SUPPORTING INFORMATION

Bifunctional Thiosquaramide Catalyzed Asymmetric Reduction of Dihydro-β-carbolines and Enantioselective Synthesis of (–)-Coerulescine and (–)-Horsfiline by Oxidative Rearrangement

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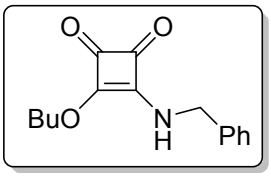
Experimental Section.

General

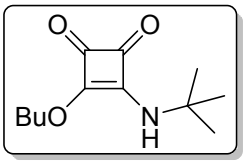
All the solvents were of commercial grade and were purified prior to use when necessary. NMR spectra were measured on Bruker 400 MHz for ^{1}H and 100 MHz for ^{13}C spectra, respectively, and calibrated to either TMS (δ = 0 for ^{1}H) or residual DMSO (δ = 2.50 for ^{1}H), residual $CHCl_3$ (δ = 7.26 for ^{1}H and δ = 77.23 for ^{1}H and δ = 39.51 for ^{13}C). Spin multiplicities are described as s (singlet), br s (broad singlet), d (doublet), dd (double doublet), t (triplet), td (triple doublet), q (quartet), or m (multiplet). Coupling constants are reported in hertz (Hz). TLC analyses were performed with silica gel plates (0.25 mm, E. Merck, 60 F254) using iodine and a UV lamp for visualization. Specific rotations were measured on a Perkin-Elmer 341MC polarimeter. Enantiomeric excesses were determined on a HP-1100 instrument (chiral column; mobile phase: hexane/i-PrOH/diethylamine). Mass spectra were recorded by electrospray ionization mass spectrometry (ESI-MS). HRMS was performed on a Varian QFT-ESI instrument. IR spectra were measured on Bruker FT-IR Equinox 55 and Bruker TENSOR 27 instruments.

3-(Benzylamino)-4-butoxycyclobut-3-ene-1,2-dione (13a).[1]



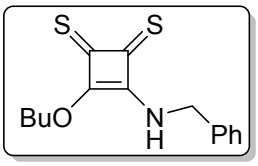
To a stirred solution of dibutylsquarate **12** (500 mg, 2.21 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added benzylamine (0.25 mL, 2.32 mmol, 1.05 equiv) dropwise at 0 °C. The mixture was stirred at room temperature for 16 h. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (60-120 mesh) using CH_2Cl_2 to 10% MeOH in CH_2Cl_2 to afford the desired product **13a** (550 mg, 96%) as a white solid. The product observed as two rotamers in DMSO at room temperature in a ratio of 0.54:0.46 in ^{1}H NMR spectrum. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86 – 0.93 (m, 3H), 1.28 – 1.42 (m, 2H), 0.86 – 0.93 (m, 3H), 1.64 – 1.74 (m, 2H), 4.48 (d, J = 5.6 Hz, 1H), 4.63 (t, J = 6.5 Hz, 2H), 4.69 (d, J = 5.9 Hz, 1H), 7.28 – 7.32 (m, 3H), 7.36 – 7.39 (m, 2H), 9.06 (br s, 0.46H), 9.29 (br s, 0.54H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5, 18.1, 31.5, 46.9, 47.3, 72.5, 127.3, 127.5, 127.5, 128.6, 138.1, 138.4, 172.0, 172.6, 176.9, 177.5, 182.2, 182.5, 189.1, 189.5; IR (KBr): 3214.79, 2954.81, 1813.62, 1714.85, 1641.49, 1307.39, 1058.33, 734.25 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{17}NNaO_3$ m/z 282.1106 $[M + Na]^+$, found 282.0894.

3-Butoxy-4-(*tert*-butylamino)cyclobut-3-ene-1,2-dione (13b).[1]



To a stirred solution of dibutylsquarate **12** (500 mg, 2.21 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added *tert*-butylamine (0.24 mL, 2.32 mmol, 1.05 equiv) dropwise at 0 °C. The mixture was stirred at room temperature for 6 h. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (60-120 mesh) using CH_2Cl_2 to 10% MeOH in CH_2Cl_2 to afford the desired product **13a** (382 mg, 78%) as a white solid. The product observed as two rotamers in DMSO at room temperature in a ratio of 0.56:0.44 in ^{1}H NMR spectrum. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.92 (t, J = 7.3 Hz, 3H), 1.31 (s, 9H), 1.40 (td, J = 14.9, 7.5 Hz, 2H), 1.73 (dt, J = 14.3, 6.5 Hz, 2H), 4.64 (s, 0.88H), 4.71 (s, 1.22H), 8.59 (s, 0.44H), 8.75 (s, 0.56H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 18.2, 29.6, 30.0, 31.5, 52.3, 52.9, 72.2, 72.4, 171.2, 172.9, 175.3, 178.3, 181.8, 182.7, 187.9, 189.9.; IR (KBr): 3143.97, 2937.01, 1796.46, 1622.82, 1351.00, 1192.92 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{19}NO_3$ *m/z* 225.1365 $[M]^+$, found 225.1363.

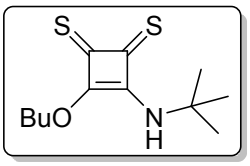
3-(Benzylamino)-4-butoxycyclobut-3-ene-1,2-dithione (14a).[1]



To a stirred solution of **13a** (400 mg, 1.54 mmol, 1.0 equiv) in dry CH_2Cl_2 (10 mL) was added Lawesson's reagent (624 mg, 1.54 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature for 3 h. The solvent evaporated and chromatographed on silica gel column (60-120 mesh) in DCM to afford product **14a** (224 mg, 50%) as an orange solid. The product exists as two rotamers

in DMSO at room temperature. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.90 (m, 3H), 1.27 – 1.83 (m, 4H), 4.58 – 5.21 (m, 4H), 7.29 – 7.41 (m, 5H), 10.20 (t, J = 6.2 Hz, 0.2H), 10.25 (t, J = 6.4 Hz, 0.2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 13.8, 17.9, 31.6, 31.7, 34.6, 45.9, 48.0, 54.8, 55.1, 73.5, 73.5, 113.4, 113.5, 127.5, 127.7, 127.8, 128.6, 128.7, 137.0, 137.2, 172.4, 174.6, 182.8, 183.5, 205.3, 205.4, 217.4, 217.7; IR (KBr): 3233.81, 2956.46, 1692.99, 1518.19, 1290.86, 1020.69 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{18}NOS_2$ m/z 292.0824 $[M + H]^+$, found 292.0827.

Synthesis of 3-(benzylamino)-4-butoxycyclobut-3-ene-1,2-dithione (14b).[1]

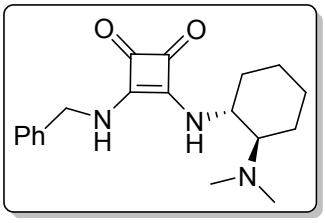


To a stirred solution of **13b** (300 mg, 1.33 mmol, 1.0 equiv) in dry CH_2Cl_2 (10 mL) was added Lawesson's reagent (538 mg, 1.33 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature for 5 h. The solvent evaporated and passed through a silica gel column (60-120 mesh) in DCM to afford product **14b** (307 mg, 90%) as an orange solid. The product exists as two rotamers in DMSO at room temperature in a ratio of 0.86:0.14. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.93 (t, J = 7.3 Hz, 3H), 1.40 (s, 8H), 1.41 – 1.48 (m, 2H), 1.54 (s, 1H), 1.78 – 1.84 (m, 2H), 5.17 (t, J = 6.5 Hz, 0.28H), 5.26 (t, J = 6.3 Hz, 1.72H), 9.45 (s, 0.86H), 9.62 (s, 0.14H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 17.9, 18.1, 29.6, 30.9, 31.7, 54.1, 54.9, 73.5, 173.5, 181.2, 205.0, 218.5; IR (KBr): 3210.90, 3164.61, 2964.05, 1688.67, 1513.85, 1432.85, 1324.86, 1238.08 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{20}NOS_2$ *m/z* 258.0981 [M + H]$^+$, found 258.0983.

(1*R*,2*R*)-*N*1,*N*1-dimethylcyclohexane-1,2-diamine (15).[2]

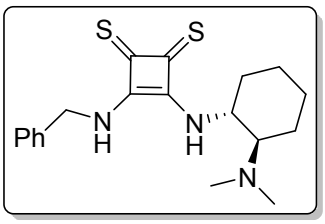
Diamine **15** was prepared as mentioned in the literature.

3-(Benzylamino)-4-(((1*R*,2*R*)-2-(dimethylamino)cyclohexyl)amino)cyclobut-3-ene-1,2-dione (11a).



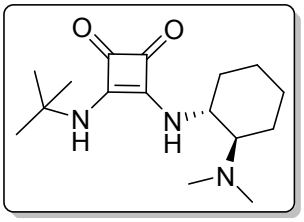
To a stirred solution of **13a** (100 mg, 0.34 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added **15** (48.79 mg, 0.34 mmol, 1.0 equiv) in 2 mL CH_2Cl_2. The reaction mixture was stirred at room temperature for 4 h. The solvent most was evaporated and the residue was washed with ice-cold CH_2Cl_2 to afford the desired product **11a** (90.72 mg, 72%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.16 – 1.23 (m, 4H), 1.51 – 1.92 (m, 3H), 2.06 (br s, 1H), 2.16 (s, 6H), 2.32 (m, 1H), 3.75 (s, 1H), 4.72 (br s, 2H), 7.31 (br s, 1H), 7.36 – 7.38 (m, 5H), 7.84 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.4, 24.3, 24.4, 34.7, 46.8, 54.0, 66.1, 127.4, 127.7, 128.6, 138.9, 167.1, 167.5, 181.9, 182.2; IR (KBr): 3502.88, 3185.49, 2935.23, 1797.61, 1644.48, 1585.70, 1430.16, 1348.69 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{26}N_3O_2$ *m/z* 328.2020 [M + H]$^+$, found 328.2013.

3-(Benzylamino)-4-(((1R,2R)-2-(dimethylamino)cyclohexyl)amino)cyclobut-3-ene-1,2-dithione (11b).[1]



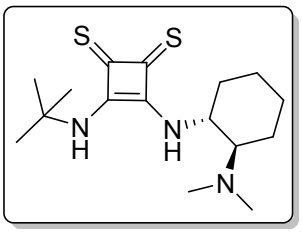
To a stirred solution of **14a** (150 mg, 0.51 mmol, 1.00 equiv.) in CH_2Cl_2 (10 mL) at 0 °C was added **15** (73.2 mg, 0.51 mmol, 1.0 equiv.) in 2 mL CH_2Cl_2. The reaction mixture was at room temperature for 1 h. The solvent most was evaporated and the orange solid was washed with Et_2O to afford the desired product **11b** (120 mg, 65%) as an orange solid. The product exists as two rotamers in DMSO at room temperature in a ratio of 0.90:0.10.^{1}H NMR (400 MHz, DMSO-d_6): δ 1.20 – 1.22 (m, 3H), 1.31 – 1.36 (m, 1H), 1.64 (br s, 1H), 1.74 (br s, 1H), 1.89 (br s, 1H), 2.10 (m, 1H), 2.26 (s, 6H), 2.50 (m, 1H), 4.55 – 4.71 (m, 0.1H), 4.81 (m, 0.9H), 5.10 – 5.39 (m, 1.8H), 5.60 – 5.71 (m, 0.2H), 7.34 – 7.45 (m, 5H), 8.65 (br s, 1H), 8.98 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 22.1, 24.1, 24.3, 24.5, 24.7, 30.6, 35.3, 46.5, 50.9, 54.0, 65.3, 66.4, 128.2, 128.45, 129.2, 137.8, 170.53, 170.9, 203.4, 204.4; IR (KBr): 3176.46, 2933.80, 1713.23, 1571.75, 1450.72, 1280.37 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{26}N_3S_2$ *m/z* 360.1563 $[M + H]^+$, found 360.1572.

3-(*tert*-Butylamino)-4-(((1*R*,2*R*)-2-(dimethylamino)cyclohexyl)amino)cyclobut-3-ene-1,2-dione (11c).[1]



To a stirred solution of **13b** (100 mg, 0.44 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added **15** (63.11 mg, 0.44 mmol, 1.0 equiv) in 2 mL CH_2Cl_2. The reaction mixture was stirred at room temperature for 18 h. The solvent most was evaporated and the residue was washed with ice-cold CH_2Cl_2 to afford the desired product **11c** (110.68 mg, 85%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.28 – 1.12 (m, 4H), 1.38 (s, 9H), 1.63 (m, 1H), 1.72 (m, 1H), 1.81 (m, 1H), 2.03 (m, 1H), 2.17 (s, 6H), 2.30 (m, 1H), 3.79 (m, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.59 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.2, 24.3, 24.4, 30.3, 35.0, 52.1, 54.1, 66.2, 167.5, 167.9, 180.4, 181.9; IR (KBr): 3207.96, 2934.87, 1791.35, 1647.94, 1570.98, 1446.34, 1363.82, 1214.60 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{28}N_3O_2$ *m/z* 294.2176 $[M + H]^+$, found 294.2186.

3-(*tert*-Butylamino)-4-(((1*R*,2*R*)-2-(dimethylamino)cyclohexyl)amino)cyclobut-3-ene-1,2-dithione (11d).[1]



To a stirred solution of **14b** (100 mg, 0.38 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added **15** (55.25 mg, 0.38 mmol, 1.0 equiv) in 2 mL CH_2Cl_2. The reaction mixture was at room temperature for 1 h. The solvent most was evaporated and the orange solid was washed with ice-cold CH_2Cl_2 to afford the desired product **11d** (94.83 mg, 75%) as an orange solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.15 – 1.28 (m, 3H), 1.30 – 1.40 (m, 1H), 1.60 (s, 9H), 1.63 (m, 1H), 1.74 (m, 1H), 1.87 (d, J = 9.8 Hz, 1H), 2.05 (d, J = 10.1 Hz, 1H), 2.23 (s, 6H), 2.50 (s, 1H), 4.92 (m, 1H), 8.71 (s, 0.9H), 8.71 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.0, 24.1, 31.1, 35.3, 53.8, 54.5, 65.6, 170.6, 171.2, 201.8, 204.5; IR (KBr): 3453.44, 3172.72, 2933.85, 1696.12, 1566.08, 1464.04, 1332.43 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{28}N_3S_2$ *m/z* 326.1719 [M + H]$^+$, found 326.1723.

General procedure for the synthesis of DHBCs 17a, 17b and 17c.

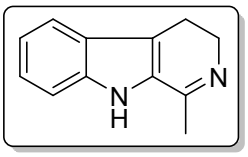
To a stirred solution of tryptamine (**16a**, 1 mmol) in DCM (10 vol) was added triethylamine (2 mmol) followed by corresponding acid chloride (1.1 mmol) at 0 °C. The reaction was stirred for 6 h, diluted with cold water after completion of starting material and extracted twice with DCM. The combined organic phase was washed once with 1N HCl solution and once with cold water before dried over with Na_2SO_4. The solvents were removed under reduced pressure and the obtained amides were reacted directly with $POCl_3$ (3 mmol) in the mixture of dry toluene and acetonitrile (3:1). The reaction mixture was heated to reflux for 2 h, cooled to room temperature, and then concentrated. The residue was basified with cold 20% NaOH solution up to pH = 10 and extracted twice with DCM and dried over Na_2SO_4. After the concentration of solvent, the resulting viscous oil was purified by chromatography (10% MeOH/$CHCl_3$) to afford DHBCs **17a**, **17b** and **17c**.

General procedure for the synthesis of DHBCs 17d, 17e and 17f.

To a stirred solution of tryptamine (**16a**, 1 mmol) and corresponding acids (1.1 mmol) in DCM (10 vol) were added EDC.HCl (1.2 mmol), HOBt (1.2 mmol) followed by

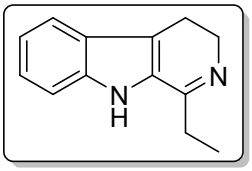
triethylamine (3 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 18 h and diluted with DCM, washed with water and brine solution. Then the organic phase was dried over Na_2SO_4 and concentrated in vacuo to a□ord the corresponding amides which were reacted directly with $POCl_3$ (3 mmol) in the mixture of dry toluene and acetonitrile (3:1). The reaction mixture was heated to reflux for 2 h, cooled to room temperature, and then concentrated. The residue was basified with cold 20% NaOH solution up to pH = 10 and extracted twice with DCM and dried over Na_2SO_4. After the concentration of solvent, the resulting viscous oil was purified by chromatography (10% MeOH/$CHCl_3$) to afford DHBCs **17d, 17e** and **17f.**

1-Methyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17a).



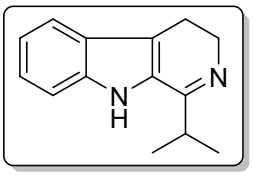
Yellow solid, 317mg, yield 92%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3H), 2.86 (t, *J* = 8.4 Hz, 2H), 3.81 (t, *J* = 8.3 Hz, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.24 (m, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 9.42 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 21.6, 47.2, 112.4, 117.6, 120.3, 120.6, 125.2, 125.4, 128.8, 137.7, 159.4 ppm; FT-IR (KBr): 3417.24, 2933.20, 1620.26, 1548.56, 744.86 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{12}N_2$ *m/z* 184.1000 $[M]^+$, found 184.1004.

1-Ethyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17b).



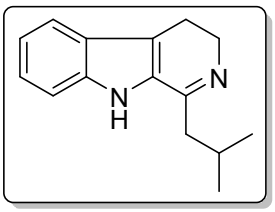
Pale yellow solid, 330 mg, yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, *J* = 7.4 Hz, 3H), 2.74 (q, *J* = 7.4 Hz, 2H), 2.91 (t, *J* = 8.4 Hz, 2H), 3.89 (t, *J* = 8.4 Hz, 2H), 7.10–7.63 (m, 4H), 8.81 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.9, 19.3, 28.4, 48.2, 111.9, 116.8, 120.0, 120.3, 124.4, 125.6, 128.6, 136.6, 161.7 ppm; FT-IR (KBr): 3428.81, 2936.01, 1630.87, 1540.68, 744.39 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{15}N_2$ *m/z* 199.1230 $[M + H]^+$, found 199.1228.

1-Isopropyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17c).



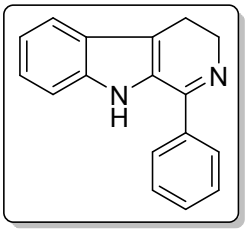
Pale yellow solid, 357 mg, yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.37 (d, *J* = 6.9 Hz, 6H), 2.99 (t, *J* = 8.5 Hz, 2H), 3.56 (dt, *J* = 13.6, 6.8 Hz, 1H), 3.92 (t, *J* = 8.5 Hz, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 7.9, 4.9 Hz, 2H), 10.87 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5, 20.4, 32.9, 45.2, 113.3, 120.2, 120.6, 120.8, 121.15, 124.9, 126.7, 139.5, 170.2 ppm; FT-IR (KBr): 3416.10, 2966.83, 1601.20, 1544.81, 742.12 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{17}N_2$ *m/z* 213.1386 $[M + H]^+$, found 213.1388.

1-Isobutyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17d).



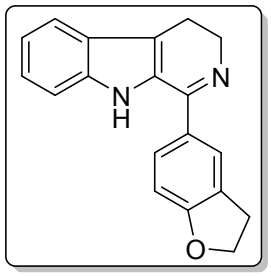
Pale yellow solid, 394 mg, yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.95 (d, *J* = 6.6 Hz, 6H), 2.14 (q, *J* = 13.5, 6.7 Hz, 1H), 2.53 (d, *J* = 7.4 Hz, 2H), 2.84 (t, *J* = 8.4 Hz, 2H), 3.87 (t, *J* = 8.3 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 8.97 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5, 22.8, 27.2, 44.8, 48.2, 112.1, 116.9, 120.0, 120.3, 124.5, 125.6, 129.1, 136.8, 160.9 ppm; FT-IR (KBr): 3419.17, 2925.48, 1619.91, 1546.63, 742.46 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}N_2$ *m/z* 227.1543 $[M + H]^+$, found 227.1553.

1-Phenyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17e).



Pale yellow solid, 419 mg, yield 91%; ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.89 (t, *J* = 8.2 Hz, 2H), 3.92 (t, *J* = 8.2 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.59 – 7.53 (m, 3H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.83 – 7.74 (m, 2H), 11.14 (br s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 19.1, 48.6, 113.0, 116.6, 119.7, 119.8, 123.9, 125.0, 127.7, 128.2, 128.7, 129.9, 137.2, 137.7, 158.8 ppm; FT-IR (KBr): 3419.17, 2933.44, 1616.40, 1534.08, 741.80 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}N_2$ *m/z* 246.1157 $[M]^+$, found 246.1153.

1-(2,3-dihydrobenzofuran-5-yl)-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole (17f).

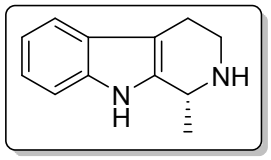


Yellow solid, 459 mg, yield 85%; ^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$): δ 2.90 (t, J = 7.8 Hz, 2H), 3.18 (t, J = 7.8 Hz, 2H), 3.89 (t, J = 8.0 Hz, 2H), 4.55 (t, J = 8.0 Hz, 2H), 6.78 (d, J = 8.0 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.54 (dd, J = 15.4, 8.3 Hz, 2H), 7.63 (s, 1H), 10.14 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4, 29.4, 47.8, 71.9, 109.3, 112.3, 118.8, 120.1, 120.6, 125.0, 125.3, 125.5, 127.7, 128.2, 128.9, 137.2, 159.4, 162.3 ppm; FT-IR (KBr): 3401.82, 2929.34, 1610.27, 1535.06, 742.46 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}N_2O$ *m/z* 289.1335 $[M + H]^+$, found 289.1343.

General procedure for the thiosquaramide 11b catalyzed asymmetric reduction of DHBCs to form chiral THBCs 18a-f.

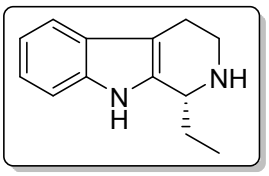
To a solution of DHBC (**17**, 1 mmol) in DCE (10 vol) was added thiosquaramide **11b** (10 mol%) and stirred at room temperature for 1 h. Then the reaction mixture was cooled to 10 ^{o}C and added $PdCl_2$ (15 mol%) followed Et_3SiH (4 mmol), the reaction mixture was stirred at same temperature for 24 h. Upon completion of starting material, the reaction mixture was filtered on celite pad, washed with DCM and evaporated in vacuo. The crude product was purified by preparative TLC using 5% MeOH/DCM to afford the chiral THBCs **18a-f**.

(*R*)-1-Methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18a).[3]



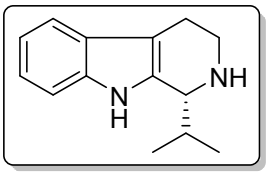
Cream solid, 7.3 mg, yield 73%; $[\alpha]_D$ = +50 (c 1.0, MeOH); Chiral HPLC: 95% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 90/10/0.1, flow rate: 1.0 mL/min, λ = 254 nm, R_t = 6.1 min (major) and 8.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (d, J = 6.7 Hz, 3H), 2.75 – 2.63 (m, 2H), 3.02 – 2.96 (m, 1H), 3.33 – 3.28 (m, 1H), 4.11 (q, J = 6.6 Hz, 1H), 7.10 – 7.02 (m, 2H), 7.24 (d, J = 7.8 Hz, 1H) 7.42 (d, J = 7.6 Hz, 1H), 7.82 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8, 22.8, 42.9, 48.3, 108.6, 110.8, 118.2, 119.5, 121.6, 127.6, 135.7, 137.2 ppm; FT-IR (KBr): 3409.53, 2977.65, 1614.15, 1502.73, 738.75 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{15}N_2$ *m/z* 187.1230 $[M + H]^+$, found 187.1236.

