Supporting Information

Concise Total Synthesis of (±)-Pseudotabersonine via Double Ring-Closing Metathesis Strategy

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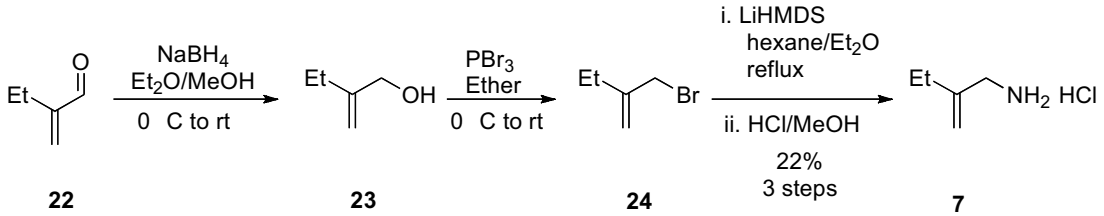
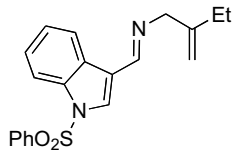
Experimental Section

General methods. Unless otherwise noted, all other reagents and solvents were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and ether (Et_2O) were dried by passage through two columns of activated neutral alumina. Methanol (MeOH) and *N*, *N*-dimethylformamide (DMF) were dried by passage through two columns of activated molecular sieves. Dichloromethane (CH_2Cl_2), triethylamine (Et_3N), and N,N-diisopropylamine(iPr_2NH) were distilled from calcium hydride. N,N-diisopropylethylamine(iPr_2NEt) was distilled from KOH. Dimethoxyethane (DME) was dried by 4 Å molecular sieves. $AlCl_3$ and KO^{t}Bu were sublimed under reduced pressure. Removal of solvent or concentration under reduced pressure was performed using a rotary evaporator. Unless otherwise indicated, all ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$, C_6D_6 or DMSO-d_6. Chemical shifts were reported in parts per million (ppm, δ) downfield from TMS (δ = 0.00 ppm) and referenced relative to $CDCl_3$ (7.26 ppm for ^1H and 77.0 ppm for ^{13}C), C_6D_6 (7.15 ppm for ^1H and 128.0 ppm for ^{13}C) and DMSO-d_6 (2.50 ppm for ^1H and 39.4 ppm for ^{13}C). Coupling constants were reported in hertz (Hz). Splitting patterns were designated as: s = singlet; d = doublet; dd = doublet of doublet; ddd = doublet of doublet of doublets; t = triplet; q = quartet; p = pentuplet; hep = heptet; m = multiplet; comp = overlapping multiplets of non-magnetically equivalent protons; br = broad; app = apparent. Melting points were determined on a melting point apparatus and are uncorrected. Infrared (IR) spectra were obtained as thin films on sodium chloride plates and reported in wave numbers (cm^{-1}). Column chromatography was performed on Merck 250-400 mesh silica gel with the indicated solvents. Analytical thin-layer chromatography (TLC) was performed on Merck-60 TLC plates with the indicated solvents. Visualization was accomplished by UV light or stained with $KMnO_4$ solution.



2-Methylenebutan-1-amine hydrochloride (7). $NaBH_4$ (7.1 g, 0.19 mol) was added portionwise to a solution of 2-ethylacrolein (**22**) (18.5 mL, 15.89 g, 0.19 mol) in Et_2O (125 mL) and

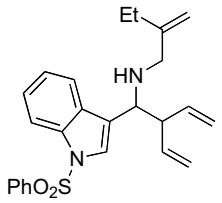
MeOH (35 mL) at 0 ºC. The reaction was stirred for 1 h at 0 ºC and then for 1 h at room temperature. The reaction was partitioned between H_2O (200 mL) and Et_2O (100 mL). The aqueous layer was backwashed with Et_2O (3 x 100 mL), and the combined organics were dried ($MgSO_4$), filtered, and concentrated by simple distillation to give 15.6 g of **23** as a ~78% solution in Et_2O (by NMR). An additional volume of Et_2O (200 mL) was added, and the solution was cooled to 0 ºC. PBr_3 (13.5 mL, 38.88 g, 0.14 mol) was added dropwise, and the reaction was warmed to room temperature and stirred for 15 h. The reaction was then cooled to 0 ºC, and ice water (100 mL) was slowly added. Additional H_2O (100 mL) and Et_2O (100 mL) were then added, and the phases were separated. The organic phase was washed sequentially with H_2O (50 mL), saturated aqueous $NaHCO_3$ (50 mL) and brine (2 x 50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated by simple distillation to give 23.1 g of **24** as a ~70% solution in Et_2O (by NMR). This solution of crude **24** was added to LiHMDS (1.44 M in hexane, 90 mL) at -40 ºC. The reaction was warmed to room temperature and then heated under reflux for 24 h. The reaction was cooled to room temperature and filtered through a pad of celite that was washed with pentane (3 x 20 mL). The filtrates and washings were concentrated under reduced pressure, and the residue was diluted with pentane (100 mL). The suspension was filtered through a pad of celite that was washed with pentane (3 x 20 mL). The filtrates and washings were concentrated under reduced pressure, and the crude bis(silyl)amine was added dropwise to a solution of HCl in MeOH/Et_2O [prepared from AcCl (35 mL) and MeOH (100 mL) in Et_2O (100 mL) at 0 ºC]. The reaction was warmed to room temperature and stirred for 15 h, whereupon the reaction was concentrated under reduced pressure. The residue was crystallized from EtOH (~15 mL) to give 5.27 g (22%) of **7** as a white waxy solid, mp = 158-159 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 3 H), 5.22 (s, 1 H), 5.11 (s, 1 H), 3.58 (s, 2 H), 2.17 (q, *J* = 7.4 Hz, 2 H), 1.08 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 113.6, 43.8, 27.0, 11.7; IR (film) 3409, 2971, 1603, 1515, 1458, 1378, 909, 736 cm^{-1}; Mass spectrum (CI) *m/z* 86.0973 [$C_5H_{12}N$ $(M+H)^+$ requires 86.0970].



8

Imine 8. A mixture of indole-3-carboxaldehyde (**6**) (4.28 g, 15.0 mmol), 2-ethylallylamine hydrochloride (**7**) (3.65 g, 30.0 mmol), Et_3N (4.32 mL, 3.13 g, 31.0 mmol) and activated 4 Å molecular

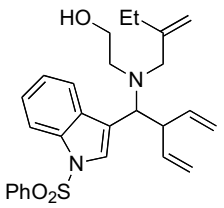
sieves (~2 g) in CH_2Cl_2 (50 mL) was stirred for 20 h at room temperature under argon, and then Et_2O (250 mL) was added. The mixture was stirred for 10 min at room temperature and filtered through a pad of celite that was washed with Et_2O (3 x 50 mL). The combined filtrates and washings were concentrated under reduced pressure to give ~5.4 g crude imine **8** as an orangish brown oil that was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1 H), 8.37 (d, *J* = 7.6 Hz, 1 H), 7.98 (d, *J* = 8.2 Hz, 1 H), 7.92 (d, *J* = 8.0 Hz, 2 H), 7.85 (s, 1 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.45 (t, *J* = 8.0 Hz, 2 H), 7.38 (td, *J* = 8.2, 1.0 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 4.96 (s, 1 H), 4.87 (s, 1 H), 4.19 (s, 2 H), 2.19 (q, *J* = 7.4 Hz, 2 H), 1.21 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 149.5, 137.8, 135.5, 134.1, 129.5, 129.4, 128.0, 126.8, 125.6, 124.2, 123.2, 120.8, 113.2, 109.0, 66.8, 27.5, 12.1; IR (film) 1642, 1446, 1378, 1177, 1126, 1100, 979 cm^{-1}; Mass spectrum (CI) *m/z* 353.1316 [$C_{20}H_{21}N_2O_2S$ $(M+H)^+$ requires 353.1310].



10

Amine 10. *n*-BuLi (7.97 mL, 2.5 M in hexane, 20.0 mmol) was added to a solution of 1,4-pentadiene (2.1 mL, 1.36 g, 20.0 mmol) in THF (10 mL) at -78 ºC under N_2. The reaction was stirred at -78 ºC for 15 min, whereupon the bath was replaced with a 0 ºC bath, and the reaction was stirred for 30 min at 0 ºC. A solution of $AlCl_3$ (2.86 g, 21.4 mmol) in Et_2O (10 mL) was added, and the reaction was stirred for 1 h at 0 ºC. The pentadienyl Al reagent **9** thus prepared was added to a solution of imine **8** (~5.4 g, 15.0 mmol) in CH_2Cl_2 (50 mL) under argon, and the reaction was stirred for 24 h at room temperature, whereupon the reaction was open to air, and 1 N NaOH (200 mL) was added. The mixture was stirred vigorously for 5 min and then filtered through a pad of celite, and the pad was washed with CH_2Cl_2 (3 x 50 mL). The filtrates were combined, and the aqueous layer was separated and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were concentrated under reduced pressure to give ~6.5 g crude **10** as an orangish brown oil that was used without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 1 H), 7.82-7.80 (m, 2 H), 7.70 (d, *J* = 7.8 Hz, 1 H), 7.49 (t, *J* = 7.5

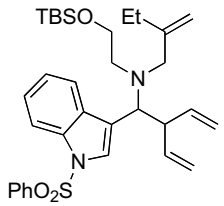
Hz, 1 H), 7.42 (s, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.29 (t, *J* = 7.8 Hz, 1 H), 7.20 (t, *J* = 7.8 Hz, 1 H), 5.75 (ddd, *J* = 17.1, 10.2, 8.7 Hz, 1 H), 5.65-5.59 (m, 1 H), 5.14 (dd, *J* = 10.2, 1.7 Hz, 1 H), 5.09 (d, *J* = 17.1 Hz, 1 H), 4.83 (d, *J* = 1.1 Hz, 1 H), 4.82-4.80 (m, 1 H), 4.77 (s, 1 H), 4.74 (s, 1 H), 3.82 (d, *J* = 7.7 Hz, 1 H), 3.14 (app q, *J* = 7.7 Hz, 1 H), 3.02 (d, *J* = 14.3 Hz, 1 H), 2.91 (d, *J* = 14.3 Hz, 1 H), 1.97 (dq, *J* = 23.1, 7.4 Hz, 1 H), 1.92 (dq, *J* = 23.1, 7.4 Hz, 1 H), 1.61 (s, 1 H), 0.93 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.4, 138.2, 137.8, 137.7, 135.8, 133.6, 130.3, 129.0, 126.6, 124.8, 124.6, 123.8, 123.1, 120.9, 117.7, 116.1, 113.9, 108.9, 57.7, 53.7, 52.0, 27.0, 12.2. IR (film) 3073, 2964, 1446, 1368, 1176, 1120, 918, 747 cm^{-1}; Mass spectrum (CI) *m/z* 421.1949 [$C_{25}H_{29}N_2O_2S$ $(M+H)^+$ requires 421.1950].



