Supporting Information

Melting point were 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).

Methyl (6*S*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-6-oxopiperidine-1-carboxylate

To a stirred solution of **1** (1.85 g, 5.40 mmol) in THF (22 mL) was added a solution of *n*-BuLi (1.6 m in hexane, 3.5 mL, 5.54 mmol) at –78 °C, and the resulting mixture was stirred at –78 °C for 30 min. To the reaction mixture was added $ClCO_2Me$ (0.43 mL, 5.54 mmol) at –78 °C, and then the reaction mixture was warmed to 0 °C for 2 h. The reaction was quenched with satd. $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2 (50 mL x1, 15 mL x 2). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (50 g, hexane:acetone=30:1~20:1) to give the imide (2.10 g, 98%) as a colorless solid (mp 97-102 °C).

IR (KBr) 2958, 1718, 1113 cm^{-1}; ^1H NMR (500 MHz) δ 1.06 (9H, s), 1.69-1.75 (1H, m), 1.86-1.99 (2H, m), 2.12-2.17 (1H, m), 2.49-2.52 (2H, m), 3.72-3.76 (2H, m), 3.76 (3H, s), 4.41-4.44 (1H, m), 7.37-7.45 (6H, m), 7.63-7.67 (4H, m); ^{13}C NMR (125 MHz) δ 17.44 (t), 18.96 (s), 24.18 (t), 26.63 (q), 34.64 (t), 53.52 (q), 56.16 (d), 64.10 (t), 127.60 (d), 129.65 & 129.68 (each d), 132.63 & 132.81 (each s), 135.36 & 135.42 (each d), 154.69 (s), 171.69 (s); MS: 425 (M^+), 115 (100); HRMS: Calcd for $C_{24}H_{31}NO_4Si$ 425.2022; Found 425.2006; $[\alpha]_D^{26}$ –41.6 (*c* 5.67, $CHCl_3$).

Mehtyl (6*S*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-6-trifluoromethanesulfonyloxy-3,4-dihydro-2*H*-pyridine-1-carboxylate

To a stirred solution of hexamethyldisilazane (1.5 mL, 6.97 mmol) in THF (5 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 4.4 mL, 6.97 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min. To a stirred solution of the above imide (2.47 g, 5.81 mmol) in THF (15 mL) was added a solution of LiHMDS prepared above at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. To the above reaction mixture was added a solution of 2-[*N*,*N*-bis(trifluoromethylsulfonyl)amino]5-chloropyridine (Comins' reagent) (97%, 2.73 g, 6.97 mmol) in THF (6 mL) at –78 °C, and the resulting mixture was warned to –40 °C for 1 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was extracted with Et_2O (20 mL x 4). The organic extracts were combined, dried, and evaporated to give pale yellow solid, which was chromatographed on SiO_2 (60 g, hexane:acetone=100:1-50:1) to give enol triflate (3.0 g, 96%) as a colorless oil.

IR (neat) 2962, 1733, 1423, 1213, 1114 cm^{-1}; ^1H NMR (500 MHz) δ 1.06 (9H, s), 1.69-1.76 (1H, m), 1.91-2.04 (2H, br m), 2.13-2.19 (1H, m), 3.57 (2H, dd, *J* = 10.2, 8.1 Hz), 3.79 (3H, s), 4.64-4.68 (1H, m), 5.17 (1H, t, *J* = 3.8 Hz), 7.37-7.46 (6H, m), 7.63-7.67 (4H, m); ^{13}C NMR (125 MHz) δ 19.09 (t), 19.29 (s), 22.22 (t), 26.81 (q), 53.69 (q), 55.63 (d), 60.79 (t), 106.05 (d), 127.63 (d), 129.69 (d), 133.06 & 133.11 (each s), 135.42 & 135.44 (each d), 138.05 (s), 154.69 (s); MS: 557 (M^+), 422 (100); HRMS: Calcd for $C_{25}H_{30}F_3NO_6Si$ 557.1515; Found 557.1518; $[\alpha]_D^{26}$ –18.8 (*c* 1.57, $CHCl_3$).

Dimethyl (*S*)-(-)-6-(*tert*-butyldiphenylsilyloxymethyl)-5,6-dihydro-4*H*-pyridine-1,2-dicarboxylate (2)

To a stirred solution of the above enol triflate (5.30 g, 9.52 mmol) in DMF (25 mL) was added $Pd(Ph_3P)_4$ (550 mg, 0.48 mmol), and the resulting mixture was stirred at room temperature under CO balloon pressure for 30 min. To the reaction mixture were added Et_3N (5.3 mL, 38.1 mmol) and MeOH (15.4 mL, 381.0 mmol), and then the reaction mixture was stirred at 70 °C under CO balloon pressure for 15 h. After cooling, the reaction mixture was diluted with H_2O (100 mL) and brine (25 mL), and the aqueous mixture was extracted with Et_2O (50 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (80 g, hexane:acetone=50:1-30:1) to give **2** (3.91 g, 88%) as a colorless oil.

IR (neat) 2968, 1732, 1652, 1240 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (9H, s), 1.77-1.85 (1H, m), 1.91-1.99 (1H, br m), 2.04-2.16 (1H, m), 3.52 (2H, dd, *J* = 10.2, 8.5 Hz), 3.70 (3H, s), 3.77 (1H, dd, *J* = 10.2, 6.3 Hz), 4.55 (1H, br), 5.96 (1H, t, *J* = 3.5 Hz), 7.37-7.45 (6H, m), 7.65-7.67 (4H, m); ^{13}C NMR (125 MHz) δ 19.43 (t), 19.55 (s), 22.48 (t), 26.95 (q), 52.16 (q), 52.69 (d), 53.30 (q), 61.39 (t), 121.98 (s), 127.72 (d), 129.72 & 129.75 (each d), 130.59 (s), 133.31 & 133.41 (each s), 135.58 (d), 154.52 (s), 165.49 (s); MS: 467 (M^+, 100); HRMS: Calcd for $C_{26}H_{33}NO_5Si$ 467.2128; Found 467.2134; $[\alpha]_D^{26}$ –53.3 (*c* 1.33, $CHCl_3$).

Dimethyl (2*R*, 3*S*, 6*S*)-(+)-6-(*tert*-butyldiphenylsilyloxymethyl)-3-vinylpiperidine-1,2-dicarboxylate

To a stirred suspension of CuI (1.71 g, 9.00 mmol) in Et_2O (15 mL) was added a solution of vinyl lithium, prepared from tetravinyltin (0.37 mL, 4.50 mmol) and MeLi (1.0 M in Et_2O, 18 mL, 18.0 mmol) in Et_2O (15 mL) at 0 °C for 30 min, at –78 °C, and the resulting suspension was warmed to –35 °C for 20 min. The resulting suspension was re-cooled to –78 °C, and a solution of **2** (1.05 g, 2.25 mmol) in Et_2O (5 mL) was added to the resulting suspension. The reaction mixture was warmed to -30 °C for 1 h, and the reaction was quenched with satd. NH_4Cl (aq). The aqueous mixture was diluted with CH_2Cl_2 (100 mL), and the resulting suspension was filtered. The filtrate was separated, and the aqueous layer was extracted

with CH_2Cl_2 (20 mL x 2). The organic layer and extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (40 g, hexane:acetone=40:1-30:1) to give the adduct (1.07 g, 96%) as a colorless oil.

IR (neat) 3071, 2935, 2890, 1750, 1705, 1113 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (9H, s), 1.41-1.43 (1H, m), 1.59 (1H, br), 1.74-1.81 (1H, br m), 1.85-1.88 (1H, m), 3.00 (1H, br), 3.45 (3H, s), 3.65 (3H, s), 3.67-3.70 (1H, m), 4.28 (1H, br), 4.78 (1H, br), 5.09-5.30 (2H, m), 5.81-5.88 (1H, m), 7.36-7.44 (6H, m), 7.65-7.67 (4H, m); ^{13}C NMR (125 MHz) δ 18.68 (t), 19.56 (s), 21.03 (t), 27.15(q), 37.06 (d), 52.27 (d), 52.34 (q), 53.19 (q), 56.05 (d), 62.34 (t), 115.56 (t), 127.74 (d), 129.72 (d), 133.76 (s), 135.63 (d), 138.91 (d), 157.63 (s), 172.66 (s); MS: 495 (M^+); HRMS: Calcd for $C_{28}H_{37}NO_5Si$ 495.2441; Found 495.2464; $[\alpha]_D^{26}$ +2.1 (*c* 1.57, $CHCl_3$).

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

To a stirred solution of the above adduct (2.0 g, 4.04 mmol) in THF (15 mL) was added Super-Hydride (1M in THF, 8.9 mL, 8.9 mmol) at 0 °C, and the resulting solution 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 (15 mL x 6). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (40 g, hexane:acetone=30:1-6:1) to give **3** (1.8 g, 96%) as a colorless oil.

IR (neat) 3449, 3070, 2937, 2862, 1679 cm^{-1}; ^1H NMR (500 MHz) δ 1.05 (9H, s), 1.26-1.39 (2H, m), 1.63-1.70 (1H, m), 1.79-1.86 (1H, br m), 2.35 (1H, br), 2.96 (1H, br), 3.55-3.69 (4H, m), 3.67 (3H, br s), 4.25-4.29 (1H, m), 4.39 (1H, br), 5.06-5.12 (2H, m), 5.79-5.86 (1H, m), 7.39-7.46 (6H, m), 7.66-7.72 (4H, m); ^{13}C NMR (125 MHz) δ 19.03 (s), 19.95 (t), 21.27 (t), 26.67 & 26.72 (each q), 36.70 (d), 50.83 (d), 52.72 (q), 56.14 (d), 64.43 (t), 64.88 (t), 115.05 (t), 127.67 & 127.70 (each d), 129.74 (d), 132.93 & 133.02 (each s), 135.44 & 135.49 (each d), 140.18 (d), 157.97 (s); MS: 410 (M^+-57), 378 (100); HRMS: Calcd for $C_{23}H_{28}NO_4Si$ 410.1787; Found 410.1807; $[\alpha]_D^{26}$ +19.7 (*c* 1.53, $CHCl_3$).

Methyl (2*S*, 3*S*, 6*S*)-(-)-6-(*tert*-butyldiphenylsilyloxymethyl)-2-propenyl-3-vinylpiperidine-1-carboxylate

To a stirred solution of $(COCl)_2$ (0.24 mL, 2.77 mmol) in CH_2Cl_2 (5 mL) was added DMSO (0.38 mL, 5.43 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of **3** (857 mg, 1.84 mmol) in CH_2Cl_2 (4 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (1.1 mL, 7.98 mmol) 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 (10 mL x 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of $EtP^+Ph_3Br^-$ (2.73 g, 7.35 mmol) in THF (15 mL) was added a solution of *n*-BuLi (1.6M ih hexane, 4 mL, 6.4 mmol) at 0 °C, and the resulting orange solution was stirred at 0 °C for 30 min. To the solution was added a solution of the above oil in THF (6 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=100:1-80:1) to give the olefin (691 mg, 79% in 2 steps) as a colorless oil.

IR (neat) 3070, 2938, 2860, 1697 cm^{-1}; ^1H NMR (500 MHz) δ 1.06 (9H, s), 1.33-1.38 (1H, m), 1.67 (3H, t-like, *J* = 6.8 Hz), 1.69-1.75 (2H, br m), 1.81-1.88 (1H, m), 2.19 (1H, br), 3.58-3.69 (2H, m), 3.63 (3H, br s), 4.35 (1H, m), 4.90 (1H, d-like, *J* = 9.4 Hz), 5.05-5.10 (2H, m), 5.29-5.33 (1H, m), 5.38-5.43 (1H, m), 5.85-5.91 (1H, m), 7.38-7.45 (6H, m), 7.67-7.68 (4H, m); ^{13}C NMR (125 MHz) δ 13.02 (q), 19.18 (s), 19.47 (t), 20.73 (t), 26.78 (q), 41.73 (d), 51.01 (d), 51.71 (d), 52.46 (q), 64.35 (t), 114.70 (t), 127.62 (d), 129.62 (d), 131.10 (d), 133.50 & 133.64 (each s), 135.56 & 135.59 (each d), 140.22 (d), 156.81 (s); MS: 420 (M^+-57), 423 (100); HRMS: Calcd for $C_{25}H_{30}NO_3Si$ 420.1995; Found 420.2017; $[\alpha]_D^{26}$ –64.5 (*c* 2.09, $CHCl_3$).

Methyl (2*S*, 3*R*, 6*S*)-(-)-3-ethyl-6-hydroxymethyl-2-propylpiperidine-1-carboxylate (4)

To a solution of the above olefin (704 mg, 1.48 mmol) in EtOAc (15 mL) was added 5% Pd-C (50 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 48 h. The catalyst was removed by filtration, and the filtrate was evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in THF (10 mL) was added a solution of TBAF (1M in THF, 1.9 mL, 1.9 mmol) at 0 °C, and the resulting solution was stirred at room temperature for 1 h. The reaction was quenched eith satd. NH_4Cl (aq), and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 8). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=20:1-7:1) to give **4** (276 mg, 77% in 2 steps) as a colorless oil.

IR (neat) 3447, 2956, 2872, 2672 cm^{-1}; ^1H NMR (500 MHz) δ 0.87-0.91 (6H, m), 1.23-1.59 (9H, br m), 1.71-1.81 (2H, m), 2.94 (1H, br), 3.57-3.64 (2H, m), 3.68 (3H, s), 3.92 (1H, br), 4.25 (1H, br); ^{13}C NMR (125 MHz) δ 11.96 (q), 13.98 (q), 19.92 (t), 20.15 (t), 25.73 (t), 37.93 (d), 38.87 (t), 52.67 (q), 52.89 (d), 54.46 (d), 52.46 (q), 65.77 (t), 158.85 (s); MS: 243 (M^+), 131 (100); HRMS: Calcd for $C_{13}H_{25}NO_3$ 243.1833; Found 243.1821; $[\alpha]_D^{26}$ –21.8 (*c* 1.05, $CHCl_3$).

Dimethyl (2*S*, 5*R*, 6*S*)-(-)-5-ethyl-6-propylpiperidine-1,2-dicarboxylate

To a stirred solution of $(COCl)_2$ (0.53 mL, 6.12 mmol) in CH_2Cl_2 (12 mL) was added DMSO (0.88 mL, 12.38 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of **4** (1 g, 4.12 mmol) in CH_2Cl_2 (9 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (2.6 mL, 18.47 mmol) 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 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of NaH_2PO_4 (4.9 g, 40.83 mmol), 2-methyl-2-butene (8.8 mL, 82.5 mmol), and the above oil in *t*-BuOH (20 mL) was added a solution of $NaClO_2$ (80%, 2.7 g, 24.3 mmol) in H_2O (8 mL), and the resulting suspension was stirred at room temperature for 45 min. The reaction was quenched with satd. $NaHSO_3$ (aq) and 10% HCl at 0 °C, and the aqueous mixture was extracted with EtOAc (15 mL x 10). The organic extracts were combined, dried, and evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in EtOAc (20 mL) was added a solution of CH_2N_2 in Et_2O at 0 °C, and the reaction mixture was stirred at room temperature for 20 h. The solvent was evaporated, and the residue was chromatographed on SiO_2 (40 g, hexane:acetone=20:1) to give the methyl ester (1.008 g, 90% in 3 steps) as a colorless oil.

IR (neat) 2957, 2872, 1740, 1701 cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (6H, t-like, *J* = 6.8 Hz), 1.24-1.42 (7H, br m), 1.46-1.52 (1H, m), 1.71-1.87 (2H, m), 1.96 (1H, br), 3.66 (3H, s), 3.69 (3H, br s), 3.88-4.05 (1H, br), 4.63 & 4.84 (1H, br); ^{13}C NMR (125 MHz) δ 11.87 (q), 13.86 (q), 19.91 (t), 20.31 (t), 25.02 (t), 36.19 (t), 37.75 (d), 51.92 (q), 52.72 (q), 54.79 (d), 157.80 (s), 173.24 (s); MS: 271 (M^+), 228 (100); HRMS: Calcd for $C_{14}H_{25}NO_4$ 271.1784; Found 271.1816; $[\alpha]_D^{26}$ –65.1 (*c* 2.17, $CHCl_3$).

Dimethyl (5*R*, 6*S*)-(+)-5-ethyl-6-propyl-5,6-dihydro-4*H*-pyridine-1,2-dicarboxylate (5)

To a stirred solution of hexamethyldisilazane (0.32 mL, 1.5 mmol) in THF (3 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 0.94 mL, 1.5 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min. To a stirred solution of the above methyl ester (271 mg, 1 mmol) in THF (2 mL) was added a solution of LiHMDS prepared above at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. To a stirred solution of PhSeCl (610 mg, 3 mmol) in THF (5 mL) was added a solution of Li enolate prepared above at –78 °C, and the resulting suspension was stirred at room temperature for 20 h. The solvent was evaporated and the residue was chromatographed on SiO_2 (30 g, hexane:acetone=40:1-35:1) to give **5** (207 mg, 77%) as a colorless oil.

