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First Total Synthesis of Alkaloid 205B**

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Melting point was determined with a Yanaco micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were taken on a Varian Gemini 300 or Unity Plus 500 spectrometer. ^{1}H NMR spectra were recorded at the indicated field strength as solutions in $CDCl_3$ unless otherwise indicated. Chemical shifts are given in parts per million (ppm, δ) downfield from TMS and are referenced to $CHCl_3$ (7.26 ppm) as internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded at the indicated field strength as solutions in $CDCl_3$ unless otherwise indicated. Chemical shifts are given in parts per million (ppm, δ) downfield from TMS and are referenced to the center line of $CDCl_3$ (77.0 ppm) as internal standard. Carbon signals were assigned by a DEPT pulse sequence, q = methyl, t = methylene, d = methine, and s = quaternary carbons. Infrared spectra (IR) were measured with a Perkin-Elmer 1600 series FT-IR spectrophotometer. Mass spectra (MS) and high-resolution mass spectra (HRMS) were measured on a JEOL JMS-AX505HAD mass spectrometer. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. Column chromatography was performed on Merck silica gel 60 (No 7734-5B) or (No 9385).

Dimethyl (2*R*, 3*R*, 6*S*)-(+)-6-(*tert*-Butyldiphenylsilyloxymethyl)-3-methylpiperidine-1,2-dicarboxylate (5)

To a stirred suspension of CuI (5.95 g, 31.25 mmol) in Et_2O (20 mL) was added a solution of MeLi (1.14 M in Et_2O, 55 mL, 62.5 mmol) at –78 °C, and the resulting suspension was stirred at –78°C~-35 °C for 20 min. The resulting solution was cooled to –78°C, and a solution of **4** (2.92 g, 6.25 mmol) in Et_2O (10 mL) was added to the above reaction mixture at –78°C. The temperature was gradually raised to –35 °C, and then the reaction was quenched with satd. NH_4Cl (aq). The reaction mixture was diluted with CH_2Cl_2, and the insoluble material was removed through a celite pad. The filtrate was separated and the aqueous layer was extracted with CH_2Cl_2. The filtrate and organic layers were combined, dried, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (60 g, hexane:acetone=30:1~20:1) to give **5** (2.96 g, 98%) as a colorless oil.

IR (neat) 2955, 1861, 1708 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (9H, s), 1.07 (3H, d, *J* = 6.8 Hz), 1.18-1.25 (1H, m), 1.54-1.57 (1H, br), 1.81-1.85 (2H, m), 2.45 (1H, br), 3.45 (3H, s), 3.49 (1H, t-like, *J* = 9.9 Hz), 3.65 (3H, s), 3.68 (1H, dd, *J* = 9.9, 4.3 Hz), 4.28 (1H, br), 4.44 (1H, br), 7.35-7.44 (6H, m), 7.64-7.68 (4H, m); ^{13}C NMR (125 MHz) δ 17.98 (q), 18.13 (t), 19.19 (s), 21.87 (t), 26.78 (q), 28.02 (d), 51.77 (q), 52.06 (d), 52.80 (q), 58.48 (d), 127.53 & 127.56 (each d), 129.53 & 129.54 (each d), 133.58 & 133.63 (each s), 135.47 (d), 157.36 (s), 172.82 (s); MS: 483 (M^+), 426 (100); HRMS: Calcd for $C_{23}H_{28}NO_5Si$ (M^+-C_4H_9) 426.1736; Found 426.1744; $[\alpha]_D^{26}$ +13.6 (*c* 5.12, $CHCl_3$).

Methyl (2*R*, 3*R*, 6*S*)-(+)-6-(*tert*-Butyldiphenylsilyloxymethyl)-2-hydroxymethyl-3-methylpiperidine-1-carboxylate

To a stirred solution of **5** (2.96 g, 6.13 mmol) in THF (15 mL) was added a solution of Super-Hydride (1M in THF, 13.5 mL, 13.48 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched with satd. $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2. The organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (45 g, hexane:acetone=30:1~6:1) to give the alcohol (2.58 g, 92%) as a colorless oil.

IR (neat) 3450, 3070, 2956, 1680 cm^{-1}; ^1H NMR (500 MHz) δ 1.04 (9H, s), 1.05 (3H, d, *J* = 7.7 Hz), 1.15-1.18 (1H, m), 1.43 (1H, br), 1.58-1.64 (1H, m), 1.78-1.90 (2H, m), 2.99 (1H, br), 3.53-3.64 (4H, m), 3.67 (3H, s), 4.01-4.04 (1H, m), 4.39 (1H, br), 7.37-7.46 (6H, m), 7.66-7.72 (4H, m); ^{13}C NMR (125 MHz) δ 18.98 (q), 19.14 (s), 19.49 (t), 22.37 (t), 26.63 (q), 27.28 (d), 50.81 (d), 52.63 (q), 58.79 (d), 64.89 (t), 127.62 & 127.65 (each d), 129.68 & 129.69 (each d), 133.03 (s), 135.39 & 135.45 (each d), 158.32 (s); MS: 398, 366 (100); HRMS: Calcd for $C_{22}H_{28}NO_4Si$ (M^+-C_4H_9) 398.1787; Found 398.1787; $[\alpha]_D^{26}$ +19.8 (*c* 1.89, $CHCl_3$).

