A Nine-Step Enantioselective Total Synthesis of (–)-Vincorine

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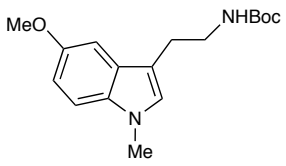
Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[i] All solvents were purified according to the method of Grubbs.[ii] Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel according to the method of Still, utilizing approximately 100 mL of silica gel per gram of crude material.[iii] Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching or ceric ammonium molybdate stain. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) or Varian 500 (500 and 125 MHz, for variable-temp experiments) instrument, and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced to δ 7.27 and 77.0 ppm respectively, d_8-PhMe referenced to δ 7.00 and 128.3 ppm, respectively, central aromatic

peak, C_6D_6 referenced to δ 7.16 and 128.4 ppm, respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm $^{-1}$). High resolution mass spectra were obtained at Princeton University mass spectrometry facilities on an Agilent 6210 High-Resolution Time-of-Flight LC/MS using electrospray ionization (ESI+). Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 254 nm) using a chiral column (25 cm) and guard column (5 cm) as noted.

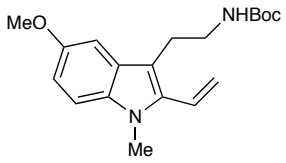
IV. Experimental Details



S1

***tert*-butyl-(2-(5-methoxy-1-methyl-1*H*-indol-3-yl)ethyl)carbamate (S1).** To a stirred solution of tert-butyl (2-(5-methoxy-1*H*-indol-3-yl)ethyl)carbamate (3.51 g, 12.1 mmol) in DMF (24 mL, 0.5 M) at 0 °C was added solid sodium hydride (0.56 g, 60 wt% mineral oil dispersion, 13.9 mmol, 1.15 equiv.). The resulting suspension was warmed to ambient temperature for 30 minutes then cooled to 0 °C and methyl iodide (0.87 mL, 13.9 mmol, 1.15 equiv.) was added dropwise *via* syringe over 2 minutes. After stirring an additional

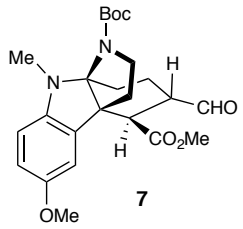
30 minutes at 0 °C, the reaction was quenched by the addition of saturated aqueous ammonium chloride (25 mL). The resulting biphasic mixture was extracted with ethyl acetate (4 x 20 mL) and the combined organic extracts were washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. The resulting light brown oil was purified by flash column chromatography (silica gel, gradient elution: 20 to 30% ethyl acetate in hexanes) to afford the title compound as a colorless, viscous oil (3.55 g, 11.7 mmol, 96%). IR (film) 3355 (br), 2932, 1693, 1490, 1365, 1249, 1225, 1165, 1036, 790, 730 cm $^{-1}$. δ_H (500 MHz, $CDCl_3$) 7.21 (d, J = 8.8, 1H), 7.05 (bs, 1H), 6.91 (dd, J = 8.8, 2.4, 1H), 6.89 (s, 1H), 4.66 (bs, 1H), 3.89 (s, 3H), 3.75 (s, 3H), 3.47 (d, J = 6.2, 2H), 2.93 (t, J = 6.6, 2H), 1.46 (s, 9H); δ_C (125 MHz, $CDCl_3$) 156.0, 153.8, 132.5, 128.0, 127.5, 111.95 (C6), 111.0, 110.1, 100.7, 79.1, 56.1, 40.9, 32.8, 28.5, 25.7; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{17}H_{25}N_2O_3$) requires *m/z* 305.18597, found 305.18601.



4

tert-butyl 2-(5-methoxy-1-methyl-2-vinyl-1H-indol-3-yl)ethylcarbamate (2). In a Schlenk tube under nitrogen equipped with a rubber septum, a solution of tryptamine **S1** (544 mg, 1.79 mmol) in dimethoxyethane (9 mL, 0.2M) was cooled to -78 °C and butyl lithium (2.86 mL of a 2.5 M solution, 7.15 mmol, 4 equivalents) was added via syringe.

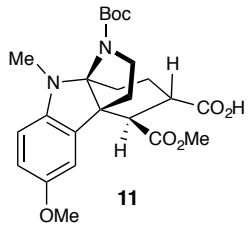
The resulting yellow solution was warmed to -40 °C and stirred for 3 hours, at which point the reaction vessel was cooled to -78 °C, the septum was removed and solid zinc chloride (1.1 g, 8.04 mmol, 4.5 equivalents, taken fresh from a glove box into a capped vial) was added in a single portion, followed by replacement of the septum. The resulting white suspension was stirred at -78 °C for 30 minutes, then warmed to ambient temperature and stirred for 1 hour, at which point 0.5 mL of a solution of (2-Dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2-aminoethyl)phenyl)]palladium(II) chloride (40 mg, .05 mmol, 3 mol%) in 1 mL DME was added via syringe, follow by vinyl iodide (0.53 mL, 7.15 mmol, 4 equivalents) and finally the remaining 0.5 mL of the palladium precatalyst solution. The resulting yellow suspension was stirred for 1 hour at ambient temperature, quenched with ammonium chloride and water, extracted with dichloromethane (5 x 20 mL), dried over magnesium sulfate, concentrated and purified by flash column chromatography (gradient elution, 10 to 15% ethyl acetate in hexanes) yielding 419 mg of the title compound (1.27 mmol, 71%) as a yellow oil which often solidified to a white solid upon standing or concentration from diethyl ether. IR (film) 3364 (br), 2935, 1701, 1488, 1365, 1247, 1163, 1034, 794. δ_H (500 MHz, $CDCl_3$) 7.18 (d, J = 8.9, 1H), 7.02 (bs, 1H), 6.89 (dd, J = 8.8, 2.4, 1H), 6.76 (dd, J = 17.9, 11.8, 1H), 5.6 (d, J = 17.9, 1H), 5.5 (d, J = 11.8, 1H), 4.67 (bs, 1H), 3.87 (s, 3H), 3.72 (s, 3H), 3.40 (d, J = 6.4, 2H), 3.01 (t, J = 6.7, 2H), 1.44 (s, 9H); δ_C (125 MHz, $CDCl_3$) 156.1, 154.1, 135.7, 132.9, 127.9, 126.0, 118.2, 112.6, 110.8, 110.1, 100.7, 79.1, 56.1, 41.2, 31.0, 28.5, 25.4; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{19}H_{27}N_2O_3$) requires *m/z* 331.20217 found *m/z* 331.20228.



7

Aldehyde 7: Taking no care to exclude oxygen or moisture, to a solution of (*E*)-methyl 4-oxobut-2-enoate (285 mg, 2.5 mmol, 2.5 equiv) (available from TCI or in two steps from commercial materials[iv]) in acetonitrile (5 mL, 0.2 M) at -20 °C was added (*S*)-5-benzyl-2,2,3-trimethyl-4-oxoimidazolidin-1-ium tetrafluoroborate (57.2 mg, 0.2 mmol, 0.2 equiv); the reaction was stirred for 5 minutes, at which point tert-butyl 2-(5-methoxy-1-methyl-2-vinyl-1H-indol-3-yl)ethylcarbamate (**4**) (330 mg, 1.0 mmol, 1.0 equiv) was added in a single portion to provide a yellow solution which was maintained at -20 °C for 6 hours. The reaction was then quenched via the addition of 20 mL of saturated aqueous sodium bicarbonate, extracted with dichloromethane (2 x 20 mL), the combined organic layers washed with brine, and the combined aqueous washes extracted once more with 20 mL dichloromethane. The combined organics were then dried over magnesium sulfate and concentrated to provide a red oil, which was purified by flash column chromatography (silica gel, 10% acetone in hexanes as eluent, repurification of mixed fractions after the first column) to afford the title compound (310 mg, 0.7 mmol, 70%) as a white foam. IR (film) 2949, 1726, 1693, 1495, 1364, 1218, 1155, 1027, 905, 730; ^{1}H NMR (500 MHz, Toluene-d_8, 80 ºC) δ 9.23 (t, J = 0.9 Hz, 1H), 6.69 (d, J = 2.6 Hz, 1H), 6.62 (ddd, J = 8.4, 2.5, 0.6 Hz, 1H), 6.22 (d, J = 8.4 Hz, 1H), 3.49 (d, J = 0.6 Hz, 3H), 3.39 (d, J = 0.7 Hz, 3H), 3.00 – 2.91 (m, 1H), 2.89 (s, 5H), 2.52 (d, J = 11.8 Hz, 1H), 2.50

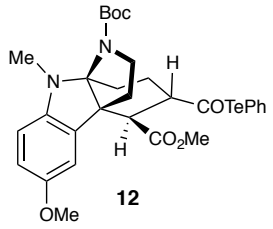
– 2.39 (m, 1H), 1.98 (ddd, J = 13.0, 11.4, 8.2 Hz, 1H), 1.88 (dd, J = 13.0, 6.3 Hz, 1H), 1.65 (ddd, J = 15.2, 11.6, 3.8 Hz, 1H), 1.55 – 1.44 (m, 1H), 1.44 – 1.31 (s, 9H), 1.13 (dddd, J = 13.7, 12.0, 10.3, 3.3 Hz, 1H); ^{13}C NMR (125 MHz, Toluene-d_8, 80 ºC) δ 200.6, 173.4, 154.6, 153.6, 144.4, 133.6, 113.5, 111.7, 107.8, 91.0, 78.9, 55.9, 55.8, 51.3, 48.6, 48.4, 47.9, 31.4, 28.9, 28.7, 28.3, 28.2, 21.7; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{24}H_{33}N_2O_6$) requires *m/z* 445.23331, found 445.23380; $[\alpha]_D^{20}$ = -258.7 (c = 2.37, d_8-PhMe); The enantiomeric ratio was determined by SFC analysis using a Chiralcel IC (25 cm x 0.46 cm) column (30% (1% diethylamine in isopropanol), 100 bar, 50 °C oven, flow = 3.0 mL/min); t_r = 3.15 min (minor) and 5.54 min (major).



11

Acid 11: To a solution of aldehyde **7** (1.12 g, 2.52 mmol) in 3:3:3:1 THF:*tert*-butanol:2-methyl-2-butene:water (0.09M, 7.5 mL THF, *tert*-butanol, 2-methyl-2-butene, 2.5 mL water) at 0 °C was added sodium dihydrogen phosphate hydrate (0.74 g, 5.04 mmol, 2 equivalents). To the resulting suspension was added a solution of sodium chlorite (0.37g, 80% purity, 3.3 mmol, 1.3 equivalents) in water (1.25 mL). The resulting suspension was stirred for 80 minutes at 0 °C then extracted with ethyl acetate. The combined organics were dried over magnesium sulfate, concentrated *in vacuo* and purified by flash chromatography (silica gel, gradient elution: 20 to 30% acetone in hexanes) to provide

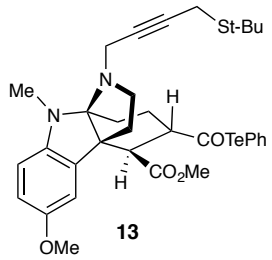
the title compound (1.11 g, 2.41 mmol, 96%) as a light pink foam. IR (film) 3200 (br), 2951, 1731, 1698, 1496, 1366, 1222, 1156, 910, 731 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 6.73 (d, *J* = 6.2 Hz, 1H), 6.59 (d, *J* = 1.8 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.56 – 3.49 (m, 1H), 3.23 (d, *J* = 15.2 Hz, 1H), 2.97 (s, 1H), 2.91 (s, 3H), 2.86 (s, 1H), 2.62 (t, *J* = 11.9 Hz, 1H), 2.17 (s, 1H), 2.10 – 1.99 (m, 1H), 1.95 (d, *J* = 6.0 Hz, 1H), 1.75 (dd, *J* = 29.0, 14.1 Hz, 1H), 1.56 (d, *J* = 14.4 Hz, 1H), 1.35 (s, 9H). δ_C (125 MHz, $CDCl_3$) 179.8, 179.7, 173.6, 173.4, 154.5, 152.7, 152.3, 144.0, 143.4, 132.7, 113.2, 113.0, 111.3, 111.2, 107.1, 90.1, 89.6, 80.8, 79.2, 56.6, 56.3, 56.2, 55.4, 51.9, 49.9, 49.7, 47.7, 47.4, 41.4, 41.3, 36.7, 30.9, 29.0, 28.7, 28.5, 28.2, 27.4, 26.7, 25.2, 25.0, 24.8; Apparent "doubling" of some peaks is due to carbamate geometrical isomerism. HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{24}H_{33}N_2O_7$) requires *m/z* 461.22823, found 461.22781. $[\alpha]_D^{20}$ = -220.5 (c = 3.98, d_8-PhMe).



12

Acyl telluride 12: To a suspension of diphenyl ditelluride (148 mg, 1.0 equivalents) and sodium borohydride (41 mg, 3.0 equivalents) in degassed THF (1.8 mL, 0.2M, degassed by bubbling through with nitrogen for 20 minutes) was added degassed methanol (180 μL) dropwise, causing an evolution of gas. After 40 minutes, a separate vial was charged with acid **11** (166 mg, 0.36 mmol) in degassed THF (1.8 mL, 0.2 M), cooled to -10 °C, and N-methyl morpholine (40 μL, 1.0 equivalents) was added via syringe, followed by

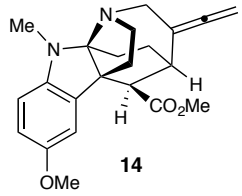
isobutyl chloroformate (57 μL, 1.2 equivalents). After stirring for 20 minutes at this temperature, the colorless solution containing the mixed anhydride was transferred via syringe to the sodium telluride solution prepared above, along with two 0.3 mL rinses with additional degassed THF. TLC analysis indicated complete conversion to a single new spot (TLC in 20% acetone in hexanes). The reaction was loaded directly onto a silica gel column with the aid of dichloromethane, and purified by flash chromatography (silica gel, 20% acetone in hexanes as eluent) to provide the title compound (203 mg, 87%) as a white foam. IR (film) 2973, 1729, 1694, 1495, 1363, 1154, 9376, 885, 733 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.1 Hz, 2H), 7.37 (t, *J* = 6.8 Hz, 1H), 7.35 – 7.27 (m, 2H), 6.72 (td, *J* = 7.1, 6.4, 2.3 Hz, 1H), 6.57 (d, *J* = 2.5 Hz, 1H), 6.36 (apparent dd, *J* = 17.0, 8.3 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.55 – 3.44 (m, 1H), 3.26 – 3.14 (m, 1H), 2.95 (dt, *J* = 11.3, 5.6 Hz, 1H), 2.88 (apparent d, *J* = 28.0 Hz, 3H), 2.70 (t, *J* = 11.3 Hz, 1H), 2.19 – 2.07 (m, 1H), 2.05 – 1.99 (m, 1H), 1.94 (dd, *J* = 13.0, 6.4 Hz, 1H), 1.81 – 1.64 (m, 1H), 1.63 – 1.53 (m, 1H), 1.42 (apparent d, *J* = 65.5 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 172.9, 172.6, 154.3, 152.6, 152.3, 143.8, 143.3, 140.4, 140.2, 138.7, 137.6, 132.4, 129.8, 129.7, 129.3, 129.0, 128.9, 128.1, 115.2, 114.0, 113.1, 113.0, 111.0, 110.0, 107.1, 90.1, 89.6, 80.6, 79.2, 58.9, 58.6, 57.0, 56.2, 56.1, 55.7, 51.8, 49.7, 49.4, 47.6, 47.4, 34.7, 31.6, 30.9, 28.7, 28.4, 27.6, 24.7, 22.7, 14.2; Apparent "doubling" of some peaks is due to carbamate geometrical isomerism. HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{30}H_{37}N_2O_6Te$) requires *m/z* 651.17084, found 651.17245. $[\alpha]_D^{20}$ = -145.4 (c = 5.16, $CDCl_3$).



13

Propargyl amine 13: Boc-protected acyl telluride **15** (165 mg, 0.255 mmol) was taken up in trifluoroacetic acid (2.5 mL, 0.1M), swirled for two minutes and then concentrated *in vacuo*. The resulting brown oil was taken up in dichloromethane (10 mL), washed with sodium bicarbonate (10 mL), and the aqueous layer was extracted with 3 x 10 mL dichloromethane. The combined organics were then dried over magnesium sulfate and concentrated. The crude amine was taken up in dichloromethane (5 mL, 0.05M) and sodium triacetoxyborohydride (270 mg, 5.0 equivalents) was added, followed by a solution of 4-(tert-butylthio)but-2-ynal[v] in 0.5 mL dichloromethane dropwise over 2 minutes. The resulting suspension was stirred for 5 minutes, quenched with 10 mL saturated aqueous sodium bicarbonate, extracted with 3 x 10 mL dichloromethane, the combined organic dried over magnesium sulfate, concentrated, and the resulting brown oil purified by flash column chromatography (gradient elution, hexanes to 5 to 10% acetone in hexanes) to provide the title compound as a light brown gum (113 mg, 0.164 mmol, 65%). IR (film) 2951, 2174, 1729, 1499, 1435, 1280, 1168, 1034, 734. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 2H), 7.41 – 7.34 (m, 1H), 7.34 – 7.27 (m, 2H), 6.66 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.46 (d, *J* = 2.5 Hz, 1H), 6.26 (d, *J* = 8.5 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 4H), 3.46 – 3.37 (m, 1H), 3.36 – 3.27 (m, 2H), 3.26 (dt, *J* = 4.1, 2.0 Hz, 3H), 2.83 (d, *J* = 11.5 Hz, 1H), 2.81 (s, 3H), 2.51 (ddd, *J* = 10.7, 8.7, 5.7 Hz, 1H), 2.26 – 2.18 (m,

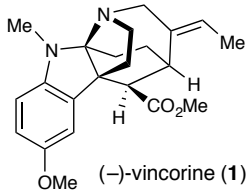
1H), 2.13 (dddd, *J* = 13.9, 11.0, 7.8, 3.2 Hz, 1H), 2.02 – 1.91 (m, 2H), 1.79 – 1.65 (m, 2H), 1.34 (s, 10H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.6, 173.7, 152.1, 145.4, 140.1, 140.1, 133.2, 129.7, 129.0, 114.3, 113.3, 111.1, 105.9, 90.0, 80.2, 79.8, 77.4, 57.7, 57.0, 56.2, 51.8, 50.1, 47.8, 37.6, 31.1, 30.8, 30.8, 25.5, 21.3, 17.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{33}H_{41}N_2O_4STe$) requires *m/z* 691.18438, found 691.18269. $[\alpha]_D^{20}$ = -50.2 (c = 2, $CDCl_3$).



