solution was filtered through Celite and washed with methanol. The solvent was removed under reduced pressure. For compound **10**, the residue was purified by silica gel chromatography (EtOAc–MeOH). And for compound **12**, the residue was neutralized by $NH_3{\cdot}H_2O$ (25%, 10 mL), then purified by acid ion exchange resin column to give colourless syrup **12**.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10aa)

Following general procedure, starting from **9aa** (0.21 g, 0.50 mmol) to give **10aa** (0.11 g, 94%) as colourless oil; $[\alpha]_D^{20}$

+104.0 (*c* 0.50 in CH_3OH); ν_{max}/cm^{-1} 3342, 1658, 1125; δ_H (D_2O, 300 MHz) 7.47–7.35 (m, 3H), 7.19 (d, *J* = 6.9 Hz, 2H), 4.33 (q, *J* = 7.2 Hz, 1H), 4.25 (t, *J* = 7.8 Hz, 1H), 3.94 (t, *J* = 7.8 Hz, 1H), 3.61 (dd, J_1 = 8.1 Hz, J_2 = 12.0 Hz, 1H), 3.28 (dd, J_1 = 8.4 Hz, J_2 = 17.2 Hz, 1H), 3.20–3.10 (m, 2H), 2.62 (d, *J* = 17.2 Hz, 1H); δ_C (D_2O, 75 MHz) 176.0, 139.5, 128.9, 127.5, 127.4, 77.3, 74.5, 67.8, 48.8, 46.0, 40.2; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1230, found 264.1229.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-1-(4-methoxyphenyl) tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10ab)

Following general procedure, starting from **9ab** (0.12 g, 0.27 mmol) to give **10ab** (70 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +80.0 (*c* 0.20 in CH_3OH); ν_{max}/cm^{-1} 3329, 2919, 1667, 1514, 1456, 1251, 1123, 618; δ_H (D_2O, 300 MHz) 7.04 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 4.26 (q, *J* = 7.2 Hz, 1H), 4.14 (t, *J* = 7.8 Hz, 1H), 3.83–3.78 (m, 1H), 3.76 (s, 3H), 3.57–3.48 (m, 1H), 3.19 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 3.11–3.03 (m, 2H), 2.49 (dd, J_1 = 0.9 Hz, J_2 = 17.1 Hz, 1H); δ_C (D_2O, 75 MHz) 176.3, 158.0, 132.2, 128.7, 114.3, 77.3, 74.5, 68.0, 55.2, 46.0, 40.4, 39.6; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1230, found 264.1229.

(1*S*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-1-propyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10ad)

Following general procedure, starting from **9ad** (0.11 g, 0.29 mmol) to give **10ad** (57 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +40.0 (*c* 0.20 in CH_3OH); ν_{max}/cm^{-1} 3313, 2929, 1660, 1448, 1123, 618; δ_H (D_2O, 300 MHz) 4.41–4.34 (m, 1H), 3.97 (t, *J* = 3.0 Hz, 2H), 3.61–3.54 (m, 1H), 3.25 (dd, J_1 = 6.0 Hz, J_2 = 12.0 Hz, 1H), 2.86 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 2.63–2.61 (m, 1H), 2.22 (dd, J_1 = 5.7 Hz, J_2 = 17.1 Hz, 1H), 1.56–1.26 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); δ_C (D_2O, 75 MHz) 177.2, 77.5, 74.1, 67.2, 46.3, 38.6, 33.2, 31.5, 19.8, 13.2; HRMS (ESI) calcd for $C_{10}H_{18}NO_3^+$ $[M + H]^+$ 200.1281, found 200.1281.

(1*R*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-1-((*E*)-prop-1-en-1-yl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10ad′)

To a solution of **9ad** (36 mg, 0.095 mmol) in dried CH_2Cl_2 (5 mL) at 0 °C was added BBr_3 (37 μL, 4 eq.) under N_2 atmosphere. The resulting mixture was stirred for 1 h, and then quenched with MeOH (2 mL) at 0 °C. $NH_3{\cdot}H_2O$ was added and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (EtOAc–MeOH, 20 : 1 v/v) give colourless syrup **10ad′** (18 mg, 96%) as colourless oil; $[\alpha]_D^{20}$ +33.3 (*c* 0.30 in CH_3OH); ν_{max}/cm^{-1} 3341, 2924, 1656, 1456, 1093; δ_H (D_2O, 300 MHz) 5.65–5.58 (m, 1H), 5.50–5.42 (m, 1H), 4.32 (t, *J* = 6.0 Hz, 1H), 3.99–3.88 (m, 2H), 3.50 (q, *J* = 7.5 Hz, 1H), 3.26–3.20 (m, 2H), 2.96 (dd, J_1 = 7.5 Hz, J_2 = 17.1 Hz, 1H), 2.21 (d, *J* = 16.8 Hz, 1H), 1.67–1.65 (m, 3H); δ_C (D_2O, 75 MHz) 176.5, 128.6, 128.0, 127.6, 77.6, 74.5, 68.0, 46.5, 39.6, 37.6, 17.1; HRMS (ESI) calcd for $C_{36}H_{40}NO_4^+$ $[M + H]^+$ 550.2957, found 550.2947.

(1*R*,5*S*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10ba)

Following general procedure, starting from **9ba** (0.19 g, 0.35 mmol) to give **10ba** (93 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +27.6 (*c* 1.45 in CH_3OH); ν_{max}/cm^{-1} 3316, 1659, 1406, 1123, 618; δ_H (D_2O, 300 MHz) 7.44–7.32 (m, 3H), 7.16 (d, *J* = 7.2 Hz, 2H), 4.23–4.13 (m, 2H), 3.96–3.87 (m, 2H), 3.69 (dd, J_1 = 3.3 Hz, J_2 = 12.3 Hz, 1H), 3.51–3.49 (m, 1H), 3.27 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 3.11 (t, *J* = 8.4 Hz, 1H), 2.57 (d, *J* = 17.1 Hz, 1H); δ_C (D_2O, 75 MHz) 177.2, 139.6, 129.1, 127.7, 127.6, 78.9, 74.3, 67.2, 60.6, 59.5, 40.25, 40.18; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1230, found 264.1229.

(1*R*,5*S*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10bb)

Following general procedure, starting from **9bb** (0.17 g, 0.29 mmol) to give **10bb** (85 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +108.0 (*c* 0.50 in CH_3OH); ν_{max}/cm^{-1} 3338, 2931, 1662, 1514, 1437, 1122, 830, 618; δ_H (D_2O, 300 MHz) 7.11 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 4.22–4.16 (m, 2H), 3.95 (dd, J_1 = 3.6 Hz, J_2 = 12.3 Hz, 1H), 3.86 (t, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 3.72 (dd, J_1 = 3.6 Hz, J_2 = 12.0 Hz, 1H), 3.54–3.51 (m, 1H), 3.27 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 3.17–3.11 (m, 1H), 2.53 (dd, J_1 = 1.2 Hz, J_2 = 17.1 Hz, 1H); δ_C (D_2O, 75 MHz) 177.2, 158.1, 132.2, 128.8, 114.4, 78.9, 74.3, 67.4, 60.5, 59.4, 55.4, 40.4, 39.5; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ $[M + H]^+$ 294.1336, found 294.1334.