(*R*)-1-Ethyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18b).[3b,4]



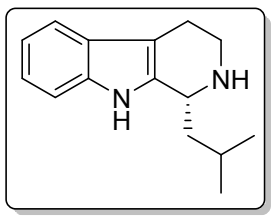
Cream solid, 8.6 mg, yield 85%; $[\alpha]_D$ = +59 (*c* 1.0, MeOH); Chiral HPLC: 92% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 90/10/0.1, flow rate: 1.0 mL/min, λ = 254 nm, R_t = 4.7 min (major) and 7.9 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (t, *J* = 7.4 Hz, 3H), 1.75 – 1.68 (m, 2H), 1.97 – 1.91 (m, 1H), 2.78 – 2.75 (m, 2H), 3.08 – 3.01 (m, 1H), 3.41 – 3.35 (m, 1H), 4.03 – 4.01 (m, 1H), 3.08 – 3.01 (m, 1H), 7.18 – 7.09 (m, 2H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.87 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.3, 22.8, 27.8, 42.7, 54.0, 109.2, 110.8, 118.1, 119.4, 121.5, 127.6, 135.7, 136.3 ppm; FT-IR (KBr): 3409.53, 2929.34, 1621.84, 1590.27, 741.40 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{17}N_2$ *m/z* 201.1386 $[M + H]^+$, found 201.1394.

(*R*)-1-Isopropyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18c).[3b,5]



Off white solid, 8.8 mg, yield 88%; $[\alpha]_D$ = +55.7 (*c* 1.0, MeOH); Chiral HPLC: 93% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 90/10/0.1, flow rate: 1.0 mL/min, λ = 254 nm, R_t = 8.0 min (major) and 11.6 min (minor); ^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$): δ 0.81 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 6.5 Hz, 3H), 2.30 – 2.33 (m, 1H), 2.68 – 2.81 (m, 2H), 2.94 – 3.00 (m, 1H), 3.41 (d, *J* = 12.3 Hz, 1H), 3.96 – 4.00 (m, 1H), 6.93 – 7.09 (m, 2H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 9.30 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.0, 19.1, 21.6, 31.5, 42.4, 57.8, 109.9, 110.7, 118.1, 119.5, 121.8, 127.2, 133.5, 135.8 ppm; FT-IR (KBr): 3415.31, 2961.74, 1627.63, 1566.40, 736.09 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}N_2$ *m/z* 215.1543 $[M + H]^+$, found 215.1547.

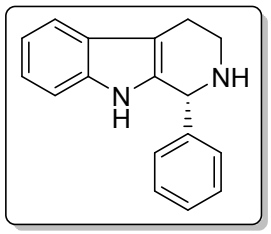
(*R*)-1-Isobutyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18d).[3b]



Cream solid, 6.5 mg, yield 65%; $[\alpha]_D$ = +33.8 (*c* 1.0, MeOH), Chiral HPLC: 86% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 95/5/0.1, flow rate: 0.8 mL/min, λ = 254 nm, R_t = 6.4 min (major) and 9.0 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 – 1.07 (m, 6H), 1.59 – 1.64 (m, 3H), 1.97 – 2.02 (m, 1H), 2.71 – 2.81 (m,

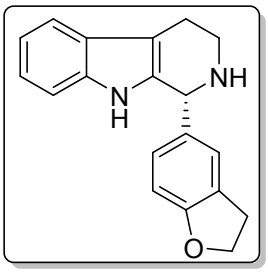
2H), 3.01 – 3.07 (m, 1H), 3.35 – 3.38 (m, 1H), 4.12 (br s, 1H), 7.09 – 7.17 (m, 2H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.80 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 22.8, 23.9, 24.7, 42.5, 44.5, 50.6, 108.9, 110.7, 118.1, 119.4, 121.5, 127.7, 135.7, 136.8 ppm; FT-IR (KBr): 3415.31, 2927.41, 1449.68, 1240.00, 736.09 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}N_2$ *m/z* 229.1699 $[M + H]^+$, found 229.1703.

(*R*)-1-Phenyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18e).[3]



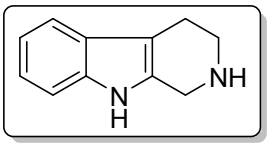
Cream solid, 7.3 mg, yield 73%; $[\alpha]_D$ = –3.8 (*c* 1.0, $CHCl_3$); Chiral HPLC: 91% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 85/15/0.1, flow rate: 1.0 mL/min, λ = 254 nm, R_t = 2.9 min (minor) and 4.5 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (s, 1H), 2.81 – 2.85 (m, 1H), 2.90 – 2.97 (m, 1H), 3.10 – 3.17 (m, 1H), 3.35 – 3.38 (m, 1H), 5.15 (s, 1H), 7.10 – 7.20 (m, 3H), 7.31 – 7.36 (m, 5H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.67 (br s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6, 42.9, 58.1, 110.3, 110.9, 118.3, 119.5, 121.8, 127.5, 128.3, 128.6, 128.9, 134.5, 136.0, 141.8 ppm; FT-IR (KBr): 3411.46, 2935.21, 1561.09, 1454.06, 742.46 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}N_2$ *m/z* 249.1386 $[M + H]^+$, found 249.1392.

(*R*)-1-(2,3-dihydrobenzofuran-5-yl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (18f).[3b,6]



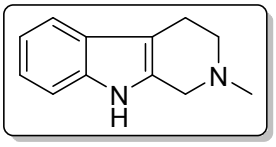
Cream solid, 7.0 mg, yield 70%; $[\alpha]_D$ = +20.3 (*c* 1.0, MeOH); Chiral HPLC: 96% *ee*, Chiralcel OD-H, n-hexane/2-propanol/diethylamine = 85/15/0.1, flow rate: 1.0 mL/min, λ = 254 nm, R_t = 4.9 min (minor) and 6.9 min (major); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.79 – 2.83 (m, 1H), 2.89 – 2.96 (m, 1H), 3.10 – 3.14 (m, 3H), 3.35 – 3.38 (m, 1H), 4.55 (t, *J* = 8.7 Hz, 2H), 5.08 (s, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 7.09 – 7.17 (m, 3H), 7.21 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.72 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6, 29.7, 43.0, 57.8, 71.5, 109.2, 110.1, 110.9, 118.3, 119.4, 121.7, 125.1, 127.5, 127.8, 128.5, 133.9, 135.0, 135.9, 160.1 ppm; FT-IR (KBr): 3394.10, 2916.64, 1690.70, 1490.70, 142.46 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}N_2O$ *m/z* 291.1492 $[M + H]^+$, found 291.1498.

2,3,4,9-Tetrahydro-1*H*-pyrido[3,4-*b*]indole (19a).[7]



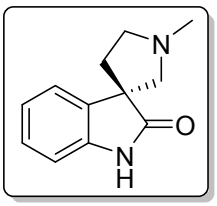
To a stirred solution of tryptamine (**16a**, 1.0 g, 6.2 mmol, 1 equiv.) in AcOH/MeOH (10/1, 10 mL) was added polyformaldehyde (0.20 g, 6.8 mmol, 1.1 equiv.). The reaction mixture was then heated to 80 °C for 1 h and cooled to room temperature and basified to pH 9−10 using aqueous ammonia solution. The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give the desired product (990 mg, 93%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 2.74 (t, J = 5.5 Hz, 2H), 3.17 (t, J = 5.6 Hz, 2H), 4.02 (s, 2H), 7.11 – 6.99 (m, 2H), 7.32 – 7.28 (m, 1H), 7.44 (d, J = 7.5 Hz, 1H), 9.35 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 22.4, 43.2, 43.9, 107.7, 110.8, 117.5, 118.7, 120.8, 127.4, 133.2, 135.8 ppm; IR (KBr): 3397.52, 3298.17, 2922.40, 1584.24, 1449.13, 1238.27 cm^{-1}; HRMS (ESI) cald for $C_{11}H_{13}N_2$ *m/z* 173.1073 $[M + H]^+$, found 173.1078.

2-Mmethyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (20a).[8]



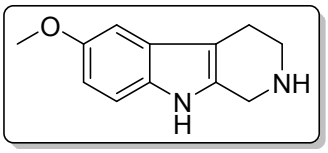
To a stirred solution of tetrahydro-β-carboline **19a** (0.50 g, 2.9 mmol, 1 equiv.) in MeOH (10 mL) was added $NaCNBH_3$ (0.36 g, 5.8 mmol, 2 equiv.) and treated with 3.2 mL of formaldehyde solution (27% in water). The reaction mixture was stirred for 2 h and added 2N HCl (50 mL) then stirred for 15 min. The reaction mixture was basified with concentrated NaOH solution (pH = 11). The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give crude product, which was purified by silica gel column chromatography using CH_2Cl_2/MeOH (10:1) to obtain desire product **20a** (481 mg, 89%) as off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 2.49 (s, 3H), 2.82 – 2.77 (m, 4H), 7.08 – 6.99 (m, 2H), 3.58 (s, 2H), 7.28 (d, J = 7.3 Hz, 1H), 7.42 (d, J = 7.6 Hz, 1H), 9.69 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 21.5, 45.7, 52.4, 53.0, 106.9, 110.8, 117.5, 118.5, 120.6, 127.0, 132.4, 136.1 ppm; IR (KBr): 3138.73, 2940.43, 1625.41, 1451.65, 1248.79, 1167.22 cm^{-1}; HRMS (ESI): cald for $C_{12}H_{15}N_2$ *m/z* 187.1230 $[M + H]^+$, found 187.1235.

(–)-Coerulescine (5).[9]



To a stirred solution of **20a** (30 mg, 0.16 mmol, 1.0 equiv) in mixture of THF/water/AcOH (1:1:1, 0.6 mL) was added thiosquaramide **11b** (5.7 mg, 10 mol%) and stirred for 10 min. Then the reaction mixture was cooled to 0 °C and added NBS (28.7 mg, 0.16 mmol, 1 equiv.). The reaction mixture was then stirred for 20 min at 0 °C. After complete consumption of starting material, the reaction mixture was basified with cold saturated $NaHCO_3$ solution. The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give crude product, which was purified by silica gel column chromatography using CH_2Cl_2/MeOH/TEA (10:1:0.5) to obtain desire product (27.6 mg, 85%) as colorless thick liquid. $[\alpha]^{25}_D$ = –1.37 (*c* = 0.4, MeOH); Chiral HPLC: 98% *ee*, Chiralcel OD-H, hexane/*i*PrOH 95/5, flow rate 1 mL/min; λ = 254 nm, Rt = 2.7 (major) and 3.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.14 – 2.07 (m, 1H), 2.44 – 2.39 (m, 1H), 2.47 (s, 3H), 2.92 – 2.78 (m, 3H), 3.04 – 2.98 (m, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 9.20 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 38.0, 41.9, 53.8, 56.9, 66.5, 109.7, 122.8, 123.3, 128.0, 136.3, 140.5, 183.4 ppm; IR (KBr): 3137.01, 2932.14, 2778.87, 1715.99, 1616.97, 1470.48, 1345.05 cm^{-1}; HRMS (ESI): cald for $C_{12}H_{15}N_2O$ *m/z* 203.1179 $[M + H]^+$, found: 203.1185.

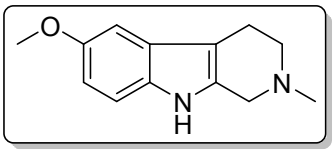
6-Methoxy-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (19b).[7]



To a stirred solution of 5-methoxytryptamine (**16b**, 1.0 g, 5.2 mmol, 1 equiv.) in AcOH/MeOH (10/1, 10 mL) was added polyformaldehyde (189 mg, 6.3 mmol, 1.2 equiv.). The reaction mixture was then heated to 80 °C for 1 h and cooled to room temperature and basified to pH 9−10 using aqueous ammonia solution. The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give crude product, which was purified by silica gel column chromatography using CH_2Cl_2/MeOH (10:1) to obtain desire product **19b** (797 mg, 75%)

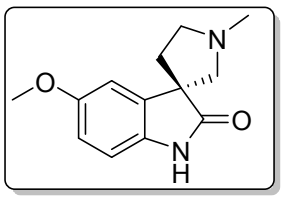
as a pale yellow solid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 2.55 (t, J = 5.6 Hz, 2H), 2.96 (t, J = 5.6 Hz, 2H), 3.73 (s, 3H), 3.82 (s, 2H), 6.62 (dd, J = 8.7, 2.5 Hz, 1H), 6.84 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 8.6 Hz, 1H), 10.43 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO–d_6): δ 22.1, 42.6, 43.34, 55.2, 99.5, 106.7, 109.5, 111.1, 127.5, 130.4, 134.9, 152.8 ppm; IR (KBr): 3290.94, 3152.20, 2746.74, 1702.47, 1592.25, 1450.71, 1322.48, 1218.88 cm^{-1}; HRMS (ESI): cald for $C_{12}H_{15}N_2O$ *m/z* 203.1179 $[M + H]^+$, found 203.1189.

6-Methoxy-2-methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (20b).[8]



To a stirred solution of tetrahydro-β-carboline **19b** (0.50 g, 2.4 mmol, 1 equiv.) in MeOH (10 mL) was added $NaCNBH_3$ (0.30 g, 4.9 mmol, 2 equiv.) and treated with 3.2 mL of formaldehyde solution (27% in water). The reaction mixture was stirred for 2 h and added 2N HCl (50 mL) then stirred for 15 min. The reaction mixture was basified with concentrated NaOH solution (pH = 11). The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give crude product, which was purified by silica gel column chromatography using CH_2Cl_2/MeOH (10:1) to obtain desire product (491 mg, 92%) as pale yellow solid. ^{1}H NMR (400 MHz, DMSO–d_6): δ 2.39 (s, 3H), 2.66 (s, 4H), 3.50 (s, 2H), 3.73 (s, 3H), 6.64 (dd, J = 8.7, 2.4 Hz, 1H), 6.85 (d, J = 2.3 Hz, 1H), 7.15 (d, J = 8.7 Hz, 1H), 10.51 (s, 1H) ppm; ^{13}C NMR (100 MHz, DMSO–d_6): δ 21.3, 45.4, 52.1, 52.6, 55.3, 99.7, 105.9, 109.7, 111.3, 127.0, 130.8, 133.6, 152.9 ppm; IR (KBr): 3140.10, 2787.63, 1589.47, 1485.34, 1377.25, 1221.25 cm^{-1}; HRMS (ESI): cald for $C_{13}H_{17}N_2O$ m/z 217.1335 $[M + H]^+$, found 217.1337.

(–)-Horsfiline (6).[9]



To a stirred solution of **20b** (30 mg, 0.13 mmol, 1.0 equiv) in mixture of THF/water/AcOH (1:1:1, 0.6 mL) was added thiosquaramide **11** (4.9 mg, 10 mol%) and stirred for 10 min. Then the reaction mixture was cooled to 0 ^{o}C and added NBS (24.7 mg, 0.13 mmol, 1 equiv.). The reaction mixture was then stirred for 20 min at 0 ^{o}C. After complete consumption of starting material, the reaction mixture was basified with cold

saturated $NaHCO_3$ solution. The basic solution was extracted with CH_2Cl_2 and the combined organic phases were washed with brine solution, dried over with Na_2SO_4, filtered, and concentrated to give crude product, which was purified by silica gel column chromatography using CH_2Cl_2/MeOH/TEA (10:1:0.5) to obtain desire product (29.0 mg, 90%) as white solid. $[\alpha]^{25}_D$ = –5.01 (*c* = 0.8, MeOH); Chiral HPLC: 93.0% *ee*, Chiralcel OD-H, hexane/*i*PrOH 95/5, flow rate 1 mL/min; λ = 254 nm, Rt = 4.4 (major) and 6.2 (minor); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.12 – 2.03 (m, 1H), 2.44 – 2.37 (m, 1H), 2.45 (s, 3H), 2.74 (q, *J* = 16.3, 1H), 2.89 – 2.83 (m, 2H), 3.04 – 2.99 (m, 1H), 3.80 (s, 3H), 6.77 – 6.71 (m, 2H), 7.04 (s, 1H), 7.42 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 38.1, 41.9, 54.3, 56.9, 56.8, 66.4, 110.0, 110.4, 112.5, 133.7, 137.7. 183.2, 156.2 ppm; IR (KBr): 3166.37, 2935.55, 2782.39, 1701.84, 1601.31, 1479.17, 1318.78, 1206.04 cm^{-1}; HRMS (ESI): cald for $C_{13}H_{17}N_2O_2$ *m/*z 233.1285 $[M + H]^+$, found: 233.1288.

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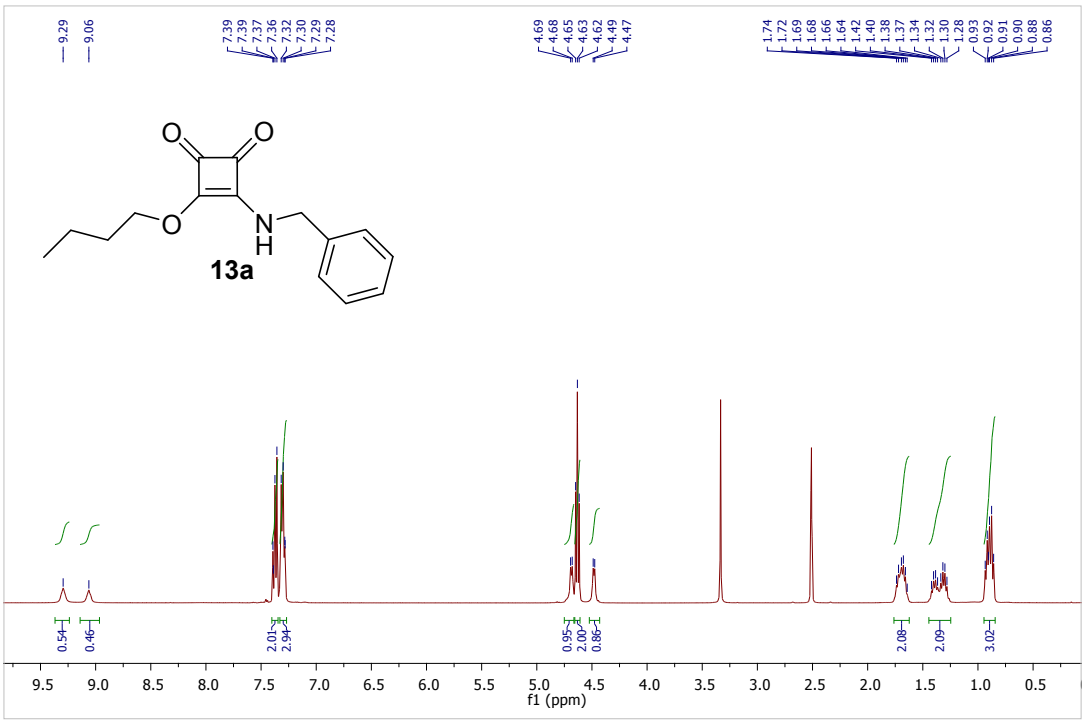
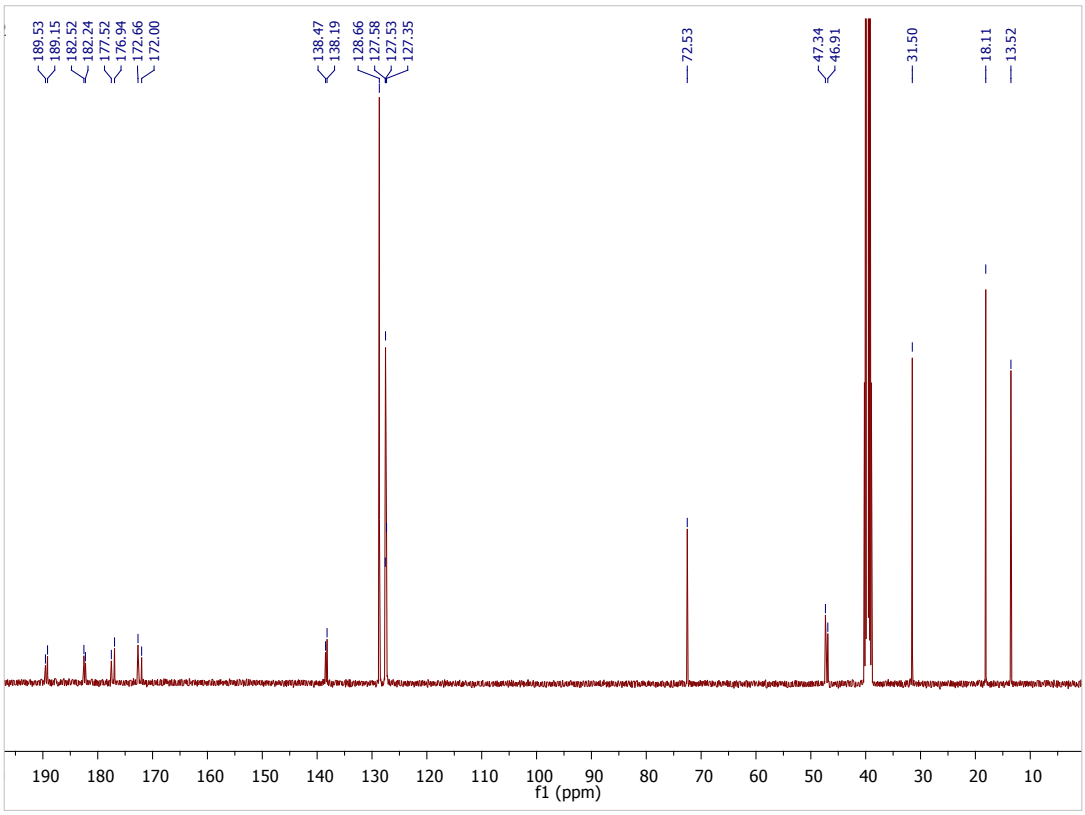
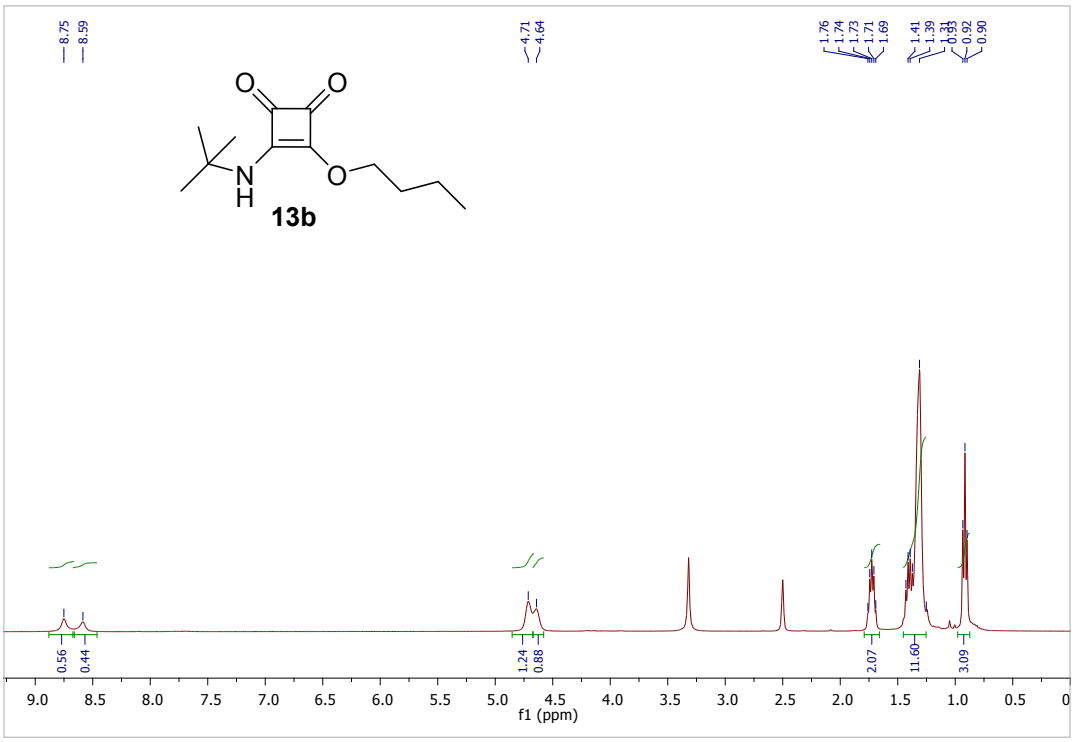


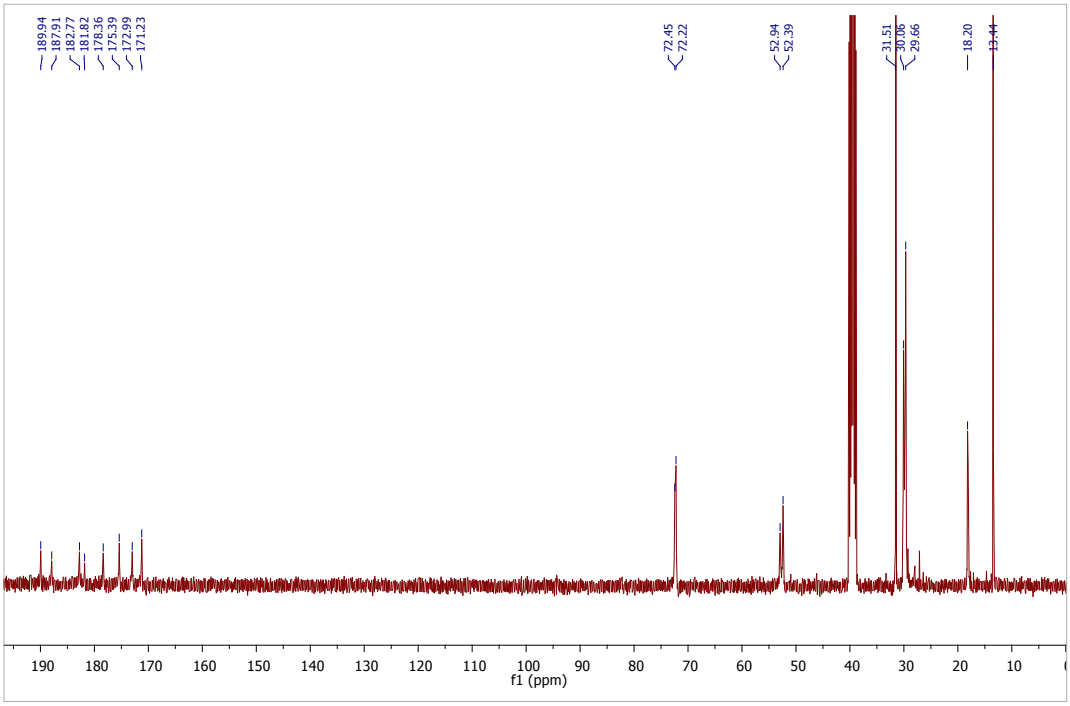
^{1}H NMR (400 MHz, DMSO-d_6) for compound **13a**.



