Efficient access to sp^3–rich tricyclic amine scaffolds through Diels-Alder reactions of azide−containing silyloxydienes

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Supporting Information

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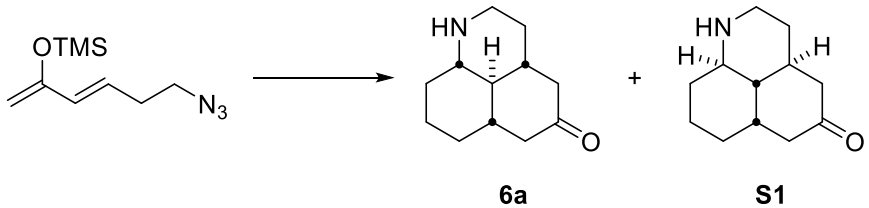
Note: For the convenience of the reader, the entire experimental details embodied in the paper are also included here.

1. General experimental

Unless stated, all solvents and reagents were used as supplied from commercial sources. Dichloromethane and tetrahydrofuran were dried by being passed through two packed columns of neutral ammonia using a commercial solvent purification system prior to use. Parallel library syntheses were performed on a Bohdan Miniblock XT parallel solution phase syntheziser obtained from Mettler-Toledo Auto Chem. Parallel evaporation was performed on a GeneVac EZ-2 plus evaporation system. Purification of the libraries was performed by mass-directed fractionalization: the HPLC analysis was carried out using a Waters Acquity system with UV and mass detection with a linear gradient of 5% acetonitrile in pH 9.8 buffered aqueous NH_4HCO_2 to 100% MeCN at a flow rate of 0.6 mL/min. Preparative reverse-phase purification was carried out using a Waters 2767 preparative system with UV detection (Waters 2996 PAD) and mass detection (Waters Micromass ZQ) with a Waters X-Bridge C18 column (19 x 150 mm, with 19 x 10 mm guard column) eluting with a water (or pH 9.8 aqueous NH_4OH)/ acetonitrile gradient with a flow rate of 20 mL/min, and sample dilution in DMSO. Flash chromatography was performed using Sorbent Technologies standard grade silica gel (40-63 µm particle size, 230 Å 400 mesh). Automated column chromatography was performed on a Teledyne CombiFlashRf system with pre-packed RediSepRf columns for normal phase, and RediSepRf C18 high performance Gold columns for reverse phase separations. Infrared spectra were acquired on a PerkinElmer Spectrum 100 FT-IR spectrophotometer. NMR spectra were recorded at the frequencies stated using a Bruker AM 400 or Bruker 500 MHz AVIII with 13C-observe cryogenically-cooled probe spectrometer. Chemical shifts were referenced to δ 7.26 and 77.0 ppm from chloroform for ^1H and ^{13}C respectively. The multiplicities of ^1H signals are designated by the following abbreviations: s = singlet; d = doublet; t = triplet; m = multiplet; br = broad. All ^{13}C NMR spectra were acquired using broadband decoupled mode and assignments were determined using DEPT sequences. Mass spectra were obtained by electrospray ionization in positive ion mode.

2. Experimental procedures for scaffold synthesis

Amine scaffolds 6a & S1



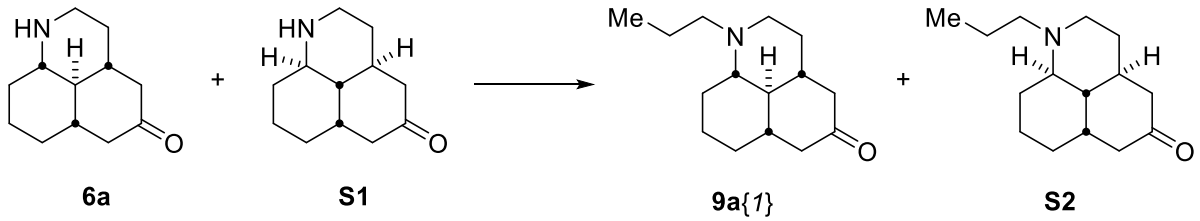
6a **S1**

$BF_3{\cdot}OEt_2$ (4.60 mL, 37.1 mmol) was added to a solution of cyclohexenone (3.60 mL, 37.1 mmol) in anhydrous CH_2Cl_2 (300 mL) with 4Å MS (~8.5 g) at −78 °C under argon. The mixture was stirred at −78 °C

for 5 min, then a solution of silyloxydiene **3a** [1] (11.8 g, 55.6 mmol) in CH_2Cl_2 (50 mL) was added over 10 min. The reaction was allowed to warm from −78 °C to rt and stirred for 18 h. The reaction was quenched with H_2O (200 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil. The crude product was purified by automated chromatography (2 x 40 g silica columns, 0 to 10% MeOH in CH_2Cl_2 over 20 min). All of the fractions containing the correct mass were combined to afford an orange oil (4.00 g).

The diastereomeric mixture of above azides was dissolved in anhydrous THF (200 mL) and PPh_3 (8.90 g, 34.0 mmol) added. The reaction mixture was stirred at rt for 18 h, then 2M NaOH (50 mL) added and the mixture extracted with EtOAc (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil. The residue was dissolved in CH_2Cl_2 (200 mL) and acetic acid (970 µL, 17.0 mmol) added, followed by sodium triacetoxyborohydride (7.20 g, 34.0 mmol). The reaction was stirred at rt for 18 h, then quenched with 2M NaOH (50 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown solid. The crude product was purified by chromatography (silica gel, 90:9:1 CH_2Cl_2:MeOH:NH_4OH) to afford the title compound (800 mg, 7% from diene **3a**, inseparable mixture of diastereoisomers) as a brown oil.

Amines 9a{*1*} & **S2**

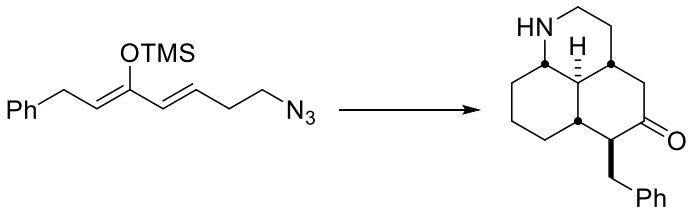


Propionaldehyde (450 µL, 6.21 mmol) was added to a solution of the diastereomeric mixture of amines **6a** and **S1** (800 mg, 4.14 mmol) in anhydrous CH_2Cl_2 (30 mL) at rt under argon. Acetic acid (240 µL, 4.14 mmol) was then added, followed by sodium triacetoxyborohydride (1.75 g, 8.28 mmol). The reaction mixture was stirred at rt for 18 h, then quenched with 2 M NaOH (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil (850 mg). The crude product was purified by automated reverse-phase chromatography (50 g C18 column, 10% MeCN in basic H_2O to 100% over 20 min), to afford **9a**{*1*} (286 mg, 29%) and **S2** (152 mg, 16%) as pale yellow solids.

9a{*1*}**:** ν_{max} (film)/cm^{-1} 2926, 1711; δ_H (500 MHz, $CDCl_3$) 2.95 – 2.90 (m, 1H), 2.66 – 2.58 (m, 1H), 2.45 – 2.38 (m, 1H), 2.33 – 2.24 (m, 3H), 2.12 – 2.00 (m, 3H), 1.88 – 1.77 (m, 2H), 1.65 – 1.59 (m, 2H), 1.51 – 1.26 (m, 6H), 1.18 – 1.04 (m, 3H), 0.82 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.2 (C), 63.8 (CH), 55.1 (CH_2), 52.6 (CH_2), 50.5 (CH), 48.5 (CH_2), 48.4 (CH_2), 41.01 (CH), 40.99 (CH), 33.8 (CH_2), 33.3 (CH_2), 30.0 (CH_2), 24.5 (CH_2), 17.5 (CH_2), 12.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 236.2001. $C_{15}H_{26}NO^+$ requires 236.2009.

S2: ν_{max} (film)/cm^{-1} 2926, 1710; δ_H (500 MHz, $CDCl_3$) 2.96 – 2.90 (m, 1H), 2.60 – 2.53 (m, 2H), 2.49 – 2.37 (m, 2H), 2.28 – 2.21 (m, 2H), 2.19 – 1.99 (m, 5H), 1.75 – 7.64 (m, 2H), 1.62 – 1.50 (m, 2H), 1.48 – 1.24 (m, 5H), 1.14 (ddd, *J* = 16.5, 12.5, 4.0 Hz, 1H), 0.85 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 211.5 (C), 59.2 (CH), 54.4 (CH_2), 53.1 (CH_2), 48.6 (CH_2), 47.6 (CH_2), 45.1 (CH), 39.1 (CH), 34.9 (CH_2), 32.6 (CH), 29.7 (CH_2), 28.1 (CH_2), 19.8 (CH_2), 17.1 (CH_2), 12.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 236.1999. $C_{15}H_{26}NO^+$ requires 236.2009.

Amine scaffold 6c



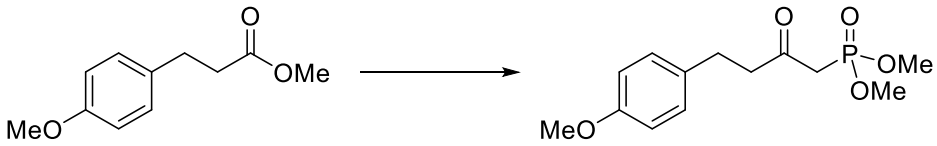
$BF_3{\cdot}OEt_2$ (5.20 mL, 42.4 mmol) was added to a solution of cyclohexenone (4.10 mL, 42.4 mmol) in anhydrous CH_2Cl_2 (350 mL) with 4Å MS (~20 g) at −78 °C under argon. The mixture was stirred at −78 °C for 5 min, then a solution of silyloxydiene **3c** [1] (17.9 g, 59.4 mmol) in CH_2Cl_2 (50 mL) was added over 10 min. The reaction was allowed to warm from −78 °C to rt and stirred for 18 h. The reaction was quenched with H_2O (200 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil (19.5 g). The crude product was purified by automated chromatography (40 g silica column, 0 to 10% MeOH in CH_2Cl_2 over 20 min). All of the fractions containing the correct mass were combined to afford an orange oil (6.60 g).

The diastereomeric mixture of above azides was dissolved in anhydrous THF (400 mL) and PPh_3 (10.6 g, 40.6 mmol) added. The reaction mixture was stirred at rt for 18 h, then 2M NaOH (60 mL) added and the mixture extracted with EtOAc (3 x 200 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil. The residue was dissolved in CH_2Cl_2 (350 mL) and acetic acid (1.20 mL, 20.3 mmol) added, followed by sodium triacetoxyborohydride (8.60 g, 40.6 mmol). The reaction was stirred at rt for 18 h, then quenched with 2M NaOH (70 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil. The crude product was purified by chromatography (silica gel, 90:9:1 CH_2Cl_2:MeOH:NH_4OH) to afford the title compound (3.30 g, 20% from diene **3c**, mixture of diastereoisomers) as a brown oil.

The diastereomeric mixture was dissolved in MeOH (150 mL) and K_2CO_3 (7.20 g, 52.4 mmol) added. The reaction was stirred at rt for 18 h, then concentrated to a brown oil, which was dissolved in CH_2Cl_2 (100 mL) and H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (4 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford the title compound (2.44 g, 74%, >9:1 dr) as a yellow solid foam. δ_H (500 MHz, $CDCl_3$) 7.26 – 7.12 (m, 5H), 3.11 – 3.05 (m, 2H), 2.79 (dd, *J* = 14.5, 2.6 Hz, 1H), 2.72 (ddd, *J* = 12.2, 12.2, 2.7 Hz, 1H), 2.43 (ddd, *J* = 10.8, 8.1, 1.9 Hz, 1H), 2.37 (dd, *J* = 12.8, 3.8 Hz, 1H),

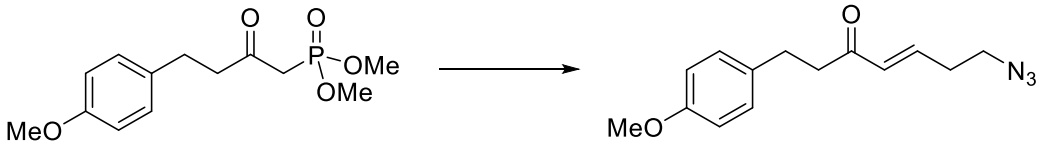
2.31 – 2.22 (m, 1H), 2.18 – 2.12 (m, 2H), 1.89 – 1.83 (m, 2H), 1.81 – 1.76 (m, 1H), 1.66 (ddd, *J* = 12.9, 5.9, 2.5 Hz, 1H), 1.58 – 1.49 (m, 1H), 1.42 – 1.23 (m, 4H), 1.19 – 1.05 (m, 2H); δ_C (125 MHz, $CDCl_3$) 209.9 (C), 141.5 (C), 129.3 (CH), 128.2 (CH), 125.7 (CH), 59.9 (CH), 58.0 (CH), 52.3 (CH), 48.9 (CH_2), 46.2 (CH_2), 46.0 (CH), 41.5 (CH), 34.3 (CH_2), 33.2 (CH_2), 31.9 (CH_2), 31.2 (CH_2), 24.3 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 284.1991. $C_{19}H_{26}NO^+$ requires 284.2009.

Dimethyl (4-(4-methoxyphenyl)-2-oxobutyl)phosphonate (7d)



n-Butyllithium (2.5 M in hexanes, 22.0 mL, 55.1 mmol) was added slowly to a solution of dimethyl methylphosphonate (6.00 mL, 55.1 mmol) in anhydrous THF (100 mL) at −78 °C under argon. The reaction mixture was stirred at −78 °C for 1 h, then a solution methyl 3-(4-methoxyphenyl)propanoate[2] (10.7 g, 55.1 mmol) in THF (50 mL) was added dropwise. The mixture was stirred at −78 °C for 5 min, then at rt for 30 min, after which the reaction was quenched with saturated aqueous NH_4Cl (100 mL) and extracted with Et_2O (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a pale yellow oil (15.8 g). The crude product was purified by chromatography (silica gel, 100% EtOAc) to afford the title compound (9.00 g, 57%) as a colourless oil. ν_{max} (film)/cm^{-1} 2956, 1712, 1243, 1021; δ_H (400 MHz, $CDCl_3$) 7.23 – 7.06 (m, 2H), 6.93 – 6.76 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.09 (d, *J* = 22.7 Hz, 2H), 2.98 – 2.84 (m, 4H); δ_C (100 MHz, $CDCl_3$) 201.1 (C, d, *J* = 6.1 Hz), 158.0 (C), 132.6 (C), 129.3 (CH), 113.9 (CH), 55.3 (CH_3), 53.1 (CH_3), 53.0 (CH_3), 45.8 (CH_2), 41.5 (CH_2, d, *J* = 128 Hz), 28.6 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 287.1049. $C_{13}H_{20}O_5P^+$ requires 287.1043.

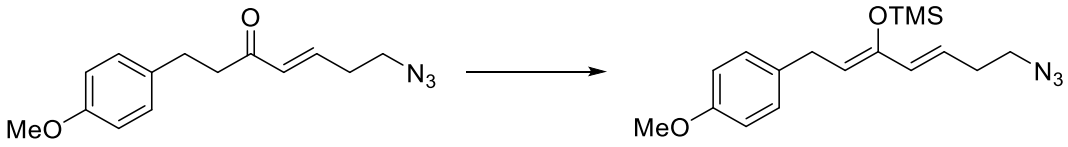
(*E*)-7-Azido-1-(4-methoxyphenyl)hept-4-en-3-one (S3)



Sodium hydride (60% dispersion in oil, 1.54 g, 38.6 mmol) was added portionwise to a solution of **7d** (8.50 g, 29.7 mmol) in anhydrous THF (100 mL) at −50 °C under argon. The resulting suspension was warmed from −78 °C to 0 °C over 2.5 h, then cooled to −10 °C and a solution of 3-azidopropanal[3] (3.82 g, 38.6 mmol) in THF (20 mL) was added over 5 min. The reaction mixture was stirred between 0 and −10 °C for 1 h, then at rt for 45 min. Water (50 mL) was then added and extracted with Et_2O (2 x 50 mL). The combined organics were washed with brine (50 mL), dried (Na_2SO_4) and concentrated to afford a brown oil (10.1 g). The crude product was purified by automated chromatography (2 x 40 g columns, 0 to 25%

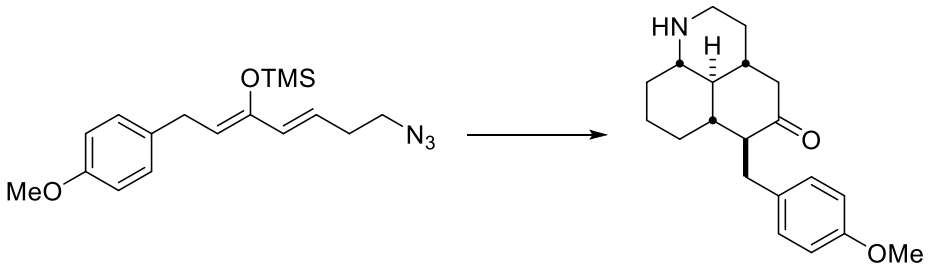
EtOAc in hexanes over 15 min) to afford the title compound (4.5 g, 58%) as a yellow oil. ν_{max} (film)/cm^{-1} 2935, 2094, 1511; δ_H (400 MHz, $CDCl_3$) 7.17 – 7.05 (m, 2H), 6.86 – 6.81 (m, 2H), 6.76 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.19 (dt, *J* = 15.9, 1.5 Hz, 1H), 3.79 (s, 3H), 3.42 (t, *J* = 6.7 Hz, 2H), 3.04 – 2.80 (m, 4H), 2.49 (dtd, *J* = 6.9, 6.9, 1.5 Hz, 2H); δ_C (100 MHz, $CDCl_3$) 199.1 (C), 158.0 (C), 142.0 (CH), 133.1 (C), 132.3 (CH), 129.3 (CH), 113.9 (CH), 55.3 (CH_3), 49.7 (CH_2), 42.2 (CH_2), 31.8 (CH_2), 29.1 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 260.1421. $C_{14}H_{18}N_3O_2^+$ requires 260.1394.

(((2Z,4E)-7-azido-1-(4-methoxyphenyl)hepta-2,4-dien-3-yl)oxy)trimethylsilane (3d)



TMSOTf (4.65 mL, 25.7 mmol) was added dropwise to a solution of azide **S3** (4.45 g, 17.2 mmol) and Et_3N (7.18 mL, 51.5 mmol) in anhydrous CH_2Cl_2 (150 mL) at −30 °C under argon. The resulting yellow solution was stirred at −30 °C for 15 min then at 0 °C for 15 min, then quenched with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (2 x 50 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil, which was dissolved in 4:1 hexanes: EtOAc and passed through a Florisil plug with 4:! hexanes: EtOAc washings. The filtrate was concentrated to afford the title compound (5.50 g, 96%) as a yellow oil that was used immediately in the next step. δ_H (400 MHz, $CDCl_3$) 6.93 – 6.88 (m, 2H), 6.65 – 6.60 (m, 2H), 5.80 (d, *J* = 15.4 Hz, 1H), 5.55 (dt, *J* = 15.0, 7.1 Hz, 1H), 4.71 (t, *J* = 7.1 Hz, 1H), 3.58 (s, 3H), 3.20 (d, *J* = 7.1 Hz, 2H), 3.12 (t, *J* = 7.1 Hz, 2H), 2.19 (dt, *J* = 7.1, 7.1 Hz, 2H), 0.05 (s, 9H).

Amine scaffold 6d



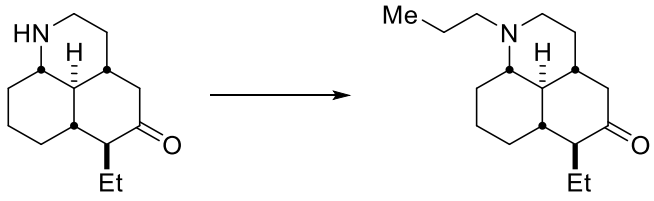
$BF_3{\cdot}OEt_2$ (1.47 mL, 11.9 mmol) was added to a solution of cyclohexenone (1.15 mL, 11.9 mmol) in anhydrous CH_2Cl_2 (100 mL) with 4Å MS (~5 g) at −78 °C under argon. The mixture was stirred at −78 °C for 5 min, then a solution of silyloxydiene **3d** (5.50 g, 16.6 mmol) in CH_2Cl_2 (20 mL) was added over 10 min. The reaction was allowed to warm from −78 °C to rt and stirred for 18 h. The reaction was quenched with H_2O (50 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oily solid (5.72 g). The crude product was purified by

automated chromatography (40 g silica column, 0 to 10% MeOH in CH_2Cl_2 over 20 min). All of the fractions containing the correct mass were combined to afford a brown oil (4.85 g).

The diastereomeric mixture of above azides was dissolved in anhydrous THF (200 mL) and PPh_3 (7.16 g, 27.3 mmol) added. The reaction mixture was stirred at rt for 18 h, then 2M NaOH (50 mL) added and the mixture extracted with EtOAc (3 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil. The residue was dissolved in CH_2Cl_2 (200 mL) and acetic acid (780 µL, 13.6 mmol) added, followed by sodium triacetoxyborohydride (5.79 g, 27.3 mmol). The reaction was stirred at rt for 18 h, then quenched with 2M NaOH (50 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a brown oil (15 g). The crude product was purified by chromatography (silica gel, 90:9:1 CH_2Cl_2:MeOH:NH_4OH) to afford the title compound (1.70 g, 46% from silyloxydiene **3d**, 4:1 dr) as a brown oil.

The diastereomeric mixture was dissolved in MeOH (50 mL) and K_2CO_3 (3.37 g, 24.4 mmol) added. The reaction was stirred at rt for 18 h, then concentrated to a brown oil, which was dissolved in CH_2Cl_2 (100 mL) and H_2O (30 mL). The aqueous layer was extracted with CH_2Cl_2 (4 x 100 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford the title compound (1.65 g, 97%, 9:1 dr) as a brown solid foam. ν_{max} (film)/cm^{-1} 2925, 1707, 1511, 1245; δ_H (400 MHz, $CDCl_3$) 7.12 – 7.07 (m, 2H), 6.81 – 6.75 (m, 2H), 3.77 (s, 3H), 3.32 (d, *J* = 12.4 Hz, 1H), 2.96 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.88 – 2.78 (m, 2H), 2.65 – 2.58 (m, 1H), 2.49 – 2.39 (m, 2H), 2.25 – 2.07 (m, 3H), 1.94 – 1.87 (m, 1H), 1.80 – 1.52 (m, 5H), 1.42 – 1.26 (m, 2H), 1.24 – 1.13 (m, 1H); δ_C (100 MHz, $CDCl_3$) 208.4 (C), 157.7 (C), 132.6 (C), 130.2 (CH), 113.7 (CH), 59.0 (CH), 57.4 (CH), 55.2 (CH_3), 48.0 (CH), 47.7 (CH_2), 45.2 (CH), 43.7 (CH_2), 39.5 (CH), 30.9 (CH_2), 30.1 (CH_2), 30.1 (CH_2), 29.7 (CH_2), 23.8 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 314.2137. $C_{20}H_{28}NO_2^+$ requires 314.2115.

Amine 9b{*1*}



Propionaldehyde (1.22 mL, 16.8 mmol) was added to a solution of amine **6b** (2.48 g, 11.2 mmol) in anhydrous CH_2Cl_2 (100 mL) at rt under argon. Acetic acid (640 µL, 11.2 mmol) was then added, followed by sodium triacetoxyborohydride (4.75 g, 22.4 mmol). The reaction mixture was stirred at rt for 48 h, then quenched with 2 M NaOH (50 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford the title compound (2.94 g, 100%) as a yellow oil, which was used without further purification. ν_{max} (film)/cm^{-1} 2929, 1711; δ_H (400 MHz, $CDCl_3$) 3.04-2.99 (1H, m), 2.74-2.66 (1H, m), 2.58-2.51 (1H, m), 2.40-2.32 (2H, m), 2.17-1.87 (6H, m), 1.70-1.41 (7H, m), 1.36-

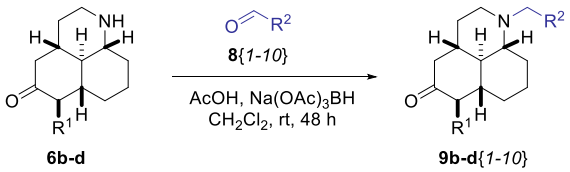
1.19 (4H, m), 1.10-1.00 (1H, m), 0.87 (3H, t, *J* 7.2), 0.85 (3H, t, *J* 7.6); δ_C (100 MHz, $CDCl_3$) 210.8 (C), 63.9 (CH), 56.1 (CH), 54.8 (CH_2), 52.4 (CH_2), 50.4 (CH), 48.8 (CH_2), 44.7 (CH), 41.4 (CH), 32.9 (CH_2), 31.2 (CH_2), 29.5 (CH_2), 24.6 (CH_2), 17.9 (CH_2), 17.1 (CH_2), 12.0 (CH_3), 11.2 (CH_3);); *m/z* (ESI+) found $[M+H]^+$ 264.2314. $C_{17}H_{30}NO^+$ requires 264.2322.

Alcohol S4

L-Selectride (1 M in THF, 8.10 mL) was added dropwise to a solution of **9b**{*1*} (850 mg, 3.23 mmol) in anhydrous THF (20 mL) at −78 °C under argon. The reaction mixture was allowed to warm slowly to rt and stirred for 18 h, then quenched with 30% aq H_2O_2 (5.1 mL) and 2 M NaOH (6.8 mL). The mixture was stirred at rt for 1 h, then extracted with CH_2Cl_2 (3 x 20 mL). The combined organics were dried (Na_2SO_4) and concentrated to afford a yellow oil. The crude product was purified by chromatography (silica gel, 90:9:1 CH_2Cl_2:MeOH:NH_4OH) to afford the title compound (825 mg, 96%) as a yellow oil. δ_H (500 MHz, $CDCl_3$) 4.03 (br s, 1H), 2.93 (ddd, *J* = 11.3, 3.8, 3.8 Hz, 1H), 2.70 – 2.56 (m, 1H), 2.55 – 2.40 (m, 1H), 2.32 (ddd, *J* = 12.0, 12.0, 2.5 Hz, 1H), 2.14 – 2.00 (m, 1H), 1.96 – 1.76 (m, 4H), 1.68 – 1.60 (m, 1H), 1.53 (ddd, *J* = 12.6, 2.7, 2.7 Hz, 1H), 1.50 – 1.40 (m, 3H), 1.41 – 0.94 (m, 7H), 0.94 – 0.87 (m, 3H), 0.84 (t, *J* = 7.4 Hz, 3H), 0.81 – 0.71 (m, 2H); δ_C (125 MHz, $CDCl_3$) 66.5 (CH), 63.5 (CH), 55.3 (CH_2), 52.7 (CH_2), 51.4 (CH), 47.6 (CH), 40.3 (CH_2), 38.6 (CH), 33.3 (CH), 32.8 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 24.5 (CH_2), 21.4 (CH_2), 17.1 (CH_2), 12.0 (CH_3), 11.7 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 266.2480. $C_{17}H_{32}NO^+$ requires 266.2478

3. Experimental procedures for library synthesis

General procedure for the preparation of amines.

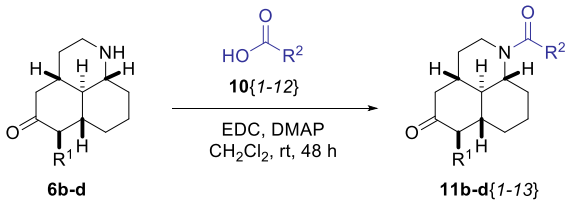


3{*1*} R = Et
3{*2*} R = thiozol-2-yl
3{*3*} R = *N*-methylimidazol-2-yl
3{*4*} R = $(CH_2)_2Ph$
3{*5*} R = Ph
3{*6*} R = 4-ClC_6H_4
3{*7*} R = 4-$MeOC_6H_4$
3{*8*} R = 4-MeC_6H_4
3{*9*} R = 2-$O_2NC_6H_4$
3{*10*} R = 2-$F_3CC_6H_4$

Each reaction tube of a 24-position Bohdan Miniblock XT was flushed with argon, then a solution of the amine scaffold **6b-d** (70 mg) in anhydrous dichloromethane (2 mL) was added, followed by the appropriate aldehyde (1.5 equiv), acetic acid (1 equiv) and $Na(OAc)_3BH$ (2 equiv). The reactions were shaken at 500 rpm at rt for 48 h, then 2 M NaOH (1 mL) added. The reactions were passed through Isolute® hydrophobic phase separator tubes, which allowed the halogenated solvent layer to pass through. The aqueous layers were extracted with dichloromethane (2 x 2 mL). The combined organics were evaporated in a Genevac EZ-2 Plus parallel evaporator and subjected to mass-directed preparative HPLC purification to afford pure amines **9b-d**{*1-10*}.

Compound	Calculated m/w	Found m/w	Recovered mass (mg)	Yield (%)	Purity (%)
9b{*2*}	319.1839	319.1847	42.8	42	94.1
9b{*3*}	316.2384	316.2376	33.5	33	100.0
9b{*4*}	340.2635	340.2598	55.2	51	95.0
9b{*5*}	312.2322	312.2325	24.6	25	100.0
9b{*6*}	346.1932	346.1959	37.8	34	100.0
9b{*7*}	342.2428	342.2430	36.7	34	97.7
9b{*8*}	326.2479	326.2480	12.8	12	95.2
9b{*9*}	357.2173	357.2193	11.9	10	12.5
9b{*10*}	380.2196	380.2229	23.8	20	97.3
9c{*1*}	326.2479	326.2516	37.8	46	100.0
9c{*2*}	381.1995	381.2039	49.6	52	100.0
9c{*3*}	378.2540	378.2560	71.9	76	100.0
9c{*4*}	402.2792	402.2818	56.8	56	100.0
9c{*5*}	374.2479	374.2523	61.7	66	100.0
9c{*6*}	408.2089	408.2108	60.2	59	98.2
9c{*7*}	404.2584	404.2609	52.4	52	100.0
9c{*9*}	419.2329	419.2354	55.5	53	97.4
9c{*10*}	442.2352	442.2374	45.6	41	94.5
9d{*1*}	356.2584	356.2596	44.6	66	98.2
9d{*2*}	411.2101	411.2119	4.7	6	1.0
9d{*3*}	408.2646	408.2629	18.7	24	98.0
9d{*4*}	432.2897	432.2902	25.1	31	93.8
9d{*5*}	404.2584	404.2580	2.8	4	63.7
9d{*6*}	438.2195	438.2191	25.2	30	97.9
9d{*7*}	434.2690	434.2690	22.1	27	48.7

General procedure for the preparation of amides.



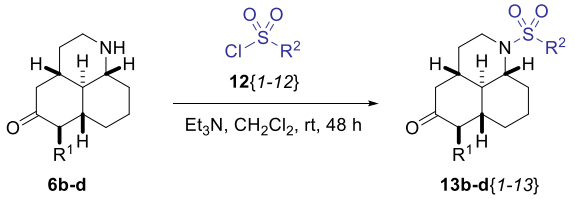
5{*1*} R^2 = Ph
5{*2*} R^2 = 4-ClC_6H_4
5{*3*} R^2 = 4-$MeOC_6H_4$
5{*4*} R^2 = 4-MeC_6H_4
5{*5*} R^2 = 3,4-$Cl_2C_6H_3$
5{*6*} R^2 = 3-$Me_2NC_6H_4$
5{*7*} R^2 = nBu
5{*8*} R^2 = cyclobutyl
5{*9*} R^2 = cyclohexyl
5{*10*} R^2 = thiophen-3-ylmethyl
5{*11*} R^2 = pyridin-3-yl
5{*12*} R^2 = phenylethynyl

Each reaction tube of a 24-position Bohdan Miniblock XT was flushed with argon, then a solution of the amine scaffold **6b-d** (70 mg) in anhydrous dichloromethane (2 mL) was added, followed by the appropriate acid (1.2 equiv), EDC (1.2 equiv) and DMAP (1.2 equiv). The reactions were shaken at 500 rpm at rt for 48 h, then water (2 mL) added. The reactions were passed through Isolute® hydrophobic phase separator tubes, which allowed the halogenated solvent layer to pass through. The aqueous layers were extracted with dichloromethane (2 x 2 mL). The combined organics were evaporated in a Genevac EZ-2 Plus parallel evaporator and subjected to mass-directed preparative HPLC purification to afford pure amides **11b-d**{*1-13*}.

Compound	Calculated m/w	Found m/w	Recovered mass (mg)	Yield (%)	Purity(%)
11b{*1*}	326.2115	326.2130	39.5	38	98.0
11b{*2*}	360.1725	360.1729	40.5	35	96.6
11b{*3*}	356.2220	356.2238	49.1	43	100.0
11b{*4*}	340.2271	340.2284	38.8	36	95.3
11b{*5*}	394.1335	394.1352	56.5	45	91.6
11b{*6*}	369.2537	369.2548	41.5	35	85.9
11b{*7*}	306.2428	306.2446	26.3	27	88.7
11b{*8*}	304.2271	304.2273	31.3	32	90.6
11b{*9*}	332.2584	332.2583	3.9	4	84.8
11b{*10*}	346.1835	346.1855	35.5	32	97.5
11b{*11*}	327.2067	327.2074	3.3	3	100.0
11c{*1*}	388.2271	388.2291	43.2	45	100.0
11c{*2*}	422.1882	422.1902	60.6	57	97.8
11c{*3*}	418.2377	418.2392	54.8	52	100.0
11c{*4*}	402.2428	402.2451	50.0	50	97.9
11c{*5*}	456.1492	456.1538	25.6	22	100.0
11c{*6*}	431.2693	431.2729	59.3	55	96.3
11c{*7*}	368.2584	368.2603	40.7	44	98.6
11c{*8*}	366.2428	366.2454	43.3	47	100.0
11c{*9*}	394.2741	394.2754	46.2	47	100.0
11c{*10*}	408.1992	408.2026	48.6	48	100.0
11c{*11*}	389.2224	389.2241	46.6	48	100.0

11c{*12*}	412.2271	412.2288	20.6	20	99.0
11d{*1*}	418.2377	418.2359	22.0	28	98.6
11d{*2*}	452.1987	452.1982	25.5	30	100.0
11d{*7*}	398.2690	398.2692	25.6	34	98.7
11d{*8*}	396.2533	396.2527	29.2	39	100.0
11d{*10*}	438.2098	438.2088	29.7	36	100.0

General procedure for the preparation of sulfonamides.