(1*S*,5*S*,6*S*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-propyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10bd)

Following general procedure, starting from **9bd** (0.25 g, 0.51 mmol) to give **10bd** (99 mg, 84%) as colourless oil; $[\alpha]_D^{20}$ +32.0 (*c* 0.25 in CH_3OH); ν_{max}/cm^{-1} 3342, 2929, 1661, 1418, 1085; δ_H (D_2O, 300 MHz) 4.24–4.20 (m, 1H), 4.00–3.97 (m, 2H), 3.93 (dd, J_1 = 3.6 Hz, J_2 = 12.0 Hz, 1H), 3.75 (dd, J_1 = 3.9 Hz, J_2 = 12.0 Hz, 1H), 3.64–3.60 (m, 1H), 2.91 (dd, J_1 = 8.6 Hz, J_2 = 17.1 Hz, 1H), 2.66–2.65 (m, 1H), 2.25 (dd, J_1 = 3.3 Hz, J_2 = 8.2 Hz, 1H), 1.64–1.55 (m, 1H), 1.49–1.30 (m, 3H), 0.95 (t, *J* = 6.9 Hz, 3H); δ_C (D_2O, 75 MHz) 178.2, 79.0, 73.9, 66.2, 60.7, 59.9, 38.3, 31.5, 19.9, 13.2; HRMS (ESI) calcd for $C_{11}H_{20}NO_4^+$ $[M + H]^+$ 230.1387, found 230.1386.

(1*R*,5*S*,6*R*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10ca)

Following general procedure, starting from **9ca** (0.11 g, 1.27 mmol) to give **10ca** (51 mg, 91%) as colourless oil; $[\alpha]_D^{20}$ +120.0 (*c* 0.30 in CH_3OH); ν_{max}/cm^{-1} 3374, 2946, 1660, 1418, 1122, 703; δ_H (D_2O, 300 MHz) 7.51–7.42 (m, 3H), 7.25–7.22 (m, 2H), 4.49 (t, *J* = 7.2 Hz, 1H), 4.24 (t, *J* = 4.8 Hz, 1H), 4.03–3.96 (m, 2H), 3.92–3.86 (m, 2H), 3.42 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 3.34 (dd, J_1 = 4.8 Hz, J_2 = 8.7 Hz, 1H), 2.67 (d, *J* = 17.1 Hz, 1H); δ_C (D_2O, 75 MHz) 178.3, 139.8, 129.0, 127.8, 127.6, 74.2, 70.2, 68.2, 58.9, 58.5, 41.1, 40.6; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1230, found 264.1229.

(1*R*,5*S*,6*R*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10cb)

Following general procedure, starting from **9cb** (0.17 g, 0.31 mmol) to give **10cb** (80 mg, 89%) as colourless oil; $[\alpha]_D^{20}$+90.0 (*c* 0.20 in CH_3OH); ν_{max}/cm^{-1} 3175, 1653, 1123, 618; δ_H (D_2O, 300 MHz) 7.13 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 4.42 (t, *J* = 7.5 Hz, 1H), 4.19 (t, *J* = 4.8 Hz, 1H), 3.95–3.90 (m, 2H), 3.88–3.84 (m, 5H), 3.42–3.36 (m, 1H), 3.33–3.28 (m, 1H), 2.58 (d, *J* = 17.1 Hz, 1H); δ_C (D_2O, 75 MHz) 178.3, 158.1, 132.3, 128.8, 114.3, 74.1, 70.2, 68.3, 58.9, 58.4, 55.4, 41.2, 39.9; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ $[M + H]^+$ 294.1336, found 294.1334.

(1*S*,5*S*,6*R*,7*S*,7*aS*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-propyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10cd)

Following general procedure, starting from **9cd** (90 mg, 0.18 mmol) to give **10cd** (41 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +20.0 (*c* 0.60 in CH_3OH); ν_{max}/cm^{-1} 3353, 2933, 1662, 1417, 1119; δ_H (D_2O, 300 MHz) 4.47 (t, *J* = 4.5 Hz, 1H), 4.19–4.07 (m, 2H), 3.97–3.93 (m, 1H), 3.84 (m, 2H), 2.94 (dd, J_1 = 8.4 Hz, J_2 = 17.1 Hz, 1H), 2.66–2.64 (m, 1H), 2.23 (d, *J* = 17.1 Hz, 1H), 1.58–1.28 (m, 4H), 0.92 (t, *J* = 6.6 Hz, 3H); δ_C (D_2O, 75 MHz) 179.1, 74.0, 69.5, 66.4, 59.2, 58.3, 39.4, 33.1, 19.8, 13.3; HRMS (ESI) calcd for $C_{11}H_{20}NO_4^+$ $[M + H]^+$ 230.1387, found 230.1387.

(1*S*,5*S*,6*R*,7*R*,7*aR*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-phenyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10da)

Following general procedure, starting from **9da** (0.20 g, 0.36 mmol) to give **10da** (96 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ −128.4 (*c* 0.95 in CH_3OH); ν_{max}/cm^{-1} 3343, 2927, 1654, 1453, 1122, 703; δ_H (D_2O, 300 MHz) 7.45–7.37 (m, 3H), 7.28–7.25 (m, 2H), 4.36 (t, *J* = 8.4 Hz, 1H), 4.17 (t, *J* = 8.1 Hz, 1H), 4.03 (dd, J_1 = 3.3 Hz, J_2 = 12.0 Hz, 1H), 3.90–3.86 (m, 2H), 3.73 (d, *J* = 12.0 HZ, 1H), 3.28 (dd, J_1 = 8.1 Hz, J_2 = 17.1 Hz, 1H), 3.14 (t, *J* = 8.7 Hz, 1H), 2.69 (d, *J* = 17.1 Hz, 1H); δ_C (D_2O,75 MHz) 175.7, 139.3, 128.7, 128.0, 127.5, 78.1, 72.4, 66.3, 56.8, 56.7, 41.0, 40.0; HRMS (ESI) calcd for $C_{14}H_{18}NO_4^+$ $[M + H]^+$ 264.1230, found 264.1229.