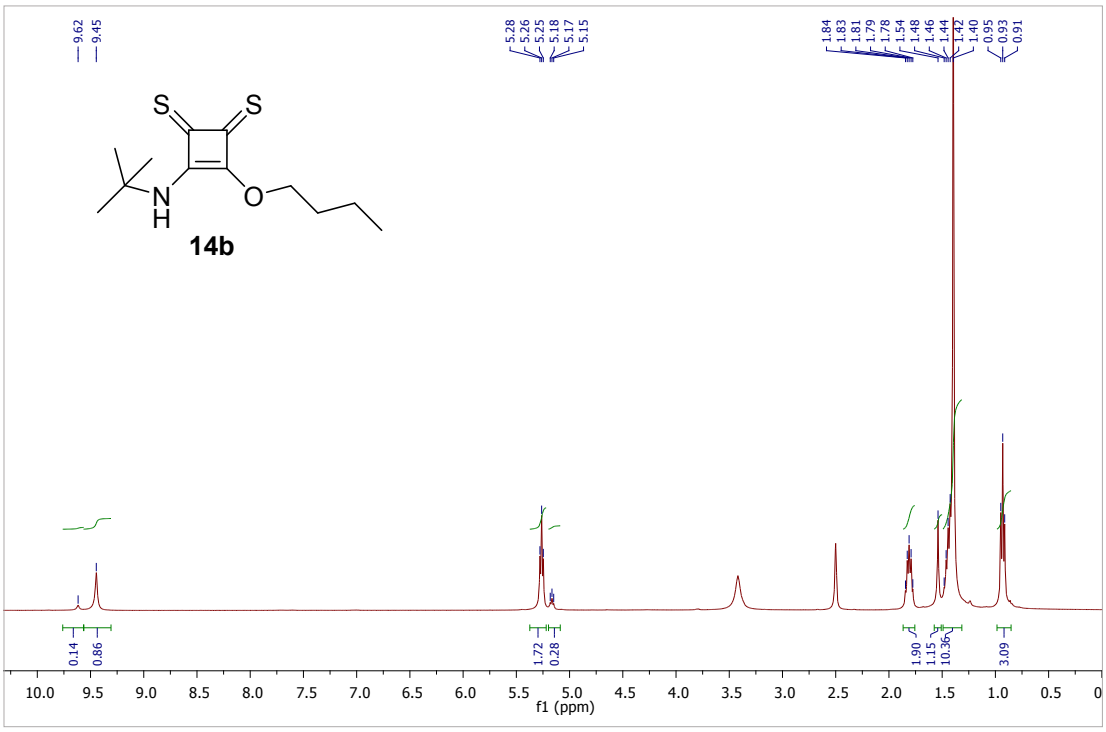
^{13}C NMR (100 MHz, DMSO-d_6) for compound **13a**.



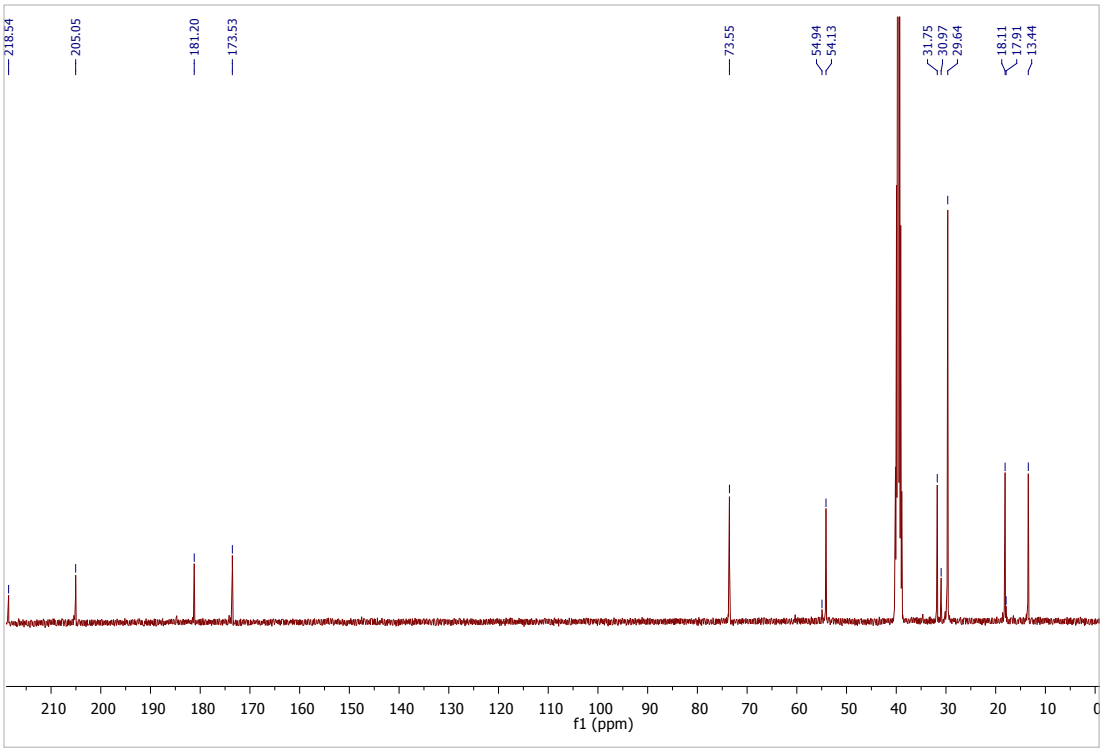
^{1}H NMR (400 MHz, DMSO-d_6) for compound **13b**.



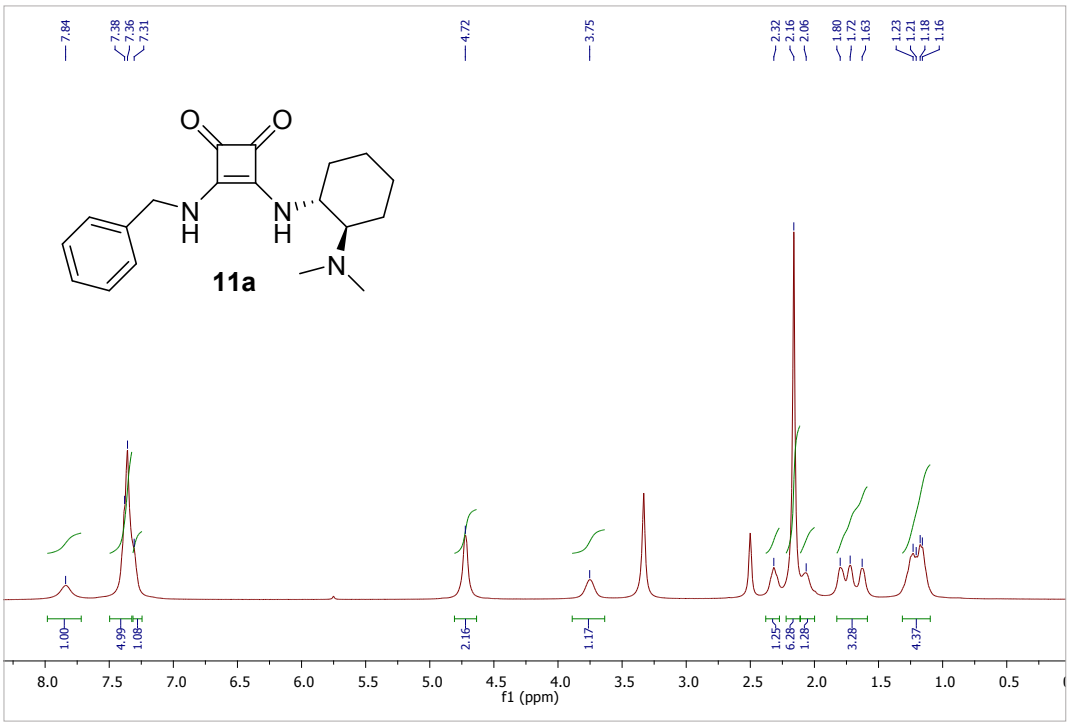
^{13}C NMR (100 MHz, DMSO-d_6) for compound **13b**.



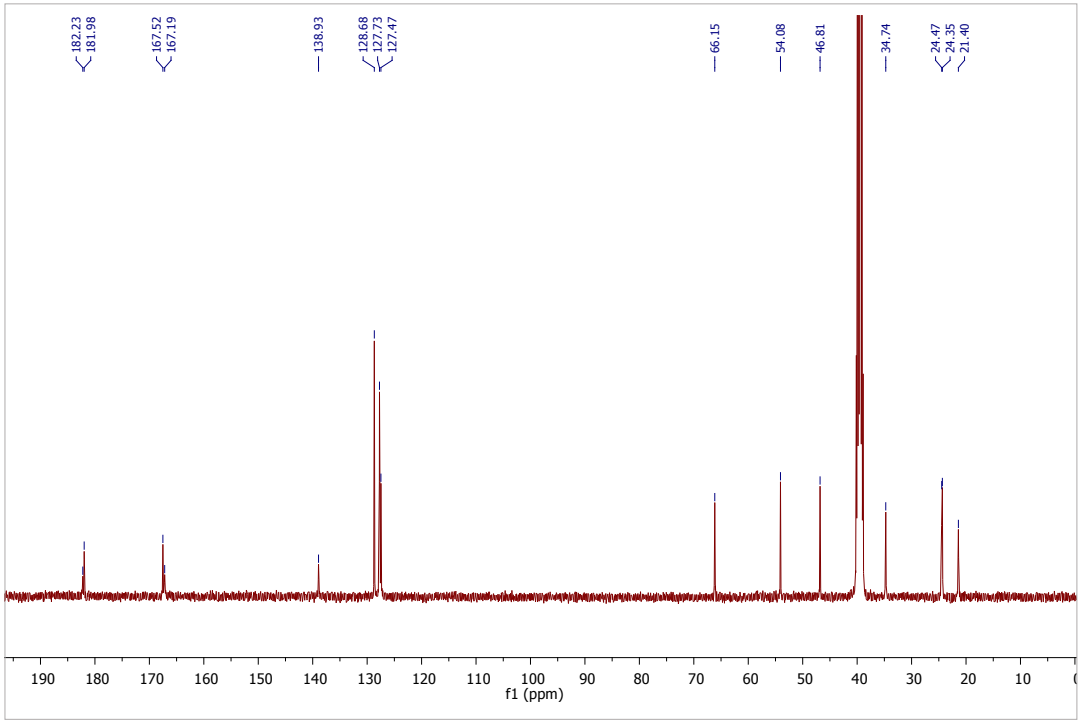
^{1}H NMR (400 MHz, DMSO-d_6) for compound **14b**.



^{13}C NMR (100 MHz, DMSO-d_6) for compound **14b**.



^{1}H NMR (400 MHz, DMSO-d_6) for compound **11a**.



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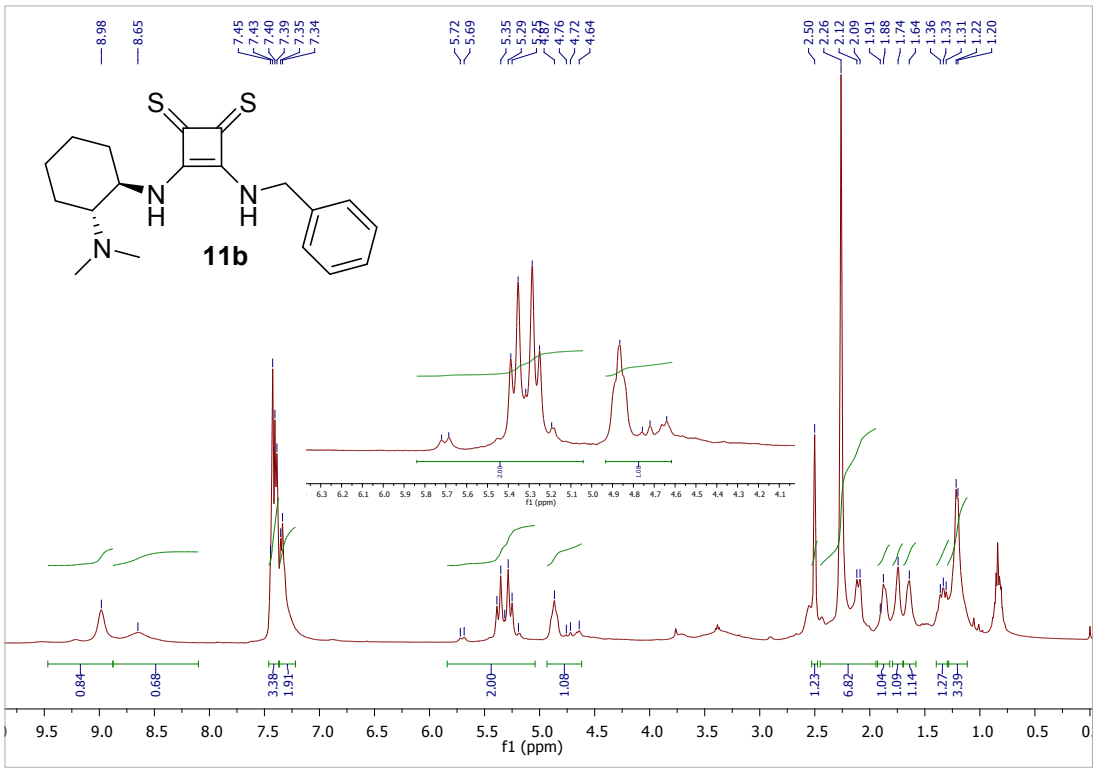
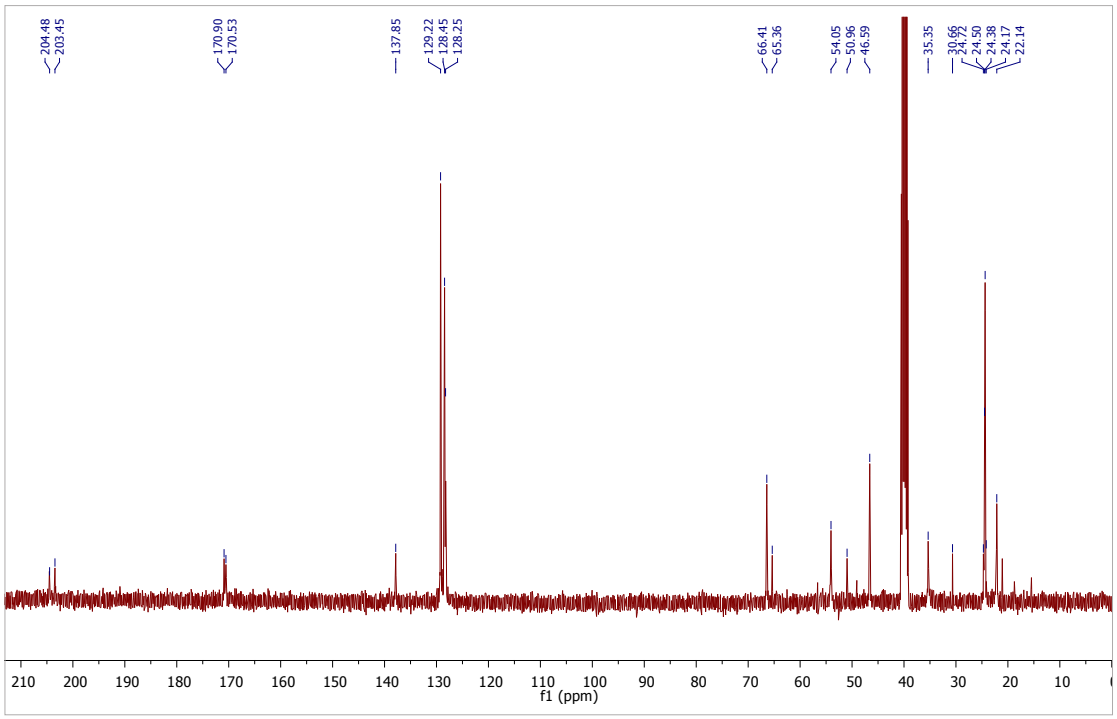
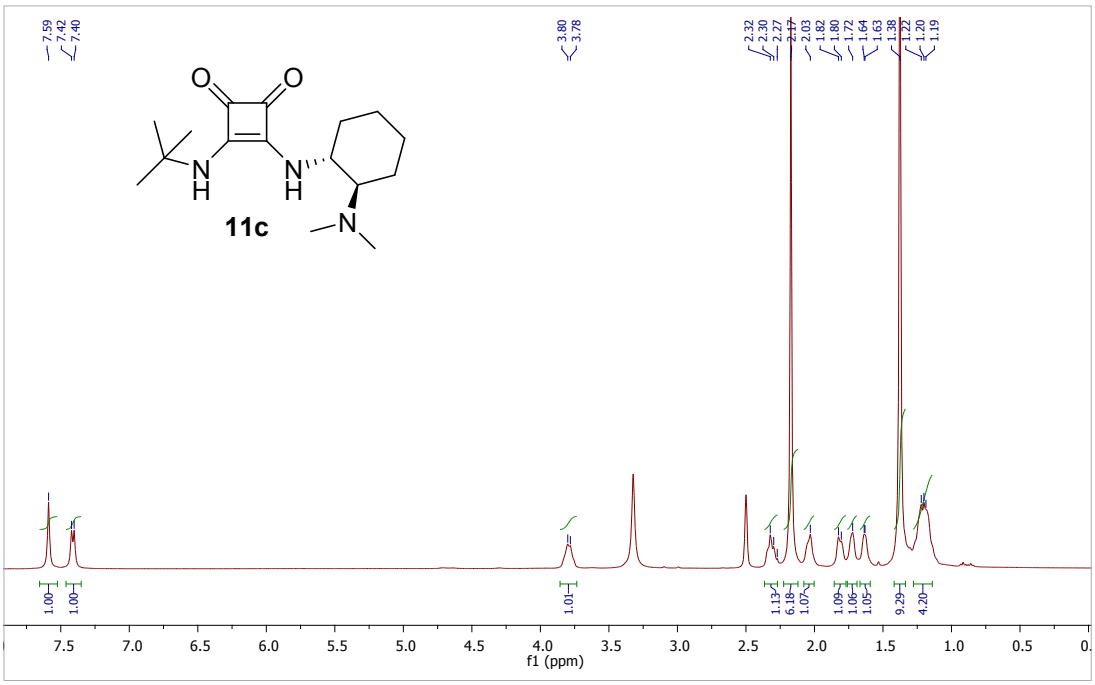


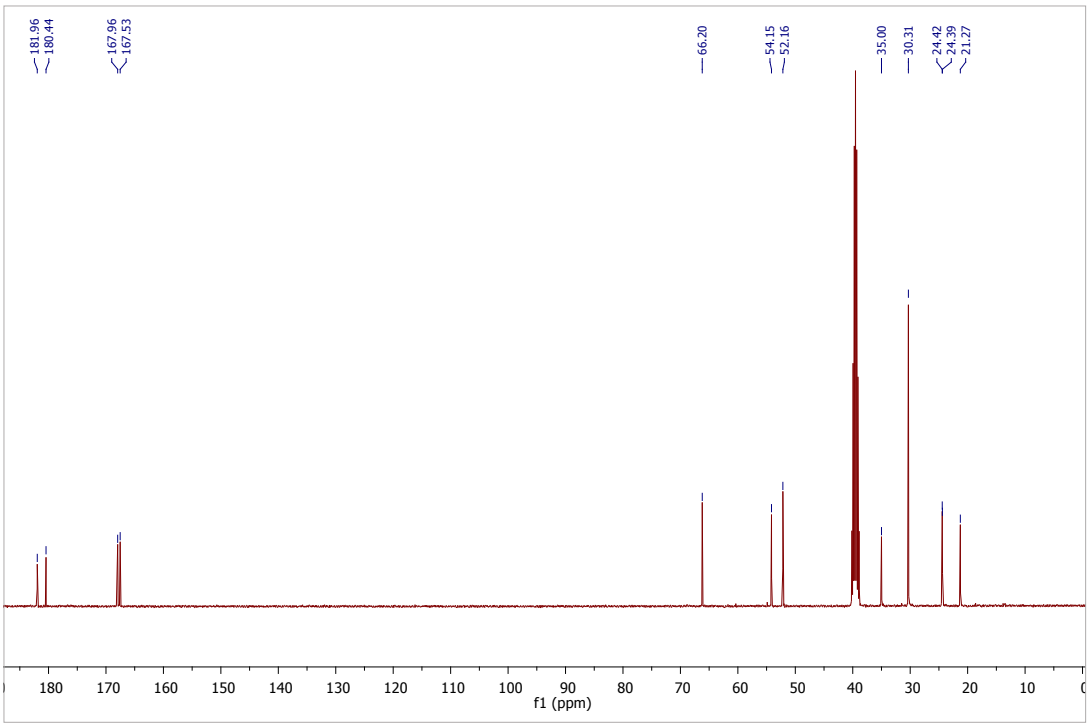
^{1}H NMR (400 MHz, DMSO-d_6) for compound **11b**.



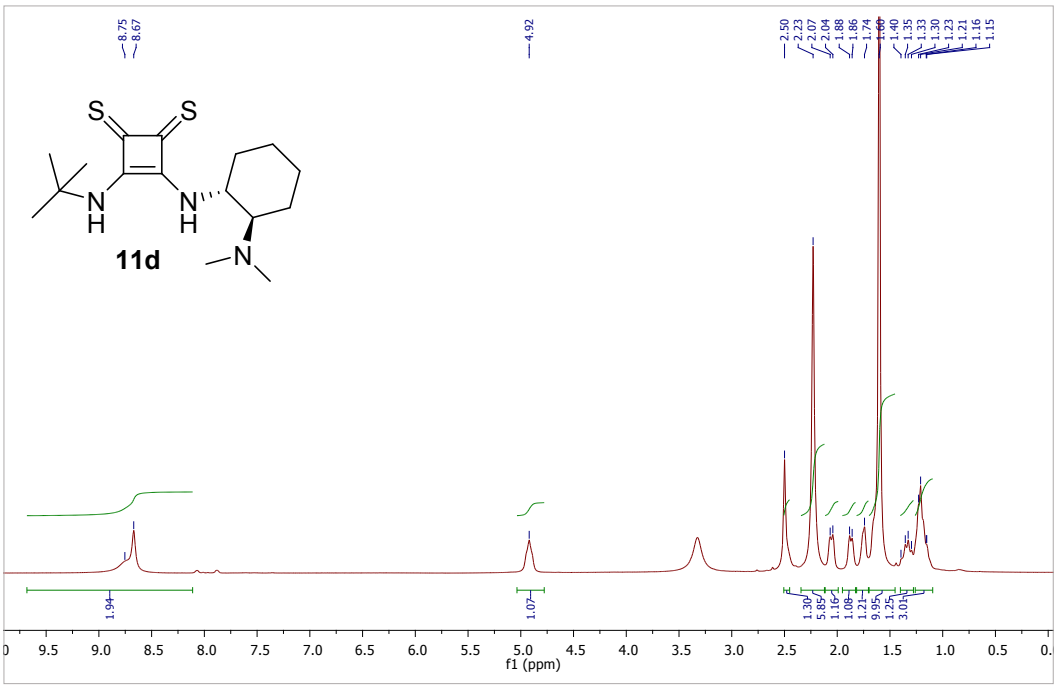
^{13}C NMR (100 MHz, DMSO-d_6) for compound **11b**.



