Synthesis of (−)-Swainsonine and (−)-8-*epi*-Swainsonine from (*S*)- and (*R*)-Glutamic Acid Derivatives[1,2]

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(−)-Swainsonine (1) and (−)-8-*epi*-swainsonine were synthesized from (*S*)- and (*R*)-glutamic acid derivatives. (2*R*,3*S*,4*R*)-3,4-Dihydroxy-2-hydroxymethylpyrrolidine derivatives (9a and 9g) were prepared by *cis*-dihydroxylation of α,β-unsaturated compounds 6, 10 and 15 with OsO_4 as the key reaction. The diastereoselective allylation of the aldehydes 18 derived from 9a and 9g, followed by cyclization, gave 1 and (−)-8-*epi*-swainsonine.

Keywords chiral synthesis; optically active glutamic acid; (−)-swainsonine; immunoregulating activity; chelation-controlled allylation; *cis*-dihydroxylation

Swainsonine (**1**) ((1*S*,2*R*,8*R*,8a*R*)-trihydroxyindolizidine) is a plant indolizidine alkaloid first isolated from the fungus *Rhizoctonia leguminicola*,[3] which exhibits remarkable physiological effects such as an α-mannosidase inhibitory activity and an immunoregulating activity.[4] Because of this physiological activity, the synthesis and biological evaluation of swainsonine and its stereoisomers have been studied by several authors.[5] As a continuation of our work to utilize optically active glutamic acid derivatives for natural product synthesis[6] and for asymmetric synthesis,[7] we have already reported the synthesis of (−)-swainsonine from (*S*)- and (*R*)-glutamic acid derivatives.[1,2] The details of this work and further synthetic studies in this area are presented here.

According to our retrosynthetic analysis as shown in Chart 1, swainsonine (**1**) could be available from **2**, which in turn might be obtained by allylation of the aldehyde **3** derived from a (2*R*,3*S*,4*R*)-3,4-dihydroxy-2-hydroxymethylpyrrolidine derivative (**4**). Since optically active polyhydroxylated pyrrolidines have interesting biological activity[8] including α-glucosidase and α-mannosidase inhibitory activity, the synthesis of (2*R*,3*S*,4*R*)-3,4-dihydroxy-2-hydroxymethylpyrrolidine derivatives such as **9a** and **9g** was first examined using **6**, **10**, and **15** prepared from (*S*)-

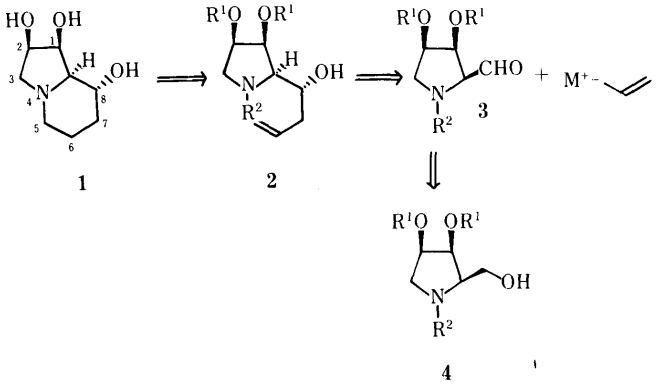

Chart 1

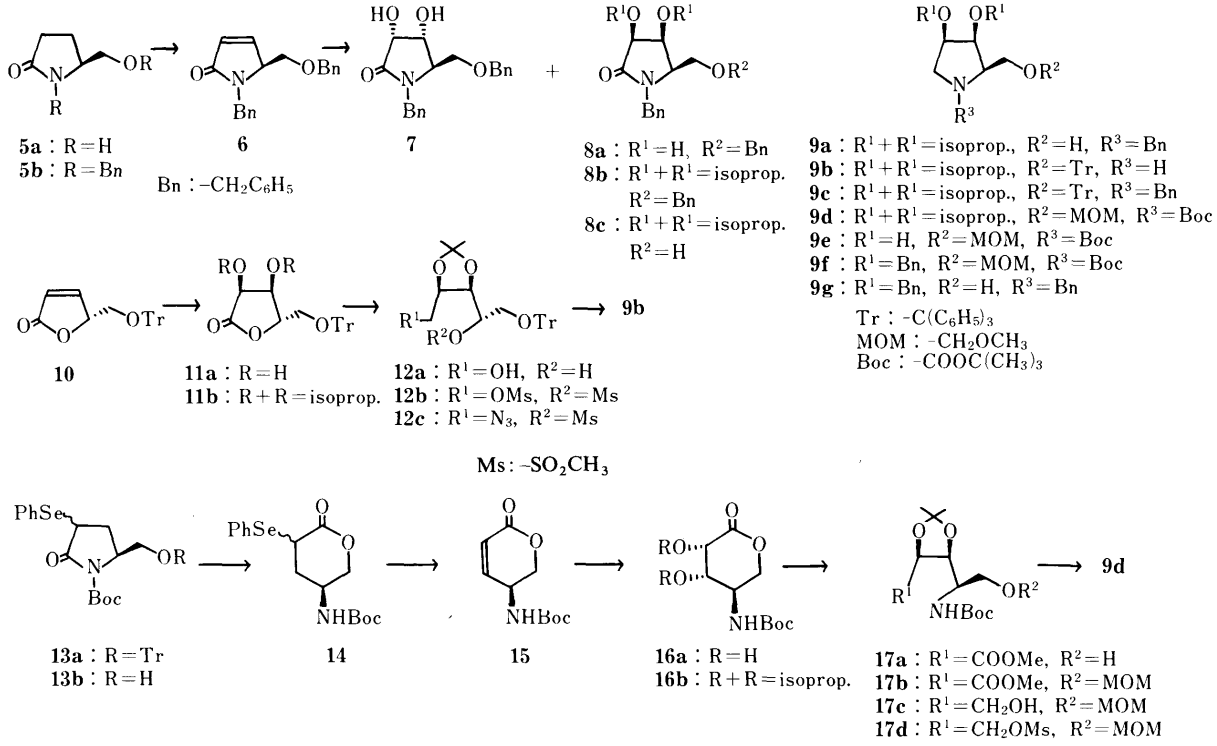

Chart 2

and (*R*)-glutamic acid derivatives as shown in Chart 2.

The α,β-unsaturated lactam **6** was prepared from (*S*)-5-hydroxymethyl-2-pyrrolidinone (**5a**)[9] by *N*,*O*-dibenzylation followed by a selenation-deselenation procedure[10a] in 50% yield. The butenolide **10**[11] was analogously prepared from (*R*)-glutamic acid. The α,β-unsaturated lactone **15**[10b] was prepared from a diastereomeric mixture of the 3-phenylseleno-2-pyrrolidinone derivative **13a**.[6d] After removal of the trityl group of **13a** by acidic treatment, hydrolysis of **13b** with aqueous lithium hydroxide in tetrahydrofuran (THF) followed by lactonization with acetic anhydride and pyridine in benzene–methylene chloride gave the 2-phenylseleno-δ-lactone **14** as a diastereomeric mixture, which was oxidatively deselenized with 30% H_2O_2 in AcOEt to provide **15** in 38% yield. *cis*-Dihydroxylation of **6** with a catalytic amount of OsO_4 in aqueous acetone in the presence of *N*-methylmorpholine *N*-oxide (NMO) gave **7** and **8a** (**7** : **8a** = 85 : 15) in 71% yield. On the other hand, **11a** and **16a** were obtained from **10**[12] and **15** by same reaction in 52 and 58% yields, respectively, and the other isomers were not detected.

Isopropylidenation of **8a** followed by removal of the benzyl group of **8b** by hydrogenolysis with palladium black in MeOH gave **8c** in 77% yield. Reduction of **8c** with borane–dimethyl sulfide (Me_2S) complex in THF afforded **9a** in 72% yield. Compound **9a** was also efficiently prepared from **11a**. The *cis*-diol of **11a** was protected with the isopropylidene group to give **11b**, which was successively treated with lithium aluminum hydride in THF, mesyl chloride in pyridine, and sodium azide in dimethylformamide (DMF) at 140—145 °C to provide the azidomesylate **12c** in 31% yield. Hydrogenation of the azido group of **12c** with palladium black in EtOH gave the pyrrolidine **9b**, which was benzylated with benzyl bromide in acetone in the presence of K_2CO_3 followed by selective removal of the trityl group of **9c** with acidic hydrolysis (concentrated HCl : MeOH = 1 : 40, room temperature) to give **9a** in 52% yield. After protection of the diol **16a** with an isopropylidene group, **16b** was hydrolyzed with aqueous base followed by treatment with diazomethane to provide the hydroxy-ester **17a** in 74% yield. Protection of the secondary hydroxy group of **17a** as the methoxymethyl (MOM) ether followed by reduction of **17b** with $NaBH_4$ in EtOH gave the alcohol **17c** in 68% yield. Mesylation of **17c** and subsequent cyclization of the mesylate **17d** with *tert*-BuOk in THF afforded the fully protected pyrrolidine **9d** in 77% yield. Selective removal of the isopropylidene group in **9d** under acidic condition (10% aqueous HCl : MeOH = 1 : 1, room temperature) followed by di-*O*-benzylation of **9e** (benzyl bromide, NaH, THF–DMF) provided **9f**, which was converted to **9g** in 33% yield from **9d** by removal of the Boc and MOM groups by acidic hydrolysis (10% aqueous HCl : MeOH = 1 : 1, 70 °C) followed by *N*-benzylation (benzyl bromide, K_2CO_3, acetone).