11

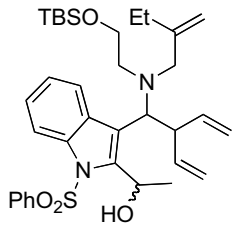
Triene 11. A solution of **10** (~6.5 g, ~15 mmol) and ethylene oxide (7.7 mL, 6.8 g, 154 mmol) in MeOH (15 mL) was heated at 65 °C in a sealed tube for 64 h. After cooling to room temperature, the reaction was concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (1: 3) to give 6.39 g (89%) of a mixture (>10:1) of branched and linear adducts as a slightly brown gum that was crystallized from MeOH (~2 mL) to give 5.1 g (71%) **11** as a pale yellow solid (mp = 90-92 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.8 Hz, 1 H), 7.83-7.81 (m, 2 H), 7.54-7.51 (m, 1 H), 7.43-7.40 (comp, 3 H), 7.32 (ddd, *J* = 8.4, 7.2, 0.9 Hz, 1 H), 7.24 (ddd, *J* = 8.4, 7.2, 0.9 Hz, 1 H), 5.91-5.85 (m, 1 H), 5.40-5.35 (m, 1 H), 5.24-5.20 (comp, 2 H), 4.95 (m, 1 H), 4.91 (m, 1 H), 4.84 (dt, *J* = 16.8, 1.2 Hz, 1 H), 4.66 (ddd, *J* = 16.2, 1.5, 0.9 Hz, 1 H), 4.00 (d, *J* = 12.0 Hz, 1 H), 3.67 (td, *J* = 10.8, 3.0 Hz, 1 H), 3.53 (app d, *J* = 10.8 Hz, 1 H), 3.47-3.43 (m, 1 H), 3.12 (d, *J* = 13.8 Hz, 1 H), 2.97 (ddd, *J* = 13.2, 10.8, 4.8 Hz, 1 H), 2.64 (app d, *J* = 13.8 Hz, 2 H), 2.18 (dt, *J* = 13.2, 2.4 Hz, 1 H), 2.16-2.10 (m, 1 H), 2.06-2.00 (m, 1 H), 1.05 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.5, 139.7, 138.0, 137.9, 134.9, 133.8, 132.1, 129.1, 126.6, 125.1, 124.8, 123.3, 120.2,

118.7, 116.6, 116.1, 113.8, 112.2, 58.8, 58.2, 56.2, 51.5, 51.2, 26.6, 12.1; IR (film) 3468, 3077, 2965, 2921, 2833, 1447, 1369, 1177, 1121, 914 cm^{-1}; Mass spectrum (CI) *m/z* 465.2215 [$C_{27}H_{33}N_2O_3S$ $(M+H)^+$ requires 465.2212].



12

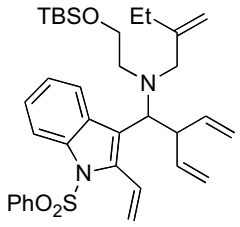
TBS ether 12. A solution of amino alcohol **11** (5.1 g, 11.0 mmol), TBSCl (1.99 g, 13.2 mmol) and imidazole (1.12 g, 16.5 mmol) in DMF (12 mL) was stirred for 6 h at room temperature. The reaction was partitioned between H_2O (100 mL) and Et_2O (100 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (2 x 100 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (1: 4) to give 6.23 g (98%) **12** as a white solid (mp = 58-59.5 ºC). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 1 H), 7.82-7.80 (m, 2 H), 7.59 (app d, *J* = 7.7 Hz, 1 H), 7.50 (t, *J* = 7.5 Hz, 1 H), 7.40 (s, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.29 (t, *J* = 7.7 Hz, 1 H), 7.21 (t, *J* = 7.7 Hz, 1 H), 6.06 (ddd, *J* = 17.5, 10.4, 7.4 Hz, 1 H), 5.43 (ddd, *J* = 17.5, 10.3, 7.4, Hz, 1 H), 5.12-5.07 (comp, 2 H), 4.84-4.82 (comp, 3 H), 4.70 (d, *J* = 10.3 Hz, 1 H), 4.07 (d, *J* = 10.9 Hz, 1 H), 3.71-3.62 (comp, 2 H), 3.40 (dt, *J* = 10.3, 7.4 Hz, 1 H), 3.12 (d, *J* = 13.9 Hz, 1 H), 2.76 (dt, *J* = 13.2, 6.7 Hz, 1 H), 2.62 (d, *J* = 13.9 Hz, 1 H), 2.30 (dt, *J* = 13.2, 6.5 Hz, 1 H), 2.03 (dq, *J* = 23.2, 7.4 Hz, 1 H), 2.00 (dq, *J* = 23.2, 7.4 Hz, 1 H), 0.98 (t, *J* = 7.4 Hz, 3 H), 0.90 (s, 9 H), 0.059 (s, 3 H), 0.056 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.6, 139.9, 138.4, 138.1, 134.9, 133.7, 132.5, 129.1, 126.7, 124.7, 124.6, 123.2, 120.7, 120.1, 116.0, 115.1, 113.7, 110.8, 62.9, 59.6, 57.3, 52.3, 50.9, 26.5, 26.0, 18.4, 12.2, -5.30, -5.31; IR (film) 2928, 1446, 1370, 1255, 1176, 1095, 835 cm^{-1}; Mass spectrum (CI) *m/z* 579.3087 [$C_{33}H_{47}N_2O_3SSi$ $(M+H)^+$ requires 579.3077].



13

Alcohols 13. TBS ether **12** (1.16 g, 2.0 mmol) was azeotroped from benzene (3 x ~10 mL), dissolved in THF (8 mL) and cooled to -78 ºC under N_2. LDA (1.0 M in THF/hexane, 4.0 mL, 4.0 mmol) was added, and the reaction was stirred for 10 min at -78 ºC. The -78 ºC bath was exchanged for a 0 ºC bath, and the reaction was stirred for 2 h at 0 ºC. The reaction was then cooled to -78 ºC, and freshly distilled acetaldehyde (0.45 mL, 353 mg, 8.0 mmol) was added. The reaction was allowed to slowly warm to -30 ºC over 2 h. The reaction was cooled to -78 ºC, and saturated NH_4Cl (3 mL) was added. The reaction was partitioned between Et_2O (20 mL) and brine (15 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (gradient elution, 1:49 to 1:19 to 1:9) to give 0.71 g (56%) of **13a** (major diastereomer, less polar) as a colorless oil, and 0.27 g (22%) of **13b** (minor diastereomer, more polar) as a colorless oil. **13a** (Major diastereomer). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.99 (d, J = 8.2 Hz, 1 H), 7.90-7.88 (m, 1 H), 7.69 (d, J = 7.5 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 7.45 (d, J = 7.5 Hz, 1 H), 7.22 (t, J = 7.7 Hz, 1 H), 7.16 (t, J = 7.7 Hz, 1 H), 6.04-6.00 (m, 1 H), 5.56-5.53 (m, 1 H), 5.46-5.40 (m, 1 H), 5.27 (d, J = 4.7 Hz, 1 H), 5.05 (d, J = 17.5 Hz, 1 H), 5.00 (d, J = 10.3 Hz, 1 H), 4.84 (s, 1 H), 4.71 (s, 1 H), 4.65 (d, J = 9.3 Hz, 1 H), 4.56 (d, J = 16.7 Hz, 1 H), 4.43 (d, J = 9.4 Hz, 1 H), 3.70 (app q, J = 8.3 Hz, 1 H), 3.52 (t, J = 6.8 Hz, 1 H), 3.14 (d, J = 13.8 Hz, 1 H), 2.75 (d, J = 13.8 Hz, 1 H), 2.61 (dt, J = 13.4, 6.8 Hz, 1 H), 2.44 (dt, J = 13.4, 6.8 Hz, 1 H), 2.01 (dq, J = 14.9, 7.4 Hz, 1 H), 1.91 (dq, J = 14.9, 7.4 Hz, 1 H), 1.57 (d, J = 6.6 Hz, 3 H), 0.86 (t, J = 7.4 Hz, 3 H), 0.81 (s, 9 H), -0.06 (s, 6 H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 150.0, 142.4, 140.9, 138.4, 137.0, 136.5, 134.1, 130.2, 129.1, 126.1, 124.3, 123.4, 123.3, 122.2, 114.8, 114.6, 114.3, 109.9, 62.5, 61.2, 60.9, 57.6, 52.2, 49.1, 25.72, 25.71, 24.7, 17.8, 11.9, -5.5; IR (film) 3551, 2930, 1447, 1362, 1254, 1174, 1092, 835 cm^{-1}; Mass spectrum (CI) *m/z* 623.3331 [$C_{35}H_{51}N_2O_4SSi$ $(M+H)^+$ requires 623.3339]. **13b** (Minor diastereomer). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.02 (d, J = 8.3 Hz, 1 H), 7.86-7.84 (m, 1 H), 7.63 (d, J = 7.5 Hz, 2 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.43 (t, J = 7.5 Hz, 1 H), 7.24 (t, J = 7.3 Hz, 1 H), 7.17 (t, J =

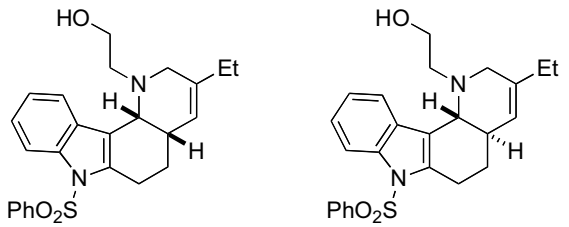
7.3 Hz, 1 H), 6.01 (ddd, J = 17.2, 10.3, 6.9 Hz, 1 H), 5.69 (br, 1 H), 5.45-5.39 (comp, 2 H), 5.08 (d, J = 17.2 Hz, 1 H), 5.03 (d, J = 10.3 Hz, 1 H), 4.75 (m, 1 H), 4.71 (s, 1 H), 4.68 (d, J = 17.4 Hz, 1 H), 4.65 (s, 1 H), 4.57 (d, J = 10.3 Hz, 1 H), 3.74-3.72 (m, 1 H), 3.50-3.42 (comp, 2 H), 3.08 (d, J = 13.8 Hz, 1 H), 2.61 (d, J = 13.8 Hz, 1 H), 2.52-2.47 (m, 1 H), 2.35 (dt, J = 12.6, 5.8 Hz, 1 H), 1.99 (dq, J = 15.1, 7.2 Hz, 1 H), 1.88 (dq, J = 15.1, 7.2 Hz, 1 H), 1.48 (d, J = 5.4 Hz, 1 H), 0.83 (t, J = 7.2 Hz, 3 H), 0.82 (s, 9 H), -0.05 (s, 3 H), -0.06 (s, 3 H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 150.4, 142.8, 140.7, 138.1, 136.9, 136.5, 134.0, 131.0, 129.1, 126.1, 124.2, 123.5, 122.2, 115.4, 115.1, 114.7, 109.4, 63.1, 61.3, 60.0, 57.5, 51.9, 48.4, 26.1, 25.8, 25.6, 17.9, 11.8, -5.41, -5.42; IR (film) 3555, 2929, 1448, 1362, 1173, 1091, 914, 836 cm^{-1}; Mass spectrum (CI) *m/z* 623.3333 [$C_{35}H_{51}N_2O_4SSi$ $(M+H)^+$ requires 623.3339].



