

***Diastereoselective Nitrenium Ion-Mediated  
Alkene Bis-Cyclofunctionalization  
Total Synthesis of (-)-Swainsonine***

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***Supporting Information, Part 1***

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## 1.1 General Procedures

All non-aqueous reactions were carried out in oven- or flame-dried glassware under an atmosphere of dry argon or nitrogen, unless otherwise noted. Except as otherwise indicated, all reactions were magnetically stirred and monitored by analytical thin-layer chromatography using Merck pre-coated silica gel plates with F<sub>254</sub> indicator. Visualization was accomplished by UV light, phosphomolybdic acid, and/or potassium permanganate solution. Flash column chromatography was performed according to the method of Still<sup>1</sup> using silica gel 60 (mesh 230-400) supplied by E. Merck. Yields refer to chromatographically and spectrographically pure compounds, unless otherwise noted.

## 1.2 Materials

All solvents were reagent grade. 1,4-Dioxane and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. Dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>) was freshly distilled from calcium hydride under nitrogen. Saturated solutions of ammonia in methanol (NH<sub>3</sub>-MeOH) were prepared by bubbling anhydrous NH<sub>3</sub>(g) through cold (0 °C), anhydrous MeOH for 20 min. The molarity of this solution was titrated against a standardized aqueous solution of HCl using bromocresol blue as an indicator (average of three determinations). Phenyliodine(III) bis(trifluoroacetate) (PIFA) was prepared from phenyliodine(III) bis(acetate) using the method of Vargolis.<sup>2</sup> Brine refers to a saturated aqueous solution of NaCl. All other reagents and starting materials, unless otherwise noted, were purchased from commercial vendors and used without further purification.

## 1.3 Instrumentation

All melting points were determined in Pyrex capillaries with a Thomas Hoover Unimelt melting point apparatus and are uncorrected. Infrared spectra were recorded as thin films on barium fluoride plates using an ATI Mattson genesis series FTIR spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker Avance 400 (400 MHz <sup>1</sup>H, 100 MHz <sup>13</sup>C), a Bruker Avance 500 (500 MHz <sup>1</sup>H, 125 MHz <sup>13</sup>C), or a Bruker AM-400 (400 MHz <sup>1</sup>H, 100 MHz <sup>13</sup>C) spectrometer. Chemical shift values (δ) are reported in ppm relative to residual chloroform (δ 7.27 ppm for <sup>1</sup>H; δ 77.23 ppm for <sup>13</sup>C) and methanol (δ 3.31 ppm for <sup>1</sup>H; δ 49.15 ppm for <sup>13</sup>C). The <sup>1</sup>H NMR spectra are reported as follows: δ (multiplicity, coupling constant, integration). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (heptet), m (multiplet) and br (broad). The identification of <sup>1</sup>H and <sup>13</sup>C signals was achieved using a combination of <sup>1</sup>H, <sup>13</sup>C, DEPT, COSY, HMBC, HMQC and NOESY experiments. In those situations where products are

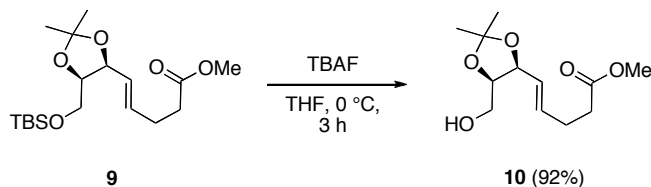
a mixture of rotamers or diastereomers,  $^1\text{H}$  resonances arising from the *same* proton in *different* rotamers (or diastereomers) are reported as follows: [ $\delta$  downfield resonance, (multiplicity, coupling constant),  $\delta$  upfield resonance (multiplicity, coupling constant), total integration for *both* resonances]; the signals arising from the minor rotamers/diastereomers are designated by asterisks (\*). Optical rotations were measured with a Perkin-Elmer model 241 polarimeter and reported as follows:  $[\alpha]_{\text{wavelength}}^{\text{temperature}}$  ( $c$ , solvent);  $[\alpha]_{\text{D}}$  is reported in  $10^{-1} \text{ deg cm}^{-2}\text{g}^{-1}$ ; concentration ( $c$ ) is reported g in per 100 mL. High-resolution electron impact (HRMS-EI) mass spectra were obtained on a Kratos Concept 1H spectrometer at the Mass Spectrometry Service Laboratory, University of Minnesota with a typical ionization voltage of 70 eV. High-resolution chemical ionization (HRMS-CI) mass spectra were obtained on a FINNIGAN MAT 95 and high-resolution fast atom bombardment (HRMS-FAB) spectra were obtained on a VG 7070-HF at the Mass Spectrometry Service Laboratory, University of Minnesota. High-resolution electron impact (EI) mass spectra were obtained on a Kratos Concept 1H spectrometer at the University of Illinois Research Resources Center with a typical ionization voltage of 70 eV. High-resolution chemical ionization (CI) mass spectra were obtained on a FINNIGAN MAT 95 and high-resolution fast atom bombardment (FAB) spectra were obtained on a VG 7070-HF at the Mass Spectrometry Service Laboratory, University of Minnesota. High-resolution electrospray ionization (HRMS-ESI) mass spectra were obtained on a Micro Mass QTOF II instrument at the University of Illinois Research Resources Center.