The diastereoselective allylation for the introduction of the three-carbon unit required for the indolizidine skeleton was examined by reaction of the aldehyde **18** with allylmagnesium chloride in THF, organocopper reagent[13] [derived from copper(I) and allylmagnesium chloride] in THF, and allyltrimethylsilane/$TiCl_4$[14] in CH_2Cl_2 at −78 °C. The aldehydes **18a** and **18b** were prepared from **9g** and **9a** by the method of Swern[15] and used for allylation without purification. The results are summarized in Table I. The ratio of the isomers was determined by high-performance liquid chromatographic analysis of the crude products. The reaction of **18b** with Grignard reagent gave **19b** and **20b** in a 1 : 1.3 ratio in 80% yield, while the reaction with the organocopper reagent afforded a 1 : 3.2 ratio of **19b** and **20b** in 71% yield. In the case of **18a**, addi-

TABLE I. Diastereoselective Allylation of **18**

Run	Aldehyde	Conditions	Products	(ratio)[a]	Yield (%)[b]
1	**18a**	Allyl-MgCl, THF	**19a** : **20a**	(3 : 1)	85
2	**18a**	Allyl-MgCl, CuI, THF–Me_2S	**19a** : **20a**	(1 : 3.8)	56
3	**18a**	Allyl-TMS, $TiCl_4$, CH_2Cl_2	**20a**		48
4	**18b**	Allyl-MgCl, THF	**19b** : **20b**	(1 : 1.3)	80
5	**18b**	Allyl-MgCl, CuI, THF–Me_2S	**19b** : **20b**	(1 : 3.2)	71
6	**18b**	Allyl-TMS, $TiCl_4$, CH_2Cl_2	**19b** : **20b**	(1 : 18)	32

a) The ratio of the isomers was determined by HPLC (Waters, Radial pak cartridge silica (10 μ), AcOEt : hexane = 1 : 4 for **19a** and **20a**, and AcOEt : hexane = 1 : 3 for **19b** and **20b** as eluants). *b*) Refers to isolated yield after column chromatography.

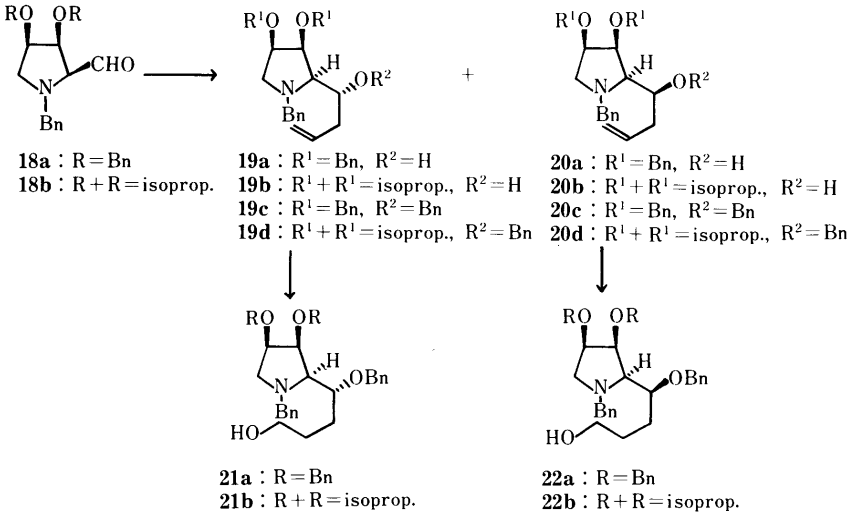

Chart 3

tion of allylmagnesium chloride gave a 3:1 ratio of **19a** and **20a** in 85% yield, and opposite diastereoselectivity was observed when the organocopper reagent was used (**19a**:**20a**=1:3.8, 56% yield). On the other hand, the condensation of **18a** and **18b** with allyltrimethylsilane (2.4 eq) in the presence of $TiCl_4$ (3.4 eq) in methylene chloride produced only **20a**, and a 1:18 ratio of **19b** and **20b** in 48 and 32% yields, respectively. This high diastereoselectivity could be explained by cyclic chelate formation between $TiCl_4$ and the α-aminocarbonyl group of **18a** and **18b**, in which the nucleophile approaches from the less hindered α-side to yield **20a** and **20b** exclusively.[14b)]

The structure of **19a** was established by hydroboration–oxidation to the alcohol **21a** after protection of the hydroxy group of **19a** as the benzyl ether, as shown in Chart 3. Mesylation of **21a** followed by hydrogenolysis with 10% palladium carbon yielded (−)-swainsonine (**1**) (mp 141—142 °C; $[\alpha]_D^{20}$ −85.1° (*c*=0.6, MeOH), lit.[3b)] mp 144—145 °C; $[\alpha]_D^{20}$ −87.2° (*c*=2.1, MeOH)) in 41% yield after treatment with Dowex 50W-X8 (H^+ form). Its spectral data (^{1}H- and ^{13}C-nuclear magnetic resonance (NMR)) were identical with those of natural (−)-swainsonine. Similarly **19b**, **20a**, and **20b** were converted to **1** and (−)-8-*epi*-swainsonine (mp 92—93 °C; $[\alpha]_D^{20}$ −22.1° (*c*=0.25, MeOH)), lit.[5g)] mp 93—95°C; $[\alpha]_D^{20}$ −24.8° (*c*=0.67, MeOH) in 35, 33, and 39% yields respectively.

Thus *cis*-dihydroxylation of **10** and **15** followed by diastereoselective allylation of the aldehyde **18** provides a facile synthesis of swainsonine and (−)-8-*epi*-swainsonine. Further synthetic studies on utilizing optically active glutamic acid derivatives are in progress.

Experimental[16)]

(*S*)-1-Benzyl-5-benzyloxymethyl-2-pyrrolidinone (5b) A suspension of NaH (5.12 g, 128 mmol, 60% oil suspension, washed with hexane) in THF (50 ml) was added at 0 °C to a solution of (*S*)-5-hydroxymethyl-2-pyrrolidinone (**5a**) (7.0 g, 60.9 mmol) in DMF (50 ml). The mixture was stirred at room temperature for 1 h, then benzyl bromide (18.1 ml, 152 mmol) was added and the whole was stirred at room temperature for 20 h. After dilution with AcOEt–benzeme (3:1, 200 ml), the reaction mixture was washed with half-saturated aqueous NaCl (×6). Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane=1:2) gave **5b** (16.1 g, yield 90%) as an oil, $[\alpha]_D^{20}$ +31° (*c*=2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1700, 1430. ^{1}H-NMR ($CDCl_3$): 2.60—3.75 (4H, m, 2×CH_2), 3.35—3.50 (2H, m, CH_2O), 3.58 (1H, m, CH), 4.13 and 4.85 (2H, AB, *J*=15 Hz, $NC\underline{H}_2Ph$), 4.39 (2H, s, $OC\underline{H}_2Ph$), 7.30 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 21.68 (t), 30.25 (t), 44.52 (t), 56.80 (d), 70.79 (t), 73.07 (t), 127.32, 127.60, 127.89, 128.46 (aromatic carbons), 136.74 (s), 137.59 (s), 175.28 (s). MS *m/z*: 295 (M^+), 174.

(*S*)-1-Benzyl-5-benzyloxymethyl-2-oxo-3-pyrroline (6) Butyl lithium (17.2 ml of a 1.10 M solution in hexane) was added to a solution of diisopropylamine (2.65 ml, 18.9 mmol) in THF (20 ml) at −78 °C. The mixture was stirred at −78 °C for 10 min, then a solution of **5b** (5.0 g, 16.9 mmol) in THF (15 ml) was added over a period of 10 min. The whole was stirred at −78 °C for 40 min and then a solution of PhSeBr in THF (20 ml) prepared from diphenyl diselenide (3.04 g, 9.7 mmol) and bromine (0.50 ml, 9.7 mmol) was added at −78 °C. Stirring was continued at −78 °C for 5 min, then 15 ml of 10% aqueous NH_4Cl was added and the aqueous layer was extracted with AcOEt. The combined 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=1:3) gave the 3-phenylseleno-2-pyrrolidinone derivative (4.94 g, 65% yield) as a diastereomeric mixture. ^{1}H-NMR ($CDCl_3$): 1.60—2.7 (2H, m, CH_2), 3.12—3.42 (2H, m, CH_2O), 3.56 (1H, m, CH), 3.78—4.50 (4H, m, $OC\underline{H}_2Ph$, PhSeC$\underline{H}$, $NC\underline{H}Ph$), 4.70—5.00 (1H, $NC\underline{H}Ph$), 6.80—7.75 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 29.73 and 30.21 (t), 39.81 and 40.45 (d), 44.37 and 44.64 (t), 55.11 and 55.50 (d), 69.34 and 70.85 (t), 72.81 (t), 126.99—137.23 (aromatic carbons), 173.04 (s), 173.48 (s). A mixture of the 3-phenylseleno-2-pyrrolidinone derivative (4.0 g, 8.9 mmol) and 30% H_2O_2 (15 ml) in AcOEt (50 ml) was stirred at 15—20 °C for 30 min, and then the organic 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=1:2) gave **6** (2.1 g, yield 81%) as an oil, $[\alpha]_D^{20}$ −57.1° (*c*=0.9, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1700, 1605. ^{1}H-NMR ($CDCl_3$): 3.52 (2H, d, *J*=5.4 Hz, CH_2O), 4.18 (1H, m, CH), 4.30 and 4.98 (2H, AB, *J*=15 Hz, $NC\underline{H}_2Ph$), 4.40 (2H, s, $OC\underline{H}_2Ph$), 6.22 (1H, dd, *J*=1.7, 6 Hz, vinyl proton), 7.00 ((1H, dd, *J*=1.5, 6 Hz, vinyl proton), 6.95—7.50 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 44.40 (t), 61.86 (d), 69.20 (t), 73.14 (t), 126.98, 127.45, 127.51, 128.08 (vinyl carbon and aromatic carbons), 137.00 (s), 137.29 (s), 145.12 (d), 171.39 (s). MS *m/z*: 293 (M^+).