5

Tetraene 5. Freshly distilled Tf_2O (0.92 mL, 1.53 g, 5.4 mmol) and Hünig's base (2.3 mL, 1.74 g, 13.4 mmol) were added in rapid succession to a solution of alcohol **13** (2.8 g, 4.5 mmol) in CH_2Cl_2 (15 mL) at -78 ºC under N_2. The reaction was stirred for 30 min at -78 ºC and then partitioned between 1 M NaOH (6 mL) and CH_2Cl_2 (10 mL). The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (1:10) to give 2.5 g (92%) of **5** as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, J = 7.7 Hz, 1 H), 7.77 (d, J = 7.7 Hz, 1 H), 7.60-7.58 (m, 2 H), 7.45 (t, J = 7.5 Hz, 1 H), 7.32-7.25 (comp, 3 H), 7.21 (t, J = 7.7 Hz, 1 H), 6.96 (dd, J = 17.7, 11.4 Hz, 1 H), 5.92 (ddd, J = 16.8, 10.8, 7.4 Hz, 1 H), 5.59 (dd, J = 11.4, 1.8 Hz, 1 H), 5.35 (ddd, J = 17.3, 10.3, 7.4 Hz, 1 H), 5.31 (dd, J = 17.7, 1.8 Hz, 1 H), 5.10-5.06 (comp, 2 H), 4.84 (s, 1 H), 4.73 (s, 1 H), 4.71 (d, J = 17.3 Hz, 1 H), 4.54 (d, J = 10.3 Hz, 1 H), 4.14 (d, J = 10.7 Hz, 1 H), 3.70 (dt, J = 10.7, 7.4 Hz, 1 H), 3.56-3.51 (m, 1 H), 3.48-3.44 (m, 1 H), 3.15 (d, J = 14.0 Hz, 1 H), 2.74 (ddd, J = 13.1, 8.4, 6.5 Hz, 1 H), 2.65 (d, J = 14.0 Hz, 1 H), 2.23 (ddd, J = 13.1, 7.8, 5.0 Hz, 1 H), 2.00 (dq, J = 15.1, 7.5 Hz, 1 H), 1.91 (dq, J =15.1, 7.5 Hz, 1 H), 0.94 (t, J = 7.4 Hz, 3 H), 0.86 (s, 9 H), -0.011 (s, 3 H), -0.014 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.7,

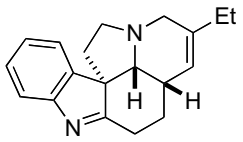
139.8, 138.2, 138.1, 137.8, 136.9, 133.5, 128.7, 128.1, 126.6, 124.7, 123.5, 122.9, 122.1, 120.7, 115.5, 115.34, 115.33, 110.0, 61.6, 60.7, 57.3, 52.2, 48.7, 26.5, 26.0, 18.3, 12.1, -5.30, -5.31; IR (film) 2928, 1448, 1374, 1253, 1175, 1091, 987, 916, 836, 751 cm^{-1}; Mass spectrum (CI) *m/z* 605.3246 [$C_{35}H_{49}N_2O_3SSi$ $(M+H)^+$ requires 605.3233].



4 **16**

C/D *cis* tetracycle 4 and C/D *trans* tetracycle 16. A solution of tetraene **5** (326 mg, 0.57 mmol) and Hoveyda-Grubbs II catalyst (18 mg, 0.029 mmol) in toluene (56 mL) was placed in a pre-heated oil bath (100 °C) and heated for 3.5 h under nitrogen. The mixture was then cooled to room temperature, and toluene was removed under reduced pressure. The residue was dissolved in degassed EtOH (3 mL) containing PtO_2 (13 mg, 0.057 mmol), and the mixture was stirred under H_2 (1 atm) for 21 h at room temperature. The reaction was filtered through a pad of celite, and the pad was washed with MeOH (10 mL). The combined filtrates and washings were concentrated under reduced pressure. The residue was dissolved in MeOH (5 mL), and 1.25 M HCl in MeOH (5 mL) was added. The reaction was stirred for 1 h at room temperature and then partitioned between 1 N NaOH (10 mL) and CH_2Cl_2 (20 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/hexanes (1:6) and EtOAc/hexanes (1:4) to give 45 mg (26%) **4** as a white foam and 76 mg (44%) **16** as a white foam. **C/D *cis* tetracycle 4**. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.8 Hz, 1 H), 7.68 (dd, *J* = 8.7, 0.9 Hz, 2 H), 7.63 (d, *J* =7.2 Hz, 1 H), 7.49 (tt, *J* = 7.5, 1.2 Hz, 1 H), 7.37 (app t, *J* = 8.1 Hz, 2 H), 7.26 (app td, *J* = 7.8, 1.2 Hz, 1 H), 7.21 (td, *J* = 7.4, 1.2 Hz, 1 H), 5.36 (s, 1 H), 4.03 (d, *J* = 4.8 Hz, 1 H), 3.63-3.50 (m, 2 H), 3.00-2.97 (m, 2 H), 2.90-2.83 (comp, 2 H), 2.76-2.69 (comp, 2 H), 2.60 (app br s, 1 H), 2.02 (m, 1 H), 1.86-1.77 (comp, 3 H), 0.92 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.1, 137.9, 136.7, 133.5, 130.2, 129.1, 126.1, 124.1, 123.6, 120.3, 119.6, 118.4, 114.6, 58.9, 55.8, 53.7, 49.0 (br), 30.3 (br), 27.6, 26.7, 22.3, 12.0; IR (film) 3419, 2960, 2923, 2875, 1449, 1369, 1187, 1170, 1146, 1092,

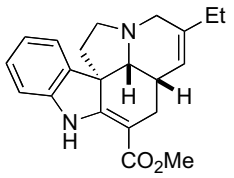
1051 cm^{-1}; Mass spectrum (ESI) m/z 437.1895 [$C_{25}H_{29}N_2O_3S$ $(M+H)^+$ requires 437.1893]. **C/D *trans* tetracycle 16**. ^1H NMR (600 MHz, $CDCl_3$) δ 8.14 (dt, *J* = 7.8, 0.90 Hz, 1 H), 7.90 (d, *J* = 7.8 Hz, 1 H), 7.77-7.75 (comp, 2 H), 7.52 (tt, *J* = 7.5, 1.2 Hz, 1 H), 7.43-7.40 (comp, 2 H), 7.26 (app td, *J* = 7.8, 1.2 Hz, 1 H), 7.21 (td, *J* = 7.5, 1.2 Hz, 1 H), 5.49 (s, 1 H), 3.93 (d, *J* = 9.6 Hz, 1 H), 3.69 (ddd, *J* = 10.8, 9.6, 4.8 Hz, 1H), 3.60 (d, *J* = 18.0 Hz, 1 H), 3.48 (ddd, *J* = 10.8, 9.6, 3.0 Hz, 1 H), 3.22 (d, *J* = 17.4 Hz, 1 H), 3.16 (ddt, *J* = 18.0, 5.4, 1.8 Hz, 1 H), 3.02-2.96 (m, 1 H), 2.45 (dt, *J* = 12.6, 3.9 Hz, 1 H), 2.42-2.37 (m, 1 H), 2.29 (ddd, *J* = 15.0, 9.0, 6.0 Hz, 1 H), 2.07 (app ddt, *J* = 13.2, 6.0, 2.1 Hz, 1 H), 2.01-1.90 (comp, 2 H), 1.53 (qd, *J* = 13.2, 5.4 Hz, 2 H), 1.04 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ139.0, 138.2, 137.4, 136.8, 133.6, 129.2, 128.8, 126.3, 124.2, 123.4, 122.2, 120.5, 119.5, 114.4, 61.6, 59.9, 53.1, 48.2, 31.4, 28.5, 27.4, 25.6, 12.2; IR (film) 3416 (br), 2960, 2926, 2855, 1449, 1370, 1173, cm^{-1}; Mass spectrum (CI) *m/z* 437.1906 [$C_{25}H_{29}N_2O_3S$ $(M+H)^+$ requires 437.1889].



18

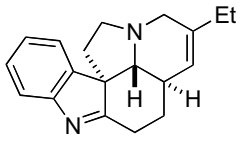
C/D *cis* pentacycle 18. A solution of KO^{t}Bu (40 mg, 0.36 mmol) in THF (2 mL) was added to a solution of **4** (62 mg, 0.14 mmol) in DME (4 mL) at -20 °C under N_2, and the reaction was slowly warmed to -5 °C over 10 min. After being stirred for 15 min at -5 °C, the reaction was quenched with brine (1.5 mL). The reaction was partitioned between brine (5 mL) and Et_2O (10 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with EtOAc/hexanes (2:1), DCM/MeOH (50:1) and DCM/MeOH (25:1) to give 26 mg (66%) of **18** as a yellow oil. ^1H NMR (600 MHz, C_6D_6) δ 7.76 (d, *J* = 7.8 Hz, 1 H), 7.21 (app dq, *J* = 7.2, 0.6 Hz, 1 H), 7.17 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.05 (td, *J* = 7.2, 1.2 Hz, 1 H), 5.19-5.17 (m, 1 H), 3.13 (d, *J* = 15.0 Hz, 1 H), 2.93 (t, *J* = 7.2 Hz, 1H), 2.89-2.82 (comp, 2 H), 2.74-2.70 (comp, 2 H), 2.57 (ddd, *J* = 10.8, 8.4, 4.8 Hz, 1 H), 2.28-2.20 (m, 1 H), 2.03 (ddd, *J* = 12.6, 10.8, 6.6 Hz, 1 H), 1.78 (q, *J* = 7.6 Hz, 2 H), 1.60-1.54 (comp, 2 H), 1.52-1.46 (m, 1 H), 0.88 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (150 MHz, C_6D_6) δ 188.5, 156.2, 147.9, 138.7, 128.0, 125.2, 123.1, 121.7, 120.6,

70.7, 61.5, 54.5, 53.6, 35.1, 34.2, 27.9, 26.9, 25.9, 12.8. IR (film) 2962, 2931, 2872, 2783, 1576, 1455, 1535, 1239, 1148; Mass spectrum (CI) *m/z* 279.1861 [$C_{19}H_{23}N_2$ $(M+H)^+$ requires 279.1861].



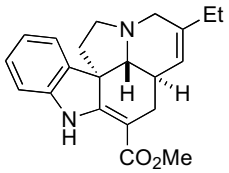
3
pseudotabersonine

Pseudotabersonine (3). Pentacycle **18** (26 mg, 0.09 mmol) was azeotroped from benzene (3 x ~10 mL), dissolved in THF (2 mL) and cooled to -78 ºC under N_2. LDA (1.0 M in THF/hexane, 0.28 mL, 0.28 mmol) was added. The reaction was allowed to warm slowly to -20 ºC over 1 h and then stirred at -20 °C for 30 min. The solution was cooled to -78 ºC, freshly distilled methyl cyanoformate (37 μL, 40 mg, 0.46 mmol) was added, and the reaction was stirred for 30 min at -78 ºC. Brine (2 mL) was added, and the reaction was partitioned between Et_2O (10 mL) and brine (5 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (1:5) to give 19 mg (61%) of **3** as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.98 (s, 1 H), 7.30 (d, *J* = 7.2 Hz, 1 H), 7.15 (td, *J* = 7.8, 1.2 Hz, 1 H), 6.88 (td, *J* = 7.2, 0.6 Hz, 1 H), 6.81 (d, *J* = 7.8 Hz, 1 H), 5.51 (app d, *J* = 6.0 Hz, 1 H), 3.77 (s, 3 H), 3.36 (d, *J* = 15.6 Hz, 1 H), 3.27 (d, *J* = 15.6 Hz, 1 H), 3.05-3.01 (comp, 2 H), 2.83-2.77 (m, 1 H), 2.68 (dd, *J* = 15.0, 3.0 Hz, 1 H), 2.15 (dd, *J* = 15.0, 11.4 Hz, 1 H), 2.09-2.03 (comp, 3 H), 1.90 (ddd, *J* = 11.6, 4.8, 2.0 Hz, 1 H), 1.77 (app br s, 1 H), 1.06 (t, *J* = 7.8 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.7, 165.9, 143.6, 139.3, 138.0, 127.7, 121.9, 121.4, 120.6, 109.1, 95.4, 65.2, 55.5, 53.2, 51.0, 51.0, 44.4, 36.8, 27.8, 26.4, 12.5; IR (film) 3367.4, 2965, 2916, 1675, 1609, 1465, 1436, 1240, 1203, 1118 cm^{-1}; Mass spectrum (CI) *m/z* 336.1833 [$C_{21}H_{24}N_2O_2$ $(M)^+$ requires 336.1838].