(5*S*, 8*R*, 9*R*)-(-)-5-(*tert*-Butyldiphenylsilyloxymethyl)-8-methylhexahydrooxazolo[3,4-*a*]pyridin-3-one (6)

To a stirred solution of the above alcohol (493 mg, 1.08 mmol) in THF (8 mL) was added NaH (60%, 48 mg, 1.19 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 1 h. The reaction was quenched with 10% AcOH (aq), and the aqueous mixture was extracted with CH_2Cl_2. The organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=30:1~15:1) to give **6** (456 mg, 99%) as a colorless solid (mp 81~83 °C).

IR (KBr) 2958, 2859, 1751, 757cm^{-1}; ^1H NMR (500 MHz) δ 0.88 (3H, d, *J* = 6.4 Hz), 1.03 (9H, s), 1.11-1.20 (1H, m), 1.41-1.48 (2H, m), 1.90 (1H, dq, *J* = 13.7, 3.4 Hz), 2.07 (1H, dq, *J* = 13.4, 3.4 Hz), 3.12-3.20 (2H, m), 3.89 (1H, dd, *J* = 8.6, 7.3 Hz), 4.18 (1H, dd, *J* = 10.2, 8.1 Hz), 4.33 (1H, dd, *J* = 8.6, 7.7

Hz), 4.48 (1H, dd, *J* = 10.2, 4.3 Hz), 7.36-7.43 (6H, m), 7.66-7.69 (4H, m); ^{13}C NMR (125 MHz) δ 16.87 (q), 19.14 (s), 26.75 (q), 28.39 (t), 31.72 (t), 35.09 (t), 56.93 (d), 62.38 (d), 63.16 (t), 66.64 (t), 127.48 (d), 129.45 (d), 133.38 & 133.50 (each s), 135.40 & 135.46 (each d), 156.20 (s); MS: 366 (100); HRMS: Calcd for $C_{21}H_{24}NO_3Si$ (M^+-C_4H_9) 366.1526; Found 366.1526; $[\alpha]_D^{26}$ –43.5 (*c* 1.46, $CHCl_3$).

(5*S*, 8*R*, 9*R*)-(-)-5-Hydroxymethyl-8-methylhexahydrooxazolo[3,4-*a*]pyridin-3-one

To a stirred solution of **6** (1.49 g, 3.51 mmol) in THF (20 mL) was added a solution of TBAF (1M in THF, 4.6 mL, 4.6 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was extracted with $CHCl_3$. The organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (18 g, hexane:acetone=10:1~4:1) to give the alcohol (648 mg, 99%) as a colorless oil.

IR (neat) 3420, 2930, 2875, 1723 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.78-0.83 (3H, m), 1.06-1.16 (1H, m), 1.26-1.37 (2H, m), 1.51-1.57 (1H, m), 1.76-1.82 (1H, m), 3.04-3.13 (1H, m), 3.13-3.21 (1H, m), 3.66-3.71 (1H, m), 3.73-3.84 (1H, m), 3.86-3.91 (1H, m), 4.37-4.41 (1H, m), 4.57-4.62 (1H, m); ^{13}C NMR (125 MHz) δ 16.52 (q), 27.46 (t), 31.40 (t), 35.70 (d), 58.44 (d), 62.02 (d), 63.23 (t), 67.52 (t), 157.40 (s); MS: 185 (M^+), 155 (100); HRMS: Calcd for $C_9H_{15}NO_3$ 185.1052; Found 185.1050; $[\alpha]_D^{26}$ –39.7 (*c* 1.32, $CHCl_3$).

Methyl (5*S*, 8*R*, 9*R*)-(-)-8-Methyl-3-oxohexahydrooxazolo[3,4-*a*]pyridine-5-carboxylate (7)

To a stirred solution of $(COCl)_2$ (0.65 mL, 7.47 mmol) in CH_2Cl_2 (10 mL) was added DMSO (1.1 mL, 15.41 mmol) at –78 °C, and the resulting mixture was stirred at –78 °C for 5 min. To the mixture was added a solution of the above alcohol (923 mg, 4.99 mmol) in CH_2Cl_2 (5 mL) via canule at –78 °C, and then stirring was continued for 30 min. To the reaction mixture was added Et_3N (3. 1 mL, 22.62 mmol) at –78 °C, and the temperature was gradually raised to 0 °C. The reaction mixture was diluted with Et_2O

and water, and the organic layer was separated. The aqueous layer was extracted with Et_2O and the organic layer and extracts were combined, dried, and evaporated to give a pale yellow oil, which was used directly in the next step. To a stirred solution of the above oil in *t*-BuOH (21 mL) were added $NaHPO_4$ (5.9 g, 49.17 mmol) and 2-methyl-2-butene (21 mL, 192.92 mmol) at room temperature, and then a solution of $NaClO_2$ (80%, 3.3 g, 29.18 mmol) in water (8 mL) was added dropwise to the reaction mixture at 0 °C. The resulting suspension was stirred at room temperature for 30 min., and the reaction was quenched with satd. $NaHSO_3$ (aq) at 0 °C. To the mixture was added 10% HCl (aq), and the aqueous mixture was saturated with NaCl. The aqueous mixture was extracted with EtOAc, and the organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was used direcly in the next step.

To a stirred solution of the above pale yellow oil in EtOAc (10 mL) was added a solution of CH_2N_2 in Et_2O (10 mL) at 0 °C, and then the resulting solution was stirred at room temparature for 23 h. The solvent was evaporated and the residue was chromatographed on SiO_2 (40 g, hexane:acetone=15:1~12:1) to give **7** (1.06 g, 86% in 2 steps) as a colorless solid (mp 74~76 °C).