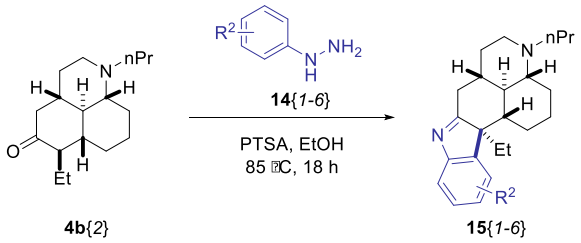
7{*1*} R^2 = Ph
7{*2*} R^2 = 4-ClC_6H_4
7{*3*} R^2 = 4-$MeOC_6H_4$
7{*4*} R^2 = 4-MeC_6H_4
7{*5*} R^2 = 3,5-$Cl_2C_6H_3$
7{*6*} R^2 = 4-$F_3CC_6H_4$
7{*7*} R^2 = 4-FC_6H_4
7{*8*} R^2 = 4-nBuC_6H_4
7{*9*} R^2 = 2,4-$(NO_2)_2C_6H_3$
7{*10*} R^2 = benzyl
7{*11*} R^2 = naphthyl
7{*12*} R^2 = *N*-methylimidazol-2-yl

Each reaction tube of a 24-position Bohdan Miniblock XT was flushed with argon, then a solution of the amine scaffold **6b-d** (70 mg) in anhydrous dichloromethane (2 mL) was added, followed by the appropriate sulfonyl chloride (1.5 equiv) and Et_3N (1.5 equiv). The reactions were shaken at 500 rpm at rt for 48 h, then water (2 mL) added. The reactions were passed through Isolute® hydrophobic phase separator tubes, which allowed the halogenated solvent layer to pass through. The aqueous layers were extracted with dichloromethane (2 x 2 mL). The combined organics were evaporated in a Genevac EZ-2 Plus parallel evaporator and subjected to mass-directed preparative HPLC purification to afford pure sulfonamides **13b-d**{*1-13*}.

Compound	Calculated m/w	Found m/w	Recovered mass (mg)	Yield (%)	Purity (%)
13b{*1*}	362.1785	362.1800	30.6	26	95.7
13b{*2*}	396.1395	396.1426	55.6	44	98.9
13b{*3*}	392.1890	392.1899	47.6	38	93.4
13b{*4*}	376.1941	376.1953	51.0	42	98.9
13b{*5*}	430.1005	430.1036	56.8	41	100.0
13b{*6*}	430.1658	430.1689	58.2	42	98.5
13b{*7*}	380.1690	380.1705	47.4	39	97.3
13b{*8*}	418.2411	418.2436	51.6	39	97.3
13b{*9*}	452.1486	N/A	0.0	0	-
13b{*10*}	376.1941	376.1960	6.8	6	87.8
13b{*11*}	412.1941	412.1971	22.8	17	98.2

13b{*12*}	366.1846	366.1856	46.9	40	93.5
13c{*1*}	424.1941	424.1954	56.7	53	100.0
13c{*2*}	458.1551	458.1566	64.1	56	98.9
13c{*3*}	454.2047	454.2046	61.2	54	98.9
13c{*4*}	438.2098	438.2108	44.8	41	100.0
13c{*5*}	492.1162	492.1176	57.5	47	98.2
13c{*6*}	492.1815	492.1849	66.5	54	100.0
13c{*7*}	442.1847	442.1869	57.7	52	98.9
13c{*8*}	480.2567	480.2560	1.9	2	92.9
13c{*9*}	514.1643	N/A	0.0	0	-
13c{*10*}	438.2098	438.2118	39.8	36	100.0
13c{*11*}	474.2098	474.2117	56.0	47	100.0
13c{*12*}	428.2003	428.2030	67.3	63	97.7
13d{*1*}	454.2047	454.2047	14.6	17	98.7
13d{*2*}	488.1657	488.1643	39.8	43	100.0
13d{*3*}	484.2152	484.2137	22.7	25	100.0
13d{*12*}	458.2108	458.2125	12.3	14	100.0

General procedure for the preparation of *3H*-indoles.



4b{*2*} **15**{*1-6*}

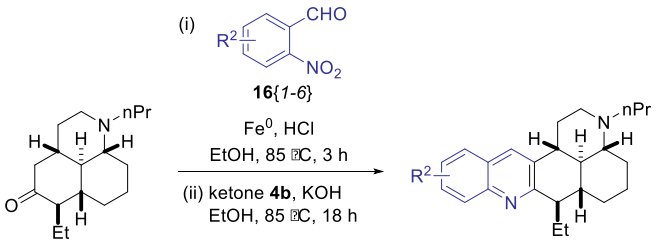
14{*1*} R^2 = H
14{*2*} R^2 = 4-iPr
14{*3*} R^2 = 4-OMe
14{*4*} R^2 = 2,5-Cl_2
14{*5*} R^2 = 2-Cl
14{*6*} R^2 = 4-Cl

PTSA (510 mg, 2.3 mmol) was added to a solution of amine scaffold **4b**{*2*} (60 mg, 0.23 mmol) in EtOH (1.5 mL) in a microwave vial, followed by the appropriate hydrazine (hydrochloride) (2.5 equiv). The vial was sealed then heated in an oil bath at 90 ^{o}C for 4 h, then cooled to rt, 2 M NaOH (2 mL) added and the mixture extracted with CH_2Cl_2 (3 x 5 mL). The combined organics were dried (Na_2SO_4) and concentrated under reduced pressure. The residues were subjected to mass-directed preparative HPLC purification to afford pure *3H*-indoles **15**{*1-6*}.

Compound	Calculated m/z	Found m/z	Recovered weight (mg)	Yield (%)	Purity (%)
15{*1*}	337.2638	337.2645	31.9	41	98.3
15{*2*}	379.3108	379.3119	33.9	39	100.0

15{*3*}	367.2744	367.2767	23.0	27	98.9
15{*4*}	405.1859	405.1856	9.3	10	48.6
15{*5*}	371.2249	371.2259	29.2	34	100.0
15{*6*}	371.2249	371.2258	48.6	57	100.0

General procedure for the preparation of quinolines.



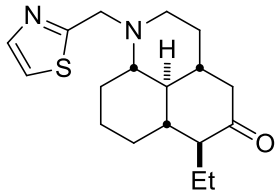
16{*1*} R^2 = H
16{*2*} 1-nitro-2-naphthaldehyde
16{*3*} R^2 = 4,5-(-OCH_2O-)
16{*4*} R^2 = 5-Cl
16{*5*} R^2 = 3-OMe
16{*6*} R^2 = 4-CF_3

Fe^0 powder (77 mg, 1.4 mmol) was added to a solution of nitrobenzaldehyde **16**{*1-6*} (0.35 mmol) in ethanol (1 mL) in a microwave vial, followed by 0.1 M HCl (180 µL). The vial was sealed, then heated in an oil bath at 85 °C until complete by TLC (~2 h). The mixture was cooled to rt, then a solution of ketone scaffold **4b**{*2*} (0.27 mmol) in EtOH (2 mL) added, followed by powdered KOH (18 mg, 0.32 mmol). The mixture was heated at 85 °C for 18 h, then cooled to rt, passed through a celite plug and eluted with dichloromethane, and concentrated under reduced pressure. The residues were subjected to mass-directed preparative HPLC purification to afford pure quinolines **17**{*1-6*}.

Compound	Calculated m/w	Found m/w	Recovered weight (mg)	Yield (%)	Purity (%)
17{*1*}	349.2638	349.2640	41.6	44	97.4
17{*2*}	399.2795	399.2809	40.7	38	100.0
17{*3*}	393.2537	393.2561	27.7	26	94.8
17{*4*}	383.2249	383.2255	27.6	27	97.9
17{*5*}	379.2744	379.2762	54.1	53	91.7
17{*6*}	417.2512	417.2518	70.0	62	100.0

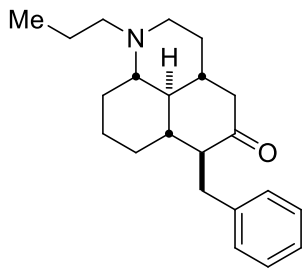
4. Characterization for representative library examples

Amine **9b**{*2*}



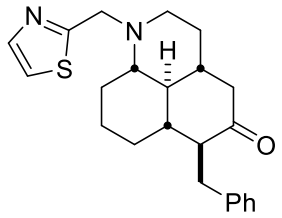
δ_H (500 MHz, $CDCl_3$) 7.72 (d, *J* = 3.3 Hz, 1H), 7.26 (d, *J* = 3.3 Hz, 1H), 4.23 (d, *J* = 15.8 Hz, 1H), 3.94 (d, *J* = 15.8 Hz, 1H), 3.05 – 2.93 (m, 1H), 2.53 – 2.40 (m, 1H), 2.34 (dd, *J* = 13.1, 3.3 Hz, 1H), 2.30 – 2.20 (m, 1H), 2.20 – 2.10 (m, 1H), 2.10 – 1.99 (m, 2H), 1.99 – 1.91 (m, 1H), 1.91 – 1.82 (m, 1H), 1.70 – 1.45 (m, 5H), 1.40 – 1.14 (m, 4H), 1.05 (qd, *J* = 13.0, 3.6 Hz, 1H), 0.84 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.7 (C), 170.7 (C), 142.4 (CH), 119.1 (CH), 64.3 (CH), 56.1 (CH), 54.3 (CH_2), 53.9 (CH_2), 50.9 (CH), 48.7 (CH_2), 44.4 (CH), 41.3 (CH), 33.2 (CH_2), 31.4 (CH_2), 30.3 (CH_2), 24.4 (CH_2), 17.9 (CH_2), 11.1 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 319.1847. $C_{18}H_{27}N_2OS^+$ requires 319.1839.

Amine **9c**{*1*}



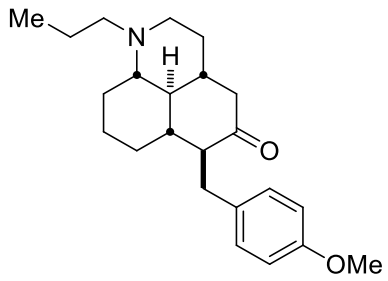
δ_H (500 MHz, $CDCl_3$) 7.26 – 7.11 (m, 5H), 3.08 (dd, *J* = 14.2, 8.1 Hz, 1H), 2.97 – 2.92 (m, 1H), 2.80 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.69 – 2.61 (m, 1H), 2.52 – 2.45 (m, 1H), 2.45 – 2.38 (m, 1H), 2.38 – 2.28 (m, 2H), 2.17 – 2.10 (m, 3H), 1.92 – 1.86 (m, 2H), 1.66 – 1.61 (m, 1H), 1.52 – 1.41 (m, 4H), 1.37 – 1.07 (m, 5H), 0.85 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.1 (C), 141.6 (C), 129.3 (CH), 128.2 (CH), 125.6 (CH), 63.8 (CH), 57.8 (CH), 55.2 (CH_2), 52.5 (CH_2), 51.2 (CH), 48.9 (CH_2), 46.5 (CH), 41.6 (CH), 33.4 (CH_2), 32.0 (CH_2), 31.2 (CH_2), 30.0 (CH_2), 24.6 (CH_2), 17.4 (CH_2), 12.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 326.2516. $C_{22}H_{32}NO^+$ requires 326.2478.

Amine 9c{*2*}



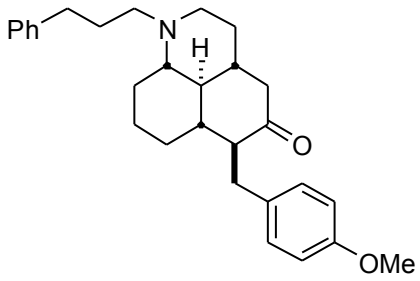
δ_H (400 MHz, $CDCl_3$) 7.72 (d, *J* = 3.3 Hz, 1H), 7.28 – 7.12 (m, 6H), 4.23 (d, *J* = 15.8 Hz, 1H), 3.94 (d, *J* = 15.4 Hz, 1H), 3.08 (dd, *J* = 14.2, 8.1 Hz, 1H), 3.03 – 2.95 (m, 1H), 2.82 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.51 – 2.40 (m, 2H), 2.37 (dd, *J* = 12.9, 3.2 Hz, 1H), 2.29 – 2.23 (m, 1H), 2.20 – 2.01 (m, 3H), 1.94 – 1.87 (m, 1H), 1.67 – 1.61 (m, 1H), 1.57 – 1.42 (m, 2H), 1.40 – 1.20 (m, 4H), 1.19 – 1.08 (m, 1H); δ_C (100 MHz, $CDCl_3$) 209.8 (C), 170.9 (C), 142.5 (CH), 141.4 (C), 129.3 (CH), 128.2 (CH), 125.7 (CH), 119.1 (CH), 64.2 (CH), 57.7 (CH), 54.4 (CH_2), 53.9 (CH_2), 51.2 (CH), 48.7 (CH_2), 46.2 (CH), 41.3 (CH), 33.3 (CH_2), 32.0 (CH_2), 31.2 (CH_2), 30.4 (CH_2), 24.4 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 381.2039. $C_{23}H_{29}N_2OS^+$ requires 381.1995.

Amine **9d**{*1*}



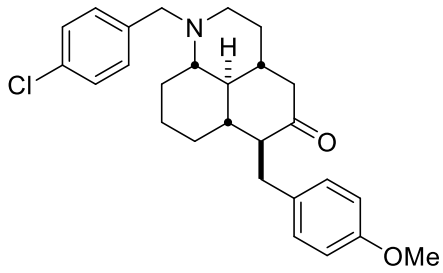
δ_H (500 MHz, $CDCl_3$) 7.15 – 7.10 (m, 2H), 6.80 – 6.76 (m, 2H), 3.77 (s, 3H), 3.01 – 2.91 (m, 2H), 2.78 (dd, *J* = 14.2, 2.5 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.54 – 2.44 (m, 1H), 2.39 – 2.27 (m, 3H), 2.17 – 2.08 (m, 3H), 1.93 – 1.85 (m, 2H), 1.67 – 1.60 (m, 1H), 1.54 – 1.38 (m, 4H), 1.36 – 1.05 (m, 5H), 0.85 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.2 (C), 157.6 (C), 133.4 (C), 130.3 (CH), 113.5 (CH), 63.8 (CH), 57.9 (CH), 55.21 (CH_3), 55.18 (CH_2), 52.5 (CH_2), 51.1 (CH), 48.9 (CH_2), 46.2 (CH), 41.5 (CH), 33.3 (CH_2), 31.9 (CH_2), 30.2 (CH_2), 30.0 (CH_2), 24.6 (CH_2), 17.4 (CH_2), 12.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 356.2596. $C_{23}H_{34}NO_2^+$ requires 356.2584.

Amine **9d**{*4*}



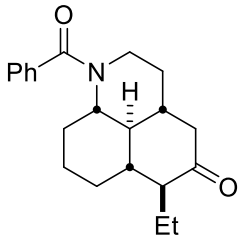
δ_H (500 MHz, $CDCl_3$) 7.32 – 7.28 (m, 2H), 7.23 – 7.18 (m, 3H), 7.15 – 7.12 (m, 2H), 6.81 – 6.77 (m, 2H), 3.78 (s, 3H), 3.01 – 2.95 (m, 2H), 2.84 – 2.77 (m, 2H), 2.65 – 2.53 (m, 3H), 2.40 – 2.32 (m, 3H), 2.18 – 2.04 (m, 3H), 1.97 – 1.74 (m, 4H), 1.67 – 1.62 (m, 1H), 1.61 – 1.41 (m, 2H), 1.39 – 1.08 (m, 5H); δ_C (125 MHz, $CDCl_3$) 210.1 (C), 157.6 (C), 141.9 (C), 133.3 (C), 130.3 (CH), 128.4 (CH), 128.3 (CH), 125.9 (CH), 113.5 (CH), 63.9 (CH), 57.8 (CH), 55.2 (CH_3), 52.5 (CH_2), 52.4 (CH_2), 50.8 (CH), 48.7 (CH_2), 46.1 (CH), 41.3 (CH), 33.8 (CH_2), 33.0 (CH_2), 31.8 (CH_2), 30.2 (CH_2), 29.7 (CH_2), 26.0 (CH_2), 24.5 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 432.2902. $C_{29}H_{38}NO_2^+$ requires 432.2897.

Amine **9d**{*6*}



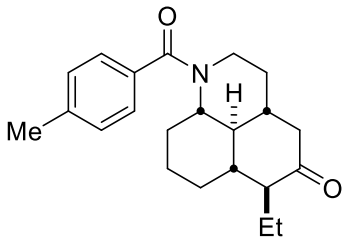
δ_H (500 MHz, $CDCl_3$) 7.29 – 7.23 (m, 4H), 7.15 – 7.12 (m, 2H), 6.81 – 6.77 (m, 2H), 4.09 (d, *J* = 13.7 Hz, 1H), 3.78 (s, 3H), 3.16 (d, *J* = 13.5 Hz, 1H), 2.98 (dd, *J* = 14.2, 8.1 Hz, 1H), 2.84 – 2.77 (m, 2H), 2.41 – 2.31 (m, 2H), 2.29 – 2.23 (m, 1H), 2.19 – 2.10 (m, 2H), 2.06 – 2.00 (m, 1H), 1.95 – 1.87 (m, 2H), 1.57 – 1.52 (m, 1H), 1.50 – 1.10 (m, 7H); δ_C (125 MHz, $CDCl_3$) 210.1 (C), 157.6 (C), 138.1 (C), 132.4 (C), 133.4 (C), 130.3 (CH), 130.2 (CH), 128.3 (CH), 113.5 (CH), 65.2 (CH), 57.9 (CH), 56.7 (CH_2), 55.2 (CH_3), 52.9 (CH_2), 51.1 (CH), 48.8 (CH_2), 46.1 (CH), 41.5 (CH), 33.0 (CH_2), 32.0 (CH_2), 30.6 (CH_2), 30.3 (CH_2), 24.5 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 438.2191. $C_{27}H_{33}ClNO_2^+$ requires 438.2194.

Amide **11b**{*1*}



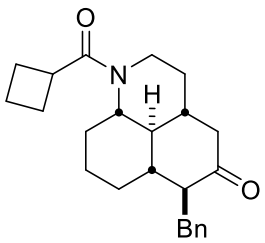
δ_H (500 MHz, $CDCl_3$) 7.43 – 7.35 (m, 5H), 3.56 – 3.46 (m, 2H), 3.41 (ddd, *J* = 13.9, 6.1, 4.1 Hz, 1H), 2.46 (dd, *J* = 13.1, 4.4 Hz, 1H), 2.31 – 2.24 (m, 1H), 2.17 – 2.06 (m, 2H), 2.03 – 1.98 (m, 1H), 1.95 – 1.86 (m, 2H), 1.82 – 1.52 (m, 5H), 1.51 – 1.33 (m, 2H), 1.26 – 1.19 (m, 1H), 1.18 – 1.08 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.0 (C), 171.7 (C), 137.2 (C), 129.6 (CH), 128.5 (CH), 126.9 (CH), 60.2 (CH), 55.9 (CH), 49.0 (CH_2), 46.4 (CH), 45.7 (CH), 43.0 (CH_2), 37.0 (CH), 32.1 (CH_2), 31.4 (CH_2), 29.7 (CH_2), 24.7 (CH_2), 17.9 (CH_2), 11.3 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 326.2130. $C_{21}H_{28}NO_2^+$ requires 326.2115.

Amide **11b**{*4*}



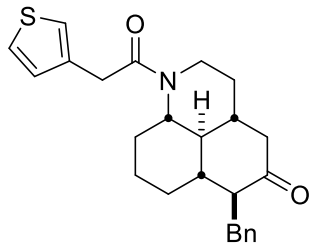
δ_H (500 MHz, $CDCl_3$) 7.30 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 3.54 – 3.46 (m, 2H), 3.43 (ddd, *J* = 13.8, 6.1, 4.3 Hz, 1H), 2.45 (dd, *J* = 13.1, 4.4 Hz, 1H), 2.36 (s, 3H), 2.28 – 2.23 (m, 1H), 2.17 – 2.06 (m, 2H), 2.03 – 1.97 (m, 1H), 1.94 – 1.85 (m, 2H), 1.81 – 1.51 (m, 5H), 1.50 – 1.33 (m, 2H), 1.25 – 1.18 (m, 1H), 1.17 – 1.08 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.1 (C), 172.0 (C), 139.7 (C), 134.3 (C), 129.0 (CH), 127.0 (CH), 60.2 (CH) , 55.9 (CH), 49.0 (CH_2), 46.4 (CH), 45.7 (CH), 43.3 (CH_2), 37.1 (CH), 32.2 (CH_2), 31.4 (CH_2), 29.7 (CH_2), 24.7 (CH_2), 21.4 (CH_3), 17.9 (CH_2), 11.3 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 340.2284. $C_{22}H_{30}NO_2^+$ requires 340.2271.

Amide **11c**{*8*}



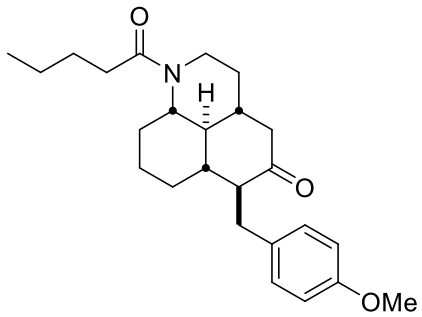
δ_H (500 MHz, $CDCl_3$) 7.26 – 7.12 (m, 5H), 3.56 – 3.38 (m, 2H), 3.30 – 3.16 (m, 2H), 3.05 (dd, *J* = 14.2, 8.5 Hz, 1H), 2.76 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.51 – 2.44 (m, 2H), 2.38 – 2.27 (m, 2H), 2.22 – 2.07 (m, 5H), 2.06 – 1.80 (m, 4H), 1.75 – 1.64 (m, 1H), 1.61 – 1.33 (m, 4H), 1.29 – 1.13 (m, 2H); δ_C (125 MHz, $CDCl_3$) 209.3 (C), 173.8 (C), 141.2 (C), 129.2 (CH), 128.2 (CH), 125.8 (CH), 59.3 (CH), 57.3 (CH), 49.1 (CH_2), 47.4 (CH), 46.4 (CH), 37.8 (CH), 35.9 (CH), 32.3 (CH_2), 31.7 (CH_2), 31.1 (CH_2), 30.2 (CH_2), 25.3 (CH_2), 25.1 (CH_2), 24.5 (CH_2), 18.0 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 366.2454. $C_{24}H_{32}NO_2^+$ requires 366.2428.

Amide **11c**{*10*}



δ_H (500 MHz, $CDCl_3$) 7.29 – 7.27 (m, 1H), 7.25 – 7.21 (m, 2H), 7.19 – 7.12 (m, 3H), 7.05 – 7.03 (m, 1H), 6.99 (dd, *J* = 4.9, 1.3 Hz, 1H), 3.69 (s, 1H), 3.64 (br s, 1H), 3.52 – 3.45 (m, 1H), 3.30 – 3.21 (m, 1H), 3.04 (dd, *J* = 14.2, 8.5 Hz, 1H), 2.75 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.49 – 2.41 (m, 2H), 2.22 – 2.15 (m, 2H), 2.08 (t, *J* = 12.3 Hz, 2H), 1.93 – 1.86 (m, 1H), 1.84 – 1.73 (m, 1H), 1.67 – 1.31 (m, 5H), 1.22 – 1.12 (m, 2H); δ_C (125 MHz, $CDCl_3$) 209.2 (C), 169.8 (C), 141.2 (C), 135.1 (C), 129.2 (CH), 128.2 (CH), 128.0 (CH), 126.0 (CH), 125.8 (CH), 121.7 (CH), 59.4 (CH), 57.1 (CH), 48.9 (CH_2), 47.4 (CH), 46.3 (CH), 39.0 (CH_2), 36.7 (CH_2), 35.7 (CH), 32.2 (CH_2), 31.2 (CH_2), 31.1 (CH_2), 30.1 (CH_2), 24.5 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 408.2026. $C_{25}H_{30}NO_2S^+$ requires 408.1992.

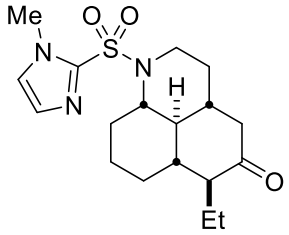
Amide **11d**{*7*}



δ_H (500 MHz, $CDCl_3$) 7.13 – 7.09 (m, 2H), 6.80 – 6.76 (m, 2H), 3.76 (s, 3H), 3.76 – 3.67 (m, 1H), 3.44 (dt, *J* = 10.7, 5.5 Hz, 1H), 3.31 – 3.21 (m, 1H), 2.96 (dd, *J* = 14.2, 8.5 Hz, 1H), 2.73 (dd, *J* = 14.2, 2.5 Hz, 1H), 2.48 (dd, *J* = 12.8, 4.6 Hz, 1H), 2.42 (ddd, *J* = 11.0, 8.6, 2.0 Hz, 1H), 2.34 – 2.16 (m, 3H), 2.15 – 2.03 (m, 3H), 1.91 – 1.85 (m, 1H), 1.75 – 1.65 (m, 1H), 1.63 – 1.55 (m, 3H), 1.54 – 1.24 (m, 6H), 1.23 – 1.13 (m, 1H),

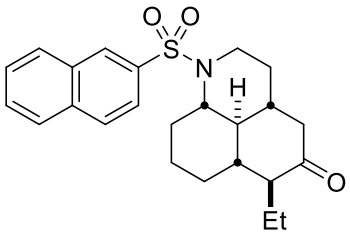
0.92 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 209.5 (C), 172.4 (C), 157.7 (C), 133.1 (C), 130.2 (CH), 113.6 (CH), 59.3 (CH), 57.4 (CH), 55.2 (CH_3), 49.1 (CH_2), 47.2 (CH), 46.4 (CH), 38.1 (CH_2), 35.7 (CH), 33.6 (CH_2), 32.3 (CH_2), 31.5 (CH_2), 30.4 (CH_2), 30.1 (CH_2), 27.6 (CH_2), 24.5 (CH_2), 22.6 (CH_2), 14.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 398.2692. $C_{25}H_{36}NO_3^+$ requires 398.2690.

Sulfonamide **13b**{*12*}



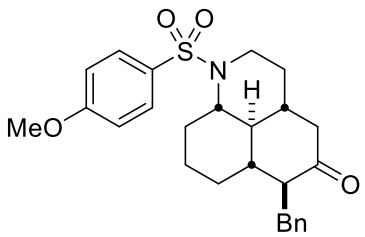
δ_H (500 MHz, $CDCl_3$) 7.46 (d, *J* = 1.2 Hz, 1H), 7.39 (d, *J* = 1.2 Hz, 1H), 4.15 (dt, *J* = 13.1, 3.9 Hz, 1H), 3.75 (s, 3H), 2.97 – 2.91 (m, 1H), 2.70 (ddd, *J* = 11.8, 9.5, 3.8 Hz, 1H), 2.47 – 2.42 (m, 1H), 2.33 (dd, *J* = 13.4, 3.1 Hz, 1H), 2.17 – 2.10 (m, 1H), 2.07 – 2.02 (m, 1H), 1.90 – 1.82 (m, 2H), 1.80 – 1.61 (m, 3H), 1.57 – 1.42 (m, 4H), 1.31 – 1.14 (m, 2H), 1.07 – 0.98 (m, 1H), 0.80 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 210.0 (C), 140.9 (C), 138.8 (CH), 123.6 (CH), 63.6 (CH), 55.8 (CH), 49.8 (CH), 48.6 (CH_2), 48.5 (CH_2), 44.8 (CH), 40.9 (CH), 34.1 (CH_3), 32.8 (CH_2), 31.0 (CH_2), 30.6 (CH_2), 24.8 (CH_2), 17.8 (CH_2), 10.9 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 366.1856. $C_{18}H_{28}N_3O_3S^+$ requires 366.1846.

Sulfonamide **13b**{*11*}



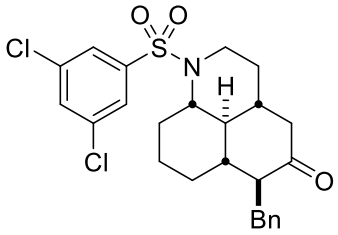
δ_H (500 MHz, $CDCl_3$) 8.38 – 8.36 (m, 1H), 7.99 – 7.95 (m, 2H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.77 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.67 – 7.60 (m, 2H), 4.35 (dt, *J* = 13.0, 3.7 Hz, 1H), 2.96 – 2.89 (m, 1H), 2.73 – 2.67 (m, 1H), 2.36 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.20 – 2.13 (m, 2H), 2.09 – 2.03 (m, 1H), 1.88 – 1.73 (m, 4H), 1.70 – 1.46 (m, 5H), 1.29 – 1.22 (m, 1H), 1.17 – 0.98 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 209.6 (C), 138.4 (C), 134.7 (C), 132.2 (C), 129.3 (CH), 129.2 (CH), 128.7 (CH), 128.0 (CH), 127.9 (CH), 127.5 (CH), 122.4 (CH), 63.8 (CH), 55.9 (CH), 49.8 (CH), 48.7 (CH_2), 48.5 (CH_2), 44.8 (CH), 41.2 (CH), 33.2 (CH_2), 30.7 (CH_2), 30.5 (CH_2), 24.8 (CH_2), 17.8 (CH_2), 10.9 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 412.1971. $C_{24}H_{30}NO_3S^+$ requires 412.1941.

Sulfonamide **13c**{*3*}



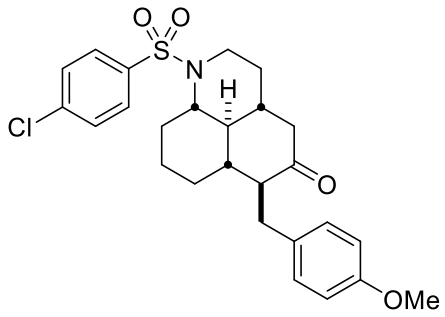
δ_H (500 MHz, $CDCl_3$) 7.73 – 7.69 (m, 2H), 7.24 – 7.20 (m, 2H), 7.18 – 7.11 (m, 3H), 6.98 – 6.94 (m, 2H), 4.20 (dt, *J* = 12.9, 3.8 Hz, 1H), 3.87 (s, 3H), 3.01 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.84 – 2.76 (m, 2H), 2.57 (ddd, *J* = 11.9, 9.7, 3.7 Hz, 1H), 2.45 (ddd, *J* = 10.8, 8.0, 2.3 Hz, 1H), 2.37 (dd, *J* = 13.3, 3.4 Hz, 1H), 2.20 – 2.13 (m, 2H), 2.07 – 2.03 (m, 1H), 1.86 – 1.81 (m, 1H), 1.75 – 1.66 (m, 2H), 1.57 – 1.43 (m, 3H), 1.29 – 1.21 (m, 1H), 1.18 – 1.05 (m, 2H); δ_C (125 MHz, $CDCl_3$) 208.9 (C), 162.6 (C), 141.0 (C), 132.5 (C), 129.2 (CH), 129.1 (CH), 128.2 (CH), 125.8 (CH), 114.2 (CH), 63.4 (CH), 57.4 (CH), 55.6 (CH_3), 49.9 (CH), 48.4 (CH_2), 48.2 (CH_2), 46.4 (CH), 41.0 (CH), 32.9 (CH_2), 31.1 (CH_2), 31.1 (CH_2), 30.9 (CH_2), 24.7 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 454.2046. $C_{26}H_{32}NO_4S^+$ requires 454.2047.

Sulfonamide **13c**{*5*}



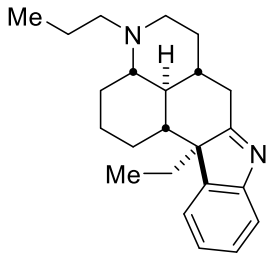
δ_H (500 MHz, $CDCl_3$) 7.65 (d, *J* = 1.8 Hz, 2H), 7.54 (t, *J* = 1.8 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.19 – 7.13 (m, 3H), 4.24 (dt, *J* = 13.2, 3.6 Hz, 1H), 3.03 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.94 – 2.83 (m, 2H), 2.76 (ddd, *J* = 13.0, 9.4, 3.7 Hz, 1H), 2.48 (ddd, *J* = 10.9, 7.9, 2.4 Hz, 1H), 2.42 (dd, *J* = 13.4, 2.7 Hz, 1H), 2.25 – 2.17 (m, 1H), 2.11 – 2.05 (m, 1H), 1.98 – 1.92 (m, 1H), 1.90 – 1.75 (m, 3H), 1.65 – 1.52 (m, 3H), 1.33 – 1.25 (m, 1H), 1.21 – 1.07 (m, 2H); δ_C (125 MHz, $CDCl_3$) 208.5 (C), 144.7 (C), 140.9 (C), 136.0 (C), 132.4 (CH), 129.2 (CH), 128.2 (CH), 125.8 (CH), 125.2 (CH), 63.8 (CH), 57.3 (CH), 49.8 (CH), 48.8 (CH_2), 48.3 (CH_2), 46.3 (CH), 41.0 (CH), 33.2 (CH_2), 31.1 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 24.7 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 492.1176. $C_{25}H_{28}Cl_2NO_3S^+$ requires 492.1161.

