

Stereoselective Synthesis of (+)-1,8-Di-*epi*- and (–)-1-*epi*-Swainsonine from an (*S*)-Pyroglutamic Acid Derivative¹⁾

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(+)-1,8-Di-*epi*-swainsonine (**15**) and (–)-1-*epi*-swainsonine (**17**) were synthesized stereoselectively from an (*S*)-pyroglutamic acid derivative (**1a**). A (2*R*,3*R*,4*R*)-3,4-dihydroxy-2-hydroxymethylpyrrolidine derivative (**6a**) was prepared by *cis*-dihydroxylation of an α,β -unsaturated lactam (**2**) followed by epimerization of the di-*O*-benzyl derivative (**3b**) as the key reactions. The diastereoselective allylation of the aldehyde **6b** obtained from **6a** and subsequent cyclization of **13** and **16** gave **15** and **17**, respectively. It proved that 1,8-di-*epi*-swainsonine (**15**) is dextrorotatory.

Keywords stereoselective synthesis; (*S*)-pyroglutamic acid; (+)-1,8-di-*epi*-swainsonine; immunoregulating activity; diastereoselective allylation; epimerization

Polyhydroxylated indolizidines such as (–)-swainsonine and (+)-castanospermine exhibit remarkable physiological effects including mannosidase- and glucosidase-inhibitory activity. More recently, it has been reported that (–)-swainsonine has an interesting immunoregulatory activity.²⁾ The synthesis and biological evaluation of (–)-swainsonine and its stereoisomers have been the focus of a number of research programs.³⁾ In connection with our synthetic studies on the utility of optically active glutamic acid derivatives for natural product synthesis⁴⁾ and asymmetric reactions,⁵⁾ we have already reported the synthesis of (+)-1,8-di-*epi*-swainsonine (**15**) and (–)-1-*epi*-swainsonine (**17**) from an (*S*)-pyroglutamic acid derivative.¹⁾ The details of this work and further synthetic studies in this field are presented here.

As shown in Chart 1, the synthesis of **15** and **17** starting from the (*S*)-pyroglutamic acid derivative (**1a**) involves firstly our previously developed *cis*-dihydroxylation of the α,β -unsaturated lactam (**2**) followed by epimerization of the benzyloxy group in **3b**. Secondly, diastereoselective allylation of **6b** is employed to construct the indolizidine skeleton. *cis*-Dihydroxylation of **2**, prepared from (*S*)-5-methoxymethoxymethyl-2-pyrrolidinone^{5c)} by *N*-benzylation (NaH, benzyl bromide, and tetrahydrofuran (THF)–*N,N*-dimethylformamide (DMF)) followed by selenation and oxidative deselenation, with a catalytic amount of OsO₄ in aqueous acetone in the presence of *N*-methylmorpholine *N*-oxide (NMO), gave a diol (**3a**) as a single isomer in 65% yield. A small amount of trihydroxy compound (**4**, about 6%; its configurations were tentatively determined as 3*S*,4*S*,5*S*) was obtained during the oxidation procedure.⁶⁾ Di-*O*-benzylation of the diol **3a** (NaH, benzyl bromide, THF–DMF; 85% yield), followed by epimerization of the α -benzyloxy group with sodium methoxide in MeOH–THF gave **5a** in 65% yield with 11% recovery of **3b**. Compound **5a** was also prepared from **3c**,^{4e)} obtained from **3a** as a minor product by *O*-monobenzylation using Ohno's procedure (dibutyltin oxide, toluene, then cesium fluoride, benzyl bromide, and DMF).⁷⁾ Mitsunobu reaction⁸⁾ of **3c** (triphenylphosphine, benzoic acid, diethyl azodicarboxylate, and THF) followed by debenzoylation of **5b** with aqueous sodium hydroxide in MeOH and subsequent *O*-benzylation of **5c** (NaH, benzyl bromide, and THF–DMF) gave **5a** in 73% yield. Compound **5a** was then

converted to the 2-hydroxymethylpyrrolidine derivative **6a** by reduction with borane–dimethyl sulfide complex in THF followed by removal of methoxymethoxy group by acidic hydrolysis (aqueous HCl and THF–MeOH, 70 °C) in 82% yield. The structure of **6a** was confirmed by the conversion of **6a** into the hydrochloride of (2*R*,3*R*,4*R*)-3,4-dihydroxy-2-hydroxymethylpyrrolidine (**7**) (10% Pd–C, H₂, HCl–EtOH), which is a potent α -glucosidase inhibitor.⁹⁾

On the other hand, 3,4-dihydroxyprolines¹⁰⁾ have also been isolated from nature and showed interesting biological activity. Therefore (2*S*,3*R*,4*S*)-3,4-dihydroxyproline (**10**) was synthesized using the (*S*)-pyroglutamic acid derivative (**8**).^{4g)} The hydrolysis of **8** with aqueous lithium hydroxide in THF gave the corresponding carboxylic acid, which was converted to the mixed anhydride (ethyl chloroformate, triethylamine (TEA), and THF) and reduced with NaBH₄ in THF–H₂O¹¹⁾ to afford the corresponding alcohol. Mesylation of the alcohol (methanesulfonyl chloride (MsCl), TEA, and CH₂Cl₂) followed by cyclization (potassium *tert*-butoxide, and THF) gave a fully protected pyrrolidine **9a** in 77% overall yield. Selective cleavage of the trityl group of **9a** under acidic condition (MeOH–concentrated HCl=40:1) followed by oxidation of **9b** using the Sharpless method (NaIO₄, catalytic RuCl₃, CH₃CN–CCl₄–H₂O)¹²⁾ and subsequent removal of the protecting groups in **9c** with 80% aqueous trifluoroacetic acid gave **10** in 37% yield.