IR (KBr) 2960, 2932, 1762, 1205 cm^{-1}; ^1H NMR (500 MHz) δ 0.90 (3H, d, *J* = 6.4 Hz), 1.13 (1H, qd, *J* = 12.8, 3.4 Hz), 1.54-1.60 (1H, m), 1.71-1.80 (1H, m), 1.88-1.98 (2H, m), 3.14-3.20 (1H, m), 3.67 (1H, dd, *J* = 11, 3.5 Hz), 3.77 (3H, s), 3.95 (1H, t-like, *J* = 8.5 Hz), 4.41 (1H, t-like, *J* = 8.5 Hz); ^{13}C NMR (125 MHz) δ 16.88 (q), 27.70 (t), 30.66 (t), 34.08 (d), 52.44 (q), 55.82 (d), 61.40 (d), 67.97 (t), 156.79 (s), 170.36 (s); MS: 213 (M^+), 211 (100); HRMS: Calcd for $C_{10}H_{15}NO_4$ 213.0101; Found 213.0991; $[\alpha]_D^{26}$ – 96.7 (*c* 1.08, $CHCl_3$).

Methyl (8*R*, 9*R*)-(-)-8-Methyl-3-oxo-5-phenylsulfanylhexahydrooxazolo[3,4-*a*]pyridine-5-carboxylate

To a stirred solution of hexamethyldisilazane (1.01 mL, 4.73 mmol) in THF (6 mL) was added *n*-BuLi (1.M in hexane, 3.0 mL, 4.73 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 30 min. To a stirred solution of **7** (871 mg, 4.09 mmol) in THF (6 mL) was added a solution of LiHMDS in THF prepared above at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. To the reaction mixture was added a solution of $(PhS)_2$ in THF (4 mL) via canule at –78 °C, and the temperature was gradually raised to 0 °C. The volatiles were removed and the residue was chromatographed on SiO_2 (50 g, hexane:acetone=10:1) to give the phenylthio ether (1.3 g, 99%) as a colorless oil.

IR (neat) 2956, 1762, 1269, 1202, 758 cm^{-1}; ^1H NMR (500 MHz) δ 0.94 (3H, d, *J* = 6.4 Hz), 1.52-1.59 (1H, m), 1.65-1.73 (2H, m), 1.87 (1H, dt-like, *J* = 14.5, 3 Hz), 2.05-2.11 (1H, m), 3.65-3.70 (1H, m), 3.74 (3H, s), 3.88 (1H, t-like, *J* = 8.5 Hz), 4.40 (1H, t-like, *J* = 8.5 Hz), 7.25-7.29 (2H, m), 7.31-7.33 (1H, m), 7.66-7.68 (2H, m); ^{13}C NMR (125 MHz) δ 16.74 (q), 27.93 (t), 32.82 (t), 34.59 (d), 53.08 (q), 57.42 (d), 67.96 (t), 71.98 (s), 128.57 (d), 129.25 (s), 129.57 (d), 137.10 (d), 155.17 (s), 169.56 (s); MS: 321 (M^+), 213 (100); HRMS: Calcd for $C_{16}H_{19}NO_4S$ 321.1035; Found 321.1038; $[\alpha]_D^{26}$ –13.3 (*c* 1.38, $CHCl_3$).

Methyl (8*R*, 9*R*)-(-)-8-Methyl-3-oxo-1,7,8,8a-tetrahydrooxazolo[3,4-*a*]pyridine-5-carboxylate (8)

To a stirred solution of the above phenylthio ether (160 mg, 0.50 mmol) in CH_2Cl_2 (2 mL) was added 2,6-lutidine (0.15 mL, 1.29 mmol), and then *m*CPBA (65%, 320 mg, 1.20 mmol) was added to the resulting mixture in four portions in 15 min. interval at room temperature. The reaction was quenched with 10% $Na_2S_2O_3$ in satd. $NaHCO_3$ (aq), and the aqueous mixture was diluted with EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc. The organic layer and extracts were combined, washed with brine, 10% HCl, and brine, successively, dried and evaporated to give a colorless oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=10:1) to give **8** (89 mg, 85%) as a colorless solid (mp 101~103 °C).

IR (KBr) 2989, 2956, 1763, 1730, 1411, 1249, 1214 cm^{-1}; ^1H NMR (500 MHz) δ 1.01 (3H, d, *J* = 6.4 Hz), 1.85-1.87 (1H, m), 1.89-1.96 (1H, m), 2.48 (1H, dt, *J* = 19.7, 5.1 Hz), 3.39-3.44 (1H, m), 3.83 (3H, s), 4.23 (1H, dd, *J* = 9.0, 3.0 Hz), 4.55 (1H, t-like, *J* = 8.5 Hz), 6.25 (1H, dd, *J* = 4.9, 2.8 Hz); ^{13}C NMR (125 MHz) δ 16.43 (q), 30.64 (d), 31.42 (t), 52.44 (q), 57.98 (d), 123.56 (d), 154.76 (s), 163.25 (s); MS:211 (M^+); HRMS: Calcd for $C_{10}H_{13}NO_4$ 211.0844; Found 211.0870; $[\alpha]_D^{26}$ –34.4 (*c* 0.46, $CHCl_3$).

