EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201300308

Asymmetric Formal Synthesis of (–)-Swainsonine by a Highly Regioselective and Diastereoselective Allylic Amination Using Chlorosulfonyl Isocyanate

Qing Ri Li,[a][‡] Guang Ri Dong,[a][‡] Sook Jin Park,[a] Yong Rae Hong,[a] In Su Kim,[a] and Young Hoon Jung*[a]

Keywords: Synthesis design / Nitrogen heterocycles / Alkaloids / Amination / Allylation / Diastereoselectivity

A concise asymmetric formal synthesis of (–)-swainsonine from readily available D-erythronolactone is described. The key steps include a highly diastereoselective amination of a chiral benzylic ether, which occurs with the retention of stereochemistry using chlorosulfonyl isocyanate, and a palladium-catalyzed decarboxylative *N*-allylation of an allyl carbamate.

Introduction

Polyhydroxylated indolizidine alkaloids are among the most interesting discoveries in the field of natural products.[1] They are widely distributed in many plants and microorganisms and have been reported to exhibit a range of biological activities that include immunoregulatory, anti-HIV, and anticancer activities.[2] Consequently, a variety of natural or non-natural polyhydroxylated indolizidine alkaloids have been prepared and evaluated for their clinical applications.[3] (–)-Swainsonine (**1**, see Figure 1) is a polyhydroxylated indolizidine alkaloid that was isolated first from the fungal plant pathogen *Rhizoctonia leguminicola*[4] and later from the Australian plant *Swainsona canescens*,[5] the North American spotted locoweed plant *Astragalus lentiginosus*,[6] and the fungus *Metarhizium anisoplia*.[7] (–)-Swainsonine is a potent inhibitor of the Golgi enzyme α-mannosidase II, an enzyme required for the maturation of *N*-linked oligosaccharides of newly formed glycoproteins.[8] Compound **1** is also reported to block lysosomal α-mannosidase, which causes the accumulation of oligomannoside chains in cells exposed to the drug.[9] Furthermore, this molecule exhibits interesting activity against some mammalian tumor cell lines[10] and possesses immunomodulatory and antiviral activities.[11,12] Although the structurally related indolizidine alkaloid (+)-castanospermine (**2**) has received considerable attention as an immunoregulatory substance,[13] the synthesis and biological evaluation of swainsonine and analogues thereof have been the subjects of intensive research. Because of the unique structural features and interesting biological activities, several methods have been developed for the synthesis of **1**.[14–18] Given the structural relationship of swainsonine to carbohydrates[15] and α-amino acids,[16] it is not surprising that most of the syntheses use these compounds as starting materials. One synthesis relies on a series of asymmetric synthetic reactions to construct the stereogenic centers.[17] In a recent example that uses a carbohydrate as a chiral pool, Wardrop and co-workers reported the total synthesis of **1** from 2,3-*O*-isopropylidene-D-erythrose through the diastereoselective addition of an acylnitrenium ion to an alkene to form the pyrrolidine framework.[15h] In another example that uses a chiral pool, Chemla et al. described the asymmetric total synthesis of **1** from readily available D-erythronolactone through the addition of allenylmetals to chiral α,β-alkoxy sulfinylimines.[15i] In a representative example of an asymmetric synthesis, Ham and co-workers demonstrated the asymmetric total synthesis of **1** through a palladium-catalyzed formation of an oxazoline, a diastereoselective dihydroxylation, and a diastereoselective allylation reaction as the key steps.[17k] Bates and Dewey reported the asymmetric formal synthesis of **1** that started from tetrahydrofuran and employed a gold-catalyzed allene cyclization and palladium-catalyzed alloc contraction as the key steps.[18d]

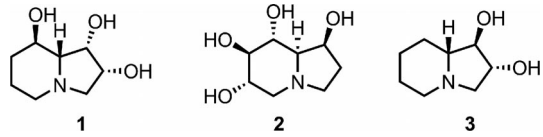


Figure 1. Structures of (–)-swainsonine (**1**), (+)-castanospermine (**2**), and (–)-lentiginosine (**3**).

As part of an ongoing research program that is aimed at developing asymmetric total syntheses of biologically active alkaloids,[19] we recently described a facile strategy for the

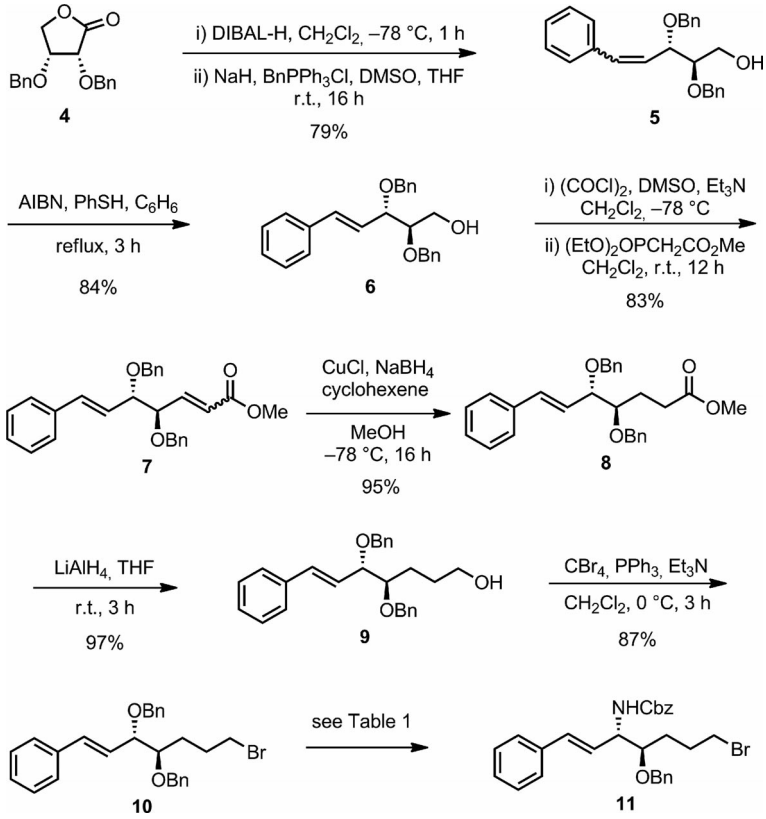
[a] School of Pharmacy, Sungkyunkwan University, Suwon 440-746, Republic of Korea
Fax: +82-31-290-7773
E-mail: yhjung@skku.edu
Homepage: http://pharm.skku.edu/
[‡] These authors contributed equally
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300308.

construction of the indolizidine alkaloid (–)-lentiginosine (**3**) based on the regioselective and diastereoselective allylic amination of polybenzyl ethers using chlorosulfonyl isocyanate (CSI).[20] In connection with our previous work regarding the stereoselective amination of various allylic ethers using CSI, we herein describe an asymmetric formal synthesis of (–)-swainsonine (**1**) that starts from commercially available D-erythronolactone. The key steps include a highly stereoselective amination of 1,2-*anti*-substituted benzyl ether using chlorosulfonyl isocyanate and a palladium-catalyzed decarboxylative *N*-allylation of an allyl carbamate.