Sulfonamide **13d**{*2*}



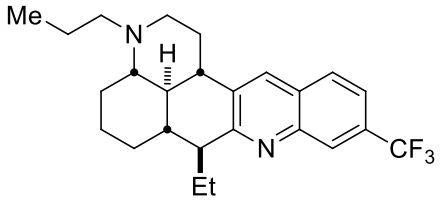
δ_H (500 MHz, $CDCl_3$) 7.74 – 7.70 (m, 2H), 7.49 – 7.46 (m, 2H), 7.11 – 7.07 (m, 2H), 6.79 – 6.75 (m, 2H), 4.23 (dt, *J* = 13.0, 3.6 Hz, 1H), 3.76 (s, 3H), 2.92 (dd, *J* = 14.3, 7.8 Hz, 1H), 2.86 – 2.79 (m, 2H), 2.67 – 2.60 (m, 1H), 2.43 – 2.36 (m, 2H), 2.20 – 2.14 (m, 1H), 2.08 – 2.02 (m, 2H), 1.88 – 1.79 (m, 1H), 1.78 – 1.69 (m, 2H), 1.59 – 1.45 (m, 3H), 1.28 – 1.20 (m, 1H), 1.18 – 1.04 (m, 2H); δ_C (125 MHz, $CDCl_3$) 208.9 (C), 157.7 (C), 139.9 (C), 138.9 (C), 132.8 (C), 130.2 (CH), 129.4 (CH), 128.4 (CH), 113.6 (CH), 63.6 (CH), 57.5 (CH), 55.2 (CH_3), 49.8 (CH), 48.5 (CH_2), 48.4 (CH_2), 46.0 (CH), 40.9 (CH), 33.0 (CH_2), 31.0 (CH_2), 30.7 (CH_2), 30.1 (CH_2), 24.7 (CH_2); *m/z* (ESI+) found $[M+H]^+$ 488.1643. $C_{26}H_{31}ClNO_4S^+$ requires 488.1657.

Indolenine **15**{*1*}



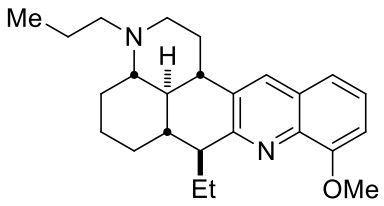
δ_H (500 MHz, $CDCl_3$) 7.64 (d, *J* = 7.7 Hz, 1H), 7.32 (td, *J* = 7.6, 1.4 Hz, 1H), 7.25 – 7.16 (m, 2H), 3.37 (d, *J* = 11.4 Hz, 1H), 2.98 – 2.63 (m, 4H), 2.36 (td, *J* = 11.5, 3.2 Hz, 1H), 2.30 – 2.14 (m, 3H), 2.11 – 1.94 (m, 2H), 1.94 – 1.74 (m, 4H), 1.73 – 1.35 (m, 5H), 1.26 (h, *J* = 14.3, 13.2 Hz, 1H), 1.11 – 1.00 (m, 1H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.37 (q, *J* = 8.2, 7.8 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 188.5 (C), 155.0 (C), 144.0 (C), 127.8 (CH), 125.1 (CH), 121.4 (CH), 120.5 (CH), 64.5 (CH), 58.3 (C), 53.3 (CH_2, br), 51.9 (CH_2, br), 51.5 (CH, br), 42.7 (CH_2), 41.6 (CH), 35.0 (CH), 29.6 (CH_2, br), 28.1 (CH_2), 27.9 (CH_2), 26.1 (CH_2), 23.6 (CH_2), 16.3 (CH_2), 11.5 (CH_3), 8.0 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 337.2645. $C_{23}H_{33}N_2^+$ requires 337.2638.

Quinoline **17**{*6*}



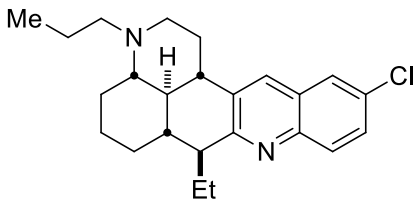
δ_H (500 MHz, $CDCl_3$) 8.31 (s, 1H), 7.94 (s, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 8.5, 1.5 Hz, 1H), 3.23 – 3.17 (m, 1H), 2.91 – 2.86 (m, 1H), 2.73 (dt, *J* = 13.4, 7.8 Hz, 1H), 2.60 – 2.47 (m, 4H), 2.34 – 2.26 (d, 1H), 2.20 – 2.11 (m, 2H), 2.09 – 2.03 (m, 1H), 1.95 – 1.82 (m, 2H), 1.75 – 1.59 (m, 2H), 1.56 – 1.43 (m, 3H), 1.29 – 1.11 (m, 3H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.73 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 163.3 (C), 145.6 (C), 136.9 (C), 130.6 (CH), 130.2 (C, q, *J* = 32 Hz), 128.4 (CH), 128.2 (C), 126.4 (CH, q, *J* = 4.2 Hz), 124.2 (C, q, *J* = 270 Hz), 121.1 (CH, q, *J* = 3.1 Hz), 65.4 (CH), 54.8 (CH_2), 52.3 (CH_2), 48.9 (CH), 47.0 (CH), 40.3 (CH), 39.4 (CH), 33.3 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 27.0 (CH_2), 24.8 (CH_2), 17.5 (CH_2), 12.0 (CH_3), 9.7 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 417.2518. $C_{25}H_{32}F_3N_2^+$ requires 417.2512.

Quinoline **17**{*5*}



δ_H (500 MHz, $CDCl_3$) 7.85 (s, 1H), 7.37 – 7.30 (m, 2H), 6.96 (d, *J* = 7.4 Hz, 1H), 4.05 (s, 3H), 3.21 (d, *J* = 11.3 Hz, 1H), 3.08 – 3.03 (m, 1H), 2.77 – 2.70 (m, 1H), 2.62 – 2.45 (m, 4H), 2.27 – 2.13 (m, 3H), 2.05 – 1.99 (m, 1H), 1.94 – 1.81 (m, 2H), 1.74 – 1.42 (m, 5H), 1.30 – 1.12 (m, 3H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.73 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 160.6 (C), 154.9 (C), 138.8 (C), 135.1 (C), 130.7 (CH), 127.9 (C), 125.5 (CH), 119.3 (CH), 106.9 (CH), 65.5 (CH), 56.1 (CH_3), 54.7 (CH_2), 52.3 (CH_2), 48.5 (CH), 47.1 (CH), 40.7 (CH), 39.1 (CH), 33.4 (CH_2), 29.7 (CH_2), 28.1 (CH_2), 25.0 (CH_2), 17.5 (CH_2), 12.0 (CH_3), 9.8 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 379.2762. $C_{25}H_{35}N_2O^+$ requires 379.2744.

Quinoline **17**{*4*}



δ_H (500 MHz, $CDCl_3$) 7.91 (d, *J* = 9.0 Hz, 1H), 7.80 (s, 1H), 7.72 (s, 1H), 7.55 (d, *J* = 9.0, 1.5 Hz, 1H), 3.30 (d, *J* = 11.4 Hz, 1H), 2.90 – 2.85 (m, 1H), 2.84 – 2.73 (m, 1H), 2.71 – 2.61 (m, 2H), 2.57 – 2.44 (m, 2H), 2.31 – 2.22 (m, 2H), 2.20 – 2.14 (m, 1H), 2.05 (d, *J* = 12.9 Hz, 1H), 1.97 – 1.91 (m, 1H), 1.89 – 1.72 (m, 2H), 1.65 – 1.43 (m, 4H), 1.38 – 1.12 (m, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.72 (t, *J* = 7.4 Hz, 3H); δ_C (125 MHz, $CDCl_3$) 161.7 (C), 145.2 (C), 135.2 (C), 131.1 (C), 130.1 (CH), 130.0 (CH), 129.5 (CH), 127.3 (C), 125.9 (CH), 65.3 (CH), 54.2 (CH_2), 51.9 (CH_2), 48.7 (CH), 46.3 (CH), 40.5 (CH), 39.1 (CH), 33.1 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 27.1 (CH_2), 24.8 (CH_2), 17.1 (CH_2), 11.9 (CH_3), 9.7 (CH_3); *m/z* (ESI+) found $[M+H]^+$ 383.2255. $C_{24}H_{32}ClN_2^+$ requires 383.2249.

5. Cheminformatic details

The structural and physiochemical properties for each of the prepared 95 library compounds and 4 scaffolds were determined as described in Table S1.

Table S1. Structural and physiochemical properties used in the cheminformatic analysis

Parameter	Description	Method of Determination
MW	molecular weight	chemdraw
XLogP	calc n-octanol/water partition coefficient	chemdraw
HBD	number of hydrogen bond donors	chemdraw
HBA	number of hydrogen bond acceptors	chemdraw
RotB	number of rotatable bonds	chemdraw
tPSA	topological polar surface area	chemdraw
Fsp^3	fraction sp^3 carbon atoms	manual inspection

The properties of these scaffolds and library compounds were then compared to Tan's dataset of 40 drugs, 20 commercial drug-like screening compounds, and 60 natural products[4]; and to our group's previously reported set of 20 alkaloid natural products[nat chem.](Table S2).

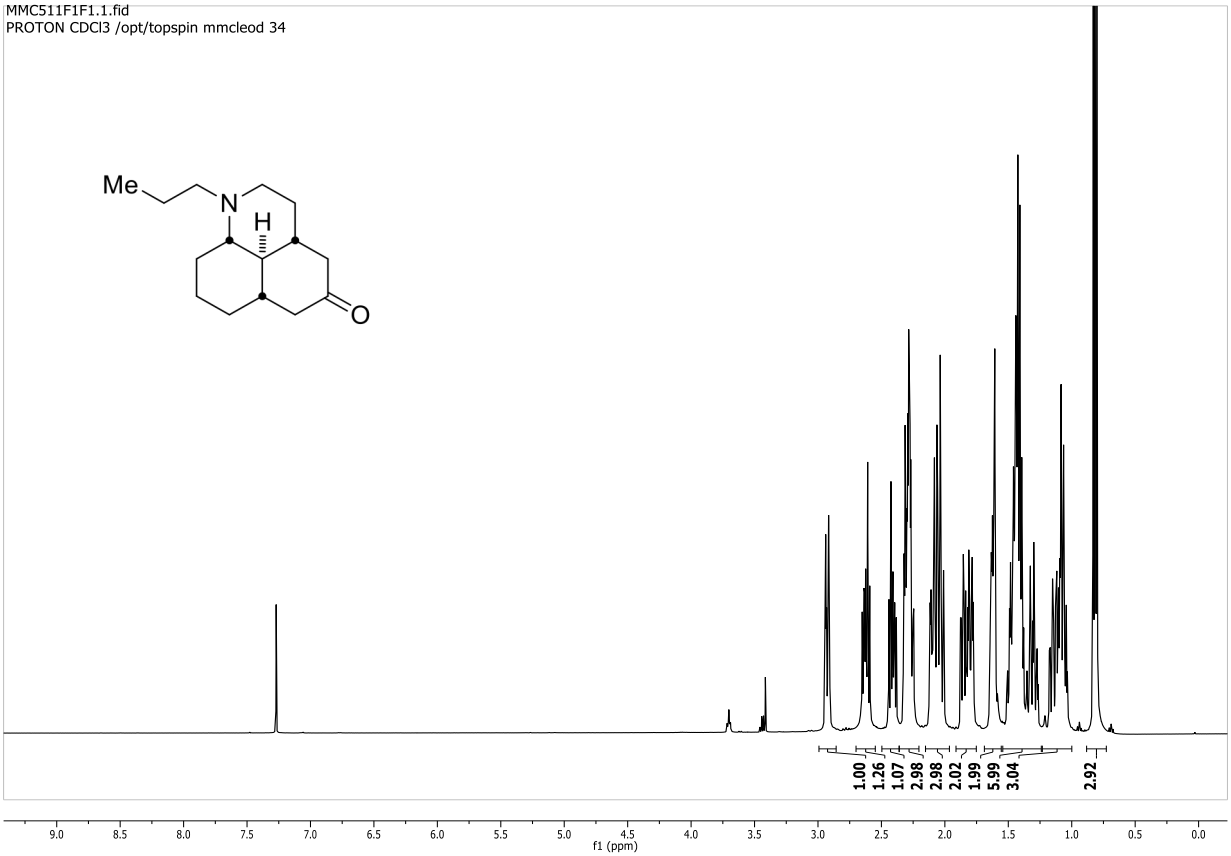
Table S2. Composition of reference set of drugs, commercial drug-like screening libraries, natural products and alkaloid natural products used in the cheminformatic analysis[4+Nat. chem].

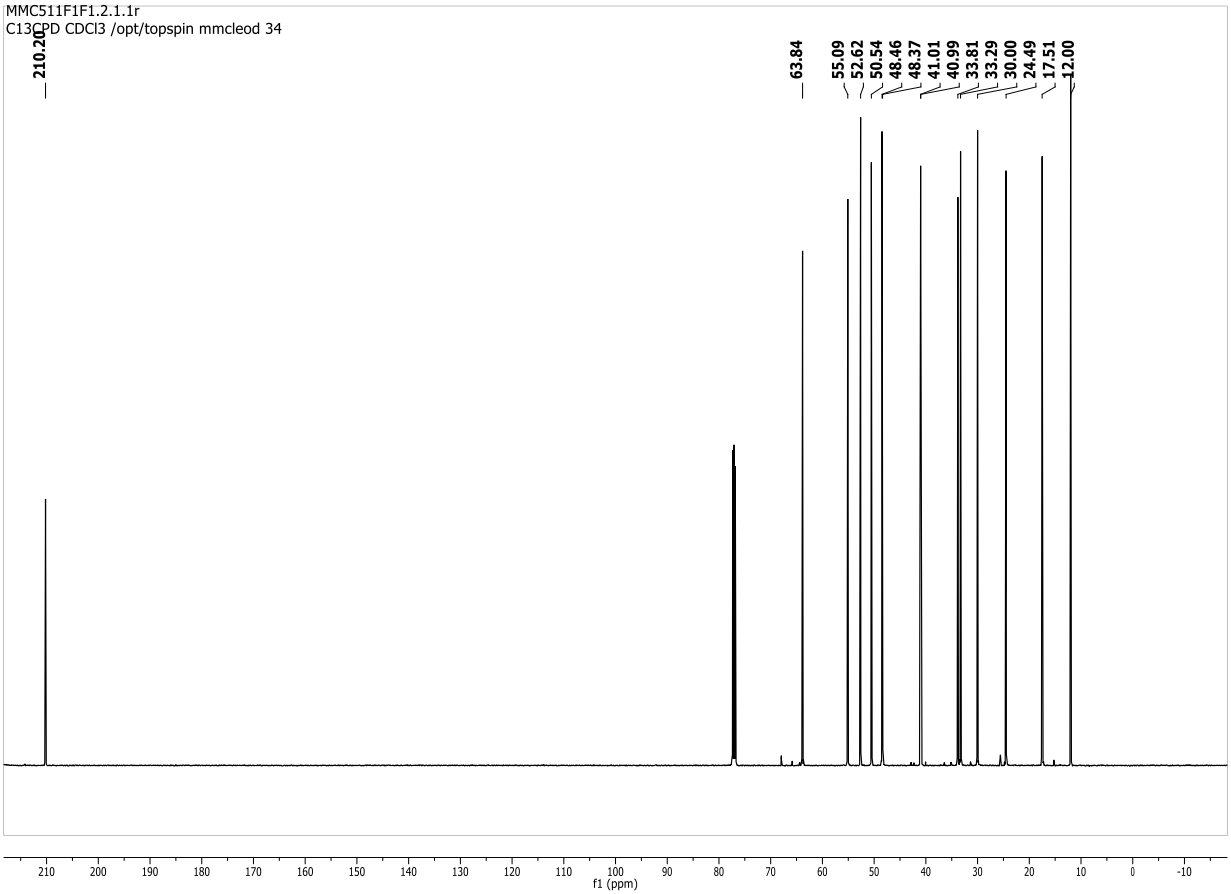
	Compounds			
Drugs (40 compounds)	Lipitor	Lexapro	Topamax	Coreg
	Nexium	Seroquel	Toprol	Valtrex
	Prevacid	Protonix	Zetia	Adderall
	Flonase	Ambien	Fosamax	Aciphex
	Serevent	Actos	Abilify	Cymbalta

	Singulair	Zoloft	Levaquin	Crestor
	Effexor	Wellbutrin	Lamictal	Diovan
	Plavix	Avandia	Celebrex	Tricor
	Zocor	Risperdal	Benazepril	Concerta
	Norvasc	Zyprexa	Zyrtec	Imitrex
Commercial screening libraries (20 compounds; pubchem compound CIDs)	**ChemBridge:**	5771429	5309975	5308431
	5771374	5309772	5309246	5771496
	5771371	5309762	5309020	
	ChemDiv:	2529482	2474145	2490046
	2474174	1340935	2490068	2529498
	2471337	2490059	1342784	
Natural products (60 compounds)	cephamycin C	mizoribine	coformycin	compactin
	spergualin	SQ26180	arglabin	artemisinin
	forskolin	thienamycin	bestatin	plaunotol
	daptomycin	validamycin	midecamycin A1	rapamycin
	echinocandin B	avermectin B1a	taxol	FK506
	calicheamicin g1	cyclosporin A	pseudomonic acid A	
	lipstatin	geldanamycin	trapoxin B	talaromycin B
	bleomycin	actinonin	vincristine	spongistatin 1
	brefeldin A	discodermolide	colchicines	radicicol
	cytochalasin B	monensin	trichostatin	salicylihalamide A
	epothilone A	calyculin A	fumagillin	brevetoxin B
	apoptolidin	amphotericin B	staurosporine	rifamycin B
	lactacystin	adriamycin	erythromycin A	quinine
	duocarmycin A	ginkgolide B	streptomycin	mycobactin S
	zaragozic acid A			
Alkaloid Natural Products (20 compounds)	neostenine	cylindricine C	mesembrine	sparteine
	morphine	harringtonine	nicotine	atropine
	quinine	monomorine	halichlorine	strychnine
	epibatidine	physostigmine	pumiliotoxin A	α-ergocryptine
	cocaine	tetracycline	yohimbine	galantamine

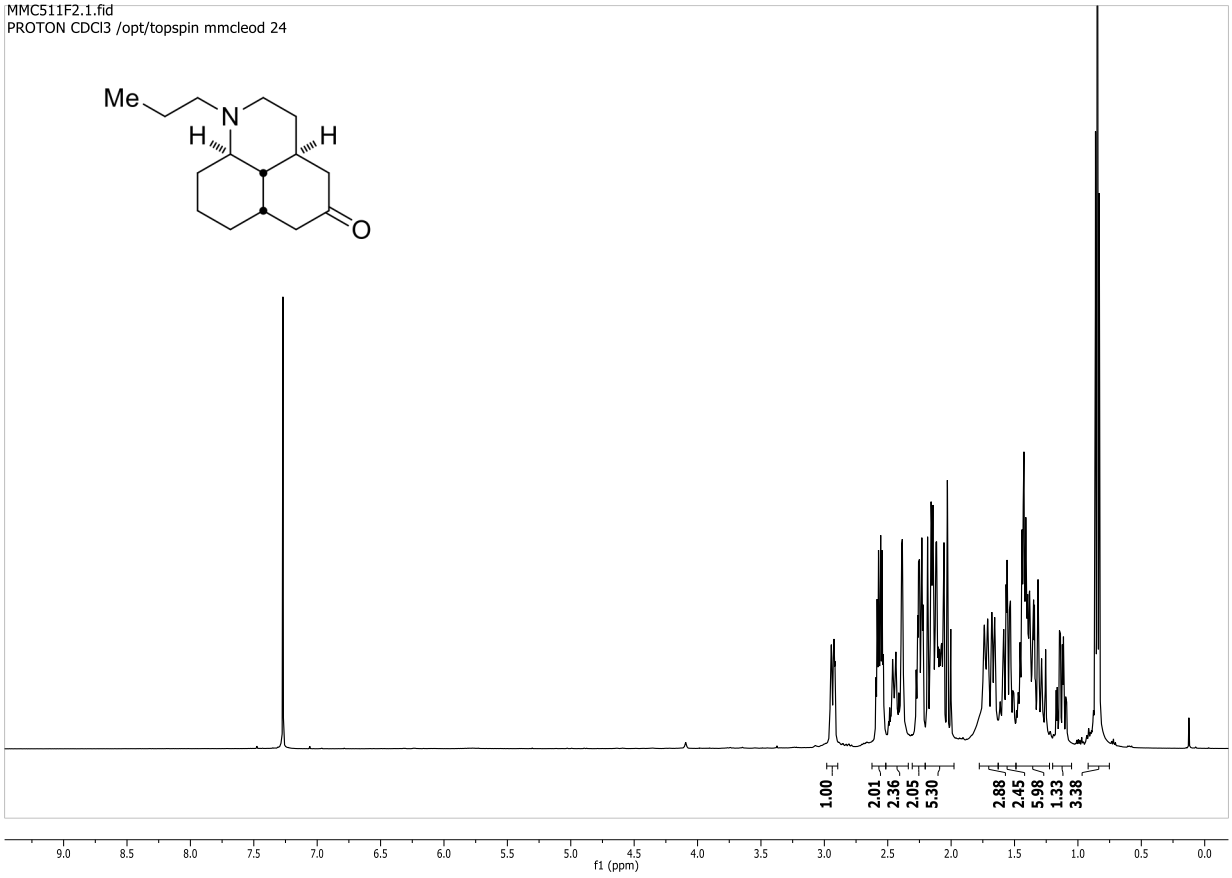
6. Copies of ^{1}H and ^{13}C spectra

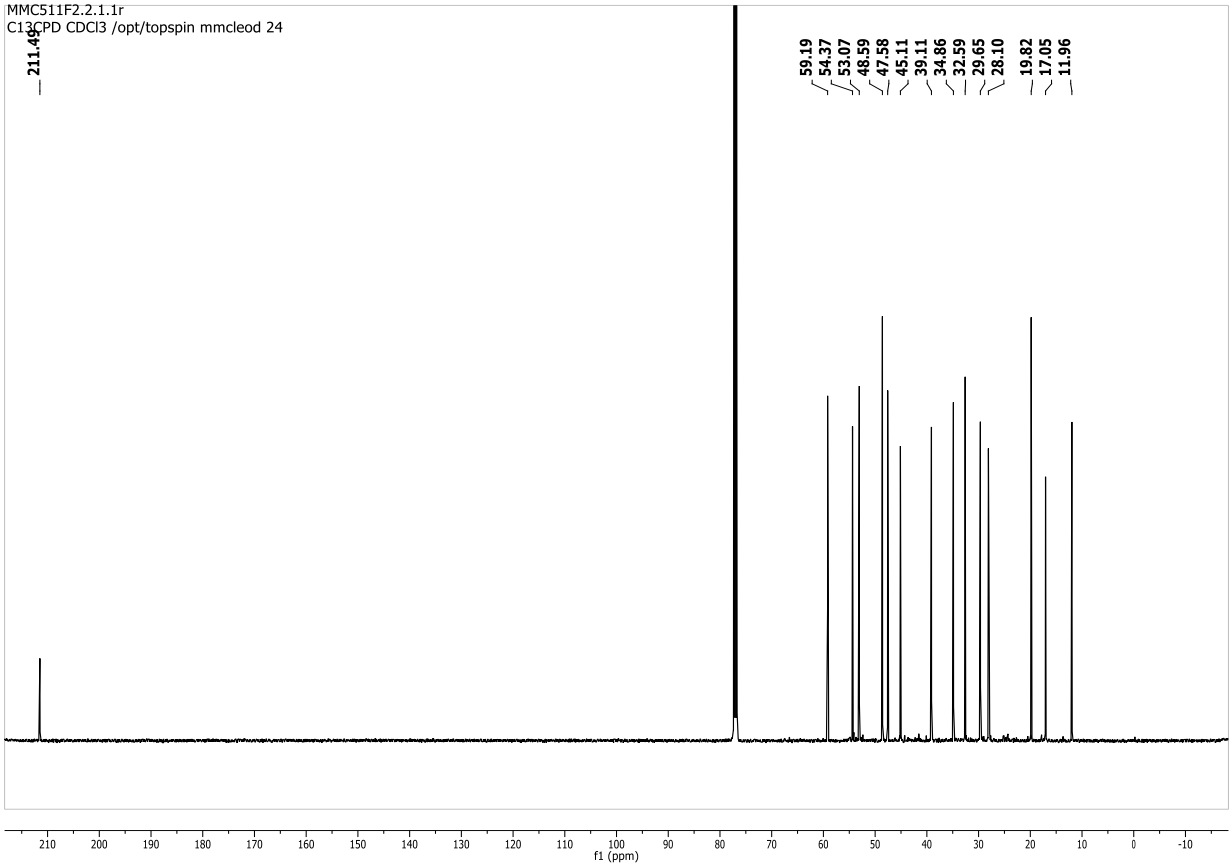
Scaffold **6a**



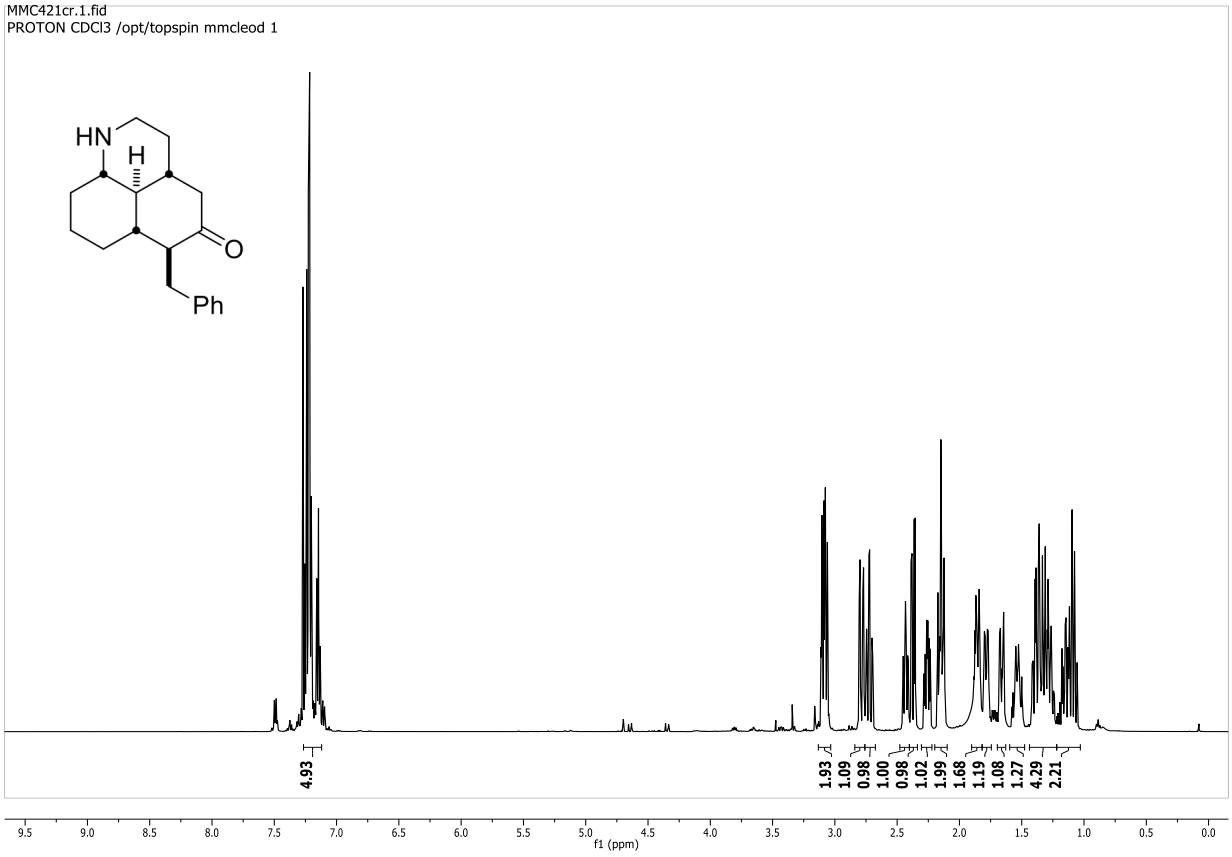


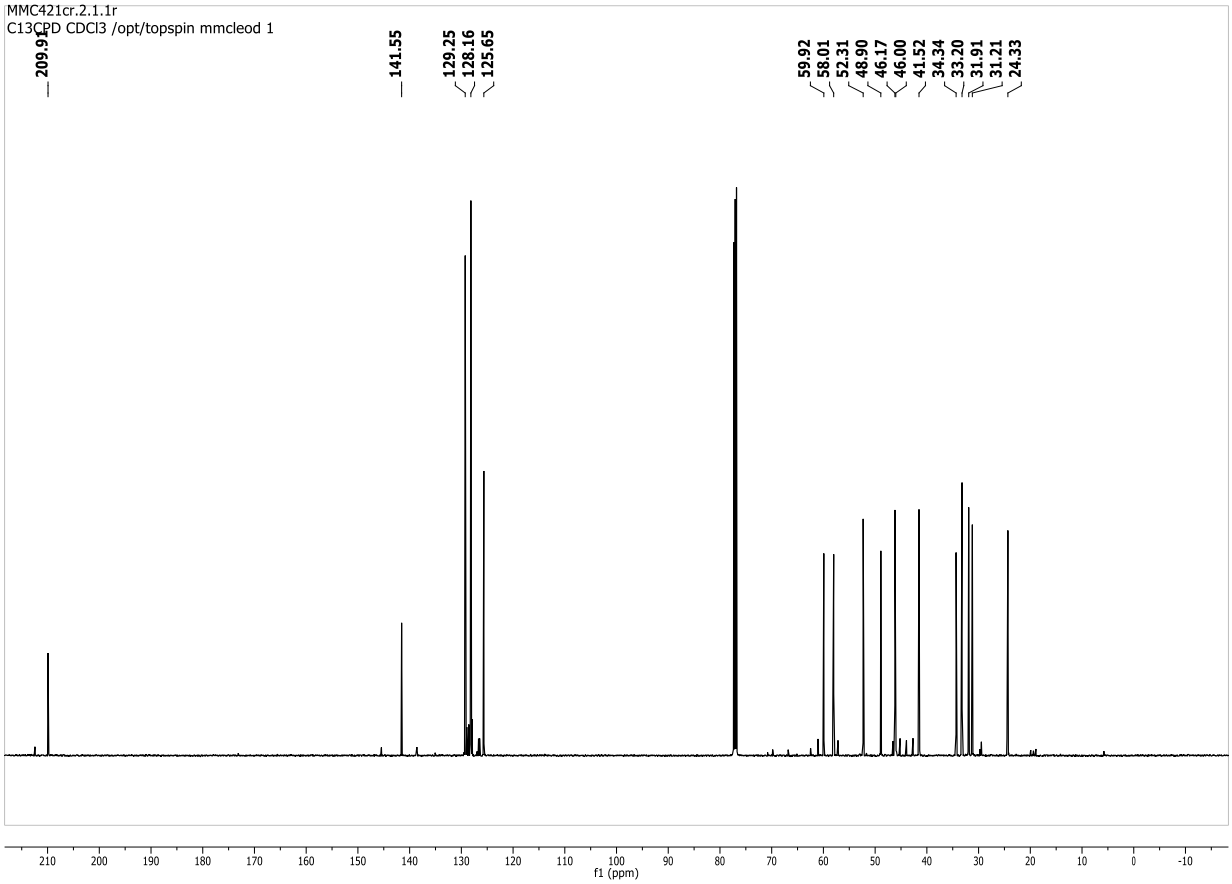
Scaffold **S1**


MMC511F2.1.fid
PROTON CDCl3 /opt/topspin mmcleod 24
Me
N
H
H
O
1.00
2.01
2.36
2.05
5.30
2.88
2.45
5.98
1.33
3.38
f1 (ppm)

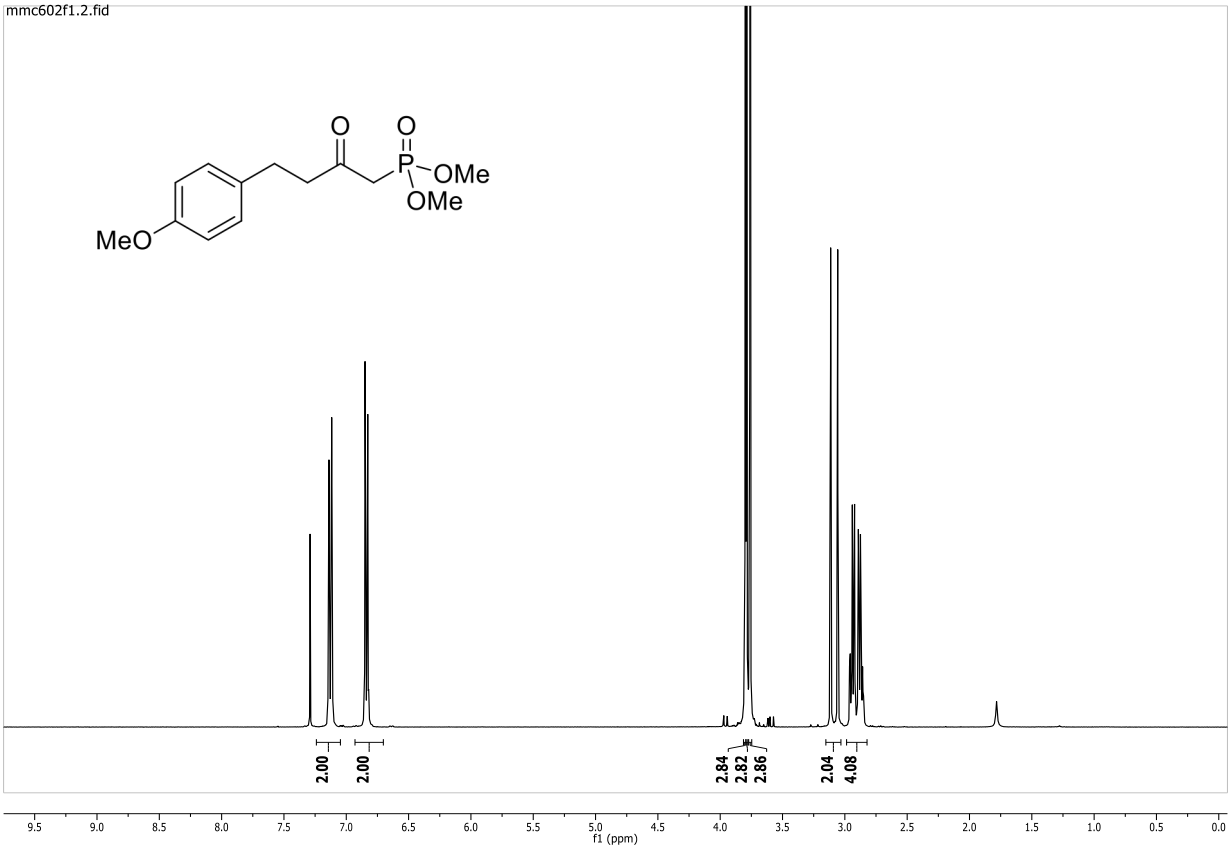

MMC511F2.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 24
211.49
59.19
54.37
53.07
48.59
47.58
45.11
39.11
34.86
32.59
29.65
28.10
19.82
17.05
11.96
f1 (ppm)