#### 1.4 Literature Preparations

Compound **9** was prepared in three steps (71% overall yield) from 2,3-*O*-isopropylidene-D-erythronolactone following a sequence of reactions reported by Pearson and Hembre.<sup>3</sup>

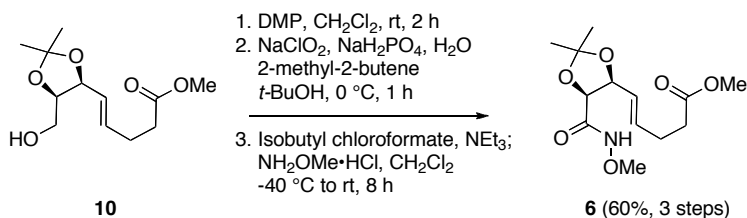
## 1.5 Total Synthesis of Total (-)-Swainsonine

### (4'*S*,5'*R*,*E*)-5-(5'-Hydroxymethyl-2',2'-dimethyl-[1',3']dioxolan-4'-yl)-pent-4-enoic acid methyl ester (**10**).



To a stirred, cooled (0 °C) solution of **9** (3.76 g, 10.5 mmol) in THF (50 mL) was added tetrabutylammonium fluoride (1.0 M solution in CH<sub>2</sub>Cl<sub>2</sub>, 21.0 mL, 21.0 mmol). After 3 h, the reaction was quenched with silica gel and stirred for 1 h. The mixture was then filtered through Celite 521 and silica gel, and washed with Et<sub>2</sub>O/EtOAc (10:3) 300 mL. The combined filtrates were concentrated under reduced pressure and purified by flash chromatography on silica gel (EtOAc/hexanes, 1:2) to afford **10** (2.56 g, 92%): colorless oil; *R<sub>f</sub>* 0.39 (EtOAc/hexanes, 1:1); [α]<sub>D</sub><sup>24</sup> +38.4 (*c* 1.2, CHCl<sub>3</sub>); IR (film/NaCl)  $\nu_{\max}$  3470, 2987, 2950, 2935, 2880, 1737, 1438, 1371, 1249, 1214, 1166, 1117, 1046, 974, 887, 859, 790, 518 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.81 (ddd, *J* = 6.1, 6.1, 15.4 Hz, 1 H, HC-4), 5.56 (dd, *J* = 8.0, 15.4 Hz, 1 H, HC-5), 4.61 (dd, *J* = 7.3, 7.3 Hz, 1 H, HC-4'), 4.20 (ddd, *J* = 6.4, 6.4, 6.4 Hz, 1 H, HC-5'), 3.66 (s, 3 H, OMe), 3.59-3.50 (m, 2 H, H<sub>2</sub>C-6'), 2.48-2.35 (m, 4 H, H<sub>2</sub>C-2, H<sub>2</sub>C-3), 2.03 (bs, 1 H, OH), 1.48 (s, 3 H), 1.36 (s, 3 H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 173.4 (C-1), 133.8 (d, C-4), 125.9 (d, C-5), 108.6 (s, C-2'), 78.2, (d), 77.8 (d), 61.9 (t, C-6'), 51.7 (q, OMe), 33.1 (t), 27.8 (q), 27.4 (t), 25.1 (q); HRMS-ESI calcd for C<sub>12</sub>H<sub>20</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup>: 267.1208, found: 267.1201.

