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Synthesis of pyrrolidine iminosugars, (−)-lentiginosine, (−)-swainsonine and their 8a-epimers from D-glycals†

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Synthesis of pyrrolidine iminosugars has been described from D-glycals *via* dihydroxylation, oxidative cleavage and double nucleophilic displacement as the key steps. The pyrrolidines obtained have been utilized for the synthesis of important bicyclic iminosugars, *viz.* (−)-lentiginosine and (−)-swainsonine and their 8a-epimers, which are known to be glycosidase inhibitors.

Introduction

Several polyhydroxylated pyrrolidines found in nature have shown splendid biological properties.[1a] Naturally occurring pyrrolidine iminosugars such as 1,4-dideoxy-1,4-imino-D-arabinitol (DAB) **1** (Fig. 1), 3,4-dihydroxy-2,5-bis(hydroxymethyl)pyrrolidine (DMDP) **2**, 2,5-dideoxy-2,5-imino-L-glucitol (DGDP) **3**, and radicamines A **4** and B **5**, have displayed good and yet a broad range of glycosidase inhibition activity,[1b–f] while codonopsine **6** and codonopsinine **7** are known for their hypotensive pharmacological activity with no side effects on the mammalian nervous systems.[1g] There is an ever-growing interest in the synthesis of such molecules owing to their immense potential from therapeutic as well as synthetic points of view. A number of methods are reported in the literature for the synthesis of pyrrolidine iminosugars from both carbohydrate[2a–c] and non-carbohydrate[2d–f] starting materials. From our group also, we have recently reported the synthesis and glycosidase inhibition studies of novel synthetic pyrrolidines.[3]

The synthetic strategies leading to polyhydroxylated pyrrolidines have often been extended to the synthesis of pyrrolizidines, indolizidines, *etc.*[4] Among the many known classes of bicyclic glycosidase inhibitors, indolizidines such as lentiginosine **8**, swainsonine **9**, castanospermine **10**, steviamine **11** (Fig. 2), as well as their unnatural analogues,[5] have received considerable attention in recent years from both synthetic and biological communities. (−)-Lentiginosine **8** is a potent and specific inhibitor of amyloglucosidase,[6a] albeit weaker than its enantiomer, while its 8a-epimer **12** is a weak β-glucosidase inhibitor.[6b] (−)-Swainsonine is an important inhibitor of Golgi α-mannosidase,[6c] and has gained more significance due to its potential anti-cancer activity.[6d] Swainsonine analogue **13** is known to be an inhibitor of α-D-mannosidase,[6e] very much like its parent compound. We have been interested in the synthesis of this class of compounds.[7]

In this paper, we report a new concise route towards pyrrolidine iminosugars from the easily available D-glycals, and demonstrate the utility of the pyrrolidines hence obtained, for

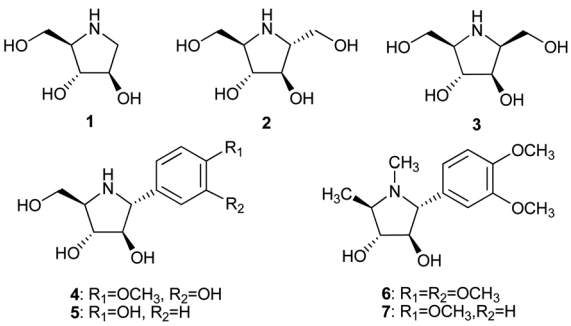

Fig. 1 Naturally occurring pyrrolidine iminosugars.

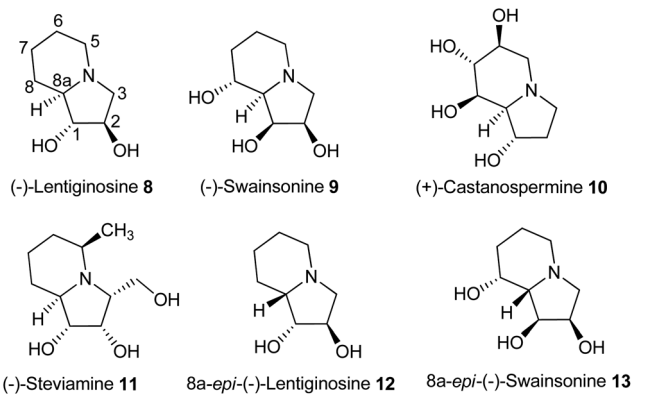

Fig. 2 Examples of important indolizidine iminosugars.

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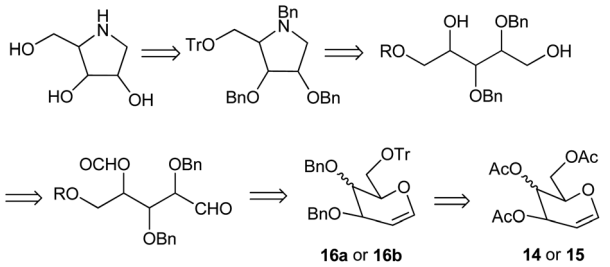
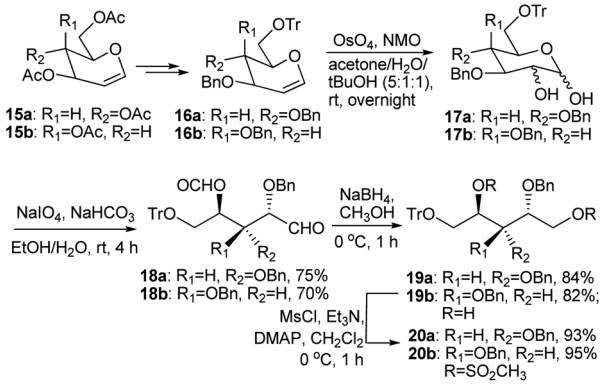
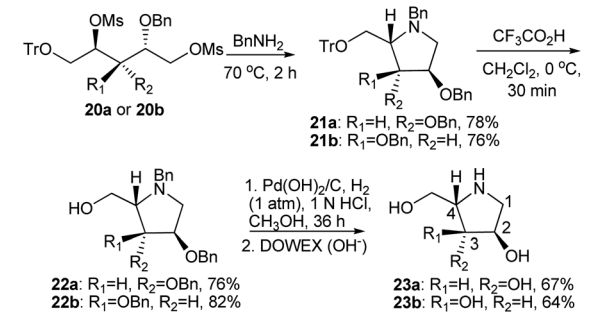
† Electronic supplementary information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra for all new compounds. See DOI: 10.1039/c3ra47555g



Scheme 1 Retrosynthetic strategy for pyrrolidines.



Scheme 2 Synthesis of dimesylate derivatives **20a** and **20b**.



Scheme 3 Cyclisation and deprotection reactions.

the synthesis of polyhydroxylated indolizidine iminosugars **8**, **9**, **12** and **13** shown in Fig. 2.

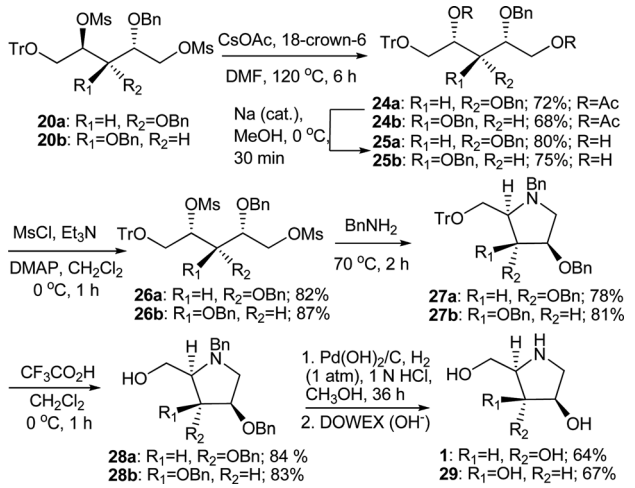
Results and discussion

We have recently reported the synthesis of dihydroxymethyl dihydroxypyrrolidines from C-2 formyl glycals using dihydroxylation, oxidative cleavage and double nucleophilic displacement as the key steps, and further synthesized steviamine analogues, which showed good inhibitory activity.[7d] Following a somewhat similar strategy, we planned the synthesis of the pyrrolidine skeletons from D-glycals, using dihydroxylation, oxidative cleavage and double nucleophilic displacement as the key steps. The retrosynthetic strategy is illustrated in Scheme 1.

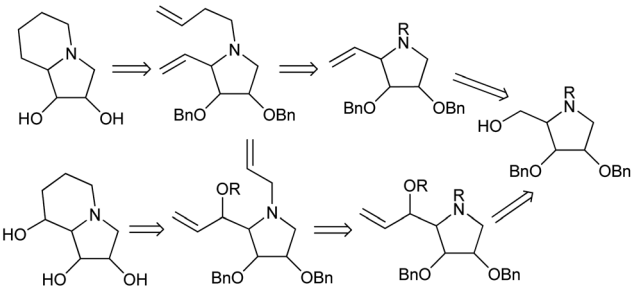
Our synthesis commenced from 3,4,6-tri-*O*-acetyl-D-glycals **14** and **15** which were converted to their corresponding 6-*O*-trityl-3,4-dibenzyl-D-glycals **16a** and **16b**, following a literature procedure.[8] Glucal **16a** was subjected to dihydroxylation reaction using a catalytic amount of OsO_4 along with *N*-methylmorpholine *N*-oxide (NMO) as the reoxidant (Scheme 2) to obtain a 2.2 : 1 mixture of diols **17a** which were not separated at this stage. Subsequent oxidative cleavage of the diol was carried out using $NaIO_4$ in an EtOH–H_2O (5 : 1) solvent system, resulting in the dicarbonyl compound **18a** which was characterized by proton peaks at δ 7.88 and 9.65 in the ^{1}H NMR spectrum, corresponding to the formate and aldehyde protons respectively. Compound **18a** on reduction using $NaBH_4$ in MeOH at 0 °C furnished the diol **19a**. Mesylation of **19a** was carried out using mesyl chloride and triethylamine as a base in CH_2Cl_2 at 0 °C. The resulting compound **20a** was not very stable in nature and hence it was quickly purified and treated with benzylamine at 70 °C (Scheme 3) for a double nucleophilic displacement reaction to obtain pyrrolidine **21a**. Attempts at cyclisation using other N-protected amines such as tosylamine, benzyl carbamate or *tert*-butylcarbamate were not successful possibly due to the poorer nucleophilicity of the amines. The trityl protection on the primary alcohol was removed successfully using trifluoroacetic acid (TFA) to yield **22a**. The benzyl groups were deprotected using $Pd(OH)_2$/C and 1 N HCl in methanol, which required around 36 h, to give 1,4-dideoxy-1,4-imino-L-xylitol **23a**[9a] in 67% yield. In a similar manner, tri-*O*-acetyl-D-galactal **15b** was converted to 1,4-dideoxy-1,4-imino-L-ribitol **23b**[9b] using the same series of steps. The spectral data of compounds **23a** and **23b** were found to be in agreement with literature reports.[9]

In order to diversify this strategy and to obtain other pyrrolidine iminosugars, we contemplated inversion of stereochemistry at the C-4 position of pyrrolidines **23a** and **23b**. At first, we made an unsuccessful attempt to displace the formate group in **18a** with iodide using sodium iodide in refluxing acetone. Attempts using Mitsunobu conditions[10] on diol **19a** also failed in spite of using excess of reagents and longer reaction times. Next, we tried to replace mesylate groups in **20a** with iodides by refluxing with NaI or tetrabutylammonium iodide in acetone or acetonitrile. In both the cases, only the primary mesylate was displaced by iodide, while the secondary mesylate did not get affected at all. However, following a report by Jung and Sun,[11] prolonged heating of the dimesylate **20a** with KOAc in DMF at 140 °C, along with addition of KOAc in portions, gave us the desired product **24a** albeit in 55% yield. Further optimisation studies were carried out and portionwise addition of CsOAc (5 equiv.) over 6 hours with heating at 120 °C in DMF gratifyingly afforded the doubly substituted compound **24a** in 72% yield. Compound **24a** was characterized by the presence of two acetate peaks at δ 1.97 and 2.07 in the ^{1}H NMR spectrum, and a strong carbonyl peak at 1742 cm^{-1} in the IR spectrum. The same reaction was performed on D-galactal-derived dimesylate compound **20b** to obtain the corresponding diacetate **24b** in 68% yield (Scheme 4).