The carbon unit required for the indolizidine skeleton was introduced using the diastereoselective allylation previously described.^{1,13)} The aldehyde **6b** was prepared from **6a** by the method of Swern¹⁴⁾ and used without purification. The reaction of **6b** with allylmagnesium chloride at –78 °C in THF gave **11a** and **12a** in a 1:1.6 ratio (the ratio of the isomers was determined by HPLC analysis (Waters, Radial pak cartridge, silica (10 μ), AcOEt:hexane=1:4 as the eluent) in 81% yield. On the other hand, opposite diastereoselectivity was observed when an organocopper reagent was used. The reaction of **6b** with lithium diallylcuprate¹⁵⁾ at –78 °C in ether afforded a 2.2:1 ratio of **11a** and **12a** in 68% yield, while the condensation of **6b** with allyltrimethylsilane in the presence of TiCl₄ in methylene chloride at –78 °C¹⁶⁾ gave only **11a** in 56% yield. This high diastereoselectivity may be rationalized in terms of cyclic chelate formation between TiCl₄ and the amino-

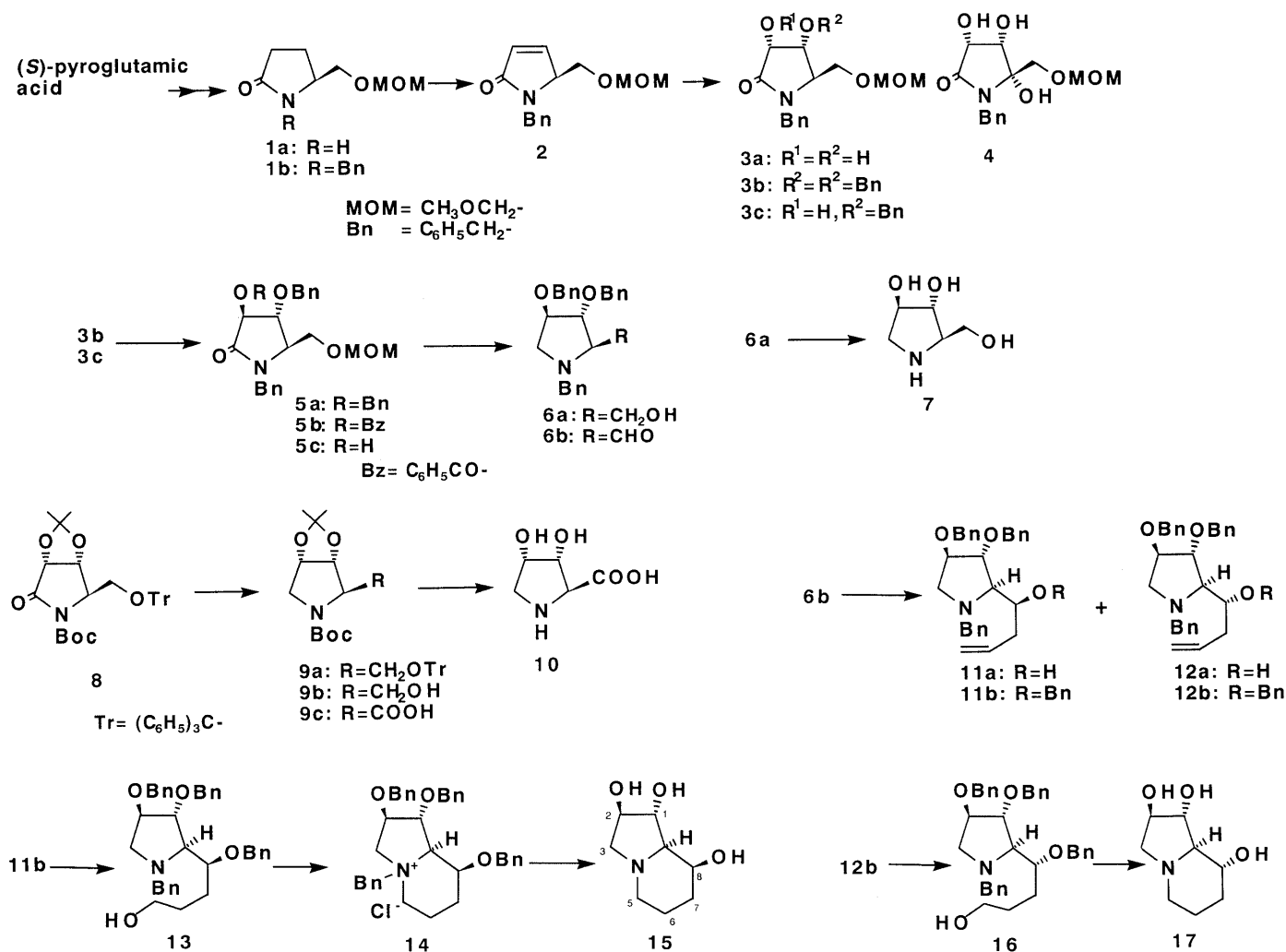


Chart 1

carbonyl group, in which the allyl group reacts from the less hindered side.¹³⁾ The hydroxy group in **11a** was protected as a benzyl ether (NaH, benzyl bromide, THF-DMF) to give **11b** in 82% yield, and this was converted to the alcohol **13** in 78% yield by hydroboration-oxidation (BH₃, THF, 40 °C, then 3 N NaOH, 30% H₂O₂). Mesylation of **13** (MsCl, TEA, CH₂Cl₂) leads to a bicyclic compound **14**, which was debenzylated by catalytic hydrogenation (10% Pd-C, H₂, HCl-EtOH) and subsequent purification with Dowex 50W-X8 (H⁺ form) to afford (+)-1,8-di-*epi*-swainsonine (**15**, mp 142–143 °C; [α]_D²⁰ +24.2° (MeOH), lit.^{1b,3g,h)} mp 138–140 °C; [α]_D²⁰ +18.2° (MeOH)) in 67% yield. Its spectral data were identical with those reported.^{3g,h)} Similarly **12a** was converted to (–)-1-*epi*-swainsonine (**17**, mp 109–110 °C; [α]_D²⁰ –33.2° (MeOH), lit.³ⁱ⁾ mp 120–121 °C) in 39% yield.

Thus, stereocontrolled syntheses of **15** and **17** from an (*S*)-pyroglutamic acid derivative allow a facile access to polyhydroxylated indolizidine alkaloids. Further synthetic studies using optically active pyroglutamic acid derivatives are in progress in this laboratory.

Experimental

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectral measurements were performed on a JASCO IRA-1 grating infrared spectrometer and a JEOL JIR-110 FT-IR spectrophotometer. Proton and carbon-13 nuclear

magnetic resonance (¹H- and ¹³C-NMR) spectra were measured with a JEOL JNM FX-100 (100 MHz) spectrometer. Data were recorded in parts per million (ppm) downfield from internal tetramethylsilane (TMS) unless otherwise stated. The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Optical rotations were determined with a JASCO DIP-360 digital polarimeter. Mass spectra (MS) were recorded with JEOL JMS-D302 and JEOL JMS-HX110 mass spectrometers. Organic extracts were dried over MgSO₄ before vacuum evaporation.