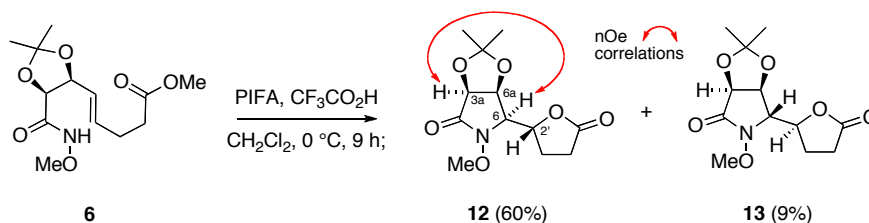
### *E*-(4'*S*,5'*S*,*E*)-5-(5'-Methoxycarbonyl-2',2'-dimethyl-[1',3']dioxolan-4'-yl)-pent-4-enoic acid methyl ester (**6**).



To a stirred solution of **10** (2.32 g, 9.51 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) was added Dess-Martin Periodinane (8.06 g, 19 mmol). After 2 h, the reaction was quenched with a 10% aqueous solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (20 mL), stirred for 30 min, then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 ×

50 mL). The combined organic extracts were then dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure to provide the aldehyde, which was dissolved in 2-methyl-2-butene (10 mL) and *tert*-BuOH (40 mL) and cooled to 0 °C. A solution of NaClO<sub>2</sub> (1.48 g, 16.4 mmol) in aqueous NaH<sub>2</sub>PO<sub>4</sub> (1 M, 13.9 mL, 13.9 mmol) was then added to the stirred solution of crude aldehyde. After 1 h, the reaction was quenched with citric acid (0.5 M, 20 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated under reduced pressure. The crude acid was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and cooled to -40 °C. To this was added triethylamine (1.19 mL, 8.6 mmol) and isobutyl chloroformate (1.02 mL, 7.85 mmol) and the reaction stirred for 30 min. Methoxylamine hydrochloride (770 mg, 9.3 mmol) and triethylamine (1.19 mL, 8.6 mmol) were then added to the stirred mixture, which was allowed to warm to room temperature over 8 h. The reaction was then quenched with citric acid (0.5 M, 20 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated under reduced pressure, and the residue purified by flash chromatography on silica gel (EtOAc/hexanes, 1:1) to afford **6** (1.62 g, 60%): colorless oil; *R*<sub>f</sub> 0.50 (EtOAc); [α]<sub>D</sub><sup>24</sup> -30.4 (*c* 0.84, CHCl<sub>3</sub>); IR (film/NaCl)  $\nu_{\max}$  3216, 2987, 2939, 1735, 1684, 1437, 1374, 1214, 1163, 1071, 972, 879 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD)  $\delta$  5.83 (ddd, *J* = 6.4, 6.4, 14.1 Hz, 1 H, HC-4), 5.44 (dd, *J* = 7.7, 15.4 Hz, 1 H, HC-5), 4.83-4.75 (m, 1 H, HC-4'), 4.55 (d, *J* = 7.5 Hz, 1 H, HC-5'), 3.68 (s, 3 H, OMe), 3.66 (s, 3 H, OMe), 2.44-2.36 (m, 2 H), 2.36-2.28 (m, 2 H), 1.55 (s, 3 H), 1.35 (s, 3 H); <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD)  $\delta$  173.5 (s, C-1), 166.6 (s, C-1'), 133.6 (d, C-4), 125.7 (d, C-5), 110.2 (s, C-2'), 78.3 (d), 77.0 (d), 63.2 (q), 50.8 (q), 32.7 (t), 27.1 (t), 25.8 (q), 23.6 (q); HRMS-ESI calcd for C<sub>13</sub>H<sub>21</sub>NO<sub>6</sub>Na [M+Na]<sup>+</sup>: 310.12614, found: 310.1259.