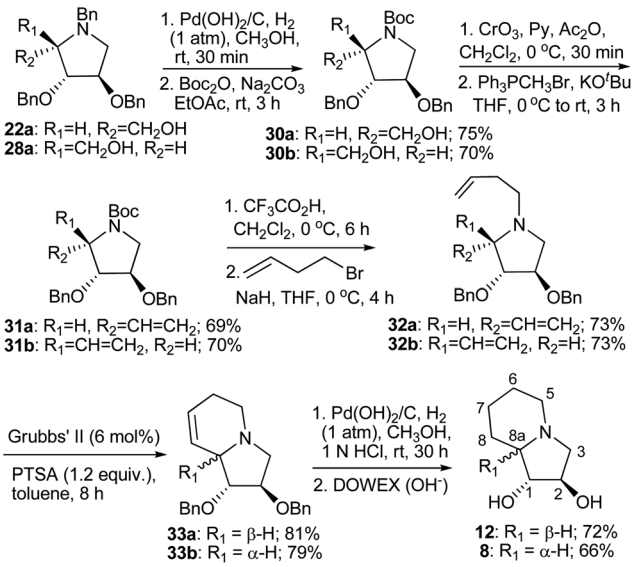
Further, the acetate protecting groups in **24a** were removed using NaOMe and the diol **25a** was again converted to mesylate **26a**. Subsequently, nucleophilic displacement with benzylamine,



Scheme 4 Synthesis of pyrrolidines **1** and **29**.



Scheme 5 Retrosynthetic plan for indolizidines.



Scheme 6 Synthesis of lentiginosine **8** and its 8a-epimer **12**.

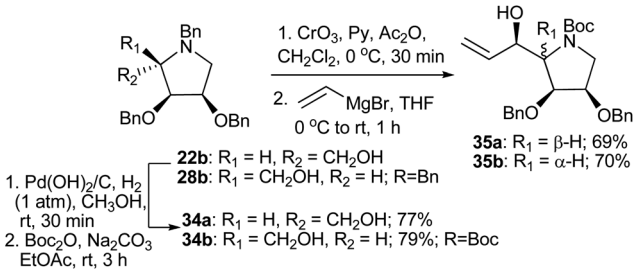
acidic deprotection and hydrogenolysis of benzyl groups in the same manner led to pyrrolidine **1**.[9a] Similarly, pyrrolidine **29**[9c] was prepared from **20b**, as shown in Scheme 4.

For the construction of the bicyclic molecules, the pyrrolidines **22** and **28** bearing the free primary hydroxyl group seemed to be suitable precursors since they could be easily obtained on gram-scale from glycals using this strategy. These pyrrolidines could be utilized for the synthesis of analogues of lentiginosine and swainsonine *via* simple manipulations as outlined in the retrosynthetic analysis (Scheme 5).

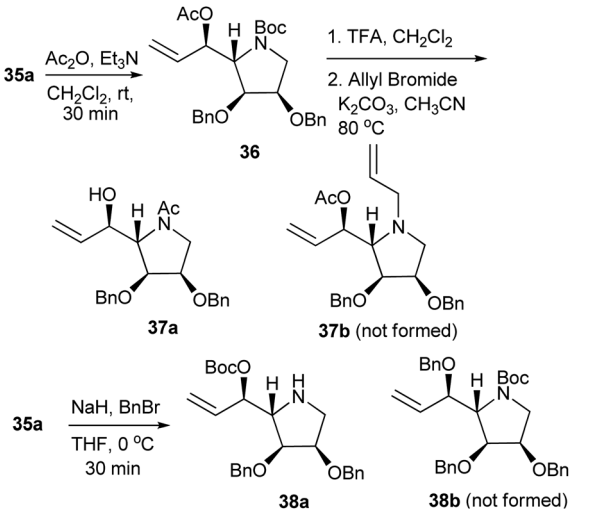
Thus, we proceeded with pyrrolidine **22a** for the synthesis of lentiginosine analogues, since the stereochemistry of C-2 and C-3 was similar to (−)-lentiginosine **8**. For this purpose, we attempted to oxidise hydroxyl using modified Cornforth oxidation conditions,[12] wherein the reaction was found to be slow and unclean on TLC, possibly because of the basic amine moiety present in the molecule. Hence we replaced the benzyl group protection on the amine with the *tert*-butylcarbamate (Scheme 6) using $Pd(OH)_2/C$ and 1 atm H_2, followed by treatment with Boc_2O in the presence of sodium carbonate as a base to furnish **30a**. Next, the primary alcohol was oxidized using Cornforth conditions to obtain aldehyde in a facile manner within 15 minutes. The crude aldehyde was directly subjected to Wittig olefination using methyltriphenylphosphonium bromide and potassium *tert*-butoxide in THF to furnish alkene **31a**. Subsequently, the carbamate group was deprotected using trifluoroacetic acid in dichloromethane following which the crude amine was treated with butenyl bromide in the presence of sodium hydride. The diene **32a** was subsequently subjected to ring closing metathesis using 6 mol% of the Grubbs' second generation catalyst in the presence of *para*-toluenesulfonic acid (PTSA)[13] to give the cyclised product **33a** in 81% yield. One-pot double bond reduction and benzyl group deprotection was achieved under hydrogenation conditions to afford 8a-*epi*-(−)-lentiginosine **12** in 70% yield. In the same manner, pyrrolidine **28a** was converted to (−)-lentiginosine **8** using the same sequence of reactions, as delineated in Scheme 6. The spectral data of the obtained indolizidine compounds were found to be in complete agreement with the literature reports.[6a,b]

The synthesis of swainsonine analogues emanated from analogous pyrrolidines **22b** and **28b**, that were obtained from D-galactal. The protecting group on amine **22b** was changed from benzyl to Boc using the same method as earlier (Scheme 7). The primary alcohol in the so-obtained pyrrolidine **34a** was oxidized and the resulting aldehyde was treated with vinyl magnesium bromide at 0 °C to give a single isomer **35a**. Similarly, alcohol **35b** was obtained from pyrrolidine **28b**.

Protection of the alcohol moiety in **35a** proved to be rather difficult contrary to our expectations. Acetylation of **35a** took place quite easily, using acetic anhydride and triethylamine (Scheme 8). Deprotection of the carbamate group on the nitrogen of **36** was done using trifluoroacetic acid, and the corresponding crude free amine obtained was treated with allyl bromide and potassium carbonate for *N*-allylation. Instead of the desired *N*-allylated product **37b**, we obtained the *N*-acetyl product **37a**. Its formation can be rationalized as a consequence of the facile migration of the acetate group from secondary hydroxyl to amine due to a favourable 5-membered transition state **B** under basic conditions (Fig. 3). Benzylation of the hydroxyl group of **35a** was then attempted using benzyl bromide



Scheme 7 Grignard reaction on alcohols **34a** and **34b**.



Scheme 8 Attempts for the protection of alcohol **35a**.

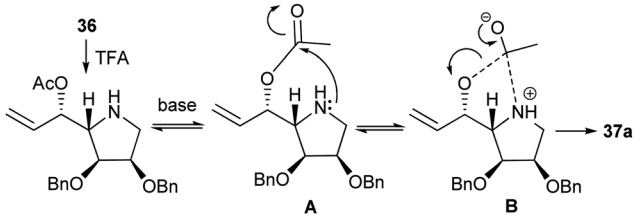


Fig. 3 Rationale for formation of **37a**.

and sodium hydride, however it led to the migration of the *tert*-butylcarbonyl group to free hydroxy group, giving **38a** instead of **38b**. This problem was overcome by carrying out protection under acidic conditions, albeit in low yield. Thus, we protected the hydroxyl group of **35a** as its benzyl ether by using benzyl trichloroacetimidate using a catalytic amount of triflic acid,[14] and we obtained only 27% of the required compound **39a** (Scheme 9). Under these conditions, the Boc group was partially deprotected to yield **39b**, so we proceeded with the crude mixture for Boc deprotection using trifluoroacetic acid. The amine hence obtained was treated with allyl bromide in the presence of K_2CO_3 in acetonitrile at 50 °C to obtain **40a**. Finally ring closing metathesis of diene **40a** was performed using the procedure used earlier (*vide supra*) to furnish **41a**, and hydrogenation conditions were employed for the reduction of double bond and deprotection of benzyl groups to obtain the fully deprotected compound **13**. Using the same series of reactions, pyrrolidine **25b** was converted to swainsonine analogue **9**. The spectral data of swainsonine analogues **13** and **9** were found to be identical to literature data.[6e,f]

Conclusion

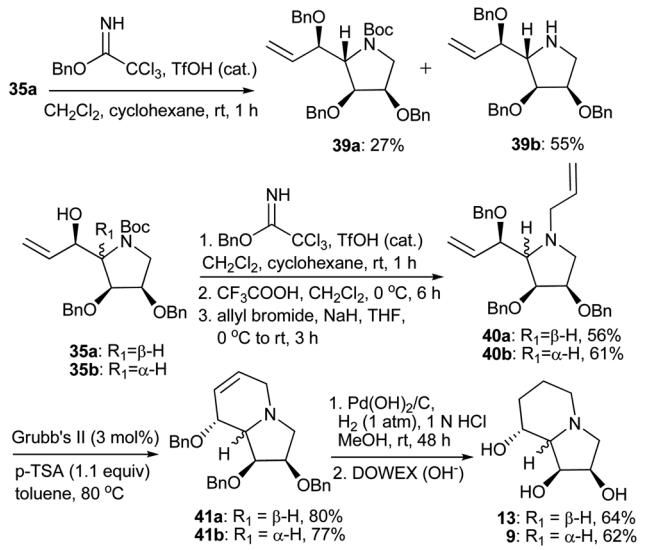
We have developed a concise method for the synthesis of 1-deoxypyrrolidine azasugars from D-glycals. Also, inversion of stereochemistry has been performed successfully, to obtain other isomers in a practical manner. The pyrrolidines could be easily prepared on gram-scale and their utility has been demonstrated by efficient conversion to indolizidine azasugars *via* simple manipulations. Hence, this strategy has helped to conveniently achieve the synthesis of (−)-lentiginosine, (−)-swainsonine and their 8a-epimers.

Experimental section

General experimental methods

All experiments were performed in a oven dried apparatus and under nitrogen atmosphere in dry solvents unless indicated otherwise. Commercial grade solvents were distilled or dried by known methods and dry solvents were stored over 4 Å molecular sieves. IR spectra were recorded on a Bruker Vector 22 FT-IR as a thin film or using KBr pellets and are expressed in cm^{-1}. NMR data were recorded on a 400 or 500 MHz JEOL JNM-LA spectrometer using $CDCl_3$ as a solvent. Chemical shifts are reported in ppm downfield to tetramethylsilane. Coupling constants are reported and expressed in Hz; splitting patterns are designated as br (broad), s (singlet), d (doublet), dd (doublet of doublets), t (triplet), dt (doublet triplets) or m (multiplet). Optical rotations were measured using a polarimeter (Autopol II) at 28 °C. TLC plates were prepared using thin layers of Acme silica gel on microscope slides and visualization of spots was effected by exposure to iodine or spraying with 10% H_2SO_4 and charring. Column chromatography was performed over silica gel (100–200 mesh) using hexane and ethyl acetate as eluent. High resolution mass spectra were recorded by Q-TOF using the electrospray ionization (ESI) method.