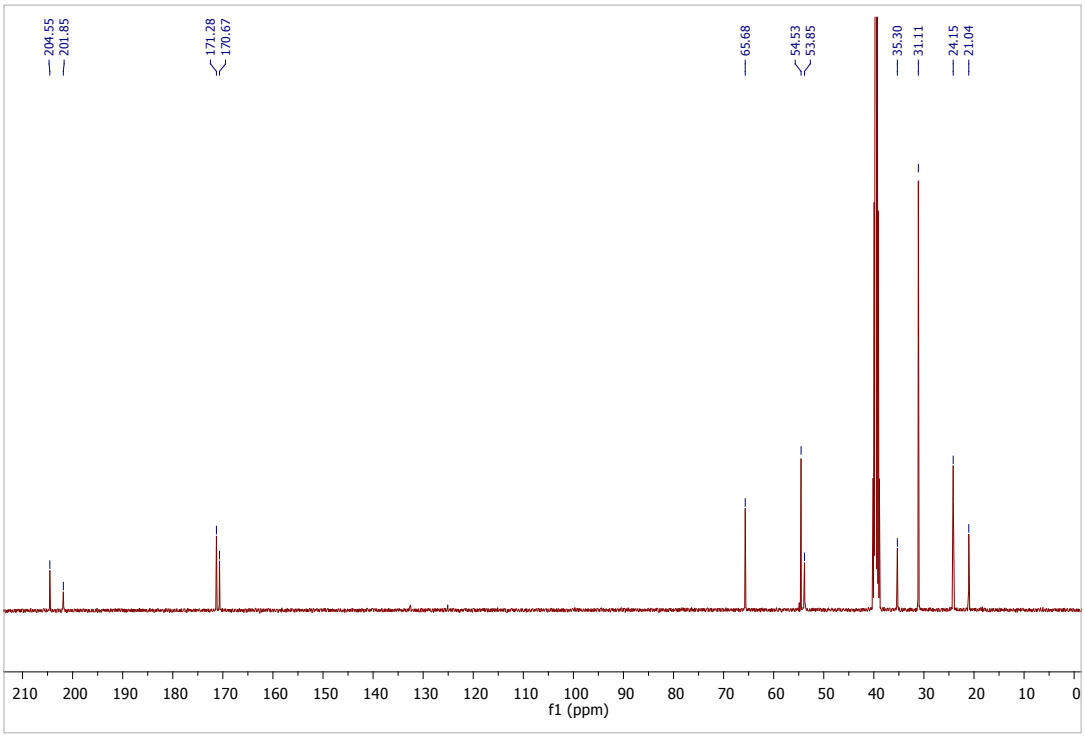
^{1}H NMR (400 MHz, DMSO-d_6) for compound **11c**.



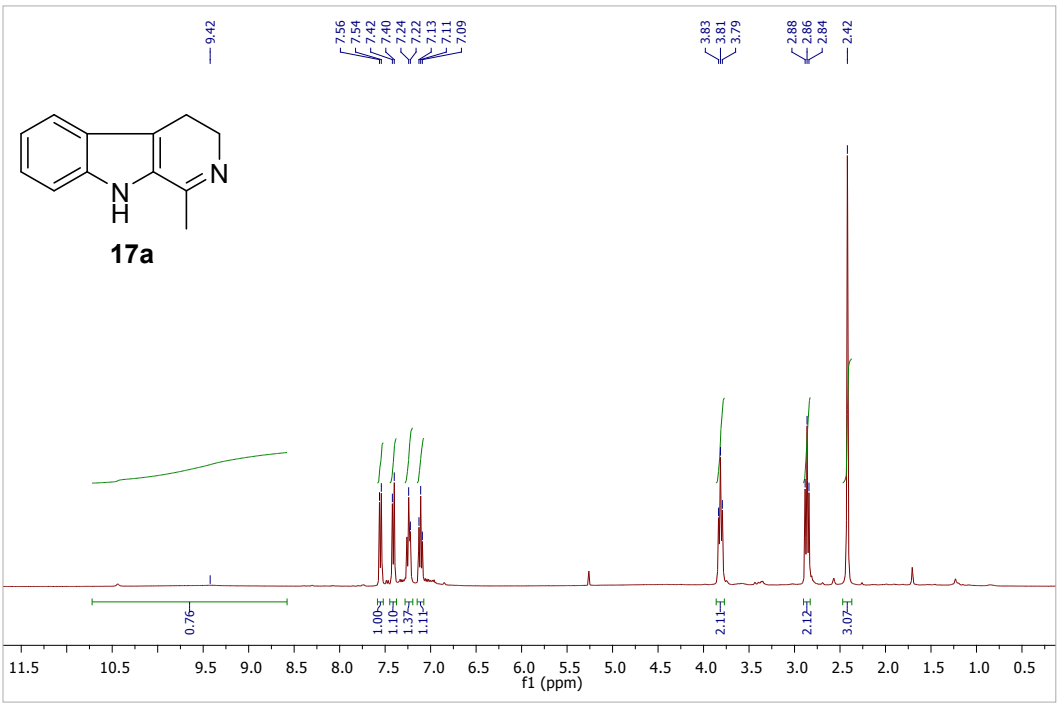
^{13}C NMR (100 MHz, DMSO-d_6) for compound **11c**.



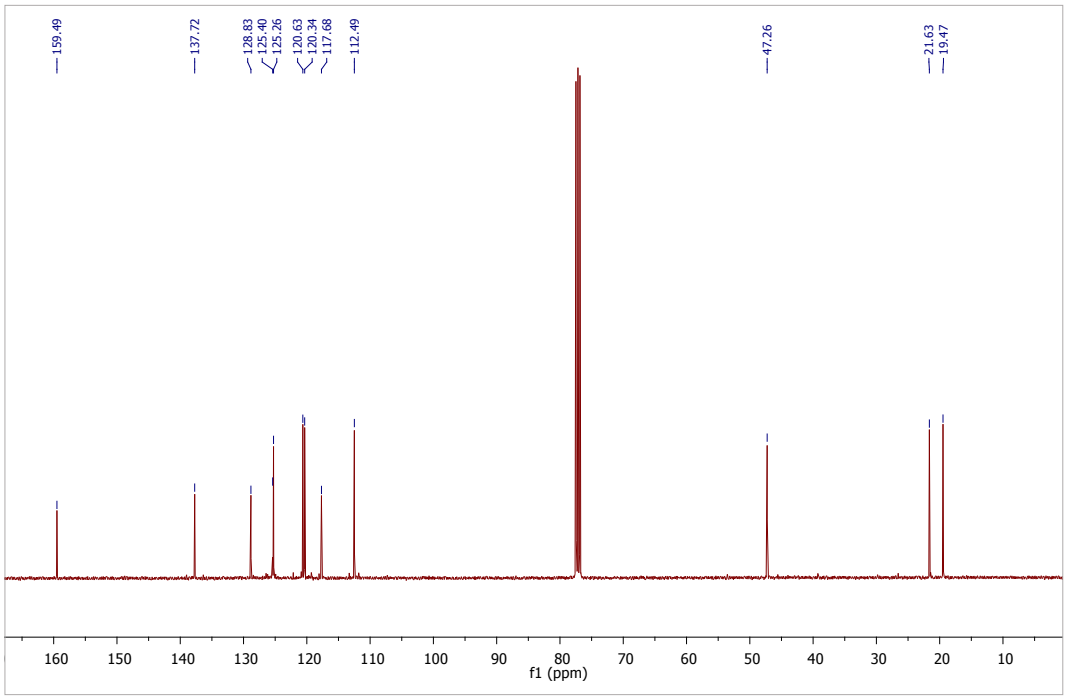
^{1}H NMR (400 MHz, DMSO-d_6) for compound **11d**.



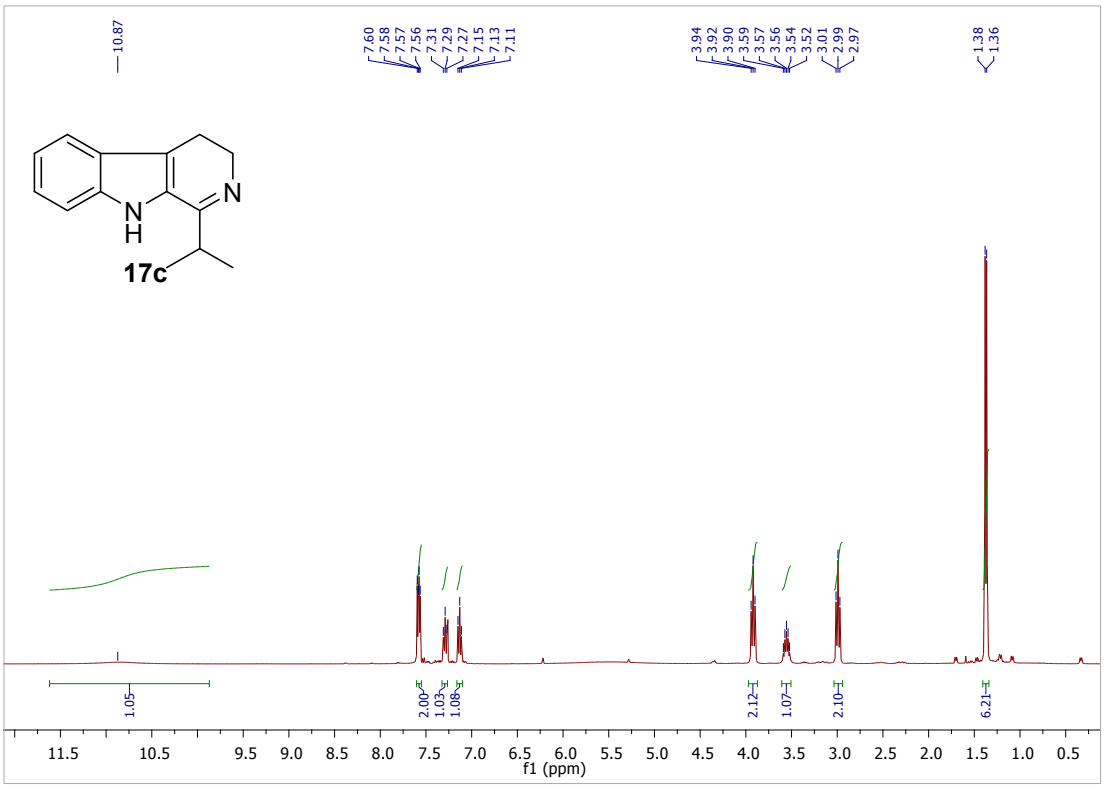
^{13}C NMR (100 MHz, DMSO-d_6) for compound **11d**.



^{1}H NMR (400 MHz, $CDCl_3$) for compound **17a**.



^{13}C NMR (100 MHz, $CDCl_3$) for compound **17a**.



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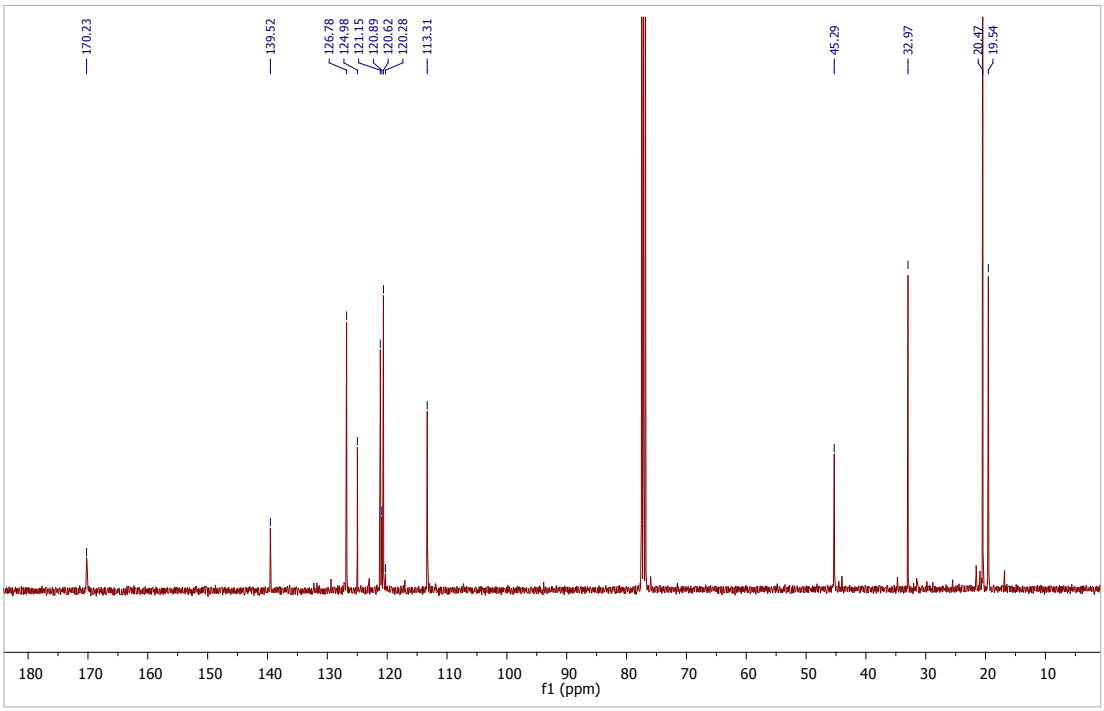

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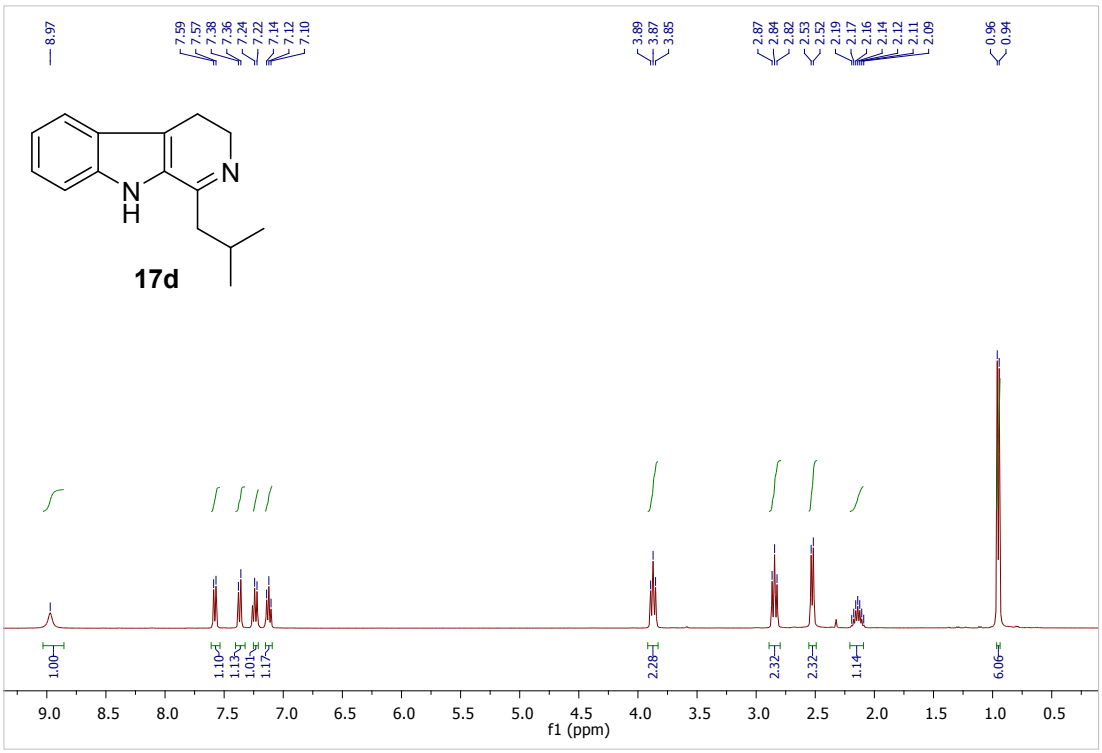
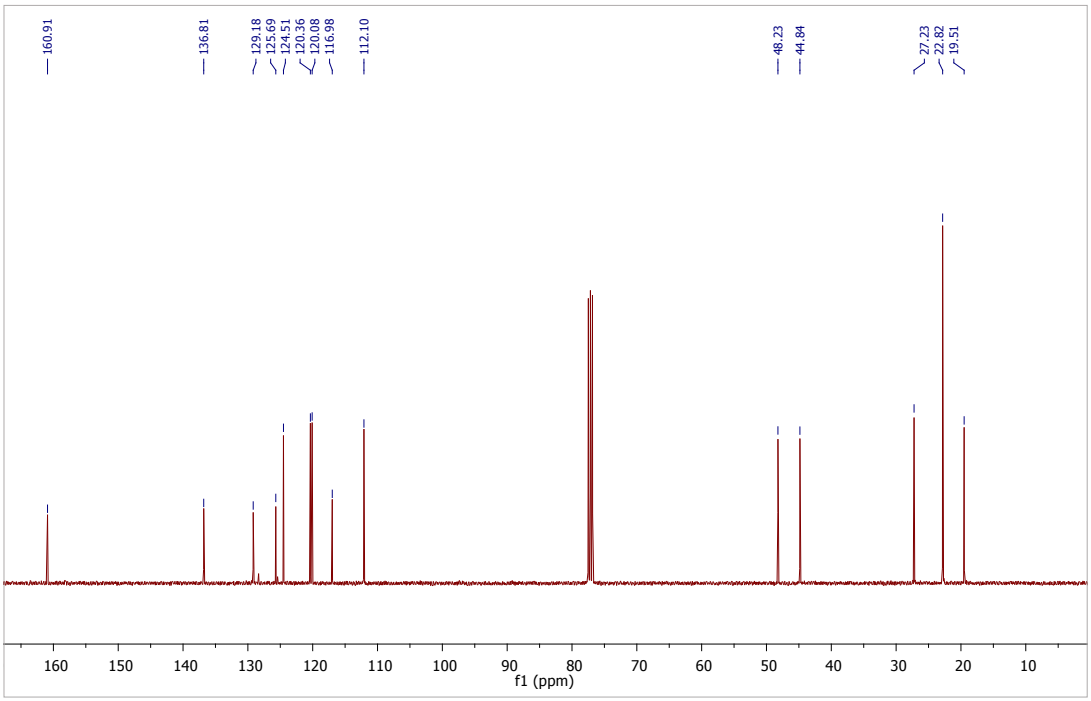
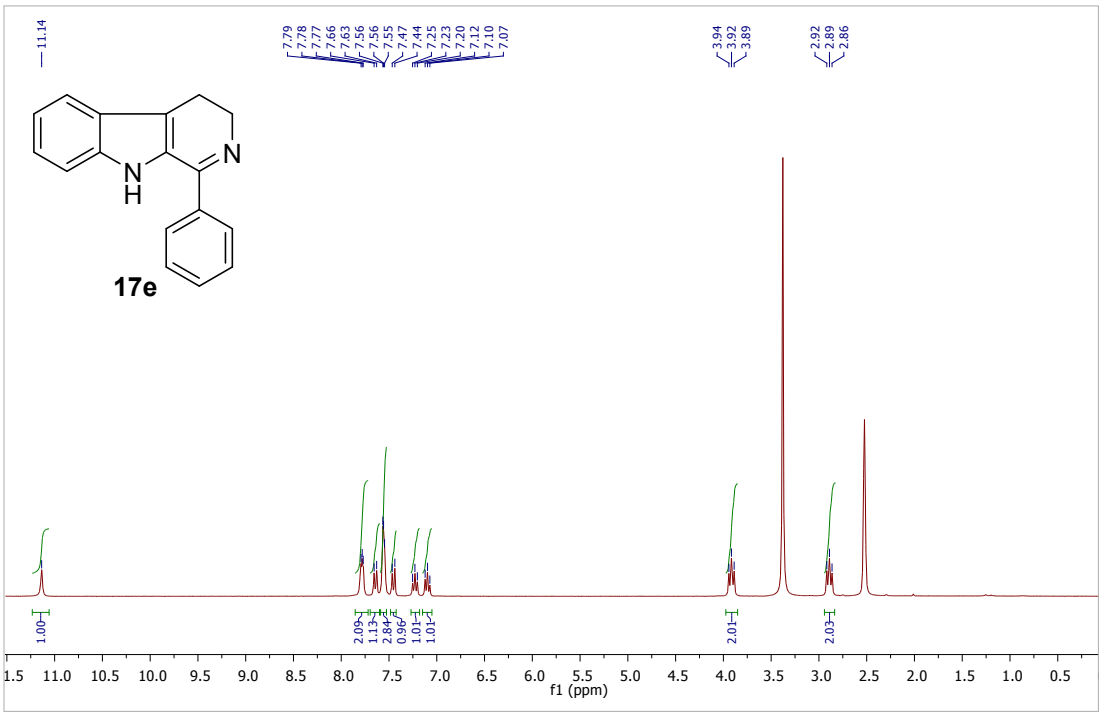


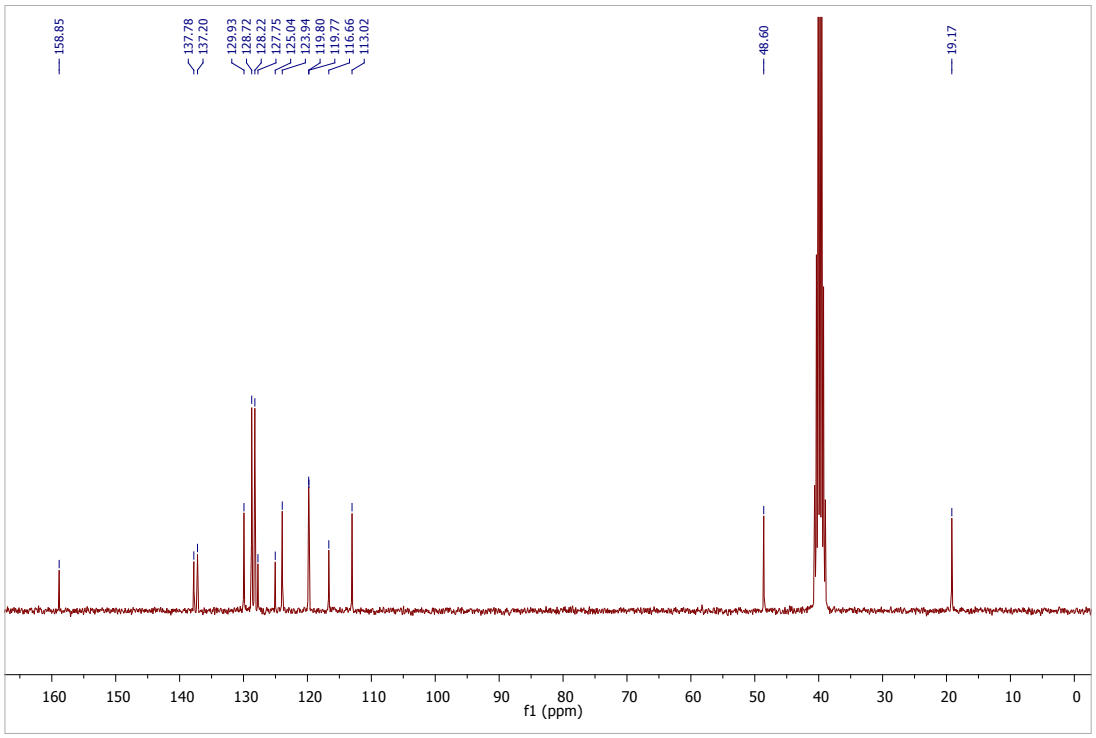
^{1}H NMR (400 MHz, $CDCl_3$) for compound **17d**.



