Supporting Information:

Highly Enantioenriched Tetrahydropyridines From Chiral Organsilanes: Application to the Synthesis of Quinolizidine (-)-217A

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General Information: ^1H - and ^{13}C -NMR were taken in CDCl_3 at 400 MHz and 75.0 MHz respectively unless specified otherwise. Chemical shifts are reported in parts per million using the solvent resonance internal standard (chloroform, 7.24 and 77.0 ppm, unless specified otherwise). Data are reported as follows: chemical shift, multiplicity (app = apparent, par obsc = partially obscured, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, abq = ab quartet), coupling constant, and integration. For compounds which appeared with significant amount of amide rotamer in NMR spectrum, resonances associated with the major amide rotamer are indicated with *, those for the minor amide rotamer with **; resonances compromising portions from both rotamers bear no asterisk. Ratios of diastereomers (dr) were determined by ^1H -NMR (400 MHz) operating at a signal/noise ratio of $>200:1$. Infrared Resonance spectra were recorded on a Nicolet Impact 400 FT-IR spectrometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm, and are reported as $[\alpha]_D$ (concentration in grams/100 mL solvent). High resolution mass spectra (HRMS) were obtained on a Figan MAT-90 spectrometer on the Boston University Mass Spectrometry Laboratory. Tetrahydrofuran (THF) and ethyl ether (Et_2O) were distilled under nitrogen from sodium-benzophenone ketyl. Methylene chloride (CH_2Cl_2) was distilled under nitrogen from CaH_2 . TiCl_4 was freshly distilled over copper powder before use. All other reagents were used as supplied. All reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted. Analytical thin layer chromatography was performed on Whatman Reagent silical gel 60-A plates. Flash chromatography was performed on E. Merck silica gel 230-400 mesh.

Typical experimental procedure for the TiCl_4 promoted [4+2]-annulation reaction illustrated for the synthesis of 1,2,5,6-tetrahydropyridine **2c**: A

suspension of crotylsilane **1a** (100 mg, 0.36 mmol), 2-furylaldehyde (34 μ L, 0.40 mmol), and MgSO_4 (87 mg, 0.72 mmol) was stirred at rt for 0.5h. The reaction mixture was filtered through a pad of celite and concentrated *in vacuo*. The resulting pale yellow oil was dissolved in CH_2Cl_2 (1 mL, 0.4 M) and the solution was cooled to -78°C . After 10 minutes, 79 μ L of TiCl_4 (0.72 mmol) was added to the cooled solution. The resulting red colored solution was allowed to slowly warm to room temperature and stirred for 12 hours. The reaction mixture was cooled to -78°C and a solution of saturated aqueous NaHCO_3 (4 mL) was added. After stirring at -78°C for 15 minutes, the reaction mixture was warmed to room temperature and stirred for 1h. The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over MgSO_4 and concentrated *in vacuo*. The generated brown color oil was dissolved in CH_2Cl_2 (1 mL, 0.4 M) and 73 μ L of pyridine (0.90 mmol) was added. The resulting crude reaction mixture was cooled to -78°C and 55 μ L of $(\text{CF}_3\text{CO})_2\text{O}$ (0.36 mmol) was added. After stirring at -78°C for 2 hours, the reaction was quenched by the addition of 3 mL of H_2O . The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried over MgSO_4 and concentrated *in vacuo*. Flash column on silica gel (10%, EtOAc/Hexanes eluant) gave 102 mg of clear colorless oil (89% yield). $[\alpha]_{\text{D}}^{20} -70.2^\circ$ (c 0.41, CHCl_3). IR (neat) 2958, 1755, 1693, 1533, 1435, 1365, 1340, 1276, 1149 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.28 (s, 1H), 6.28 (dd, $J = 2.0, 3.3$ Hz, 1H), 6.02 (m, 2H), 5.63 (dd, $J = 3.6, 10.2$ Hz, 1H), 5.14 (s, 1H), 4.70 (brs, 1H), 3.75 (s, 3H) 2.94 (m, 1H), 1.37 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.6, 152.7, 142.0, 131.8, 120.0, 110.2, 106.1, 57.1, 55.8, 52.8, 33.2, 18.8; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{F}_3\text{NO}_4$ 317.0875, found 317.0874.

(2S, 5S, 6R)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-isopropyl-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (2a). $[\alpha]_{\text{D}}^{20} -84.2^\circ$ (c 0.55, CHCl_3). IR (neat) 2970, 1756, 1691, 1438, 1338, 1340, 1273, 1197, 1150 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.01 (t, $J = 7.9$ Hz, 1H), 5.64 (dd, $J = 3.0, 10.1$ Hz, 1H), 4.59 (brs, 1H), 3.73 (s, 3H) 3.51 (d, $J = 9.6$ Hz, 1H), 2.51 (m, 1H), 1.85 (m, 1H), 1.23 (d, $J = 6.92$ Hz, 3H), 0.93 (d, $J = 6.59$ Hz, 3H), 0.82 (d, $J = 6.92$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.7, 132.6, 120.1, 63.8, 57.2, 52.7, 31.8, 31.6, 20.8, 19.4, 19.3; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{13}\text{H}_{18}\text{F}_3\text{NO}_4$ 293.1239, found 293.1234.