(4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-(trityloxymethyl)tetrahydro-2*H*-pyran-2,3-diol (17a). The olefin **16a** (3.00 g, 5.28 mmol) was dissolved in acetone–H_2O–^{t}BuOH (4 : 1 : 1, 30 mL) and to this solution at room temperature was added NMO (680 mg, 5.81 mmol) followed by OsO_4 (0.05 mmol) and the mixture was stirred overnight. Then saturated sodium metabisulphite solution (20 mL) was added and stirred for 1 h. The reaction mixture was filtered through a Celite® pad and the filtrate was extracted with EtOAc (3 × 30 mL). Combined organic extracts were washed with brine (1 × 60 mL), dried over Na_2SO_4 and evaporated *in vacuo*. A small portion of the crude was purified through a short silica gel column to obtain diol **17a** as a colourless oil: R_f = 0.4 (hexane–EtOAc = 2 : 1); IR (neat) ν_{max}: 3400, 2926, 1492, 1449, 1358, 1050, 737, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 2.2 : 1 mixture of diols): δ 7.49–7.47 (m, 6H, both isomers), 7.38–7.20 (m, 17H, both isomers), 6.91–6.88 (m, 2H, both isomers),



Scheme 9 Synthesis of (−)-swainsonine **9** and its 8a-epimer **13**.

5.34 (br s, 1H, major isomer), 4.88–4.82 (m, 2H, both isomers), 4.70–4.68 (m, 1H, both isomers), 4.58 (br s, 1H, minor isomer), 4.36–4.30 (m, 1H, both isomers), 4.04 (br s, 1H, major isomer), 3.79–3.78 (m, 2H major isomer, 3H minor isomer), 3.66 (br s, 1H, minor isomer), 3.60–3.51 (m, 2H, both isomers), 3.25 (br s, 2H major isomer, 1H minor isomer), 2.56 (br s, 1H, minor isomer), 2.33 (br s, 1H, major isomer); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 143.8, 138.5, 137.9, 137.7, 128.9, 128.6, 128.5, 128.3, 128.1, 127.9, 127.8, 127.7, 127.1, 96.9, 92.4, 86.6, 86.4, 84.4, 82.4, 77.7, 75.8, 75.6, 75.4, 75.3, 75.0, 74.8, 72.8, 71.0, 62.5, 62.3; HRMS calcd for $C_{39}H_{38}NaO_6$ $[M + Na]^+$ 625.2566, found: 625.2567.

(2*R*,3*R*,4*S*)-3,4-Bis(benzyloxy)-5-oxo-1-(trityloxy)pentan-2-yl formate (18a). To a well stirred solution of diol **17a** (2.92 g, 4.86 mmol) in EtOH–H_2O (5 : 1, 30 mL), was added in portions $NaIO_4$ (3.12 g, 14.58 mmol) and $NaHCO_3$ (5 mL) over 2 h, followed by vigorous stirring for another 2 h. The solids were filtered out and the filtrate was extracted with dichloromethane (3 × 20 mL). The organic layer was washed with brine (1 × 45 mL), concentrated under vacuum and the residue was purified through a short silica gel column and compound **18a** (2.45 g, 75% over 2 steps) was obtained as a colourless oil: R_f = 0.5 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −31.7 (*c* 0.85, CH_2Cl_2); IR (neat) ν_{max}: 3440, 2925, 1728, 1492, 1449, 1167, 1091, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.65 (s, 1H), 7.88 (s, 1H), 7.40–7.38 (m, 6H), 7.31–7.21 (m, 17H), 6.99–6.98 (m, 2H), 5.32–5.29 (m, 1H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.38–4.29 (m, 3H), 3.91–3.90 (m, 1H), 3.59 (dd, *J* = 2.5, 11.0 Hz, 1H), 3.38 (dd, *J* = 4.5, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.6, 159.8, 143.5, 136.8, 136.4, 128.9, 128.7, 128.5, 128.4, 128.3, 128.1, 128.0, 127.2, 127.0, 86.9, 82.2, 74.3, 73.5, 71.4, 61.5; HRMS calcd for $C_{39}H_{36}NaO_6$ $[M + Na]^+$ 623.2410, found: 623.2416.

(2*R*,3*R*,4*R*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diol (19a). The aldehyde **18a** (2.45 g, 4.08 mmol) was dissolved in dry CH_3OH (25 mL) and cooled to 0 °C. To this solution, $NaBH_4$ (465 mg, 12.25 mmol) was added in 3 portions over 5 min and then stirred for 1 h with gradual warming to room temperature. The reaction mixture was quenched with aq. NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). Organic extracts were washed with brine (1 × 40 mL) and dried over Na_2SO_4. Concentration *in vacuo* gave a residue which was purified by column chromatography to get 1.98 g (84%) of **19a** as a colourless oil: R_f = 0.3 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −4.0 (*c* 1.50, CH_2Cl_2); IR (neat) ν_{max}: 3431, 3086, 3060, 2929, 2878, 1492, 1449, 1071, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44–7.42 (m, 6H), 7.31–7.23 (m, 17H), 7.14 (br s, 2H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.50–4.44 (m, 3H), 4.05 (q, *J* = 5.5 Hz, 1H), 3.79–3.75 (m, 2H), 3.71 (dd, *J* = 4.5, 12.0 Hz, 1H), 3.64 (dd, *J* = 4.5, 9.0 Hz, 1H), 3.39–3.32 (m, 2H), 3.12 (br s, 1H), 2.30 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 137.8, 137.6, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.2, 86.8, 79.2, 78.3, 73.3, 72.6, 70.6, 64.6, 61.5; HRMS calcd for $C_{38}H_{38}NaO_5$ $[M + Na]^+$ 597.2617, found: 597.2618.

(2*R*,3*S*,4*R*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl dimethanesulfonate (20a). The diol **19a** (1.20 g, 2.08 mmol) was dissolved in dry CH_2Cl_2 (12 mL) under N_2 at 0 °C and then Et_3N (1.46 mL, 10.45 mmol), DMAP (2.4 mg, 0.02 mmol) and MsCl (0.40 mL, 5.20 mmol) were added to the reaction mixture. It was stirred for 30 min and then aq. $NaHCO_3$ (6 mL) was added and again stirred for 10 min. The reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL) and extracts were dried over Na_2SO_4. Evaporation of solvent gave a residue which was purified by column chromatography to yield 1.41 g (93%) of **20a** as a colourless viscous liquid: R_f = 0.4 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = +1.64 (*c* 3.65, CH_2Cl_2); IR (neat) ν_{max}: 3031, 1492, 1450, 1357, 1176 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41–7.38 (m, 5H), 7.31–7.20 (m, 18H), 7.16–7.14 (m, 2H), 5.03–5.00 (m, 1H), 4.55–4.53 (m, 3H), 4.45 (d, *J* = 11.1 Hz, 1H), 4.24 (dd, *J* = 4.6, 11.2 Hz, 1H), 4.16–4.09 (m, 1H), 3.84–3.80 (m, 2H), 3.55–3.50 (m, 2H), 3.01 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 137.3, 137.0, 129.0, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 127.6, 127.4, 127.2, 87.6, 81.4, 76.6, 74.0, 73.6, 68.2, 62.8, 38.7, 37.3; HRMS calcd for $C_{40}H_{42}NaO_9S_2$ $[M + Na]^+$ 753.2168, found: 753.2169.

(2*S*,3*R*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)-2-(trityloxymethyl)-pyrrolidine (21a). The dimesylate compound **20a** (1.10 g, 1.53 mmol), was heated in neat benzylamine (10 mL) at 70 °C for 2 h. After the complete consumption of starting material (TLC monitoring), excess amine was neutralised with 1 N HCl (20 mL) and compound **21a** was extracted from the aqueous layer using EtOAc (3 × 12 mL). Organic extracts were washed with brine (1 × 20 mL) and dried over Na_2SO_4. The solvent was removed and residue was purified by column chromatography to afford compound **21a** (770 mg, 78%) as a yellow oil: R_f = 0.8 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = +22.70 (*c* 2.60, CH_2Cl_2); IR (neat) ν_{max}: 3402, 3029, 2924, 1492, 1450, 1072 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45–7.44 (m, 6H), 7.35–7.17 (m, 24H), 4.54 (d, *J* = 11.9 Hz, 1H), 4.46 (d, *J* = 12.2 Hz, 1H), 4.42–4.39 (m, 2H), 4.09 (d, *J* = 4.5 Hz, 1H), 3.99–3.97 (m, 2H), 3.41–3.37 (m, 3H), 3.25 (dd, *J* = 6.4, 10.0 Hz, 1H), 3.14 (dd, *J* = 5.5, 11.0 Hz, 1H), 2.35 (dd, *J* = 4.6, 10.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 139.0, 138.4, 138.2, 128.9, 128.8, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 126.9, 126.8, 87.1, 83.6, 82.3, 72.2, 71.4, 65.9, 62.5, 59.3, 57.5; HRMS calcd for $C_{45}H_{44}NO_3$ $[M + H]^+$ 646.3321, found: 646.3326.

((2*S*,3*R*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)methanol (22a). The trityl ether **21a** (750 mg, 1.16 mmol) was dissolved in dry CH_2Cl_2 (8 mL) and cooled to 0 °C and then TFA (0.44 mL, 5.80 mmol) was added dropwise *via* a syringe. After 30 min, solvent was evaporated and the residue was dissolved in EtOAc (5 mL) and aq. $NaHCO_3$ (5 mL) was added. The compound was extracted using EtOAc (3 × 5 mL) and extracts were dried over Na_2SO_4. The residue resulting after concentration was purified by column chromatography and 355 mg (76%) of alcohol **22a** was obtained as a pale yellow oil: R_f = 0.4 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = +36.4 (*c* 1.40, CH_2Cl_2); IR (neat) ν_{max}: 3400, 3029, 2923, 2855, 1670, 1495, 1453, 1362, 1072 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7.25 (m, 15H), 4.68 (d, J = 12.0 Hz, 1H), 4.54–4.45 (m, 3H), 4.16–4.08 (m, 3H), 3.88 (d, J = 10.7 Hz, 1H), 3.76 (dd, J = 3.3, 12.0 Hz, 1H), 3.58 (d, J = 12.8 Hz, 1H), 3.35 (dd, J = 6.1, 8.9 Hz, 1H), 3.13 (br s, 1H), 2.50 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7, 137.6, 129.5, 128.6, 128.0, 127.8, 127.7, 83.5, 81.7, 72.2, 72.0, 66.7, 59.5, 55.5; HRMS calcd for $C_{26}H_{30}NO_3$ $[M + H]^+$ 404.2226, found: 404.2226.

(2*R*,3*S*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl diacetate (24a). The dimesylate compound **20a** (410 mg, 0.57 mmol) and 18-crown-6 (15 mg, 0.057 mmol) were dissolved in dry DMF (5 mL) and heated to 120 °C. To this, CsOAc (655 mg, 3.42 mmol) was added in portions over 6 h and heating continued for another 2 h. Once the reaction was complete (TLC monitoring), the reaction was cooled to room temperature and the contents were poured into ice-cold water (10 mL). The target compound was extracted with EtOAc (3 × 8 mL) and extracts were washed again with ice-cold water (1 × 15 mL), brine (1 × 15 mL) and then dried over Na_2SO_4. Solvent was evaporated and the residue was purified by column chromatography to yield 243 mg (72%) of diacetate **24a** as a colourless oil: R_f = 0.7 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −1.54 (*c* 0.65, CH_2Cl_2); IR (neat) ν_{max}: 3030, 2926, 1742, 1491, 1449, 1370, 1230 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.40–7.39 (m, 6H), 7.29–7.19 (m, 17H), 7.15–7.14 (m, 2H), 5.31 (q, J = 4.9 Hz, 1H), 4.65 (d, J = 11.3 Hz, 1H), 4.59 (d, J = 11.3 Hz, 1H), 4.47 (d, J = 11.6 Hz, 1H), 4.24–4.19 (m, 2H), 4.13 (dd, J = 5.2, 11.6 Hz, 1H), 4.04 (t, J = 5.2 Hz, 1H), 3.62 (q, J = 5.2 Hz, 1H), 3.36 (dd, J = 4.6, 10.4 Hz, 1H), 3.19 (dd, J = 4.9, 10.0 Hz, 1H), 2.07 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 170.3, 143.6, 138.0, 137.8, 128.6, 128.4, 128.3, 127.9, 127.8, 127.2, 127.0, 86.7, 76.7, 74.8, 73.1, 72.9, 62.8, 62.0, 21.2, 20.9; HRMS calcd for $C_{42}H_{42}NaO_7$ $[M + Na]^+$ 681.2828, found: 681.2829.