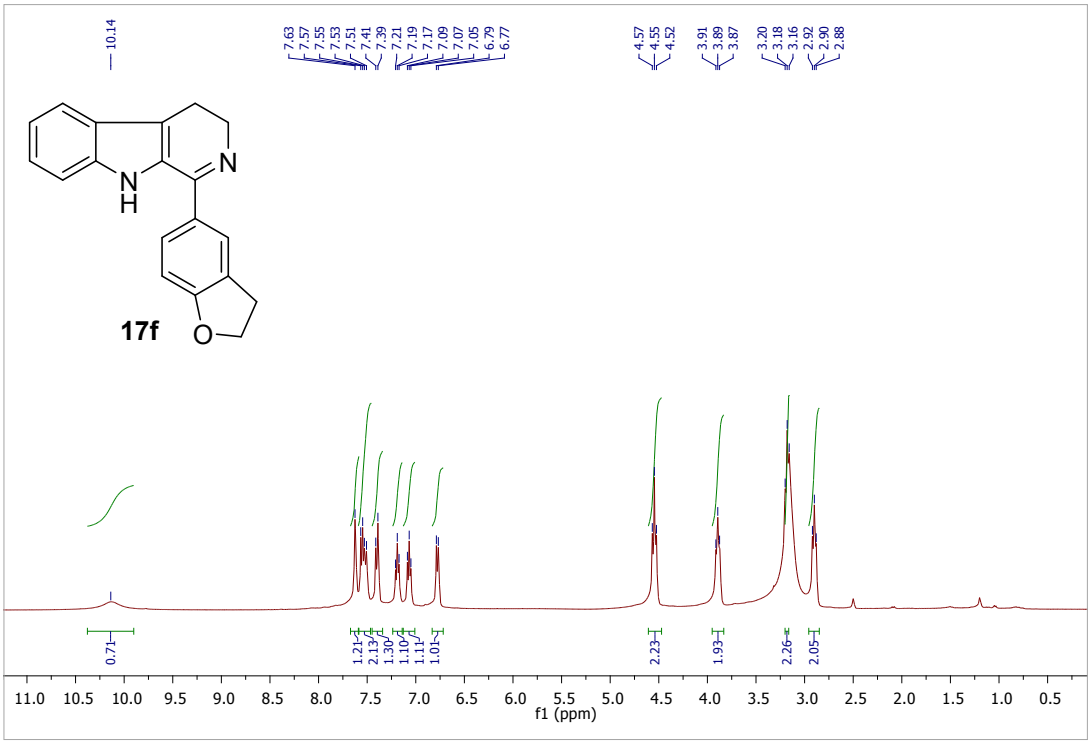
^{13}C NMR (100 MHz, $CDCl_3$) for compound **17d**.



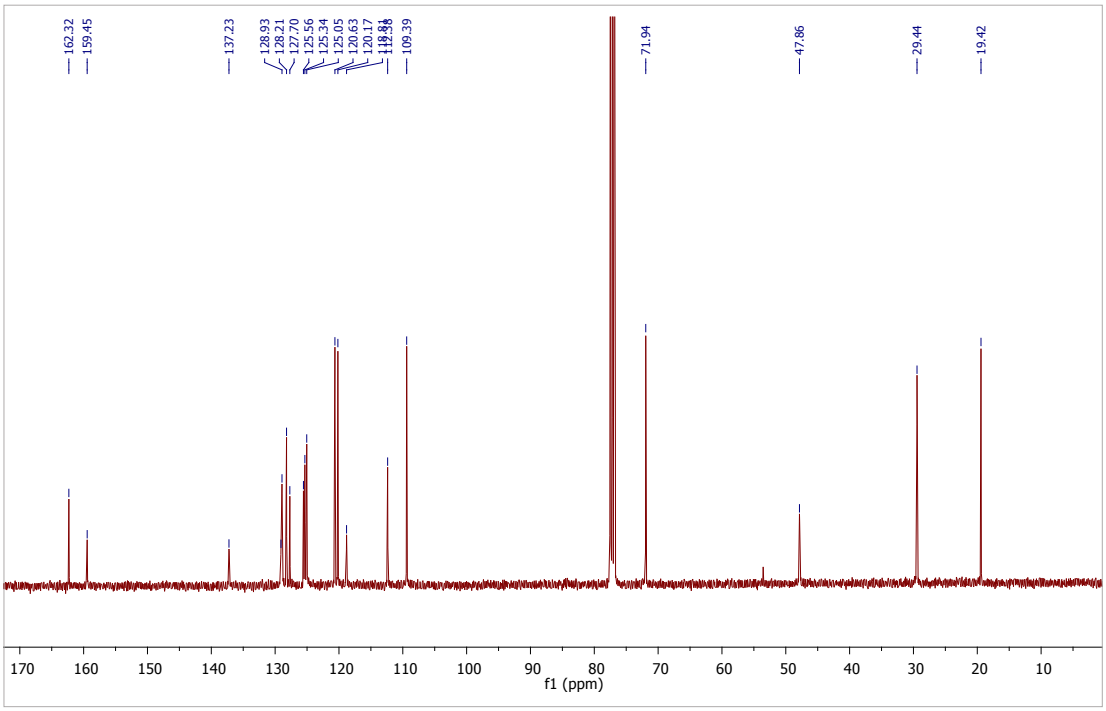
^{1}H NMR (400 MHz, DMSO-d_6) for compound **17e**.



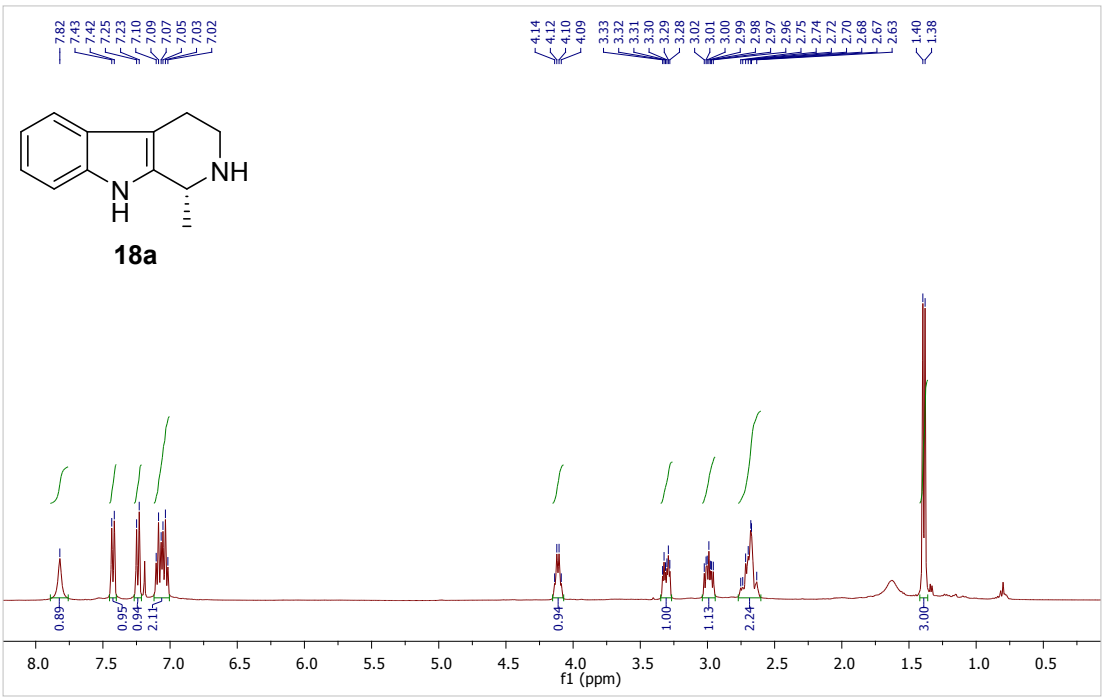
^{13}C NMR (100 MHz, DMSO-d_6) for compound **12e**.



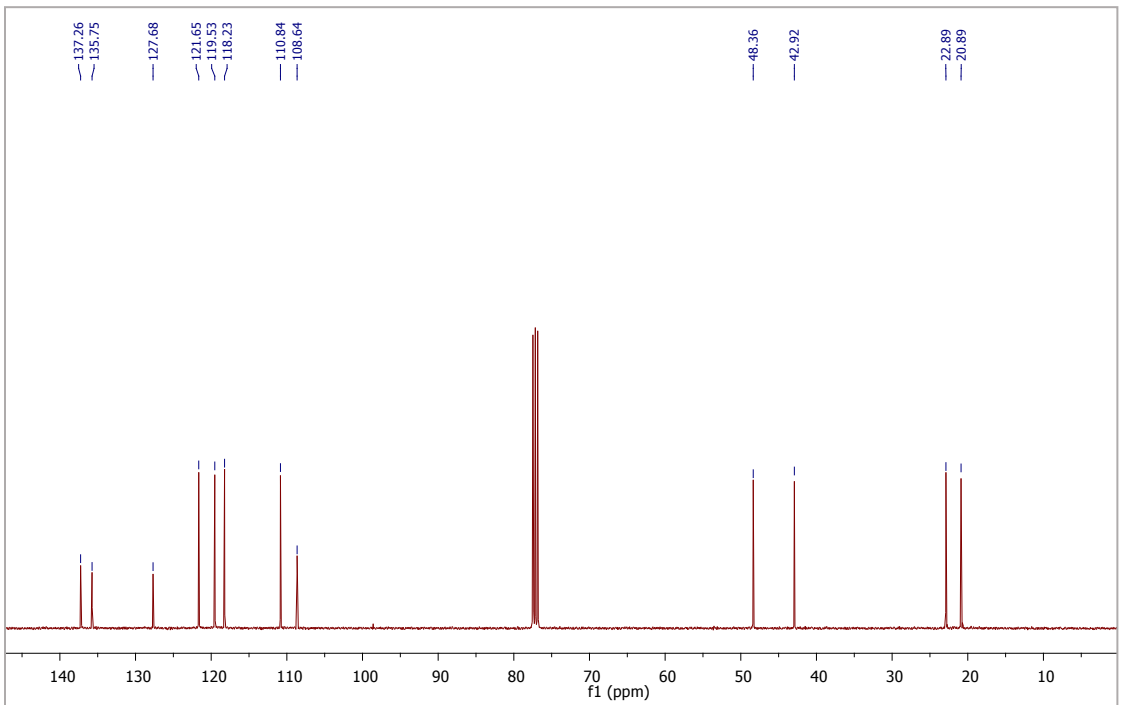
^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$) for compound **17f**.



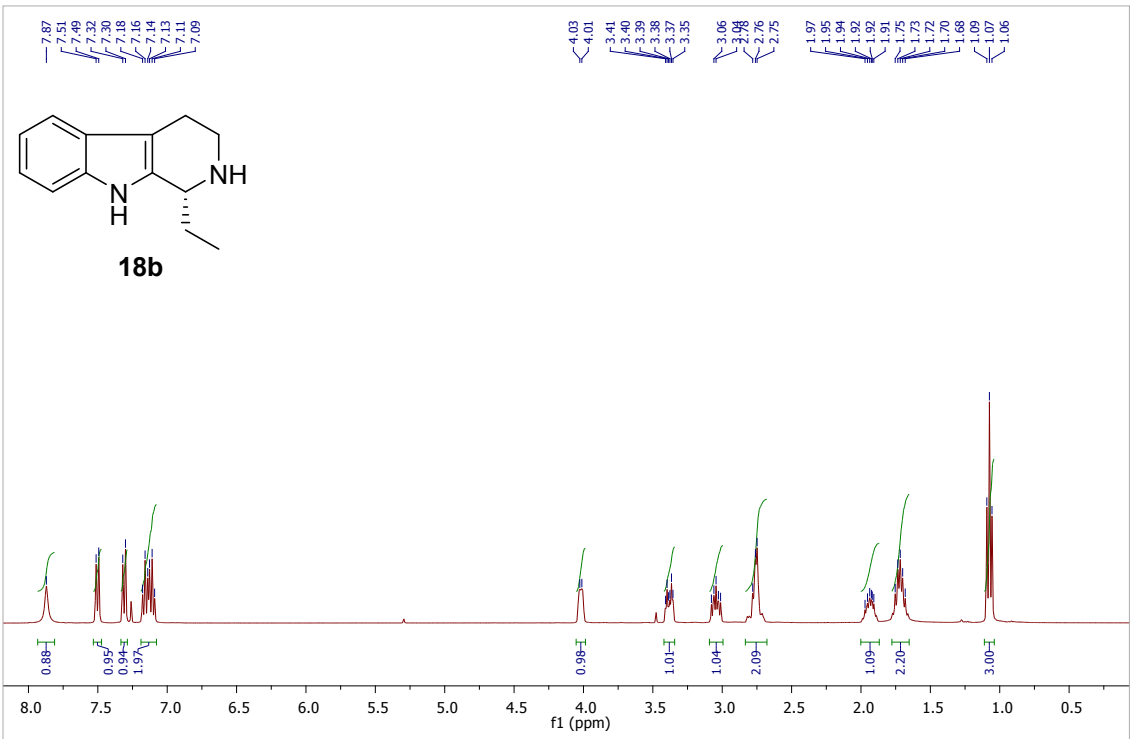
^{13}C NMR (100 MHz, $CDCl_3$) for compound **17f**.



^{1}H NMR (400 MHz, $CDCl_3$) for compound **18a**.



^{13}C NMR (100 MHz, $CDCl_3$) for compound **18a**.



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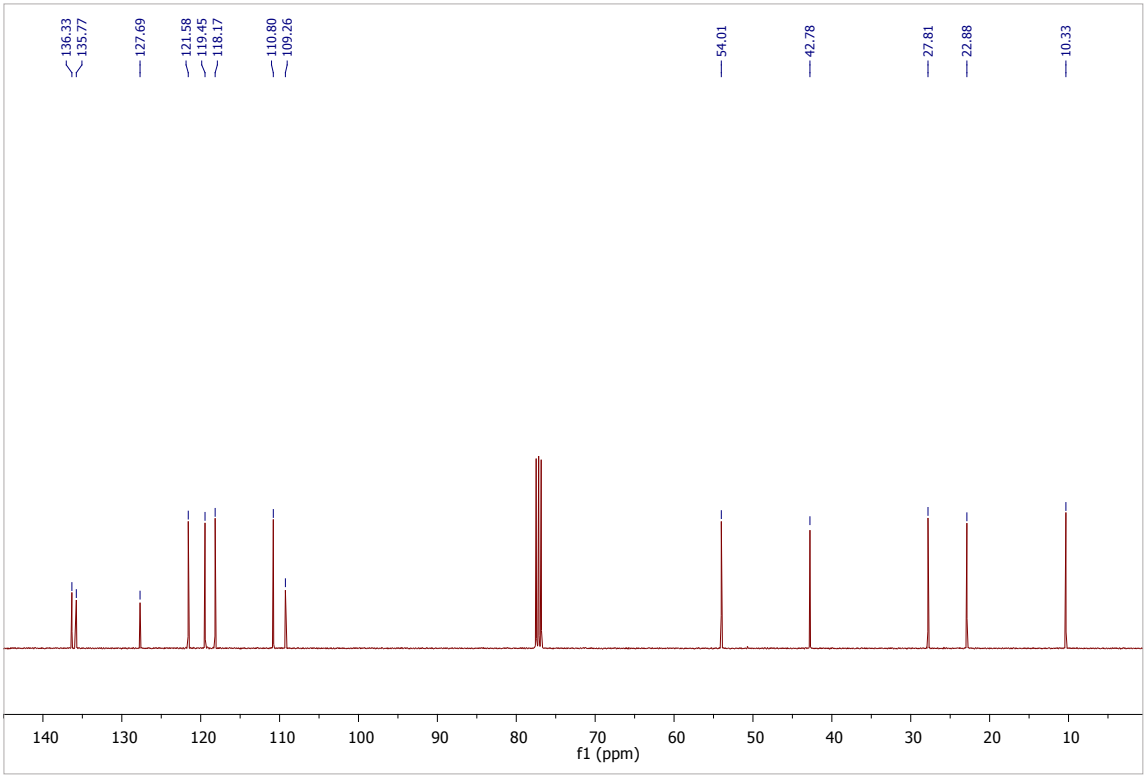

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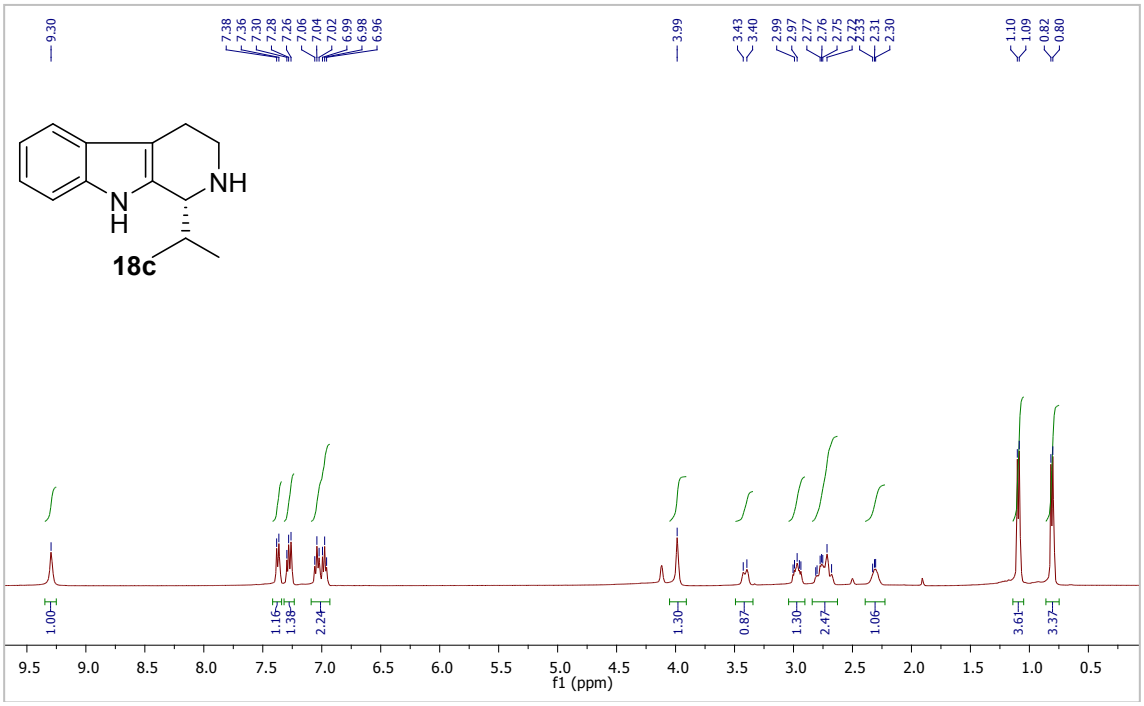
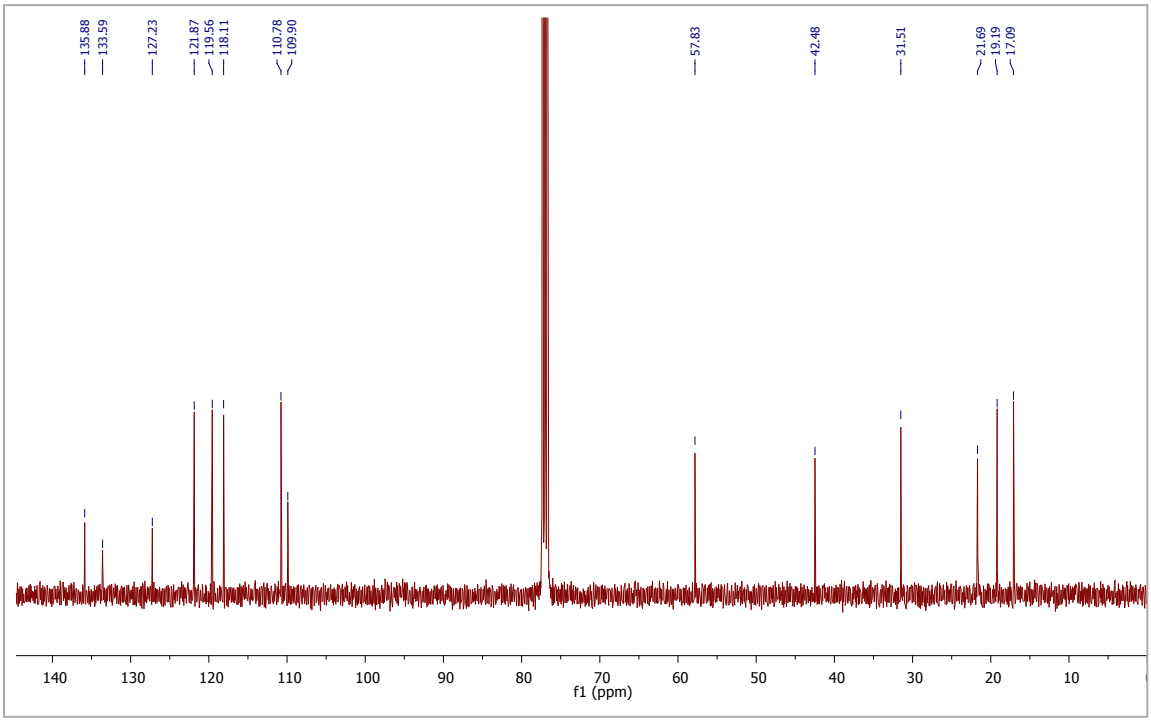
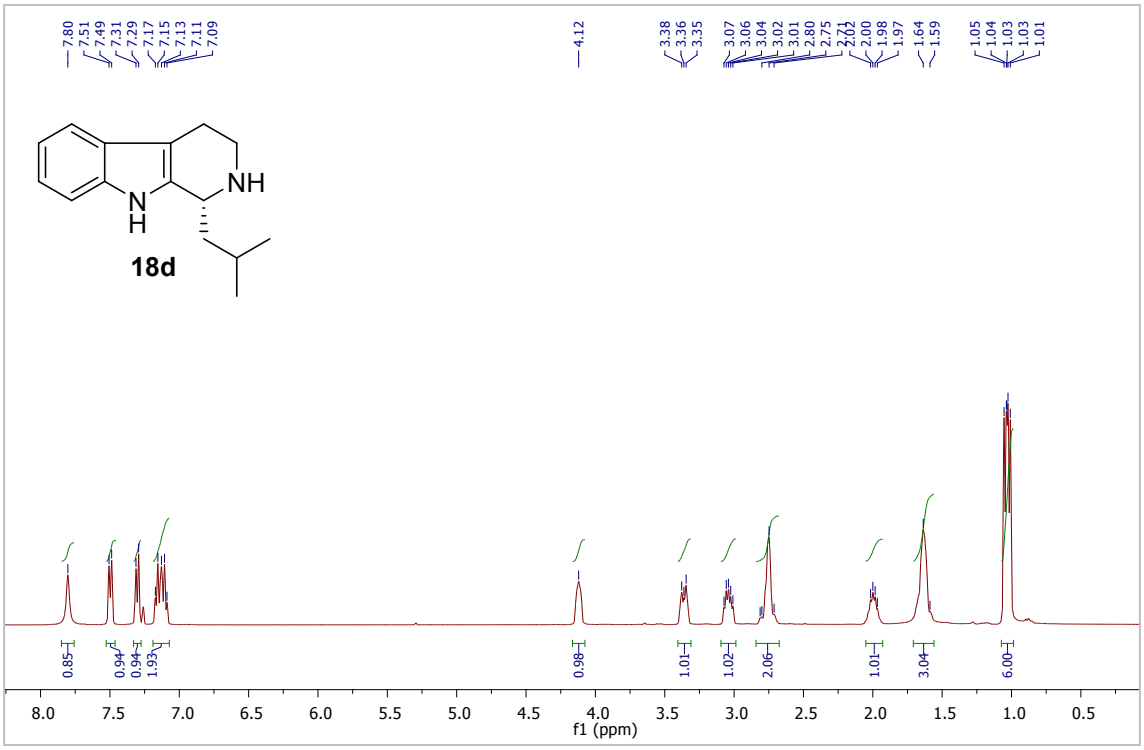


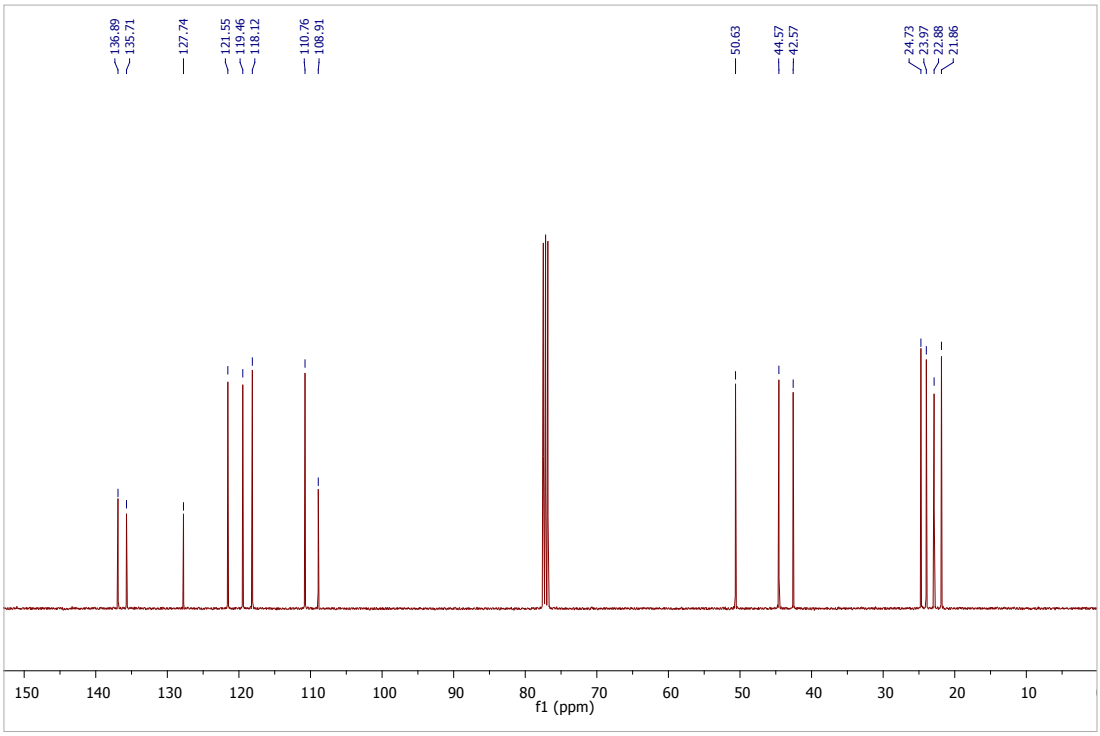
^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$) for compound **18c**.