(S)-1-Benzyl-5-methoxymethoxymethyl-2-pyrrolidinone (1b) A suspension of NaH (60% oil suspension, hexane-washed, 1.1 g, 27.5 mmol) in THF (15 ml) was added at 0 °C to a solution of (*S*)-5-methoxymethoxymethyl-2-pyrrolidinone^{5c)} (**1a**, 4.0 g, 25.2 mmol) in THF-DMF (1:1, 30 ml), and the mixture was stirred at room temperature for 1 h. Then benzyl bromide (3.6 ml, 30.3 mmol) was added. After being stirred at room temperature for 15 h, the mixture was diluted with AcOEt-benzene (2:1, 150 ml), and washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane=1:1) gave **1b** (5.96 g, 95% yield) as an oil, [α]_D²⁰ +70.5° (c=1.7, CHCl₃). IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 1700, 1430, 1045. ¹H-NMR (CDCl₃): 1.57–2.86 (4H, m, 2 × CH₂), 3.29 (3H, s, OCH₃), 3.30–3.71 (3H, m, CH, CH₂O), 4.12 and 4.92 (2H, AB, *J*=15 Hz, NCH₂Ph), 4.46, 4.50 (2H, m, OCH₂O), 7.25 (5H, s, aromatic protons). HR-MS *m/z*: Calcd for C₁₄H₁₉NO₃ (M⁺): 249.1363. Found: 249.1355.

(S)-1-Benzyl-5-methoxymethoxymethyl-2-oxo-3-pyrroline (2) A solution of **1b** (3.0 g, 12.1 mmol) in THF (20 ml) was added to a solution of lithium diisopropylamide [prepared from butyl lithium (12.7 ml of a 1.1 M solution in hexane) and diisopropylamine (2.0 ml, 14.6 mmol) in 13 ml of THF] at –78 °C. The mixture was stirred at –78 °C for 40 min and then a solution of PhSeCl (2.78 g, 14.5 mmol) in THF (18 ml) was added. Stirring was continued at –78 °C for 15 min, then 15 ml of 10% aqueous NH₄Cl was added and the aqueous layer was extracted with AcOEt. The organic

extracts were washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:3) gave the 3-phenylseleno-2-pyrrolidinone derivative (4.01 g, 82% yield) as a diastereomeric mixture (2.1:1). Less polar isomer: oil, $[\alpha]_D^{20} + 79.2^\circ$ ($c = 0.7$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1700, 1450. $^1\text{H-NMR}$ (CDCl_3): 1.80–2.20 (1H, m, CH_2), 2.40–2.90 (1H, m, CH_2), 3.35 (3H, s, OCH_3), 3.30–3.50 (2H, m, CH_2O), 3.68 (1H, m, CH), 4.00 (1H, m, CH), 4.30 and 5.00 (2H, AB, $J = 14.3$ Hz, NCH_2Ph), 4.52 (2H, s, OCH_2O), 7.20–7.85 (10H, m, aromatic protons). More polar isomer: oil, $[\alpha]_D^{20} + 14.5^\circ$ ($c = 1.0$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1700, 1450. $^1\text{H-NMR}$ (CDCl_3): 1.90–2.70 (1H, m, CH_2), 3.38 (3H, s, OCH_3), 3.30–3.80 (3H, m, CH_2O , CH), 4.12 and 5.08 (2H, AB, $J = 14.3$ Hz, NCH_2Ph), 4.20 (1H, m, CH), 4.60 (2H, s, OCH_2O), 7.15–7.85 (10H, m, aromatic protons). A mixture of 3-phenylselenopyrrolidinone (3.0 g, 7.43 mmol) and 30% H_2O_2 (6 ml) in AcOEt (24 ml) was stirred at 15–20°C for 20 min, then the AcOEt layer was separated and washed with H_2O , saturated aqueous NaHCO_3 , and saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:1) gave **2** (1.54 g, 84% yield) as an oil, $[\alpha]_D^{20} - 28.7^\circ$ ($c = 1.8$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1700. $^1\text{H-NMR}$ (CDCl_3): 3.29 (3H, s, OCH_3), 3.63 (2H, m, CH_2), 4.14 (1H, m, CH), 4.43 and 5.06 (2H, AB, $J = 14.3$ Hz, NCH_2Ph), 4.49 (2H, s, OCH_2O), 6.23 (1H, dd, $J = 1.7$, 6.0 Hz, vinyl proton), 7.03 (1H, dd, $J = 1.5$, 6.0 Hz, vinyl proton), 7.23 (5H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 44.21 (t), 55.20 (q), 61.76 (d), 66.29 (t), 96.24 (t), 127.54 (d), 126.35, 127.43, 128.28 (aromatic carbons), 145.32 (d), 171.0 (s). *Anal.* Calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_2$: C, 67.99; H, 6.93; N, 5.66. Found: C, 67.75; H, 6.90; N, 5.41.

