Supporting Information

Total Synthesis of the Neotropical Poison-Frog Alkaloid (-)-205B.

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Experimental

I. Materials and Methods

Except as otherwise indicated, reactions were carried out under an argon atmosphere in flame- or oven-dried glassware. In aqueous work-up, all organic solutions were dried over sodium sulfate or magnesium sulfate, and filtered prior to rotary evaporation at water aspirator pressure. All solvents were freshly distilled and dried by standard techniques just before use. Diethyl ether and THF were distilled from sodium/benzophenone. After storing over 4A molecular sieves for several days, HPLC grade dichloromethane was used without further purification. Hexamethylphosphoramide (HMPA), and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU) were freshly distilled from calcium hydride under vacuum. Triethylamine was distilled from calcium hydride and stored over potassium hydroxide or sodium hydroxide. TMSCl was distilled and stored over 4A molecular sieves activated with microwave. Anhydrous 1,2-dimethoxyethane and benzene were purchased from Aldrich and used without further purification. HPLC grade methanol was used without further purification. 5% sodium amalgam and *t*-BuLi were purchased from Aldrich. Reactions were monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck pre-coated silica gel plates (Kieselgel 60F₂₅₄, Merck). Spots were detected by viewing under a UV light, putting into an iodine chamber, or coloring with charring after dipping in an anisaldehyde solution composed of acetic acid, sulfuric acid, and MeOH. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by Silicycle and Sorvent technologies. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ¹H and ¹³C spectra were recorded on a Bruker AM-500 spectrometer. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.26 for ¹H and δ 77.0 for ¹³C) or benzene (δ 7.16 for ¹H and δ 128.39 for ¹³C). IR spectra were measured as neat oils on a Perkin-Elmer Model 1600 FTIR. Optical rotations were measured on a Jasco polarimeter. High resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Service Center.

II. Procedure

Aziridine (+)-8. To a suspension of (D)-serine methyl ester hydrochloride (-)-7 (4.76 g, 30.6 mmol) in CH_2Cl_2 (50 mL) at 0 °C were added dropwise triethyl amine (8.60 mL, 61.2 mmol, 2.0 equiv) and a solution of *p*-toluene sulfonyl chloride (5.83 g, 30.6 mmol, 1.0 equiv) in CH_2Cl_2 (60 mL). After 12 h at 0 °C, the suspended white precipitate was filtered off under suction, and the filtrate was evaporated in *vacuo* to yield a white solid. The solid was then dissolved in ethyl acetate (50 mL), washed with NaHCO_3 (1.0 M aq. 40 mL), citric acid (10% w/v aq. 40 mL) and water (40 mL). Then, the organic layer was dried over Na_2SO_4 , filtered, and concentrated *in vacuo* to yield a white powder. Recrystallization from ethyl acetate/hexanes (1/1) provided the *N*-tosyl serine methyl ester (7.49 g, 27.2 mmol, 89%): R_f 0.70 (ethyl acetate); mp 92-93 °C; $[\alpha]_D^{20}$ -11.6° (c 1.00, CHCl_3); IR (film) 3496 (s), 3270 (s), 2950 (m), 1747 (s), 1598 (m), 1435 (m), 1332 (s), 1160 (s), 1092 (m), 818 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.74 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 5.63 (d, J = 7.5 Hz, 1H), 4.01-3.97 (m, 1H), 3.89 (d, J = 3.7 Hz, 2H), 3.62 (s, 3H), 2.42 (s, 3H), 2.34 (br s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 170.10, 143.93, 136.44, 129.78, 127.22, 63.69, 57.58, 52.92, 21.52; high resolution mass spectrum (CI) m/z 274.0744 [(M+H) $^+$; calcd for $\text{C}_{11}\text{H}_{16}\text{NO}_5\text{S}$: 274.0749].

To a solution of the *N*-tosyl serine methyl ester (2.00 g, 7.31 mmol) in THF (10 mL) at 0 °C were added PPh_3 (2.11 g, 8.04 mmol, 1.10 equiv) and diethyl azodicarboxylate (1.27 mL, 8.04 mmol, 1.10 equiv) and the resulting mixture was warmed to ambient temperature, stirred for 15 h and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:3) as eluent, provided aziridine (+)-8 (1.71 g, 6.70 mmol, 92%) as a pale yellow oil: R_f 0.60 (1/1 ethyl acetate/hexanes); $[\alpha]_D^{20}$ +51.3° (c 1.00, CHCl_3); IR (film) 3031(w), 2955 (w), 1748 (s), 1597 (m), 1440 (m), 1394 (m), 1331 (s), 1231 (s), 1163 (s), 1094 (m), 907 (s), 780 (m), 691 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 3.74 (s, 3H), 3.34 (dd,

$J = 7.1, 4.1$ Hz, 1H), 2.76 (d, $J = 7.1$ Hz, 1H), 2.56 (d, $J = 4.1$ Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.22, 145.24, 134.08, 129.87, 128.22, 52.85, 35.71, 31.99, 21.67; high resolution mass spectrum m/z 278.0466 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_4\text{SNa}$: 278.0463].

Ketone (+)-9. To a solution of (+)-**8** (3.10 g, 12 mmol) in THF (25 mL) at -78 °C was added MeLi (1.6 M in ether, 8.0 mL, 1.05 equiv) dropwise over 5 min. After 10 min, saturated NH_4Cl aqueous solution (10 mL) was added at -78 °C. The mixture was poured into a separatory funnel and extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo* to yield a white solid. Recrystallization from ethyl acetate/hexanes (1/5) and flash chromatography of the residue on silica gel, using ethyl acetate-hexanes (1:2) as eluent, provided ketone (+)-**9** (2.65 g, 11.1 mmol, 92%) as a white solid: R_f 0.50 (ethyl acetate/hexanes 1/1); mp 93 °C; $[\alpha]_D^{20} +47.3^\circ$ (c 1.00, CHCl_3); IR (film) 3102 (w), 3034 (w), 1705 (s), 1597 (w), 1492 (w), 1355 (m), 1318 (s), 1255 (m), 1206 (m), 1153 (s), 913 (s), 819 (s), 720 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.83 (d, $J = 8.3$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 3.28 (dd, $J = 7.4, 4.1$ Hz, 1H), 2.79 (d, $J = 7.4$ Hz, 1H), 2.49 (d, $J = 4.1$ Hz, 1H), 2.46 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 201.35, 145.33, 133.99, 129.93, 128.15, 41.97, 31.83, 25.84, 21.66; high resolution mass spectrum m/z 240.0702 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{11}\text{H}_{14}\text{NO}_3\text{S}$: 240.0694].