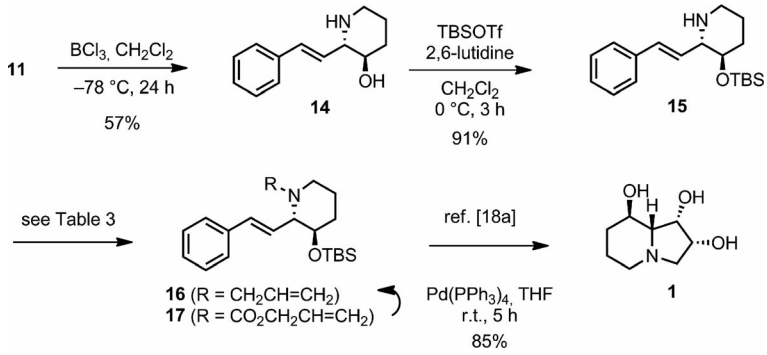
Results and Discussion

The total synthesis of indolizidine alkaloid **1** was achieved by starting with **4**, which was prepared from commercially available D-erythronolactone according to a literature report (see Scheme 1).[21] The reduction of lactone **4** with diisobutylaluminum hydride (DIBAL-H) in CH_2Cl_2 at –78 °C followed by a Wittig reaction of the resulting lactol afforded olefin **5** as an inseparable mixture of *cis* and *trans* isomers (*cis*/*trans*, 1.9:1) in 79% yield. The isomerization of the olefin in the diastereomeric mixture of **5** by treatment with 2,2′-azobis(isobutyronitrile) (AIBN) and thiophenol exclusively gave *trans* olefin **6**. The homologation of two carbons to construct the piperidine ring was performed by the oxidation of alcohol **6** and a subsequent Wittig reaction using a stabilized ylide to afford **7** as a separable mixture of *cis* and *trans* isomers (*cis*/*trans*, 1:2) in 83% yield. We then sought the selective reduction of α,β-unsaturated ester **7** to give saturated primary alcohol **9**, which left the internal alkene intact and was accomplished in either a single step or over two consecutive steps. An attempt to perform a one-pot reduction of α,β-unsaturated ester **7** with $LiAlH_4$ afforded a 1:1 mixture of the desired saturated alcohol **9** and the undesired allylic alcohol concomitant with ester **8** in a 71% combined yield. In view of these unsuccessful results, we changed our synthetic plan to a two-step transformation, which involved a partial reduction of the olefin in α,β-unsaturated ester **7** and subsequent reduction of the ester group. After an extensive screening of the optimal reaction conditions, we found that a combination of sodium borohydride and cuprous chloride in the presence of cyclohexene furnished our desired α,β-saturated ester **8** in 95% yield.[22] The reduction of ester **8** under standard conditions [$LiAlH_4$, tetrahydrofuran (THF)] afforded primary alcohol **9**, which was subjected to an Appel reaction (PPh_3, CBr_4, and Et_3N) to furnish compound **10** in 87% yield.

Next, the diastereoselectivity of the reaction of **10** and chlorosulfonyl isocyanate was examined under various conditions, and the selected results are summarized in Table 1. As shown in Entry 1, the reaction in dichloromethane at 0 °C gave the desired product **11** and its diastereomer in a ratio of 10:1. After screening different solvents under otherwise identical conditions, toluene was found to be most effective for this reaction. As shown in Entry 4, the reaction in toluene exclusively afforded compound **11** in 83% yield



Scheme 1.



Scheme 3.

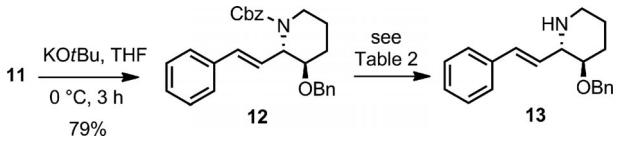
with an excellent diastereoselectivity (*dr* 16:1). The diastereoselectivity of compound **11** can be explained by a neighboring group effect, whereby the orientation of the NHCbz (Cbz = benzyloxycarbonyl) group retains the original configuration by double inversion of the configuration.[19]

Table 1. Selected results for optimization of the diastereoselective amination of **10**.[a]

Entry	Solvent	Time [h]	% Yield[b]	*dr*[c]
1	CH_2Cl_2	10	87	10:1
2	CCl_4	18	75	10:1
3	*n*-hexane	24	85	12:1
4	toluene	12	83	16:1

[a] Reagents and conditions: (i) **10** (1 equiv.), chlorosulfonyl isocyanate (3 equiv.), Na_2CO_3 (4.5 equiv.), solvent (0.25 M), 0 °C; (ii) aqueous saturated solution of Na_2SO_3, room temp., 12 h. [b] Isolated yield by flash column chromatography. [c] Diastereomeric ratio (*dr*) was determined by ^1H NMR analysis of the crude reaction mixture.

First, we envisioned the selective removal of the Cbz protecting group in compound **12** to give piperidine **13**, which can then be converted into the indolizidine framework through an *N*-allylation and a ring-closing metathesis reaction (see Scheme 2). Thus, compound **11** was treated with KO*t*Bu to afford compound **12**, which was then subjected to various reaction conditions to remove the Cbz protecting group as shown in Table 2. Nevertheless, these attempts



Scheme 2.

Table 2. Reaction conditions for removing Cbz protecting group of **12**.

Entry	Reaction conditions	% Yield
1	LiOH (10 equiv.), 1,4-dioxane/H_2O (4:1), 120 °C, 18 h	n.r.[a]
2	KOH (10 equiv.), 1,4-dioxane/H_2O (4:1), 120 °C, 18 h	n.r.
3	$Pd(OAc)_2$, Et_3SiH, Et_3N, CH_2Cl_2, reflux, 24 h	n.r.