(3R,4R,5R)-1-Benzyl-3,4-dihydroxy-5-methoxymethoxymethyl-2-pyrrolidinone (3a) A mixture of **2** (2.1 g, 8.5 mmol), OsO_4 (213 mg, 0.85 mmol), and NMO monohydrate (1.49 g, 11 mmol) in acetone– H_2O (1:1, 25 ml) was stirred at room temperature for 13 h. After addition of sodium hydrosulfite (2.0 g), the acetone was evaporated off *in vacuo*, and the mixture was extracted with AcOEt. The organic layer was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 5:1) gave **3a** (1.55 g, 65% yield) and **4** (150 mg, 6% yield). **3a**: Oil, $[\alpha]_D^{20} + 89.1^\circ$ ($c = 0.5$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3363, 1681, 1114. $^1\text{H-NMR}$ (CDCl_3): 3.25 (3H, s, OCH_3), 3.52 (3H, m, CH_2 , CH), 3.77 (1H, brs, OH), 4.23 and 4.80 (2H, AB, $J = 14.3$ Hz, NCH_2Ph), 4.31 (1H, m, CH), 4.33 and 4.47 (2H, AB, $J = 5.7$ Hz, OCH_2O), 4.58 (1H, m, CH), 5.60 (1H, m, OH), 7.26 (5H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 44.89 (t), 55.30 (q), 63.32 (d), 64.73 (t), 69.69 (t), 70.37 (t), 96.20 (t), 127.51, 127.56, 128.39 (aromatic carbons), 135.05 (s), 174.15 (s). HR-MS m/z : Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_5$ (M^+): 281.1262. Found: 281.1273. **4**: mp 135–138°C (CHCl_3 –hexane), $[\alpha]_D^{20} + 3.3^\circ$ ($c = 1$, MeOH). IR $\nu_{\text{max}}^{\text{solid}}$ cm^{-1} : 3334, 1680, 1155, 1075, 1030. $^1\text{H-NMR}$ (CDCl_3): 3.20 (3H, s, OCH_3), 2.50–3.80 (4H, m, CH_2 , 2 $\times$ OH), 4.03 (1H, m, CH), 4.10–4.80 (4H, m, OH, CH_2 , CH), 4.61 (2H, s, OCH_2), 7.29 (5H, s, aromatic protons). $^{13}\text{C-NMR}$ (CD_3OD): 42.49 (t), 55.75 (q), 70.02 (t), 71.19 (d), 72.95 (d), 89.51 (s), 97.56 (t), 128.16, 129.04, 129.28 (aromatic carbons), 139.46 (s), 175.57 (s). *Anal.* Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_6$: C, 56.56; H, 6.44; N, 4.71. Found: C, 56.38; H, 6.52; N, 4.48.

(3R,4R,5R)-1-Benzyl-3,4-bis(benzyloxy)-5-methoxymethoxymethyl-2-pyrrolidinone (3b) A suspension of NaH (660 mg, 16.5 mmol, 60% oil suspension) in THF (15 ml) was added at 0°C to a solution of **3a** (2.2 g, 7.8 mmol) in DMF (10 ml). Stirring was continued at room temperature for 30 min, then benzyl bromide (2.1 ml, 17.7 mmol) was added and the mixture was stirred at room temperature for 3 h. After dilution with AcOEt–benzene (2:1, 150 ml), the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **3b** (3.07 g, 85% yield) as an oil, $[\alpha]_D^{20} + 84.3^\circ$ ($c = 1$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1705. $^1\text{H-NMR}$ (CDCl_3): 3.19 (3H, s, OCH_3), 3.49 (3H, m, CH_2 , CH), 3.97 (2H, m, 2 $\times$ CH), 4.17 and 5.04 (2H, AB, $J = 12.8$ Hz, NCH_2Ph), 4.39 and 4.47 (2H, AB, $J = 10$ Hz, OCH_2Ph), 4.45 and 4.57 (2H, AB, $J = 15$ Hz, OCH_2Ph), 4.80 and 5.00 (2H, AB, $J = 11.4$ Hz, OCH_2O), 7.29 (5H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 43.91 (t), 55.31 (t), 59.87 (d), 64.43 (t), 71.84 (d), 72.41 (t), 75.43 (d), 75.83 (d), 96.35 (t), 127.54, 127.60, 127.80, 127.82, 128.39 (aromatic carbons), 135.47 (s), 137.46 (s), 171.19 (s). HR-MS m/z : Calcd for $\text{C}_{28}\text{H}_{32}\text{NO}_5$ ($(M+1)^+$): 462.2279. Found: 462.2279.

(3S,4R,5R)-1-Benzyl-3,4-bis(benzyloxy)-5-methoxymethoxymethyl-2-pyrrolidinone (5a) A mixture of **3b** (2.5 g, 5.42 mmol) and freshly prepared sodium methoxide (360 mg, 6.78 mmol) in MeOH–THF (1:5, 20 ml) was stirred at room temperature for 5 h. After dilution with AcOEt, the mixture

was washed with H_2O , 5% aqueous HCl, and saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **5a** (1.63 g, 65% yield) and **3b** (0.28 g, 11% recovery) as an oil. **5a**: $[\alpha]_D^{20} + 16.7^\circ$ ($c = 1$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1705, 1380, 1050. $^1\text{H-NMR}$ (CDCl_3): 3.25 (3H, s, OCH_3), 3.52 (3H, m, CH_2 , CH), 3.98–4.30 (3H, m, NCH_2Ph , 2 $\times$ CH), 4.44 (2H, s, OCH_2Ph), 4.50 and 4.60 (2H, AB, $J = 10$ Hz, OCH_2Ph), 4.80–5.23 (3H, m, OCH_2O , NCH_2Ph), 7.25 (5H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 43.96 (d), 55.39 (q), 59.14 (t), 64.59 (t), 71.89 (t), 72.32 (t), 78.35 (d), 80.68 (d), 96.24 (t), 127.40, 127.56, 128.10, 128.12 (aromatic carbons), 135.73 (s), 137.09 (s), 137.34 (s), 171.00 (s). HR-MS m/z : Calcd for $\text{C}_{28}\text{H}_{32}\text{NO}_5$ ($(M+1)^+$): 462.2279. Found: 462.2283.

(3S,4R,5R)-3-Benzoyloxy-1-benzyl-4-benzyloxy-5-methoxymethoxymethyl-2-pyrrolidinone (5b) A mixture of **3c**^{4e} (700 mg, 1.89 mmol), triphenylphosphine (1.81 g, 4.73 mmol), benzoic acid (575 mg, 4.73 mmol), and diethyl azodicarboxylate (820 mg, 4.73 mmol) in THF (10 ml) was stirred at room temperature for 14 h. After dilution with AcOEt, the mixture was washed with saturated aqueous NaHCO_3 and saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:3) gave **5b** (840 mg, 94% yield) as an oil, $[\alpha]_D^{20} + 33.2^\circ$ ($c = 0.6$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1726, 1708, 1446, 1261, 1110. $^1\text{H-NMR}$ (CDCl_3): 3.27 (3H, s, OCH_3), 3.46–3.83 (3H, m, CH_2 , CH), 4.03–4.37 (2H, m, 2 $\times$ CH), 4.44 (2H, s, OCH_2Ph), 4.14 and 5.12 (2H, AB, $J = 14.9$ Hz, NCH_2Ph), 4.48 (2H, s, OCH_2Ph), 4.56 and 4.72 (2H, AB, $J = 11.7$ Hz, OCH_2Ph), 7.23–8.20 (15H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 43.95 (t), 54.97 (q), 59.35 (d), 63.74 (t), 71.58 (t), 75.53 (d), 77.09 (d), 95.95 (t), 127.14, 127.38, 127.34, 127.82, 128.16, 128.64, 129.43 (aromatic carbons), 132.89 (s), 135.08 (s), 136.44 (s), 164.9 (s), 167.77 (s). HR-MS m/z : Calcd for $\text{C}_{28}\text{H}_{29}\text{NO}_6$ (M^+): 475.1993. Found: 475.1985.