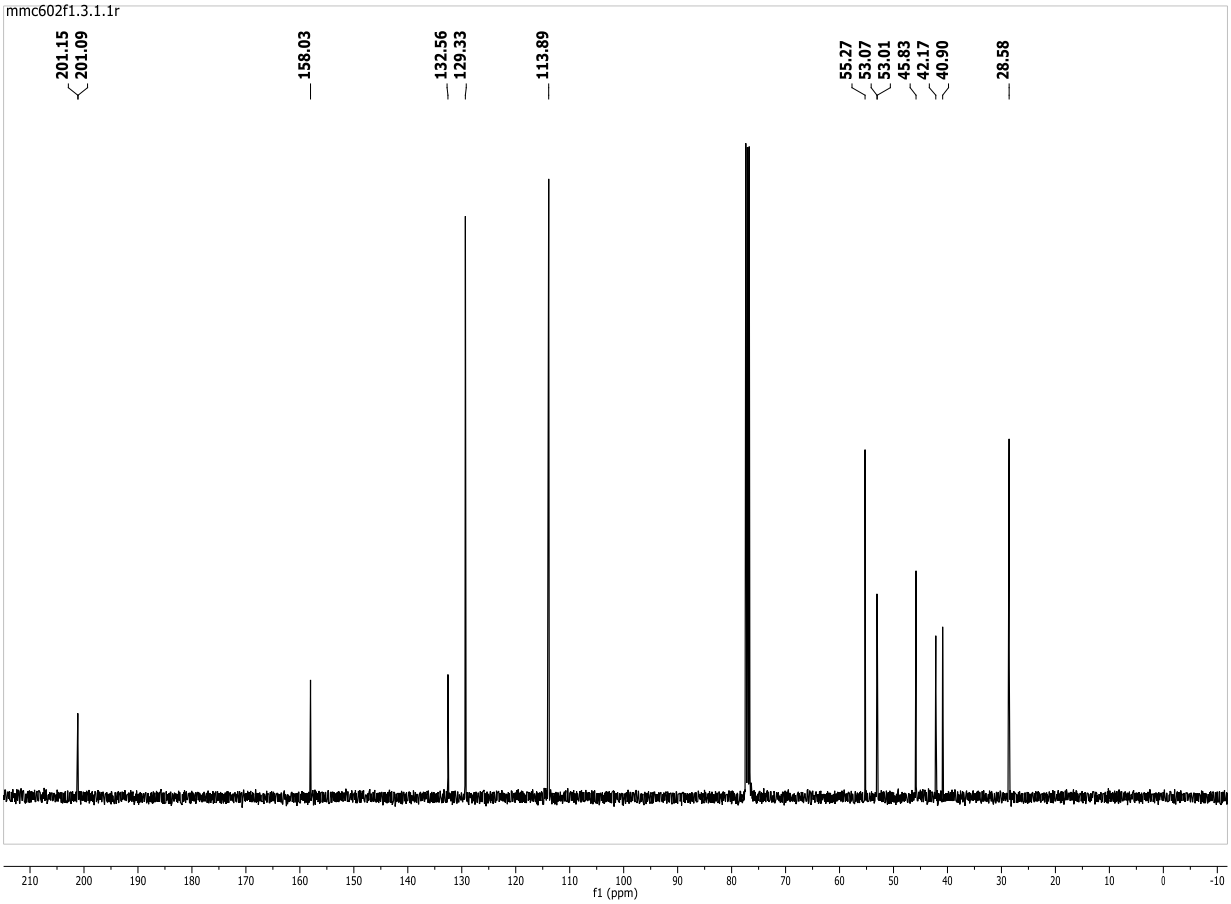
Scaffold **6b**


MMC421cr.1.fid
PROTON CDCl3 /opt/topspin mmcleod 1
HN
H
O
Ph
4.93
1.93
1.09
0.98
1.00
0.98
1.02
1.99
1.68
1.19
1.08
1.27
4.29
2.21
f1 (ppm)

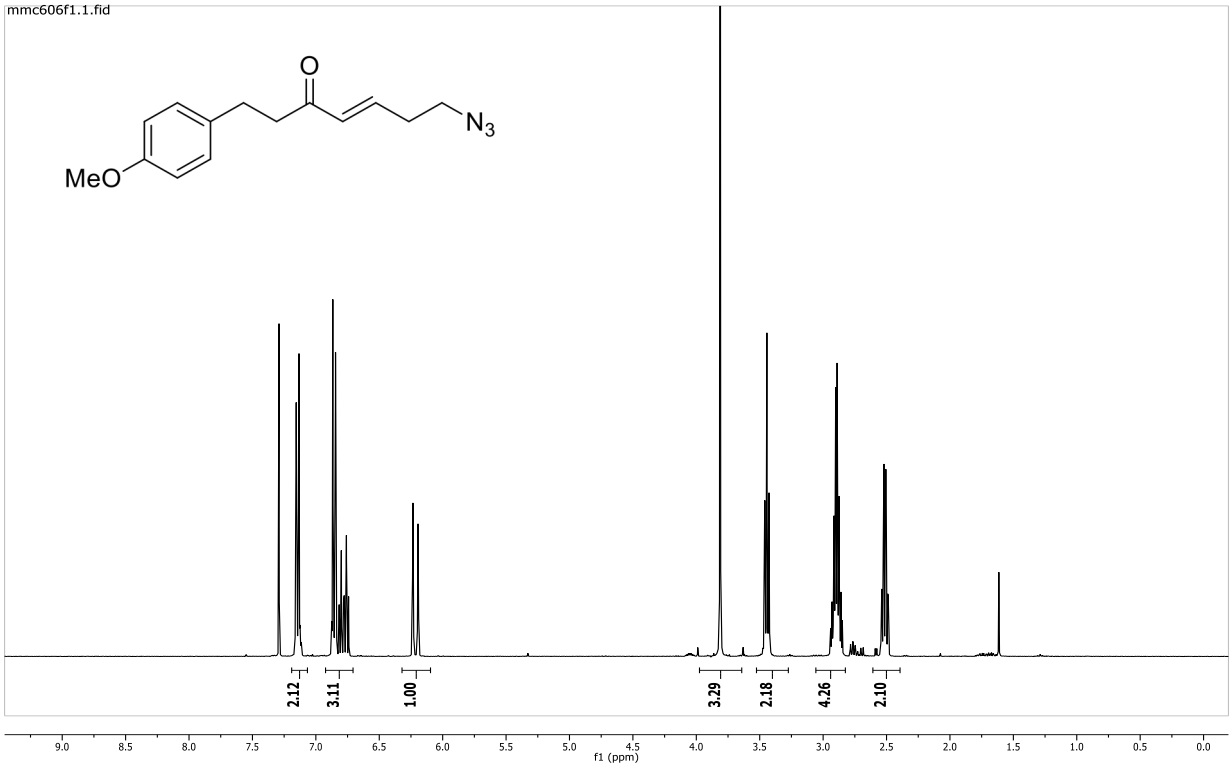

MMC421cr.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 1
209.91
141.55
129.25
128.16
125.65
59.92
58.01
52.31
48.90
46.17
46.00
41.52
34.34
33.20
31.91
31.21
24.33
f1 (ppm)

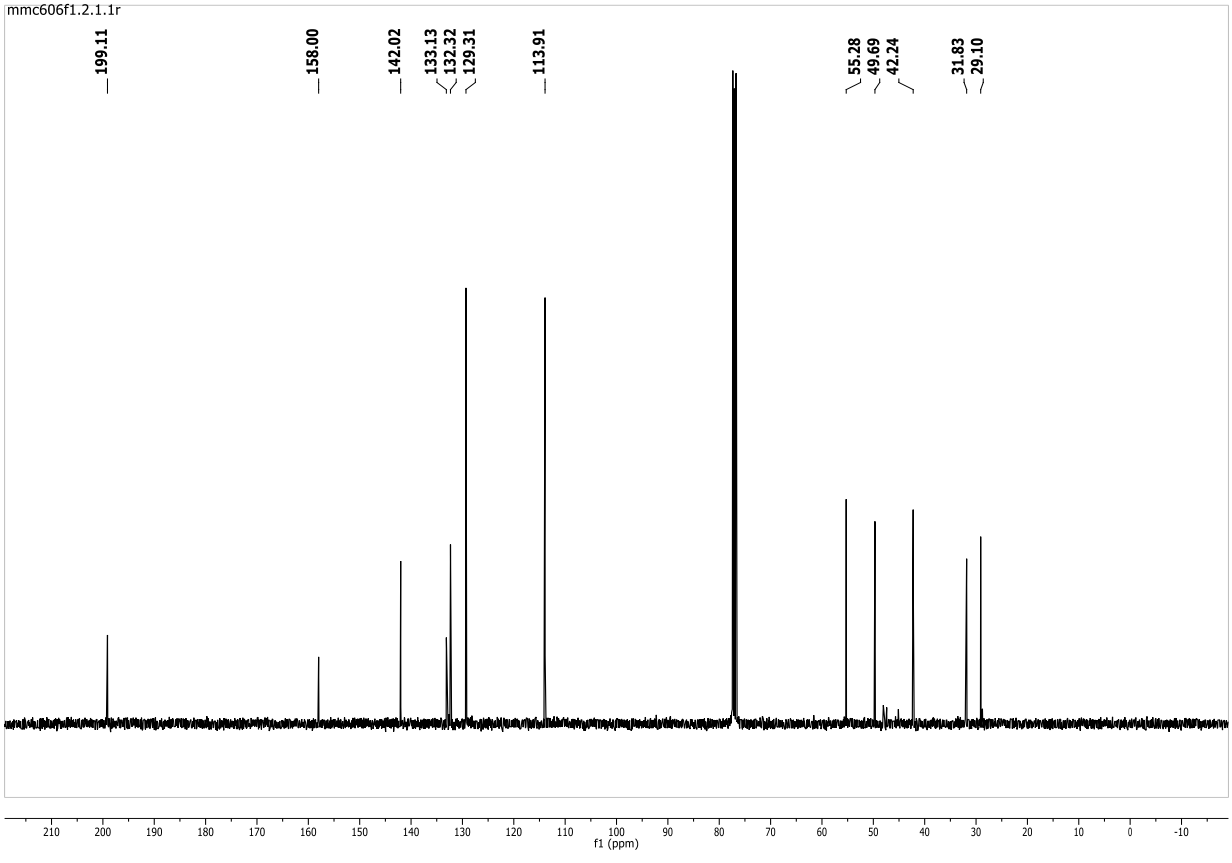
Phosphonate **7d**



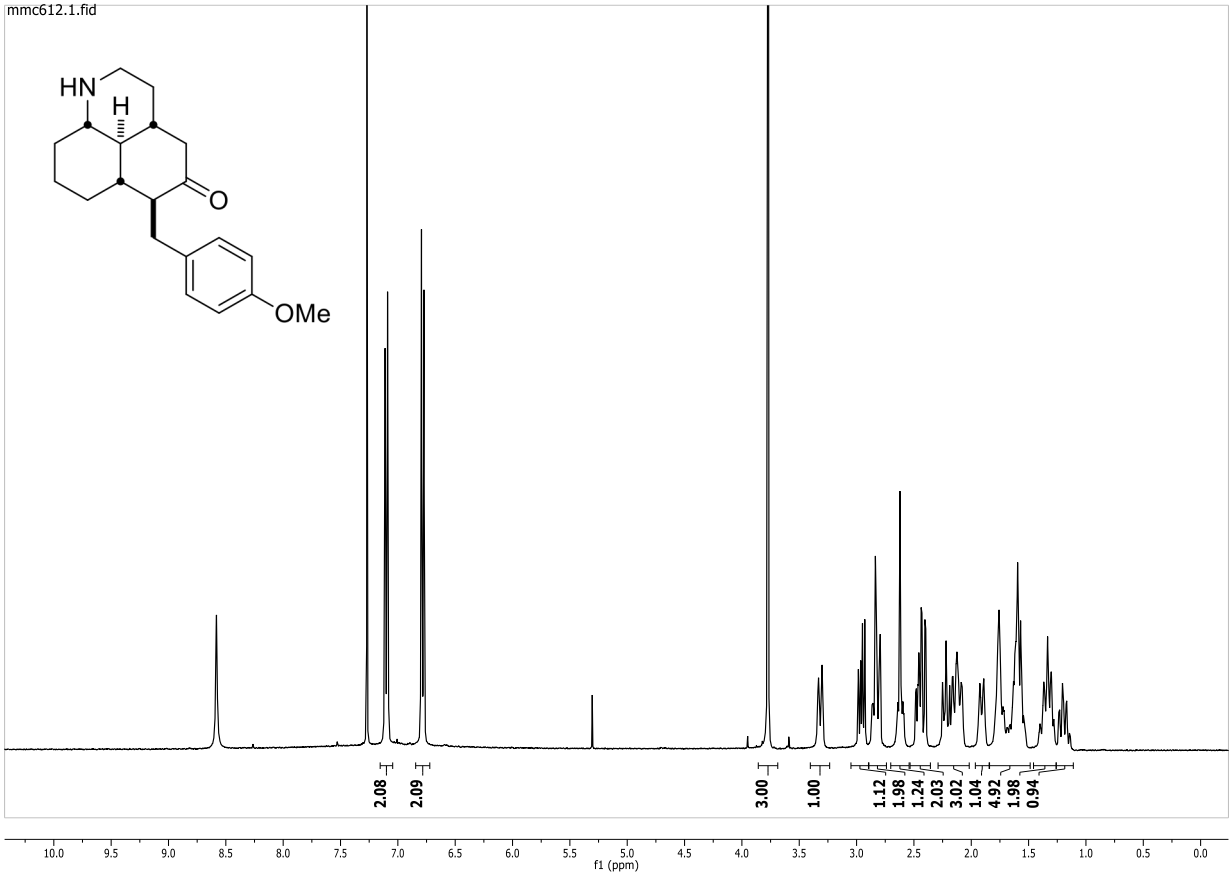


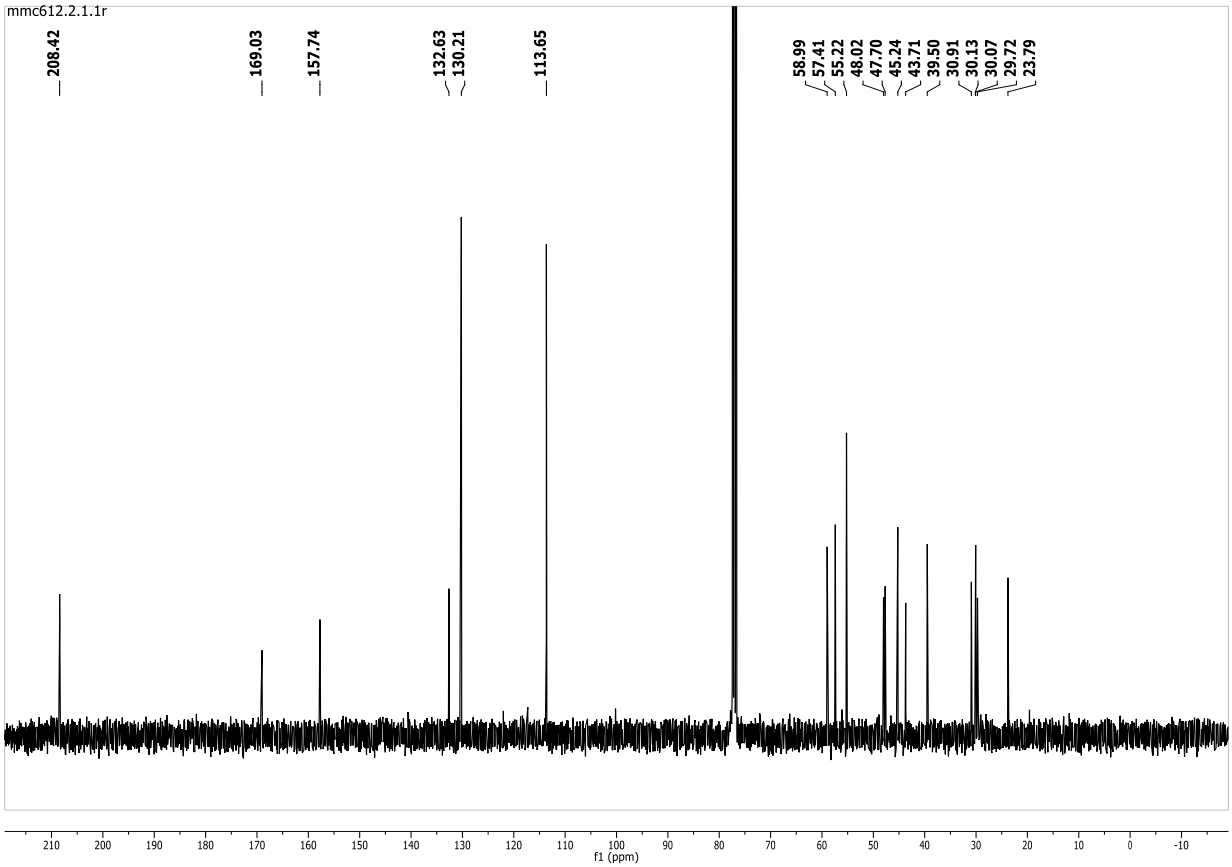
Azide **S3**


mmc606f1.1.fid
O
N3
MeO
2.12
3.11
1.00
3.29
2.18
4.26
2.10
f1 (ppm)

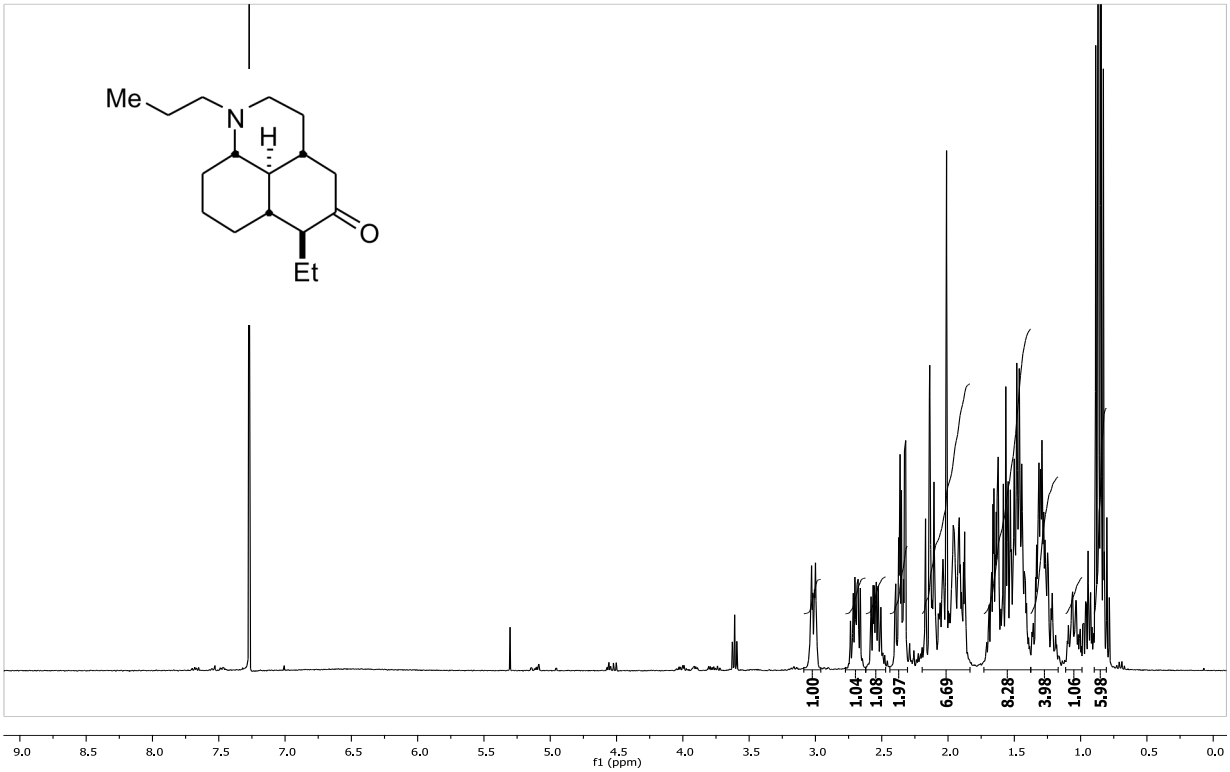

mmc606f1.2.1.1r
199.11
158.00
142.02
133.13
132.32
129.31
113.91
55.28
49.69
42.24
31.83
29.10
f1 (ppm)

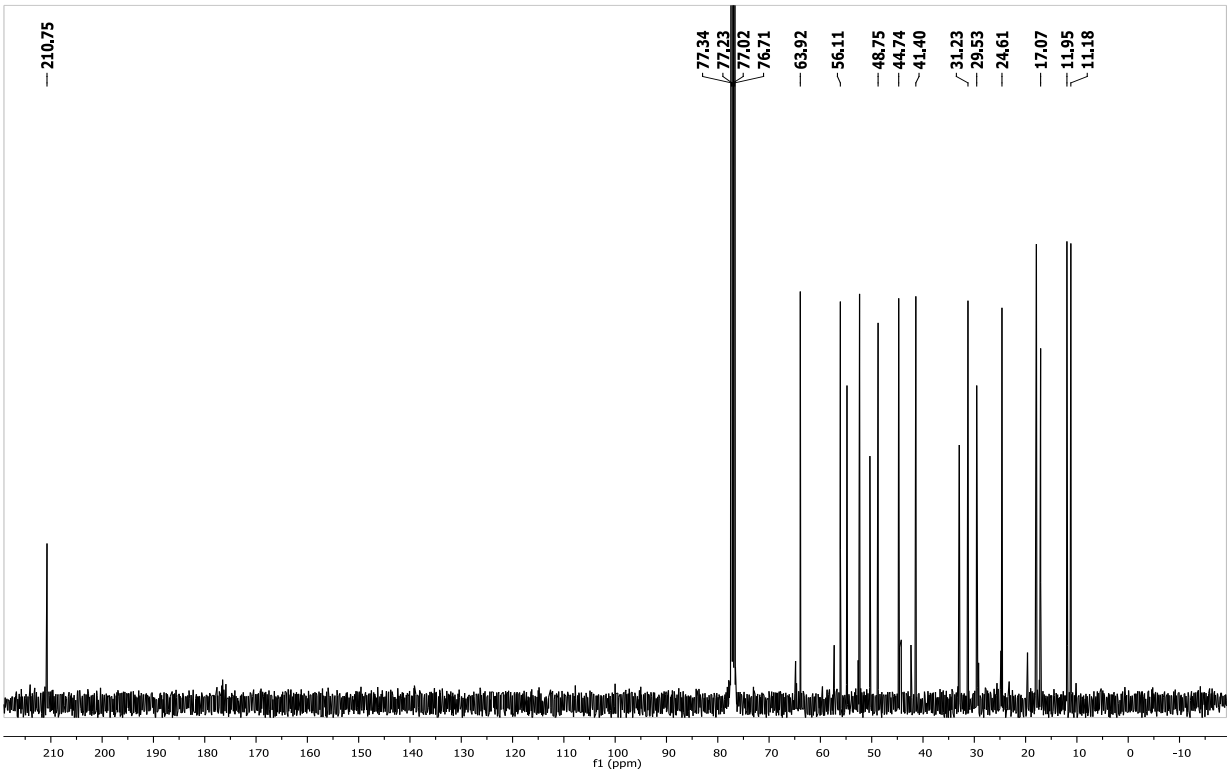
Scaffold **6d**


mmc612.1.fid
HN
H
O
OMe
2.08
2.09
3.00
1.00
1.12
1.98
1.24
2.03
3.02
1.04
4.92
1.98
0.94
f1 (ppm)

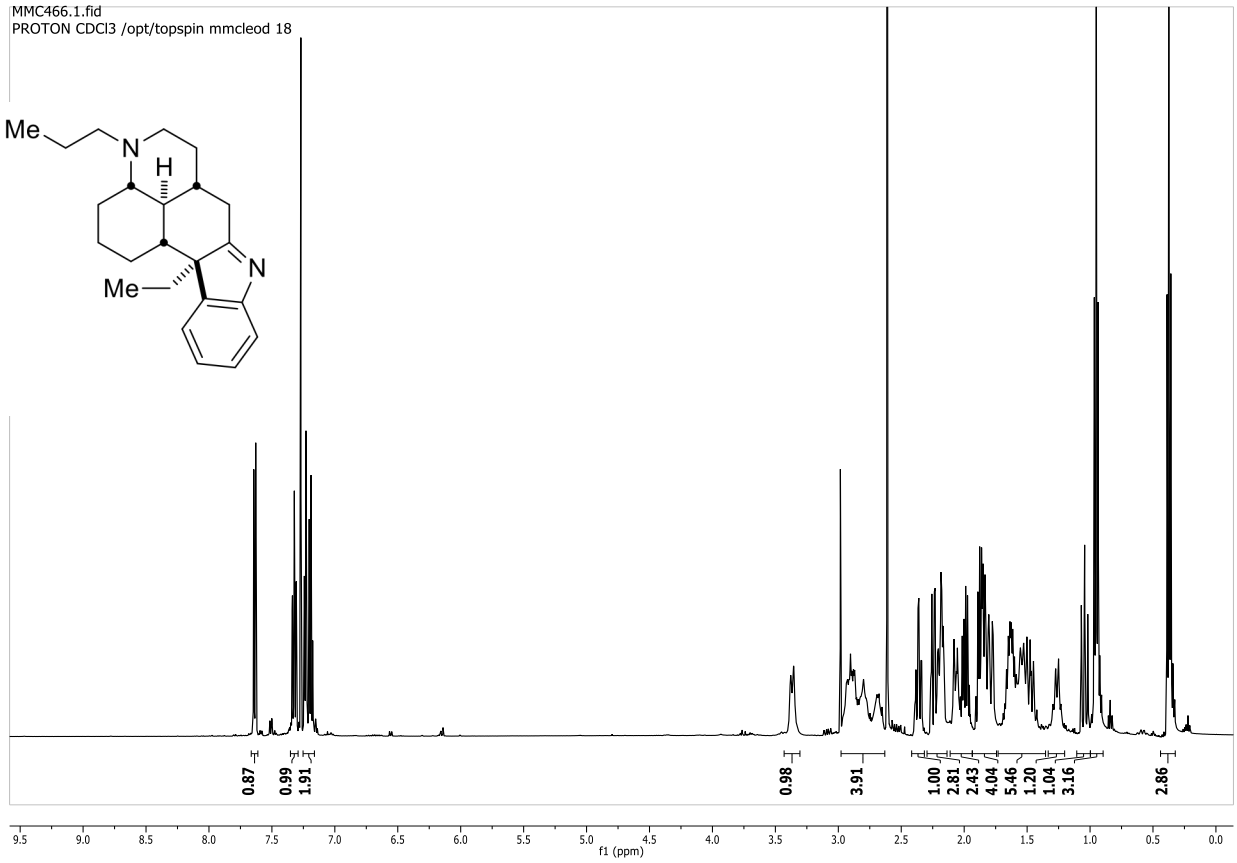

mmc612.2.1.1r
208.42
169.03
157.74
132.63
130.21
113.65
58.99
57.41
55.22
48.02
47.70
45.24
43.71
39.50
30.91
30.13
30.07
29.72
23.79
f1 (ppm)

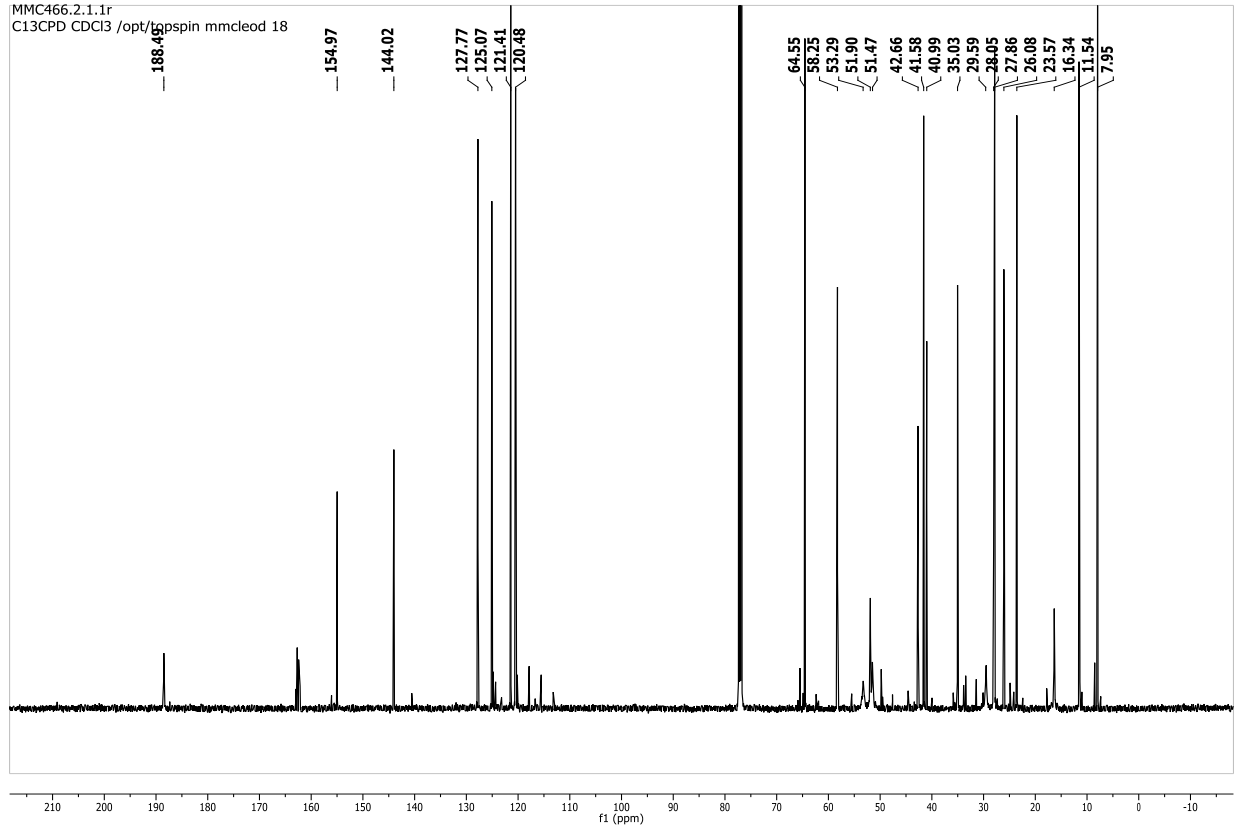
Amine **9b**{*1*}


Me
N
H
O
Et
1.00
1.04
1.08
1.97
6.69
8.28
3.98
1.06
5.98
f1 (ppm)

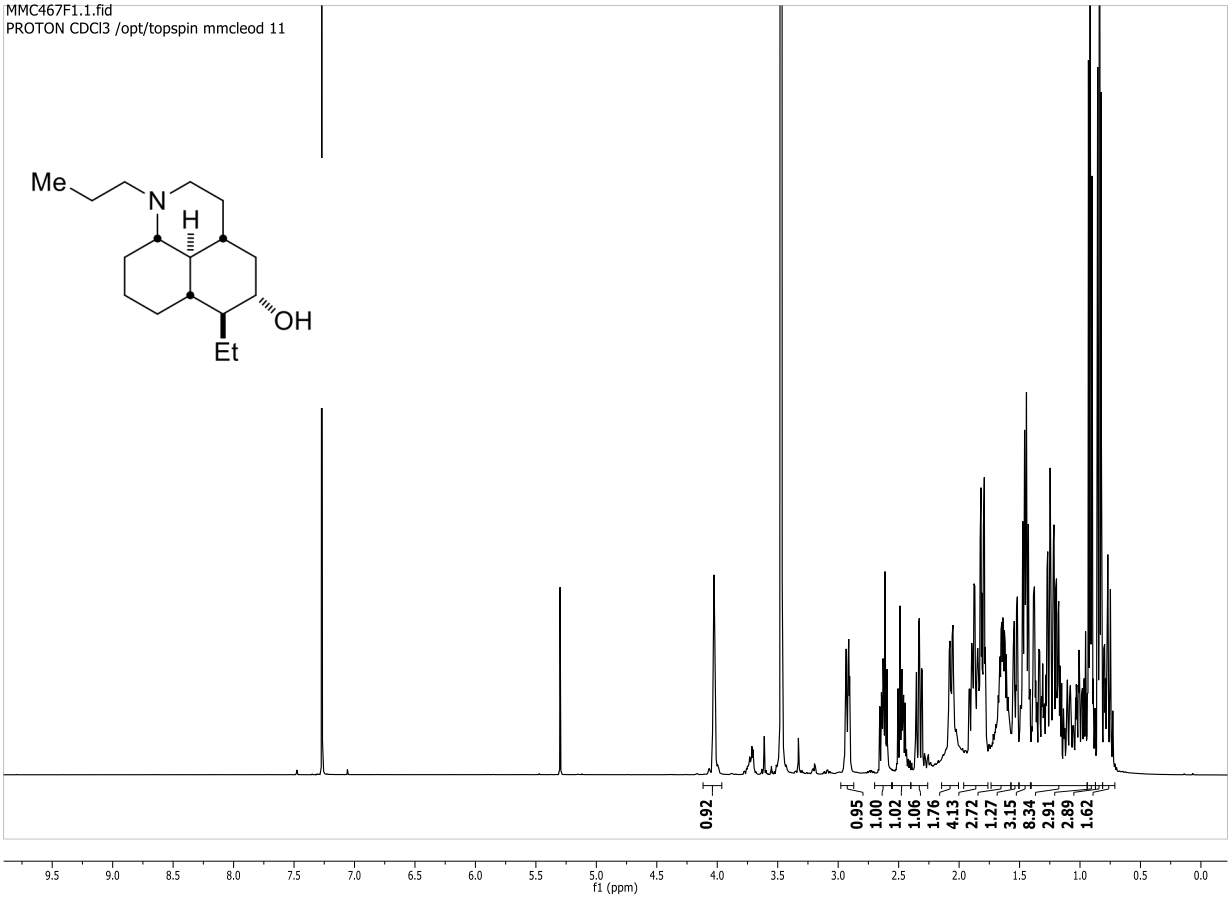

210.75
77.34
77.23
77.02
76.71
63.92
56.11
48.75
44.74
41.40
31.23
29.53
24.61
17.07
11.95
11.18
f1 (ppm)