[a] n.r.: no reaction.

were unsuccessful and led to recovery of most of the starting material or decomposition of the starting material.[23]

Thus, we focused our synthetic protocol to the removal of the Cbz and benzyl protecting groups followed by an intramolecular cyclization to obtain the piperidine ring (see Scheme 3). To our delight, the treatment of **11** with BCl_3 in dichloromethane removed the Cbz and benzyl groups followed by an intramolecular cyclization to provide piperidine **14**. To obtain target compound **16** for the formal synthesis of (–)-swainsonine (**1**), the introduction of a *tert*-butyldimethylsilyl (TBS) group to **14** and subsequent *N*-allylation was performed under standard reaction conditions. However, the direct *N*-allylation of **15** by using allyl iodide or allyl bromide provided poor yields of the desired compound **16** (see Table 3). On the other hand, the introduction of an allyloxycarbonyl group (see Table 3, Entry 5) followed by a palladium-catalyzed decarboxylative *N*-allylation[24] of allyl carbamate **17** proved to be a highly satisfactory route, which provided compound **16** in 85% yield. The spectroscopic data and the specific rotation of **16** were in full agreement with the reported literature value.[18a]

Table 3. Reaction conditions for allylation and allyloxycarbonylation of **15**.

Entry	Reaction conditions	% Yield **16**[a]	**17**[a]
1	allyl iodide, K_2CO_3, MeCN, 50 °C, 10 h	6	
2	allyl iodide, KO*t*Bu, 80 °C, 10 h	4	
3	allyl bromide, NaH, DMF,[b] r. t., 10 h	5	
4	allyl iodide, NaH, DMF, r. t.., 10 h	10	
5	allyl chloroformate, Na_2CO_3, CH_2Cl_2, r. t., 4 h		83

[a] Isolated yield by flash column chromatography. [b] DMF = *N*,*N*-dimethylformamide.

Conclusions

In summary, we have described a concise formal synthesis of (–)-swainsonine from readily available D-erythronolactone in 11 linear steps (13.4% overall yield) through a highly diastereoselective amination of a chiral benzylic ether, which occurs with the retention of stereochemistry using chlorosulfonyl isocyanate, and a palladium-catalyzed

decarboxylative *N*-allylation of an allyl carbamate. It is believed that this synthetic strategy can be applied to the preparation of a broad range of biologically active compounds that contain a chiral amine moiety.

Experimental Section

General Methods: Commercially available reagents were used without additional purification, unless otherwise stated. All reactions were performed under an inert atmosphere of nitrogen or argon. The ^1H and ^{13}C NMR spectroscopic data were recorded with a Varian Unit 500 MHz spectrometer using $CDCl_3$ solutions, and the chemical shifts are reported in parts per million (ppm) relative to the residual $CHCl_3$ δ_H (δ = 7.26 ppm for ^1H NMR) and $CDCl_3$ δ_C (δ = 77.0 ppm for ^{13}C NMR) as internal standards. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation br. is used to indicate a broad signal. Coupling constants (*J*) are reported in Hertz (Hz). IR spectra were recorded with a Bruker Infrared spectrophotometer and are reported in cm^{-1}. Optical rotations were measured with a Jasco P1020 polarimeter. Thin layer chromatography was carried out using plates coated with Kieselgel $60F_{254}$ (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230–400 mesh) was used. High resolution mass spectra were recorded with a JEOL JMS-600 spectrometer.

(2*R*,3*S*)-2,3-Bis(benzyloxy)-5-phenylpent-4-en-1-ol (5): To a stirred solution of **4** (9.0 g, 30.0 mmol) in dichloromethane (300 mL) cooled to –78 °C was added DIBAL-H (1.0 M in toluene, 42 mL). The resulting solution was mixed at –78 °C for 1 h and then was quenched with a mixture of $Na_2SO_4{\cdot}10H_2O$/Celite (2:1) until mixing became difficult. At this time, the cooling bath was removed, and a sufficient amount of dichloromethane was added to afford a vigorously stirring solution. The stirring was then continued for 10 h. The solution was then filtered, and the filter cake was washed with EtOAc (2 × 500 mL). Concentration of the filtrate afforded the crude lactol (8.8 g) as an oil, which was used without further purification. To a stirred solution of dimethyl sulfoxide (DMSO, 10.4 mL, 146.5 mmol) in anhydrous THF (100 mL) was added NaH (60% in mineral oil, 3.5 g, 87.9 mmol) at 0 °C under N_2. The reaction mixture was stirred for 1 h at room temperature and then cooled to 0 °C. Benzyltriphenylphosphonium chloride (34.2 g, 87.9 mmol) was added in one portion, and the reaction mixture was stirred for 2 h at room temperature and then cooled to 0 °C. A solution of lactol (8.8 g, 29.3 mmol) in anhydrous THF (46 mL) was slowly added, and the reaction mixture was stirred for 12 h at room temperature. After cooling, the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (50 mL). The aqueous layer was extracted with EtOAc (200 mL), and the organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 4:1) to afford **5** (8.87 g, 23.7 mmol, 79% yield; *cis*/*trans*, 1.9:1) as a colorless syrup; R_f = 0.26 (*n*-hexanes/EtOAc, 4:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 2.18–2.38 (m, 1 H), 3.59–3.63 (m, 1 H), 3.76–3.83 (m, 2 H), 4.11–4.14 (m, 0.34 H), 4.17 (d, *J* = 11.5 Hz, 0.66 H), 4.44 (d, *J* = 11.5 Hz, 0.34 H), 4.51–4.73 (m, 3.66 H), 5.69 (dd, *J* = 11.5, 10.0 Hz, 0.66 H), 6.18 (dd, *J* = 16.0, 7.5 Hz, 0.34 H), 6.63 (d, *J* = 16.0 Hz, 0.34 H), 6.88 (d, *J* = 11.5 Hz, 0.66 H), 7.08–7.42 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 62.4, 62.7, 70.5, 70.9, 73.1, 74.6, 80.9, 81.1, 81.5, 126.9, 127.3, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 129.1, 129.2, 130.2, 134.5, 135.0, 136.7, 138.0, 138.3, 138.4 ppm. HRMS [chemical ionization (CI)]: calcd. for $C_{25}H_{25}O_3$ $[M - H]^+$ 373.1806; found 373.1804.