**(3a*S*,6a*S*,6*R*,2'*R*)-5-Methoxy-2,2-dimethyl-6-(5'-oxo-tetrahydro-furan-2'-yl)-tetrahydro-[1,3]dioxolo[4,5-*c*]pyrrol-4-one (12) and (3a*S*,6a*S*,6*S*,2'*S*)-5-Methoxy-2,2-dimethyl-6-(5'-oxo-tetrahydro-furan-2'-yl)-tetrahydro-[1,3]dioxolo[4,5-*c*]pyrrol-4-one (13).**



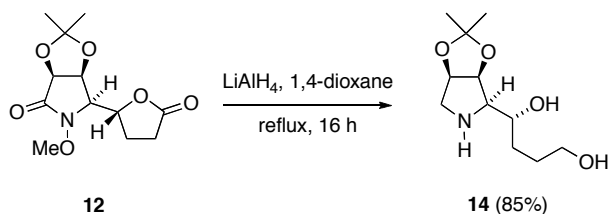
To a stirred, cooled (0 °C) solution of **6** (757.4 mg, 2.64 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (25 mL) was added trifluoroacetic acid (0.27 mL, 3.69 mmol) and bis(trifluoroacetoxy)iodobenzene

(1.56 g, 3.96 mmol). After 9 h, the reaction was concentrated and the residue purified by flash chromatography on silica gel (EtOAc/hexanes, 1:1→1:0) to afford **12** (452.1 mg, 60%) and **13** (65.4 mg, 9%):

Analytical Data for **12**: white needles; mp 192-194 °C (CH<sub>2</sub>Cl<sub>2</sub>/hexanes); *R<sub>f</sub>* 0.30 (EtOAc);  $[\alpha]_D^{24} +73.0$  (*c* 1.0, CHCl<sub>3</sub>); IR (film/NaCl)  $\nu_{\max}$  2990, 2945, 1780, 1757, 1712, 1461, 1390, 1318, 1271, 1205, 1155, 1096, 1045, 1026, 983, 958, 877, 849, 740 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  4.96 (ddd, *J* = 3.4<sub>6</sub>, 7.0<sub>3 $\alpha$</sub> , 8.1<sub>3 $\beta$</sub>  Hz, 1 H, HC-2'), 4.83 (dd, *J* = 5.4<sub>6</sub>, 6.4<sub>3 $\alpha$</sub>  Hz, 1 H, HC-6a), 4.61 (d, *J* = 6.5<sub>6 $\alpha$</sub>  Hz, 1 H, HC-3a), 4.25 (dd, *J* = 3.4<sub>2</sub>, 5.3<sub>6 $\alpha$</sub>  Hz, 1 H, HC-6), 3.79 (s, 3 H, OMe), 2.66 (ddd, *J* = 4.8<sub>3 $\beta$</sub> , 10.7<sub>3 $\alpha$</sub> , 18.0<sub>4 $\alpha$</sub>  Hz, 1 H, HHC-4' $\beta$ ), 2.55 (ddd, *J* = 8.3<sub>3 $\alpha$</sub> , 10.6<sub>3 $\beta$</sub> , 18.4<sub>4 $\beta$</sub>  Hz, 1 H, HHC-4' $\alpha$ ), 2.43 (dddd, *J* = 4.8<sub>4 $\beta$</sub> , 8.2<sub>2</sub>, 10.6<sub>4 $\alpha$</sub> , 13.2<sub>3 $\alpha$</sub>  Hz, 1 H, HHC-3' $\beta$ ), 2.26 (dddd, *J* = 7.0<sub>2</sub>, 8.2<sub>4 $\alpha$</sub> , 10.7<sub>4 $\beta$</sub> , 13.5<sub>3 $\beta$</sub>  Hz, 1 H, HHC-3' $\alpha$ ), 1.46 (s, 3 H), 1.36 (s, 3 H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  176.4 (s, C-5'), 165.6 (s, C-4), 113.5 (s, C-2), 77.6 (d, C-2'), 74.5 (d, C-3a), 71.5 (d, C-6a), 61.8 (q, OCH<sub>3</sub>), 59.2 (d, C-6), 27.9 (t, C-4'), 26.5 (q), 25.3 (q), 23.5 (t, C-3'); HRMS-ESI calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>6</sub>Na [M+Na]<sup>+</sup>: 294.09484, found: 294.09464.