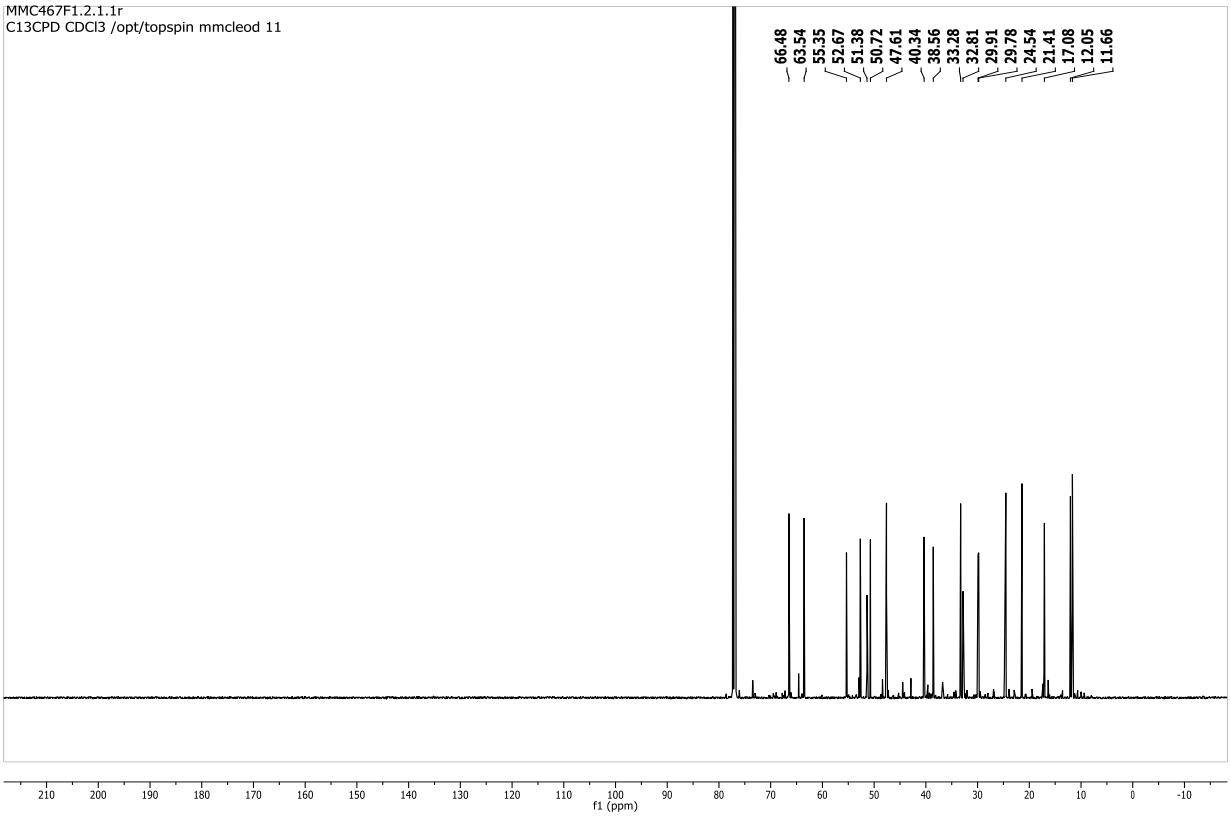
Indolenine **15**{*1*}



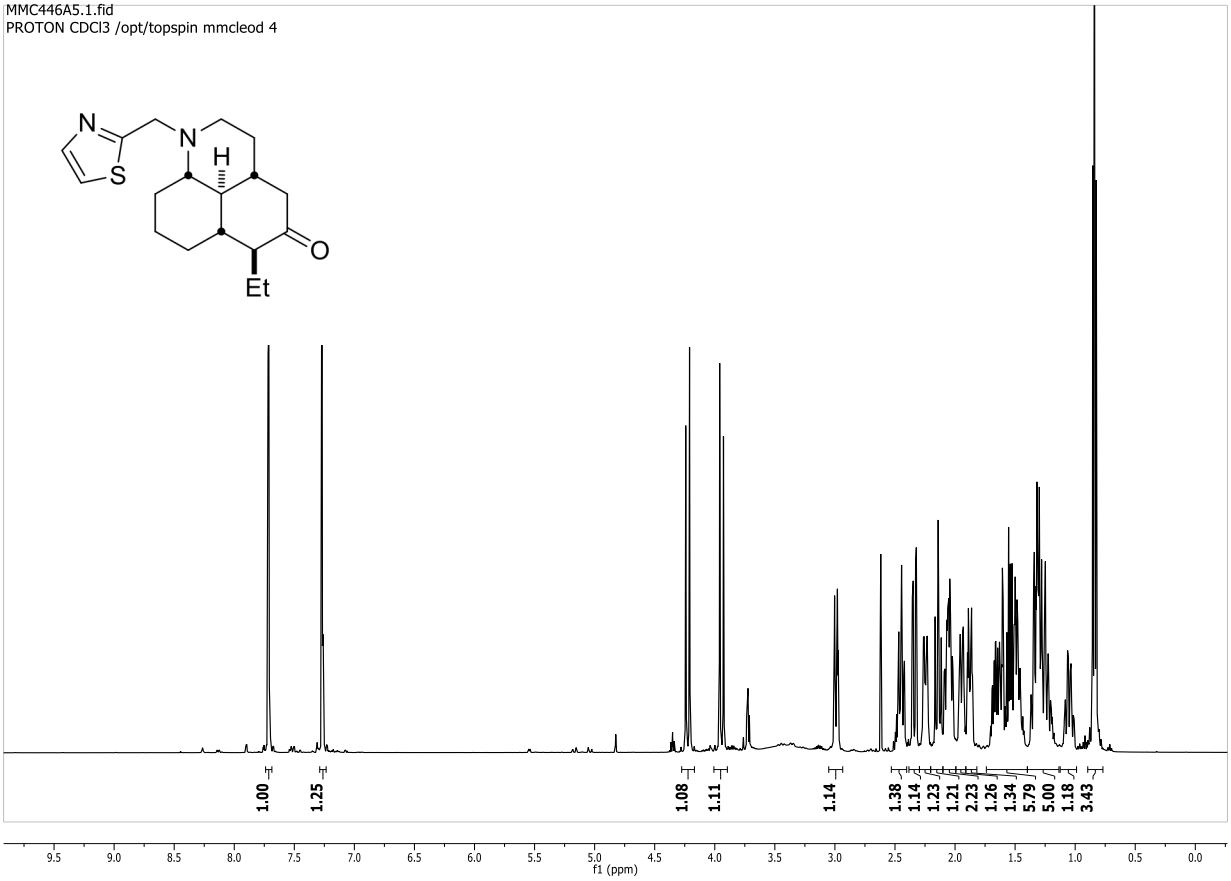


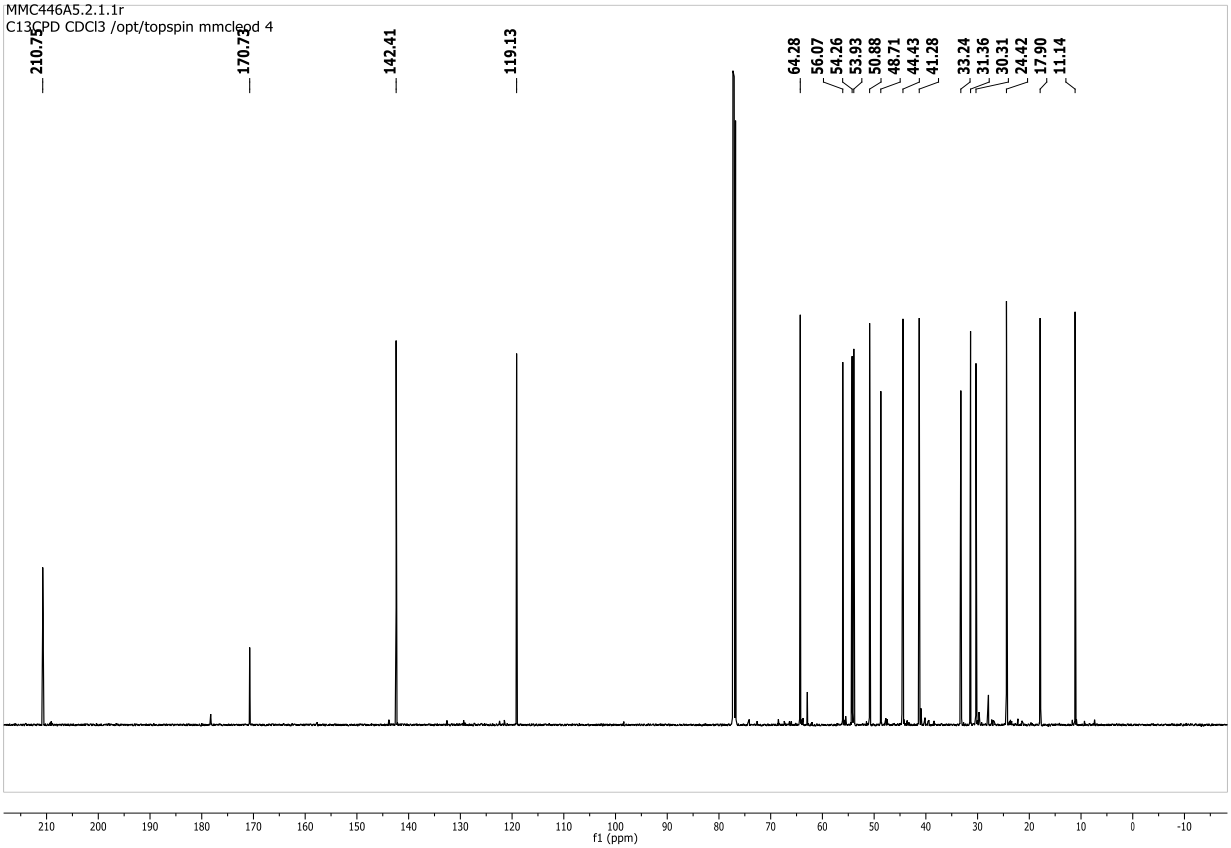
Alcohol **S4**


MMC467F1.1.fid
PROTON CDCl3 /opt/topspin mmcleod 11
Me
N
H
OH
Et
0.92
0.95
1.00
1.02
1.06
1.76
4.13
2.72
1.27
3.15
8.34
2.91
2.89
1.62
f1 (ppm)

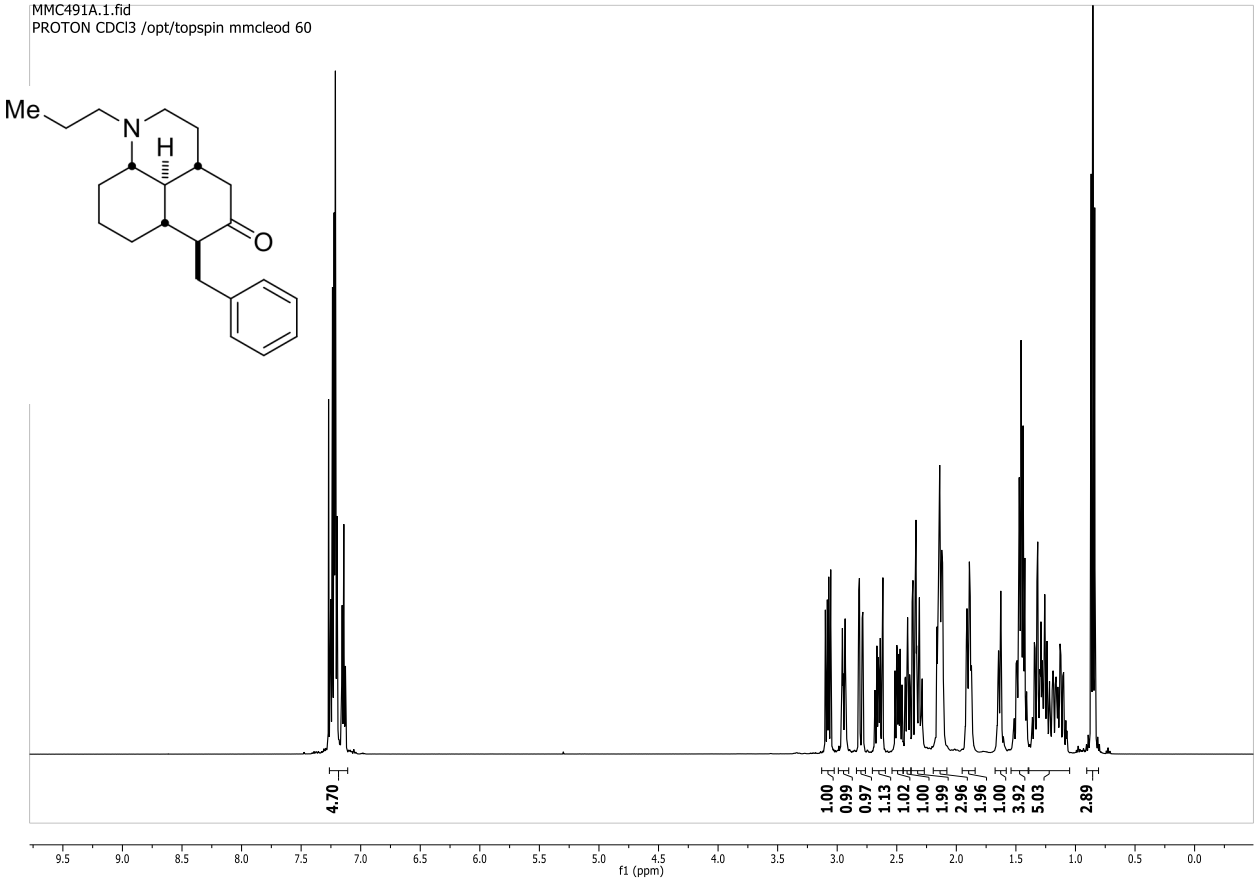

MMC467F1.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 11
66.48
63.54
55.35
52.67
51.38
50.72
47.61
40.34
38.56
33.28
32.81
29.91
29.78
24.54
21.41
17.08
12.05
11.66
f1 (ppm)

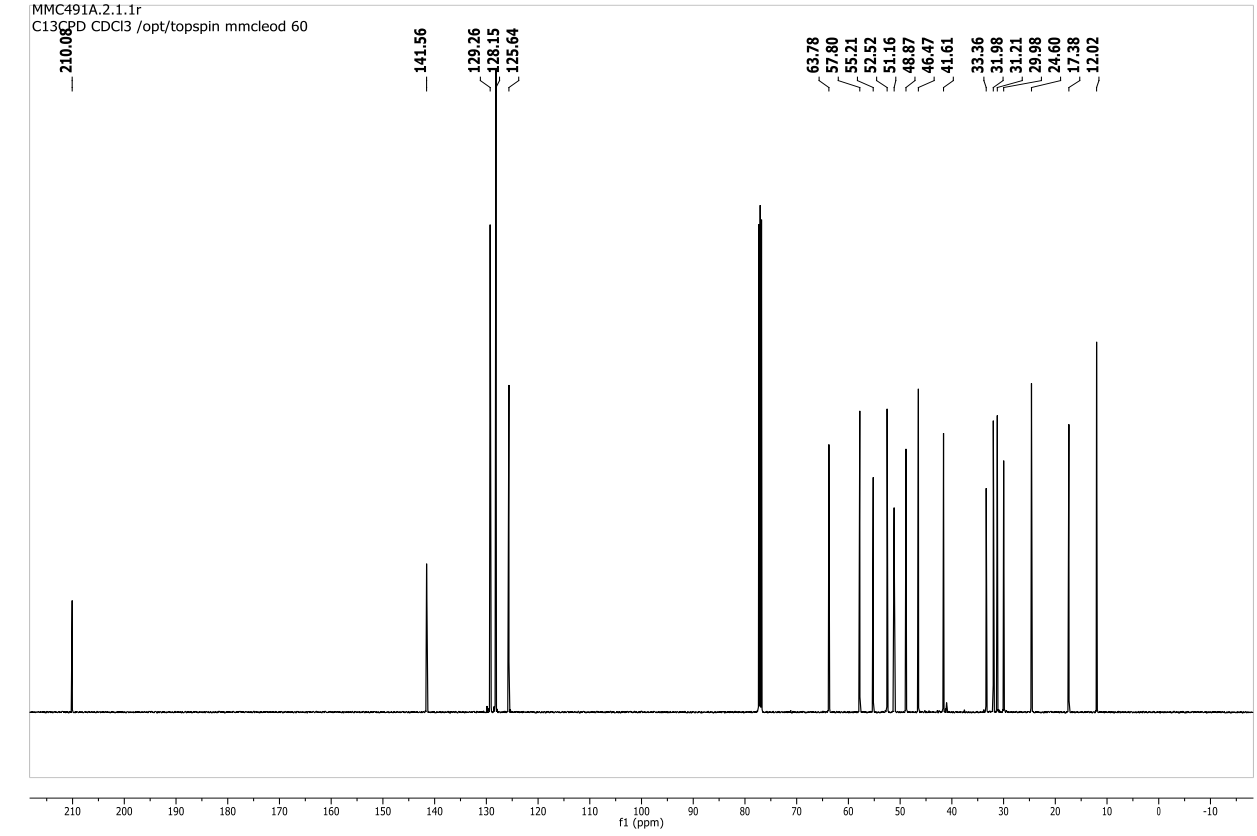
Amine **9b**{*2*}


MMC446A5.1.fid
PROTON CDCl3 /opt/topspin mmcleod 4
N
S
N
H
O
Et
1.00
1.25
1.08
1.11
1.14
1.38
1.14
1.23
1.21
2.23
1.26
1.34
5.79
5.00
1.18
3.43
f1 (ppm)


MMC446A5.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 4
210.75
170.75
142.41
119.13
64.28
56.07
54.26
53.93
50.88
48.71
44.43
41.28
33.24
31.36
30.31
24.42
17.90
11.14
f1 (ppm)

Amine **9c**{*1*}


MMC491A.1.fid
PROTON CDCl3 /opt/topspin mmcleod 60
Me
N
H
O
4.70
1.00
0.99
0.97
1.13
1.02
1.00
1.99
2.96
1.96
1.00
3.92
5.03
2.89
f1 (ppm)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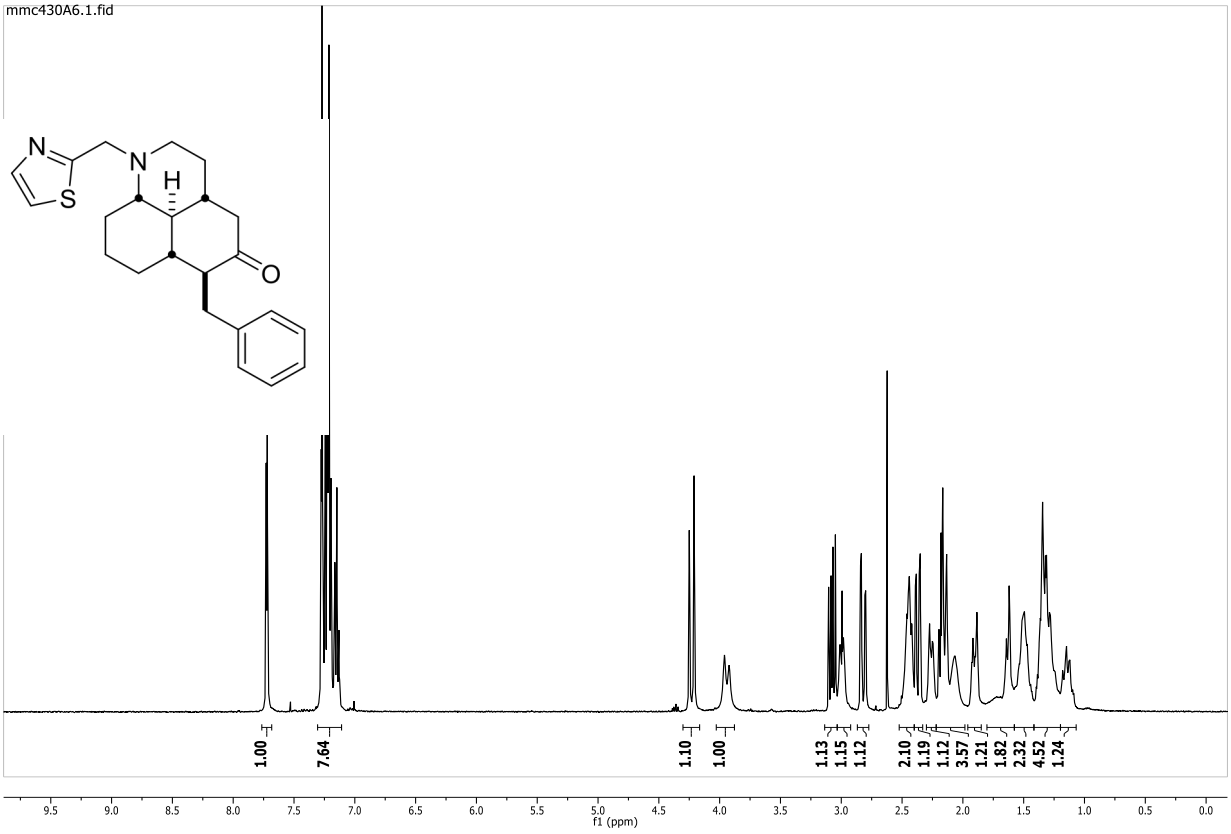
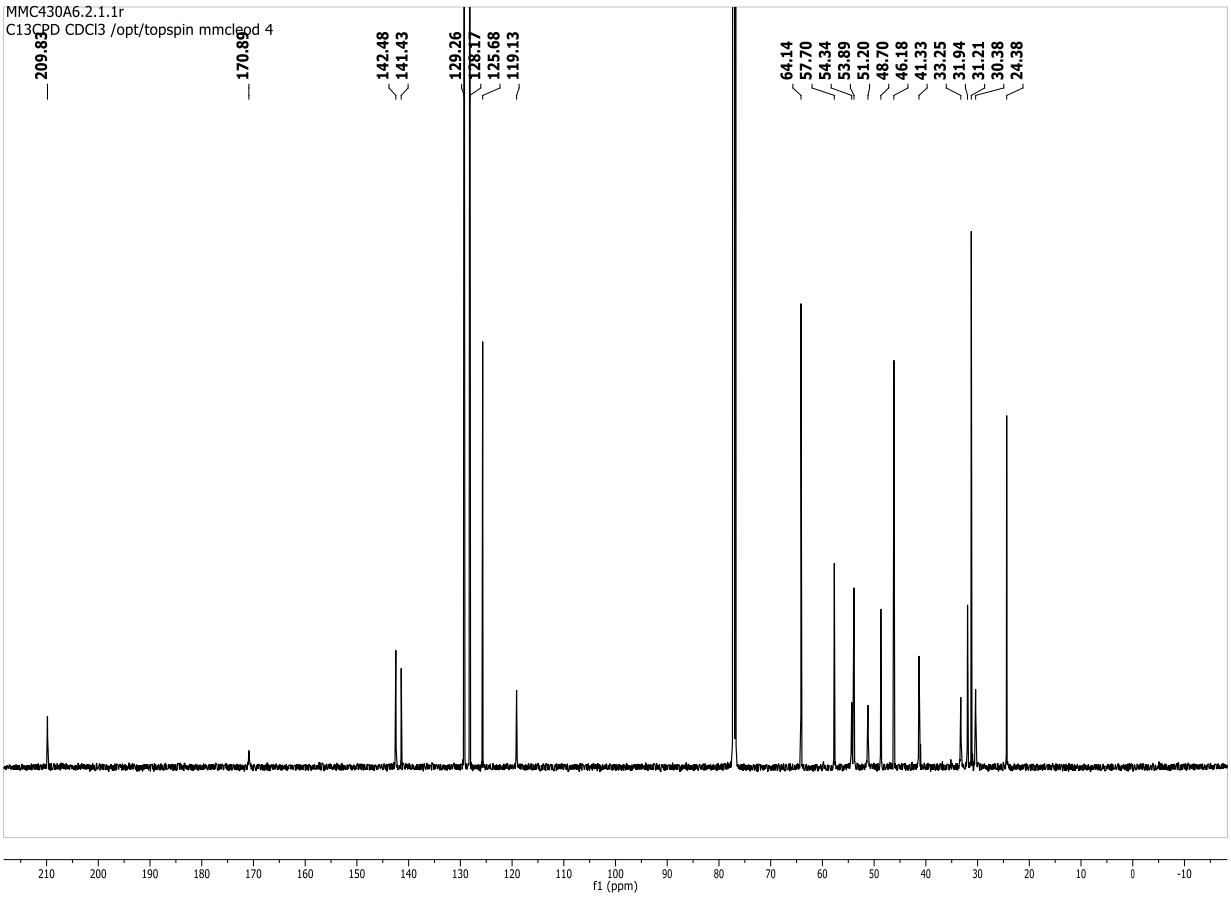
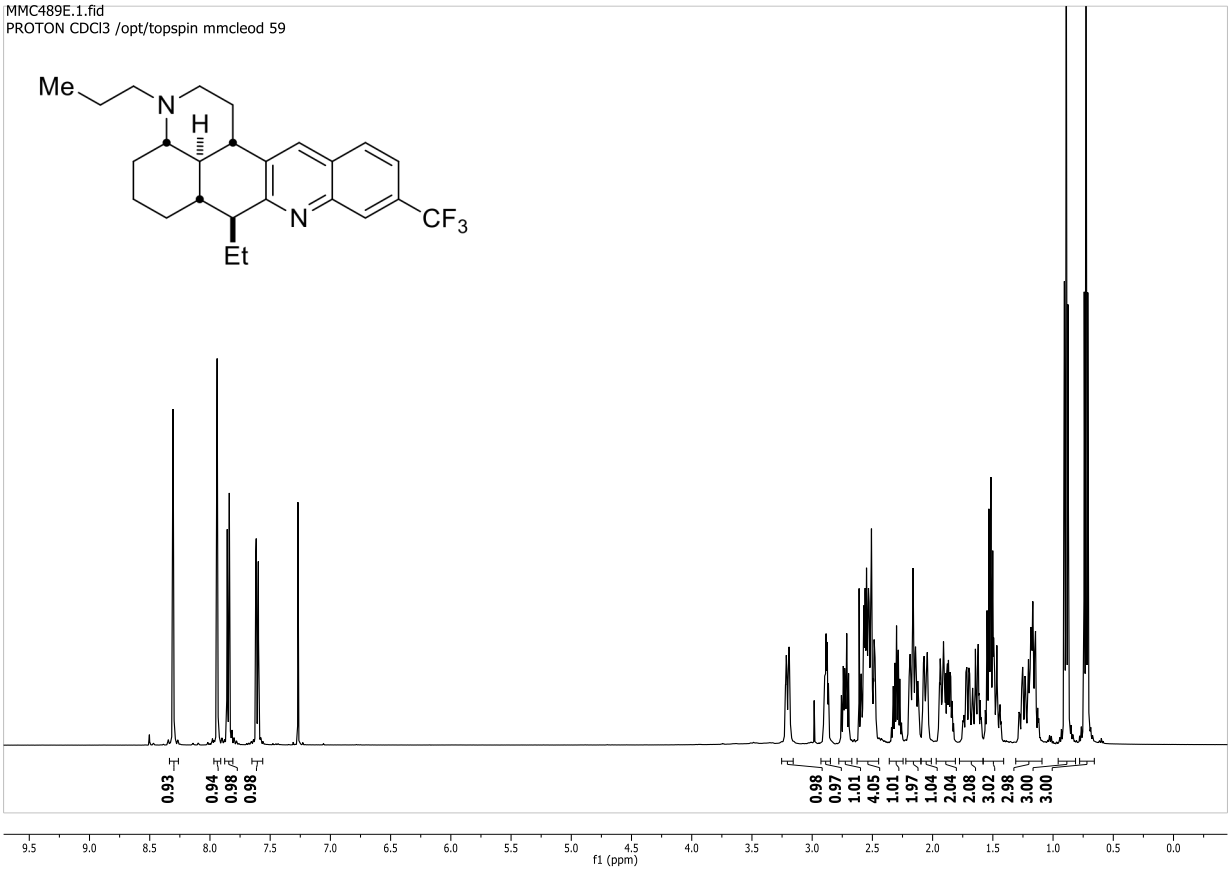
C13CPD CDCl3 /opt/topspin mmcleod 60
210.08
141.56
129.26
128.15
125.64
63.78
57.80
55.21
52.52
51.16
48.87
46.47
41.61
33.36
31.98
31.21
29.98
24.60
17.38
12.02
f1 (ppm)

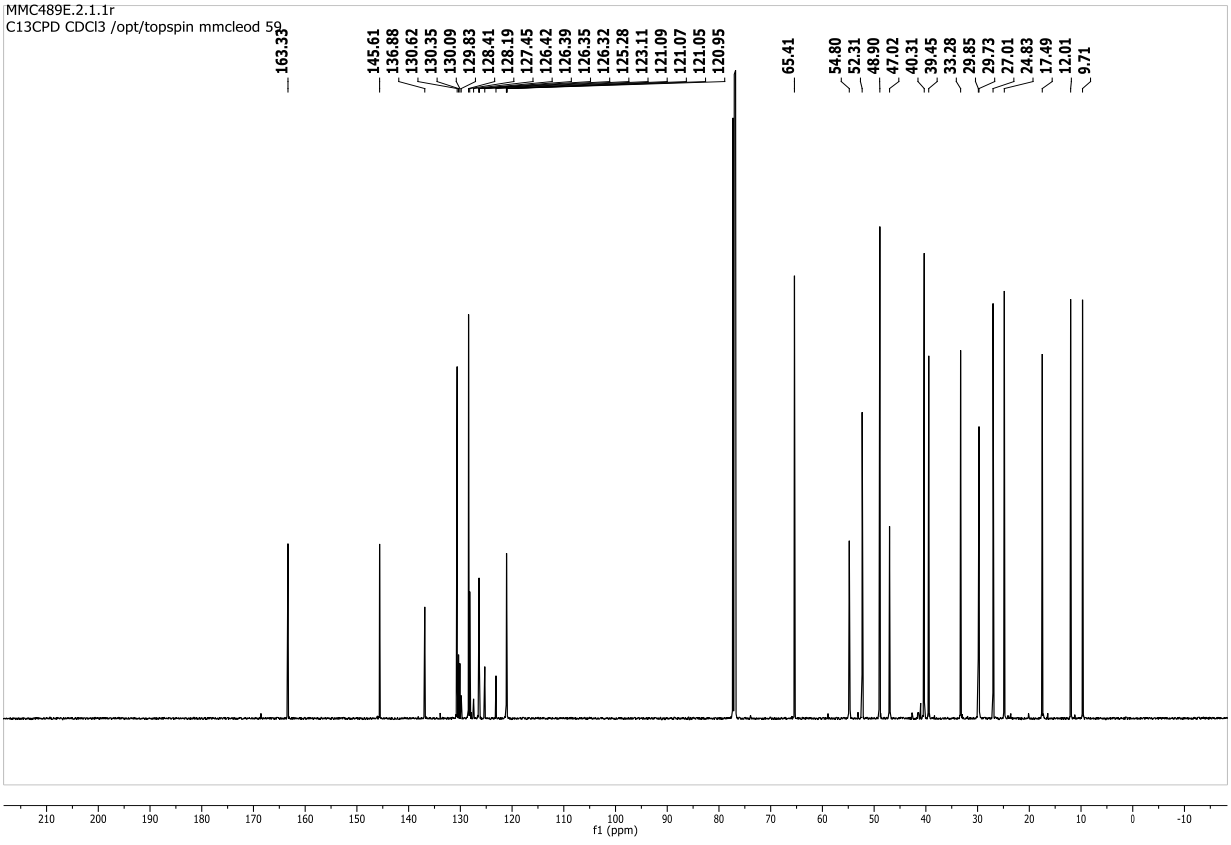
Amine **9c**{*2*}


mmc430A6.1.fid
1.00
7.64
1.10
1.00
1.13
1.15
1.12
2.10
1.19
1.12
3.57
1.21
1.82
2.32
4.52
1.24
f1 (ppm)

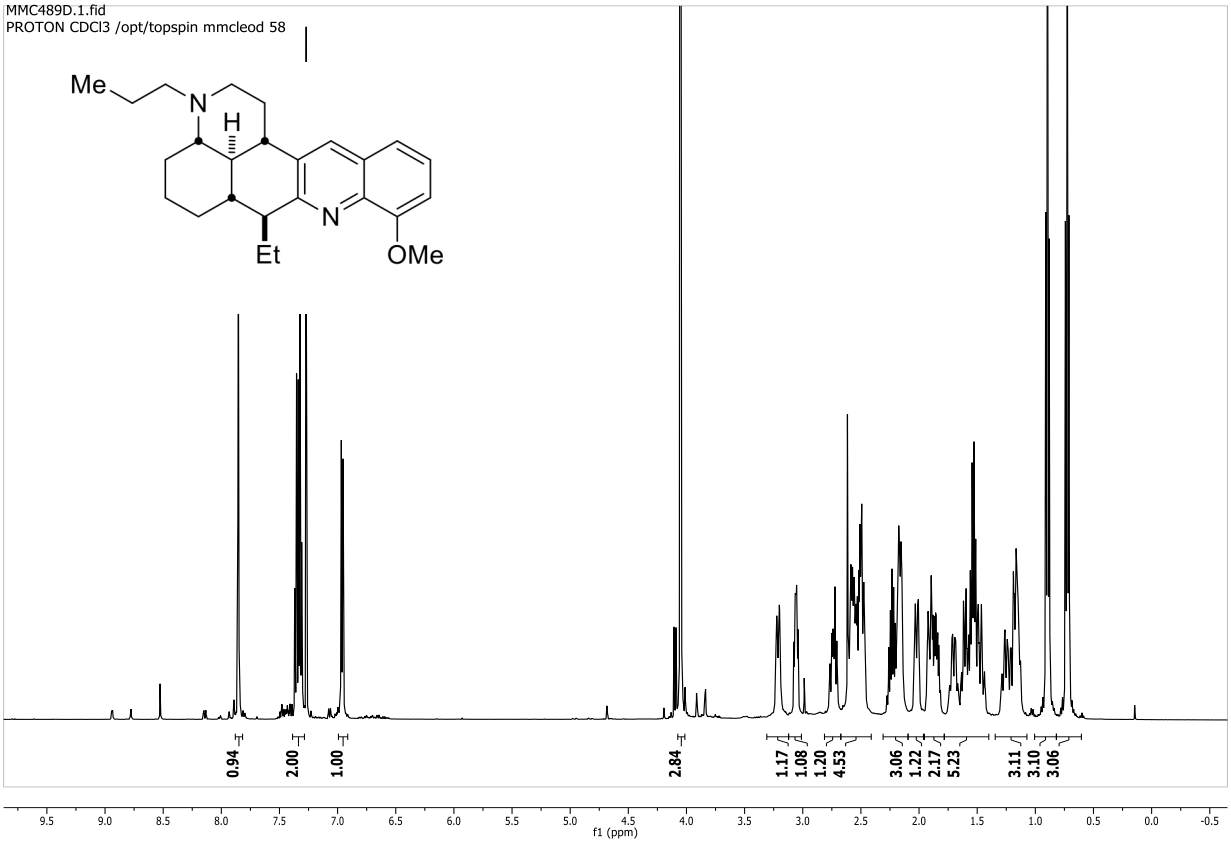

MMC430A6.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 4
209.83
170.89
142.48
141.43
129.26
128.17
125.68
119.13
64.14
57.70
54.34
53.89
51.20
48.70
46.18
41.33
33.25
31.94
31.21
30.38
24.38
f1 (ppm)