(2*R*,3*S*,*E*)-2,3-Bis(benzyloxy)-5-phenylpent-4-en-1-ol (6): To a stirred solution of **5** (4.5 g, 12.0 mmol) in anhydrous benzene (120 mL) were added PhSH (0.6 mL, 6.0 mmol) and AIBN (394 mg, 2.4 mmol) at room temperature under N_2. The reaction mixture was heated at reflux for 3 h. The resulting mixture was cooled to room temperature and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 4:1) to afford **6** (3.78 g, 10.08 mmol, 84% yield) as a colorless syrup; R_f = 0.26 (*n*-hexanes/EtOAc, 4:1). $[\alpha]_D^{22}$ = +51.8 (*c* = 2.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3448, 3030, 2872, 1721, 1602, 1494, 1452, 1365, 1094, 971, 747, 697, 610 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.23 (br. s, 1 H), 3.60–3.63 (m, 1 H), 3.79 (br. s, 2 H), 4.11–4.14 (m, 1 H), 4.45 (d, *J* = 11.5 Hz, 1 H), 4.59–4.71 (m, 2 H), 6.18 (dd, *J* = 16.0, 8.0 Hz, 1 H), 6.63 (d, *J* = 16.0 Hz, 1 H), 7.20–7.43 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 62.4, 70.9, 73.1, 80.8, 81.5, 126.8, 127.3, 127.9, 128.0, 128.1, 128.2, 128.3, 128.7, 128.8, 128.9, 134.6, 136.6, 138.3, 138.4 ppm. HRMS (CI): calcd. for $C_{25}H_{25}O_3$ $[M - H]^+$ 373.1806; found 373.1804.

(4*R*,5*S*,6*E*)-Methyl 4,5-Bis(benzyloxy)-7-phenylhepta-2,6-dienoate (7): To a stirred solution of oxalyl chloride (2 M in CH_2Cl_2, 10.6 mL, 21.15 mmol) in dry CH_2Cl_2 (60 mL) at –78 °C was added DMSO (3.3 mL, 47 mmol) in CH_2Cl_2 (10 mL) over 20 min, and the mixture was stirred for 40 min. Then, alcohol **6** (3.52 g, 9.4 mmol) in CH_2Cl_2 (10 mL) was added over 30 min, and the mixture was stirred for an additional 1 h. Triethylamine (7.2 mL, 51.7 mmol) in CH_2Cl_2 (10 mL) was added over 20 min, and the white slurry was stirred for 30 min at –78 °C. To the reaction mixture was added methyl(triphenylphosphoranylidene) acetate (7.3 g, 21.6 mmol) in one portion, and the resulting mixture was stirred for 12 h as it warmed to room temperature. Water (50 mL) was added to the reaction mixture, and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 8:1) to afford **7** (3.34 g, 7.80 mmol, 83% yield; *cis*/*trans*, 1:2) as a colorless oil. Data for *cis* isomer: R_f = 0.37 (*n*-hexanes/EtOAc, 8:1). $[\alpha]_D^{22}$ = –2.3 (*c* = 1.2, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3258, 3030, 2862, 1723, 1495, 1452, 1199, 1074, 825, 772, 697 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.64 (s, 3 H), 4.12–4.15 (m, 1 H), 4.54–4.71 (m, 4 H), 5.34–5.37 (m, 1 H), 5.96 (d, *J* = 11.5 Hz, 1 H), 6.19–6.28 (m, 2 H), 6.54 (d, *J* = 16.0 Hz, 1 H), 7.22–7.39 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.5, 70.7, 72.0, 76.9, 116.5, 122.3, 126.7, 126.9, 127.6, 127.7, 127.8, 127.9, 128.4, 128.7, 133.9, 136.8, 138.7, 138.8, 147.2, 166.4 ppm. Data for *trans* isomer: R_f = 0.35 (*n*-hexanes/EtOAc, 8:1). $[\alpha]_D^{22}$ = +23.1 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3258, 2864, 1724, 1452, 1274, 1219, 1170, 1072, 772, 697 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.76 (s, 3 H), 4.02–4.13 (m, 2 H), 4.44–4.68 (m, 4 H), 6.09–6.18 (m, 2 H), 6.61 (d, *J* = 15.5 Hz, 1 H), 7.01 (dd, *J* = 16.0, 6.5 Hz, 1 H), 7.18–7.40 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.8, 70.8, 71.9, 80.6, 81.9, 123.3, 126.6, 126.9, 127.8, 127.9, 128.0, 128.1, 128.2, 128.5, 128.6, 128.8, 134.7, 136.6, 138.0, 138.3, 145.8, 166.7 ppm. HRMS (CI): calcd. for $C_{28}H_{27}O_4$ $[M - H]^+$ 427.1919; found 427.1909.

(4*R*,5*S*,*E*)-Methyl 4,5-Bis(benzyloxy)-7-phenylhept-6-enoate (8): To a stirred solution of α,β-unsaturated ester **7** (3.0 g, 7.0 mmol) in MeOH (117 mL) were added $NaBH_4$ (1.32 g, 35 mmol), CuCl (0.55 g, 5.6 mmol), and cyclohexene (2.8 mL, 28 mmol) at –78 °C. The reaction was stirred at –78 °C for 24 h, and during this period of time, it turned from green to brown. Then, the reaction mixture

was concentrated in vacuo. The residue was partitioned between a saturated aqueous solution of NH_4Cl (50 mL) and Et_2O (150 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (4 × 120 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 8:1) to afford **8** (2.86 g, 6.65 mmol, 95% yield) as a colorless oil; R_f = 0.30 (*n*-hexanes/EtOAc, 8:1). $[\alpha]_D^{22}$ = +68.7 (*c* = 1.4, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3259, 3029, 2863, 1737, 1603, 1495, 1447, 1364, 1218, 1171, 1077, 772, 698, 611 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.89–1.99 (m, 2 H), 2.34–2.47 (m, 2 H), 3.60 (s, 3 H), 3.61–3.65 (m, 1 H), 3.99–4.01 (m, 1 H), 4.49 (dd, *J* = 12.0, 11.5 Hz, 2 H), 4.67–4.73 (m, 2 H), 6.24 (dd, *J* = 16.0, 8.0 Hz, 1 H), 6.61 (d, *J* = 16.0 Hz, 1 H), 7.24–7.42 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.6, 30.3, 51.7, 70.6, 73.1, 80.6, 82.3, 126.8, 127.2, 127.7, 127.8, 127.9, 128.1, 128.3, 128.5, 128.6, 128.8, 134.5, 136.7, 138.7, 138.8, 174.3 ppm. HRMS (CI): calcd. for $C_{28}H_{29}O_4$ $[M - H]^+$ 429.2058; found 429.2066.