IR (neat) 2958, 2874, 1708, 1646 cm^{-1}; ^1H NMR (500 MHz) δ 0.91 & 0.93 (each 3H, each t, *J* = 7.2 Hz), 1.17-1.34 (4H, br m), 1.42-1.51 (3H, m), 1.99 (1H, dd, *J* = 19.2, 3.9 Hz), 2.27 (1H, ddd, *J* = 19.2, 7.3, 3.9 Hz), 3.70 (3H, br s), 3.76 (3H, s), 4.26 (1H, br), 5.97 (1H, t, *J* = 3.9 Hz); ^{13}C NMR (125 MHz) δ 11.91 (q), 14.02 (q), 19.30 (t), 25.12 & 26.20 (each t), 33.04 (t), 36.30 (t), 37.99 & 38.66 (each d), 52.10 (q), 53.07 (q), 55.29 (d), 121.05 (d), 129.05 & 129.28 (each s), 155.49 (s), 165.40 (s); MS: 269 (M^+, 100); HRMS: Calcd for $C_{14}H_{23}NO_4$ 269.1627; Found 269.1604; $[\alpha]_D^{26}$ +63.4 (*c* 0.68, $CHCl_3$).

Dimethyl (2*S*, 3*R*, 5*R*, 6*S*)-(-)-5-ethyl-6-propyl-3-vinylpiperidine-1,2-dicarboxylate (6)

To a stirred suspension of CuI (622 mg, 3.27 mmol) in Et_2O (5 mL) was added a solution of vinyl lithium, prepared from tetravinyltin (0.31 mL, 1.63 mmol) and MeLi (1.01 M in Et_2O, 6.5 mL, 6.6 mmol) in Et_2O (3 mL) at 0 °C for 30 min, at –78 °C, and the resulting suspension was warmed to –35 °C for 20 min. The resulting suspension was re-cooled to –78 °C, and a solution of **5** (176 mg, 0.65 mmol) in Et_2O (4 mL) was added to the resulting suspension. The reaction mixture was warmed to 0 °C for 1 h, and the reaction was quenched with satd. NH_4Cl (aq). The aqueous mixture was diluted with CH_2Cl_2 (50 mL), and the resulting suspension was filtered. The filtrate was separated, and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 2). The organic layer and extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=70:1-40:1) to give **6** (174 mg, 90%) as a colorless oil.

IR (neat) 2957, 2873, 1747, 1702 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 & 0.89 (each 3H, each t, *J* = 7.3 Hz), 0.96 (1H, q, *J* = 12 Hz), 1.24-1.46 (6H, br m), 1.62-1.70 (1H, m), 1.70-1.77 (1H, m), 2.64 (1H, q-like, *J* = 8 Hz), 3.67 (3H, s), 3.69 (3H, s), 3.92 (1H, br), 4.29 (1H, br), 5.00-5.08 (2H, m), 5.71-5.78 (1H, m); ^{13}C NMR (125 MHz) δ 11.31 (q), 13.98 (q), 19.86 (t), 29.56 (t), 31.76 (t), 39.68 (d), 40.50 (t), 40.86 (d), 51.73 (q), 52.81 (q), 55.40 (d), 59.78 (d), 115.31 (t), 139.95 (d), 157.35 (s), 173.20 (s); MS: 254 (M^+-43, 100); HRMS: Calcd for $C_{13}H_{20}NO_4$ (M^+-C_3H_7) 254.1392; Found 254.1353; $[\alpha]_D^{26}$ –65.9 (*c* 0.91, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(-)-5-ethyl-2-hydroxymethyl-6-propyl-3-vinylpiperidine-1-carboxylate

To a stirred solution of **6** (45 mg, 0.15 mmol) in THF (1 mL) was added a solution of Super-Hydride (1 M in THF, 0.4 mL, 0.4 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 1 hr. The reaction was quenched with satd $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 5). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=30:1-15:1) to give the alcohol (41 mg, 99%) as a colorless oil.

IR (neat) 3456, 3078, 2958, 2873, 1672 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 & 0.92 (each 3H, each t, *J* = 7.3 Hz), 1.00 (1H, q, *J* = 10.7 Hz), 1.28-1.47 (6H, br m), 1.53-1.59 (1H, m), 1.62-1.66 (2H, m), 2.12 (1H, br q-like, *J* = 9.8 Hz), 3.54-3.59 (1H, m), 3.71 (3H, s), 3.72-3.85 (1H, br), 3.97 (2H, br), 5.03-5.29 (2H, m), 5.69 (1H, ddd, *J* = 17.1, 9.8, 8.1 Hz); ^{13}C NMR (125 MHz) δ 11.22 (q), 13.88 (q), 19.65 (t), 29.56 (t), 32.50 (t), 40.51 (d), 41.63 (t), 41.74 (d), 52.98 (q), 55.65 (d), 60.40 (d), 67.09 (t), 115.63 (t), 141.02 (d); MS: 238 (M^+-31), 117 (100); HRMS: Calcd for $C_{14}H_{24}NO_2$ (M^+-MeO), 238.1808; Found 238.1792; $[\alpha]_D^{26}$ –93.4 (*c* 1.86, $CHCl_3$).

(5*S*, 6*R*, 8*R*, 9*S*)-(-)-6-Ethyl-5-propyl-8-vinylhexahydrooxazolo[3,4-*a*]pyridin-3-one (7)

To a stirred solution of the above alcohol (41 mg, 0.15 mmol) in THF (1 mL) was added NaH (60%, 7.9 mg, 0.20 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 1 h. The reaction was quenched with 10% AcOH, and the aqueous mixture was extracted with CH_2Cl_2 (5 mL x 4). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=20:1) to give **7** (30.3 mg, 84%) as a colorless oil.

IR (neat) 3078, 2962, 2872, 1751 cm^{-1}; ^1H NMR (500 MHz) δ 0.87 (3H, t, *J* = 7.5 Hz), 0.93 (3H, *t*, J = 7.3 Hz), 1.06-1.16 (2H, m), 1.26-1.33 (1H, br m), 1.51 (1H, qm, *J* = 11.5 Hz), 1.54-1.62 (2H, m), 1.73-1.80 (1H, m), 3.54-3.59 (1H, m), 1.97 (1H, dt, *J* = 13, 3.5 Hz), 2.17 (1H, qm, *J* = 11 Hz), 2.21-2.29 (1H, m), 2.82 (1H, td, *J* = 10, 3.5 Hz), 3.24 (1H, ddd, *J* = 13, 7, 3 Hz), 3.96 (1H, dd, *J* = 8, 3 Hz), 4.16 (1H, dd, *J* =

8, 7 Hz), 5.10-5.14 (2H, m), 5.52 (1H, ddd, *J* = 16.5, 10, 8 Hz); ^{13}C NMR (125 MHz) δ 10.20 (q), 14.01 (q), 19.49 (t), 24.19 (t), 29.34 (t), 35.98 (t), 39.97 (d), 44.78 (d), 61.16 (d), 61.20 (d), 64.87 (t), 117.44 (t), 137.61 (d), 155.82 (s); MS: 237 (M^+, 100); HRMS: Calcd for $C_{14}H_{23}NO_2$, 237.1728; Found 237.1740; $[\alpha]_D^{26}$ –31.9 (*c* 1.52, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(-)-2-(2-ethoxycarbonylvinyl)-5-ethyl-6-propyl-3-vinylpiperidine-1-carboxylate (8)

To a stirred solution of $(COCl)_2$ (0.11 mL, 1.26 mmol) in CH_2Cl_2 (2 mL) was added DMSO (0.18 mL, 2.52 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of the above alcohol (150 mg, 0.56 mmol) in CH_2Cl_2 (3 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (0.52 mL, 3.78 mmol) 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 (10 mL x 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of NaH (60%, 25 mg, 0.61 mmol) in THF (2 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (0.12 mL, 0.59 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 15 min. To the reaction mixture was added a slolution of the above oil in THF (4 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (12 g, hexane:acetone=80:1) to give **8** (181 mg, 96%) as a colorless oil.

IR (neat) 3078, 2958, 2873, 1697 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.86-0.92 (6H, m), 1.00 (1H, q, *J* = 11.1 Hz), 1.25 (3H, t, J = 7.3 Hz), 1.29-1.45 (7H, br m), 1.51-1.58 (1H, m), 1.68-1.72 (1H, m), 2.30 (1H, q-like, *J* = 11.1 Hz), 3.67 (3H, s), 4.16 (2H, q, *J* = 7.3 Hz), 4.18 (1H, br), 5.03-5.07 (2H, m), 5.59-5.66 (1H, m), 5.79-5.87 (1H, m), 6.77 (1H, dd, *J* = 15.8, 6.9 Hz); ^{13}C NMR (125 MHz) δ 11.20 (q), 13.80 (q), 14.15 (q),

19.76 (t), 29.70 (t), 32.23 (t), 41.17 (t), 41.51 (d), 41.82 (d), 52.69 (q), 55.37 (d), 58.29 (d), 60.35 (t), 116.19 (t), 122.33 (d), 139.72 (d), 147.09 (d), 157.17 (s), 166.42 (s); MS: 337 (M^+), 294 (100); HRMS: Calcd for $C_{19}H_{31}NO_4$, 337.2253; Found 337.2231; $[\alpha]_D^{26}$ –42.1 (*c* 1.08, $CHCl_3$).

Methyl (2*R*, 3*S*, 5*R*, 6*S*)-(-)-3,5-diethyl-2-(3-hydroxypropyl)-6-propylpiperidine-1-carboxylate

To a solution of **8** (200 mg, 0.59 mmol) in EtOAc (10 mL) was added 5% Pd-C (50 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 72 h. The catalyst was removed by filtration, and the filtrate was evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of the above in THF (8 mL) was added a solution of Super-Hydride (1 M in THF, 1.3 mL, 1.3 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 1 hr. The reaction was quenched with satd $NaHCO_3$ (aq), and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 5). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=30:1-8:1) to give the alcohol (157 mg, 89%) as a colorless oil.

IR (neat) 3448, 2957, 2872, 1674 cm^{-1}; ^1H NMR (500 MHz) δ 0.63 (1H, q-like, *J* = 11.1 Hz), 0.86-0.89 (6H, m), 1.18-1.66 (15H, br m), 2.01 (1H, br), 2.60 (1H, br), 3.63 (3H, s), 3.76 (1H, br), 3.92 (1H, br); ^{13}C NMR (125 MHz) δ 11.46 (q), 14.02 (q), 20.09 (t), 28.45 (t), 28.82 (t), 29.73 (t), 30.60 (t), 34.41 (t), 40.46 (t), 42.12 (d), 52.43 (q), 55.23 (d), 56.74 (d), 62.70 (t), 158.40 (s); MS: 299 (M^+), 256 (100); HRMS: Calcd for $C_{17}H_{33}NO_3$, 299.2460; Found 299.2459; $[\alpha]_D^{26}$ –7.2 (*c* 3.00, $CHCl_3$).

Methyl (2*R*, 3*S*, 5*R*, 6*S*)-(+)-3,5-diethyl-2-(3-methoxymethoxypropyl)-6-propylpiperidine-1-carboxylate (9)

To a stirred solution of the above alcohol (217 mg, 0.73 mmol) in $CHCl_3$ (5 mL) were added MOMCl (0.22 mL, 2.9 mmol) and Hünig base (0.56 mL, 3.19 mmol), and the resulting mixture was refluxed for 2 h. After cooling, the solvent was evaporated and the residue was chromatographed on SiO_2 (15 g, hexane:acetone=30:1) to give **9** (215 mg, 86%) as a colorless oil.

IR (neat) 2955, 2873, 1693, 1110 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.60 (1H, q-like, *J* = 8.8 Hz), 0.83-0.86 (6H, m), 1.19-1.62 (15H, br m), 2.04 (1H, br), 3.30 (3H, br s), 3.46 (2H, br), 3.60 (3H, br s), 3.71 (1H, br), 3.91 (1H, br), 4.55 (2H, br s); ^{13}C NMR (125 MHz) δ 11.42 (q), 14.00 (q), 20.10 (t), 27.17 (t), 28.60 (t), 30.60 (t), 34.38 (t), 40.21 (t), 42.08 (d), 52.22 (q), 54.91 (q), 56.76 (d), 67.52 (t), 96.20 (t), 158.13 (s); MS: 343 (M^+), 300 (100); HRMS: Calcd for $C_{19}H_{37}NO_4$, 343.2721; Found 343.2709; $[\alpha]_D^{26}$ +0.126 (*c* 6.28, $CHCl_3$).

(5*S*, 6*R*, 8*S*, 9*R*)-(+)-6,8-Diethyl-5-propyloctahydroindolizine (10)

To a stirred solution of *n*-PrSLi, prepared from *n*-PrSH (0.11 mL, 1.17 mmol) and *n*-BuLi (1.6 M in hexane, 0.69 mL, 1.13 mmol) in HMPA (0.5 mL) at 0 °C for 30 min. To the reaction mixture was added a solution of **9** (40 mg, 0.17 mmol) in THF (2 mL) at 0 °C, and the resulting solution was stirred at room temperature for 48 h. The reaction was quenched with NH_3 (aq), and the aqueous mixture was extracted with Et_2O (5 mL x 10). 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 MeOH (4 mL) was added c. HCl (3 drops), and the resulting mixture was refluxed for 1 h. After cooling, the solvent was evaporated, and the residue was washed with Et_2O. To the residue was added NH_3 (aq), and the aqueous mixture was extracted with $CHCl_3$ (5 mL x 8). The organic extracts were combined, dried over K_2CO_3, and evaporated to give colorless oil, which was used directly in the next step.

Carbontetrabromide (55 mg, 0.16 mmol) and Ph_3P (46 mg, 0.17 mmol) were added to a solution of the above oil in CH_2Cl_2 (1 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 2 h. To the reaction mixture was added Et_3N (0.26 mL, 1.87 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 10 min. The solvent was evaporated, and the residue was extracted with *n*-pentane (5 mL x 5). The organic extracts were combined and evaporated to give colorless solid, which was chromatographed on SiO_2 (7 g, hexane:acetone:Et_3N=50:1:5 drops) to give **10** (14 mg, 52%) as a pale yellow oil.

IR (neat) 2959, 2872, 2778, 1461, 1379, 1324, 1247, 1172, 934, 901, 733 cm^{-1}; ^1H NMR (500 MHz) δ 0.61 (1H, q-like, *J* = 12 Hz), 0.89 (9H, t, *J* = 7 Hz), 1.07 (2H, m), 1.20-1.80 (13H, br m), 1.93 (3H, br dt-like, J = 13, 3.5 Hz), 3.18 (1H, br); ^{13}C NMR (75 MHz) δ 11.08 (q), 14.76 (q), 18.00 (t), 20.71 (t), 24.71 (t), 26.03 (t), 28.80 (t), 32.98 (t), 35.23 (t), 39.94 (d), 52.06 (t), 67.49 (d); MS: 223 (M^+), 190 (100); $[\alpha]_D^{26}$ +60.4 (*c* 0.25, $CHCl_3$).

DCl salt: ^1H NMR (500 MHz, D_2O) δ 0.84-0.91 (9H, m), 1.01 (1H, q-like, *J* = 12.5 Hz), 1.23 (3H, m), 1.39 (1H, m), 1.55 (3H, br m), 1.65 (2H, m), 1.75 (2H, m), 1.94 (1H, quint-like, *J* = 11 Hz), 2.05 (2H, dm, *J* = 14 Hz), 2.33 (1H, m), 2.89 (1H, dt-like, *J* = 12, 2.5 Hz), 2.93 (1H, m), 3.03 (1H, q-like, *J* = 10 Hz), 3.65 (1H, td-like, *J* = 10, 3 Hz); ^{13}C NMR (75 MHz, D_2O) δ 9.79 (q), 9.99 (q), 13.79 (q), 16.49 (t), 19.45 (t), 23.74 (t), 25.13 (t), 27.12 (t), 30.15 (t), 33.20 (t), 38.53 (d), 40.21 (d), 51.42 (t), 67.89 (d), 71.87 (d); $[\alpha]_D^{26}$ +17.2 (*c* 0.3, $CHCl_3$).

(2*S*)-2-(2-Ethylbut-3-enyloxy)tetrahydropyran

To a stirred solution of (2*R*)-2-(hydroxymethyl)butyl acetate (730 mg, 5 mmol) in CH_2Cl_2 (5 mL) were added 3,4-dihydro-2H-pyran (0.55 mL, 6 mmol) and PPTS (251 mg, 1 mmol), and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched with satd $NaHCO_3$ (a), and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 4). The organic extracts were combined, dried, and evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of the above oil in MeOH (5 mL) was added solid K_2CO_3 (414 mg, 3 mmol) at 0 °C, and the resulting suspension was stirred at room temperature for 3 h. The reaction was quenched with 10% AcOH, and the aqueous mixture was extracted with $CHCl_3$ (10 mL x 6). The organic extracts were combined, drie, and evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of $(COCl)_2$ (0.65 mL, 7.5 mmol) in CH_2Cl_2 (7 mL) was added DMSO (1.06 mL, 15.0 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of the above oil in CH_2Cl_2 (6 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30

min. Triethylamine (3.1 mL, 22.5 mmol) 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 (15 mL x 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of $MeP^+Ph_3Br^-$ (8.08g, 20.0 mmol) in THF (20 mL) was added a solution of *n*-BuLi (1.6M ih hexane, 12 mL, 19.0 mmol) at 0 °C, and the resulting orange solution was stirred at 0 °C for 30 min. To the solution was added a solution of the above oil in THF (10 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 1.5 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (25 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (40 g, hexane:acetone=100:1-80:1) to give **3** (695 mg, 76% in 4 steps) as a colorless oil.