(2S, 5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-(3-nitrophenyl)-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (2b). $[\alpha]_{\text{D}}^{20} -88.7^\circ$ (c 1.3, CHCl_3). IR (neat) 3028, 2957, 1755, 1697, 1533, 1436, 1350, 1217, 1148 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.12 (d, J = 6.6 Hz, 1H), 7.95 (s, 1H), 7.5 (t, J = 8.1 Hz, 1H), 7.36 (d, J = 7.3 Hz, 1H), 5.95 (t, J = 6.9 Hz, 1H), 5.83 (dd, J = 4.3, 9.9 Hz, 1H), 5.23 (s, 1H), 5.06 (d, J = 3.6 Hz, 1H), 3.80 (s, 3H) 2.82 (m, 1H), 1.49 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.1, 148.6, 144.2, 131.4, 131.1, 129.8, 122.7, 120.5, 60.5, 57.5, 53.0, 37.1, 20.0; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{16}\text{H}_{15}\text{F}_3\text{N}_2\text{O}_5$ 372.0933, found 372.0917.

(2S, 5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-(E-2-phenylethyl-1-enyl)-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (2d). $[\alpha]_{\text{D}}^{20}$ -53.2° (c 0.5, CHCl_3). IR (neat) 3028, 2957, 1754, 1692, 1437, 1275, 1216, 1153, 757 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.57-7.24 (m, 5H), 6.36 (d, J = 15.8 Hz, 1H), 6.13-6.07 (overlap, 2H), 5.73 (dd, J = 3.6, 9.89 Hz, 1H), 4.77 (s, 1H), 4.70 (d, J = 5.3 Hz, 1H), 3.77 (s, 3H) 2.56-2.52 (m, 1H), 1.34 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.6, 135.9, 132.1, 131.5, 128.7, 128.1, 127.9, 126.5, 120.2, 59.2, 56.8, 52.8, 35.5, 19.1; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{18}\text{H}_{18}\text{F}_3\text{NO}_3$ 353.1239, found 353.1256.

(2R, 5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-cyclohexyl-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (3a). (containing 4 : 1 rotamer) $[\alpha]_{\text{D}}^{20}$ $+181.3^\circ$ (c 0.525, CHCl_3). IR (neat) 2929, 2854, 1762, 1688, 1439, 1207, 1148 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.96-5.89 (m, 1H), 5.86* (dd, J = 2.9, 10.2 Hz, 1H), 5.78** (dd, J = 3.3, 9.89 Hz, 1H), 4.26* (brs, 1H), 4.98** (t, J = 2.0 Hz, 1H), 4.31** (d, J = 10.2 Hz, 1H), 3.75** (s, 3H), 3.73* (s, 3H), 3.54* (d, J = 8.9 Hz, 3H), 2.58-2.53 (m, 1H), 2.04 (d, J = 12.9 Hz, 1H), 1.73-1.70 (m, 2H), 1.61-1.55 (m, 2H), 1.45-1.37 (m, 1H), 1.31-1.01 (m, 4H), 0.95** (d, J = 6.9 Hz, 3H), 0.92** (d, J = 6.9 Hz, 3H), 0.90-0.79 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4**, 168.7*, 131.0**, 130.0*, 120.2*, 119.0**, 63.0*, 60.4**, 55.2**, 54.4*, 52.8**, 52.5*, 39.2*, 37.9**, 31.5**, 31.2*, 29.9*, 29.7*, 29.3*, 28.7*, 26.4, 26.2, 25.9**, 19.5**, 19.0*; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{16}\text{H}_{23}\text{F}_3\text{NO}_3$ 334.1629, found 336.1646.

(2R, 5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-(4-bromophenyl)-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (3b). (containing ca. 1 : 1 rotamer) $[\alpha]_{\text{D}}^{20}$ $+74.4^\circ$ (c 0.45, CHCl_3). IR (neat) 2966, 2878, 1746, 1696, 1491, 1439, 1216, 1076, 1034, 802, 756, 727 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.40-7.36

(m, 4H), 7.29-7.26 (m, 2H), 6.23-6.20** (m, 1H), 6.14-6.10* (m, 1H), 6.0 (m, 2H), 5.76** (s, 1H), 5.42** (s, 1H), 5.05* (s, 1H), 4.95* (brs, 1H), 3.31* (s, 3H), 3.20** (s, 3H), 2.85-2.76 (m, 2H), 1.18* (d, J = 6.9 Hz, 3H), 1.13** (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 168.0, 167.7, 137.1, 136.3, 131.6, 131.3, 131.0, 130.3, 130.2, 122.3, 122.1, 121.3, 120.3, 58.8, 55.9, 53.6, 52.3, 51.9, 32.7, 32.6, 19.4, 18.7; HRMS (CI/NH₃) m/z calcd for C₁₆H₁₅BrF₃NO₃ 405.0187, found 405.0208.