14

Allene 14: Cyclization precursor **13** (82 mg, 0.12 mmol) was dissolved in 238 mL 1,2-dichlorobenzene (0.5 mM), and the solution was degassed via three cycles of the freeze-pump-thaw method. The system was allowed to remain sealed under static vacuum, then heated to 200 °C for 10 hours. The resulting solution was cooled to ambient temperature, concentration via rotary evaporation (2 torr, 50 ºC water bath) to a red oil, then purified by flash column chromatography (gradient elution, 10 to 15% ethyl acetate in hexanes) to give 22.2mg, 51% of the title compound as a colorless oil. IR (film) 2948, 1954, 1730, 1492, 1279, 1240, 1160, 1033, 794; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 2.7 Hz, 1H), 6.64 (dd, *J* = 8.3, 2.7 Hz, 1H), 6.19 (d, *J* = 8.3 Hz, 1H), 4.59 (qdt, *J* = 5.0, 3.4, 1.4 Hz, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 3.51 – 3.32 (m, 2H), 3.19 (d, *J* = 15.0 Hz, 1H), 2.86 (d, *J* = 1.8 Hz, 1H), 2.80 (ddd, *J* = 11.6, 9.3, 2.0 Hz, 1H), 2.55 (s, 3H), 2.35 – 2.17 (m, 2H), 2.00 (ddd, *J* = 13.8, 9.1, 1.9 Hz, 1H), 1.84 (dddd, *J* = 12.1, 10.3, 5.4, 1.6 Hz, 1H),

1.76 – 1.55 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.9, 173.3, 152.2, 143.7, 138.7, 112.8, 111.6, 105.4, 99.9, 98.1, 77.4, 72.9, 57.6, 56.1, 55.2, 53.5, 51.7, 51.7, 41.9, 36.1, 28.1, 24.9, 20.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{22}H_{26}N_2O_3$) requires 367.20162 found 367.20177; $[\alpha]_D^{20}$ = -260 (c = 1, $CDCl_3$).

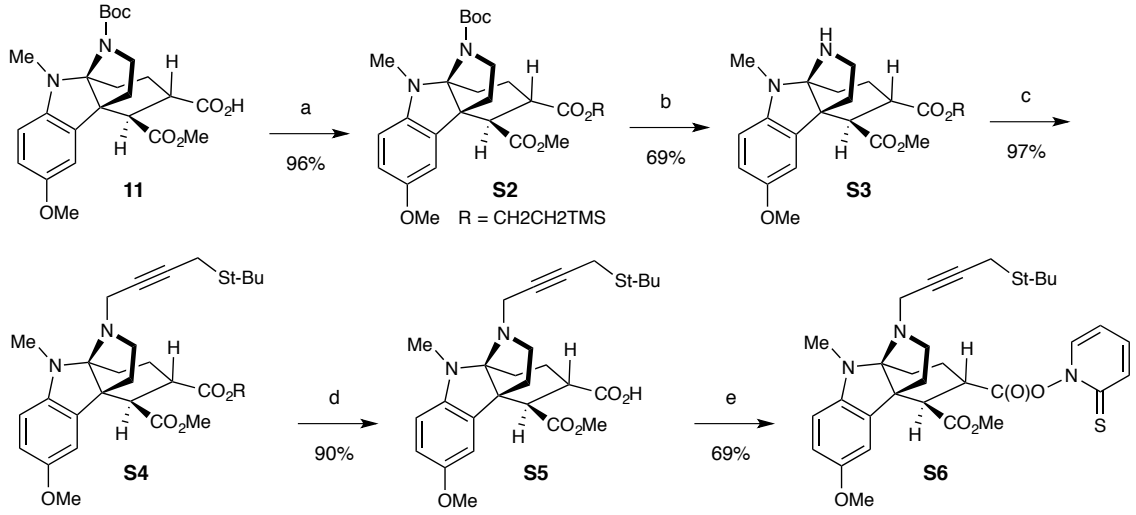


(–)-vincorine (**1**)

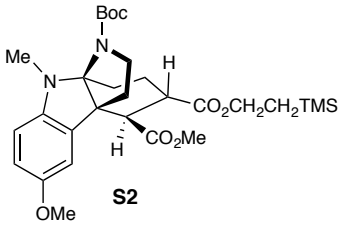
Vincorine (**1**): To a solution of allene **14** (16 mg, 44 μmol) in THF (1.5 mL, 0.03 M) was added 16 mg Pd/C, and the resulting heterogeneous suspension was cooled to -15 °C, flushed with hydrogen for 5 minutes, then left under a hydrogen atmosphere for 75 minutes, at which point 8 mg more Pd/C was added, and the reaction was stirred 20 more minutes (periodically flushing with hydrogen). The resulting suspension was filtered through a short pad of celite, which was eluted with 40 mL ethyl acetate, then the combined filtrate was concentrated and purified by flash column chromatography (gradient elution, 20 to 30 to 40% ethyl acetate in hexanes) to provide 12.9 mg of vincorine, 80%. IR (film) 2947, 1732, 1667, 1486, 1434, 1277, 1111, 1032, 792, 765; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (d, *J* = 2.6 Hz, 1H), 6.62 (dd, *J* = 8.3, 2.6 Hz, 1H), 6.18 (d, *J* = 8.3 Hz, 1H), 5.39 (q, *J* = 6.9 Hz, 1H), 3.79 (s, 4H), 3.73 (s, 3H), 3.66 – 3.54 (m, 1H), 3.36 (td, *J* = 11.0, 8.9 Hz, 1H), 2.99 (d, *J* = 15.2 Hz, 1H), 2.79 (s, 0H), 2.72 (ddd, *J* = 11.3, 9.3, 1.6 Hz, 1H), 2.57 (s, 3H), 2.46 (ddd, *J* = 13.9, 10.5, 9.1 Hz, 1H), 2.33 – 2.23 (m, 1H), 2.05 – 1.93 (m, 1H), 1.75 (tdd, *J* = 9.8, 5.1, 2.2 Hz, 2H), 1.65 (ddd, *J* = 14.4, 12.1, 6.1 Hz, 1H), 1.58 (dd, *J* = 6.9, 1.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8,

152.1, 143.9, 139.1, 138.7, 122.5, 112.4, 111.4, 105.2, 97.9, 58.4, 57.3, 56.2, 55.2, 51.8, 50.9, 41.1, 34.9, 28.1, 26.4, 20.6, 13.7; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{22}H_{28}N_2O_3$) requires 369.21727, found 369.21622; $[\alpha]_D^{20}$ = -113.6 (c = 0.5, EtOH) whereas $[\alpha]_D^{20}$ = -142 (c = 1.0, EtOH) is reported for natural vincorine.[vi]

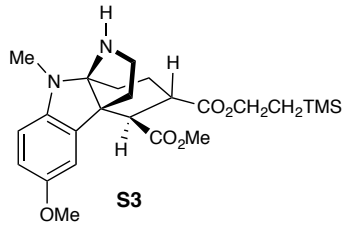
Scheme S1: Synthesis of Barton Ester cyclization precursor.



Reagent and conditions: (a) EDCI, 2-(trimethylsily)ethanol, DMAP, CH_2Cl_2. (b) TMSI, MeCN, rt. (c) 4-(*tert*-butylthio)but-2-ynal, $NaBH(OAc)_3$, CH_2Cl_2, rt. (d) TAS-F, DMF, rt. (e) 2-thiopyridine-N-oxide, EDCI, DMAP, PhH.

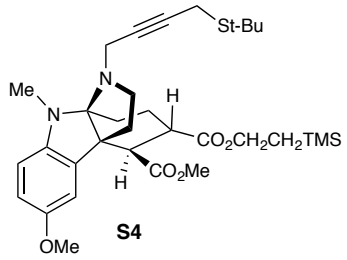


TMSE ester S2: To a solution of (+/-) acid **11** (209.5 mg, 0.455 mmol) in dichloromethane (2.3 mL, 0.2 M) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (131 mg, 0.68 mmol, 1.5 equivalents) and 2-dimethylaminopyridine (14mg, 0.115 mmol, 0.25 equivalents) followed by 2-(trimethylsilyl)ethanol (1 mL, 7 mmol, 15 equivalents) and the resulting solution was stirred for 48 hours. The reaction was quenched with pH 4 buffer, extracted with ethyl acetate, and the combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. Purification of the resulting oil was achieved *via* flash column chromatography (silica gel, gradient elution: 8 to 10 to 12% acetone in hexanes) to provide the title compound (244.9 mg, 96%) as a colorless gum. IR (film) 2932, 2119, 1731, 1698, 1496, 1364, 1157, 860, 837. δ_H (500 MHz, $CDCl_3$) 6.73 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.58 (d, *J* = 2.1 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 4.16 – 4.00 (m, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.57 – 3.49 (m, 1H), 3.20 (d, *J* = 15.2 Hz, 1H), 2.97 (dd, *J* = 11.3, 6.3 Hz, 1H), 2.92 (s, 3H), 2.81 (td, *J* = 11.7, 3.6 Hz, 1H), 2.66 (d, *J* = 11.7 Hz, 1H), 2.21 (dd, *J* = 11.8, 9.1 Hz, 1H), 1.98 (ddd, *J* = 13.4, 7.6, 3.5 Hz, 1H), 1.85 – 1.70 (m, 1H), 1.54 (d, *J* = 12.9 Hz, 1H), 1.35 (s, 9H), 0.99 – 0.87 (m, 2H), 0.01 (apparent d, *J* = 4.4 Hz, 9H). δ_C (125 MHz, $CDCl_3$) 174.2, 174.2, 173.7, 173.4, 154.5, 152.6, 152.3, 144.0, 143.5, 132.9, 113.1, 112.9, 111.1, 111.1, 107.0, 90.1, 89.5, 80.6, 79.1, 63.3, 60.3, 56.8, 56.3, 56.2, 55.5, 51.7, 50.1, 49.9, 47.7, 47.5, 46.2, 41.7, 41.6, 30.9, 29.0, 28.7, 28.5, 28.2, 27.5, 26.8, 25.2, 25.0, 22.3, 17.4, -1.3, -1.4. HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{29}H_{45}N_2O_7Si$) requires *m/z* 561.29905, found 561.28163.



S3

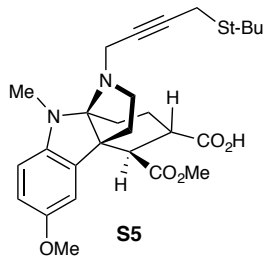
Amine S3: To a solution of TMSE-protected **S2** (38.5mg, 0.069 mmol) in acetonitrile (0.7 mL, 0.1M) was added trimethylsilyl iodide (36 μL, 0.25 mmol, 3.6 equivalents) and the reaction was stirred for 5 minutes. At this point, the reaction was quenched with saturated aqueous sodium bicarbonate, extracted with ethyl acetate, and the combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. Purification by flash chromatography (triethylamine saturated silica gel, gradient elution: 50% ethyl acetate in hexanes to ethyl acetate) yielded the title compound (21.7 mg, 0.047 mmol, 69%) as a colorless gum. IR (film) 2951, 1728, 1490, 1250, 1176, 1037, 838. δ_H (500 MHz, $CDCl_3$) 6.71 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.63 (d, *J* = 2.5 Hz, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 4.18 – 4.00 (m, 2H), 3.74 (s, 3H), 3.71 (s, 3H), 3.01 (ddd, *J* = 12.1, 9.2, 3.2 Hz, 1H) (H13), 2.86 – 2.73 (m, 2H) (H13, H16), 2.70 (s, 4H) (H 11, H17), 2.31 (dt, *J* = 13.3, 8.9 Hz, 1H) (H12), 2.22 (ddd, *J* = 14.3, 4.7, 2.7 Hz, 1H) (H14), 2.08 (ddd, *J* = 13.2, 8.0, 3.2 Hz, 1H) (H12), 2.01 – 1.92 (m, 1H) (H15), 1.79 – 1.66 (m, 1H) (H15), 1.61 (ddd, *J* = 15.8, 12.1, 2.9 Hz, 1H) (H14), 0.97 – 0.86 (m, 2H) (H22), 0.01 (s, 9H) (TMS). δ_C (125 MHz, $CDCl_3$) 174.4, 174.3, 152.8, 144.2, 135.4, 112.8, 112.2, 108.7, 90.7, 63.2, 56.1, 55.4, 51.6, 49.6, 44.4, 41.7, 31.6, 29.5, 29.3, 24.8, 17.4, -1.4. HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{24}H_{37}N_2O_5Si$) requires *m/z* 461.24663, found 461.24679.



S4

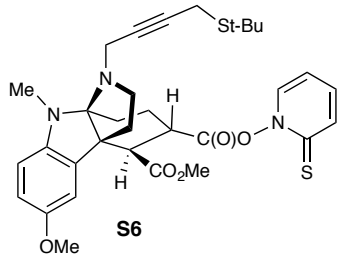
Propargyl amine S4: To a solution of amine **S3** (139.5 mg, 0.303 mmol) in dichloromethane (6 mL, 0.05 M) was added sodium triacetoxyborohydride (321 mg, 1.51 mmol, 5 equivalents) followed by a solution of 4-(*tert*-butylthio)but-2-ynal (57 mg, 0.365 mmol, 1.2 equivalents) in dichloromethane (1.5 mL) dropwise over two minutes. After stirring for a further five minutes, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate. The resulting biphasic solution was extracted with ethyl acetate, the combined organic phases were dried over magnesium sulfate, concentrated *in vacuo*, and purified by flash chromatography (silica gel, gradient elution: 8 to 10 to 12% acetone in hexanes) to provide the title compound (176.6 mg, 0.294 mmol, 97%) as a colorless gum. IR (film) 2953, 1731, 1500, 1173, 1038, 838. δ_H (500 MHz, $CDCl_3$) 6.66 (dd, *J* = 8.4, 2.6 Hz, 1H) (H6), 6.48 (d, *J* = 2.5 Hz, 1H) (H4), 6.27 (d, *J* = 8.4 Hz, 1H) (H7), 4.10 (td, *J* = 7.8, 5.0 Hz, 2H) (H21), 3.71 (s, 3H) (H19), 3.70 (s, 3H) (H10), 3.47 – 3.27 (m, 2H) (H24), 3.25 (d, *J* = 1.9 Hz, 1H) (H27), 2.96 (ddd, *J* = 12.2, 8.0, 4.1 Hz, 2H) (H13, H16), 2.83 (s, 3H) (H11), 2.74 (d, *J* = 11.9 Hz, 1H) (H17), 2.61 – 2.51 (m, 1H) (H13), 2.36 – 2.24 (m, 1H) (H12), 2.20 – 2.06 (m, 1H) (H15), 2.03 – 1.87 (m, 2H) (H14, H12), 1.86 – 1.69 (m, 2H) (H15, H14), 1.33 (s, 9H) (SC(**C**H_3), 0.93 (dd, *J* = 9.8, 7.6 Hz, 2H) (H22), 0.00 (d, *J* = 9.3 Hz, 9H) (H 23). δ_C (125 MHz, $CDCl_3$) 175.1, 174.3, 152.1, 145.3, 133.8, 113.2, 111.1, 105.9, 90.0, 80.2, 80.0, 63.3, 56.8, 56.2, 51.7, 50.1, 48.6, 43.2,

40.2, 37.8, 30.9, 30.7, 30.6, 25.8, 21.7, 17.4, 17.1, 0.1, -1.4. HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{32}H_{49}N_2O_5SSi$) requires *m/z* 601.31260, found 601.31447.



S5

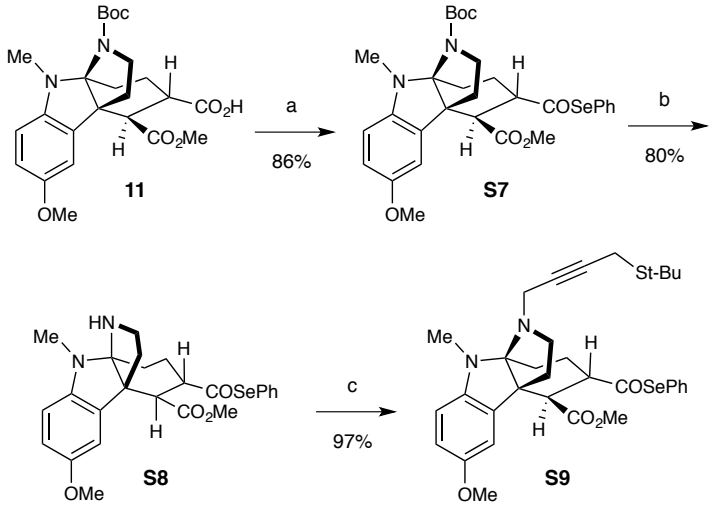
Acid S5: To a solution of propargyl amine **S4** (100.7 mg, 0.168 mmol) in DMF (1.5 mL, ~ 0.1 M) was added tris(dimethylamino)sulfonium difluorotrimethylsilicate (TAS-F) (92.3mg, 0.335 mmol, 2 equivalents). The resulting solution was stirred at ambient temperature for 2 hours, then purified directly by flash column chromatography (silica gel, gradient elution: 30 to 35% acetone in hexanes) to provide the title compound (75.6 mg, 0.151 mmol, 90%) as a light brown gum. IR (film) 2956, 1730, 1496, 1365, 1167, 1034, 737. δ_H (500 MHz, $CDCl_3$) 6.67 (dd, *J* = 8.4, 2.6 Hz, 1H) (H6), 6.50 (d, *J* = 2.5 Hz, 1H) (H4), 6.28 (d, *J* = 8.4 Hz, 1H) (H7), 3.71 (s, 6H) (H10, H19), 3.48 – 3.27 (m, 2H) (H21), 3.24 (s, 2H) (H24), 3.07 – 2.91 (m, 2H) (H16, H13), 2.83 (s, 3H) (H11), 2.75 (d, *J* = 11.9 Hz, 1H) (H17), 2.62 – 2.52 (m, 1H) (H13), 2.35 – 2.24 (m, 1H) (H12), 2.18 (s, 1H) (H15), 2.04 – 1.90 (m, 2H) (H12, H14), 1.89 – 1.80 (m, 1H) (H14), 1.79 – 1.67 (m, 1H) (H15), 1.33 (s, 9H) ($SC(\mathbf{C}H_3)_3$). δ_C (125 MHz, $CDCl_3$) 178.6, 174.2, 152.1, 145.2, 133.7, 113.2, 111.2, 106.1, 56.6, 56.2, 51.8, 50.0, 48.5, 43.2, 39.7, 37.9, 30.8, 30.6, 30.5, 29.9, 25.7, 21.9, 17.1. HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{27}H_{37}N_2O_5S$) requires *m/z* 501.24177, found 501.24296.