^{1}H NMR (500 MHz) δ 0.88 (3H, t, *J* = 7.3 Hz), 1.22-1.35 (1H, m), 1.46-1.62 (5H, br m), 1.69 (1H, m), 1.80 (1H, m), 2.22 (1H, br), 3.31 (1H, m), 3.50 (1H, br), 3.68 (1H, m), 3.80 (1H, m), 4.59 (1H, br), 5.07 (2H, m), 5.63 (1H, m).

(2*R*, 3*R*)-3-(Tetrahydropyran-2-yloxymethyl)pentane-1,2-diol

To a stirred solution of the above olefin (690 mg, 3.75 mmol) in *t*-BuOH (10 mL) and H_2O (10 mL) was added $(DHQD)_2PYR$ (4 g) at 0 °C, and the resulting suspension was stirred at 0 °C for 24 h. The reaction was quenched with Na_2SO_3 (4 g), and the reaction mixture was extracted with EtOAc (20 mL x 5). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=10:1-4:1) to give **3** (654 mg, 80%) as a colorless oil.

IR (neat) 3405, 2940, 2877, 1124 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.91-0.94 (3H, m), 1.31-1.78 (9H, br m), 2.22 & 2.28 (1H, each br), 3.46-3.65 (3H, m), 3.66-3.72 (3H, m), 3.78 (1H, br), 3.82-3.93 (2H, br m), 4.52 & 4.57 (1H, each br), 3.91 (1H, br); ^{13}C NMR (125 MHz) δ 11.60 & 11.61 (each q), 19.37 & 19.76 (each

t), 21.22 & 21.43 (each t), 25.13 (t), 30.41 & 30.55 (each t), 42.13 & 42.27 (each d), 62.38 & 62.99 (each t), 65.11 (t), 67.74 & 68.15 (each t), 73.61 & 73.59 (each d), 98.88 & 99.74 (each d).

(2*R*, 3*R*)-1-(*tert*-Butyldiphenylsilyloxy)-3-(tetrahydropyran-2-yloxymethyl)pentan-2-ol

To a stirred solution of the above diol (590 mg, 2.71 mmol) in CH_2Cl_2 (5 mL) were added TBDPSCl (0.8 mL, 2.98 mmol), Et_3N (0.5 mL, 3.52 mmol), and DMAP (70 mg, 0.54 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 20 h. The solvent was evaporated and the redisue was chromatographed on SiO_2 (30 g, hexane:acetone=50:1-30:1) to give **3** (1.21 g, 98%) as a colorless oil.

IR (neat) 3486, 3069, 2935, 2864, 1113 cm^{-1}; ^1H NMR (500 MHz) δ 0.95 & 0.96 (3H, each t, each *J* = 7.7 Hz), 1.06 (9H, s), 1.42-1.76 (9H, br m), 3.01-3.05 (1H, m), 3.44-3.52 (2H, m), 3.72-3.95 (5H, br m), 4.52 (1H, br), 7.40-7.46 (6H, m), 7.69-7.72 (4H, m); ^{13}C NMR (125 MHz) δ 11.62 & 11.76 (each q), 19.12 & 19.14 (each t), 19.32 (s), 21.02 & 21.08 (each t), 25.24 & 25.27 (each t), 26.77 (q), 30.38 & 30.41 (each t), 41.57 (d), 61.77 & 61.82 (each t), 66.33 (t), 66.97 (t), 73.18 & 73.24 (each d), 98.55 & 99.12 (each d), 127.61 (d), 129.61 & 129.62 (each d), 133.27 & 133.28 (each s), 135.47 (d).

(2*S*, 3*S*)-1-(*tert*-Butyldiphenylsilyloxy)-3-(tetrahydropyran-2-yloxymethyl)pentan-2-azide

To a stirred solution of the above silyl ether (1.49 g, 3.27 mmol) in CH_2Cl_2 (4 mL) were added MsCl (0.28 mL) and Et_3N (0.68 mL) at 0 °C, and the resulting suspension was stirred at 0 °C for 1 h. The reaction was quenched with satd $NaHCO_3$ (aq), and aqueous mixture was extracted with CH_2Cl_2 (10 mL x 4). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred solution of the above oil in DMF (10 mL) was added NaN_3 (2.1 g, 32.65 mmol), and the resulting suspension was stirred at 80 °C for 15 h. After cooling, the insoluble material was filtered, washed with CH_2Cl_2, and filtrate was evaporated to give pale yellow oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=50:1-40:1) to give **3** (1.3 g, 83%) as a colorless oil.

IR (neat) 3070, 2936, 2098, 1112, 1032 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.88 & 0.90 (3H, each t, each *J* = 7.3 Hz), 1.10 (9H, s), 1.44-1.75 (9H, br m), 3.22-3.29 (1H, m), 3.44-3.52 (1H, m), 3.66-3.83 (5H, br m), 4.46 & 4.51 (1H, each br), 7.39-7.47 (6H, m), 7.70-7.74 (4H, m); ^{13}C NMR (125 MHz) δ 11.82 & 11.91 (each q), 19.06 & 19.14 (each t), 19.42 (s), 20.09 & 20.26 (each t), 25.35 & 25.38 (each t), 26.66 (q), 30.45 & 30.49 (each t), 41.26 & 41.32 (each d), 61.76 & 62.22 (each t), 65.49 & 65.55 (each d), 65.68 (t), 66.19 (t), 66.83 (t), 98.32 & 99.35 (each d), 127.70 (d), 129.70 & 129.72 (each d), 133.03 & 133.14 (each s), 135.58 & 135.60 (each d).

Ethyl (4*R*, 5*S*)-5-azide-6-(*tert*-butyldiphenylsilyloxy)-4-ethyl-2-hexenoate

To a stirred solution of the above azide (1.1 g, 2.29 mmol) in EtOH (5 mL) was added PPTS (115 mg, 0.46 mmol), and the reaction mixture was stirred at 60 °C for 2 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, and evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of $(COCl)_2$ (0.3 mL, 3.43 mmol) in CH_2Cl_2 (6 mL) was added DMSO (0.5 mL, 6.86 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of the above alcohol in CH_2Cl_2 (8 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (1.4 mL, 10.29 mmol) 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 (15 mL x 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of NaH (60%, 100 mg, 2.52 mmol) in THF (5 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (0.5 mL, 2.52 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 15 min. To the reaction mixture was added a solution of the above aldehyde in THF (6 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O, and the

aqueous mixture was extracted with CH_2Cl_2 (15 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (25 g, hexane:acetone=80:1) to give **9** (935 mg, 88% in 3 steps) as a colorless oil.

IR (neat) 3070, 2962, 2934, 2861, 1720, 1110 cm^{-1}; ^1H NMR (500 MHz) δ 0.84-0.92 (3H, m), 1.11 (9H, s), 1.31 (3H, t, *J* = 6.0 Hz), 1.33-1.40 (1H, m), 1.69-1.77 (1H, m), 2.30-2.44 (1H, m), 3.36-3.40 (1H, m), 3.56-3.74 (1H, m), 3.78-3.81 (1H, m), 4.21 (2H, q, *J* = 6.0 Hz),5.83 (1H, d, *J* = 15.4 Hz), 6.63 (1H, dd, *J* = 15.4, 7.7 Hz), 7.40-7.48 (6H, m), 7.69-7.73 (4H, m); ^{13}C NMR (125 MHz) δ 11.35 (q), 14.17 (q), 19.00 (s), 23.36 (t), 26.62 (q), 44.97 (d), 60.28 (t), 65.37 (t), 66.12 (d), 123.73 (d), 127.71 & 127.75 (each d), 129.78 & 129.80 (each d), 132.64 & 132.66 (each s), 135.47 & 135.50 (each d), 139.33 (d), 147.35 (d), 165.79 (s).

(5*R*, 6*S*)-(+)-6-(*tert*-butyldiphenylsilyloxymethyl)-5-ethylpiperidin-2-one (12)

To a solution of **9** (3.88 g, 8.34 mmol) in EtOAc (100 mL) was added 5% Pd-C (800 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 4 atm for 72 h. The catalyst was removed by filtration, and the filtrate was evaporated to give colorless oil, which was chromatographed on SiO_2 (80 g, hexane:acetone=40:1-8:1) to give **12** (2.4 g, 73%) as a colorless oil.

IR (neat) 3402, 3206, 2933, 1666, 1108 cm^{-1}; ^1H NMR (500 MHz) δ 0.81 (3H, t, *J* = 7.5 Hz), 1.05 (9H, s), 1.17-1.26 (2H, m), 1.66-1.70 (2H, m), 1.72-1.76 (1H, m), 2.30-2.39 (2H, m), 3.53-3.57 (1H, m), 3.58 (1H, t-like, *J* = 9 Hz), 3.63 (1H, dd, *J* = 9, 3 Hz), 7.37-7.46 (6H, m), 7.62-7.65 (4H, m); ^{13}C NMR (125 MHz) δ 11.57 (q), 19.05 (s), 21.19 (t), 23.00 (t), 26.73 (q), 29.48 (t), 35.73 (d), 56.78 (d), 64.42 (t), 127.79 & 127.81 (each d), 129.85 & 129.88 (each d), 132.79 (s), 135.44 & 135.46 (each d), 171.89 (s); MS: 338 (M^+-57), 199 (100); HRMS: Calcd for $C_{20}H_{24}NO_2Si$ (M^+-C_4H_9) 338.1577; Found 338.1592; $[\alpha]_D^{26}$ +28.2 (*c* 2.94, $CHCl_3$).

Methyl (2*S*, 3*R*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-3-ethyl-6-oxopiperidine-1-carboxylate

To a stirred solution of **12** (1.7 g, 4.30 mmol) in THF (15 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 3.0 ml, 4.80 mmol) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. To the reaction mixture was added $ClCO_2Me$ (0.5 mL, 6.33 mmol) at –78 °C, and the resulting mixture was warmed to 0 °C for 1 h. 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, and evaporated to give colorless oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=20:1-15:1) to give the imide (1.88 g, 97%) as a colorless oil.

IR (neat) 3069, 3049, 2957, 2883, 2860, 1774, 1719, 1108 cm^{-1}; ^1H NMR (300 MHz) δ 0.93 (3H, t, *J* = 7.4 Hz), 1.02 (9H, s), 1.23-1.44 (2H, m), 1.81-1.88 (2H, m), 1.99-2.06 (1H, m), 2.49-2.70 (2H, m), 3.73 (1H, dd, *J* = 11, 3.3 Hz), 3.80 (3H, s), 3.83 (1H, dd, *J* = 11, 4.4 Hz), 4.28 (1H, br), 7.35-7.47 (6H, m), 7.61-7.68 (4H, m); ^{13}C NMR (75 MHz) δ 12.02 (q), 18.96 (s), 24.53 (t), 25.68 (t), 26.71 (q), 34.38 (t), 39.11 (d), 53.69 (q), 59.25 (d), 61.48 (t), 127.55 & 127.58 (each d), 129.62 (d), 132.08 & 132.63 (each s), 135.41 & 135.52 (each d), 154.82 (s), 171.78 (s); MS: 396 (M^+-57), 84 (100); HRMS: Calcd for $C_{22}H_{26}NO_4Si$ (M^+-C_4H_9) 396.1631; Found 396.1631; $[\alpha]_D^{26}$ –34.9 (*c* 3.38, $CHCl_3$).

Methyl (2*S*, 3*R*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-3-ethyl-6-trifluoromethanesulfonyl-oxy-3,4-dihydro-2*H*-pyridine-1-carboxylate

To a stirred solution of hexamethyldisilazane (1.03 mL, 4.87 mmol) in THF (8 mL) was added a solution of *n*-BuLi (1.6 M in hexane, 3.03 mL, 4.86 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 30 min. To a stirred solution of the above imide (1.84 g, 4.06 mmol) in THF (10 mL) was added a solution of LiHMDS prepared above at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. To the above reaction mixture was added a solution of 2-[*N*,*N*-bis(trifluoromethylsulfonyl)amino]5-chloropyridine (Comins' reagent) (97%, 1.96 g, 4.85 mmol) in THF (6 mL) at –78 °C, and the resulting mixture was warned to –45 °C for 1 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was extracted with Et_2O (20 mL x 4). The organic extracts were combined, dried, and

evaporated to give pale yellow solid, which was chromatographed on SiO_2 (40 g, hexane:acetone=50:1-40:1) to give the enol triflate (2.3 g, 97%) as a colorless oil.

IR (neat) 3070, 2959, 2933, 2887, 2860, 1733, 1684, 1213, 1111 cm^{-1}; ^1H NMR (300 MHz) δ 0.83 (3H, t, *J* = 7.4 Hz), 1.06 (9H, s), 1.13-1.30 (2H, m), 1.60-1.81 (2H, m), 2.32 (1H, dm, *J* = 16.4 Hz), 3.57-3.63 (1H, m), 3.71-3.78 (1H, m), 3.85 (3H, s), 4.61-4.67 (1H, m), 5.23 (1H, t, *J* = 3.4 Hz), 7.38-7.48 (6H, m), 7.67-7.75 (4H, m); ^{13}C NMR (75 MHz) δ 11.89 (q), 19.11 (s), 25.44 (t), 26.49 (t), 26.59 (q), 37.62 (d), 53.46 (q), 59.25 (d), 58.43 (t), 59.75 (d), 105.51 (d), 127.51 & 127.56 (each d), 129.52 & 129.60 (each d), 133.09 & 133.14 (each s), 135.42 & 135.51 (each d), 138.13 (s), 153.80 (s); MS: 528 (M^+-57), 308 (100); HRMS: Calcd for $C_{23}H_{25}NO_6F_3SiS$ (M^+-C_4H_9) 528.1124; Found 528.1115; $[\alpha]_D^{26}$ –43.8 (*c* 5.73, $CHCl_3$).

Dimethyl (5*R*, 6*S*)-(-)-6-(*tert*-butyldiphenylsilyloxymethyl)-5-ethyl-5,6-dihydro-4*H*-pyridine-1,2-dicarboxylate (13)

To a stirred solution of the above enol triflate (2.3 g, 3.93 mmol) in DMF (15 mL) was added $Pd(Ph_3P)_4$ (230 mg, 0.20 mmol), and the resulting mixture was stirred at room temperature under CO balloon pressure for 30 min. To the reaction mixture were added Et_3N (2.2 mL, 15.73 mmol) and MeOH (6.4 mL, 157.26 mmol), and then the reaction mixture was stirred at 70 °C under CO balloon pressure for 14 h. After cooling, the reaction mixture was diluted with H_2O (50 mL) and brine (10 mL), and the aqueous mixture was extracted with Et_2O (50 mL x 4). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (40 g, hexane:acetone=40:1-20:1) to give **13** (1.46 g, 75%) as a colorless oil.

IR (neat) 3048, 2955, 2882, 2859, 1919, 1650 cm^{-1}; ^1H NMR (500 MHz) δ 0.87 (3H, t, *J* = 7.5 Hz), 1.04 (9H, s), 1.18-1.32 (2H, m), 1.66-1.72 (1H, m), 1.82-1.86 (1H, m), 2.27-2.33 (1H, m), 3.59-3.71 (2H, m), 3.74 (3H, s), 3.75 (3H, s), 4.54 (1H, br), 6.01 (1H, br), 7.36-7.45 (6H, m), 7.66-7.73 (4H, m); ^{13}C NMR (125 MHz) δ 11.80 (q), 19.14 (s), 26.02 (t), 26.55 (q), 27.43 (t), 37.51 (d), 51.89 (q), 53.04 (q), 56.29 (d), 59.14 (t), 121.34 (d), 127.43 & 127.46 (each d), 129.41 & 129.47 (each d), 133.28 (s), 133.26 (s), 135.44

& 135.47 (each d), 154.42 (s), 165.58 (s); MS: 438 (M^+-57), 68 (100); HRMS: Calcd for $C_{24}H_{28}NO_5Si$ (M^+-C_4H_9) 438.1736; Found 438.1741; $[\alpha]_D^{26}$ –47.1 (*c* 4.22, $CHCl_3$).