(3*R*,4*R*,5*R*)- and (3S,4*S*,5*R*)-1-Benzyl-5-benzyloxymethyl-3,4-dihydroxy-2-pyrrolidinone (7 and 8a) A mixture of **6** (1.9 g, 6.48 mmol), OsO_4 (81 mg, 0.32 mmol) and NMO monohydrate (1.05 g, 7.8 mmol) in acetone (16 ml) and H_2O (5 ml) was stirred at room temperature for 14 h. After addition of sodium hydrosulfite (1.6 g), the acetone was remove *in vacuo*, and the mixture was extracted with AcOEt. The combined 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=4:1) gave **7** (1.275 g, yield 60%) and **8a** (223 mg, yield 11%) as crystals. A small amount of 1-benzyl-5-benzyloxymethyl-3,4,5-trihydroxy-2-pyrrolidinone (mp 153 °C (MeOH–$CHCl_3$), *Anal.* Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.36; H, 6.15; N, 3.83) was present as a contaminant of **7** after column chromatography and was removed by filtration due to its low solubility in $CHCl_3$. **7**: mp 56—57 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +35.0° (*c*=0.6, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3432, 1619, 1110. ^{1}H-NMR ($CDCl_3$): 3.22—3.56 (4H, m, $C\underline{H}_2OBn$, OH, CH), 4.22 (1H, m, CH), 4.20 and 4.72 (2H, AB, *J*=16 Hz, $NC\underline{H}_2Ph$), 4.32 (2H, s, $OC\underline{H}_2Ph$), 4.60 (1H, m, CH), 4.90 (1H, m, OH), 7.24 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 44.99 (t), 63.56 (d), 66.97 (t), 69.69 (d), 70.32 (d), 73.09 (t), 127.27, 127.51, 128.20, 128.34 (aromatic carbons), 135.15 (s), 137.05 (s), 173.91 (s). *Anal.* Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.47; N, 4.28. Found: C, 69.50; H, 6.49: N, 4.21. **8a**: mp 116—118 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +2.4° (*c*=1.6, MeOH). IR ν_{max}^{Nujol} cm^{-1}: 3450, 1690, 1110. ^{1}H-NMR ($CDCl_3$): 3.30—3.78 (3H, m, $C\underline{H}_2OBn$, CH), 3.80—4.48 (7H, m, $OC\underline{H}_2Ph$, 2×OH, 2×CH, $NC\underline{H}Ph$), 4.75 (1H, AB, *J*=14.5 Hz, $NC\underline{H}Ph$) 6.90—7.50 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 44.79 (t), 59.09 (d), 67.02 (t), 70.52 (d), 73.24 (d), 127.78, 128.07, 128.64 (aromatic carbons), 136.12 (s), 136.76 (s), 173.23 (s). *Anal.* Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.47; N, 4.28. Found: C, 69.46; H, 6.49; N, 4.27.

(3*S*,4*S*,5*R*)-1-Benzyl-5-benzyloxymethyl-3,4-isopropylidenedioxy-2-pyrrolidinone (8b) A mixture of **8a** (690 mg, 2.1 mmol) and 2,2-dimethoxypropane (5 ml) in acetone (12 ml) was stirred in the presence of a catalytic amount of *p*-TsOH at room temperature for 2 h. After dilution with AcOEt, the mixture was washed with saturated aqueous $NaHCO_3$ and H_2O. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt:hexane=1:2) gave **8b** (700 mg, yield 90%) as an oil, $[\alpha]_D^{20}$ +25.3° (*c*=2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1705, 1090. ^{1}H-NMR ($CDCl_3$): 1.45 (3H, s, CH_3), 1.53 (3H, s, CH_3), 3.38—3.98 (3H, m, $C\underline{H}_2OBn$, CH), 4.46 (2H, s, $OC\underline{H}_2Ph$), 4.47 and 4.80 (2H, AB, *J*=15 Hz, $NC\underline{H}_2Ph$), 4.73—4.80 (2H, m, 2×CH), 6.95—7.50 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.58 (q), 26.75 (q), 44.80 (t), 57.94 (d), 68.71 (t), 73.14 (t), 73.39 (d), 77.14 (d), 112.54 (s), 127.14, 127.48, 127.87, 128.11 (aromatic carbons), 136.39 (s), 137.27 (s), 171.53 (s). MS *m/z*: 366 (M^+).

(3*S*,4*S*,5*R*)-1-Benzyl-5-hydroxymethyl-3,4-isopropylidenedioxy-2-pyrrolidinone (8c) **8b** (700 mg, 1.91 mmol) was hydrogenated using palladium black (190 mg) in EtOH (16 ml) under hydrogen at atmospheric pressure at room temperature for 13 h. After removal of the catalyst by filtration, the filtrate was concentrated *in vacuo* in give a residue, which was purified by column chromatography (silica gel, AcOEt:hexane=2.5:1) to give **8c** (454 mg, yield 86%) as an oil, $[\alpha]_D^{20}$ +79.1° (*c*=0.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1690. ^{1}H-NMR ($CDCl_3$): 1.39 (3H, s, CH_3), 1.49 (3H, s, CH_3), 2.88 (1H, br s, OH), 3.53 (1H, m, CH), 3.61—4.08 (2H, m, $C\underline{H}_2OH$), 4.13 and 5.18 (2H, AB, *J*=15 Hz, $NC\underline{H}_2Ph$), 4.63—4.89 (2H, m, 2×CH), 7.27 (5H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.39 (q), 26.65 (q), 44.30 (t), 57.14 (d), 59.14 (t), 74.85 (d), 77.27 (d), 112.64 (s), 127.37, 127.62, 128.34 (aromatic carbons), 135.34 (s), 170.89 (s). MS *m/z*: 277 (M^+), 245.

(2*R*,3*S*,4*R*)-*N*-Benzyl-2-hydroxymethyl-3,4-(isopropylidenedioxy)pyrrolidine (9a) Borane–Me_2S complex (0.52 ml) was added to a solution of **8c** (350 mg, 1.26 mmol) in THF (7 ml). The solution was stirred at 70 °C

for 1 h. After cooling to room temperature, the mixture was acidified with 10% aqueous HCl and stirred at 50 °C for 10 min. After cooling to room temperature, the mixture was basified with 10% aqueous NaOH and extracted with AcOEt. The AcOEt 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 : 1) gave **9a** (240 mg, yield 72%) as an oil, $[\alpha]_D^{20}$ −80.3° (c = 1.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1100, 1040. ^{1}H-NMR ($CDCl_3$): 1.36 (3H, s, CH_3), 1.54 (3H, s, CH_3), 2.12 (1H, dd, J = 4.5, 11 Hz, H-5), 2.36 (1H, m, H-2), 2.59 (1H, br s, OH), 3.08 (1H, d, J = 11 Hz, H-5′), 3.27 and 3.98 (2H, AB, J = 13 Hz, NC$\underline{H}_2$Ph), 3.88—4.00 (2H, m, CH_2), 4.56—4.74 (2H, m, 2 × CH), 7.29 (5H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.75 (q), 25.92 (q), 56.53 (t), 58.48 (t), 59.35 (t), 66.90 (d), 77.58 (d), 81.52 (d), 111.90 (s), 126.57, 128.00, 128.57 (aromatic carbons), 137.71 (s). MS m/z: 263 (M^+), 262 ($(M-1)^+$).

(2*S*,3*S*,4*S*)-2,3-Dihydroxy-4-trityloxymethyl-4-butanolide (11a) This sample was obtained from **10** in 52% yield after purification by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 1) in the same manner as described above for the preparation of **8a**, mp 168—170 °C, $[\alpha]_D^{20}$ −53.1° (c = 1, CH_2Cl_2), lit.[17] for the antipode of **11a**, mp 170—172 °C, $[\alpha]_D^{20}$ +50° (c = 3.8, CH_2Cl_2). ^{1}H-NMR ($CDCl_3$): 2.91 (2H, br s, 2 × OH), 3.29 (1H, dd, J = 2.2, 11 Hz, C$\underline{H}$OTr), 3.72 (1H, dd, J = 3, 11 Hz, C$\underline{H}$OTr), 4.30 (1H, d, J = 5.4 Hz, CH), 4.55 (1H, m, CH), 4.87 (1H, m, CH), 7.20—7.40 (15H, m, aromatic protons). ^{13}C-NMR (20% $CD_3OD/CDCl_3$): 62.52 (t), 68.80 (d), 69.68 (d), 84.06 (d), 87.26 (s), 126.88, 127.46, 128.02 (aromatic carbons), 143.44 (s), 177.70 (s).

(2*S*,3*S*,4*S*)-2,3-Isopropylidenedioxy-4-trityloxymethyl-4-butanolide (11b) This sample was prepared in 80% yield after purification by column chromatography (silica gel, AcOEt : hexane = 1 : 3) from **11a** in the same manner as described above for the preparation of **8b**, $[\alpha]_D^{20}$ +0.9° (c = 0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1790. ^{1}H-NMR ($CDCl_3$): 1.33 (3H, s, CH_3), 1.45 (3H, s, CH_3), 3.07 (1H, dd, J = 2, 11 Hz, C$\underline{H}$OTr), 3.71 (1H, dd, J = 2.5, 11 Hz, C$\underline{H}$OTr), 4.42 (1H, d, J = 5.6 Hz, CH), 4.56 (1H, m, CH), 4.98 (1H, d, J = 5.6 Hz, CH), 7.17—7.49 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.34 (q), 26.56 (q), 62.57 (t), 75.53 (d), 78.36 (d), 81.09 (d), 87.57 (s), 112.91 (s), 127.19, 127.87, 128.16 (aromatic carbons), 142.63 (s), 174.11 (s). MS m/z: 430 (M^+), 353 ($(M-77)^+$).