Aziridine (+)-4. To a solution of ketone (+)-**9** (2.00 g, 8.36 mmol) and 1,2-bis (trimethylsilyloxy)ethane (6.2 mL, 24.9 mmol, 2.98 equiv) in CH_2Cl_2 (25 mL) at 0 °C was added trimethylsilyl triflate (0.2 mL, 1.0 mmol, 0.12 equiv). After being stirred at 0 °C for 24 h, the mixture was poured into a sat'd aqueous NaHCO_3 solution (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , filtered,

and concentrated *in vacuo*. Flash chromatography of the residue on silica gel, using ethyl acetate-hexanes (1:2) as eluent, provided aziridine (+)-**4** (1.76 g, 6.22 mmol, 74%) as a white solid. Further purification was done by recrystallization from hexanes/ether (5/1) to afford 1.56 g (5.51 mmol, 66%): R_f 0.3 (ethyl acetate/hexanes 1/2); mp 42 °C; $[\alpha]_D^{20} +49.0^\circ$ (c 1.00, CHCl_3); IR (film) 2986 (m), 1597 (m), 1449 (w), 1380 (m), 1325 (s), 1162 (s), 1041 (s), 941 (s), 725 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 3.91-3.80 (m, 3H), 3.71-3.66 (m, 1H), 2.90 (dd, J = 7.0, 4.5 Hz, 1H), 2.56 (d, J = 7.0 Hz, 1H), 2.45 (s, 3H), 2.29 (d, J = 4.5 Hz, 1H), 1.31 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.63, 134.83, 129.62, 128.18, 105.85, 65.84, 65.25, 43.83, 29.71, 22.92, 21.63; high resolution mass spectrum m/z 284.0952 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{13}\text{H}_{18}\text{NO}_4\text{S}$: 284.0957].

Aldehyde (-)-10. To a solution of commercial ethyl (*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate (5.00 g, 25.0 mmol) in ethanol (40 mL) was added 2M HCl (20 mL) at ambient temperature. After 2 h, the reaction mixture was cooled to 0 °C and NaHCO_3 (4.0 g) was added slowly. The resulting suspensions were filtered, and the filtrate was concentrated *in vacuo* to afford an oil accompanied by precipitates which were removed by filtration through a Celite pad. The Celite pad was rinsed with EtOAc and the combined organic solution was concentrated to give a crude diol (4.00 g), which was used without further purification.

A suspension of the above crude diol (4.00 g) and Pd/C (5% w/w, 0.100 g) in ethanol (20 mL) was hydrogenated at atmospheric pressure and ambient temperature. After being stirred overnight, the mixture was filtered through celite. The Celite pad was rinsed with EtOAc and the combined organic solution was concentrated to give a hydrogenated diol (4.00 g), which was used without further purification. The crude NMR of the diol matched the reported.^{9b}

To a solution of the diol (2.65 g) in CH_2Cl_2 (30 mL) at 0 °C were added imidazole (6.60 g, 96.9 mmol), DMAP (0.100 g, 0.818 mmol) and TBSCl (7.40 g, 49.1 mmol). After being stirred

overnight, the mixture was poured into saturated aqueous NH_4Cl (50 mL) and extracted with CH_2Cl_2 (3 X 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:20) as eluent, provided the TBS protected diol (6.16 g, 15.8 mmol, 97% yield over 3 steps) as a colorless oil: R_f 0.80 (4/1 hexanes/ethyl acetate); $[\alpha]_D^{20}$ -20.5° (c 1.00, CHCl_3); IR (film) 2954 (s), 2858 (s), 1739 (s), 1470 (s), 1364 (m), 1254 (s), 1173 (s), 1080 (s), 835 (s), 777 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.13 (q, $J = 7.1$ Hz, 2H), 3.73-3.70 (m, 1H), 3.47 (ABX, $J_{AB} = 10.0$, $J_{AX} = 6.6$, $J_{BX} = 5.2$, $\Delta\nu_{AB} = 70.7$ Hz, 2H), 2.40-2.36 (m, 2H), 1.96-1.90 (m, 1H), 1.74-1.68 (m, 1H), 1.26 (t, $J = 7.1$ Hz, 3H), 0.89 (s, 9H), 0.89 (s, 9H), 0.061 (s, 6H), 0.052 (s, 3H), 0.048 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.79, 71.97, 67.05, 60.12, 29.83, 29.38, 25.94, 25.86, 18.32, 18.07, 14.21, -4.34, -4.85, -5.37, -5.42; high resolution mass spectrum m/z 391.2709 [(M+H) $^+$; calcd for $\text{C}_{19}\text{H}_{43}\text{O}_4\text{Si}_2$: 391.2700].

To a solution of the ester (3.20 g, 8.19 mmol) in CH_2Cl_2 (20 mL) at -78°C was added DIBAL-H (1.0 M in hexanes, 10 mL, 10 mmol, 1.2 equiv) dropwise. After 1 h at -78°C , the reaction was quenched by adding acetone (2 mL), then water (10 mL) and saturated Rochelle's solution (20 mL) were added. After 2 h at ambient temperature, the mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:10) as eluent, provided aldehyde (-)-**10** (2.78 g, 8.03 mmol, 98%) as a colorless oil: R_f 0.80 (4/1 hexanes/ethyl acetate); $[\alpha]_D^{20}$ -22.0° (c 1.00, CHCl_3); IR (film) 2954 (s), 2858 (s), 2712 (w), 1729 (s), 1471 (m), 1389 (w), 1255 (s), 1097 (s), 836 (s), 777 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 9.78 (s, 1H), 3.75-3.70 (m, 1H), 3.47 (ABX, $J_{AB} = 10.0$, $J_{AX} = 7.1$, $J_{BX} = 5.1$, $\Delta\nu_{AB} = 78.1$ Hz, 2H), 2.51-2.48 (m, 2H), 1.96-1.92 (m, 1H), 1.78-1.72 (m, 1H), 0.89 (s, 9H), 0.88 (s, 9H), 0.058 (s, 3H), 0.053 (s, 3H), 0.050 (s, 3H), 0.046 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.68, 71.84, 66.69, 39.42, 26.62, 25.93, 25.84, 18.31,

18.06, -4.37, -4.78, -5.37, -5.42; high resolution mass spectrum m/z 347.2451 $[(M+H)^+]$; calcd for $C_{17}H_{39}O_3Si_2$: 347.2438].