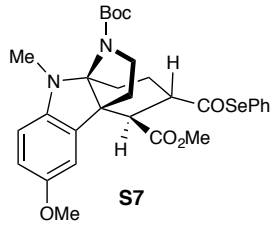
S6

Barton Ester S6: To a solution of **acid S5** (31.7 mg, 0.063 mmol) in benzene (0.32 mL, 0.2 M) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (22.2 mg, 0.116 mmol, 1.84 equivalents) followed by 2-thiopyridine-*N*-oxide (11.7 mg, 0.092 mmol, 1.46 equivalents) followed by 4-dimethylaminopyridine (8.9 mg, 0.073 mmol, 1.16 equivalents) and the reaction was stirred for 11 hours. Direct purification by flash column chromatography (silica gel, gradient elution: hexanes to 20 to 30% acetone in hexanes) provided the title compound (26.5mg, 0.043 mmol, 69%) as an amorphous, sticky yellow solid. IR (film) 2933, 2125, 1644, 1602, 1453, 1216, 1140, 995, 807; ^{1}H NMR (500 MHz, Benzene-d6) δ 7.42 (dd, *J* = 8.9, 1.7 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.69 (dd, *J* = 7.0, 1.5 Hz, 1H), 6.21 (d, *J* = 8.4 Hz, 1H), 6.12 (s, 1H), 5.98 (ddd, *J* = 8.6, 6.7, 1.6 Hz, 1H), 5.35 (td, *J* = 6.9, 1.8 Hz, 1H), 3.45 (s, 3H), 3.40 (dt, *J* = 11.8, 7.3 Hz, 1H), 3.34 (s, 3H), 3.27 – 3.11 (m, 3H), 3.09 (d, *J* = 2.2 Hz, 2H), 2.96 – 2.84 (m, 1H), 2.75 (ddd, *J* = 10.2, 8.6, 6.0 Hz, 1H), 2.51 – 2.41 (m, 2H), 2.40 (s, 3H), 2.22 (ddd, *J* = 12.6, 10.3, 7.9 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.54 (s, 1H), 1.19 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 177.2, 174.3, 171.2, 153.3, 146.2, 138.0, 137.6, 134.3, 132.7, 128.7, 113.6, 112.2, 111.4, 107.1, 90.6, 80.8, 80.4, 57.2, 55.9, 51.7, 50.5, 49.2, 39.2, 38.3, 31.5, 31.1, 30.8, 25.2, 22.3, 17.6;

Figure S2: Synthesis of acyl selenide.

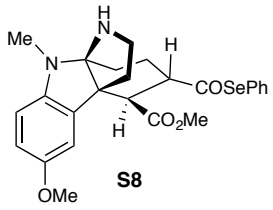


Reagent and conditions: (a) carbonyl diimidazole, DMF; Benzene selenol. (b) TFA, rt. (c) 4-(*tert*-butylthio)but-2-ynal, $NaBH(OAc)_3$, CH_2Cl_2, rt.



Acyl selenide S7: To a solution of (+/-) carboxylic acid **11** (299mg, 0.65 mmol) in DMF (0.65 mL, 1.0 M) was added carbonyldiimidazole (139 mg, 0.86 mmol, 1.32 equivalents) and the resulting solution was stirred for 30 minutes, at which point benzene selenol (0.172 mL, 1.6 mmol, 2.5 equivalents) was added and the reaction stirred for an additional 1 hour. Direct purification *via* flash column chromatography (silica gel, gradient elution: hexanes to 10% acetone in hexanes) provided the title compound (336.5

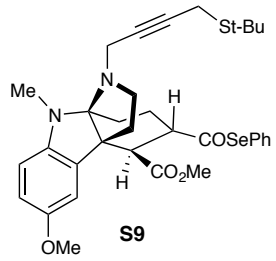
mg, 0.56 mmol, 86%) as a colorless foam. IR (film) 3364, 2949, 1729, 1697, 1496, 1365, 1220, 1154, 885, 739; δ_H (500 MHz, $CDCl_3$) 7.38 (d, *J* = 7.1 Hz, 3H), 7.28 (d, *J* = 6.3 Hz, 2H), 6.73 – 6.62 (m, 1H), 6.51 (s, 1H), 6.30 (dd, *J* = 17.1, 8.4 Hz, 1H), 3.67 (s, 1H), 3.64 (s, 2H), 3.48 (t, *J* = 9.4 Hz, 1H), 3.16 (td, *J* = 11.4, 3.3 Hz, 1H), 2.96 – 2.88 (m, 1H), 2.86 (s, 3H), 2.68 (d, *J* = 11.6 Hz, 1H), 2.14 (dd, *J* = 11.3, 8.5 Hz, 1H), 2.09 – 2.00 (m, 1H), 1.92 (dd, *J* = 12.6, 6.1 Hz, 1H), 1.78 (d, *J* = 15.2 Hz, 1H), 1.57 (s, 1H), 1.29 (s, 9H); δ_C (125 MHz, $CDCl_3$) 202.4, 202.3, 173.0, 172.7, 154.4, 152.7, 152.4, 144.0, 143.4, 135.9, 132.5, 129.5, 129.1, 129.1, 126.1, 113.2, 113.0, 111.1, 111.0, 107.2, 90.1, 89.5, 80.7, 79.2, 60.6, 57.0, 56.3, 56.2, 55.8, 53.2, 53.0, 51.9, 50.1, 49.9, 47.7, 47.5, 31.0, 29.8, 28.8, 28.7, 28.5, 28.0, 27.7, 27.0, 25.9, 25.7; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{17}H_{25}N_2O_3$) requires *m/z* 601.18114, found 601.18423.



S8

Deprotected S8: To neat **S7** (336.5 mg, 0.56 mmol) was added trifluoroacetic acid (2.5 mL, 0.2 M) and the smoking solution is swirled (no stir bar) for two minutes and then concentrated. The resulting viscous oil is purified by flash column chromatography (triethylamine saturated silica gel, gradient elution: hexanes to 50% ethyl acetate in hexanes to 100% ethyl acetate) to provide the title compound (224 mg, 0.45 mmol, 80%) as a sticky light-brown amorphous solid. IR (film) 3360, 3947, 1725, 1489, 1437, 1279, 1220, 1033, 955, 802, 737, 690; δ_H (500 MHz, $CDCl_3$) 7.53 – 7.41 (m, 3H), 7.35 (d, *J* =

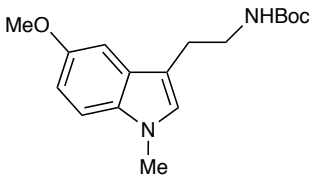
6.3 Hz, 2H), 6.71 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.62 (d, *J* = 2.5 Hz, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 3.73 (s, 1H), 3.71 (s, 2H), 3.20 (td, *J* = 11.3, 4.0 Hz, 1H), 3.09 (q, *J* = 7.3 Hz, 1H), 3.06 – 2.97 (m, 1H), 2.78 (d, *J* = 11.5 Hz, 1H), 2.70 (d, *J* = 4.1 Hz, 2H), 2.36 – 2.22 (m, 1H), 2.16 – 2.04 (m, 1H), 1.83 – 1.70 (m, 1H), 1.67 – 1.57 (m, 1H); δ_C (125 MHz, $CDCl_3$) 202.3, 173.5, 152.9, 144.1, 135.9, 134.9, 129.5, 129.1, 126.2, 113.0, 112.1, 108.7, 90.7, 56.1, 55.6, 53.2, 51.8, 49.7, 45.6, 44.3, 31.7, 29.4, 29.4, 29.0, 25.4, 8.7; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{17}H_{25}N_2O_3$) requires *m/z* 501.12871, found 501.12888.



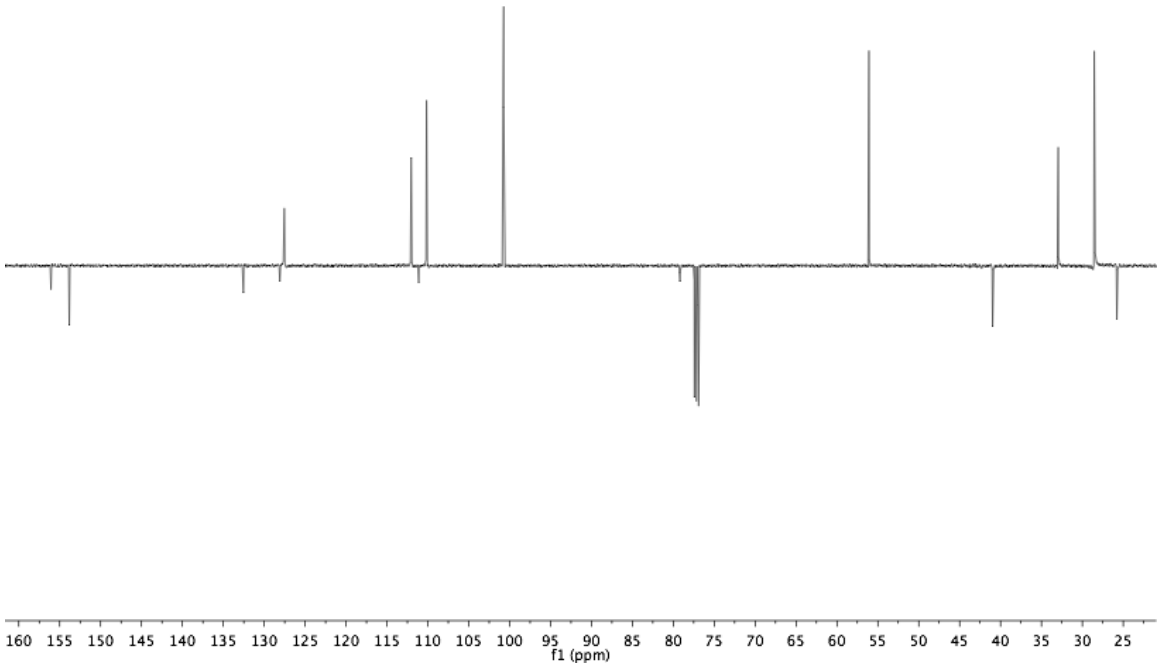
S9

Propargyl sulfide S9: To a solution of amine **S8** (224 mg, 0.45 mmol) in dichloromethane (10 mL, 0.05 M) was added sodium triacetoxyborohydride (475 mg, 2.24 mmol, 5 equivalents) followed by a solution of 4-(*tert*-butylthio)but-2-ynal (84 mg, 0.54 mmol, 1.2 equivalents) in dichloromethane (2 mL) dropwise over two minutes. After stirring for a further five minutes, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate. The resulting biphasic solution was extracted with ethyl acetate, the combined organics were dried over magnesium sulfate, concentrated *in vacuo*, and purified by flash chromatography (silica gel, gradient elution: 8 to 10 to 12% acetone in hexanes) to provide the title compound (176.6 mg, 0.294 mmol, 97%) as a colorless gum. IR (film) 2951, 1728, 1498, 1438, 1364, 1280, 1164, 1022, 959, 800, 739;

δ_H (500 MHz, $CDCl_3$) 7.46 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.36 (d, *J* = 6.1 Hz, 1H), 6.66 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.48 (d, *J* = 2.5 Hz, 1H), 6.26 (d, *J* = 8.4 Hz, 1H), 3.72 (s, 1H), 3.70 (s, 1H), 3.48 – 3.27 (m, 1H), 3.26 (s, 1H), 2.98 (t, *J* = 7.9 Hz, 1H), 2.87 (d, *J* = 11.6 Hz, 1H), 2.82 (s, 1H), 2.57 – 2.48 (m, 1H), 2.33 – 2.16 (m, 1H), 2.05 – 1.95 (m, 1H), 1.83 – 1.74 (m, 1H), 1.34 (s, 1H); δ_C (125 MHz, $CDCl_3$) 202.9, 173.7, 152.1, 145.4, 135.7, 133.2, 129.4, 129.0, 126.3, 113.2, 111.0, 105.8, 89.8, 80.1, 79.8, 57.0, 56.1, 51.8, 51.7, 50.0, 48.3, 43.1, 37.6, 31.1, 30.8, 30.7, 25.5, 22.1, 17.0; HRMS (ESI-TOF) exact mass calculated for [M+H]+ ($C_{33}H_{41}N_2O_4SSe$) requires *m/z* 641.19468, found 641.19774. HRMS found 641.19774.



S1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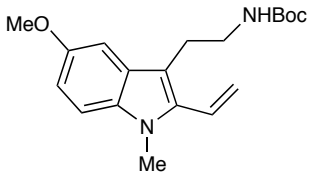
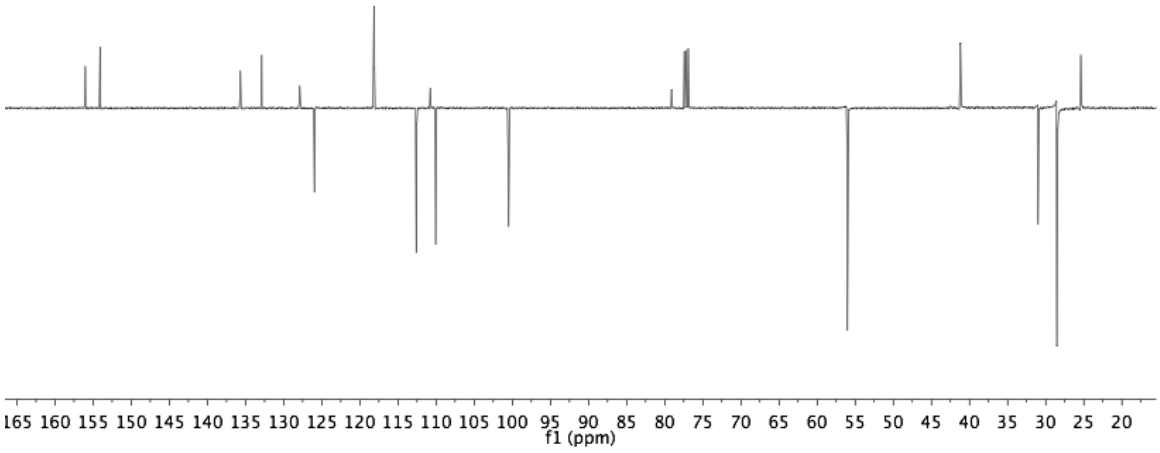
f1 (ppm)



4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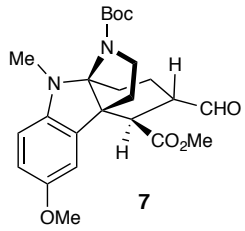
f1 (ppm)


Boc
N
Me
N
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CHO
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CO2Me
OMe