3,4-*O*-Isopropylidene-1-*O*-trityl-D-ribitol (12a) Lithium aluminum hydride (300 mg, 7.7 mmol) was added to a solution of **11b** (2.95 g, 6.87 mmol) in THF (30 ml) at 0 °C. After being stirred at room temperature for 2 h, 0.3 ml of H_2O, 0.3 ml of 15% aqueous NaOH, and 0.9 ml of H_2O were successively added and the mixture was stirred for 30 min. The insoluble materials were filtered off and washed with THF. The combined filtrates were dried, followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 1) to give **12a** (2.8 g yield 84%) as an oil, $[\alpha]_D^{20}$ −14.9° (c = 0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1100, 1050, ^{1}H-NMR ($CDCl_3$): 1.28 (6H, s, 2 × CH_3), 2.93—3.47 (4H, m, 2 × OH, 2 × CH), 3.47—3.96 (3H, m, 3 × CH), 3.96—4.44 (2H, m, 2 × CH), 6.81—7.60 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.19 (q), 27.68 (q), 60.57 (t), 65.01 (t), 68.85 (d), 76.65 (d), 77.38 (d), 86.88 (s), 108.33 (s), 126.99—128.45 (aromatic carbons), 143.56 (s). MS m/z: 434 (M^+), 357 ($(M-77)^+$).

2,5-Di-*O*-Methylsulfonyl-3,4-*O*-isopropylidene-1-*O*-trityl-D-ribitol (12b) A mixture of **12a** (2.67 g, 6.14 mmol) and methanesulfonyl chloride (1.77 g, 15.3 mmol) in pyridine (35 ml) was stirred at 0 °C for 13 h. After dilution with AcOEt, the mixture was washed with 10% aqueous HCl, and H_2O. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 3) gave **12b** (3.3 g, yield 91%) as crystals, mp 139—140 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +9.8° (c = 0.4, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1340, 1180. ^{1}H-NMR ($CDCl_3$): 1.34 (3H, s, CH_3), 1.41 (3H, s, CH_3), 2.87 (3H, s, SO_2CH_3), 2.97 (3H, s, SO_2CH_3), 3.30—3.76 (2H, m, C$\underline{H}_2$OTr), 4.22—4.66 (4H, m, 2 × CH, C$\underline{H}_2$OMs), 4.91 (1H, m, C$\underline{H}$OMs), 7.10—7.52 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.95 (q), 27.04 (q), 37.01 (q), 38.86 (q), 59.87 (t), 62.30 (t), 73.83 (d), 74.46 (d), 77.91 (d), 86.91 (s), 108.99 (s), 126.79, 127.37, 128.00 (aromatic carbons), 145.25 (s). *Anal.* Calcd for $C_{29}H_{34}O_9S_2$: C, 58.96; H, 5.80. Found: C, 58.72; H, 5.97.

5-Azide-5-deoxy-3,4-isopropylidene-2-*O*-methylsulfonyl-1-*O*-trityl-D-ribitol (12c) A mixture of **12b** (800 mg, 1.36 mmol) and sodium azide (194 mg, 2.98 mmol) in DMF (8 ml) was stirred at 140—145 °C for 25 min. After dilution with AcOEt–benzene (2 : 1), the mixture was washed with half-saturated aqueous NaCl (× 5). Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 3) gave **12c** (372 mg, yield 51%) as crystals, mp 91—92 °C (AcOEt–hexane), $[\alpha]_D^{20}$ +18.5° (c = 1, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 2050, 1350, 1180. ^{1}H-NMR ($CDCl_3$): 1.33 (3H, s, CH_3), 1.39 (3H, s, CH_3), 2.84 (3H, s, SO_2CH_3), 3.24—3.64 (4H, m, C$\underline{H}_2$OTr, C$\underline{H}_2N_3$), 4.24—4.50 (2H, m, 2 × CH), 4.88 (1H, m, C$\underline{H}$OMs), 7.10—7.52 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.05 (q), 27.38 (q), 39.10 (q), 50.48 (t), 60.16 (t), 74.26 (d), 76.06 (d), 78.83 (d), 87.15 (s), 108.84 (s), 126.98, 127.61, 128.24 (aromatic carbons), 142.54 (s). *Anal.* Calcd for $C_{28}H_{31}N_3O_6S$: C, 62.55; H, 5.81; N, 7.82. Found: C, 62.31; H, 5.97; N, 7.66.

(2*R*,3*S*,4*R*)-3,4-(Isopropylidenedioxy)-2-(trityloxymethyl)pyrrolidine (9b) **12c** (1.39 g, 2.60 mmol) was hydrogenated using palladium black (280 mg) in EtOH (30 ml) under hydrogen at atmospheric pressure at room temperature for 14 h. After removal of the catalyst by filtration and washing with EtOH and AcOEt, the filtrates were concentrated *in vacuo* to give a residue, to which AcOEt and 10% aqueous NaOH were added. The mixture was vigorously stirred and the organic layer was separated and washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : $CHCl_3$ = 3 : 1) gave **9b** (700 mg, yield 65%) as an oil, $[\alpha]_D^{20}$ −35.3° (c = 0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1440, 1380, 1210. ^{1}H-NMR ($CDCl_3$): 1.26 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.98 (1H, br s, NH), 2.58 (1H, dd, J = 3, 13 Hz, H-5), 2.86 (1H, m, H-2), 3.05 (1H, d, J = 13 Hz, H-5′), 3.15—3.48 (2H, m, C$\underline{H}_2$OTr), 4.58—4.64 (2H, m, 2 × CH), 6.95—7.50 (15H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 23.98 (q), 25.68 (q), 52.86 (t), 61.62 (t), 63.42 (d), 80.88 (d), 81.32 (d), 86.42 (s), 110.15 (s), 126.49, 127.32, 128.44 (aromatic carbons), 143.66 (s). MS m/z: 415 (M^+).

(2*R*,3*S*,4*R*)-*N*-Benzyl-3,4-(isopropylidenedioxy)-2-(trityloxymethyl)-pyrrolidine (9c) A mixture of **9b** (695 mg, 1.67 mmol) and benzyl bromide (490 mg, 2.85 mmol) in acetone (11 ml) was stirred in the presence of anhydrous K_2CO_3 (550 mg) at room temperature for 1 h and filtered. Evaporation of the filtrate followed by purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 4) gave **9c** (845 mg, yield quant.) as an oil, $[\alpha]_D^{20}$ −72.1° (c = 0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1500, 1380, 1210. ^{1}H-NMR ($CDCl_3$): 1.40 (3H, s, CH_3), 1.49 (3H, s, CH_3), 2.08 (1H, dd, J = 4.4, 11 Hz, H-5), 2.48 (1H, m, H-2), 3.06 (1H, d, J = 11 Hz, H-5′), 3.23 and 4.27 (2H, AB, J = 14 Hz, NC$\underline{H}_2$Ph), 3.41 (1H, dd, J = 5.4, 10 Hz, C$\underline{H}$OTr), 3.77 (1H, dd, J = 6, 10 Hz, C$\underline{H}$OTr), 4.56—4.91 (2H, m, 2 × CH), 6.96—7.76 (20H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.92 (q), 26.21 (q), 57.73 (t), 59.48 (t), 62.15 (d), 67.31 (t), 77.95 (d), 80.93 (d), 86.76 (s), 110.88 (s), 126.54, 127.37, 128.53 (aromatic carbons), 138.31 (s), 143.85 (s). MS m/z: 505 (M^+), 504 ($(M-1)^+$).

(2*R*,3*S*,4*R*)-*N*-Benzyl-2-hydroxymethyl-3,4-(isopropylidenedioxy)-pyrrolidine (9a) A mixture of **9c** (710 mg, 1.41 mmol) and 35 ml of concentrated HCl–MeOH (1 : 40) was stirred at room temperature for 14 h, and then basified with 10% aqueous NaOH and extracted with AcOEt. The AcOEt 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 : 1) gave **9a** (296 mg, yield 80%) as an oil, $[\alpha]_D^{20}$ −76.0° (c = 1.2, $CHCl_3$). Spectral data were identical with those of **9a** prepared from **8c**.

(3*RS*,5*S*)-1-(*tert*-Butoxycarbonyl)-5-hydroxymethyl-3-phenylseleno-2-pyrrolidinone (13b) A mixture of **13a** (10.0 g, 16.3 mmol) and 140 ml of concentrated HCl–MeOH (1 : 20) was stirred at 40 °C for 2 h. After neutralization with saturated aqueous $NaHCO_3$, the MeOH was evaporated *in vacuo*. The aqueous layer was extracted with AcOEt. The AcOEt extracts were washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 3 : 2) gave **13b** (4.90 g, yield 81%) as a diastereomeric mixture (1 : 1). IR ν_{max}^{film} cm^{-1}: 3460, 1772, 1724, 1060. ^{1}H-NMR ($CDCl_3$): 1.47 (9H, s, *tert*-butyl), 1.73—2.66 (2H, m, CH_2), 3.02 (1H, br s, OH), 3.35—4.00 (4H, m, 2 × CH, CH_2OH), 7.09—7.75 (5H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 27.44 and 27.83 (q), 28.65 and 28.90 (t), 40.69 and 41.03 (d), 57.60 and 58.23 (d), 62.72 and 64.08 (t), 82.74 and 83.67 (s) 126.55—128.98 (aromatic carbons), 134.30 and 134.89 (d), 149.36 and 134.30 (s), 149.36 and 150.62 (s), 173.33 and 173.43 (s). MS m/z: 370 (M^+).