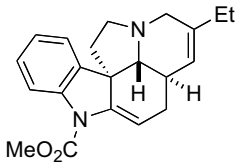


19

C/D *trans* pentacycle 19. A solution of KO^{t}Bu (191 mg, 1.7 mmol) in THF (5 mL) was added to a solution of **16** (313 mg, 0.71 mmol) in THF (10 mL) at 0 °C under N_2, and the reaction was stirred for 30 min at 0 ºC. Brine (5 mL) was added, and the reaction was partitioned between brine (5 mL) and Et_2O (10 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (basic Al_2O_3) eluting with EtOAc/hexanes (1:10) to give 151 mg (75%) of **19** as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.0 Hz, 1 H), 7.54 (d, *J* = 7.5 Hz, 1 H), 7.30 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.19 (td, *J* = 7.5, 1.0 Hz, 1 H), 5.49 (app dd, *J* = 3.0, 1.5 Hz, 1 H), 3.65-3.59 (comp, 2 H), 3.24 (dt, *J* = 18.5, 2.5 Hz, 1 H), 3.08 (ddd, *J* = 11.0, 9.0, 5.0 Hz, 1H), 2.98 (ddd, *J* = 13.5, 3.7, 2.5 Hz, 1 H), 2.67 (td, *J* = 13.0, 5.5 Hz, 1 H), 2.46 (ddd, *J* = 13.3, 10.8, 5.0 Hz, 1 H), 2.40-2.33 (m, 1 H), 2.32 (d, *J* = 9.5 Hz, 1 H), 2.11 (dp, *J* = 13.0, 2.5 Hz, 1 H), 1.96-1.89 (comp, 3 H), 1.25 (qd, *J* = 12.5, 3.5 Hz, 1 H), 1.00 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.4, 153.8, 146.2, 104.1, 127.4, 125.3, 123.2, 121.0, 119.6, 72.0, 63.1, 51.4, 51.3, 31.5, 31.0, 30.9, 30.7, 27.3, 12.4; IR (film) 3248, 3047, 2963, 2928, 2877, 1574, 1454, 1338, 1145; Mass spectrum (ESI) *m/z* 279.1858 [$C_{19}H_{23}N_2$ $(M+H)^+$ requires 279.1856].



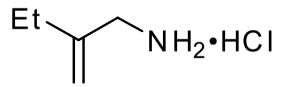
20
14-*epi* pseudotabersonine



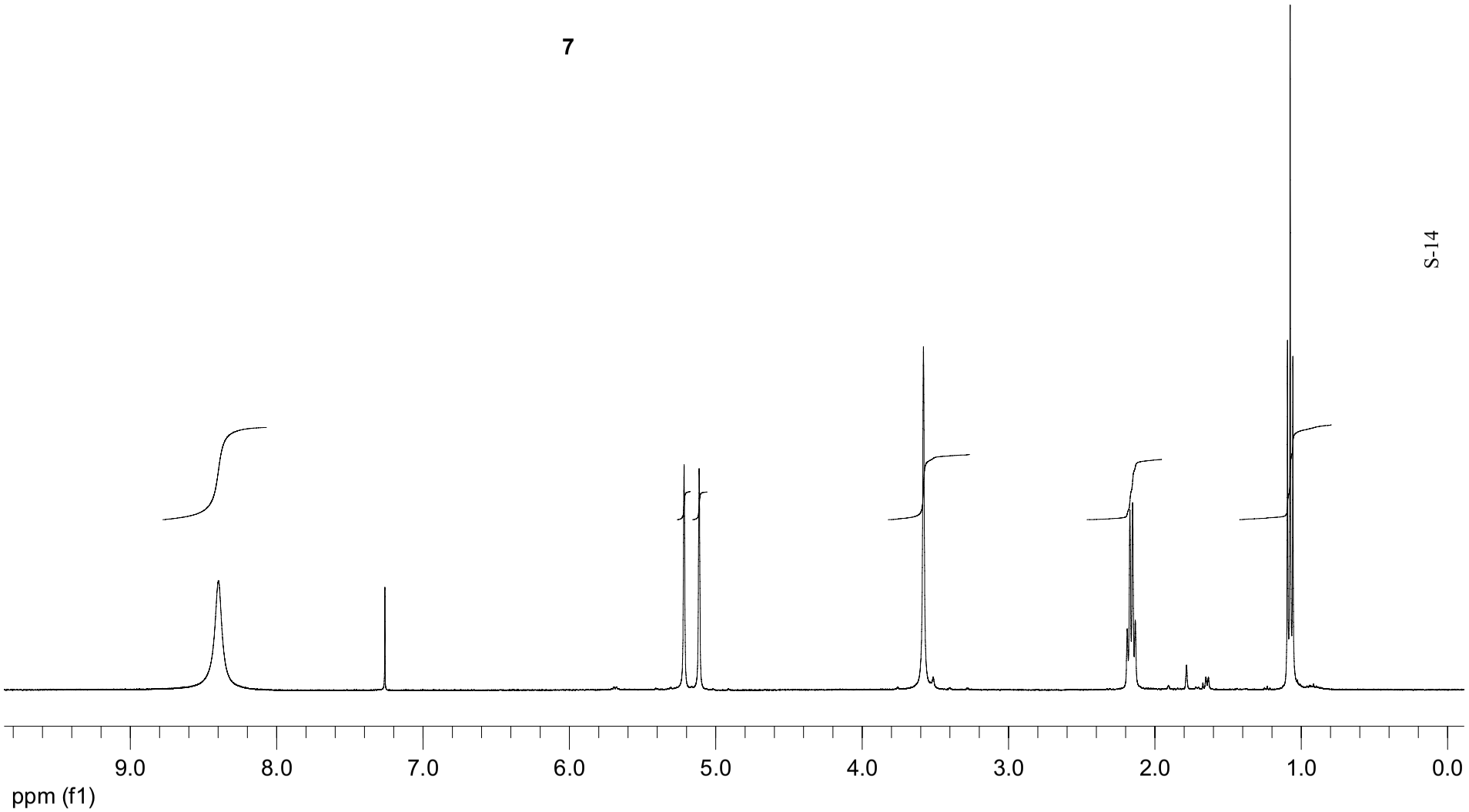
21

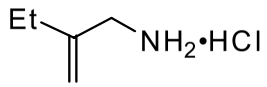
14-*epi* Pseudotabersonine (20) and Carbamate 21. Pentacycle **19** (70 mg, 0.25 mmol) was azeotroped from benzene (3 x ~10 mL), dissolved in THF (3 mL) and cooled to -78 ºC. LDA (1.0 M in THF/hexane, 0.75 mL, 0.75 mmol) was added, and the reaction was stirred for 1 h while warming to -20 ºC. Stirring was continued at -20 ºC for 1 h, whereupon the reaction was cooled to -78 ºC, and methyl

cyanoformate (0.09 mL, 96 mg, 1.13 mmol) was added. The reaction was stirred for 1 h at -78 ºC. The reaction was then partitioned between CH_2Cl_2 (5 mL) and saturated aqueous NH_4Cl (5 mL). The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/Hexane (3:97) to give 39 mg (46%) of **20** as a viscous oil and 22 mg (26%) of **21**. **14-*epi* pseudotabersonine (20)**. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (s, 1 H), 7.52 (d, *J* = 7.5 Hz, 1 H), 7.08 (td, *J* = 7.5, 1.3 Hz, 1 H), 6.83 (td, *J* = 7.5, 1.0 Hz, 1 H), 6.75 (d, *J* = 7.5 Hz, 1 H), 5.51 (d, *J* = 1.5 Hz, 1 H), 3.75 (s, 3 H), 3.70 (d, *J* = 18.5 Hz, 1 H), 3.39 (ddd, *J* = 9.0, 9.0, 5.5 Hz, 1 H), 3.20 (d, *J* = 18.5 Hz, 1 H), 2.92 (ddd, *J* = 10.8, 9.0, 4.7 Hz, 1 H), 2.81 (d, *J* = 9.8 Hz, 1 H), 2.71 (dd, *J* = 15.6, 5.5 Hz, 1 H), 2.56-2.50 (comp, 2 H), 2.06 (dd, *J* = 15.6, 12.8 Hz, 1 H), 1.99-1.96 (comp, 2 H), 1.91 (ddd, *J* = 13.3, 9.0, 4.7 Hz, 1 H), 1.05 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.1, 165.3, 144.2, 138.9, 138.2, 127.3, 123.1, 121.2, 120.8, 109.2, 95.0, 63.4, 55.0, 51.5, 51.0, 49.8, 40.7, 29.3, 28.1, 27.3, 12.3; IR (film) 3354, 2963, 1677, 1606, 1463, 1283, 1233, 1215, 1163 cm^{-1}; Mass spectrum (CI) *m/z* 337.1910 [$C_{21}H_{25}N_2O_2$ $(M+H)^+$ requires 337.1916]. **Carbamate 21**.^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.5 Hz, 1 H), 7.62 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.16 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.00 (dt, *J* = 7.5, 1.0 Hz, 1 H), 5.91 (s, 1 H), 5.47 (d, *J* = 1.5 Hz, 1 H), 3.91 (s, 3 H), 3.69 (d, *J* = 18.3 Hz, 1 H), 3.32 (ddd, *J* = 9.1, 9.1, 4.9 Hz, 1 H), 3.17 (d, *J* = 18.3 Hz, 1 H), 2.91 (ddd, *J* = 10.6, 9.0, 5.2 Hz, 1 H), 2.75 (d, *J* = 9.5 Hz, 1 H), 2.55-2.50 (comp, 2 H), 2.41 (ddd, *J* = 13.1, 10.6, 4.9 Hz, 1 H), 1.99-1.91 (comp, 3 H), 1.84 (ddd, *J* = 13.1, 9.1, 5.2 Hz, 1 H), 1.05 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.0, 143.4, 140.5, 139.5, 139.1, 127.1, 123.7, 123.0, 120.9, 114.8, 111.3, 64.2, 52.7, 51.7, 51.3, 50.3, 39.7, 29.9, 27.4, 27.3, 12.3; IR (film) 2961, 1715, 1603, 1475, 1380, 1303, 1211, 754 cm^{-1}; Mass spectrum (CI) *m/z* 337.1913 [$C_{21}H_{25}N_2O_2$ $(M+H)^+$ requires 337.1916] .



7




Et
NH2•HCl

7

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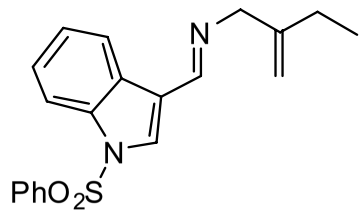

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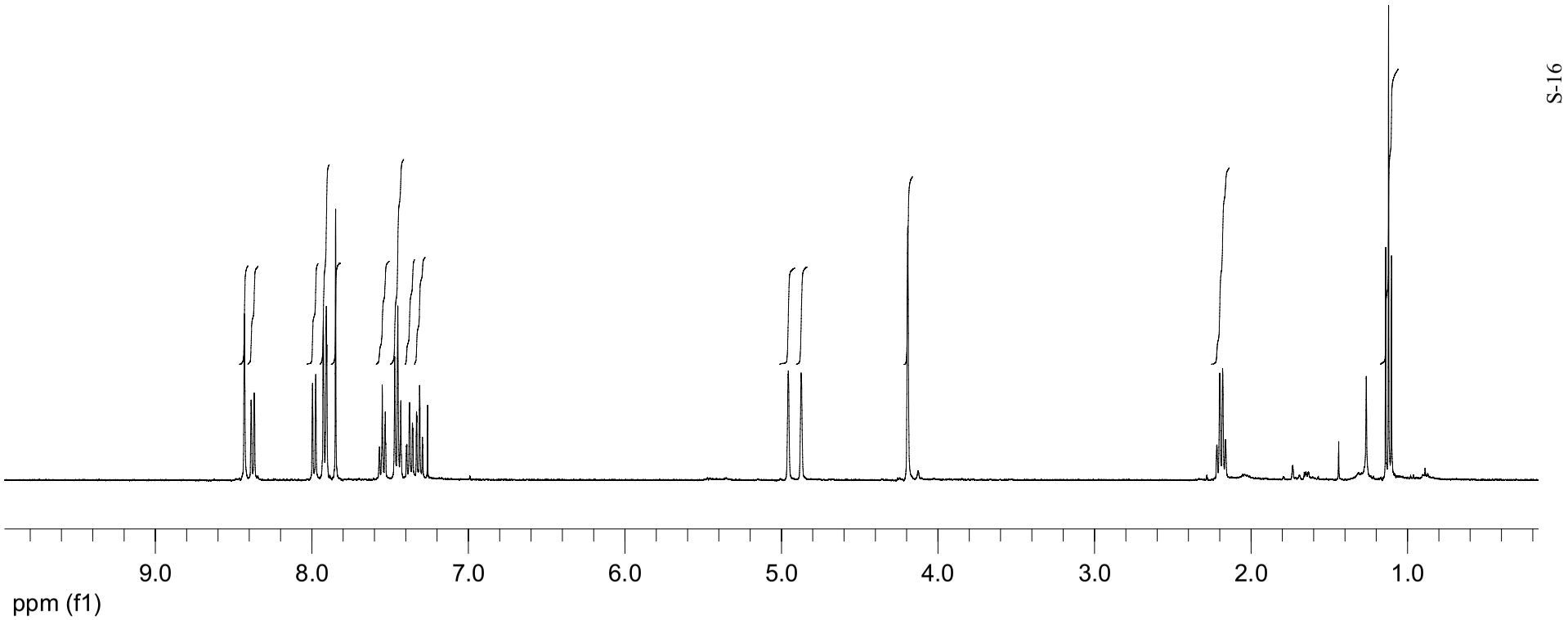