^{13}C NMR (100 MHz, $CDCl_3$) for compound **18c**.



^{1}H NMR (400 MHz, $CDCl_3$) for compound **18d**.



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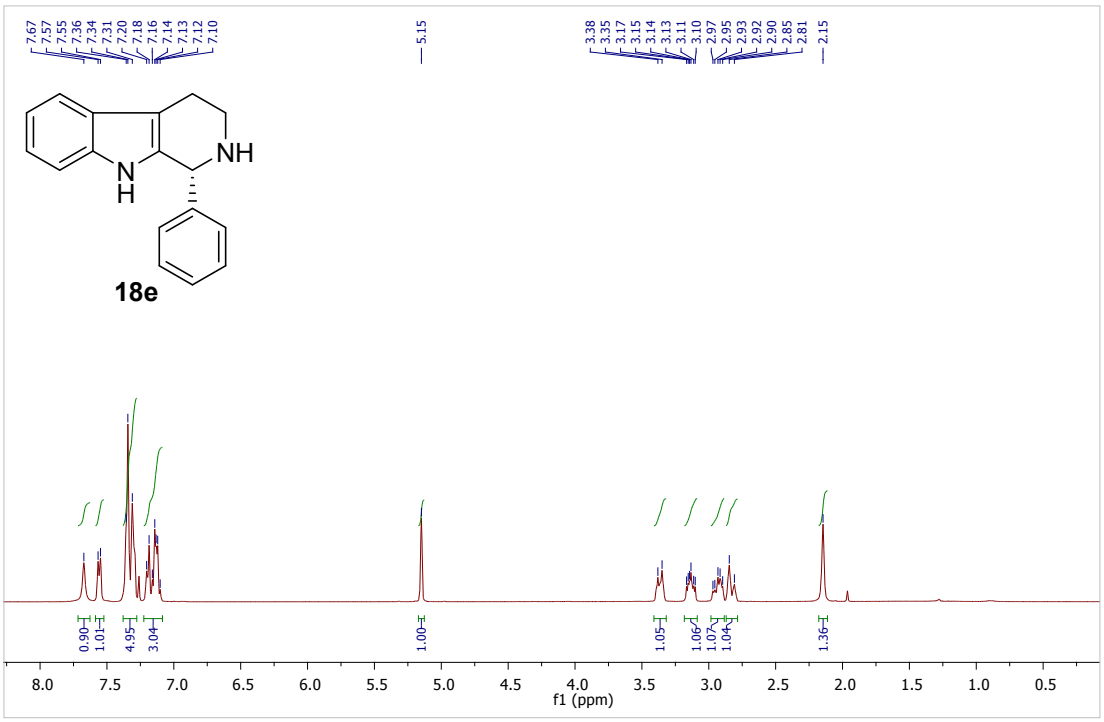
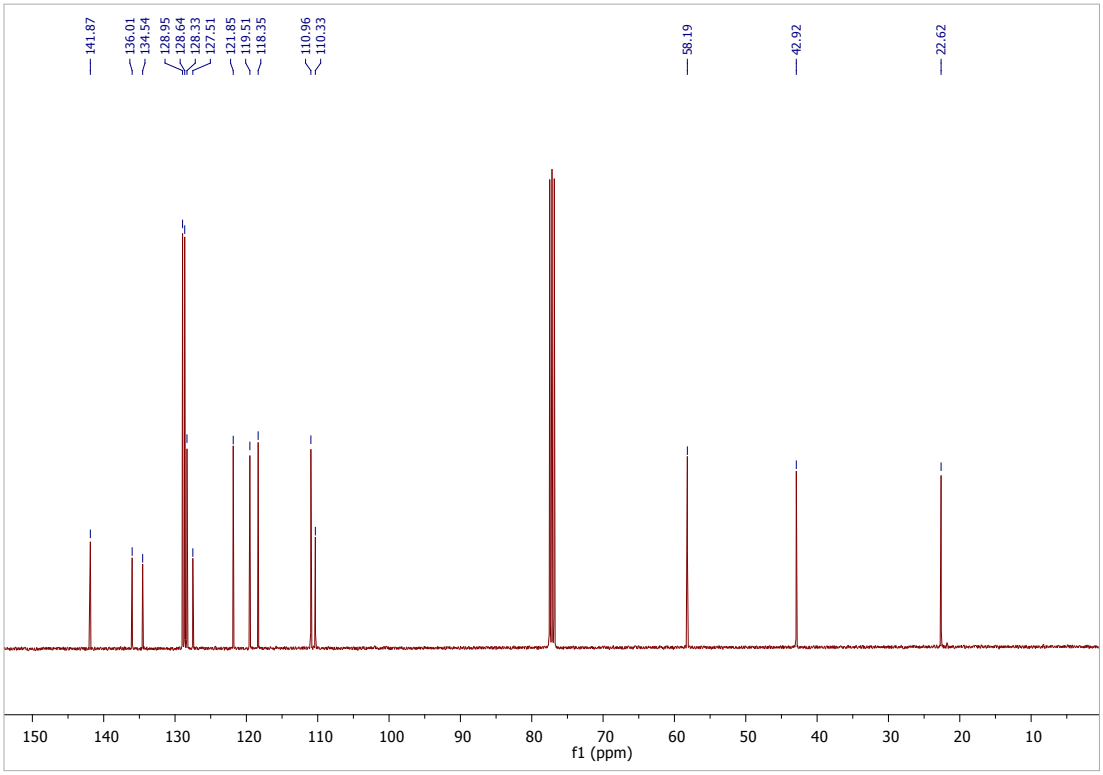
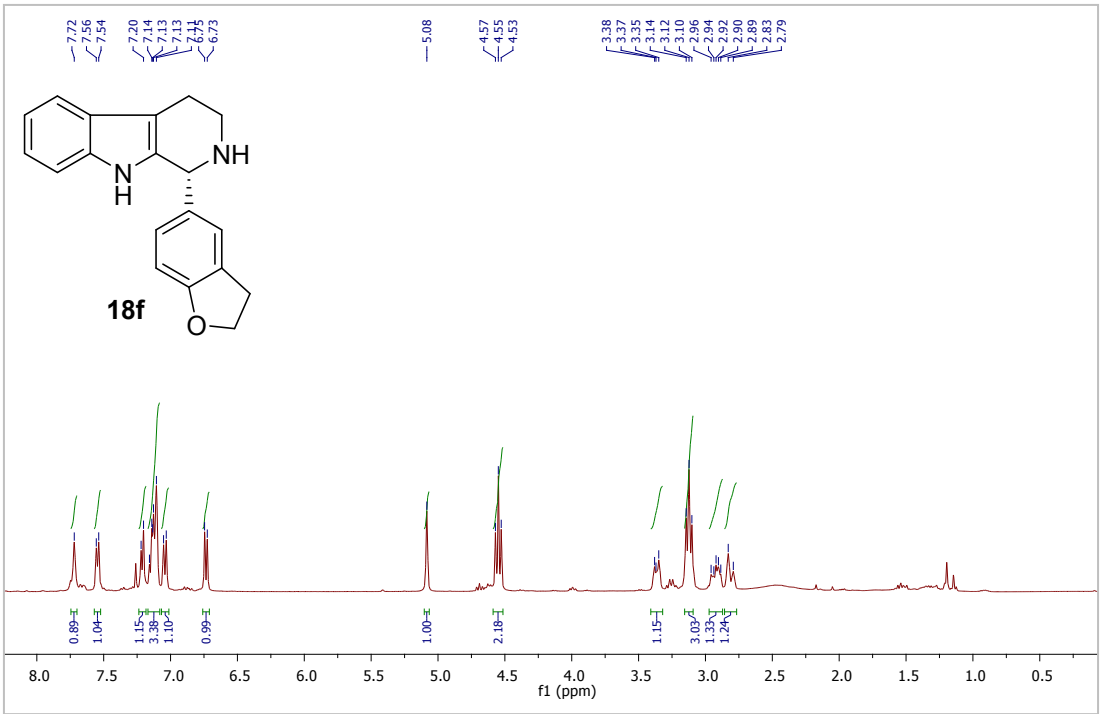


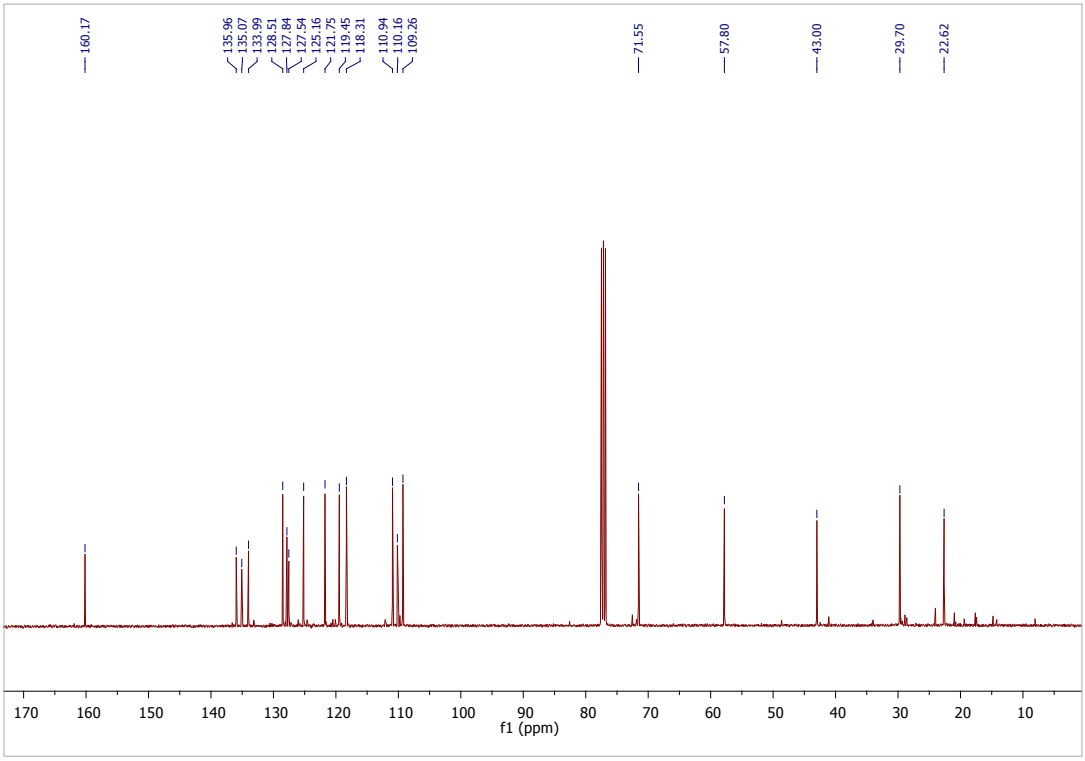
^{1}H NMR (400 MHz, $CDCl_3$) for compound **18e**.



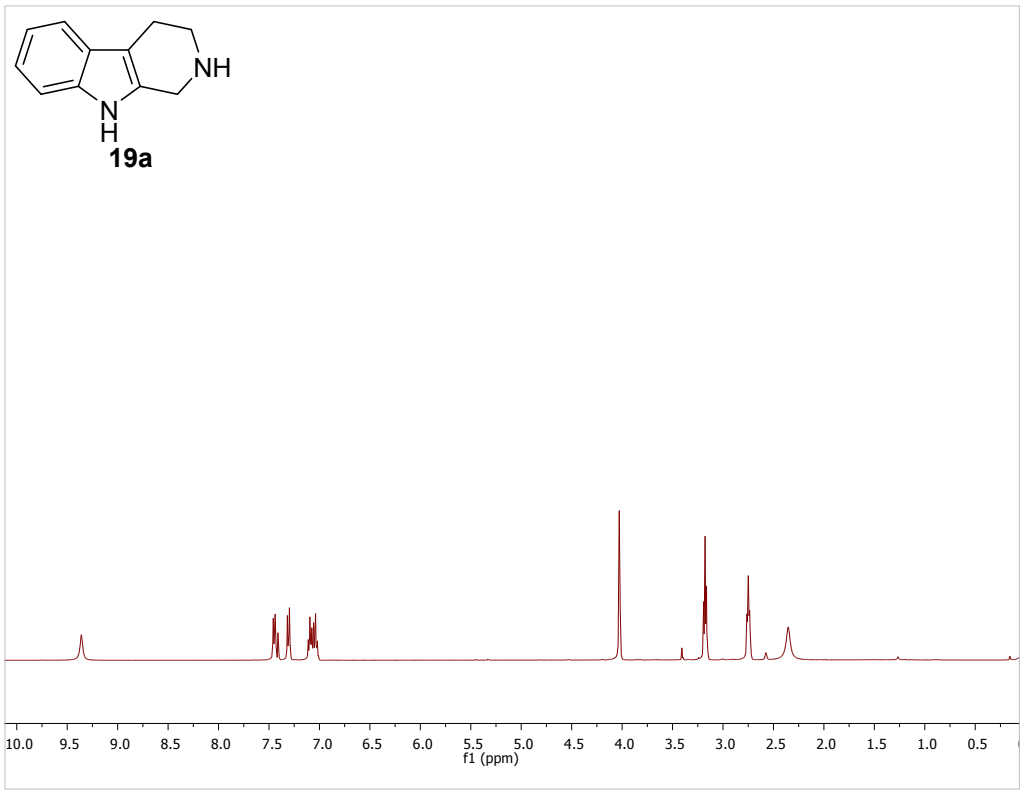
^{13}C NMR (100 MHz, $CDCl_3$) for compound **18e**.



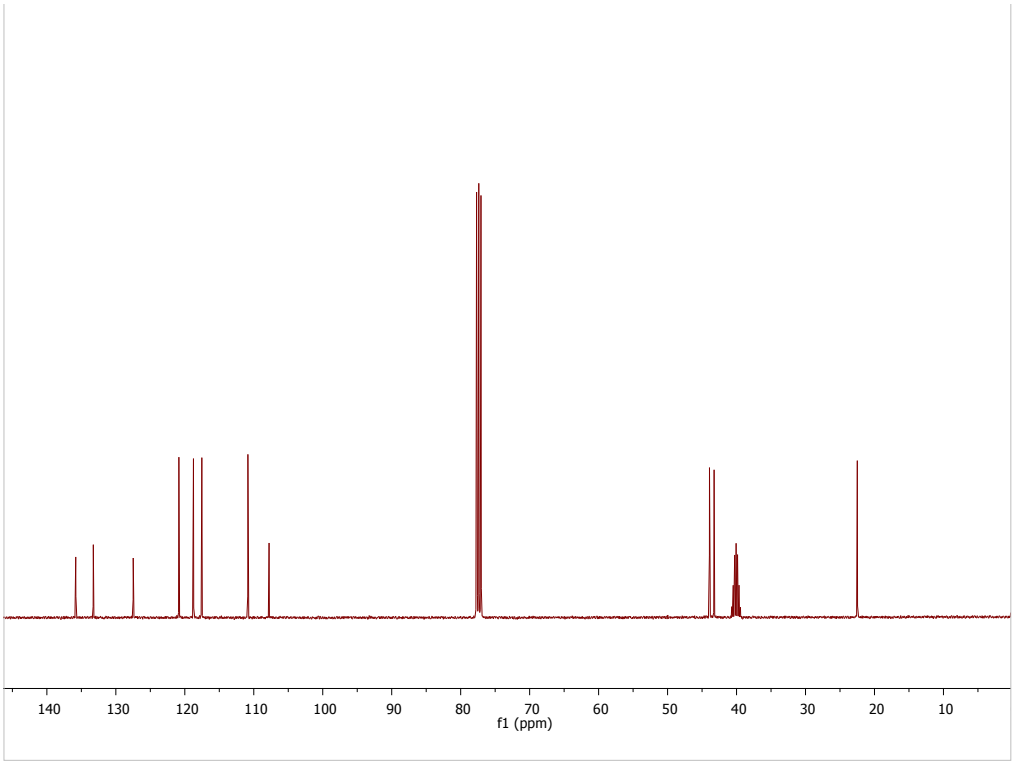
^{1}H NMR (400 MHz, $CDCl_3$) for compound **18f**.



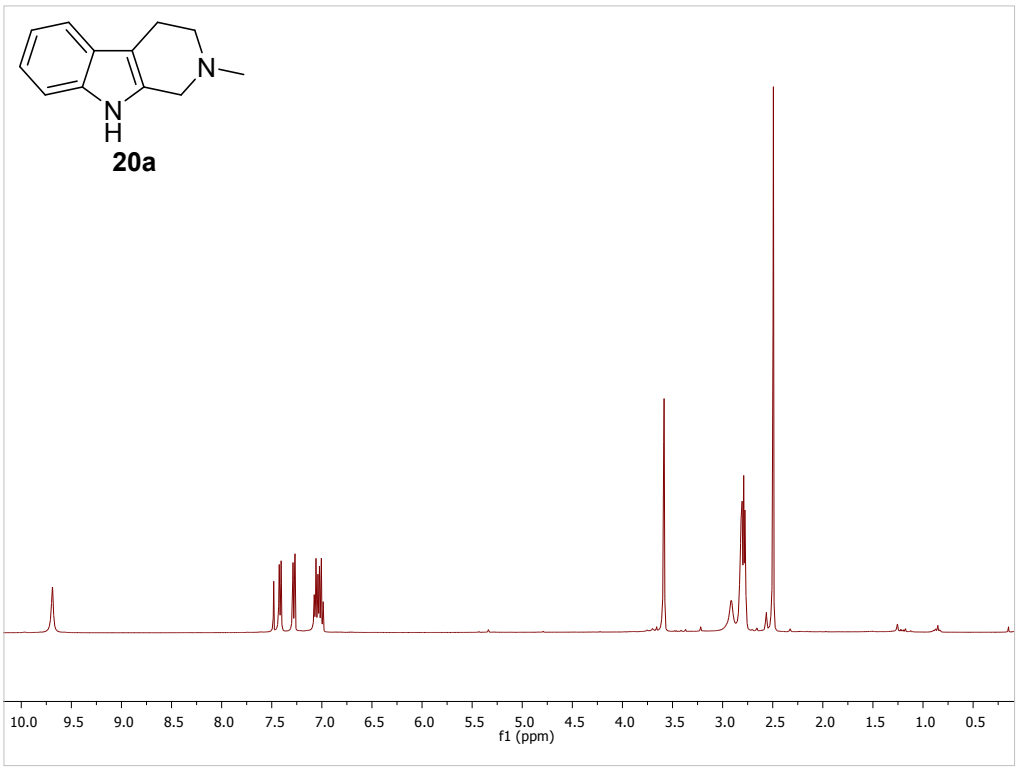
^{13}C NMR (100 MHz, $CDCl_3$) for compound **18f**.



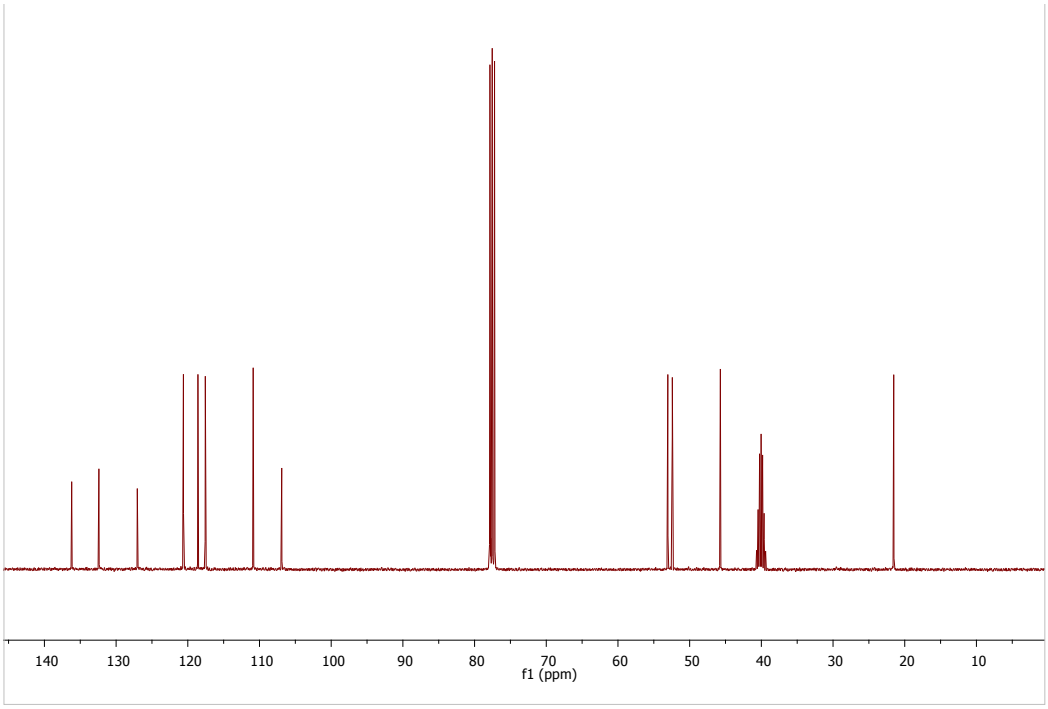
^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) for compound **19a**.



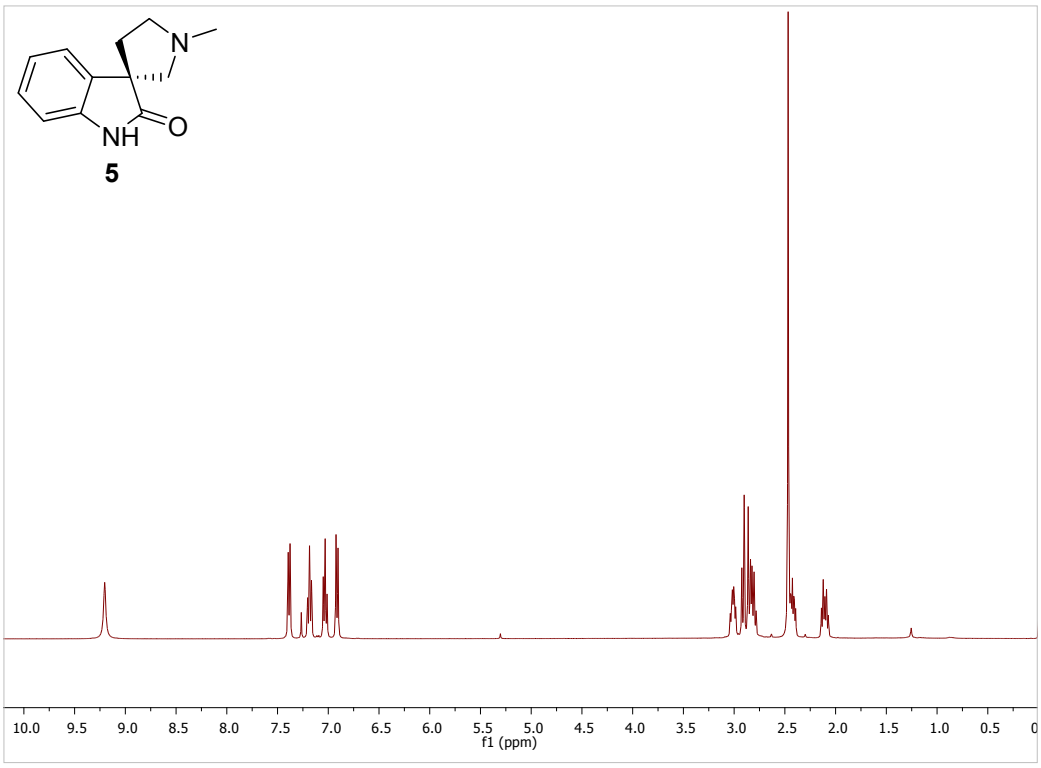
^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) for compound **19a**.