(2*RS*,4*S*)-4-[(*tert*-Butoxycarbonyl)amino]-2-phenylseleno-5-pentanolide (14) A mixture of **13b** (4.5 g, 12.2 mmol) and 13.5 ml of 2 N solution of lithium hydroxide in 70 ml of THF–MeOH (1 : 1) was stirred at room temperature for 3 h. After removal of the solvents *in vacuo*, the aqueous layer was acidified with 10% aqueous citric acid and extracted with AcOEt. The AcOEt extracts were washed with saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was treated with acetic anhydride (2.48 g, 24.8 mmol) and pyridine (1.86 g, 24.8 mmol) in 50 ml of benzene–CH_2Cl_2 (4 : 1) at room temperature for 20 h. After dilution with AcOEt, the mixture was washed with 5% aqueous HCl, 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 **14** (3.23 g, yield 72% as a diastereomeric mixture (1 : 1). IR ν_{max}^{film} cm^{-1}: 1732, 1682. ^{1}H-NMR ($CDCl_3$): 1.40 (9H, s, *tert*-butyl), 1.65—2.75 (2H, m, CH_2), 3.81—3.56 (4H, m, 2 × CH CH_2OH), 5.00 (1H, br s, NH), 7.10—7.73 (5H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 28.16 (q), 33.23 and 33.67 (t), 36.01 and 36.60 (d), 43.27 and 44.15 (d), 70.80 and 70.95 (t), 80.11 (s), 127.24, 128.79, 129.18 (aromatic carbons), 135.52 (d), 154.67 and 154.86 (s). MS *m/z*: 370 (M^+).

(*S*)-4-[(*tert*-Butoxycarbonyl)amino]-2-penten-5-olide (15) This sample was obtained from **14** in 65% yield after column chromatography (silica gel, AcOEt : hexane = 1 : 1) in the same manner as described above for the preparation of **6**, mp 123 °C, $[\alpha]_D^{20}$ +108° (*c* = 0.5, $CHCl_3$), lit.[10b] mp 128—129 °C, $[\alpha]_D^{20}$ +113° (*c* = 1.07, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1714, 1687, ^{1}H-NMR ($CDCl_3$): 1.46 (9H, s, *tert*-butyl), 4.14—4.68 (3H, m, CH_2), 5.07 (1H, m, NH), 6.08 (1H, d, *J* = 9.5 Hz, vinyl proton), 6.89 (1H, dd, *J* = 9.5, 4.7 Hz, vinyl proton). ^{13}C-NMR ($CDCl_3$): 28.17 (q), 42.69 (d), 70.32 (t), 80.65 (s), 122.56 (d), 144.53 (d), 162.51 (s), 169.33 (s).

(2*S*,3*S*,4*R*)-2,3-Dihydroxy-4-[(*tert*-butoxycarbonyl)amino]-5-pentanolide (16a) This sample was obtained as crystals in 58% crude yield from **15** in the same manner as described above for the preparation of **8a**, and the crude material was used for next step, mp 169—170 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −8.1° (*c* = 0.6, AcOEt). IR ν_{max}^{Nujol} cm^{-1}: 3409, 1716, 1677, 1182. ^{1}H-NMR (20% $CD_3OD/CDCl_3$): 1.33 (9H, s, *tert*-butyl), 3.79 (1H, m, CH), 3.93—4.25 (2H, m, 2 × CH), 4.35—4.54 (2H, m, 2 × CH). ^{13}C-NMR (20% $CD_3OD/CDCl_3$): 27.78 (q), 51.02 (d), 67.35 (t), 67.98 (d), 71.19 (d), 79.96 (s), 155.84 (s), 173.43 (s). *Anal.* Calcd for $C_{10}H_{17}NO_6$: C, 48.58; H, 6.93; N, 5.67. Found: C, 48.30; H, 6.96; N, 5.40.

(2*S*,3*S*,4*R*)-4-[(*tert*-Butoxycarbonyl)amino]-2,3-isopropylidenedioxy-5-pentanolide (16b) This sample was obtained from **16a** in 84% as crystals after column chromatography (silica gel, AcOEt : hexane = 1 : 3) in the same manner as described above for the preparation of **8b**, mp 125 °C (AcOEt–hexane), $[\alpha]_D^{20}$ −17.5° (*c* = 0.6, $CHCl_3$), IR ν_{max}^{Nujol} cm^{-1}: 1759, 1705. ^{1}H-NMR ($CDCl_3$): 1.36 (9H, s, *tert*-butyl), 1.43 (3H, s, CH_3), 1.51 (3H, s, CH_3), 3.57—3.91 (1H, m, H-5), 4.00—4.74 (4H, m, 3 × CH, H-5′), 5.43 (1H, br s, NH). ^{13}C-NMR ($CDCl_3$): 23.98 (q), 25.97 (q), 28.02 (q), 49.41 (d), 66.32 (t), 71.97 (d), 75.38 (d), 80.31 (s), 111.11 (s), 154.91 (s), 167.44 (s). *Anal.* Calcd for $C_{13}H_{21}NO_6$: C, 54.34; H, 7.36; N, 4.88. Found: C, 54.27; H, 7.13; N, 4.62.

1,1-Dimethylethyl *N*-[(1*R*,2*S*,3*S*)-1-Hydroxymethyl-2,3-(isopropylidenedioxy)-3-(methoxycarbonyl)propyl]carbamate (17a) A 2 N solution of NaOH (3.5 ml) was added to a solution of **16b** (1.0 g, 3.48 mmol) in 16 ml of THF–MeOH (1 : 1). After being stirred at room temperature for 1 h, the mixture was acidified with 5% aqueous HCl and extracted with AcOEt. The AcOEt extracts were washed with half-saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was treated with ethereal diazomethane to afford the methyl ester **17a** (980 mg, yield 88%) as an oil after purification by column chromatography (silica gel, AcOEt : hexane = 1 : 2.5), $[\alpha]_D^{20}$ +1.1° (*c* = 2, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3446, 1756, 1706, 1099. ^{1}H-NMR ($CDCl_3$): 1.36 (3H, s, CH_3), 1.39 (9H, s, *tert*-butyl), 1.59 (3H, s, CH_3), 3.41 (1H, s, OH), 3.40—3.71 (2H, m, CH_2), 3.69 (3H, s, $COOCH_3$), 4.50—4.90 (3H, m, 2 × CH, NH). ^{13}C-NMR ($CDCl_3$): 24.46 (q), 26.12 (q), 28.02 (q), 49.95 (d), 51.85 (q), 62.81 (t), 74.56 (d), 74.95 (d), 79.63 (s), 109.98 (s), 155.35 (s), 169.78 (s). MS *m/z*: 320 ($(M+1)^+$).

1,1-Dimethylethyl *N*-[(1*R*,2*S*,3*S*)-2,3-(Isopropylidenedioxy)-3-(methoxycarbonyl)-1-[(methoxymethoxy)methyl]propyl]carbamate (17b) A mixture of **17a** (900 mg, 2.82 mmol), *N*,*N*-diethylaniline (840 mg, 5.63 mmol), and chloromethyl methyl ether (454 mg, 5.63 mmol) in CH_2Cl_2 (10 ml) was stirred at room temperature for 20 h. After dilution with AcOEt, the mixture was washed with 5% aqueous HCl, and saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 2.5) gave **17b** (850 mg, yield 83%) as an oil, $[\alpha]_D^{20}$ +0.23° (*c* = 4, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1761, 1711. ^{1}H-NMR ($CDCl_3$): 1.35 (3H, s, CH_3), 1.40 (9H, s, *tert*-butyl), 1.59 (3H, s, CH_3), 3.32 (3H, s, CH_2OCH_3), 3.30—3.59 (2H, m, CH_2), 3.69 (3H, s, $COOCH_3$), 4.04 (1H, m, CH), 4.42—4.79 (3H, m, 2 × CH, NH), 4.60 (2H, s, OCH_2O). ^{13}C-NMR ($CDCl_3$): 24.41 (q), 26.17 (q), 28.02 (q), 47.71 (d), 51.85 (q), 54.97 (q), 66.76 (t), 74.46 (d), 74.75 (d), 79.35 (s), 96.10 (t), 109.84 (s), 154.62 (s), 169.48 (s). MS *m/z*: 363 (M^+).

1,1-Dimethylethyl *N*-[(1*R*,2*S*,3*R*)-3-Hydroxymethyl-2,3-(isopropylidenedioxy)-1-[(methoxymethoxy)methyl]propyl]carbamate (17c) $NaBH_4$ (210 mg, 5.52 mmol) was added to a solution of **17b** (800 mg, 2.20 mmol) in EtOH (10 ml) at 20 °C and the mixture was stirred at room temperature for 2 h. After neutralization with 10% aqueous HCl, the mixture was diluted with AcOEt and washed with saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 1) gave **17c** (605 mg, yield 82%) as an oil, $[\alpha]_D^{20}$ −0.32° (*c* = 3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3448, 1706, 1045. ^{1}H-NMR ($CDCl_3$): 1.37 (3H, s, CH_3), 1.45 (9H, s, *tert*-butyl), 1.49 (3H, s, CH_3), 2.71 (1H, s, OH), 3.36 (3H, s, $CH_2OC\underline{H}_3$), 3.40—3.86 (4H, m, 2 × CH_2), 3.98 (1H, m, CH), 4.21—4.42 (2H, m, 2 × CH), 4.64 (2H, s, $OC\underline{H}_2O$), 4.90 (1H, br s, NH). ^{13}C-NMR ($CDCl_3$): 24.41 (q), 27.00 (q), 28.17 (q), 48.05 (d), 55.16 (q), 61.25 (t), 67.88 (t), 74.12 (d), 77.48 (d), 79.82 (s), 96.24 (t), 107.99 (s). MS *m/z*: 335 (M^+).