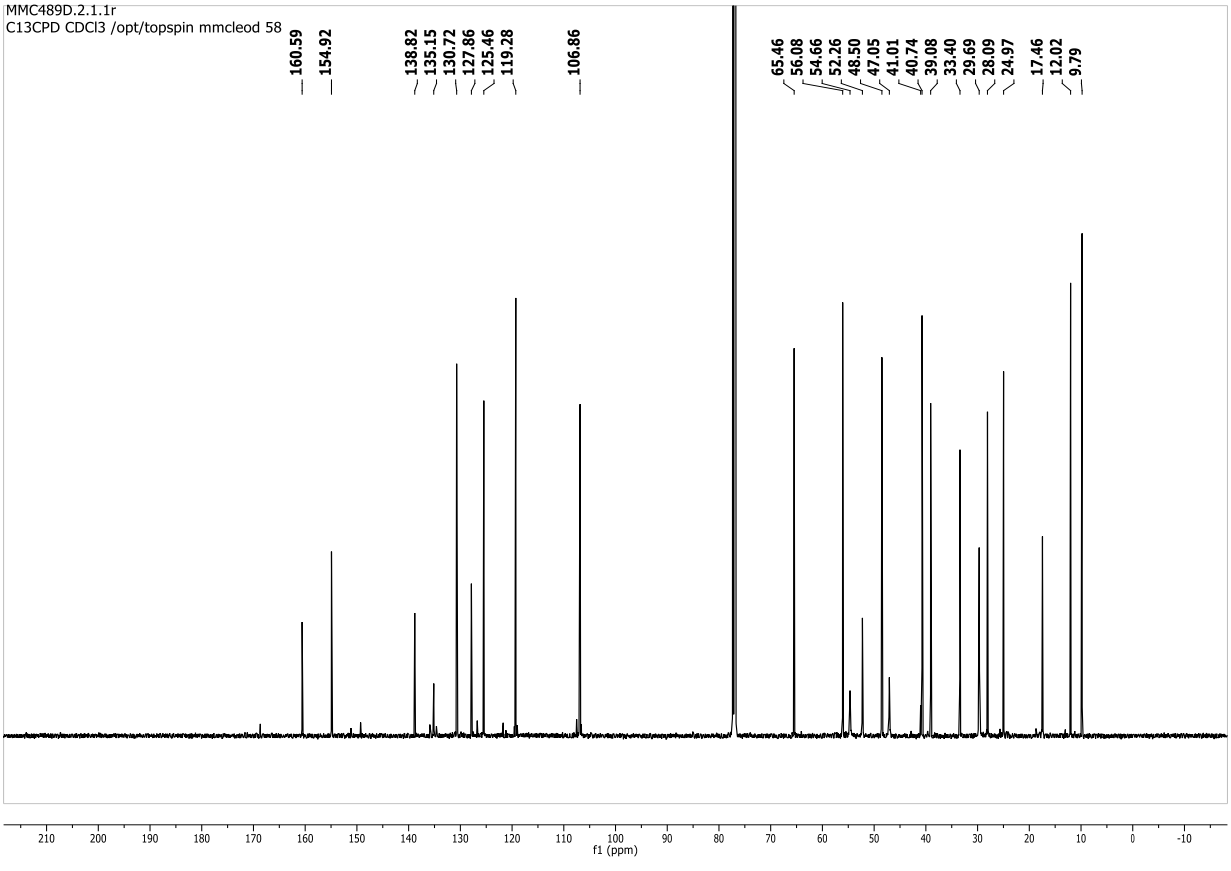
Quinoline **17**{*6*}



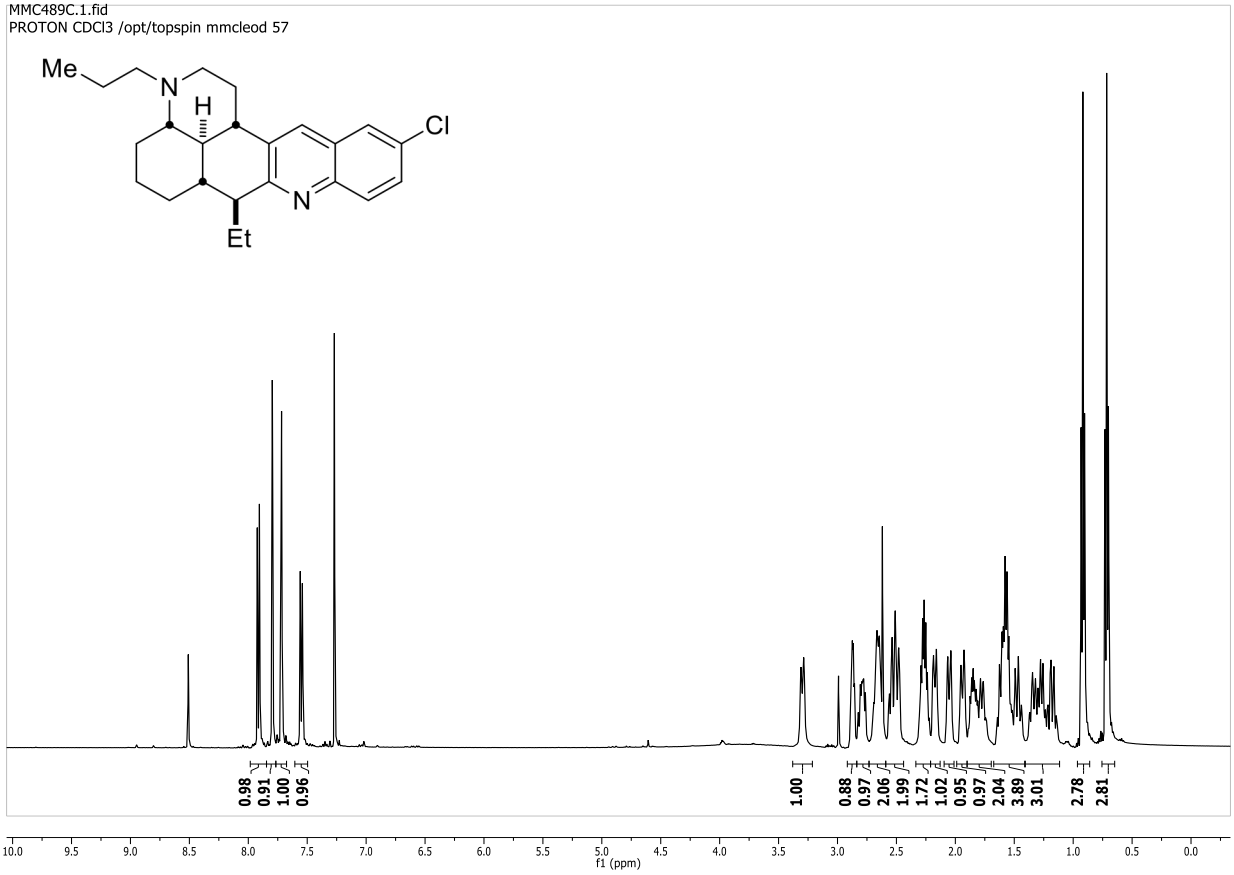


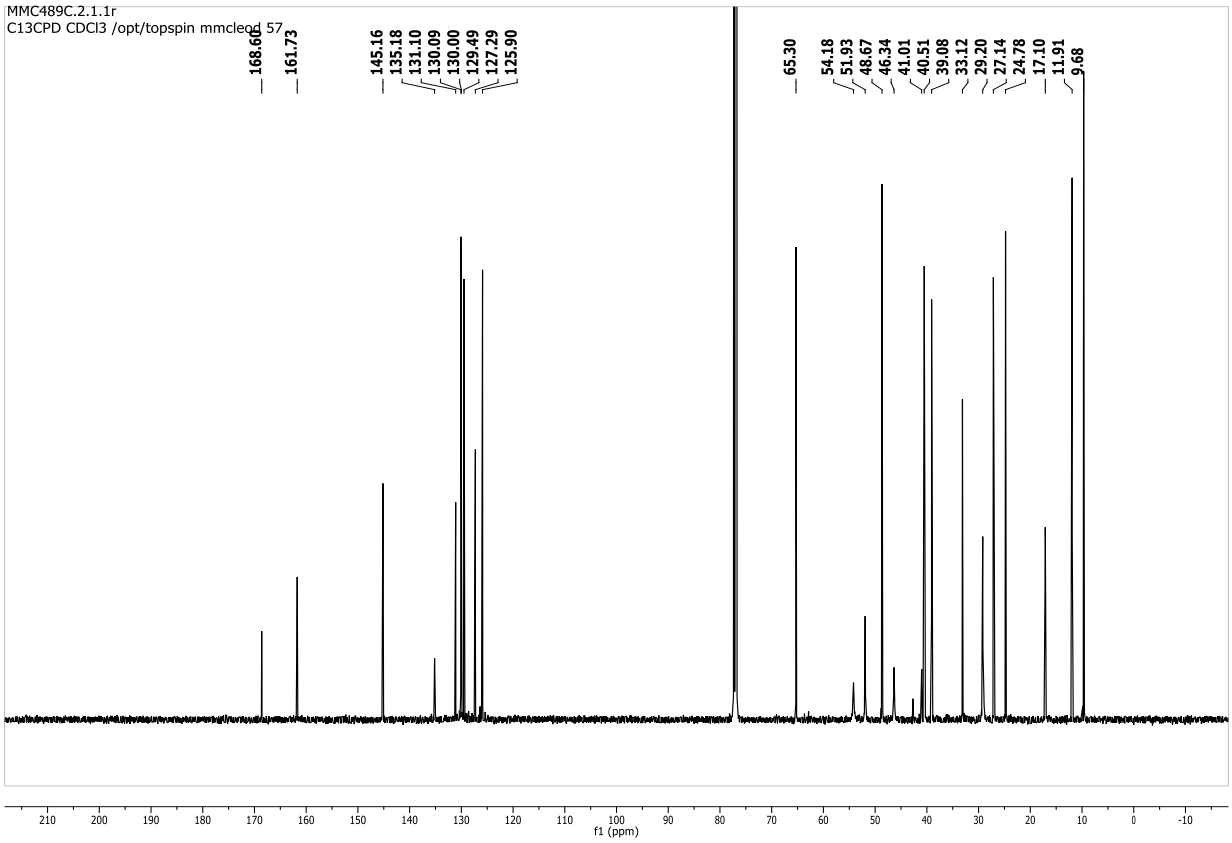
Quinoline **17**{*5*}



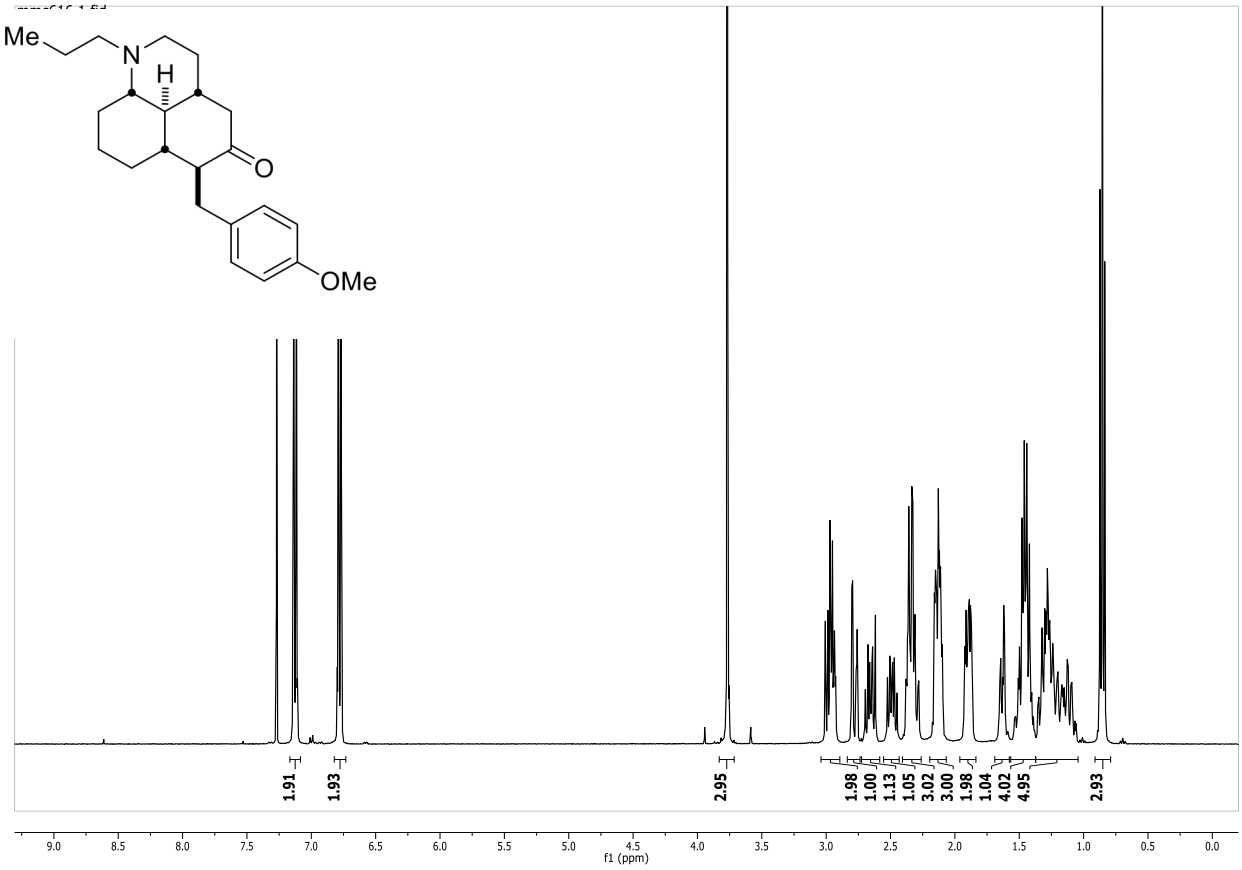


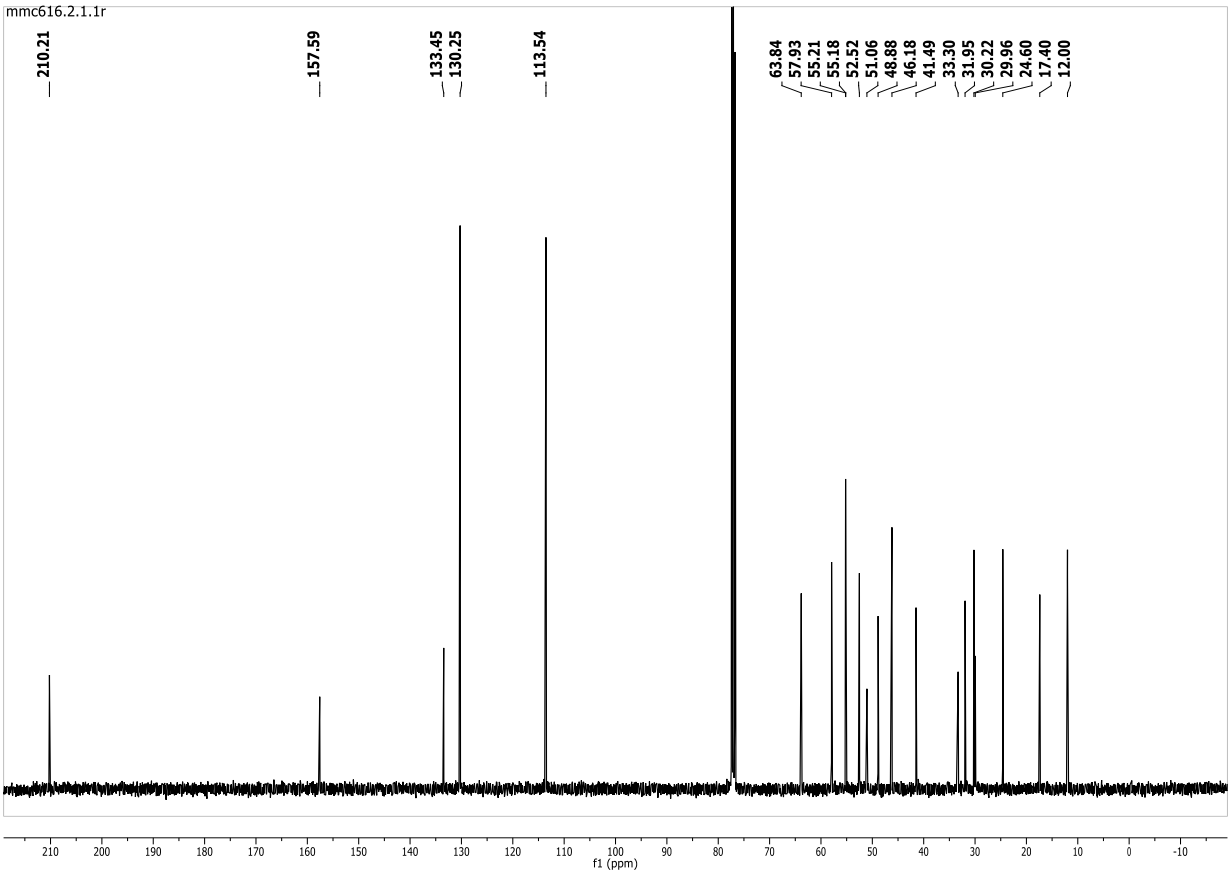
Quinoline **17**{*4*}



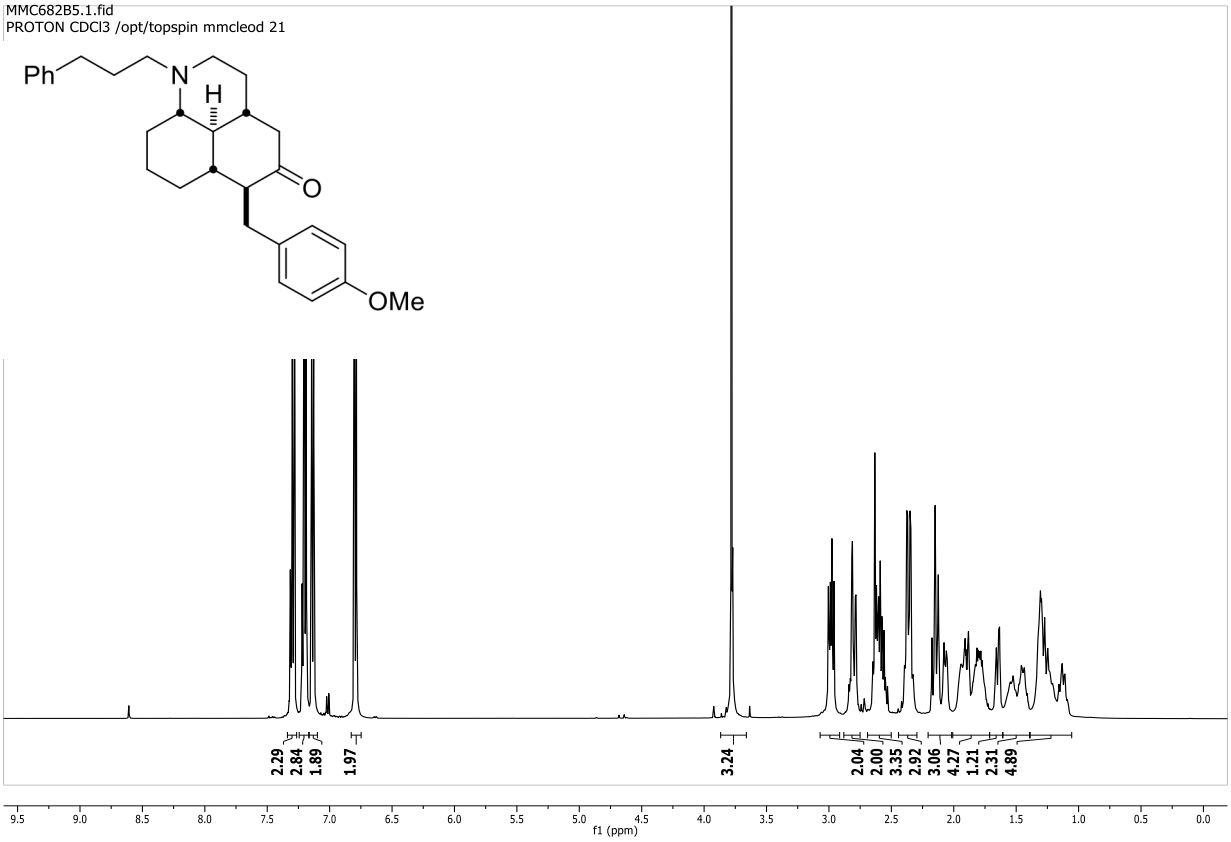


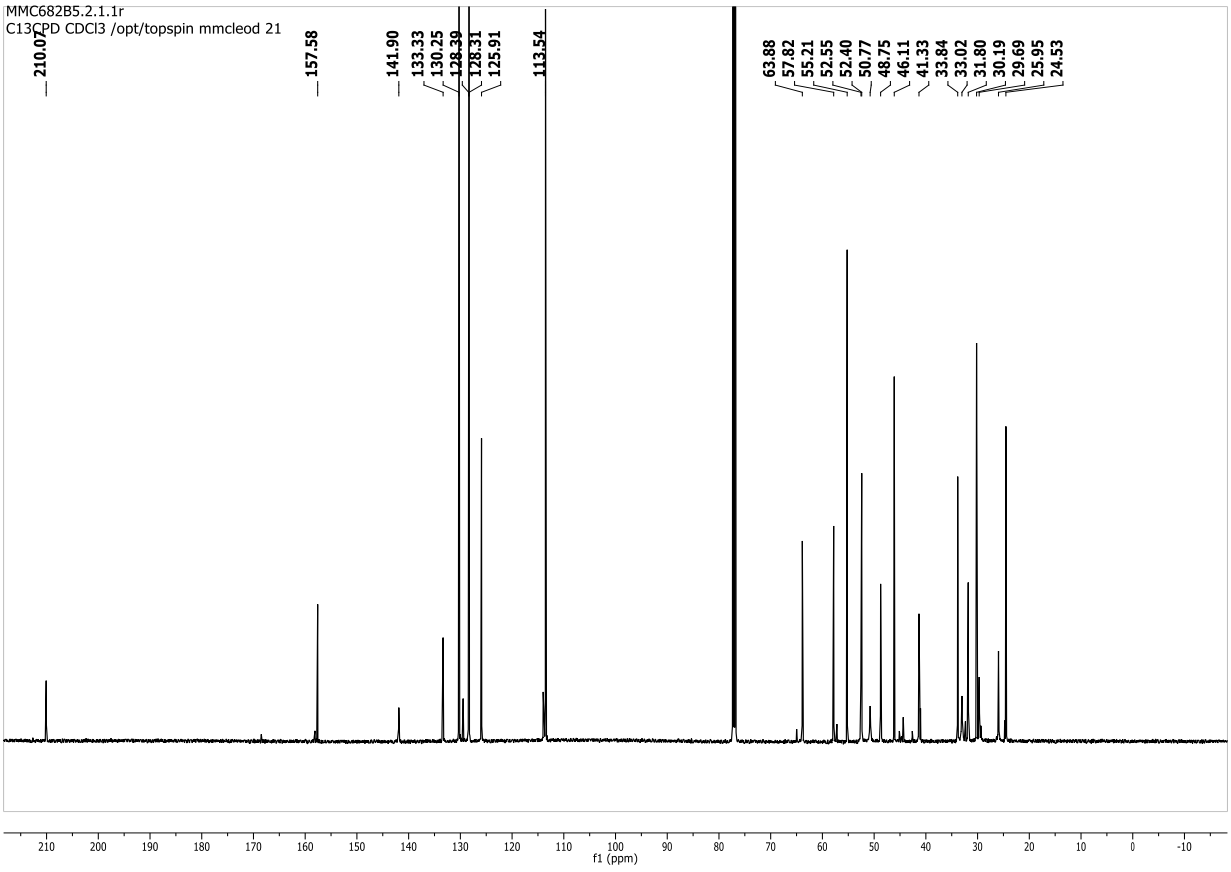
Amine **9d**{*1*}


Me
N
H
O
OMe
1.91
1.93
2.95
1.98
1.00
1.13
1.05
3.02
3.00
1.98
1.04
4.02
4.95
2.93
f1 (ppm)

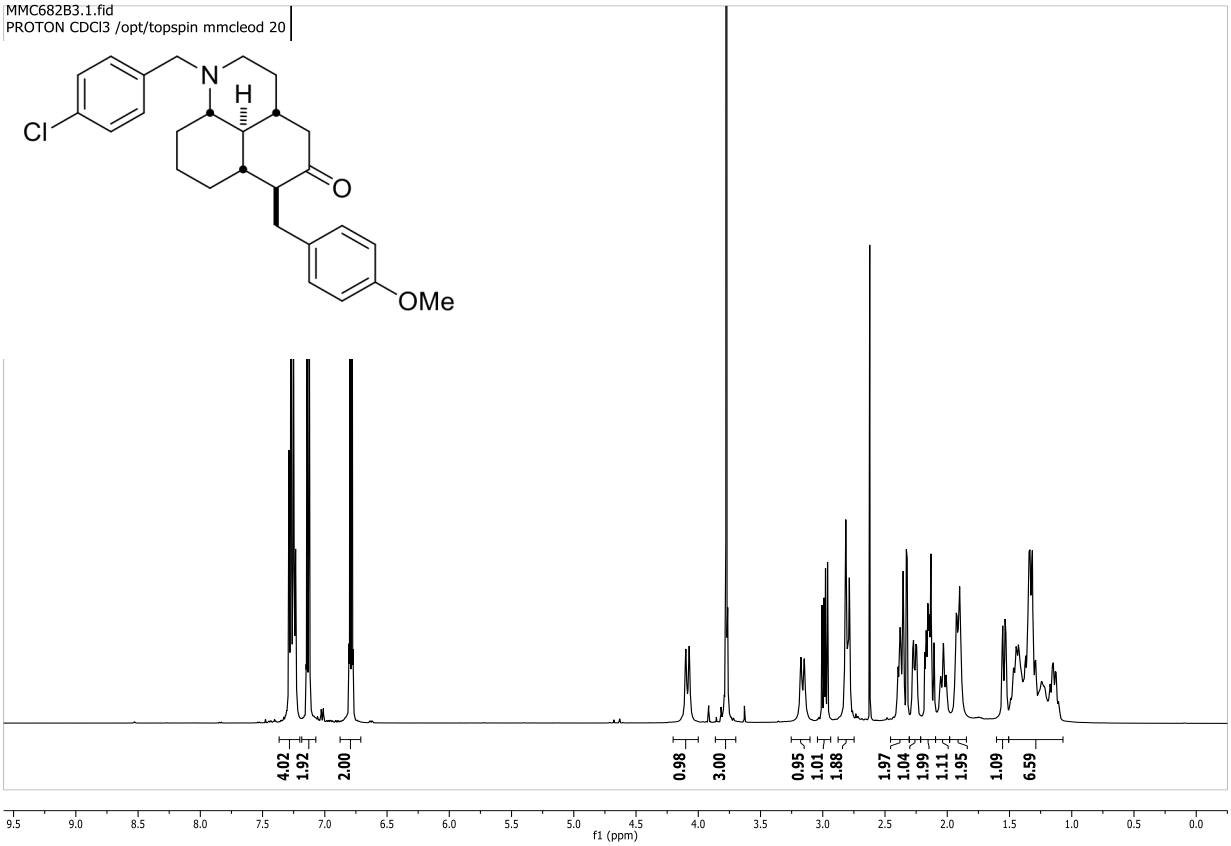

mmc616.2.1.1r
210.21
157.59
133.45
130.25
113.54
63.84
57.93
55.21
55.18
52.52
51.06
48.88
46.18
41.49
33.30
31.95
30.22
29.96
24.60
17.40
12.00
f1 (ppm)

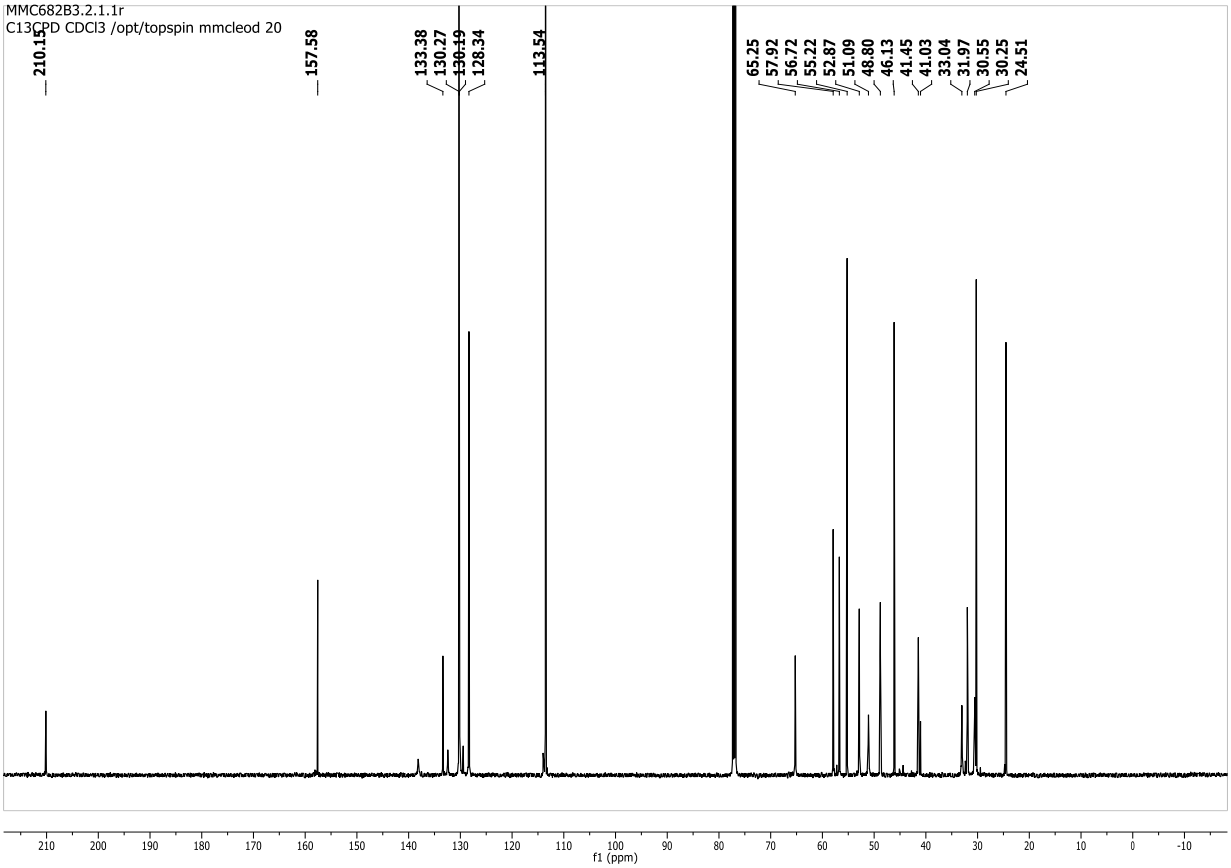
Amine **9d**{*4*}


MMC682B5.1.fid
PROTON CDCl3 /opt/topspin mmcleod 21
Ph
N
H
O
OMe
2.29
2.84
1.89
1.97
3.24
2.04
2.00
3.35
2.92
3.06
4.27
1.21
2.31
4.89
f1 (ppm)