(3S,4R,5R)-1-Benzyl-4-benzyloxy-3-hydroxy-5-methoxymethoxymethyl-2-pyrrolidinone (5c) A mixture of **5b** (800 mg, 1.68 mmol) and aqueous 2N NaOH (1.5 ml) in MeOH (7 ml) was stirred at room temperature for 30 min. After dilution with AcOEt, the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:2) gave **5c** (580 mg, 93% yield) as an oil, $[\alpha]_D^{20} + 60.3^\circ$ ($c = 0.6$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3642, 1693, 1110. $^1\text{H-NMR}$ (CDCl_3): 3.25 (3H, s, OCH_3), 3.34–3.80 (3H, m, CH_2 , CH), 4.10 and 5.03 (2H, AB, $J = 15$ Hz, NCH_2Ph), 4.07 (1H, m, CH), 4.43 (2H, s, OCH_2Ph), 4.50 (1H, m, CH), 4.66 and 4.83 (2H, AB, $J = 9.5$ Hz, OCH_2O), 5.04 (1H, brs, OH), 7.25 and 7.30 (10H, each s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 43.86 (t), 55.16 (q), 58.67 (d), 63.74 (t), 71.68 (t), 75.33 (d), 79.53 (d), 96.10 (t), 127.28, 127.43, 127.53, 127.67, 128.01, 128.31 (aromatic carbons), 135.47 (s), 137.27 (s), 173.04 (s). HR-MS m/z : Calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_5$ (M^+): 371.1731. Found: 371.1722.

Preparation of 5a from 5c This sample was obtained in 83% yield from **5c** in the same manner as described above for the preparation of **3b**. Physical and spectral data were identical with those of the sample prepared from **3b**.

(2R,3R,4R)-N-Benzyl-3,4-bis(benzyloxy)-2-hydroxymethylpyrrolidine (6a) Borane–dimethyl sulfide complex (1.2 ml) was added to a solution of **5a** (1.5 g, 3.25 mmol) in THF (15 ml). The solution was stirred at 70°C for 1 h, and then acidified with 10% aqueous HCl. After addition of 10 ml of MeOH, the mixture was stirred at 70°C for 1 h. After cooling to room temperature, the whole was basified with 10% aqueous NaOH and extracted with AcOEt. The AcOEt extract was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (AcOEt:hexane = 1:1) gave **6a** (1.07 g, 82% yield) as an oil, $[\alpha]_D^{20} - 24.2^\circ$ ($c = 0.9$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3500, 1080. $^1\text{H-NMR}$ (CDCl_3): 2.45–3.25 (3H, m, CH_2 , CH), 3.40 and 3.97 (2H, AB, $J = 14$ Hz, NCH_2Ph), 3.63–4.15 (3H, m, 2 $\times$ CH, OH), 4.45 and 4.53 (4H, each s, 2 $\times$ OCH_2Ph), 7.25 (15H, s, aromatic protons). $^{13}\text{C-NMR}$ (CDCl_3): 56.95 (t), 57.73 (t), 59.48 (t), 70.13 (d), 70.62 (t), 71.69 (t), 80.29 (d), 85.11 (d), 127.00, 127.48, 128.05, 128.12 (aromatic carbons), 137.54 (s), 137.92 (s). HR-MS m/z : Calcd for $\text{C}_{26}\text{H}_{28}\text{NO}_3$ ($(M-1)^+$): 402.2069. Found: 402.2066.

(2R,3R,4R)-3,4-Dihydroxy-2-hydroxymethylpyrrolidine Hydrochloride (Hydrochloride of 7) A solution of **6a** (100 mg, 0.25 mmol) in EtOH (3 ml) was hydrogenated using 10% palladium carbon (40 mg) in the presence of ethanolic HCl at room temperature for 13 h under hydrogen at atmospheric pressure. The mixture was filtered and concentrated *in vacuo* to give a residue, which was crystallized from MeOH–ether to afford the hydrochloride of **7**, mp 113°C; $[\alpha]_D^{20} + 36.3^\circ$ ($c = 0.3$, H_2O), lit.⁹ mp 113–115°C; $[\alpha]_D^{20} + 37.9^\circ$ ($c = 0.53$, H_2O). *Anal.* Calcd for $\text{C}_5\text{H}_{12}\text{ClNO}_3$:

C, 35.41; H, 7.13; N, 8.26. Found: C, 35.17; H, 7.09; N, 7.99. Spectral data (^1H and ^{13}C -NMR) were identical with those reported.⁹⁾

(2R,3R,4S)-N-(tert-Butoxycarbonyl)-3,4-isopropylidenedioxy-2-trityloxymethylpyrrolidine (9a) A mixture of **8** (1 g, 1.89 mmol) and aqueous 2N LiOH (1.9 ml) in THF (14 ml) was stirred at room temperature for 2 h. After acidification with 5% aqueous HCl, the mixture was extracted with AcOEt. The organic extracts were washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a crude carboxylic acid. A solution of ethyl chloroformate (205 mg, 1.89 mmol) in THF (8 ml) was added at 0 °C to a solution of the above carboxylic acid and triethylamine (190 mg, 1.89 mmol) in THF (8 ml), and the mixture was stirred at 0 °C for 30 min. The precipitate was filtered off, and washed with THF. The combined organic solutions were added to a solution of sodium borohydride (200 mg, 5.3 mmol) in water (5 ml) at 0 °C. After being stirred at room temperature for 1 h, the mixture was diluted with AcOEt and washed with half-saturated aqueous NaCl. Drying followed by evaporation gave the corresponding alcohol (0.93 g, 93% yield), which was mesylated with methanesulfonyl chloride (270 mg, 2.36 mmol) and triethylamine (240 mg, 2.37 mmol) in methylene chloride (8 ml) at 0 °C for 30 min. After dilution with AcOEt, the mixture was washed with saturated aqueous NaHCO_3 and H_2O . Drying followed by evaporation gave a crude mesylate, which was dissolved in 10 ml of THF. Potassium *tert*-butoxide (350 mg, 0.31 mmol) was added at 0 °C and the mixture was stirred at 0 °C for 15 min. After dilution with AcOEt, the mixture was washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **9a** (805 mg, 83% yield), $[\alpha]_{\text{D}}^{20} - 37.2^\circ$ ($c = 0.55$, CHCl_3), lit.⁴⁰⁾ for the enantiomer, $[\alpha]_{\text{D}}^{20} + 31.0^\circ$ ($c = 0.7$, CHCl_3). ^1H -NMR (CDCl_3): 1.27, 1.34, 1.41, 1.47 (15H, 4 × s, 5 × CH_3), 2.88–4.21 (5H, m, 2 × CH_2 , CH), 4.55 (1H, d, $J = 6$ Hz, CH), 4.73–4.99 (1H, m, CH), 6.98–7.53 (15H, m, aromatic protons). ^{13}C -NMR (CDCl_3): 24.90 (q), 26.85 (q), 28.21 (q), 53.07 and 53.85 (t), 63.11 (d), 63.45 and 63.64 (t), 78.85 and 79.82 (d), 79.38 (s), 82.35 and 83.13 (d), 86.84 (s), 111.15 (s), 126.84, 127.67, 128.26 (aromatic carbons), 143.31 (s), 153.74 (s), in good agreement with the data for the enantiomer of **9a**.