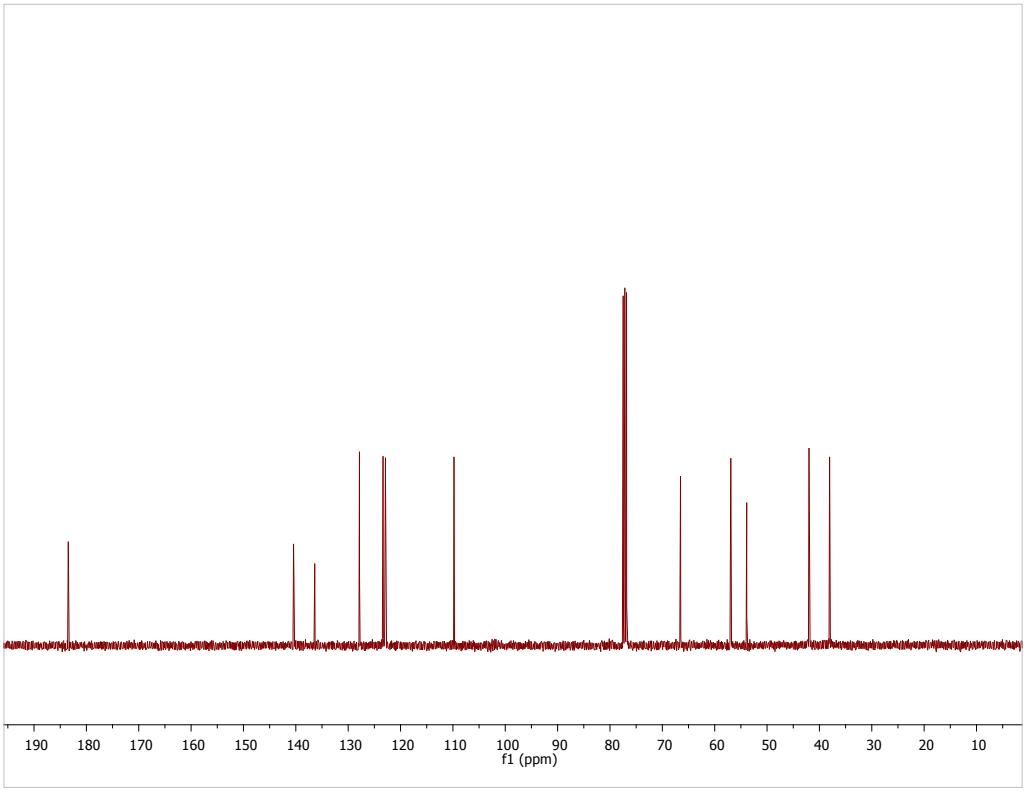
^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) for compound **20a**.



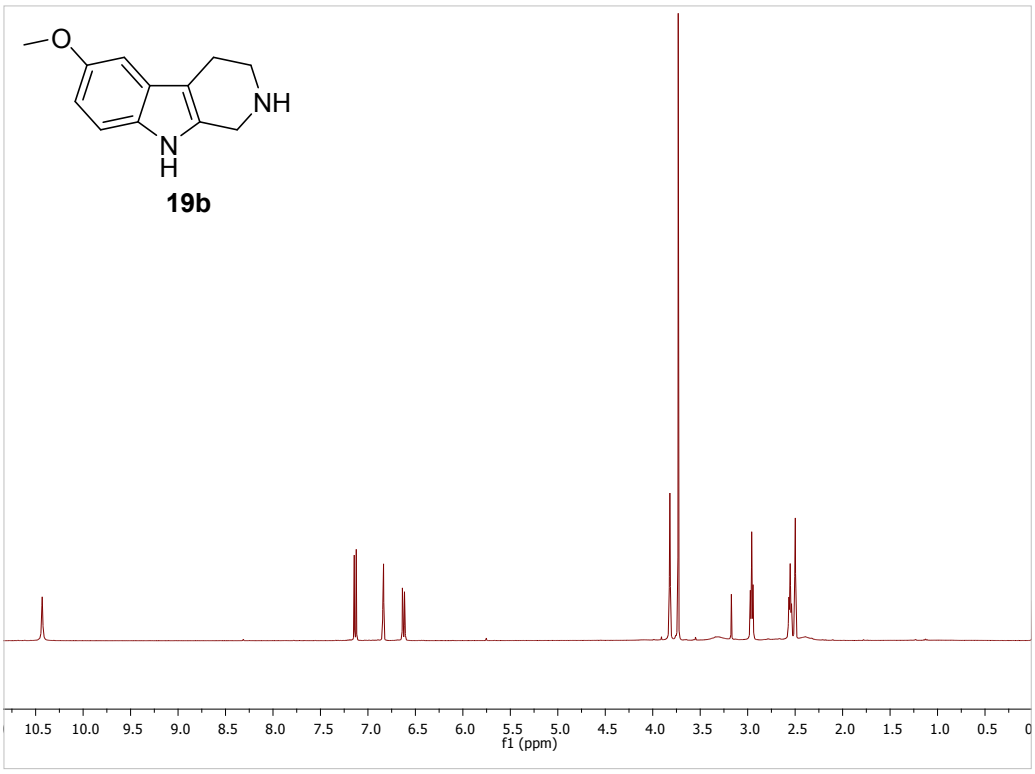
^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) for compound **20a**.



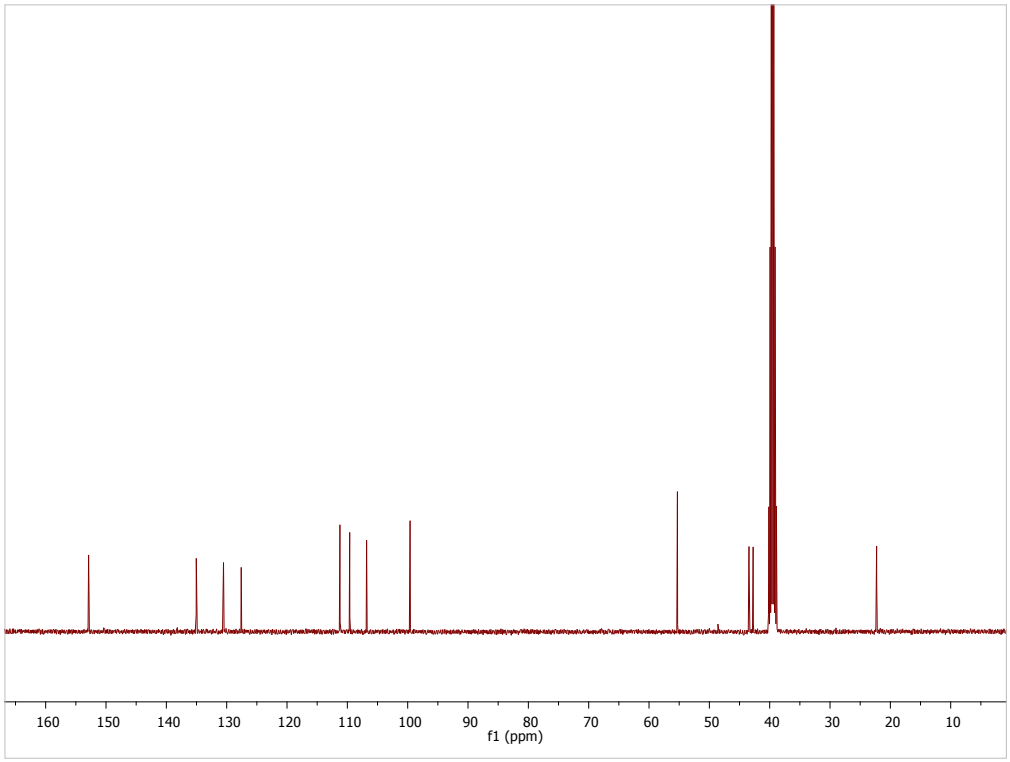
^{1}H NMR (400 MHz, $CDCl_3$) for (–)-coerulescine (**5**).



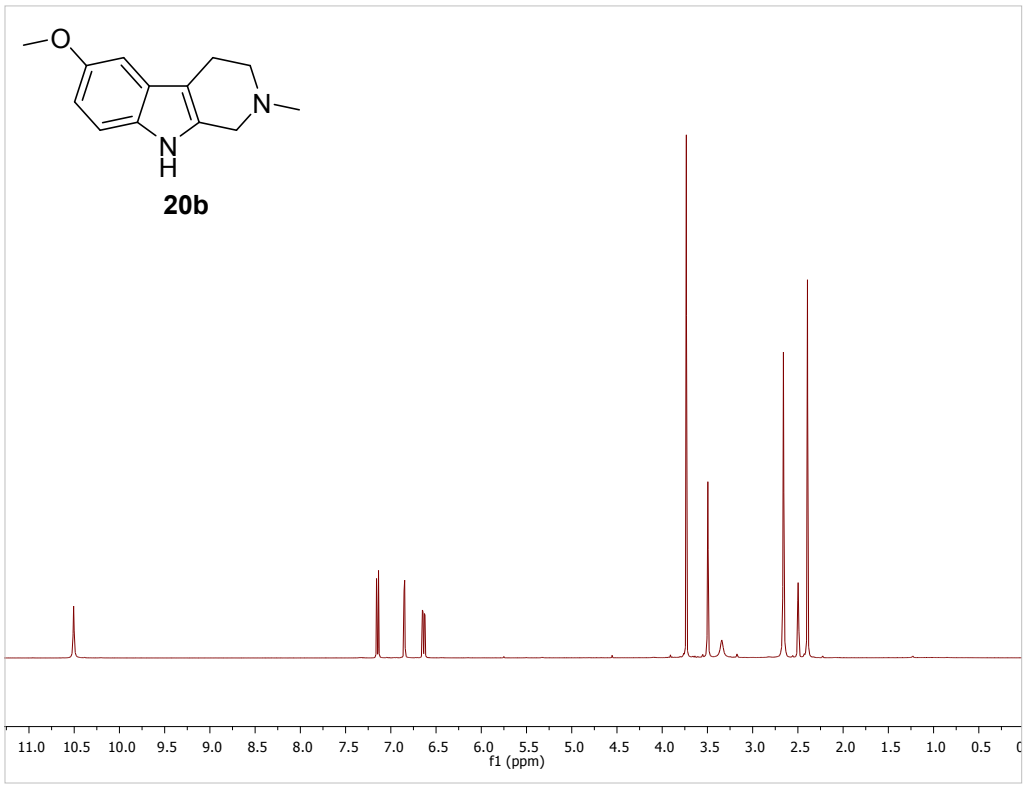
^{13}C NMR (100 MHz, $CDCl_3$) for (–)-coerulescine (**5**).



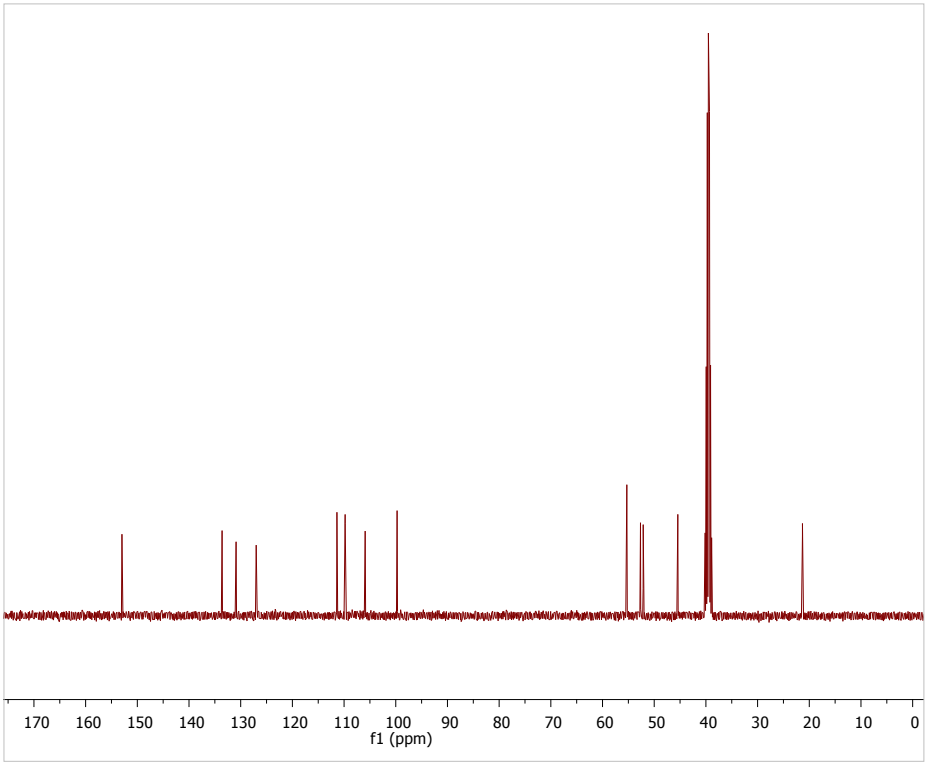
^{1}H NMR (400 MHz, DMSO–d_6) for compound **19b**.



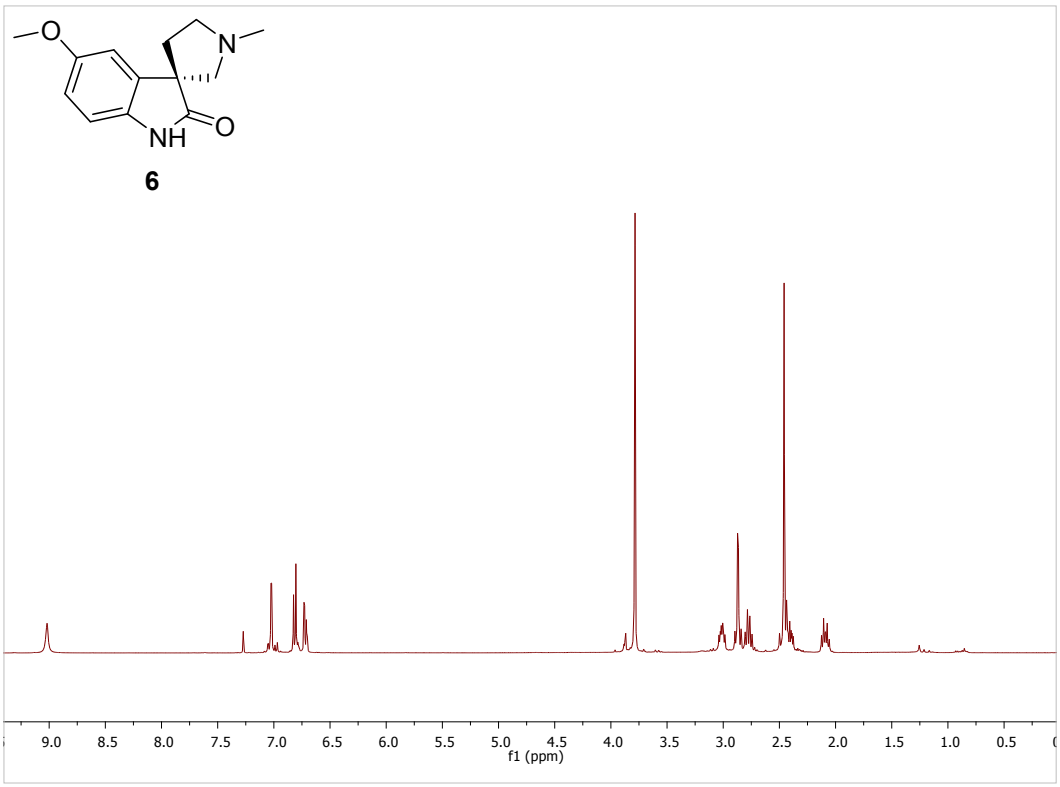
^{13}C NMR (100 MHz, DMSO–d_6) for compound **19b**.



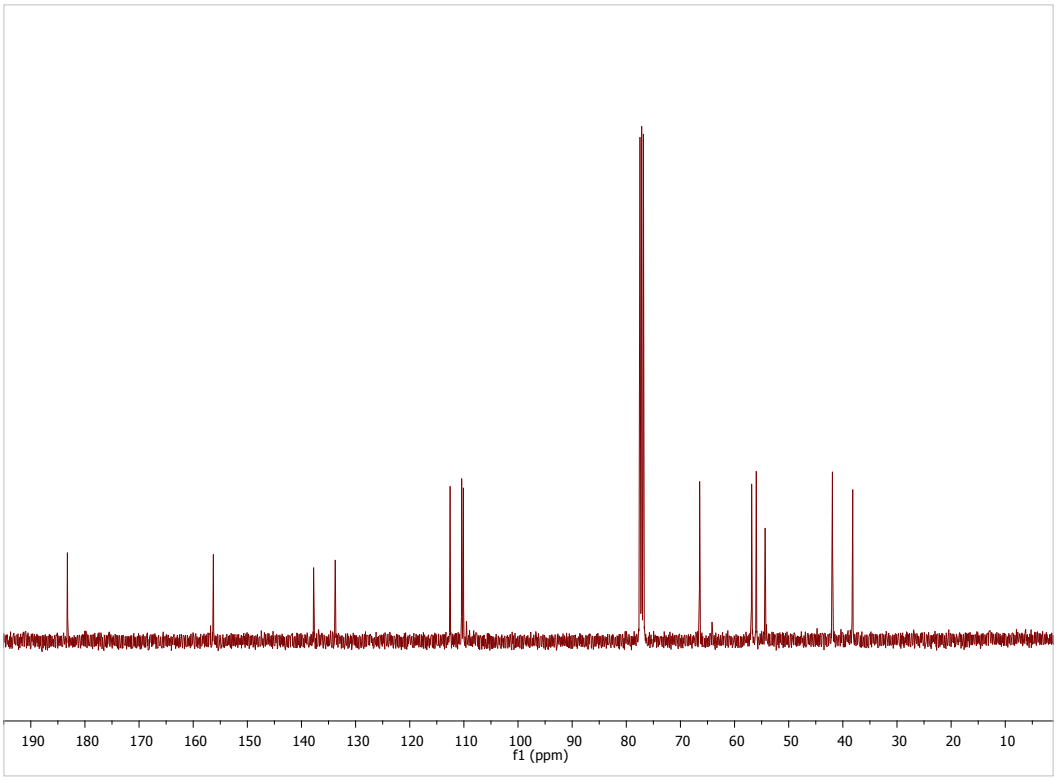
^{1}H NMR (400 MHz, DMSO–d_6) for compound **20b**.



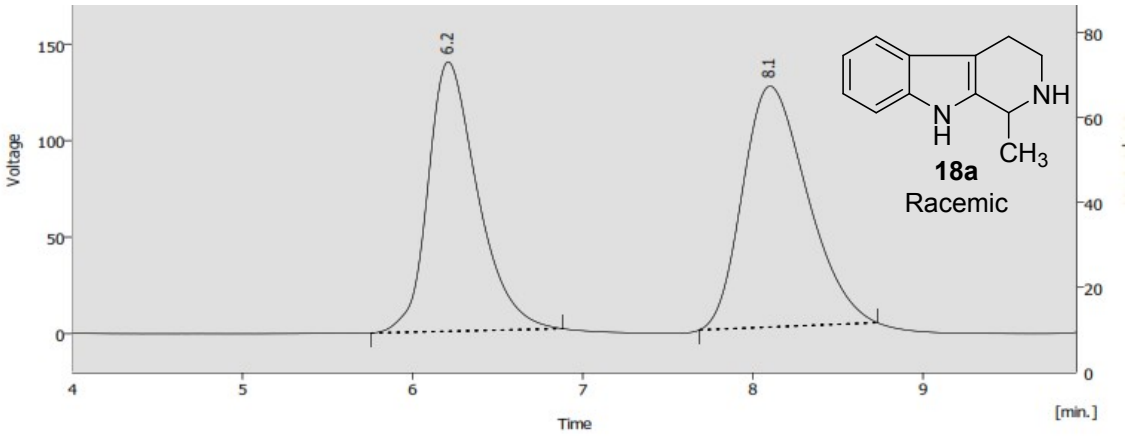
^{13}C NMR (100 MHz, DMSO–d_6) for compound **20b**.



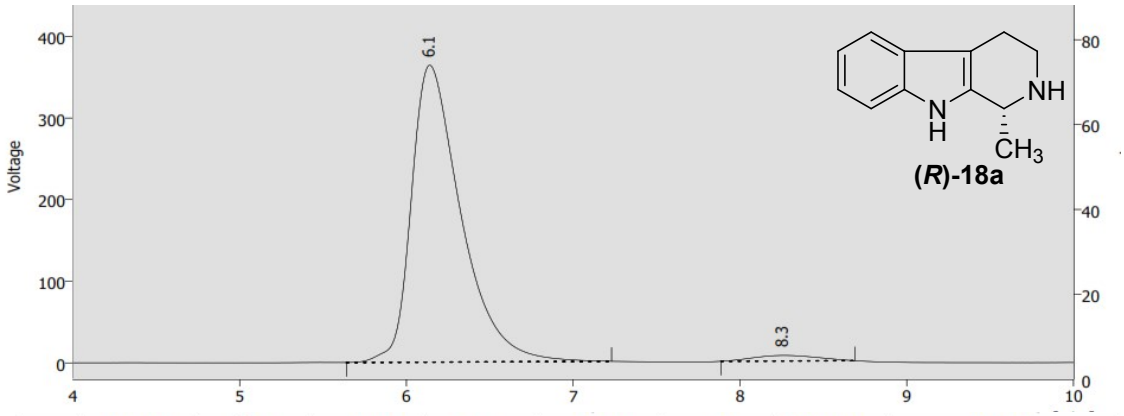
^{1}H NMR (400 MHz, $CDCl_3$) for (–)-horsfiline (**6**).



^{13}C NMR (100 MHz, $CDCl_3$) for (–)-horsfiline (**6**).

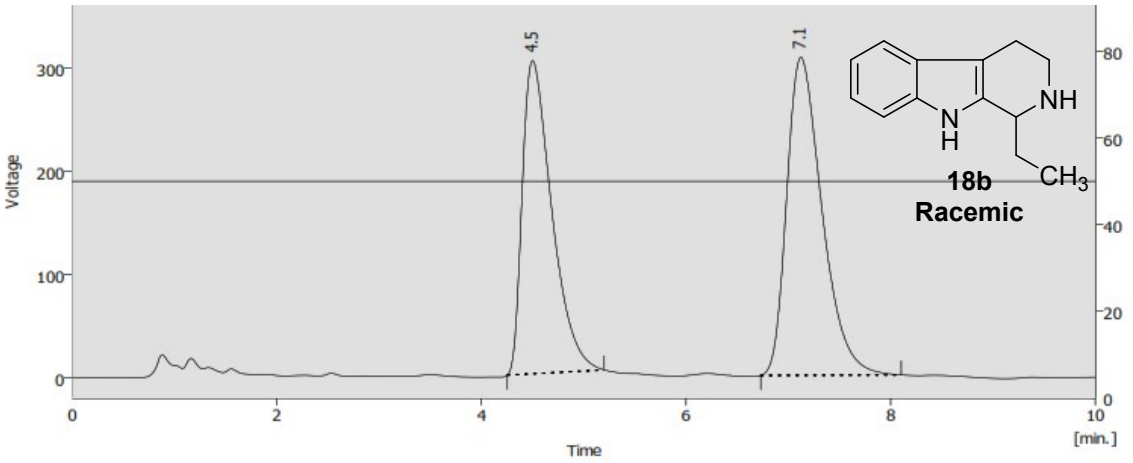


HPLC chromatogram for racemic-**18a.**

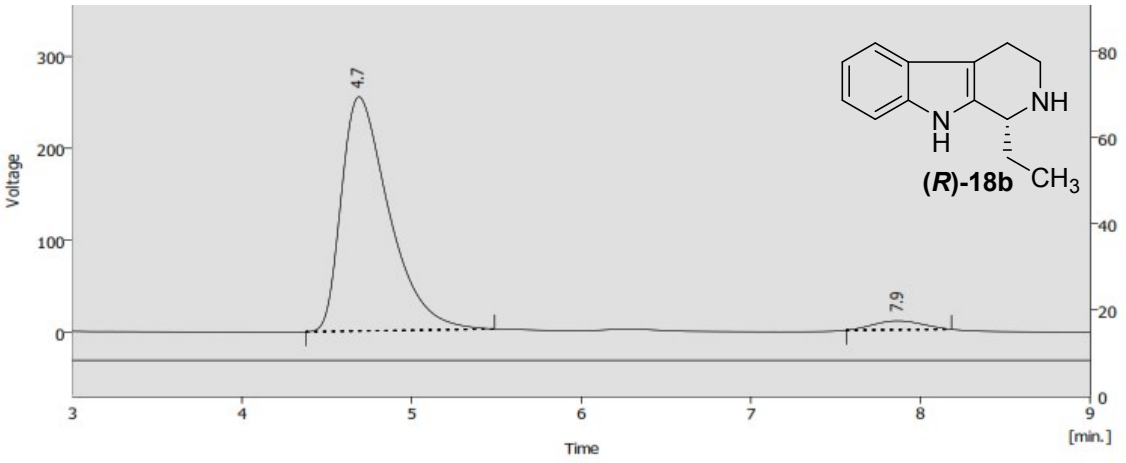


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	6.140	7549.858	363.935	97.7	98.2	0.31	988	
2	8.260	181.575	6.859	2.3	1.8	0.45	990	
	Total	7731.433	370.794	100.0	100.0			

HPLC chromatogram for (*R*)-**18a**.