7

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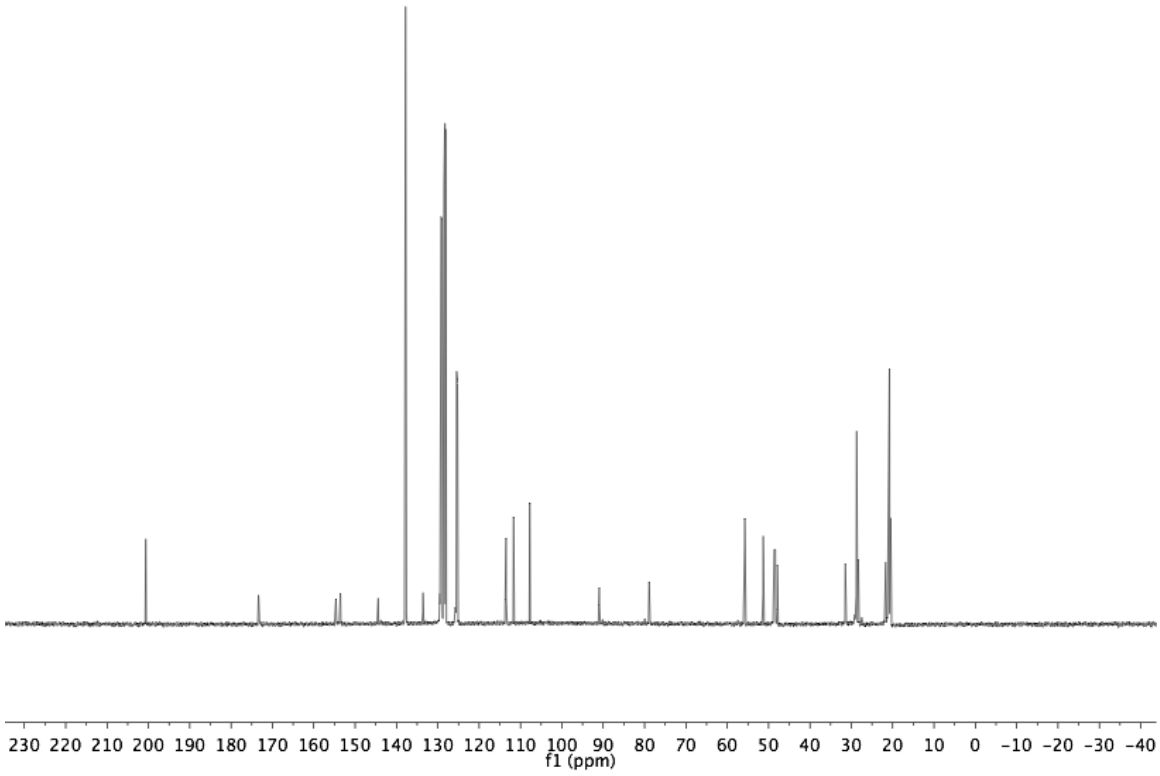
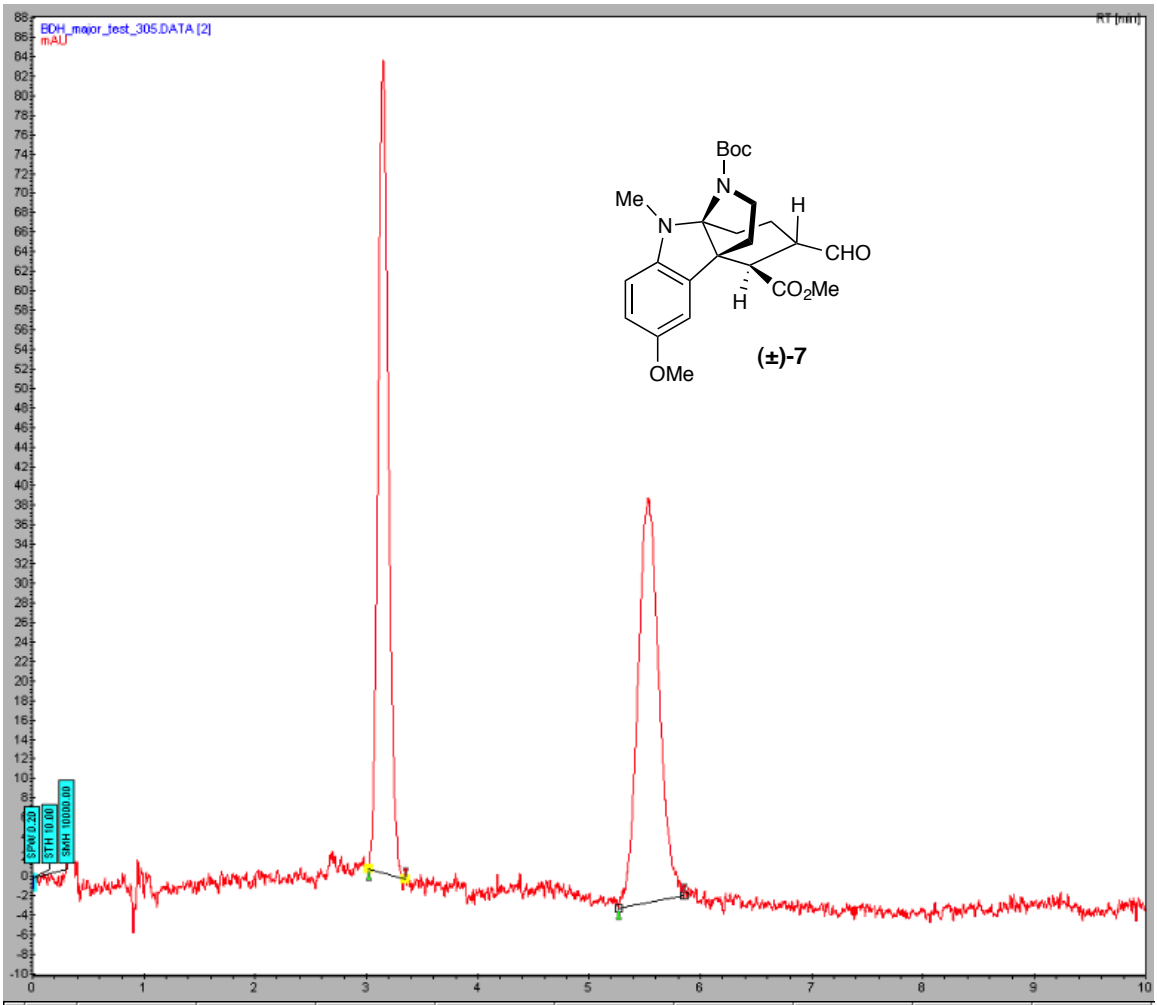
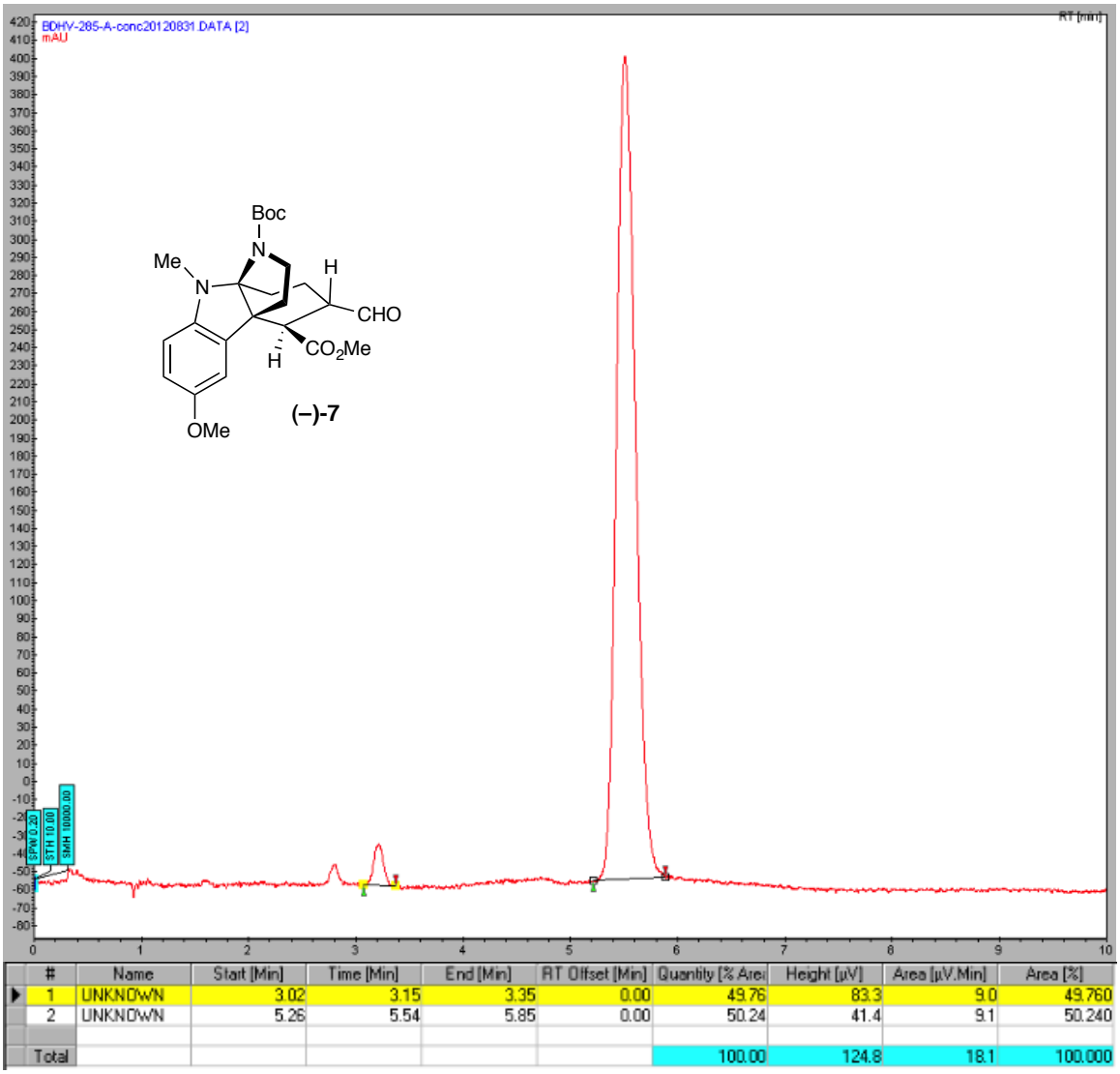
0.5
f1 (ppm)

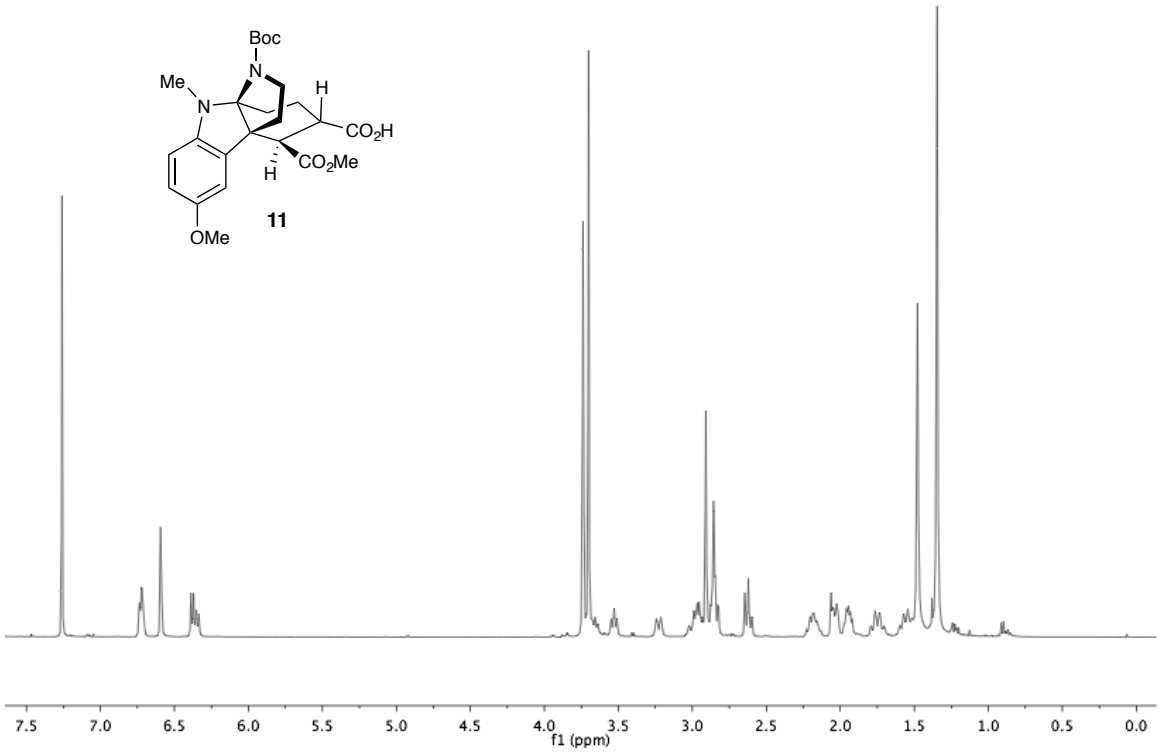

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

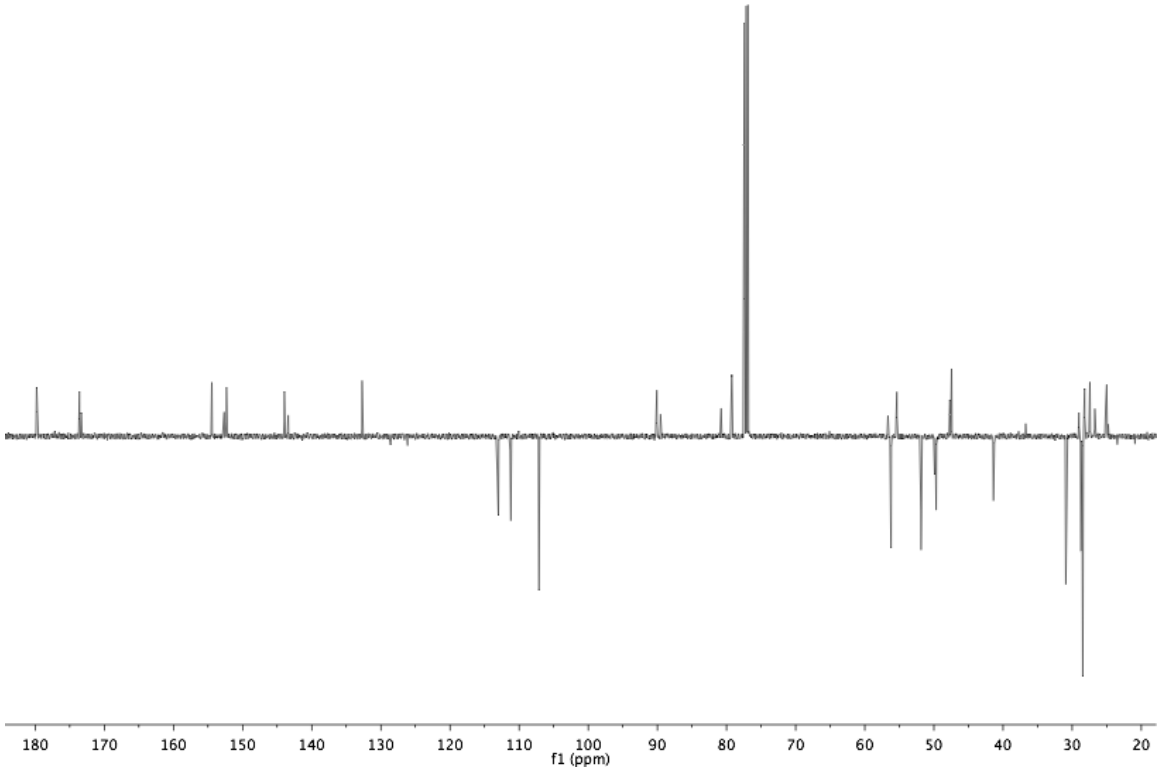


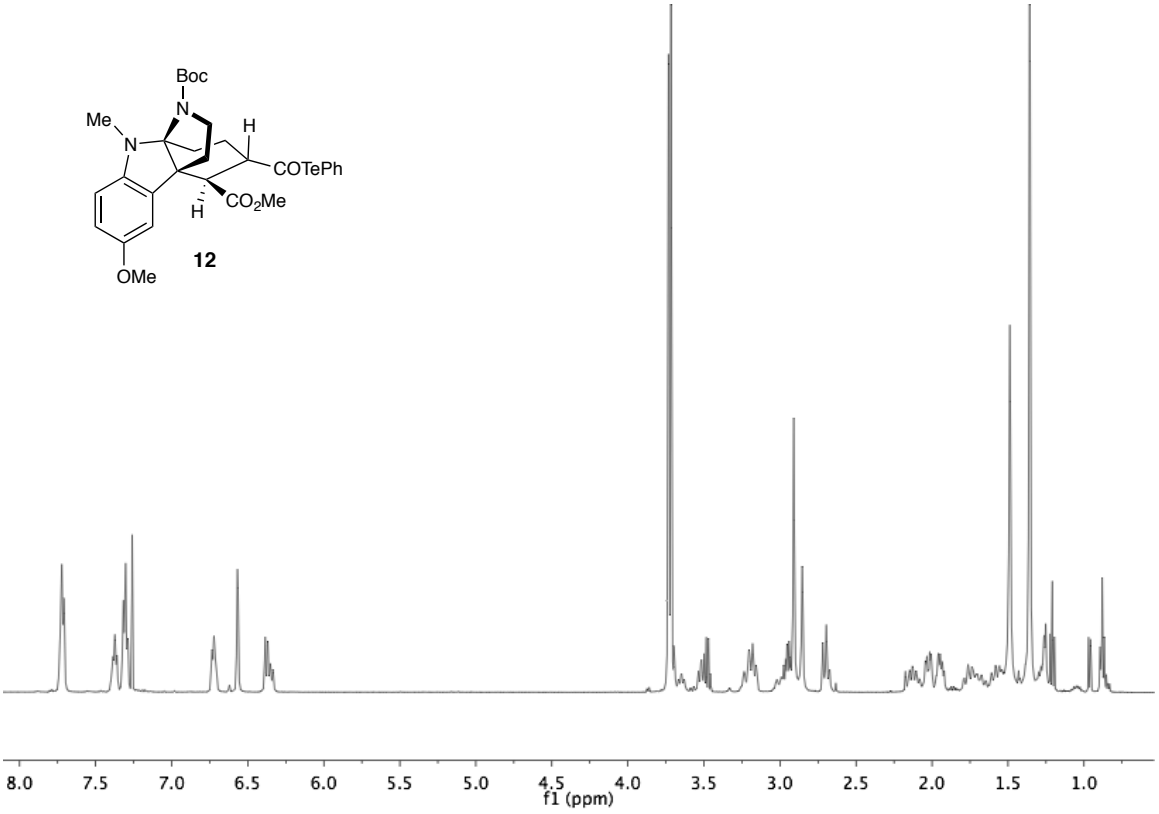
#	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	3.02	3.15	3.35	0.00	49.76	83.3	9.0	49.760
2	UNKNOWN	5.26	5.54	5.85	0.00	50.24	41.4	9.1	50.240
Total						100.00	124.8	18.1	100.000