Alcohol (-)-11. The potassium *tert*-butoxide (2.58 g, 23.0 mmol, 2.1 equiv) was heated at 80 °C under high vacuum overnight to dry. Then, THF (10 mL) was added and cooled to -78 °C. *Cis*-2-butene (~ 3mL) was then added *via* cannula, followed by *n*-BuLi (1.6 M in hexane, 14.4 mL, 2.1 equiv) dropwise to produce an orange suspension. After 10 min at -45 °C, the reaction mixture was cooled to -78 °C and treated with (+)-Ipc₂BOMe (8.54 g, 27 mmol, 2.5 equiv) in THF (30 mL) dropwise over 15 min. After an additional 30 min at -78 °C, the colorless slurry was treated with BF₃·OEt₂ (3.7 mL, 29 mmol, 2.7 equiv) dropwise over 10 min, the aldehyde (-)-10 (3.76 g, 10.8 mmol) over 20 min and 2 x 5 mL THF rinse. After an additional 3 h, the pale yellow slurry was charged with 3N NaOH (20 mL) and allowed to slowly warm to ambient temperature. During this time, H₂O₂ (30% aq., 6 mL) was added in 1 mL portions to control bubbling and the resulting mixture was heated at reflux for 1 h. The biphasic solution was then cooled to ambient temperature and diluted with water (30 mL). The aqueous phase was then washed with ether (2 X 30 mL) and the combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Short flash chromatography on silica gel, using ethyl acetate-hexanes (1:10) as eluent, provided an 11:1 diastereomeric mixture of homoallylic alcohol **11** (3.52 g, 8.74 mmol, 81%). Additional flash chromatography on silica gel, using ethyl acetate-hexanes (1:20) as eluant, provided higher de alcohol (-)-11 (de > 90%, 1.6 g) and lower de alcohol (-)-11 (de < 78%, 1.9 g). Both were used in the subsequent steps since the isomers were easily separable by flash chromatography after removal of the two silyl groups in (+)-3: R_f 0.50 (9/1 hexanes/ethyl acetate); $[\alpha]_D^{20}$ -24.6° (c 3.20, CHCl₃); IR (film) 3426 (br s), 3078 (w), 2955 (s), 2858 (s), 1829 (w), 1639 (w), 1470 (s), 1362 (m), 1254 (s), 1101 (s), 835 (s), 776 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.79 (ddd, *J* = 17.6, 10.5, 7.5 Hz, 1H), 5.10-5.05 (m, 2H), 3.72-3.69 (m,

1H), 3.48 (ABX, $J_{AB} = 10.0$, $J_{AX} = 6.6$, $J_{BX} = 5.4$, $\Delta\nu_{AB} = 59.9$ Hz, 2H), 3.47 (ddd, $J = 9.3$, 5.3, 3.4 Hz, 1H), 2.30-2.26 (m, 1H), 1.67-1.54 (m, 3H), 1.51-1.43 (m, 1H), 1.04 (d, $J = 6.9$ Hz, 3H), 0.894 (s, 9H), 0.888 (s, 9H), 0.064 (s, 6H), 0.053 (s, 3H), 0.048 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.14, 115.03, 74.90, 72.97, 67.16, 43.55, 30.52, 29.27, 25.98, 25.91, 18.37, 18.14, 14.36, -4.29, -4.66, -5.32, -5.36; high resolution mass spectrum m/z 425.2864 $[(M+\text{Na})^+]$; calcd for $\text{C}_{21}\text{H}_{46}\text{O}_3\text{Si}_2\text{Na}$: 425.2883].

Diol (-)-12. To a solution of alcohol (-)-11 (2.50 g, 6.21 mmol) in CH_2Cl_2 (25 mL) at 0 °C were added imidazole (0.45 g, 6.6 mmol, 1.5 equiv), DMAP (0.100 g, 0.818 mmol, 0.13 equiv) and BPSCI (2.00 mL, 7.64 mmol, 1.2 equiv). After stirring for 20 h at ambient temperature, the mixture was poured into saturated aqueous NH_4Cl (30 mL) and extracted with CH_2Cl_2 (3 X 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was dissolved in $\text{MeOH}/\text{CH}_2\text{Cl}_2$ (15/5 mL) and treated with CSA (0.300g, 1.29 mmol, 0.2 equiv) at ambient temperature. After 4 h, triethyl amine (0.50 mL) was added and the mixture was concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:1) as eluant, provided diol (-)-12 (2.26 g, 5.48 mmol, 88% yield over 2 steps) as a colorless oil: R_f 0.30 (1/1 hexanes/ethyl acetate); $[\alpha]_D^{20}$ -7.20 (c 1.00, CHCl_3); IR (film) 3379 (br s), 3071 (m), 2957 (s), 2932 (s), 2858 (s), 1960 (w), 1895 (w), 1824 (w), 1640 (w), 1589 (w), 1471 (m), 1427 (m), 1109 (s), 1064 (s), 913 (m), 822 (m), 703 (s) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.70-7.67 (m, 4H), 7.44-7.41 (m, 2H), 7.39-7.36 (m, 4H), 5.97-5.91 (m, 1H), 5.02 (s, 1H), 5.00 (d, $J = 7.4$, 1H), 3.69 (q, $J = 5.1$ Hz, 1H), 3.34-3.29 (m, 1H), 3.29 (ABX, $J_{AB} = 10.9$, $J_{AX} = 7.4$, $J_{BX} = 2.9$, $\Delta\nu_{AB} = 90.33$ Hz, 2H), 2.40-2.36 (m, 1H), 1.65 (br s, 2H), 1.49-1.36 (m, 2H), 1.32-1.19 (m, 2H), 1.06 (s, 9H), 0.96 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 141.10, 136.09, 136.01, 134.74, 134.15, 129.59, 129.56, 127.47, 127.46, 114.15, 76.79, 72.12,

66.57, 42.41, 29.29, 28.69, 27.13, 19.59, 14.89; high resolution mass spectrum m/z 435.2331 [(M+Na)⁺; calcd for C₂₅H₃₆O₃SiNa: 435.2331].