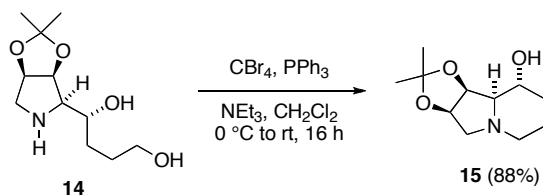
Analytical Data for **13**: white needles; mp 132-134 °C (EtOAc/hexanes); *R<sub>f</sub>* 0.40 (EtOAc);  $[\alpha]_D^{24} +56.7$  (*c* 2.1, CHCl<sub>3</sub>); IR (film/NaCl)  $\nu_{\max}$  2989, 2941, 1781, 1720, 1214, 1183, 1154, 1100, 1029, 920 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  4.77 (ddd, *J* = 3.1<sub>6</sub>, 7.0<sub>3 $\beta$</sub> , 9.7<sub>3 $\alpha$</sub>  Hz, 1 H, HC-2'), 4.63 (d, *J* = 6.4<sub>6 $\alpha$</sub>  Hz, 1 H, HC-3a), 4.50 (d, *J* = 6.2<sub>3 $\alpha$</sub>  Hz, 1 H, HC-6a), 3.87 (d, *J* = 3.2<sub>2</sub> Hz, 1 H, HC-6), 3.83 (s, 3 H, OMe), 2.65 (dd, *J* = 3.5<sub>3 $\beta$</sub> , 10.2<sub>3 $\alpha$</sub> , 18.4<sub>4 $\alpha$</sub>  Hz, 1 H, HHC-4' $\beta$ ), 2.64 (d, *J* = 8.4<sub>3 $\beta$</sub> , 10.2<sub>3 $\alpha$</sub> , 18.4<sub>4 $\beta\alpha$</sub>  Hz, 1 H, HHC-4' $\alpha$ ), 2.43 (dddd, *J* = 5.3<sub>4 $\beta$</sub> , 7.4<sub>2</sub>, 7.4<sub>4 $\alpha$</sub> , 13.9<sub>3 $\alpha$</sub>  Hz, 1 H, HHC-3' $\beta$ ), 2.13 (dddd, *J* = 10.0<sub>2</sub>, 10.0<sub>4 $\alpha$</sub> , 10.0<sub>4 $\alpha$</sub> , 13.2<sub>3 $\beta$</sub>  Hz, 1 H, HHC-3' $\alpha$ ), 1.45 (s, 3 H), 1.36 (s, 3 H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  175.3 (s, C-5'), 165.0 (s, C-4), 113.0 (s, C-2), 76.2 (d), 74.5 (d), 71.6 (d), 63.9 (d), 62.3 (q), 28.4 (t), 27.1 (q), 25.5 (q), 24.0 (t); HRMS-ESI calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>6</sub> [M+H]<sup>+</sup>: 272.11286, found: 272.11279.