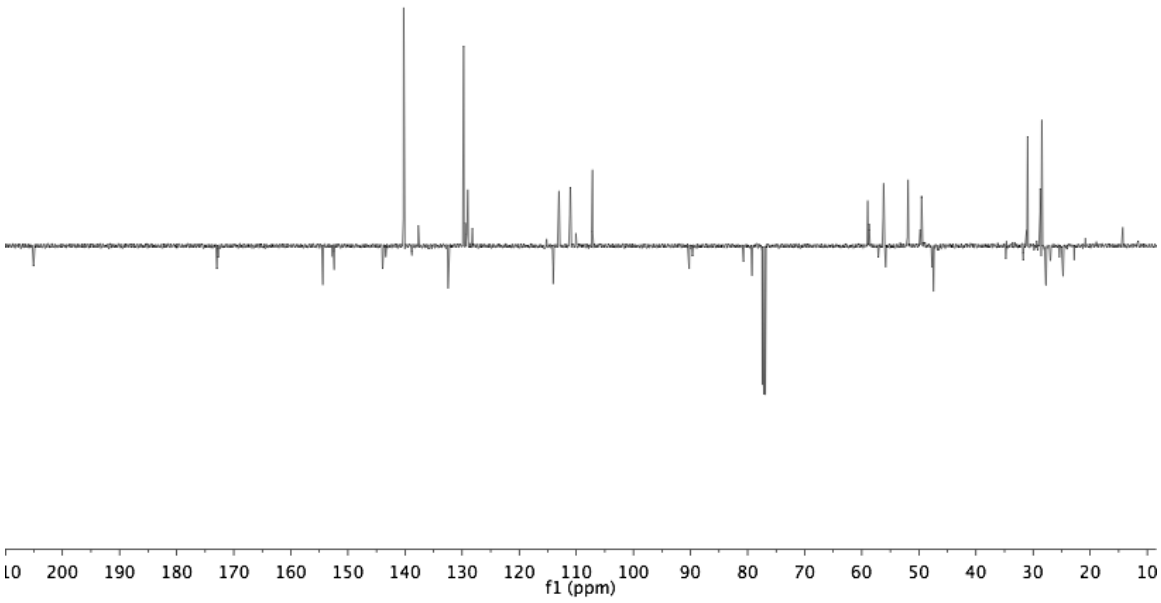


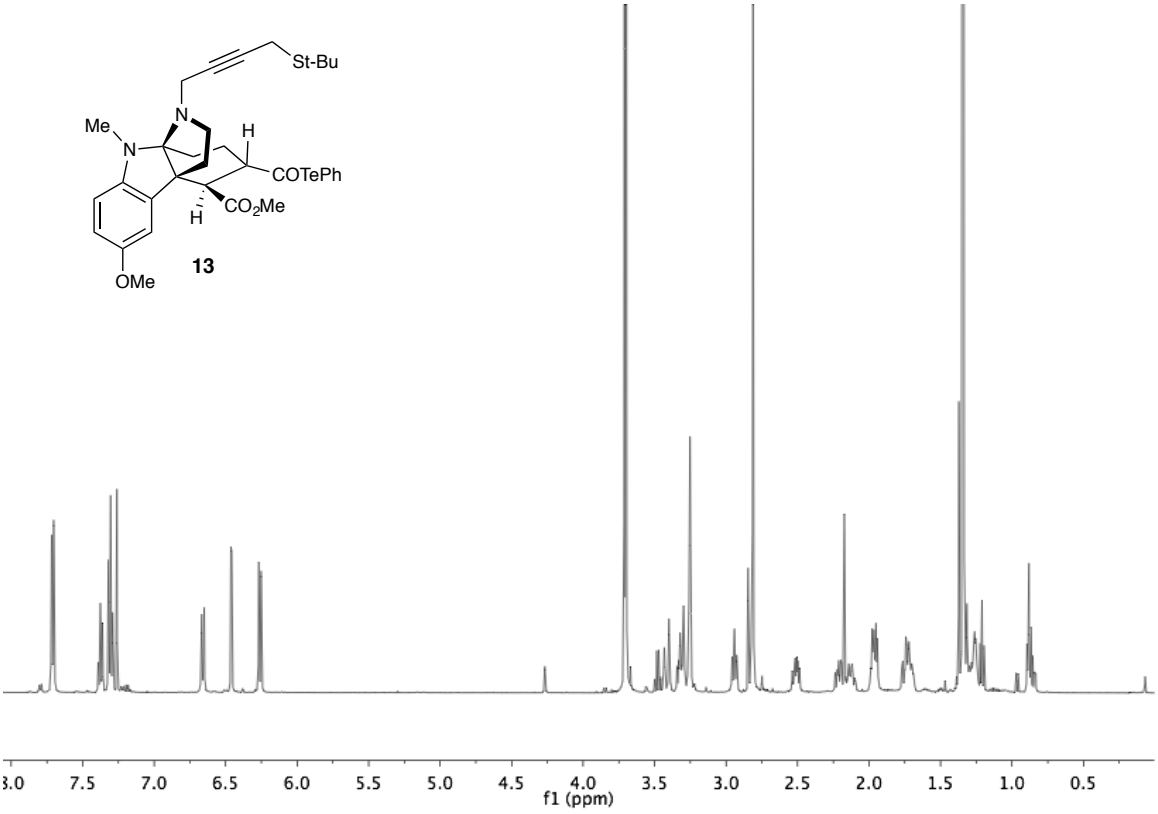
#	Name	Start [Min]	Time [Min]	End [Min]	RT Offset [Min]	Quantity [% Area]	Height [µV]	Area [µV.Min]	Area [%]
1	UNKNOWN	3.02	3.15	3.35	0.00	49.76	83.3	9.0	49.760
2	UNKNOWN	5.26	5.54	5.85	0.00	50.24	41.4	9.1	50.240
Total						100.00	124.8	18.1	100.000

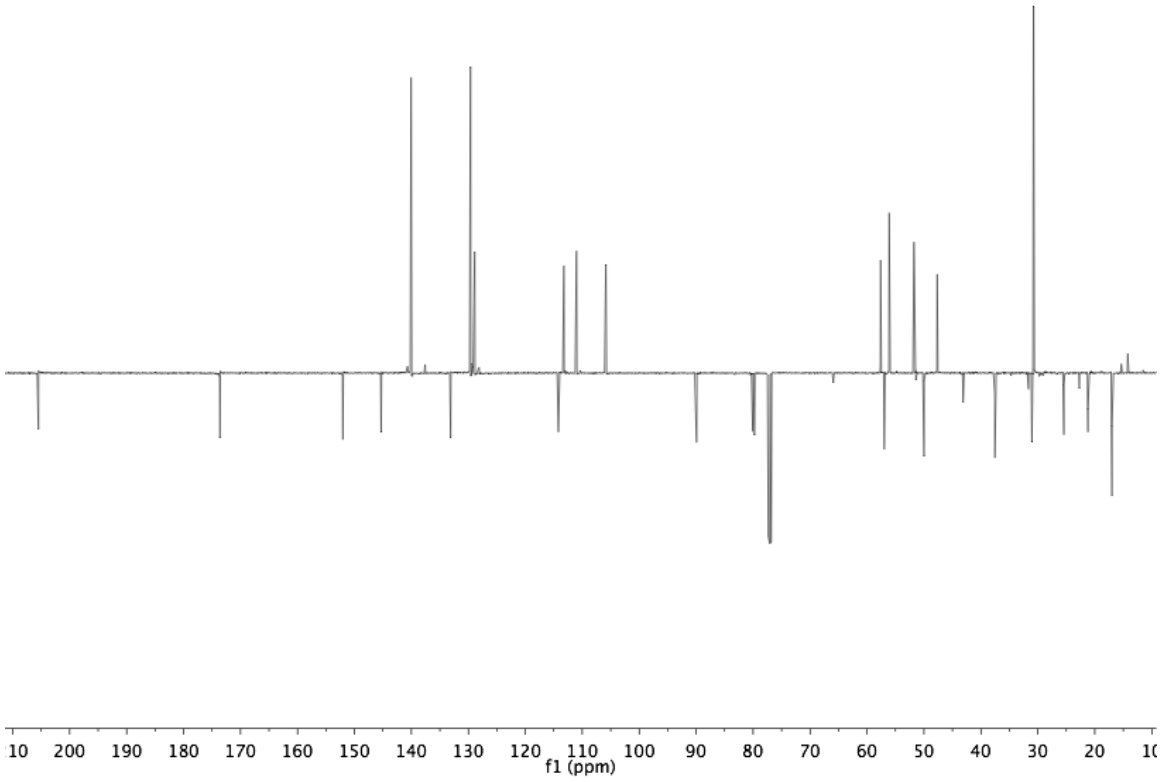

Boc
N
Me
N
H
CO2H
H
CO2Me
OMe
11
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

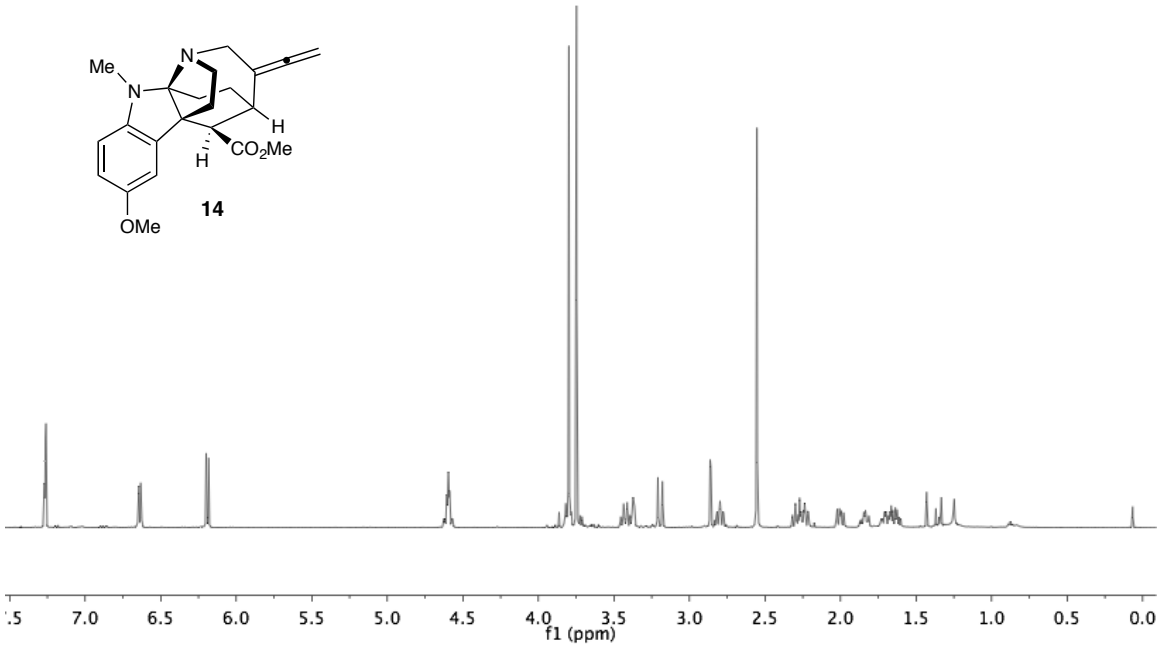

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

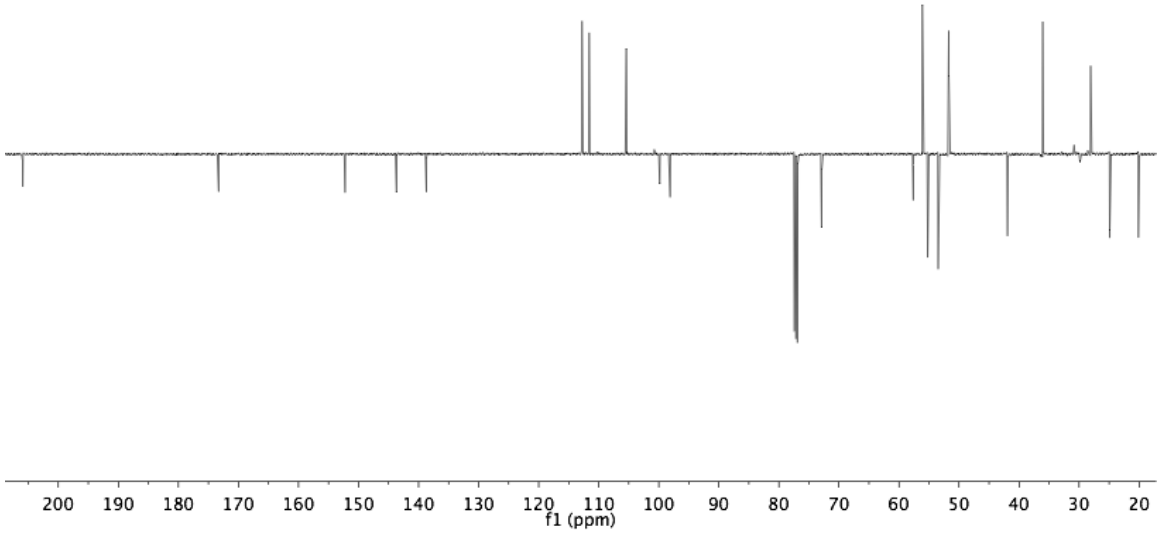

Boc
N
Me
N
H
COTePh
H
CO2Me
OMe
12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

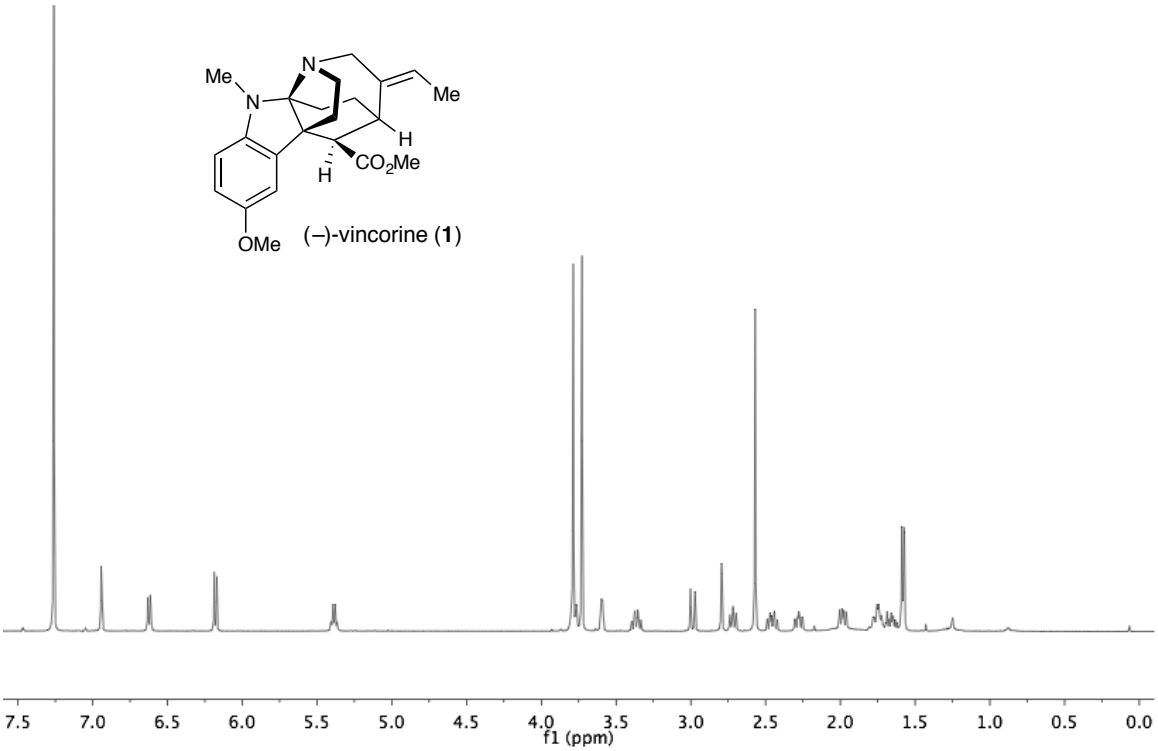

10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

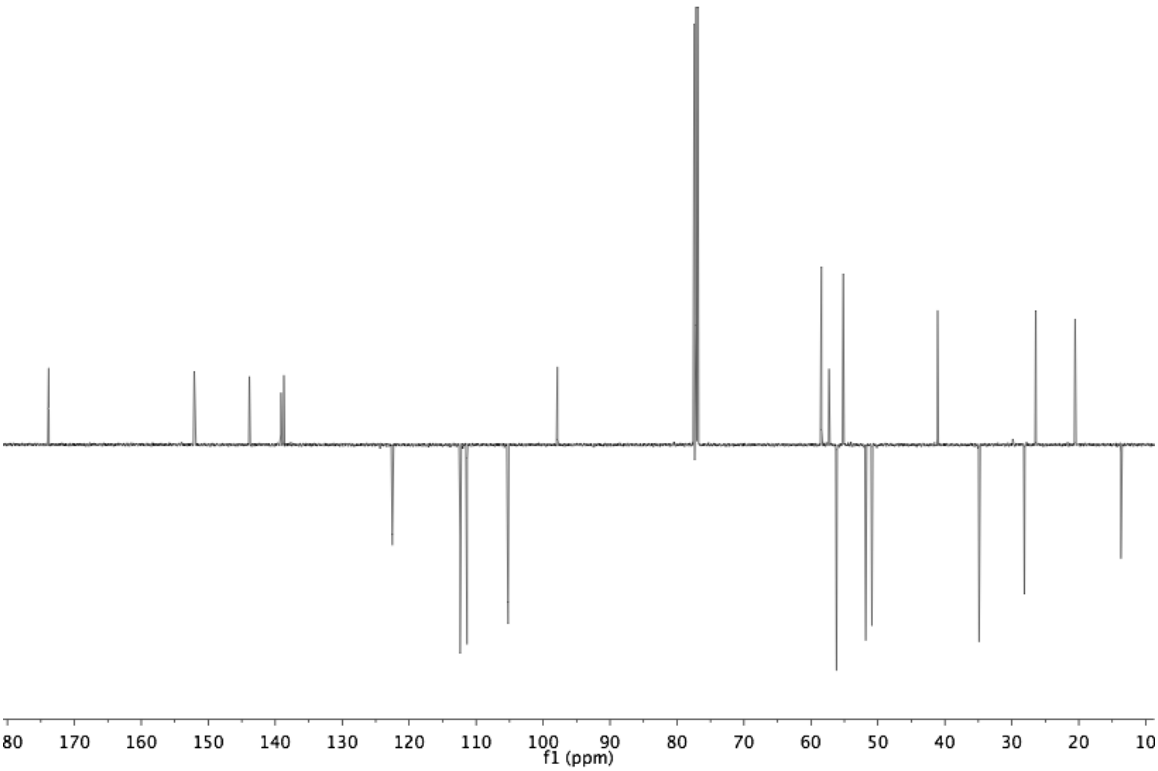

St-Bu
N
Me
N
H
COTePh
CO2Me
H
OMe
13
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