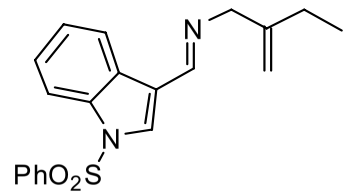
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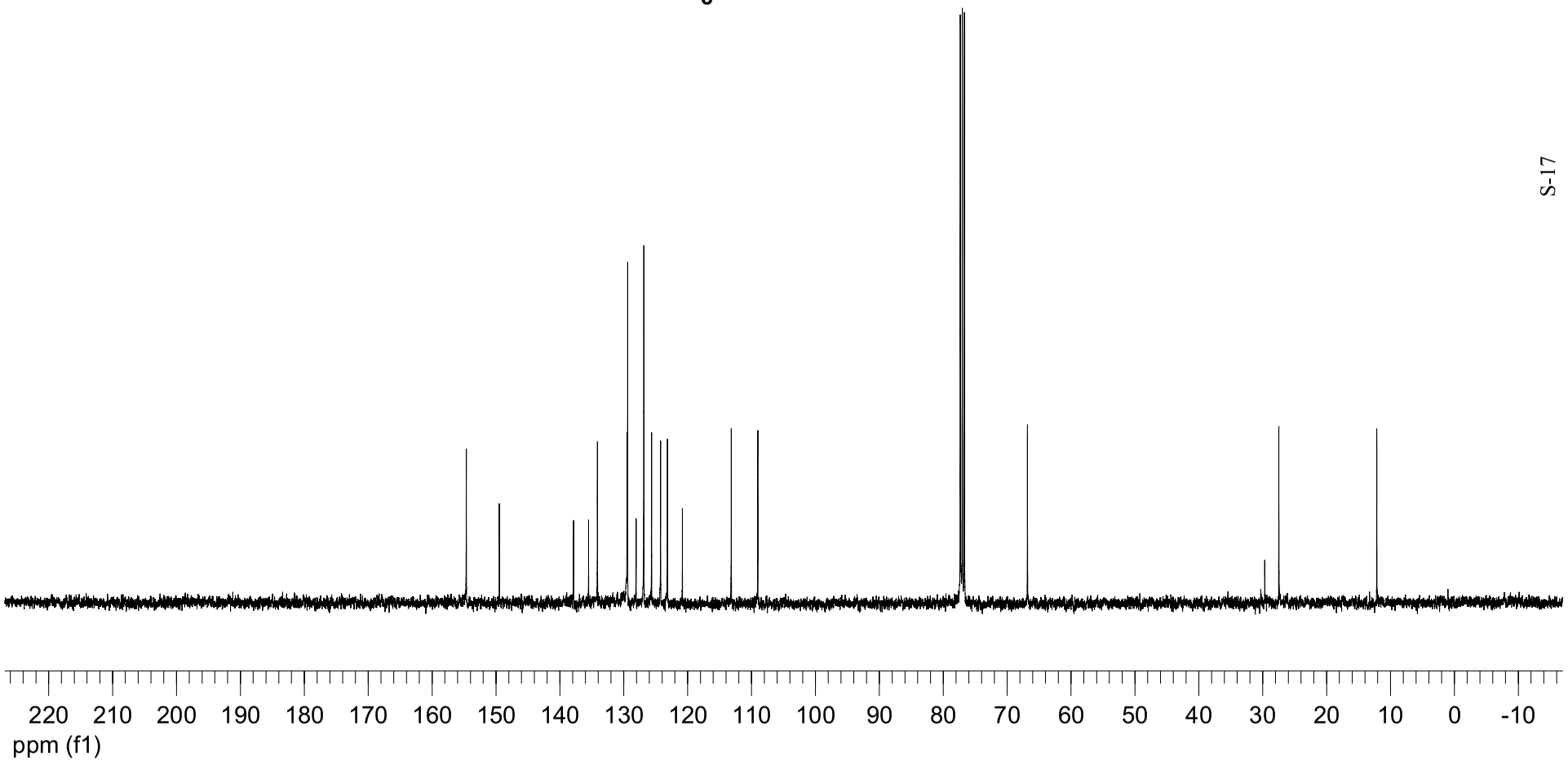
N
PhO2S

8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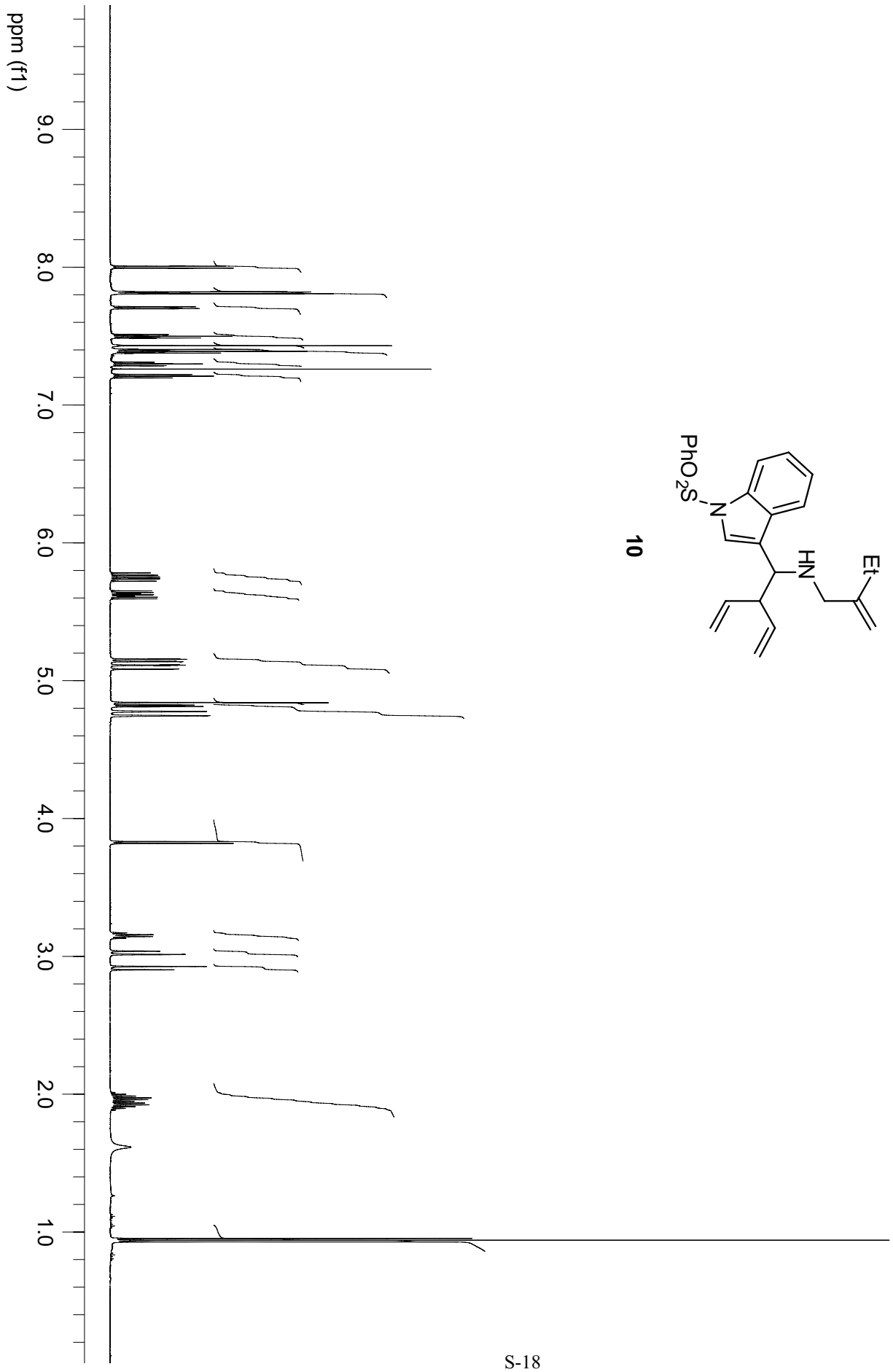
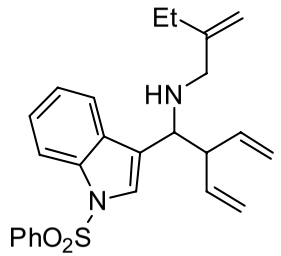
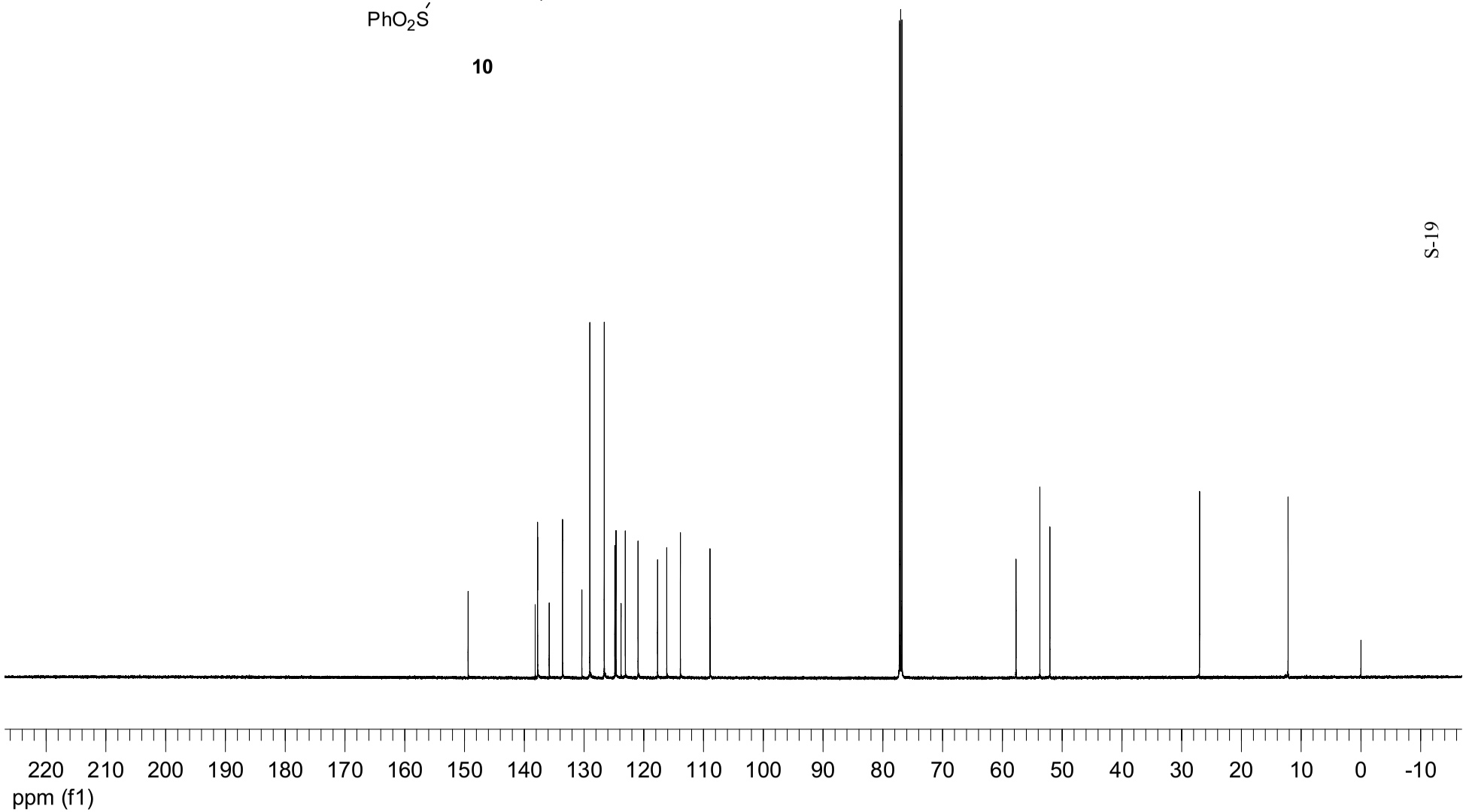
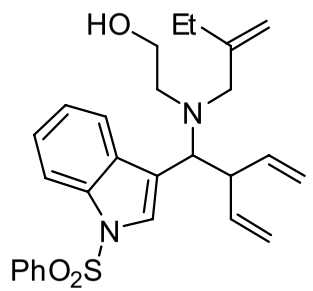