(2R,3R,4S)-N-(tert-Butoxycarbonyl)-3,4-isopropylidenedioxy-2-hydroxymethylpyrrolidine (9b) A mixture of **9a** (330 mg, 0.64 mmol) and 15 ml of concentrated HCl–MeOH solution (1:40) was stirred at room temperature for 1 h. After addition of AcOEt–benzene (1:1, 200 ml) and aqueous NaOH (5 ml), the mixture was washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 2:1) gave **9b** (110 mg, 62% yield) as an oil, $[\alpha]_{\text{D}}^{20} - 41.7^\circ$ ($c = 0.8$, CHCl_3). ^1H -NMR (CDCl_3): 1.28 (3H, s, CH_3), 1.42 (12H, s, CH_3 , $(\text{CH}_3)_3$), 2.84 (1H, brs, OH), 3.30–3.89 (4H, m, 2 × CH_2), 3.98 (1H, m, CH), 4.47–4.81 (2H, m, 2 × CH). ^{13}C -NMR (CDCl_3): 24.49 (q), 26.95 (q), 28.31 (q), 52.68 (t), 62.81 (t), 64.96 (d), 78.94 (d), 80.11 (s), 81.91 and 82.74 (d), 114.50 (s). MS m/z : 274 ($(\text{M} + 1)^+$), 273 (M^+).

(2S,3R,4S)-N-(tert-Butoxycarbonyl)-3,4-isopropylidenedioxyproline (9c) RuCl_3 (10 mg) was added to a solution of **9b** (100 mg, 0.37 mmol), NaIO_4 (320 mg, 1.5 mmol), 0.8 ml of CH_3CN , 0.8 ml of CCl_4 , and 1.1 ml of H_2O . The mixture was stirred at room temperature for 30 min, diluted with H_2O (5 ml), and extracted with ether. The organic layers were washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:MeOH = 10:1) gave **9c** (85 mg, 80% yield) as an oil, $[\alpha]_{\text{D}}^{20} - 31.2^\circ$ ($c = 0.8$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2723, 1714, 1672. ^1H -NMR (CDCl_3): 1.35 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.49 (9H, s, $(\text{CH}_3)_3$), 3.42–4.00 (2H, m), 4.40–4.66 (1H, m, CH), 4.66–5.04 (2H, m), 7.26 (1H, brs, COOH). ^{13}C -NMR (CDCl_3): 24.76 (q), 26.66 (q), 28.02 and 28.12 (q), 51.70 and 52.14 (t), 65.69 and 66.08 (d), 80.36 and 80.09 (d), 80.74 and 81.04 (s), 82.41 and 83.08 (d), 112.18 and 112.28 (s), 154.28 and 155.21 (s), 173.92 and 174.26 (s). MS (FAB) m/z : 288 ($(\text{M} + 1)^+$).

(2S,3R,4S)-3,4-Dihydroxyproline (10) A mixture of **9c** (60 mg, 0.21 mmol) and 3.5 ml of 80% aqueous trifluoroacetic acid was stirred at room temperature for 20 h. The trifluoroacetic acid was removed *in vacuo* and the residue was purified by ion exchange chromatography (Dowex 50W-X8, H^+ form, eluted with 1N aqueous NH_4OH) to give **10** (23 mg, 74% yield) as a solid after freeze drying, mp 235–240 °C (dec.), $[\alpha]_{\text{D}}^{20} + 7.2^\circ$ ($c = 0.5$, H_2O), lit.^{10a)} mp 240–250 °C (dec.), $[\alpha]_{\text{D}}^{20} + 7.5^\circ$ ($c = 0.16$, H_2O). ^{13}C -NMR (D_2O , internal standard: dioxane $\delta = 67.40$): 49.18 (t), 65.11 (d), 70.78 (d), 74.91 (d), 172.90 (s), in good agreement with the data reported.^{10a)} Anal. Calcd for $\text{C}_5\text{H}_9\text{NO}_4$: C, 40.81; H, 6.17; N, 9.52. Found: C, 40.55; H, 6.36; N, 9.28.