(2R, 5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-furyl-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (3c). (containing 4 : 1 rotamer) [α]_D²⁰ +156.1° (c 0.8, CHCl₃). IR (neat) 3123, 2965, 2880, 1741, 1696, 1501, 1440, 1208, 1147, 1073, 1018, 801, 750, 722 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.32 (s, 1H), 6.24-6.21 (m, 2H), 6.13-6.04 (m, 1H), 6.00-5.93 (m, 1H), 5.82** (s, 1H), 5.34* (t, J = 3.0 Hz, 1H), 5.10* (s, 1H), 4.95** (t, J = 3.3 Hz, 1H), 3.43* (s, 3H), 3.41** (s, 3H), 2.80-2.74 (m, 1H), 1.15* (d, J = 6.9 Hz, 3H), 1.10** (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 168.1**, 167.5*, 151.5**, 151.0*, 142.3, 131.1**, 131.0*, 120.5*, 119.7**, 110.1*, 110.0**, 109.8**, 109.2*, 54.4*, 53.4**, 52.8, 52.6, 50.5**, 32.7*, 32.4**, 19.5**, 19.1*; HRMS (CI/NH₃) m/z calcd for C₁₄H₁₅F₃NO₄ 318.0952, found 318.0936.

Typical experimental procedure for DBU promoted isomerization illustrated for the synthesis of 1,4,5,6-tetrahydropyridine **4d**: To a solution of **2** (102 mg, 0.33 mmol) in THF (1 mL, 0.3 M), was added 49 μL of DBU (0.90 mmol). After stirring 1h at room temperature, the reaction was quenched by addition of 3 mL of H₂O. The aqueous layer was extracted with CH₂Cl₂ (3 x 5 mL). The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. Flash column on silica gel (10%, EtOAc/Hexanes eluant) gave 97 mg of clear colorless oil (95% yield). [α]_D²⁰ -120.6° (c 0.9, CHCl₃). IR (neat) 3027, 2965, 1734, 1703, 1654, 1491, 1433, 1383, 1354, 1324, 1274, 1251, 1207, 1154, 1074, 1009, 753 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.6 Hz, 2H), 6.23 (brs, 1H), 5.05 (s, 1H), 3.83 (s, 3H), 2.69 (m, 1H), 2.12-2.07 (m, 1H), 1.96 (dd, J = 3.9, 19.8 Hz, 1H), 1.11 (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 136.6, 132.0, 129.0, 127.4, 126.5, 121.8, 61.2, 52.6, 31.2, 26.5, 18.5; HRMS (CI/NH₃) m/z calcd for C₁₆H₁₅BrF₃NO₃ 405.0187, found 405.0155.

(5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-(3-nitrophenyl)-1,4,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (4a). $[\alpha]_D^{20} -159.8^\circ$ (c 0.5, CHCl_3). IR (neat) 3088, 3027, 2962, 1705, 1654, 1533, 1426, 1383, 1351, 1276, 1233, 1208, 1152 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.28 (s, 1H), 8.15 (d, $J = 8.2\text{ Hz}$, 1H), 7.74 (d, $J = 7.6\text{ Hz}$, 1H), 7.54 (t, $J = 8.2\text{ Hz}$, 1H), 6.26 (brs, 1H), 5.18 (s, 1H), 3.87 (s, 3H), 2.79 (m, 1H), 2.05-2.02 (m, 2H), 1.17 (d, $J = 6.9\text{ Hz}$, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 163.1, 148.9, 139.9, 131.9, 130.0, 129.0, 126.6, 122.8, 121.0, 61.1, 57.8, 31.4, 26.6, 18.5; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{16}\text{H}_{16}\text{F}_3\text{N}_2\text{O}_5$ 373.1011, found 373.0975.

(5S, 6R)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-furyl-1,4,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (4b). $[\alpha]_D^{20} -146.4^\circ$ (c 0.57, CHCl_3). IR (neat) 3124, 2963, 1705, 1654, 1505, 1429, 1385, 1352, 1327, 1277, 1257, 1210, 1153, 1077, 1012, 944, 750 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, $J = 0.7\text{ Hz}$, 1H), 6.32-6.28 (overlap m, 3H), 5.10 (brs, 1H), 3.87 (s, 3H), 2.79 (m, 1H), 2.26 (m, 1H), 1.98 (dd, $J = 4.3, 20.1\text{ Hz}$, 1H), 1.08 (d, $J = 6.9\text{ Hz}$, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 163.2, 150.7, 142.3, 128.6, 126.7, 110.6, 107.3, 57.1, 52.4, 29.7, 27.4, 18.2; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{14}\text{H}_{14}\text{F}_3\text{NO}_4$ 317.0875, found 317.0895.