**(3a'S,6a'R,4'R,1R)-1-(2',2'-Dimethyl-tetrahydro-[1',3']dioxolo[4,5-c]pyrrol-4'-yl)-butane-1,4-diol (14).**



To a stirred solution of **12** (386.7 mg, 1.427 mmol) in 1,4-dioxane (20 mL) at room temperature was added  $\text{LiAlH}_4$  (542 mg, 14.3 mmol) portionwise. Upon completion of addition, the reaction mixture was heated to reflux for 16 h, then cooled to room temperature, sequentially quenched with saturated aqueous  $\text{Na}_2\text{SO}_4$  (0.5 mL), aqueous  $\text{NaOH}$  (0.5 mL, 1 M) and  $\text{Et}_2\text{O}$  (20 mL) then stirred at 40 °C for 2 h. The mixture was then filtered through a pad of Celite 521, the filtrates reserved and the filter cake itself placed in a Soxhlet apparatus and extracted with  $\text{Et}_2\text{O}$  for 24 h. After cooling, the ethereal extracts and initial filtrates were combined and concentrated, and the residue purified by flash chromatography on silica gel ( $\text{NH}_3$ - $\text{MeOH}/\text{CH}_2\text{Cl}_2$ , 1:20) to afford **14** (273.5 mg, 85%): colorless oil;  $R_f$  0.19 ( $\text{NH}_3$ - $\text{MeOH}/\text{CH}_2\text{Cl}_2$ , 1:15);  $[\alpha]_D^{24}$  -48.4 ( $c$  1.8,  $\text{CHCl}_3$ ); IR (film/ $\text{NaCl}$ )  $\nu_{\text{max}}$  3323, 2982, 2934, 2868, 1444, 1374, 1271, 1206, 1163, 1039, 980, 907, 518  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  4.72 (dd,  $J = 4.2, 5.5$  Hz, 1 H), 4.67 (dd,  $J = 3.9, 5.6$  Hz, 1 H), 3.85 (ddd,  $J = 3.1, 5.5, 8.6$  Hz, 1 H, HC-1), 3.69-3.60 (m, 2 H,  $\text{H}_2\text{C}$ -4), 3.12 (d,  $J = 13.5$  Hz, 1 H,  $\text{HHC}$ -6'), 3.09-2.81 (bs, 3 H, OH, NH), 2.64-2.57 (m, 2 H, HC-4',  $\text{HHC}$ -6'), 1.85-1.65 (m, 4 H,  $\text{H}_2\text{C}$ -2,  $\text{H}_2\text{C}$ -3), 1.45 (s, 3 H), 1.29 (s, 3 H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  110.9 (s, C-2'), 82.0 (d), 81.9 (d), 71.1 (d), 66.8 (d), 62.4 (t, C-4), 52.4 (t, C-6'), 32.5 (t), 29.4 (t), 25.7 (q), 23.5 (q); HRMS-ESI calcd for  $\text{C}_{11}\text{H}_{22}\text{NO}_4$   $[\text{M}+\text{H}]^+$ : 232.15433, found: 232.15428.

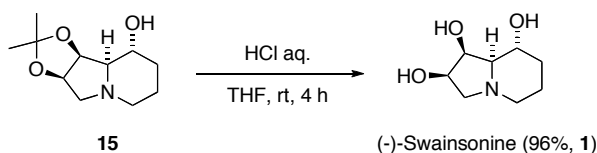
**(3aR,9R,9aR,9bS)-2,2-Dimethyl-octahydro-[1,3]dioxolo[4,5-a]indolizin-9-ol (15).**



To a stirred, cooled (0 °C) solution of **14** (44.0 mg, 0.190 mmol) in  $\text{CH}_2\text{Cl}_2$  (6 mL) was added carbon tetrabromide (143 mg, 0.430 mmol). A solution of triphenylphosphine (180 mg, 0.69 mmol) and triethylamine (140  $\mu\text{L}$ , 1.0 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) was then added

to the reaction at a rate of 1.0 mL/h. After 4 h, the reaction was quenched with NH<sub>3</sub>-MeOH (5 mL), concentrated and the residue purified by flash chromatography on silica gel (NH<sub>3</sub>-MeOH/CH<sub>2</sub>Cl<sub>2</sub>, 1:30) to afford **15** (35.5 mg, 88%): white needles; mp 103-104 °C (hexanes) [*lit.* 100-103 °C<sup>4</sup>]; *R<sub>f</sub>* 0.40 (NH<sub>3</sub>-MeOH/CH<sub>2</sub>Cl<sub>2</sub>, 1:15); [ $\alpha$ ]<sub>D</sub><sup>24</sup> -52.9 (*c* 0.54, CHCl<sub>3</sub>) [*lit.* [ $\alpha$ ]<sub>D</sub><sup>24</sup> -72.8 (*c* 0.43, CHCl<sub>3</sub>)<sup>5</sup>]; IR (film/NaCl)  $\nu_{\max}$  3190, 2980, 2941, 2857, 2792, 1371, 1345, 1260, 1211, 1173, 1144, 1114, 1069, 1027, 1004, 928, 903, 867, 866, 839 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  4.71 (dd, *J* = 4.7, 6.2 Hz, 1 H, HC-9b), 4.62 (dd, *J* = 4.3, 6.2 Hz, 1 H, HC-3a), 3.84 (m, 1 H, HC-9), 3.16 (d, *J* = 10.7 Hz, 1 H, HHC-4 $\alpha$ ), 2.99 (d, *J* = 10.6 Hz, 1 H, HHC-6), 2.13 (dd, *J* = 4.2, 10.7 Hz, 1 H, HHC-4 $\beta$ ), 2.05 (dddd, *J* = 3.8, 3.8, 7.5, 7.5 Hz, 1 H, HHC-8), 2.03-1.99 (m, 1 H, OH), 1.86 (ddd, *J* = 4.0, 10.8, 10.8 Hz, 1 H, HHC-6), 1.75-1.60 (m, 3 H, H<sub>2</sub>C-7, HC-9a), 1.51 (s, 3 H), 1.34 (s, 3 H), 1.26-1.18 (m, 1 H, HHC-8); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  111.3 (s, C-2), 79.1 (d), 78.2 (d), 73.6 (d), 67.5 (d), 59.8 (t), 51.6 (t), 33.0 (t), 25.9 (q), 24.7 (q), 24.1 (t); HRMS-ESI calcd for C<sub>11</sub>H<sub>20</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 214.14377, found: 214.14373.