10

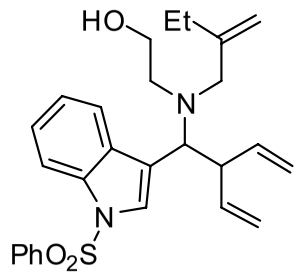

Et
HN
N
PhO2S

10


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



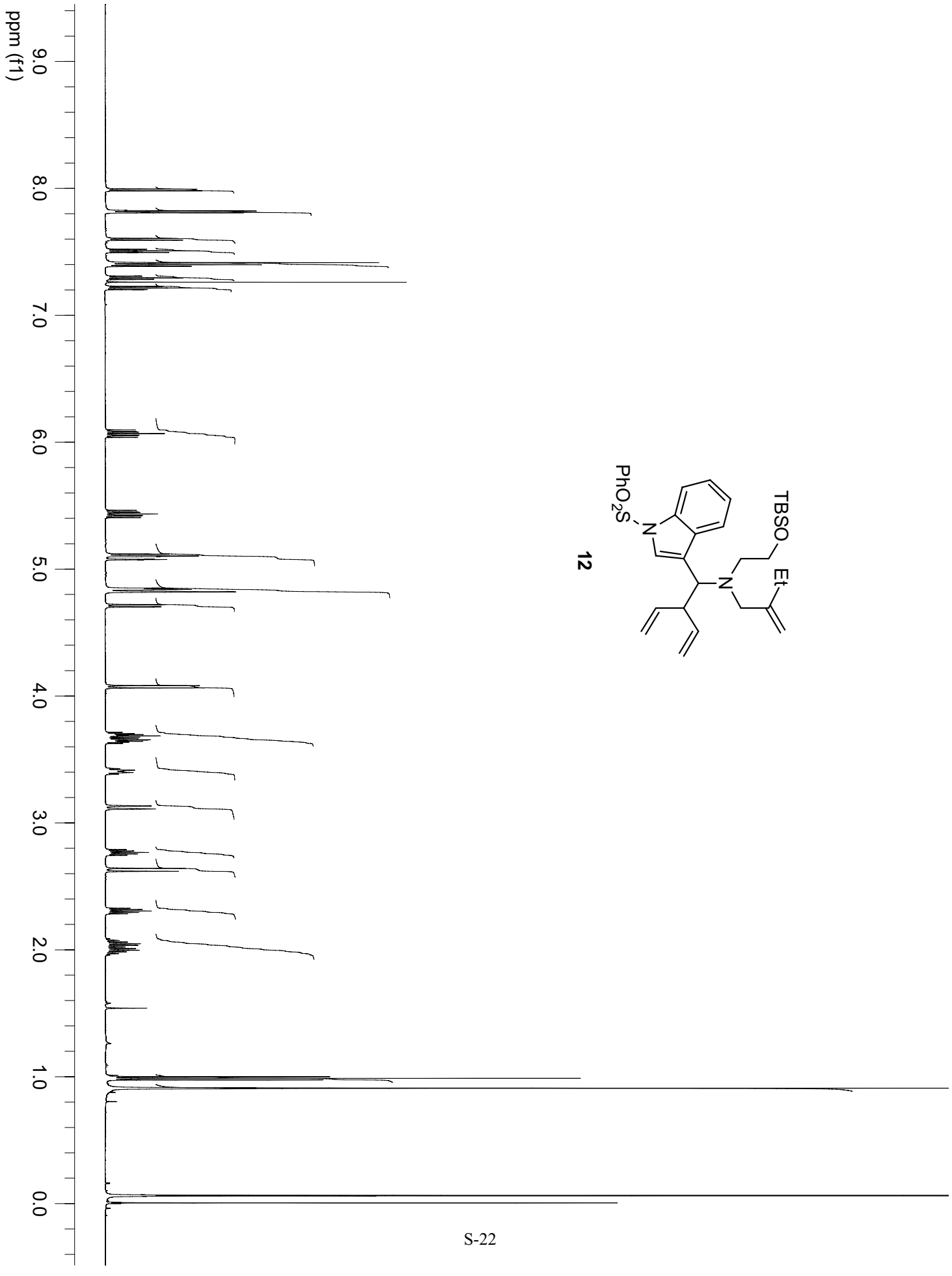
11



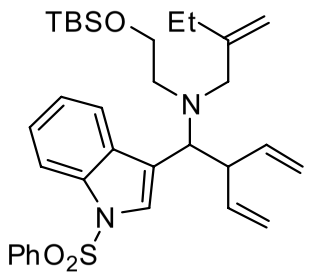
11

240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

ppm (f1)



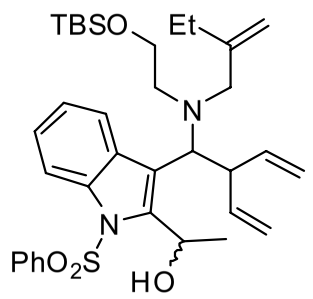
12



12

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

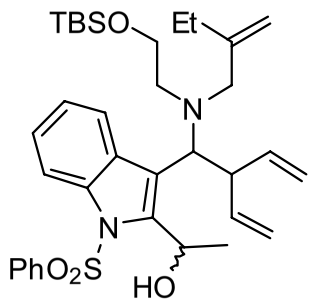
ppm (f1)



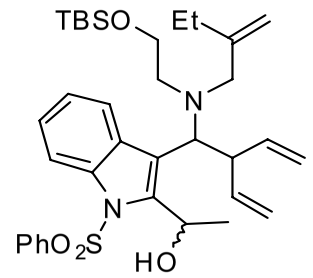
13a (major diastereomer)

9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

ppm (f1)



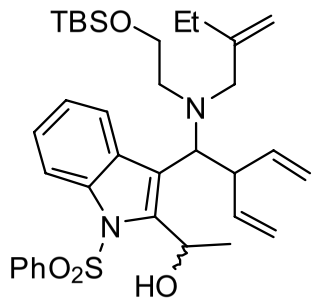
13a (Major diastereomer)



13b (minor diastereomer)

9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

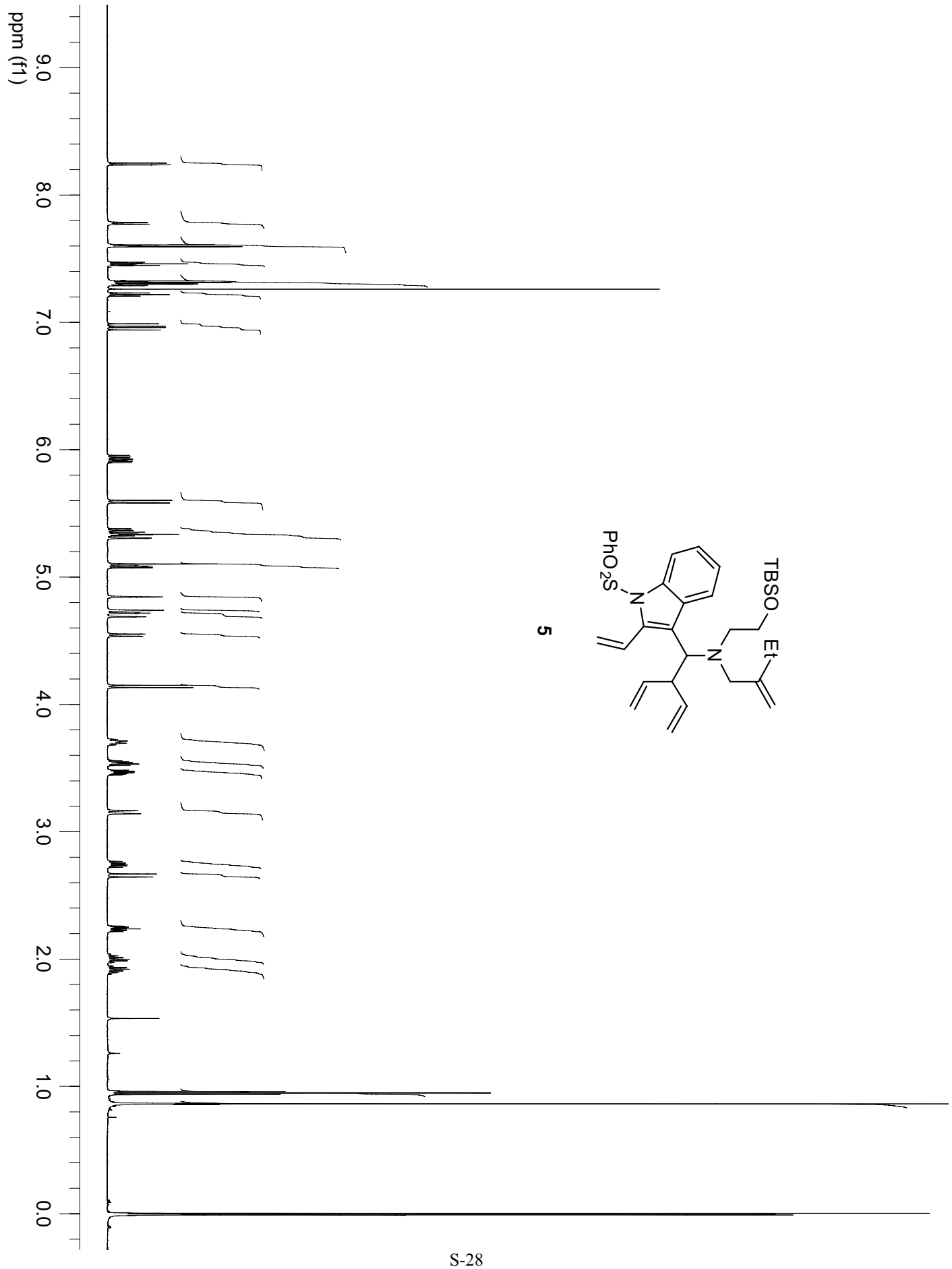
ppm (f1)