(5S, 6S)-1-(2, 2, 2-trifluoroacetyl)-5-Methyl-6-isopropyl-1,4,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (4c). $[\alpha]_D^{20} -18.8^\circ$ (c 0.5, CHCl_3). IR (neat) 2967, 2881, 1736, 1693, 1653, 1427, 1387, 1349, 1322, 1273, 1201, 1155, 1122, 751 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.40 (brs, 1H), 3.76 (s, 3H), 3.44 (d, $J = 8.6\text{ Hz}$, 1H), 2.43-2.36 (m, 1H), 2.29 (m, 1H), 1.95 (dd, $J = 3.9, 20.4\text{ Hz}$, 1H), 1.70 (m, 1H), 1.01 (d, $J = 4.6\text{ Hz}$, 1H), 0.96 (d, $J = 6.9\text{ Hz}$, 1H), 0.93 (d, $J = 6.9\text{ Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 163.4, 127.4, 65.4, 65.1, 52.3, 27.9, 27.7, 27.2, 19.7, 19.3; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{13}\text{H}_{18}\text{F}_3\text{NO}_3$ 293.1239, found 293.1244.

(5S, 6R)-1-(2, 2, 2-Trifluoroacetyl)-5-methyl-6-cyclohexyl-1,4,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (4e). $[\alpha]_D^{20} -69.8^\circ$ (c 0.55, CHCl_3).

CHCl₃). IR (neat) 2932, 1735, 1694, 1437, 1205, 1152 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.40 (brs, 1H), 3.76 (s, 3H), 3.50 (d, J = 8.0 Hz, 1H), 2.41-2.30 (overlap m, 2H), 1.97-1.91 (overlap m, 2H), 1.74-1.64 (m, 6H), 1.32-0.97 (m, 7H), 0.91 (d, J = 6.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 163.4, 127.5, 64.4, 52.3, 37.1, 29.8, 27.3, 26.3, 19.2; HRMS (CI/NH₃) m/z calcd for C₁₆H₂₃F₃NO₃ 334.1629, found 334.1614.

(2S, 5R, 6S)-1-Benzyloxycarbonyl-5-methyl-6-(5'-acetoxypentanyl)-1,2,5,6-tetrahydropyridine-2-carboxylic acid methyl ester (6). (containing 1 : 1 rotamer) A suspension of crotylsilane **1c** (280 mg, 1 mmol), 5-acetoxypentanal (140 mg, 1 mmol), and MgSO₄ (240 mg, 2 mmol) was stirred at rt for 0.5h. The resulted reaction mixture was filtered through celite and concentrated *in vacuo*. The pale yellow residue was dissolved in CH₂Cl₂ (4 mL, 0.25 M) and the solution was cooled to -78 °C. After 10 minutes, 220 mL of TiCl₄ (2 mmol) was added to the cooled solution. The resulted red color solution was allowed to slowly warm to room temperature and stirred for 12 hours. After which time, the reaction mixture was cooled to -78 °C and a solution of saturated aqueous Na₂CO₃ (8 mL) was added. The reaction mixture was allowed to warm to rt by 2h, then recool to 0°C. After addition of 0.157 mL of benzyl chloroformate, it was allowed to stir at this temperature for 4h. After the partition of the mixture, the aqueous was extracted with CH₂Cl₂ (3 X 6 mL). The combined organic phase was dried over MgSO₄ and concentrated *in vacuo*. Flash column on silica gel (2%, EtOAc/CH₂Cl₂ eluant) gave 242 mg of the title compound as clear colorless oil (60% yield). [α]_D²⁰ -32.6° (c 0.65, CHCl₃). IR (neat) 3024, 2957, 2871, 1737, 1454, 1411, 1309, 1246, 1107, 1032, 756 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34-2.26 (m, 10H), 5.92-5.84 (m, 2H), 5.78 (dd, J = 3.3, 10.2 Hz, 1H), 5.69 (dd, J = 3.3, 9.9 Hz, 1H), 5.20 (d, J = 12.4 Hz, 1H), 5.18 (s, 1H), 5.06 (d, J = 12.4 Hz, 1H), 5.02 (t, J = 2.2, H), 4.93 (t, J = 2.5 Hz, 1H), 4.16 (t, J = 7.0 Hz, 1H), 4.05 (overlp t, J = 5.9 Hz, 1H), 4.02 (overlp t, J = 6.6 Hz, 2H), 3.95 (t, J = 6.6 Hz, 2H), 3.72 (s, 3H), 3.61 (s, 1H), 2.25-2.20 (m, 1H), 2.17-2.14 (m, 1H), 2.01 (s, 3H), 2.00 (s, 3H), 1.63-1.21 (m, 12H), 0.99 (d, J = 7.0 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 170.6, 156.5, 156.2, 136.5, 131.0, 130.5, 128.4, 127.7, 119.8, 119.2, 67.4, 64.4, 56.3, 55.5, 54.9, 54.4, 54.2, 52.2, 33.4, 33.0, 28.5, 23.3, 21.0, 19.6; HRMS (CI/NH₃) m/z calcd for C₂₂H₂₉NO₆ 403.1995, found 403.2002.