(1*S*,5*S*,6*R*,7*R*,7*aR*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-(4-methoxyphenyl)tetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10db)

Following general procedure, starting from **9db** (0.21 g, 0.37 mmol) to give **10db** (96 mg, 87%) as colourless oil; $[\alpha]_D^{20}$ −44.0 (*c* 0.50 in CH_3OH); ν_{max}/cm^{-1} 3131, 1652, 1404, 1123, 618; δ_H (D_2O, 300 MHz) 7.17 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 4.33 (t, *J* = 8.7 Hz, 1H), 4.10 (dd, J_1 = 6.6 Hz, J_2 = 9.3 Hz, 1H), 3.99 (dd, J_1 = 3.9 Hz, J_2 = 12.3 Hz, 1H), 3.85–3.82 (m, 1H), 3.81 (s, 3H), 3.70 (dd, J_1 = 3.3 Hz, J_2 = 12.3 Hz, 1H), 3.23 (dd, J_1 = 8.1 Hz, J_2 = 17.1 Hz, 1H), 3.11 (t, *J* = 8.7 Hz, 1H), 2.60 (d, *J* = 17.1 Hz, 2H); δ_C (D_2O, 75 MHz) 175.7, 158.0, 131.9, 129.2, 114.0, 78.1, 72.4, 66.4, 56.8, 56.7, 55.3, 41.2, 39.3; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ $[M + H]^+$ 294.1336, found 294.1338.

(1*R*,5*S*,6*R*,7*R*,7*aR*)-6,7-Dihydroxy-5-(hydroxymethyl)-1-propyltetrahydro-1*H*-pyrrolizin-3(2*H*)-one (10dd)

Following general procedure, starting from **9dd** (0.20 g, 0.40 mmol) to give **10dd** (84 mg, 92.8%) as colourless oil; $[\alpha]_D^{20}$ −5.3 (*c* 1.50 in CH_3OH); ν_{max}/cm^{-1} 3341, 2958, 2927, 1654, 1119; δ_H (D_2O, 300 MHz) 4.37 (t, *J* = 8.1 Hz, 1H), 4.14–4.06 (m, 2H), 3.92–3.71 (m, 3H), 2.84 (dd, J_1 = 7.2 Hz, J_2 = 13.5 Hz, 1H), 2.49 (m, 1H), 2.25 (d, *J* = 17.1 Hz, 1H), 1.54–1.25 (m, 4H), 0.89 (t, *J* = 6.6 Hz, 3H); δ_C (D_2O, 75 MHz) 175.7, 78.1, 71.5, 65.6, 56.6, 56.2, 39.9, 33.9, 30.8, 19.6, 13.3; HRMS (ESI) calcd for $C_{11}H_{20}NO_4^+$ $[M + H]^+$ 230.1387, found 230.1387.

(1*S*,6*R*,7*R*,8*R*,8*aR*)-6,7,8-Trihydroxy-1-phenylhexahydroindolizin-3(2*H*)-one (10ea)

Following general procedure, starting from **9ea** (0.10 g, 0.19 mmol) to give **10ea** (43 mg, 90%) as colourless oil; $[\alpha]_D^{20}$ −75.0 (*c* 0.40 in CH_3OH); ν_{max}/cm^{-1} 3315, 1653, 1406, 1123, 618; δ_H (D_2O, 300 MHz) 7.46–7.38 (m, 3H), 7.27 (d, *J* = 6.9 Hz, 2H), 4.37 (t, *J* = 8.4 Hz, 1H), 4.21–4.18 (m, 1H), 4.03 (dd, J_1 = 3.6 Hz, J_2 = 12.3 Hz, 1H), 3.92–3.87 (m, 2H), 3.74 (dd, J_1 = 3.0 Hz, J_2 = 12.3 Hz, 1H), 3.30 (dd, J_1 = 7.8 Hz, J_2 = 17.1 Hz, 1H), 3.14 (t, *J* = 8.7 Hz, 1H), 2.70 (d, *J* = 17.4 Hz, 1H); δ_C (D_2O, 75 MHz) 175.7, 139.3, 128.7, 128.0, 127.5, 78.1, 72.4, 66.3, 56.8, 56.7, 41.0, 40.0; HRMS (ESI) calcd for $C_{15}H_{19}NO_5Na^+$ $[M + Na]^+$ 316.1155, found 316.1153.

(1*S*,6*R*,7*R*,8*R*,8*aR*)-6,7,8-Trihydroxy-1-(4-methoxyphenyl)-hexahydroindolizin-3(2*H*)-one (10eb)

Following general procedure, starting from **9eb** (90 mg, 0.16 mmol) to give **10eb** (46 mg, 98%) as colourless oil; $[\alpha]_D^{20}$ −120.0 (*c* 0.40 in CH_3OH); ν_{max}/cm^{-1} 3326, 1653, 1406, 1123, 618; δ_H (D_2O, 300 MHz) 7.19 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 4.35 (t, *J* = 8.4 Hz, 1H), 4.15–4.12 (m, 1H), 4.01 (dd, J_1 = 3.6 Hz, J_2 = 12.3 Hz, 1H), 3.90–3.80 (m, 5H), 3.72 (dd, J_1 = 3.3 Hz, J_2 = 12.3 Hz, 1H), 3.25 (dd, J_1 = 8.1 Hz, J_2 = 17.4 Hz, 1H), 3.14 (d, *J* = 17.4 Hz, 1H), 2.63 (d, *J* = 17.4 Hz, 1H); δ_C (D_2O, 75 MHz) 175.7, 158.0, 131.9, 129.2, 114.0, 78.1, 72.4, 66.4, 56.9, 56.7, 55.4, 41.2, 39.3; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ $[M + H]^+$ 294.1342, found 294.1334.

(1*S*,6*R*,7*R*,8*R*,9*R*,9*aR*)-6,7,8,9-Tetrahydroxy-1-phenylhexahydro-1*H*-pyrrolo[1,2-*a*]azepin-3(2*H*)-one (10fa)

Following general procedure, starting from **9fa** (87 mg, 0.13 mmol) to give **10fa** (37 mg, 95%) as colourless oil; $[\alpha]_D^{20}$ +13.3 (*c* 0.15 in CH_3OH); ν_{max}/cm^{-1} 3357, 2923, 1660, 1455, 1093, 702; δ_H (D_2O, 300 MHz) 7.50–7.42 (m, 5H), 4.20–4.17 (m, 2H), 4.13–4.05 (m, 2H), 4.03–3.98 (m, 2H), 3.36 (q, *J* = 9.6 Hz, 1H), 3.14 (d, *J* = 13.5 Hz, 1H), 2.88 (dd, J_1 = 8.7 Hz, J_2 = 17.1 Hz, 1H), 2.71 (dd, J_1 = 10.5 Hz, J_2 = 16.8 Hz, 1H); δ_C (D_2O, 75 MHz) 176.9, 139.5, 129.1, 128.0, 127.7, 72.6, 70.9, 69.7, 68.3, 42.4, 42.2, 38.5; HRMS (ESI) calcd for $C_{15}H_{20}NO_5^+$ $[M + H]^+$ 294.1336, found 294.1335.