(2*R*,3*R*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diol (25a). The diacetate compound **24a** (230 mg, 0.35 mmol) was dissolved in dry MeOH (5 mL). The solution was cooled to 0 °C and a catalytic amount of sodium was added to it. The reaction mixture was stirred with gradual warming to room temperature over 30 min, following which water (5 mL) was added. Extraction was done with EtOAc (3 × 5 mL), and the extracts were dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the residue purified using column chromatography to obtain diol **25a** (160 mg, 80%) as a colourless oil: R_f = 0.5 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −5.0 (*c* 0.40, CH_2Cl_2); IR (neat) ν_{max}: 3424, 3031, 2926, 1491, 1449, 1214, 1072 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.43–7.42 (m, 6H), 7.31–7.22 (m, 17H), 7.08–7.06 (m, 2H), 4.60 (s, 2H), 4.51 (d, J = 11.0 Hz, 1H), 4.33 (d, J = 11.3 Hz, 1H), 4.08 (m, 1H), 3.84 (dd, J = 1.2, 5.8 Hz, 1H), 3.79–3.74 (m, 2H), 3.64–3.61 (m, 1H), 3.35 (dd, J = 6.1, 8.8 Hz, 1H), 3.09 (dd, J = 6.1, 8.8 Hz, 1H), 2.69–2.64 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 138.1, 137.7, 128.7, 128.6, 128.4, 128.3, 127.9, 127.2, 86.8, 78.7, 74.3, 72.4, 68.9, 64.4, 60.6; HRMS calcd for $C_{38}H_{38}NaO_5$ $[M + Na]^+$ 597.2617, found: 597.2619.

(2*R*,3*S*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl dimethanesulfonate (26a). Dimesylation of diol **25a** (150 mg, 0.26 mmol) was performed in the same manner as is described for **19a**, to afford 156 mg (82%) of compound **25a** as a thick viscous liquid: R_f = 0.5 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = +7.9 (*c* 1.20, CH_2Cl_2); IR (neat) ν_{max}: 3031, 1742, 1492, 1450, 1371, 1232 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.40–7.38 (m, 6H), 7.30–7.25 (m, 17H), 7.12–7.10 (m, 2H), 4.92–4.89 (m, 1H), 4.62 (s, 2H), 4.45 (d, J = 11.3 Hz, 1H), 4.27 (dd, J = 5.5, 11.0 Hz, 1H), 4.22 (dd, J = 4.9, 11.0 Hz, 1H), 4.17 (d, J = 11.3 Hz, 1H), 3.97–3.95 (m, 1H), 3.69 (dd, J = 5.5, 10.4 Hz, 1H), 3.55 (dd, J = 3.0, 11.3 Hz, 1H), 3.24 (dd, J = 5.5, 11.3 Hz, 1H), 2.97 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.4, 137.0, 136.9, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 81.5, 76.0, 74.0, 73.4, 72.4, 68.7, 67.6, 38.6, 37.7; HRMS calcd for $C_{40}H_{42}NaO_9S_2$ $[M + Na]^+$ 753.2168, found: 753.2167.

(2*S*,3*R*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)-2-(trityloxymethyl)-pyrrolidine (27a). The double nucleophilic displacement as mentioned for dimesylate **20a** was carried out on 165 mg (0.23 mmol) of compound **26a** to obtain 124 mg (78%) of product **27a** as a pale yellow oil: R_f = 0.8 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −10.6 (*c* 2.45, CH_2Cl_2); IR (neat) ν_{max}: 3060, 3029, 1493, 1449, 1090, 1075 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.45–7.43 (m, 6H), 7.30–7.19 (m, 24H), 4.50 (s, 2H), 4.39 (d, J = 12.5 Hz, 1H), 4.34 (d, J = 12.5 Hz, 1H), 4.09 (d, J = 13.1 Hz, 1H), 3.94–3.89 (m, 2H), 3.38 (d, J = 13.1 Hz, 1H), 3.29–3.28 (m, 2H), 3.02 (d, J = 10.6 Hz, 1H), 2.87 (q, J = 5.2 Hz, 1H), 2.54 (dd, J = 5.2, 10.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.2, 139.0, 138.3, 128.9, 128.8, 128.7, 128.4, 128.2, 127.8, 127.7, 127.6, 126.9, 86.8, 86.0, 81.6, 71.5, 70.8, 69.1, 64.6, 59.3, 57.2; HRMS calcd for $C_{45}H_{44}NO_3$ $[M + H]^+$ 646.3321, found: 646.3328.

((2*R*,3*R*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)methanol (28a). The trityl ether moiety of compound **27a** (120 mg, 0.18 mmol) was deprotected using the same method as was adopted for trityl ether **21a**, to afford 61 mg of compound **28a** (84%) as a pale yellow oil: R_f = 0.4 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −8.29 (*c* 2.05, CH_2Cl_2); IR (neat) ν_{max}: 3205, 3031, 1670, 1454, 1202, 1133 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.44–7.21 (m, 15H), 4.59–4.53 (m, 3H), 4.49–4.43 (m, 2H), 4.29 (d, J = 12.8 Hz, 1H), 4.13 (dd, J = 4.2, 7.9 Hz, 1H), 4.10–4.08 (m, 1H), 3.90 (dd, J = 8.2, 10.4 Hz, 1H), 3.83 (td, J = 3.0, 7.9 Hz, 1H), 3.71 (dd, J = 3.0, 10.1 Hz, 1H), 3.63 (br s, 1H), 3.59–3.51 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.5, 137.3, 131.2, 129.0, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 78.3, 73.6, 72.6, 68.1, 61.8, 59.0; HRMS calcd for $C_{26}H_{30}NO_3$ $[M + H]^+$ 404.2226, found: 404.2223.

(2*S*,3*R*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-(hydroxymethyl)-pyrrolidine-1-carboxylate (30a). The amine **22a** (1.05 g, 2.60 mmol) was dissolved in dry CH_3OH (10 mL) and $Pd(OH)_2/C$ (20% w/w, 50 mg) was added to it. The solution was degassed and then stirred under 1 atm H_2 (balloon) for 1 h. The catalyst

was filtered through a Celite® pad and the filtrate concentrated *in vacuo*. The crude amine so obtained was subjected to the next step without purification.

Thus, the crude amine was dissolved in ethyl acetate (8 mL) and to this solution Boc_2O (0.63 mL, 2.73 mmol) and Na_2CO_3 (828 mg, 7.81 mmol) were added, and the reaction mixture stirred for 2 h. On complete consumption of amine (TLC monitoring), water (10 mL) was added to it. The desired compound was extracted with EtOAc (3 × 8 mL), and the extracts dried over Na_2SO_4. The solvent was evaporated using a rotary evaporator, and the residue purified by column chromatography to obtain 810 mg (75% over 2 steps) of compound **30a** as a white solid: mp = 67–69 °C R_f = 0.5 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = +28.2 (*c* 1.10, CH_2Cl_2); IR (neat) ν_{max}: 3410, 2930, 1692, 1495, 1454, 1408, 1365, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 2 : 1 mixture of rotamers): δ 7.37–7.25 (m, 10H, both rotamers), 4.72 (d, J = 11.6 Hz, 1H, minor rotamer), 4.61–4.49 (m, 4H, major rotamer, 3H, minor rotamer), 4.32 (d, J = 6.1 Hz, 1H, major rotamer), 4.21–4.16 (m, 2H, minor rotamer), 4.06–3.98 (m, 3H, major rotamer, 2H, minor rotamer), 3.88–3.76 (m, 2H, both rotamers), 3.62–3.59 (m, 1H, both rotamers), 3.49–3.42 (m, 1H, both rotamers), 1.45 (s, 9H, both rotamers); ^{13}C NMR (125 MHz, $CDCl_3$, 2 : 1 mixture of rotamers): δ 156.3, 154.4, 137.7, 137.4, 128.6, 128.2, 128.0, 127.9, 127.7, 83.4, 82.2, 80.5, 80.3, 79.6, 78.9, 72.9, 72.7, 71.9, 71.7, 63.1, 61.9, 61.4, 59.0, 50.4, 48.9, 28.5; HRMS calcd for $C_{24}H_{32}NO_5$ $[M + H]^+$ 414.2280, found: 414.2281.

(2*S*,3*R*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-vinylpyrrolidine-1-carboxylate (31a). To a well stirred suspension of CrO_3 (296 mg, 2.96 mmol) in CH_2Cl_2 (5 mL) at 0 °C were added Ac_2O (0.56 mL, 5.92 mmol), and pyridine (0.94 mL, 11.84 mmol) and stirred for 15 min. To the resulting brown suspension the alcohol **30a** (765 mg, 1.85 mmol) dissolved in CH_2Cl_2 (3 mL), was added at 0 °C. The reaction mixture was stirred vigorously for 1 h with gradual warming to room temperature, following which it was filtered quickly through a short silica gel column and eluted with EtOAc (60 mL). The filtrate was concentrated using a rotavapor and the crude aldehyde was used for the next step without any further purification.

Methyltriphenylphosphonium bromide (1.39 g, 3.88 mmol) was dissolved in dry THF (4 mL) and KO^{t}Bu (845 mg, 5.55 mmol) was added and stirred at room temperature for 1 hour. The colour of the solution became bright yellow, indicating the formation of ylide. The crude aldehyde was dissolved in dry THF (2 mL) and added dropwise to this ylide solution under N_2, at 0 °C. The reaction mixture was stirred for 3 h at room temperature. The contents were then poured into ice-cold water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic portions were washed with brine (1 × 20 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The residue hence obtained was purified by column chromatography to give olefin **31a** (525 mg, 69% over 2 steps) as a colourless oil: R_f = 0.7 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −47.5 (*c* 0.80, CH_2Cl_2); IR (neat) ν_{max}: 3379, 2976, 1696, 1476, 1454, 1393, 1174, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 6 : 1 mixture of rotamers): δ 7.35–7.25 (m, 10H, both rotamers), 5.82 (br s, 1H, both rotamers), 5.23–5.12 (m, 2H, both rotamers), 4.64–4.21 (m, 5H, both rotamers), 4.07–4.02 (m, 2H, both rotamers), 3.89 (br s, 1H, minor isomer), 3.65 (dd, J = 6.4, 11.6 Hz, 1H, major rotamer), 3.51 (d, J = 11.6 Hz, 1H, minor rotamer), 3.43–3.32 (m, 1H, major rotamer), 1.42 (s, 9H, both rotamers); ^{13}C NMR (125 MHz, $CDCl_3$, 2 : 1 mixture of rotamers): δ 154.7, 138.0, 137.7, 134.4, 133.7, 128.5, 127.8, 127.7, 127.5, 116.8, 116.6, 83.4, 82.9, 79.8, 79.6, 79.0, 72.4, 72.1, 71.4, 60.6, 59.8, 48.8, 48.1, 28.4; HRMS calcd for $C_{25}H_{31}NNaO_4$ $[M + Na]^+$ 432.2151, found: 432.2156.

(2*S*,3*R*,4*R*)-3,4-Bis(benzyloxy)-1-(but-3-enyl)-2-vinylpyrrolidine (32a). The protected amine **31a** (500 mg, 1.22 mmol) was dissolved in dry CH_2Cl_2 (6 mL) and cooled to 0 °C. To this solution was added trifluoroacetic acid (0.47 mL, 6.11 mmol) and stirred for 6 h at room temperature. The solvent was removed *in vacuo* and the residue dissolved in EtOAc (5 mL). The acid was quenched by the gradual addition of aq. $NaHCO_3$ (5 mL) and the compound was then extracted from the aqueous layer using EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (1 × 10 mL) and dried over Na_2SO_4. Concentration led to the crude amine which was used for the next step without purification.