(2S, 5R, 6S)- 5-Methyl-6-(5'-hydroxypentanyl)-piperidine -2-carboxylic acid methyl ester (7). To solution of **6** (0.22 g) in 3 mL of methanol, was added 20 mg of PtO₂ and 10 mg NaNO₂. The suspension was stirred under hydrogen balloon

atmosphere for 12hrs. After which time, it was filtered through celite and concentrated *in vacuo*. The residue was dissolved in 3 mL of methanol and then treated with 20 mg Pd/C and 10 mg of K₂CO₃. After stirring under hydrogen balloon atmosphere for 6hrs, it was filtered through celite and concentrated *in vacuo*. Flash column on silica gel (90 : 9 : 1 CHCl₃/MeOH/NH₄OH) gave 126 mg of the title compound as clear colorless oil (90% yield). [α]_D²⁰ –46.8° (c 1.0, CHCl₃). IR (neat) 3327, 2933, 2860, 1739, 1437, 1375, 1216, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.86 (s, 3H), 3.69 (t, J = 10.5 Hz, 2H), 3.30 (dd, J = 2.8, 11.9 Hz, 1H), 2.17-2.13 (m, 1H), 1.84-1.73 (m, 3H), 1.69-1.62 (m, 1H), 1.58-1.50 (m, 3H), 1.49-1.39 (m, 1H), 1.38-1.29 (m, 2H), 1.26-1.06 (m, 3H), 0.83 (d, J = 6.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 173.8, 62.7, 62.2, 59.3, 51.8, 35.8, 33.9, 33.2, 32.9, 29.9, 21.7, 18.4; HRMS (CI/NH₃) m/z calcd for C₁₂H₂₃NO₃ 229.1678, found 229.1678.

(1R, 4S, 9aS)- 1-Methyldodecahydroquinolizidine-4-carboxylic acid methyl ester (8). To a cold (0 °C) stirred mixture of piperidine **7** (115 mg, 0.5 mmol) and CBr₄ (200 mg, 0.6 mmol) in 2.5 mL of CH₂Cl₂, was added PPh₃ (197 mg, 0.75 mmol). The mixture was stirred at 0 °C for 30 min, and then Et₃N was added. Ten min later the mixture was concentrated *in vacuo*. Flash column on silica gel (3% Et₃N/Hexanes) gave 100 mg of the title compound as clear colorless oil (94% yield). [α]_D²⁰ –52.3° (c 0.39, CHCl₃). IR (neat) 2934, 2857, 2806, 2758, 1743, 1440, 1276, 1199, 1170, 1130, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.71 (s, 3H), 3.76 (dd, J = 3.6, 10.9 Hz, 2H), 1.91-1.82 (m, 2H), 1.79-1.69 (m, 2H), 1.65-1.57 (m, 2H), 1.50-1.41 (m, 2H), 1.34-1.23 (m, 3H), 1.18-1.02 (m, 1H), 0.84 (d, J = 6.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 174.6, 69.5, 68.7, 54.7, 51.8, 35.8, 33.1, 29.8, 29.6, 25.7, 24.8, 18.7; HRMS (CI/NH₃) m/z calcd for C₁₂H₂₁NO₂ 211.1572, found 211.1507.

(1R, 4S, 9aS)- 1-Methyldodecahydro-4-(E-2-methoxyethenyl)quinolizidine (9). To a solution of **8** (100 mg, 0.47 mmol) in dry Et₂O (1.5 mL) was added dropwise of 1 M DIBAH in hexane (0.95 mL, 0.95 mmol) at –78 °C. The mixture was stirred for 1h at –78 °C, the quenching with MeOH (0.1 mL), and allowed to warm to rt. A saturated aqueous potassium-sodium tartrate solution (1.0 mL) was added and the mixture vigorously stirred for 1h. The aqueous layer was extracted by Et₂O (3 X 3 mL) and the combined organic phase was dried over MgSO₄ and concentrated *in vacuo*. The crude pale yellow aldehyde was dissolved in 1.5 mL of dry THF. In a separate flask, a solution of KHMDS in toluene (3.1 mL, 0.5 M, 1.55 mmol) was added to a suspension of (methoxymethyl)triphenylphosphonium chloride