(1*S*,2*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-7-phenylhexahydro-1*H*-pyrrolizine (11aa)

Following general procedure, starting from **9aa** (0.52 g, 1.26 mmol) to give **11aa** (0.46 g, 92%) as colourless oil; $[\alpha]_D^{20}$ +113.3 (*c* 0.90 in CH_2Cl_2); ν_{max}/cm^{-1} 3029, 2905, 2865, 1603, 1453, 1122, 737, 697, 619; δ_H ($CDCl_3$, 300 MHz) 7.32–7.12 (m, 13H), 6.98–6.95 (m, 2H), 4.44 (s, 2H), 4.10 (d, *J* = 11.1 Hz, 1H),

4.02 (q, J = 5.1 Hz, 1H), 3.72–3.65 (m, 3H), 3.49 (t, J = 4.5 Hz, 1H), 3.35 (dd, J_1 = 5.4 Hz, J_2 = 11.4 Hz, 1H), 3.18–3.09 (m, 1H), 2.96–2.83 (m, 2H), 2.28–2.14 (m, 1H), 1.96–1.88 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 140.1, 138.28, 138.25, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.5, 126.6, 85.0, 84.9, 73.0, 72.0, 71.9, 58.2, 54.8, 47.5, 27.8; HRMS (ESI) calcd for $C_{27}H_{30}NO_2^+$ $[M + H]^+$ 400.2279, found 400.2271.

(1*S*,2*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-7-(4-methoxyphenyl)-hexahydro-1*H*-pyrrolizine (11ab)

Following general procedure, starting from **9ab** (0.32 g, 0.72 mmol) to give **11ab** (0.31 g, 99%) as colourless oil; $[\alpha]_D^{20}$ +89.3 (c 1.50 in CH_2Cl_2); ν_{max}/cm^{-1} 2906, 2870, 1611, 1513, 1454, 1248, 1120, 830, 737, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.19 (m, 10H), 7.00–6.97 (m, 2H), 6.84 (d, J = 8.7 Hz, 2H), 4.45 (s, 2H), 4.15 (d, J = 11.1 Hz, 1H), 4.03 (q, J = 4.8 Hz, 1H), 3.81–3.77 (m, 4H), 3.63–3.59 (m, 2H), 3.50 (t, J = 4.5 Hz, 1H), 3.35 (dd, J_1 = 5.4 Hz, J_2 = 11.4 Hz, 1H), 3.15–3.08 (m, 1H), 2.95–2.83 (m, 2H), 2.23–2.09 (m, 1H), 1.93–1.87 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 158.2, 138.3, 138.2, 132.1, 129.2, 128.5, 128.2, 127.8, 127.7, 127.6, 127.4, 113.7, 85.0, 84.7, 73.0, 71.9, 71.8, 58.2, 55.3, 54.7, 46.6, 28.1;HRMS (ESI) calcd for $C_{28}H_{32}NO_3^+$ $[M + H]^+$ 430.2382, found 430.2375.

(1*S*,2*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-7-((*E*)-prop-1-en-1-yl)-hexahydro-1*H*-pyrrolizine (11ad)

Following general procedure, starting from **9ad** (0.19 g, 0.52 mmol) to give **11ad** (0.16 g, 85%) as colourless oil; $[\alpha]_D^{20}$ +120.0 (c 0.25 in CH_2Cl_2); ν_{max}/cm^{-1} 3328, 3030, 2922, 2856, 1668, 1454, 1092, 736, 696; δ_H ($CDCl_3$, 300 MHz) 7.37–7.25 (m, 10H), 5.56–5.42 (m, 2H), 4.63–4.49 (m, 4H), 4.19–4.13 (m, 1H), 3.92–3.85 (m, 1H), 3.51–3.46 (m, 1H), 3.42–3.37 (m, 1H), 3.09–3.03 (m, 1H), 2.89–2.86 (m, 1H), 2.79–2.70 (m, 2H), 1.80–1.74 (m, 2H), 1.65 (d, J = 6.3 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 138.4, 138.2, 130.6, 128.57, 128.45, 128.40, 127.9, 127.88, 127.78, 127.73, 126.7, 84.9, 83.5, 72.3, 72.0, 71.8, 57.8, 54.1, 44.9, 30.7, 18.2; HRMS (ESI) calcd for $C_{24}H_{30}NO_2^+$ $[M + H]^+$ 364.2276, found 364.2266.

(1*S*,2*S*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-phenylhexahydro-1*H*-pyrrolizine (11ba)

Following general procedure, starting from **9ba** (0.25 g, 0.47 mmol) to give **11ba** (0.23 g, 90%) as colourless oil; $[\alpha]_D^{20}$ +51.7 (c 1.20 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2871, 1603, 1496, 1453, 1119, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.33–6.92 (m, 20H), 4.60–4.48 (m, 4H), 4.08–3.96 (m, 2H), 3.74 (t, J = 7.5 Hz, 1H), 3.66–3.46 (m, 5H), 3.19–3.00 (m, 3H), 2.22–2.03 (m, 1H), 1.93–1.86 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 139.8, 138.5, 138.4, 138.3, 128.6, 128.44, 128.39, 128.2, 127.8, 127.7, 127.6, 127.4, 126.6, 86.1, 84.9, 73.5, 72.8, 72.0, 70.9, 69.0, 54.6, 47.7, 27.9; HRMS (ESI) calcd for $C_{35}H_{38}NO_3^+$ $[M + H]^+$ 520.2852, found 520.2850.

(1*S*,2*S*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (11bb)

Following general procedure, starting from **9bb** (0.53 g, 0.95 mmol) to give **11bb** (0.48 g, 91%) as colourless oil; $[\alpha]_D^{20}$ +64.3 (c 1.40 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2863, 1611, 1513, 1454, 1121, 736, 698; δ_H ($CDCl_3$, 300 MHz) 7.31–7.18 (m, 15H), 6.98–6.93 (m, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.56–4.49 (m, 4H), 4.08 (d, J = 11.1 Hz, 1H), 3.98 (t, J = 6.0 Hz, 1H), 3.76 (s, 3H), 3.72–3.67 (m, 1H), 3.61–3.52 (m, 5H), 3.19–2.99 (m, 3H), 2.13–2.04 (m, 1H), 1.92–1.85 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 158.3, 138.5, 138.4, 138.3, 131.9, 129.4, 128.4, 128.39, 128.2, 127.8, 127.7, 127.66, 127.60, 127.4, 113.8, 86.1, 84.9, 73.4, 72.8, 72.0, 71.0, 69.1, 55.3, 54.6, 46.9, 28.2; HRMS (ESI) calcd for $C_{36}H_{40}NO_4^+$ $[M + H]^+$ 550.2957, found 550.2963.