Methyl (5*R*, 6*R*, 8*R*, 9*R*)-(-)-6,8-Dimethyl-3-oxohexahydrooxazolo[3,4-*a*]pyridine-5-carboxylate (9)

To a stirred suspension of CuI (744 mg, 3.91 mmol) in Et_2O (25 mL) was added a solution of MeLi (1.18 M in Et_2O, 6.6 mL, 7.82 mmol) at –78 °C, and the reaction mixture was warmed to –35 °C for 30 min. To a solution of **8** (165 mg, 0.78 mmol) in Et_2O (70 mL) was added a solution of $(Me)_2CuLi$, prepared above, at –78 °C, and the reaction mixture was warmed to –10 °C for 1 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was diluted with CH_2Cl_2 (300 mL). The resulting suspension was filtered, and the filtrate was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 2), and the filtrate and organic extracts were combined, dried, and evaporated to give a colorless oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=14:1) to give **9** (165 mg, 93%) as a colorless oil.

IR (neat) 2961, 1748, 1420, 1272, 1243 cm^{-1}; ^1H NMR (500 MHz) δ 0.84 (3H, d, *J* = 6.4 Hz), 1.13 (3H, d, *J* = 7.3 Hz), 1.28 (1H, td, *J* = 13, 4.3 Hz), 1.53 (1H, dt, *J* = 14, 3 Hz), 1.65-1.72 (1H, m), 2.49-2.51 (1H, m), 3.59 (1H, dt, *J* = 10, 8 Hz), 3.74 (3H, s), 3.97 (1H, t-like, *J* = 8.5 Hz), 4.26 (1H, br), 4.52 (1H, t-like, *J* = 8.5 Hz); ^{13}C NMR (125 MHz) δ 17.18 (q), 18.17 (q), 29.51 (d), 29.73 (d), 34.82 (t), 52.39 (q), 57.21 (d), 57.67 (d), 68.12 (t), 157.68 (s), 170.97 (s); MS: 227 (M^+), 169 (100); HRMS: Calcd for $C_{11}H_{17}NO_4$ 227.1158; Found 227.1168; $[\alpha]_D^{26}$ –36.4 (*c* 0.96, $CHCl_3$).

Methyl (5*S*, 6*R*, 8*R*, 9*R*)-(-)-(6,8-Dimethyl-3-oxohexahydrooxazolo[3,4-*a*]pyridin-5-yl)acetate (10)

To a stirred solution of **9** (211 mg, 0.93 mmol) in MeOH (3 mL) and H_2O (1 mL) was added LiOH•H_2O (84 mg, 1.99 mmol), and the resulting solution was refluxed for 2 h. After cooling, the MeOH was evaporated, and the aqueous residue was acidified with 10% HCl and saturated with NaCl. The aqueous layer was extracted with EtOAc (10 mL x 7), and the organic extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in THF (8 mL) were added $ClCO_2Et$ (0.15 mL, 1.56 mmol) and Et_3N (0.23 mL, 1.66 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 1 h. The insoluble material was filtered off, and the filtrate was evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in Et_2O (15 mL) was added a solution of CH_2N_2 in Et_2O at 0 °C, and the resulting mixture was stirred at room temperature for 19 h. The solvent was evaporated to give a pale yellow oil, which was used directly in the next step.

To a stirred solution of the above oil in MeOH (10 mL) were added $PhCO_2Ag$ (48 mg, 0.21 mmol) and Et_3N (0.3 mL, 2.17 mmol) at 0 °C, and the resulting suspension was stirred in the dark at room temperature for 27 h. The insoluble material was filtered, and the filtrate was evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=14:1) to give **10** (160 mg, 71% in 4 steps) as a colorless oil.

IR (neat) 2960, 2923, 1750 cm^{-1}; ^1H NMR (500 MHz) δ 0.85 (3H, d, *J* = 6.8 Hz), 1.08 (3H, d, *J* = 7.3 Hz), 1.42-1.53 (2H, m), 1.64-1.70 (1H, m), 1.84-1.89 (1H, m), 2.53 (1H, dd, *J* = 14.5, 7.7 Hz), 2.61 (1H, dd, *J* = 14.5, 8.2 Hz), 3.28-3.34 (1H, m), 3.66 (3H, s), 3.95 (1H, dd, *J* = 8.5, 6.4 Hz), 4.09 (1H, t-like, *J* = 7.9 Hz), 4.41 (1H, t-like, *J* = 8.5 Hz); ^{13}C NMR (125 MHz) δ 17.25 (q), 18.56 (q), 29.95 (d), 30.85 (d), 33.46 (t), 36.15 (t), 51.70 (d), 51.94 (q), 56.32 (d), 67.34 (t), 157.16 (s), 170.96 (s); MS: 241 (M^+), 197 (100); HRMS: Calcd for $C_{12}H_{19}NO_4$ 241.1314; Found 241.1312; $[\alpha]_D^{26}$ –37.7 (*c* 1.01, $CHCl_3$).