(2R,3R,4R)-N-Benzyl-3,4-bis(benzyloxy)-2-[(1S)-1-hydroxy-3-butenyl]-

pyrrolidine (11a) and (2R,3R,4R)-N-Benzyl-3,4-bis(benzyloxy)-2-[(1R)-1-hydroxy-3-butenyl]pyrrolidine (12a) A) Allylation with Allylmagnesium Chloride: Swern oxidation¹⁴⁾ of **6a** (500 mg, 1.24 mmol) was performed using 2 eq of oxalyl chloride and 4 eq of dimethylsulfoxide in methylene chloride at –20 °C. A solution of the crude aldehyde in THF (6 ml) was treated with allylmagnesium chloride (1.2 ml of a 2 M solution in THF) at –78 °C for 1 h, then the reaction was quenched with 5 ml of 10% aqueous NH_4Cl and the mixture was extracted with AcOEt. The organic layers were washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **11a** (166 mg, 30% yield) and **12a** (279 mg, 51% yield) as an oil. **11a**: $[\alpha]_{\text{D}}^{20} - 9.57^\circ$ ($c = 0.8$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3500, 1450. ^1H -NMR (CDCl_3): 2.05–3.48 (6H, m, $\text{CH}_2\text{CH}=\text{CH}_2$, CH_2 , OH, CH), 3.71 and 4.17 (2H, AB, $J = 14.3$ Hz, NCH_2Ph), 3.66–4.20 (3H, m, 3 × CH), 4.51 and 4.58 (4H, s, 2 × OCH_2Ph), 4.95–5.29 (2H, m, $\text{CH}_2=\text{CH}$), 5.66–6.14 (1H, m, $\text{CH}_2=\text{CH}$), 7.31 (15H, s, aromatic protons). ^{13}C -NMR (CDCl_3): 39.10 (t), 57.05 (t), 61.81 (t), 70.37 (d), 71.00 (t), 71.30 (t), 72.90 (d), 81.61 (d), 85.64 (d), 116.77 (t), 126.96, 127.37, 128.14 (aromatic carbons), 134.95 (d and s), 138.65 (s). HR-MS m/z : Calcd for $\text{C}_{29}\text{H}_{33}\text{NO}_3$ (M^+): 443.2459. Found: 443.2450. **12a**: $[\alpha]_{\text{D}}^{20} - 8.1^\circ$ ($c = 1.0$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3500, 1450. ^1H -NMR (CDCl_3): 2.08–2.91 (5H, m, $\text{CH}_2\text{CH}=\text{CH}_2$, CH_2 , OH, CH), 3.11 (1H, m, CH), 3.37 and 4.09 (2H, AB, $J = 14.0$ Hz, NCH_2Ph), 3.77–4.20 (3H, m, 3 × CH), 4.47 (4H, s, 2 × OCH_2Ph), 4.95–5.26 (2H, m, $\text{CH}_2=\text{CH}$), 5.63–6.17 (1H, m, $\text{CH}_2=\text{CH}$), 7.30 (15H, s, aromatic protons). ^{13}C -NMR (CDCl_3): 37.69 (t), 56.61 (t), 57.78 (t), 67.74 (d), 70.42 (t), 71.49 (t), 73.19 (d), 79.56 (d), 82.58 (d), 116.84 (t), 126.84, 127.42, 127.47, 127.66, 128.10, 128.14, 128.38 (aromatic carbons), 134.71 (d), 137.34 (s), 137.83 (s). HR-MS m/z : Calcd for $\text{C}_{29}\text{H}_{33}\text{NO}_3$ (M^+): 443.2458. Found: 443.2443.

B) Allylation with Lithium Diallylcuprate: A solution of **6b** in ether (4 ml) prepared from **6a** (250 mg, 0.62 mmol) as described above was treated with 1.5 eq of an ethereal solution of lithium diallylcuprate¹⁴⁾ at –78 °C for 30 min. The mixture was allowed to warm to 0 °C and then was partitioned between ether and an aqueous solution (pH 8) of ammonia and NH_4Cl . The organic layer was washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **11a** (133 mg, 48% yield) and **12a** (55 mg, 20% yield).

C) Allylation with Allyltrimethylsilane and TiCl_4 : TiCl_4 (0.17 ml, 1.5 mmol) was added to a solution of allyltrimethylsilane (0.17 ml, 1.1 mmol) and **6b** [prepared from **6a** (200 mg, 0.5 mmol)] in methylene chloride (5 ml) at –78 °C. The mixture was stirred at –78 °C for 1 h, and then 5 ml of aqueous NaOH was added and the whole was extracted with AcOEt. The organic layer was washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane = 1:4) gave **11a** (124 mg, 56% yield).

(2R,3R,4R)-N-Benzyl-2-[(1S)-1-benzyloxy-3-butenyl]-3,4-bis(benzyloxy)pyrrolidine (11b) This sample was obtained from **11a** in 82% yield as an oil after column chromatography (silica gel, AcOEt:hexane = 1:6) in the same manner as described above for the preparation of **3b**, $[\alpha]_{\text{D}}^{20} - 43.9^\circ$ ($c = 1.0$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1500, 1460, 1100. ^1H -NMR (CDCl_3): 2.07–3.23 (5H, m, $\text{CH}_2=\text{CHCH}_2$, CH_2 , CH), 3.55 and 4.16 (2H, AB, $J = 14.0$ Hz, NCH_2Ph), 3.56 (1H, m, CH), 3.91 (1H, m, CH), 4.02 (1H, m, CH), 4.42–4.83 (6H, m, 3 × OCH_2Ph), 4.96–5.22 (2H, m, $\text{CH}_2=\text{CH}$), 5.69–6.18 (1H, m, $\text{CH}_2=\text{CH}$), 7.32 (20H, s, aromatic protons). ^{13}C -NMR (CDCl_3): 35.41 (t), 57.34 (t), 59.87 (t), 70.37 (t), 71.20 (t), 71.64 (d), 72.12 (t), 79.32 (d), 80.78 (d), 84.47 (d), 115.79 (t), 127.23, 127.42, 127.91, 128.29 (aromatic carbons), 136.36 (d), 137.82 (s), 138.31 (s), 138.94 (s). MS m/z : 533 (M^+), 532 ($(\text{M} - 1)^+$).

(2R,3R,4R)-N-Benzyl-2-[(1S)-1-benzyloxy-4-hydroxybutyl]-3,4-bis(benzyloxy)pyrrolidine (13) A mixture of **11b** (120 mg, 0.23 mmol) and borane–THF complex (1.0 ml of a 1 M solution in THF) in THF (6 ml) was stirred at 40 °C for 45 min, then 0.6 ml of 3N NaOH and 0.7 ml of 30% H_2O_2 were added and the mixture was stirred at 60 °C for 30 min. After cooling to room temperature, the mixture was acidified (pH 2) with 10% aqueous HCl and heated at 70 °C for 10 min. Then, the mixture was basified with aqueous NaOH and extracted with AcOEt. The organic layers were washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (AcOEt: = 1:1) gave **13** (97 mg, 78% yield) as an oil, $[\alpha]_{\text{D}}^{20} - 44.3^\circ$ ($c = 1.0$, CHCl_3). IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3400, 1060. ^1H -NMR (CDCl_3): 1.05–2.10 (6H, m), 2.60 (1H, m), 2.90–3.27 (2H, m), 3.30–3.62 (2H, m), 3.72–4.20 (3H, m), 4.40–4.91 (6H, m, 3 × OCH_2Ph), 7.31 (20H, s, aromatic protons). ^{13}C -NMR (CDCl_3): 26.85 (t), 29.62 (t), 57.53 (t), 59.97 (t), 62.40 (t), 70.32 (t), 71.20

(t), 71.34 (d), 71.88 (t), 79.08 (d), 80.68 (d), 84.28 (d), 126.64, 127.27, 127.95, 128.39 (aromatic carbons), 136.70 (d), 137.92 (s), 137.73 and 137.68 (s). HR-MS m/z : Calcd for $C_{36}H_{41}NO_4$ (M^+): 551.3033. Found: 551.3025.