(1*S*,2*S*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-((*E*)-prop-1-en-1-yl)hexahydro-1*H*-pyrrolizine (11bd)

Following general procedure, starting from **9bd** (0.29 g, 0.59 mmol) to give **11bd** (0.26 g, 90%) as colourless oil yield; $[\alpha]_D^{20}$ +23.2 (c 0.95 in CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2859, 1453, 1096, 735, 697; δ_H ($CDCl_3$, 300 MHz) 7.32–7.25 (m, 15H), 5.50–5.36 (m, 2H), 4.65–4.50 (m, 6H), 4.07 (t, J = 6.3 Hz, 1H), 3.93 (t, J = 6.3 Hz, 1H), 3.59–3.48 (m, 3H), 3.10–3.02 (m, 1H), 2.96–2.91 (m, 1H), 2.84–2.77 (m, 2H), 1.90–1.70 (m, 2H), 1.65 (d, J = 5.7 Hz, 3H); δ_C ($CDCl_3$, 75 MHz) 138.6, 138.56, 138.50, 131.2, 128.5, 128.43, 128.41, 127.9, 127.85, 127.79, 127.7, 127.60, 126.4, 86.4, 84.1, 73.5, 73.0, 72.09, 70.4, 69.1, 53.8, 45.2, 31.5, 18.2; HRMS (ESI) calcd for $C_{32}H_{38}NO_3^+$ $[M + H]^+$ 484.2852, found 484.2850.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-phenylhexahydro-1*H*-pyrrolizine (11ca)

Following general procedure, starting from **9ca** (0.24 g, 0.45 mmol) to give **11ca** (0.23 g, 98%) as colourless oil; $[\alpha]_D^{20}$ +35.2 (c 1.25 in CH_2Cl_2); ν_{max}/cm^{-1} 3061, 3029, 2914, 2865, 1603, 1496, 1453, 1367, 1095, 734, 698; δ_H ($CDCl_3$, 300 MHz) 7.32–7.18 (m, 18H), 6.85–6.82 (m, 2H), 4.70 (d, J = 12.0 Hz, 1H), 4.53–4.43 (m, 3H), 4.03–3.94 (m, 2H), 3.83–3.78 (m, 2H), 3.67–3.55 (m, 2H), 3.48 (d, J = 7.8 Hz, 1H), 3.41 (dd, J_1 = 3.6 Hz, J_2 = 9.0 Hz, 1H), 3.13–3.04 (m, 1H), 2.97–2.86 (m, 2H), 2.11–2.01 (m, 1H), 1.93–1.86 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 139.1, 138.9, 138.3, 137.6, 128.4, 128.3, 128.12, 128.1, 128.0, 127.85, 127.76, 127.5, 127.3, 126.5, 81.7, 73.52, 73.49, 71.9, 69.9, 68.9, 67.4, 53.2, 46.6, 27.1; HRMS (ESI) calcd for $C_{35}H_{38}NO_3^+$ $[M + H]^+$ 520.2852, found 520.2843.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (11cb)

Following general procedure, starting from **9cb** (0.29 g, 0.52 mmol) to give **11cb** (0.25 g, 88%) as colourless oil; $[\alpha]_D^{20}$+31.1 (c 0.90, CH_2Cl_2); ν_{max}/cm^{-1} 3030, 2903, 2864, 1610, 1513, 1453, 1249, 1096, 734, 697; δ_H ($CDCl_3$, 300 MHz) 7.31–7.20 (m, 15H), 6.89–6.80 (m, 4H), 4.72 (d, J = 11.7 Hz, 1H), 4.53–4.44 (m, 3H), 4.04 (m, 1H), 3.93–3.89 (m, 2H), 3.80 (t, J = 8.4 Hz, 1H), 3.74 (s, 3H), 3.56–3.52 (m, 3H), 3.39 (dd, J_1 = 3.6 Hz, J_2 = 9.0 Hz, 1H), 3.08–2.99 (m, 1H), 2.95–2.83 (m, 2H), 2.04–1.94 (m, 1H), 1.89–1.84 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 158.3, 139.0, 138.4, 137.8, 131.3, 129.3, 128.5, 128.2, 128.1, 128.0, 127.89, 27.88, 127.7, 127.5, 127.4, 113.7, 82.0, 77.8, 73.6,

73.58,, 72.1, 70.3, 69.1, 67.5, 55.3, 53.4, 46.0, 27.6; HRMS (ESI) calcd for $C_{36}H_{40}NO_4^+$ $[M + H]^+$ 550.2957, found 550.2942.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-((*E*)-prop-1-en-1-yl)hexahydro-1*H*-pyrrolizine (11cd)

Following general procedure, starting from **9cd** (0.19 g, 0.39 mmol) to give **11cd** (0.61 g, 87%) as colourless oil; $[\alpha]_D^{20}$ +22.9 (*c* 0.35 in CH_2Cl_2);ν_{max}/cm^{-1} 3030, 2914, 2860, 1453, 1120, 734, 697; δ_H ($CDCl_3$, 300 MHz) 7.33–7.24 (m, 15H), 5.56–5.39 (m, 2H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.64 (t, *J* = 11.4 Hz, 1H), 4.54–4.45 (m, 3H), 4.33 (d, *J* = 11.4 Hz, 1H), 4.17 (t, *J* = 3.0 Hz, 1H), 3.79 (t, *J* = 8.7 Hz, 1H), 3.73–3.67 (m, 1H), 3.62 (dd, J_1 = 3.3 Hz, J_2 = 8.7 Hz, 1H), 3.51 (dd, J_1 = 5.1 Hz, J_2 = 9.0 Hz, 1H), 2.95–2.79 (m, 3H), 2.70–2.63 (m, 1H), 1.78–1.71 (m, 1H), 1.66 (d, *J* = 5.7 Hz, 3H), 1.63–1.52 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 139.1, 138.4, 138.1, 130.1, 128.5, 128.2, 128.1, 128.0, 127.95, 127.8, 127.7, 127.4, 125.7, 81.4, 78.1, 73.7, 73.6, 72.2, 68.6, 67.9, 53.3, 44.2, 29.9, 18.3; HRMS (ESI) calcd for $C_{32}H_{38}NO_3^+$ $[M + H]^+$ 484.2852, found 484.2846.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-phenylhexahydro-1*H*-pyrrolizine (11da)

Following general procedure, starting from **9da** (0.50 g, 0.94 mmol) to give **11da** (0.44 g, 90%) as colourless oil; $[\alpha]_D^{20}$ −47.5 (*c* 0.80 in CH_2Cl_2); ν_{max}/cm^{-1} 3061, 3029, 2910, 2866, 1603, 1496, 1454, 1098, 735, 697; δ_H ($CDCl_3$, 300 MHz) 7.34–7.19 (m, 18H), 7.01–6.97 (m, 2H), 4.62–4.54 (m, 2H), 4.38 (d, *J* = 12.0 Hz, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 3.93–3.91 (m, 3H), 3.86 (d, *J* = 6.6 Hz, 2H), 3.73 (q, *J* = 7.5 Hz, 1H), 3.66–3.62 (m, 1H), 3.56–3.50 (m, 1H), 3.42 (d, *J* = 4.5 Hz, 1H), 3.28–3.21 (m, 1H), 2.86 (q, *J* = 8.4 Hz, 1H), 2.15–2.02 (m, 2H); δ_C ($CDCl_3$, 75 MHz) 141.2, 138.5, 138.46, 138.1, 128.44, 128.41, 128.3, 127.8, 127.65, 127.63, 127.60, 127.3, 126.5, 86.4, 85.1, 76.5, 73.4, 71.8, 71.4, 67.1, 64.6, 46.9, 45.0, 29.6. HRMS (ESI) calcd for $C_{35}H_{38}NO_3^+$ $[M + H]^+$ 520.2851, found 520.2841.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (11db)