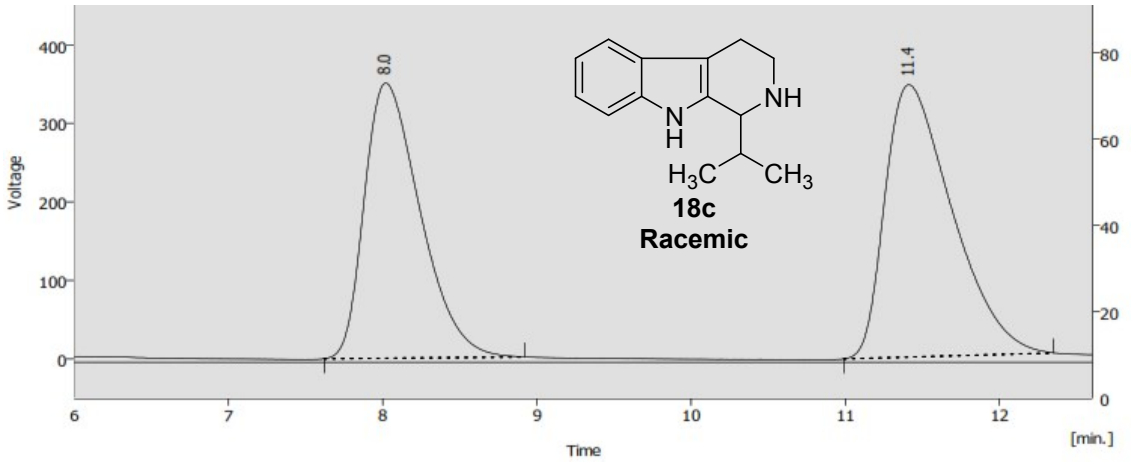


HPLC chromatogram for racemic-**18b**.

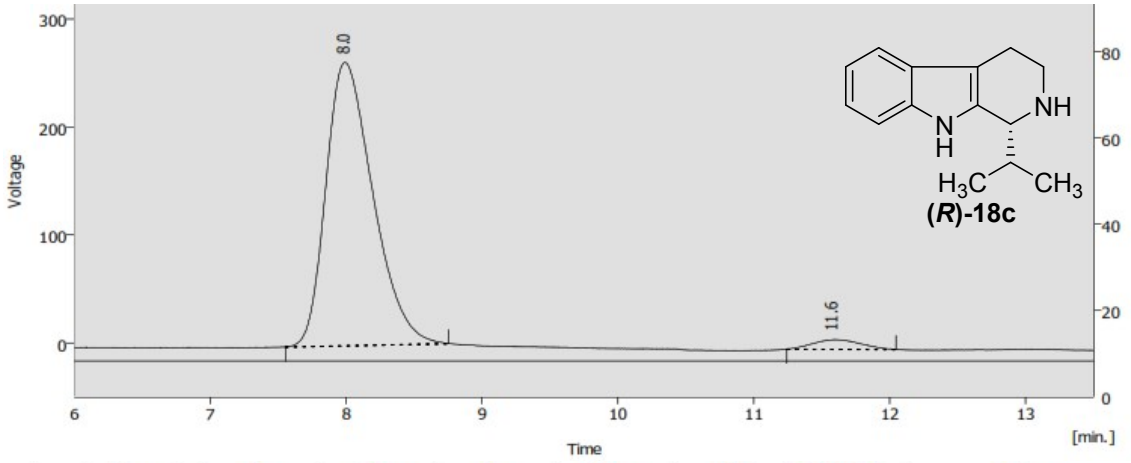


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	4.690	4992.381	254.946	96.2	96.3	0.30	969	
2	7.867	194.535	9.679	3.8	3.7	0.34	984	
	Total	5186.916	264.625	100.0	100.0			

HPLC chromatogram for (*R*)-**18b**.

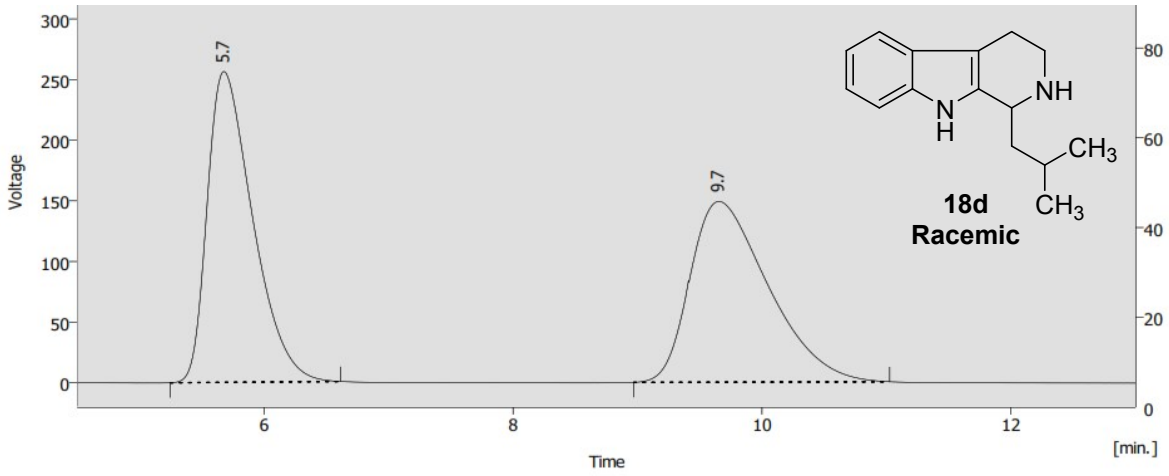


HPLC chromatogram for racemic-**18c**.

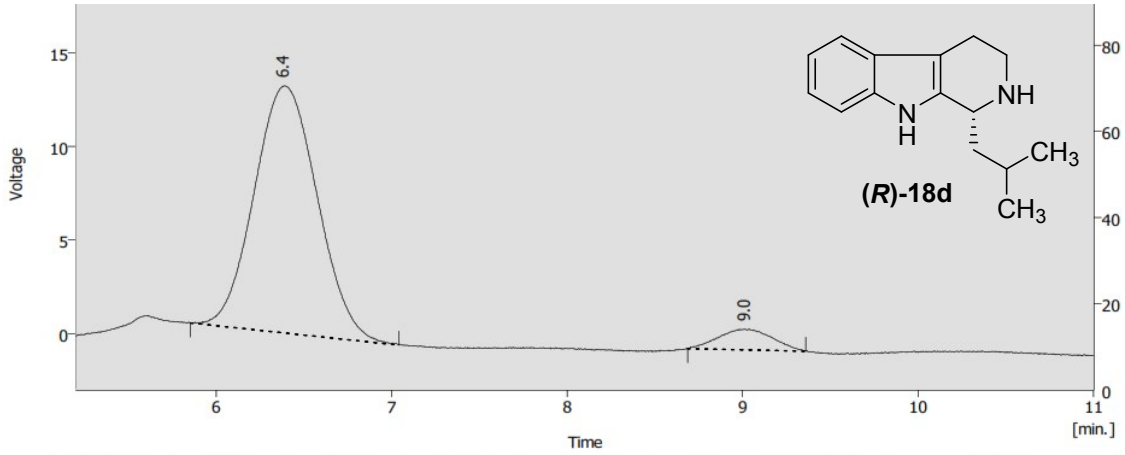


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	7.990	6330.970	262.815	96.6	96.6	0.38	885	
2	11.583	222.885	9.219	3.4	3.4	0.40	721	
	Total	6553.856	272.034	100.0	100.0			

HPLC chromatogram for (*R*)-**18c**.

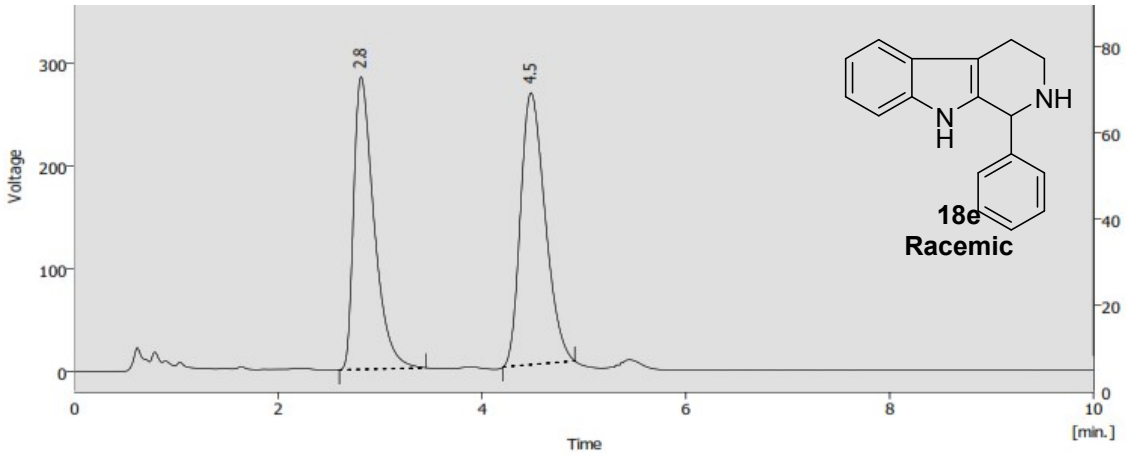


HPLC chromatogram for racemic-**18d**.

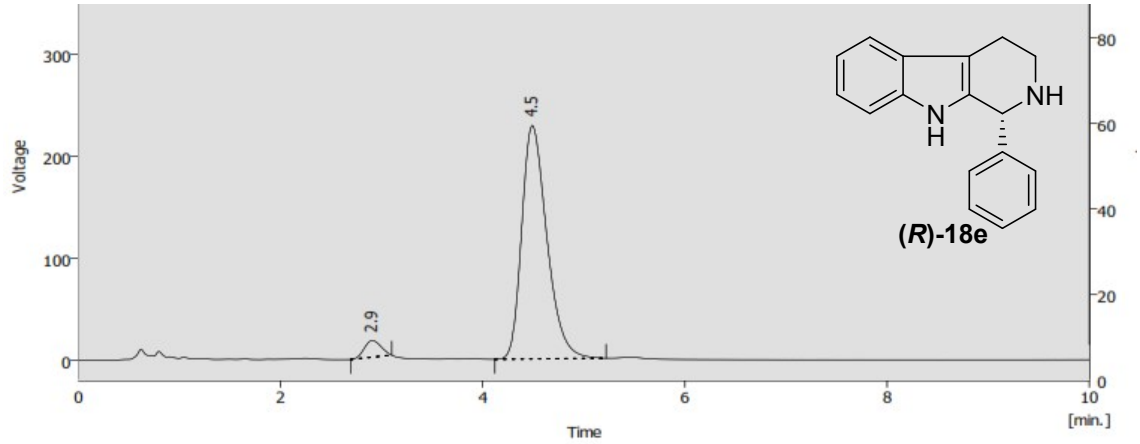


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	6.387	330.891	13.212	93.3	92.3	0.40	870	
2	9.013	23.635	1.109	6.7	7.7	0.35	959	
	Total	354.526	14.321	100.0	100.0			

HPLC chromatogram for (*R*)-**18d**.

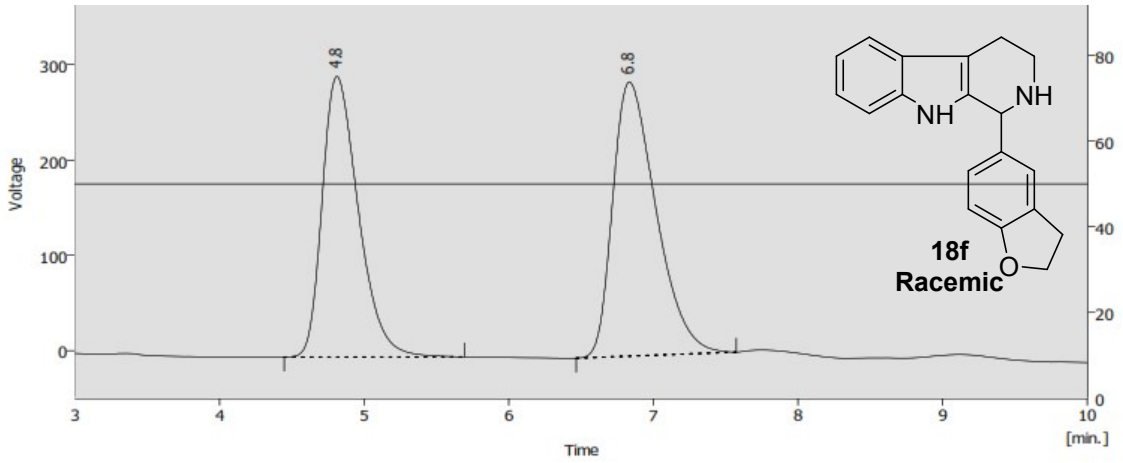


HPLC chromatogram for racemic-**18e**.

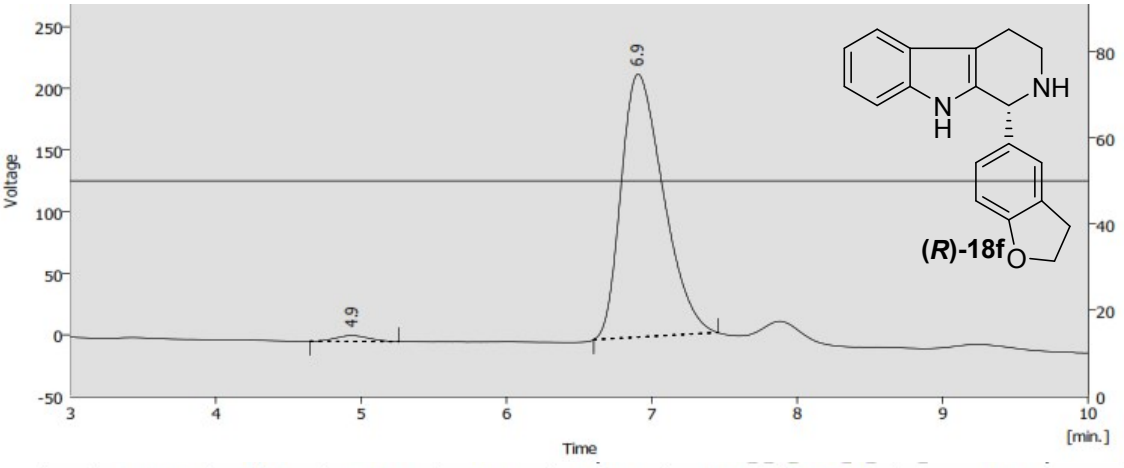


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	2.910	186.006	16.292	4.5	6.6	0.19	955	
2	4.490	3963.477	228.988	95.5	93.4	0.26	901	
	Total	4149.482	245.281	100.0	100.0			

HPLC chromatogram for (*R*)-**18e**.

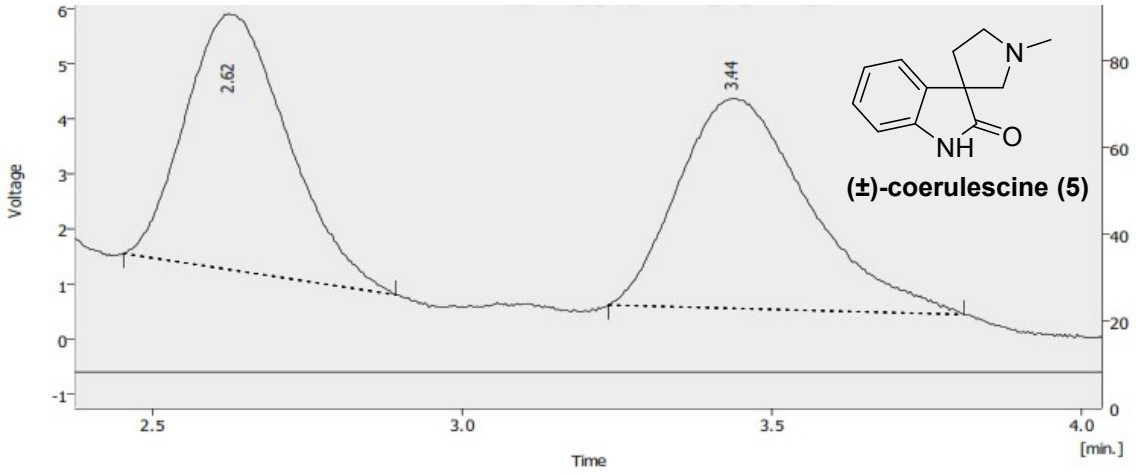


HPLC chromatogram for racemic-**18f**.

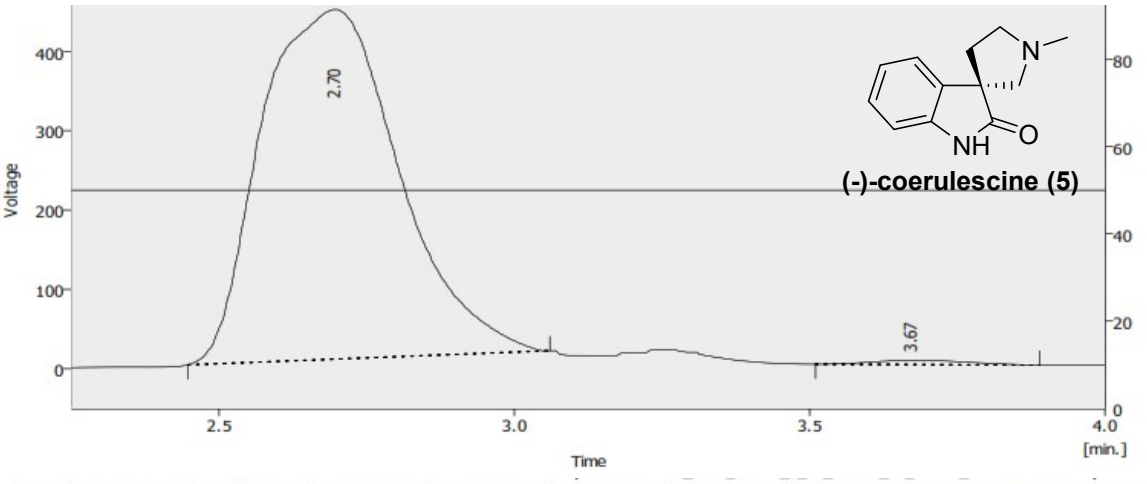


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	4.943	75.616	4.787	1.7	2.2	0.25	422	
2	6.907	4319.586	213.532	98.3	97.8	0.32	968	
	Total	4395.202	218.319	100.0	100.0			

HPLC chromatogram for (*R*)-**18f**.

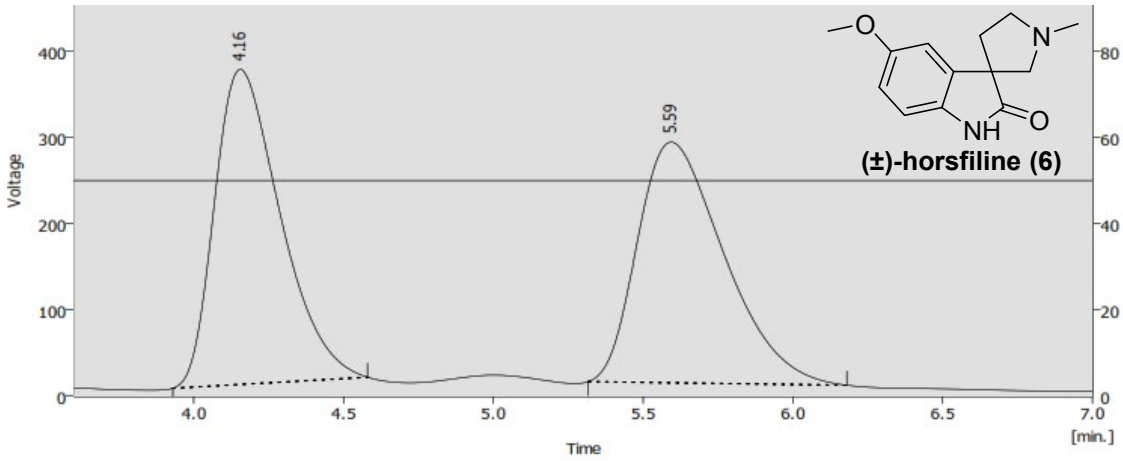


HPLC chromatogram for (±)-coerulescine (**5**).

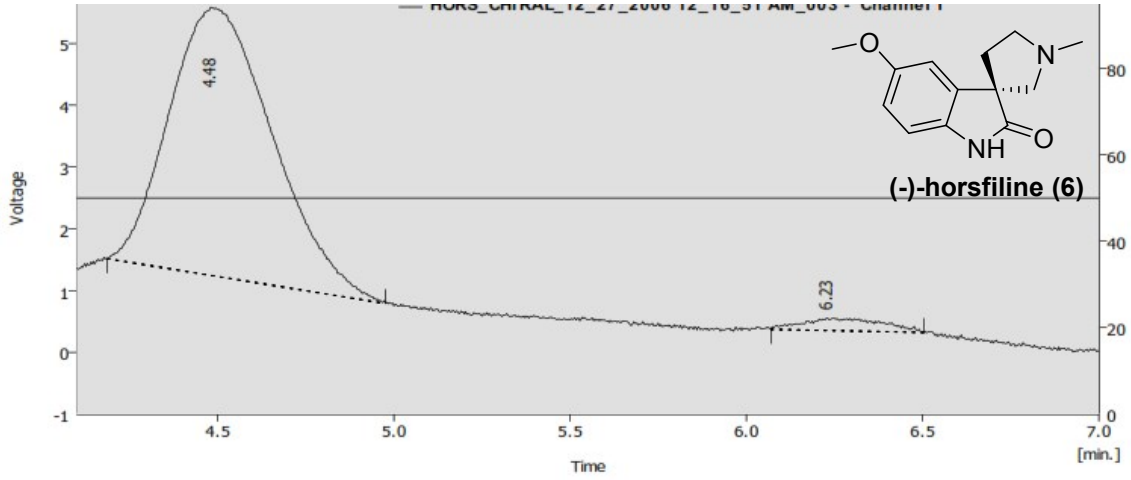


	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	2.697	7140.334	440.453	99.1	98.8	0.26	998	
2	3.673	61.659	5.459	0.9	1.2	0.18	999	
	Total	7201.993	445.911	100.0	100.0			

HPLC chromatogram for (-)-coerulescine (**5**).



HPLC chromatogram for (±)-horsfiline (**6**).



	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	4.480	89.015	4.344	96.5	95.5	0.32	988	
2	6.230	3.259	0.205	3.5	4.5	0.26	979	
	Total	92.274	4.550	100.0	100.0			

HPLC chromatogram for (-)-horsfiline (**6**).