Dimethyl (2*R*, 3*S*, 5*R*, 6*S*)-(+)-6-(*tert*-butyldiphenylsilyloxymethyl)-5-ethyl-3-vinylpiperidine-1,2-dicarboxylate (14)

To a stirred suspension of CuI (2.69 g, 14.14 mmol) in Et_2O (15 mL) was added a solution of vinyl lithium, (prepared from tetravinyltin (1.2 mL, 7.07 mmol) and MeLi (1.0 M in Et_2O, 28 mL, 28.0 mmol) in Et_2O (10 mL) at 0 °C for 30 min), at –78 °C, and the resulting suspension was warmed to –35 °C for 20 min. The resulting suspension was re-cooled to –78 °C, and a solution of **13** (1.4 g, 2.82 mmol) in Et_2O (8 mL) was added to the resulting suspension. The reaction mixture was warmed to -20 °C for 1 h, and the reaction was quenched with satd. NH_4Cl (aq). The aqueous mixture was diluted with CH_2Cl_2 (100 mL), and the resulting suspension was filtered. The filtrate was separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL x 2). The organic layer and extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=50:1-30:1) to give **14** (1.41 g, 95%) as a colorless oil.

IR (neat) 3070, 2954, 2860, 1704, 1112 cm^{-1}; ^1H NMR (500 MHz) δ 0.80 (3H, t-like, *J* = 7 Hz), 1.05 (9H, s), 1.11-1.18 (1H, m), 1.36 (1H, quint-like, *J* = 7.2 Hz), 1.52 (1H, d-like, *J* = 13.7 Hz), 1.64 (1H, td, *J* = 13.2, 4.7 Hz), 1.72-1.77 (1H, m), 3.09 (1H, br), 3.45 (3H, s), 3.63 (2H, d, *J* = 6.8 Hz), 3.70 (3H, br s), 4.40 (1H, br), 4.98 (1H, br), 5.07-5.13 (2H, m), 5.79-5.85 (1H, m), 7.36-7.45 (6H, m), 7.68-7.69 (4H, br); ^{13}C NMR (75 MHz) δ 11.91 (q), 19.21 (s), 25.70 (t), 26.83 (q), 27.81 (t), 34.63 (d), 36.99 (d), 52.00 (q), 52.97 (q), 54.80 (d), 61.18 (t), 115.07 (t), 127.46 (d), 129.49 (d), 133.34 & 133.39 (each s), 135.42 (d), 139.15 (d), 156.91 (s), 172.52 (s); MS: 466 (M^+-57, 100); HRMS: Calcd for $C_{26}H_{32}NO_5Si$ (M^+-C_4H_9) 466.2050; Found 466.2035; $[\alpha]_D^{26}$ +26.6 (*c* 5.52, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*S*, 6*R*)-(+)-2-(*tert*-butyldiphenylsilyloxymethyl)-3-ethyl-6-hydroxymethyl-5-vinylpiperidine-1-carboxylate (15)

To a stirred solution of **14** (1.38 g, 2.64 mmol) in THF (15 mL) was added a solution of Super-Hydride (1 M in THF, 6 mL, 6.0 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 (15 mL x 6). The organic extracts were combined, dried, and evaporated to give a colorless oil, which was chromatographed on SiO_2 (25 g, hexane:acetone=40:1-15:1) to give **15** (1.26 g, 96%) as a colorless oil.

IR (neat) 3459, 3071, 2957, 2932, 1692, 1111 cm^{-1}; ^1H NMR (500 MHz) δ 0.53 & 0.64 (3H, br), 0.90-0.99 (2H, br), 1.02 (9H, s), 1.40-1.44 (1H, br), 1.56 (1H, td, *J* = 13.7, 4.7 Hz), 1.71-1.77 (1H, br), 2.30 & 2.41 (1H, br), 3.61-3.91 (5H, br), 4.44-4.69 (2H, br), 5.00-5.14 (2H, m), 5.83-5.90 (1H, m), 7.39-7.46 (6H, m), 7.65-7.88 (4H, m); ^{13}C NMR (75 MHz) δ 11.04 (q), 18.95 (s), 25.11 (t), 26.65 (q), 27.43 (t), 33.67 (d), 36.62 (d), 52.81 (q), 54.61 (d), 61.95 (t), 64.36 (t), 114.75 (t), 127.58 & 127.69 (each d), 129.68 & 129.78 (each d), 132.66 (s), 135.21 (d), 140.12 (d), 157.90 (s); MS: 438 (M^+-57), 407 (100); HRMS: Calcd for $C_{25}H_{32}NO_4Si$ (M^+-C_4H_9) 438.2101; Found 438.2099; $[\alpha]_D^{26}$ +22.7 (*c* 2.37, $CHCl_3$).

(5*S*, 6*R*, 8*R*, 9*R*)-(-)-5-(*tert*-butyldiphenylsilyloxymethyl)-6-ethyl-8-vinyl-hexahydrooxazolo-[3,4-*a*]pyridin-3-one (16)

To a stirred solution of **15** (50 mg, 0.10 mmol) in THF (0.5 mL) was added NaH (60%, 4.8 mg, 0.12 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 1 h. The reaction was quenched with 10% AcOH, and the aqueous mixture was extracted with CH_2Cl_2 (10 mL x 4). The organic extracts were combined, dried, and evaporated to give colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=40:1-25:1) to give **16** (44 mg, 94%) as a colorless oil.

IR (neat) 3070, 2958, 2933, 1753, 1110 cm^{-1}; ^1H NMR (500 MHz) δ 0.92 (3H, t, *J* = 7.4 Hz), 1.09 (9H, s), 1.25-1.32 (1H, m), 1.41 (1H, ddd, *J* = 15, 12, 5 Hz), 1.49-1.57 (1H, m), 2.01-2.05 (2H, m), 2.27 (1H, ddd, *J* = 12, 10, 5 Hz), 3.35 (1H, ddd, *J* = 10.5, 8.5, 5 Hz), 3.42 (1H, ddd, *J* = 8.5, 5.5, 3 Hz), 3.94 (1H, dd, *J* =

8.5, 5 Hz), 4.25 (1H, t, *J* = 8.5 Hz), 4.32 (1H, dd, *J* = 10.5, 8.5 Hz), 4.35 (1H, dd, *J* = 10.5, 5.5 Hz), 5.05-5.16 (2H, m), 5.48-5.55 (1H, m), 7.37-7.45 (6H, m), 7.65-7.73 (4H, m); ^{13}C NMR (75 MHz) δ 11.89 (q), 18.25 (t), 19.34 (s), 26.99 (q), 32.81 (t), 35.42 (d), 40.53 (d), 59.77 (d), 60.11 (d), 60.42 (t), 66.44 (t), 117.09 (t), 127.55 (d), 129.55 (d), 133.35 & 133.42 (each s), 135.41 & 135.44 (each d), 137.46 (d), 156.38 (s); MS: 406 (M^+-57, 100); HRMS: Calcd for $C_{24}H_{28}NO_3Si$ (M^+-C_4H_9) 406.1839; Found 406.1841; $[\alpha]_D^{26}$ –32.8 (*c* 2.03, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*S*, 6*R*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-3,5-diethyl-6-(2-ethoxycarbonylvinyl)piperidine-1-carboxylate

To a stirred solution of $(COCl)_2$ (0.26 mL, 3.03 mmol) in CH_2Cl_2 (8 mL) was added DMSO (0.43 mL, 6.06 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of **15** (1.0 g, 2.02 mmol) in CH_2Cl_2 (10 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (1.26 mL, 9.09 mmol) 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 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of NaH (60%, 90 mg, 2.22 mmol) in THF (10 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (0.44 mL, 2.22 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 15 min. To the reaction mixture was added a solution of the above oil in THF (10 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with CH_2Cl_2 (30 mL x 3). The organic extracts were combined, dried, and evaporated to give pale yellow oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=80:1-40:1) to give the α,β-unsaturated ester (1.05 g, 92%) as a colorless oil.

IR (neat) 3070, 2957, 2932, 1703, 1111 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.62 (3H, br t-like, *J* = 7 Hz), 0.95 (2H, quint-like, *J* = 7.5 Hz), 1.07 (9H, s), 1.20 (3H, t, *J* = 7.5 Hz), 1.44 (1H, d-like, *J* = 14 Hz), 1.60 (1H,

td, *J* = 13, 4.7 Hz), 1.76 (1H, br), 2.71 (1H, br), 3.49 (1H, dd, *J* = 11, 5.2 Hz), 3.64-3.76 (3H, br m), 4.10-4.24 (2H, m), 5.09-5.28 (2H, m), 5.88-5.94 (1H, m), 6.16 (1H, d-like, *J* = 16 Hz), 7.26 (H, d-like, *J* = 16 Hz), 7.36-7.45 (6H, m), 7.67-7.81 (4H, m); ^{13}C NMR (75 MHz) δ 11.30 (q), 14.27 (q), 19.01 (s), 25.29 (t), 26.71 (q), 27.46 (t), 33.70 (d), 39.16 (d), 52.81 (q), 53.41 (d), 54.32 (d), 60.16 (t), 60.37 (t), 115.15 (t), 121.36 (d), 129.42 & 129.50 (each d), 133.35 (s), 135.38 (d), 139.62 (d), 149.26 (d), 157.15 (s), 166.12 (s); MS: 506 (M^+-57), 69 (100); HRMS: Calcd for $C_{29}H_{36}NO_5Si$ (M^+-C_4H_9) 506.2363; Found 506.2363; $[\alpha]_D^{26}$ –10.8 (*c* 4.43, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(+)-2-(*tert*-butyldiphenylsilyloxymethyl)-3,5-diethyl-6-(3-hydroxypropyl)piperidine-1-carboxylate (17)

To a solution of the above α,β-unsaturated ester (1.0 g, 1.78 mmol) in EtOAc (30 mL) was added 5% Pd-C (100 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 72 h. The catalyst was removed by filtration, and the filtrate was evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of the above in THF (12 mL) was added a solution of Super-Hydride (1 M in THF, 4.0 mL, 4.0 mmol) at 0 °C, and the resulting mixture was stirred at 0 °C for 1 hr. 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, and evaporated to give colorless oil, which was chromatographed on SiO_2 (25 g, hexane:acetone=40:1-12:1) to give **17** (913 mg, 98%) as a colorless oil.

IR (neat) 3448, 2998, 2962, 2839, 1738, 1240 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.76-0.95 (6H, m), 1.04 (9H, s), 1.15-1.86 (10H, br m), 1.98-2.23 (1H, br), 2.72 (1H, br), 3.58-3.71 (4H, br m), 3.62 (3H, s), 3.91-4.08 (1H, br), 4.41-4.45 (1H, br), 7.39-7.41 (6H, m), 7.63-7.69 (4H, m); ^{13}C NMR (75 MHz) δ 11.89 (q), 12.38 & 12.54 (each q), 19.16 (s), 22.67 (t), 25.53 (t), 25.71 (t), 26.78 (q), 29.53 (t), 31.16 (t), 33.51 (d), 33.67 (d), 52.59 (q), 53.54 (d), 54.74 (d), 59.25 (t), 61.99 (t), 127.50 & 127.56 (each d), 129.49 & 129.58 (each

d), 133.21 & 133.35 (each s), 135.33 & 135.41 (each d), 158.23 (s); MS: 468 (M^+-57), 256 (100); HRMS: Calcd for $C_{27}H_{38}NO_4Si$ (M^+-C_4H_9) 468.2570; Found 468.2568; $[\alpha]_D^{26}$ +10.6 (*c* 1.57, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(-)-2-(*tert*-butyldiphenylsilyloxymethyl)-3,5-diethyl-6-(3-methoxymethoxypropyl)piperidine-1-carboxylate

To a stirred soultion of **17** (913 mg, 1.74 mmol) in $CHCl_3$ (12 mL) were added MOMCl (0.52 mL, 6.96 mmol) and Hünig base (1.4 mL, 7.66 mmol), and the resulting mixture was refluxed for 2 h. After cooling, the solvent was evaporated and the residue was chromatographed on SiO_2 (25 g, hexane:acetone=40:1) to give the MOM ether (878 mg, 89%) as a colorless oil.

IR (neat) 2932, 1692, 1111 cm^{-1}; ^1H NMR (500 MHz) δ 0.73 & 0.79 (3H, each t, each *J* = 7.3 Hz), 0.90 (3H, t-like, *J* = 7.3 Hz), 1.02 (9H, s), 1.14-1.77 (12H, br m), 3.30 (3H, s), 3.41-3.45 (1H, m), 3.49-3.58 (1H, m), 3.64 (3H, s), 3.61-3.69 (2H, m), 3.93 & 4.12 (1H, m), 4.42 & 4.68 (1H, m), 4.57 (2H, s), 7.37-7.44 (6H, m), 7.67-7.78 (4H, m); ^{13}C NMR (75 MHz) δ 11.70 & 11.86 (each q), 12.36 & 12.48 (each q), 19.09 (s), 25.47 (t), 25.66 (t), 26.70 (q), 27.81 (t), 31.81 (t), 33.41 & 33.77 (each d), 37.59 & 38.01 (each d), 52.39 (q), 54.38 (d), 54.75 (d), 54.98 (q), 62.12 (t), 67.70 (t), 96.27 (t), 127.43 & 127.48 (each d), 129.41 (d), 133.27 & 133.37 (each s), 135.28 & 135.33 (each d), 157.53 (s); MS: 512 (M^+-57, 100); HRMS: Calcd for $C_{17}H_{33}NO_5$ (M^+-C_4H_9) 512.2832; Found 512.2829; $[\alpha]_D^{26}$ –0.98 (*c* 3.37, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(+)-3,5-diethyl-2-hydroxymethyl-6-(3-methoxymethoxy-propyl)-piperidine-1-carboxylate (18)

To a stirred solution of the above MOM ether (240 mg, 0.42 mmol) in THF (8 mL) was added a solution of TBAF (1 M in THF, 1.5 mL, 1.5 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 22 h. The reaction was quenched with satd. NH_4Cl (aq), and the aqueous mixture was extracted with $CHCl_3$ (10 mL x 5). The organic extracts were combined, dried, and evaporated to give a

colorless oil, which was chromatographed on SiO_2 (15 g, hexane:acetone=30:1-6:1) to give **18** (110 mg, 79%) as a colorless oil.

IR (neat) 3461, 2955, 2878, 1680, 1114, 1042 cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (3H, t-like, *J* = 7.3 Hz), 0.90 (3H, t, *J* = 7.2 Hz), 1.12 (1H, m), 1.22-1.38 (2H, m), 11.40-1.59 (3H, m), 1.61-1.72 (4H, m), 2.17 (1H, br), 2.46 (1H, br), 3.32 (3H, s), 3.50 (2H, m), 3.57-3.66 (1H, m), 3.67 (3H, s), 3.69-3.76 (1H, br), 3.93-4.14 (1H, br), 4.31-4.46 (1H, br), 4.58 (2H, s); ^{13}C NMR (75 MHz) δ 11.93 (q), 12.30 (q), 25.29 (t), 25.50 (t), 27.43 (t), 32.15 (t), 33.28 (d), 37.94 (d), 52.84 (q), 54.43 (d), 55.11 (q), 55.21 (d), 62.12 (t), 67.47 (t), 96.25 (t), 159.39 (s); MS: 330 (M^+-1), 300 (100); HRMS: Calcd for $C_{17}H_{33}NO_5$ (M^+-H) 330.2279; Found 330.2291; $[\alpha]_D^{26}$ +3.6 (*c* 4.85, $CHCl_3$).

Methyl (2*S*, 3*R*, 5*R*, 6*S*)-(+)-3,5-diethyl-2-(3-methoxymethoxypropyl)-6-propenylpiperidine-1-carboxylate

To a stirred solution of $(COCl)_2$ (0.12 mL, 1.41 mmol) in CH_2Cl_2 (4 mL) was added DMSO (0.2 mL, 2.82 mmol) at –78 °C, and the resulting solution was stirred at –78 °C for 10 min. To the mixture was added a solution of **18** (311 mg, 0.94 mmol) in CH_2Cl_2 (4 mL) at –78 °C, and the reaction mixture was stirred at –78 °C for 30 min. Triethylamine (0.58 mL, 4.23 mmol) 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 (10 mL x 4). The organic extracts were combined, dried and evaporated to give pale yellow oil, which was used directly in the next step.

To a stirred suspension of $EtP^+Ph_3Br^-$ (1.7 g, 4.70 mmol) in THF (15 mL) was added a solution of *n*-BuLi (1.6M ih hexane, 2.6 mL, 4.22 mmol) at 0 °C, and the resulting orange solution was stirred at 0 °C for 30 min. To the solution was added a solution of the above oil in THF (6 mL) at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched with H_2O, and the aqueous mixture was extracted with Et_2O (15 mL x 3). The organic extracts were combined, dried, and evaporated

to give pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=100:1-30:1) to give the olefin (266 mg, 83% in 2 steps) as a colorless oil.