(644 mg, 1.88 mmol) in 7 mL of THF at $-78\text{ }^{\circ}\text{C}$. The cooling bath was removed and the mixture allowed to warm to rt over 30 min. Then, with further cooling at $-78\text{ }^{\circ}\text{C}$, the above prepared crude aldehyde solution was added. The mixture was stirred at rt overnight. The reaction was quenched with H_2O (10 mL) and extracted with Et_2O (3 X 8 mL). The combined organic phase was dried over MgSO_4 and concentrated *in vacuo*. Flash column on silica gel (3% Et_3N /Hexanes) gave 66 mg of the title compound as clear colorless oil (67% yield). $[\alpha]_{\text{D}}^{20} -26.75^{\circ}$ (c 0.4, CHCl_3). IR (neat) 2929, 2853, 2782, 1653, 1457, 1209, 1130, 1106 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.36 (d, $J = 12.9$ Hz, 1H), 4.64 (dd, $J = 9.6, 12.5$ Hz, 1H), 3.49 (s, 3H), 1.79-1.69 (m, 2H), 3.30 (br d, $J = 11.5$ Hz, 2H), 2.31-2.25 (m, 1H), 1.90 (br d, $J = 12.2$ Hz, 1H), 1.73-1.40 (m, 8H), 1.37-1.28 (m, 1H), 1.26-1.00 (m, 3H), 0.84 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 148.0, 107.3, 69.4, 64.1, 55.7, 53.6, 36.4, 34.8, 33.6, 30.2, 29.7, 25.9, 24.8, 19.1; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{13}\text{H}_{24}\text{NO}$ 210.1864, found 210.1848.

(1R, 4S, 9aS)- 1-Methyldodecahydro-4-(Z)-(5-(trimethylsilyl)pent-2-en-4-ynyl)quinolizidine (10). A solution of **9** (50 mg, 0.24 mmol) in Et_2O (2.7 mL) was treated with aq. 6N HCl (0.9 mL) and stirred at rt overnight. The mixture was diluted with H_2O (2 mL), basified with solid Na_2CO_3 , and extracted with Et_2O (3 X 5 mL) and the combined organic phase was dried over MgSO_4 and concentrated *in vacuo*. The crude pale yellow aldehyde was dissolved in 0.2 mL of dry THF. In a separate flask, $t\text{-BuLi}$ (180 μL , 1.69 M solution in hexane) was added to a solution of 3-(tert-butyl dimethylsilyl)-1-(trimethylsilyl)-1-propyne (45 mg, 0.23 mmol) in 0.45 mL of THF at $-78\text{ }^{\circ}\text{C}$. After 1h, $\text{Ti}(\text{O}i\text{Pr})_4$ (89 μL , 0.30 mmol) was added to the mixture. After 10 min, the above prepared solution of aldehyde in THF was added to the organotitanium reagent and the resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1h, $-20\text{ }^{\circ}\text{C}$ for 1h and at room temperature for 1h, after which saturated NH_4Cl (3 mL) was added and the mixture was extracted with Et_2O (3 X 8 mL). The combined organic phase was dried over MgSO_4 and concentrated *in vacuo*. Flash column on silica gel (20:1 $\text{CHCl}_3/\text{MeOH}$) gave 40 mg of the title compound as yellow oil (60% yield). $[\alpha]_{\text{D}}^{20} -17.3^{\circ}$ (c 0.3, CHCl_3). IR (neat) 2927.1, 2854.9, 2787.4, 2149.4, 1902.0, 1734.2, 1461.7, 1249.5, 841.8, 758.9 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.04 (dt, $J = 7.4, 10.8$ Hz, 1H), 5.53 (dt, $J = 1.3, 10.8$ Hz, 1H), 3.28 (br d, $J = 10.9$ Hz, 1H), 2.64-2.57 (m, 1H), 2.49-2.41 (m, 1H), 2.08-2.02 (m, 1H), 1.89 (br d, $J = 11.2$ Hz, 1H), 1.74-0.87 (m, 12H), 0.83 (d, $J = 6.3$ Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 142.8, 110.3, 102.4, 99.1, 69.6, 63.4, 51.9, 36.3, 35.0, 33.4, 32.0, 30.2, 26.2, 24.7, 19.2, 0.03; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{18}\text{H}_{32}\text{NSi}$ 290.2304, found 290.2293.

(1R, 4S, 9aS)- 1-Methyldodecahydro-4-(Z)-(pent-2-en-4-ynyl)quinolizidine **217A (11)**. To a solution of **10** (21 mg, 0.073 mmol) in 0.5 mL of MeOH was added anhydrous potassium carbonate (10 mg, 0.073 mmol) at rt. After 1.5 h, the solution was diluted with H₂O (2 mL) and extracted with Et₂O (3 X 8 mL). The combined organic phase was dried over MgSO₄ and concentrated *in vacuo*. Flash column on silica gel (10:1 CHCl₃/MeOH) gave 15 mg of the title compound as pale yellow oil (95% yield). $[\alpha]_D^{20}$ -13.75° (c 0.4, CHCl₃). IR (neat) 3312.6, 2924.4, 2853.5, 2786.0, 2149.4, 1736.7, 1454.2, 1376.4, 1264.4, 1127.4, 1107.6, 1086.9, 1056.5, 960.0, 634.5 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.09 (dt, J = 7.25, 10.8 Hz, 1H), 5.49 (dt, J = 1.3, 10.8 Hz, 1H), 3.25 (br d, J = 10.5 Hz, 1H), 3.05 (d, J = 1.6 Hz, 1H), 2.62-2.47 (m, 2H), 2.03 (m, 1H), 1.89 (br d, J = 11.9 Hz, 1H), 1.75-0.94 (m, 12H), 0.83 (d, J = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 143.4, 109.2, 81.5, 69.5, 63.0, 51.7, 36.3, 34.9, 33.8, 31.7, 30.1, 26.2, 24.6, 19.2; HRMS (CI/NH₃) m/z calcd for C₁₅H₂₃N 217.1830, found 217.1832.