**(1*S*,2*R*,8*R*,8*aR*)-1,2,8-Trihydroxyindolizidine [(-)-Swainsonine (**1**)].**



To a stirred solution of **15** (28.9 mg, 0.136 mmol) in THF (2.5 mL) was added HCl (6 M, 2.5 mL, 15 mmol). After stirring 4 h, the reaction was concentrated under reduced pressure and the residue then purified by ion-exchange chromatography on Dowex 1X8-50 resin (OH form) eluting with H<sub>2</sub>O to afford (-)-swainsonine (**1**) (23.0 mg, 96%): white crystals; mp 143-144 °C dec (MeOH/Et<sub>2</sub>O) [*lit.* 144-145 °C dec (sublimation),<sup>6</sup> 139-142 °C (MeOH/Et<sub>2</sub>O),<sup>7</sup> 138-140 °C dec (sublimation)<sup>8</sup>]; *R<sub>f</sub>* 0.51 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH/conc. NH<sub>3</sub>OH, 1:1:0.3); [ $\alpha$ ]<sub>D</sub><sup>24</sup> -86.0 (*c* 0.1, MeOH) [*lit.* [ $\alpha$ ]<sub>D</sub><sup>25</sup> -87.2 (*c* 2.1, MeOH),<sup>9</sup> [ $\alpha$ ]<sub>D</sub><sup>23</sup> -74.0 (*c* 0.98, MeOH),<sup>10</sup> [ $\alpha$ ]<sub>D</sub><sup>27</sup> -85.2 (*c* 0.50, MeOH)<sup>11</sup>]; IR (film/ZnSe)  $\nu_{\max}$  3367, 2943, 2885, 2806, 1346, 1318, 1257, 1221, 1149, 1126, 1105, 1074, 1024, 1005, 938, 895 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O)  $\delta$  4.39 (ddd, *J* = 2.5, 6.2, 8.2 Hz, 1 H, HC-2), 4.29 (dd, *J* = 3.7, 6.0 Hz, 1 H, HC-1), 3.84 (ddd, *J* = 4.6, 9.6, 11.0 Hz, 1 H, HC-8), 2.97-2.91 (m, 1 H, HHC-5), 2.92 (dd, *J* = 2.4, 11.0 Hz, 1 H, HHC-3), 2.59 (dd, *J* = 7.9, 11.0 Hz, 1 H, HHC-3), 2.10 (dddd, *J* = 3.3, 3.3, 3.3, 11.4 Hz, 1 H, HHC-7), 1.99 (ddd, *J* = 2.8, 12.4, 12.4 Hz, 1 H, HHC-3), 1.96 (dd, *J* = 3.7, 9.5 Hz, 1 H, HC-8a), 1.81-1.72 (m, 1 H, HHC-6), 1.56



(dddd,  $J = 4.2, 4.2, 13.7, 13.7, 13.7$  Hz, 1 H, *HHC-6*), 1.27 (dddd,  $J = 4.5, 13.0, 13.0, 13.0$  Hz, 1 H, *HHC-7*);  $^{13}\text{C}$  NMR (125 MHz,  $\text{D}_2\text{O}$ )  $\delta$  72.4 (d, C-8a), 69.2 (d, C-1), 68.6 (d, C-2), 66.0 (d, C-8), 60.2 (t, C-3), 51.2 (t, C-5), 32.1 (t, C-7), 22.8 (t, C-6); HRMS-ESI calcd for  $\text{C}_8\text{H}_{16}\text{O}_3\text{Si}$   $[\text{M}+\text{H}]^+$ : 174.1130, found: 174.1122.