IR (neat) 2929, 1693 cm^{-1}; ^1H NMR (500 MHz) δ 0.80 (3H, t, *J* = 7.3 Hz), 0.86 (3H, m), 1.01-1,08 (1H, m), 1.09-1.15 (1H, m), 1.22-1.74 (12H, br m), 1.77 (1H, d-like, *J* = 6 Hz), 3.31 (3H, s), 3.44-3.48 (2H, br), 3.63 & 3.66 (3H, each s), 3.94 & 4.27 (1H, each br), 4.56 (2H, s), 4.93 & 5.11 (1H, each br), 5.48 (1H, q-like, *J* = 9.4 Hz), 5.54 (1H, br); ^{13}C NMR (75 MHz) δ 11.44 (q), 12.38 (q), 13.19 & 13.63 (each q), 25.37 & 25.42 (each t), 25.76 (t), 26.99 & 27.20 (each t), 32.60 (t), 34.14 (d), 38.07 & 38.65 (each d), 49.96 (d), 52.38 (q), 54.15 (d), 55.01 (q), 67.54 (t), 96.17 (t), 126.28 & 126.51 (each d), 127.37 & 128.42 (each d), 156.83 (s); MS: 341 (M^+), 239 (100); HRMS: Calcd for $C_{19}H_{35}NO_4$ 341.2564; Found 341.2583; $[\alpha]_D^{26}$ +34.7 (*c* 1.50, $CHCl_3$).

(5*R*, 6*R*, 8*R*, 9*S*)-(-)-6,8-Diethyl-5-propyloctahydroindolizine (11)

To a solution of the above olefin (120 mg, 0.35 mmol) in EtOAc (12 mL) was added 5% Pd-C (100 mg), and the resulting suspension was hydrogenated under hydrogen atmosphere at 1 atm for 84 h. The catalyst was removed by filtration, and the filtrate was evaporated to give colorless oil, which was used directly in the next step.

To a stirred solution of *n*-PrSLi, prepared from *n*-PrSH (0.32 mL, 3.50 mmol) and *n*-BuLi (1.6 M in hexane, 2.1 mL, 3.33 mmol) in HMPA (3 mL) at 0 °C for 30 min. To the reaction mixture was added a solution of the above oil in THF (3 mL) at 0 °C, and the resulting solution was stirred at room temperature for 60 h. The reaction was quenched with NH_3 (aq), and the aqueous mixture was extracted with Et_2O (10 mL x 10). 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.

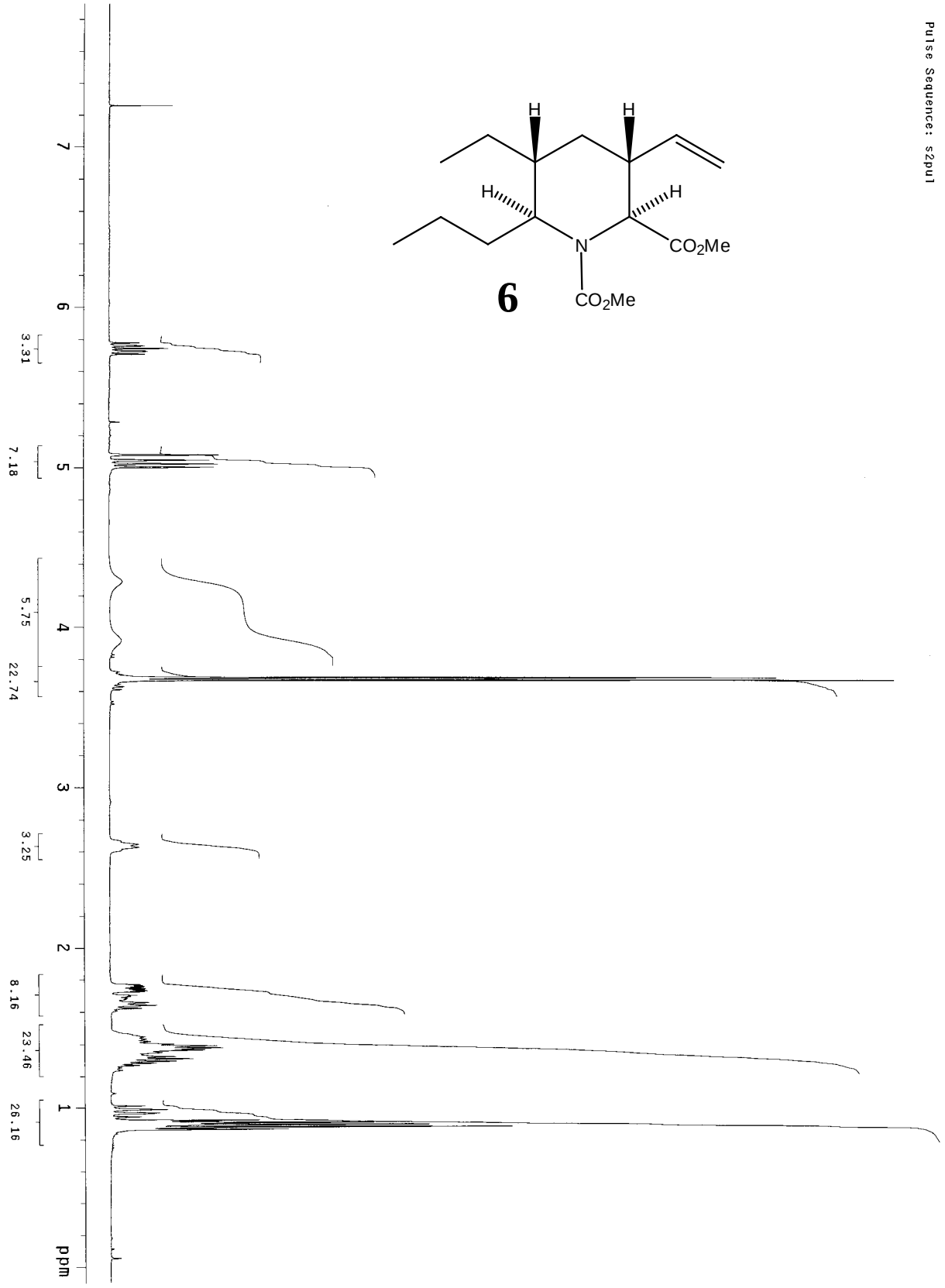
To a stirred solution of the above oil in MeOH (10 mL) was added c. HCl (8 drops), and the resulting mixture was refluxed for 2 h. After cooling, the solvent was evaporated, and the residue was washed with Et_2O. To the residue was added NH_3 (aq), and the aqueous mixture was extracted with $CHCl_3$ (10 mL x

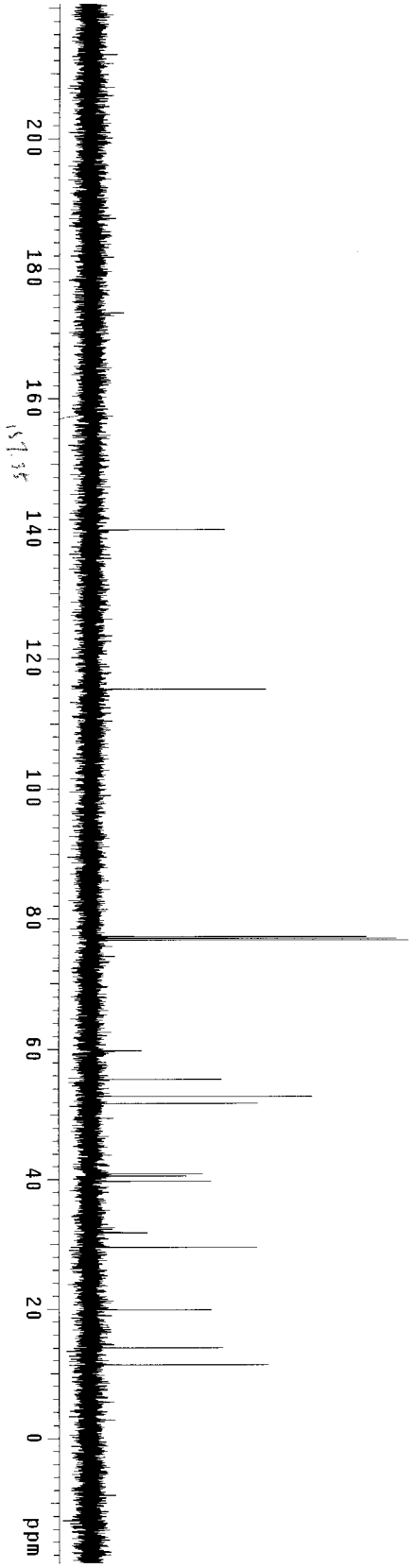
8). The organic extracts were combined, dried over K_2CO_3, and evaporated to give colorless oil, which was used directly in the next step.

Carbontetrabromide (163 mg, 0.49 mmol) and Ph_3P (138 mg, 0.53 mmol) were added to a solution of the above oil in CH_2Cl_2 (6 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 2 h. To the reaction mixture was added Et_3N (0.77 mL, 5.60 mmol) at 0 °C, and the resulting suspension was stirred at 0 °C for 30 min. The solvent was evaporated, and the residue was extracted with *n*-pentane (10 mL x 5). The organic extracts were combined and evaporated to give colorless solid, which was chromatographed on SiO_2 (15 g, hexane:acetone:Et_3N=50:1:5 drops) to give **11** (40 mg, 51%) as a pale yellow oil.

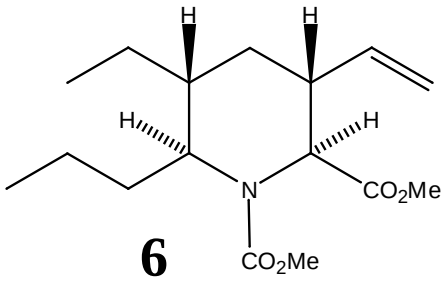
IR (neat) 2958, 2874, 2776, 1460, 1378, 1316, 1180, 1112, 928, 888 cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (3H, t, *J* = 7.5 Hz), 0.87 (3H, t, *J* = 7.5 Hz), 0.91 (3H, *t*, J = 7 Hz), 0.97-1.06 (1H, m), 1.13-1.21 (1H, m), 1.21-1.52 (11H, br m), 1.55-1.62 (1H, m), 1.70-1.77 (1H, m), 1.86 (1H, q, *J* = 9 Hz), 1.86-1.92 (1H, m), 1.94 (1H, dt, *J* = 13, 3 Hz), 1.95-1.99 (1H, m), 3.12 (1H, td, *J* = 8, 2 Hz); ^{13}C NMR (75 MHz) δ 11.23 (q), 12.56 (q), 14.68 (q), 18.45 (t), 19.17 (t), 20.49 (t), 26.00 (t), 29.29 (t), 32.49 (t), 33.51 (t), 37.28 (d), 37.86 (d), 52.13 (t), 66.82 (d), 71.34 (d); MS: 223 (M^+, 100); $[\alpha]_D^{26}$ –100.9 (*c* 1.76, $CHCl_3$).

DCl salt: ^1H NMR (500 MHz, D_2O) δ 0.83-0.89 (9H, m), 1.10-1.23 (4H, m), 1.32-1.39 (1H, m), 1.42-1.51 (2H, br m), 1.53-1.62 (3H, m), 1.66-1.74 (1H, m), 1.85-2.01 (3H, m), 2.07 (1H, dm, *J* = 13.5 Hz), 2.27-2.34 (1H, m), 2.85 (1H, td-like, *J* = 11, 6 Hz), 2.94 (1H, q-like, *J* = 10 Hz), 3.14 (1H, dm, *J* = 11 Hz), 3.58 (1H, tm, *J* = 10 Hz); ^{13}C NMR (75 MHz, D_2O) δ 9.47 (q), 11.10 (q), 12.77 (q), 16.57 (t), 17.35 (t), 18.27 (t), 24.06 (t), 26.39 (t), 29.43 (t), 29.48 (t), 34.92 (d), 35.00 (d), 51.08 (t), 66.13 (d), 71.82 (d); $[\alpha]_D^{26}$ –40.9 (*c* 0.25, $CHCl_3$).

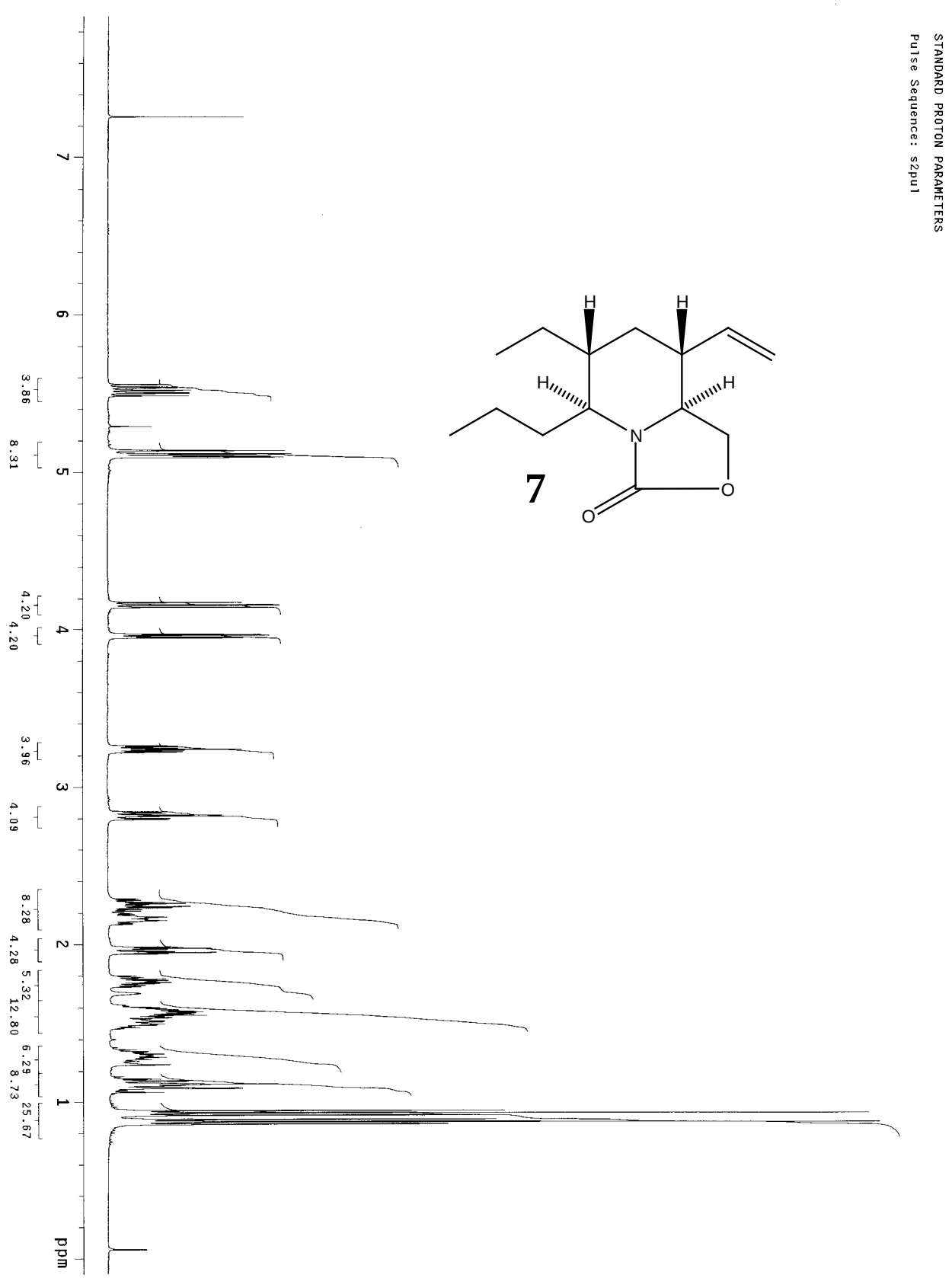

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
H
H
H
N
CO2Me
CO2Me
6
ppm
3.31
7.18
5.75
22.74
3.25
8.16
23.46
26.16



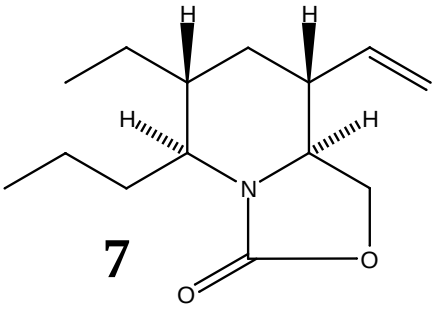
INDEX	FREQUENCY	PPM	HEIGHT
1	21771.510	173.197	5.2
2	17591.901	139.947	21.1
3	14494.940	115.310	27.6
4	9711.405	77.256	43.5
5	9679.183	77.000	48.2
6	9646.962	76.744	50.1
7	7513.888	59.775	8.0
8	6964.279	55.402	20.6
9	6638.380	52.810	34.9
10	6502.128	51.726	26.3
11	5135.930	40.857	17.6
12	5090.820	40.499	15.1
13	4987.711	39.678	18.9
14	3992.522	31.761	8.9
15	3715.416	29.557	26.2
16	2496.516	19.860	19.0
17	1757.260	13.979	20.7
18	1421.234	11.306	28.0