Chiral GC analysis of Synthetic (-) – 217A: Racemic 217A was resolved into two enantiomers on a beta cyclodextrin column (Supelco beta-Dex 120, fused silica 30m x 0.25 μm film thickness). Typical retention times were 11.99; 12.29 with a program 135->175 at 2°C/min. Synthetic (-) – 217A cochromatographed with the peak of longer retention time. An extract of skin of the Madagascan frog *Mantella baroni* containing natural 217A cochromatographed with the same longer retention time.

Assignment of Absolute Stereochemistry of Tetrahydropyridines as Illustrated for **12**.

The absolute stereochemistry of the tetrahydropyridines was assigned by Mosher analysis after conversion of piperidine **12** to corresponding (R) and (S)-MTPA amides.^{1,2} Comparison of ¹H NMR spectra of the individual MTPA amide established the absolute configuration of **12** to be (2R, 5S, 6R) as shown.

Preparation of (2R, 5S, 6R)-1-((S)-2-methoxy-2-trifluoromethylphenylacetyl)-5-Methyl-6-isopropylpiperidine -2-carboxylic acid methyl ester (**13**).

(R)-MTPA-Cl (11.2 μ L, 0.06 mmol) was added to a stirred solution of the piperidine **12** (8 mg, 0.04 mmol) and Hunig's base (10.4 μ L, 0.06 mmol) in 0.2 mL of CH_2Cl_2 . The reaction mixture was stirred at room temperature for 48h. The mixture was dilute with H_2O and extracted with CH_2Cl_2 . The combined organic phase was dried over MgSO_4 and concentrated *in vacuo*. Flash column on silica gel (10% EtOAc/Hexanes) gave 8 mg of the title compound as colorless oil (48% yield). $[\alpha]_{\text{D}}^{20} +8.0^\circ$ (c 0.25, CHCl_3). IR (neat) 3001, 2954, 2870, 1756, 1659, 1454, 1414, 1198, 1176, 1122, 711 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.61 (br s, 2H), 7.39 (m, 3H), 4.62 (br d, $J = 4.4\text{ Hz}$, 1H), 4.28 (d, $J = 11.2\text{ Hz}$, 3H), 3.72 (q, $J = 2.3\text{ Hz}$, 3H), 3.70 (s, 3H), 2.07 (m, 1H), 2.51 (m, 1H), 1.68-1.58 (m, 3H), 1.41-1.37 (m, 1H), 1.04 (d, $J = 6.27\text{ Hz}$, 3H), 0.96 (d, $J = 6.92\text{ Hz}$, 3H), 0.89 (d, $J = 6.26\text{ Hz}$, 3H), 0.71-0.61 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.2, 134.0, 129.5, 128.3, 126.9, 62.1, 57.6, 54.3, 51.9, 29.2, 28.1, 21.9, 21.4, 20.8, 19.4, 19.1; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{21}\text{H}_{29}\text{F}_3\text{NO}_4$ 416.2048, found 416.2026.

Preparation of (2R, 5S, 6R)-1-((R)-2-methoxy-2-trifluoromethylphenylacetyl)-5-Methyl-6-isopropylpiperidine -2-carboxylic acid methyl ester (14).