(+)-1,8-Di-*epi*-swainsonine (15) A mixture of **13** (80 mg, 0.15 mmol), methanesulfonyl chloride (20 mg, 0.17 mmol), and triethylamine (18 mg, 0.18 mmol) in 3 ml of methylene chloride was stirred at room temperature for 14 h. Washing with H_2O followed by drying and evaporation gave an oily residue, which was hydrogenated using 10% palladium carbon (50 mg) in EtOH (4 ml) in the presence of ethanolic HCl at room temperature for 12 h under hydrogen at atmospheric pressure. The mixture was filtered and concentrated *in vacuo*, and the residue was placed on a Dowex 50W-X8 (H^+ form) column, washed with 20 ml of water, and eluted with 0.7 N NH_4 OH. Freeze drying of the appropriate fractions gave a residue, which was crystallized from MeOH-ether to afford **15** (17 mg, 67% yield) as crystals, mp 142–143 °C, $[\alpha]_D^{20} + 24.2^\circ$ ($c=0.3$, MeOH). IR ν_{max}^{KBr} cm^{-1} : 3600–3000, 2920, 2810, 1330, 1240, 1210, 1150, 1135, 1100, 1095. 1H -NMR (D_2O): 1.22–2.27 (6H, m), 2.60 (1H, dd, $J=6, 11$ Hz), 2.75–3.10 (2H, m), 3.83–4.30 (3H, m). ^{13}C -NMR (CD_3OD): 20.22 (t), 32.03 (t), 54.04 (t), 62.62 (t), 64.37 (d), 74.85 (d), 77.63 (d), 79.97 (d), in good agreement with the data for **15** reported.^{3g,h} HR-MS m/z : Calcd for $C_8H_{15}NO_3$ (M^+): 173.1049. Found: 173.1039.

Preparation of 12b This sample was obtained from **12a** in 80% yield as an oil after column chromatography (silica gel, AcOEt:hexane=1:6) in the same manner as described above for the preparation of **3b**, $[\alpha]_D^{20} - 24.5^\circ$ ($c=2.0$, $CHCl_3$). IR ν_{max}^{film} cm^{-1} : 1550, 1450, 1100. 1H -NMR ($CDCl_3$): 2.36–2.67 (3H, m), 2.87 (1H, m, CH), 3.12 (1H, m, CH), 3.36 and 4.27 (2H, AB, $J=13.7$ Hz, NCH_2Ph), 3.75 (1H, m, CH), 3.97 (1H, m, CH), 4.14 (1H, m, CH), 4.26 and 4.38 (4H, $2 \times s$, $2 \times CH_2Ph$), 4.52 and 4.70 (2H, AB, $J=7$ Hz, OCH_2Ph), 5.00–5.22 (2H, m, $CH_2=CH$), 5.72–6.21 (1H, m, $CH_2=CH$), 7.34 (20H, s, aromatic protons). ^{13}C -NMR ($CDCl_3$): 36.18 (t), 57.39 (t), 59.63 (t), 70.57 (t), 71.34 (t), 72.07 (d), 72.27 (t), 81.22 (d), 84.67 (d), 116.43 (t), 126.42, 126.93, 127.02, 127.22, 128.00 (aromatic carbons), 135.59 (d), 137.80 (s), 138.30 and 138.92 (s). MS m/z : 533 (M^+).

Preparation of 16 This sample was obtained from **12b** in 76% yield as an oil after column chromatography (silica gel, AcOEt:hexane=1:1) in the same manner as described above for the preparation of **13**, $[\alpha]_D^{20} - 13.1^\circ$ ($c=1.1$, $CHCl_3$). IR ν_{max}^{film} cm^{-1} : 3450, 1070. 1H -NMR ($CDCl_3$): 1.43–2.10 (5H, m, $2 \times CH_2$, OH), 2.46 (1H, m, CH), 2.84 (1H, m, CH), 3.07–3.37 (2H, m, NCH_2Ph , CH), 3.40–3.69 (3H, m), 3.72–4.40 (3H, m, NCH_2Ph , $2 \times CH$), 4.43–5.04 (6H, m, $3 \times OCH_2Ph$), 7.30 (20H, s, aromatic protons). ^{13}C -NMR ($CDCl_3$): 28.01 (t), 29.42 (t), 57.34 (t), 59.48 (t), 62.40 (t), 70.57 (t), 71.39 (t), 72.22 (d, s), 77.86 (d), 81.02 (d), 84.82 (d), 126.29, 126.86, 126.90, 127.71, 128.00 (aromatic carbons), 137.68 (s), 137.82 (s), 138.31 (s), 138.70 (s). MS m/z : 551 (M^+).

Preparation of (–)-1-*epi*-Swainsonine (17) This sample was obtained from **16** in 64% yield in the same manner as described above for the preparation of **15**, mp 109–110 °C, $[\alpha]_D^{20} - 33.2^\circ$ ($c=0.85$, MeOH). IR ν_{max}^{KBr} cm^{-1} : 3600–3000, 2920, 2800, 1330, 1270, 1250, 1150, 1130, 1090. 1H -NMR (CD_3OD): 0.80–2.12 (6H, m), 2.44 (1H, dd, $J=6.4, 10.6$ Hz), 2.05 (2H, m), 3.35 (1H, m, CHOH), 3.61–4.18 (2H, m, $2 \times CHOH$). ^{13}C -NMR (CD_3OD): 20.41 (t), 32.20 (t), 54.08 (t), 62.76 (t), 64.61 (d), 74.99 (d), 77.86 (d), 80.15 (d). HR-MS m/z : Calcd for $C_8H_{15}NO_3$ (M^+): 173.1049. Found: 173.1021.

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