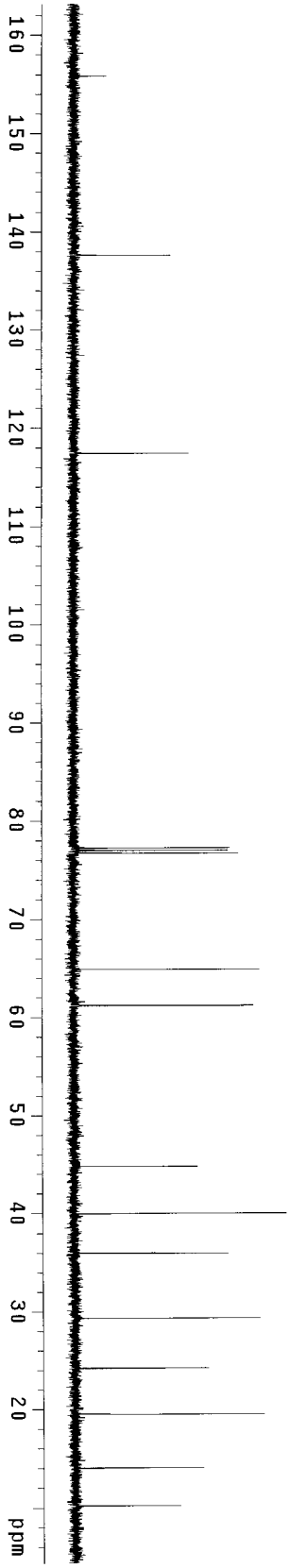
6

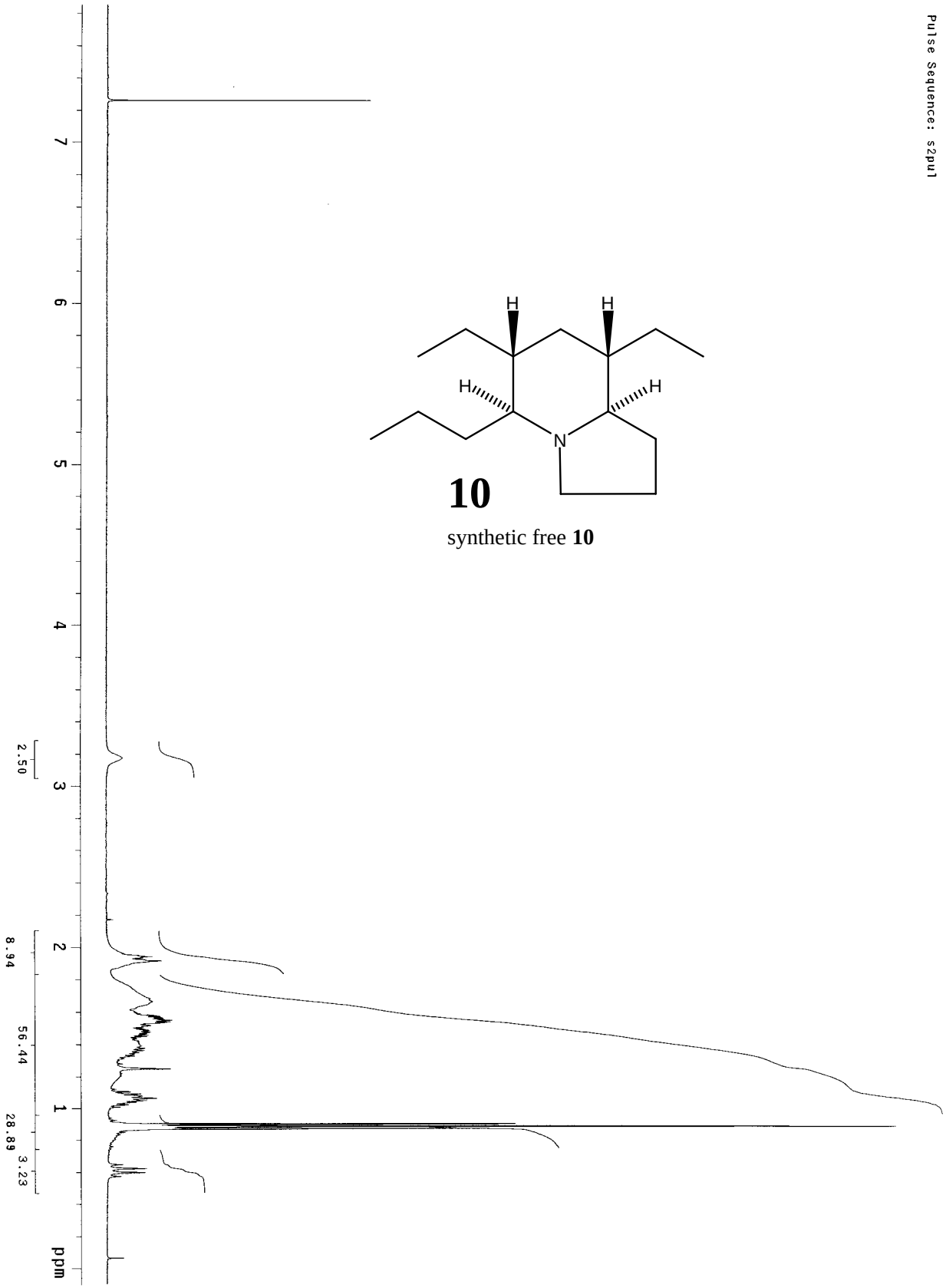

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
H
H
H
N
O
O
7
ppm
1
2
3
4
5
6
7
3.86
8.31
4.20
4.20
3.96
4.09
8.28
4.28
5.32
12.80
6.29
8.73
25.67

INDEX	FREQUENCY	PPM	HEIGHT
1	19586.882	155.818	5.1
2	17298.224	137.611	15.2
3	14762.840	117.442	18.2
4	9710.485	77.249	24.5
5	9679.184	77.000	24.3
6	9646.962	76.744	25.9
7	8154.639	64.872	29.2
8	7694.330	61.210	28.3
9	7687.885	61.159	27.0
10	5629.382	44.783	19.4
11	5024.535	39.971	33.3
12	4522.798	35.980	24.2
13	3687.797	29.337	29.2
14	3040.602	24.189	21.0
15	2450.486	19.494	29.7
16	1760.942	14.009	20.2
17	1282.220	10.200	16.5



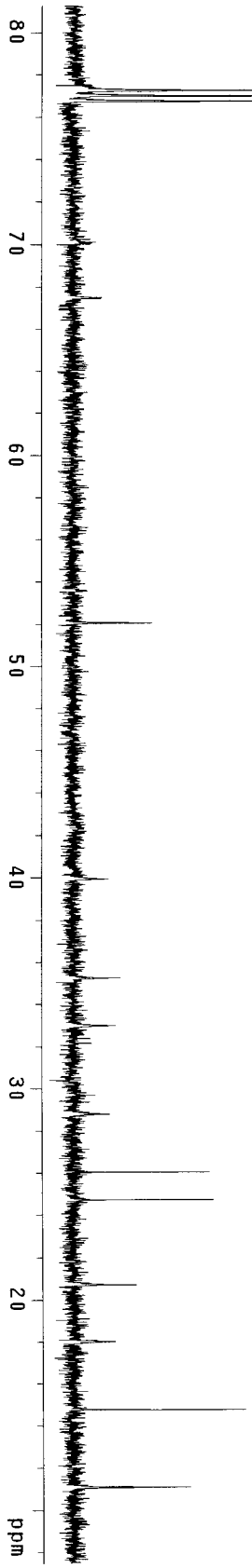
7



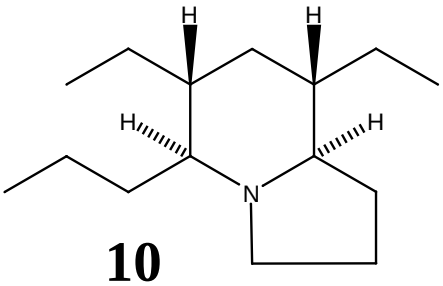


10

synthetic free **10**

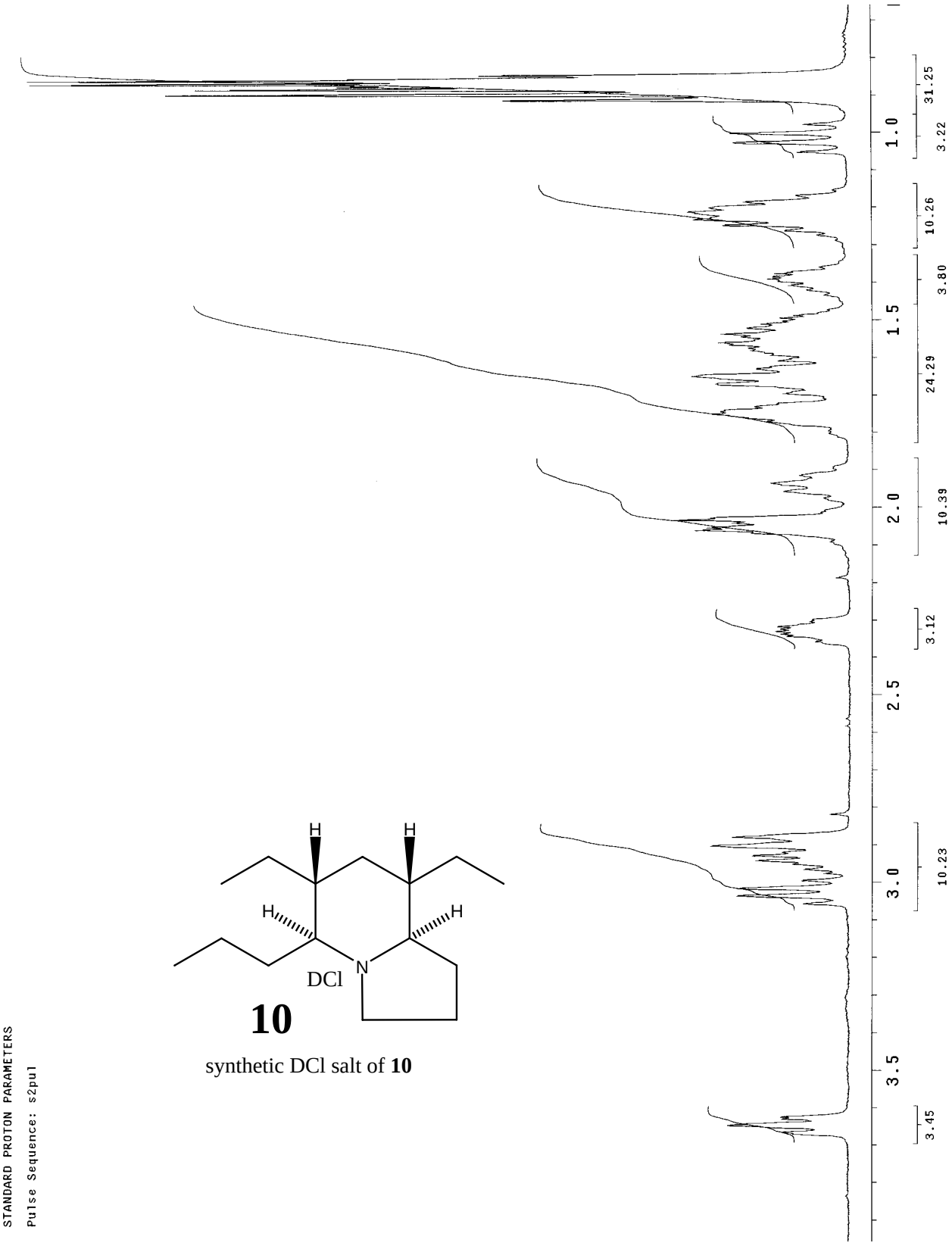


INDEX	FREQUENCY	PPM	HEIGHT
1	9711.405	77.256	146.5
2	9679.183	77.000	151.3
3	9646.962	76.744	136.8
4	8483.300	67.486	4.5
5	6543.556	52.055	12.4
6	5019.932	39.935	5.4
7	4428.895	35.233	7.3
8	4146.265	32.984	6.6
9	3619.671	28.795	5.6
10	3271.677	26.027	21.3
11	3105.966	24.709	21.8
12	2603.308	20.710	9.7
13	2262.679	18.000	6.3
14	1854.845	14.756	26.7
15	1392.695	11.079	18.0



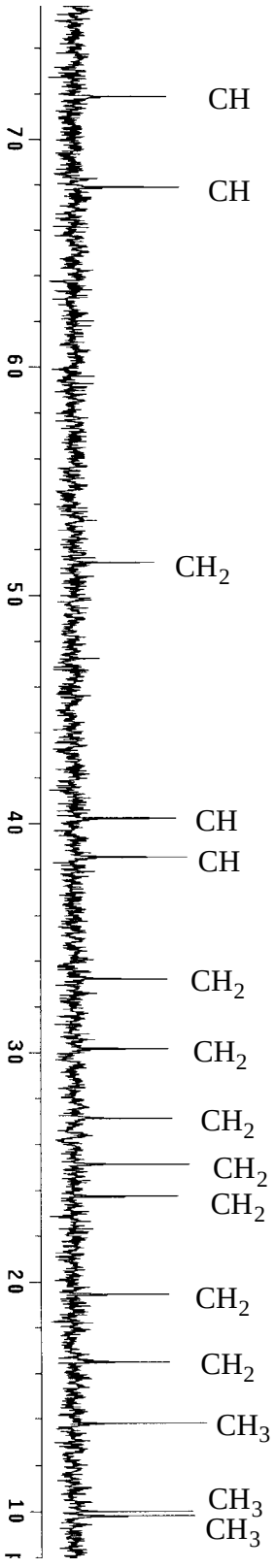
10

synthetic free **10**



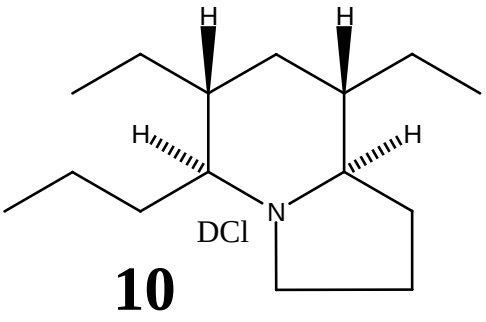
10

synthetic DCl salt of **10**



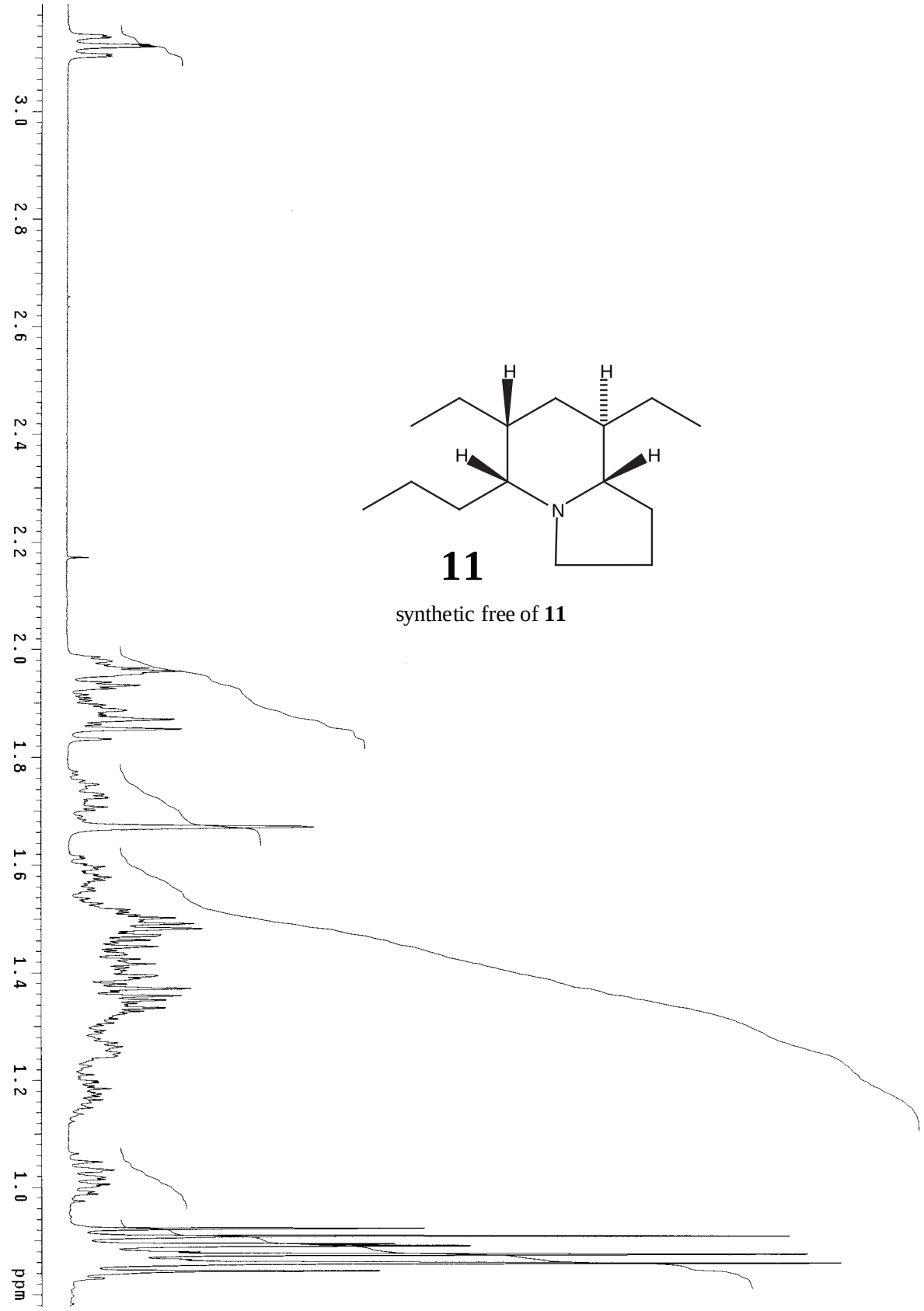
From DEPT

INDEX	FREQUENCY	PPM	HEIGHT
1	5422.937	71.873	14.4
2	5122.626	67.892	16.5
3	3879.874	51.422	12.5
4	3033.875	40.209	15.9
5	2906.914	38.527	17.6
6	2505.279	33.204	14.5
7	2274.552	30.146	14.7
8	2046.266	27.120	15.3
9	1896.110	25.130	17.8
10	1791.124	23.739	16.2
11	1467.618	19.451	14.7
12	1244.215	16.490	14.8
13	1040.345	13.788	20.4
14	753.463	9.986	18.3
15	738.813	9.792	18.6