The crude amine was dissolved in dry THF (4 mL) and cooled to 0 °C. Sodium hydride (146 mg, 60% in oil, 3.66 mmol) was added carefully to the solution, followed by the addition of butenyl bromide (0.19 mL, 1.83 mmol). When the reaction was complete (TLC monitoring), the contents were carefully poured into ice-water (5 mL). Extraction was done with EtOAc (3 × 5 mL) and the extracts were washed with brine (1 × 10 mL) and dried over Na_2SO_4. The solvent was evaporated and the residue purified by column chromatography to afford diene **32a** (322 mg, 73% over 2 steps) as a colourless oil: R_f = 0.7 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = + 23.33 (*c* 1.50, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1697, 1640, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7.25 (m, 10H), 5.97–5.90 (m, 1H), 5.81–5.73 (m, 1H), 5.27 (dd, J = 1.8, 3.7 Hz, 1H), 5.25 (dd, J = 1.8, 10.4 Hz, 1H), 5.02 (ddd, J = 1.5, 3.0, 17.1 Hz, 1H), 4.96 (dt, J = 0.9, 10.1 Hz, 1H), 4.57–4.50 (m, 2H), 4.42 (s, 2H), 4.06 (dt, J = 2.4, 6.7 Hz, 1H), 3.89 (dd, J = 2.4, 5.8 Hz, 1H), 3.51 (dd, J = 6.7, 9.8 Hz, 1H), 3.07 (dd, J = 5.5, 9.1 Hz, 1H), 2.77–2.71 (m, 1H), 2.25–2.12 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 138.1, 136.7, 135.7, 128.5, 128.3, 127.9, 127.8, 127.7, 127.6, 119.1, 115.5, 85.2, 82.5, 71.9, 71.6, 71.0, 57.5, 53.3, 32.3; HRMS calcd for $C_{24}H_{30}NO_2[M + H]^+$ 364.2277, found: 364.2276.

(1*R*,2*R*,8a*S*)-1,2-Bis(benzyloxy)-1,2,3,5,6,8a-hexahydroindolizine (33a). The diene (320 mg, 0.89 mmol) was dissolved in dry toluene (8 mL), and to this solution was added PTSA (344 mg, 1.79 mmol), and the Grubbs' second generation catalyst (38 mg, 0.045 mmol). The mixture was heated to reflux for 8 h, following which it was treated with aq. $NaHCO_3$ solution (5 mL). Extraction was done with EtOAc (3 × 5 mL). Organic extracts were washed with brine (1 × 10 mL), dried and concentrated. The residue was purified by column chromatography to afford **33a** as a colourless oil (240 mg, 81%): R_f = 0.5 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = + 13.3 (*c* 1.10, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1697, 1640, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7.25 (m, 10H), 5.97–5.90 (m, 1H), 5.81–5.73 (m, 1H), 4.71–4.63 (m, 2H), 4.57–4.50 (m, 2H), 4.06 (dt, J = 2.4, 6.7 Hz, 1H), 3.89 (dd, J = 2.4, 5.8 Hz, 1H), 3.51 (dd, J = 6.7, 9.4 Hz, 1H), 3.34 (m, 1H), 3.25 (m, 1H), 3.07 (dd, J = 5.8, 9.4 Hz, 1H), 2.77–2.71 (m, 1H), 2.25–2.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 138.1, 136.7, 135.7, 128.5, 128.3, 127.9, 127.8,

127.7, 127.6, 119.1, 115.5, 85.2, 82.5, 71.9, 71.6, 71.0, 57.5, 53.3; HRMS calcd for $C_{22}H_{25}NNaO_2[M + Na]^+$ 358.1783, found: 358.1786.

(2*R*,3*R*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-(hydroxymethyl)-pyrrolidine-1-carboxylate (30b). The procedure used for converting **22a** to **30a** was followed to obtain **30b** (215 mg, 70% over 2 steps) from **28a** (300 mg, 0.74 mmol) as a colourless oil: $R_f = 0.4$ (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28} = -16.5$ (*c* 2.85, CH_2Cl_2); IR (neat) ν_{max}: 3419, 2928, 1691, 1454, 1400, 1366, 1170, 1098 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.36–7.24 (m, 10H), 4.62–4.45 (m, 4H), 4.04–3.97 (m, 2H), 3.84–3.75 (m, 3H), 3.67–3.64 (m, 1H), 3.49–3.47 (m, 1H), 1.46 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.8, 137.4, 128.6, 128.0, 127.8, 82.9, 80.6, 80.3, 71.7, 71.6, 65.3, 65.2, 51.3, 28.5; HRMS calcd for $C_{24}H_{31}NNaO_5[M + Na]^+$ 436.2100, found: 436.2100.

(2*R*,3*R*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-vinylpyrrolidine-1-carboxylate (31b). The same procedure used for obtaining **31a** from **30a** was followed to obtain **31b** (145 mg, 70% over 2 steps) from **30b** (210 mg, 0.51 mmol) as a colourless oil: $R_f = 0.7$ (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28} = -2.85$ (*c* 1.40, CH_2Cl_2); IR (neat) ν_{max}: 2976, 2928, 1695, 1496, 1454, 1393, 1365, 1171, 1098 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.36–7.25 (m, 10H), 5.85 (br s, 1H), 5.29–5.09 (m, 2H), 4.61–4.41 (m, 4H), 4.21 (br s, 1H), 4.06–4.01 (m, 1H), 3.89 (br s, 1H), 3.78–3.63 (m, 1H), 3.52–3.50 (m, 1H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.7, 137.7, 137.1, 128.5, 127.9, 127.7, 115.7, 86.7, 85.4, 81.2, 80.1, 79.8, 79.7, 71.8, 71.7, 71.6, 71.4, 65.3, 51.0, 49.9, 29.7, 28.5; HRMS calcd for $C_{25}H_{31}NNaO_4$ $[M + Na]^+$ 432.2151, found: 432.2152.

(2*R*,3*R*,4*R*)-3,4-Bis(benzyloxy)-1-(but-3-enyl)-2-vinylpyrrolidine (32b). The procedure used for converting **31a** to **32a** was used to obtain **32b** (90 mg) from **31b** (140 mg, 0.34 mmol) in 73% yield as a colourless oil: $R_f = 0.4$ (hexane–EtOAc = 9 : 1); $[\alpha]_D^{28} = +11.0$ (*c* 1.00, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1695, 1638, 1496, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.35–7.24 (m, 10H), 5.86–5.70 (m, 2H), 5.12–5.00 (m, 4H), 4.64–4.51 (m, 4H), 3.76 (dd, $J = 4.6$, 6.8 Hz, 1H), 3.70–3.61 (m, 3H), 3.57 (dd, $J = 2.9$, 4.6 Hz, 1H), 2.99 (br s, 1H), 2.69 (br s, 1H), 2.34–2.17 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6, 135.4, 132.7, 132.8, 128.0, 127.6, 127.5, 84.5, 79.8, 76.4, 67.8, 63.9, 60.7, 32.7; HRMS calcd for $C_{24}H_{30}NO_2[M + H]^+$ 364.2277, found: 364.2272.

(1*R*,2*R*,8a*R*)-1,2-Bis(benzyloxy)-1,2,3,5,6,8a-hexahydroindolizine (33b). The diene **32b** was subjected to ring closing metathesis using the same procedure as described for diene **32a** (80 mg, 0.22 mmol) to obtain **33b** (58 mg, 79%) as a colorless oil: $R_f = 0.7$ (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28} = +11.0$ (*c* 1.00, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1695, 1638, 1496, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7.25 (m, 10H), 5.91–5.88 (m, 1H), 5.82–5.78 (m, 1H), 4.71–4.68 (m, 2H), 4.63–4.52 (m, 2H), 4.35 (dd, $J = 2.4$, 6.5 Hz, 1H), 4.26 (dd, $J = 3.1$, 8.2 Hz, 1H), 3.92 (br s, 1H), 3.50 (dd, $J = 6.7$, 9.8 Hz, 1H), 3.39 (d, $J = 11.2$ Hz, 1H), 3.14 (d, $J = 11.2$ Hz, 1H), 2.97 (m, 1H), 2.50 (dd, $J = 5.5$, 8.2 Hz, 1H), 2.25 ($J = 5.5$, 8.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 138.2, 136.5, 135.8, 128.5, 128.3, 127.9, 127.8, 127.7, 127.6, 121.2, 119.6, 82.3, 81.3, 71.9, 71.6, 71.0, 57.6, 53.5; HRMS calcd for $C_{22}H_{25}NNaO_2[M + Na]^+$ 358.1783, found: 358.1782.

(4*R*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-(trityloxymethyl)tetrahydro-2*H*-pyran-2,3-diol (17b). The olefin **16b** (3.00 g, 5.28 mmol) was subjected to dihydroxylation using the same procedure as **16a**, and the diol **17b** was obtained as a colourless oil: $R_f = 0.4$ (hexane–EtOAc = 2 : 1); IR (neat) ν_{max}: 3402, 3060, 3030, 2925, 1491, 1448, 1077 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 1.4 : 1 mixture of diols): δ 7.40–7.36 (m, 6H, both isomers), 7.33–7.19 (m, 17H, both isomers), 7.13–7.08 (m, 2H, both isomers), 5.28 (d, $J = 3.7$ Hz, 1H, major isomer), 4.73–4.63 (m, 2H major isomer, 4H minor isomer), 4.48–4.40 (m, 1H major isomer, 2H minor isomer), 4.13 (t, $J = 6.7$ Hz, 1H, major isomer), 4.09 (dd, $J = 3.6$, 10.2 Hz, 1H, minor isomer), 4.04 (br s, 1H, major isomer), 3.97 (d, $J = 2.7$ Hz, 1H, major isomer), 3.78 (dd, $J = 7.9$, 9.5 Hz, 1H, minor isomer), 3.75 (dd, $J = 2.7$, 10.0 Hz, 1H, major isomer), 3.49–3.47 (m, 2H, minor isomer), 3.42–3.38 (m, 2H, major isomer), 3.29 (t, $J = 10.2$ Hz, 1H, minor isomer) 3.24–3.21 (m, 1H, major isomer), 2.97 (br s, 1H, major isomer), 2.55 (br s, 1H minor isomer), 2.33 (br s, 1H, major isomer); 1.88 (br s, 1H, minor isomer) ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 138.5, 138.4, 128.7, 128.6, 128.2, 128.1, 127.9, 127.8, 127.5, 127.2, 97.3, 92.8, 87.3, 87.2, 82.1, 79.0, 74.6, 74.1, 73.1, 72.9, 72.4, 70.2, 68.9, 62.5, 62.2; HRMS calcd for $C_{39}H_{38}NaO_6$ $[M + Na]^+$ 625.2566, found: 625.2563.

(2*R*,3*S*,4*S*)-3,4-Bis(benzyloxy)-5-oxo-1-(trityloxy)pentan-2-yl formate (18b). Following the procedure for oxidative cleavage of diol **17a**, crude diol **17b** was converted to **18b** (2.20 g, 70% over 2 steps) as a colourless oil: $R_f = 0.5$ (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28} = -7.8$ (*c* 0.90, CH_2Cl_2); IR (neat) ν_{max}: 3060, 3031, 2928, 1728, 1491, 1449, 1170, 1070 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.55 (s, 1H), 8.00 (s, 1H), 7.39–7.37 (m, 6H), 7.31–7.22 (m, 17H), 7.14–7.12 (m, 2H), 5.40 (dd, $J = 5.1$, 10.0 Hz, 1H), 4.60–4.55 (m, 2H), 4.40–4.46 (m, 2H), 4.15 (t, $J = 4.9$ Hz, 1H), 3.85 (dd, $J = 5.1$, 2.0 Hz, 1H), 3.38 (dd, $J = 5.1$, 10.3 Hz, 1H), 3.32 (dd, $J = 5.1$, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.6, 160.3, 143.4, 137.1, 136.7, 129.0, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 87.2, 82.2, 77.7, 74.4, 72.9, 72.1, 61.7; HRMS calcd for $C_{39}H_{36}NaO_6$ $[M + Na]^+$ 623.2410, found: 623.2416.