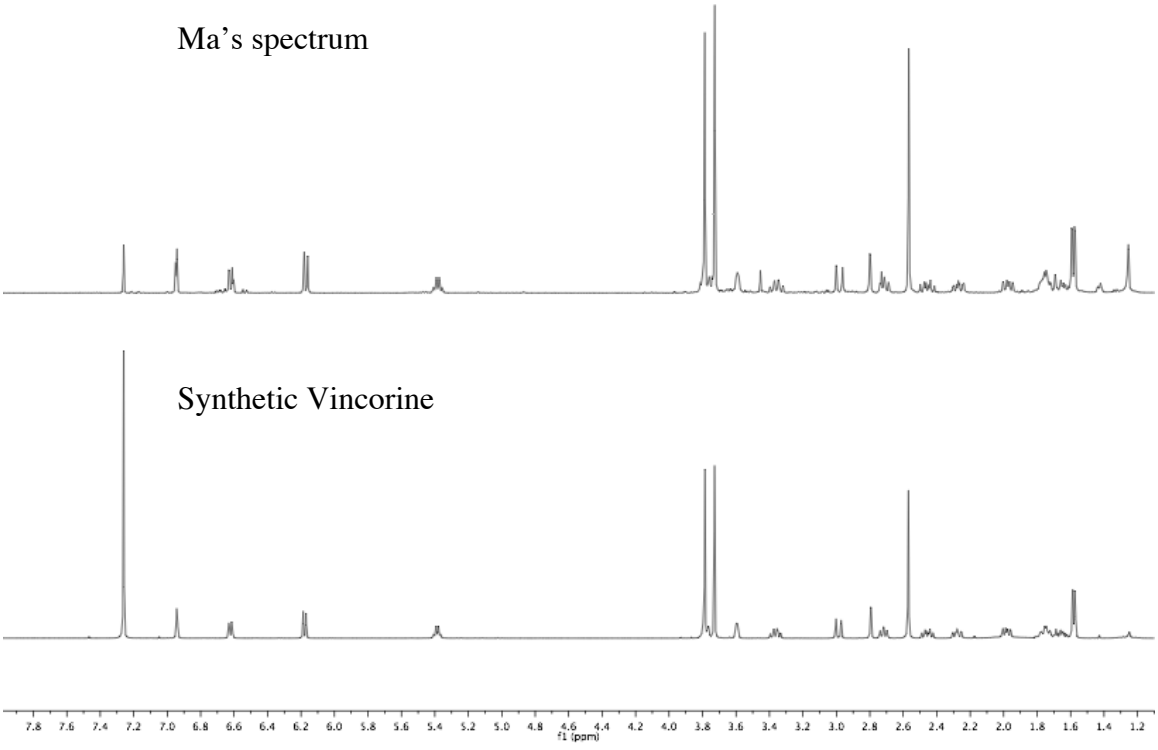

10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 1
f1 (ppm)


Me
N
N
H
H
CO2Me
OMe
14
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

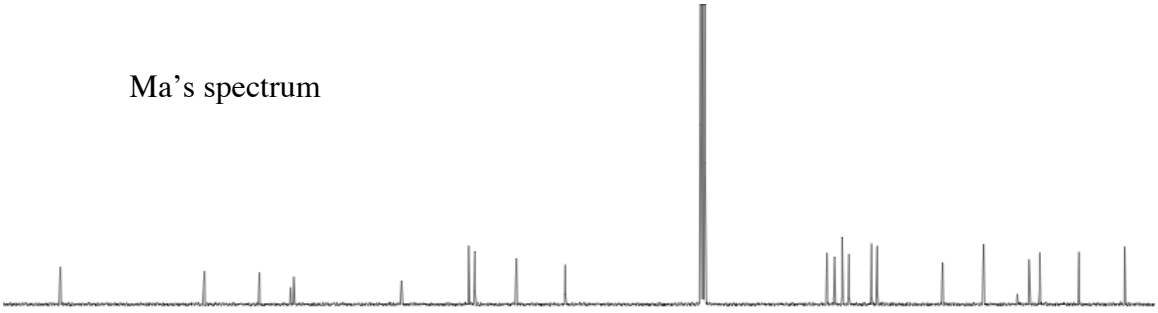

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


Me
N
N
Me
H
H
CO_2Me
OMe
(–)-vincorine (**1**)
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

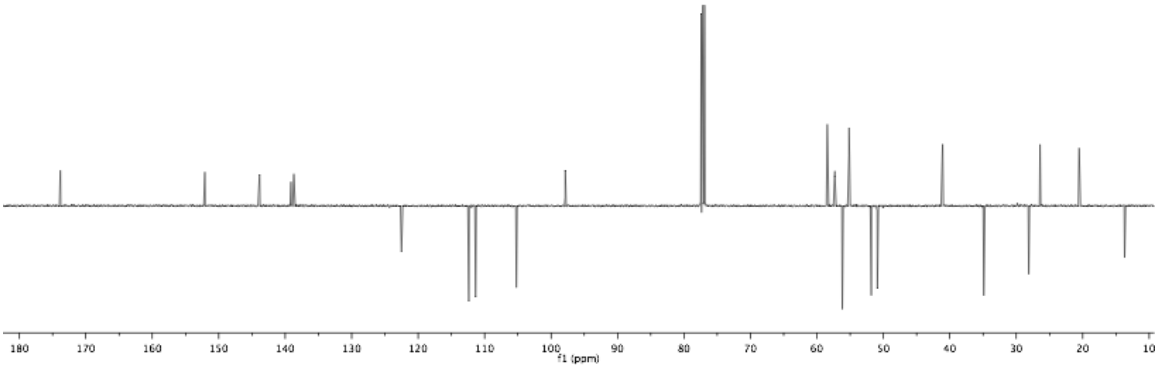

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

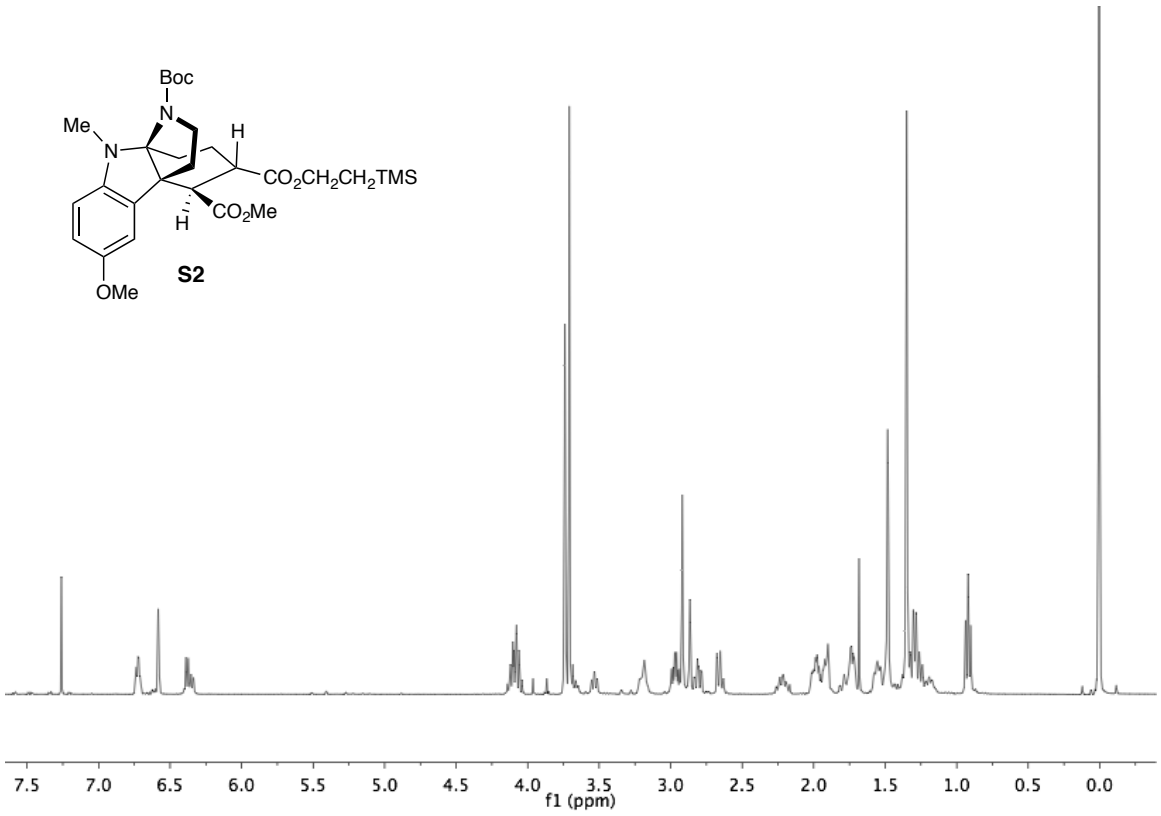

Ma's spectrum
Synthetic Vincorine
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)