Following general procedure, starting from **9db** (0.35 g, 0.62 mmol) to give **11db** (0.33 g, 97%) as colourless oil; $[\alpha]_D^{20}$ −13.3 (*c* 0.90 in CH_2Cl_2); ν_{max}/cm^{-1} 3358, 3062, 3031, 2928, 2866, 1603, 1496, 1453, 1367, 1095, 734, 698; δ_H ($CDCl_3$, 300 MHz) 7.34–7.18 (m, 15H), 7.02–7.00 (m, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.03–3.97 (m, 2H), 3.92 (d, *J* = 4.5 Hz, 1H), 3.85 (d, *J* = 6.6 Hz, 2H), 3.79 (s, 3H), 3.68–3.60 (m, 3H), 3.56–3.51 (m, 1H), 3.44 (d, *J* = 4.2 Hz, 1H), 3.26–3.19 (m, 1H), 2.90–2.81 (m, 1H), 2.07–2.02 (m, 2H), 1.66–1.62 (m, 1H); δ_C ($CDCl_3$, 75 MHz) 158.2, 138.38, 138.36, 138.0, 132.9, 129.2, 128.4, 128.3, 127.8, 127.75, 127.6, 127.59, 127.3, 113.8, 86.0, 84.8, 73.4, 71.7, 71.4, 66.9, 64.6, 62.6, 55.3, 46.8, 44.3, 30.2; HRMS (ESI) calcd for $C_{36}H_{40}NO_4$ $[M + H]^+$ 550.2957, found 550.2947.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-7-((*E*)-prop-1-en-1-yl)hexahydro-1*H*-pyrrolizine (11dd)

Following general procedure, starting from **9dd** (0.31 g, 0.62 mmol) to give **11dd** (0.26 g, 85%) as colourless oil; $[\alpha]_D^{20}$ −3.3 (*c* 0.60 in CH_2Cl_2); ν_{max}/cm^{-1} 3032, 2917, 2859, 1452, 1097, 735, 697; δ_H ($CDCl_3$, 300 MHz) 7.33–7.24 (m, 15H), 5.53–5.35 (m, 2H), 4.60–4.49 (m, 3H), 4.45–4.38 (m, 3H), 4.02–4.00 (m, 1H), 3.87–3.76 (m, 3H), 3.52–3.47 (m, 1H), 3.39–3.33 (m, 1H), 3.10–3.03 (m, 1H), 2.99–2.90 (m, 1H), 2.74–2.66 (m, 1H), 1.93–1.83 (m, 1H), 1.67–1.60 (m, 4H); δ_C ($CDCl_3$, 75 MHz) 138.5, 138.4, 131.6, 128.45, 128.43, 127.8, 127.7, 127.6, 127.4, 126.1, 86.5, 84.0, 75.3, 73.4, 71.7, 71.6, 67.0, 64.0, 46.7, 43.0, 31.6, 18.1. HRMS (ESI) calcd for $C_{32}H_{38}NO_3^+$ $[M + H]^+$ 484.2852, found 484.2828.

(1*S*,2*S*,7*R*,7*aS*)-1,2-Dihydroxy-7-phenylhexahydro-1*H*-pyrrolizine (12aa)

Following general procedure, starting from **11aa** (0.38 g, 0.94 mmol) to give **12aa** (0.20 g, 97%) as colourless oil; $[\alpha]_D^{20}$ +108.6 (*c* 0.35 in CH_3OH); ν_{max}/cm^{-1} 3342, 2919, 1122; δ_H (D_2O, 300 MHz) 7.46–7.40 (m, 4H), 7.37–7.31 (m, 1H), 4.05–3.97 (m, 1H), 3.67–3.59 (m, 1H), 3.57–3.52 (m, 1H), 3.49–3.44 (m, 1H), 3.38–3.32 (m, 1H), 3.04–2.89 (m, 2H), 2.60 (t, *J* = 9.6 Hz, 1H), 2.37–2.22 (m, 1H), 2.01–1.92 (m, 1H); δ_C (D_2O, 75 MHz) 138.2, 128.6, 128.4, 126.9, 76.5, 75.3, 69.8, 56.8, 53.5, 46.4, 26.4; HRMS (ESI) calcd for $C_{13}H_{18}NO_2^+$ $[M + H]^+$ 220.1332, found 220.1332.

(1*S*,2*S*,7*R*,7*aS*)-1,2-Dihydroxy-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (12ab)

Following general procedure, starting from **11ab** (0.23 g, 0.53 mmol) to give **12ab** (0.13 g, 97%) as colourless oil; $[\alpha]_D^{20}$ +115.6 (*c* 1.80 in CH_3OH); ν_{max}/cm^{-1} 3358, 2916, 1612, 1514, 1463, 1248, 1035, 831; δ_H (D_2O, 300 MHz) 7.22 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 4.00–3.93 (m, 1H), 3.74 (s, 3H), 3.47–3.40 (m, 2H), 3.38–3.34 (m, 1H), 3.32–3.22 (m, 1H), 2.87–2.75 (m, 2H), 2.49 (t, *J* = 9.6 Hz, 1H), 2.16–2.04 (m, 1H), 1.85–1.75 (m, 1H); δ_C (D_2O, 75 MHz) 157.5, 130.9, 129.4, 113.8, 76.7, 75.5, 69.9, 57.0, 55.2, 53.4, 45.7, 26.8; HRMS (ESI) calcd for $C_{14}H_{20}NO_3^+$ $[M + H]^+$ 250.1438, found 250.1434.

(1*S*,2*S*,7*S*,7*aS*)-1,2-Dihydroxy-7-propylhexahydro-1*H*-pyrrolizine (12ad)

Following general procedure, starting from **11ad** (0.10 g, 0.27 mmol) to give **12ad** (55 mg, 100%) as colourless oil; $[\alpha]_D^{20}$ +40.0 (*c* 0.20 in CH_3OH); ν_{max}/cm^{-1} 3328, 2958, 2928, 1457, 1123, 618; δ_H (D_2O, 300 MHz) 4.16–4.09 (m, 1H), 3.98 (t, *J* = 7.5 Hz, 1H), 3.64–3.53 (m, 2H), 3.17–3.07 (m, 1H), 3.02–2.96 (m, 1H), 2.76–2.70 (m, 1H), 2.37–2.26 (m, 1H), 2.04–1.92 (m, 1H), 1.77–1.42 (m, 5H), 0.93 (t, *J* = 7.2 Hz, 3H); δ_C (D_2O, 75 MHz) 75.0, 74.6, 70.1, 56.7, 54.6, 40.6, 30.4, 28.3, 21.3, 13.4; HRMS (ESI) calcd for $C_{10}H_{20}NO_2^+$ $[M + H]^+$ 186.1489, found 186.1487.