1,1-Dimethylethyl *N*-[(1*R*,2*S*,3*R*)-1-[(Methoxymethoxy)methyl]-2,3-(isopropylidenedioxy)-3-(methylsulfonyloxy)propyl]carbamate (17d) A mixture of **17c** (1.37 g, 4.1 mmol), methanesulfonyl chloride (935 mg, 8.16 mmol), and triethylamine (TEA, 825 mg, 8.16 mmol) in CH_2Cl_2 (15 ml) was stirred at 0 °C for 15 min and then diluted with AcOEt. Washing with saturated aqueous $NaHCO_3$ and H_2O, drying, and evaporation, followed by purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 1) gave **17d** (1.60 g, yield 95%) as an oil, $[\alpha]_D^{20}$ +6.1° (*c* = 3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1710, 1357, 1170. ^{1}H-NMR ($CDCl_3$): 1.33 (3H, s, CH_3), 1.41 (9H, s, *tert*-butyl), 1.48 (3H, s, CH_3), 3.03 (3H, s, CH_3SO_2), 3.32 (3H, s, $CH_2OC\underline{H}_3$), 3.30—3.60 (2H, m, CH_2), 3.97 (1H, m, CH), 4.20—4.50 (4H, m, CH_2, 2 × CH), 4.58 (2H, s, OCH_2O), 4.90 (1H, d, *J* = 9 Hz, NH).

(2*R*,3*S*,4*R*)-*N*-(*tert*-Butoxycarbonyl)-3,4-(isopropylidenedioxy)-2-[(methoxymethoxy)methyl]pyrrolidine (9d) Potassium *tert*-butoxide (780 mg, 6.97 mmol) was added to a solution of **17d** (1.44 g, 3.49 mmol) in THF (20 ml) at 0 °C. After being stirred at 0 °C for 10 min, the mixture was diluted with AcOEt and washed with half-saturated NaCl. Drying followed by evaporation and purification by column chromatography (silica gel, AcOEt : hexane = 1 : 2) gave **9d** (903 mg, yield 81%) as an oil, $[\alpha]_D^{20}$ −53.8° (*c* = 1.9, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1700, 1382, 1170. ^{1}H-NMR ($CDCl_3$): 1.38 (3H, s, CH_3), 1.48 (9H, s, *tert*-butyl), 1.56 (3H, s, CH_3), 3.07—3.40 (1H, m, CH), 3.33 (3H, s, $CH_2OC\underline{H}_3$), 3.61—4.11 (4H, m), 4.58—4.87 (2H, m, s × CH), 4.61 (2H, s, OCH_2O). ^{13}C-NMR ($CDCl_3$): 24.51 (q), 26.12 (q), 27.73 (q), 50.73 (t), 54.43 (q), 58.38 (d), 64.47 (t), 77.09 (d), 79.19 (s and d), 95.95 (t), 111.98 (s), 153.69 (s). MS *m/z*: 318 ($(M+1)^+$).

(2*R*,3*S*,4*R*)-*N*-(*tert*-Butoxycarbonyl)-3,4-dihydroxy-2-[(methoxymethoxy)methyl]pyrrolidine (9e) A mixture of **9d** (870 mg, 2.73 mmol) in 18 ml of 10% aqueous HCl–MeOH (1 : 1) was stirred at room temperature for 15 min. After dilution with AcOEt, the mixture was washed with aqueous $NaHCO_3$ and half-saturated NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 2) gave **9e** (650 mg, yield 86%) as an oil, $[\alpha]_D^{20}$ −42.5° (*c* = 0.7, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3429, 1619, 1404, 1164. ^{1}H-NMR ($CDCl_3$): 1.45 (9H, s, *tert*-butyl), 3.08—3.60 (3H, m, CH, 2 × OH), 3.37 (3H, s, $CH_2OC\underline{H}_3$), 3.65—4.46 (6H, m), 4.64 and 4.69 (2H, AB, *J* = 7 Hz, OCH_2O). ^{13}C-NMR ($CDCl_3$): 27.97 (q), 52.09 (t), 55.16 (q), 57.79 (d), 63.30 (t), 69.24 and 69.93 (d), 71.15 (d), 79.63 (s), 96.05 (t), 154.04 (s). MS *m/z*: 278 ($(M+1)^+$).

(2*R*,3*S*,4*R*)-3,4-Bis(benzyloxy)-*N*-(*tert*-butoxycarbonyl)-2-[(methoxymethoxy)methyl]pyrrolidine (9f) A suspension of NaH (260 mg, 6.5 mmol, 60% oil suspension, washed with hexane) in THF (5 ml) was added to a solution of **9e** (600 mg, 2.16 mmol) in DMF (5 ml) at 0 °C. The mixture was stirred at room temperature for 30 min, then benzyl bromide (1.10 g, 6.48 mmol) was added and the whole was stirred at room temperature for 2 h. After dilution with 50 ml of AcOEt–benzene (1 : 1), the mixture was washed with half-saturated NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 2 : 3) gave **9f** (890 mg, yield 90%) as an oil, $[\alpha]_D^{20}$ +2.4° (*c* = 0.7, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1695. ^{1}H-NMR ($CDCl_3$): 1.48 (9H, s, *tert*-butyl), 3.33 (3H, s, $CH_2OC\underline{H}_3$), 3.40—3.59 (2H, m, CH_2), 3.78—4.19 (5H, m, CH_2, 3 × CH), 4.63 (4H, s, 2 × CH_2), 4.70 (2H, s, CH_2), 7.22—7.44 (10H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 28.02 (q), 48.68 (t), 54.63 (q), 57.21 (d), 66.13 (t), 71.68 (t), 72.36 (t), 77.14 (d), 78.21 (d), 96.10 (t), 127.04, 127.14, 127.87 (aromatic carbons), 137.76 (s), 137.96 (s), 154.23 (s). MS *m/z*: 457 (M^+).

(2*R*,3*S*,4*R*)-*N*-Benzyl-3,4-bis(benzyloxy)-2-hydroxymethylpyrrolidine (9g) A mixture of **9f** (840 mg, 1.84 mmol) in 16 ml of 10% aqueous HCl–MeOH (1 : 1) was stirred at 70 °C for 40 min. The mixture was cooled, basified with 10% aqueous NaOH, and extracted with AcOEt. The AcOEt extracts were washed with saturated aqueous NaCl. Drying followed by evaporation gave a residue, which was treated with benzyl bromide (750 mg, 4.65 mmol) in acetone (25 ml) in the presence of K_2CO_3 (700 mg) at room temperature for 2.5 h. Filtration of the insoluble materials followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : hexane = 1 : 1) provided **9g** (310 mg, yield 42%) as an

oil, $[\alpha]_D^{20}$ −62.5° (c=0.6, $CHCl_3$). Spectral data (IR, NMR) and $[\alpha]_D$ value were identical of those of an authentic sample.[6b]

(2*R*,3*S*,4*R*)-*N*-Benzyl-3,4-bis(benzyloxy)-2-[(1*R*)-1-hydroxy-3-butenyl]-pyrrolidine (19a) and (2*R*,3*S*,4*R*)-*N*-Benzyl-3,4-bis(benzyloxy)-2-[(1*S*)-1-hydroxy-3-butenyl]pyrrolidine (20a) A) Allylation with Grignard Reagent: The dimethylsulfoxide (194 mg, 2.48 mmol) was added at −60 °C to a solution of oxalyl chloride (0.11 ml, 1.24 mmol) in CH_2Cl_2 (4 ml). The mixture was stirred at −60 °C for 2 min and then a solution of **9g** (250 mg, 0.62 mmol) in CH_2Cl_2 (3 ml) was added at −20 °C over a period of 5 min. The whole was stirred at −20 °C for 20 min, then TEA (0.52 ml, 3.73 mmol) was added and the reaction mixture was stirred at −20 °C for 5 min, then allowed to warm to room temperature. H_2O (4 ml) was then added and the aqueous layer was extracted with CH_2Cl_2. The organic layers were washed with half-saturated aqueous NaCl. Drying followed by evaporation gave the crude aldehyde **18a.** Allylmagnesium chloride (0.63 ml of a 2 M solution in THF) was added at −78 °C to a solution of **18a** in THF (4 ml). After being stirred at −78 °C for 1 h, the mixture was quenched with 3 ml of 10% aqueous NH_4Cl and extracted with AcOEt. The organic layers 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 **19a** (173 mg, yield 63%) and **20a** (61 mg, yield 22%) as an oil. **19a**: $[\alpha]_D^{20}$ −53.2° (c=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 1120. ^{1}H-NMR ($CDCl_3$): 2.08—2.80 (3H, m, C<u>H</u>$_2$CH=CH$_2$, OH), 2.89 (1H, m, H-2), 3.16 (1H, dd, J=2.5, 11 Hz, H-5), 3.53 and 4.03 (2H, AB, J=14 Hz, NC<u>H</u>$_2$Ph), 3.98—4.27 (3H, m, 3×CH), 4.40—4.83 (5H, m, 2×OC<u>H</u>$_2$Ph, CH), 4.98—5.30 (2H, m, CH=C<u>H</u>$_2$), 5.66—6.43 (1H, m, C<u>H</u>=CH$_2$), 7.30 (15H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 38.20 (t), 54.09 (t), 60.02 (t), 66.42 (d), 71.19 (t), 71.73 (d), 72.31 (t), 76.21 (d), 80.35 (d), 116.17 (t), 126.17, 128.16 (aromatic carbons), 136.06 (d), 137.22 (s), 137.23 (s), 138.40 (s). MS m/z: 443 (M^+). **20a**: $[\alpha]_D^{20}$ −37.8° (c=0.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 1130. ^{1}H-NMR ($CDCl_3$): 2.23—2.57 (3H, m, C<u>H</u>$_2$CH=CH$_2$, OH), 2.97—3.25 (2H, m, H-2, 5), 3.60 and 4.05 (2H, AB, J=14 Hz, NC<u>H</u>$_2$Ph), 3.87—4.19 (3H, m, 3×CH), 4.38—4.74 (5H, m, 2×OC<u>H</u>$_2$Ph, CH), 4.91—5.22 (2H, m, CH=C<u>H</u>$_2$), 5.69—6.17 (1H, m, C<u>H</u>=C<u>H</u>$_2$), 7.32 (15H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 39.23 (t), 54.43 (t), 61.64 (t), 65.83 (d), 68.46 (d), 71.49 (t), 71.88 (t), 76.07 (d), 78.99 (d), 116.22 (t), 126.89, 128.31 (aromatic carbons), 136.10 (d), 137.76 (s), 137.82 (s), 138.44 (s). MS m/z: 443 (M^+).