(5*S*, 6*R*, 8*R*, 9*R*)-(-)-2-(6,8-Dimethyl-3-oxohexahydrooxazolo[3,4-*a*]pyridin-5-yl)-*N*-methoxy-*N*-methylacetamide

To a stirred solution of **10** (267 mg, 1.11 mmol) in MeOH (3 mL) and H_2O (1 mL) was added LiOH•H_2O (94 mg, 2.22 mmol), and the resulting solution was refluxed for 1 h. After cooling, the MeOH was evaporated, and the aqueous residue was acidified with 10% HCl and saturated with NaCl. The aqueous layer was extracted with EtOAc (10 mL x 8), and the organic extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in CH_2Cl_2 (5 mL) was added 1,1'-carbonyldiimidazole (234 mg, 1.44 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 30 min. To the reaction mixture were added Me(MeO)NH•HCl (141 mg, 1.44 mmol) and Et_3N (0.2 mL, 1.44 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 22 h. The solvent was evaporated and the rsidue was chromatographed on SiO_2 (15 g, hexane:acetone=10:1-4:1) to give the Weinreb amide (292 mg, 98%) as a colorless oil.

IR (neat) 2961, 2926, 1746, 1656, 1416 cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (3H, d, *J* = 6.4 Hz), 1.09 (3H, d, *J* = 7.3 Hz), 1.49-1.50 (2H, m), 1.64-1.68 (1H, m), 1.93-1.95 (1H, m), 2.62 (1H, dd, *J* = 13.7, 7.6 Hz), 2.73 (1H, dd, *J* = 13.7, 7.7 Hz), 3.15 (3H, s), 3.39 (1H, q-like, *J* = 8.1 Hz), 3.72 (3H, s), 3.92 (1H, t-like, *J* = 7.3 Hz), 4.10 (1H, t-like, *J* = 7.2 Hz), 4.42 (1H, t-like, *J* = 7.3 Hz; ^{13}C NMR (125 MHz) δ 17.26 (q), 18.65 (q), 30.07 (d), 30.74 (d), 32.14 (q), 33.56 (t), 34.31 (t), 51.36 (d), 56.60 (d), 61.41 (d), 67.52 (t), 157.27 (s), 171.23 (s); MS: 270 (M^+), HRMS: Calcd for $C_{13}H_{22}N_2O_4$ 270.1578; Found 270.1563; $[\alpha]_D^{26}$ – 53.3 (*c* 1.28, $CHCl_3$).

(5*S*, 6*R*, 8*R*, 9*R*)-(-)-6,8-Dimethyl-5-(2-oxopropyl)hexahydrooxazolo[3,4-*a*]pyridin-3-one (11)

To a stirred solution of the above Weinreb amide (51 mg, 0.19 mmol) in THF (2 mL) was added a solution of MeMgBr (0.9 m in THF, 0.31 mL, 0.28 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 3). The organic extracts were combined, dried, and evaporated to give a colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=10:1-7:1) to give **11** (31 mg, 73%) as a colorless solid (mp 53-56 °C).

IR (KBr) 2962, 1748 cm^{-1}; ^1H NMR (500 MHz) δ 0.83 (3H, d, *J* = 6.4 Hz), 1.07 (3H, d, *J* = 7.3 Hz), 1.40-1.50 (2H, m), 1.62-1.69 (1H, m), 1.82-1.84 (1H, br), 2.13 (3H, s), 2.63 (1H, dd, *J* = 15.4, 7.6 Hz), 2.68 (1H, dd, *J* = 15.4, 7.7 Hz), 3.23-3.28 (1H, m), 3.95 (1H, dd, *J* = 8.5, 6.4 Hz), 4.12 (1H, t-like, *J* = 7.7 Hz), 4.36 (1H, dd, *J* = 8.5, 6.4 Hz); ^{13}C NMR (125 MHz) δ 17.22 (q), 18.52 (q), 29.68 (q), 29.77 (d), 30.86 (d), 33.40 (t), 45.30 (t), 50.99 (d), 56.41 (d), 67.25 (t), 157.24 (s), 206.19 (s); MS: 225 (M^+), 182 (100); HRMS: Calcd for $C_{12}H_{19}NO_3$ 225.1364; Found 225.1364; $[\alpha]_D^{26}$ –13.9 (*c* 1.48, $CHCl_3$).

(5*S*, 6*R*, 8*R*, 9*R*)-(-)-6,8-Dimethyl-5-(2-methyl-[1,3]dioxolan-2-ylmethyl)hexahydrooxazolo-[3,4-*a*]pyridin-3-one

To a stirred solution of **11** (161 mg, 0.72 mmol) in benzene (15 mL) were added *p*-TsOH•H_2O (30 mg, 0.16 mmol) and ethyleneglycol (0.3 mL, 5.39 mmol), and the reaction mixture was refluxed using Dean-Stark apparatus for 18 h. After cooling, the reaction was quenched with satd. $NaHCO_3$ (aq) and the organic layer was separated. The aqueous layer was extracted with benzene (10 mL x 3), and the organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=10:1-7:1) to give the acetal (166 mg, 86%) as a colorless solid (mp 82-84 °C).

IR (KBr) 2961, 2922, 1740, 1060 cm^{-1}; ^1H NMR (500 MHz) δ 0.82 (3H, d, *J* = 6.5 Hz), 1.04 (3H, d, *J* = 7.3 Hz), 1.33 (3H, s), 1.45-1.47 (2H, m), 1.63-1.69 (1H, m), 1.76 (1H, dd, *J* = 14.5, 4.7 Hz), 1.83-1.88 (1H, m), 2.06 (1H, dd, *J* = 14.5, 9 Hz), 3.28-3.33 (1H, m), 3.87-3.99 (6H, m), 4.36 (1H, t-like, *J* = 8.5 Hz); ^{13}C NMR (125 MHz) δ 17.35 (q), 18.34 (q), 23.76 (q), 30.16 (d), 32.20 (d), 33.75 (t), 39.65 (t), 50.72 (d), 56.25 (d), 64.26 (t), 66.91 (t), 109.03 (s), 157.09 (s); MS: 269 (M^+), 254 (100); HRMS: Calcd for $C_{14}H_{23}NO_4$ 269.1627; Found 269.1641; $[\alpha]_D^{26}$ –20.4 (*c* 1.59, $CHCl_3$).