Epoxide (-)-6. To a solution of diol (-)-12 (0.690 g, 1.67 mmol) in THF (30 mL) at 0 °C was added NaH (60% wt. in mineral oil, 0.20 g, 5.0 mol, 3.0 equiv). The resulting mixture was then warmed to ambient temperature and stirred for 40 min. The mixture was then cooled to 0 °C and *N*-(2,4,6-triisopropylbenzenesulfonyl)imidazole (0.587 g, 1.75 mmol, 1.05 equiv) was added in one portion. The reaction mixture was then allowed to warm to ambient temperature and stirred for 1 h. The reaction was quenched with water (30 mL) and extracted with Et₂O (3 X 50 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:20) as eluent, provided epoxide (-)-6 (0.650g, 1.65 mmol, 99% yield) as a colorless oil: *R*_f 0.60 (4/1 hexanes/diethyl ether); $[\alpha]_D^{20}$ -11.6° (*c* 3.07, CHCl₃); IR (film) 3048 (m), 2959 (s), 2859 (s), 1963 (w), 1895 (w), 1829 (w), 1640 (w), 1590 (w), 1468 (m), 1427 (m), 1108 (s), 915 (m), 703 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.71-7.69 (m, 4H), 7.45-7.36 (m, 6H), 5.95 (ddd, *J* = 17.3, 10.7, 6.7 Hz, 1H), 5.03-4.98 (m, 2H), 3.72-3.69 (m, 1H), 2.59-2.56 (m, 2H), 2.40-2.36 (m, 1H), 2.23 (dd, *J* = 3.8, 3.4 Hz, 1H), 1.56-1.44 (m, 3H), 1.38-1.32 (m, 1H), 1.08 (s, 9H), 0.96 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 140.90, 136.08, 135.99, 134.54, 134.07, 129.57, 129.53, 127.45, 114.17, 76.50, 51.96, 46.82, 42.30, 29.48, 28.01, 27.13, 19.57, 14.86; high resolution mass spectrum m/z 417.2233 [(M+Na)⁺; calcd for C₂₅H₃₄O₂SiNa: 417.2226].

Dithiane (+)-3: A solution of 2-TBS-1,3-dithiane (**5**) (0.086 g, 0.367 mmol, 1.20 equiv) in Et₂O (1.5 mL) was cooled to –78 °C and treated with a 1.7 M solution of *t*-BuLi (0.22 mL, 0.374 mmol, 1.30 equiv) dropwise via syringe. The resulting solution was warmed to –45 °C over 1 h and then cooled to –78 °C. The solution of epoxide (–)-**6** (0.120 g, 0.304 mmol) in Et₂O (1.5 mL) was added dropwise to the reaction mixture at –78 °C via cannula. The resulting solution was warmed to –20 °C over 0.5 h, stirred an additional 1.5 h at –20 °C and cooled to –78 °C. A solution of aziridine (+)-**4** (0.112 g, 0.395 mmol, 1.30 equiv) in THF (4 mL) and DME (0.10 mL) was added dropwise to the reaction mixture at –78 °C via cannula. After 10 min, the reaction vessel was transferred to a ice bath and stirred for 2 h at 0 °C. The resulting mixture was poured into saturated aqueous NH₄Cl (5 mL) and extracted with Et₂O (3 X 10 mL). The combined organic layers were washed with brine (5 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (hexanes/ethyl acetate, 20/1 → 3/1) provided (+)-**3** (0.148 g, 0.163 mmol, 53% yield) as a pale yellow oil: R_f 0.4 (3/1 hexanes/ethyl acetate); $[\alpha]_D^{20} +7.50^\circ$ (*c* 1.00, CHCl₃); IR (film) 3207 (m, br), 3070 (w), 2956 (s), 2932 (s), 2892 (s), 2857 (s), 1640 (w), 1599 (w), 1471 (m), 1427 (m), 1323 (m), 1255 (m), 1153 (s), 1107 (s), 1090 (s), 1043 (s), 919 (m), 837 (m), 756 (m), 704 (s) cm^{–1}; ¹H NMR (500 MHz, CDCl₃) δ 7.72–7.69 (m, 6H), 7.42–7.35 (m, 6H), 7.20 (d, *J* = 8.1 Hz, 2H), 6.34 (d, *J* = 3.5 Hz, 1H), 5.95 (ddd, *J* = 17.3, 10.7, 7.0 Hz, 1H), 5.00–4.97 (m, 2H), 4.07 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.97–3.89 (m, 2H), 3.75–3.68 (m, 2H), 3.66–3.61 (m, 2H), 2.86 (ddd, *J* = 14.4, 8.4, 2.7 Hz, 1H), 2.73 (ddd, *J* = 14.1, 8.5, 2.6 Hz, 1H), 2.62 (ddd, *J* = 14.3, 7.7, 2.9 Hz, 1H), 2.51–2.47 (m, 1H), 2.46 (dd, *J* = 15.6, 10.8 Hz, 1H), 2.38 (s, 3H), 2.27–2.30 (m, 2H), 2.25 (dd, *J* = 15.0, 9.8 Hz, 1H), 2.0–1.87 (m, 2H), 1.86 (d, *J* = 15.3 Hz, 1H), 1.62–1.50 (m, 2H), 1.44–1.38 (m, 1H), 1.27–1.21 (m, 1H), 1.11 (s, 3H), 1.05 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.10 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 141.77, 141.64, 140.68, 136.06, 135.99, 134.84, 134.21, 129.52, 129.49, 128.64, 127.49, 127.46, 126.87, 114.08, 110.30, 77.62, 72.26, 64.48, 64.17, 54.50, 51.92, 41.94, 40.08, 37.07, 34.61, 29.54, 27.14, 26.27, 25.79, 25.36, 21.47, 19.66, 19.54, 18.23, 14.24, –2.88, –4.82; high resolution mass spectrum *m/z* 934.4049 [(M+Na)⁺; calcd for C₄₈H₇₃NO₆NaSi₂S₃: 934.4036].