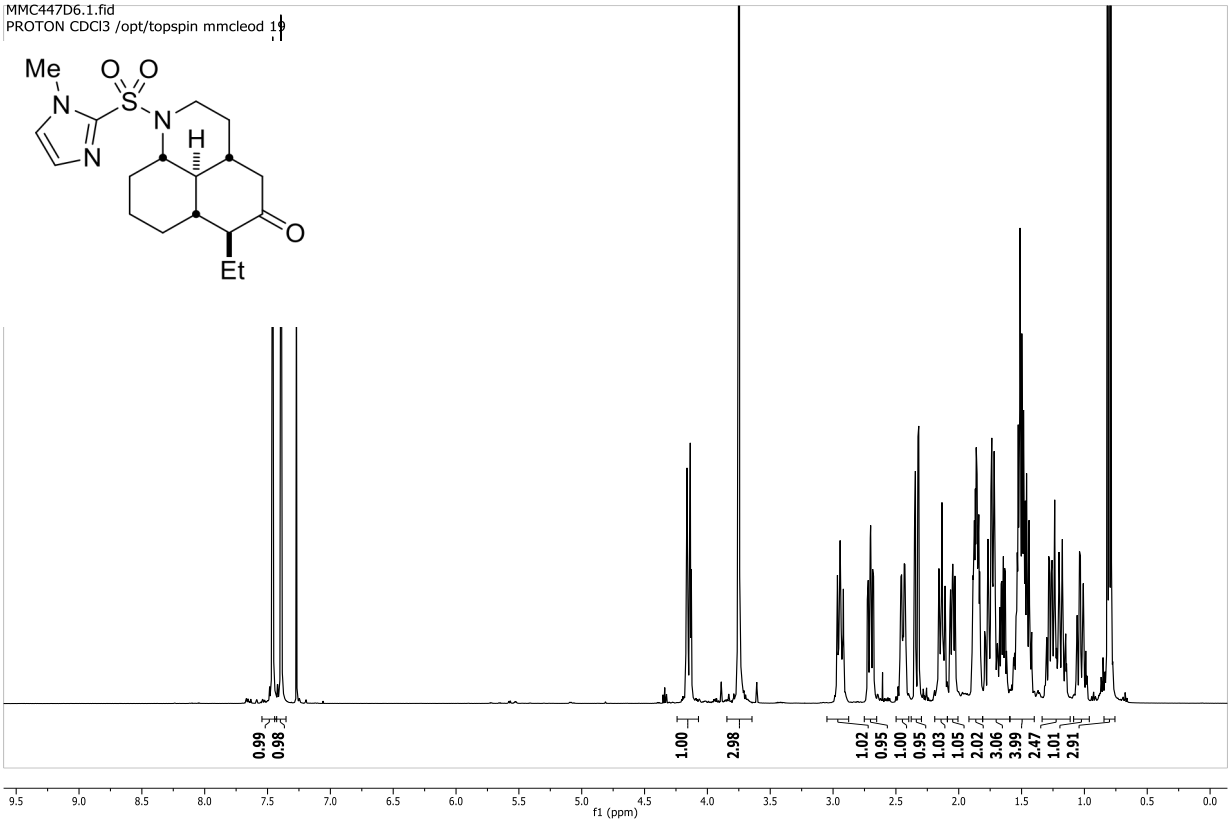

MMC682B5.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 21
210.07
157.58
141.90
133.33
130.25
128.39
128.31
125.91
113.54
63.88
57.82
55.21
52.55
52.40
50.77
48.75
46.11
41.33
33.84
33.02
31.80
30.19
29.69
25.95
24.53
f1 (ppm)

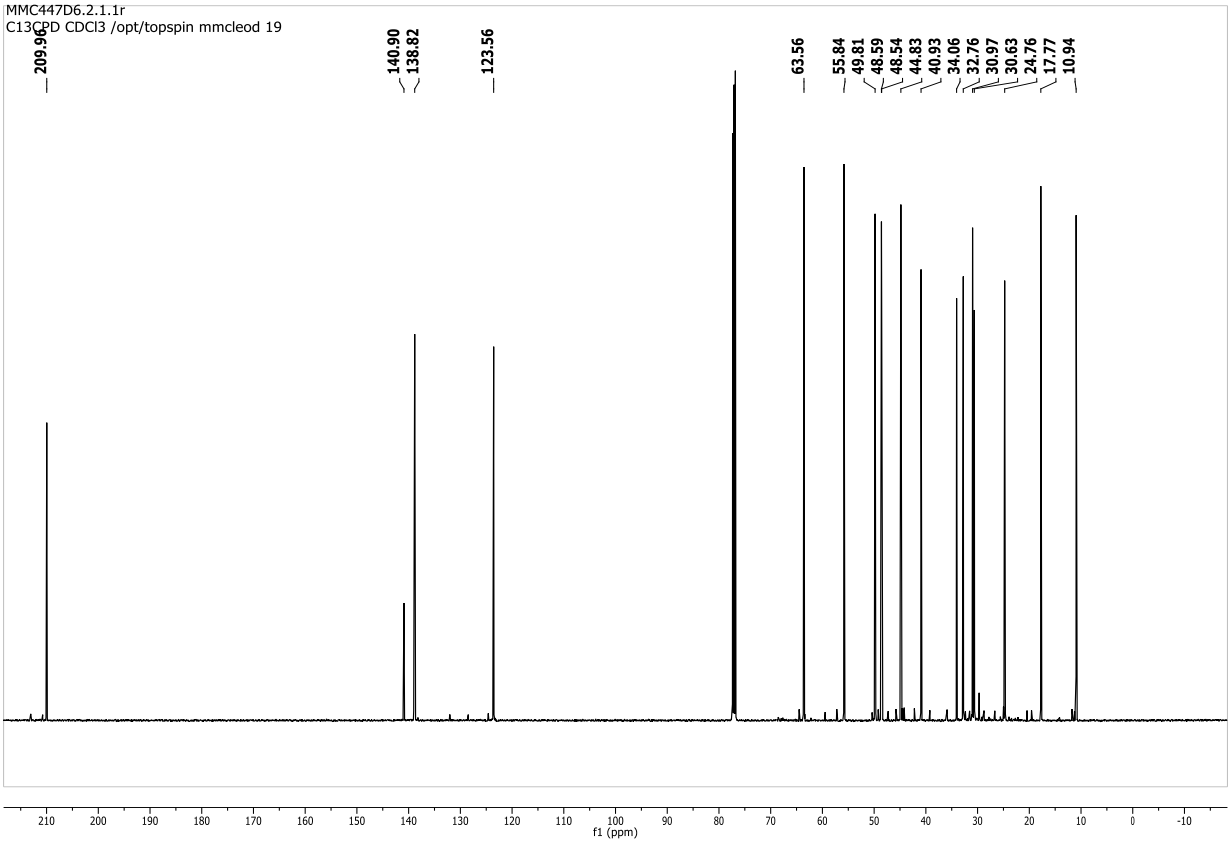
Amine **9d**{*6*}


MMC682B3.1.fid
PROTON CDCl3 /opt/topspin mmcleod 20
Cl
N
H
O
OMe
4.02
1.92
2.00
0.98
3.00
0.95
1.01
1.88
1.97
1.04
1.99
1.11
1.95
1.09
6.59
f1 (ppm)

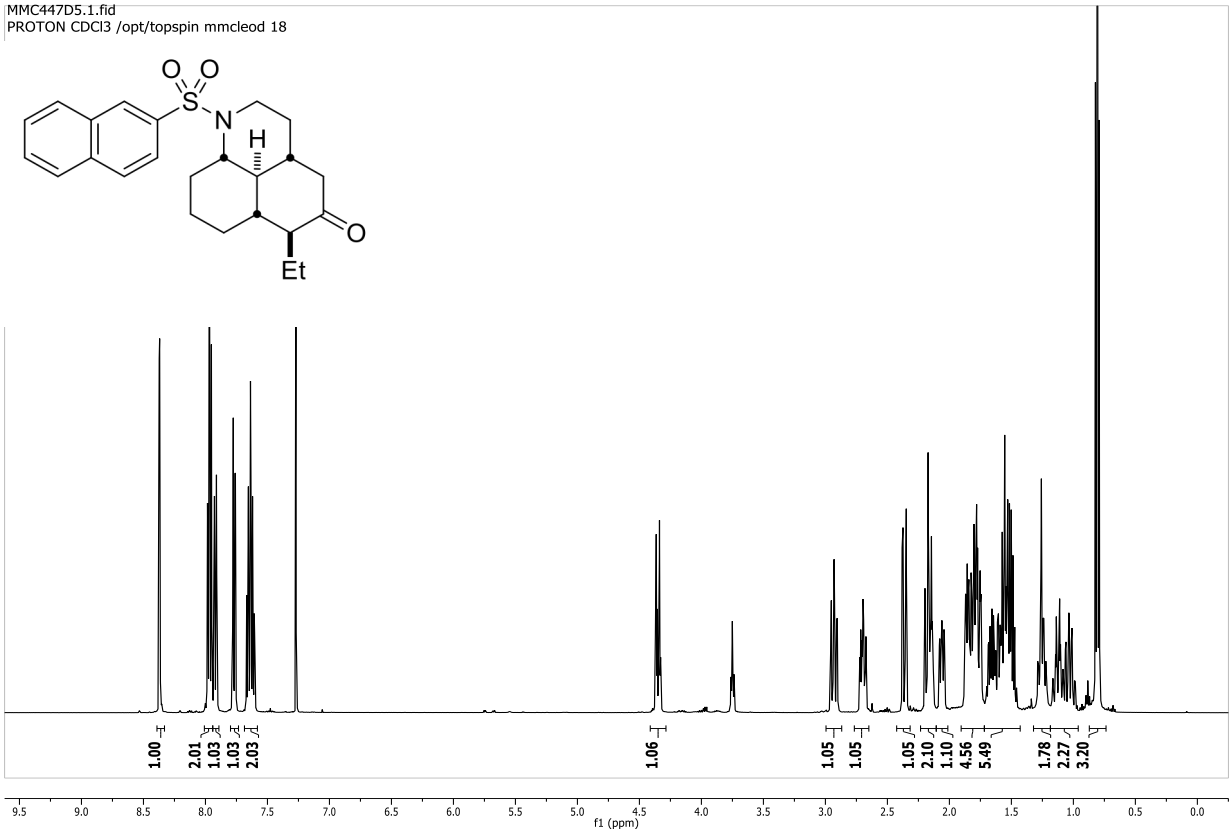

MMC682B3.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 20
210.15
157.58
133.38
130.27
130.19
128.34
113.54
65.25
57.92
56.72
55.22
52.87
51.09
48.80
46.13
41.45
41.03
33.04
31.97
30.55
30.25
24.51
f1 (ppm)