B) Allylation with Organocopper Reagent: Allylmagnesium chloride (0.5 ml of a 2 M solution in THF) was added at −78 °C to a solution of CuI (209 mg, 1.1 mmol) in 4 ml of THF–Me_2S (5 : 1) and the mixture was stirred at −78°C for 5 min. A solution of **18a** in THF (3 ml) prepared from **9g** (200 mg, 0.50 mmol) as described above was added to a solution of the organocopper reagent at −78 °C, and the mixture was stirred at −78 °C for 1 h and then allowed to warm to room temperature. After addition of 10% aqueous NH_4Cl (3 ml), the reaction mixture was diluted with AcOEt, and 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 **19a** (26 mg, yield 12%) and **20a** (97 mg, yield 44%) as an oil.

C) Allylation with Allytrimethylsilane and $TiCl_4$: $TiCl_4$ (0.19 ml, 1.7 mmol) was added to a solution of allytrimethylsilane (0.19 ml, 1.20 mmol) and **18a** prepared from **9g** (200 mg, 0.50 mmol) in CH_2Cl_2 (5 ml) at −78 °C over a period of 5 min. After being stirred at −78 °C for 2 h, the mixture was basified with 10% aqueous NaOH and extracted with AcOEt. The AcOEt 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 : 4) gave **20a** (105 mg, yield 48%) as an oil.

(2*R*,3*S*,4*R*)-*N*-Benzyl-2-[(1*R*)-1-benzyloxy-3-butenyl]-3,4-bis(benzyloxy)pyrrolidine (19c) This sample was obtained from **19a** in 78% yield as an oil after column chromatography (silica gel, AcOEt : hexane = 1 : 4) in the same manner as described above for the preparation of **9f**, $[\alpha]_D^{20}$ −48.8° (c=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1455, 1100. ^{1}H-NMR ($CDCl_3$): 2.25—2.70 (2H, m, C<u>H</u>$_2$CH=CH$_2$), 2.82 (1H, m, CH), 2.90—3.30 (2H, m, 2×CH), 3.47 and 4.21 (2H, AB, J=14 Hz, NC<u>H</u>$_2$Ph), 3.80—4.20 (3H, m, 3×CH), 4.56 (4H, s, 2×OC<u>H</u>$_2$Ph), 4.52 and 4.81 (2H, AB, J=8.8 Hz, OC<u>H</u>$_2$Ph), 4.90—5.20 (2H, m, CH=C<u>H</u>$_2$), 5.80—6.20 (1H, m, C<u>H</u>=CH$_2$), 7.00—7.40 (20H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 40.42 (t), 56.75 (t), 62.84 (t), 67.80 (d), 72.07 (t), 72.33 (d), 73.20 (t), 77.51 (d), 79.25 (d), 79.42 (d), 111.80 (t), 121.04, 121.85, 121.87, 122.59 (aromatic carbons), 130.51 (d), 131.86 (s), 132.12 (s), 132.38 (s), 132.94 (s). MS m/z: 533 (M^+).

(2*R*,3*S*,4*R*)-*N*-Benzyl-2-[(1*R*)-1-benzyloxy-4-hydroxybutanyl]-3,4-bis-(benzyloxy)pyrrolidine (21a) Borane–THF complex (1.4 ml of a 1 M solution in THF) was added to a solution of **19c** (160 mg, 0.3 mmol) in THF (5 ml) at room temperature and the mixture was stirred at 45 °C for 1 h, and allowed to cool to room temperature. Then 0.5 ml of 3 N NaOH and 0.5 ml of 30% H_2O_2 were added and the mixture was stirred at 60 °C for 1 h, allowed to cool, acidified with 10% aqueous HCl (pH 2) and stirred again at 60 °C for 5 min. After cooling to room temperature, the mixture was basified with 10% aqueous NaOH and extracted with AcOEt. The AcOEt extracts were washed with half-saturated aqueous NaCl. Drying followed by evaporation and purification of the residue by column chromatography (silica gel, AcOEt : $CHCl_3$ = 1 : 2) gave **21a** (125 mg, yield 76%) as an oil, $[\alpha]_D^{20}$ −40.9° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1050. ^{1}H-NMR ($CDCl_3$): 1.50—2.42 (6H, m, 2×CH_2, CH, OH), 3.00—3.62 (5H, m), 3.70—4.20 (3H, m), 4.20—4.85 (7H, m, 3×OC<u>H</u>$_2$Ph, NC<u>H</u>Ph), 7.30 (20H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 27.33 (t), 29.18 (t), 54.13 (t), 60.55 (t), 62.30 (t), 65.31 (d), 71.20 (t), 71.54 (t), 72.41 (t), 76.00 (d), 79.22 (d), 79.66 (d), 126.45, 127.23, 127.47, 127.95, 128.14 (aromatic carbons), 138.02 (s), 138.41 (s), 139.14 (s). MS m/z: 551 (M^+).

(−)-Swainsonine (1) A mixture of **21a** (90 mg, 0.16 mmol), methanesulfonyl chloride (30 mg, 0.26 mmol), and TEA (27 mg, 0.26 mmol) in CH_2Cl_2 (4 ml) was stirred at room temperature for 16 h. After addition of 20 ml of CH_2Cl_2, the mixture was washed with H_2O. Drying followed by evaporation gave a residue, which was hydrogenated using 10% palladium carbon (45 mg) in EtOH (5 ml) in the presence of methanolic HCl at room temperature for 6 h under hydrogen at atmospheric pressure. The mixture was filtered and concentrated *in vacuo*, and the residue was dissolved in water, placed on a Dowex 50W-X8 (H^+ form) column (12 ml), washed with 30 ml of water, and eluted with 1 N NH_4OH. Evaporation of the appropriate fractions gave a residue, which was crystallized from MeOH–ether to give **1** (19.5 mg, yield 69%) as crystals, mp 141—142 °C, $[\alpha]_D^{20}$ −85.1° (c=0.6, MeOH), ^{1}H-NMR (D_2O, internal standard: dioctyl sodium sulfosuccinate): 0.99—2.17 (6H, m, H-5, 6, 6′, 7,7′, 8a), 2.54 (1H, dd, J=7, 11 Hz, H-3), 2.72—3.15 (2H, m, H-3′, 5′), 3.78 (1H, ddd, J=4.4, 10, 10 Hz), 4.17—4.43 (2H, m). ^{13}C-NMR (D_2O, internal standard: MeOH, δ 49.02): 22.95 (t), 32.26 (t), 51.41 (t), 60.38 (t), 66.13 (d), 68.76 (d), 69.44 (d), 72.56 (d), in good agreement with the data for natural (−)-swainsonine.

(2*R*,3*S*,4*R*)-*N*-Benzyl-2-[(1*R*)-1-hydroxy-3-butenyl]-3,4-(isopropylidenedioxy)pyrrolidine (19b) and (2*R*,3*S*,4*R*)-*N*-Benzyl-2-[(1*S*)-1-hydroxy-3-butenyl]-3,4-(isopropylidenedioxy)pyrrolidine (20b) These samples were obtained from **9a** in 32—80% yields after column chromatography (silica gel, AcOEt : hexane = 1 : 3) in the same manner as described above for the preparation of **19a** and **20a**. **19b**: $[\alpha]_D^{20}$ −43.8° (c=0.4, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1080. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, s, CH_3), 1.54 (3H, s, CH_3), 2.05 (1H, dd, J=5, 11 Hz, H-5), 2.13 (1H, m, H-2), 2.33—2.71 (2H, m, C<u>H</u>$_2$CH=CH$_2$), 3.03 (1H, d, J=11 Hz, H-5′), 3.13 and 4.16 (2H, AB, J=13 Hz, NC<u>H</u>$_2$Ph), 3.52 (1H, d, J=7 Hz, OH), 4.10 (1H, m, CH), 4.41—4.74 (2H, m, 2×CH), 5.01—5.31 (2H, m, CH=C<u>H</u>$_2$), 5.70—6.19 (1H, m, C<u>H</u>=CH$_2$), 7.30 (5H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.51 (q), 26.02 (q), 39.62 (t), 55.50 (t), 58.28 (t), 67.98 (d), 68.13 (d), 77.19 (d), 80.74 (d), 111.11 (s), 116.66 (t), 126.80, 128.01, 128.70 (aromatic carbons), 135.17 (d), 137.66 (s). MS m/z: 303 (M^+). **20b**: $[\alpha]_D^{20}$ −65.5° (c=0.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1110. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, s, CH_3), 1.54 (3H, s, CH_3), 2.13 (1H, dd, J=4.4, 11 Hz, H-5), 2.36—2.62 (3H, m, H-2, C<u>H</u>$_2$CH=CH$_2$), 2.72 (1H, br s, OH), 3.05 (1H, d, J=11 Hz, H-5′), 3.21 and 4.34 (2H, AB, J=13 Hz, NC<u>H</u>$_2$Ph), 4.09 (1H, m, CH), 4.45—4.84 (2H, m, 2×CH), 4.95—5.32 (2H, m, CH=C<u>H</u>$_2$), 5.60—6.12 (1H, m, C<u>H</u>=CH$_2$), 7.30 (5H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.75 (q), 26.07 (q), 40.15 (t), 58.62 (t), 58.77 (t), 69.00 (d), 69.68 (d), 77.48 (d), 81.33 (d), 111.01 (s), 117.58 (t), 126.75, 128.11 128.31 (aromatic carbons), 135.22 (d), 138.54 (s). MS m/z: 303 (M^+).