Indolizidine (+)-13. To a solution of (+)-**3** (0.550 g, 0.603 mmol) in THF (15 mL) was added tetrabutyl ammonium fluoride (1.0 M in THF, 3.0 mL, 5 equiv) at ambient temperature. The mixture was stirred for 20 h, then poured into saturated aqueous NaHCO₃ solution (10 mL) and extracted with Et₂O (4 X 10 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:1) as eluent, provided a diol (0.329 g, 0.588 mmol, 98% yield) as a colorless oil: R_f 0.40 (1/1 hexanes/ethyl acetate); $[\alpha]_D^{20}$ -7.6° (*c* 1.00, CHCl₃); IR (film) 3477(s, br), 3287 (s, br), 3161 (s, br), 2933 (s), 1764 (w), 1598 (w), 1441 (m), 1317 (s), 1237 (m), 1153 (s), 1093 (s), 1045 (s), 915 (m), 754 (m), 665 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 3.4 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 5.81-5.74 (m, 1H), 5.10 (br s, 1H), 5.07 (br s, 1H), 4.17-4.11 (m, 1H), 4.00 (dd, *J* = 9.5, 2.3 Hz, 1H), 3.94 (q, *J* = 6.8 Hz, 1H), 3.78-3.72 (m, 3H), 3.56 (ddd, *J* = 9.4, 5.2, 1.4 Hz, 1H), 2.96 (ddd, *J* = 13.7, 10.7, 2.5 Hz, 2H), 2.72 (ddd, *J* = 14.5, 5.4, 3.0 Hz, 1H), 2.65 (ddd, *J* = 14.3, 5.8, 2.9 Hz, 1H), 2.50 (dd, *J* = 16.0, 7.2 Hz, 2H), 2.39 (s, 3H), 2.36 (dd, *J* = 15.2, 10.0 Hz, 1H), 2.29 (q, *J* = 6.5 Hz, 1H), 2.08-2.04 (m, 1H), 1.95 (d, *J* = 15.2 Hz, 1H), 1.92-1.90 (m, 1H), 1.83-1.78 (m, 1H), 1.78-1.70 (m, 2H), 1.51-1.43 (m, 1H), 1.16 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 141.90, 140.60, 140.54, 128.75, 126.66, 115.59, 110.40, 75.50, 68.95, 64.64, 64.11, 55.08, 52.00, 44.01, 43.71, 36.51, 35.77, 30.83, 26.06, 25.54, 25.38, 21.47, 19.23, 14.39; high resolution mass spectrum *m/z* 582.2019 [(M+Na)⁺; calcd for C₂₆H₄₁NO₆NaS₃: 582.1994].

The diol (1.37 g, 2.45 mmol) was dissolved in THF (40 mL) and triethyl amine (2.10 mL, 14.9 mmol, 6.1 equiv) was added. The mixture was cooled to 0 °C and methanesulfonyl chloride (0.58 mL, 7.49 mmol, 3.0 equiv) was added dropwise. The solution was warmed to ambient temperature and stirred for 0.5 h. The resultant mixture was poured into water (30 mL) and

extracted with Et₂O (4 X 30 mL). The combined organic layers were washed with brine (30 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude mesylate was dissolved in MeOH (60 mL) and K₂CO₃ (1.50 g, 10.9 mmol, 4.43 equiv) was added. After the mixture was stirred for 12h at ambient temperature, Na₂HPO₄ (14 g, 99 mmol, 40 equiv) was added. Then, 5% Na-Hg (22 g, 48 mol, 20 equiv) was added in 3 portions (10, 6 and 6 g over 2 h) and the mixture was stirred for an additional 30 h. The mixture was filtered through celite and washed with EtOAc. Brine (30 mL) was added to the mixture, and the layers were separated. The aqueous layer was extracted with Et₂O (3 x 30 mL) and the combined organic layers were dried over MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:10) as eluent, afforded (+)-**13** (0.634 g, 1.72 mmol, 70% over 2 steps) as a white solid: R_f 0.60 (4/1 hexanes/ethyl acetate); mp 122 °C; $[\alpha]_D^{20} +53.0^\circ$ (c 1.00, CHCl₃); IR (film) 3074 (w), 2949 (s), 1636 (m), 1422 (m), 1379 (m), 1137 (m), 1049 (s) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.83-5.76 (m, 1H), 4.95 (ddd, *J* = 6.8, 1.9, 1.6 Hz, 1H), 4.92 (d, *J* = 1.6 Hz, 1H), 4.10-3.96 (m, 1H), 3.95-3.87 (m, 3H), 3.47-3.41 (m, 2H), 3.35 (dd, *J* = 11.2, 3.1 Hz, 1H), 3.09-3.05 (m, 1H), 3.01 (ddd, *J* = 14.3, 9.2, 3.2 Hz, 1H), 2.86-2.79 (m, 2H), 2.71 (ddd, *J* = 14.4, 7.1, 3.3 Hz, 1H), 2.58 (dt, *J* = 13.6, 2.9 Hz, 1H), 2.20 (dt, *J* = 12.9, 2.9 Hz, 1H), 2.03-1.96 (m, 2H), 1.76-1.70 (m, 2H), 1.61-1.55 (m, 2H), 1.37-1.26 (m, 2H), 1.32 (s, 3H), 0.99 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 144.14, 112.24, 111.92, 64.54, 64.18, 60.76, 57.17, 54.60, 49.59, 42.98, 37.53, 36.69, 29.91, 26.20, 26.03, 25.40, 22.76, 19.94, 14.23; high resolution mass spectrum *m/z* 370.1861 [(M+H)⁺; calcd for C₁₉H₃₂NO₂S₂: 370.1874].