(2*R*,3*S*,4*R*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diol (19b). In the same way as **18a** was reduced using $NaBH_4$, the aldehyde **18b** (2.45 g, 4.08 mmol) was reduced to furnish 1.92 g (82%) of **19b** as a colourless oil: $R_f = 0.3$ (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28} = -5.40$ (*c* 2.05, CH_2Cl_2); IR (neat) ν_{max}: 3437, 3060, 3030, 2936, 2876, 1491, 1449, 1074 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.51–7.43 (m, 6H), 7.36–7.23 (m, 17H), 7.12–7.10 (m, 2H), 4.68–4.61 (m, 3H), 4.37 (d, $J = 10.6$ Hz, 1H), 4.01 (t, $J = 5.8$ Hz, 1H), 3.90 (dd, $J = 1.4$, 6.4 Hz, 1H), 3.85 (dd, $J = 3.9$, 11.9 Hz, 1H), 3.72 (dd, $J = 3.3$, 11.9 Hz, 1H), 3.67–3.65 (m, 1H), 3.37 (dd, $J = 6.1$, 9.2 Hz, 1H) 3.12 (dd, $J = 7.0$, 9.2 Hz, 1H); 2.43 (br s, 1H), 2.30 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 138.0, 137.7, 128.7, 128.6, 128.4, 128.3, 128.0, 127.9, 127.2, 86.9, 79.5, 77.2, 74.6, 72.5, 70.0, 64.7, 60.8; HRMS calcd for $C_{38}H_{38}NaO_5$ $[M + Na]^+$ 597.2617, found: 597.2615.

(2*R*,3*R*,4*R*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl dimethanesulfonate (20b). The diol **19b** (1.20 g, 2.08 mmol) was converted to its mesylate in the same manner as diol **19a**, to yield 1.42 g (95%) of **20b** as a colourless viscous liquid: $R_f = 0.4$ (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28} = +16.4$ (*c* 0.65, CH_2Cl_2); IR (neat) ν_{max}: 3031, 1492, 1450, 1357, 1176 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.45–7.14 (m, 25H), 5.10–5.07 (m, 1H), 3.65–3.58 (m, 3H), 4.54 (dd, $J = 2.8$, 11.4 Hz, 1H), 4.44 (d, $J = 10.9$ Hz, 1H), 4.31 (dd, $J = 3.7$, 11.4 Hz, 1H), 3.92 (dd, $J = 3.7$, 8.3 Hz, 1H), 3.79–3.77

(m, 1H), 3.46 (dd, J = 4.0, 10.6 Hz, 1H), 3.38 (dd, J = 2.8, 6.6 Hz, 1H), 2.98 (s, 3H), 2.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 137.3, 136.9, 129.5, 129.1, 128.6, 128.4, 128.1, 127.4, 87.7, 80.6, 76.6, 75.0, 72.5, 67.4, 63.4, 39.0, 37.6; HRMS calcd for $C_{40}H_{42}NaO_9S_2$ $[M + Na]^+$ 753.2168, found: 753.2165.

(2*S*,3*S*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)-2-(trityloxymethyl)-pyrrolidine (21b). The same method for double nucleophilic displacement for **20a** was applied to compound **20b** (1.10 g, 1.53 mmol) to afford compound **21a** (750 mg, 76%) as a yellow oil: R_f = 0.8 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = +15.0 (c 0.40, CH_2Cl_2); IR (neat) ν_{max}: 2923, 1492, 1450, 1355, 1173 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45–7.41 (m, 6H), 7.31–7.20 (m, 24H), 4.61 (s, 2H), 4.49–4.43 (m, 2H), 3.98 (d, J = 13.2 Hz, 1H), 3.86–3.80 (m, 2H), 3.52 (d, J = 13.2 Hz, 1H), 3.09–3.05 (m, 4H), 2.65 (t, J = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 137.3, 136.9, 128.6, 128.5, 128.4, 128.2, 128.1, 127.4, 87.7, 80.6, 82.3, 76.6, 75.0, 72.5, 67.4, 63.4; HRMS calcd for $C_{45}H_{44}NO_3$ $[M + H]^+$ 646.3321, found: 646.3323.

((2*S*,3*S*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)methanol (22b). The trityl ether **21b** (740 mg, 1.14 mmol) was subjected to deprotection following the same procedure as used for **21a**, and 375 mg (82%) of alcohol **22b** was obtained as a pale yellow oil: R_f = 0.4 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −25.7 (c 0.35, CH_2Cl_2); IR (neat) ν_{max}: 3332, 3032, 2925, 1672, 1496, 1455, 1202, 1133 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41–7.25 (m, 15H), 4.69–4.63 (m, 2H), 4.59–4.55 (m, 2H), 4.44 (d, J = 12.6 Hz, 1H), 4.33 (d, J = 12.6 Hz, 1H), 4.19–4.14 (m, 2H), 3.66 (dd, J = 5.1, 13.1 Hz, 1H), 3.62–3.60 (m, 1H), 3.54-3.49 (m, 1H), 3.25 (dd, J = 3.7, 12.6 Hz, 1H), 2.50 (br s,1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.9, 131.0, 130.3, 129.4, 128.8, 128.5, 128.1, 128.0, 78.4, 75.6, 73.3, 73.0, 71.2, 62.7, 58.7, 55.1; HRMS calcd for $C_{26}H_{30}NO_3$ $[M + H]^+$ 404.2226, found: 404.2222.

(2*R*,3*R*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl diacetate (24b). The dimesylate **20b** (410 mg, 0.57 mmol) was subjected to treatment with CsOAc in the same manner as **20a**, to yield 254 mg (68%) of diacetate **24b** as a colourless oil: R_f = 0.5 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = +36.4 (c 1.40, CH_2Cl_2); IR (neat) ν_{max}: 3030, 1742, 1491, 1449, 1370, 1230 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42–7.36 (m, 4H), 7.30–7.20 (m, 19H), 7.13–7.09 (m, 2H), 5.45–5.42 (m, 1H), 4.64–4.52 (m, 3H), 4.46 (d, J = 11.7 Hz, 1H), 4.40 (dd, J = 3.4, 12.0 Hz, 1H), 4.16–4.10 (m, 1H), 3.94 (t, J = 5.4 Hz, 1H), 3.72 (dd, J = 4.8, 8.6 Hz, 1H), 3.39 (dd, J = 6.0, 10.3 Hz, 1H), 3.32 (dd, J = 2.8, 10.3 Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 143.8, 137.8, 128.7, 128.4, 128.3, 128.2, 128.0, 127.8, 127.1, 86.6, 76.8, 76.5, 75.4, 73.6, 72.3, 72.2, 72.1, 63.0, 62.6, 21.2, 21.0; HRMS calcd for $C_{42}H_{42}NaO_7$ $[M + Na]^+$ 681.2828, found: 681.2829.

(2*R*,3*S*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diol (25b). The diacetate **24b** (230 mg, 0.35 mmol) was subjected to hydrolysis in the same way as **24a**, to obtain diol **25b** (150 mg, 75%) as a colourless oil: R_f = 0.5 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −2.06 (c 1.45, CH_2Cl_2); IR (neat) ν_{max}: 3430, 3060, 3030, 2878, 1491, 1449, 1214, 1070 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44–7.41 (m, 6H), 7.33–7.22 (m, 17H), 7.12–7.11 (m, 2H), 4.64 (d, J = 11.1 Hz, 1H), 4.58 (d, J = 11.4 Hz, 1H), 4.51 (d, J = 11.4 Hz, 1H), 4.47 (d, J = 11.1 Hz, 1H), 4.01 (td, J = 3.4, 6.3 Hz, 1H), 3.82 (dd, J = 4.3, 11.7 Hz, 1H), 3.79–3.75 (m, 2H), 3.71 (dd, J = 4.3, 8.5 Hz, 1H), 3.39 (dd, J = 3.4, 9.7 Hz, 1H), 3.29 (dd, J = 6.6, 9.7 Hz, 1H), 2.73 (br s, 1H), 2.40 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 138.0, 137.9, 128.7, 128.5, 128.4, 128.1, 127.9, 127.8, 127.2, 86.9, 79.5, 79.3, 73.9, 72.0, 71.2, 64.7, 61.1; HRMS calcd for $C_{38}H_{38}NaO_5$ $[M + Na]^+$ 597.2617, found: 597.2617.

(2*R*,3*R*,4*S*)-2,3-Bis(benzyloxy)-5-(trityloxy)pentane-1,4-diyl dimethanesulfonate (26b). Dimesylation of diol **25b** (150 mg, 0.26 mmol) was performed in the same way as described for **19a** to afford 160 mg (87%) of compound **26b** as a thick viscous liquid: R_f = 0.5 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = −8.08 (c 2.65, CH_2Cl_2); IR (neat) ν_{max}: 3400, 3061, 2934, 2874, 1597, 1492, 1449, 1357, 1175, 1095, 917 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41–7.39 (m, 4H), 7.34–7.22 (m, 19H), 7.17–7.15 (m, 2H), 5.03 (br s, 1H), 4.66 (d, J = 11.0 Hz, 1H), 4.61 (d, J = 11.0 Hz, 1H), 4.47–4.40 (m, 3H), 4.20 (dd, J = 2.7, 6.1 Hz, 1H), 3.87–3.81 (m, 2H), 3.73–3.71 (m, 2H), 2.91 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.1, 137.4, 137.3, 128.8–127.4 (m, aromatic C), 87.4, 81.5, 81.4, 77.9, 77.8, 74.7, 74.5, 73.5, 69.7, 63.6, 38.7, 38.4; HRMS calcd for $C_{40}H_{42}NaO_9S_2$ $[M + Na]^+$ 753.2168, found: 753.2166.

(2*S*,3*S*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)-2-(trityloxymethyl)-pyrrolidine (27b). The double nucleophilic displacement as mentioned for dimesylate **20a** was done on 165 mg (0.23 mmol) of compound **26a** to obtain 120 mg (81%) of product **27b** as a pale yellow oil: R_f = 0.8 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −18.2 (c 0.55, CH_2Cl_2); IR (neat) ν_{max}: 2923, 2854, 1664, 1492, 1448, 1344, 1152, 1064 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45–7.44 (m, 6H), 7.30–7.17 (m, 24H), 4.65 (d, J = 12.0 Hz, 1H), 4.53 (d, J = 12.0 Hz, 1H), 4.49–4.43 (m, 1H), 4.10 (t, J = 5.0 Hz, 1H), 3.99 (d, J = 13.7 Hz, 1H), 3.92 (dd, J = 6.3, 10.6 Hz, 1H), 3.52–3.47 (m, 3H), 3.10 (dd, J = 6.0, 11.7 Hz, 1H), 3.02 (dd, J = 5.7, 10.6 Hz, 1H), 2.58 (dd, J = 6.6, 10.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 139.4, 138.8, 128.9, 128.7, 128.3, 128.2, 127.8, 127.4, 127.3, 126.9, 126.8, 87.0, 78.7, 77.6, 72.9, 71.6, 65.3, 63.5, 59.9, 54.9; HRMS calcd for $C_{45}H_{44}NO_3$ $[M + H]^+$ 646.3321, found: 646.3324.

((2*R*,3*S*,4*R*)-1-Benzyl-3,4-bis(benzyloxy)pyrrolidin-2-yl)methanol (28b). The trityl ether of compound **27b** (120 mg, 0.18 mmol) was deprotected using the same method as for trityl ether **21a**, to afford 60 mg of compound **28b** (83%) as a pale yellow oil: R_f = 0.4 (hexane–EtOAc = 3 : 1); $[\alpha]_D^{28}$ = +24.29 (c 0.70, CH_2Cl_2); IR (neat) ν_{max}: 3424, 3292, 2865, 1601, 1494, 1453, 1117, 1045, 1027 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.20 (m, 15H), 4.55 (d, J = 12.0 Hz, 1H), 4.51–4.42 (m, 3H), 4.14–4.09 (m, 2H), 4.01 (d, J = 6.1 Hz, 1H), 3.97–3.93 (m, 1H), 3.76 (br s, 2H), 3.45 (dd, J = 3.4, 7.1 Hz, 1H), 3.37 (dd, J = 3.7, 9.7 Hz, 1H), 3.27–3.24 (m, 1H), 3.21 (dd, J = 7.4, 9.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.1, 138.3, 138.1, 137.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.4, 126.9, 78.9, 77.8, 73.4, 71.8, 71.3, 67.8, 61.6, 58.4, 52.7; HRMS calcd for $C_{26}H_{30}NO_3$ $[M + H]^+$ 404.2226, found: 404.2224.