## 1.6 <sup>1</sup>H and <sup>13</sup>C NMR Chemical Shifts for Natural and Synthetic (-)-Swainsonine

Position	Natural (-)-Swainsonine ( <b>1</b> ) <sup>12</sup>		Synthetic (-)-Swainsonine [Pearson] <sup>13</sup>		Synthetic (-)-Swainsonine [Bowen]	
	<sup>1</sup> H NMR <sup>a</sup> (ppm)	<sup>13</sup> C NMR <sup>b</sup> (ppm)	<sup>1</sup> H NMR <sup>c</sup> (ppm)	<sup>13</sup> C NMR <sup>d</sup> (ppm)	<sup>1</sup> H NMR <sup>e</sup> (ppm)	<sup>13</sup> C NMR <sup>f</sup> (ppm)
1	4.44-4.18 (m)	69.4	4.29 (dd, <i>J</i> = 3.5, 5.8 Hz)	69.4	4.29 (dd, <i>J</i> = 3.7, 6.0 Hz)	69.2 (d)
2	4.44-4.18 (m)	68.8	4.39 (ddd, <i>J</i> = 2.8, 5.9, 8.0 Hz)	68.9	4.39 (ddd, <i>J</i> = 2.5, 6.2, 8.2 Hz)	68.6 (d)
3 $\alpha$	2.89 (dd)	60.4	2.97 (dd, <i>J</i> = 2.8, 11.3 Hz)	60.3	2.92 (dd, <i>J</i> = 2.4, 11.0 Hz)	60.2 (t)
3 $\beta$	2.53 (dd)		2.70 (dd, <i>J</i> = 8.1, 11.3 Hz)		2.59 (dd, <i>J</i> = 7.9, 11.0 Hz)	
5 $\alpha$	2.14-0.98 (m)	51.4	2.04-2.15 (m)	51.6	1.99 (ddd, <i>J</i> = 2.8, 12.4, 12.4 Hz)	51.2 (t)
5 $\beta$	2.89 (dd)		3.0 (m)		2.97-2.91 (m)	
6 $\alpha$	2.14-0.98 (m)	22.9	1.55 (tq, <i>J</i> = 4.1, 13.2 Hz)	22.9	1.56 (dddd, <i>J</i> = 4.2, 4.2, 13.7, 13.7, 13.7 Hz)	22.8 (t)
6 $\beta$	2.14-0.98 (m)		1.76 (m)		1.81-1.72 (m)	
7 $\alpha$	2.14-0.98 (m)	32.2	1.28 (qd, <i>J</i> = 4.5, 12.3 Hz)	32.2	1.27 (dddd, <i>J</i> = 4.5, 13.0, 13.0, 13.0 Hz)	32.1 (t)
7 $\beta$	2.14-0.98 (m)		2.04-2.15 (m)		(dddd, <i>J</i> = 3.3, 3.3, 3.3, 11.4 Hz)	
8	3.80 (ddd)	66.1	3.84 (app td, <i>J</i> = 4.6, 10.3 Hz)	66.0	3.84 (ddd, <i>J</i> = 4.6, 9.6, 11.0 Hz)	66.0 (d)
8a	2.14-0.98 (m)	72.6	2.04-2.15 (m)	72.6	1.96 (dd, <i>J</i> = 3.7, 9.5 Hz)	72.4 (d)

<sup>a</sup>(90 MHz, D<sub>2</sub>O). <sup>b</sup>(22.5 MHz, D<sub>2</sub>O). <sup>c</sup>(300 MHz, D<sub>2</sub>O). <sup>d</sup>(90 MHz, D<sub>2</sub>O). <sup>e</sup>(500 MHz, D<sub>2</sub>O). <sup>f</sup>(125 MHz, D<sub>2</sub>O).

## 1.7 References.

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