2-Methyl-2-propyl (2*R*, 3*R*, 5*R*, 6*S*)-(+)-2-Hydroxymethyl-3,5-dimethyl-6-(2-methyl-[1,3]dioxolan-2-ylmethyl)piperidine-1-carboxylate (12)

A solution of 2M KOH in *i*-PrOH (50 mL) was added to the above acetal (1.9 g, 7.06 mmol), and the resulting mixture was heated at 120 °C in the sealed tube for 2 days. After cooling, the solvent was evaporated, and the residue was dissolved in H_2O. The aqueous mixture was extracted with $CHCl_3$ (20 mL x 10), and the organic extracts were combined, dried over K_2CO_3, and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred solution of the above oil in H_2O (24 mL) and dioxane (48 mL) were added NaOH (950 mg, 23.75 mmol) and Boc_2O (4.8 g, 21.99 mmol) at 0 °C, and the resulting solution was stirred at room temperature for 18 h. The aqueous layer was extracted with $CHCl_3$ (10 mL x 5). The organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (50 g, hexane:acetone=20:1) to give **12** (1.8 g, 74% in 2 steps) as a colorless oil.

IR (neat) 3425, 2963, 2928, 1669 cm^{-1}; ^1H NMR (500 MHz) δ 0.91 (3H, d, *J* = 6.4 Hz), 0.98 (3H, d, *J* = 6.8 Hz), 1.33 (3H, s), 1.38 (1H, br), 1.44 (9H, s), 1.72 (1H, br), 1.76 (1H, dd, *J* = 14.5, 4.1 Hz), 2.00-2.16 (2H, br), 2.83 (1H, br), 3.89 (2H, br), 3.92 (4H, m), 4.19 (1H, br), 5.29 (1H, br); ^{13}C NMR (125 MHz) δ 18.34 (q), 18.95 (q), 23.88 (q), 26.58 (d), 28.37 (q), 33.42 (d), 36.36 (t), 41.79 (t), 55.75 (d), 60.60 (t), 61.31 (d), 64.31 (t), 64.51 (t), 79.92 (s), 109.53 (s), 157.60 (s); MS: 343 (M^+), 212 (100); HRMS: Calcd for $C_{18}H_{33}NO_5$ 343.2357; Found 343.2345; $[\alpha]_D^{26}$ +22.8 (*c* 9.84, $CHCl_3$).

(2*R*, 3*R*, 5*R*, 6*S*)-(+)-2-Methyl-2-propyl 2(2-Ethoxycarbonylvinyl)-3,5-dimethyl-6-(2-methyl-[1,3]-dioxolan-2-ylmethyl)piperidine-1-carboxylate (13)

To a stirred solution of $(COCl)_2$ (0.7 mL, 8.06 mmol) in CH_2Cl_2 (20 mL) was added DMSO (1.2 mL, 17.0 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of **12** (1.8 g, 5.25 mmol) in CH_2Cl_2 (10 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (3.3 mL, 23.92 mmol) was added to the reaction mixture at –78 °C, and the reaction mixture was warmed to 0 °C for 1 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (20 mL x 5). The organic extracts were combined, dried, and evaporated to give a pale yellow oil, which was used directly in the next step.

To a stirred suspension of NaH (60%, 330 mg, 8.05 mmol) in THF (20 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (1.6 mL, 7.87 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min. To the mixture was added a solution of the above aldehyde in THF (9 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 6 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with CH_2Cl_2 (20 mL x 4). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (50 g, hexane:acetone=20:1) to give **13** (2.16 g, 73% in 2 steps) as a colorless oil.

IR (neat) 2972, 2929, 2881, 1716, 1690 cm^{-1}; ^1H NMR (500 MHz) δ 0.81 (3H, d, *J* = 6.4 Hz), 0.98 (3H, d, *J* = 6.8 Hz), 1.26 (3H, t, *J* = 7.2 Hz), 1.33 (3H, s), 1.35-1.42 (1H, m), 1.40 (9H, s), 1.80-1.86 (4H, m), 2.14-2.18 (1H, m), 3.46 (1H, t-like, *J* = 8.5 Hz), 3.88-3.95 (5H, m), 4.18 (2H, q, *J* = 7.2 Hz), 5.80 (1H, d, *J* = 15.8 Hz), 7.10 (1H, dd, *J* = 15.8, 7.7 Hz); ^{13}C NMR (125 MHz) δ 14.18 (q), 18.67 (q), 18.85 (q), 23.82 (q), 28.28 (q), 29.28 (d), 31.70 (d), 35.36 (t), 39.46 (t), 55.18 (d), 60.06 (t), 64.24 (t), 64.34 (t), 79.87 (s), 109.32 (s), 120.12 (d), 148.59 (d), 155.75 (s), 166.58 (s); MS: 411 (M^+), 253 (100); HRMS: Calcd for $C_{22}H_{37}NO_6$ 411.2619; Found 411.2932; $[\alpha]_D^{26}$ +37.0 (*c* 1.39, $CHCl_3$).