(2*S*,3*R*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-(hydroxymethyl)-pyrrolidine-1-carboxylate (34a). The amine **22b** (1.05 g, 2.60 mmol) was dissolved in dry CH_3OH (10 mL) and $Pd(OH)_2/C$ (20% w/w, 50 mg) was added to it. The solution was degassed and then stirred under 1 atm H_2 (balloon) for 1 h. The catalyst was filtered through a Celite® pad and the filtrate was

concentrated *in vacuo*. The crude amine obtained was subjected to the next step without purification. The crude amine was dissolved in ethyl acetate (8 mL) and to this solution, Boc_2O (0.63 mL, 2.73 mmol) and Na_2CO_3 (828 mg, 7.81 mmol) were added and the reaction mixture was stirred for 2 h. On complete consumption of amine (TLC monitoring), water (10 mL) was added. The compound was extracted with EtOAc (3 × 8 mL), and the extracts dried over Na_2SO_4. The solvent was evaporated using rotary evaporator, and the residue purified by column chromatography to obtain 772 mg (74% over 2 steps) of compound **34a** as a white solid: mp = 67–69 °C; R_f = 0.5 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = +5.12 (*c* 2.15, CH_2Cl_2); IR (neat) ν_{max}: 3447, 2928, 2867, 1694, 1496, 1454, 1394, 1365, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 1.7 : 1 mixture of rotamers): δ 7.32–7.22 (m, 10H, both rotamers), 4.46–4.41 (m, 3H, both rotamers), 4.21 (br s, 1H, major rotamer), 4.11–3.97 (m, 2H, both rotamers), 3.90–3.86 (m, 2H major rotamer, 3H minor rotamer), 3.75 (br s, 1H, major rotamer), 3.50–3.45 (m, 2H, both rotamers), 3.02 (br s, 1H, minor rotamer), 1.47–1.40 (m, 9H, both rotamers); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.8, 138.0, 137.7, 137.0, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 80.6, 80.3, 78.2, 78.0, 77.8, 77.5, 73.4, 71.9, 71.7, 68.6, 68.4, 64.4, 63.0, 61.8, 61.4, 28.4; HRMS calcd for $C_{24}H_{32}NO_5$ $[M + H]^+$ 414.2280, found: 414.2281.

(2*S*,3*S*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-((*R*)-1-hydroxyallyl)-pyrrolidine-1-carboxylate (35a). To a well stirred suspension of CrO_3 (296 mg, 2.96 mmol) in CH_2Cl_2 (5 mL) at 0 °C were added Ac_2O (0.56 mL, 5.92 mmol), and pyridine (0.94 mL, 11.84 mmol) and stirred for 15 min. To the resulting brown suspension, the alcohol **34a** (765 mg, 1.85 mmol) dissolved in CH_2Cl_2 (3 mL) was added at 0 °C. The reaction mixture was stirred vigorously for 1 h with gradual warming to room temperature, following which it was filtered quickly through a short silica gel column and eluted with EtOAc (60 mL). The filtrate was concentrated using a rotavapor and the crude aldehyde was used for the next step without any further purification. R_f = 0.6 (hexane–EtOAc = 4 : 1). The aldehyde was dissolved in dry THF (4 mL) and cooled to 0 °C. Vinylmagnesium bromide (5.55 mL, 5.55 mmol, 1.0 M solution in THF) was added to this solution and stirred at room temperature for 2 h. The contents were then poured into saturated NH_4Cl solution (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic portions were washed with brine (1 × 20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue hence obtained was purified by column chromatography to give olefin **35a** (515 mg, 69% over 2 steps) as a colourless oil: R_f = 0.3 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −47.5 (*c* 0.80, CH_2Cl_2); IR (neat) ν_{max}: 3379, 2976, 1696, 1476, 1454, 1393, 1174, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 3 : 1 mixture of rotamers): δ 7.36–7.28 (m, 10H, both rotamers), 5.99–5.92 (m, 1H, both rotamers), 5.38–5.14 (m, 2H, both rotamers), 4.80–4.73 (m, 1H, both rotamers), 4.64–4.41 (m, 5H, both rotamers), 4.35–4.26 (m, 1H, both rotamers), 4.15–4.00 (m, 2H, major rotamer, 1H minor rotamer), 3.82–3.81 (m, 1H, minor isomer), 3.63–3.48 (m, 2H, both rotamers), 1.47 (s, 9H, minor rotamer), 1.44 (s, 9H, major rotamer); ^{13}C NMR (125 MHz, $CDCl_3$, 3 : 1 mixture of rotamers): δ 156.3, 154.4, 137.7, 137.4, 128.6, 128.2, 128.0, 127.9, 127.7, 83.4, 82.4, 80.5, 80.3, 79.6, 78.9, 72.9, 72.7, 71.9, 71.7, 63.1, 61.9, 61.4, 59.0, 50.4, 48.9, 28.5; HRMS calcd for $C_{26}H_{34}NO_5$ $[M + H]^+$ 440.2437, found: 440.2436.

(2*S*,3*S*,4*R*)-1-Allyl-3,4-bis(benzyloxy)-2-((*R*)-1-(benzyloxy)allyl)-pyrrolidine (40a). To a stirred solution of alcohol **35a** (500 mg, 1.14 mmol) in dry cyclohexane–CH_2Cl_2 (2 : 1, 8 mL), was added benzyl trichloroacetimidate (2.28 mL, 1 M solution in hexane), followed by triflic acid (50 μL), and stirred at room temperature for 2 h. The reaction mixture was quenched using aq. $NaHCO_3$ (5 mL) and extraction was done using EtOAc (3 × 5 mL). Organic extracts were dried and concentrated and the crude residue was dissolved in dry CH_2Cl_2 (5 mL). After cooling to 0 °C, CF_3CO_2H (0.45 mL, 5.70 mmol) was added and the reaction mixture stirred at room temperature for 6 h. The solvent was removed by evaporation and crude residue was dissolved in dry THF (5 mL) and cooled to 0 °C. To the solution was added butenyl bromide (0.3 mL, 2.28 mmol) followed by NaH (135 mg, 3.42 mmol, 60% in oil), and stirred with gradual warming to room temperature over 4 h. The solution was poured carefully over ice-water and extraction was done using EtOAc (3 × 5 mL). Organic extracts were dried and concentrated and the crude residue was subjected to column chromatography to furnish **40a** (300 mg, 56% over 3 steps) as a pale yellow oil: R_f = 0.6 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −4.8 (*c* 1.40, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1695, 1638, 1496, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.37–7.24 (m, 15H), 5.98–5.83 (m, 2H), 5.30–5.22 (m, 1H), 5.14–5.05 (m, 1H), 4.56–4.38 (m, 6H), 4.16 (t, *J* = 7.2 Hz, 1H), 3.97–3.95 (m, 1H), 3.89 (dd, *J* = 2.0, 5.1 Hz, 1H), 3.79 (dd, *J* = 5.1, 13.7 Hz, 1H), 3.44 (dd, *J* = 5.4, 11.2 Hz, 1H), 3.15 (dd, *J* = 7.4, 13.7 Hz, 1H), 3.02 (dd, *J* = 5.1, 6.8 Hz, 1H), 2.57 (dd, *J* = 2.9, 11.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.8, 135.6, 132.3, 131.7, 129.0, 128.7, 127.6, 127.5, 119.8, 116.5, 76.4, 73.5, 68.5, 65.4, 43.3; HRMS calcd for $C_{26}H_{34}NO_5$ $[M + H]^+$ 470.2695, found: 470.2696.

(1*S*,2*R*,8*R*,8a*S*)-1,2,8-Tris(benzyloxy)-1,2,3,5,8,8a-hexahydroindolizine (41a). The diene **40a** (290 mg, 0.62 mmol) was subjected to ring closing metathesis using the same procedure as described for diene **32a** to obtain **41a** (220 mg, 80%) as a colorless oil: R_f = 0.4 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −4.8 (*c* 1.40, CH_2Cl_2); IR (neat) ν_{max}: 2922, 1695, 1638, 1496, 1454, 1363, 1206, 1096 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.22 (m, 15H), 5.91–5.88 (m, 1H), 5.82–5.78 (m, 1H), 4.49–4.34 (m, 7H), 4.18–4.13 (m, 1H), 4.01–3.99 (m, 2H), 3.91–3.87 (m, 1H), 3.84 (dd, *J* = 4.0, 8.6 Hz, 1H), 3.39 (dd, *J* = 2.8, 10.3 Hz, 1H), 3.32–3.30 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.8, 138.7, 136.4, 136.2, 128.6, 128.4, 128.3, 128.1, 128.0, 127.8, 127.6, 127.4, 127.3, 126.6, 108.7, 85.6, 83.5, 74.8, 73.4, 69.3, 58.1, 51.9; HRMS calcd for $C_{29}H_{31}NNaO_3$ $[M + Na]^+$ 464.2202, found: 464.2201.

(2*R*,3*S*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-(hydroxymethyl)-pyrrolidine-1-carboxylate (34b). The benzylamine **28b** (450 mg, 1.12 mmol) was converted to Boc amine **34b** (365 mg, 79%, colorless oil) following the procedure used to obtain **34a**. R_f = 0.6 (hexane–EtOAc = 7 : 3); $[\alpha]_D^{28}$ = +5.1 (*c* 2.15, CH_2Cl_2); IR (neat) ν_{max}: 3447, 2928, 2867, 1694, 1496, 1454, 1394, 1365, 1106 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 1.7 : 1 mixture of rotamers): δ 7.32–7.22 (m, 10H, both rotamers), 4.55–4.53 (m, 3H, both rotamers), 4.46–4.41 (m, 3H, both rotamers), 4.21 (br s, 1H, major rotamer), 4.11–3.97 (m, 1H, both rotamers), 3.90–3.86

(m, 1H major rotamer, 2H minor rotamer), 3.75 (br s, 1H, major rotamer), 3.50–3.45 (m, 2H, both rotamers), 3.02 (br s, 1H, minor rotamer), 1.47–1.40 (m, 9H, both rotamers); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.8, 138.0, 137.7, 137.0, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 80.6, 80.3, 78.2, 78.0, 77.8, 77.5, 73.4, 71.9, 71.7, 68.6, 68.4, 64.4, 63.0, 61.8, 61.4, 28.4; HRMS calcd for $C_{24}H_{32}NO_5$ $[M + H]^+$ 414.2280, found: 414.2283.

(2*R*,3*S*,4*R*)-*tert*-Butyl-3,4-bis(benzyloxy)-2-((*R*)-1-hydroxyallyl)-pyrrolidine-1-carboxylate 35b. Compound **34b** (350 mg, 0.85 mmol) was subjected to oxidation and vinyl Grignard reactions, using the same procedure as described for **34a**, to furnish **35b** (260 mg, 70%) as a pale yellow oil: R_f = 0.7 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −1.3 (*c* 0.75, CH_2Cl_2); IR (neat) ν_{max}: 3331, 2976, 2929, 1692, 1453, 1391, 1105 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 3.5 : 1 mixture of rotamers): δ 7.36–7.18 (m, 10H, both rotamers), 6.14–6.07 (m, 1H, major rotamer), 5.70 (br s, 1H, minor rotamer), 5.32–5.05 (m, 1H, both rotamers), 4.75–4.40 (7H, both rotamers), 4.31 (t, *J* = 8.5 Hz, 1H, major rotamer), 4.15–4.11 (m, 1H, both rotamers), 4.06 (d, *J* = 4.0 Hz, 1H, minor rotamer), 4.02 (d, *J* = 4.0 Hz, 1H, major rotamer), 3.95 (dd, *J* = 2.7, 6.7 Hz, 1H, minor rotamer), 3.79 (br s, 1H, minor rotamer), 3.65–3.47 (m, 2H, major rotamer), 3.34–3.30 (m, 1H, minor rotamer), 1.41 (br s, 9H, major rotamer), 1.38 (s, 9H, minor rotamer); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.5, 138.3, 138.0, 136.0, 135.3, 128.5–127.5 (m, aromatic), 118.5, 117.9, 80.0, 79.9, 78.7, 78.0, 77.7, 73.2, 72.2, 71.7, 71.5, 69.5, 68.7, 62.6, 61.9, 61.7, 61.5, 53.5, 28.5, 28.4; HRMS calcd for $C_{26}H_{34}NO_5$ $[M + H]^+$ 440.2437, found: 440.2431.