Ketone (+)-2. To a solution of (+)-**13** (0.330g, 0.893 mmol) in acetone (10 mL) was added 2M HCl (10 mL) and the mixture was heated at reflux for 24 h. The mixture was then cooled to 0 °C and 30 mL ether and 20 mL water were added. NaHCO₃ (3 g) was added carefully at 0 °C with

stirring. The organic layer was separated and the aqueous layer was extracted with ether (3 X 20 mL). The combined organic layers were then dried over Na₂SO₄, filtered, and concentrated in *vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:7) as eluant, afforded (+)-**2** (0.240 g, 0.737 mmol, 83% yield) as a white solid: R_f 0.4 (4/1 hexanes/ethyl acetate); mp 97 °C, $[\alpha]_D^{20} +48.9^\circ$ (*c* 1.00, CHCl₃); IR (film) 3071 (w), 2955 (s), 1711 (s), 1637 (w), 1422 (m), 1350 (m), 1158 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.62 (ddd, *J* = 17.0, 10.6, 6.3 Hz, 1H), 4.95-4.91 (m, 2H), 4.03 (dd, *J* = 11.5, 2.6 Hz, 1H), 3.49-3.46 (m, 1H), 3.31-3.27 (m, 1H), 2.95 (ddd, *J* = 12.7, 9.3, 3.0 Hz, 1H), 2.87-2.79 (m, 2H), 2.74 (ddd, *J* = 14.4, 7.0, 3.2 Hz, 1H), 2.45 (dt, *J* = 13.1, 2.4 Hz, 1H), 2.33-2.29 (m, 2H), 2.22 (s, 3H), 2.06-1.96 (m, 2H), 1.85-1.80 (m, 2H), 1.73 (t, *J* = 2.7 Hz, 1H), 1.61-1.50 (m, 1H), 1.47 (t, *J* = 12.3 Hz, 1H), 1.43-1.38 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 209.51, 141.97, 113.71, 63.48, 60.44, 54.32, 48.93, 43.05, 39.20, 38.71, 30.30, 26.29, 26.29, 25.77, 25.42, 22.80, 14.26; high resolution mass spectrum *m/z* 326.1600 [(M+H)⁺; calcd for C₁₇H₂₈NOS₂: 326.1612].

(+)-**15**

Ketone (+)-15. To a solution of LiHMDS (1.0 M in THF, 0.29 mL, 1.5 equiv) in THF (3 mL) at -78 °C was added trimethylsilyl chloride (0.074 mL, 0.583 mmol, 3.0 equiv) and a solution of ketone (+)-**2** (63 mg, 0.194 mmol) in THF (2 mL). After 2 h at -78 °C, the reaction was quenched by addition of saturated NaHCO₃ aqueous solution (2 mL) and the mixture was allowed to warm to ambient temperature. The mixture was poured into water (5 mL) in a separatory funnel and extracted with ether (3 X 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄ and concentrated in *vacuo* to afford the crude enol ether. To a solution of the crude enol ether in benzene (150 mL) was added Grubbs 2nd generation catalyst (**14**) (16 mg, 0.019 mmol, 0.10 equiv). The reaction mixture was stirred at 65 °C overnight, then cooled to ambient temperature and concentrated in *vacuo*. Flash chromatography on silica gel

(hexanes/ethyl acetate, 10/1 -> 5/1 -> 2/1) afforded (+)-**15** (0.047 g, 0.158 mmol, 81% yield) as a white solid: R_f 0.25 (hexanes/ethyl acetate 1/1); mp 101 °C; $[\alpha]_D^{20} +93.5^\circ$ (c 1.00, CHCl_3); IR (film) 2951 (s), 1714 (s), 1424 (m), 1241 (m), 1144 (m) cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.98 (dd, J = 12.2, 3.0 Hz, 1H), 3.57-3.52 (m, 1H), 3.04 (ddd, J = 13.9, 10.6, 2.7 Hz, 1H), 2.91-2.83 (m, 2H), 2.74 (ddd, J = 14.2, 6.1, 3.0 Hz, 1H), 2.66 (ddd, J = 14.4, 5.8, 3.1 Hz, 1H), 2.47 (dd, J = 17.0, 4.5 Hz, 1H), 2.25 (dt, J = 13.5, 2.6 Hz, 1H), 2.10-2.00 (m, 4H), 1.98-1.84 (m, 3H), 1.83-1.73 (m, 1H), 1.64 (t, J = 12.7 Hz, 1H), 1.47-1.40 (m, 2H), 0.95 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 210.11, 63.06, 59.14, 54.64, 49.88, 45.81, 39.50, 35.88, 33.35, 29.18, 28.52, 26.22, 26.13, 25.93, 18.82; high resolution mass spectrum m/z 297.1221 $[(M)^+]$; calcd for $\text{C}_{15}\text{H}_{23}\text{NOS}_2$: 297.1221].

Alcohol (+)-16. To a mixture of methoxymethyl triphenylphosphonium chloride (0.356g, 1.04 mmol, 10 equiv) and potassium *tert*-butoxide (0.111 g, 0.989 mmol, 9.5 equiv) was added THF (7 mL) at ambient temperature. After 2 min, a solution of (+)-**15** (31 mg, 0.104 mmol) in THF (3 mL) was added dropwise via cannular. After 20min, water (1 mL) was added and the mixture was diluted with EtOAc (70 mL), washed with brine (2 X 5 mL) and dried over K_2CO_3 . The solvent was removed in *vacuo*. Quick flash chromatography on silica gel, using acetone-hexanes (1:1) as eluent, afforded a mixture (*ca* 4:3) of methyl enol ether containing some phosphine impurity. The mixture was then dissolved (without further purification) in THF (4 mL), cooled to 0 °C and pre-cooled 6 M HCl (4 mL) was added. After the reaction mixture was stirred for 24 h at 0 °C, saturated NaHCO_3 aqueous solution (40 mL) was added slowly. The resulting solution was extracted with ether (3 X 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in *vacuo* to afford the crude aldehyde. To a solution of the crude aldehyde in MeOH (5 mL) at 0 °C was added NaBH_4 (0.019 g, 0.50 mmol, 4.8 equiv). After 40 min, saturated NH_4Cl

aqueous solution (1 mL) was added and solvents were removed in *vacuo*. The residue was partitioned between ethyl acetate (50 mL) and water (5 mL) and the organic layer was separated. The aqueous layer was then extracted with ethyl acetate (2 X 5 mL), and the combined organic layers were dried over Na₂SO₄ and concentrated in *vacuo*. Purification by preparative-TLC (hexanes/acetone, 1/1, 500 μ m plate) afforded (+)-**16** (24.0 mg, 0.0765 mmol, 74% yield for 3 steps) as a colorless oil and (+)-**17** (5.7 mg, 0.018 mmol, 18% yield for 3 steps) as a colorless oil.