(2a*S*, 5a*S*, 6*R*, 8*R*, 8a*S*)-(+)-6,8-Dimethyldecahydropyrrolo[2,1,5-de]quinolizin-4-one (14) and Its acetal (15)

To a stirred solution of **13** (165 mg, 0.40 mmol) in EtOAc (20 mL) was added 10% Pd-C (50 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 45 h. The catalyst was removed by filtration and the filtrate was evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in CH_2Cl_2 (2 mL) was added a solution of DIBAL (0.93 M in hexane, 0.43 mL, 0.4 mmol) at –78 °C, and the resulting mixture was stirred at –78 °C for 30 min. The reaction was quenched with MeOH (1 mL) and satd. Rochelle solution in H_2O (1 mL). The organic layer was seperated, and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 3). The organic layer and extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in benzene (24 mL) and acetone (4 mL) was added *p*-TsOH•H_2O (228 mg, 1.2 mmol), and the reaction mixture was heated at reflux using Dean-Stark apparatus for 5 h. After cooling, the reaction was quenched with satd. $NaHCO_3$ (aq), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 5), and the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=30:1-15:1) to give **14** (52 mg, 62% in 3 steps) as a colorless solid (mp 57~58 °C) and its acetal **15** (15 mg, 15% in 3 steps) as a pale yellow oil.

Ketone **14**: IR (KBr) 2959, 2920, 2867, 1707 cm^{-1}; ^1H NMR (500 MHz) δ 0.91 (3H, d, *J* = 6.3 Hz), 1.18 (3H, d, *J* = 7 Hz), 1.38-1.53 (4H, m), 1.63 (1H, m), 1.75 (1H, m), 2.02-2.08 (2H, m), 2.13-2.20 (2H, m), 2.29 (1H, dd, *J* = 13.5, 11 Hz), 2.58 (1H, td, *J* = 10, 6.4 Hz), 2.64 (1H, t, *J* = 13 Hz), 3.08 (1H, dt, *J* = 12, 2.5 Hz), 3.39 (1H, m); ^{13}C NMR (125 MHz) δ 18.74 (q), 20.42 (q), 28.88 (t), 29.00 (t), 32.13 (d), 33.23 (d), 35.68 (t), 42.67 (t), 45.14 (t), 59.59 (d), 61.05 (d), 61.55 (d), 210.34 (s); MS: 207 (M^+), 91 (100); HRMS: Calcd for $C_{13}H_{21}NO$ 207.1622; Found 207.1642; $[\alpha]_D^{26}$ +27.1 (*c* 2.29, $CHCl_3$).

Acetal **15**: IR (neat) 2951, 2921, 2878, 1152 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.84 (3H, d, *J* = 6.4 Hz), 1.15 (3H, d, *J* = 7.3 Hz), 1.27-1.39 (5H, m), 1.42-1.44 (1H, m), 1.51-1.56 (2H, m), 1.68 (1H, br), 1.83 (1H, t, *J* = 12.8 Hz), 1.94 (1H, m), 2.04 (1H, m), 2.44 (1H, m), 3.00 (1H, d-like, *J* = 12.7 Hz), 3.26 (1H, m), 3.96 (4H, s-like); ^{13}C NMR (125 MHz) δ 18.82 (q), 20.42 (q), 28.07 (t), 28.95 (t), 32.18 (d), 32.93 (d), 34.19 (t), 36.36 (t), 36.57 (t), 57.33 (d), 57.73 (d), 58.96 (d), 63.83 (t), 64.41 (t), 109.17 (s); MS: 251 (M^{+}), 250 (100); HRMS: Calcd for $C_{15}H_{25}NO_2$ 251.1884; Found 251.1889; $[\alpha]_D^{26}$ –4.6 (*c* 1.48, $CHCl_3$).

Deprotection of the acetal (**15**) with acid: To a stirred solution of **15** (179 mg, 0.71 mmol) in acetone (20 mL) was added *p*-TsOH•H_2O (1 g, 5.71 mmol), and the reaction mixture was heated at reflux for 20 h. After cooling, the reaction was quenched with satd. $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2 (20 mL x 4). The organic extracts were combined, dried over K_2CO_3, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=30:1-15:1) to give **14** (118 mg, 80%) as a colorless solid, whose spectral data were identical with those of the authentic sample.

(2a*S*, 5a*S*, 6*R*, 8*R*, 8a*R*)-(-)-6,8-Dimethyl-2,2a,5,5a,6,7,8,8a-octahydro-1*H*-pyrrolo[2,1,5-de]-quinolizin-4-yl Trifluoromethanesulfonate (16)

To a stirred solution of *R*-(*R**,*R**)-(+)-bis(α-methylbenzyl)amine (110 mg, 0.49 mmol) in THF (1 mL) was added *n*-BuLi (1.6 M in hexane, 0.3 mL, 0.49 mmol) at 0 °C, and the resulting solution was stirred at 0 ° C for 30 min. To the above solution was added a solution of **14** (66 mg, 0.32 mmol) in THF (2 mL) at – 78 °C, and the reaction mixture was stirred at – 78 °C for 30 min. To the reaction mixture was added a solution of 2[*N*,*N*-Bis(trifluoromethylsulfonyl)amino]-5-chloropyridie (Comins' reagent) (194 mg, 0.49 mmol) at –78 °C, and the reaction mixture was warmed to –40 °C for 30 min. The reaction was quenched with satd. $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2 (15 mL x 5). The organic extracts were combined, dried over K_2CO_3, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=150:1) to give **16** (58 mg, 54%) as a colorless oil.