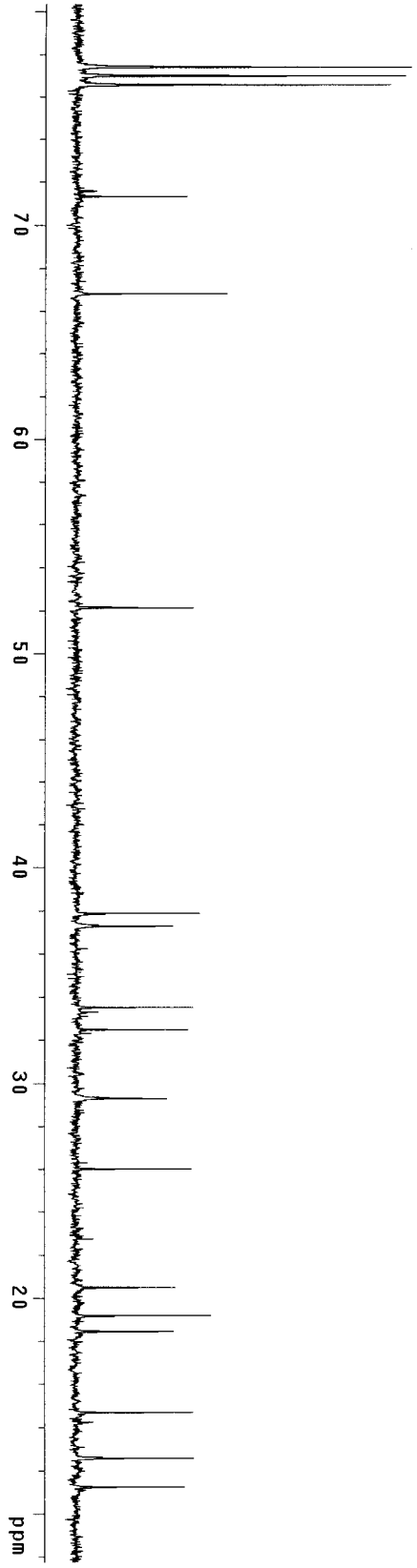
10

synthetic DCl salt of **10**

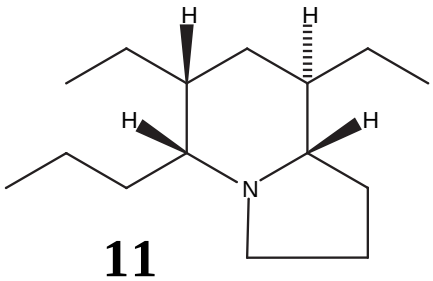


11

synthetic free of **11**

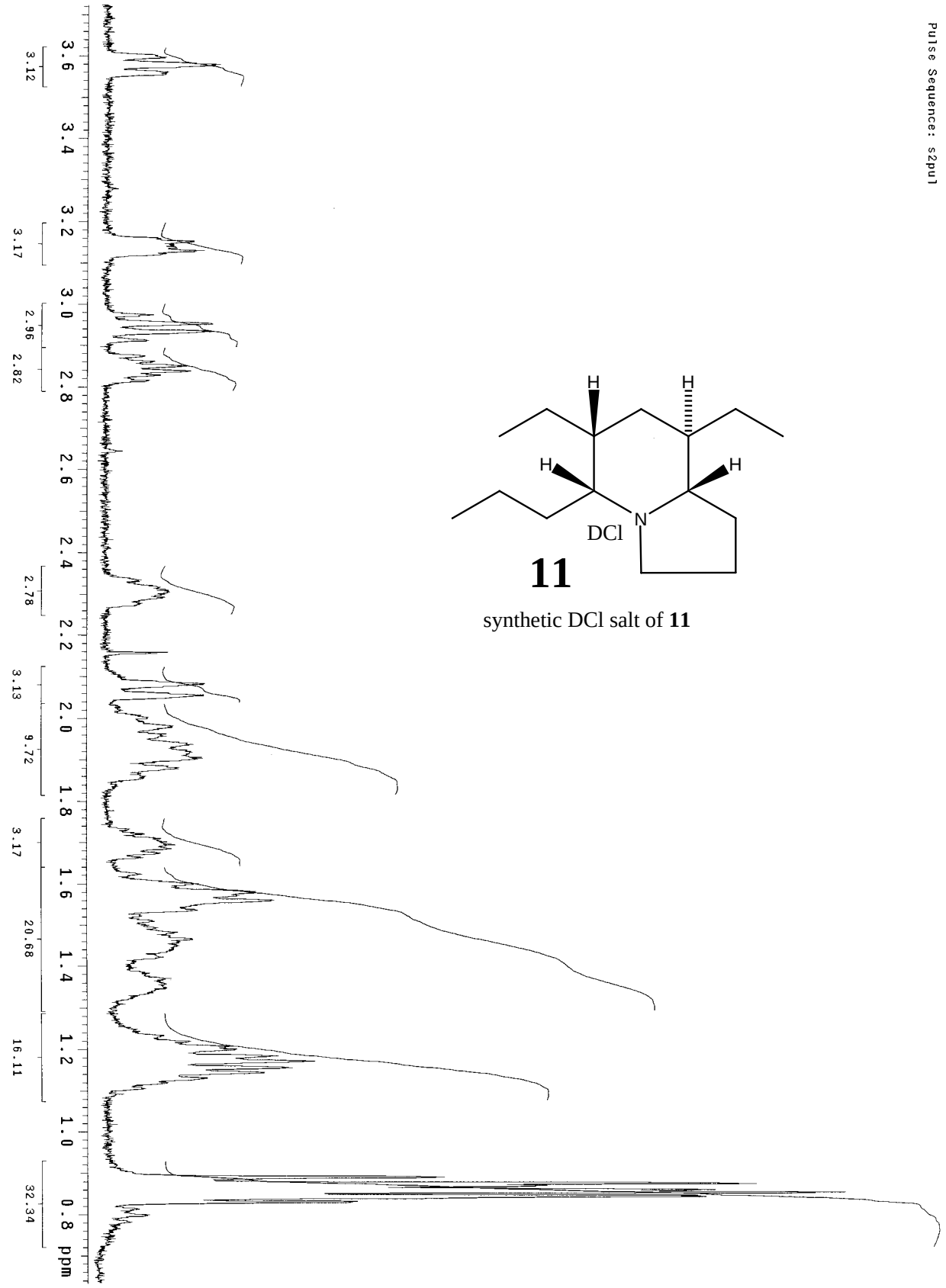


INDEX	FREQUENCY	PPM	HEIGHT
1	5841.541	77.421	53.0
2	5809.800	77.000	52.1
3	5778.060	76.579	49.7
4	5382.528	71.337	17.6
5	5041.931	66.823	23.9
6	3933.465	52.132	18.6
7	2856.739	37.862	19.6
8	2812.791	37.279	15.5
9	2528.350	33.509	18.5
10	2451.441	32.490	17.8
11	2209.727	29.287	14.5
12	1961.909	26.002	18.3
13	1545.624	20.485	15.7
14	1446.741	19.174	21.5
15	1391.806	18.446	15.5
16	1107.365	14.676	18.6
17	947.443	12.557	18.6
18	847.339	11.230	17.2