(+)-**16**: R_f 0.2 (hexanes/acetone 1/1); $[\alpha]_D^{20} +4.8^\circ$ (*c* 0.50, CHCl₃); IR (film) 3378 (m br), 2925 (s), 1456 (m), 1375 (w), 1275 (w), 1144 (w), 1040 (w), 754 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.85 (ABX, *J*_{AB} = 10.1, *J*_{AX} = 4.8, *J*_{BX} = 3.5, $\Delta\nu_{AB}$ = 76.3 Hz, 2H), 3.73 (d, *J* = 12.7 Hz, 1H), 3.65-3.58 (m, 1H), 2.95-2.86 (m, 2H), 2.82-2.73 (m, 2H), 2.54-2.49 (m, 1H), 2.10 (t, *J* = 13.1 Hz, 1H), 2.04-1.92 (m, 4H), 1.86 (d, *J* = 13.6 Hz, 1H), 1.76 (d, *J* = 14.3 Hz, 1H), 1.75-1.70 (m, 1H), 1.70 (dd, *J* = 13.9, 11.9 Hz, 1H), 1.64 (ddd, *J* = 13.8, 3.5, 2.0 Hz, 1H), 1.59 (br s, 1H), 1.36-1.23 (m, 3H), 0.86 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, C₆D₆) δ 67.69, 57.97, 54.93, 51.73, 50.51, 39.92, 37.29, 34.00, 33.89, 33.29, 28.09, 27.11, 25.90, 25.41, 25.35, 18.86; high resolution mass spectrum *m/z* 314.1614 [(M+H)⁺; calcd for C₁₆H₂₈NOS₂: 314.1612].

(+)-**17**: R_f 0.1 (hexanes/acetone 1/1); $[\alpha]_D^{20} +23.9^\circ$ (*c* 0.285, CHCl₃); IR (film) 3377 (m br), 2922 (s), 1454 (m), 1376 (w), 1275 (w), 1241 (w), 1146 (m), 1065 (m), 754 (s) cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 3.99 (ddd, *J* = 12.3, 5.4, 2.8 Hz, 1H), 3.84-3.79 (m, 1H), 3.23-3.19 (m, 2H), 2.66 (ddd, *J* = 14.2, 8.3, 3.6 Hz, 1H), 2.54 (ddd, *J* = 10.8, 8.3, 3.6 Hz, 1H), 2.48 (ddd, *J* = 14.2, 6.9, 4.0 Hz, 1H), 2.35-2.29 (m, 2H), 2.12-2.06 (m, 1H), 2.01 (dt, *J* = 13.3, 2.4 Hz, 1H), 1.94-1.86 (m, 1H), 1.84 (dd, *J* = 13.4, 12.9 Hz, 1H), 1.84-1.79 (m, 1H), 1.72 (dd, *J* = 13.8, 11.7 Hz, 1H), 1.71-1.65 (m, 1H), 1.64-1.57 (m, 2H), 1.32-1.24 (m, 3H), 1.04 (dddd, *J* = 16.6, 9.6, 6.8, 1.3 Hz, 1H), 0.91 (br s, 1H), 0.77 (d, *J* = 6.4 Hz, 3H), 0.57 (q, *J* = 12.6 Hz, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 64.79,

59.13, 55.55, 51.57, 51.16, 42.28, 38.64, 37.81, 33.17, 29.08, 28.82, 28.30, 26.70, 26.11, 26.03, 19.06; high resolution mass spectrum m/z 314.1605 $[(M+H)^+]$; calcd for $C_{16}H_{28}NOS_2$: 314.1612].

(+)-**18**

Dithiane (+)-**18**. Alcohol (+)-**16** (16.5 mg, 0.0526 mmol) was dissolved in CH_2Cl_2 (1 mL) and triethyl amine (0.037 mL, 0.263 mmol, 5.0 equiv) was added. The mixture was cooled to 0 °C and methanesulfonyl chloride (0.012 mL, 0.155 mmol, 3.0 equiv) was added dropwise. The solution was warmed to ambient temperature and stirred for 20 min. The resultant mixture was poured into saturated $NaHCO_3$ aqueous solution (3 mL) and extracted with CH_2Cl_2 (3 X 10 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude mesylate was then dissolved in THF (5 mL) and $LiHBEt_3$ (1.0 M in THF, 0.26 mL, 5.0 equiv) was added. After the mixture was heated at reflux for 36 h, it was poured into saturated $NaHCO_3$ aqueous solution (10 mL) and extracted with Et_2O (3 X 12 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:1) as eluant, afforded (+)-**18** (13 mg, 0.044 mmol, 83% yield for 2 steps) as a colorless oil: R_f 0.4 (ethyl acetate); $[\alpha]_D^{20} +6.4^\circ$ (c 0.50, $CHCl_3$); IR (film) 2927 (s), 1458 (m), 1370 (m), 1148 (m) cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 3.72-3.67 (m, 1H), 3.52 (d, J = 12.3 Hz, 1H), 2.54-2.51 (m, 2H), 2.35 (dd, J = 9.7, 6.3 Hz, 1H), 2.32-2.29 (m, 2H), 2.10 (t, J = 12.9 Hz, 1H), 1.90-1.85 (m, 2H), 1.81 (dt, J = 13.2, 2.4 Hz, 1H), 1.73 (dd, J = 13.6, 11.7 Hz, 1H), 1.72-1.67 (m, 1H), 1.61-1.46 (m, 4H), 1.30-1.13 (m, 3H), 1.19 (d, J = 7.1 Hz, 3H), 1.08-1.01 (m, 1H), 0.74 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 59.33, 56.00, 55.60, 51.57, 38.42, 37.07, 35.90, 33.58, 32.88, 29.22, 28.17, 26.65, 26.10, 26.05, 21.04, 19.22; high resolution mass spectrum m/z 298.1671 $[(M+H)^+]$; calcd for $C_{16}H_{28}NS_2$: 298.1663].