(4*R*,5*S*,*E*)-4,5-Bis(benzyloxy)-7-phenylhept-6-en-1-ol (9): To a stirred solution of **8** (2.8 g, 6.5 mmol) in anhydrous THF (43 mL) was added $LiAlH_4$ (0.74 g, 19.5 mmol) at 0 °C under N_2. The reaction mixture was stirred at room temperature for 4 h and then was carefully quenched with H_2O (5 mL) and HCl (1 M solution, 10 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL). The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 2:1) to afford **10** (2.54 g, 6.31 mmol, 97% yield) as a colorless oil; R_f = 0.33 (*n*-hexanes/EtOAc, 2:1). $[\alpha]_D^{22}$ = +59.2 (*c* = 1.2, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3259, 3029, 2866, 1495, 1452, 1362, 1218, 1066, 971, 772, 697, 613 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.56–1.73 (m, 4 H), 3.60–3.64 (m, 3 H), 4.02 (dd, *J* = 8.0, 4.0 Hz, 1 H), 4.45–4.76 (m, 4 H), 6.26 (dd, *J* = 16.0, 8.5 Hz, 1 H), 6.61 (d, *J* = 16.0 Hz, 1 H), 7.20–7.42 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.9, 29.1, 63.2, 70.7, 73.1, 81.6, 82.5, 126.8, 127.4, 127.7, 127.8, 127.9, 128.0, 128.3, 128.5, 128.6, 128.8, 134.4, 136.7, 138.7, 138.8 ppm. HRMS (CI): calcd. for $C_{27}H_{31}O_3$ $[M + H]^+$ 403.2280; found 403.2273.

[(3*S*,4*R*,*E*)-7-Bromo-1-phenylhept-1-ene-3,4-diyl]bis(oxy)bis(methylene)dibenzene (10): To a stirred solution of **9** (2.3 g, 5.71 mmol) in anhydrous CH_2Cl_2 (29 mL) were added PPh_3 (4.94 g, 18.8 mmol), CBr_4 (3.1 g, 9.42 mmol), and Et_3N (14 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 3 h and then quenched with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 10:1) to afford **10** (2.31 g, 4.97 mmol, 87% yield) as a colorless oil; R_f = 0.32 (*n*-hexanes/EtOAc, 10:1). $[\alpha]_D^{23}$ = +57.1 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3259, 3061, 3029, 2926, 2864, 1739, 1602, 1495, 1452, 1363, 1256, 1207, 1098, 1029, 971, 742 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.71–2.04 (m, 4 H), 3.32–3.37 (m, 2 H), 3.58–3.61 (m, 1 H), 3.98–4.01 (m, 1 H), 4.44 (d, *J* = 12.0 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 4.68–4.73 (m, 2 H), 6.26 (dd, *J* = 16.0, 8.0 Hz, 1 H), 6.62 (d, *J* = 16.0 Hz, 1 H), 7.25–7.43 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 29.1, 30.0, 34.2, 70.6, 73.0, 80.8, 82.3, 126.8, 126.9, 127.3, 127.7, 127.8, 127.9, 128.1, 128.3, 128.5, 128.6, 128.8, 134.5, 136.7, 138.7 ppm. HRMS (CI): calcd. for $C_{27}H_{28}BrO_2$ $[M - H]^+$ 463.1273; found 463.1273.

Benzyl (3*S*,4*R*,*E*)-4-(Benzyloxy)-7-bromo-1-phenylhept-1-en-3-ylcarbamate (11): To a stirred solution of **10** (2.2 g, 4.73 mmol) in anhydrous toluene (19 mL) was added Na_2CO_3 (2.3 g, 21.3 mmol), and the reaction mixture was stirred at room temperature for 1 h. This mixture was added to chlorosulfonyl isocyanate (1.2 mL, 14.2 mmol) at 0 °C under N_2. It was stirred at 0 °C for 12 h and then quenched with H_2O (3 mL). The aqueous layer was extracted with EtOAc (2 × 30 mL). The organic layer was added to a solution of aqueous saturated Na_2SO_3 (30 mL), and the reaction mixture was stirred at room temperature for 12 h. The organic layer was washed with H_2O and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 5:1) to afford **11** (2.0 g, 3.93 mmol, 83% yield) as a pale yellow syrup; R_f = 0.32 (*n*-hexanes/EtOAc, 5:1). $[\alpha]_D^{22}$ = +22.2 (*c* = 0.4, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3259, 1720, 1219, 1074, 773 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.65–1.75 (m, 2 H), 1.94 (br. s, 2 H), 3.37 (br. s, 2 H), 3.60 (br. s, 1 H), 4.51 (br. s, 1 H), 4.55–4.64 (m, 2 H), 5.07–5.13 (m, 3 H), 6.17 (dd, *J* = 16.0, 7.5 Hz, 1 H), 6.58 (br. s, 1 H), 7.22–7.37 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.9, 29.4, 33.7, 55.7, 67.1, 72.4, 80.3, 121.3, 125.5, 126.8, 128.0, 128.1, 128.3, 128.8, 133.3, 136.7, 156.0 ppm. HRMS (CI): calcd. for $C_{28}H_{31}BrNO_3$ $[M + H]^+$ 508.1483; found 508.1487.

(2*S*,3*R*)-Benzyl 3-(Benzyloxy)-2-styrylpiperidine-1-carboxylate (12): To a stirred solution of **11** (1.8 g, 3.54 mmol) in THF (18 mL) was slowly added potassium *tert*-butoxide (0.47 g, 4.2 mmol) at 0 °C under N_2. The reaction mixture was stirred at room temperature for 2 h and then was quenched with H_2O (10 mL). The aqueous layer was extracted with EtOAc (30 mL). The organic layer was washed with H_2O, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 8:1) to afford **12** (1.2 g, 2.80 mmol, 79% yield) as a colorless syrup; R_f = 0.30 (*n*-hexanes/EtOAc, 8:1). $[\alpha]_D^{23}$ = +49.3 (*c* = 2.3, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3029, 2947, 1697, 1650, 1496, 1424, 1307, 1264, 1199, 1127, 874, 750 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.42 (br. s, 1 H), 1.60–1.71 (m, 1 H), 1.89–2.15 (m, 2 H), 3.05 (t, *J* = 10.0 Hz, 1 H), 3.64 (br. s, 1 H), 4.09–4.17 (m, 1 H), 4.52–4.67 (m, 2 H), 5.09–5.22 (m, 2 H), 5.25 (br. s, 1 H), 6.10 (dd, *J* = 16.0, 5.0 Hz, 1 H), 6.45 (d, *J* = 16.0 Hz, 1 H), 7.18–7.44 (m, 15 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.8, 25.0, 40.0, 67.4, 70.5, 74.9, 77.1, 125.4, 126.6, 127.6, 127.7, 127.8, 127.9, 128.0, 128.5, 128.6, 128.7, 128.8, 128.9, 132.3, 136.8, 137.2, 138.8, 156.6 ppm. HRMS (EI): calcd. for $C_{28}H_{29}NO_3$ $[M]^+$ 427.2147; found 427.2136.