(S)-MTPA-Cl (11.2 μ L, 0.06 mmol) was added to a stirred solution of the piperidine **12** (8 mg, 0.04 mmol) and Hunig's base (10.4 μ L, 0.06 mmol) in 0.2 mL of CH_2Cl_2 . The reaction mixture was stirred at room temperature for 96h. The mixture was dilute with H_2O and extracted with CH_2Cl_2 . The combined organic phase was dried over MgSO_4 and concentrated *in vacuo*. Flash column on silica gel (10% EtOAc/Hexanes) gave 10 mg of the title compound as colorless oil (60% yield). $[\alpha]_{\text{D}}^{20} +59.2^\circ$ (c 0.5, CHCl_3). IR (neat) 3063, 2955, 2873, 1759, 1734, 1655, 1452, 1411, 1295, 1252, 1181, 1114, 1023, 998, 708 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.58 (m, 2H), 7.33 (m, 3H), 5.17 (t, $J = 4.29\text{ Hz}$, 1H), 4.15 (d, $J = 10.9\text{ Hz}$, 1H), 3.83 (d, $J = 2.0\text{ Hz}$, 3H), 3.04 (s, 3H), 2.13 (m, 1H), 1.94-1.89 (m, 2H), 1.73-1.61 (m, 2H), 1.22-1.21 (m, 1H), 1.04 (d, $J = 7.25\text{ Hz}$, 3H), 1.00 (d, $J = 6.59\text{ Hz}$, 3H), 0.89 (d, $J = 6.59\text{ Hz}$, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.0, 166.6, 132.9, 128.9, 127.8, 127.2, 62.7, 56.8, 53.0, 51.4, 30.1, 27.3, 22.0, 21.2, 21.1, 21.0, 19.1; HRMS (CI/ NH_3) m/z calcd for $\text{C}_{21}\text{H}_{29}\text{F}_3\text{NO}_4$ 416.2048, found 416.2049.

Enantiomeric Excess Analysis (Chiral HPLC): compound ent-**3b**.

Enantiomeric excess (ee) analysis of tetrahydropyridines **2** and **3** is illustrated for tetrahydropyridine ent-**3b**. In this case, the starting vinylsilane reagent employed in the synthesis of ent-**3b** was used in 95% ee (chiralcel OD column, eluant n-hexane/2-propanol

99:1, flow rate 0.8 mL/min, 250 × 46 mm).³ Accordingly, the ee analysis has determined that during the annulation process nearly complete transfer of chirality is observed. Ee analysis for compound ent-**3b**, the 95% ee measurement was determined by HPLC analysis (chiralcel OD column, eluant n-hexane/2-propanol 99.75:0.25, flow rate 0.8 mL/min, 250 × 46 mm).

Reference and Notes:

¹ Earlier studies have shown that Mosher amides derived from 2-methylpiperidine often favor a conformation in which the substituent in the 2-position is axial and H (2) is equatorial in an attempt to minimize A^{1,3}-strain. See: (a) Lunazzi, L.; Macciantelli, D.; Tassi, D.; Dondoni, A. *J. Chem. Soc. Perkin Trans. 2* **1980**, 217. (b) Chow, Y. L.; Colon, C. J.; Tam, J. N. S. *Can. J. Chem.* **1968**, 46, 2821.

² Hoye, T. R.; Renner, M. K. *J. Org. Chem.* **1996**, 61, 8489-8495.

³ For the preparation of vinylsilane, see Beresis, R. T.; Solomon, J. S.; Yang, M. G.; Jain, N. F.; Panek, J. S. *Org. Syn.* **1997**, 75, 78-86.

Channel A Results -- PDA Channel 1, 213 nm, 8 nm Band

Peak	Time	Area	Area %
1	11.02	181195	3.206
2	13.59	183323	3.244
3	20.81	2631288	46.561
4	25.60	2655444	46.989

Totals :

5651250 100.000

racemate

(2,5-trans-2,6-cis)

Peak	Time	Area	Area %
1	10.13	19795	0.108
2	11.57	7140	0.039
3	12.35	143491	0.786
4	14.43	20370	0.112
5	20.02	452578	2.481
6	23.97	17601494	96.474

Totals :

18244868 100.000

ent-3b

2a

¹H NMR (400 MHz, CDCl₃)

2a
¹³C NMR (75 MHz, CDCl₃)

2b

^1H NMR (400 MHz, CDCl_3)

2c
¹H NMR (400 MHz, CDCl₃)

2c

^{13}C NMR (75 MHz, CDCl_3)

3a
 ^1H NMR (400 MHz, CDCl_3)

3a

^{13}C NMR (75 MHz, CDCl_3)

^1H NMR (400 MHz, CDCl_3)

3b

^{13}C NMR (75 MHz, CDCl_3)

3c

¹H NMR (400 MHz, CDCl₃)

3c

^{13}C NMR (75 MHz, CDCl_3)

4a

¹H NMR (400 MHz, CDCl₃)

4a

^{13}C NMR (75 MHz, CDCl_3)

4b

^1H NMR (400 MHz, CDCl_3)

4b

^{13}C NMR (75 MHz, CDCl_3)

4c
¹H NMR (400 MHz, CDCl₃)

4d

^1H NMR (400 MHz, CDCl_3)

4d

^{13}C NMR (75 MHz, CDCl_3)

4e

^1H NMR (400 MHz, CDCl_3)

4e

^{13}C NMR (75 MHz, CDCl_3)

6
¹H NMR (400 MHz, CDCl₃)

8

^{13}C NMR (75 MHz, CDCl_3)

10

^1H NMR (400 MHz, CDCl_3)

10

^{13}C NMR (75 MHz, CDCl_3)

(-) - 217A

^1H NMR (400 MHz, CDCl_3)