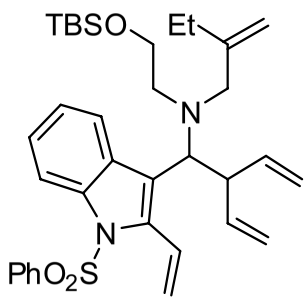
13b (Minor diastereomer)

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

ppm (f1)

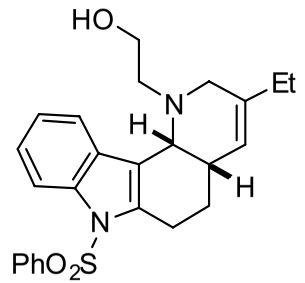


5

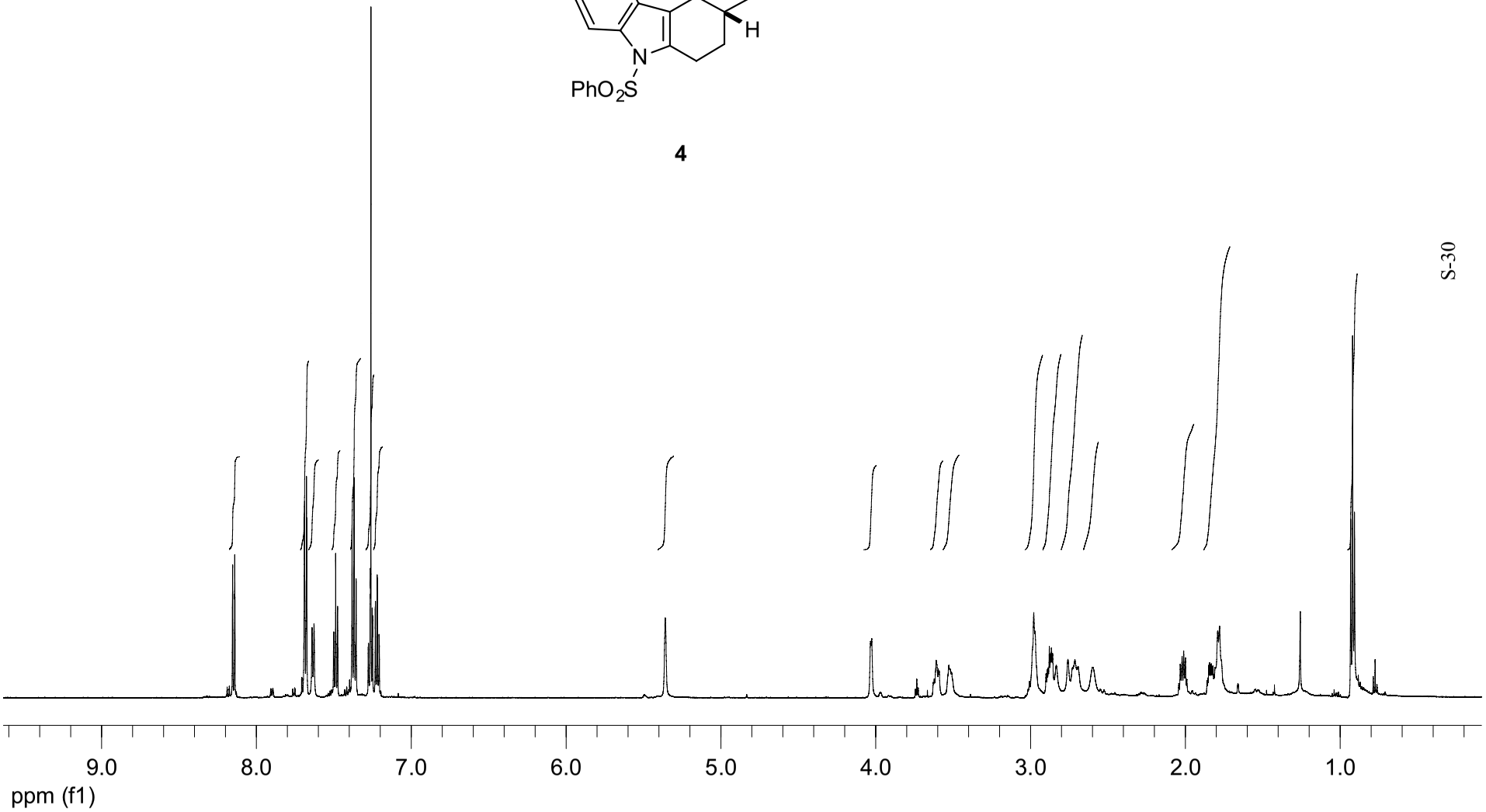

TBSO
Et
N
N
PhO2S

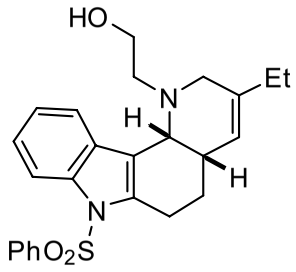
5

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



4

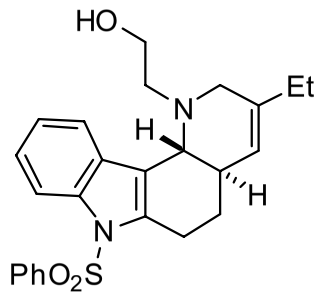




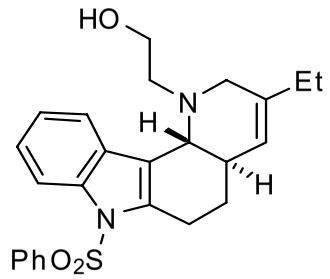
4

240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

ppm (f1)