(2*S*,3*R*)-2-Styrylpiperidin-3-ol (14): To a stirred solution of **11** (0.54 g, 1.061 mmol) in anhydrous CH_2Cl_2 (21 mL) was added BCl_3 (1.0 M in CH_2Cl_2, 66 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 24 h and then quenched with MeOH (20 mL). The resulting mixture was stirred at –78 °C for an additional 1 h. The resulting mixture was warmed to room temperature and concentrated in vacuo. The residue was purified by ion-exchange resin DOWEX 50WX8–100 (NH_4OH, 0.5 M solution) to afford **14** (123 mg, 0.605 mmol, 57% yield) as a white solid; m.p. 174.6 °C. R_f = 0.13 (CH_2Cl_2/CH_3OH/NH_4OH, 90:10:0.15). $[\alpha]_D^{27}$ = +66.4 (*c* = 0.4, CH_3OH). IR (neat): $\tilde{\nu}$ = 3269, 2926, 2826, 1354, 1070, 924, 864, 744, 692 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ = 1.59–1.67 (m, 1 H), 1.77–1.85 (m, 1 H), 2.01–2.09 (m, 1 H), 2.13–2.18 (m, 1 H), 3.01–3.02 (m, 1 H), 3.31 (t, *J* = 3.0 Hz, 2 H), 3.33–3.37 (m, 1 H), 3.66 (t, *J* = 8.4 Hz, 1 H), 3.73–3.78 (m, 1 H), 6.29 (dd, *J* = 16.0, 8.2 Hz, 1 H), 6.89 (d, *J* = 16.0 Hz, 1 H), 7.29–7.39 (m, 3 H), 7.45–7.51 (m, 2 H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 20.4, 30.3, 43.0, 63.2, 67.7, 121.4, 126.7, 128.6, 128.7, 135.7, 138.3 ppm. HRMS (EI): calcd. for $C_{13}H_{17}NO$ $[M]^+$ 203.1310; found 203.1312.

(2*S*,3*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-styrylpiperidine (15): To a stirred solution of **14** (349 mg, 0.837 mmol) in anhydrous CH_2Cl_2

(11 mL) were added 2,6-lutidine (0.44 mL, 1.842 mmol) and TBSOTf (0.790 mL, 1.675 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 5 h and then was quenched with a solution of aqueous saturated $NaHCO_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (CH_2Cl_2/CH_3OH/NH_4OH, 90:10:0.15) to afford **15** (242 mg, 0.762 mmol, 91% yield) as a colorless oil; R_f = 0.42 (CH_2Cl_2/CH_3OH/NH_4OH, 90:10:0.15). $[\alpha]_D^{27}$ = +185.9 (c = 0.03, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2926, 2854, 1739, 1464, 1364, 1253, 1099, 969, 926, 837, 776, 747 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 3 H), 0.07 (s, 3 H), 0.88 (s, 9 H), 1.45–1.50 (m, 1 H), 1.74–1.80 (m, 2 H), 2.04–2.08 (m, 2 H), 2.68 (dt, J = 11.8, 2.8 Hz, 1 H), 3.08 (d, J = 11.8 Hz, 1 H), 3.13 (t, J = 7.8 Hz, 1 H), 3.44–3.46 (m, 1 H), 6.31 (dd, J = 16.0, 7.1 Hz, 1 H), 6.60 (d, J = 16.0 Hz, 1 H), 7.24–7.40 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.3, –4.1, 18.2, 25.3, 26.0, 26.0, 29.9, 34.8, 45.9, 66.1, 72.9, 126.4, 127.5, 128.7, 131.7, 137.3 ppm. HRMS (EI): calcd. for $C_{19}H_{31}NOSi$ $[M]^+$ 317.2175; found 317.2177.

(2*S*,3*R*)-Allyl 3-(*tert*-Butyldimethylsilyloxy)-2-styrylpiperidine-1-carboxylate (17): To a stirred solution of **15** (51 mg, 0.161 mmol) in anhydrous CH_2Cl_2 (1.1 mL) were added allyl chloroformate (0.05 mL, 0.481 mmol) and sodium carbonate (426 mg, 0.402 mmol) at room temperature. The reaction mixture was stirred at room temperature for 4 h and then was quenched with a solution of saturated aqueous NH_4Cl (3 mL). The resulting mixture was then diluted with CH_2Cl_2 (5 mL). The mixture was washed with H_2O, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc, 20:1) to afford **17** (53.8 mg, 0.134 mmol, 83% yield) as a colorless oil; R_f = 0.41 (*n*-hexanes/EtOAc, 10:1). $[\alpha]_D^{27}$ = +224.6 (c = 0.1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2952, 2929, 2856, 1701, 1465, 1417, 1375, 1252, 1197, 1129, 1091, 1304, 964, 923, 891, 836 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.07 (s, 3 H), 0.09 (s, 3 H), 0.89 (s, 9 H), 1.35 (d, J = 13.1 Hz, 1 H), 1.64–1.69 (m, 2 H), 1.98–2.02 (m, 1 H), 2.98 (dt, J = 13.3, 2.9 Hz, 1 H), 2.95–3.01 (m, 1 H), 4.12 (d, J = 12.6 Hz, 1 H), 4.55–4.65 (m, 2 H), 4.88 (br. s, 1 H), 5.16–5.19 (m, 1 H), 5.27–5.31 (m, 1 H), 5.91–5.96 (m, 1 H), 6.13 (dd, J = 16.1, 5.2 Hz, 1 H), 6.46 (dd, J = 16.1, 1.8 Hz, 1 H), 7.22–7.38 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.7, –4.6, 18.3, 19.2, 25.9, 27.8, 39.9, 60.0, 66.1, 68.9, 117.2, 125.4, 126.5, 127.9, 128.8, 132.0, 133.5, 136.8, 156.4 ppm. HRMS (EI): calcd. for $C_{23}H_{35}NO_3Si$ $[M]^+$ 401.2386; found 401.2384.