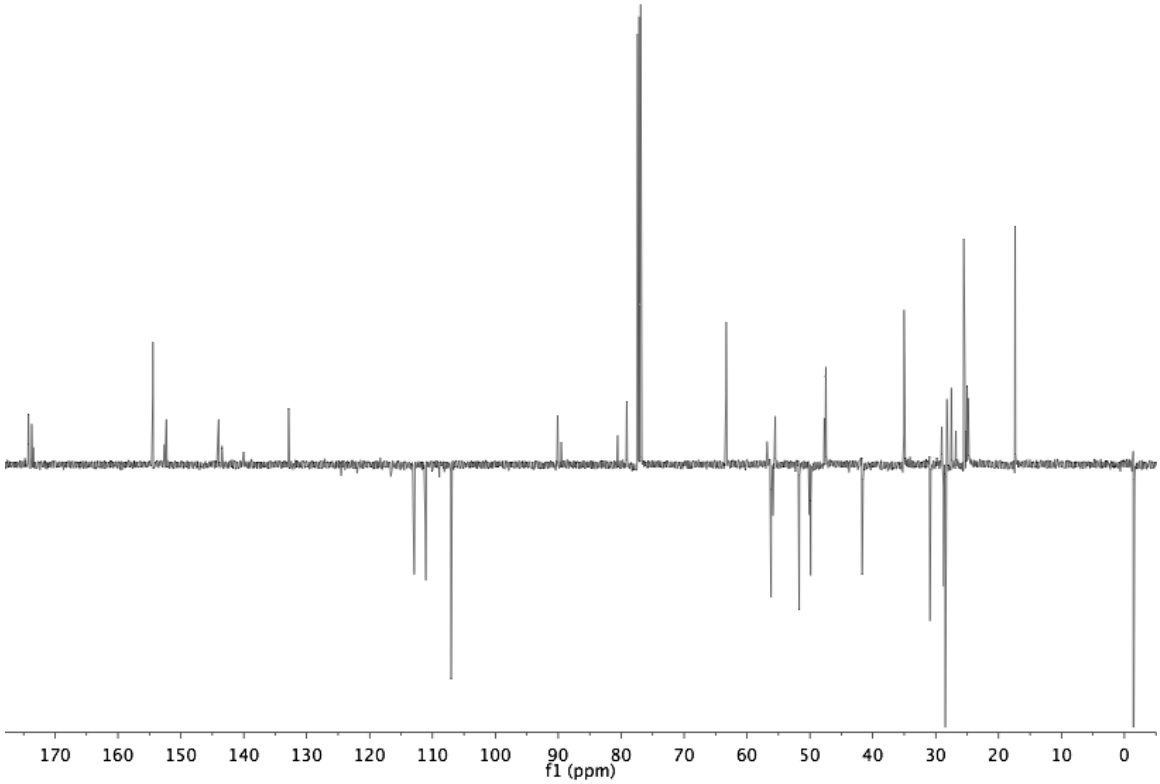
Ma's spectrum

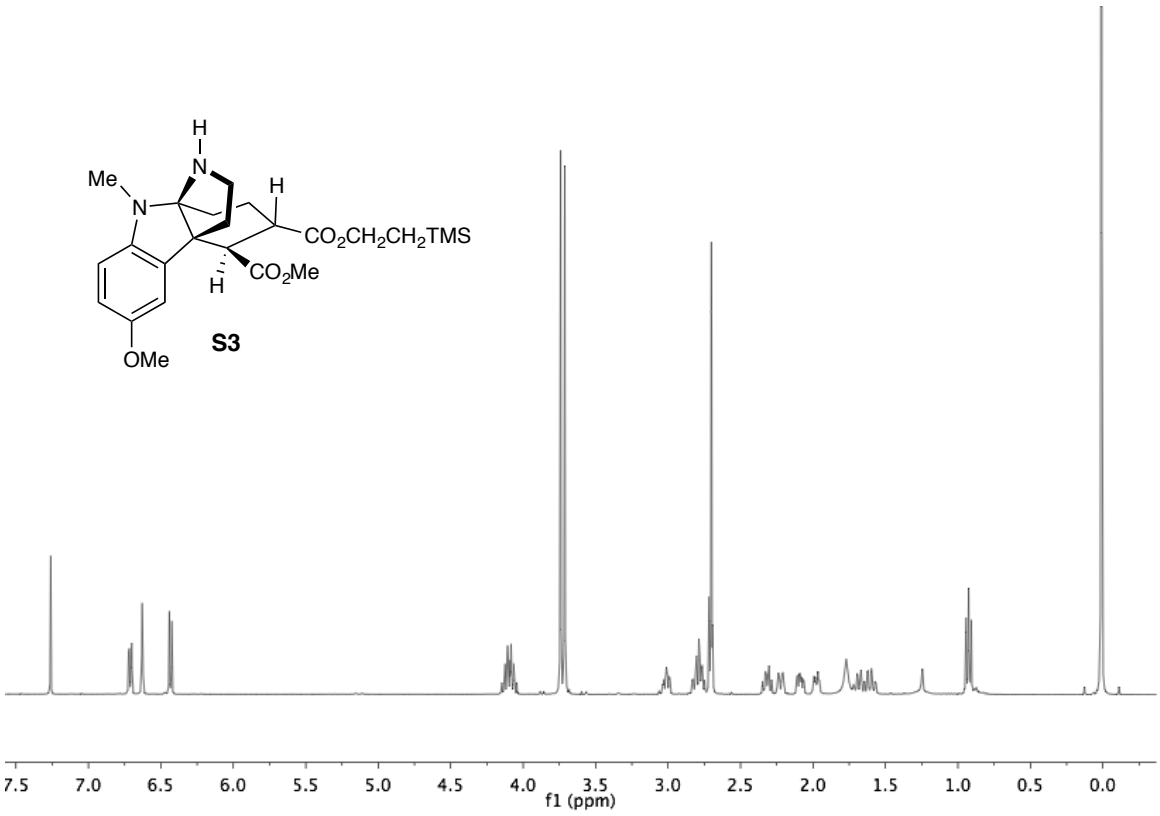


Synthetic vincorine

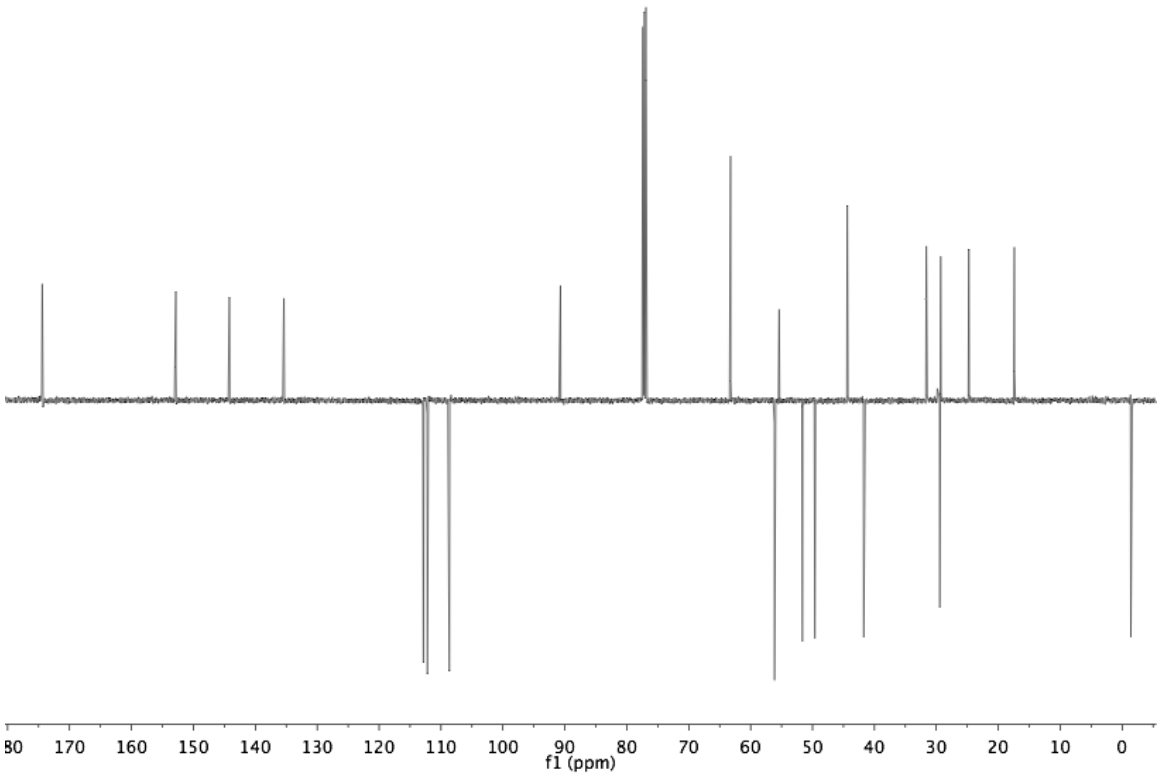


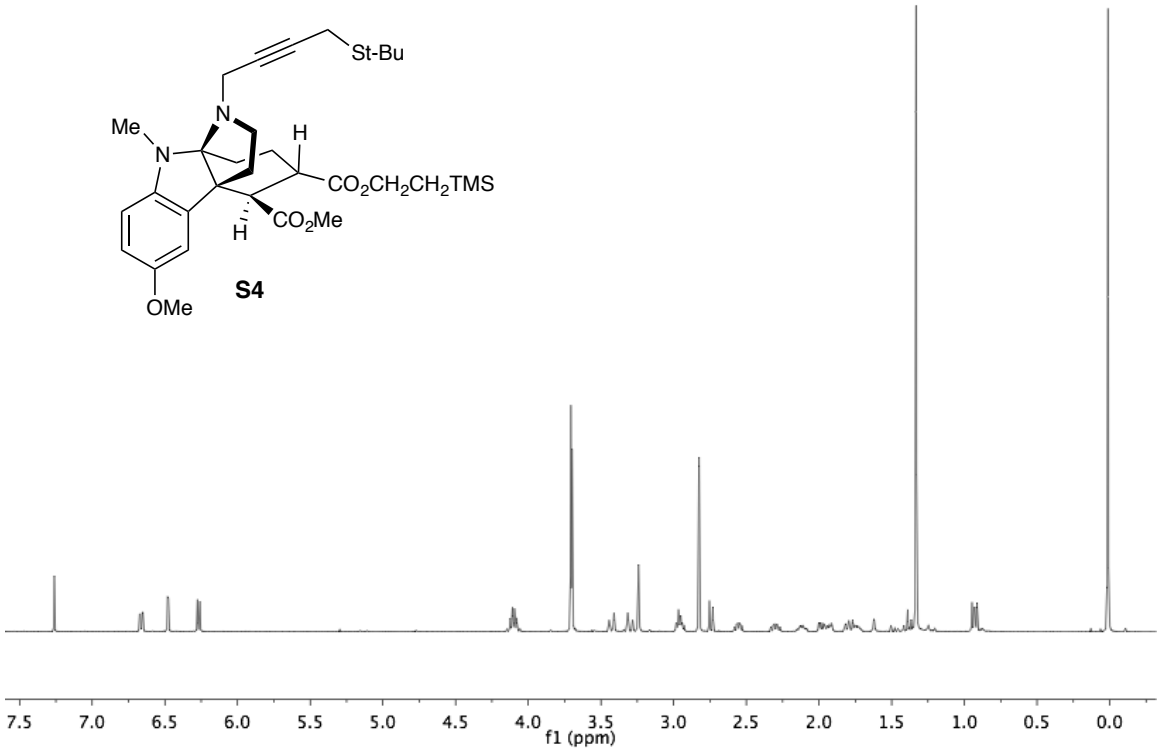

Boc
N
Me
N
H
CO2CH2CH2TMS
CO2Me
H
OMe
S2
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

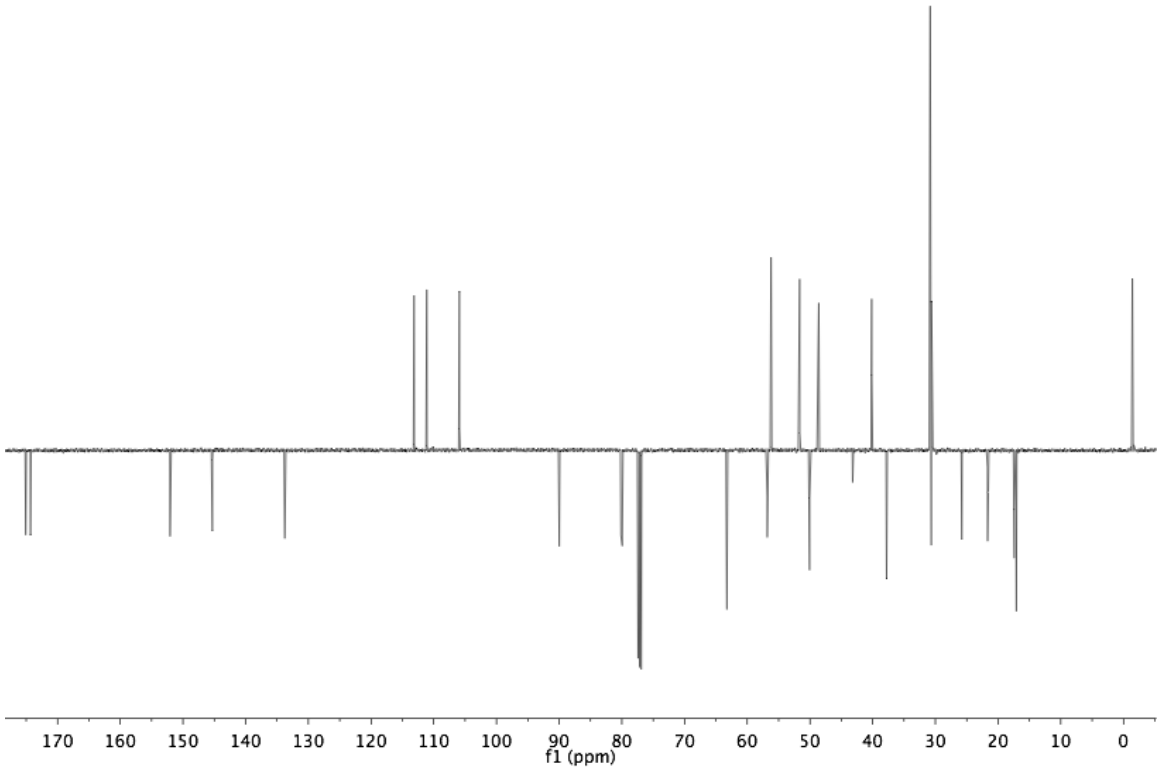

H
N
Me
N
H
CO2CH2CH2TMS
CO2Me
H
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

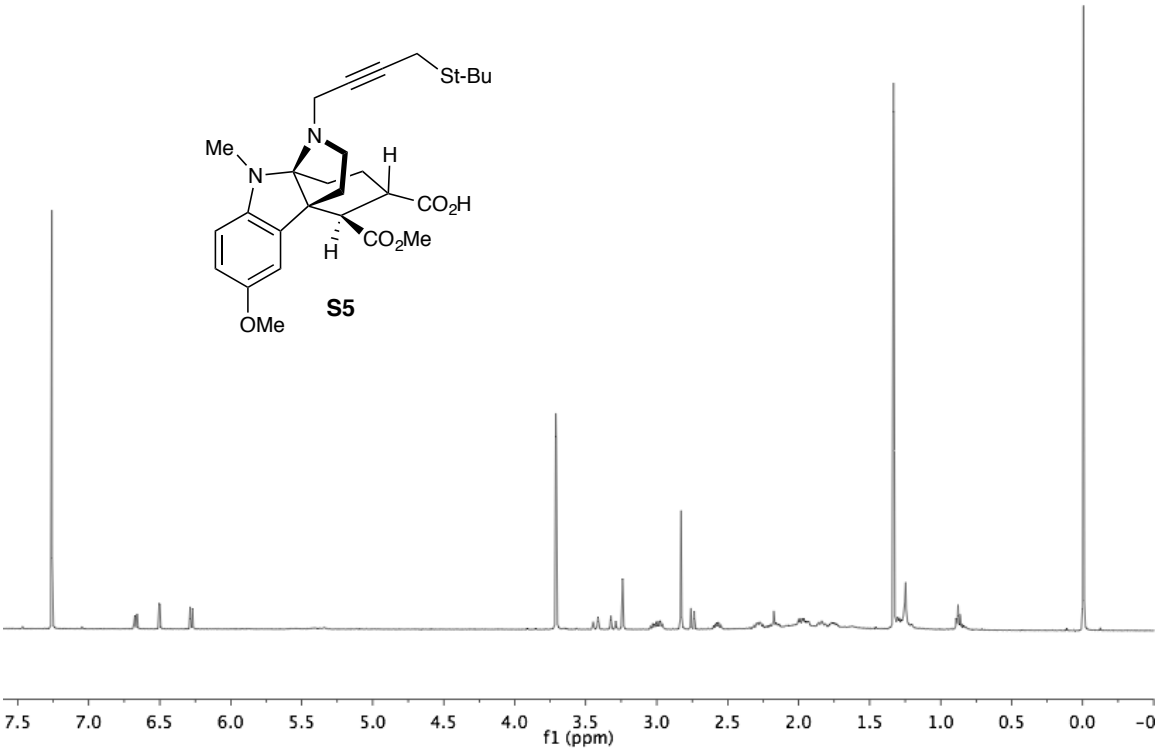
S3

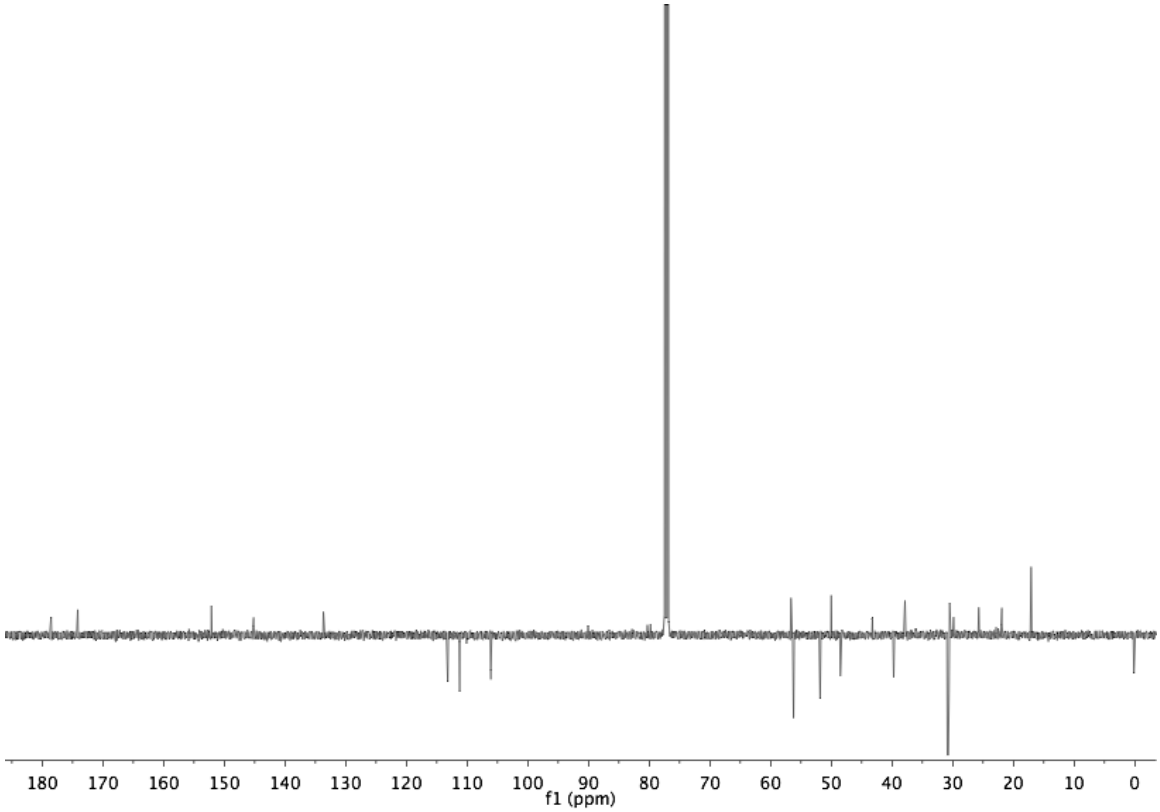

80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

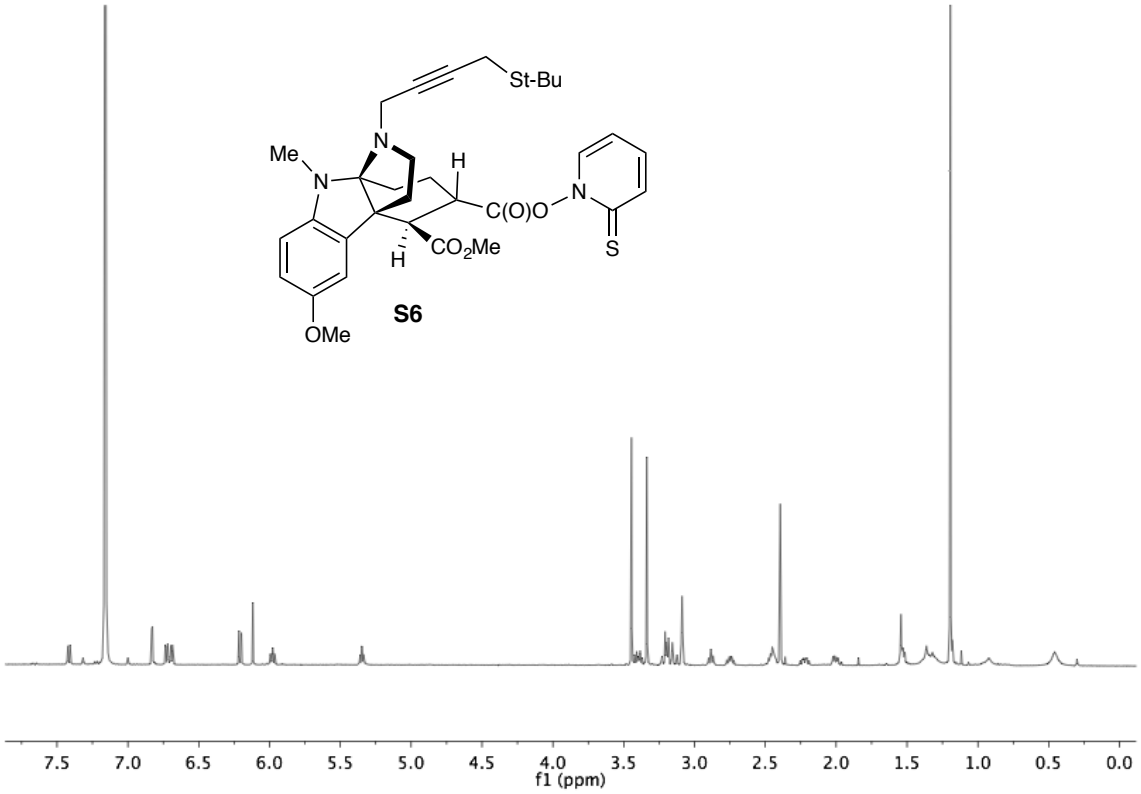

St-Bu
N
Me
N
H
CO2CH2CH2TMS
CO2Me
H
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

S4

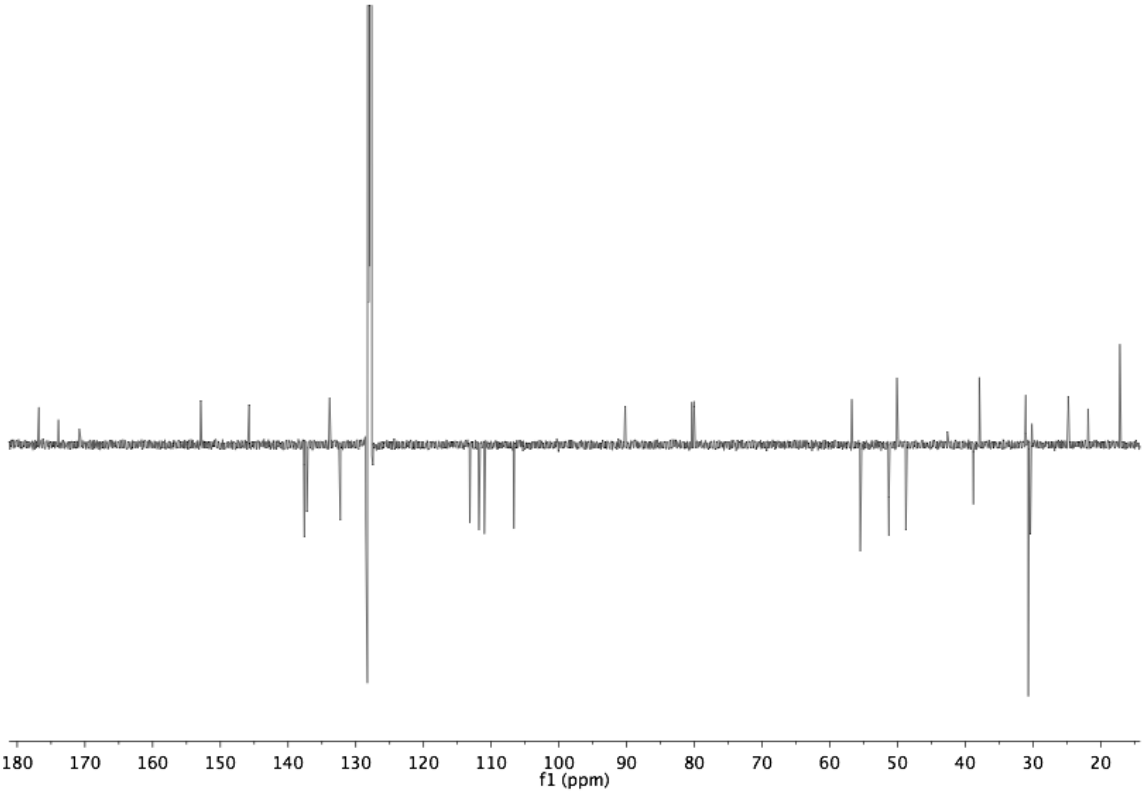

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

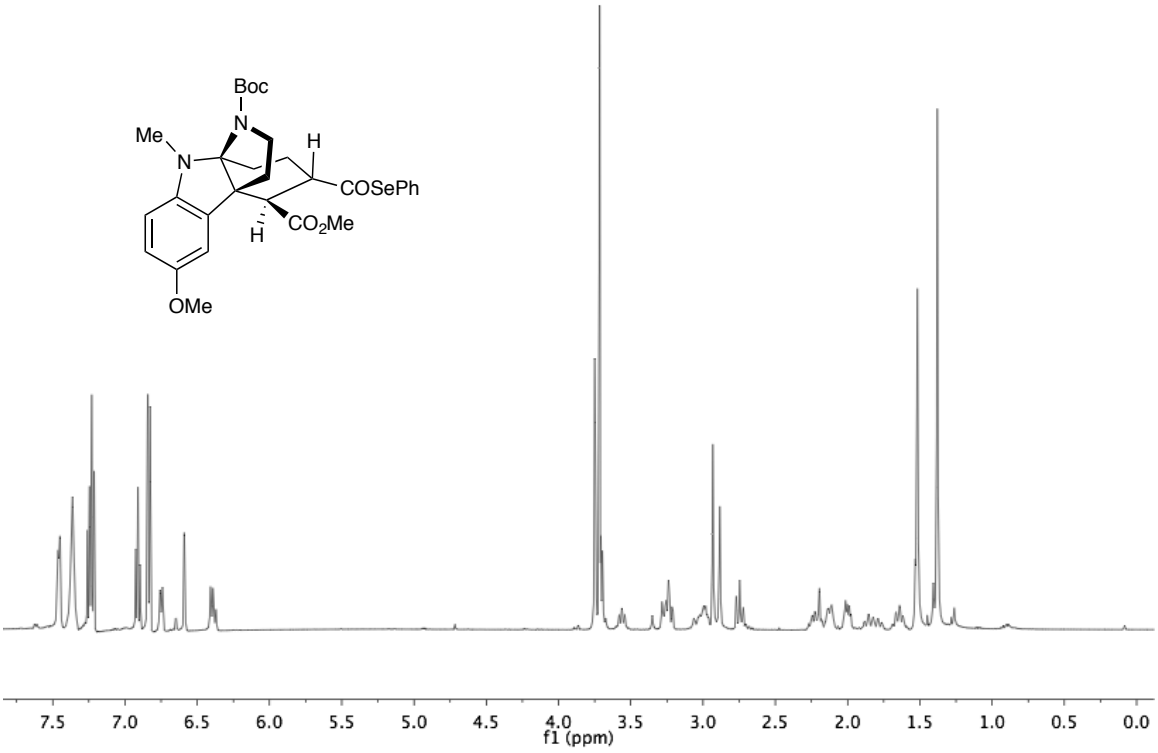

St-Bu
N
Me
N
H
CO2H
CO2Me
H
OMe
S5
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