(-)-**19**

Ketone (-)-19. To a solution of (+)-**18** (10 mg, 0.0336 mmol) in CH₃CN/H₂O (1/1 mL) at ambient temperature was added trifluoroacetic acid (0.026 mL, 0.337 mmol, 10 equiv) and PhI(O₂CCF₃)₂ (43 mg, 0.10 mmol, 3.0 equiv). After being stirred for 4 h at ambient temperature, the reaction mixture was extracted with hexanes (3 X 1 mL). The aqueous phase was neutralized with solid K₂CO₃ (~ 0.1 g) until basic to litmus paper and then neat EtSH (0.10 mL) was added. After the mixture was stirred for 5 min, it was poured into saturated NaHCO₃ aqueous solution (5 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in *vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:1) as eluent, afforded (-)-**19** (6.4 mg, 0.031 mmol, 91 %) as a viscous oil: R_f 0.55 (ethyl acetate); $[\alpha]_D^{20}$ -26.4° (c 0.50, CHCl₃); IR (film) 2955 (s), 2910 (s), 1711 (s), 1460 (m), 1323 (m), 1267 (m), 1225 (m), 1144 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.39-3.34 (m, 1H), 3.05 (dt, *J* = 12.6, 2.6 Hz, 1H), 2.61 (t, *J* = 12.7 Hz, 1H), 2.56 (dd, *J* = 9.7, 6.3 Hz, 1H), 2.27 (dd, *J* = 13.4, 11.3 Hz, 1H), 2.17 (ddd, *J* = 13.4, 4.2, 2.0 Hz, 1H), 2.14-2.00 (m, 3H), 1.76-1.70 (m, 1H), 1.64-1.56 (m, 1H), 1.52-1.34 (m, 4H), 1.16 (d, *J* = 7.1 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 210.45, 61.53, 61.03, 59.58, 45.12, 42.64, 35.66, 33.17, 32.08, 28.94, 28.84, 20.29, 18.60; high resolution mass spectrum *m/z* 207.1629 [(M)⁺; calcd for C₁₃H₂₁NO: 207.1623].

(-)-**1**

Alkaloid 205B (-)-1. To a stirred suspension of CH₃PPh₃Br (0.110 g, 0.308 mmol, 10 equiv) in THF (1 mL) was added *n*-BuLi (1.6 M in hexanes, 0.19 mL, 9.5 equiv) at 0 °C and the resulting yellow suspension was stirred at 0 °C for 10 min. To the suspension was then added a solution of (-)-**19** (6.2 mg, 0.030 mmol) in THF (1 mL) at 0 °C and the reaction mixture was stirred for 40 min

at ambient temperature. The reaction was quenched with H₂O (3 mL) and the aqueous mixture was extracted with Et₂O (3 X 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in *vacuo*. Flash chromatography on silica gel, using ethyl acetate-hexanes (1:1) as eluent, afforded an alkene (5.6 mg, 0.027 mmol, 91% yield) as a colorless oil: R_f 0.35 (ethyl acetate); $[\alpha]_D^{20}$ -12.8° (c 0.280, CHCl₃); IR (film) 3070 (w), 2954 (s), 2927 (s), 1646 (m), 1460 (m), 1144 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.63 (br s, 2H), 3.03 (br s, 1H), 2.71 (d, *J* = 12.1 Hz, 1H), 2.57 (q, *J* = 6.9 Hz 1H), 2.29 (t, *J* = 12.3 Hz, 1H), 2.05-1.96 (m, 4H), 1.83 (d, *J* = 12.0 Hz, 1H), 1.71 (br s, 1H), 1.56-1.48 (m, 1H), 1.38-1.29 (m, 4H), 1.12 (d, *J* = 7.1 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 148.61, 106.50, 61.95, 61.61, 59.46, 37.63, 36.55, 35.13, 33.24, 32.30, 29.09, 28.54, 20.39, 18.68; high resolution mass spectrum *m/z* 205.1825[(M)⁺; calcd for C₁₄H₂₃N: 205.1831].

To a solution of the alkene (5.6 mg, 0.027 mmol) in benzene (3 mL) was added *p*-TsOH·H₂O (26 mg, 0.137 mmol, 5.1 equiv) and the reaction mixture was heated at reflux for 20 h. After cooling, the reaction was quenched with saturated NaHCO₃ aqueous solution (3 mL) and the organic layer was separated. The aqueous layer was extracted with Et₂O (4 X 5 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in *vacuo*. Flash chromatography on silica gel (hexanes/ethyl acetate 3/1 -> 1/1) afforded (-)-**1** (3.9 mg, 0.019 mmol, 70 % yield) as a colorless oil: R_f 0.2 (ethyl acetate); $[\alpha]_D^{20}$ -8.3° (c 0.12, CHCl₃); IR (film) 2959 (m), 2924 (m), 2841 (m), 1655 (w), 1458 (m), 1376 (m), 1170 (m) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.18 (br s, 1H), 3.79 (br s, 1H), 2.98 (dd, *J* = 11.4, 4.6 Hz, 1H), 2.17-2.10 (m, 3H), 1.93-1.88 (m, 1H), 1.71-1.79 (m, 1H), 1.62 (s, 3H), 1.49-1.26 (m, 6H), 1.18 (d, *J* = 7.2 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H); ¹H NMR (500 MHz, C₆D₆) δ 5.19 (br s, 1H), 3.87 (br s, 1H), 2.95 (dd, *J* = 11.5, 4.6 Hz, 1H), 2.15 (dd, *J* = 9.8, 5.2 Hz, 1H), 2.06 (br t, *J* = 14.3 Hz, 1H), 2.02-1.95 (m, 1H), 1.84-1.79 (m, 1H), 1.59 (s, 3H), 1.60-1.53 (m, 1H), 1.39-1.21 (m, 6H), 1.29 (d, *J* = 7.1 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 129.54, 125.56, 60.53, 58.12, 56.54, 35.51, 32.61, 32.43, 29.23, 28.43, 28.43, 23.52, 20.19, 18.82; ¹³C NMR (125 MHz, C₆D₆) δ 129.94, 126.85,

60.99, 59.00, 57.02, 36.39, 33.36, 33.16, 30.18, 29.20, 28.74, 24.15, 20.79, 19.41; high resolution mass spectrum m/z 205.1830[(M)⁺; calcd for C₁₄H₂₃N: 205.1831].

Synthetic alkaloid (-)-205B (**1**)
 125 MHz ^{13}C NMR in C_6D_6