(1*S*,2*S*,3*S*,7*R*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-phenylhexahydro-1*H*-pyrrolizine (12ba)

Following general procedure, starting from **11ba** (50 mg, 0.096 mmol) to give **12ba** (22 mg, 92%) as colourless oil; $[\alpha]_D^{20}$ +66.7 (*c* 0.75 in CH_3OH); ν_{max}/cm^{-1} 3297, 1403, 1123, 618; δ_H (D_2O, 300 MHz) 7.44–7.43 (m, 4H), 7.38–7.34 (m, 1H), 3.86 (dd, J_1 = 3.3 Hz, J_2 = 12.0 Hz, 1H), 3.78–3.57 (m, 5H), 3.16–3.11 (m, 2H), 2.93–2.87 (m, 1H), 2.41–2.27 (m, 1H), 2.09–2.01 (m, 1H); δ_C (D_2O, 75 MHz) 137.0, 128.6, 128.5, 127.1, 75.4, 74.9, 68.5, 68.4, 61.2, 53.7, 45.9, 26.3; HRMS (ESI) calcd for $C_{15}H_{20}NO_3^+$ $[M + H]^+$ 250.1438, found 250.1434.

(1*S*,2*S*,3*S*,7*R*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (12bb)

Following general procedure, starting from **11bb** (0.38 g, 0.69 mmol) to give **12bb** (0.19 g, 96%) as colourless oil; $[\alpha]_D^{20}$ +64.0 (*c* 0.50 in CH_3OH); ν_{max}/cm^{-1} 3327, 2924, 1613, 1514, 1456, 1248, 1124; δ_H (D_2O, 300 MHz) 7.37 (d, J = 8.7 Hz, 2H), 7.03 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H), 3.83 (d, J = 8.4 Hz, 1H), 3.80–3.71 (m, 2H), 3.70–3.51 (m, 2H), 3.45–3.38 (m, 1H), 3.04–2.99 (m, 2H), 2.80–2.74 (m, 1H), 2.30–2.16 (m, 1H), 1.97–1.93 (m, 1H); δ_C (D_2O, 75 MHz) 157.6, 130.4, 129.5, 114.0, 76.2, 75.4, 68.5, 68.3, 62.6, 55.4, 53.6, 45.5, 26.8; HRMS (ESI) calcd for $C_{15}H_{22}NO_4^+$ $[M + H]^+$ 280.1543, found 280.1539.

(1*S*,2*S*,3*S*,7*S*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-propylhexahydro-1*H*-pyrrolizine (12bd)

Following general procedure, starting from **11bd** (96 mg, 0.20 mmol) to give **12bd** (43 mg, 99%) as colourless oil yield; $[\alpha]_D^{20}$ +20.0 (*c* 0.20 in CH_3OH); ν_{max}/cm^{-1} 3310, 1404, 1124, 618; δ_H (D_2O, 300 MHz) 4.01 (t, J = 8.1 Hz, 1H), 3.93–3.76 (m, 3H), 3.56 (t, J = 8.1 Hz, 1H), 3.14–3.11 (m, 2H), 3.00–2.94 (m, 1H), 2.36–2.28 (m, 1H), 2.09–2.03 (m, 1H), 1.76–1.37 (m, 5H), 0.94 (t, J = 6.9 Hz, 3H); δ_C (D_2O, 75 MHz) 74.6, 73.8, 69.0, 68.2, 59.4, 54.2, 40.5, 29.7, 28.1, 21.3, 13.4; HRMS (ESI) calcd for $C_{11}H_{22}NO_3$ $[M + H]^+$ 216.1594, found 216.1593.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-phenylhexahydro-1*H*-pyrrolizine (12ca)

Following general procedure, starting from **11ca** (0.18 g, 0.34 mmol) to give **12ca** (86 mg, 100%) as colourless oil; $[\alpha]_D^{20}$ +106.7 (*c* 0.60 in CH_3OH); ν_{max}/cm^{-1} 3201, 2938, 2878, 1520, 1144, 1050, 765, 701; δ_H (D_2O, 300 MHz) 7.42–7.32 (m, 5H), 4.11 (t, J = 3.3 Hz, 1H), 3.94–3.86 (m, 2H), 3.76–3.70 (m, 1H), 3.67–3.57 (m, 2H), 3.05–3.02 (m, 3H), 2.26 (t, J = 10.2 Hz, 1H), 1.99–1.95 (m, 1H); δ_C (D_2O, 75 MHz) 137.5, 128.5, 128.4, 127.0, 72.4, 72.0, 69.4, 68.8, 59.7, 53.2, 45.7, 26.3; HRMS (ESI) calcd for $C_{14}H_{20}NO_3^+$ $[M + H]^+$ 250.1438, found 250.1434.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (12cb)

Following general procedure, starting from **11cb** (0.14 g, 0.52 mmol) to give **12cb** (73 mg, 99%) as colourless oil; $[\alpha]_D^{20}$ +104.0 (*c* 0.50 in CH_3OH); ν_{max}/cm^{-1} 3297, 2943, 1612, 1514, 1250, 1034, 826; δ_H (D_2O, 300 MHz) 7.31 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 4.08 (t, J = 3.3 Hz, 1H), 3.90–3.76 (m, 4H), 3.70–3.65 (m, 1H), 3.55–3.47 (m, 2H), 2.92–2.90 (m, 3H), 2.19–2.05 (m, 1H), 1.84 (d, J = 9.1 Hz, 1H); δ_C (D_2O, 75 MHz) 157.5, 130.6, 129.5, 113.8, 72.5, 72.2, 69.3, 68.6, 60.0, 55.3, 53.1, 45.2, 26.6; HRMS (ESI) calcd for $C_{15}H_{22}NO_4^+$ $[M + H]^+$ 280.1543, found 280.1541.

(1*S*,2*R*,3*S*,7*S*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-propylhexahydro-1*H*-pyrrolizine (12cd)

Following general procedure, starting from **11cd** (0.14 g, 0.39 mmol) to give **12cd** (60 mg, 95%) as colourless oil; $[\alpha]_D^{20}$ +22.5 (*c* 0.80 in CH_3OH); ν_{max}/cm^{-1} 3357, 2957, 2927, 1124; δ_H (D_2O, 300 MHz) 4.23–4.17 (m, 2H), 3.96–3.90 (m, 1H), 3.77 (dd, J_1 = 6.6 Hz, J_2 = 11.4 Hz, 1H), 3.61 (t, J = 8.4 Hz, 1H), 3.13–3.09 (m, 1H), 2.98 (d, J = 6.9 Hz, 2H), 2.28–2.24 (m, 1H), 1.98–1.94 (m, 1H), 1.66–1.36 (m, 5H), 0.93 (t, J = 6.9 Hz, 3H); δ_C (D_2O, 75 MHz) 72.5, 71.4, 69.3, 69.0, 59.2, 53.8, 40.1, 30.0, 28.2, 21.4, 13.5; HRMS (ESI) calcd for $C_{11}H_{22}NO_3^+$ $[M + H]^+$ 216.1594, found 216.1596.