(2*S*,3*R*)-1-Allyl-3-(*tert*-butyldimethylsilyloxy)-2-styrylpiperidine (16): To a stirred solution of **17** (38.3 mg, 0.095 mmol) in THF (2.5 mL) was added tetrakis(triphenylphosphane)palladium (11 mg, 0.01 mmol) at room temperature. The reaction mixture was stirred at room temperature for 5 h and then concentrated in vacuo. The residue was purified by flash chromatography (*n*-hexanes/EtOAc, 20:1) to afford **16** (28.9 mg, 0.081 mmol, 85%) as a colorless oil; R_f = 0.28 (*n*-hexanes/EtOAc, 20:1). $[\alpha]_D^{27}$ = +73.6 (c = 1.3, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3079, 3027, 2929, 2790, 2709, 1739, 1642, 1600, 1494, 1463, 1360, 1253, 1101, 969, 916, 836 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = –0.14 (s, 3 H), –0.01 (s, 3 H), 0.77 (br. s, 9 H), 1.31–1.39 (m, 1 H), 1.54–1.62 (m, 1 H), 1.68–1.72 (m, 1 H), 1.96–2.01 (m, 2 H), 2.60 (t, J = 8.7 Hz, 1 H), 2.80 (dd, J = 13.9, 8.2 Hz, 1 H), 2.95 (d, J = 11.5 Hz, 1 H), 3.47–3.52 (m, 2 H), 5.08–5.13 (m, 2 H), 5.81–5.89 (m, 1 H), 6.00 (dd, J = 15.9, 9.0 Hz, 1 H), 6.52 (dd, J = 15.9 Hz, 1 H), 7.18–7.36 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.3, –4.2, 18.1, 23.6, 25.9, 34.3, 41.8, 51.9, 58.8, 72.2, 73.3, 117.9, 126.4, 127.4, 128.7, 129.1, 129.3, 130.8, 134.2, 135.2, 137.2 ppm. HRMS (EI): calcd. for $C_{22}H_{35}NOSi$ $[M]^+$ 357.2488; found 357.2492.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra for all compounds.

Acknowledgments

This work was supported by the Postdoctoral Research Program of Sungkyunkwan University (2012) and the National Research Foundation of Korea (NRF-2012-002506) and funded by the Ministry of Education, Science, and Technology, Korea.

[1] A. A. Watson, G. W. J. Fleet, N. Asano, R. J. Molyneux, R. J. Nash, *Phytochemistry* **2001**, *56*, 265.
[2] For selected reviews, see: a) E. B. de Melo, A. da Silveria Gomes, I. Carvalho, *Tetrahedron* **2006**, *62*, 10277; b) S. Gerber-Lemaire, L. Juillerat-Jeanneret, *Mini-Rev. Med. Chem.* **2006**, *6*, 1043; c) N. Asano, *Glycobiology* **2003**, *13*, 93R; d) V. H. Lillelund, H. H. Jensen, X. F. Liang, M. Bols, *Chem. Rev.* **2002**, *102*, 515.
[3] For a selected review, see: J. P. Michael, *Nat. Prod. Rep.* **2007**, *24*, 191.
[4] a) F. P. Guengerich, S. J. DiMari, H. P. Broquist, *J. Am. Chem. Soc.* **1973**, *95*, 2055; b) M. J. Schneider, F. S. Ungemach, H. P. Broquist, T. M. Harris, *Tetrahedron* **1983**, *39*, 29.
[5] S. M. Colegate, P. R. Dorling, C. R. Huxtable, *Aust. J. Chem.* **1979**, *32*, 2257.
[6] R. J. Molyneux, L. F. James, *Science* **1982**, *216*, 190.
[7] M. Hino, O. Nakayama, Y. Tsurumi, K. Adachi, T. Shibata, H. Terano, M. Kohsaka, H. Aoki, H. Imanaka, *J. Antibiot.* **1985**, *38*, 926.
[8] a) A. D. Elbein, R. Solf, P. R. Dorling, K. Vosbeck, *Proc. Natl. Acad. Sci. USA* **1981**, *78*, 7393; b) D. R. Tulsiani, T. M. Harris, O. Touster, *J. Biol. Chem.* **1982**, *257*, 7936.
[9] a) P. E. Goss, C. L. Reid, D. Bailey, J. W. Dennis, *Clin. Cancer Res.* **1997**, *3*, 11077; b) I. Cenci di Bello, G. Fleet, S. K. Namgoong, K. Tadano, B. Winchester, *Biochem. J.* **1989**, *259*, 855.
[10] J. Y. Sun, H. Yang, S. Miao, J. P. Li, S. W. Wang, M. Z. Zhu, Y. H. Xie, J. B. Wang, Z. Liu, Q. Yang, *Phytomedicine* **2009**, *16*, 1070.
[11] a) T. Kino, N. Inamura, K. Nakahara, S. Kiyoto, T. Goto, H. Terno, M. Kohsaka, H. Aoki, H. Imanaka, *J. Antibiot.* **1985**, *38*, 936; b) M. J. Humphries, K. Matsumoto, S. L. White, R. J. Molyneux, K. Olden, *Cancer Res.* **1988**, *48*, 1410.
[12] A. D. Elbein, P. R. Dorling, K. Vosbeck, M. Horisberger, *J. Biol. Chem.* **1982**, *257*, 1573.
[13] For isolation of **2**, see: a) L. D. Hohenschutz, E. A. Bell, P. J. Jewess, D. P. Leworthy, R. J. Pryce, E. Arnold, J. Clardy, *Phytochemistry* **1981**, *20*, 811; for biologial activity of **2**, see: b) R. A. Gruters, J. J. Neefjes, M. Tersmette, R. E. Y. de Goede, A. Tulp, H. G. Huisman, F. Miedema, H. L. Ploegh, *Nature* **1987**, *330*, 74.
[14] For reviews about the synthesis of (–)-swainsonine, see: a) M. D. López, J. Cobo, M. Nogueras, *Curr. Org. Chem.* **2008**, *12*, 718; b) S. Pyne, *Curr. Org. Synth.* **2005**, *2*, 39; c) A. El Nemr, *Tetrahedron* **2000**, *56*, 8579.
[15] For recent selected examples of the total synthesis of (–)-swainsonine, see: a) S. A. Miller, A. R. Chamberlin, *J. Am. Chem. Soc.* **1990**, *112*, 8100; b) W. H. Pearson, K.-C. Lin, *Tetrahedron Lett.* **1990**, *31*, 7571; c) S. H. Kang, G. T. Kim, *Tetrahedron Lett.* **1995**, *36*, 5049; d) W. H. Pearson, E. J. Hembre, *J. Org. Chem.* **1996**, *61*, 7217; e) H. Zhao, S. Hans, X. Cheng, D. R. Mootoo, *J. Org. Chem.* **2001**, *66*, 1761; f) W. H. Pearson, Y. Ren, J. D. Powers, *Heterocycles* **2002**, *58*, 421; g) P. K. Sharma, R. N. Shah, J. P. Carver, *Org. Process Res. Dev.* **2008**, *12*, 831; h) D. J. Wardrop, E. G. Bowen, *Org. Lett.* **2011**, *13*, 2376; i) J. Louvel, F. Chemla, E. Demont, F. Ferreira, A. Pérez-Luna, *Org. Lett.* **2011**, *13*, 6452.
[16] For recent selected examples of the total synthesis of (–)-swainsonine, see: a) N. Ikota, A. Hanaki, *Chem. Pharm. Bull.* **1990**,