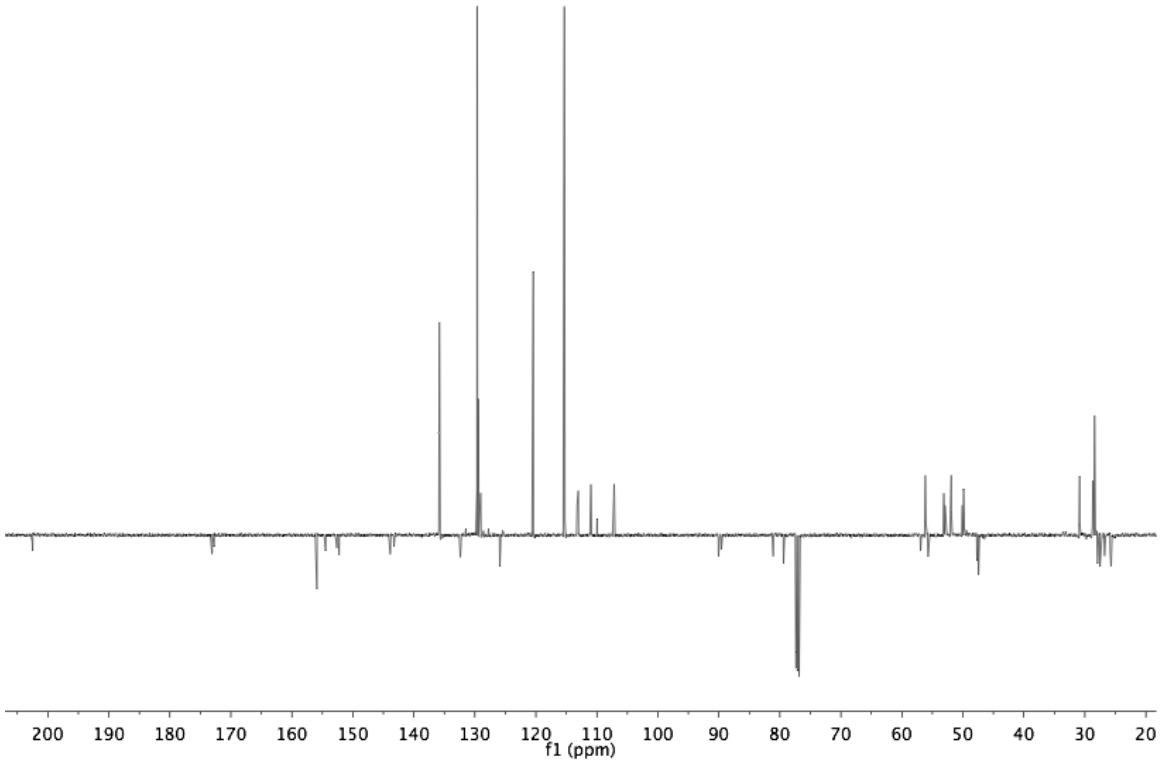

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

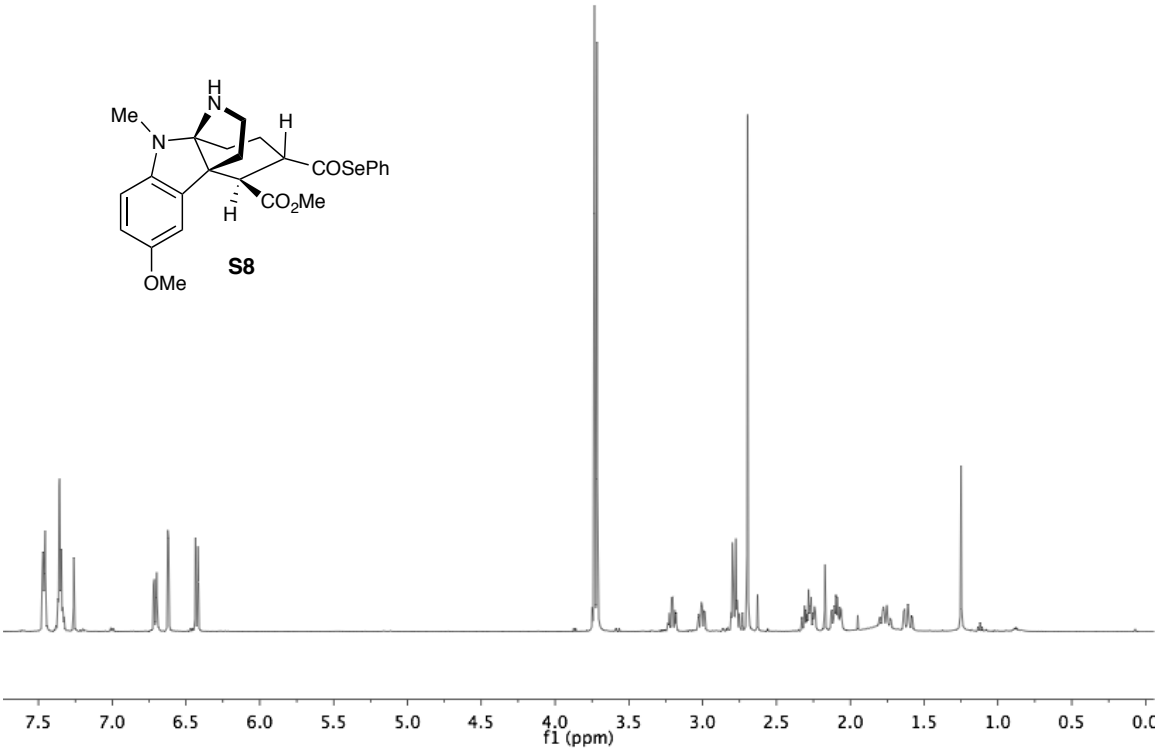

St-Bu
N
Me
N
H
C(O)O
N
S
CO2Me
H
OMe
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

S6

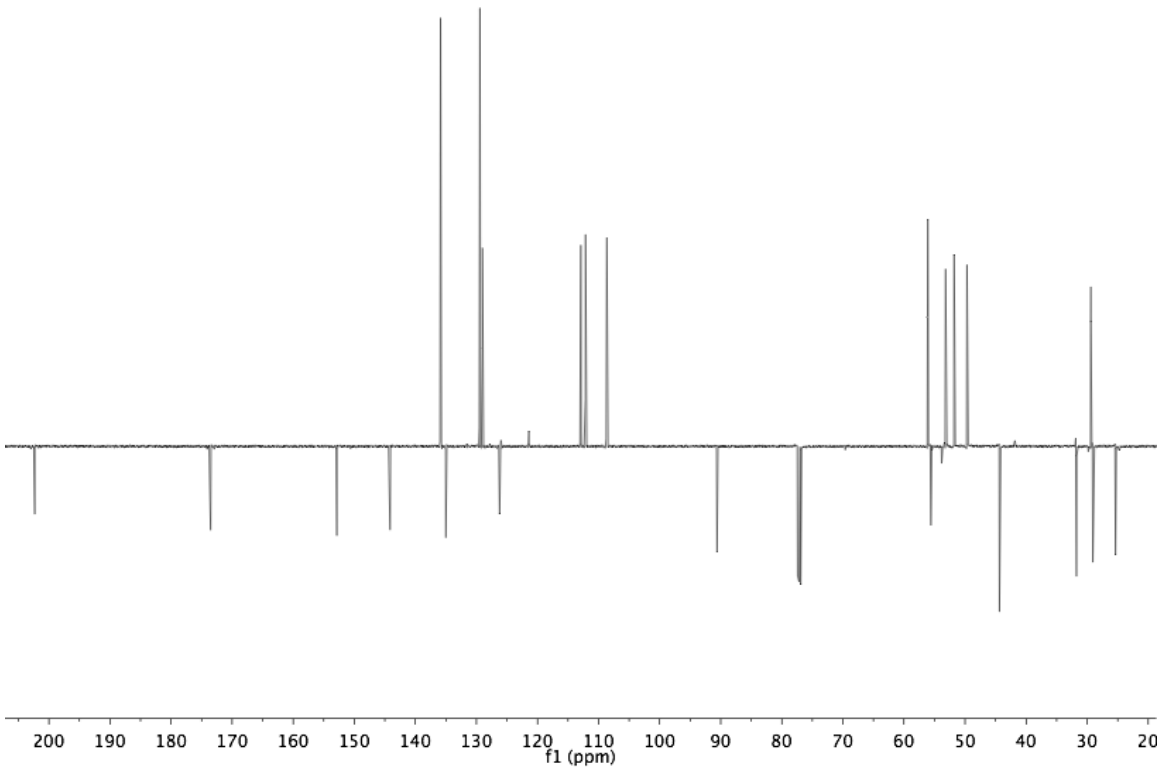

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

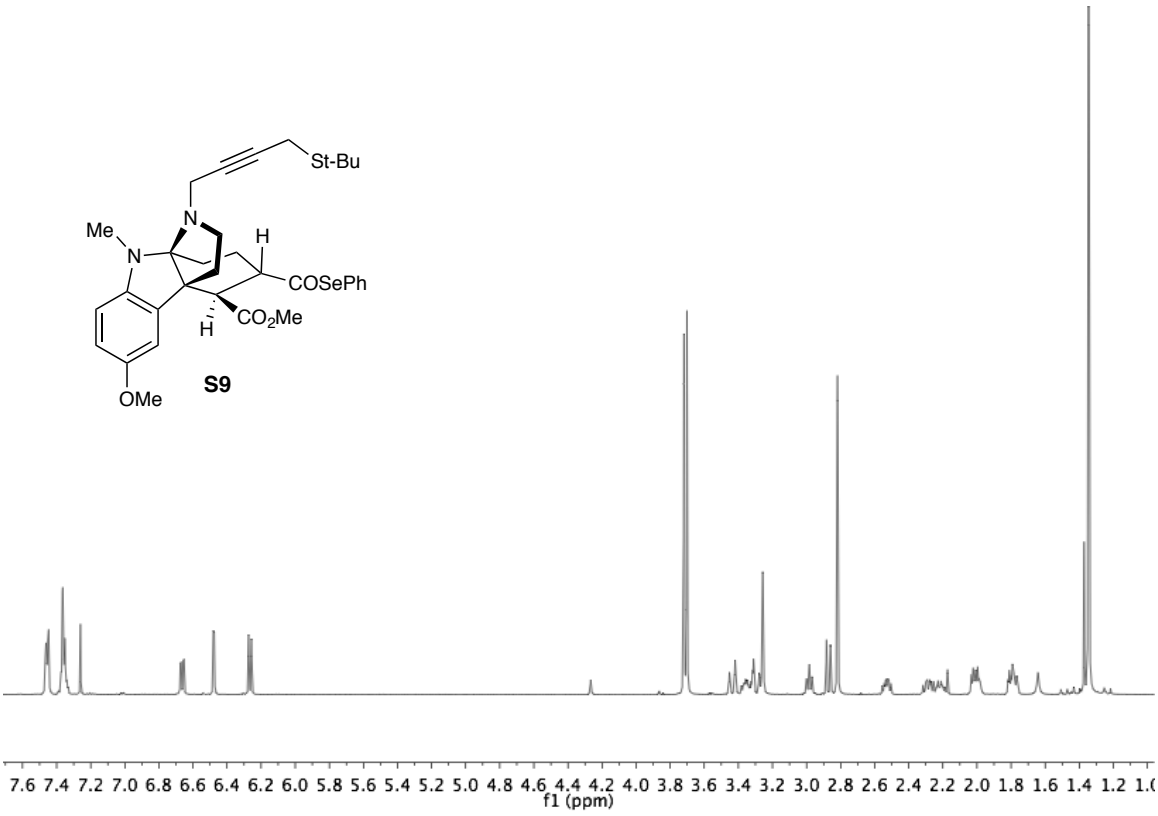

Boc
N
Me
N
H
COSePh
H
CO2Me
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

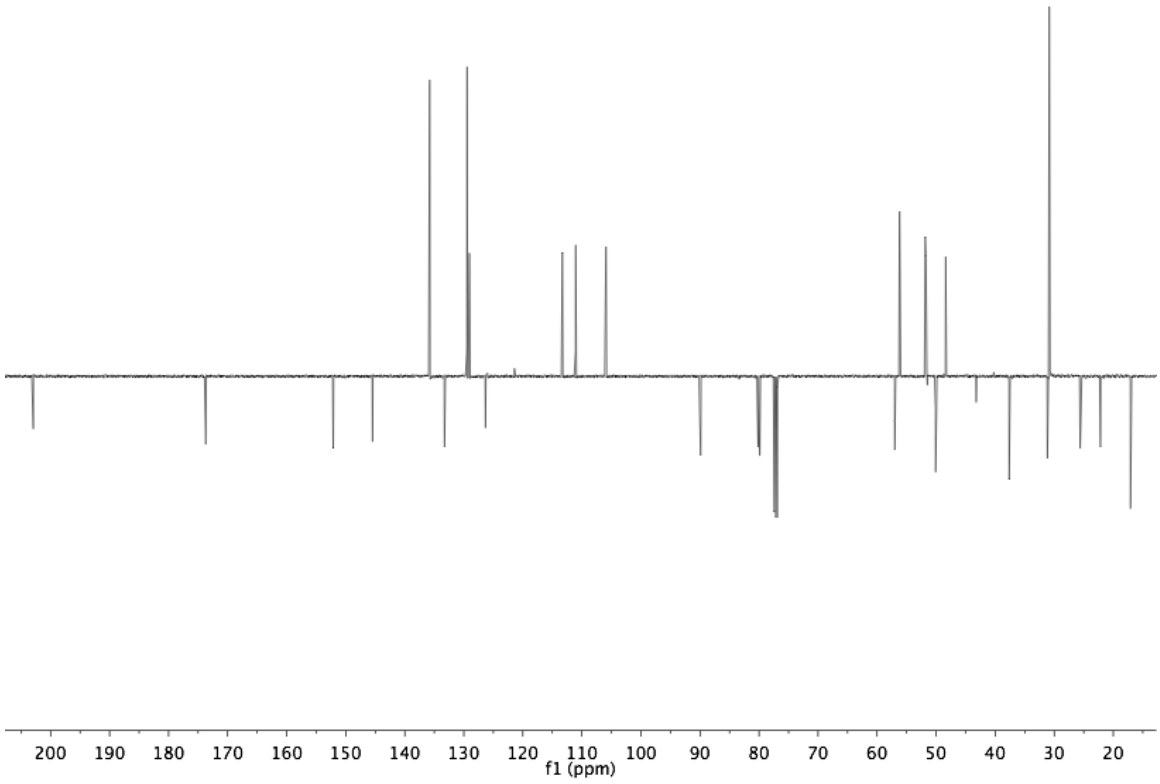

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


H
N
Me
N
H
COSePh
CO2Me
H
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

S8


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


St-Bu
N
Me
N
H
COSePh
H
CO2Me
OMe
S9
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)



[i] Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals* (Pergamon Press, Oxford, 1988) ed. 3.
[ii] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[iii] Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978,** *43*, 2923.
[iv] Satoh, T.; Hanaki, N.; Kuramochi, Y.; Inoue, Y.; Hosoya, K.; Sakai, K. *Tetrahedron* **2002**, *58*(13), 2533.
[v] Prepared according to Jones, S. B.; Simmons, B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131* (38), 13606.
[vi] Mokrý, J.; Dúbravková, L.; Šefčovič, P. *Experientia* **1962**, *18*, 564.