Preparation of 19d, 20c, 20d, 21b, 22a, 22b These samples were prepared in 65—80% yields from **19b**, **20a**, **20b**, **19d**, **20c**, and **20d** in the same manner as described above for the preparation of **19c** and **21a**. **19d**: mp 37—38°C, $[\alpha]_D^{20}$ −49.0° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1380, 1205, 1100. ^{1}H-NMR ($CDCl_3$): 1.27 (3H, s, CH_3), 1.52 (3H, s, CH_3), 1.92 (1H, dd, J=4, 11 Hz, H-5), 2.30—2.70 (2H, m, CH_2), 2.75—3.02 (3H, m, H-2, H-5′, NC<u>H</u>Ph), 3.88 (1H, m, CH), 4.40—4.80 (5H, m, 2×CH, NC<u>H</u>Ph, OC<u>H</u>$_2$Ph), 4.90—5.22 (2H, m, CH=C<u>H</u>$_2$), 6.01 (1H, m, C<u>H</u>=CH$_2$), 7.32 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.56 (q), 25.82 (q), 37.00 (t), 58.51 (t), 58.99 (t), 68.62 (d), 72.17 (d), 77.86 (d), 79.17 (d), 81,26 (d), 110.74 (s), 115.45 (t), 126.30, 127.08, 127.27, 127.90 (aromatic carbons), 137.19 (d), 138.45 (s), 138.80 (s). MS m/z: 393 (M^+). **20c**: $[\alpha]_D^{20}$ −18.3° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1500, 1455, 1100. ^{1}H-NMR ($CDCl_3$): 2.00—2.46 (2H, m, C<u>H</u>$_2$CH=CH$_2$), 2.69 (1H, m, CH), 2.97 (1H, m, CH), 33.29 (1H, m, CH), 3.60 and 4.29 (2H, AB, J=14 Hz, NC<u>H</u>$_2$Ph), 3.79—4.13 (3H, m, 3×CH), 4.45—4.78 (5H, m, 2×OC<u>H</u>$_2$Ph, CH), 4.90—5.12 (2H, m, CH=C<u>H</u>$_2$), 5.70—6.12 (1H, m, C<u>H</u>=CH$_2$), 7.26—7.30 (20H, s,

aromatic protons). ^{13}C-NMR ($CDCl_3$): 36.82 (t), 54.42 (t), 61.91 (t), 67.99 (d), 71.69 (d), 73.19 (d), 78.64 (d), 78.83 (d), 80.93 (d), 116.28 (t), 126.16, 126.98, 127.81 (aromatic carbons), 135.15 (d), 138.02 (s), 138.41 (s), 138.55 (s), 140.26 (s). MS *m/z*: 533 (M^+). **20d**: $[\alpha]_D^{20}$ −20.3° (*c*=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1620, 1380. ^{1}H-NMR ($CDCl_3$): 1.35 (3H, s, CH_3), 1.59 (3H, s, CH_3), 2.02 (1H, dd, *J*=5, 11 Hz, H-5), 2.53—2.80 (2H, m, CH_2), 2.46 (1H, m, CH), 3.09 (1H, d, *J*=11 Hz, H-5′), 3.20 (1H, AB, *J*=14 Hz, NC<u>H</u>Ph), 3.99 (1H, m, CH), 4.40—4.82 (5H, m, 2×CH, NC<u>H</u>Ph, OCH_2Ph), 5.06—5.29 (2H, m, CH=C<u>H</u>$_2$), 6.09 (1H, m, C<u>H</u>=CH_2), 7.30 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.29 (q), 26.17 (q), 35.72 (t), 58.38 (t), 59.94 (t), 68.42 (d), 71.88 (d), 77.33 (d), 79.57 (d), 80.70 (d), 116.51 (s), 126.31 (t), 127.28—128.20 (aromatic carbons), 135.42 (d), 138.26 (s), 139.12 (s). MS *m/z*: 393 (M^+). **21b**: $[\alpha]_D^{20}$ −35.6° (*c*=0.7, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1050. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, s, CH_3), 1.52 (3H, s, CH_3), 1.60—2.42 (6H, m, 2×CH_2, CH, OH), 2.67 (1H, m, CH), 2.92—3.20 (2H, m, CH, NC<u>H</u>Ph), 3.61 (2H, m, CH_2), 3.88 (1H, m, CH), 4.40—4.80 (5H, m, 2×CH, $OC\underline{H}_2$Ph, NC<u>H</u>Ph), 7.10—7.40 (10H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 24.46 (q), 25.73 (q), 28.16 (t), 29.47 (t), 58.55 (t), 62.35 (t), 67.80 (d), 71.98 (d), 78.15 (d), 78.69 (d), 81.46 (d), 110.83 (s), 126.40—128.10 (aromatic carbons), 138.12 (s), 138.70 (s). MS *m/z*: 411 (M^+). **22a**: mp 61 °C, $[\alpha]_D^{20}$ −35.1° (*c*=0.7, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1040. ^{1}H-NMR ($CDCl_3$): 1.27—1.95 (5H, m, 2×CH_2, OH), 2.39 (1H, dd, *J*=11 Hz, CH), 3.00 (1H, m, CH), 3.30 (1H, dd, *J*=8, 11 Hz,CH), 3.35—3.60 (2H, m, 2×CH), 3.62 and 4.26 (2H, AB, *J*=14 Hz, NC<u>H</u>$_2$Ph), 3.75—4.10 (3H, m, CH_2, CH), 4.40—4.66 (4H, m, 2×$OC\underline{H}_2$Ph), 4.75 and 4.96 (2H, AB, *J*=12 Hz, OCH_2Ph), 7.10—7.35 (20H, m, aromatic protons). ^{13}C-NMR ($CDCl_3$): 28.45 (t), 29.18 (t), 54.27 (t), 61.19 (t), 62.64 (t), 68.23 (d), 73.73 (t), 73.14 (t), 71.68 (t), 78.35 (d), 79.22 (d), 80.63 (d), 126.45—128.14 (aromatic carbons), 138.02 (s), 138.41 (s), 139.14 (s). MS *m/z*: 551 (M^+). **22b**: $[\alpha]_D^{20}$ −59.7° (*c*=0.66, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1050. ^{1}H-NMR ($CDCl_3$): 1.30 (3H, s, CH_3), 1.57 (3H, s, CH_3), 1.50—2.20 (6H, m, 2×CH_2, CH, OH), 2.46 (1H, m, CH), 3.04—3.22 (2H, m, CH, NC<u>H</u>Ph), 3.54—3.68 (2H, m, 2×CH), 3.99 (1H, m, CH), 4.44—4.72 (5H, m, 2×CH, NC<u>H</u>Ph, $OC\underline{H}_2$Ph), 7.25 (10H, s, aromatic protons). ^{13}C-NMR ($CDCl_3$): 25.39 (q), 26.27 (q), 28.26 (t), 28.46 (t), 60.18 (t), 62.62 (t), 68.86 (t), 72.71 (d), 75.73 (t), 77.58 (d), 79.67 (d), 81.28 (d), 111.10 (s), 126.55, 127.62, 128.06, 128.31 (aromatic carbons), 138.15 (s), 139.12 (s). MS *m/z*: 411 (M^+).

Preparation of (−)-Swainsonine (1) from 21b and (−)-8-*epi*-Swainsonine from 22a and 22b These samples were prepared in 60—70% yields in the same manner as described above for the preparation of **1** from **21a**. In the cases of **21b** and **22b**, the crude reaction mixture was heated in 10% aqueous HCl–MeOH (1:1) at 70 °C for 1 h after removal of the benzyl group by hydrogenolysis with 10% palladium carbon. (−)-8-*epi*-Swainsonine: mp 92—93 °C; $[\alpha]_D^{20}$ −22.1° (*c*=0.25, MeOH). ^{1}H-NMR (CD_3OD): 1.20—2.20 (6H, m, H-5, 6, 6′, 7, 7′, 8a), 2.31 (1H, dd, *J*=7, 11 Hz, H-3), 2.80—3.20 (2H, m, H-3′, 5′), 4.10—4.50 (3H, m, H-1, 2, 8). ^{13}C-NMR (CD_3OD): 20.61 (t), 31.97 (t), 54.24 (t), 62.91 (t), 67.44 (d), 69.29 (d), 69.83 (d), 74.17 (d), in good agreement with reported data.[5g]

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