IR (neat) 2947, 2926, 2875, 1283 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.88 (3H, d, *J* = 6.4 Hz), 1.20 (3H, d, *J* = 7.3 Hz), 1.34-1.46 (4H, m), 1.52 (1H, m), 1.78 (1H, m), 1.99 (2H, m), 2.10 (1H, td, *J* = 10, 5 Hz), 2.20 (1H, m), 2.59 (1H, m), 3.11 (1H, dd, *J* = 11, 5 Hz), 3.99 (1H, dd-like, *J* = 7, 2.5 Hz), 5.62 (1H, t-like, *J* = 2.5 Hz); ^{13}C NMR (125 MHz) δ 18.77 (q), 20.03 (q), 26.65 (t), 27.86 (t), 29.19 (t), 32.22 (d), 35.19 (t), 57.23 (d), 57.46 (d), 60.79 (d), 100.57 (s), 121.95 (d), 144.71 (s); MS: 339 (M^+), 69 (100); HRMS: Calcd for $C_{14}H_{20}F_3NO_3S$ 339.1115; Found 339.1137; $[\alpha]_D^{26}$ –13.8 (*c* 1.84, $CHCl_3$).

(2a*S*, 5a*S*, 6*R*, 8*R*, 8a*S*)-(+)-3,5-Dimethyl-7-methylenedecahydropyrrolo[2,1,5-de]quinolizine (17)

To a stirred suspension of $MeP^+Ph_3I^-$ (1.22 g, 3.01 mmol) in THF (5 mL) was added *n*-BuLi (1.6 M in hexane, 1.65 mL, 2.63 mmol) at 0 °C, and the resulting yellow suspension was stirred at 0 °C for 15 min. To the suspension was added a solution of **14** (78 mg, 0.38 mmol) in THF (2 mL) at 0 °C, and the resulting suspension was stirred at room temperature for 21 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 4). The organic extracts were combined, dried over K_2CO_3, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=100:1) to give **17** (65 mg, 84%) as a colorless oil.

IR (neat) 3070, 2954, 2927, 2791 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.86 (3H, d, *J* = 6.9 Hz), 1.14 (3H, d, *J* = 7.3 Hz), 1.34-1.38 (4H, m), 1.54 (1H, m), 1.74 (1H, br), 1.85 (1H, d, *J* = 11.5 Hz), 1.96-2.07 (4H, m), 2.32 (1H, t, *J* = 12.4 Hz), 2.59 (1H, q-like, *J* = 6.9 Hz), 2.74 (1H, dm, *J* = 12.4 Hz), 3.05 (1H, br), 4.66 (2H, br); ^{13}C NMR (125 MHz) δ 18.79 (q), 20.49 (q), 28.54 (t), 29.11 (t), 32.31 (d), 33.25 (d), 35.13 (t), 36.52 (t), 37.60 (t), 59.45 (d), 61.58 (d), 61.92 (d), 106.48 (t), 148.42 (s); MS: 205 (M^+), 150 (100); HRMS: Calcd for $C_{14}H_{23}N$ 205.1829; Found 205.1844; $[\alpha]_D^{26}$ +12.4 (*c* 3.01, $CHCl_3$).

(2a*S*, 5a*S*, 6*R*, 8*R*, 8a*S*)-(+)-3,5,7-Trimethyl-2,2a,3,4,5,5a,6,8a-octahydro-1*H*-pyrrolo[2,1,5-de]-quinolizidine (205B, 3)

To a stirred solution of **17** (60 mg, 0.29 mmol) in benzene (6 mL) was added *p*-TsOH•H_2O (167 mg, 0.88 mmol), and the reaction mixture was heated at reflux for 24h. After cooling, the reaction was quenched with satd. $NaHCO_3$ (aq), and the organic layer was separated. The aqueous layer was extracted with Et_2O (10 mL x 4), the organic layer and extracts were combined, dried over K_2CO_3, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=100:1) to give **3** (38 mg, 63%) as a pale yellow oil.

IR (neat) 2956, 2905, 2790, 1660, 1458, 1375, 1317, 1216, 1169 cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (3H, d, *J* = 6.4 Hz), 1.19 (3H, d, *J* = 7.3 Hz), 1.27-1.52 (4H, br m), 1.64 (3H, s), 1.72 (1H, m), 1.92 (1H, m), 2.12-2.18 (3H, m), 3.00 (1H, dd, *J* = 11.2, 4.5 Hz), 3.80 (1H, br), 5.20 (1H, br); ^{13}C NMR (125 MHz) δ 18.83 (q), 20.19 (q), 23.56 (q), 28.35 (t), 28.38 (t), 29.22 (t), 32.44 (d), 32.55 (d), 35.42 (d), 56.49 (d), 58.04 (d), 60.46 (d), 125.52 (d), 129.52 (d); MS: 205 (M^+), 71 (100); HRMS: Calcd for $C_{14}H_{23}N$ 205.1829; Found 205.1828; $[\alpha]_D^{26}$ +8.1 (*c* 1.05, $CHCl_3$).