(1*S*,2*R*,3*S*,7*R*,7*aS*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-((*E*)-prop-1-en-1-yl)hexahydro-1*H*-pyrrolizine (12cd′)

To a solution of **11ad** (0.19 g, 0.095 mmol) in dried CH_2Cl_2 (5 mL) at 0 °C was added BBr_3 (0.20 mL, 6 eq.) under N_2 atmosphere. The resulting mixture was stirred for 1 h, and then quenched with MeOH (2 mL) at 0 °C. The solvent was removed under reduced pressure. The residue was neutralized by $NH_3{\cdot}H_2O$ (25%, 10 mL), then purified by acid ion exchange resin column to give **12cd′** (0.089 g, 91%) as colourless oil; $[\alpha]_D^{20}$ +70.8 (c 0.65, CH_3OH); ν_{max}/cm^{-1} 3342, 2920, 1123, 618; δ_H (D_2O, 300 MHz) 5.75–5.54 (m, 2H), 4.18 (t, J = 3.0 Hz, 1H), 4.09–4.04 (m, 1H), 3.88–3.82 (m, 1H), 3.65 (dd, J_1 = 6.0 Hz, J_2 = 11.1 Hz, 1H), 3.37 (t, J = 8.7 Hz, 1H), 2.95–2.82 (m, 4H), 1.76–1.66 (m, 5H); δ_C (D_2O, 75 MHz) 128.1, 127.9, 72.7, 71.9, 69.1, 68.9, 59.9, 53.1, 43.4, 28.7, 17.3; HRMS (ESI) calcd for $C_{11}H_{20}NO_3^+$ $[M + H]^+$ 214.1438, found 214.1437.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-phenylhexahydro-1*H*-pyrrolizine (12da)

Following general procedure, starting from **11da** (0.38 g, 0.94 mmol) to give **12da** (0.17 g, 91%) as colourless oil; $[\alpha]_D^{20}$ −57.1 (*c* 0.35 in CH_3OH); ν_{max}/cm^{-1} 3357, 2949, 1455, 1029, 699; δ_H (D_2O, 300 MHz) 7.47–7.35 (m, 5H), 4.08 (d, J = 4.2 Hz, 1H), 3.98–3.94 (m, 2H), 3.79–3.67 (m, 2H), 3.59–3.55 (m, 1H), 3.47–3.41 (m, 1H), 3.32 (t, J = 9.9 Hz, 1H), 3.02–2.93 (m, 1H), 2.37–2.13 (m, 2H); δ_C (D_2O, 75 MHz) 141.7, 131.2, 130.7, 129.4, 82.0, 78.4, 68.0, 60.0, 48.5, 47.2, 30.1; HRMS (ESI) calcd for $C_{14}H_{20}NO_3$ $[M + H]^+$ 250.1438, found 250.1435.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-(4-methoxyphenyl)hexahydro-1*H*-pyrrolizine (12db)

Following general procedure, starting from **11db** (140 mg, 0.25 mmol) to give **12db** (65 mg, 92.0%) as colourless oil; $[\alpha]_D^{20}$ −40.0 (*c* 0.40 in CH_3OH); ν_{max}/cm^{-1} 3332, 2919, 1515, 1112; δ_H (D_2O, 300 MHz) 7.34 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 8.7 Hz, 2H), 4.08 (dd, J_1 = 0.9 Hz, J_2 = 4.2 Hz, 1H), 3.96 (dd, J_1 =

3.3 Hz, J_2 = 6.9 Hz, 1H), 3.83 (s, 3H), 3.74–3.60 (m, 3H), 3.55–3.49 (m, 1H), 3.40–3.33 (m, 1H), 3.06–2.97 (m, 1H), 2.35–2.11 (m, 2H); δ_C (D_2O, 75 MHz) 157.6, 131.2, 129.3, 114.0, 79.1, 78.9, 76.1, 65.8, 57.2, 55.3, 46.2, 43.8, 27.6; HRMS (ESI) calcd for $C_{36}H_{40}NO_6$ $[M + H]^+$ 280.1543, found 280.1543.

(1*R*,2*R*,3*S*,7*R*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-propylhexahydro-1*H*-pyrrolizine (12dd)

Following general procedure, starting from **11dd** (0.19 g, 0.38 mmol) to give **12dd** (73 mg, 89%) as colourless oil; $[\alpha]_D^{20}$ −13.3 (*c* 0.75 in CH_3OH); ν_{max}/cm^{-1} 3311, 2955, 1123, 618; δ_H (D_2O, 300 MHz) 4.16 (d, *J* = 3.6 Hz, 1H), 4.08 (d, *J* = 5.1 Hz, 1H), 3.96–3.82 (m, 2H), 3.50–3.46 (m, 1H), 3.30 (t, *J* = 6.0 Hz, 1H), 3.14 (t, *J* = 9.0 Hz, 1H), 2.84 (q, *J* = 9.0 Hz, 1H), 2.35–2.30 (m, 1H), 1.98–1.95 (m, 1H), 1.67–1.36 (m, 5H), 0.90 (t, *J* = 7.8 Hz, 3H); δ_C (D_2O, 75 MHz) 79.5, 78.4, 74.6, 65.2, 57.3, 45.9, 39.2, 31.8, 29.3, 21.2, 13.5; HRMS (ESI) calcd for $C_{11}H_{22}NO_3^+$ $[M + H]^+$ 216.1594, found 216.1594.

(1*R*,2*R*,3*S*,7*S*,7*aR*)-1,2-Dihydroxy-3-(hydroxymethyl)-7-((*E*)-prop-1-en-1-yl)hexahydro-1*H*-pyrrolizine (12dd′)

Following the procedure of **12cd′**, starting from **11dd** (0.10 g, 0.20 mmol) to give **12dd′** (50 mg, 96%) as colourless oil; $[\alpha]_D^{20}$ −33.8 (*c* 0.65 in CH_3OH); ν_{max}/cm^{-1} 3326, 2921, 1123, 618; δ_H (D_2O, 300 MHz) 5.79–5.55 (m, 2H), 4.21 (d, *J* = 4.5 Hz, 1H), 4.14 (d, *J* = 4.5 Hz, 1H), 4.03–3.90 (m, 2H), 3.63–3.57 (m, 1H), 3.55–3.48 (m, 1H), 3.37–3.28 (m, 1H), 3.13–2.97 (m, 2H), 2.05–1.87 (m, 2H), 1.72 (d, *J* = 6.3 Hz, 3H); δ_C (D_2O, 75 MHz) 128.7, 128.4, 78.6, 78.1, 75.4, 65.5, 56.9, 46.5, 42.2, 29.7, 17.3; HRMS (ESI) calcd for $C_{11}H_{20}NO_3^+$ $[M + H]^+$ 214.1438, found 214.1438.

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