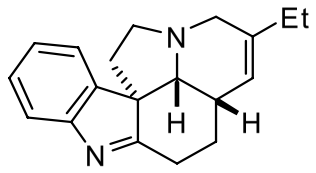


16

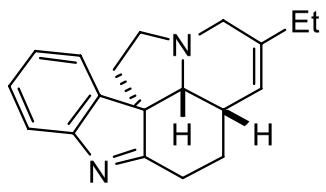

HO
N
Et
H
H
N
PhO2S

16

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



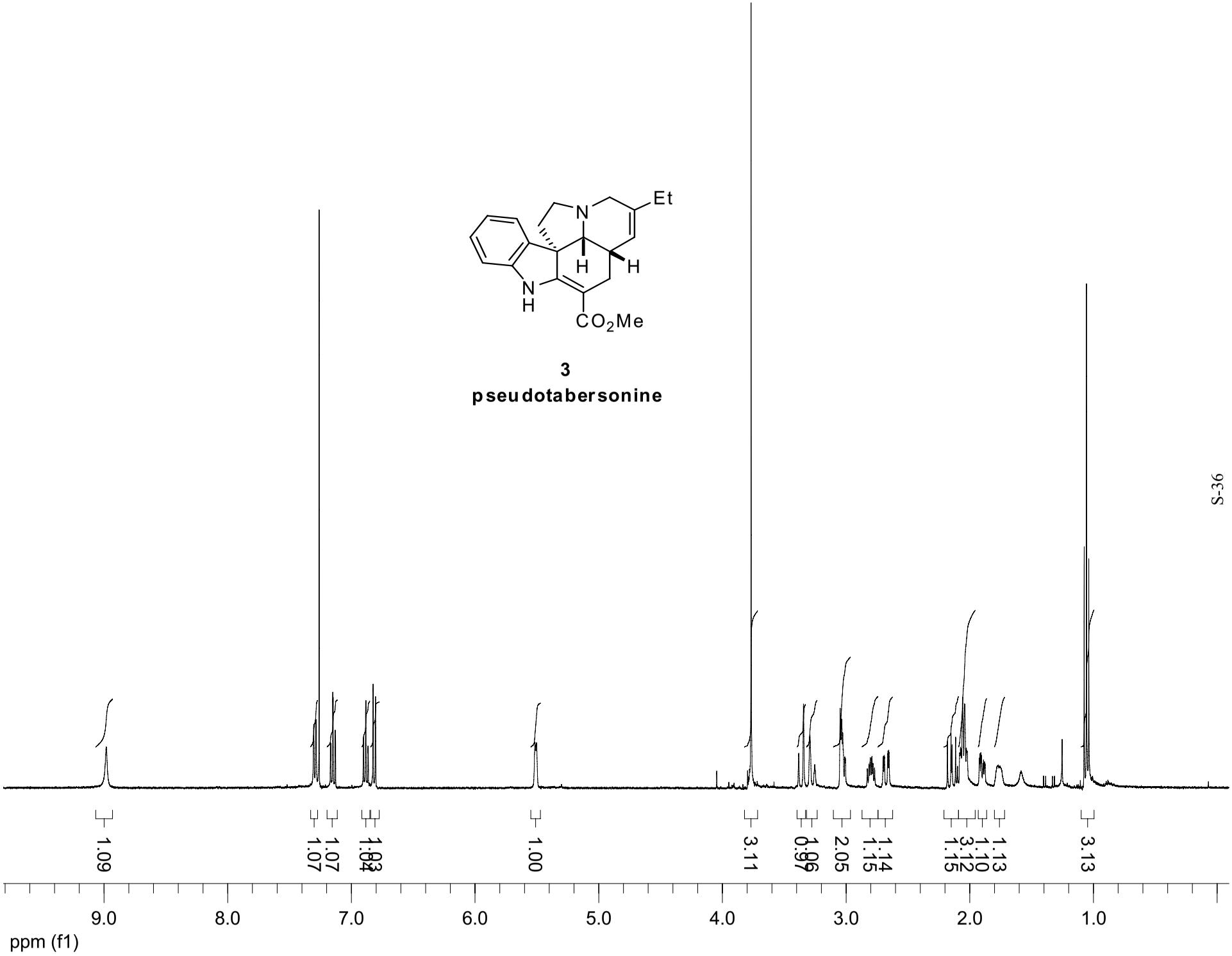
18

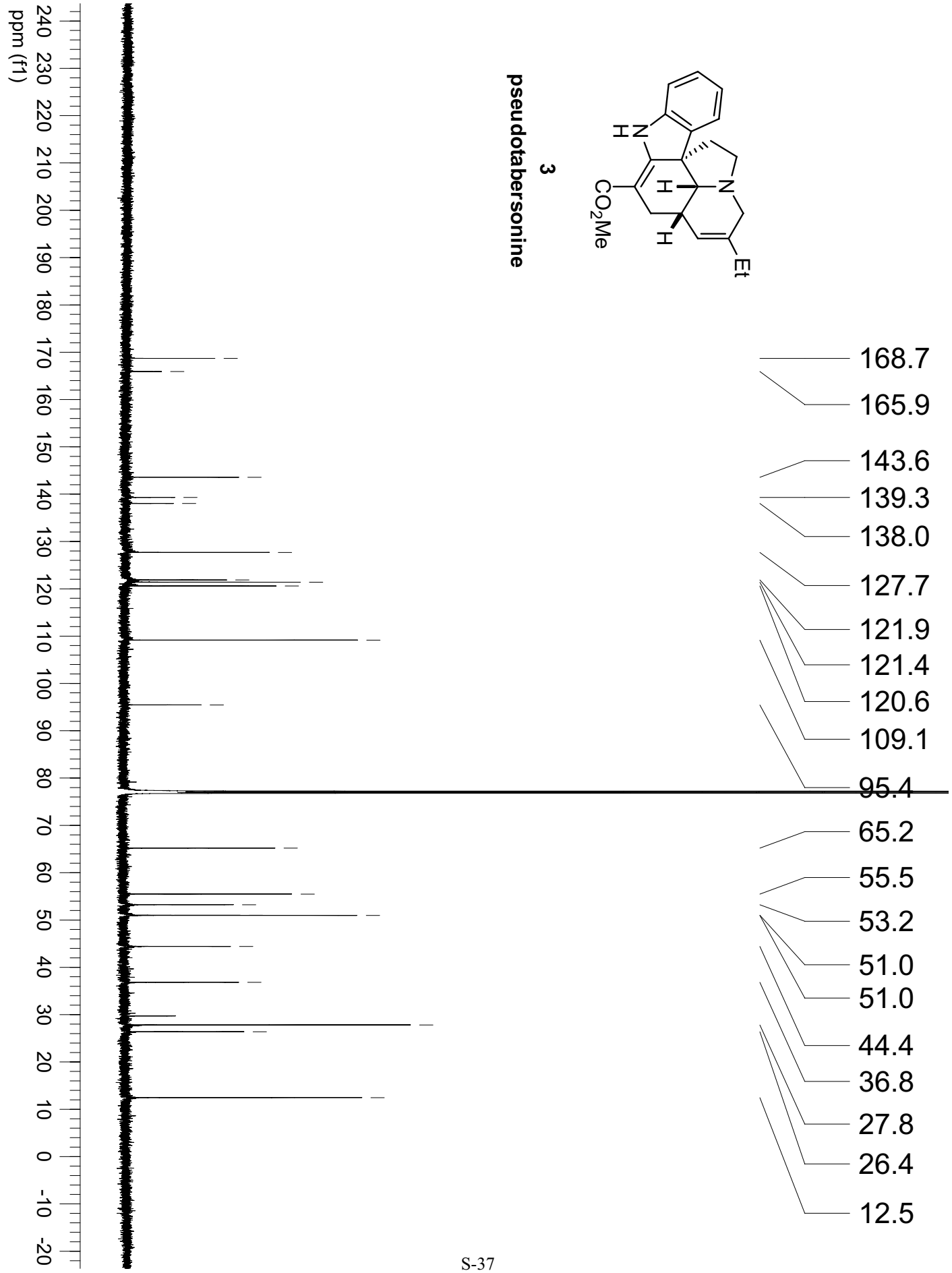


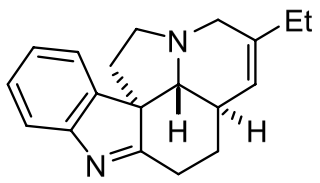
18

240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

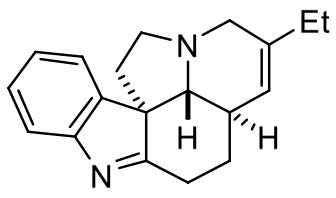
ppm (f1)


Et
N
H
H
N
H
CO2Me
3
pseudotabersonine
1.09
1.07
1.07
1.00
3.11
2.05
1.14
1.15
1.13
3.13
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)


3
pseudotabersonine
CO2Me
Et
ppm (f1)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
168.7
165.9
143.6
139.3
138.0
127.7
121.9
121.4
120.6
109.1
95.4
65.2
55.5
53.2
51.0
51.0
44.4
36.8
27.8
26.4
12.5

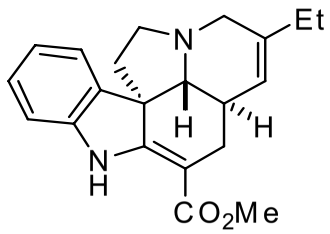


19


Et
N
H
H
N

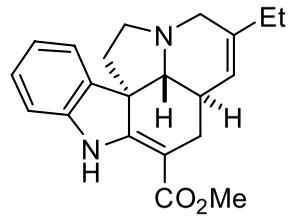
19

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



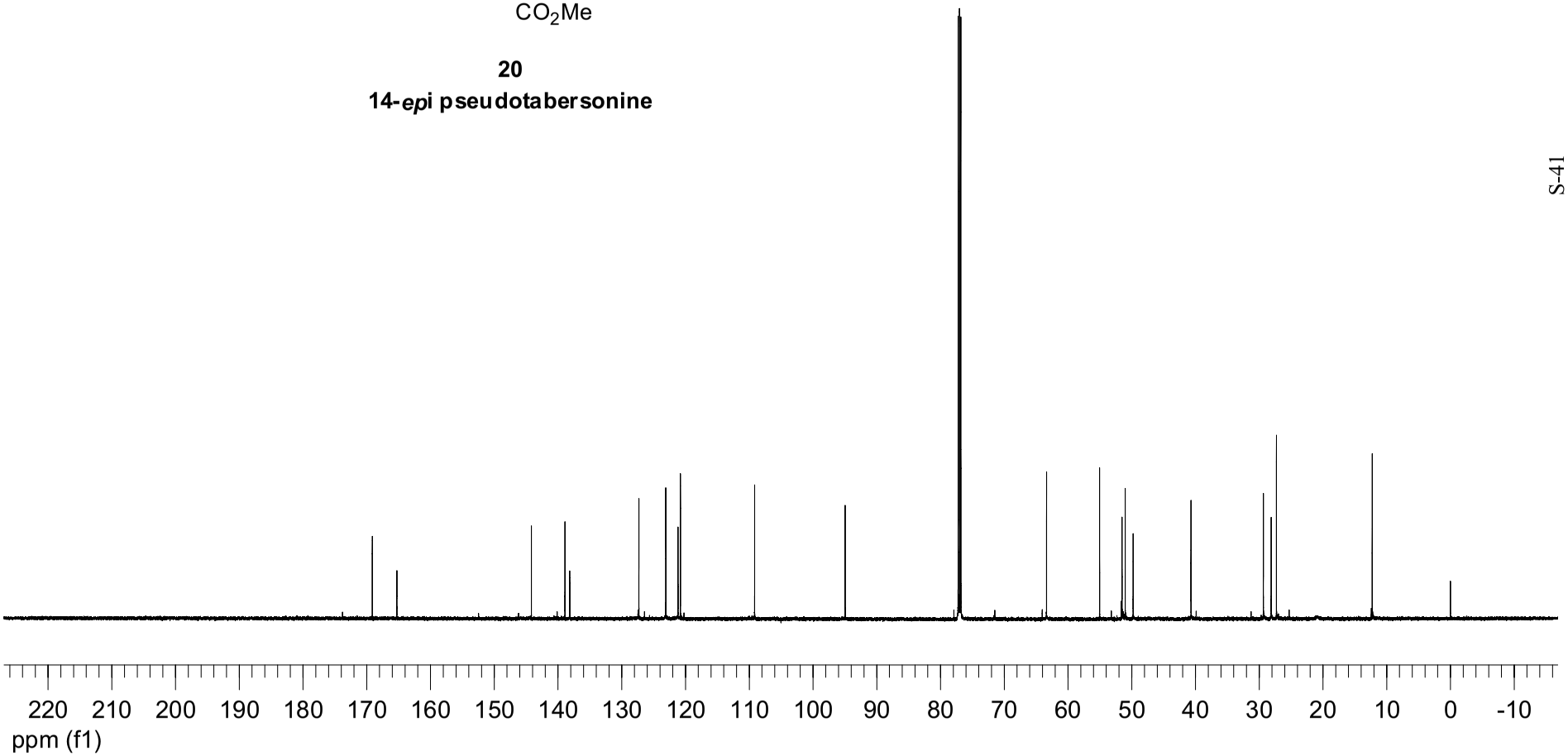
20

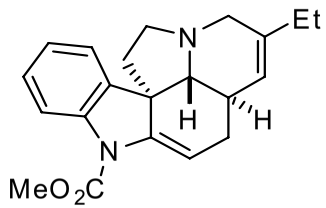
14-*epi* pseudotabersonine



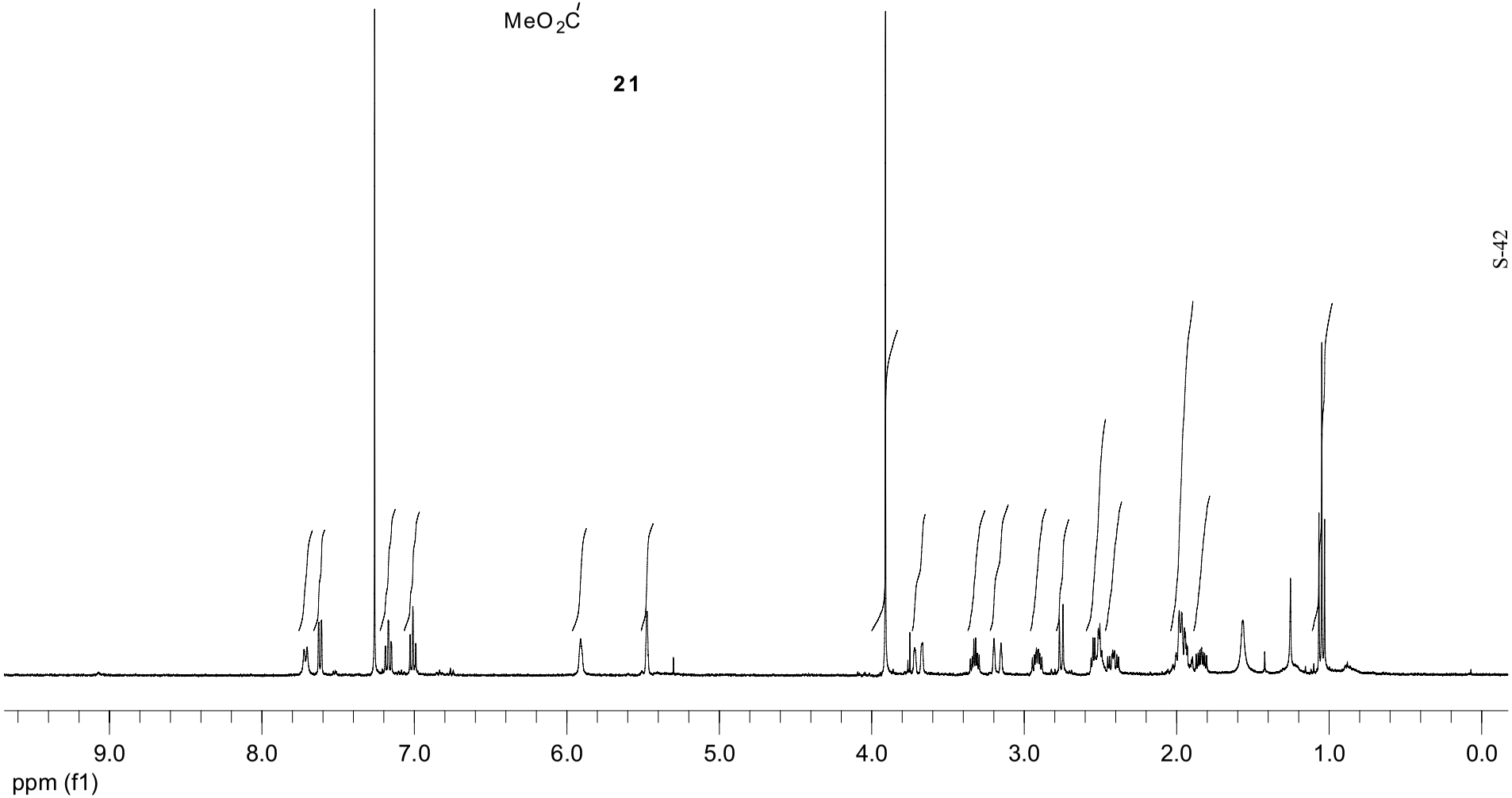
20

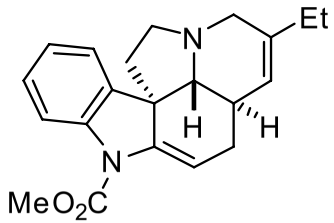
14-*epi* pseudotabersonine





21




Et
N
H
H
N
MeO2C

21

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