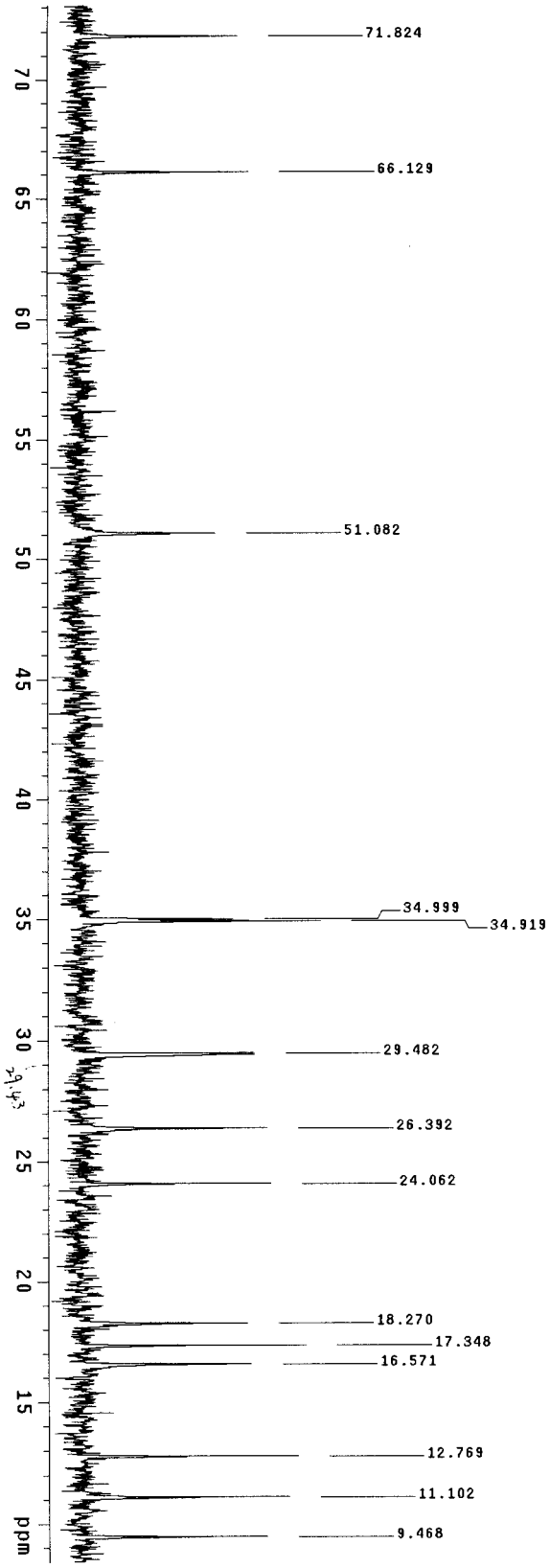
11

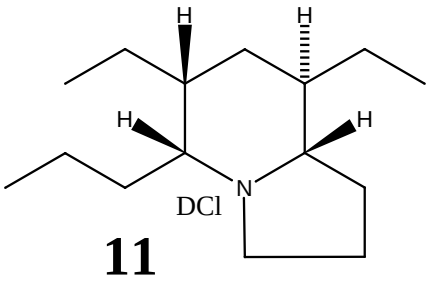
synthetic free of **11**



11

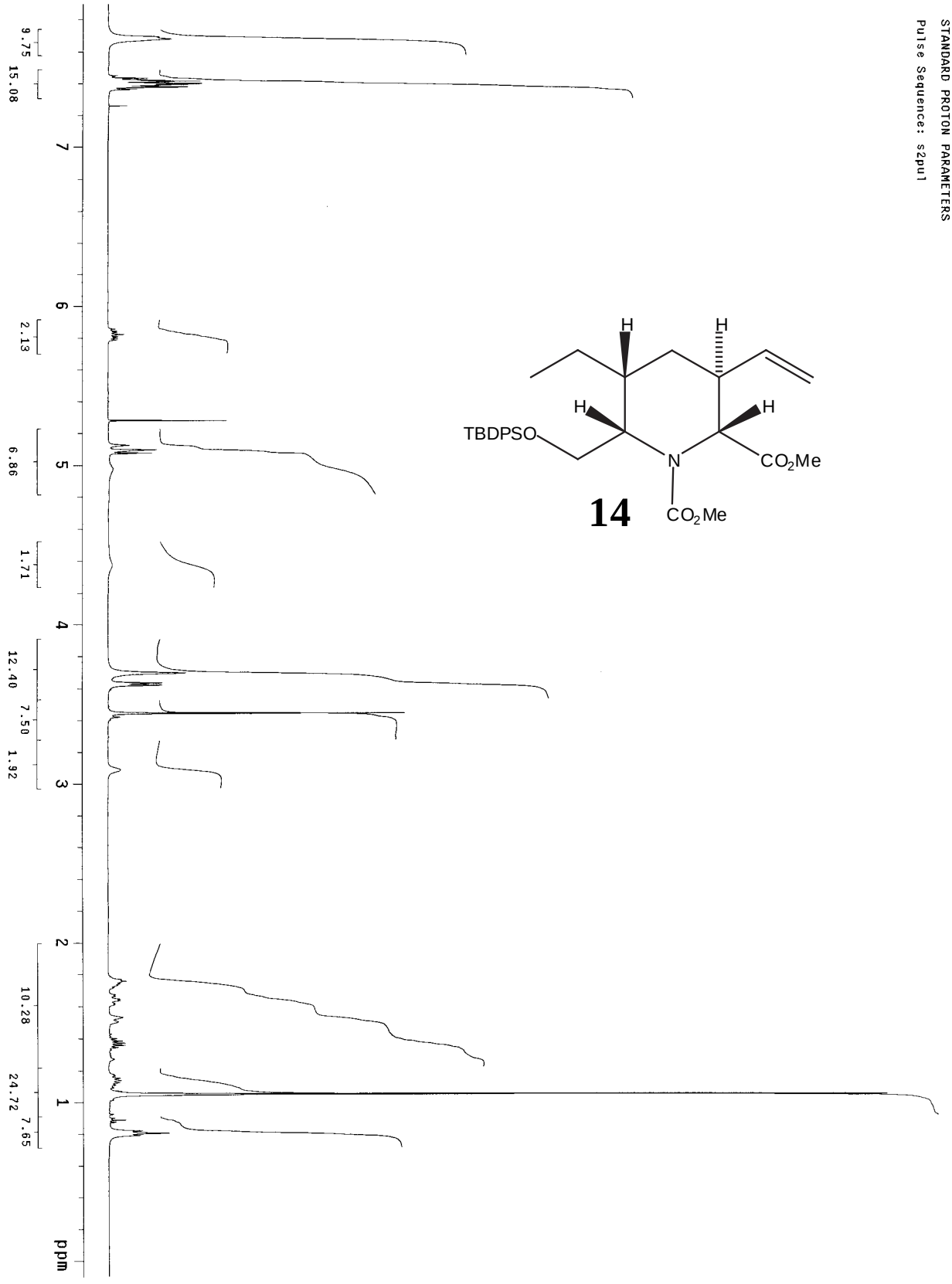
synthetic DCl salt of **11**

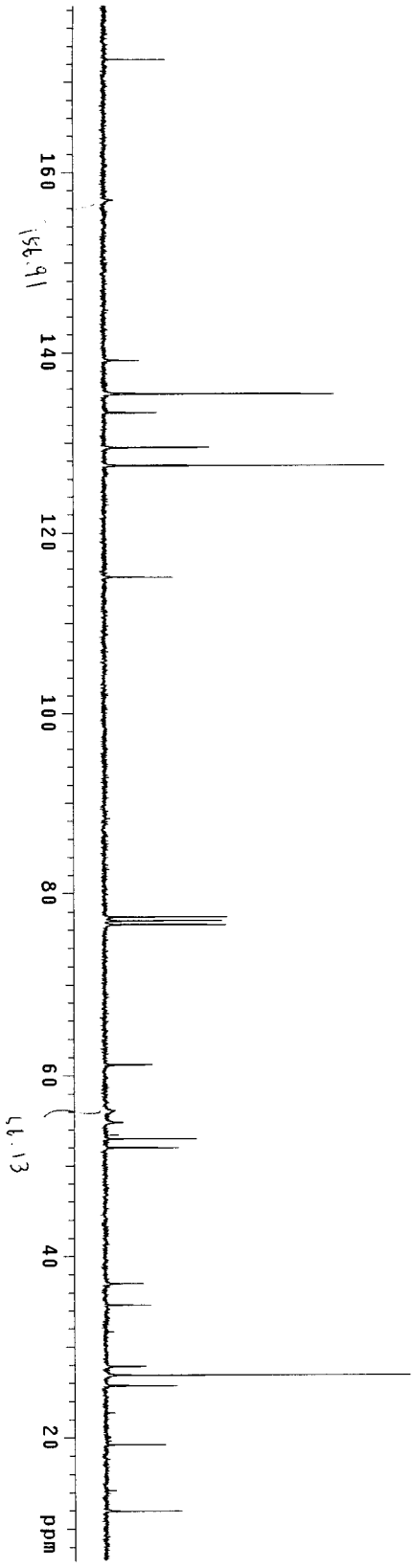




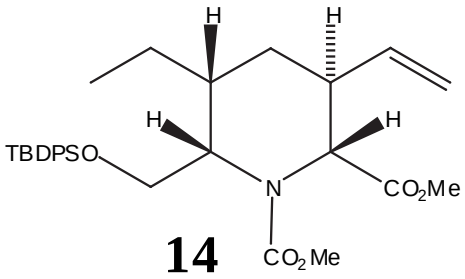
11

synthetic DCl salt of **11**

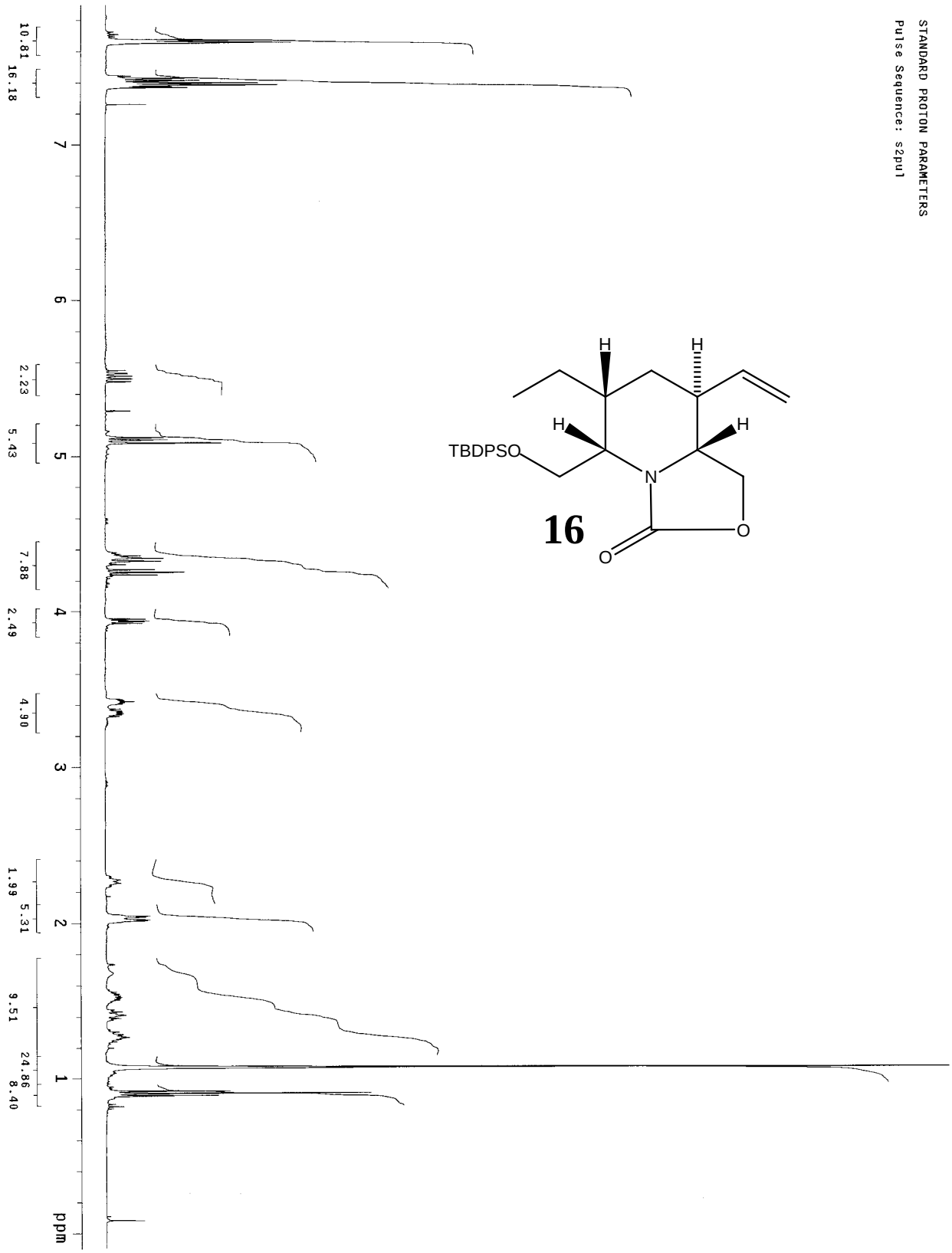

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
H
H
H
H
TBDPSO
N
CO2Me
CO2Me
14
9.75
15.08
2.13
6.86
1.71
12.40
7.50
1.92
10.28
24.72
7.65
ppm



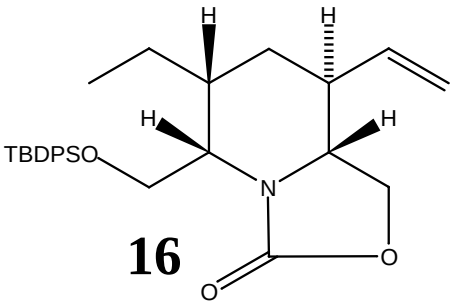
INDEX	FREQUENCY	PPM	HEIGHT
1	13017.272	172.524	9.7
2	10498.808	139.146	5.6
3	10218.029	135.424	36.4
4	10064.211	133.386	8.4
5	10060.549	133.337	6.5
6	9770.003	129.486	16.7
7	9617.406	127.464	44.4
8	8682.291	115.070	10.8
9	5841.541	77.421	19.4
10	5809.801	77.000	18.5
11	5776.840	76.563	19.2
12	4615.880	61.176	7.5
13	4134.894	54.802	2.8
14	3996.946	52.973	14.5
15	3923.699	52.003	11.6
16	2790.818	36.988	6.0
17	2612.584	34.626	7.2
18	2098.637	27.814	6.5
19	2024.169	26.827	48.3
20	1938.715	25.695	11.4
21	1449.183	19.207	9.4
22	898.612	11.910	11.9



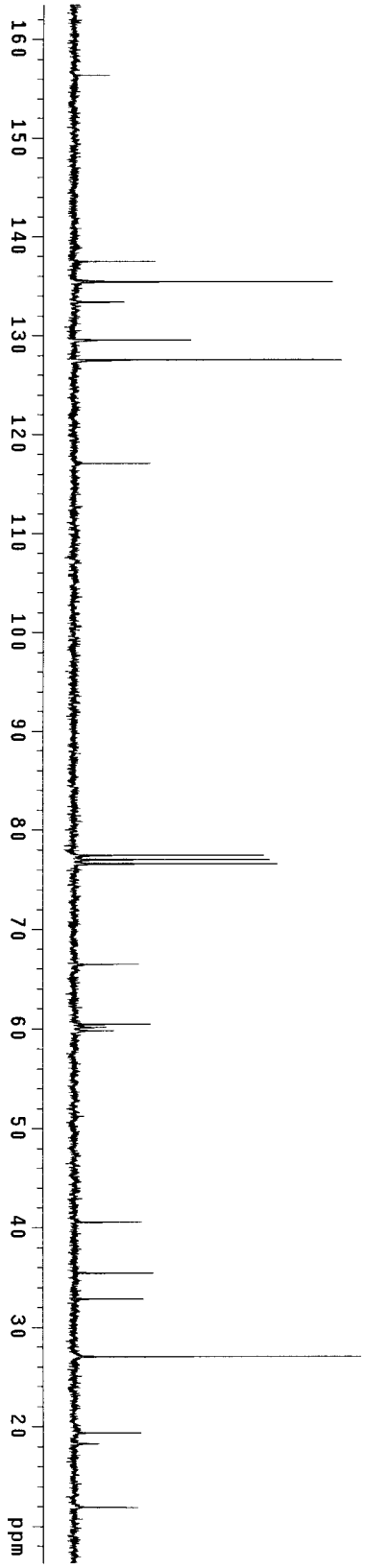
14

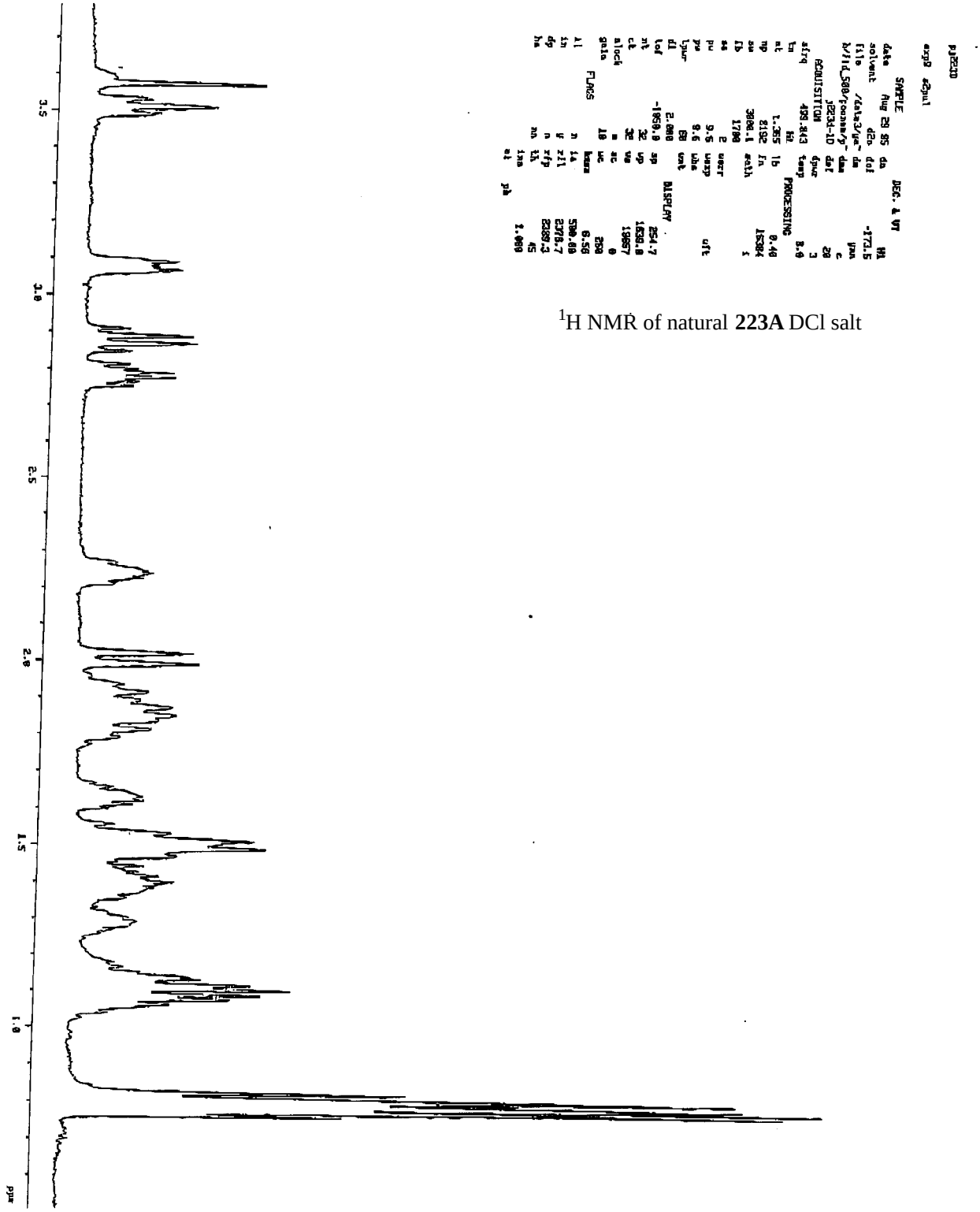

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
TBDPSO
H
H
H
H
N
O
O
16
10.81
16.18
2.23
5.43
7.88
2.49
4.90
1.99
5.31
9.51
24.86
8.40
7
6
5
4
3
2
1
ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	11798.936	156.377	5.5
2	10371.847	137.463	12.8
3	10219.249	135.440	31.0
4	10216.808	135.408	40.9
5	10066.652	133.418	7.9
6	10061.769	133.353	5.5
7	9774.886	129.551	18.5
8	9623.510	127.545	42.3
9	9616.185	127.448	5.7
10	8834.888	117.093	12.0
11	5842.762	77.437	30.0
12	5809.801	77.000	30.9
13	5778.060	76.579	32.1
14	5012.633	66.435	10.2
15	4558.504	60.416	12.1
16	4535.309	60.109	5.1
17	4509.672	59.769	6.2
18	3058.168	40.531	10.7
19	2672.402	35.419	12.6
20	2475.857	32.814	11.0
21	2036.377	26.989	45.3
22	1458.949	19.336	10.6
23	1377.157	18.252	3.9
24	897.391	11.894	10.1

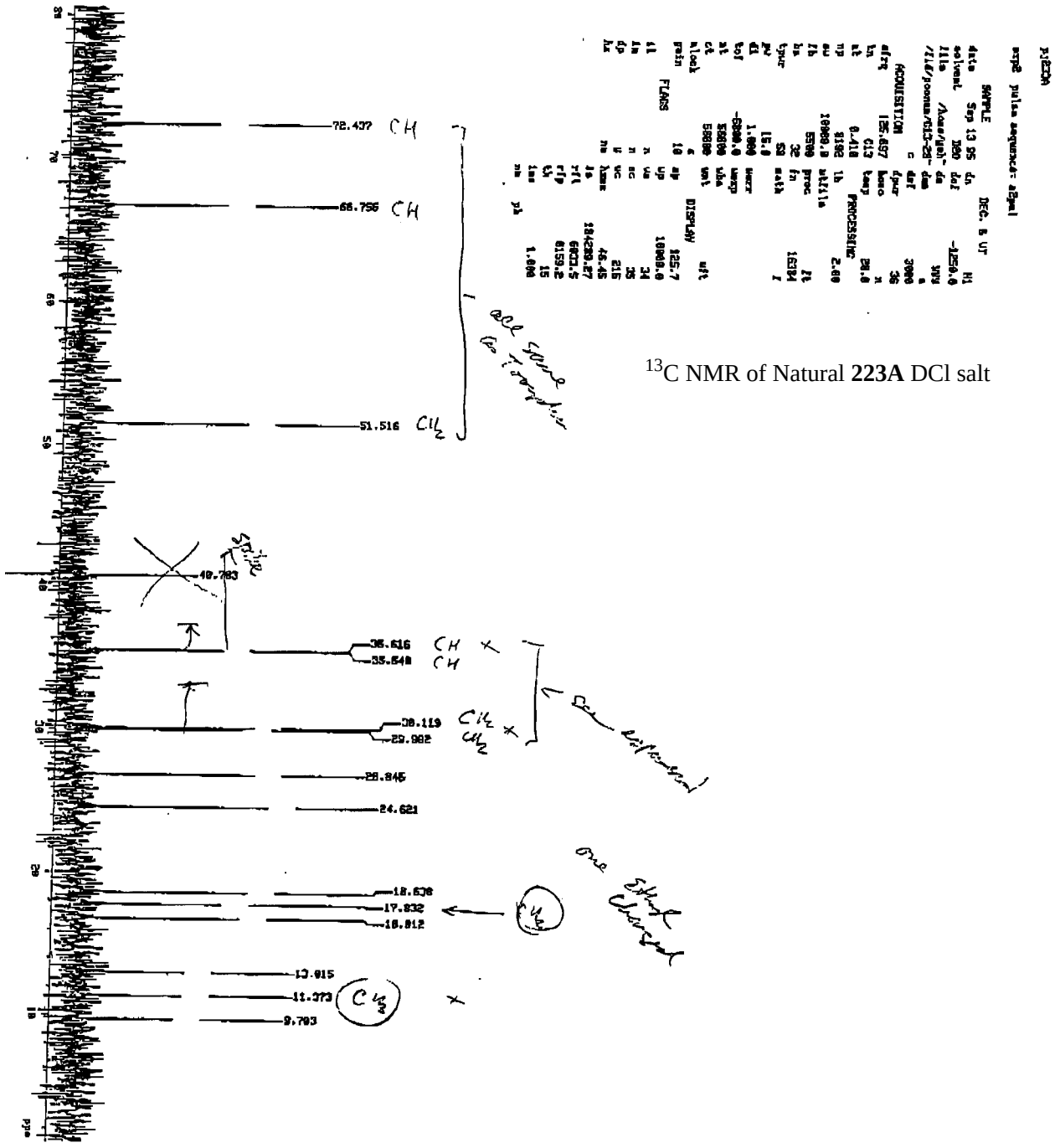


16





^{1}H NMR of natural **223A** DCl salt



^{13}C NMR of Natural **223A** DCl salt