38, 2712; b) M. Naruse, S. Aoyagi, C. Kibayashi, *J. Org. Chem.* **1994**, *59*, 1358; c) M.-J. Blanco, F. J. Sardina, *J. Org. Chem.* **1996**, *61*, 4748; d) I. Déchamps, D. G. Pardo, J. Cossy, *ARKIVOC* **2007**, *5*, 38.

[17] For recent selected examples of the total synthesis of (–)-swainsonine, see: a) T. Punniyamurthy, R. Irie, T. Katsuki, *Chirality* **2000**, *12*, 464; b) N. Buschmann, A. Rückert, S. Blechert, *J. Org. Chem.* **2002**, *67*, 4325; c) K. B. Lindsay, S. G. Pyne, *J. Org. Chem.* **2002**, *67*, 7774; d) K. B. Lindsay, S. G. Pyne, *Aust. J. Chem.* **2004**, *57*, 669; e) L. Song, E. N. Duesler, P. S. Mariano, *J. Org. Chem.* **2004**, *69*, 7284; f) R. Martín, C. Murruzzu, M. A. Pericás, A. Riera, *J. Org. Chem.* **2005**, *70*, 2325; g) G. Heimgärtner, D. Raatz, O. Reiser, *Tetrahedron* **2005**, *61*, 643; h) H. Guo, G. A. O'Doherty, *Org. Lett.* **2006**, *8*, 1609; i) J. Ceccon, A. E. Greene, J.-F. Poisson, *Org. Lett.* **2006**, *8*, 4739; j) G.-F. Shi, J.-Q. Li, X.-P. Jiang, Y. Cheng, *Tetrahedron* **2008**, *64*, 5005; k) Y.-S. Tian, J.-E. Joo, B.-S. Kong, V.-T. Pham, K.-Y. Lee, W.-H. Ham, *J. Org. Chem.* **2009**, *74*, 3962; l) S. Chooprayoon, C. Kuhakarn, P. Tuchinda, V. Reutrakul, M. Pohmakotr, *Org. Biomol. Chem.* **2011**, *9*, 531.

[18] For recent selected examples of the formal synthesis of (–)-swainsonine, see: a) C. W. G. Au, S. G. Pyne, *J. Org. Chem.* **2006**, *71*, 7097; b) I. Déchamps, D. G. Pardo, J. Cossy, *Tetrahedron* **2007**, *63*, 9082; c) H. Kwon, C. Park, S. Lee, J.-H. Youn, S. Kang, *Chem. Eur. J.* **2008**, *14*, 1023; d) R. W. Bates, M. R. Dewey, *Org. Lett.* **2009**, *11*, 3706; e) H. G. Choi, J. H. Kwon, J. C. Kim, W. K. Lee, H. Eum, H.-J. Ha, *Tetrahedron Lett.* **2010**, *51*, 3284; f) S. J. Oxenford, S. P. Moore, G. Carbone, G. Barker, P. O'Brien, M. R. Shipton, J. Gilday, K. R. Campos, *Tetrahedron: Asymmetry* **2010**, *21*, 1563; g) S. N. Murthy, Y. V. D. Nageswar, *Synthesis* **2011**, 755.

[19] I. S. Kim, O. P. Zee, Y. H. Jung, *Org. Lett.* **2006**, *8*, 4101.

[20] For a review, see: a) I. S. Kim, Y. H. Jung, *Heterocycles* **2011**, *83*, 2489; for recent examples, see: b) I. S. Kim, Q. R. Li, G. R. Dong, S. H. Woo, H.-j. Park, O. P. Zee, Y. H. Jung, *Synlett* **2008**, 2985; c) I. S. Kim, Q. R. Li, G. R. Dong, Y. C. Kim, Y. J. Hong, M. Lee, K.-W. Chi, J. S. Oh, Y. H. Jung, *Eur. J. Org. Chem.* **2010**, 1569; d) S. H. Lee, I. S. Kim, Q. R. Li, G. R. Dong, L. S. Jeong, Y. H. Jung, *J. Org. Chem.* **2011**, *76*, 10011; e) G. R. Dong, S. M. Hong, S. I. Kim, I. S. Kim, Y. H. Jung, *Eur. J. Org. Chem.* **2012**, 4200; f) S. J. Kim, T. H. Jeon, I. S. Min, I. S. Kim, Y. H. Jung, *Tetrahedron Lett.* **2012**, *53*, 3680; g) S. H. Lee, S. J. Park, I. S. Kim, Y. H. Jung, *Tetrahedron* **2013**, *69*, 1877.

[21] J. A. Marshall, B. M. Seletsky, G. P. Luke, *J. Org. Chem.* **1994**, *59*, 3413.

[22] L. J. Baird, M. S. M. Timmer, P. H. Teesdale-Spittle, J. E. Harvey, *J. Org. Chem.* **2009**, *74*, 2271.

[23] For the selective cleavage of a Cbz protecting group, see: a) S. R. Angel, D. O. Arnaiz, *Tetrahedron Lett.* **1989**, *30*, 515; b) M. Sakatani, N. Kurokawa, Y. Ohfune, *Tetrahedron Lett.* **1986**, *27*, 3753; c) P. Wipf, Y. Uto, *Tetrahedron Lett.* **1999**, *40*, 5165.

[24] For selected examples, see: a) C. Torque, B. Sueur, J. Cabou, H. Bricout, F. Hapiot, E. Monflier, *Tetrahedron* **2005**, *61*, 4811; b) P. Gomez-Martinez, M. Dessolin, F. Guibé, F. Albericio, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2871.

Received: March 1, 2013
Published Online: May 31, 2013