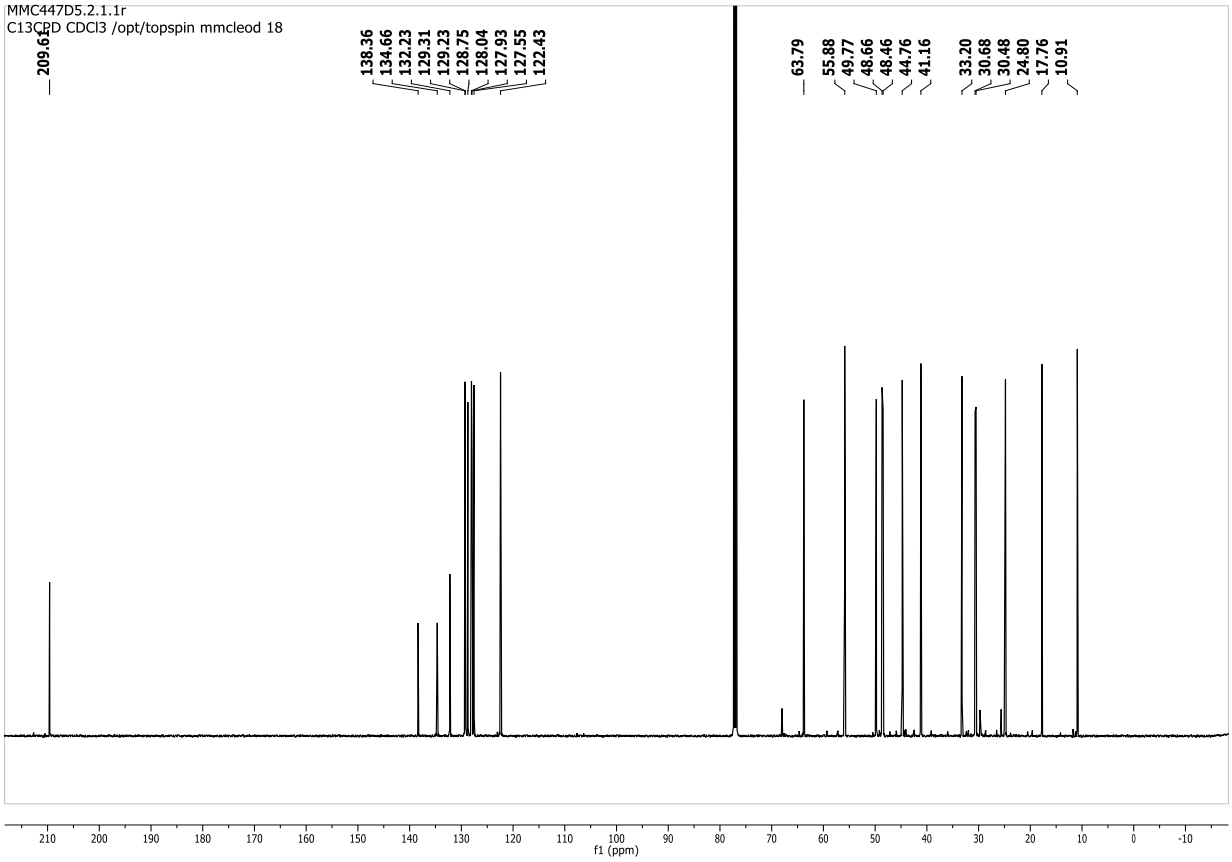
Sulfonamide **13b**{*12*}



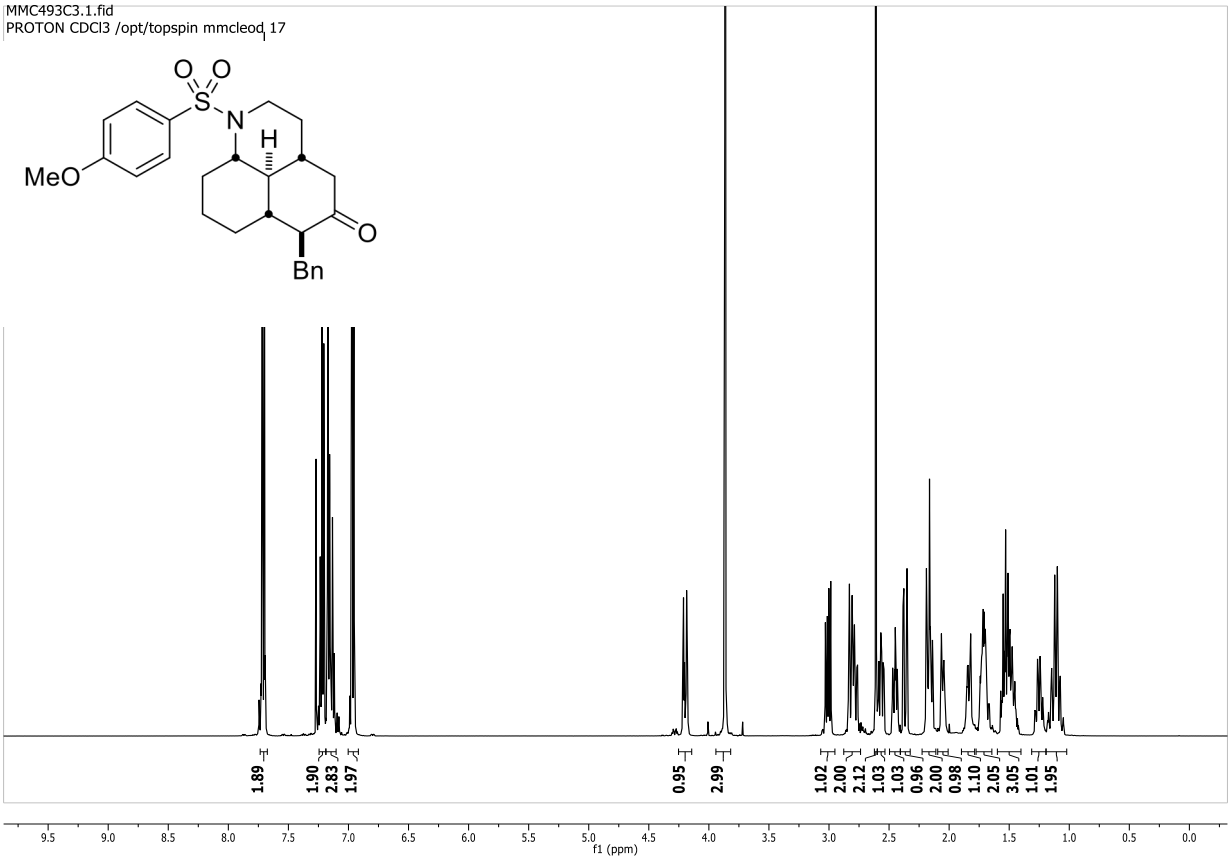


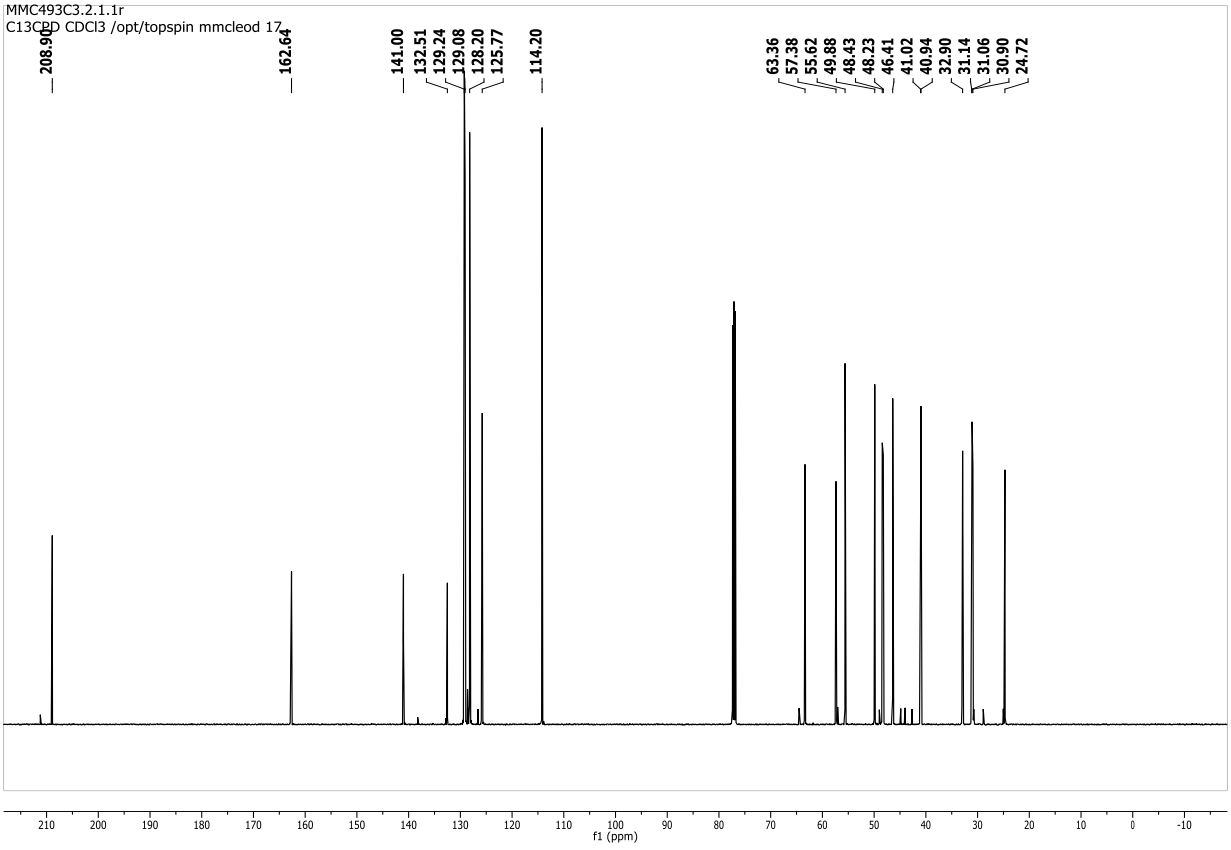
Sulfonamide **13b**{*11*}



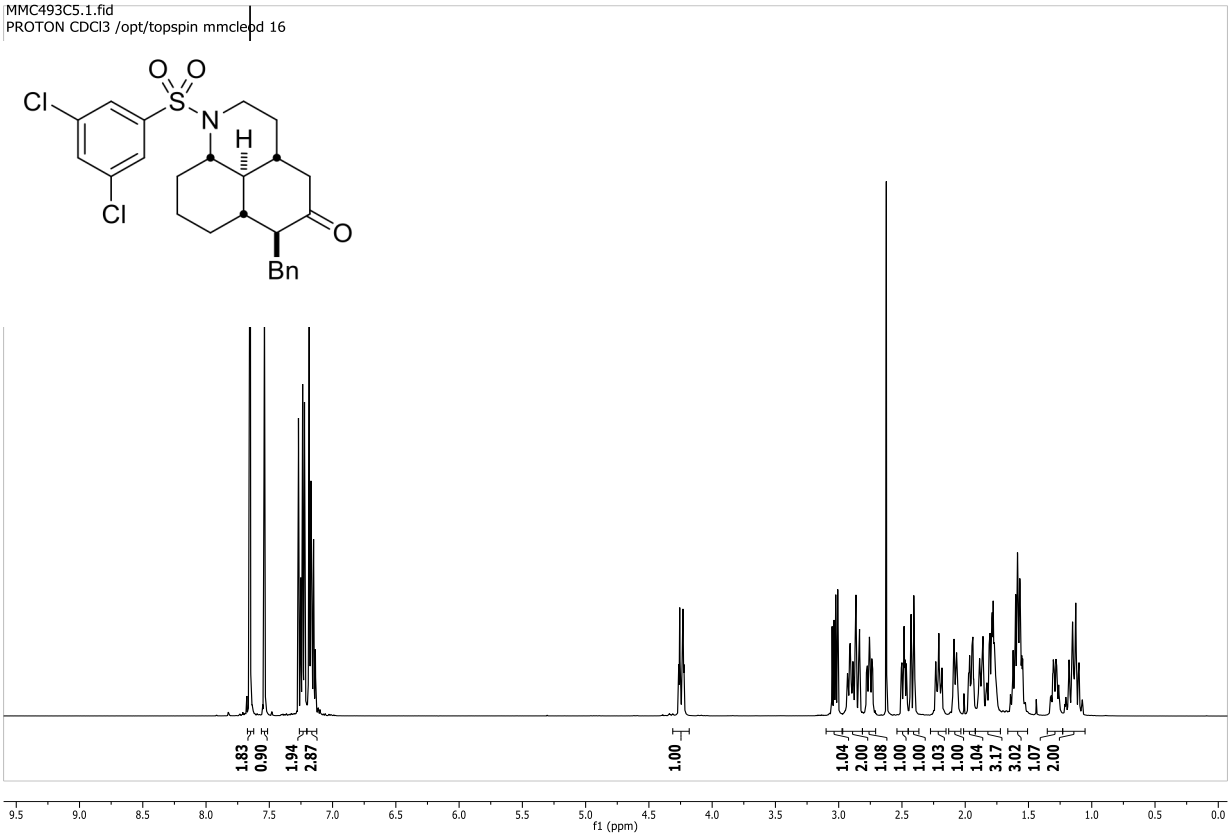


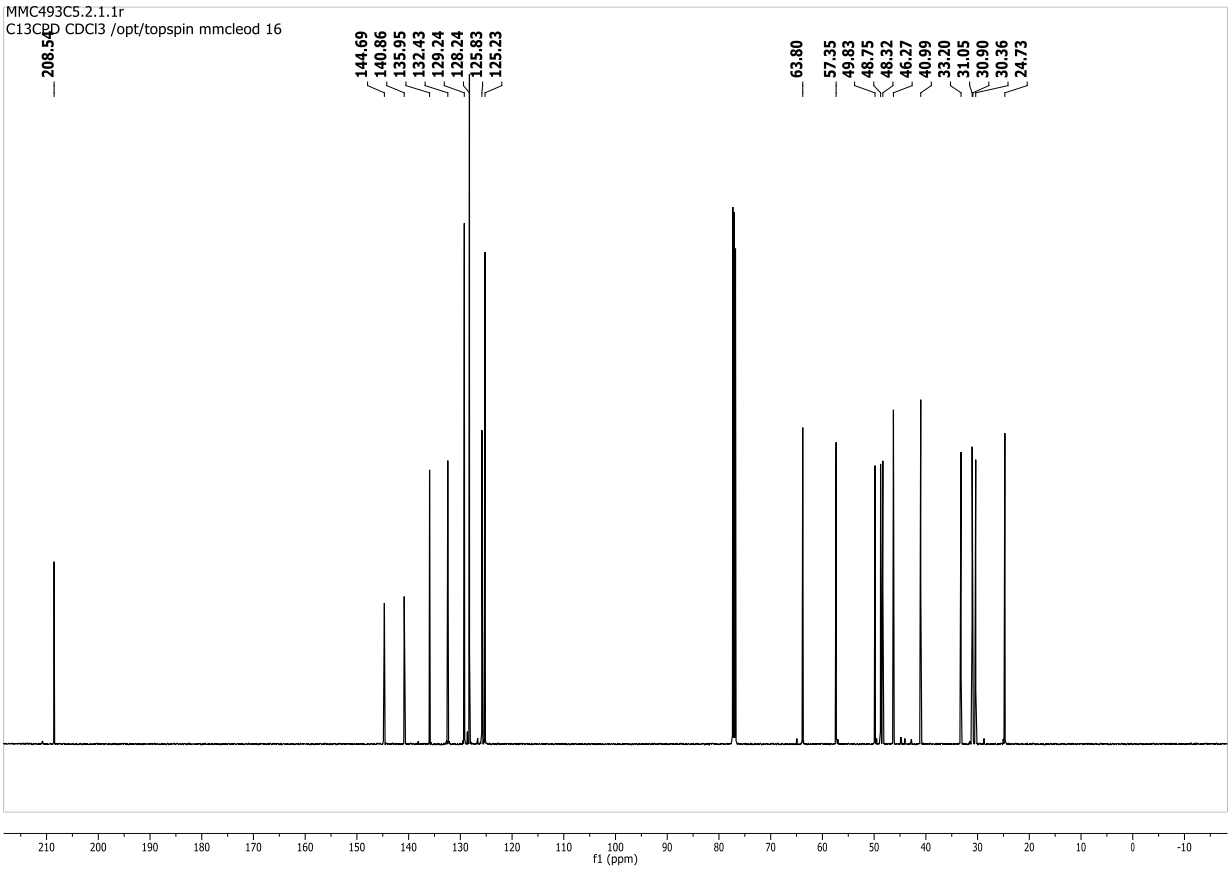
Sulfonamide **13c**{*3*}



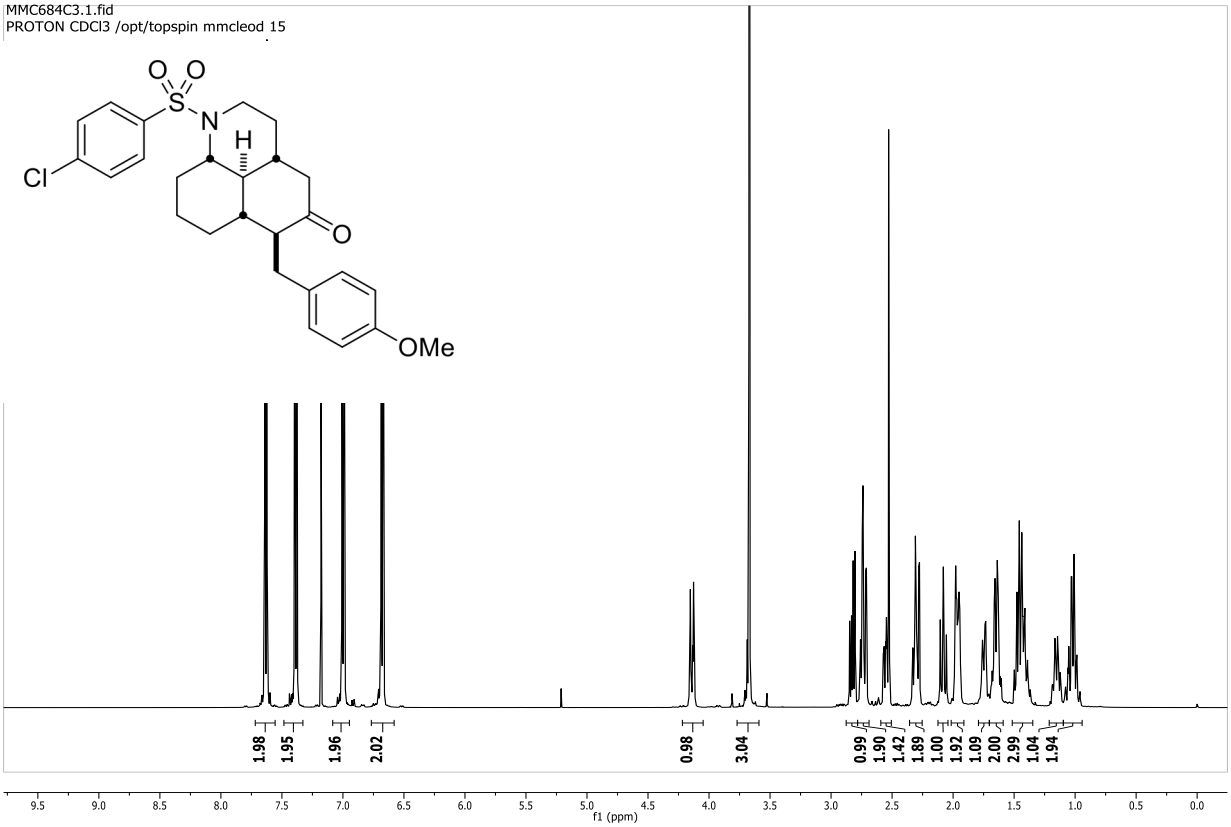


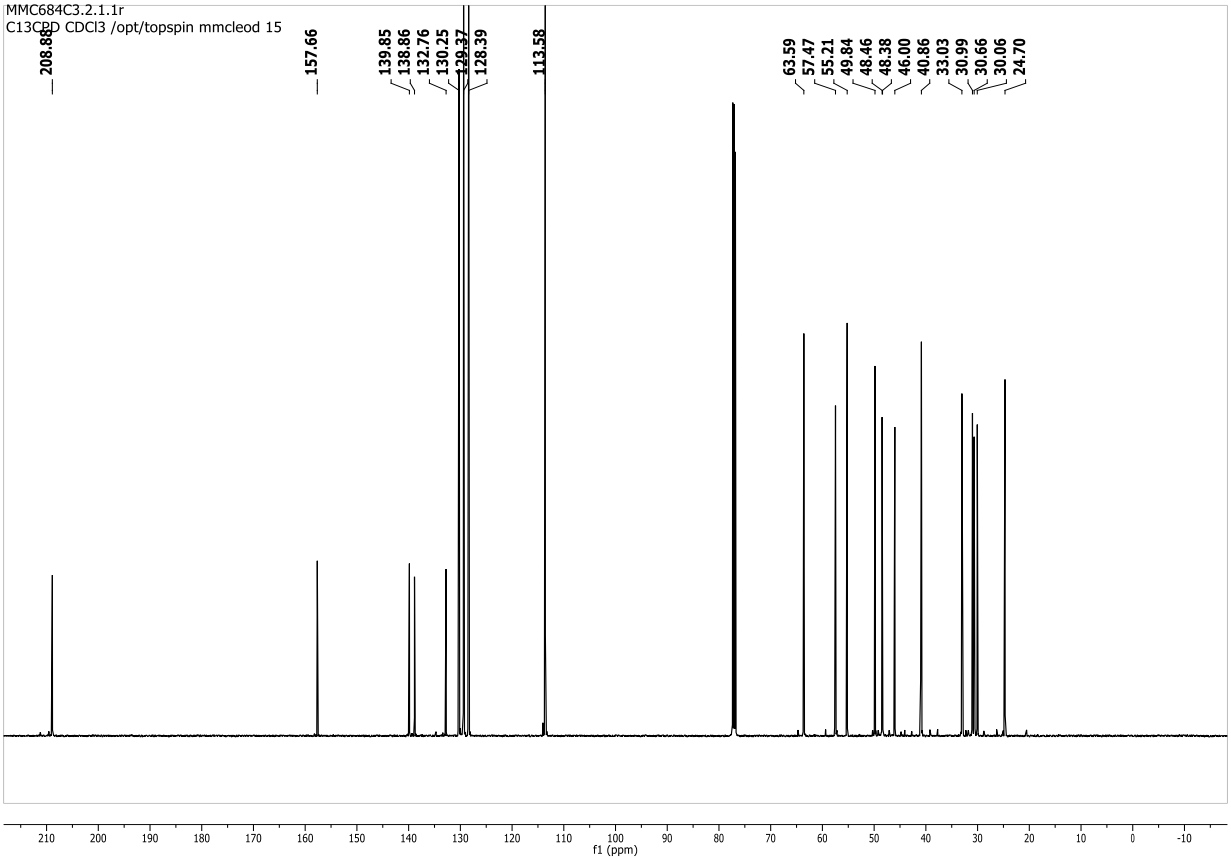
Sulfonamide **13c**{*5*}



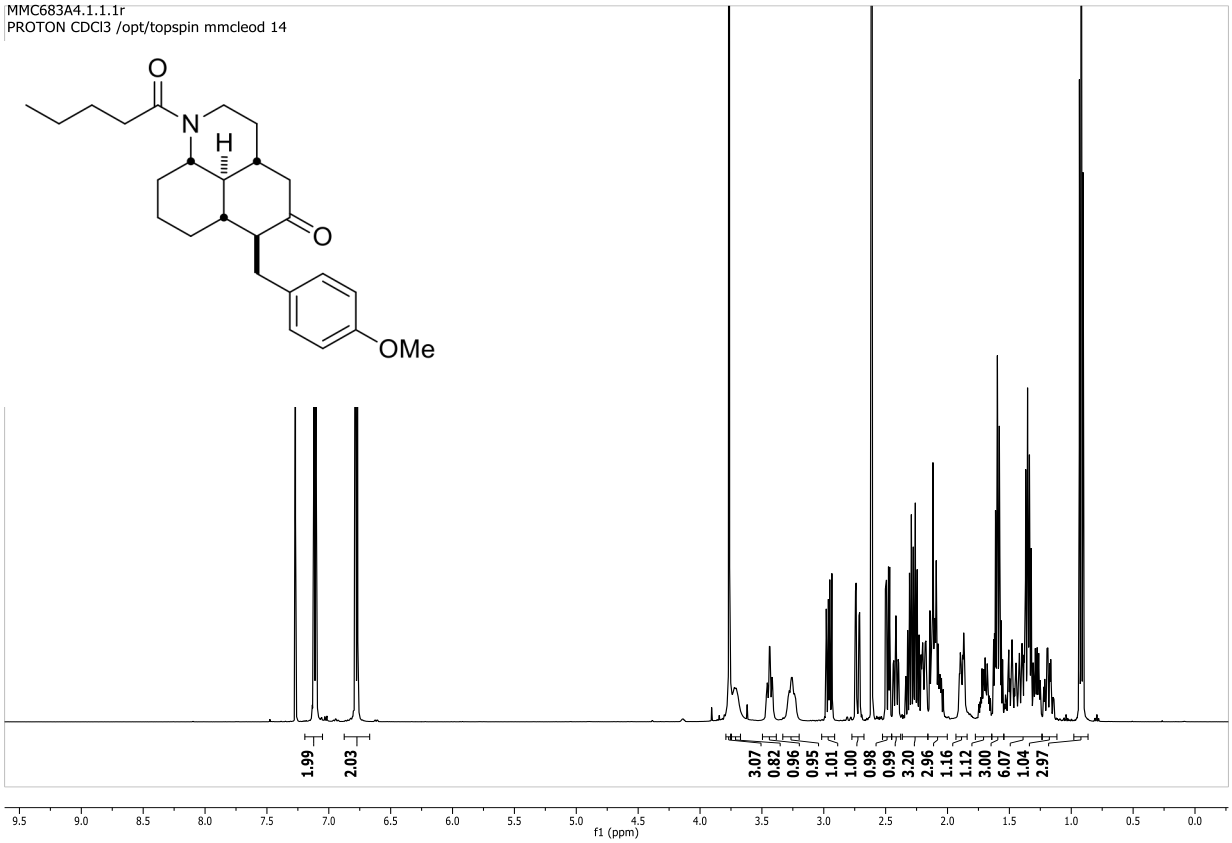


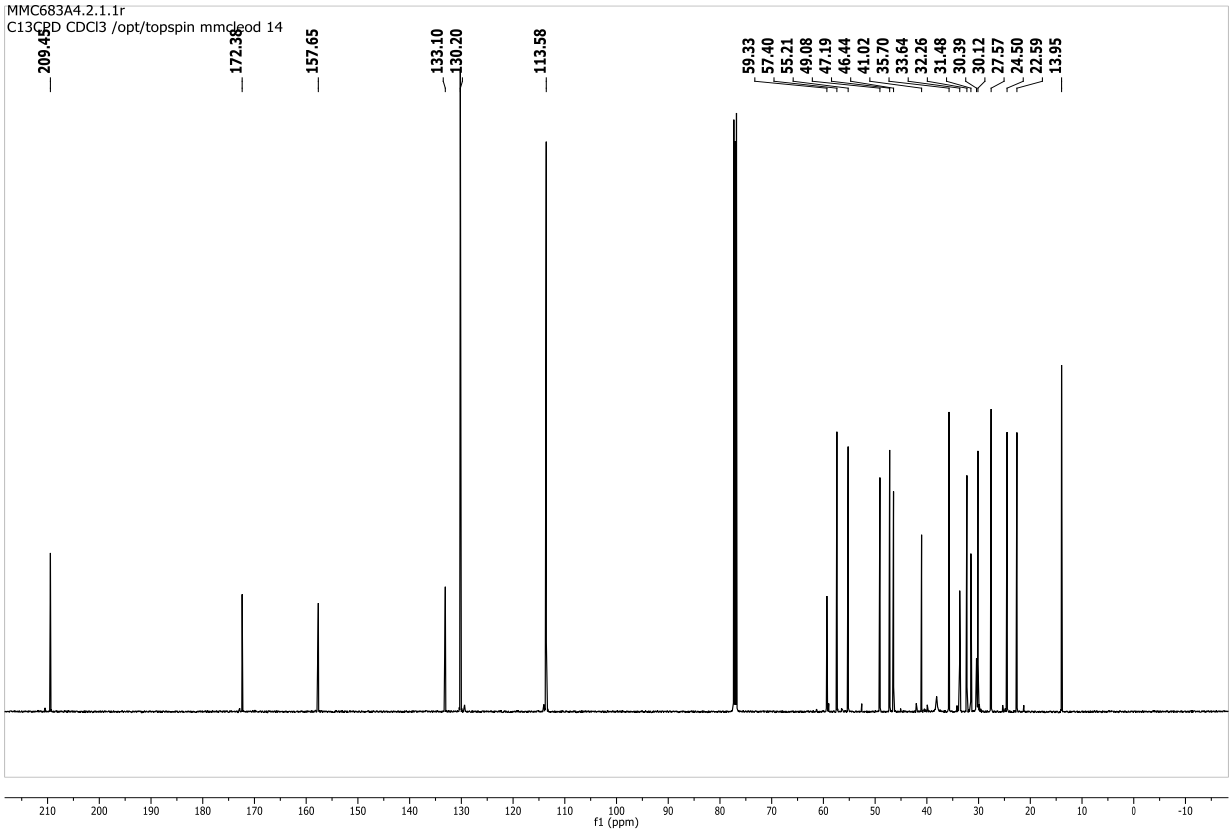
Sulfonamide **13d**{*2*}



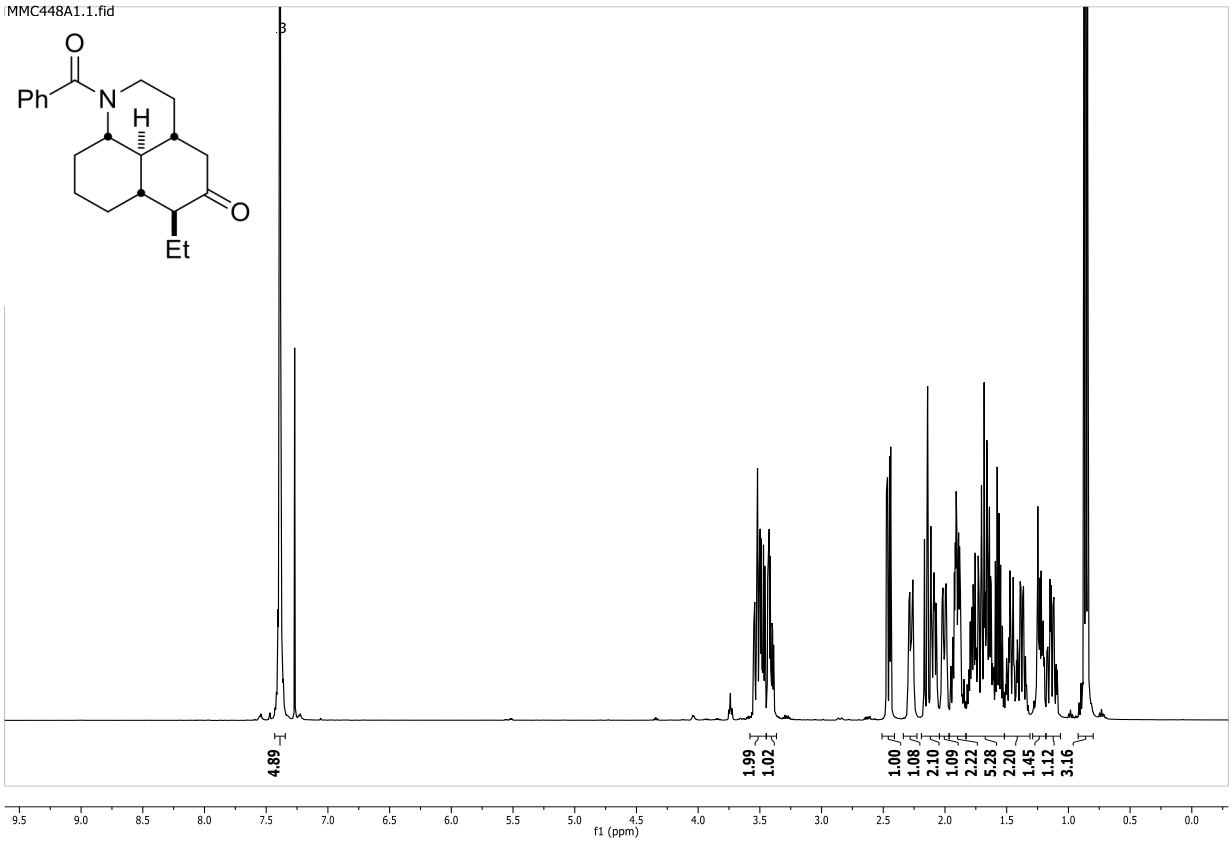


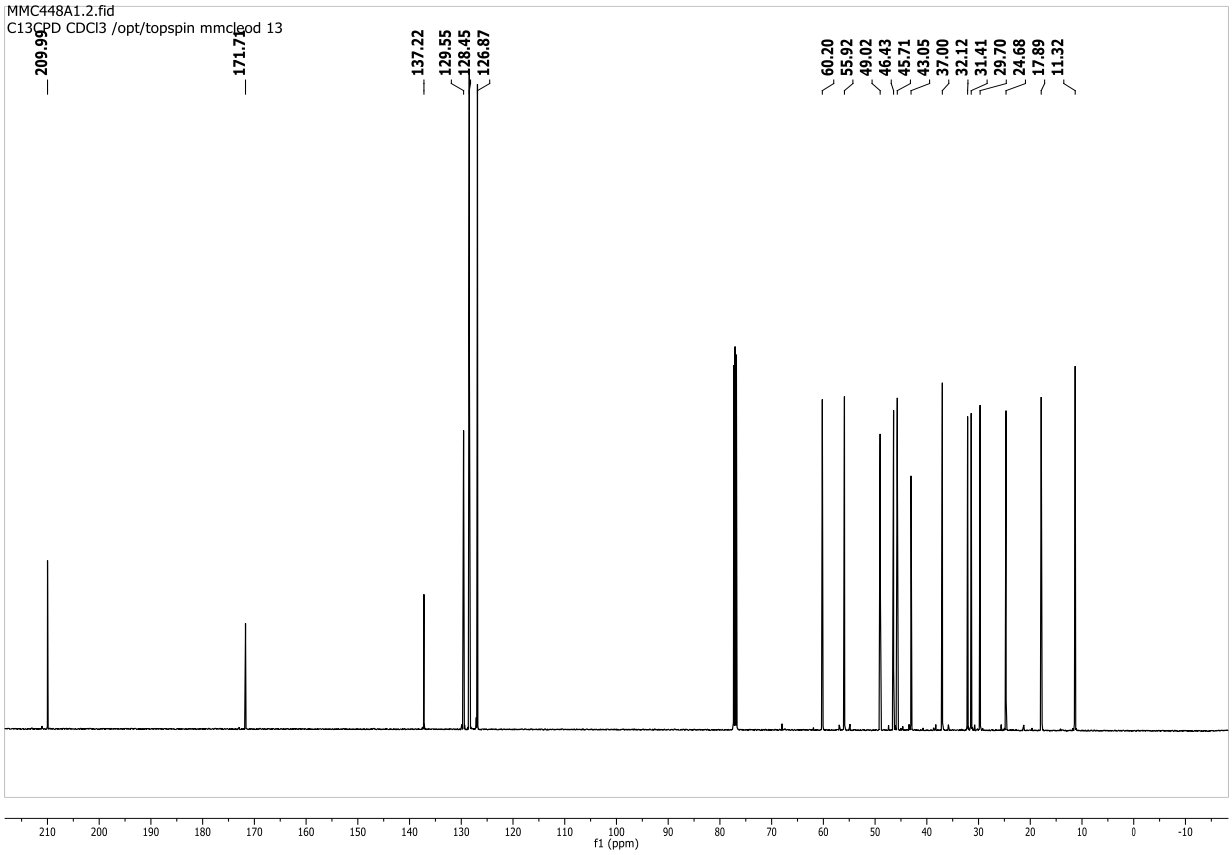
Amide **11d**{*7*}


MMC683A4.1.1.1r
PROTON CDCl3 /opt/topspin mmcleod 14
O
N
H
O
OMe
1.99
2.03
3.07
0.82
0.96
0.95
1.01
1.00
0.98
0.99
3.20
2.96
1.16
1.12
3.00
6.07
1.04
2.97
f1 (ppm)

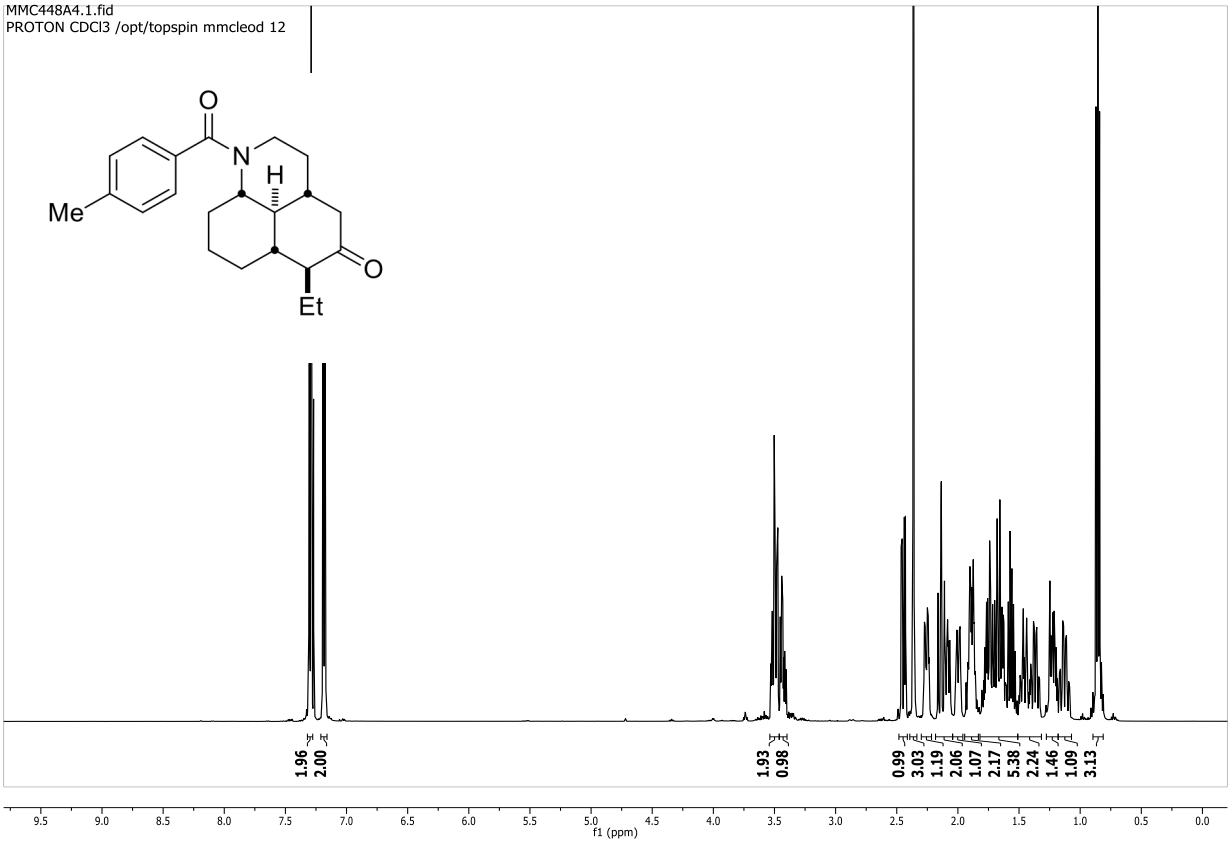

MMC683A4.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 14
209.45
172.38
157.65
133.10
130.20
113.58
59.33
57.40
55.21
49.08
47.19
46.44
41.02
35.70
33.64
32.26
31.48
30.39
30.12
27.57
24.50
22.59
13.95
f1 (ppm)

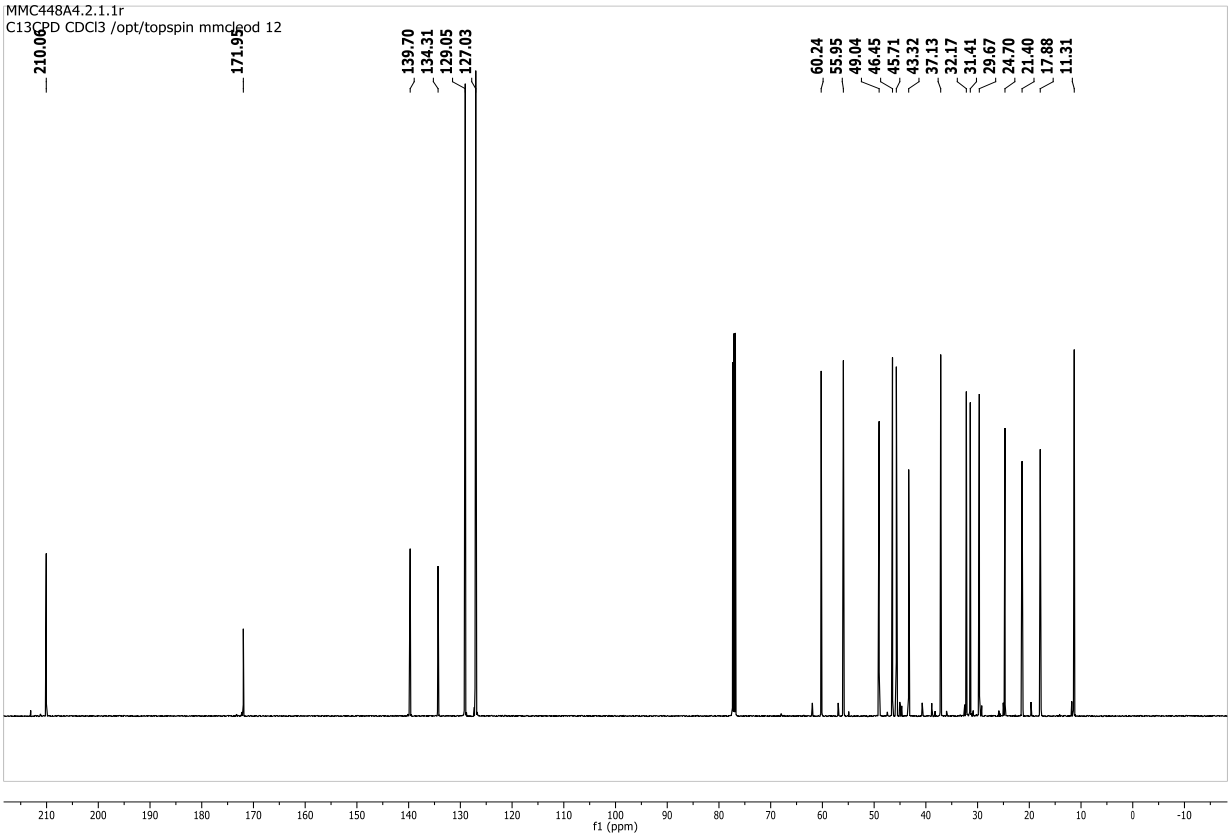
Amide **11b**{*1*}


MMC448A1.1.fid
Ph
N
H
O
O
Et
4.89
1.99
1.02
1.00
1.08
2.10
1.09
2.22
5.28
2.20
1.45
1.12
3.16
f1 (ppm)

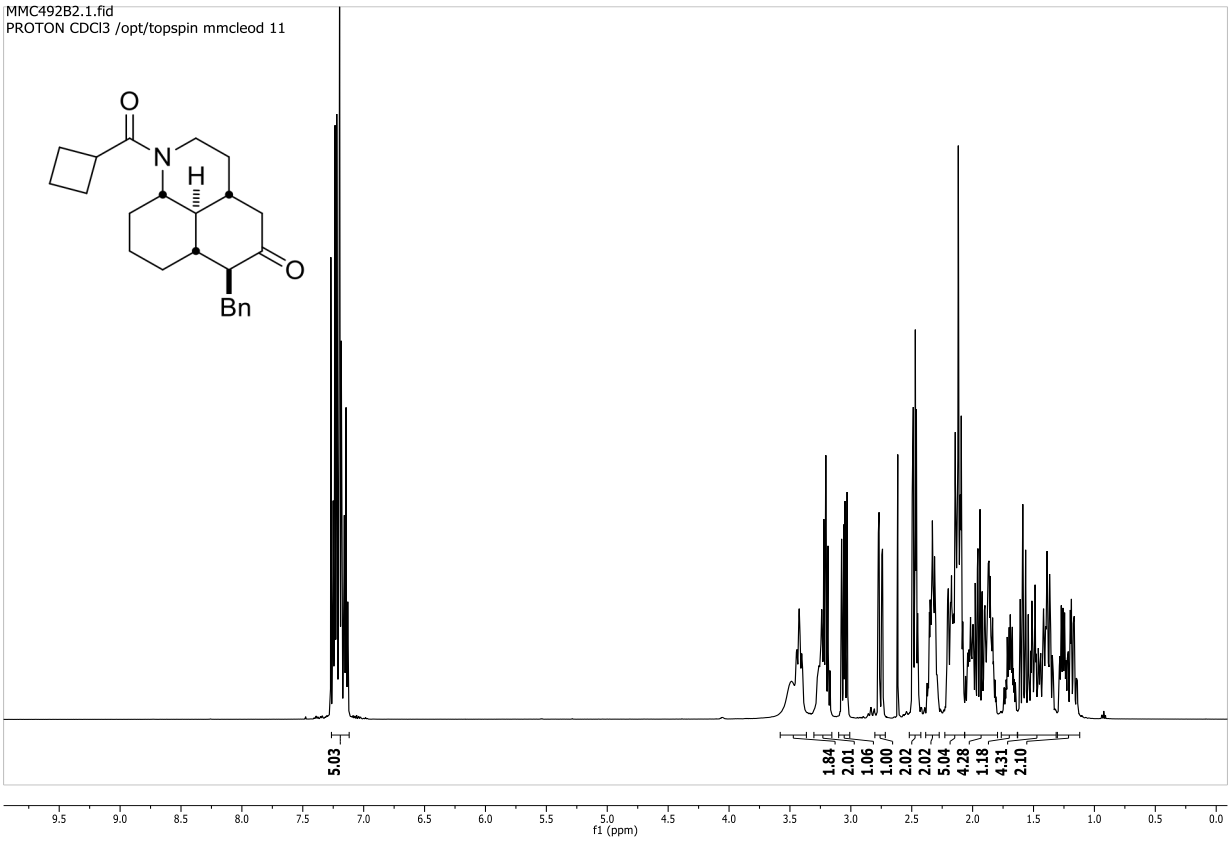

MMC448A1.2.fid
C13CPD CDCl3 /opt/topspin mmcleod 13
209.99
171.71
137.22
129.55
128.45
126.87
60.20
55.92
49.02
46.43
45.71
43.05
37.00
32.12
31.41
29.70
24.68
17.89
11.32
f1 (ppm)

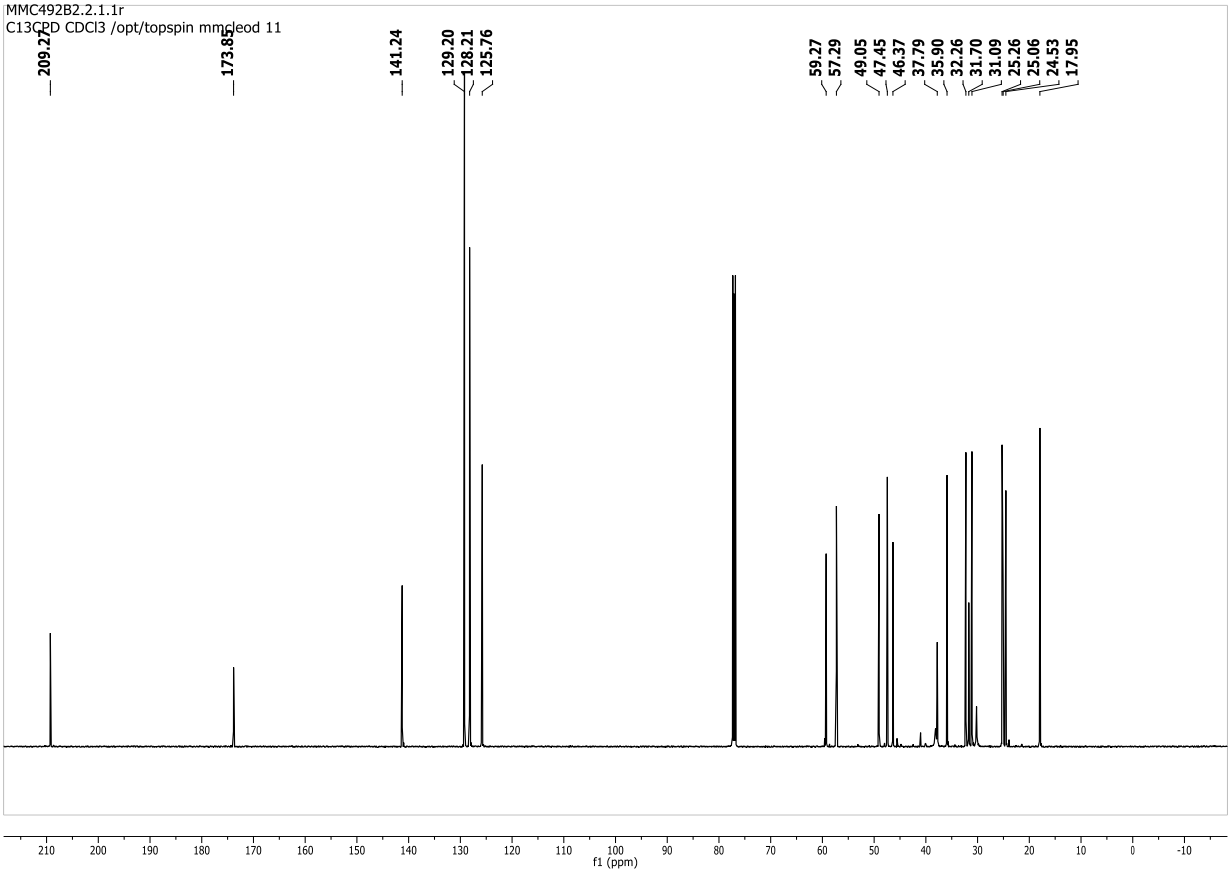
Amide **11b**{*4*}


MMC448A4.1.fid
PROTON CDCl3 /opt/topspin mmcleod 12
O
N
H
Me
O
Et
1.96
2.00
1.93
0.98
0.99
3.03
1.19
2.06
1.07
2.17
5.38
2.24
1.46
1.09
3.13
f1 (ppm)

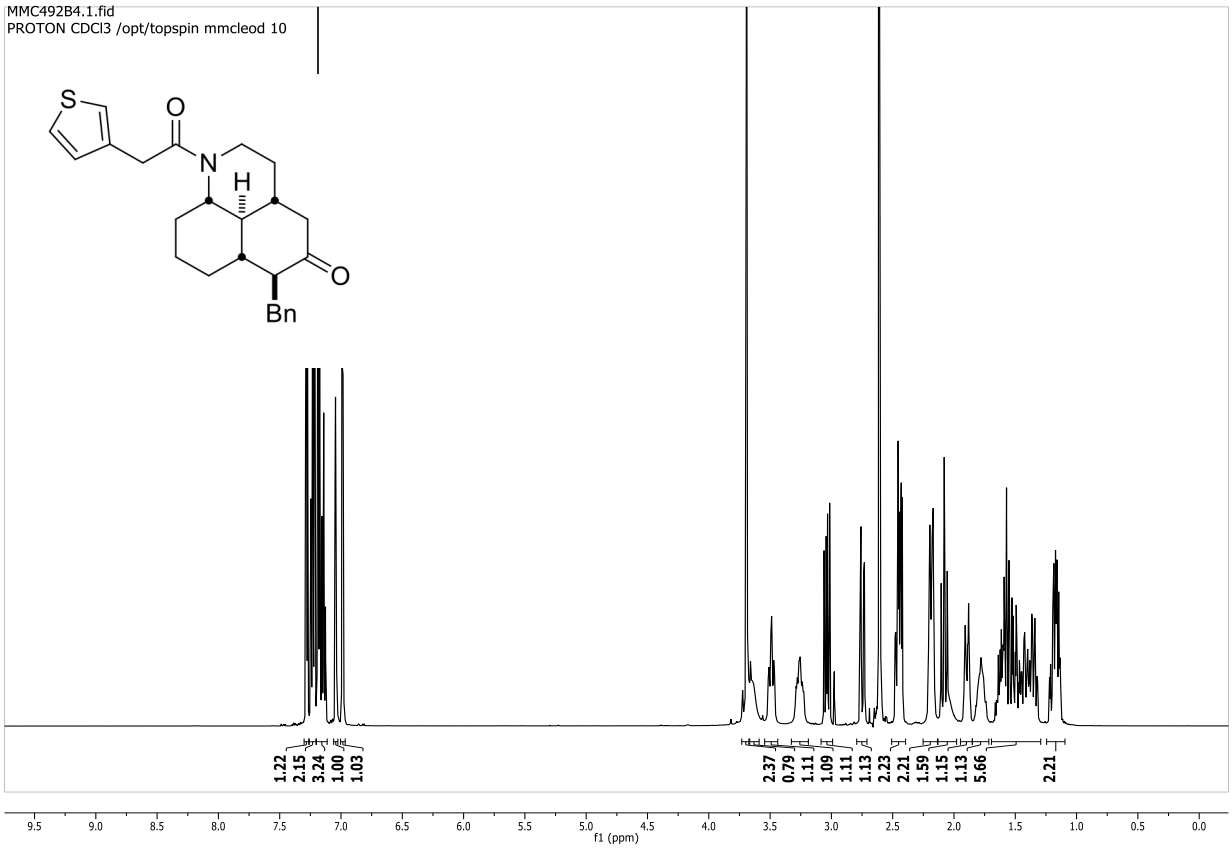

MMC448A4.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 12
210.06
171.95
139.70
134.31
129.05
127.03
60.24
55.95
49.04
46.45
45.71
43.32
37.13
32.17
31.41
29.67
24.70
21.40
17.88
11.31
f1 (ppm)

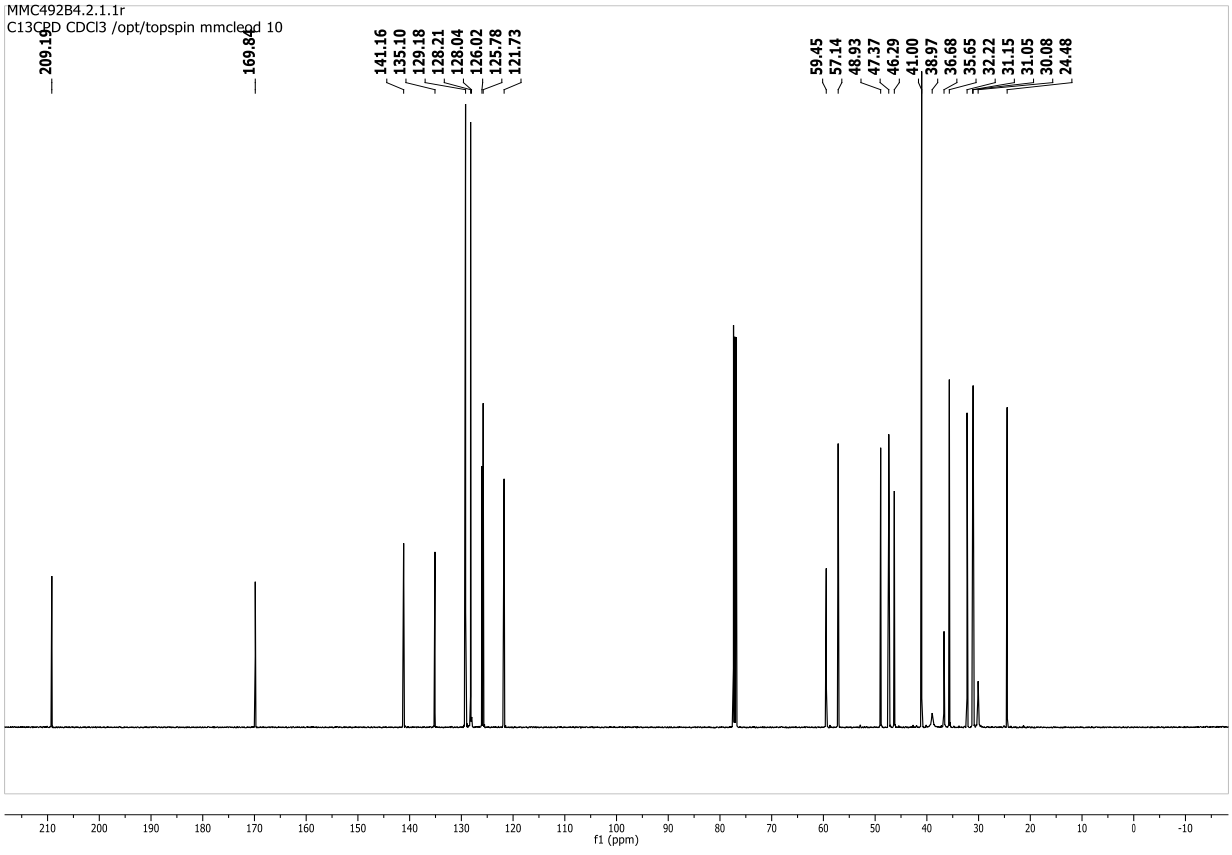
Amide **11c**{*8*}


MMC492B2.1.fid
PROTON CDCl3 /opt/topspin mmcleod 11
O
N
H
O
Bn
5.03
1.84
2.01
1.06
1.00
2.02
2.02
5.04
4.28
1.18
4.31
2.10
f1 (ppm)


MMC492B2.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 11
209.27
173.85
141.24
129.20
128.21
125.76
59.27
57.29
49.05
47.45
46.37
37.79
35.90
32.26
31.70
31.09
25.26
25.06
24.53
17.95
f1 (ppm)

Amide **11c**{*10*}


MMC492B4.1.fid
PROTON CDCl3 /opt/topspin mmcleod 10
S
O
N
H
O
Bn
1.22
2.15
3.24
1.00
1.03
2.37
0.79
1.11
1.09
1.11
1.13
2.23
2.21
1.59
1.15
1.13
5.66
2.21
f1 (ppm)


MMC492B4.2.1.1r
C13CPD CDCl3 /opt/topspin mmcleod 10
209.19
169.84
141.16
135.10
129.18
128.21
128.04
126.02
125.78
121.73
59.45
57.14
48.93
47.37
46.29
41.00
38.97
36.68
35.65
32.22
31.15
31.05
30.08
24.48
f1 (ppm)

7. References

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