(2*R*,3*S*,4*R*)-1-Allyl-3,4-bis(benzyloxy)-2-((*R*)-1-(benzyloxy)allyl)-pyrrolidine (40b). Following the procedure used to convert **35a** to **40a**, compound **40b** was obtained from **35b** (250 mg, 0.57 mmol) in 61% yield (3 steps, 160 mg) as a pale yellow oil: R_f = 0.5 (hexane–EtOAc = 9 : 1); $[\alpha]_D^{28}$ = −6.7 (*c* 0.50, CH_2Cl_2); IR (neat) ν_{max}: 2925, 1698, 1640, 1495, 1453, 1361, 1208, 1095 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.21 (m, 15H), 6.10–5.96 (m, 2H), 5.45 (d, *J* = 6.8 Hz, 1H), 5.38–5.26 (m, 2H), 5.19 (d, *J* = 8.7 Hz, 1H), 4.90–4.52 (m, 6H), 4.31 (br s, 1H), 4.10 (dd, *J* = 2.5, 6.8 Hz, 1H), 3.83–3.81 (m, 1H), 3.75–3.69 (m, 2H), 3.33 (dd, *J* = 3.1, 5.5 Hz, 1H), 3.09–2.88 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.6, 137.3, 136.2, 133.1, 133.0, 130.5, 130.0, 129.3, 129.2, 127.9, 127.8, 116.8, 116.0, 84.5, 75.4, 70.9, 65.4, 46.1; HRMS calcd for $C_{31}H_{36}NO_3$ $[M + H]^+$ 470.2695, found: 470.2691.

(1*S*,2*R*,8*R*,8a*R*)-1,2,8-Tris(benzyloxy)-1,2,3,5,8,8a-hexahydroindolizine (41b). The diene **40b** (150 mg, 0.32 mmol) was subjected to ring closing metathesis using the same procedure as described for diene **32a** to obtain **41b** (105 mg, 77%) as a colorless oil: R_f = 0.7 (hexane–EtOAc = 4 : 1); $[\alpha]_D^{28}$ = −11.5 (*c* 0.90, CH_2Cl_2); IR (neat) ν_{max}: 2925, 1698, 1640, 1495, 1453, 1361, 1208, 1095 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32–7.22 (m, 15H), 5.91–5.84 (m, 2H), 4.27–4.09 (m, 4H), 3.92–3.70 (m, 6H), 3.12 (dt, *J* = 2.1, 5.2 Hz, 1H), 3.06 (dd, *J* = 8.7, 14.3 Hz, 1H), 2.84–2.78 (m, 1H), 2.28–2.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2, 138.0, 136.5, 135.8, 128.5, 128.3, 127.9, 127.8, 127.7, 127.6, 115.5, 114.0, 84.2, 82.6, 71.9, 71.3, 57.5, 53.3; HRMS calcd for $C_{29}H_{32}NO_3[M + H]^+$ 442.2382, found: 442.2387.

General procedure for hydrogenation conditions to obtain compounds 23a, 23b, 1, 29, 8, 12, 9 and 13. The protected compound (50 mg) was dissolved in CH_3OH (1 mL) and 1 N HCl (1 mL) was added. Then $Pd(OH)_2$/C (10 mg, 20% w/w) was added and the mixture stirred under 1 atm H_2 (balloon) for 2–3 days. The catalyst was filtered out using Celite® and the filtrate stirred with Dowex (OH^-) resin (20–30 mg) and then concentrated. The residue was purified by repeated washing with 50% EtOAc–hexane.

(2*S*,3*R*,4*R*)-2-(Hydroxymethyl)pyrrolidine-3,4-diol (23a). Colourless viscous liquid. Yield = 11 mg, 67%; R_f = 0.4 (EtOAc–MeOH = 19 : 1); $[\alpha]_D^{28}$ = −3.3 (*c* 0.80, H_2O); IR (neat) ν_{max}: 3353, 3060, 1420, 1232, 1101, 1029 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.10–4.12 (m, 1H), 4.06 (dd, *J* = Hz, 1H), 3.78 (dd, *J* = Hz, 1H), 3.63 (dd, *J* = Hz, 1H), 3.51–3.48 (m, 1H), 3.35 (dd, *J* = Hz, 1H), 2.53 (br s, 1H); ^{13}C NMR (125 MHz, D_2O): δ 76.5, 76.3, 63.1, 58.8, 51.0; HRMS calcd for $C_5H_{12}NO_3$ $[M + H]^+$ 134.0817, found: 134.0815.

(2*S*,3*S*,4*R*)-2-(Hydroxymethyl)pyrrolidine-3,4-diol (23b). Pale yellow viscous liquid. Yield = 10 mg, 64%; R_f = 0.3 (EtOAc–MeOH = 19 : 1); $[\alpha]_D^{28}$ = −50.8 (*c* 0.45, H_2O); IR (neat) ν_{max}: 3351, 3064, 1229, 1101, 1027 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.05 (m, 1H), 3.82 (dd, *J* = 4.9, 7.3 Hz, 1H), 3.67 (dd, *J* = 4.2, 12.0 Hz, 1H), 3.54–3.53 (m, 1H), 3.08 (dd, *J* = 4.9, 12.0 Hz, 1H), 3.00 (m, 1H), 2.72 (dd, *J* = 3.9, 12.0 Hz, 1H); ^{13}C NMR (125 MHz, D_2O): δ 72.8, 71.2, 62.5, 61.6, 50.2; HRMS calcd for $C_5H_{12}NO_3$ $[M + H]^+$ 134.0817, found: 134.0814.

(2*R*,3*R*,4*R*)-2-(Hydroxymethyl)pyrrolidine-3,4-diol (1). Colourless viscous liquid. Yield = 10 mg, 64%; R_f = 0.4 (EtOAc–MeOH = 19 : 1); $[\alpha]_D^{28}$ = +6.9 (*c* 0.50, H_2O); IR (neat) ν_{max}: 3349, 3062, 1237, 1100, 1028 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.08–4.05 (m, 1H), 3.80–3.76 (m, 1H), 3.63 (dd, *J* = 5.1, 12.0 Hz, 1H), 3.08–3.06 (m, 1H), 2.94 (dd, *J* = 5.7, 11.3 Hz, 1H), 2.79–2.76 (m, 2H); ^{13}C NMR (125 MHz, D_2O): δ 76.5, 75.2, 63.8, 59.8, 48.7; HRMS calcd for $C_5H_{12}NO_3$ $[M + H]^+$ 134.0817, found: 134.0817.

(2*R*,3*S*,4*R*)-2-(Hydroxymethyl)pyrrolidine-3,4-diol (29). Colourless viscous liquid. Yield = 11 mg, 67%; R_f = 0.3 (EtOAc–MeOH = 19 : 1); $[\alpha]_D^{28}$ = +15.5 (*c* 0.20, H_2O); IR (neat) ν_{max}: 3352, 3060, 1233, 1098, 1025 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.45–4.39 (m, 1H), 4.30 (dd, *J* = 3.5, 4.9 Hz, 1H), 3.92 (dd, *J* = 5.4, 11.6 Hz, 1H), 3.80 (dd, *J* = 7.9, 11.6 Hz, 1H), 3.68–3.66 (m, 1H), 3.49–3.45 (m, 1H), 3.16 (dd, *J* = 6.9, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, D_2O): δ 70.1, 69.8, 62.8, 57.5, 46.9; HRMS calcd for $C_5H_{12}NO_3$ $[M + H]^+$ 134.0817, found: 134.0815.

(1*R*,2*R*,8a*S*)-Octahydroindolizine-1,2-diol (12). White solid. Yield = 17 mg, 72%; mp = 128–130 °C; R_f = 0.5 (EtOAc–MeOH = 9 : 1); $[\alpha]_D^{28}$ = +3.9 (*c* 0.25, MeOH); IR (neat) ν_{max}: 3356, 2962, 1237, 1100,cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.35–4.32 (m, 1H), 4.20 (d, *J* = 3.8 Hz, 1H), 4.05 (dd, *J* = 5.9, 11.7 Hz, 1H), 3.69 (d, *J* = 11.7, 1H), 3.38–3.35 (d, *J* = 11.7 Hz, 1H), 3.08–3.02 (m, 1H), 2.91 (dd, *J* = 12.8, 3.1 Hz, 1H), 2.10–1.98 (m, 3H), 1.80–1.56 (m, 3H); ^{13}C NMR (125 MHz, D_2O): δ 81.1, 77.9, 67.1, 62.5, 53.2, 25.4, 24.7, 22.7; HRMS calcd for $C_8H_{16}NO_2$ $[M + H]^+$ 158.1181, found: 158.1179.

(1*R*,2*R*,8a*R*)-Octahydroindolizine-1,2-diol (8). White solid. Yield = 15 mg, 66%; mp = 98–102 °C; R_f = 0.5 (EtOAc–MeOH = 9 : 1); $[\alpha]_D^{28}$ = −2.5 (*c* 0.45, MeOH); IR (neat) ν_{max}: 3348, 3005, 1241, 1109, 1025 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.10 (m, 1H), 3.65 (m, 1H), 3.05 (m, 1H), 2.89 (dd, *J* = 2.4, 11.6 Hz, 1H), 2.67

(dd, J = 6.8, 11.6 Hz, 1H), 2.29–2.25 (m, 1H), 2.09–2.07 (m, 1H), 1.96–1.75 (m, 3H), 1.52–1.22 (m, 3H); ^{13}C NMR (125 MHz, D_2O): δ 85.0, 77.9, 71.1, 62.5, 55.2, 29.4, 26.7, 25.7; HRMS calcd for $C_8H_{16}NO_2$ $[M + H]^+$ 158.1181, found: 158.1181.

(1*S*,2*R*,8*R*,8a*S*)-Octahydroindolizine-1,2,8-triol (13). White solid. Yield = 13 mg, 64%; mp = 102–107 °C; R_f = 0.4 (EtOAc–MeOH = 9 : 1); $[\alpha]_D^{28}$ = −57.5 (c 0.70, MeOH); IR (neat) ν_{max}: 3360, 3008, 1237, 1102, 1025 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.33–4.29 (m, 1H), 4.15–4.12 (m, 1H), 3.87 (dd, J = 6.0, 10.3 Hz, 1H), 3.39 (dd, J = 6.0, 11.1 Hz, 1H), 2.99–2.96 (m, 1H), 2.15–2.12 (m, 1H), 2.10–2.05 (m, 2H), 1.92–1.87 (m, 1H), 1.69–1.65 (m, 1H), 1.58–1.52 (m, 2H); ^{13}C NMR (125 MHz, D_2O): δ 71.0, 69.9, 67.1, 63.5, 60.2, 52.2, 19.6; HRMS calcd for $C_8H_{16}NO_3$ $[M + H]^+$ 174.1130, found: 174.1129.

(1*S*,2*R*,8*R*,8a*R*)-Octahydroindolizine-1,2,8-triol (9). White solid. Yield = 12 mg, 62%; mp = 139–141 °C; R_f = 0.4 (EtOAc–MeOH = 9 : 1); $[\alpha]_D^{28}$ = −82.5 (c 0.45, MeOH); IR (neat) ν_{max}: 3348, 3005, 1241, 1109, 1025 cm^{-1}; ^{1}H NMR (500 MHz, D_2O): δ 4.32–4.29 (m, 1H), 4.28 (dd, J = 4.1, 8.0 Hz, 1H), 3.85–3.82 (m, 1H), 2.95–2.86 (m, 2H), 2.57 (dd, J = 7.5, 11.0 Hz, 1H), 2.10–2.02 (m, 1H), 1.98–1.90 (m, 2H), 1.72 (br s, 1H), 1.52 (m, 1H), 1.27–1.24 (m, 1H); ^{13}C NMR (125 MHz, D_2O): δ 73.1, 69.5, 69.0, 66.2, 60.3, 51.4, 32.4, 22.7; HRMS calcd for $C_8H_{16}NO_3$ $[M + H]^+$ 174.1130, found: 174.1132.

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